Equine Ophthalmology

Third Edition

Edited by

Brian C. Gilger

North Carolina State University

WILEY Blackwell

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Editorial Offices
1606 Golden Aspen Drive, Suites 103 and 104, Ames, Iowa 50010, USA
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
9600 Garsington Road, Oxford, OX4 2DQ, UK

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List of contributors

Rachel A. Allbaugh
Diplomate ACVO
Assistant Professor
Department of Veterinary Clinical Sciences
Iowa State University
Ames, Iowa, USA

Rebecca Bellone
Associate Adjunct Professor
Department of Population Health and Reproduction
Veterinary Genetics Laboratory
School of Veterinary Medicine
University of California-Davis
Davis, California, USA

Elsa Beltran
European and Royal College Recognised Specialist in Veterinary Neurology
Lecturer in Veterinary Neurology and Neurosurgery
Department of Clinical Science and Services
The Royal Veterinary College
University of London
Hatfield, UK

Dennis E. Brooks
Professor of Ophthalmology
College of Veterinary Medicine
University of Florida
Department of Small Animal Clinical Sciences
Gainesville, Florida, USA

Alison B. Clode
Ophthalmologist
Port City Veterinary Referral Hospital
Portsmouth, New Hampshire, USA

Jennifer L. Davis
Associate Professor of Equine Internal Medicine
North Carolina State University College of Veterinary Medicine
Raleigh, North Carolina, USA

Ann E. Dwyer
Practitioner
Genesee Valley Equine Clinic PLLC
Scottsville, New York, USA

Anne J. Gemensky-Metzler
Diplomate ACVO
Professor
Department of Veterinary Clinical Sciences
The Ohio State University College of Veterinary Medicine
Columbus, Ohio, USA

Brian C. Gilger
Professor of Ophthalmology
North Carolina State University College of Veterinary Medicine
Raleigh, North Carolina, USA

Rachael A. Grundon
Clinician in Comparative Ophthalmology
Fellow ANZCVS(Ophthal)
Animal Health Trust
Newmarket, UK

Elizabeth A. Giuliano
Diplomate, ACVO
Professor of Comparative Ophthalmology
College of Veterinary Medicine
University of Missouri
Columbia, Missouri, USA

Claudia Hartley
European and Royal College Recognised Specialist in Veterinary Ophthalmology
Animal Health Trust
Newmarket, UK

Steven R. Hollingsworth
Professor of Clinical, Surgical & Radiological Sciences
University of California
Surgical and Radiological Science
Davis, California, USA

Mary Lassaline
Associate Professor of Clinical Equine Ophthalmology
Department of Surgical and Radiological Sciences
School of Veterinary Medicine
University of California, Davis
Davis, California, USA

Eric C. Ledbetter
Associate Professor of Ophthalmology
Department of Clinical Sciences
Cornell University
College of Veterinary Medicine
Hospital for Animals
Ithaca, New York, USA

Marta Leiva
Diplomate ECVO
Assistant Professor of Ophthalmology
Department of Animal Medicine and Surgery
Autonomous University of Barcelona
Barcelona, Spain

Kaspar Matiasek
Professor and Section Head of Clinical and Comparative Neuropathology
Centre for Clinical Veterinary Medicine
Ludwig-Maximilians-University
Munich, Germany

Andrew Matthews
Bents Cottage
Red Castle, Lunan Bay
Inverkeilor, Angus, Scotland, UK

Richard J. McMullen Jr
Diplomate ACVO, ECVO
Associate Professor
Department of Clinical Sciences
Auburn University
Auburn, Alabama, USA

Paul E. Miller
University of Wisconsin–Madison
Department of Surgical Sciences
Madison, Wisconsin, USA

Christopher J. Murphy
University of California
Surgical and Radiological Science
Davis, California, USA

Teresa Peña
Diplomate ECVO
Associate Professor of Ophthalmology
Department of Animal Medicine and Surgery
Autonomous University of Barcelona
Barcelona, Spain

Lynne Sheila Sandmeyer
Diplomate American College of Veterinary Ophthalmology
Professor of Veterinary Ophthalmology
Department of Small Animal Clinical Sciences
Western College of Veterinary Medicine
University of Saskatchewan
Saskatoon, Saskatchewan, Canada

Riccardo Stoppini
Consultant in Equine Ophthalmology
Calvagese della Riviera, Italy

Wendy M. Townsend
Diplomate ACVO
Associate Professor
Department of Veterinary Clinical Sciences
Purdue University
West Lafayette, Indiana, USA

Ruth A. Van Hatten
Staff Radiologist
Angell Animal Medical Center
Boston, Massachusetts, USA

David A. Wilkie
Diplomate ACVO
Professor
Department of Veterinary Clinical Sciences
The Ohio State University
Columbus, Ohio, USA

Preface to the third edition

It has been over a decade since the first edition of *Equine Ophthalmology* was published. The field of equine ophthalmology has grown through the efforts of pioneers, such as Drs Dennis Brooks, Andy Matthews, Dan Lavach, and Bill Rebhun, to name a few. Also, the International Equine Ophthalmology Consortium (IEOC), an organization created in 2009, has pushed the advancement of equine ophthalmology through sharing of information and development of collaborations among interested practitioners and researchers throughout the world. My hope is that this organization continues to grow and spurs the further study of equine ophthalmology.

A goal of *Equine Ophthalmology* has always been to provide a comprehensive source of information to assist veterinarians in the diagnosis and treatment of ophthalmic diseases in horses. To assist this effort, the authors of individual chapters have included numerous images, figures, and detailed treatment plans. However, it is the responsibility of each practitioner to verify dosages and treatments for each individual horse. Also, most figures in this new edition have been redrawn from the second edition to improve clarity and accuracy.

Another goal of this book is to provide a comprehensive source of information and references to assist with research and publications in equine ophthalmology. I believe the previous editions of equine ophthalmology have been extremely helpful as a source of information and the basis of clinical studies, and I am sure that this new edition will be even better.

A final goal of *Equine Ophthalmology* is simply to provide education for all of us—from students to specialists. I have learned a tremendous amount from the incredible knowledge and experience of the authors of this new edition.

There are numerous changes in this third edition of *Equine Ophthalmology*. With the expanded content and information available on equine ocular disorders, we have provided online supplementary materials, including expanded content and figures to augment the print and digital versions of the textbook. Please see links in the text to view the expanded online content. We have new authors in many chapters, including the orbit, cornea, glaucoma, posterior segment, and inherited disease. I thank the authors of these chapters in previous editions who have provided the basis for these important chapters. In addition, there are new chapters for this third edition, including advanced diagnostics, foal ophthalmology, neuro-ophthalmology, and national and international regulations, and an expanded chapter on inherited ocular disease. These new chapters reflect the growing knowledge and importance of these subject areas in equine ophthalmology.

This is an excellent comprehensive textbook on equine ophthalmology, which I am very proud of—I hope you enjoy it as much as we have putting it together and I hope it is a constant resource to assist you in the management of your equine cases.

Brian C. Gilger
Raleigh North Carolina, USA

About the companion website

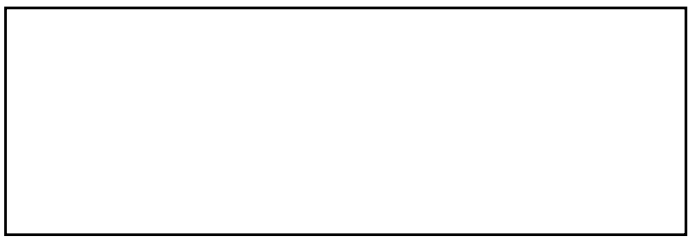
This book is accompanied by a companion website:

www.wiley.com/go/gilger/ophthalmology

The website includes additional text, figures, and tables that are not in the printed book or E-book.

How to access the website:

1. Carefully scratch away the top coating on the label, below, to reveal the PIN code.
2. Go to www.wiley.com/go/gilger/ophthalmology to register your PIN and access the site.



CHAPTER 1

Equine ocular examination basic techniques

Riccardo Stoppini and Brian C. Gilger*

Introduction

The basic and essential aspect of equine ophthalmology is a complete, thorough ocular examination. In this chapter, ophthalmic examination of the horse is discussed, with emphasis on techniques, tools, and instruments, and basic diagnostic modalities. Understanding normal equine ocular anatomy is integral to interpreting the ocular examination. Anatomy of every equine ocular compartment (Figure 1.1) is described in detail in subsequent chapters and is not discussed here, although cross-references to relevant sections in the book will augment our discussion. Excellent reviews of equine eye and head anatomy can also be found in other sources [1–6].

Routine ophthalmic diagnostic techniques are described here, while advanced diagnostic techniques are discussed in Chapter 2. Examination of the equine eye includes obtaining a detailed history and signalment, inspecting the patient in a well-lit environment, examining the ocular structures in a darkened environment, facilitating the examination with restraint, sedation, and local nerve blocks, and collecting relevant diagnostic samples or data [4, 7–10].

Medical history

A thorough medical history relevant to the ocular examination should include how the animal is used (e.g., pet or performance) and its living environment. Additional information that should be collected includes any history of travel, vaccination history, deworming schedule, and presence of concurrent or previous medical problems such as nasal discharge, presence of stridor, previous trauma to the head, and status of other horses on the premises with similar signs (Box 1.1). Characterization of the primary complaint should include the onset and initial clinical signs, treatment given and response to that treatment, progression and duration of the ocular problem, and current therapy. Signalment can provide an important clue as to the cause of many ophthalmic conditions (e.g., congenital stationary night blindness in the Appaloosa, hereditary cataracts in the Morgan horse). Existing medical therapy can also greatly influence findings on ophthalmic examination. For example, a finding of mydriasis on the ophthalmic examination could be caused by use of topical atropine, which may result in mydriasis for up to 14 days in horses [11]. Depending on the specific complaint, further information may be required, such as a thorough description of vision loss (e.g., light versus dark, moving objections, one eye or both) or changes in behavior during sport activity.

Routine and advanced equipment required for the ophthalmic examination

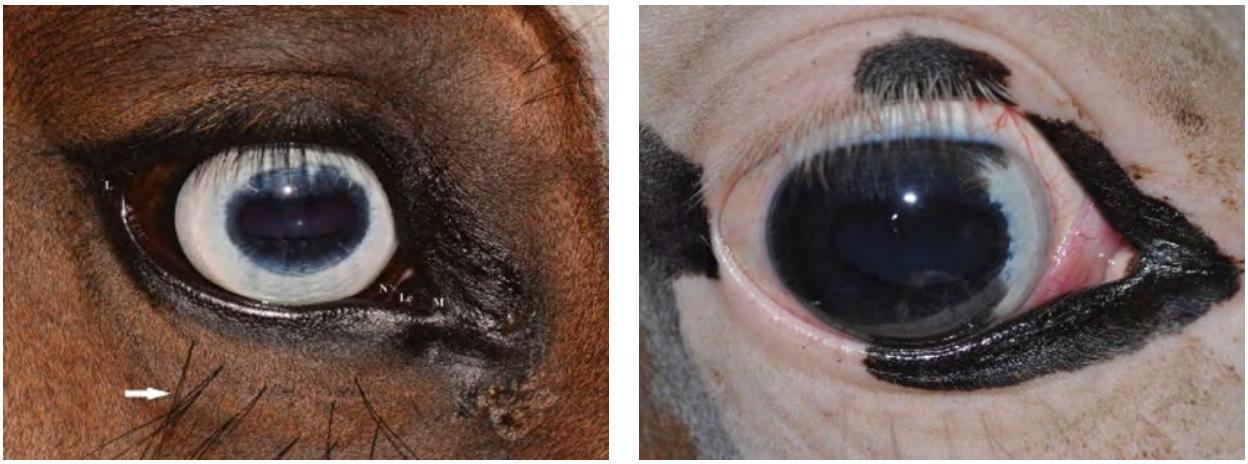
Prior to any examination, the proper equipment to perform the examination is needed. Although there are some differences in opinion and personal preferences among equine ophthalmologists, Box 1.2 lists the routine and advanced equipment a clinician should have available for the ophthalmic examination. Routine materials for the examination are shown in Figures 1.2 and 1.3.

Overview and methods of the equine ocular examination

Ocular examination in the horse, like any physical examination, should be performed in a systematic manner, and to help remember the steps, the compilation of a clinical report or

*The authors would like to thank Dr Tammy Miller Michau for her contributions. She was the author of this chapter in the first edition of *Equine Ophthalmology*.

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(A) (B)

Figure 1.1 (A) Normal external appearance of the equine eye. The horse's palpebral fissure, cornea, and pupil are oval horizontally. The lateral canthus (L) is more rounded than the medial canthus (M). There are prominent folds in the upper and lower eyelids. Numerous eyelashes are present along the lateral two-thirds of the upper eyelid, and vibrissae are located dorsonasal to the upper lid and ventral to the lower lid (**arrow**). The leading edge of the third eyelid is usually partially pigmented (N). The lacrimal caruncle (Lc) is prominent. (B) Normal external appearance of the equine eye when eyelid pigment is absent. Note the lack of pigment on the third eyelid, conjunctiva, and sclera as well.

Box 1.1 Anamnesis and horse history.

- Horse attitude and use (jumping, trotter, dressage, pleasure, etc.)
- Travel and environment history
- Medical history (previous trauma, incident, etc.)
- Time of purchase and PPE (pre-purchase examination)
- Horses in contact and eventual infectious diseases
- Vaccination status
- Deworming history
- Reaction/drug anaphylaxis events
- Breeding info (in case possible presence of heritable pathologies)
- Previous medical history (PMH) (nasal discharge, coughing, colic, etc.)
- Previous ocular history
- Previous ocular treatments (medical/surgical)
- Previous abnormal/changed behavior

examination sheet may be helpful (Box 1.3). The general order of steps to be taken is shown in Box 1.4. The initial examination of the equine eye should occur prior to sedation and should take place in a well-lit area. The examination area should be quiet, away from distractions, and if possible away from other horses. The menace response and other subjective vision testing (e.g., maze testing) and evaluation of the pupillary light reflex (PLR) should be performed before sedation. For accurate evaluation of PLRs, a bright focal light source and a darkened examination area are often required. To adequately examine the cornea and internal structures of the eye, the horse must be examined in a darkened stall or in stocks in a room where the lights can be dimmed. Ideally, stocks are preferred because they will better protect the examiner from accidental (or purposeful!) movements of the horse, which can be exaggerated and unpredictable when the horse is tranquilized.

A thorough ocular examination usually requires appropriate restraint, tranquilization, regional nerve blocks, and topical anesthesia. Methods of restraint required to examine the ocular

Box 1.2 Equipment and supplies for general equine ophthalmic examination.

Routine equipment and supplies

- Bright focal light source: Finnoff halogen transilluminator
- Direct ophthalmoscope, PanOptic ophthalmoscope, or indirect ophthalmoscope with 20-D lens
- Sterile dye strips (fluorescein, rose bengal, lissamine green)
- STT
- Sterile culture swabs for cytology and culture
- Kimura platinum spatula, #10 to #15 sterile surgical blade (cytology)
- Glass slides (cytology)
- Sterile eyewash
- Ophthalmic lubricant, artificial tears ointment
- Topical anesthetic: proparacaine HCl 0.5%
- Short-acting dilating agent: tropicamide HCl 1%
- Sedatives: detomidine HCl, xylazine, acepromazine, romifidine, etc.
- Local nerve block agents: mepivacaine HCl, lidocaine HCl, bupivacaine HCl
- Graefe fixation forceps (to manipulate conjunctiva and third eyelid)
- Digital tonometer (Tono-Pen or TonoVet tonometer)
- Open-ended tomcat urinary catheter for nasolacrimal irrigation
- 1- and 3-mL syringes, 18- and 25-G needles
- 12-mL syringes for nasolacrimal irrigation

Advanced equipment and supplies

- All supplies and instruments for routine examination
- Handheld slit-lamp biomicroscope
- Binocular indirect ophthalmoscope and lenses (15-, 20-, 30-D or 2.2 panretinal)
- Ultrasound (7.5-, 10-, and 20-MHz probe)
- Sterile methylcellulose gel for ultrasound
- Electroretinogram
- 19-G, 3½-inch spinal needle for retrobulbar block
- 27-G needle for aqueocentesis
- Digital camera (color and infrared)
- Advanced imaging: radiography, computed tomography (CT), magnetic resonance imaging (MRI)



Figure 1.2 Materials and supplies for a routine ophthalmic examination in the horse. **(A)** 18-G, 1½-inch needle, 25-G, 1-inch needle, 1 mL and 3 mL syringes. **(B)** Tranquilizer (detomidine). **(C)** 2% Lidocaine HCl. **(D)** STT strips. **(E)** Fluorescein dye strips. **(F)** 1% Tropicamide HCl. **(G)** Sterile eyewash. **(H)** Direct ophthalmoscope. **(I)** Finnoff transilluminator. **(J)** Indirect ophthalmoscopy lens (20 D). **(K)** Panoptic ophthalmoscope.



Figure 1.3 Materials for collection of corneal culture and cytology. **(A)** 0.5% Proparacaine HCl. **(B)** 25-G, 1-inch needle and 3-mL syringe. **(C)** 2% Lidocaine HCl. **(D)** Kimura platinum spatula. **(E)** #15 surgical blade. **(F)** Microscope slides. **(G)** Blood agar culture plate. **(H)** Sabouraud agar culture plate. **(I)** Thyoglycolate medium.

Box 1.3 Equine ophthalmology examination form.

Equine Ophthalmology Examination Form

Owner:

Referring Veterinarian:
Horse:

First visit:
Remote history:
Recent history:

RIGHT EYE
PLR dir:
PLR cons:
Dazzle Refl:
Corneal Rifl:
Palpebral Rifl:
Menace response:
IOP:
STT I-II:
TBUT:

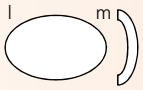
Globe and orbit:

Eyelids

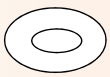
Conjunctiva:

NLD:

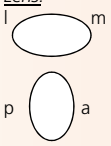
Cornea:



Iris and AC:

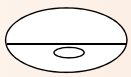


Lens:



Vitreous:

Fundus:



LEFT EYE
PLR dir:
PLR cons:
Dazzle Refl:
Corneal Rifl:
Palpebral Rifl:
Menace response:
IOP:
STT I-II:
TBUT:

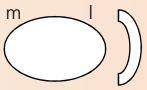
Globe and orbit:

Eyelids

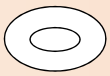
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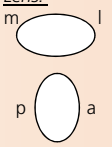
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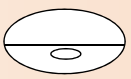


Lens:



Vitreous:

Fundus:



structures of the horse range from a halter and lead rope to mechanical restraint in stocks with use of a lip twitch. Use of restraint is dependent on temperament of the horse and experience of the handlers and examiner. Use of a tranquilizer is generally recommended, and frequently needed, to facilitate the complete routine ophthalmic examination.

Initial examination

With the examiner positioned in front of the horse, the head, bony orbits, eyelids, globes, and pupils should be examined for symmetry (Figure 1.4) before touching the eyelids, giving sedation, or use of eyelid nerve blocks. Ocular comfort may be assessed by evaluation of palpebral fissure size and symmetry,

Box 1.4 General order of steps in the routine equine ocular examination.

1. Obtain medical and ocular history.
2. Examine horse in its environment.
   - Observe walking on a lead or loose in a stall or round pen.
   - Observe horse performing activity such as jumping, cutting, etc.
3. Evaluate for symmetry from the front of the head.
   - Observe globe, orbit, pupils, eyelash direction, ear and lip position.
4. Perform vision testing.
   - Menace response, dazzle reflex, maze testing.
5. Perform palpebral and pupillary light reflexes.
6. Perform STT if indicated.
7. Administer sedation if required.
8. Perform palpebral nerve block.
9. Use direct transillumination for gross disease of eyelids, cornea, anterior chamber, and iris.
10. Collect samples for culture and cytology if indicated.
11. Perform detailed examination of the eyelids, cornea, anterior chamber, and iris with transillumination and biomicroscopy.
12. Test corneal reflex.
13. Apply topical fluorescein and examine the cornea.
14. Apply topical anesthesia if indicated.
15. Perform tonometry.
16. Induce mydriasis (tropicamide HCl) if not contraindicated.
17. Perform detailed examination of the lens and vitreous, via transillumination, retroillumination, and biomicroscopy.
18. Perform direct and/or indirect ophthalmoscopy.
19. Irrigate nasolacrimal duct(s) if indicated.

position of the eyelashes, ocular discharge, and blink rate [4, 8, 9]. The upper eyelashes of the healthy horse are nearly perpendicular to the cornea (Figure 1.5A) [8]. A ventral or downward direction of the eyelashes in relation to the cornea may indicate blepharospasm, enophthalmos, or ptosis (see Figure 1.4B–D and Figure 1.5B), while an upward deviation may indicate exophthalmos or an enlarged eye (see Figure 1.4C) [8].

The examiner should then be positioned at the side of the horse's head to examine each eye individually. An assistant may be required to elevate the head of a sedated horse to the same level as the examiner's eyes. The examiner may need to use a stool for an extremely tall horse or kneel on the ground for an extremely short horse (e.g., Miniature horse), although this should be done with great caution and never directly in front of the horse.

A cranial nerve (CN) evaluation (specifically, CN II, III, IV, V, VI, VII) is then performed before any sedation is induced. These CNs are assessed via the menace response, pupillary light and dazzle reflexes, globe and eyelid position and mobility, and sensation of ocular and adnexal structures [8, 9]. Examination of the CNs is discussed in more detail in the following section.

The cornea should be examined for abnormalities (e.g., opacities, ulceration, blood vessels, edema) by using transillumination and/or slit-lamp biomicroscopy. Evaluation of resting pupil size, shape, and mobility, and appearance of the anterior chamber structures should follow, including the assessment for aqueous flare. The attachment of the iridocorneal angle pectinate ligaments to Descemet's membrane (i.e., gray line) can be observed medially and laterally in the adult horse (Figure 1.6A, B) and allows for direct visualization of the horse's iridocorneal angle. Collection of cultures and Schirmer tear values are performed, when indicated, prior to placing any medications into the eyes. When indicated, cytology is collected next, usually after application of topical anesthetic (e.g., proparacaine HCl 0.5%, oxibuprocaine cloridrate 0.4%, tetracaine). Fluorescein staining of the cornea is then performed. Examination of the nasolacrimal system, third eyelid, and conjunctiva is performed concurrently. Fluorescein staining is followed by induction of topical anesthesia, if not already given to collect cytology and perform tonometry. The ocular media (cornea, aqueous humor, lens, and vitreous) are evaluated for clarity and transparency by transillumination and ophthalmoscopy [4, 9]. The anterior surface of the third eyelid can be examined by gently retropulsing the globe to produce passive prolapse of the nictitans. For evaluation of the posterior surface, the third eyelid can be gently grasped with Graefe fixation forceps or manipulated with a strabismus hook.

For complete examination of the lens and posterior segment, mydriasis is required. The most common mydriatic used is 1% tropicamide HCl eyedrops, which takes effect in approximately 10–20 minutes and lasts 4–6 hours [12, 13]. In the case of severe intraocular inflammation or reflex uveitis because of corneal disease or trauma, a single application of tropicamide may not be sufficient to dilate the pupil. Topical phenylephrine (2.5% or 10%) does not cause mydriasis in normal horses, nor does it enhance the mydriatic effect of tropicamide [14, 15]. The use of atropine for routine examination is not recommended because of its longer duration of action and potential adverse effects in the horse [11, 16]. After mydriasis has been achieved, the clarity, position, and size of the lens, vitreous body, optic nerve, retinal blood vessels, and the tapetal and nontapetal fundus are evaluated. With full mydriasis, the edge of the lens and attachment of the zonular fibers may be visible [17].

Cranial nerve examination

For a breakdown of the CN examination see Table 1.1.

Vision testing

Vision testing in horses is subjective. Environmental observation, menace response, dazzle reflex, and maze testing provide only rough data. Determining total blindness is possible with these tests, but determining whether a horse has decreased vision is not easily done. Advanced diagnostic testing, such as electroretinography (see section **Electroretinography**), may help to determine if there are abnormalities in retinal electrical function but do not test vision per se. If visual function is in doubt in one or both eyes, the horse can have a unilateral blindfold and be subjected to a maze test. However, horses that are depressed, are ataxic, or have vestibular disease may stumble over objects despite having vision [9]. Equine vision and vision testing are discussed more extensively in Chapter 12.



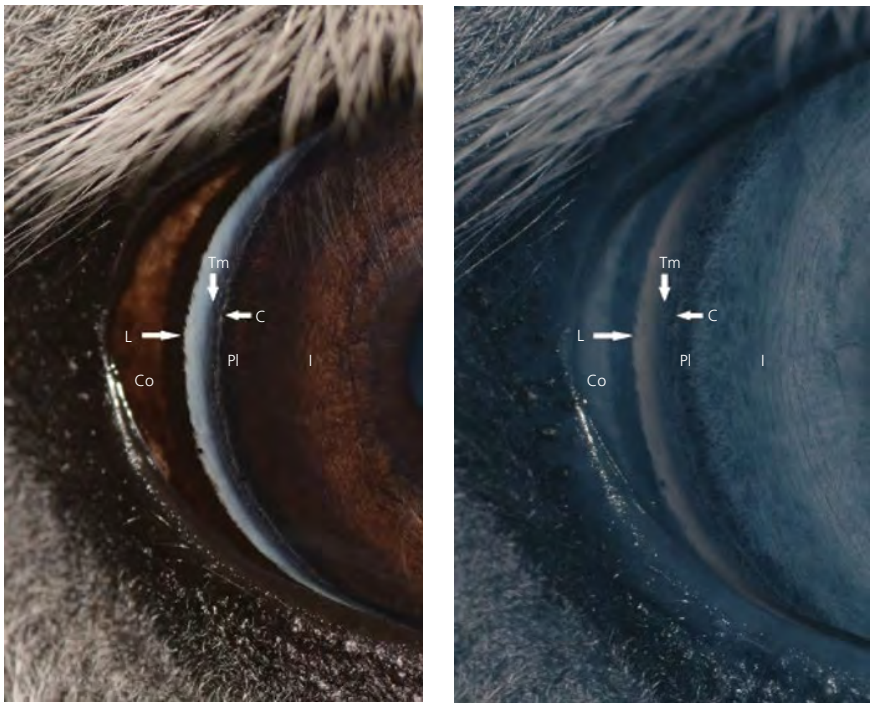
(A) (B) (C) (D)

Figure 1.4 (A) The head (including ears and nostrils), bony orbits, eyelids, globes, and pupils should be examined for symmetry, with the examiner positioned in front of the horse. (B) Horse with orbital asymmetry due to an orbital fracture on the right side. (C) Horse with asymmetry due to a retrobulbar mass resulting in exophthalmos on the left side. (D) Horse with orbital asymmetry due to an orbital fracture resulting in enophthalmos on the left side.



(A) (B)

Figure 1.5 (A) The cornea and eyelids as viewed from the front in a healthy horse. The upper eyelashes are nearly perpendicular to the cornea. (B) The cornea and eyelids as viewed from the front in a horse with ocular pain. The eyelashes are no longer at 90 degrees from the corneal surface but are pointed downward.



(A) (B)

Figure 1.6 (A) The attachment of the iridocorneal angle pectinate ligament to Descemet's membrane (i.e., gray line) can be observed medially and laterally in the adult horse. Iris (I), pectinate ligaments (Pl), attachment of pectinate ligaments to corneal endothelium (C), trabecular meshwork (Tm), limbus (L), and conjunctiva (Co). (B) More details are visible at infrared picture.

Table 1.1 Cranial nerve examination.

CN	Name	Motor (M) or sensory (S)	Function	Dysfunction	Assessment
II	Optic	S	Vision Pupillary light pathway	Blindness	Menace response Pupillary light reflex Dazzle reflex
III	Oculomotor	Medial, dorsal, ventral rectus (M), ventral oblique Pupillary sphincter muscle (M) Levator palpebrae superioris (M)	Globe movement Pupillary function Upper eyelid elevation	Lateral strabismus Mydriasis Ptosis	Eye position Pupillary light reflexes
IV	Trochlear	Superior oblique (M)	Globe movement	Dorsomedial strabismus	Move head and observe eye position
V	Trigeminal	Maxillary branches: skin of face/eyelid (S) Ophthalmic branches: eye (S)	Sensation of skin, eyelids, and cornea	Neurotrophic keratitis	Corneal reflex
VI	Abducens	Lateral rectus (M), retractor bulbi	Globe movement	Medial strabismus	Move head and observe eye position
VII	Facial	Orbicularis oculi (M) Lacrimal gland (M)	Close palpebral fissure Stimulates tear production	Exposure keratitis KCS	Observation Palpebral reflex STT
VIII	Vestibulocochlear		Equilibrium	Spontaneous nystagmus	Observation

Menace response

The menace response is a learned protective response in which a menacing movement toward the eye results in closure of the eyelids and possibly retraction of the globe or an avoidance movement of the head [12]. The threatening movement can be performed with the examiner's hand, but care should be taken to avoid contacting the vibrissae and to avoid causing an air current that could be detected even in a blind eye. For detection of a visual deficit in one field, the menacing gesture is directed first toward the nasal visual fields and then toward the temporal visual fields [18]. However, partial visual deficits can be extremely difficult to detect using a menace response. The afferent arm of the menace response is the retina and CN II, and the efferent arm is the palpebral branch of CN VII, which innervates the orbicularis oculi muscle (see Chapter 14) [19]. A horse that has intact vision but is extremely stoic, depressed,

or frightened may have a diminished menace response. Lightly tapping the medial or lateral canthus before attempting to induce the menace response again may heighten the response from an uninterested, stoic horse. A pathologic lack of menace response may result from a lesion in the retina, CN II, visual cortex, or CN VII [19]. Cerebellar disease can also cause bilateral deficiency in the menace response in the absence of blindness or CN VII paralysis, possibly because of a loss of cerebellar modulation of cerebral visual function [18, 19].

Pupillary light reflexes

Both eyes should be examined for pupil size and symmetry and for abnormalities such as synechia that may affect the PLR. One method to observe pupil symmetry in the horse is to use an indirect or direct ophthalmoscope directed at the center of the horse's head from a distance of 1.5–2.0 m. This technique will illuminate the pupils via both tapetal reflexes and make it possible to evaluate pupil symmetry (Figures 1.7 and 1.8) [20]. Anisocoria may be a normal finding in horses with bilateral heterochromia iridis or unilateral heterochromia iridis in which the larger pupil is ipsilateral to the heterochromic eye (Figure 1.9) [6].

When stimulated by light during the PLR, vertical movement of the pupil is much faster and excursion is greater than horizontal movement. The pupil's shape is a horizontal ellipse that becomes rounder when dilated (Figures 1.10 and 1.11) [21]. Pupillary light reflexes can be used to simultaneously evaluate function of the retina, CN II, midbrain, and CN III [18–20]. Light directed into one eye should result in constriction of both that pupil (direct response) and the pupil of the contralateral eye (indirect or consensual response). This results from bilateral excitation of the parasympathetic component of CN III in the pretectal region [18–20]. The normal equine pupil responds



Figure 1.7 With the examiner 1.5–2.0 m in front of the horse, an indirect ophthalmoscope directed at the center of the horse's head should illuminate both tapetal reflexes and make it possible to determine pupil symmetry.



Figure 1.8 In this case, a different pupil diameter is present (anisocoria), with slight miosis in the left eye.



Figure 1.9 Anisocoria may be a normal finding in horses with bilateral heterochromia iridis or unilateral heterochromia iridis in which the larger pupil is ipsilateral to the heterochromic eye.

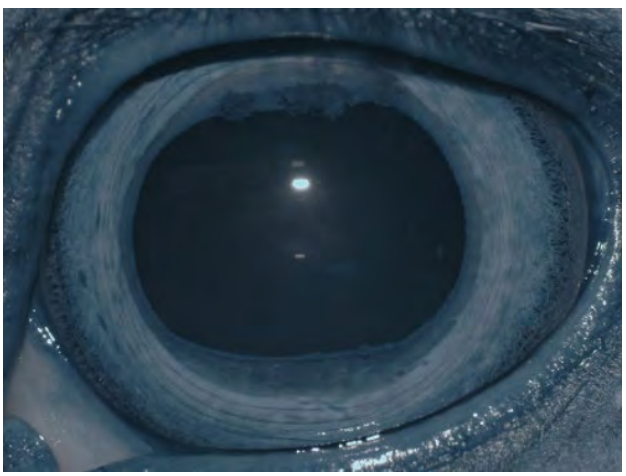
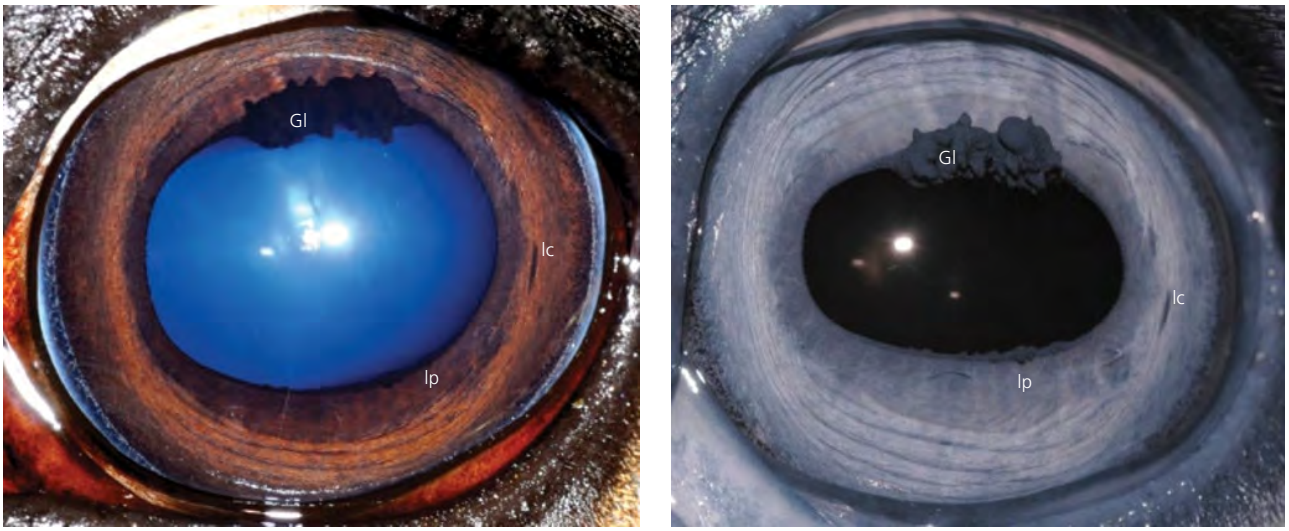


Figure 1.10 Pupil of the adult horse appears rounder when dilated. At infrared photograph, details of lateral and medial parts of the iridocorneal angle are more visible.



(A) (B)

Figure 1.11 Normal anatomy of the pupil and corpora nigra in a horse. Granula iridica (GI) are present on the dorsal and ventral pupillary margins but are normally more prominent on the dorsal margin. The iris can be separated into a pupillary zone (Ip) and a more peripheral ciliary zone (Ic). **(A)** Color photograph. **(B)** Infrared photograph.

somewhat sluggishly and incompletely to light, in a biphasic manner [8, 19]. The first part is a brisk but small reaction, followed by the second slower complete movement. The magnitude and time of response depends on the brightness of the light source and the mental state of the horse. A very focal and bright light source is required to stimulate a rapid and complete response. Pupillary light responses are most vigorous if the beam is directed towards the visual streak in a direction that is temporal (lateral) and slightly dorsal to the optic disc. Consensual responses can be difficult to evaluate in the horse because they tend to be weaker than the direct response and can be awkward for an examiner to determine alone. The indirect PLR is less prominent because of decussation at the chiasm (85%) in the horse, which results in more efferent pupillomotor fibers that return to the ipsilateral side of the brain [6, 12, 20]. This is referred to as **dynamic contraction anisocoria** [17]. Evaluation for the consensual light reflex is unnecessary if the horse has vision and a direct response in both eyes. The consensual light reflex can be extremely valuable in evaluating problems when the posterior segment cannot be visualized (e.g., corneal edema, hyphema) for assessment of retinal function in the affected eye. Pupillary escape, a slight dilation that follows constriction under direct light stimulation, is a normal response in the horse [20].

Dazzle reflex

The dazzle reflex, in contrast to the cortically mediated menace response, is a subcortical reflex that requires function of the retina, CN II, rostral colliculus, possibly the supraoptic nuclei of the hypothalamus, CN VII, and orbicularis oculi [18–20]. A very bright focal light source is directed into the eye, and blinking or blepharospasm is a normal response. Care should be taken if the light source generates heat, because this can be detected by the horse if the light source is close to the cornea and can also result in blepharospasm.

Palpebral reflex

Horses normally blink approximately 5–25 times per minute at rest [22]. The blink is synchronous between both eyes approximately 30–100% of the time [22, 23]. Two types of normal blinking occur in the horse at rest: complete and incomplete [23]. Incomplete blinking is most common and consists predominantly of upper eyelid motion downward [23]. Complete blinking is associated with an upward movement of the lower lid to meet the upper lid and is highly variable in occurrence [23]. The blink rate slows when the horse is sedated, anxious, or focused on an object of interest.

The palpebral reflex is elicited by touching the medial and lateral canthi and results in closure of the eyelids [18–20]. If CN V or CN VII is abnormal (e.g., facial nerve paralysis) or if the eyelids are unable to close (e.g., with severe trauma and swelling), the blink may be absent or incomplete.

Corneal reflex

The corneal reflex is elicited by lightly touching the unanesthetized cornea with a sterile cotton-tipped swab and results in closure of the eyelid and retraction of the globe [18–20]. This subcortical reflex occurs in response to a tactile or painful stimulus to the cornea. The afferent pathway of the corneal reflex is via the ophthalmic branch of CN V [20]. The result should be closure of the eyelid and retraction of the globe, mediated by CN VII and CN VI, respectively [20]. If CN V or CN VII is abnormal or if the eyelids are unable to close, the blink may be absent or incomplete. Corneal sensitivity can be quantitated by

a technique called **corneal esthesiometry**, which is described later in this chapter. Lack of corneal sensation may be the cause of corneal ulceration and other corneal abnormalities (see Chapter 7).

Autonomic (sympathetic and parasympathetic) nervous system

The autonomic nervous system is composed of two main divisions: the sympathetic and parasympathetic nervous systems (see Chapter 14). The sympathetic nervous system begins in the hypothalamus and extends down the intermediolateral cell columns of the spinal cord to synapse at C8 to T3. The axons from these cells exit the anterior nerve root of the spinal cord though the white ramus. The fibers (preganglionic fibers) course through the brachial plexus, through the thoracic inlet, and course cranially in the neck in the cervical sympathetic trunk. This trunk is associated with the vagus nerve forming the vagosympathetic trunk in the carotid sheath. Ventromedial to the tympanic bulla, the cervical sympathetic trunk separates from the vagus nerve and terminates in the cranial cervical ganglion. Postganglionic fibers proceed rostrally between the tympanic bulla and petrous temporal bone through the orbital fissure and form the sympathetic root of the ciliary ganglion [18–20]. Short ciliary nerves (along with contributory fibers to the long ciliary nerves) extend from the ciliary ganglion to the dilator muscle of the iris.

The sympathetic nervous system controls dilation of the pupils and other motor functions of the eyes and face. Damage to sympathetic innervation to the head may result in Horner's syndrome (miosis, ptosis, enophthalmos, increased sweating on the face and ear of the affected side, ipsilateral distention of facial blood vessels, and ipsilateral hyperemia of the conjunctiva and nasal mucosa) [24–30]. Chapter 15 offers a detailed description of the clinical signs and diagnosis of Horner's syndrome in horses. Causes reported in the horse include jugular vein and carotid artery injections, cervicothoracic spinal cord injury, cervical abscesses, guttural pouch disease or surgery, neoplasia or trauma of the neck and thorax, trauma to the vagosympathetic trunk, middle ear disease, traumatic lesions of the basisphenoid area, polyneuritis equi syndrome, equine protozoal myelitis of the cervical spinal cord, esophageal rupture, and trauma to the neck and thorax [8, 20, 24, 26, 27, 29–31].

The parasympathetic nervous system to the eye originates in the parasympathetic nucleus of the oculomotor nerve, located in the ventral part of the central gray matter next to the median plane and anteriorly to the general somatic efferent motor nucleus of the oculomotor nerve [32]. The fibers from this nucleus travel with the oculomotor nerve (CN III) and exit in the motor root of the ciliary ganglia where they synapse. The postsynaptic fibers travel to the eye in the short ciliary nerves to the constrictor muscles of the iris. Parasympathetic fibers also run with the facial nerve (CN VII) to the lacrimal gland to result in lacrimation when stimulated.

Restraint and sedation

Some horses can undergo an ocular examination without sedation, but most horses require sedation for a complete, detailed ophthalmic examination. Use of restraint and sedation depends on the temperament of the horse, availability of equipment, and comfort level of the handlers and examiner. Tranquilization with detomidine HCl 0.02–0.04 mg/kg, administered intravenously (IV) is preferred for ophthalmic examinations because it provides rapid tranquilization without an excitation phase (either on induction or during recovery) and a steady and low head position without movement (i.e., fine tremors). Xylazine 0.5–1 mg/kg IV with or without butorphanol tartrate (0.01–0.02 mg/kg IV) can also be used [8, 9]. Butorphanol is commonly added for painful procedures or additional restraint [8, 9]. However, xylazine can have a profound excitation phase on induction or recovery. Both butorphanol and xylazine are associated with fine head tremors, or head "jerks," which can be very disruptive during slit-lamp biomicroscopy and minor procedures around the eye such as cytology collection. Addition of acepromazine (0.02–0.04 mg/kg IV; 20 mg IV in a 500-kg horse) [33] 10–15 minutes prior to or together with detomidine is recommended to avoid the fine tremors when additional tranquilization is needed for extended examination or minor standing surgical procedures. For prolonged examination, need of additional tranquilization, or standing surgical procedures, addition of romifidine (50–75 µg/kg IV) may be helpful [34, 35]. Additional restraint includes lip (rope or chain) and neck twitch (manual). Although these techniques are generally very effective for short-term restraint (i.e., less than 10 minutes), some horses react adversely to these techniques, so caution is advised when using them.

Regional nerve blocks

Two ophthalmic nerves are frequently denervated ("blocked") during the equine ocular examination: the auriculopalpebral, or more precisely the palpebral branch of the facial nerve (CN VII), and the frontal (supraorbital) branch of the trigeminal nerve (CN V) [36, 37]. When these nerves are blocked, akinesia and anesthesia, respectively, of the upper eyelid occurs.

Regional akinesia

The most common nerve blocked is the palpebral branch of the auriculopalpebral nerve, which innervates the orbicularis oculi muscle, responsible in part for eyelid closure. The orbicularis oculi muscle in horses is very strong, and therefore akinesia of this muscle is required to open the eyelid for examination in many horses, especially horses that are in pain. It is extremely important in conditions in which the structural integrity of the globe can be compromised, because the pressure applied by the muscle during manipulation for examination or during blepharospasm could result in rupture of the globe. Akinesia of the eyelids may be induced for routine eye examination, diagnostic procedures (e.g., corneal cytology and culture), therapy (e.g., subconjunctival injections, placement of a subpalpebral lavage), and standing surgeries [36, 37].

A volume of 1–2 mL of an anesthetic is injected subcutaneously with a 25-gauge (G), ⅝-inch needle adjacent to the nerve, and the injection site is massaged to facilitate anesthetic diffusion [8, 9, 12, 36, 37]. Anesthetics most frequently used for eyelid blocks include 2% lidocaine HCl, which has an onset of action of 4–6 minutes and a duration of 60–90 minutes, and 2% mepivacaine, with an onset of action of 3–5 minutes and a duration of 90–120 minutes [8, 9, 12]. Procaine or bupivacaine can also be used. Repeated injections of anesthetic may result in a refractory phenomenon, requiring higher volumes of drug and longer times to achieve akinesia [12]. The auriculopalpebral nerve block results in paralysis of the orbicularis oculi muscle of the upper eyelid and variable paralysis of the lower eyelid for approximately 1–2 hours [8, 9, 12]. Duration of anesthesia can be prolonged with the addition of 1:10,000 epinephrine [12], but this is not usually required for most examinations or minor surgical procedures. Ptosis, narrowing of the palpebral fissure, and easy manual elevation of the upper eyelid should result [8, 9, 12]. Sensation to the eyelids and some palpebral function remains intact, so the horse can usually blink and continue to protect the cornea. Once the examination is concluded, if the horse is not blinking well, topical ophthalmic ointments should be used every 30 minutes to protect the cornea until palpebral function returns.

The auriculopalpebral nerve branches from the main trunk of the facial nerve, where it is protected by the parotid gland for the full length of the caudal border of the ramus of the mandible [12, 20]. It then emerges from beneath the gland just caudal to the caudal border of the condyle of the mandible, where it is covered by thin facial muscles and lies close to the rostral auricular artery and vein [12]. The branches then pass rostrally and dorsally to reach their destination (Figure 1.12).

The auriculopalpebral nerve can be blocked subfascially in the depression just anterior to the base of the ear where the caudal border of the coronoid process of the mandible meets the zygomatic process of the temporal bone. At this point, the nerve emerges from the parotid salivary gland and becomes subcutaneous on the lateral aspect of the dorsal tip of the coronoid process (Figures 1.12 and 1.13) [12, 36, 37].

The palpebral branch of the auriculopalpebral nerve can be blocked just lateral to the highest point of the caudal zygomatic arch, where the nerve can be palpated through the skin by running a finger forcefully over the dorsal border of the bone (see Figures 1.14 and 1.15) [36, 37]. The palpebral branch of the auriculopalpebral nerve can also be blocked where it lies on the zygomatic arch caudal to the bony process of the frontal bone (see Figures 1.14 and 1.15) [36, 37].

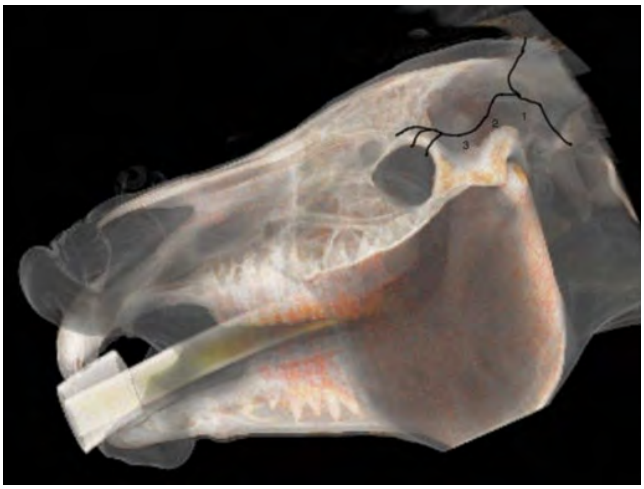


Figure 1.12 Three sites at which the auriculopalpebral nerve can be blocked: caudal to the posterior ramus of the mandible (1), dorsal to the highest point of the zygomatic arch (2), and where it lies on the zygomatic arch caudal to the bony process of the frontal bone (3).



Figure 1.13 Location of the palpebral nerve block. A 25-G needle is inserted, and 1–2 mL of lidocaine or mepivacaine is injected subcutaneously.

Regional anesthesia and analgesia

Sensation to the eyelids is provided by the ophthalmic and maxillary divisions of the trigeminal nerve (CN V) (Figure 1.14) [12]. The frontal, lacrimal, and infratrochlear nerves arise from the ophthalmic branch of CN V, and the zygomatic nerve arises from the maxillary branch of CN V [6, 12]. The frontal (supraorbital) nerve innervates most of the central upper eyelid and is the only sensory block normally required for examination [12]. The lacrimal nerve provides sensory innervation for the lateral upper eyelid [12]. The infratrochlear nerve provides sensory innervation for the medial canthus [12]. The zygomatic nerve innervates the majority of the lateral lower eyelid [12]. The nasociliary nerve, a branch of the maxillary branch of CN V, provides sensory innervation to the cornea [12]. Anesthesia of these nerves is sometimes necessary for eyelid and conjunctival biopsies or simple surgeries, as well as subpalpebral lavage placement in the horse. The anesthetics most frequently used

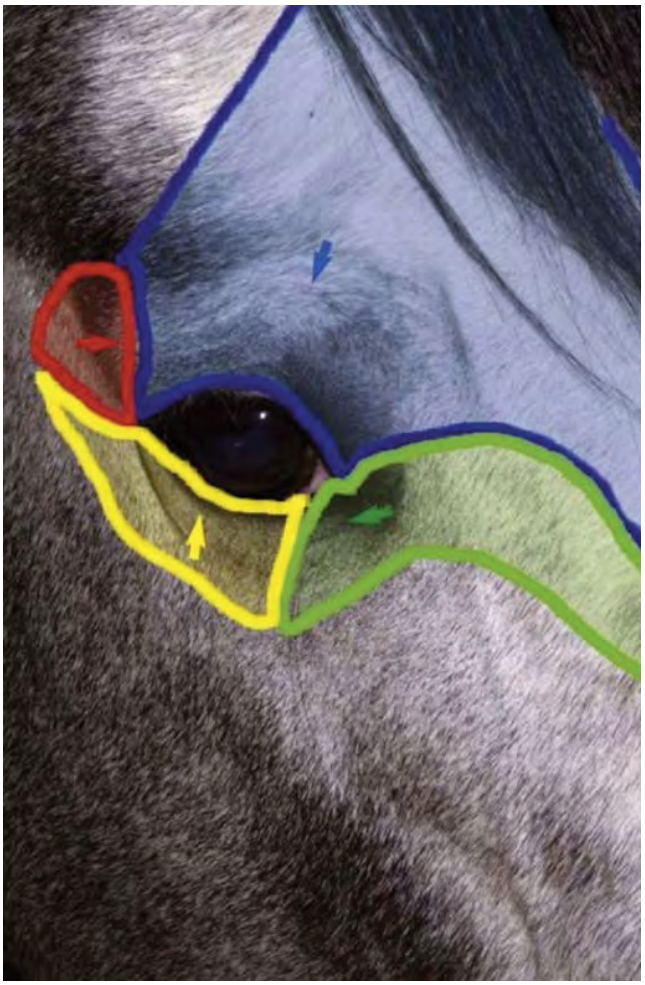


Figure 1.14 Sensation to the eyelids is provided by the ophthalmic and maxillary divisions of the trigeminal nerve (CN V). The frontal, lacrimal, and infratrochlear nerves arise from the ophthalmic branch of CN V, whereas the zygomatic nerve arises from the maxillary branch of CN V. The approximate areas of sensation that would be blocked with each nerve are indicated as follows: frontal (blue), lacrimal (red), zygomatic (yellow), infratrochlear (green).

are the same as those used for akinesia and include lidocaine HCl and mepivacaine.

The four main sensory nerve branches can be blocked directly as follows: the frontal (supraorbital) nerve is blocked as it emerges from the supraorbital foramen within the frontal bone (Figures 1.15 and 1.16) [12, 17]. This foramen can be easily palpated by placing the thumb below the dorsal orbital rim and the middle finger in the supraorbital fossa. The index finger is placed straight down, midway between the thumb and middle finger, to locate the supraorbital foramen (see Figure 1.16). A depression is usually palpable. A 25-G, ⅝-inch needle is then inserted subcutaneously over the foramen, and 1–2 mL of anesthetic is injected (Figure 1.17). Passing the needle into the foramen is not recommended because this may damage the supraorbital artery and vein, which exit the skull through the



Figure 1.15 The frontal (supraorbital) nerve is blocked as it emerges from the supraorbital foramen within the frontal bone, as indicated by the white dot.

supraorbital foramen. Furthermore, if the needle inadvertently enters the periosteum surrounding the supraorbital foramen, this can be painful and the horse may react negatively. The frontal nerve is mainly sensory, but this block can result in partial upper eyelid akinesia as well, likely by further denervating the branches of the palpebral nerve [9].

The lacrimal nerve can be blocked by injecting 1 mL of lidocaine adjacent to the lacrimal notch, a depression that can be palpated on the dorsolateral bony orbital rim, or by using a line block along the lateral third of the dorsal orbital rim (Figures 1.14 and 1.18). The zygomatic nerve can be blocked with a line block along the ventrolateral orbital rim (Figures 1.14 and 1.19).

The infratrochlear nerve can be blocked as it runs through the trochlear notch located medially on the dorsal orbital rim (Figures 1.14 and 1.20). The notch can be palpated along the orbital rim.

Globe and orbit examination

Anatomy of the globe and orbit is reviewed in detail in Chapter 5. Initial examination of the globe and orbit should be made with the examiner positioned in front of the horse (see Figure 1.4), where symmetry between the eyes is carefully assessed. Palpebral fissure size and symmetry, relative globe position, and direction of the eyelashes are evaluated. The upper eyelashes of the healthy horse are nearly perpendicular to the cornea (see Figure 1.5A) [8]. A change in the angle between the eyelashes and the cornea may indicate blepharospasm, enophthalmos, exophthalmos, or ptosis (see Figure 1.5B) [8].



Figure 1.16 The supraorbital foramen can be palpated with the thumb below the dorsal orbital rim and the middle finger in the supraorbital fossa. The examiner then places the index finger straight down midway between the thumb and middle finger to locate the supraorbital foramen.



Figure 1.17 A 25-G, ⅝-inch needle is inserted into or just over the foramen.

Apparent changes in globe size (e.g., buphthalmos (Figure 1.21)) should be differentiated from changes in globe position (e.g., exophthalmos (Figure 1.22)). Cornea globosa (Figure 1.23) has been reported in the Rocky Mountain horse and may be difficult to distinguish from buphthalmos [38, 39]. The orbit should be examined by observation, palpation of the bony orbital rim, and retropulsion of the globe through a closed eyelid [4, 8, 9]. Forceful manipulation of the eyelid and retropulsion should not be performed if the structural integrity of the cornea or globe may be compromised.

Eyelids and conjunctiva examination

Anatomy of the eyelids and conjunctiva is reviewed in detail in Chapter 6. Examination of the eyelid should include assessment of function and detailed examination using diffuse illumination with magnification (e.g., using a slit-lamp biomicroscope). The periocular tissues including the eyelids, conjunctiva, sclera, and nictitans should be inspected with transillumination [17], the technique of direct focal illumination for inspection of the



Figure 1.18 The lacrimal nerve can be blocked by using a line block along the lateral third of the dorsal orbital rim.

anterior structures of the eye. It can be performed with a Finnoff transilluminator (Welch-Allyn, Skaneateles Falls, NY), direct ophthalmoscope, slit-lamp biomicroscope, or even a penlight. Eyelids should be examined for position, movement,



Figure 1.19 The zygomatic nerve can be blocked with a line block along the ventrolateral orbital rim.



Figure 1.20 The infratrochlear nerve can be blocked as it runs through the trochlear notch, located medially on the dorsal orbital rim. The notch can be palpated.



Figure 1.21 Right eye congenital glaucoma and hydrophthalmus in a foal.



Figure 1.22 Exophthalmos of the right eye of a horse with a retrobulbar mass.

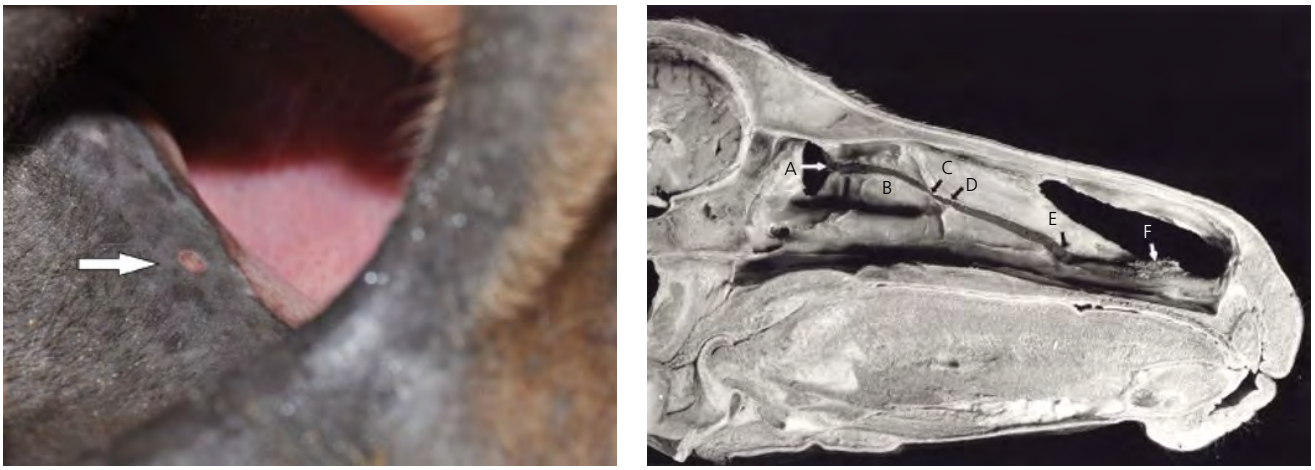


Figure 1.23 Corneal globosa of a Rocky Mountain horse with multiple congenital ocular anomalies. (*Source*: Photograph courtesy Dr David Ramsey.)

and conformation prior to the use of eyelid blocks [4, 8, 9] Attempts to forcefully elevate the upper eyelid should be avoided if a palpebral nerve block has not yet been performed, and each eye should be examined with minimal handling of the adnexal tissues. Culture and cytology should be collected prior to instillation of any medications (see section **Culture and cytology of corneal lesions** and Chapter 3). Biopsy of the eyelid or conjunctiva should be considered if indicated (see Chapter 6).

Lacrimal and nasolacrimal system examination

See anatomy of the lacrimal and nasolacrimal system in Chapter 6. Assessment of the lacrimal system is done by microscopic examination of the tear film via slit-lamp biomicroscopy



(A) (B)

Figure 1.24 (A) Normally a single distal punctum of the nasolacrimal system is present and can be located in the skin of the floor of the nostril near the mucocutaneous junction (**arrow**). (B) Methyl methacrylate cast of the left nasolacrimal duct in the horse with the medial bony orbit and medial wall of the lacrimal canal removed. (A) Lacrimal sac. (B) Duct within the lacrimal canal. (C) Narrowing of nasolacrimal duct at the exit from the lacrimal canal. (D) Exit of the duct from the lacrimal canal. (E) Duct pressed laterally by cartilaginous plate in alar fold. (F) Duct within basal fold. (*Source*: (B) Latimer et al., 1984. Reproduced with permission from American Veterinary Medical Association.)

(or other means of magnification) and adjunctive diagnostic tests, such as the Schirmer tear test (STT), the phenol red thread (PRT) tear test and Tear film Break-Up Time (TBUT) test. The examiner should also inspect the openings of the proximal (eyelid) and distal (nasal) nasolacrimal puncta (Figure 1.24).

The STT is used commonly to measure aqueous tear production [40–43]. In the test, a filter paper strip is placed in the lower conjunctival sac, and wetting is then measured in millimeters per 60 seconds (Figure 1.25). Commercial filter paper strips available include standardized Sno-Strips (Akorn) and Color Bar (Eagle Vision/Schering-Plough). Strips can also be made from Whatman filter paper (#40, 5 × 40 mm with a notch 5 mm from the end) [12]. The STT I, in which no topical anesthesia is used, measures the approximate amount of basal and reflex tearing. The STT II, performed after the application of topical anesthesia, theoretically only measures basal secretion of aqueous tears. Some residual tear volume may make both of these measurements slightly inaccurate. The STT should be performed before manipulation of the eye and orbit during examination to minimize reflex tearing. There are no reports of the effect of an auriculopalpebral nerve block on the STT in horses.

The PRT test consists of a thread of 75 mm in length with a fold 3 mm from the end, impregnated with phenol red, which is a pH indicator. The thread is placed in the lower conjunctival fornix for 15 seconds. The pale yellow thread turns orange due to the alkaline tears composition. Even if the main advantage of this test is that it can be used in small eyes (e.g., nondomestic species), it has been used in horses too, with a mean tear production of 30.22 ± 0.99 and 31.00 ± 1.4 in healthy Arabian and Thoroughbred horses [44]. The TBUT test is a noninvasive ocular diagnostic test that allows an assessment of the quality of the precorneal tear film (mucin and/or lipid layers) by observing its stability over the corneal surface. It corresponds to the time required for the ocular surface to lose cohesive surface wetting after each blink. To perform the TBUT test, fluorescein solution is applied to the corneal surface, the horse is allowed to blink, and then the eyelids are held open until a dry spot forms, which



Figure 1.25 The STT is used to measure aqueous tear production. In the test, a filter-paper strip is placed in the conjunctival sac, and wetting is then measured in millimeters per 60 seconds.

appears dark compared to the fluorescein green color in the tear film. The observation of these dark areas is facilitated by using a slit-lamp biomicroscope with the cobalt blue filter. Mean basal TBUT values reported in horses are 8.3 ± 1.3 seconds [45]. Topical use of tetracaine HCl eyedrops in a normal horse results in a quicker TBUT [45].

Deficiencies in aqueous tear production have rarely been reported in the horse [23, 42, 43, 46–51]. This may be because the STT is not a part of the routine ophthalmic examination in the horse. Specific indications to perform STT include evidence of CN VII dysfunction (e.g., after trauma, facial paralysis), desiccated cornea or conjunctiva, presence of tenacious mucoid discharge, and presence of unexplained corneal vascularization or ulceration. Keratoconjunctivitis sicca (KCS) is most commonly the result of CN V or VII trauma but has also been reported in cases of fractures of the mandible and stylohyoid bone, post anesthesia, locoweed poisoning, eosinophilic dacryoadenitis, hypothyroidism, and in association with corneal stromal sequestration [23, 41, 43, 46–51].

The effects of age, season, gender, environment, sex, time of day, and placement of strips on STT results in healthy horses and ponies have also been reported [40, 42]. In general, the STT value in the horse is much greater than that in cats and dogs [41, 52, 53]. STT values are highly variable between eyes and between the same eye during different times of the day, and this appears to be unrelated to signalment, housing, or season [40]. One study found a diurnal variation in horses housed in a 12-hour light and 12-hour dark setting [42]. These horses had STT values that gradually increased during the light phase, peaked at 4–6 hours, then decreased during the dark phase [42]. Healthy horses have been reported to have an STT I range of 11–>30 mm wetting/min and 15–20 mm/30 s. Both sick and healthy neonatal foals have been reported to have lower STT values than adults [54, 55]. STT I values for sick neonatal foals (14.2 ± 1 mm wetting/min) and healthy neonatal foals (12.8 ± 2.4 mm/min) were not significantly different but were lower than STT I values from healthy adult horses (18.3 ± 2.1 mm/min) [54, 55].

Comparisons of STT I and STT II values revealed minimal differences in one study (i.e., STT I and STT II values of 12.7 ± 9.1 mm wetting/min and 9.9 mm ± 4.25 mm wetting/min) [53], while the second study did not reveal a difference between STT I and STT II values [40]. This is in contrast to the dog, in which the STT I value is significantly higher than the STT II value [56]. Sedation with xylazine does not affect the STT value; however, general inhalant anesthesia with halothane does lower the STT value for up to 3 hours [41].

Borderline STT measurements (e.g., measurements of 10–15 mm wetting/min) should always be repeated. Comparison of tear test results between the two eyes should be cautiously interpreted in clinical assessment of decreased tearing [40]. In general, repeatable measurements of less than 10 mm wetting/min should be considered abnormal in conjunction with clinical signs [4]. See Chapters 6 and 7 for more information on KCS.



Figure 1.26 Passage of fluorescein dye to the distal punctum in the nares (Jones test I) is timed and should occur within 5 minutes but may take up to 20 minutes in the horse.

Nasolacrimal duct patency

The physiologic patency of the nasolacrimal system can be evaluated with topical sodium fluorescein, which is not rinsed from the eye [12]. Passage of the fluorescein to the distal puncta in the nares (Jones test I) is timed and should occur within 5 minutes but may take up to 20 minutes (Figure 1.26) [17]. The required time for passage is influenced by the amount of fluorescein placed, tear production, and length of the individual horse's nasolacrimal system [17]. A positive test result is definitive for a patent nasolacrimal duct but does not prove that both proximal puncta are patent [17]. A negative test result is only suggestive of a problem and may even be normal in the horse because of the large volume capacity of the nasolacrimal duct [17, 57, 58]. However, the nasolacrimal duct should be irrigated if the dye fails to appear and clinical signs suggest a problem such as epiphora (watery ocular discharge) without an obvious cause, mucopurulent ocular or nasal punctal discharge, or dacryohemorrhea [17, 57, 58].

Irrigation of the nasolacrimal duct can be performed retrograde (i.e., from the distal nares opening) or normograde (i.e., from the proximal eyelid puncta) [12]. Sedation is usually required to perform either procedure in the horse. Retrograde irrigation through the nasal meatus to the nasolacrimal duct is easiest to perform (Figure 1.27) because of the larger size of the opening [17, 58]. The distal nasolacrimal puncta can usually be cannulated by a 5 or 6 polyethylene urinary catheter [17]. Suitable catheters are 4- to 6-French canine urinary catheters, 5-French feeding tubes, or polyethylene tubing [17]. The largest catheter that will pass through the bony canal in an adult horse is a 6-French urinary catheter [17]. The tip of the catheter, after it has been coated with lidocaine gel, is inserted into the distal punctal opening for a distance of at least 5 cm. Digital pressure should be applied to the opening to close it and prevent normograde loss of fluid. A 12- to 20-mL syringe previously filled with



(A)



(B)

Figure 1.27 Retrograde irrigation through the distal opening to the nasolacrimal duct is easiest to perform. (A) The tip of the catheter, after it has been coated with lidocaine gel, is inserted into the distal punctal opening. Digital pressure should be applied to the opening to prevent normograde loss of fluid. (B) The 12-mL syringe, previously filled with eyewash, is attached; gentle irrigation of the nasolacrimal duct is performed until fluid exits the proximal punctum near the medial canthus of the eye.

Box 1.5 Supplies needed for irrigation of the nasolacrimal duct.

Retrograde irrigation

- Lidocaine gel for retrograde
- Open-ended tomcat catheter, 4- to 6-French polyethylene urinary catheter, 5-French feeding tubes, or polyethylene tubing
- A 12- to 20-mL syringe
- Sterile eyewash or balanced salt solution

Normograde irrigation

- Topical anesthetic (proparacaine HCl)
- Open-ended tomcat catheter, lacrimal cannula, 18- to 20-G IV cannula
- A 12- to 20-mL syringe
- Sterile eyewash or balanced salt solution

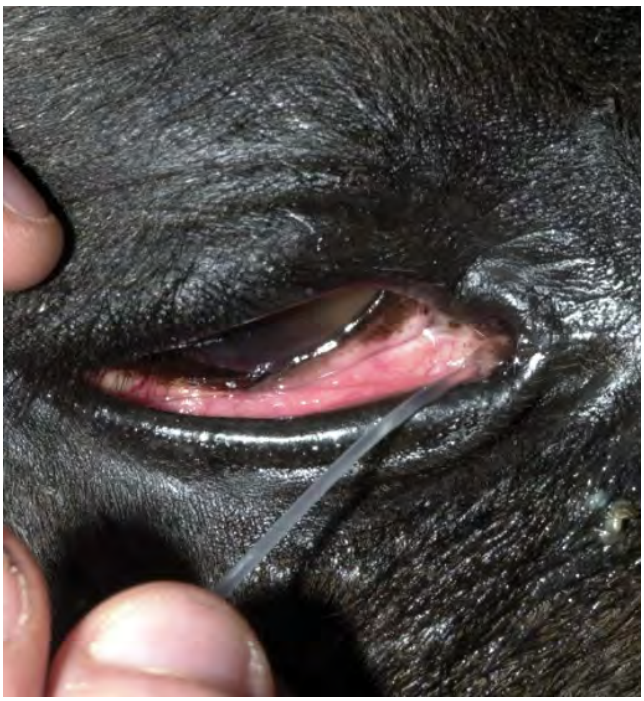


Figure 1.28 Normograde irrigation from the proximal puncta should be attempted if the result of the Jones test I is negative and the duct cannot be irrigated from the distal nasal puncta. Catheterization of the proximal punctum using an open-ended tomcat catheter in the lower eyelid is demonstrated.

eyewash is attached, and gentle irrigation of the nasolacrimal duct is performed until fluid exits the proximal puncta near the medial canthus of the eye. Sneezing by the horse is common during this procedure and may be violent. A list of supplies needed to perform nasolacrimal duct irrigation can be found in Box 1.5.

If retrograde irrigation is unsuccessful, then normograde irrigation from the proximal puncta should be attempted with a lacrimal cannula, open-ended tomcat catheter, 18- to 20-G IV cannula, or teat tube syringe (Figure 1.28) [17]. The punctum in

the lower eyelid is usually slightly larger and easier to cannulate than the punctum in the upper eyelid [17]. Gentle pulse pressure may be required to unblock an obstructed duct. Excessive force in the placement of the catheter or during irrigation should be avoided because significant damage to the nasolacrimal duct could result [17]. Ducts that are compromised by a foreign body or other anatomic obstruction (e.g., after trauma, mass effect) may not be effectively irrigated [59] Skull radiographs or computed tomography (CT) scans and a contrast dye study (e.g., dacryocystorhinography) should be performed next if the duct cannot be irrigated. Endoscopic examination of the nasolacrimal duct also has been described [60]. See descriptions of these diagnostic techniques in the Chapter 2.

Cornea and sclera examination

The anatomy and diseases of the equine cornea are described in Chapter 7. To examine the cornea of the horse, diffuse and focal direct illumination (or transillumination) with magnification is used first, followed in most cases by biomicroscopy using a slit-lamp. The corneal examination should be performed with the observer located rostral to the eye. Light directed diagonally across the cornea will reveal opacities of the cornea against the dark background of the pupil [17].

The Purkinje–Sanson reflexes are three reflections from the eye produced by the light source during transillumination (Figure 1.29) [17]. Disease may alter the sharpness and location of these reflexes. The first, largest, and most anterior originates from the cornea. The second originates from the anterior lens capsule, and the third and most posterior originates from the posterior lens capsule. If a slit-lamp biomicroscope is used, two corneal reflexes are seen, one from the anterior surface and the other from the endothelium [17]. The corneal and anterior lens capsule reflexes are virtual and noninverted and will move in the same direction as a change in the light position. The image on the posterior surface is real and inverted and will move in the opposite direction to the light [17]. The images are valuable in determining corneal clarity, depth of the anterior chamber, thickness and position of the lens (after mydriasis), and in locating lesions within the lens [17].

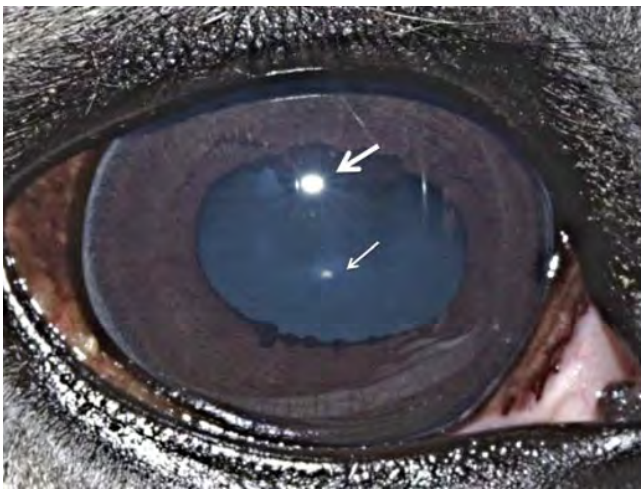


Figure 1.29 The Purkinje–Sanson reflexes are three reflections produced by the light source during transillumination. The largest is produced by the cornea (**larger arrow**). The second is produced by the anterior lens capsule (**smaller arrow**). The third is not easily visible and is produced by the posterior lens capsule.

Biomicroscopy for corneal examination

The technique of biomicroscopy, in which a slit-lamp binocular microscope with an external pivoting light source is used, is the same for horses as for humans and small animals and has been well described elsewhere [12, 61–64]. Slit-lamp biomicroscopy improves visualization and localization of lesions of the cornea, anterior chamber, lens, and anterior vitreous by means of transillumination and retroillumination [12]. It can also be used to assess corneal thickness (i.e., pachymetry), anterior chamber depth, and aqueous flare [12].

The availability of portable handheld models of the slit-lamp biomicroscope has made biomicroscopy for equine ophthalmology easy and efficient. Portable models are available from Clement-Clark, Kowa, Nippon, Dioptrix, and Zeiss. The Kowa SL-14, SL-15, and SL-17 (×10 or ×16 magnification) is light and powered by battery, and therefore of excellent use in examination of a horse. However, lack of magnification above ×16 and inherent movement of the examiner and horse limit the ability to see fine structure and lesions. An alternative to a biomicroscope is using magnification (i.e., ×2.5–3.0 magnifying head loupes) and the slit beam on the direct ophthalmoscope. Very small "slit-lamps" are also made by Heine (HSL 150 (Heine USA, Dover, NH); Eidolon Hand Held Slit Lamp Model 510 L (Eidolon Optical LLC, Natick, MA)) that resemble a penlight with a magnifier on the end (Figure 1.30). Although these instruments are inexpensive and portable, their lack of magnification and illumination limits their usefulness [12].



Figure 1.30 Use of a small, portable slit-lamp (Heine Handheld Slit Lamp (Heine USA, Dover, NH)). (*Source*: Photograph courtesy Dr David Wilkie.)

The light beam of the biomicroscope should be angled at 20–45 degrees from the axis of the microscope and thus the visual plane of the observer (Figure 1.31). The light beam width, length, orientation, and color can then be modified by a series of diaphragms and filters [12]. The focal distance of the instrument is 7–10 cm, and fine focus is achieved by moving either toward or away from the eye within this range [12].

Particular attention needs to be used during biomicroscopy examination in horses, as during this examination the examiner's eyes are in contact with the slit-lamp without direct visualization of the entire animal. In this situation, sudden head movement could be very dangerous for the examiner and for the instrument as well. To avoid possible trauma from the horse, it is important to stay in contact with the horse's head with your hand (Figure 1.31). It is also very important to remove glasses, if used, during this examination.

The initial examination of the horse should proceed with diffuse illumination: a wide, low-intensity slit beam should be used, and the microscope should be defocused from the light [12]. The surfaces of the eyelids, cornea, conjunctiva, and iris should be inspected. With the use of low magnification, a broad slit beam is focused on the cornea, creating a parallelepiped (i.e., a three-dimensional section) of illuminated tissue [12, 61]. This allows visualization of transparent structures such as the cornea and lens in three dimensions. In the cornea, the anterior surface, stroma, and posterior surface of the cornea can be visualized [61]. Nontransparent structures such as the sclera only yield a magnified two-dimensional surface or external view. The slit beam is then narrowed and intensified to reveal a two-dimensional cross-section of the cornea and lens, allowing the examiner to accurately determine lesion depth and axial positioning [61]. This is extremely important in evaluating the depth of corneal lesions (e.g., stromal ulcerative keratitis, stromal abscesses) in the horse.

Direct and indirect retroillumination are performed by reflecting the slit beam from deeper structures while focusing on more superficial structures [61]. Other techniques that can be performed with slit-lamp biomicroscopy, such as specular reflection, are difficult to impossible in a horse because of continuous slight ocular movements.

Culture and cytology of corneal lesions

See Chapter 3 and online material for detailed information on collecting and interpreting ocular cultures and cytology.

Ophthalmic dyes

Topical ophthalmic dyes are routinely used in veterinary medicine to aid in the diagnosis of corneal, conjunctival, and nasolacrimal diseases. Commonly used topical ophthalmic dyes include sodium fluorescein, rose bengal, lissamine green, alcian blue, trypan blue, and methylene blue [12, 65–67]. Sodium fluorescein and rose bengal are the two most commonly used dyes in clinical veterinary ophthalmology [12, 66, 68, 69]. Indications for the use of topical ophthalmic dyes in the horse include determining the health and integrity of the precorneal tear film, corneal epithelium, and conjunctival epithelium, and the physiologic flow of the nasolacrimal system. Intravenous sodium fluorescein is used to perform fluorescein angiography and is discussed in Chapter 2.

Sodium fluorescein

The most common use for topical sodium fluorescein is detecting ulcerative keratitis, but it will also stain conjunctival ulcerations and abrasions. In a corneal ulceration, the hydrophilic fluorescein binds to the corneal stroma but not to the lipophilic epithelium or to Descemet's membrane (Figure 1.32). Small quantities can also pool or diffuse through intact epithelial cell intercellular spaces to reveal weakly staining epithelial



Figure 1.31 The light beam of the biomicroscope should be angled at 20–45 degrees from the axis of the microscope (Kowa SL-17) and thus the visual plane of the observer. The examiner should always be in contact with the horse's head, avoiding possible trauma from head movements.

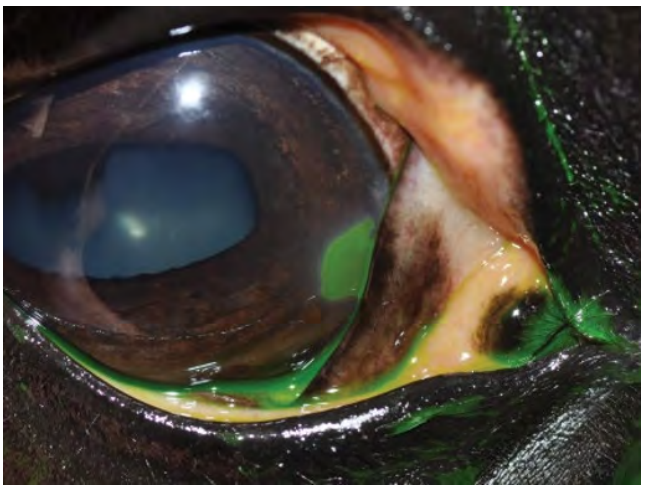


Figure 1.32 In a corneal ulceration, the hydrophilic fluorescein binds to the corneal stroma but not to the epithelium or to Descemet's membrane, resulting in a green stain.

microcysts and partial-thickness microerosions [12, 67]. From the stroma, the dye can then readily pass through Descemet's membrane and the corneal endothelium to enter the aqueous humor and can be quantified (e.g., by fluorophotometry).

Fluorescein staining of the cornea is indicated for almost every condition in the horse involving its eye and orbit—a red or painful eye, discharge from the eye, an obvious corneal irregularity, history of ocular trauma—and for assessment of the tear film stability (TBUT) and physiologic nasolacrimal function. Fluorescein is available as a sterile 0.5–2% alkaline solution or as a sterile impregnated paper strip [70]. The impregnated paper strips should be used for topical application, because the solutions have been associated with bacterial contamination [71]. Other equipment needed to perform the stain includes sterile eyewash solution and a 3-mL syringe with a 25-G needle. The easiest method of applying topical fluorescein to horses is to place a sterile fluorescein strip in a 3-mL syringe, fill the syringe with sterile eyewash, replace the plunger, and then squirt the solution through the **hub** of a 25-G needle from which the needle has been manually broken off (Figure 1.33) [8, 17]. After application, the eyelids should be closed or the animal allowed to blink to distribute the stain evenly across the ocular surfaces. Excess fluorescein can be removed with gentle irrigation with eyewash if required. Alternatively, undiluted fluorescein applied topically may allow for better visualization of corneal epithelial erosions or early corneal trauma. The use of an ultraviolet or blue light, usually available on a direct ophthalmoscope or the slit-lamp biomicroscope, may improve visualization of the stain. False-positive results may occur after the use of proparacaine topical anesthesia or if direct contact between the paper strip and cornea occurs, which may leave a mark that resembles a corneal defect [12, 17].

Fluorescein may also be used to detect leakage of aqueous humor through the cornea (i.e., the Seidel test) [12, 17]. The Seidel test can be used to detect full-thickness corneal injuries or determine whether a corneal suture is leaking. The application of sodium fluorescein without subsequent irrigation results in a high dye concentration in which the dye fluoresces at wavelengths closer to the yellow and orange spectra. With or without gentle pressure on the cornea, aqueous leakage locally dilutes the fluorescein, and the dye fluoresces green [12].



Figure 1.33 The easiest method of applying topical fluorescein to horses is to place a sterile fluorescein strip in a 3-mL syringe, fill the syringe with sterile eyewash, replace the plunger, then squirt the solution through the hub of a 25-G needle from which the needle has been manually broken off.

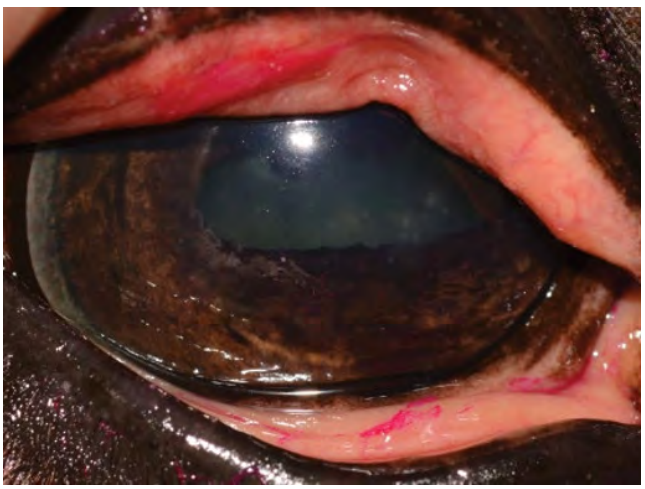


Figure 1.34 Rose bengal positive stain of epithelial multipunctate lesions suspected of superficial primary fungal infection.

Rose bengal

Rose bengal (i.e., tetrachloro-tetra-iodo-fluorescein) has been used to aid in the diagnosis of precorneal tear film disorders, mucin precorneal film deficiencies, and superficial corneal epithelial abnormalities in horses (Figure 1.34). It can be used primarily or after sodium fluorescein application. Rose bengal stains dead and degenerating cells and mucus [67]. However, rose bengal has a dose-dependent ability to stain normal cells, and this ability is normally blocked by tear film components [12, 67, 72]. Therefore stain uptake may indicate tear film abnormalities, such as a mucin deficiency, more accurately than cell viability [12, 67, 72]. Rose bengal, like sodium fluorescein, is available as both an impregnated paper strip and a solution [12, 66, 69]. Use of the 0.5% or lower concentrations can minimize the irritation that can be associated with the 1% solution [12]. The dye has also been shown to be toxic to corneal epithelium at routine concentrations [73]. Slit-lamp biomicroscopy may be necessary for adequate visualization of rose bengal stain.

The use of rose bengal would be indicated in the horse in any of the conditions in which corneal or conjunctival ulceration is suspected, but especially when a viral or fungal cause is suspected. One report suggested that rose bengal staining is present as a result of ocular surface damage in the presence of keratomycosis (Figure 1.34) [74]. Specimens obtained from horses with painful eyes should be stained with both fluorescein and rose bengal; superficial keratitis may be negative for fluorescein but positive for rose bengal [23, 74].

Other ophthalmic dyes

Lissamine green is an organic acid dye widely used in human ophthalmology [67]. It is a true vital dye as it does not stain healthy epithelial cells even in the absence of the tear film, differently from rose bengal. Despite this difference, lissamine green has a similar staining pattern to rose bengal and it has been used in the case of KCS, with the advantage that it is less toxic and irritant than rose bengal [69, 75, 76]. Different dyes can be applied alone or at the same time, as mixing of the dyes does not affect staining properties [69, 77].

Trypan blue, an azo dye derived from tuluidine, is widely used in human and veterinary cataract surgery, as it stains the anterior lens capsule and thus helps its visualization during capsulorrhexis. Also it has been used in two recent studies on equine cornea: an *in vitro* model for corneal scarring treatment with mitomycin C and a novel model method of gene delivery [78, 79].

Anterior chamber and iris examination

The intraocular portion of the ocular examination is conducted next. See Chapter 8 regarding the anatomy and diseases of the anterior chamber and uvea of the horse's eye. With a thin beam (slit) or small circular beam of light from the light source directed at a 45-degree angle to the eye, the anterior chamber depth and clarity are inspected. In a healthy horse, this will not result in any internal reflection of light from the aqueous, and the anterior chamber should appear clear (Figure 1.35). If solids (e.g., protein, cells) are present in the aqueous, there will be a reflection of light from these particles (i.e., the Tyndall effect) [12]. This turbidity results in visualization of the beam of light traversing the anterior chamber and is referred to as **aqueous flare**. Aqueous flare (and other ocular lesions such as corneal edema, corneal pigment, and conjunctival redness) can be graded on a subjective scale from 1+ to 4+, with 4+ being the greatest degree of severity.

Tonometry

Measurement of intraocular pressure (IOP) in the horse has been revolutionized by the development of handheld portable digital tonometers. Direct tonometry via a manometer is the most accurate but invasive method for recording the IOP and is not practical for clinical use. Indirect tonometry, the measurement of corneal tension, is the technique used to determine IOP in clinical veterinary ophthalmology [17]. Digital, indentation, and applanation tonometry have all been described in the horse [12]. Digital tonometry, the estimation of IOP by digital palpation, can be considered just approximate but not accurate. Indentation tonometry, commonly performed with a Schiotz tonometer, requires general anesthesia (a lateral position) in the horse and is impractical. However, normal values have been reported for the Schiotz tonometer in the horse and are 14–22 mm Hg [17]. Applanation tonometry measures the amount of flattening (area of contact) of the cornea when a weight touches it [12, 17]. The force it takes to flatten this portion of the cornea is an estimate of the IOP (pressure = force/area). Rebound tonometry (TonoVet tonometer (ICare Finland Oy, Helsinki)) is another method to measure IOP in horses. This uses a disposable probe that is electromagnetically propelled to contact the cornea, then rebound to the instrument, which then uses these rebound characteristics to estimate IOP [80]. Accurate measurement of IOP in the standing horse requires use of applanation or rebound tonometry (Figure 1.36) [8, 12]. In one study involving normal horses, the TonoVet rebound tonometer correlated well to manometry IOP measurements, and IOPs obtained with the TonoVet rebound tonometer (Figure 1.37) were higher than with the Tono-Pen applanation tonometer (Figure 1.38) [80].

Tonometry is part of routine ocular examination and it is particularly indicated in horses with focal or diffuse corneal edema, a red or painful eye, orbital trauma, ocular blunt trauma, exophthalmos or hydro-ophthalmos, a history of glaucoma in the

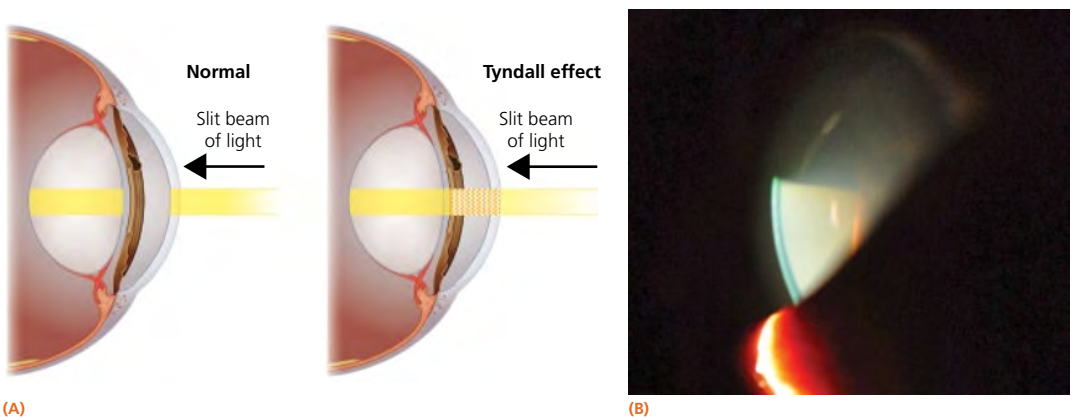


Figure 1.35 (A) With a thin beam (slit) or small circular beam of light from the light source directed at a 45-degree angle to the eye, the anterior chamber depth and clarity are inspected. In a healthy horse, this will not result in any internal reflection of light from the aqueous, and the anterior chamber should appear clear. If solids (e.g., protein, cells) are present in the aqueous, there will be reflection of light from these particles (i.e., the Tyndall effect). (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.) (B) This turbidity results in visualization of the beam of light traversing the anterior chamber and is referred to as aqueous flare.



Figure 1.36 Materials needed to perform tonometry in the horse. Accurate measurement of IOP in the standing horse requires tonometry, either using a Tono-Pen digital tonometer (TP) or a TonoVet rebound tonometer (TV), or similar instrument. The Tono-Pen tonometer requires use of a topical anesthetic, such as 0.5% proparacaine HCl (P), while the TonoVet does not.



Figure 1.37 Tonometry in the horse using a TonoVet tonometer.

opposite eye, or a lens subluxation/luxation; it is also indicated for follow-up examinations of animals with medically controlled glaucoma [8, 12] Three separate readings with less than 5% standard error are averaged to obtain the IOP in millimeters of mercury [12, 17]. If significant corneal disease is present, the most normal part of the cornea should be used to take readings [17]. A fibrotic or edematous cornea may result in a falsely elevated IOP [17]. See Chapter 10 for more information on the diagnosis and treatment of glaucoma.



Figure 1.38 Tonometry in the horse using a Tono-Pen tonometer.

Horses that require sedation for ocular examination may show dramatic decreases in IOP, as illustrated by one study in which xylazine decreased IOP by 23% [81]. In another report, the IOP range was 20.5–39.8 mm Hg and showed that both acepromazine and xylazine decreased IOP [82]. A combination of xylazine and ketamine had no effect [83, 84]. The effect of IV administration of romifidine on IOP in normal horses has been recently described by two publications. In the first report, a consistent decrease of IOP after romifidine IV administration (75 μg/kg) was noted, with the largest change from baseline values (16.7%) at 15 minutes after injection [85]. The second report describes a highly significant IOP decrease 45 minutes after IV injection of romifidine (40 μg/kg) in right eyes (58.5% decrease) and left eyes (55.2% decrease) from the baseline values. In this second report, IOP values returned to normal 120 minutes after the IV injection [86]. It has been suggested that horses without an auriculopalpebral block will have an elevated IOP due to eyelid tension [17, 84] but this has not been supported in two other studies in normal horses [81, 87]. However, horses with ocular disease such as glaucoma may be blepharospastic; therefore auriculopalpebral blocks are recommended prior to tonometry. IOP in normal horses without an auriculopalpebral nerve block has been reported as ranging from 24.5 ± 4.0 mm Hg to 28.6 ± 4.8 mm Hg, while baseline IOP values in horses with auricolopalpebral nerve block has been reported as ranging from 24.25 ± 3.5 mm Hg to 26.35 ± 5.57 mm Hg [80, 85, 86, 88]. In one study of normal horses in which horses were tranquilized with detomidine and given auriculopalpebral nerve blocks, 87% of horses with their head positioned lower than their hearts had elevated IOP [89]. In another study, circadian rhythm was shown to have an influence on horses' IOP [90]. In this study, IOP was found to be low during the dark phase and high during the light phase, with a peak at the end of the light phase [90]. Evaluating the results of these studies together, it is

recommended that the examiner be consistent when measuring IOPs in horses in terms of time of day, nerve blocks, head position, and tranquilization, especially when performing repeated IOPs on the same horse. Tranquilization (always the same drug), auriculopalpebral nerve blocks, and an elevated normal head position are recommended for tonometry in horses.

Countertop electronic applanation tonometers may also still be available (e.g., MacKay-Marg (Biotronics, Redding, CA); the Alcon pneumotonograph) and can be used to measure IOP in horses. The MacKay-Marg tonometer was shown to produce reliable results in comparison with direct tonometry in the dog, rabbit, and horse [88, 91, 92]. It has been used to study IOP in the horse [81, 83, 87, 88]. IOP measured in the normal horse using the MacKay-Marg tonometer in one report was 20.6 ± 4.7 mm Hg [81].

The Alcon pneumotonograph is an applanation tonometer-tonographer that measures IOP via a gas-suspended plunger. Measurements can be permanently recorded on heat-sensitive paper. However, pneumotonography may provide falsely elevated pressure readings in the horse [93].

Tonography

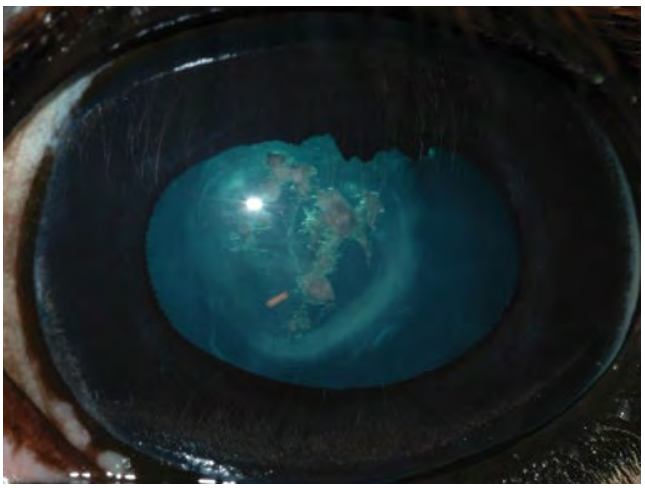
Tonography is the use of continuous tonometry to noninvasively estimate the pressure-sensitive facility of conventional aqueous humor outflow [12, 94]. In theory, the weight of the tonographic probe on the cornea increases both IOP and the rate of aqueous humor outflow without changing the rate of aqueous humor production [12]. The subsequent decline in IOP (decay curve) is measured over 2–4 minutes, thereby allowing an estimation of conventional outflow (corneoscleral trabecular outflow) [12]. The unconventional outflow (uveoscleral) is pressure independent and thus not estimated by tonography. Uveoscleral outflow in the horse is substantial and may be the major outflow pathway, but it cannot be measured by tonography [83]. Tonography has been used in the normal horse to estimate the facility of aqueous humor outflow (C-value). A measured equine C-value of 0.88 ± 0.65 mL/min per mm Hg is substantially higher than that reported for the healthy dog and cat (0.24–0.27 mL/min per mm Hg) [94–96]

Lens examination

For details on the anatomy and diseases of the lens see Chapter 9. Complete evaluation of the lens requires a dilated pupil; therefore use of 1% tropicamide HCl is recommend 15–20 minutes prior to initiating the lens examination. The lens is initially evaluated using direct focal illumination (i.e., transillumination) and retroillumination. Transillumination of the lens is performed by directing a beam of light at a 45-degree angle into the lens and directly observing the lens using this light [17]. Retroillumination is examining the lens using light reflected by the tapetum and posterior segment structures of the eye. This is done by using a direct ophthalmoscope or other focal light source (e.g., a Finnoff transilluminator) and starting about an arm's length from the horse, directing the light to obtain a bright tapetal reflex, then moving toward the animal to bring the lens structures into focus. This technique improves detection of opacities in the cornea, anterior chamber, lens, and vitreous because these opacities reflect, refract, or obstruct returning light (Figure 1.39A) [17]. Normal Y sutures can be visualized with transillumination but not with retroillumination [17]. With transillumination, nuclear sclerosis (i.e., the normal aging change of the lens due to increased lens density) will appear as a greater central translucence, with the cortex remaining clear [17]. On retroillumination, the lens will appear clear with the pupil filled with the tapetal reflex, and a junction "ring" will be seen at the nuclear–cortical junction. With transillumination, the attachment of the lens zonules may be seen in a well-dilated eye immediately behind the edge of the



(A)



(B)

Figure 1.39 (A) Retroillumination from distance with direct ophthalmosopy in this foal shows dark multipunctate central spots in the left eye. (B) Transillumination of the same lesions shows multipunctate nuclear cataracts that appear white.

pupil [17]. Cataracts will appear white on transillumination (Figures 1.39B and 1.40) and black if they are not complete (i.e., light can pass around them) when observed on retroillumination (Figure 1.41) [17]. Direct retroillumination is performed by placing the objectives in the path of the refracted light, which causes opaque lesions to appear dark against a light background and transparent lesions to appear clear within a dark halo [17]. Indirect retroillumination allows improved detection of transparent lesions by taking advantage of differences between their refractive indices and those of surrounding tissues [17]. Lesions are observed against a darker background because the reflected light is directed away from the objectives [17]. Any noted opacities should be further investigated with the slit-lamp biomicroscope.



Figure 1.40 Direct transillumination of a cataract. The lesion appears white.



Figure 1.41 Retroillumination of an incomplete cataract. The lesion appears black.

Biomicroscopy for lens examination

The light beam of the biomicroscope should be angled at 20–45 degrees from the axis of the microscope and thus the visual plane of the observer (see Figure 1.31). The initial examination of the lens should proceed with diffuse illumination; a wide, low-intensity slit-beam should be used, and the microscope should be defocused from the light [12] The anterior surfaces of the lens and vitreous should be inspected. The slit-beam is then narrowed and intensified to reveal a two-dimensional cross-section of the lens, allowing the examiner to accurately determine lesion depth and axial positioning [61] This is extremely important in evaluating the depth and location of lens opacities. Direct and indirect retroillumination are performed by reflecting the slit beam from deeper structures while focusing on more superficial structures [61].

Posterior segment ocular examination: vitreous and retina

Normal anatomy and diseases of the posterior segment of the equine eye are discussed in Chapter 11. Examination of the equine ocular posterior segment involves direct focal illumination (i.e., transillumination) using a focal light source, as previously described in the lens section. Examination of the vitreous is performed first. Transillumination of the vitreous can reveal small posterior polar remnants of the hyaloid artery and areas of light reflection between vitreous planes [17]. Neither can be seen with retroillumination. Transillumination can also be used to look directly at the ocular fundus of the horse [17]. This is done by holding a light source against the examiner's face and directing the light into the horse's pupil (Figure 1.42). The examiner moves forward toward the eye until the ocular fundus becomes visible. A large fundus area, approximately six times greater than that seen with an ophthalmoscope, can be visualized [17]. This is used as an initial screen for



Figure 1.42 Transillumination can also be used to look directly at the ocular fundus of the horse. This is done by holding a light source against the examiner's face and directing the light into the horse's pupil.

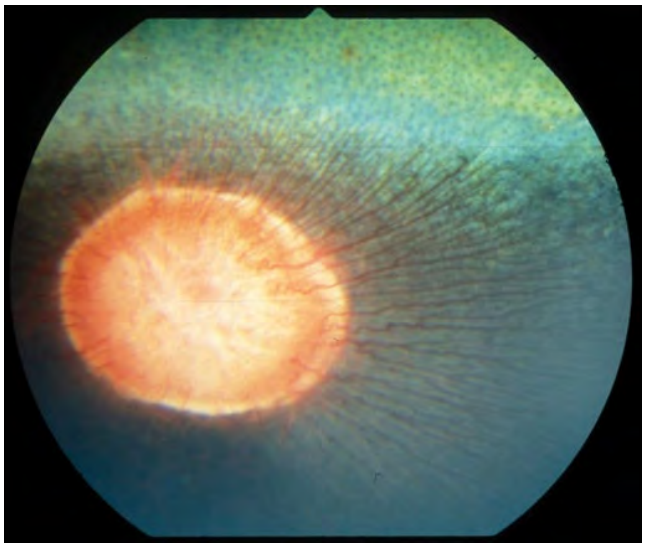


Figure 1.43 In most horses, a triangular fibrous tapetum in the dorsal choroid can be seen on ophthalmoscopic examination. End-on choroidal capillaries can be visualized as small dark dots throughout the tapetal fundus (i.e., stars of Winslow). The nontapetal area is usually dark brown.



Figure 1.44 The tapetum may be undeveloped in animals with albinotic or subalbinotic coat colors. Melanin in the retinal pigment epithelium may be absent, depending on coat and iris coloration.

disease. Details of any observed abnormality can then be evaluated with direct or indirect ophthalmoscopy.

Ophthalmoscopy is the examination of the ocular fundus (i.e., choroid, retina, and optic nerve) and is an integral part of any ophthalmic or physical examination. There are two common methods of performing ophthalmoscopy in the horse: direct and indirect. Direct ophthalmoscopy can be performed by means of transillumination, as previously described, or with the use of a direct ophthalmoscope. Indirect ophthalmoscopy requires the use of a light source and a handheld lens.

Advantages of the direct ophthalmoscope are its upright image, availability of options such as slit and graticule, ability to alter the dioptric power of the ophthalmoscope, and the high magnification provided [12, 17]. Disadvantages include the short working distance to the horse's head, a small field of view, lack of stereopsis, difficulty in examining the peripheral fundus, and greater distortion of the image when the visual axis is not clear [12, 17]. Advantages of indirect ophthalmoscopy include a wider field of view, a safer working distance from the horse's head, potential for stereopsis (i.e., depth perception) if binocular equipment is used, a greater view of the peripheral fundus, and the ability to alter the magnification by changing the diopter strength of the lens being used [12, 17]. Disadvantages of indirect ophthalmoscopy include the inverted and reversed image, the expense of binocular equipment, and the initial difficulty of mastering the technique [12, 17].

The ocular fundus can be visualized without mydriasis in the horse, but a complete examination requires mydriasis. The use of a short-acting mydriatic (1% tropicamide) is recommended, as previously described, resulting in complete mydriasis within 10–20 minutes with a duration of 4–6 hours [13]. The menace response, dazzle reflex, resting pupil size, and direct and consensual PLRs in each eye in bright and dim lighting should be evaluated before mydriasis is induced. Tonometry before pharmacologic mydriasis, indicated in small animals, is not absolutely necessary in the horse unless glaucoma is high on the list of differential diagnoses.

The normal ophthalmoscopic appearance of the ocular fundus of the horse (Figure 1.43) is described in Chapter 11 [7, 97–102]. The equine ocular fundus is dominated by the tapetum fibrosum, which occupies the dorsal two-thirds of the posterior segment, and the stars of Winslow, which are end-on views of choroidal blood vessels traversing the tapetum. The tapetal color varies from green-yellow (most common) to aquamarine or turquoise [8, 99]. Changes in tapetal color intensity from the central to peripheral tapetum have also been described [103]. The tapetum may be undeveloped in animals with albinotic or subalbinotic coat colors (Figure 1.44) [8, 104]. The nontapetal area is usually dark brown, but this melanin in the retinal pigmented epithelium (RPE) may be absent, depending on coat and iris coloration. If the pigment is absent, the choroidal vessels can be visualized. The optic disc is horizontally oval, usually located slightly temporal and ventral in the nontapetal area, and salmon pink [8, 104]. Retinal vessels radiate out only a short distance from the optic disc and are usually absent at the ventral disc border [8, 104].

Direct ophthalmoscopy

Direct ophthalmoscopy is extremely useful for rapid ocular examination in horses, and it can be used to identify most lesions of the equine ocular fundus (Figure 1.45) [8]. In the horse, direct ophthalmoscopy can be performed with a transilluminator. The light source should be held against the examiner's face, near the eye, and directed through the horse's pupil. This provides a larger view of the fundus than can be seen with the

direct ophthalmoscope, but it is not entirely in focus. This is a quick and useful method to screen for obvious signs of disease.

The direct ophthalmoscope consists of a halogen coaxial optical system and a power source [12]. A series of concave and convex lenses can be rotated through the viewing aperture by means of a dial (Figure 1.46) [7, 97, 105]. Green or black numbers represent convex or converging lenses, and red numbers represent concave or diverging lenses [7, 12, 97, 105]. The size, shape, and color of the light beam can be adjusted by a second dial which produces large and small circles of light, a slit beam of light, a graticule, and two filters [12, 17]. The size of the circular spot of white light should be adjusted to the patient's pupil size to minimize light reflections from the corneal surface [12]. The slit beam also aids in the detection of elevations or depressions in the ocular fundus, and distances can be estimated by changing the dioptric power of the ophthalmoscope [12]. When the retina is in focus at 0 diopter (D), the lesion is elevated if the lesion surface is in focus at a positive diopter setting (i.e., black numbers) and depressed if the lesion surface is in focus at a negative diopter setting (i.e., red numbers) [12]. The graticule is a grid that can be used to size the optic disc and estimate the size of fundic lesions [12]. A red-free filter (appears green) is used to evaluate retinal vessels and differentiate hemorrhage (which appears black) from pigmented lesions (which appear brown) [12].



Figure 1.45 Direct ophthalmoscopy is extremely useful for rapid ocular examination in horses and can be used to identify most lesions of the equine ocular fundus. There is a short working distance to the horse's head.

Most ocular fundi are in focus at 0 to −2 D if the examiner's vision is emmetropic, and therefore the ophthalmoscope should initially be set at 0 D [12, 17]. The direct ophthalmoscope should be placed against the examiner's brow, and using the dominant eye, the examiner should identify the horse's fundic reflex from a distance of approximately 0.5–0.75 m [12, 17]. Once the fundic reflex is identified, the examiner moves toward the horse to a point approximately 2–3 cm from the eye to visualize the fundus [12, 17]. Ophthalmoscopy should then proceed to identification and examination of the optic nerve, retinal vasculature, nontapetal fundus, and tapetal fundus in quadrants. The resulting image with a direct ophthalmoscope is upright and magnified several times above normal with a millimeter equivalent per dioptric change of 1.33 in the axial plane [12, 106]. Magnification of the image varies with working distance; lesions should be compared with optic disc diameter rather than by units of measurement [12, 17].

Welch-Allyn has developed a new monocular indirect ophthalmoscope (PanOptic (Welch-Allyn, Skaneateles Falls, NY)) that can be used in an undilated pupil and has five times greater magnification than a routine ophthalmoscope (Figure 1.47). The PanOptic ophthalmoscope also has a wider visual field than the direct ophthalmoscope, with an upright nonreversed image.

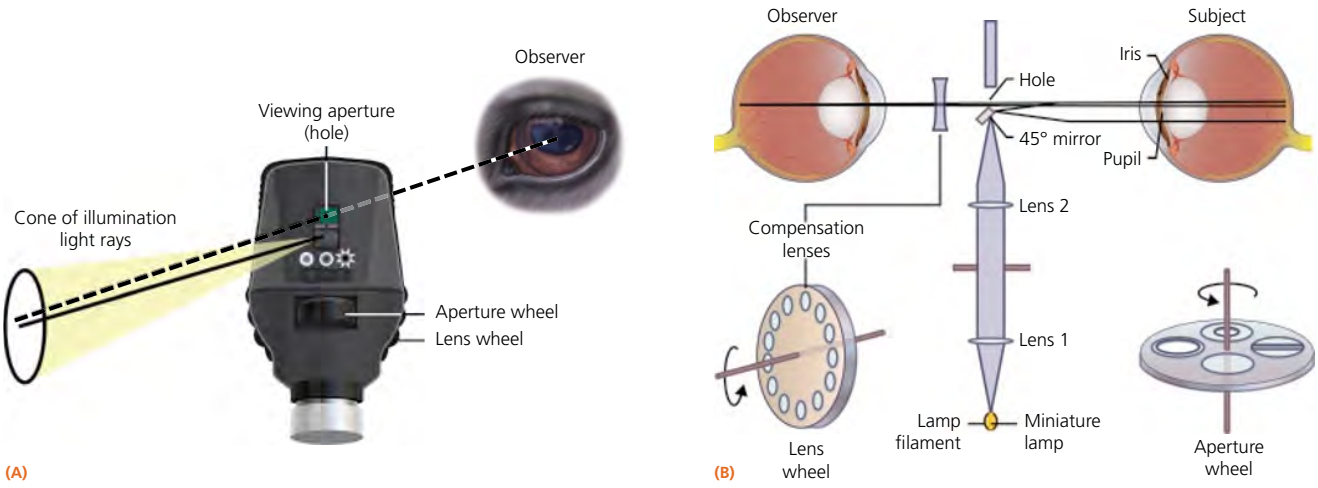


Figure 1.46 (A, B) Direct ophthalmoscope schematics. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)



Figure 1.47 PanOptic ophthalmoscope, which has a wider visual field than the direct ophthalmoscope and an upright, nonreversed image.

Indirect ophthalmoscopy

Monocular or binocular indirect ophthalmoscopy involves the use of a handheld converging lens held near the patient and a light source near the examiner's eye. A larger area of ocular fundus can be visualized with indirect versus direct ophthalmoscopy and may allow the examiner to more easily detect disease.

In binocular indirect ophthalmoscopy, a mirror and a light source fitted onto a headband are used to direct light into the patient's eye. The handheld lens is used to magnify the reflected image, and two prisms are used to split the reflected beam so it can be directed into both the examiner's eyes, permitting stereopsis (Figure 1.48) [12]. The light intensity should be adjusted to permit adequate illumination without causing patient discomfort [12].

In monocular indirect ophthalmoscopy, a handheld light source is used in addition to the handheld lens (Figure 1.49). The light source should be placed near the examiner's eye and temple so that both the head and light source function as one unit. A direct ophthalmoscope can be used for indirect ophthalmoscopy, and the dioptric power of the ophthalmoscope should be adjusted to +4 or +6 D [12].

The handheld lens provides a virtual image (i.e., the image is inverted and reversed) of the patient's fundus. A variety of lenses are available, ranging from +14 to +90 D in strength. The +20-D and +28-D lenses are the most useful in the horse, providing a fundus view of approximately 40 degrees. A +15-D is useful for a more detailed image of the fundus, while the 2.2 Pan-Retinal lens is a good compromise, giving a wide field of view (similar to +30-D lens) with magnification similar to a +20-D lens. The quality of the handheld converging lens affects the ease and clarity of the evaluation. The smaller the lens diopter rating, the greater the fundic magnification [12]. In the horse, lateral magnification has been reported for 14-D (1.18), 20-D (0.79), 30-D (0.51), and 40-D (0.38) lenses [106]. Axial magnification in the horse has also been reported for 14-D (1.86), 20-D (0.84), 30-D (0.35), and 40-D (0.19) lenses [106].



Figure 1.48 In binocular indirect ophthalmoscopy, a mirror and a light source fitted onto a headband are used to direct light into the patient's eye. The handheld lens magnifies the reflected image, and two prisms split the reflected beam so it can be directed into both the examiner's eyes, permitting stereopsis.



Figure 1.49 In monocular indirect ophthalmoscopy, a handheld light source is used in addition to the handheld lens. The light source should be placed near the examiner's eye near the temple so the head and light source function as one unit.

The refractive error of an animal can be semiqualified during indirect ophthalmoscopy by slowly withdrawing the lens toward the examiner and further from the eye and observing any change in magnification. The fundic image will get larger (myopic) or smaller (hyperopic), or it will remain static (emmetropia) [104]. For a more accurate measurement of refractive error, streak retinoscopy can be performed. This technique is described in the section **Retinoscopy (skiascopy)**.

Binocular indirect ophthalmoscopes suitable for use in horses, some with battery-powered illumination, are available from Heine, Keeler, Propper, Topcon, Welch-Allyn, Zeiss, and others.

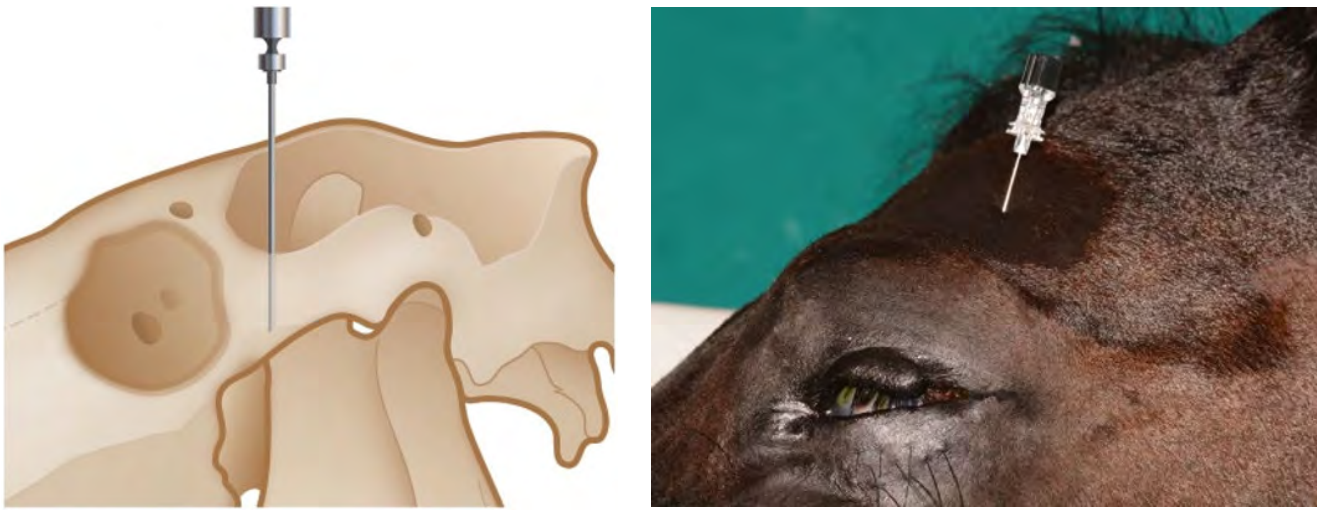
Advanced ophthalmic procedures

Retrobulbar nerve block

The retrobulbar nerve block temporarily blocks the optic (CN II) and oculomotor (CN III) nerves, the abducens nerve (CN VI), trochlear nerve (CN IV), and the maxillary and ophthalmic branches of the trigeminal nerve (CN V). Retrobulbar anesthesia can be used as an adjunct to general anesthesia in horses to reduce nystagmus and enophthalmos during corneal and intraocular surgery and prevent the need to give the horse neuromuscular blocking agents [107]. It can also be used to perform standing eyelid and corneal surgeries, as well as to perform anterior or posterior chamber paracentesis for diagnostic purposes. It can be used for the primary purpose of analgesia during the immediate post-operative period after an enucleation, and its use has been widely described for enucleation in standing sedated horses [108, 109]. A recent study reports that retrobulbar nerve block can prevent heart rate decrease and bradyarrhythmias caused by vagal stimulation occurring during enucleation [110]. Retrobulbar nerve block has been used also during cataract surgery, with the patient under general anesthesia, to provide extraocular muscle akinesia, thereby reducing the need for muscle relaxants and assisted ventilation [111]. Three methods have been described for retrobulbar anesthesia in the horse: the four-point block, modified Peterson block, and direct injection into the orbital cone above or below the zygomatic arch.

The site for the retrobulbar injection above the zygomatic arch and caudal to the temporal process of the malar bone is preferred because it requires a single needle penetration, is not located near the globe, and, if performed properly, avoids the direct location of the optic nerve. The orbital fossa above the dorsal orbital rim and zygomatic arch is clipped and aseptically prepped with povidone-iodine (Betadine) solution. Care must be taken to avoid getting surgical scrub (Betadine or Nolvasan) or alcohol on the ocular surface, because severe irritation and corneal ulceration may develop. Therefore these substances are avoided around the eye. A 22-G, 2½-inch spinal needle (BD, Franklin Lakes, NJ) is placed through the skin perpendicular to the skull, in the orbital fossa just posterior to the posterior aspect of the dorsal orbital rim (Figure 1.50). The needle is advanced posterior to the globe until it reaches the retrobulbar orbital cone. When the needle advances to this location, the eye will have a slight dorsal movement as the needle passes through the fascia of the dorsal retrobulbar cone into the retrobulbar space. The needle is advanced until it just passes into the cone, evidenced by the sudden release of the eye back to normal position or a slight "popping" sensation. Once the needle is positioned, 10–12 mL of 2% lidocaine HCl is injected into the retrobulbar space. Mepivacaine 2% (Carbocaine) and bupivacaine are also used with a longer action and reduced tissue hypersensitivity reaction. Before injection, aspiration should be performed to make sure the needle is not positioned within a blood vessel. During the injection, the globe is pushed externally (i.e., slight exophthalmos), indicating an accurate placement of anesthetic. Onset of anesthesia usually occurs within 5–10 minutes. The duration of effect is approximately 1–2 hours. Ocular sensation, blink reflex, and vision will be compromised during this time, so stall rest and protection of the eye with lubricants or a temporary tarsorrhaphy are recommended for 2–4 hours after anesthesia.

Very few complications have been documented from this procedure. The most common complication is a hypersensitivity to lidocaine, which results in generalized formation of hives and severe retrobulbar swelling after injection. These lesions will resolve with the use of systemic nonsteroidal



(A) (B)

Figure 1.50 Retrobulbar block. (A) Placement of the needle for the retrobulbar block. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.) (B) The orbital fossa above the dorsal orbital rim and zygomatic arch is clipped and aseptically prepped. A 22-G, 2½-inch spinal needle is placed through the skin perpendicular to the skull, in the orbital fossa, just posterior to the posterior aspect of the dorsal orbital rim.

anti-inflammatory and antihistamine medications within 3–5 days after the injection. Another complication is development of exposure corneal ulcers, likely caused by exposure of the cornea due to poor eyelid function and corneal desensitization. Careful monitoring of eyelid function and frequent topical lubrication until full function returns will prevent this complication. Retrobulbar block denervates the optic nerve; therefore the horse will have decreased vision or be blind in that eye for 1–3 hours after injection. Thus it is recommended that the injection be performed unilaterally so that complete blindness does not occur after injections.

The four-point block, a local muscle block, has also been described for retrobulbar anesthesia in the horse [17]. Lidocaine or mepivacaine, 5–10 mL, can be deposited laterally by passing a 20-G, 3-inch needle through the lateral canthus skin and following the globe posteriorly. Ventrally, the needle passes through the skin or bulbar conjunctiva posteriorly. The needle should be directed slightly nasally to avoid the optic nerve. Nasally, the needle passes through the base of the elevated third eyelid and posteriorly into the orbit. Dorsally, the needle is passed through the center of the upper eyelid following the globe posteriorly. This technique should not be used when intraocular surgery is performed, because it may put pressure on the globe [17]. Failure to inject anesthetic into the muscle cone or injecting it in front of the orbital septum may cause the drug to migrate forward under the conjunctiva and cause severe chemosis [17]. There is no advantage of this technique over the single-injection retrobulbar block; therefore the four-point block is not recommended unless adequate anesthesia has not been achieved with the first block.

Use of a modified Peterson block has been described in the horse, although it would rarely have application in most types of ocular surgery and is not recommended [17].

Although few complications have been seen after retrobulbar and eyelid nerve blocks in horses, rare problems associated with the injections can occur during or after the surgical procedure [107]. Bacteria can be deposited in the orbit by the spinal needle if the skin surgical site was not aseptically prepared. This may result in orbital abscess or cellulitis formation. Laceration of the extraocular muscles, optic nerve, sclera, or ophthalmic arteries by the needle is also possible during the injection. Traumatic injury during needle introduction could result in retrobulbar hemorrhage or optic neuritis. An isolated case of oculocardiac reflex elicitation during the block has also been reported [112]. These complications can be mostly avoided by use of appropriate tranquilization, eyelid nerve blocks, antiseptic technique, and added restraint methods to restrict movement by a standing horse. The relatively low complication rate associated with the injection techniques far outweighs the risks associated with general anesthesia in horses.

Orbital aspiration

Aspiration of a lesion (e.g., mass, fluid) in the equine orbit can be performed for cytology, culture, and histopathologic examination [12]. An 18-G, 4-inch, slightly curved needle is inserted 1 cm lateral to the lateral canthus and then directed posteriorly in a line parallel to the medial canthus [8, 113]. Approaching the retrobulbar space via the supraorbital fossa (as described in the section **Retrobulbar nerve block**) is also possible, especially if the lesion is in the dorsal retrobulbar area. For accurate and less risky sample collection, ultrasound- or CT-guided fine-needle aspiration, versus blind aspiration, may decrease the risk of injuring orbital structures [114].

Aqueous paracentesis

Aqueous humor fills the anterior segment of the eye, supplies nutrients to the avascular cornea and lens, and removes waste products from the interior of the eye. Small amounts of aqueous humor (0.2–0.5 mL) can be aspirated from the anterior chamber in the horse [12, 115, 116]. Aqueous paracentesis can be performed with the horse under general anesthesia or standing with sedation, topical anesthesia, and a retrobulbar block [12]. The site for aspiration should be the dorsal or dorsotemporal limbus to take advantage of the scleral extension beyond the iris base (Figure 1.51) [17]. The bulbar conjunctiva should be cleaned with dilute Betadine (5%) solution and sterile saline solution or eyewash [12]. Use of a topical broad-spectrum antibiotic, such as fluoroquinolones, before and after paracentesis is recommended to further decrease possible bacterial contamination. The bulbar conjunctiva is grasped with thumb forceps near the site of entry (0.5–0.7 mL subconjunctival injection of 2% Mepivacaine helps in this procedure), and a 27- to 30-G needle is directed through the limbal cornea or subconjunctival limbus (bevel up) anterior and parallel to the iris (see Figure 1.51) [12]. The needle should be tunneled for several millimeters through the limbus into the anterior chamber, which may facilitate rapid formation of a seal after the needle is withdrawn [12]. A small volume (0.2–0.5 mL) of aqueous humor is slowly aspirated, and the needle is withdrawn [12]. A syringe can be attached to the needle when this is first performed or after the needle is placed into the anterior chamber; or no syringe may be used, and the aqueous that fills the hub can be drawn into a capillary tube. The tip of the needle should be visualized at all times to avoid lacerating the iris or lens capsule.

Injections of therapeutics into the anterior chamber (e.g., tissue plasminogen activator, antibiotics) can also be performed using the same technique, except that injection of solution is made instead of aspiration. If an aqueous humor diagnostic sample is also required, this sample should be collected first, followed by injection of the medication.

Possible complications of aqueous paracentesis include hyphema, anterior lens capsule rupture with subsequent phacoclastic uveitis, endophthalmitis, anterior uveitis, corneal edema associated with endothelial damage, and choroidal edema and hemorrhage [12]. In an attempt to minimize development of inflammation and other complications after the procedure, the aqueous humor should be very slowly removed, and the volume removed should be 0.5 mL or less. Diagnostic procedures that can be performed with aqueous humor samples in the horse

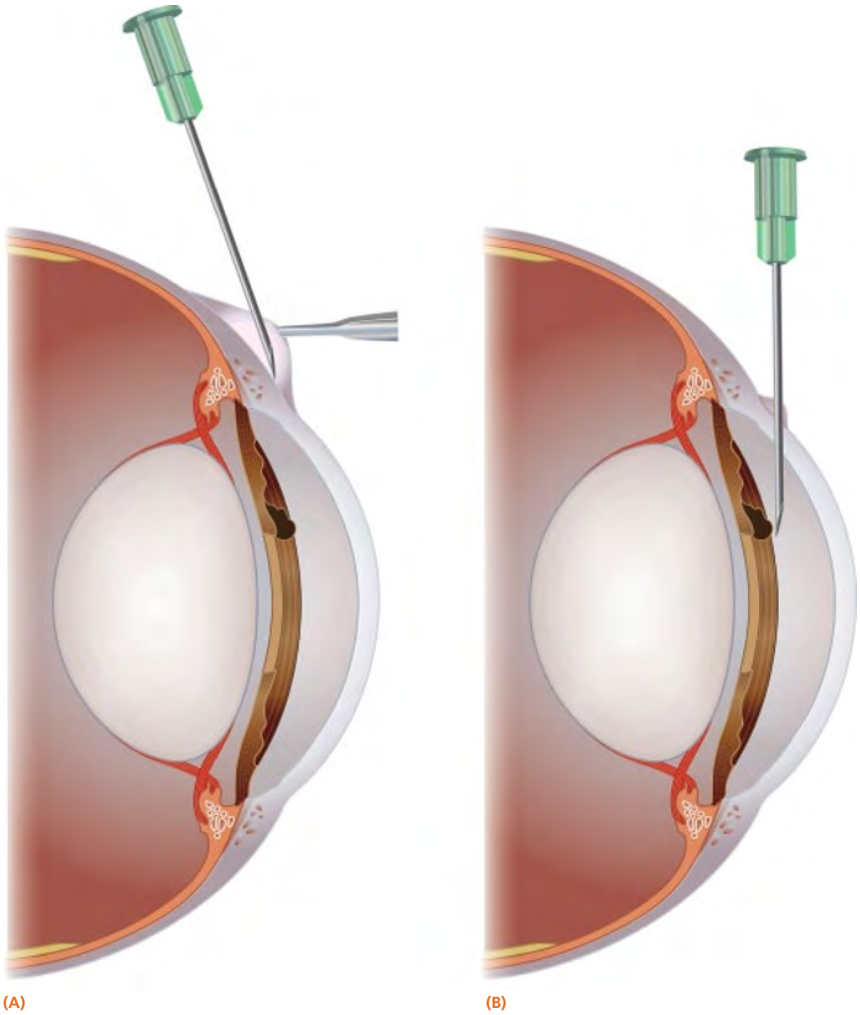


Figure 1.51 Aqueous paracentesis. (A) The bulbar conjunctiva is grasped with thumb forceps near the site of entry. (B) A 27- to 30-G needle is directed through the limbal cornea or subconjunctival limbus (bevel up) anterior and parallel to the iris, avoiding the lens. A drilling and tunneling motion will facilitate entry through the sclera and may facilitate rapid formation of a seal after the needle is withdrawn. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

include cytology, culture and sensitivity, protein measurement, antibody titers (e.g., *Leptospira* species), and polymerase chain reaction (PCR) [117–121]. See Chapter 8 for more information on the diagnostic value of aqueocentesis.

Vitreous paracentesis

The location for vitreous paracentesis is approximately 10–12 mm from the dorsolateral limbus. This will place the needle through the pars plana and avoid introducing the needle through the sensory retina [122, 123]. A 23- to 25-G needle is inserted through the conjunctiva and sclera, with the needle directed posteriorly to avoid the lens (Figure 1.52). As with aqueous humor, diagnostic procedures performed on vitreous humor samples include culture and sensitivity, cytology, protein measurement, antibody titers, and PCR [12, 124, 125]. Vitreous paracentesis can also be performed to instill therapeutic medications, such as gentamicin for ciliary body ablation in cases of chronic glaucoma and antibiotics in cases of endophthalmitis. Complications of vitreal paracentesis include hemorrhage, retinal detachment, and endophthalmitis—risks versus benefits of this procedure have to be considered.

Advanced ophthalmic diagnostics

Corneal esthesiometry

The corneal reflex is one of the most sensitive reflexes of the body, and its purpose is to protect the eye. Corneal sensitivity can be tested empirically by touching the cornea with a sterile Dacron-tipped applicator and observing a corneal reflex (response of blinking, globe retraction, or avoidance), or using an esthesiometer. The afferent arm of corneal reflex is mediated by the ophthalmic branch of the trigeminal nerve (CN V), and the efferent arm by the abducens (CN VI, globe retraction) and

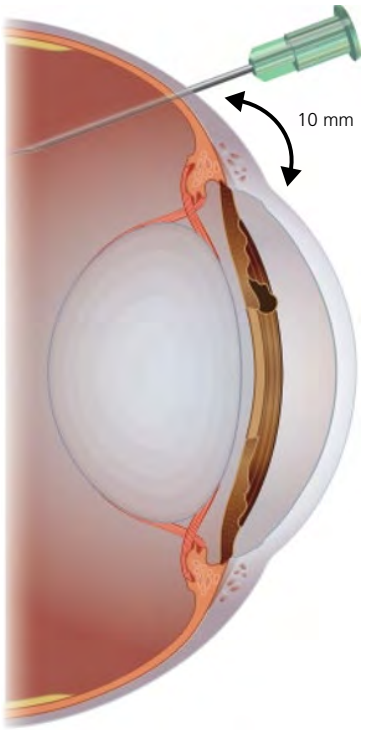


Figure 1.52 Vitreous paracentesis. The dorsal scleral overhang requires a greater distance from the limbus with a dorsal site than with a temporal site. However, 10 mm, rather than 15 mm, is probably more appropriate dorsally to avoid introducing the needle through the sensory retina. A 23-G needle is inserted through the conjunctiva and sclera, with the objective being to pass through the pars plana of the ciliary body. The needle should be directed toward the optic nerve to avoid the lens. (*Source*: Illustration by Samantha J Elmhurst BA Hons/LivingArt.)

facial nerve (CN VII, eyelid closure). Corneal esthesiometers quantitatively evaluate corneal sensitivity by measuring the corneal touch threshold (CTT), which is the threshold of the stimulus that results in a corneal reflex [126]. Estimation of corneal sensitivity may be used to diagnose and monitor corneal diseases, evaluate progression of corneal diseases after surgery, and monitor the effects of surgery and topical medications. The Cochet–Bonnet esthesiometer (Luneau Ophthalmologie, Chartres Cedex, France) has been described to evaluate CTT in horses [54, 126]. The instrument contains a nylon or platinum filament with an adjustable length (0.5–6 cm) and 0.12-mm diameter. The filament is applied in different lengths to the cornea until a corneal reflex is elicited with the same pressure or length of filament [54]. The length of the nylon filament estimates the applied pressure on the corneal surface and is readable on a millimeter scale. The shorter the filament, the more pressure is applied to the cornea, and vice versa. The pressure ranges from 5 to 180 mg/0.0113 mm (0.4 to 15.9 g/mm).

The CTT in the central area of the equine cornea, similar to that in other species, has been shown to be the most sensitive, and the dorsal region the least sensitive [54, 126, 127]. A decrease in corneal sensitivity was shown in sick neonatal foals compared with normal adults [54]. Corneas in healthy foals were slightly more sensitive than those in healthy adults [54].

In humans, it has been shown that the CTT is influenced by age, mental status, iris color, hormone cycle, gravidity, time of day, humidity, room temperature, esthesiometric method, and investigator [128–132]. A decrease in sensitivity has been described in cats with herpes keratitis, in dogs with spontaneous chronic corneal epithelial defects, and in dogs after neodymium: yttrium aluminium garnet (Nd:YAG) laser photocoagulation [133, 134]. Further investigation into the effects of corneal disease, cyclophotocoagulation, and surgeries such as penetrating or lamellar keratoplasty on CTT needs to be performed in the horse.

Ultrasonic pachymetry

Pachymetry is an accurate and reliable ultrasound technique to measure the corneal thickness *in vivo* in animals and humans [81, 135, 136]. Use of spectral-domain optical coherence tomography (SD-OCT) or *in vivo* confocal microscopy (IVCM) may be more accurate methods to measure corneal thickness, but the cost of these modalities and the lack of portable equipment make them not as practical for use in the horse [137, 138]. Prior to use of ultrasonic pachymetry, corneal thickness was measured from gross post-mortem specimens and histologic specimens, which overestimated corneal thickness because the cornea swells after death [139]. Ultrasonic pachymetry measures the time required for ultrasonic energy to traverse the cornea, with a preset constant for velocity of sound, and converts this to a measure of thickness [135, 136, 140]. A transparent cornea is required for ultrasonic pachymetry full-thickness corneal measurements [12].

A 20-MHz ultrasonic pachymeter (DGH500 (DGH Technology Inc., Exton, PA)) has been used to study the horse. It has been used to determine corneal thickness in healthy juvenile and adult horses, Rocky Mountain horses with cornea globosa, horses that have been given an auriculopalpebral nerve block and xylazine, and healthy Miniature horses [38, 81, 140, 141]. Corneal thickness of enucleated globes measured by a caliper was approximately 858 mm centrally, 914–939 mm dorsally and ventrally, and 861–898 mm laterally and medially [140]. With ultrasonic pachymetry, central corneal thickness (CCT) was reported to be 793 mm, and thicker peripherally at 831–924 mm *in vivo* [81]. Three reports indicate that the dorsal and ventral portions of the cornea are thicker than the central cornea [38, 81, 140]. CCT of healthy equine eyes has been recently measured also with high-frequency (HF) ultrasound and ultrasound microscopy (UBM), with the mean value of 818 ± 41 µm, and with SD-OCT, with the mean values of 800 ± 50 and 812.8 ± 42.9 µm [142, 143]. Eyelid block, sedation, age, and sex did not affect corneal thickness [81]. However, thickness of the central portion of the cornea may increase up to the age of 6 months in a healthy horse [38]. Corneal thickness in the normal Miniature horse is 785 mm centrally [141]. Corneal thickness was measured using a portable ultrasonic pachymeter in Quarter horses

affected by hereditary equine regional dermal asthenia (HERDA) [144, 145]. In several different corneal regions (dorsal, ventral, nasal, temporal, and central) the corneal thickness was significantly lower than in the control group, with a CCT mean value of 741.2 ± 43.6 µm compared with 819.9 ± 45.9 µm mean value in the control group [145]. See Chapter 7 for more information on corneal thickness and diseases of the cornea in the horse.

Electroretinography

Electroretinography is used to determine function in the outer layers of the retina by recording the summation of electrical response when the retina is stimulated by light [146, 147]. The electroretinogram (ERG) is the recorded total electrical response of the retina to that light. The ERG is not a measure of vision but only a measure of functional integrity of the outer portion of the retina and RPE. A blind animal (e.g., with disease of the inner retina, optic nerve, or central nervous system) can have normal ERG findings. The ganglion cells, their axons, and the optic nerve do not contribute to the ERG recording.

An ERG is indicated whenever visual problems in the outer retina are suspected. In the horse, an ERG is indicated to assess for retinal function in cases of equine recurrent uveitis (ERU), corneal or lens opacities that preclude visualization of the ocular fundus (e.g., cataracts, diffuse corneal edema), suspected congenital stationary night blindness (CSNB), neuroaxonal dystrophy (NAD), equine degenerative myeloencephalopathy (EMD), non-ERU-related retinitis and chorioretinitis, drug toxicity, retinal detachment, ocular trauma, and chronic glaucoma [12, 148–154]. A recent ERG evaluation of eyes with extensive bullet-hole lesions shows that these lesions do not appear to compromise outer retinal function [155]. See Chapter 11 for more information on these diseases and their effect on the ERG.

The primary components of an electroretinograph are a light source (photostimulator), a high-gain amplifier, and a recorder [147]. Three electrodes are needed: a positive (i.e., active) corneal electrode, a negative (i.e., reference) electrode, and a ground (i.e., indifferent) electrode (Figure 1.53A) [147]. The clinical ERG consists of three basic waveforms: the a-wave, b-wave, and c-wave (Figure 1.53B) [147]. The a-wave is an initial negative deflection. This is followed by a positive deflection, the b-wave, which has a higher potential (amplitude) and is followed by an after-negativity. In addition to the a-wave and b-wave, there is usually a second positive deflection, the c-wave, which is more prolonged. The origin of each wave component is complex and poorly understood. Latency and implicit times, the time from onset of a stimulus to the peak of a particular response, are also important in evaluating the ERG. In a diseased eye, the amplitudes typically decrease while the implicit times increase.

One of the intrinsic factors that can affect the ERG is the eye's state of light adaptation, classified as scotopic (dark-adapted) and photopic (light-adapted) [147]. The scotopic state of the eye is primarily a rod response. The photopic state of the eye is primarily a cone response. Rods are more numerous than cones in the horse, so the ERG is primarily a rod response in this species [147]. The rod and cone responses can be separated by repetitive stimuli or flickers of varying frequency, light adaptation state of the retina, and variation in the intensity of the stimulus [147]. Other intrinsic factors that may affect the ERG include age, transparency of the ocular media, retinal integrity, and retinal circulatory disturbances [147]. Amplitudes

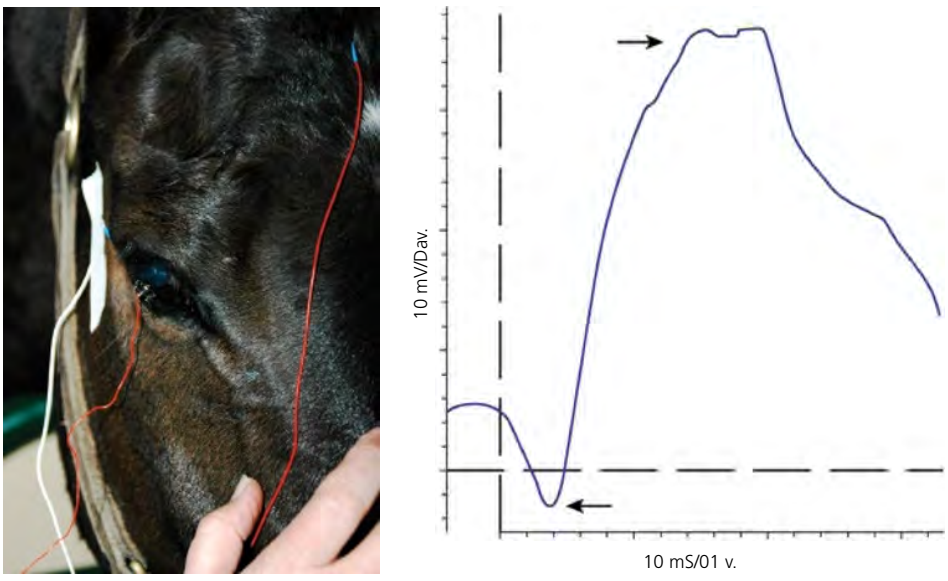


Figure 1.53 (A) Three electrodes are in place for performance of an electroretinogram (ERG) in the standing horse. (B) The clinical ERG consists of three basic waveforms (a-wave, b-wave, and c-wave). The a-wave, an initial negative deflection (**bottom arrow**), and the b-wave, positive deflection, which follows the a-wave (**top arrow**), are most prominent in the horse.

can vary according to species, state of adaptation to light, ocular movements, pupillary dilation, and pathologic state of the eye [147, 156].

Extrinsic factors that affect the ERG include the light stimulus used, electrodes used, and recording equipment [147, 156]. The light stimulus may have variations in duration of flash, light intensity, frequency, and color. The positioning and type of electrode affect the level of background noise and amplitude of the ERG. Both extrinsic and intrinsic factors can be minimized and must be monitored by establishing a protocol for evaluating the ERG in the horse [147, 156].

Three main techniques used in clinical veterinary ophthalmology are the flash ERG, pattern ERG, and visual evoked potentials. In contrast to the flash ERG, the pattern ERG originates in the inner retina and therefore is helpful in diagnosing diseases such as glaucoma. Limits to visual resolution can also be established by pattern ERG. Visual evoked potentials, although not ERGs, can be recorded with the same equipment and can record activity from the visual cortex. This activity has been mapped in dogs and cats but not in the horse [157].

Flash electroretinography is the most common method for assessment of retinal function in veterinary ophthalmology [147, 153–156]. Proper ERG recording requires general anesthesia in animals to prevent recording artifacts from muscle activity and to allow ideal positioning of the eyes. General anesthesia is inherently risky, expensive, and more labor intensive in the horse. Also, the inhalant anesthetics, halothane and isoflurane, have been shown to have a negative effect on the ERG amplitude and inner retinal function in other species [147, 158]. Electroretinography in the standing horse can be difficult because sedation will not eliminate the almost constant head movement. Sedated or unsedated, the horse may still shy from the closeness of the stimulator, and even small head movements can easily dislodge the other electrodes and require their replacement [147]. However, with proper restraint, auriculopalpebral nerve blocks, sedation, and patience, an adequate ERG can be recorded in the standing horse [147, 156].

The normal dark adaptation curve has been investigated, suggesting that full-field ERG examination should be performed after a minimum 20 min of dark adaptation [159]. Findings from flash ERGs in horses have been reported, and the implicit times and amplitudes were similar in the various reports [147, 149, 151, 156, 160, 161, 163]. Mean reported implicit times and amplitudes of the photopic a- and b-waves are 5.19 ± 1.56 and 26.63 ± 2.26 ms and 40.89 ± 20.50 and 184.75 ± 63.26 mV, respectively [147]. Mean implicit times and amplitudes of low-intensity flash (0.33 cd/m2 with 5 minutes of dark adaptation) and high-intensity flash (4.62 cd/m2 with 5 minutes of dark adaptation) scotopic a- and b-waves, with pseudo-Ganzfield stimulation, DTL (Dawson, Trick, and Litzkow) microfiber electrodes (Retinographic Technologies, Scranton, PA), and detomidine sedation in the standing horse have been reported [147]. Low-intensity flash scotopic a- and b-wave implicit times and amplitudes are 5.73 ± 1.88 and 36.95 ± 3.89 ms and 103.18 ± 120.72 and 409.30 ± 319.36 mV, respectively [147]. High-intensity flash scotopic a- and b-wave implicit times and amplitudes are 5.13 ± 1.34 and 34.75 ± 1.87 ms and 153.68 ± 94.19 and 374.09 ± 161.93 mV, respectively [147].

More recently, a study on ERG responses has been performed in 30 normal Thoroughbreds, sedated with detomidine HCl (0.015 mg/kg) using the Handheld Multispecies ERG (HMsERG) Model 1000 (RetVetCorp Inc., Columbia, MO), with its mini-Ganzfeld half-sphere bowl system and a gold foil contact lens electrode (ERG-jetTM (Fabrinal SA Tuilerie 42, 2300 La Chaux-de-Fonds, Switzerland)). After 20 min of dark adaptation, the International Society for Clinical Electrophysiology of Vision (ISCEV) standard protocol was used measuring implicit time (IT) and amplitudes (AMP). The protocol included a scotopic setting for rod function testing (10 mcd s/m2 with 0.2-s intervals, b-wave: mean IT = 57.35 ± 9.36 ms, variation 41.8–72.9 ms, AMP = 96.53 ± 46.19 μV, variation 19.8–173.3), followed by a mixed scotopic–photopic (rod and cone) stimulation (3000 mcd s/m2 with 2.5-s intervals, a-wave: mean IT = 13.94 ± 0.44 ms, range 13.2–14.7 ms, AMP = 106.20 ± 22.75 μV, range 68.4–144 μV, b-wave: mean IT = 35.13 ± 3.84 ms, range 28.7–41.5, mean AMP = 188.60 ± 49.88 μV, range 105.7–271.5 μV) and then by photopic (cone) stimulation (10,000 mcd s/m2 with 5-s intervals, a-wave: mean IT = 13.95 ± 0.56 ms, range 13–14.9, mean AMP = 136.25 ± 30.39 μV, range 85.7–186.8 μV, b-wave: mean IT = 36.01 ± 5.66 ms, range 26.6–45.4 ms, mean AMP = 177.64 ± 43.83 μV, range 104.7–250.6 μV). Lastly, after 10 minutes of light adaptation, a cone stimulation was recorded using a 30-Hz flicker response test at 3000 mcd s/m2 (b-wave: mean IT = 25.84 ± 1.86 ms, range 22.8–28.9 ms, mean AMP = 80.59 ± 21.94 μV, range 44.1–117.1 μV) [156]. ERG flicker-photometry has been used to assess the spectral sensitivities of cones in the horse, [147, 156] but oscillatory potentials have not yet been recorded [147, 149, 151, 156, 160, 161, 163].

Retinoscopy (skiascopy)

Retinoscopy, or skiascopy, is the technique used to determine the refractive state of the eye. Retinoscopy is the only clinical and practical method of refraction in horses. Commonly used in pediatric human ophthalmology, this technique has been used in veterinary medicine to define the normal, pathologic, and surgically induced refractive state of the eyes of the horse [39, 163–180]. The instrumentation and technique used can be challenging, and the reader is referred to an article by Davidson for further information [170].

Light rays projected onto an eye from infinity emerge from an emmetropic eye as parallel rays, from a myopic (near-sighted) eye as converging rays, and from a hyperopic (far-sighted) eye as diverging rays [170]. The location at which these emergent light rays form a focal point is called the **far point** [170]. The far point is at infinity, in front of infinity, and beyond infinity for emmetropic, myopic, and hyperopic eyes, respectively [170].

The retinoscope is either spot or streak, but streak retinoscopes are the most commonly used in veterinary medicine [170].



Figure 1.54 Retinoscopy with a skiascopy bar in the horse.

Both streak and spot retinoscopes are available from Copeland, Heine, Keeler, Propper, Reichert, and Welch Allyn. Plus or minus spherical lenses, available in increments of 0.25 D, are placed between the retinoscope and the horse to quantitate the refractive error of the eye [170]. A simple and inexpensive skiascopy bar or rack contains a series of plus and minus lenses in increments of 0.5–1.0 D [170].

Retinoscopy is performed in a darkened room with a handler restraining the horse's head. Mydriasis is often unnecessary and can even make the technique more difficult; the limited accommodative ability of the horse makes cycloplegia less important [170–172]. The retinoscope is placed against the examiner's brow, and the examiner is positioned 0.67 m (working distance, approximately an arm's length) from the patient's eye (Figure 1.54) [170]. The streak is swept horizontally across the horse's pupil, rotated horizontally, and then swept vertically across the pupil [170]. Finally, a trial lens or skiascopy bar is placed 1–2 cm from the patient's cornea, and the process is repeated [170].

As the streak is slowly swept across the pupil, the fundic reflex will move in either the same or the opposite direction, depending on the refractive state of the patient. With no refractive lens, the fundic reflex will move in the same direction as the sweep with emmetropic and hyperopic eyes (a **with** motion) and in the opposite direction of the sweep with more than 1.5-D myopic eyes (an **against** motion) [170]. If a with motion is observed, plus lenses of increasing dioptric strength are placed in front of the patient's eye until an against motion is observed or neutralization is reached [170] Neutralization is characterized by a fundic reflex that completely fills the pupil without any noticeable direction of movement [170]. If an against motion is observed, minus lenses of increasing dioptric strength are used to achieve neutrality [170]. At a working distance of 0.67 m, a +1.5-D lens is needed to achieve neutralization with an emmetropic eye; therefore the refractive error of an eye is determined by subtracting 1.5 D from the gross refraction needed to achieve neutrality [170].

Retinoscopy may allow selection of intraocular lens implants in horses and assist with evaluation of performance problems in working animals. However, refractive error has an unknown effect on horses, and is discussed further in Chapter 12. In healthy horses, refractive error has been reported to range from −3 to +3 D [173], but most appear to be within 1 D of emmetropia [168–176]. In one study, the mean refractive state was −0.06 ± 0.68 D, with emmetropia in 77 of 158 horses (48.7%), hyperopia, with a maximum value of +1.5 D, in 38 (24.1%), and myopia, with a maximum value of −1.5 D, in 40 (25.3%) horses. In this study, just 1.3% of horses (2/158) were myopic to the degree of −2.0 D, and 0.6% (1/158) were myopic to the degree of −3.0 D [175]. In another study on 333 horses and ponies (666 eyes), emmetropia was found in 83.63% of eyes (557/666), with 68.5% (228/333) of horses/ponies with emmetropia in both eyes. Refractive errors greater than 1.50 D were found in 2.7% of eyes tested. Ametropic eyes included hyperopia (54%) and myopia (46%). Anisometropia (when the refractive power of the two eyes differs by more than 0.5 D) was found in 30.3% of horses/ponies [176]. No significant differences in the refractive states in both axes, horizontal and vertical, were found after mydriasis induced with tropicamide 1%, but it is suggested to perform retinoscopy examination before or 40–45 min after application of topical tropicamide 1%, as mydriasis may subjectively influence a novice retinoscopist's ability to obtain accurate results [172]. The aphakic equine eye after cataract surgery has been reported to be hyperopic (+9.94 D) [177, 178]. An intraocular lens implant (IOL) with a refractive power of 25 D resulted in −3.48 D myopia at post-operative retinoscopy [177, 178]. In a second study, a 14-D IOL was placed, after cataract phacoemulsification, in five eyes with a mean post-operative refractive error of +0.4 ± 1.1 D [179]. In another study, the same +14-D IOL was placed in a foal after phacoemulsification, resulting in a post-operative refractive error of +0.31 D [180]. Astigmatism, a state of unequal refraction along the different meridians of the eye (i.e., vertical versus horizontal), has not been investigated by retinoscopy, but in horses has been measured by keratometry [145, 175]. Variation in the reported refractive error in horses can be explained by the technique used, skill of the examiner, sample size, and accommodative state of the animal.

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CHAPTER 2

Advanced ophthalmic imaging in the horse

Eric C. Ledbetter and Ruth A. Van Hatten*

Introduction

Ophthalmic imaging techniques available for use in the horse have expanded and improved rapidly in recent years. Utilization of these newer imaging modalities has permitted observation of anatomical and physiologic changes associated with many equine ocular disorders in a manner that was previously not possible. These observations have enhanced the fundamental understanding of many equine ocular conditions. In addition, advanced ophthalmic imaging techniques applied in the clinical setting permit improvements in the clinical detection, diagnosis, and treatment of equine ocular diseases. As the availability of these imaging technologies continues to expand, it is important to emphasize that, in most instances, the clinician should regard these techniques as providing supplemental information only and they should not be considered as substitutes for the ocular examination. A complete and through ocular examination remains indispensable to the clinician.

Even though the routine ocular examination is the foundation for detecting equine ophthalmic disease, advanced imaging is often required to make the definitive diagnosis. In this chapter, indications and techniques for advanced ophthalmic diagnostic imaging of the horse are discussed, with emphasis on radiology, cross-sectional imaging (computed tomography (CT) and magnetic resonance imaging (MRI)), and ultrasound. Advanced ophthalmic imaging techniques, such as high-frequency ultrasonography, ultrasound biomicroscopy, infrared photography, infrared thermography, specular microscopy, *in vivo* confocal microscopy, and ocular coherence tomography, are also described. In addition, imaging modalities used in clinical and research settings in human and veterinary ophthalmology that may hold promise for future use in the horse are briefly discussed.

Understanding normal equine ocular anatomy is integral to interpreting diagnostic imaging. A review of the basic anatomy of the equine eye is presented in Chapter 1, and excellent reviews of equine ocular and head anatomy can also be found in other sources [1–7].

Radiology

The anatomic structures in the equine head are complex, and superimposition of these structures can make radiographic interpretation difficult [1, 2, 6–11]. In addition, obtaining the images often requires multiple views and the radiographic technique can vary with the area of the head being examined [12–14]. Despite these challenges, with good knowledge of head radiographic anatomy and the radiographic signs of disease, as well as a basic understanding of disease processes, accurate radiographic interpretation is possible [8, 10–18].

Skull radiography

Radiography is a valuable diagnostic tool, and often the first step, for evaluating the equine skull, specifically for sinonasal and dental diseases, suture periostitis, and post-trauma evaluation (Figure 2.1) [12, 16, 19].

In regards to specific ophthalmologic disorders, radiographs are primarily indicated for nasolacrimal disease (e.g., chronic epiphora, dacryohemorrhea) or when bony trauma or remodeling of the orbit is suspected (Figure 2.2) [10, 20, 21]. Trauma to the skull overlying the sinuses or nasal cavity—specifically the frontal, lacrimal, nasal, and maxillary bones–often results in depression fractures that can impinge on the orbit or nasolacrimal duct [11, 11, 12, 21]. Radiographic examination can evaluate

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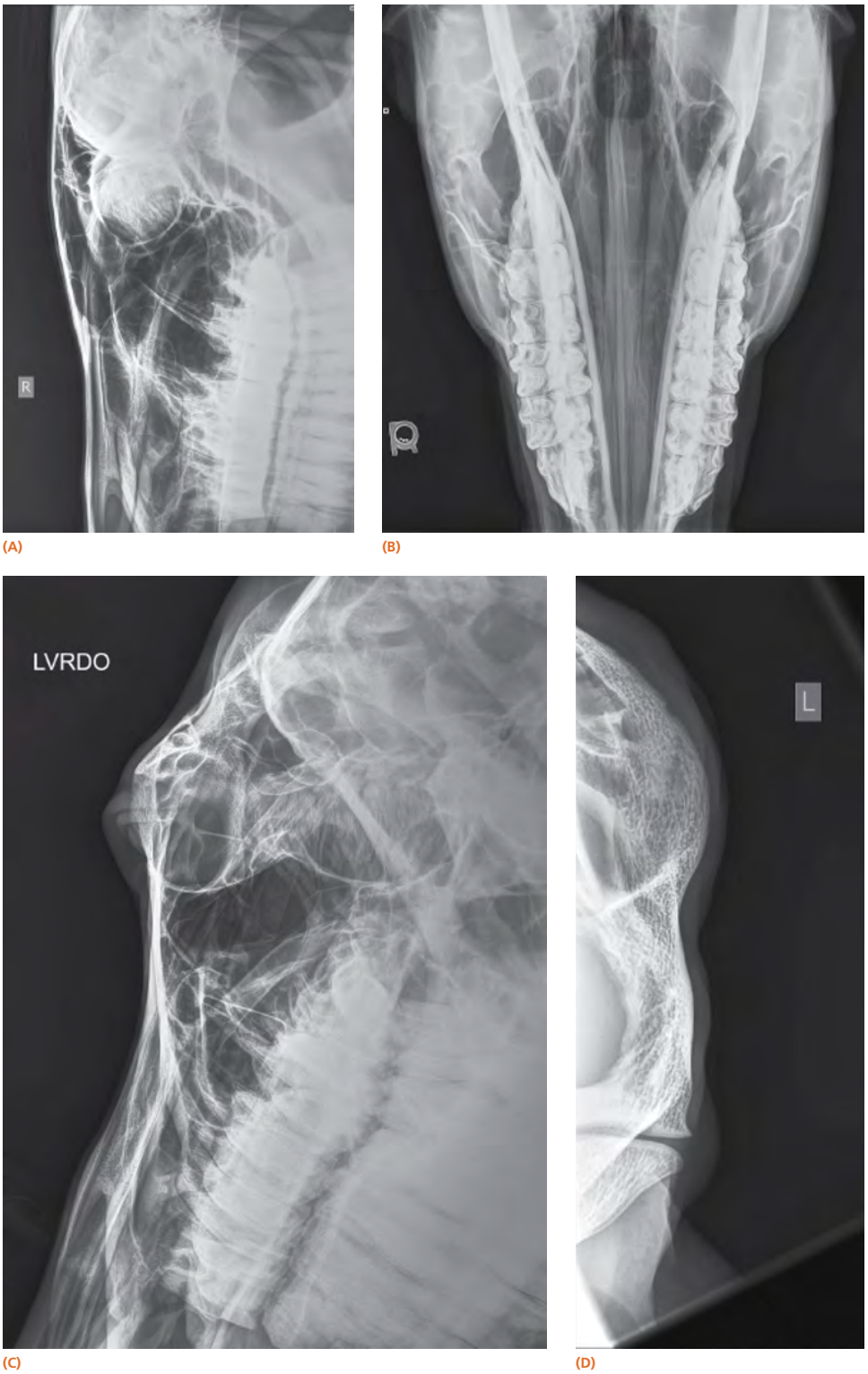


Figure 2.1 Various radiographic views of the equine head can be obtained to evaluate the orbit and sinuses. (A) Normal right lateral radiograph. (B) Normal dorsoventral radiograph. (C) Normal right dorsal–left ventral oblique radiograph. (D) Normal oblique ("skyline") radiograph of the bony orbit. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



Figure 2.2 Right dorsal–left ventral oblique radiograph of an equine skull with an acute, traumatic depression fracture of the left nasal bone with fluid in the adjacent dorsal conchal sinuses. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

fracture size, extent of displacement, sinus/nasal involvement, suitability for surgical repair, and predict post-healing contour [11, 16, 21, 22]. Often multiple radiographic views with varying degrees of obliquity, such as a "skyline" of the bony orbit, are required to best evaluate the lesion (Figure 2.1D) [8, 12, 13]. When applicable, a radiograph of the other, nonaffected, side can be performed for comparison [12]. A thorough evaluation of the eye is required with periorbital skull fractures because concurrent ophthalmic complications (e.g., corneal ulceration, corneal perforation, globe rupture, uveitis, hyphema, globe entrapment) are common [21, 22]. The advanced imaging techniques of CT and MRI remove superimposition of the skull, which is the main limiting factor of radiography, allowing for better evaluation of the equine periorbital region with improved lesion detection and extent (see descriptions later in the chapter) [12, 22].

Contrast radiography

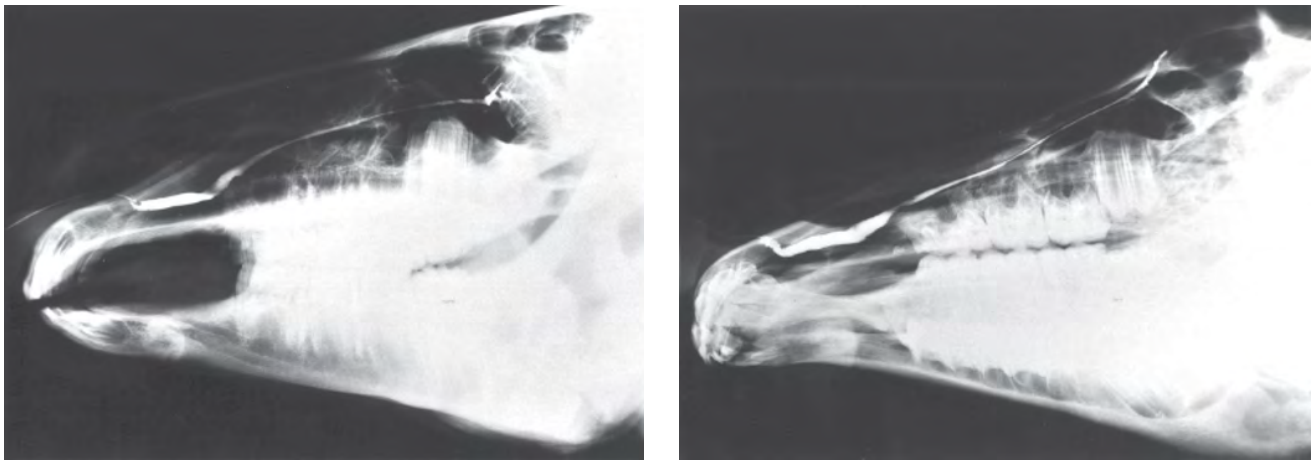
Various contrast radiograph techniques have been reported in animals and humans, including dacryocystorhinography, sialography, orbital angiography, orbitography, and thecography; however, only dacryocystorhinography and sialography have been described in the horse, and have largely been replaced by CT or MRI [10, 23–28].

Dacryocystorhinography

The entire nasolacrimal system can be outlined through contrast radiography (e.g., iodine), a process termed dacryocystorhinography [10, 24–27]. This technique has been used to characterize the anatomy and identify obstructive lesions of the nasolacrimal duct in horses and donkeys [10, 26–155]. Dacryocystorhinography highlights the nasolacrimal system, thereby revealing congenital (most often of the distal portion) or acquired obstructions, dilations, deviations, and other abnormalities [10, 17, 24, 26, 27]. The main indications for dacryocystorhinography are chronic epiphora and facial trauma [10, 24, 26, 27].

Dacryocystorhinography can be performed in a standing, tranquilized patient after successful or unsuccessful irrigation of the duct [10]. The dorsal or ventral lacrimal punctum is cannulated, and radiopaque contrast medium is injected into the catheter until it emerges from the nasolacrimal meatus or external nares (unless obstruction of the duct is present) [10]. The use of 60% barium sulfate (3–5 mL) has been previously described, while currently iodinated contrast media (5–15 mL) such as iohexol (Omnipaque (NovaPlus GE Healthcare, Princeton, NJ)) is more commonly used [10, 26, 27]. After contrast injections, lateral, dorsoventral, and oblique radiographs (Figure 2.3) are recommended [10, 24]. The lateral view provides better visualization of the entire length of the duct, specifically of the canaliculi and distal nasolacrimal duct [10]. Retrograde injections have also been reported and are described as being easier to perform due to the larger nasolacrimal meatus. For these injections, a catheter was inserted into the nasolacrimal meatus and contrast was instilled until it exited the lacrimal puncta, with little subjective difference when compared to antegrade injections [10, 26]. In cases with complete obstruction, both antegrade and retrograde studies should be performed to determine the length of the obstruction [26].

Computed tomography dacryocystography (CT-DCG) and magnetic resonance dacryocystography (MR-DCG) have been used in both animals and humans to evaluate the nasolacrimal system for underlying causes of chronic epiphora, masses either arising from or secondarily obstructing the nasolacrimal duct, and facial trauma [27, 29–31]. CT-DCG has been described in a horse with multiple facial bone fractures for evaluation of the patency of the nasolacrimal duct [27] and in a horse with nasofrontal suture exostosis and bilateral epiphora [30]. Bilateral injection of both the normal and abnormal sides is recommended for comparison [27]. The advantages of CT-DCG over skull radiography with DCG include better evaluation of the nasolacrimal duct (specifically the portion in the nasolacrimal canal) due to lack of superimposition of the skull, improved surgical planning, and ability to reconstruct three-dimensional (3D) images (Figure 2.4) [27, 29]. The disadvantages are the significant increase in cost and the requirement for general anesthesia, which has inherent risks in the horse. CT-DCG may be reserved for animals already undergoing CT for evaluation of



(A) (B)

Figure 2.3 The entire nasolacrimal system can be outlined through contrast radiography (i.e., iodine) and is termed dacryocystorhinography. (A) Left lateral dacryocystorhinography. (B) Oblique view. (*Source*: Photographs courtesy of Dr Claire Latimer.)

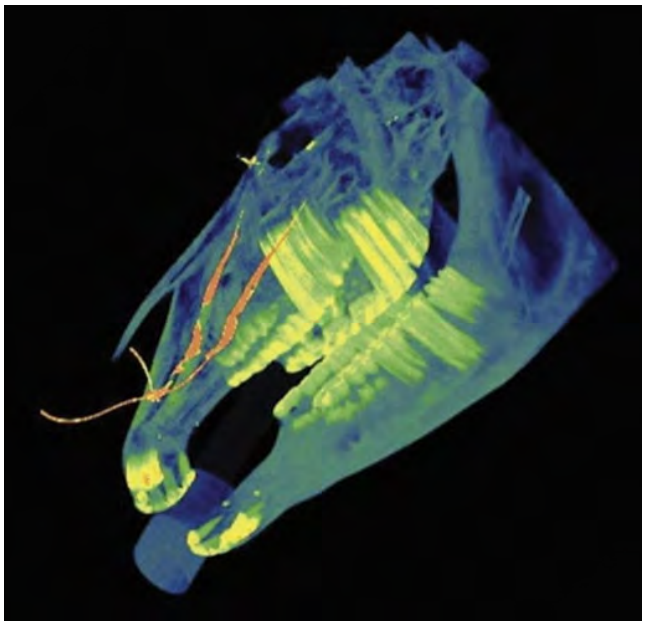


Figure 2.4 The 3D color-enhanced reconstruction of CT-DCG can assist in interpretation of the nasolacrimal duct (red).

facial and orbital bone fractures or for those cases in which routine DCG proves nondiagnostic. See Chapter 6 for more information on the diagnosis and treatment of nasolacrimal disease and below for more information on CT and MRI in the horse.

Computed tomography

CT is the acquisition of cross-sectional, two-dimensional (2D) slices (i.e., tomograms) of a tissue [23]. These tomograms are created by a rotating radiation source that transmits a highly collimated beam of X-rays, and the degree of attenuation of the X-rays within the intervening tissue is measured by a detector system [23, 32]. Both are housed within a large donut-shaped tube or gantry that the patient table moves into [32–34]. The degree of attenuation of the X-ray beam determines the object density by assigning a CT number (or Hounsfield Unit (HU)) to each image point or pixel [33]. HU range from −1000 for air to > 1000 for metal, with pure water being 0 [32, 35]. Grayscale image reconstruction of the raw data based on the HU can then be digitally performed to construct a transverse image or slice of the region [23, 33, 36]. All of the slices are then used to create a volume of data that can be reconstructed into any plane as well as create 3D reconstructions [34, 36].

Since CT imaging uses the same principles as standard radiography, the whiter the region on the image, the greater the absorption of X-rays through that tissue [23, 37]. For example, air and fat are darker (i.e., low density) and bone, mineral, and metal are various shades of bright white (i.e., high density) [23, 37]. This provides relatively good contrast between the bone, muscles, and fat within the orbit [23]. With the large range of HU, CT is able to differentiate between small differences in tissue density: for example, between fluid (HU of water is 0), soft tissue (HU between 30 and 70), and fat (HU is approximately −100) [37]. This improved contrast exceeds radiography, where fluid and soft tissue are the same opacity [20, 33]. With the large grayscale that is produced in CT images, windowing and leveling the image allows visualization of a narrow or wide range of densities, as well as focus on certain densities such as bone or soft tissue, in order to optimize the image [32, 36]. For example, using a narrow window setting allows for maximizing the differences in grayness between tissues that are similar in density, improves contrast resolution, and is best to evaluate soft tissue structures. On the other hand, using a wide window setting is necessary to display regions with a wide range of densities and inherently high contrast, such as bone, lungs, and nasal turbinates [38].

The modern spiral or helical CT is commonly used in veterinary medicine, where the X-ray beam and the table both move continuously [20, 34]. This, along with the development of multirow detectors, allows for quicker imaging, reduced motion artifacts, reduced radiation exposure, and prevents loss of image quality with reconstructions [34]. With the older CT units, some loss of image quality can occur with reconstructions made in other than the transverse plane (the plane the image was acquired) [33]. Since most CT units are human medical grade products, the size of the bore or hole in the gantry is a limiting factor in large animal diagnostic imaging, with only the head, cranial neck, and extremities of adult horses able to be imaged [20, 33]. Another limiting factor is the CT table, which has a weight limit; thus, to perform equine imaging, a special table needs to be constructed [20, 33, 39, 40]. Currently, almost all imaging facilities require general anesthesia, since the horse will be positioned on the table in either dorsal or lateral recumbency (Figure 2.5A, B) [20]. The requirement for general anesthesia is a risk that must be weighed against the gain of diagnostic information [35, 41]. Because of this risk, standing CT units are being tested, with a few in use in Europe and the USA, which require sedation instead of general anesthesia [34, 42]. The different designs consist of a dropped, movable floor (a hovercraft-design table), where the horse's head moves into the gantry versus the gantry that moves around a stationary, standing horse's head (Figure 2.5C) [34, 42, 43]. Disadvantages of the standing CT unit include increased likelihood of motion artifact, possible injury to the horse or personnel while positioning, and the increased radiation exposure to personnel restraining the horse [42, 43]. Proper radiation safety equipment is paramount (i.e., lead gown, thyroid shield), as well as proper positioning (the handler should stand at the side of the CT unit) [42, 43].

The use of cross-sectional CT imaging of the equine head removes superimposition of the complex anatomic features of the skull to allow better visualization of the head compared to conventional survey radiography [20, 32, 40, 44]. CT also provides better resolution and detail of bony structures as well as soft tissue structures based on their attenuation of the X-ray beam (Figure 2.6) [20, 35].

Clinically, CT is mainly used to evaluate dental disease, sinonasal disease, neurologic disorders localized to the head, and trauma; however, any disease process localized to the head can utilize CT imaging (Figure 2.7) [20, 32, 34, 41, 44]. Iodinated contrast medium safe for intravenous (IV) injection (doses from 0.45 to 1 mL/kg have been described) may be used in order to better evaluate the extent of inflammatory or neoplastic lesions, specifically lesions with increased vascularity or that disrupt the blood–brain barrier [20, 35, 36, 41, 44]. A good understanding of normal anatomy is required to interpret CT images, and references for normal transverse CT anatomy of the adult horse and the foal have been published, with a specific report describing the normal equine eye and orbit anatomy with CT and MRI [35, 45–48].

The large amount of low-density fat in the equine orbit provides good natural contrast for differentiating the various soft-tissue structures by CT, although the primary advantages of CT over MRI are its ability to detect osseous changes, less expense, and shorter scan times [20, 23, 33, 42]. Because of these advantages, CT is the best modality to evaluate orbital trauma [20]. Disadvantages of CT over skull radiography in the horse include the need for general anesthesia and the risks associated with recovery from anesthesia, increased cost, and limited accessibility [41]. Disadvantages of CT over MRI in the horse include the use of ionizing radiation and the superior contrast resolution seen with MRI [33, 36, 41].

Previously, most cases in the literature regarding CT of the equine head involved evaluation of the teeth, sinuses, brain abscess/mass, pituitary tumors, and skull fractures [22, 34, 35, 40, 41, 44, 49–56]. Recently, there have been multiple additional reports of CT examination of the equine head specifically involving diseases of the orbit/periorbit, retrobulbar space, and nasolacrimal duct, with most being performed for surgical planning [22, 27, 30, 44, 51, 57–60].

Magnetic resonance imaging

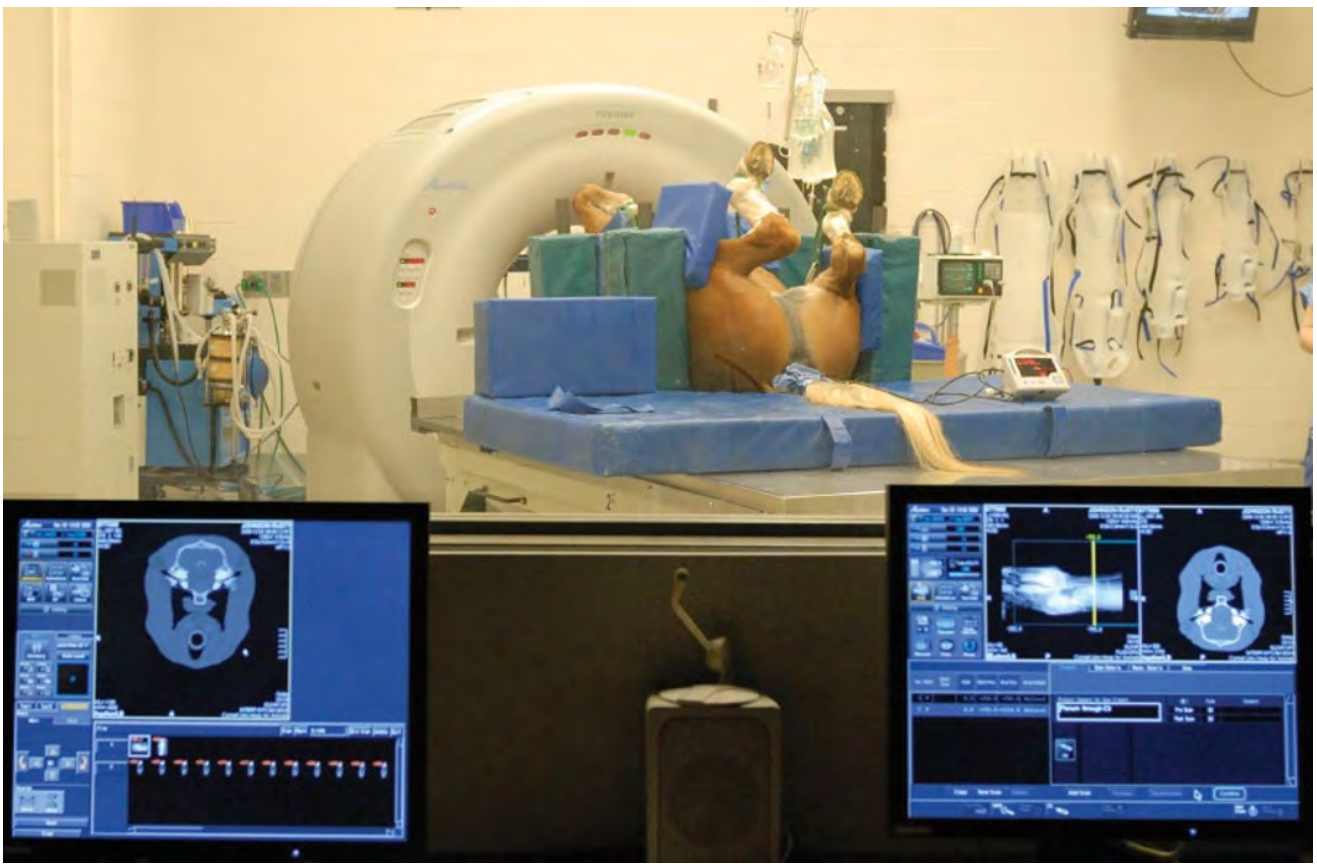
The fundamental principle of MRI is based on the behavior of hydrogen protons when placed within a strong magnetic field and how quickly the protons return to equilibrium after excitation by a radiofrequency (RF) pulse [20]. When an object is placed within a strong magnetic field, the hydrogen protons that make up that object behave like tiny magnets, and align themselves along the axis of the external magnetic field [20]. In addition, these hydrogen protons will wobble about their axis to a specific frequency (called Larmour frequency) that depends on the internal properties of the hydrogen atom and the strength of the magnetic field. An RF pulse set to this specific frequency is applied to the object from a transmitter coil. This causes excitation of the hydrogen protons, resulting in them obtaining a different orientation than the main axis of the external magnetic field [20]. When the RF pulse is discontinued, the protons begin to realign with the main axis by two methods of relaxation: longitudinal magnetic relaxation time (T1, spin–lattice relaxation time) and transverse magnetic relaxation time (T2, spin–spin relaxation time), while emitting a radiowave in the process [20]. The MRI unit detects the radiowave with a receiver coil and the computer generates a grayscale image from the collected data based on the signal intensity [20, 33]. The T1 and T2 relaxation times for hydrogen protons vary depending on the type of environment and molecular arrangement of the protons [33, 61]. This results in the various tissue types having different signal characteristics ultimately providing tissue contrast within the image [20, 33, 61]. The T1 and T2 specific relaxation times are a characteristic of the tissue type, and, along with the proton density, are a fundamental property of tissue, which can be exploited by the MRI machine by using certain acquisition techniques [61].



(A)

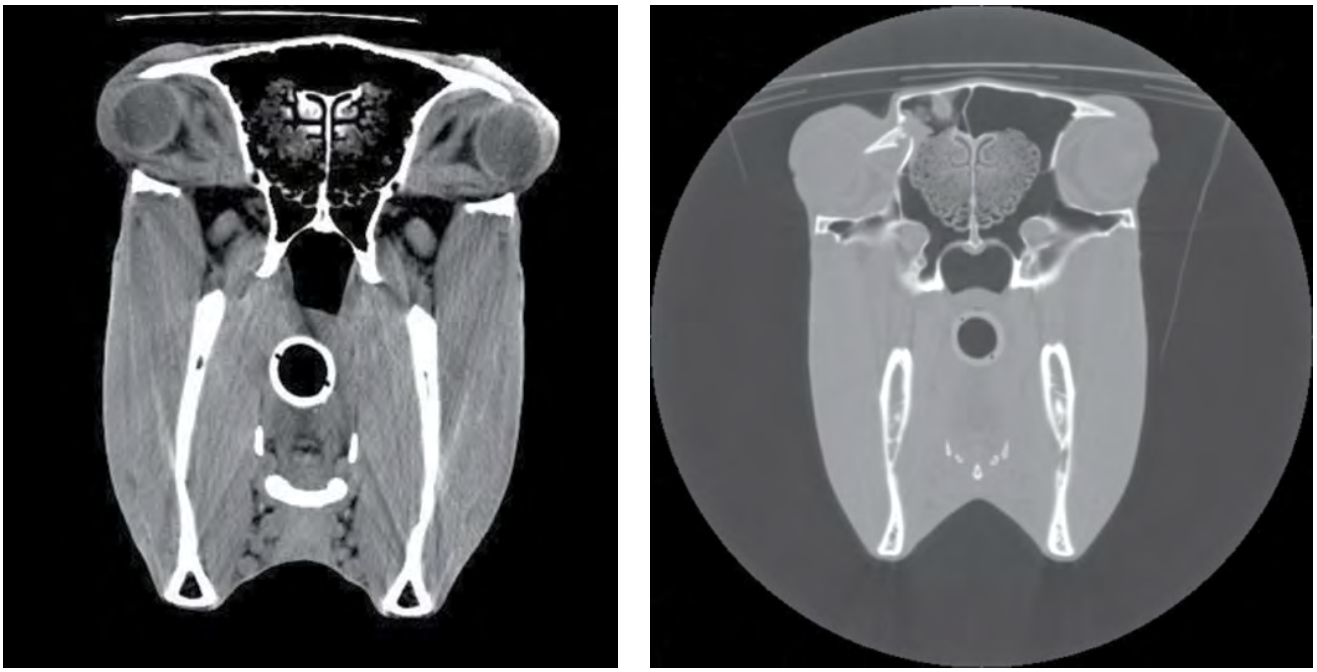


(C)



(B)

Figure 2.5 (A) and (B) A horse under general anesthesia in dorsal recumbency for CT examination of the head. (Photographs reproduced by permission of Dr Nathan Dykes, Cornell University, Ithaca, NY.) (C) A standing, sedated horse for CT examination of the head. (*Source*: Sarah Powell. Reproduced with permission from Sarah Powell, Rossdales Equine Diagnostic Centre, Suffolk, UK.)



(A) (B)

Figure 2.6 The large amount of low-density fat in the equine orbit provides good natural contrast for the differentiation of the various soft-tissue structures by CT, although the primary advantage of CT over MRI is its ability to detect osseous changes. **(A)** Normal transverse equine CT scan. **(B)** A supraorbital fracture is present on this CT scan.

Clinically, the spin echo (SE) pulse sequence is most commonly used, which allows for T1-, T2-, and proton density (PD)-weighted acquisitions. T1-weighted SE sequences produce an image based on T1 characteristics of tissues, which highlights tissue structural characteristics and is best used to evaluate anatomy, but has less tissue contrast [20, 33, 41, 61]. T2-weighted SE, similarly, produces an image based on the T2 characteristics of tissues, and is sensitive to fluid, which is bright (hyperintense) on the image [20, 33, 41, 61]. Thus T2-weighted images are best used to evaluate pathology because they highlight areas of inflammation or edema; however, they have less anatomic definition [20, 33, 41, 61]. PD-weighted images rely on differences between the concentrations of protons within tissues, and are used to highlight tissue contrast [20, 61]. Similar to T1-weighted images, PD-weighted images are best for evaluating anatomy, specifically for differentiating gray versus white matter in the brain and spinal cord and evaluating tendons and ligaments [20, 41, 61]. Other important pulse sequences include inversion recovery (IR) and gradient echo (GE). The IR sequences are useful because they allow the signal from certain tissues to be nulled. For example, a short tau IR (STIR) sequence nulls the signal from fat, making pathology in tissues adjacent to, or within, fat more detectable. In addition, a fluid-attenuated IR (FLAIR) sequence nulls the signal from low-cellular fluids such as cerebral spinal fluid (CSF) or a cystic lesion, making lesions adjacent to CSF more detectable and enabling a distinction between a cystic lesion and a hyperintense solid structure [20, 61]. The gradient echo pulse sequences are primarily used to emphasize magnetic field inhomogeneities and tissue susceptibilities that occur because of paramagnetic or diamagnetic substances [61]. A hypointense (dark) region on this sequence will occur because of these substances, which is called susceptibility artifact. The T2* sequence accentuates this artifact, making paramagnetic blood degradation products more detectable, and is an important sequence used in MRI for detecting microbleeds that are not seen on the routine sequences [61].

Contrast medium can be used in MRI, with similar principles to CT (i.e., increased vascularity, breakdown of the blood–brain barrier), although the underlying physics and contrast medium are different [20]. In MRI, pre- and post-T1-weighted images are obtained using a paramagnetic contrast material (gadolinium-based contrast agents such as gadopentetate dimeglumine (Magnevist (Bayer HealthCare, Wayne, NJ)) are commonly used) [20, 41]. The contrast material decreases the T1 relaxation time of adjacent protons, causing affected tissues to be hyperintense (brighter) on T1-weighted images [20, 41]. The standard IV dose in humans and small animals is 0.1 mmol/kg [62]; however, the reported doses in adult horses vary from 20 to 40 mL and up to 0.02 mmol/kg [41, 62–65].

The strength of the magnetic field (defined using the SI unit of Tesla (T)) plays an important role in image acquisition. Most clinical veterinary MRI units range from 0.5 to 1.5 T, with some 3 T magnets in use, as well as many "open-bore" systems that utilize low-field magnets at 0.2 T. The higher strength magnetic field MRI units are more expensive and have enhanced susceptibility artifact, but have a higher signal-to-noise ratio, faster

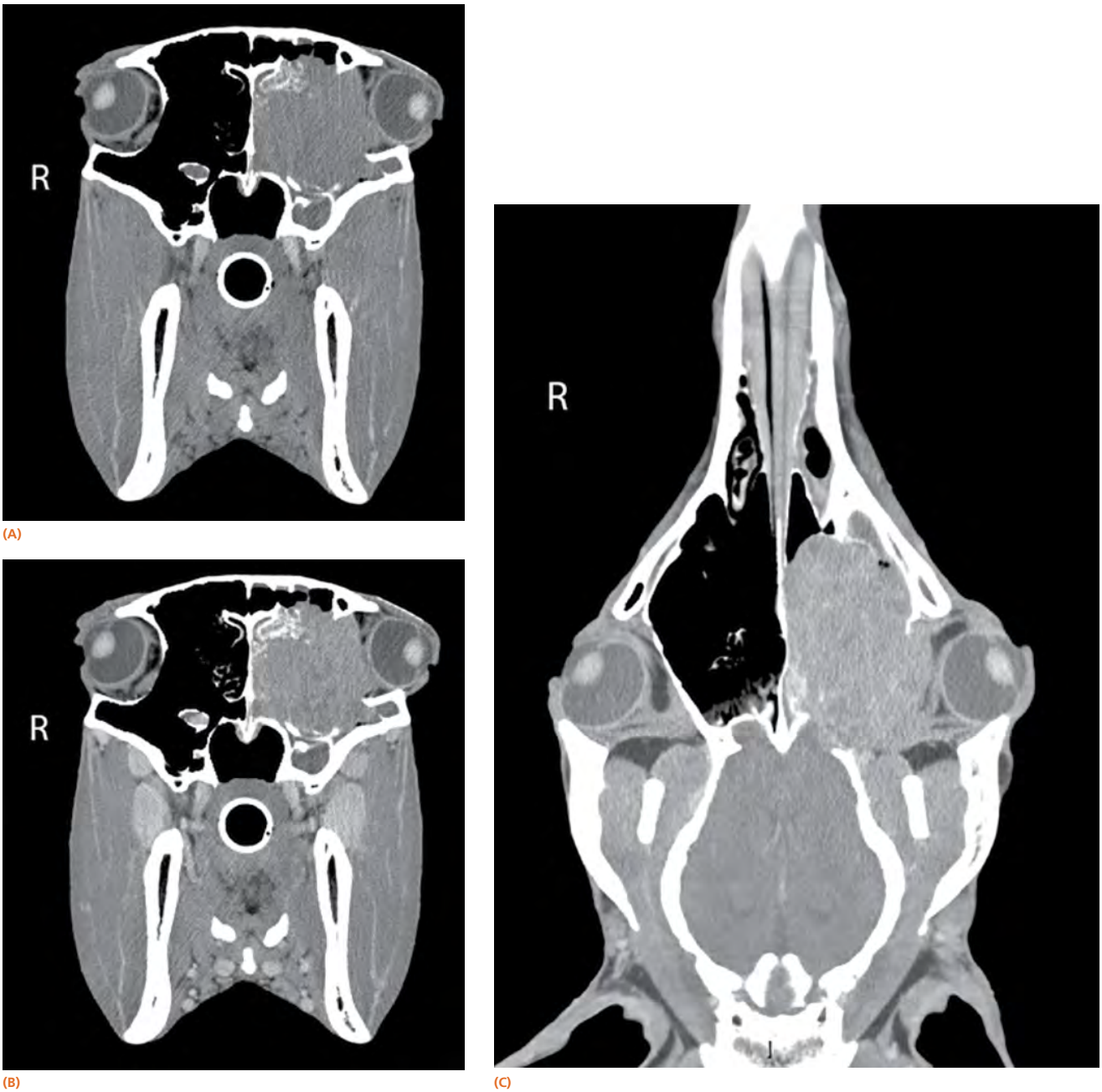


Figure 2.7 CT can be used to evaluate the underlying cause of exophthalmos in horses. A large mass (sinonasal transitional carcinoma) is seen in the left conchofrontal sinus extending into the left caudal maxillary sinus and orbit, and through the cribiform plate. CT images of the head in the transverse plane at the level of the globes in a soft tissue algorithm pre **(A)** and post **(B)** IV contrast administration. **(C)** CT image of the head in the dorsal plane at the level of the globes in a soft tissue algorithm, post IV contrast administration. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

image acquisition times, and higher resolution and tissue contrast [20, 66]. MRI safety must also be considered, as the strong magnetic field exerts an attractive force on magnetic objects that can lead to severe patient or personnel injury [33]. This means that the horse's shoes must be removed prior to MRI [33].

Standard MRI studies of the head are typically acquired in at least three orthogonal image planes (i.e., sagittal, transverse, and dorsal) relative to the central axis of the head; however, additional planes and the specific sequences performed should be chosen based on the region of interest and suspected pathology (Figure 2.8) [41, 67].

The oblique dorsal and oblique sagittal planes have been reported to be the most valuable for evaluating the orbit and optic pathways [67]. As in humans, T1-weighted images provide better spatial resolution and definition of normal anatomic detail of both the eye and orbit compared to T2-weighted

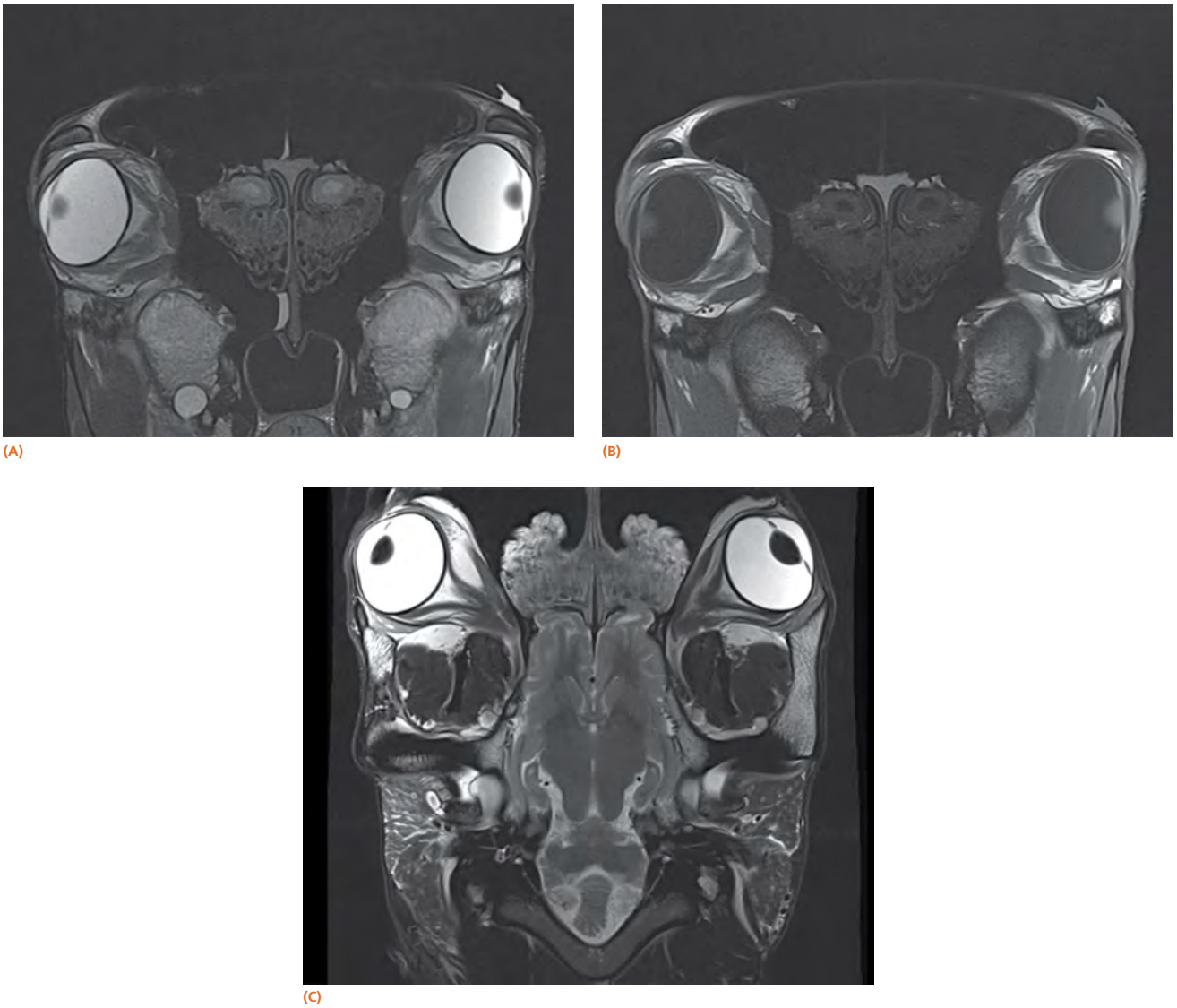


Figure 2.8 T2-weighted **(A)** and T1-weighted **(B)** MRI images of an equine head in the transverse plane at the level of the globes, demonstrating normal anatomy of the eye and periocular structures. **(C)** T2-weighted MRI image in the dorsal plane at the level of the globes. Note the vitreous cavity of the eye is bright (hyperintense) on the T2-weighted image and dark (hypointense) on the T1-weighted image, and the improved soft tissue contrast in the image compared to the CT scans (Figures 2.6 and 2.7). (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

images [67, 68]. While, pathologic processes that result in increased fluid content in regions of inflammation and edema are best evaluated as regions of hyperintensity (bright) on T2-weighted images [41, 67]. The order of signal intensity for T1-weighted images from white to black is: fat > cornea, lens capsule, iris, retina, choroid > brain > extraocular muscles, optic nerve, skin, eyelids > aqueous, vitreous humor > lens, sclera > bone, air [67]. The order of signal intensity for T2-weighted images from white to black is: vitreous, aqueous humor > brain > extraocular muscles, optic nerve, iris, eyelids, skin > fat, bone, sclera > lens, air [67]. Additional sequences used in head imaging include FLAIR to null the signal from fluid such as CSF and vitreous humor, making periventricular and intraocular lesions more detectable, and STIR to null the signal from fat, specifically in the retrobulbar space, making lesions in this location more detectable [41].

MRI in human ophthalmology is often used to evaluate space-occupying lesions, congenital and degenerative disorders, the retrobulbar space, foreign bodies, and orbital vascular lesions [20, 67]. MRI has also been reported to assist with diagnosing diseases of the nasolacrimal drainage system [31]. In veterinary medicine, MRI can be used to image the orbit to assist diagnosis of inflammatory diseases, abscesses, nonmetallic foreign bodies, and neoplasia [62]. In horses, MRI has assisted with the diagnosis of sinonasal disease, retrobulbar mass, third eyelid mass, periorbital wooden foreign body, optic

neuritis, and optic nerve atrophy [63–65, 69]. Additional magnetic resonance studies on diseased eyes are needed to determine the value of this imaging tool in equine ophthalmology. Normal anatomic atlases for the equine orbital structures and sinuses have been published for both T1-weighted and T2-weighted magnetic resonance images, as well as magnetic resonance angiography of the head [48, 67, 68, 70–73]. MRI of the equine eye was able to identify the ocular adnexa, as well as the optic nerve and different components of the eye, except the sclera which could not be differentiated from the choroid and retina [48].

Use of MRI to evaluate the equine eye and orbit suffers from the same technical difficulties as CT, including the need for general anesthesia and the risks associated with recovery, size and shape of the gantry, and limited availability [20, 33, 41, 46, 67]. The main advantages of MRI over CT include the absence of ionizing radiation, ability for direct multiplanar imaging (the image is obtained in different planes, eliminating the risk of lower quality images made from reconstructions), and, probably most importantly, better soft tissue contrast [20, 33, 67]. The superior soft tissue contrast allows for enhanced anatomic detail and characterization, better resolution of ocular and retrobulbar structures, and better assessment of the optic nerve [20, 23, 67]. Disadvantages include long data-acquisition time, which may increase the risk for post-anesthetic myopathy or neuropathy, increased slice thickness and poorer spatial resolution, failure to detect defects in cortical bone, potential for image artifacts, and the need for nonmagnetic equipment (i.e., ventilator, table, monitoring equipment) [20, 22, 23, 41, 64, 67, 74]. On all pulse sequences, cortical bone does not produce a signal (i.e., black), and if the bone is adjacent to other structures that do not produce signal, such as the nasal sinuses, the margin of the bone can be difficult to delineate [20]. This makes CT the modality of choice to evaluate bony structures, and MRI is recommended when the soft tissue structures need to be evaluated; however, sometimes both are used to evaluate a lesion, as they can complement each other, each providing valuable information [33]. Despite defects in cortical bone being difficult to discern, MRI is good at detecting bony injury or disease because certain pathologies, such as neoplasia, edema, and bruising, can cause an increase in signal, making detection easier, and may be more sensitive to early changes [33, 41].

Ultrasound

Ultrasonography is a rapid, safe, noninvasive method for examination of periocular, intraocular, and retrobulbar structures in an awake horse [20, 75–78]. Ocular ultrasonography allows examination of the globe in conditions in which opacity of the transmitting media of the eye (cornea, aqueous humor, lens, and vitreous humor) or extreme eyelid swelling otherwise prevents a complete ophthalmic examination [20, 75, 77–80]. In addition, evaluation of intraocular and retrobulbar mass lesions, differentiation between solid and cystic structures, examination for a foreign body, axial length determination of the globe and intraocular structures, and examination of orbital structures are all indications for performing ocular ultrasonography [20, 75, 79]. The most common clinical indications for ocular ultrasonography in the horse are to evaluate for the presence of retinal detachment or lens luxation after trauma and in horses with uveitis, hypopyon, hyphema, cataract, and severe corneal opacities (e.g., edema, fibrosis) [20, 75, 77–79, 81]. Orbital evaluation is also routinely performed in instances of exophthalmos or orbital trauma [20]. In addition, ultrasonography is commonly used to verify the stage and location of a cataract before surgical removal, as well as potential complications (e.g., posterior lenticonus) that would make phacoemulsification more challenging [75, 77, 82]. More thorough descriptions of the physics, equipment, techniques, and results of ultrasonography in various disease states can be found elsewhere [75, 77–79, 81–90].

Ocular ultrasonography: general features

Ultrasound is an acoustic wave with frequencies that exceed the range of human hearing. In ultrasonographic imaging, an ultrasound beam is produced by a transducer or probe that contains a piezoelectric crystal [89]. When electric energy is applied to the crystal, an ultrasound wave is created that causes oscillation of particles within a medium [89, 91]. The velocity of the wave is dependent on the medium through which it is traveling [91]. Water transmits sound waves at a slower velocity than a more solid media; thus the wave passes more quickly through the solid lens than through the liquid aqueous or vitreous [91]. The sound wave as it travels through tissue can be reflected back towards the probe, and this reflected wave is called an echo. Echoes are produced at interfaces created at the junction of two media with different acoustic impedances, which is determined by the sound velocity and density of the medium [91]. The greater the difference in the acoustic impedance between the two media, the stronger the reflection of the ultrasound wave or echo [91]. Thus the anterior lens capsule would produce a stronger echo when bordered by normal aqueous than when bordered by blood (hyphema).

The opposite is also true; if two tissues have the same acoustic impedance, the ultrasound wave is not reflected and no image is produced [89]. The reflected echoes return to the transducer and the piezoelectric crystal, which converts the ultrasound back into electric voltage and ultimately produces an image [89]. The returning echoes are affected by numerous factors, such as the angle of sound incidence; the size, shape, and smoothness of the acoustic interface; absorption; scatter; and refraction [91]. If the sound wave strikes an interface at a perpendicular angle, the entire wave is reflected back to the transducer, and a strong echo results. If the beam is angled, some of the reflected energy is diverted away from the probe and results in a weaker echo. The smoother and straighter the interface (e.g., retinal surface, lens capsule), the more reflected energy returns directly to the

probe, resulting in a strong echo. Higher frequency sound waves and greater tissue thickness increase absorption of the sound wave and weaken the echo. Refraction occurs when a sound wave is directed obliquely to an interface between two media with different sound velocities [91]. Therefore no refraction occurs when the wave is directed perpendicular to the interface or when the two media have the same sound velocities [91]. In addition, the returning echoes can be amplified by adjusting the overall gain control on the instrument screen. By increasing the gain, the intensity of the returning echo is also increased [91]. Time gain compensation (TGC) allows for modification of the intensity of the returning echoes based on the distance from the transducer. This results in the ability to amplify the weaker echoes returning from deeper tissues while decreasing the intensity of the stronger echoes from the shallow tissues [91]. TGC is often an automatic control; however, many instruments also offer a manual TGC control [91].

Deep tissue penetration is not a necessity for ocular ultrasonography, but high resolution is required [79]. The frequency of the ultrasonic waves emitted by the selected oscillating piezoelectric transducer determines the resolution of the image [91]. Transducer probes are available in a range of frequencies (e.g., 3.5, 5, 7.5, 10, 12.5, 20, 35, and 50 MHz), and the frequency is inversely proportional to the wavelength of the sound beam [79, 91]. In turn, the wavelength is directly proportional to the depth of sound beam penetration [79]. Therefore a low-frequency transducer (5 MHz) provides poor near-field axial resolution but greater tissue penetration and is therefore useful for imaging more posteriorly located structures, such as the orbit. A high-frequency transducer (50 MHz) provides lower tissue penetration but high near-field axial resolution and is therefore useful for imaging more anteriorly located structures [91].

An optimal ophthalmic transducer for general use is a 7.5- or 10-MHz transducer [79, 85]. These probes provide adequate depth of penetration to visualize the retrobulbar structures, enhanced resolution, and ability to visualize anterior intraocular structures such as the iris, ciliary body, anterior and posterior chambers, and cornea (with the use of an offset device) [79]. The 7.5-MHz transducer, with a focal range of 2–5 cm, produces good ophthalmic images and has a better depth of penetration for visualization of retrobulbar structures than the 10-MHz [79]. However, near-field reverberation artifacts will obscure the anterior segment of the globe unless an offset device or increased sterile coupling gel is used or the ultrasound examination is performed through closed eyelids [79]. The 10-MHz transducer has a focal range of 3–4 cm, and provides better resolution but less depth penetration [79]. Linear transducers provide higher frequency and thus better resolution of near-field structures, but the small footprint of a sector or convex probe is easier to manipulate [88]. The use of probes with frequencies of 20–100 MHz is referred to as **high-frequency ultrasound biomicroscopy** [92–96]. Ultrasound biomicroscopy allows for optimal visualization of the cornea, sclera, anterior and posterior chambers, iris, choroid, and lens and is described in the section **High-frequency ultrasound examination and ultrasound biomicroscopy**.

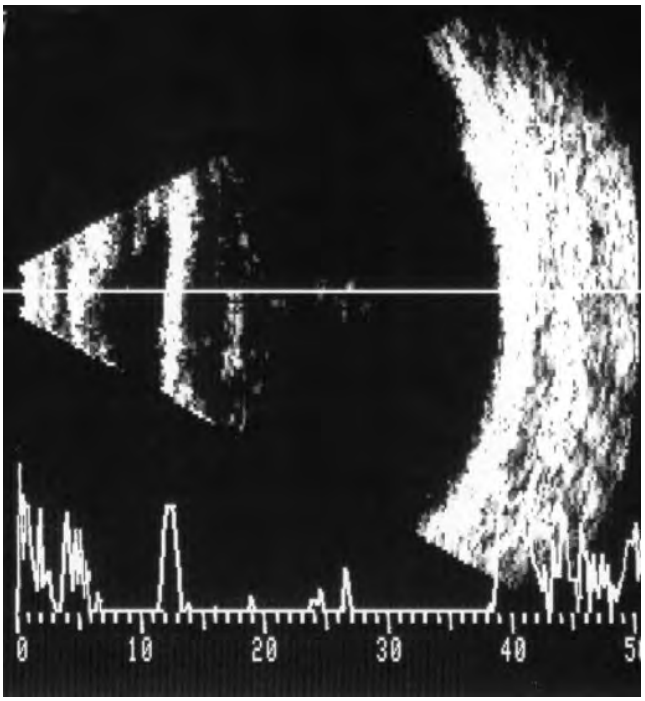


Figure 2.9 A-scan ultrasonography produces an anterior–posterior image, with peaks reflecting tissues of different identities displayed as a linear series of vertical spikes from a baseline. (*Source*: Ultrasound image courtesy of Dr David Wilkie.)

Both amplitude-mode (A-scan) and brightness-mode (B-scan) ultrasonography are useful for diagnostic purposes in ocular disease [91]. A-scan ultrasonography produces an anterior–posterior image, with peaks reflecting tissues of different identities displayed as a linear series of vertical spikes from a baseline, where the height of the peak corresponds with the strength of the echo (Figure 2.9) [20, 82, 91]. The time between two spikes can be converted into distance and used to measure anterior–posterior axial length of the globe, anterior chamber depth, axial lens thickness, and vitreous anterior–posterior axial length [91, 97]. B-scan ultrasonography provides a two-dimensional (2D) real-time image of the eye and orbit and is the most common mode of ultrasound used clinically in veterinary ophthalmology (Figure 2.10) [20, 78, 87]. Doppler ultrasound utilizes the shift of frequency that occurs in an ultrasound wave caused by a moving reflector to evaluate blood flow [61]. If the moving reflector (i.e., blood cells) is moving towards the transducer, the reflected ultrasound frequency is greater than the incident ultrasound frequency, and, conversely, if the reflector is moving away from the transducer, the reflected frequency is less than the incident frequency. The difference between the incident and reflected frequencies is called Doppler shift, and the greater the Doppler shift, the greater the velocity of the moving blood [61, 91]. Doppler ultrasound is used in ophthalmic imaging to evaluate the direction of blood flow within orbital

blood vessels and the presence of blood flow within orbital and periorbital lesions [91].

Ultrasonographic images are described as hyperechoic, hypoechoic, and anechoic [20, 87]. Four major ocular acoustic echoes (hyperechogenicities) are generated within a normal eye. These echoes originate from the cornea (seen as one or two parallel hyperechoic lines depending on the transducer frequency), the anterior and posterior lens capsules (seen as hyperechoic, convex/concave, curvilinear structure surrounding the anechoic lens), and the retina/choroid/sclera (see Figure 2.10) [20, 75, 77–80, 83, 86–88]. The retina, choroid, and sclera cannot be normally differentiated from one another by ultrasonography [77–79, 83, 86]. Additional echogenicities can be generated by the iris, corpora nigra (hyperechoic irregular structures at the edge of the pupil), ciliary body, optic nerve, orbital fat, muscles, and other orbital structures [78–80, 85, 87]. The anterior chamber is the anechoic space between the cornea and anterior lens, and the posterior chamber is the small anechoic space between the iris and the anterior lens, which is often not detectable [75, 80]. Posterior to the lens is a large anechoic space called the vitreous chamber [75, 77, 80]. The optic nerve head/lamina cribrosa appears as a hyperechoic structure, with the optic nerve itself seen as a hypoechoic structure extending posteriorly from the optic nerve head [79, 91]. The orbital muscles have a hypoechoic speckled appearance consistent with striated muscle extending posteriorly from the equatorial region of the globe and converging toward the orbital apex, while the retrobulbar fat is more echogenic and somewhat heterogeneous [20, 79, 91]. The bony orbit is hyperechoic and casts a strong acoustic shadow [85]. Ultrasonography of both eyes can be performed for comparison [79]. Normal ultrasonographic anatomy of the equine eye has been published, as well as the range of normal measurements in intact and extirpated eyes [77, 79, 80, 84–86, 92, 97–99].

The main limitation of ultrasonography is the inability of the ultrasound beam to penetrate through bone or air [20]. In addition, there are numerous ultrasonographic artifacts; however, with knowledge of these artifacts, they can be used to help make a diagnosis.

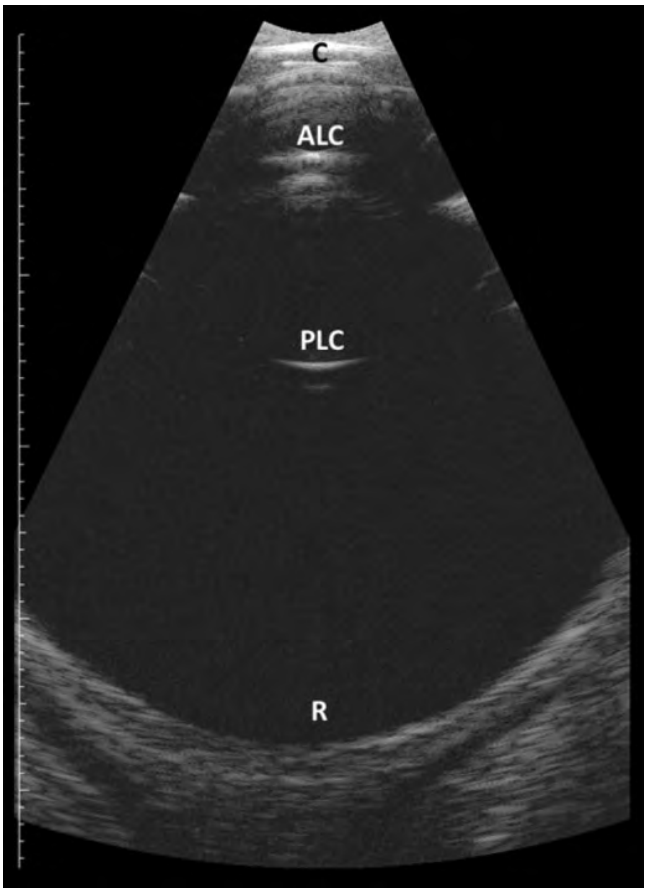


Figure 2.10 B-scan ultrasonography with anatomy provides a 2D real-time image of the eye and orbit and is the most common mode of ultrasound used in a clinical setting. Four major ocular acoustic echoes (hyperechoic) are generated within a normal eye. These echoes originate from the anterior cornea (C), the anterior lens capsule (ALC), the posterior lens capsule (PLC), and the retina/choroid/sclera (R). (*Source*: Ultrasound image courtesy of Dr David Wilkie.)

Ocular ultrasonography technique

The ultrasound transducer can be placed directly on the cornea (transcorneal), which provides superior images of the posterior segment or orbit, or the scan may be performed through closed eyelids (transpalpebral) or with an offset device to examine the anterior aspect of the globe (Figure 2.11) [20, 78]. With the transpalpebral approach, the main advantage is the horse cannot see the transducer; however, there are more ultrasonographic artifacts with this approach compared to the transcorneal approach [78, 85]. Use of a small scan head diameter allows optimal placement directly on the cornea (Figure 2.12) [79].

When ultrasound biomicroscopy is not being performed, conducting the examination through the eyelids or with an offset device, which may require an increase in gain setting, will



Figure 2.11 The ultrasound transducer can be placed directly on the cornea, which provides superior images of the posterior segment or orbit, or the scan may be performed through closed eyelids.



Figure 2.12 A small transducer head is optimal for transcorneal ultrasound examination.



Figure 2.13 A standoff pad will facilitate examination of the anterior portions of the globe; alternatively, a water-filled balloon or excess coupling gel can be used.

facilitate examination of the anterior portions of the globe [79]. A suitable tissue-equivalent offset device is available with most transducers; alternatively, a water-filled balloon or excess coupling gel can be used (Figure 2.13) [79, 85]. The transducer can be positioned to provide horizontal, vertical, and oblique scanning sections of the eye. The globe should routinely be imaged in the horizontal and vertical planes through the visual axis, with oblique positioning being performed for a complete examination [78, 83, 85, 87]. The transducer can also be positioned dorsal to the zygomatic arch in the supraorbital fossa to scan the orbit and retrobulbar space [20, 75, 90].

Sedation and/or regional nerve blocks may be required, depending on globe stability and the temperament and level of discomfort of the horse. An auriculopalpebral nerve block will block motor to the upper eyelid, preventing blinking [85, 86]. Topical anesthesia of the cornea (proparacaine 0.5% (Alcaine (Alcon Laboratories, Fort Worth, TX)) is required for a transcorneal ultrasound examination [78. 79]. Sterile methocellulose gel, such as Surgilube® (Fougera Pharm., Melville, NY), is recommended as the ultrasound coupling gel [85]. It is placed on the transducer tip or on the corneal surface and should be irrigated from the eye on completion of the examination [78, 79, 86]. Standard ultrasound coupling gels may cause corneal irritation and should be avoided [79].

Ultrasound examination of the anterior segment

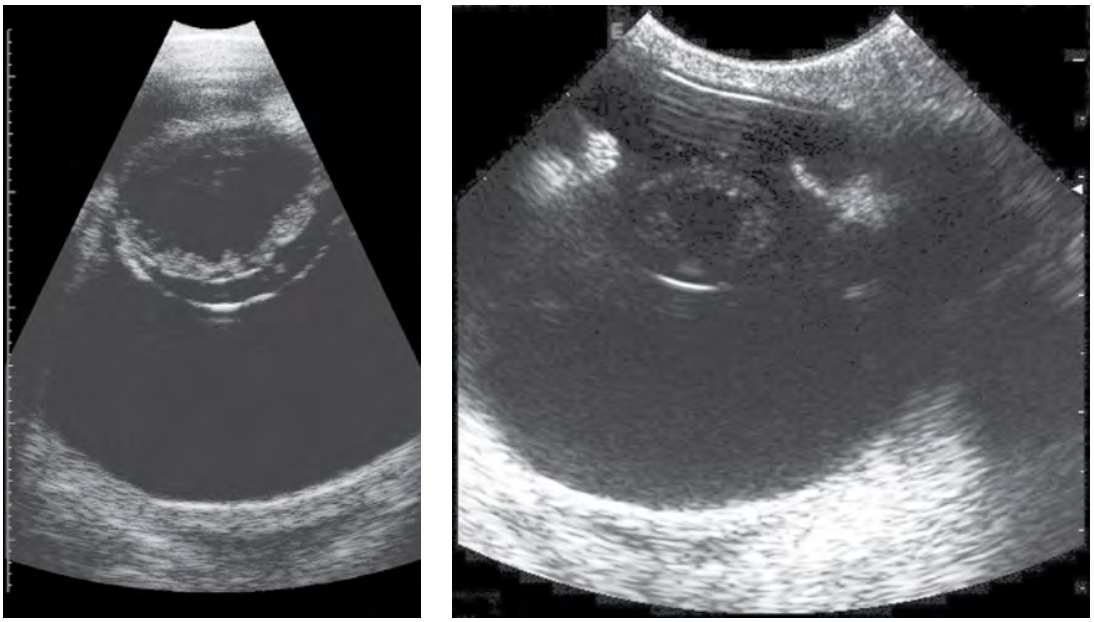
To evaluate the cornea, an offset or water-filled glove can be used in order to minimize transducer interference and allow for better resolution [86]. Corneal ulcers are best evaluated by an ophthalmic examination; however, if severe eyelid swelling is present, ultrasonography may be useful. An ulcer is seen as a concave defect or pitted appearance along the cornea. It is important to note that ultrasound should not be performed in horses with severe corneal ulceration, as there is a risk of corneal perforation [75]. Ultrasound can also be used to evaluate for foreign material within a corneal stromal abscess or corneal dermoids [75]. Synechiae imaged with ultrasonography will appear as adherence of the iris to the cornea (anterior synechiae) or the anterior lens capsule (posterior synechiae) [75].

If the cornea is opacified, ultrasound can evaluate the rest of the globe and orbit [82]. Detecting echoes in the anterior chamber is considered abnormal and can be due to exudates, hyphema, or hypopyon, for which differentiation between can be difficult [82]. Fibrin often causes flocculent hyperechogenicities, where hypopyon is usually more ventral with a uniform echogenicity [79].

Ultrasound examination of lens abnormalities

When findings of ocular ultrasound examination are normal, the lens appears as two distinct echogenicities seen at the anterior and posterior axial lens capsules (see Figure 2.10) [75. 79, 80]. The anterior echo is slightly convex, and the posterior echo is slightly concave [75, 79, 80]. Internally, the lens is anechoic, and peripherally, the echo is reflected away from the probe so the peripheral curved margins are not seen [75, 79, 80, 88].

Abnormalities of the lens that can be detected on ultrasonography include abnormalities of lens size, cataract, luxation or subluxation, and lens capsule rupture [79]. Cataracts are commonly seen in horses and can be a congenital or acquired (secondary to uveitis or trauma) abnormality [77]. A cataract appears as increased echogenicity within the lens and as increased visualization of the lens periphery other than the anterior and posterior axial portions (Figure 2.14) [77, 79]. The size and intensity of the echoes will depend on the extent and



(A) (B)

Figure 2.14 (A) A posterior cortical cataract seen as a thick, irregular echogenicity located anterior to the posterior lens capsule. (*Source*: Ultrasound image courtesy of Cornell University, Ithaca, NY.) (B) Anterior and posterior cortical cataracts.

severity of the cataract, with a direct relationship between intensity of the lens echoes and cataract stage (Figure 2.15) [77, 79].

The size of the lens, measured anterior to posterior at the axial position, can be both increased and decreased with cataracts [79, 87]. An increase in lens size occurs as a result of imbibition of fluid and secondary swelling of the lens [87]. A decrease in lens size occurs as a result of resorption of liquefied cortical material, as is seen with a hypermature cataract or microphakia (Figure 2.16) [77, 79]. Hypermature cataracts can also contain hyperechoic regions with acoustic shadowing consistent with mineral and the lens capsules can appear wrinkled [75, 88]. Examination of the posterior segments is important prior to cataract surgery to evaluate for any abnormalities that would be a contraindication for surgery [75, 77, 82].

Ultrasonography can be used to evaluate the position of the lens after trauma or during inflammation when the anterior segment is opaque because of edema or hemorrhage [79]. The echogenic capsules of the lens will be seen in an abnormal position, and may even be seen freely moving (Figure 2.17) [75]. Difficulty in obtaining a simultaneous echo of both the anterior and posterior lens capsule and changes in the anterior–posterior axial measurements of the lens or lens–posterior scleral wall distance may indicate a luxation or subluxation of the lens [79].

Ultrasound examination of the posterior segment

Ultrasonography is used to evaluate the posterior segment for abnormalities of the vitreous or retina in an eye with a cataract, after trauma, or in other conditions in which opacification of the transmitting media may be present (e.g., equine recurrent uveitis) [77, 79]. Evaluation of the posterior segment in an eye with a cataract is probably the most common indication for ocular ultrasonography in a horse, with evaluation post-trauma a close second [77, 81]. Ultrasonography has also been used to help determine the extent and size of bilateral optic disc colobomas (an absence or defect of the ocular tissue) in horses [100].

The vitreous cavity is normally anechoic, appearing dark or black on ultrasonography [79]. Echogenicities in the vitreous can be due to hemorrhage, inflammation, vitreal or retinal detachment, vitreal pseudomembranes, degeneration (synaresis), and asteroid hyalosis [75, 78, 79, 87]. Vitreal degeneration creates interfaces that result in ultrasonographic echogenicities. These appear as multiple variable echogenic lines within the vitreous cavity and are best visualized by increasing the far-field gain setting on the ultrasound unit. However, setting the gain too high can result in a false impression of hyperechogenicities [79]. Clinically, the vitreous degeneration may or may not be visible. Asteroid hyalosis appears as highly reflective, discrete, freely moving echoes (calcium phosphate crystals) that persist even as the gain setting is decreased. They are commonly seen in older animals and not considered clinically significant [75, 79, 87]. Vitreous hemorrhage appears as discrete to diffuse moderate amplitude echoes that may demonstrate a swirling motion (Figure 2.18) [85]. Vitreous inflammation, which is often associated with equine recurrent uveitis, appears as multifocal disconnected variable echogenicities within the vitreous cavity that are often larger and more hyperechoic (brighter) than blood [75, 85]. Fibrin strands and vitreal pseudomembranes appear as linear or curvilinear echogenicities that cannot be traced to the optic nerve [78].



Figure 2.15 Late immature cataract. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



Figure 2.16 A decrease in lens size occurs as a result of resorption of liquefied cortical material, as is seen with a hypermature cataract or microphakia. This hypermature cataract is smaller than normal and the fibrotic lens capsule appears hyperechoic. A reverberation artifact is also present in the vitreous (12.5-MHz probe).

Retinal detachment is most commonly due to chronic equine recurrent uveitis and trauma, with other causes (i.e., infection, neoplasia, glaucoma, congenital abnormality, or a complication secondary to phacoemulsification) reported less frequently [75, 79, 81]. The retinal echo is indistinguishable from the underlying choroidal and scleral echo in a normal eye [77–79, 83, 86]. The detached retina becomes apparent as a distinct echodensity with a separation of 0.5–1 mm [87]. Classically, the retina appears as two hyperechoic curvilinear-to-linear structures, often attached at the optic disc posteriorly and the ora ciliaris retinae anteriorly, resulting in a V-shape or gull-wing-appearing detachment (Figure 2.19) [77, 79, 87].

A complete or only partial retinal detachment, as well as disinsertion from the ora (usually dorsally), can be present [79, 87]. Initially, retinal detachments will be seen to undulate when viewed in real time, but with chronicity, the retina will become fixed and less mobile, as well as more echogenic due to dystrophic mineralization [86, 87]. Examination of the subretinal space with retinal detachment is important. Anechoic fluid in the subretinal space, such as a transudate, may resorb; however, the presence of echogenic material can indicate hemorrhage or infiltration of neoplastic or inflammatory cells, and has a poorer prognosis [75, 79, 87]. Other differential diagnoses for a hyperechoic linear structure in the vitreous include vitreous hemorrhage, degeneration, or fibrin, choroidal or vitreous detachment, traction bands, and reverberation artifacts such as from the lens (Figure 2.20) [78, 79, 87].

Ultrasound examination of intraocular masses

Intraocular masses consist of inflammatory, infectious, hematoma, neoplastic, and cystic structures and most commonly arise from the anterior segment (iris, ciliary body, lens) in the horse (Figure 2.21), but choroidal mass lesions can occur as well [75, 79, 87]. Because many of these mass lesions arise from the anterior uvea, an offset device, extra coupling gel, scanning through closed eyelids, or ultrasound biomicroscopy is required to adequately visualize the lesion [79]. In the horse, the most common tumor of the eye and adnexa is squamous cell carcinoma; however, other reported ocular tumors include melanoma, adenoma, lymphosaracoma, multiple myeloma, and primary and metastatic adenocarcinoma



Figure 2.17 The lens is luxated and mildly displaced caudally into the vitreous cavity. Adjacent to the lens, the vitreous cavity contains numerous hyperechoic strands indicating concurrent hemorrhage or inflammation. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



Figure 2.18 Vitreous hemorrhage appears as discrete to diffuse moderate-amplitude echoes, which may demonstrate motion.

[87, 101, 102]. Intraocular mass lesions that are densely pigmented and cannot be transilluminated clinically can be either cysts or melanomas [79]. A cyst will have a thin, echogenic wall but an anechoic fluid-filled center with acoustic enhancement of the far-field structures, whereas melanoma appears as a homogeneous echogenicity [75, 79, 87]. In one study, intraocular blood clots were misdiagnosed as neoplasm; thus interpretation of intraocular masses with large amounts of intraocular blood should include both neoplasm and hematomas [103].

Ultrasound examination of the orbit

Orbital contents include the extraocular muscles, fat, vascular tissues, glands, optic nerve, and bony orbit. Exophthalmos and orbital trauma are the two most common indications for orbital ultrasound examination in the horse. Differential diagnoses for exophthalmos include orbital mass lesions (e.g., neoplasia, abscess, hemorrhage) or extension of nasal or sinus disease [87]. An orbital mass lesion should be characterized as cystic, solid, or infiltrative, and its location within the orbit should be determined [79, 83, 87]. Some retrobulbar neoplasms described in horses are melanoma, lymphoma, squamous cell carcinoma, carcinoma or neuroepitheal origin, and undifferentiated sarcoma [20, 104]. Other differential diagnoses for retrobulbar masses include abscess, hematoma, cysts, hemorrhage, and cellulitis [75, 79, 104]. Epibulbar neoplasia, such as squamous cell carcinoma, sarcoid, and melanoma, are commonly described in horses [75]. Doppler ultrasound can be performed to determine if an orbital mass is vascular or nonvascular, and ultrasound-guided fine-needle aspiration or biopsy may be useful to obtain a sample for cytology or histopathology [79, 91]. After trauma to the orbit and associated structures, ultrasound may be used to evaluate the retrobulbar space for displaced fractures, hemorrhage, swelling, compression of the optic nerve, and integrity of the posterior wall of the globe [79, 87].

Ultrasonography is also useful for evaluating the presence of abscesses and foreign bodies. Foreign bodies often appear as echogenic or hyperechoic structures, with bone and metal creating an acoustic shadow and tracked gas creating a reverberation artifact [20, 79, 85]. Foreign bodies are also commonly surrounded by fluid or an abscess (Figure 2.22) [20, 79, 85]. Foreign bodies are often more easily seen with ultrasound compared to CT or MRI, whereas the adjacent soft tissue abnormalities (i.e., abscess or fluid) are more easily seen with CT or MRI.

Ultrasonic evaluation of ocular trauma

Ocular ultrasonography is of extreme importance in the evaluation of ocular trauma in the equine patient [79]. The extent and severity of the injury, prognosis, and probable therapy can be determined in many cases through ultrasound examination [79].



Figure 2.19 When detached, the retina appears as an echogenic linear structure, most often attached at the optic disc posteriorly and the ora ciliaris retinae anteriorly, resulting in the classic funnel or gull-wing-appearing detachment. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



Figure 2.20 Hyperechoic linear structures in the vitreous can be due to retinal detachment, vitreous hemorrhage, degeneration, or fibrin, choroidal, or vitreous detachment, traction bands, or reverberation artifacts such as from the lens. This example shows panuveitis with vitritis and vitreal fibrin seen as hyperechoic strands in the vitreous. Retinal detachment is also present, seen as a small gap posterior to the retina. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

Often, ultrasonography is the only examination method of value in an eye that is otherwise severely painful or opaque, or when the eyelids cannot be opened because of swelling [79, 87]. If the structural integrity of the globe is compromised, extreme care should be taken when the ultrasound examination is performed to not induce further damage to the eye. For complex osseous changes and trauma to the bone, radiographs or CT remain the best modality to better evaluate for abnormalities, but ultrasonography is good for quickly evaluating trauma to the soft tissue structures [79].

Both blunt and penetrating trauma in the horse can result in significant intraocular changes. Penetrating trauma can result in a shallow anterior chamber; fibrin in the anterior chamber; hyphema; lens capsule rupture; lens luxation, subluxation, or expulsion; vitreous hemorrhage; retinal detachment; and possibly limbal or posterior scleral rupture [79, 87]. Blunt trauma can result in expulsive rupture of the globe, hyphema, vitreous hemorrhage, cataract, lens luxation or subluxation and rupture,

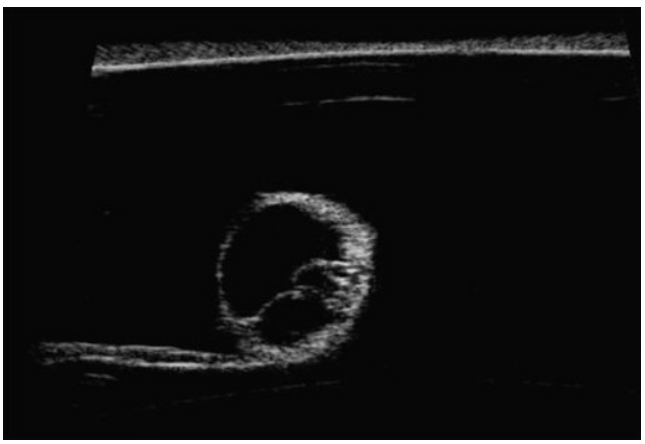


Figure 2.21 Intraocular masses consist of inflammatory, neoplastic, and cystic structures and most commonly arise from the anterior uvea (iris, ciliary body) in the horse. A corpora nigra cyst is shown with the use of a 35-MHz probe.

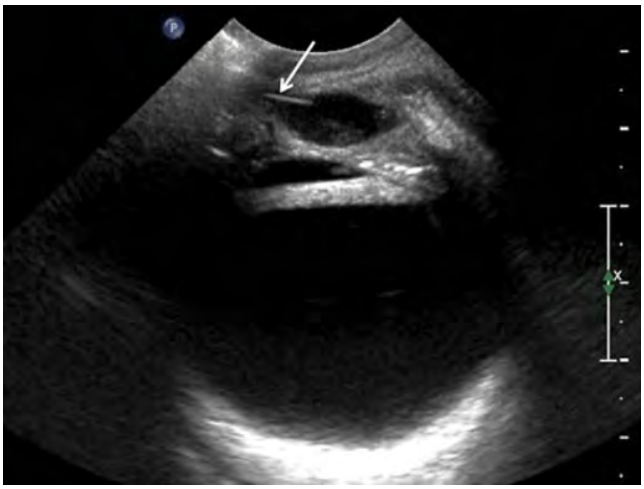


Figure 2.22 Foreign bodies can occasionally be seen surrounded by a fluid collection or abscess. Adjacent to the globe, a thin, linear, hyperechoic foreign body (**arrow**) is seen surrounded by a small amount of hypoechoic fluid. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

and retinal tear, retinal detachment, and choroidal detachment [79, 81, 87]. The eye and periorbital region should also be thoroughly evaluated for any foreign material [82].

In instances of severe trauma, measurements of identifiable structures should be obtained for assessment of the damage [79]. For example, a reduction in the lens–posterior scleral wall axial length may indicate a posterior lens luxation, whereas an increase may indicate an anterior lens luxation or a posterior scleral wall rupture [79]. With a ruptured globe, the eye will appear smaller than normal [75]. On ultrasound examination, vitreous and orbital hemorrhage can appear uniform in echogenicity, blending together because they are no longer separated by the scleral fibrous tunic in a ruptured globe [79, 87]. In addition, the normally hyperechoic posterior scleral wall is not identifiable [79, 87].

Interpretation of ocular ultrasound artifacts

Ultrasound artifacts can be useful or adversely affect the image quality, which can be caused by inaccurate technique (e.g., insufficient amount of coupling gel or air bubbles in the water bath) [20]. The most common types of artifacts that can occur during ocular examination in the horse include reverberation artifact (i.e., reduplication or multiple-signal echoes), shadowing, enhancement, and Baum's bumps [79, 91]. Reduplication echoes (reverberation artifacts) occur either between the probe and a highly reflective interface or between two highly reflective interfaces, such as air, lens capsule, cataract, sclera, foreign body, and orbital bone [78, 79, 91]. The sound beam will reverberate multiple times between the two interfaces, and because it will take longer for these echoes to reach the probe, multiple, linear echogenicities that are equidistant apart will be seen deeper in the globe than the tissue of origin (Figure 2.23) [78, 87, 91]. Reverberation artifact can occur with entrapment of air between

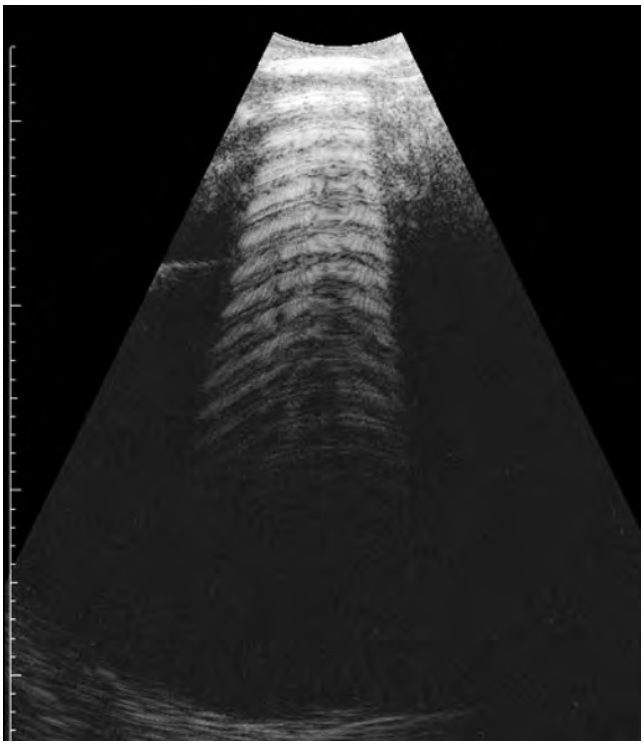


Figure 2.23 Reverberation artifact is demonstrated as multiple, parallel hyperechoic lines throughout the image due to air between the probe and the eye. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

the transducer and the eye, resulting in the display of bright echoes across the image, and can be avoided by ensuring that a sufficient amount of coupling gel is used [79, 85, 91]. Air can also be entrapped by the hair coat with a transpalpebral ultrasound approach, so the hair should be moistened with water and gel or clipped [20, 78, 79, 85]. Also with this approach, air can be trapped between the eyelid and the cornea [20, 79, 85]. The most common reduplication echo occurs between the lens capsule and the transducer and appears as linear hyperechogenicities in the mid to posterior axial vitreous which can be confused with vitreous hemorrhage, inflammatory debris, or degeneration [79, 87, 91]. The true echo and the subsequent artifacts are equidistant and decrease in strength, and the artifact may "move" with movement of the transducer [91]. Reverberation artifacts in the anterior chamber, lens, and posterior segment have been reported as a common finding in a recent study [77].

Shadowing occurs when a structure causes sound attenuation or complete reflection of the sound wave and produces an absence of echoes posterior to the hyperechoic structure [78, 79, 87, 91]. This appears as either decreased echoes or a complete loss of echoes posterior to the structure [91]. Structures that can cause "acoustic shadow" include dense cataracts, intraocular foreign bodies, bone, mineral, and large amount of gas [79, 91, 92]. This artifact can prevent evaluation of structures and lesions posterior to the shadowing structure [91]. Refraction at the edges of a smooth, curved surface can also

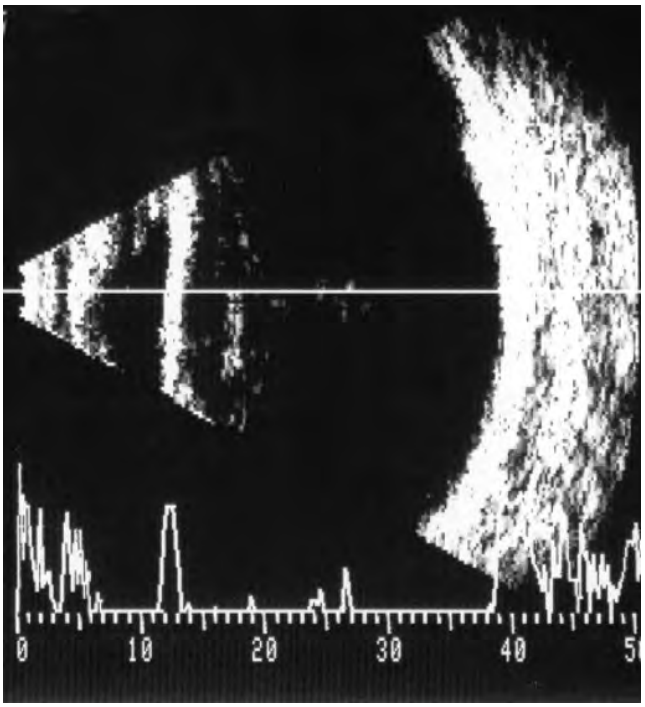


Figure 2.24 Baum's bumps occur because the normal lens refracts the sound waves from the transducer, resulting in faster passage of sound through the peripheral lens compared with the central lens. This may result in the posterior eye wall appearing to be closer to the probe and will be seen as one or two discrete retinal elevations at the retinal surface, the size of which will vary with the scan angle. Only one bump is visible on this scan. (*Source*: Ultrasound image courtesy of Dr David Wilkie.)



Figure 2.25 UBM allows imaging of the anterior ocular segment at near-microscopic resolution in living patients. The cornea (C), sclera (S), ciliary body (CB), and iris (I) can be visualized (35-MHz probe).

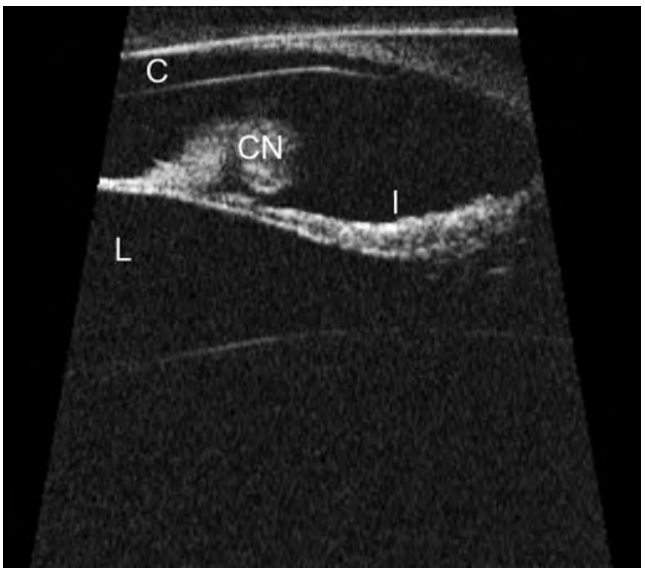


Figure 2.26 Normal appearance of the corpora nigra. Corpora nigra (CN), iris (I), cornea (C), and lens (L) can be visualized (35-MHz probe).

occur, and is most commonly seen as shadowing at the edges of the globe [91]. Acoustic enhancement, on the other hand, results in increased amplitude of echoes posterior to a weakly attenuating, fluid-filled structure [91]. For example, the tissues deep to cysts and the vitreous are brighter than those deep to solid structures [78, 79].

Baum's bumps are artifacts that appear as elevations along the fundus (Figure 2.24) [91]. They occur because of refraction of the sound beam by the lens and because the shape of the lens causes the sound waves to move more quickly through the peripheral versus central lens [75, 88, 91]. As a result, the posterior wall of the eye appears to be closer to the probe and can be seen as two discrete retinal elevations on the posterior surface of the globe [75, 88]. These bumps can be misinterpreted as masses and can be eliminated by repositioning the probe, and thus the sound beam, to avoid the lens [91].

High-frequency ultrasound examination and ultrasound biomicroscopy

Ultrasound probes with frequencies ranging from approximately 20 to 38 MHz (high-resolution ultrasound) and 40 to 100 MHz (ultrasound biomicroscopy) have been developed and allow imaging at resolutions comparable to those achieved with low-power light microscopes [105]. Routine ocular ultrasound examination with 5- to 12.5-MHz probes effectively bypasses the anterior segment of the eye. High-resolution ultrasound and high-frequency ultrasound biomicroscopy (UBM) allows imaging of the anterior ocular segment at near-microscopic resolution in living patients and provides exceptionally detailed 2D, cross-sectional grayscale images of the conjunctiva, cornea, anterior sclera, anterior chamber, iridocorneal angle, posterior chamber, ciliary body, ciliary zonules, the layers of the lens, and the anterior vitreal face (Figures 2.25, 2.26, and 2.27) [105–107].

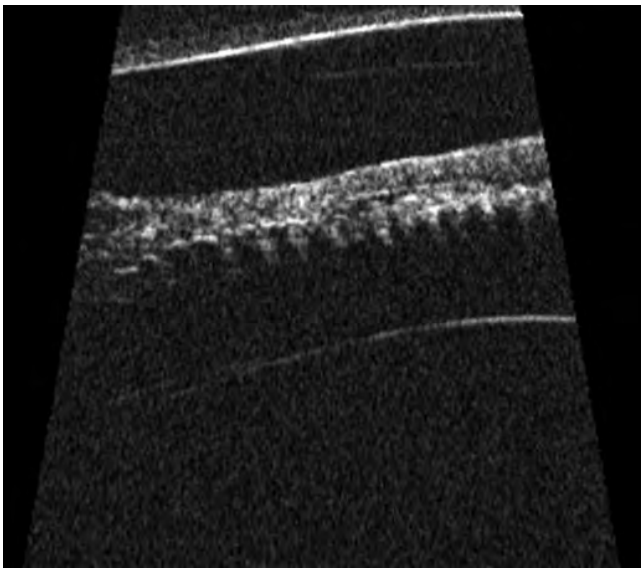


Figure 2.27 Normal appearance of the posterior surface of the iris and ciliary body (35-MHz probe).

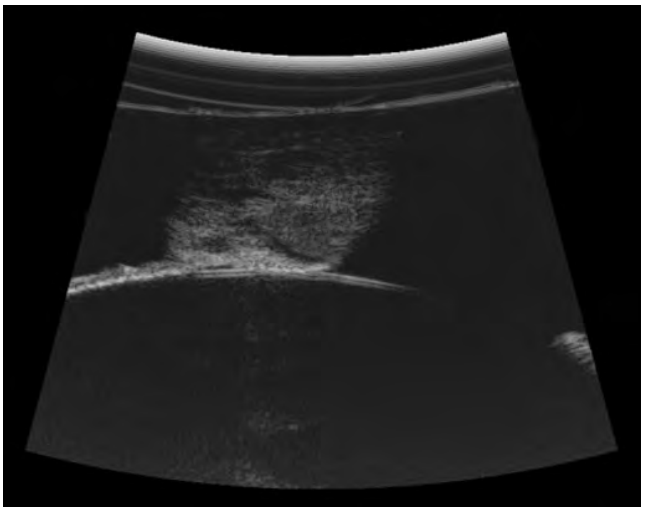


Figure 2.28 Fibrin appears as a series of disconnected echodensities throughout the anterior chamber, whereas hypopyon is most often seen ventrally and is more uniform in its echodensity. A fibrin clot is shown attached to the tip of the iris and adherent to the anterior lens capsule (25-MHz probe). (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

High-resolution ultrasound and UBM differ from conventional ultrasound examination as the transducers have a higher frequency (20–100 MHz) and provide higher image resolution [105]. The high frequency of the probes also limits tissue penetration and restricts the use of UBM to imaging of the anterior segment of the globe. In general, UBM also requires the use of a water bath. With early models, this necessitated heavy sedation or general anesthesia in most veterinary patients. Self-contained water bath systems (i.e., within the ultrasound handpiece) that can be used in an upright position are now available and allow clinical use in veterinary patients, especially large-animal patients such as the horse.

High-resolution ultrasound and UBM have been used extensively in human medicine and dogs to define the dynamic mechanism of angle-closure glaucoma, evaluate the functional status of glaucoma-filtering implants, evaluate tumors of the iris and ciliary body, assess intraocular trauma, and evaluate the position of intraocular lens implants [93–96, 108–110]. High-resolution ultrasound and UBM do not require optically clear intervening ocular structures for image formation, which provides an advantage over some other advanced imaging techniques where opacities can obscure visualization of deeper tissues.

In the horse, high-resolution ultrasound and UBM can be used to evaluate depth of corneal lesions, corneal thickness, ocular surface masses (e.g., ocular squamous cell carcinoma), uveal masses, alterations in lens position, anterior uveitis, and other anterior segment and lens changes, including trauma, foreign bodies, and cataracts (Figures 2.28 and 2.29). Evaluation of anterior segment masses can help differentiate solid tissue structures (e.g., neoplasms) from cystic structure (e.g., uveal cysts) and often helps to determine the composition of a mass and the underlying pathophysiology of the mass formation (Figures 2.29 and 2.30) [111].

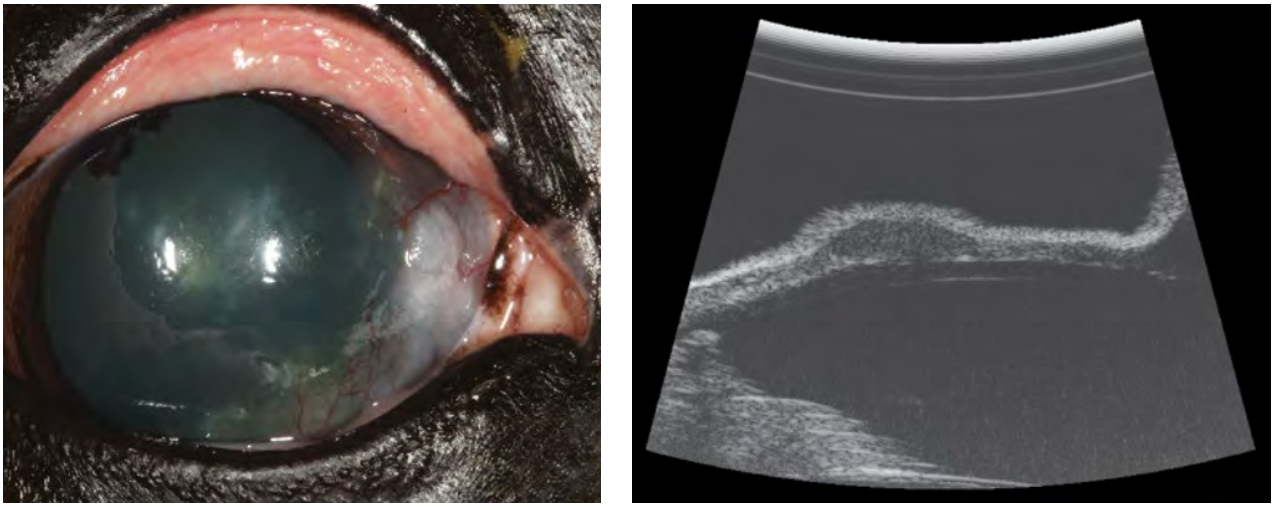
Evaluation of uveal and corpora nigra cysts prior to diode or neodymium:yttrium-aluminum-garnet laser ablation can assist in planning the procedure and help predict the response of the cyst to the laser ablation (Figures 2.31 and 2.32) [112, 113]. The depth of corneal stromal abscesses and, in some instances, the extension of the abscess into the anterior chamber can be determined with high-resolution ultrasound and UBM (Figure 2.33) [114, 115].

Scleral thickness has been measured in both fresh and formalin-fixed equine globes [116]. Caliper and UBM measurements on fresh equine tissue revealed that at all sites measured, the thickness of the sclera in fresh tissue was significantly greater than that of tissue fixed in formalin. Thickness ranged between 1.02 ± 0.19 mm at the limbus (inferior), 0.44 ± 0.06 mm at the equator (superior), and 0.79 ± 0.12 mm at the optic nerve (nasal). There were no significant differences between measurements obtained by caliper and measurements obtained by UBM [116].

Central corneal thickness measurements with high-resolution ultrasound (22-MHz transducer) and UBM (50-MHz transducer) were reported for a group of young warmblood horses [92]. The mean corneal thickness measured by both methods combined was 818 ± 41 μm and there were not significant differences between the measurements obtained with the two transducers. A positive correlation was identified between increasing age and central corneal thickness in the study horses [92].

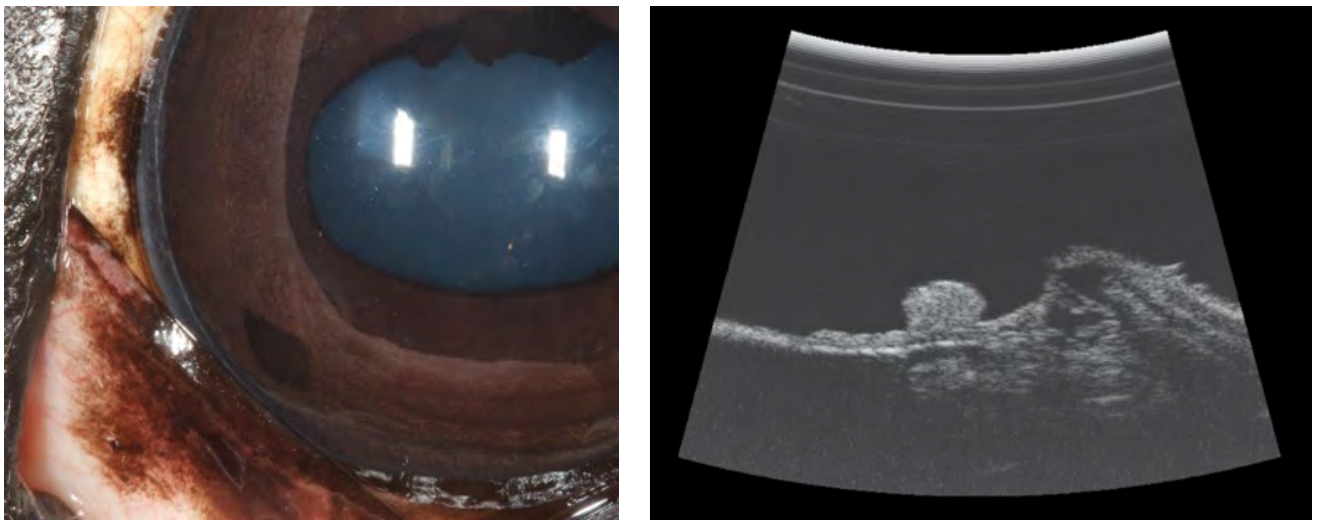
Infrared photography

Infrared radiation consists of longer wavelengths of electromagnetic radiation than those of the visible light spectrum. Because of its longer wavelengths, infrared radiation is



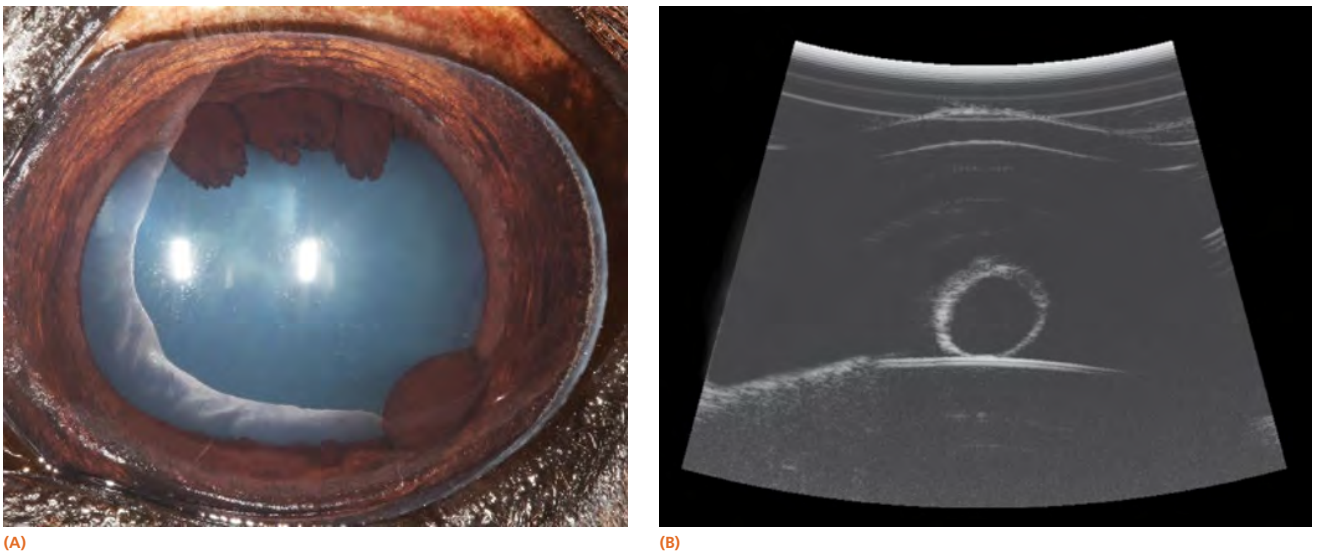
(A) (B)

Figure 2.29 Clinical photograph (A) and high-resolution ultrasound image (B) of a horse with a corneoconjunctival squamous cell carcinoma. An elevated, whitish- pink, heavily vascularized mass is extending from the nasal limbus into the cornea. The corneal component of the mass has moderate echogenicity and focally expands the affected corneal region during ultrasound (25-MHz probe). (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



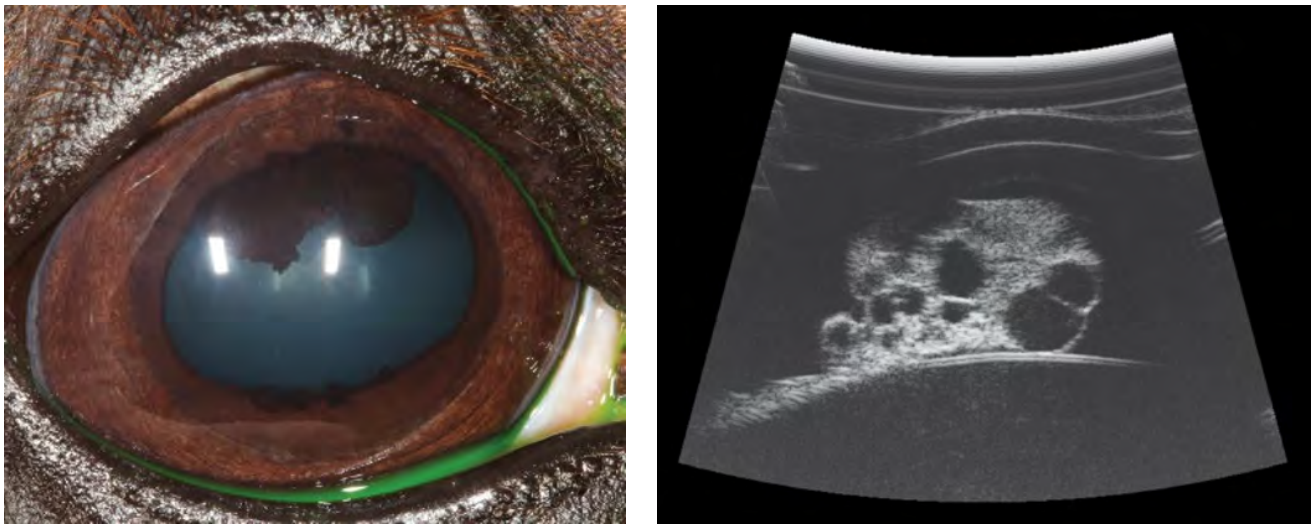
(A) (B)

Figure 2.30 Clinical photograph (A) and high-resolution ultrasound image (B) of a horse with an iris melanoma. The heavily pigmented mass on the anterior surface of the iris appears as a hyperechoic structure of homogenous echogenicity during ultrasound (25-MHz probe). (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



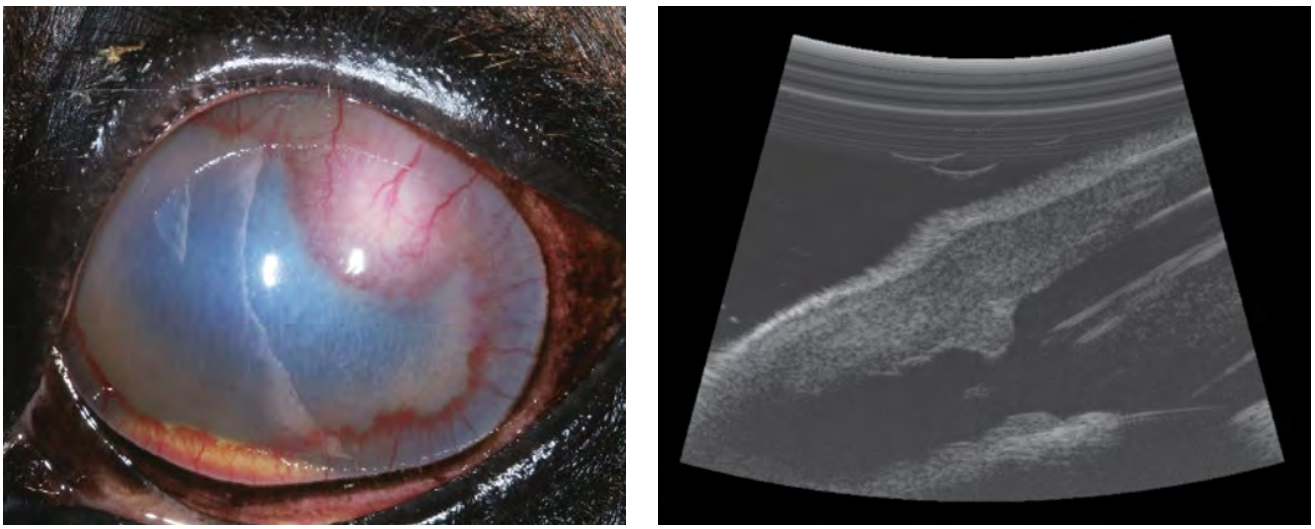
(A) (B)

Figure 2.31 Clinical photograph (A) and high-resolution ultrasound image (B) of a horse with a simple uveal cyst. A thin hyperechoic wall surrounds the single hypoechoic cyst space (25-MHz probe). (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



(A) (B)

Figure 2.32 Clinical photograph (A) and high-resolution ultrasound image (B) of a horse with a cystic corpora nigra. A thick hyperechoic wall surrounds multiple hypoechoic cysts (25-MHz probe). (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)



(A) (B)

Figure 2.33 Clinical photograph (A) and high-resolution ultrasound image (B) of a horse with keratomycosis and a deep corneal abscess that extends into the anterior chamber. Hyperechoic material is visible extending across a discontinuous Descemet's membrane into the anterior chamber (25-MHz probe). (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

able to penetrate an opaque cornea, allowing better visualization of intraocular structures [117]. Infrared images are very different in appearance than standard black-and-white or color photographs. With infrared photography, the equine iris (Figure 2.34) appears bluish-gray with a wide tonal range, thereby increasing image contrast. The corpora nigra, pupillary zone of the iris, and pectinate ligament appear darker than the anterior iridal surface, and the pupil appears black [117].

The ability of infrared wavelengths to penetrate an opaque cornea (e.g., due to edema or cellular infiltrate) makes evaluation of the uveal tract possible in ocular diseases such as glaucoma, acute or chronic anterior uveitis, superficial punctate keratopathy, immune-mediated keratitis, chronic superficial nonhealing corneal ulcers, superficial keratomycosis, and stromal abscesses (Figure 2.35) [117, 118]. In any situation where corneal edema or fibrosis prevents visualization of the anterior chamber or iridal surface, infrared digital photography can be used to obtain an image of the pupil and provide visualization of the contents of the anterior chamber (Figure 2.35) [117, 118]. The potentially valuable clinical ability of infrared

photography to permit visualization of the anterior chamber and iris through an optically opaque cornea is exemplified in a recent case series of horses with heterochromic iridocyclitis and secondary keratitis [118].

Infrared thermography

Infrared ocular thermography is a noninvasive, rapid, and potentially remote method of measuring the temperature of the ocular surface. Radiated heat is emitted from the eye in the nonvisible infrared region of the electromagnetic spectrum. An infrared thermograph is a device consisting of a system for collecting radiation emitted from a specific field and a photosensitive detector system [119]. In practical terms, an ocular infrared thermograph is typically a specialized camera used to capture the temperature distribution on the ocular surface and display it as visible information referred to as a thermal image or thermogram (Figure 2.36) [120].

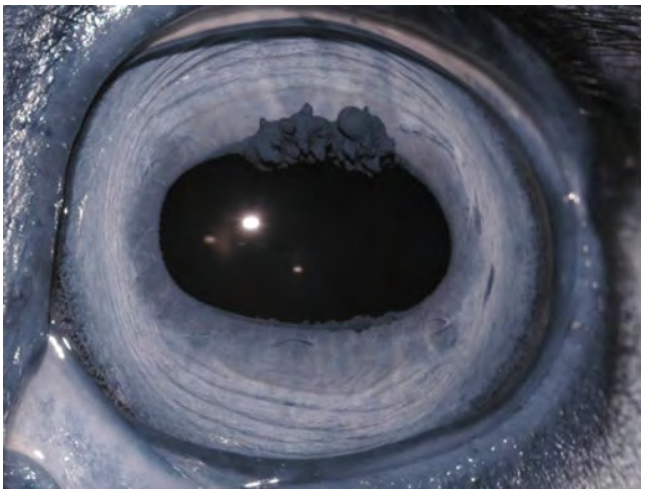
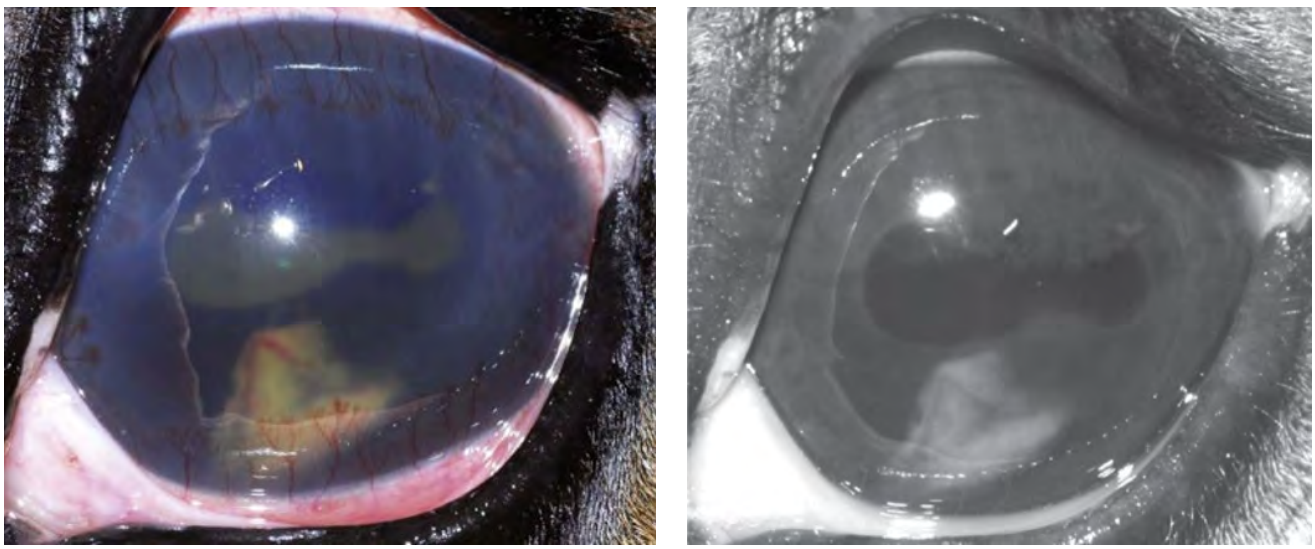


Figure 2.34 Infrared photograph of the equine iris.

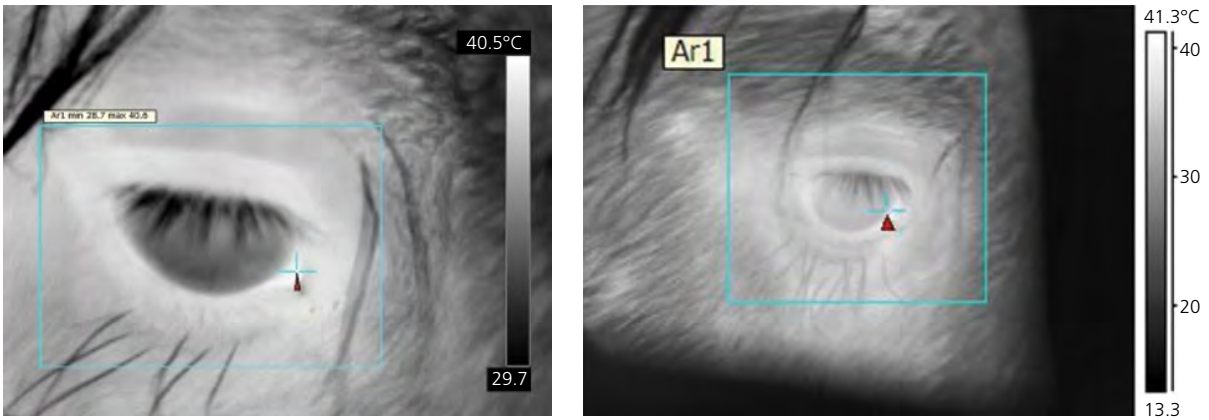
Thermographic eye surface temperatures measured in horses with an infrared camera were demonstrated to be associated with body temperature measurements collected by rectal thermometer or implanted thermal microchip, and it was suggested that infrared ocular thermography could be used as a preliminary screening tool for the detection of pyrexia in horses [121]. Similar applications are reported in other domestic and wild animal species, where infrared thermography can be issued as a mass screening tool for the identification of febrile individuals during situations such as infection epidemics, surveillance programs, and inspection stations [122–124].

Infrared ocular thermography is also being explored as an objective method of detecting and assessing physiological stress in horses, especially during athletic training or competition [125–128]. Ocular temperature measurements by a portable infrared thermography camera performed during various stages of show jump competitions suggested that maximum eye temperature is an effective method for detecting stress in horses during sport competitions [125, 126]. Maximum eye temperature increased significantly in horses exposed to an aversive animal management procedure (i.e., hair clipping) and there was a significant correlation between changes in salivary cortisol concentration and eye temperature [129]. Ocular thermal images have also been used to assess relative stress levels in horses subjected to different types of housing designs that provided varying levels of social contact [130].



(A) (B)

Figure 2.35 Because of the ability of infrared wavelengths to penetrate the opaque cornea, the uveal tract is less visible in a color photograph of an eye with a stroma abscess (A) compared to the same eye photographed with an infrared camera (B).



(A) (B)

Figure 2.36 (A) and (B) Infrared ocular thermograms of normal horses. (*Source*: Photographs courtesy of the U.S. Department of Agriculture, Wildlife Services, Shylo Johnson.)

Infrared thermography has been used to assess ocular surface temperature changes in humans and other animal species with a variety of ocular disease [131, 132]. Characterization of equine ocular surface temperature changes with different ocular pathologies, and the mechanisms through which these changes are mediated, are not yet described in horses. Further investigations exploring these relationships will be important for determining the potential future applications of this technology in equine ophthalmology.

Specular microscopy

Specular microscopy is a noninvasive imaging technique that provides a rapid method for qualitative, quantitative, and morphometric evaluation of the corneal endothelium [133]. Specular microscopes form an image from light reflected from an optical interface [134]. Specifically, specular microscopes capture light reflected with an angle of reflection equal to the angle of incidence. The corneal epithelium, stroma, and lens can all be imaged with specular microscopy; however, the optical interface between the corneal endothelium and aqueous humor is the most common application of specular microscopy in ophthalmology. Contact and noncontact specular microscopes are available and many provide automated or semi-automated analyses of corneal endothelial cell density, endothelial cell morphology, and corneal pachymetry.

Noncontact specular microscopy is described to determine corneal endothelial cell density and corneal thickness in enucleated globes from healthy horses (Topcon SP-2000P (Topcon America, Paramus, NJ)) [135]. The mean density of endothelial cells was 3155 ± 765 cells/mm^2 (Figure 2.37). Similar to dogs and humans, endothelial cell density decreased with age in horses [135, 136]. Endothelial density was not affected by sex and did not significantly differ between the individual eyes from the same horse. Although the differences were small, the mean density of endothelial cells was significantly lower in the ventral

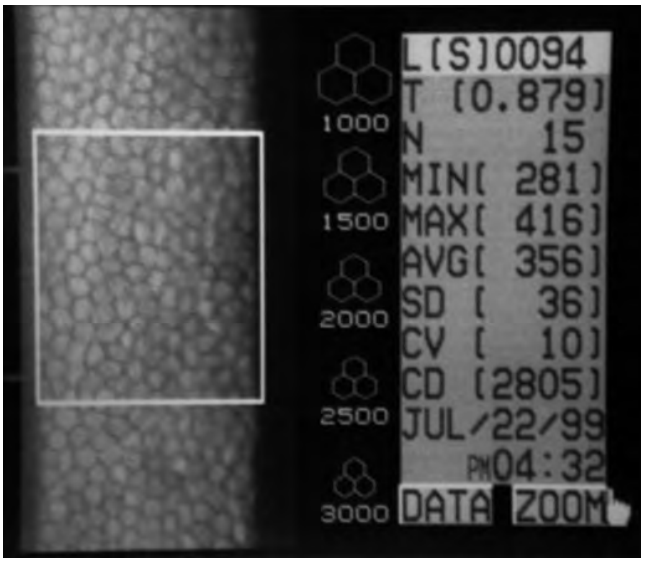


Figure 2.37 Specular photomicrograph on the normal corneal endothelium in a horse. (*Source*: Reproduced with permission from Stacy Andrew, Atlanta, GA.)

corneal quadrant compared to the medial and lateral quadrants. Mean corneal thickness in the study horses was 893 μm [135]. Age and sex had no impact on corneal thickness, but the mean corneal thickness varied between different quadrants.

Corneal edema occurs when a minimal critical endothelial cell density is reached; however, this number has not yet been established in horses [137, 138]. Determining corneal endothelial cell density would be useful in evaluating horses with unexplained corneal edema, perforating corneal injuries, and horses that have undergone penetrating keratoplasty or intraocular surgeries such as phacoemulsification [139]. The corneal endothelial cell count is also vital information in collecting and preparing donor tissue to be used for corneal transplantation [133, 140, 141].

In vivo corneal confocal microscopy

In vivo confocal microscopy permits noninvasive, high magnification, real-time imaging of the ocular surface at the cellular level. All confocal microscopes utilize the same basic design principle, where the illumination and detections paths of the instrument share the same focal plane [142]. *In vivo* confocal microscopes possess an illumination point source and observation aperture of the detector system with a common focal point in the tissue [143]. Only light originating from the tissue focal point is efficiently detected and light reflected from outside the field of view is suppressed. This design dramatically increases resolution while permitting the use of higher magnification than that achievable with standard light microscopy. Contemporary *in vivo* laser scanning confocal microscopes provide high-resolution images of the cornea with lateral resolutions of 1–2 μm [144]. Confocal microscopy systems are inherently limited by small fields of view, but this is overcome by rapidly scanning the focal point across the tissue and reconstructing the imaging for viewing. The focal plan of the confocal microscope may be optically adjusted, permitting imaging at all depths of the cornea. In general, *in vivo* confocal microscopes generate coronal optical sections through the examined tissue structures; however, it is also possible to obtain oblique sections with some microscopes.

In horses, *in vivo* confocal microscopy can be performed with either standing sedation or general anesthesia [145–147]. Normal morphologic features, corneal sublayer pachymetry, and endothelial cell density of the equine cornea and limbus are described by *in vivo* confocal microscopy using a laser scanning confocal microscope (Heidelberg Retina Tomograph II and Rostock Corneal Module (Heidelberg Engineering, Dossenheim, Germany)) [145]. In this study of clinically normal horses, the cellular and noncellular components of the corneal epithelium, stroma, endothelium, and limbus were readily detectable in all examined horses (Figure 2.38). The equine corneal epithelium was morphologically divided into four distinct cellular layers: superficial, superficial-intermediate, deep-intermediate, and basal. The basal lamina

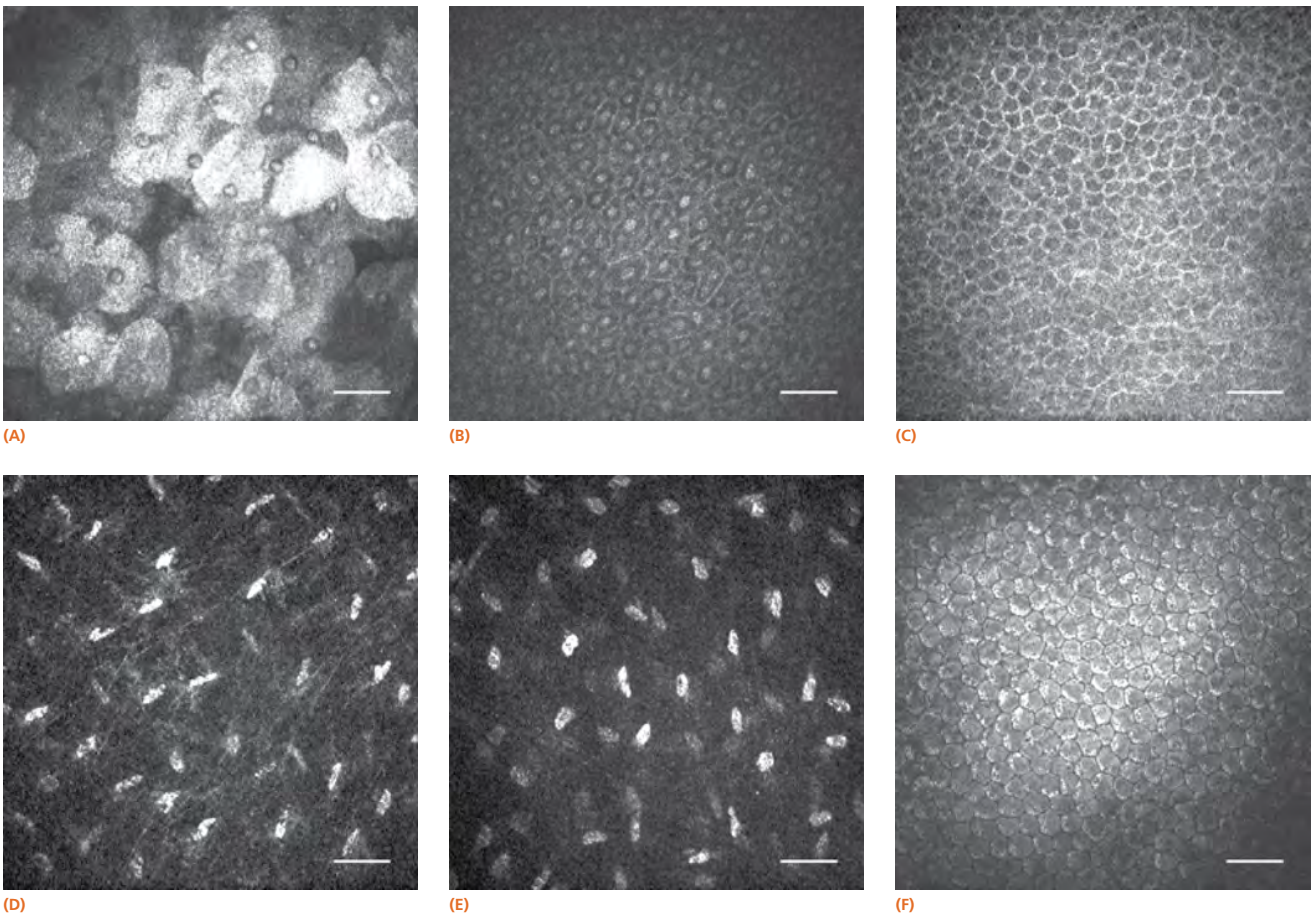


Figure 2.38 *In vivo* confocal photomicrographs of the normal equine cornea arranged from anterior to posterior: superficial epithelium (A), deep intermediate epithelium (B), basal epithelium (C), anterior stroma (D), deep stroma (E), and endothelium (F). Bars = 50 μm. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

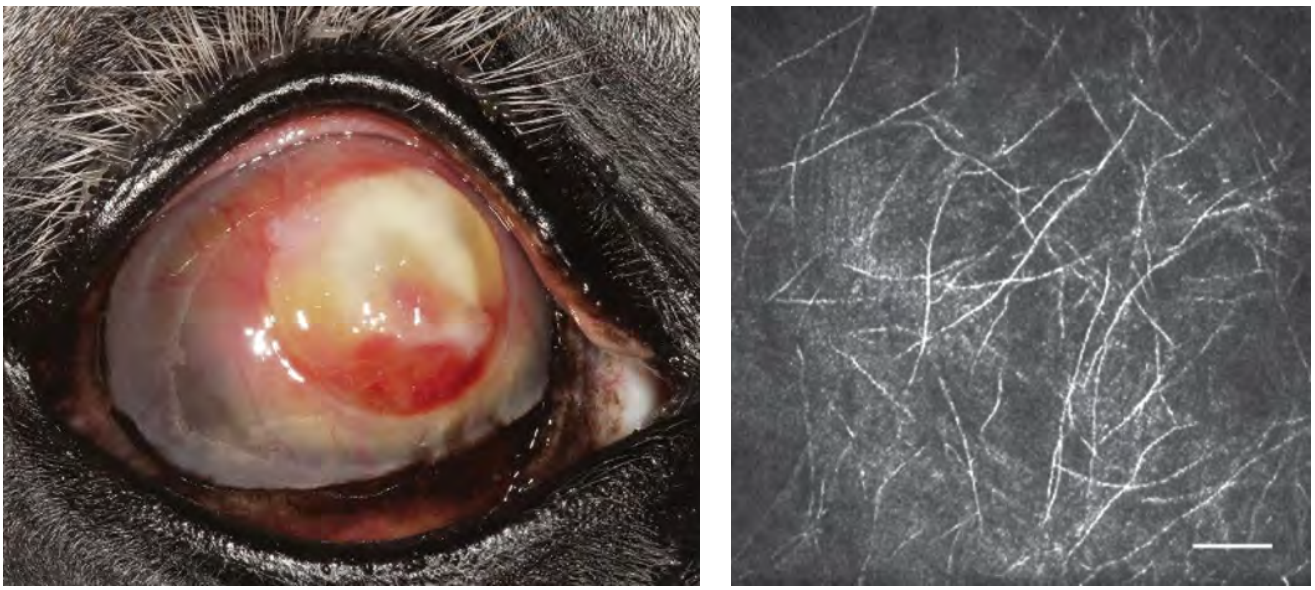
was visible immediately posterior to the basal epithelium. The stromal extracellular matrix and collagen lamellae appeared transparent and dark in color. Highly reflective keratocyte nuclei were visible throughout the corneal stroma, with the greatest density in the anterior layers [145]. Descemet's membrane appeared as a uniform, moderately reflective, amorphous or granular layer. The endothelium was composed of a monolayer of hexagonal and pentagonal cells. Corneal stromal nerves, the subepithelial nerve plexus, and the sub-basal nerve plexus were visible and appeared as highly reflective, linear, branching structures. In the examined horses, the median central total corneal thickness was 835 μm and the median central endothelial cell density was 3002 cells/mm^2 (range 2473–3581 cell/mm^2) [145].

Clinical applications of *in vivo* confocal microscopy in horses with corneal disease are also described [146–148]. *In vivo* confocal microscopy is a rapid and noninvasive method for diagnosing fungal keratitis in the horse [146]. Ulcerative and nonulcerative keratomycosis can be evaluated by this technique and fungal elements can be detected in lesions at all corneal depths. In a study of horses with naturally acquired fungal keratitis, *Aspergillus* and *Fusarium* hyphae appeared as linear, branching, or interlocking, hyper-reflective structures within the cornea that measured 2–6 μm in width and 75– > 400 μm in length (Figure 2.39) [146]. *Candida* yeast appeared as round-to-oval hyper-reflective structures that were 2–8 μm in diameter and frequently surrounded by a distinct hyporeflective outer limiting membrane [146]. In this study, fungal morphologies observed in clinical cases by *in vivo* confocal microscopy were confirmed and validated by examination of cultured fungal isolates *in vitro* and by examination of experimentally infected *ex vivo* equine corneas [146].

In vivo corneal confocal microscopy is also described as a method to detect, characterize, and localize microscopic corneal foreign bodies in horses [147]. Included in this clinical series were horses with burdock pappus bristles, other plant foreign materials, and surgical glove powder corneal foreign bodies. With confocal microscopy, the corneal foreign bodies appeared as moderately or hyper-reflective linear, circular, or oval structures that did not resemble any normal corneal anatomic structures [147]. The precise anatomic localization and depth measurements provided by *in vivo* corneal confocal microscopy can be used to assist in the selection of a therapeutic or surgical plan for corneal foreign bodies.

The *in vivo* confocal microscopic findings in a horse with primary corneal lymphoma were recently described [148]. In this horse, a dramatic infiltration of the cornea with a population of large, monomorphic leukocytes arranged in sheets within the anterior corneal stroma was observed by confocal microscopy. Histopathology and immunohistopathology of corneal samples confirmed a diagnosis of B-cell lymphoma in the horse [148].

In many situations, *in vivo* confocal microscopy possesses several advantages over standard diagnostic assays currently used in clinical practice, and additional indications for this technology in equine ophthalmology are likely to be identified in the future. Furthermore, the research applications of this technology are numerous and *in vivo* confocal microscopy may contribute to a greater understanding of equine ocular surface physiology and pathophysiology.



(A) (B)

Figure 2.39 Clinical photograph (A) and *in vivo* confocal photomicrograph (B) of a horse with fungal keratitis (*Aspergillus fumigatus* was cultured from corneal samples). Bars = 50 μm. (*Source*: Reproduced with permission from Cornell University, Ithaca, NY.)

Optical coherence tomography

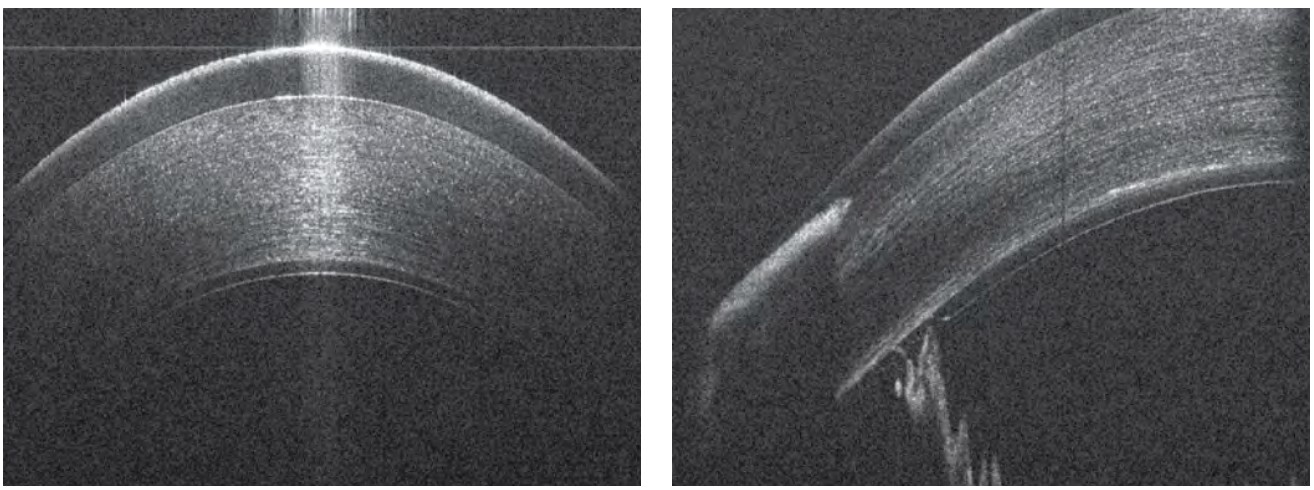
Optical coherence tomography (OCT) is a noncontact, *in vivo* technique for obtaining high-resolution cross-sectional tomographic images of the eye. This technology utilizes the optical delay of reflected light and interferometry to measure distance and produce images [149]. With OCT, a beam of light (most commonly in the infrared wavelength) is split by a beam splitter into sample (tissue) and reference beams. Sample and reference beam reflections are recombined and their interference pattern is detected by a photodetector, converted into a digital signal, and processed by a computer to produce a cross-sectional image [150]. OCT may be used for both the anterior and posterior segments of the eye, but requires clear ocular media to generate high quality images.

There are two primary methods of OCT [150]. Time-domain OCT (TD-OCT) was developed first and utilizes a reference mirror that is physically moved through a delay range where the interference pattern between the sample beams and reference beams is processed into the image. Spectral-domain OCT (SD-OCT, also known as Fourier-domain OCT and frequency-domain OCT) uses a stationary reference mirror and Fourier transformation of spectral interference patterns between the sample and reference reflections to generate the image. SD-OCT permits more rapid scanning speeds and greater image resolution compared to TD-OCT.

Examination of the anatomy of the cornea, retina, and optic nerve of clinically normal horses is described with a handheld SD-OCT device (Envisu SD-OCT (Bioptigen Inc., Morrisville, NC)) [151]. Standing, sedated horses were examined and high quality images successfully obtained of both the anterior and posterior segment. Corneal layers, including the epithelium, stroma, and endothelium–Descemet's membrane complex, were distinguished and measured (Figure 2.40). Means (± standard deviation in) total corneal thickness measurements were 800 ± 50 μm, 937 ± 61 μm, 956 ± 61 μm, 912 ± 65 μm, and 884 ± 68 μm for the axial, superior, inferior, nasal, and temporal regions of the cornea, respectively [151]. Retinal and optic nerve head images were obtained and manual measurements of the total retinal thickness, nerve fiber layer thickness, and the vertical and horizontal axis of the optic nerve head and optic cup were performed (Figure 2.41) [151]. Total retinal and nerve fiber layer thickness were highest around the optic nerve head. The highest total retinal and nerve fiber layer thickness measurements were found nasally: 459 ± 115 μm and 377 ± 116 μm, respectively. The dimensions of the optic nerve head and optic cup were 3.682 ± 0.276 mm and 2.175 ± 0.502 mm for the horizontal axis, and 3.012 ± 0.278 mm and 2.035 ± 0.488 mm for the vertical axis [151].

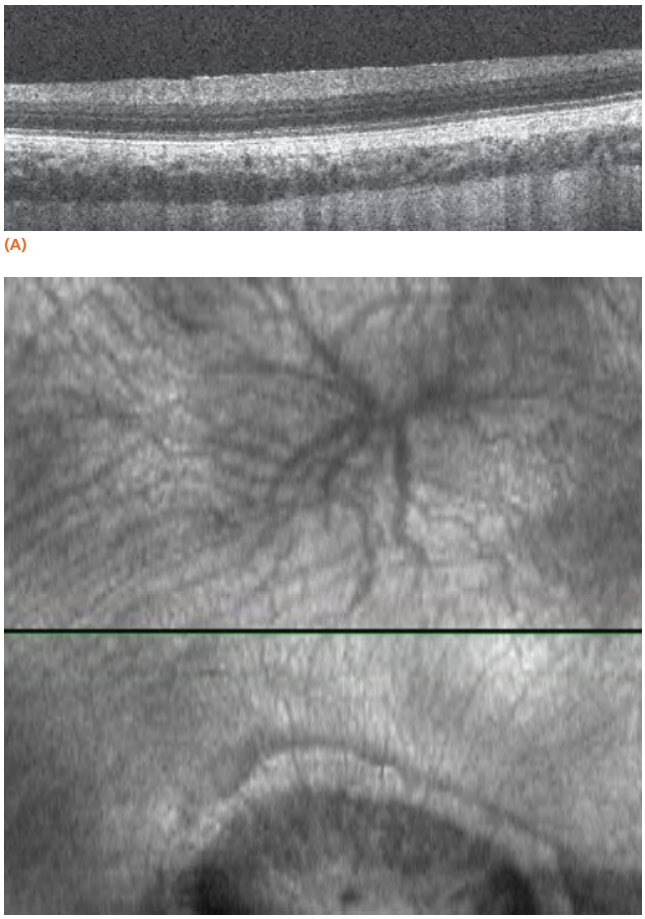
Sublayer corneal pachymetry with an SD-OCT (I-Vue (Optovue Inc., Freemont, CA)) is also reported for normal horses [152]. Total corneal thickness and the thickness of the corneal epithelium, stroma, and endothelium–Descemet's membrane complex were measured. Mean total axial corneal thickness for the examined horses was 812.4 ± 43.4 μm. A positive correlation was found between Descemet's membrane thickness and age (Descemet's membrane increased in thickness by 2 μm/year) [152]. Mean epithelial and stromal thicknesses were 175.3 ± 13.3 μm and 599.2 ± 45.0 μm, respectively [152]. Intra- and interoperator measurement reliability were determined to be clinically acceptable in the study.

There are few published descriptions of OCT imaging of equine ocular diseases. Heterochromic iridocyclitis with secondary keratitis is a recently described condition of horses that is characterized by uveal inflammation, pigment dispersion, and corneal endothelial dysfunction [118]. Horses with this condition develop retrocorneal membranes and pigmented keratic precipitates. When evaluated by SD-OCT, these pathologies



(A) (B)

Figure 2.40 Optical coherence tomography image of the axial (A) and temporal (B) cornea of a clinically normal horse. The iridocorneal angle is visible in the temporal corneal image.



(A)

(B)

Figure 2.41 Optical coherence tomography B-scan image (A) of a normal equine retina (horizontal scan superior to the optic nerve) and a volume intensity projection image (B) demonstrating the location of the B-scan image.

appeared as highly reflective areas along the inner aspect of the endothelium–Descemet's membrane complex that projected into the anterior chamber. In addition, the endothelium–Descemet's membrane complex was thickened with a highly reflective inner aspect that occasionally appeared detached (interpreted as detachment of the retrocorneal membrane) [118].

OCT is a unique and powerful ocular imaging tool. Additional clinical and research applications of OCT are expected in equine ophthalmology and this technology possesses the potential to improve the diagnosis and management of many ocular disorders of the horse.

Future imaging modalities

Advances in ocular imaging technology have been rapid in recent years in both human and veterinary ophthalmology. Although many of the more recent technologies currently used in the clinical and research setting in human and veterinary ophthalmology have yet to be reported in horses, or are not in routine use, adaption of many of these techniques holds promise in the management of equine ocular diseases. Examples of these technologies include high-resolution ocular MRI, optical coherence microscopy, optical coherence angiography, scanning laser ophthalmoscopy, scanning laser polarimetry, Scheimpflug imaging, third harmonic generation microscopy, two-photon excitation microscopy, and ultra-high-resolution ocular surface optical coherence tomography [153–155]. Difficulties posed by the size, temperament, and environment of horses will require hardware and other technological modifications for many of these techniques and instruments prior to their becoming practical for routine use in horses.

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CHAPTER 3

Practical field ophthalmology

Ann E. Dwyer*

Introduction

Routine ocular examination and treatment of ocular emergencies is an important part of equine practice. Between 5% and 10% of horses are reported to have important ophthalmic lesions that affect vision or function in the developed world [1] and more than twice that number are reported to have vision-threatening disease in the developing world [2]. At least 10% of emergency calls in most equine practices involve the ocular region [3]. Fortunately, the equine eye is easily examined with simple portable equipment and common conditions can be diagnosed with stall-side tests. Practitioners who make an effort to learn the techniques of examination, diagnostic testing, ocular imaging, and therapy described in this text will be able to diagnose the majority of ocular problems presented in their patients. Familiarity with the problems described in Chapters 4–11 will enhance skills in field therapeutics and facilitate recognition of the subset of ocular problems that could benefit from specialist oversight. Several books, compendia, reviews, and atlases are available as additional study sources [4–16].

Indications for examination

All horses benefit from baseline ocular examination during routine wellness visits on the farm (Figure 3.1). See Table 3.1 (online).

Newborn foals are commonly examined in the first 12–36 hours after birth to check for postnatal problems and assess transfer of passive immunity. The neonatal visit presents an excellent opportunity to perform the first ophthalmic examination to check for birth trauma or conditions like entropion or cataracts [17–19]. Regular repeat examination of youngstock will screen for problems that could affect future sales or training.

Inspection of mature horses serves to establish a baseline and detect conditions that may not produce signs noticed by the owner, like early adnexal disease, cataracts, insidious uveitis, and fundic abnormalities. Geriatric horses are frequently found to harbor ocular problems like chronic uveitis, cataracts, and eyelid masses not readily apparent to casual observers [20–22]. Most elderly animals have detectable changes in some ocular components that signify senescence and over 20% have Cushing's disease that may affect eye status [23]. Regular examination will provide information to owners on any functional changes that may accompany these age-related problems. Occasionally owners are unaware that a horse is blind in one or both eyes until a veterinary examination reveals the problem.

A full ophthalmic examination is an important part of every pre-purchase examination. Owners may also request an ocular examination if they suspect that spooky behavior or poor performance is related to a visual problem. All horses that present with a sudden change in performance or attitude should undergo an ophthalmic examination to screen for occult issues that might affect vision.

Horses often present with ocular signs that dictate an urgent examination [24–27]. Table 3.1 lists common differential diagnoses for the chief complaints that prompt calls for emergent ophthalmic evaluation, such as acute pain/tearing/blepharospasm of one or both eyes, eyes that are discolored or asymmetric in appearance, periorbital, adnexal, or globe trauma, and masses on the adnexa or globe (Figure 3.2).

Ocular examination should be a routine part of assessment of any horse that is systemically ill. Conditions like sepsis, systemic infection, neoplasia, immunodeficiency, autoimmune disease, endocrine problems, parasitism, and nutritional imbalances are frequently associated with ophthalmic signs and/or dysfunction.

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Figure 3.1 All horses benefit from regular ocular examination.

Chapter 15 has additional information on ocular manifestations of systemic disease. Ocular examination is also essential in any horse that presents with neurologic disturbance. Chapter 14 presents an in-depth discussion of equine neuro-ophthalmology.

Finally, many breeds of horses are at risk for ocular problems that are inherited [28–32]. Veterinarians should be familiar with the conditions that are prevalent in the breeds they service and should counsel owners to have their horses examined for the conditions of concern. Under some circumstances, genetic testing should be advised. Further information on inherited disorders is found in Chapter 13.

Education of horse owners and veterinary staff

Horse owners understand that horses need routine vaccination, parasite monitoring, and dental and foot care, but may not recognize the value of regular veterinary physical examinations that include ocular inspection [33]. They also may be unaware that some equine ophthalmic problems that compromise sight are "silent." Owners usually know that horses that present with eyes that are painful, traumatized, or abnormal in appearance require veterinary attention, but may not realize that such cases are best assessed on a "same day" basis.

Client seminars, newsletters, practice websites, and social media sites present opportunities for veterinarians to educate horse owners about the value of baseline ophthalmic examinations as part of screening physicals. These same educational outlets can be used to teach horse owners to call for an urgent examination if they notice signs of an acute ophthalmic problem.

Most horses are used for purposes where visual acuity is important, and the sale value of any horse is greatly reduced if one eye is disfigured. Client education should stress that ocular problems may cause great suffering for the horse and can quickly progress to visual compromise or altered appearance. Clients should also be counseled that the use of old medication in a "sore eye" that has not been examined may be dangerous. Case reports of poor outcomes secondary to delayed or incorrect treatment can be included in an owner education event as a

Table 3.1 Common causes of ocular complaints noted by owners.

Chief complaint	Most common causes
Eye partly closed	Corneal ulcer Allergic blepharitis Recurrent uveitis Stromal abscess Foreign body in cornea or conjunctiva Blunt trauma to orbit ± globe
Epiphora or excess ocular discharge	Allergic blepharitis or conjunctivitis Corneal ulcer Recurrent uveitis Obstruction of nasolacrimal duct
Odd appearance to eyelid	Trauma Meibomianitis/chalazion Neoplasia Foreign body Facial nerve paralysis Lacrimal gland inflammation
Mass on eyelid	Squamous cell carcinoma Sarcoid Other neoplasia Granuloma
Prominence of one or both eyes	Glaucoma Orbital trauma Space-occupying mass in adjacent sinus Space-occupying mass in orbit Multiple congenital ocular anomaly syndrome
One eye smaller than the other	Recurrent uveitis Phthisis bulbi Orbital compression
One region of the eye appears abnormal or discolored	Corneal ulcer Glaucoma Stromal abscess Corneal fibrosis Corpora nigrans cyst Cataract Chronic uveitis Immune-mediated keratopathy Eosinophilic keratitis Corneal neoplasia Nictitans neoplasia Corneal dystrophy Endotheliitis
Entire globe appears abnormal or discolored	Glaucoma Uveitis Bullous keratopathy Traumatic hyphema Advanced infectious keratitis Endophthalmitis Neoplasia (rare)

graphic and effective means of convincing owners of the importance of proper eye care and oversight.

The veterinary receptionist team must be trained to promote routine ocular examination over the phone, and to schedule horses with swollen, painful, traumatized, or acutely discolored eyes as "same day emergencies." Veterinarians must commit to see such patients promptly.



Figure 3.2 Eyelid swelling, blepharospasm, and tearing are signs that prompt an urgent ocular examination.

Being prepared

Field practice involves "barn calls" at the stables where horses live. The ambulatory vehicle must be well equipped for both routine examination and treatment of urgent ophthalmic problems [34].

Essential tools for field eye examination include a direct ophthalmoscope (Welch Allyn, Skaneatelas, NY), a bright light source (Finnoff transilluminator that attaches to an ophthalmoscope, or bright penlight), a 14- to 20-D magnifying lens, and a digital camera. Useful adjunct equipment includes a battery-powered handheld slit-lamp (SL-17 (Kowa Co, Nagoya, Japan) and a tonometer (TonoVet (Icare Vet, Helsinki, Finland) or Tono-Pen (Reichert, Depew, NY)) (Figure 3.3A, B). Consumable items commonly used for examination include topical ophthalmic anesthetic, tropicamide solution, fluorescein dye strips, rose bengal dye strips, and Schirmer tear test (STT) strips. Most ambulatory clinicians carry digital ultrasound equipment in their vehicles; many of the probes that are used for orthopedic evaluation are suitable for field examination of the globe or periocular region.

Commercial subpalpebral lavage (SPL) kits (MILA International, Erlanger, KY) are needed for management of serious corneal disease. It is helpful to carry boxes of tuberculin syringes and 25-G ⅝-inch needles to facilitate treatment of horses requiring an SPL. Pour bottles of 1 part povidone iodine/50 parts physiologic saline solution are useful for cleaning the periocular region (Figure 3.4). A supply of towels is helpful for general hygiene and may also be used as blindfolds when performing maze testing. Practitioners who have a lot of experience in assessing corneal disease will want to carry a diamond burr instrument (Algerbrush II (Alger Equipment Co., Inc., Lago Vista, TX)) to treat selected corneal conditions.



(A)



(B)

Figure 3.3 (A) Equipment commonly used for field examination (direct ophthalmoscope, bright light source, digital camera, eyewash, gloves, surface stains). (B) Useful adjunct examination equipment (slit-lamp, applanation and rebound tonometers, indirect headset, lens).



Figure 3.4 Pour bottles of 2% povidone iodine solution are useful for cleaning the periocular region.



Figure 3.5 A tote box designated for storage of ocular diagnostic and therapeutic supplies promotes efficiency in ambulatory situations.

A variety of topical ocular solutions and ointments will be required to treat the spectrum of problems encountered, including antibiotic, antifungal, anti-inflammatory, mydriatic, and hyperosmotic products. Medications that lower intraocular pressure (IOP) can be carried in the vehicle or prescribed through retail pharmacies. Test tubes for collection of autologous serum for anticollagenase therapy are essential. Systemic nonsteroidal products (phenylbutazone and flunixin) will be needed to manage painful conditions and severe inflammation.

Many of the supplies used for ophthalmic tests and treatments, such as microscope slides, scalpel blades, cytobrushes, culture materials, small gauge suture packs, sterile saline, and general surgical instruments, have multiple uses in ambulatory practice and are part of normal vehicle inventory, but having small quantities of these items stored with ophthalmic medications and treatment supplies improves efficiency. A small variety of ophthalmic surgical instruments will be handy in several field situations: these items can be autoclaved in individual packs and opened as needed. Absorbable suture material of 4-0 to 5-0 diameter on cutting semicircular needles is suitable for apposing subcutaneous and subconjunctival tissues in field settings; nonabsorbable suture material of 4-0 to 5-0 diameter on a cutting semicircular needle is suitable for apposing periocular skin.

Some clinicians carry the diagnostic and therapeutic supplies needed for ocular problems in a tote-box that is designated "just for eyes." Having all the materials gathered in one place improves efficiency when handling urgent eye conditions (Figure 3.5). Hardware and home improvement stores are good sources for rugged tote or tackle boxes that have multiple compartments well suited for the transport of ophthalmic supplies and drugs.

Horse barns often have poor lighting. Strap-on battery-powered headlamps that emit a wedge-shaped beam of light through LED bulbs are extremely useful for focal illumination during minor surgical or sampling procedures. Small portable construction lamps that can be set up on tripods or clipped to a stall wall are also useful as auxiliary light sources. These items are inexpensive and readily available in camping or hardware stores (Figure 3.6).

Creating an "examination room" in the field

Horses are commonly examined in barn aisles or stalls. Any uncluttered area that is at least 2.4 × 3 m (8 × 10 ft) can be adapted as an "examination room" as long as the area can be made dark by shutting doors and windows. Diagnostic accuracy and efficiency of ocular tests and treatments will be optimized if the clinician takes a few minutes to stage the space and assemble all needed equipment before starting the examination.

All instruments and supplies should be placed on a clean, elevated surface such as a folding table. The examination area will need to be darkened for the examination, but additional lighting may be required when actual procedures are performed. Gusts



Figure 3.6 Portable auxiliary light sources such as headlamps and electric halogen or LED lights are useful tools for practitioners who work in dark barns.

of wind and stray barn cats can upend diagnostic supplies and samples, so these disturbances must be anticipated and minimized. Personnel in the barn must be aware that an eye examination is in progress, as people leading horses or driving motorized farm vehicles in the vicinity can spook the horse at a time when sharp instruments are near the globe.

Outdoor settings and sunny sheds are not appropriate stages for ocular examination. If an urgent situation presents where no darkened shelter is available, an emergency examination can be performed if the horse's head is covered by a blanket or tarp to block external light. Such conditions compromise a thorough examination, so a sheltered site should be arranged for any subsequent follow-up.

Examination in the field

Optimizing patient restraint and position

Simple ophthalmic examinations are usually performed on awake horses. Horses with painful eyes and/or eyes that require diagnostic tests other than surface stains require sedation. Two drugs commonly used as intravenous (IV) agents for chemical restraint are xylazine (0.5–1.0 mg/kg) and detomidine hydrocloride (Dormosedan® (Zoetis Inc., Florham Park, NJ), 0.02–0.04 mg/kg). Both drugs rapidly induce levels of sedation that cause the horse to drop its head and accept manipulation of the periocular region. Detomidine produces more profound levels of sedation than xylazine. Dosage and duration of action from either agent will depend on the temperament of the animal, the pre-existing level of pain, and the length of time and manipulation needed to complete the full evaluation. "Coldblooded" breeds like draft horses generally require lower doses of sedatives than "hotblooded" breeds like Thoroughbreds and Arabians.

Sedation dosing can be minimized if the practitioner assembles all the supplies, drugs, and examination aids needed for the situation at hand, so the examination can quickly be followed by any appropriate diagnostic tests, ocular imaging, and therapy. It is wise to start with a sedative dose that is on the low end of the spectrum and then add additional dosages as behavior dictates. Butorphanol tartrate (Torbugesic® (Zoetis Inc., Florham Park, NJ), 0.01–0.02 mg/kg) is a sedative that is occasionally used in standing ophthalmic procedures in combination with small doses of detomidine. This protocol produces profound sedation, but the butorphanol can produce temporary head tremors that make working on the eye challenging. Table 3.2 lists dosages and additional information on sedatives as well as topical and local anesthetics commonly used in the field.

Restraint for complex eye examinations and standing diagnostic and therapeutic procedures is facilitated by passive head support. Bales of hay or shavings, recycling totes, and oil drums are readily available elements that can be used to create a home-made table to support the mandible of a sedated horse at a convenient working level (Figure 3.7). Stabilization of the head facilitates thorough examination, image acquisition, diagnostic testing, subpalpebral lavage (SPL) tube placement, and standing surgeries. The head of a mature horse can weigh as much as 36.3 kg (80 lb); a solid surface that provides broad support for the mandibular region is far superior to a handler struggling to raise and hold the head of a sedated horse. Flat surfaces such as "bale tables" also provide a platform that can support the clinician's elbows for procedures that require steady hands.

Handlers should be directed to stand on the opposite side of the eye being examined, and should "switch sides" when the fellow eye is inspected. Excessive physical restraint is inappropriate, but judicious use of a twitch on the upper lip may steady a horse during minor procedures. The handler can improve visualization and access to areas of the bulbar conjunctiva that are usually covered by the eyelids by rolling the head one way or another, with the mandible serving as the base of support. Exposure of the superior sclera and limbus is increased when the poll of the horse is rolled away from the clinician, and exposure of the inferior globe is increased when the poll is pushed towards the clinician. Manipulation of the head position is particularly helpful in procedures that involve the nictitans (Figure 3.8).

Table 3.2 Sedatives and topical medications used in ophthalmic examinations.

Drug	Route/dosage	Action/comments
Xylazine	Intravenous/0.5–1.0 mg/kg	Moderate sedation
Detomidine	Intravenous/0.02–0.05 mg/kg	Profound sedation
Butorphanol	Intravenous/0.01–0.02 mg/kg	Sedative and opioid. May be given in addition to detomidine in selected cases. Causes head tremors
Acepromazine	Intravenous/2–4 mg/45.4 kg (100 lb)	Light sedation. Rarely used on ocular cases
Lidocaine	Subcutaneous/infiltrate to effect	Local anesthesia of tissues. Rapid onset of action
Mepivicaine	Subcutaneous/infiltrate to effect	Local anesthesia of tissues. Slightly slower onset than lidocaine
Bupivicaine	Subcutaneous/infiltrate to effect	Local anesthesia of tissues. Very rapid onset of action
Proparicaine	Topical/0.3 mL per eye	Topical anesthethic for ocular surface. Needs refrigeration
Tetracaine	Topical/0.3 mL per eye	Topical anesthetic for ocular surface. More effective than proparicaine.
Tropicamide	Topical/0.3 mL per eye	Short-term mydriasis. Takes 20 minutes to effect



Figure 3.7 "Tables" for head support can be constructed from many items found in the stable. Stacked shavings bales provide a support that can be varied in height; a wheeled recycling bin is a lightweight alternative that can be easily repositioned.

Clinicians may need to stand on a stool or bale to examine tall horses. Examination of Miniature horses or small ponies is best done sitting on a similar prop. Examination of neonates or suckling foals should be done with the foal positioned in front of the dam so as to minimize separation anxiety (Figure 3.9). An assistant should cradle the foal gently, placing one arm around the chest and the other around the rump, or using the other hand to hold the base of the tail. The examining veterinarian squats by the foal's shoulder, supporting the mandible of the foal with one hand and holding the examining light source or ophthalmoscope with the other.



Figure 3.8 Exposure of the superior sclera and limbus increases if the horse's ear region is rolled away from the examiner.

Local and regional anesthesia

General examination of a comfortable eye in a cooperative horse does not require nerve blocks. However, motor and/or sensory denervation may be necessary for examination, diagnostic testing, and initial field therapy for eyes that are painful from keratitis, uveitis, or other serious conditions [35, 36]. Nerve blocks are also essential for handling any eye in danger of rupture due to tectonic instability. All practitioners should be skilled at performing auriculopalpebral and supraorbital nerve blocks, as described in Chapter 1.

Corneal or conjunctival topical anesthesia is necessary for many diagnostic tests and standing procedures. Short-term



Figure 3.9 Foal ocular examination is done with the foal positioned in front of the mare.



Figure 3.10 Topical anesthetic or mydriatic solutions are applied to the ocular surface using the broken-off hub of a 25-G needle attached to a small syringe as a spray device. This image shows a corneal lesion being lavaged with a spray of sterile saline to flush out surface debris.

tissue desensitization is achieved by applying the topical anesthetic ophthalmic solution onto the target surface (Figure 3.10).

Pupil dilation

Many ophthalmic examinations are enhanced when the horse is re-examined after a mydriatic has been applied. Pupil dilation should be performed after the various light responses and reflexes have been tested and the resting pupil size and shape has been noted. As described in Chapter 1, dilation is achieved by applying about 0.3 mL of a short-acting mydriatic (1% tropicamide) to each ocular surface. Complete pupil dilation takes about 20 minutes. Many conditions are well imaged by photographs that compare the undilated eye with a photograph of the eye after dilation (Figure 3.11).



Figure 3.11 This lens subluxation is an example of an ocular condition that is best imaged following pupil dilation.

The discipline of performing a complete examination

Practitioners are often called to evaluate eyes that are discolored, traumatized, or painful. In these cases, clinicians are tempted to immediately examine the obvious problem. All ocular examinations, both routine and emergent, should begin with a brief examination of the entire animal. Assessment of the vital signs, overall health and condition of the patient, and inspection of the structure and function of tissues near the eye will assure that conditions that might either accompany or be related to any discoverable ocular issue are not overlooked [37–40]. Examples of such findings are listed in the online material. The examination should proceed in checklist fashion, much as a pilot runs through a pre-flight drill. The routine of assessment of the overall patient and periocular region can be done quickly but should never be skipped. A checklist is outlined in Box 3.1 (online). Clinicians must always do a full examination of both globes, even when assessing an acute injury involving only one eye.

Performing ocular examinations in field settings

Most practitioners use simple, inexpensive equipment to carry out ocular examination of a standing animal in the field [41–44]. The examination begins after the staged "barn examination room" is darkened. A bright light source such as a Finnoff transilluminator or penlight is used to inspect the head, adnexa, and ocular surfaces and perform the standard ocular reflex testing described in Chapter 1. The same instrument is then used for transillumination, retroillumination, and direct inspection of the intraocular structures. The bright light survey is followed by direct ophthalmoscopy, which is first done from a distance to retroilluminate focal densities against the tapetal reflection, and then performed close to the eye to view detail directly and perform transillumination. The handler can provide assistance in visualization of the regions that are superior or inferior to the limbus by tilting the horse's head either towards or away from the clinician. Box 3.5 (online) lists several other practice tips that may facilitate the examination process.

Many practitioners get additional information with aids such as head loupes (Optivisor® (Donegan Optical Co. Inc., Lenexa, KS)), and handheld lenses that are used to show indirect images of the fundus. Practitioners with special interest in ophthalmology may perform slit-lamp examination and/or indirect ophthalmoscopy with a magnifying headset. Specific techniques for examination of the globe with all these pieces of equipment are covered in Chapter 1.

Pre-purchase examinations

People who are deciding whether or not to buy a horse frequently request a pre-purchase veterinary examination of that animal. Pre-purchase examinations involve a thorough inspection of all observable body systems, using basic equipment including an ophthalmoscope, stethoscope, hoof testers, weight tape, and bright light source. Pre-purchase examinations usually include observation of the horse being ridden or lunged, tests to assess the neurologic status of the horse, and orthopedic flexion tests to assess gait following joint manipulation. Buyers may request additional procedures such as diagnostic imaging of the musculoskeletal, respiratory, or reproductive systems, laboratory blood analysis, or drug testing.

Guidelines for the conduct of pre-purchase examinations have been established by the American Association of Equine Practitioners (AAEP). The AAEP guidelines, last revised in 2009, state that a veterinarian performing a pre-purchase examination should "list all abnormal or undesirable findings discovered during the examination and give his or her qualified opinions as to the functional effect of these findings" [45]. The guidelines go on to state that the veterinarian "should make no determination and express no opinions as to the suitability of the animal for the purpose intended." Contrary to popular perception, veterinarians do not "pass" or "fail" horses when they do pre-purchase examinations.

Every pre-purchase examination involves discovery and disclosure of medical findings, however. These findings will be listed in the veterinary report of the examination that the buyer evaluates when making the final purchase decision. Ophthalmic findings are frequently the focus of significant scrutiny for buyers, and the veterinarian's interpretation of the functional effect and prognosis of such findings may influence whether or not the horse changes hands.

The ophthalmic portion of the pre-purchase examination

The ophthalmologic examination is a critical part of pre-purchase examination. Between 5% and 10% of horses have been reported to have important ophthalmic lesions that may affect vision or athletic function. An additional sizable percentage of horses have observable ophthalmic variants that are clinically insignificant. It is the responsibility of the examiner to do a thorough ophthalmic examination to discover any abnormalities and variants and render a written judgment as to the significance of the findings.

The process of doing the pre-purchase ophthalmic examination is basically identical to the thorough field ocular examination described in Chapter 1 [46, 47]. Ideally, an ocular history should be taken, but this may not be possible if the seller is not present or is unfamiliar with the horse. During the moving/riding part of the examination the horse is watched for its reaction to objects in its environment and observed for its ability to navigate obstacles such as a jumping course. Sometimes inclement weather, conditions of the examination site, or the temperament or level of training of the horse may affect the ability of the examiner to complete the examination at the desired level of scrutiny. The pre-purchase report should fully document any situation where examination conditions were less than ideal.

Pupil dilation and the pre-purchase examination

No official consensus exists regarding the application of a short-term mydriatic (e.g., 1% tropicamide) to dilate the pupils during a pre-purchase examination. However, mydriasis is required for complete examination of the lens and ocular posterior segment. Response to a mydriatic also tests the range of iris mobility and checks for the presence of synechia. Pupil dilation is thus recommended for pre-purchase examinations.

Ocular reflex testing and inspection of the globes in an undilated state should precede any dilated examination. From a practical standpoint, the riding and moving part of the examination should also be completed prior to the instillation of tropicamide. A dose of 0.3 mL of mydriatic solution should be applied to each cornea after the riding examination is finished and before the standing portion of the physical examination. Mydriasis will be complete about 20 minutes after drops are applied. The dilated ophthalmic examination is then performed in a dark area after the standing physical examination is finished. The pre-purchase report should state that the pupils were dilated, and the findings of both the dilated and undilated examination should be listed.

Situations may arise where pupil dilation cannot be performed. The owner or seller's agent of the horse may not give

permission to dilate the pupils, or the horse may be participating in a competition where the use of any topical medication is forbidden. If pupil dilation is not performed, the report should state that the examination was done with the eyes undilated. The situation will dictate whether an explanation of why the pupils were not dilated is appropriate or not.

The pre-purchase examination report

A report of the pre-purchase examination is prepared after the examination is completed. The report is archived in the horse's medical record [48] and shared with the buyer and his or her agent in digital and/or printed form. The ophthalmic portion of the report should be very descriptive of any abnormalities or variants. The text of the description should be composed in such a way that future changes could be judged and compared to the status on the date of the pre-purchase examination. The results of any ophthalmic testing performed (e.g., tonometry, ocular surface staining, ocular reflexes) should be listed. As the report will be providing a baseline for the horse's future, it is helpful if any ophthalmic findings of note are photographed and images are attached to the report.

Abnormalities in ocular reflexes, cranial nerve function, periorbital region, or adnexa should be listed. Findings on the ocular surface or within the globe may be described by citing the affected side and describing the lesion or variant with respect to color, shape, size, optical properties (presence or lack of transparency), and location of the lesion in respect to other structures [49, 50].

Buyers often have an unrealistic expectation that the examiner will render an opinion in the report as to whether any finding(s) affect vision, and whether these finding(s) might progress or recur. Usually it is not possible for the veterinarian to give such an opinion with certainty. Buyers must understand that it is impossible for veterinarians to pass judgment on the visual acuity of any horse, unless that horse has been determined to be blind.

The greatest dilemmas occur when a lesion is noted that could either progress or remain static. It may be impossible to determine if such a lesion affects vision to a significant degree at the time of the examination. Such is the case with many pigmentary lesions in the peripapillary region, some corneal opacities, many focal cataracts, and a number of other findings. Box 3.1 lists findings that may be discovered during the pre-purchase examination that are uncertain in

Box 3.1 Significance of pre-purchase ocular examination findings.

Unequivocal significance

- Sarcoids, other adnexal tumors or masses
- Dysplasia of eyelid tissue or conjunctiva
- Ectropion or entropion
- Lid motility disorder
- Trichiasis, old lid repair that does not frame a normal aperture
- Chalazion
- Exophthalmos, microphthalmos, enophthalmos, buphthalmos
- Pronounced or unilateral strabismus
- Impaired pupillary light reflexes
- Large corneal scar near axis
- Multiple punctate corneal opacities
- Mineralized corneal deposits
- Corneal edema
- Multiple corneal stria, branching stria
- Corneal vascularization
- Flare, hyphema, hypopyon
- Miosis
- Eccentric pupil shape
- Synechia
- Mature cataracts
- Extensive cortical cataracts
- Lens luxation, subluxation
- Elevated IOP
- Multiple opacities in vitreous
- Vitritis
- Extensive peripapillary chorioretinitis with vessel attenuation
- Retinal detachment
- Optic nerve atrophy
- Optic neuritis
- Phthisis bulbi

Uncertain significance

- Past sinus trauma (dents or raised areas)
- Eyelid skin that lacks pigment
- Solar blepharitis
- Small focal corneal scars
- Pigment deposits on cornea or lens with no other ocular abnormalities
- Lipid deposits in the cornea
- Single corneal stria
- Large iridociliary cysts
- Iridal hypoplasia
- Large granula iridica cysts
- Small focal cataracts
- Vitreal syneresis
- Vitreal membranes
- Focal "bullet hole" chorioretinopathy without other abnormalities
- Diffuse "butterfly wing" peripapillary chorioretinopathy without other abnormalities
- Proliferative optic neuropathy
- Senile retinopathy

Variants or minor blemishes

- Healed small notches or gaps in the tarsal margin with no trichiaisis
- Persistent pupillary membranes that bridge iris stroma
- Small iris colobomas or nevi
- Heterochromia iridis
- Small granula iridica cysts
- Small vacuolations in the lens
- Mittendorf's dot
- Faint retrolenticular fibroplasia
- Prominent suture lines in the posterior lens
- Small focal inclusions in the vitreous
- Persistent hyaloid vasculature
- Variations in the color of the tapetum
- Partial albinism
- Circumpapillary marginal pigment proliferation
- A few scattered chorioretinal scars
- Ectopic myelination of the disc
- Small fundic colobomas ("window defects")

terms of prognostic significance, as well as findings of unquestionable significance.

Most practitioners opt to err on the side of caution when preparing their report on ophthalmic findings. When equivocal lesions are discovered, it is advisable to give buyers the option of obtaining a second opinion from a board-certified veterinary ophthalmologist who may be able to provide additional prognostic expertise or advanced testing. If the buyer declines this option, the report should document that referral was offered and discussed.

Ophthalmic tests in the field

Field tips for vision testing

A rough assessment of vision can often be made with maze testing. This test involves blindfolding first one eye and then the other with a towel or hood, and observing how the horse navigates a short obstacle course with only one eye receiving light signals. The maze tests should be repeated in dim light conditions after completion in good lighting, particularly in patients who are suspected to have congenital stationary night blindness (Figure 3.12A, B).

Barn aisles that have been cleared of hazards are good stages for maze testing. An obstacle course is created using overturned buckets or other smooth, solid objects that are easily rearranged, yet harmless if the horse runs into them. Stall doors and barn openings that exit the maze path should be closed off for safety concerns. Handlers and observers should be instructed to stay away from the maze area to avoid giving the horse verbal clues that might affect spatial orientation.

The horse being tested should be turned loose in the aisle and coaxed to navigate the line of obstacles on its own. This is accomplished by directing an assistant to stand at the far end of the maze shaking a bucket of grain. The clinician stands at the origin of the maze path, observing the horse's behavior and also prepared to catch the horse if it reverses direction during testing.

The noise of the grain rattling in the bucket is usually a strong incentive for a visual horse to progress through the maze confidently. Horses that are visual in the uncovered eye will show head and body movements that demonstrate recognition of the obstacles in the path. A horse blind in the uncovered eye will show a dramatic difference in maze behavior. It will freeze in place and refuse to move, or walk very tentatively forward, often running into the ground obstacles.

Maze testing is very useful in instructing owners and trainers. People who work with the animal every day may not "believe" that a damaged eye is blind until they observe the asymmetric behavior displayed during a maze test.

Field tips for tonometry

Tonometry is discussed in Chapters 1 and 10. Tonometers are moderately expensive tools, but equine practices that have invested in this equipment have found that offering this service is a valuable part of comprehensive care.



(A)



(B)

Figure 3.12 (A) A maze test can help distinguish a blind eye from a visual eye. With one eye blindfolded, the horse must pick a route through a series of harmless objects. (B) An assistant shakes grain in a bucket to motivate the horse to proceed through the maze. The test is repeated with the opposite eye blindfolded.

The two instruments most commonly used are the Tono-Pen Vet applanation tonometer (Reichert Inc., Depew, NY) and the TonoVet rebound tonometer (Icare Finland OY, Helsinki) [51]. Both instruments are portable, handheld, and battery powered. The Tono-Pen requires topical anesthesia of the cornea, while the TonoVet can be used without topical anesthesia. The Tono-Pen Vet does not operate well in conditions below freezing and should not be left in the ambulatory vehicle in cold months. The TonoVet performs well in a variety of temperatures. Research has shown that sedation with any of the alpha-2 agonists may lower the IOP by a few millimeters of mercury with either instrument [52–54], but this fact can be taken into consideration when results are interpreted.

The horse's head should be held or supported at a "normal" level (mandible slightly above the level of the point of the shoulder) for accurate readings. Care should be taken to raise the eyelid of the target globe by pinching the skin and suspending the eyelid above the cornea so as not to create digital pressure on the globe. If sequential IOP readings are performed, the conditions of the initial examination (time of day, head position, sedation with or without blocks) should be duplicated as closely as possible.

Performing culture and cytology in the field

The most common indication for ocular culture and cytology in equine practice is a corneal ulcer that is obviously infected, chronic, unresponsive to therapy, or melting. Such cases are very painful and many progress rapidly. Rational therapeutic decision-making requires prompt sample analysis to check for infectious agents and gather information on etiology. Additional diagnostic samples may be sent to reference laboratories as appropriate, but all clinicians are urged to cultivate basic skills in acquiring and interpreting samples of corneal surface cells [55].

Supplies for obtaining culture and cytology samples should be packed in the ambulatory vehicle at all times, and the practice laboratory should be equipped with materials for Diff-Quik and gram stains and a microscope that has a 100× lens. The sample collection process can be done on the same visit as other procedures including dye tests, digital imaging, debridement of the lesion, and/or instillation of an SPL system. The steps involved in prepping a patient for culture and cytology are listed in Box 3.2.

Obtaining and handling ocular culture samples

Culture samples are usually done before other procedures to optimize procurement of an uncontaminated sample. Ideally cultures should be obtained without topical anesthesia, but few horses will allow this. The operator should use a sampling instrument (scalpel blade, cytobrush, or culture swab) that has been packed in a sterile wrapper to assure sterility. The use of gloves will guard against the introduction of pathogens from the clinician's hands and avoid contamination of the swab, brush, or blade.

Box 3.2 Preparation for corneal culture and cytology.

1. Assemble all needed supplies on a raised, clean surface.
2. Construct "bale table" or similar solid support for the mandible.
3. Assure adequate illumination (headband light, assistant with flashlight).
4. Minimize traffic of humans, animals, and farm vehicles in area.
5. Shut doors to minimize wind.
6. Prep the periocular region with 2% povidone iodine solution.
7. Administer sedation and periocular nerve blocks.
8. Obtain pre-sampling photographic images.
9. Administer topical anesthetic as appropriate.

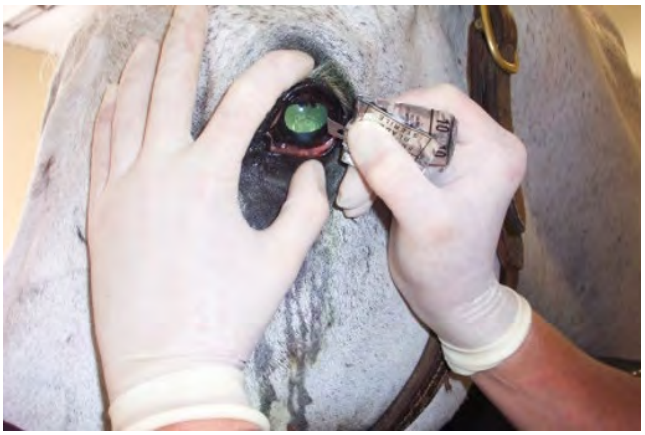


Figure 3.13 A sterile blade being used to obtain a culture sample. The same technique is used to obtain a cytology sample, and to debride the ulcer surface.

One common field sampling technique involves using a scalpel blade to obtain the culture sample. The foil wrapper of the blade, which is sterile on both surfaces due to extra packaging, is folded around the sharp edge of the blade, and used as a handle. The blunt base of the blade is scraped across the lesion to exfoliate material for culture (Figure 3.13).

The sampled material is then transferred to appropriate culture media by one of two methods:

1. The entire blade is released from the foil wrapper and dropped into a screw-topped tube of thioglycollate broth for subsequent incubation/submission, OR
2. The blunt sampling blade end is used to make multiple "C-shaped" inoculations of corneal material into the culture agar of a standard biplate for subsequent incubation/submission (Figure 3.14).

Another technique involves applying a sterile Dacron or calcium alginate swab to the corneal surface area of interest and then inserting the swab in transport media (broth or gel).

All of these sampling techniques produce a specimen that can be placed in a cooler for transport for the day and later incubated and analyzed in the practice laboratory, or shipped to a



Figure 3.14 Sabaroud agar plate that has been inoculated with a sample from a blade base.

reference laboratory for incubation, amplification, identification, and sensitivity analysis.

Samples that have been placed in thioglycollate broth and incubated at body temperature (37°C) will turn turbid in 12–24 hours if bacteria are replicating in the broth. A filamentous plaque may appear on the surface of the broth overnight if the sample contains fungus. Specimens that are plated on blood agar will grow visible bacterial colonies or fungal plaques within 12–48 hours. Saboraud's agar provides a medium that promotes fungal replication, and plates harboring positive samples will rapidly demonstrate fluffy, dustball-like plaques on the agar surface.

If a culture sample yields bacteria, it should be Gram-stained to determine morphology and staining characteristics. Characterization of the specimen properties (Are the bacteria in the colonies cocci or rods? Are they Gram-positive or Gram-negative? Do they present in chains, clusters, or solitary organisms?) guides therapeutic decision-making and dictates the best type of agar plate (Mueller Hinton plain agar v Mueller Hinton agar with blood) to use for antibiotic sensitivity analysis.

Antibiotic sensitivity testing for culture samples that yield bacterial growth can be referred to a reference laboratory or performed in-house using the Kirby-Bauer disk diffusion method of applying antibiotic-impregnated disks to agar that has been plated with diluted colonies of sample bacteria. A sensitivity wheel stocked with disks containing the antibiotics commonly used to treat corneal bacterial infections should be designated for ophthalmic sample testing. Testing a positive fungal culture sample for antifungal sensitivity patterns must be done at a reference laboratory. The process is lengthy and expensive, so most practitioners make therapeutic decisions on cases of mycotic keratitis on an empirical basis, and adjust by assessing response to treatment.

Box 3.3 Corneal cytology sampling procedure.

1. Use a Kimura spatula, blunt end of a scalpel blade, or a cytobrush as the sampling instrument. Use sterile technique.
2. Hold the sampling instrument at a 45-degree angle to the cornea and scrape the ulcer margin firmly.
3. Hold the sampling instrument at a 45-degree angle to the slide and spread the sample thinly on two to four clean microscope slides.
4. Repeat sampling if visible material is not present on the slide.
5. Label slides with date, patient and owner names, left eye or right eye (OS or OD). Store in plastic slotted box for transport.
6. Stain one slide with Diff-Quik stain. If bacteria are present in large quantities, stain another slide with Gram stain.
7. Rinse the stained slide(s) and air dry or dry in incubator.
8. Examine with microscope using oil immersion, 100× lens.

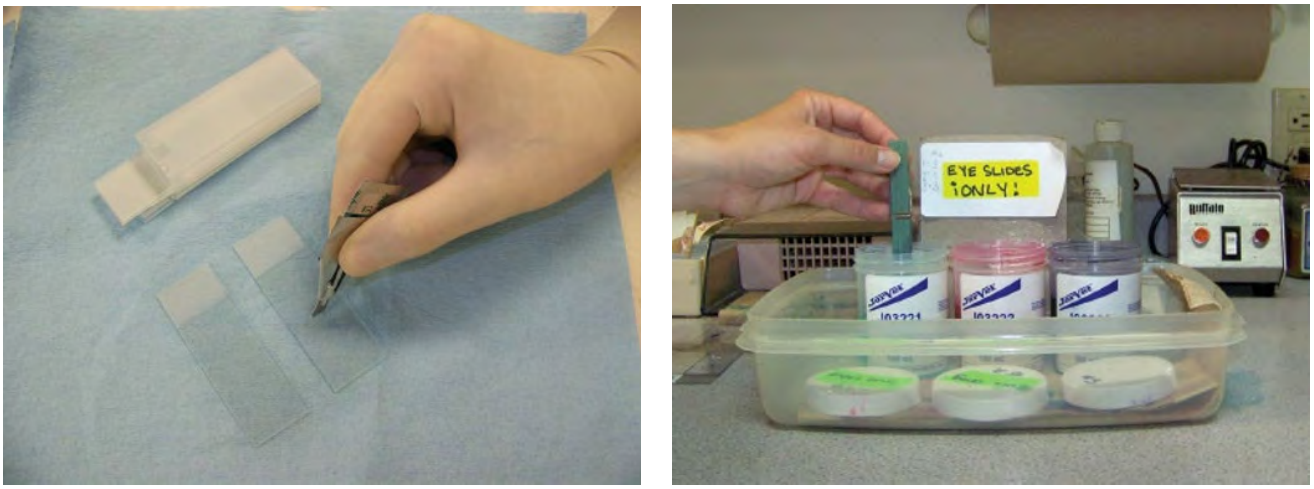
Obtaining and staining ocular cytology samples

The steps involved in obtaining cytology samples are described in Box 3.3. Two to four slides should be made from each eye that is sampled; spare slides may be sent to reference laboratories or used for additional staining at the practice laboratory (Figure 3.15A, B). Once cellular material is on the slides there is no need to apply fixative. The sampled material will dry on the slides during transport and can be stained and examined later the same day. If the clinician needs to evaluate the sample immediately, slide surface drying time can be reduced if the underside of the slide is held briefly over a low flame.

One slide should be stained with Diff-Quik stain, which involves a three-step dipping or immersion process. Many laboratories use a "rapid dip" method, where the slide is dipped five to twelve times into the jar containing Diff-Quik fixative (light blue solution), then the dipping process is repeated for each of two subsequent stain components (Diff-Quik red solution 1, then dark blue solution 2). Each dip cycle lasts approximately 1 second. This technique yields reasonable sample quality and can be performed very quickly.

However, cytologic detail and staining contrast is enhanced if a longer immersion process is used. A technique where the slide is first left in the light-blue fixative reagent for 3 minutes, then submerged in the eosinophilic red stain (Diff-Quik solution 1) for 1 minute, and finally immersed in the basophilic dark-blue stain (Diff-Quik solution 2) for 3 minutes will optimize sample staining quality. Practices that perform ocular cytology frequently will find that slide quality is optimized if a set of stain jars is designated solely for ocular samples. The stain components should be changed frequently, as accumulation of stain precipitate will produce particulate artifacts on the sample slides that can be misinterpreted as extracellular bacteria.

Whether a short dipping technique or a longer immersion process is used, the stained slide should be rinsed gently with water, and dried prior to examination. If microscopic analysis of



(A) (B)

Figure 3.15 (A) Cytology sample obtained with a blade is applied to several slides. Slides will dry inside a plastic slotted box. (B) Diff-Quik stain jars reserved for staining ocular samples.

the slide shows abundant bacteria, a second slide should be stained with Gram stain. Rational therapeutic decisions on cases harboring bacterial infections can be made with the information obtained from Diff-Quik and Gram stain analysis. Diff-Quik stain usually outlines fungal hyphal elements well, with either positive stain uptake or an outline of a silhouette of the elements by "negative staining," allowing rapid identification of cases of mycotic keratitis and facilitating prompt and appropriate treatment.

Clinicians may choose to submit additional unstained slides to reference laboratories. Reference laboratories can provide further analysis using other Romanovsky-type stains (Wright–Giemsa) or special stains like periodic acid-Schiff (PAS), Gomori methenamine silver (GMS), or Cellufluor (Calcofluor white) to identify acid-fast bacteria or confirm fungal elements.

Interpreting ocular cytology samples

The goals of analyzing a corneal sample are simple:

- assess the cells native to the sampling site;
- assess the host cellular response to the presenting condition; and
- assess whether noncellular elements are present.

Cytology samples can be read in-house by technicians or clinicians with basic training in clinical pathology. Rational choice of therapy depends on assessing the character and degree of inflammatory reaction and determining whether infectious agents or foreign bodies are present. Obtaining the answers to these questions on a same day basis will expedite appropriate treatment and guide the clinician in planning case management.

Scrapings of healthy cornea should contain nothing but sheets of epithelial cells. Cells from the most superficial layers of the epithelium are flattened with large amounts of blue cytoplasm and basophilic nuclei. Cells from intermediate layers are more polyhedral, while cells from basal layers are more cylindrical and round. Basal cells stain more darkly, showing less cytoplasm than cells from the upper layers (Figure 3.16).

Normal corneal epithelial cells do not contain bacteria and are exfoliated in sheets. Individual cells that are flat in contour may roll up in tight scrolls on the slide and must not be mistaken for hyphae or foreign bodies. Degenerate corneal material may be evidenced as "cytoplasmic streaming"—long thread-like tangles of basophilic material that are often seen mixed with intact corneal cells and neutrophils. Care must be taken not to interpret the degenerate material as fungal hyphae.

Scrapings from corneas with a cellular inflammatory response will show an infiltrate (Figure 3.17A–C). The most common finding is a suppurative infiltrate, where neutrophils with or without toxic changes predominate. A small number of lymphocytes, monocytes, or plasma cells may also be present. Although a suppurative infiltrate is not pathognomonic for infection, it is highly suggestive of it.

Occasionally a corneal sample will show an eosinophilic infiltrate. Presence of eosinophils is abnormal and suggests either acute allergic hypersensitivity or eosinophilic keratitis. Some fungal infections incite a granulomatous infiltrate consisting of epithelioid macrophages and giant cells. If hemorrhage has occurred due to the disease process or sampling trauma, red blood cells will be present in large numbers.

The most common noncellular elements found in corneal scrapings are infectious agents. Bacteria commonly seen include cocci, large rods, small rods, and bipolar rods (Figure 3.18A, B). Most cocci are Gram positive in their staining patterns, and most rods are Gram negative, but some small rods may have Gram-positive stain characteristics. Intracellular bacteria are highly correlated with infection.

The presence of even a few fungal hyphae in a cytology sample is indicative of mycotic keratitis. Hyphae are slender, septate, linear structures that branch at various intervals.

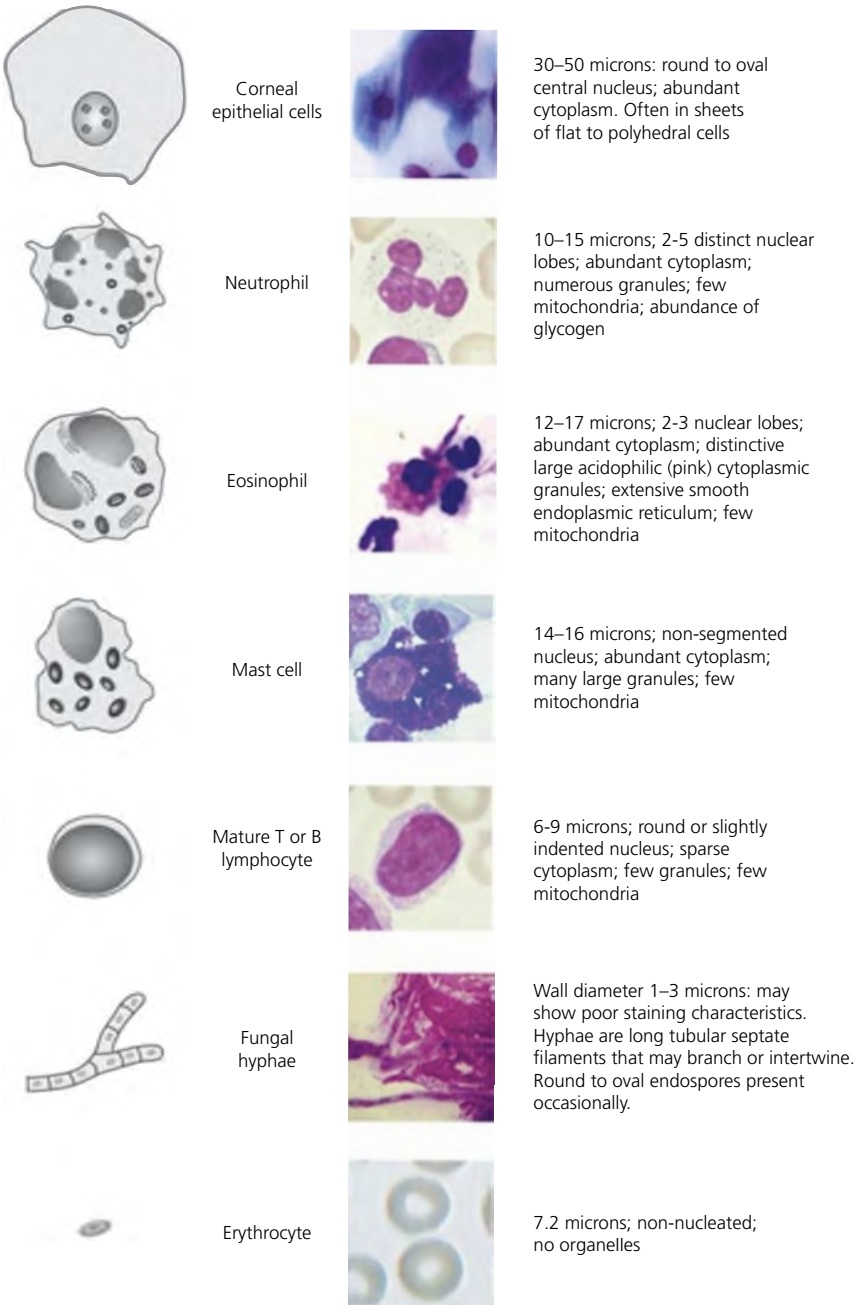
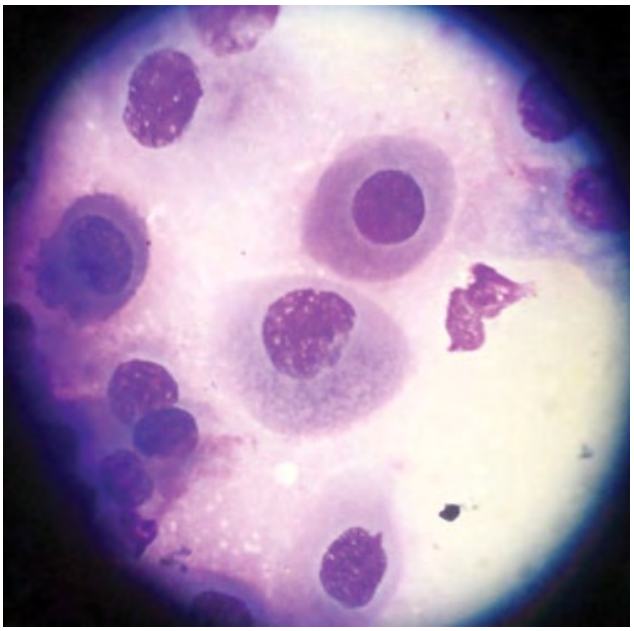


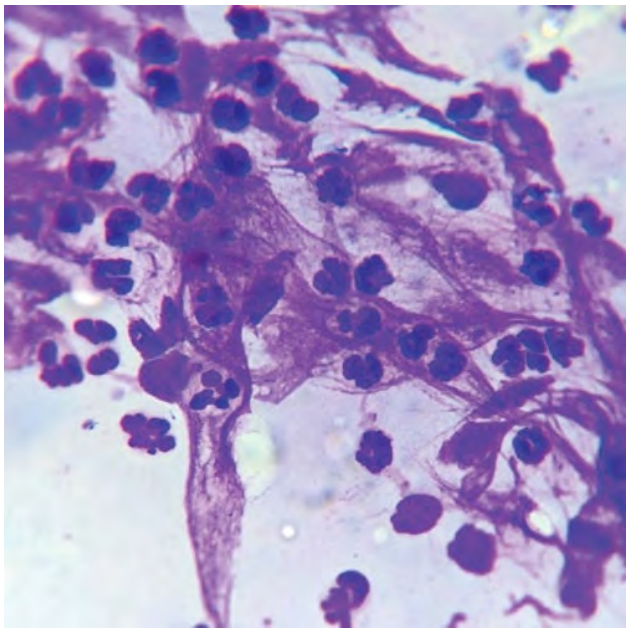
Figure 3.16 Drawing of common cellular elements. (*Source*: Gilger, 2011 [11]. Reproduced with permission from Elsevier.)

Most fungal hyphae stain well with Romanovsky stains such as Diff-Quik and can be seen as a tangle of spaghetti-like densities interspersed with native epithelial cells (Figure 3.19A, B). Care must be taken to distinguish degenerate corneal cellular elements ("scrolled" epithelial cells and long, thin strands of necrotic cellular debris that represent "cytoplasmic streaming") from true fungal hyphae (Figure 3.20A, B). Differentiation can be aided by looking for the distinctive elements that identify hyphae: parallel walls, septate compartments that are perpendicular to hyphal walls, and branching of the hyphae. Some fungal specimens demonstrate negative staining characteristics, where fungal elements appear transparent but are faintly outlined by stain adherent to the other elements of the organism that do stain. Occasionally spores are seen budding off hyphal elements.

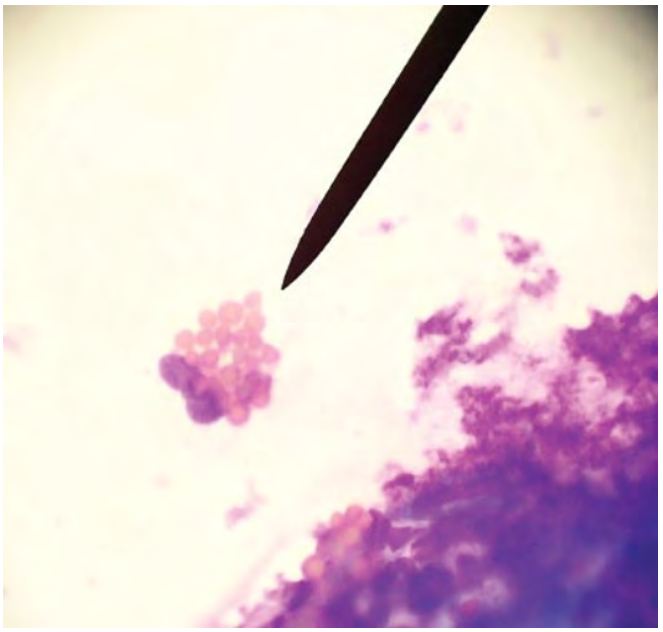
The presence of fungal elements is always significant in ulcer samples, but the absence of hyphae does not rule out infection; hyphae may be present in corneal layers deep to



(A)



(B)

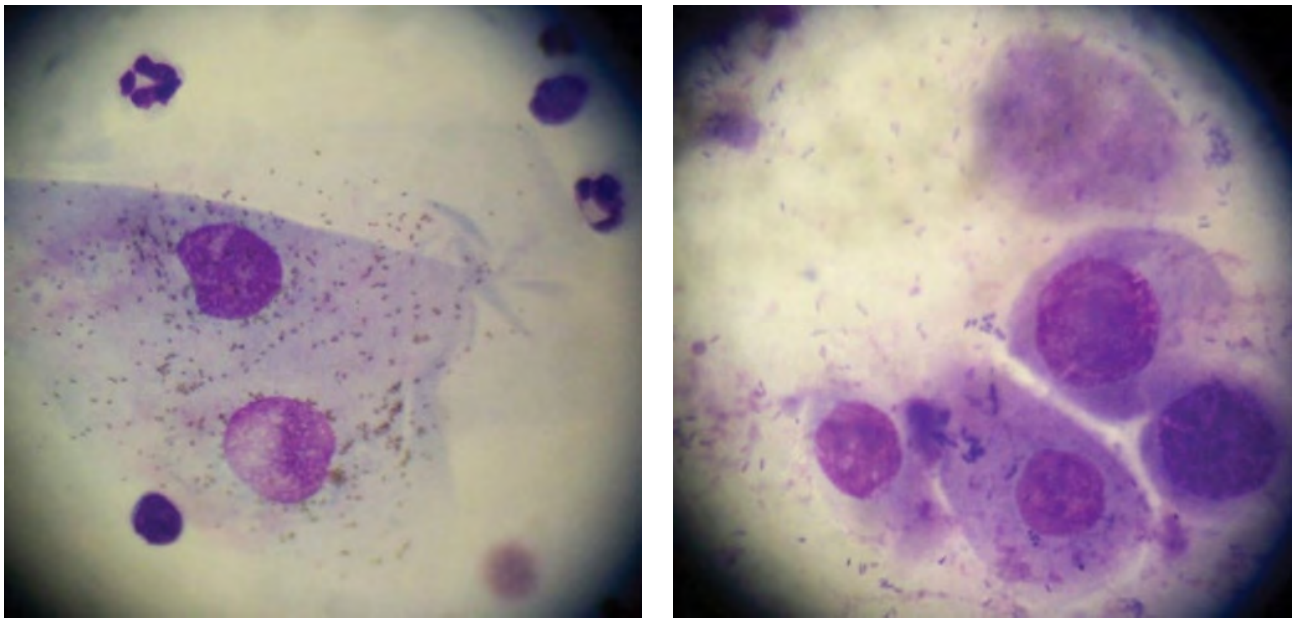


(C)

Figure 3.17 (A) Photomicrograph of normal corneal scraping. Corneal surface epithelial cells are flattened with large amounts of blue cytoplasm and basophilic nuclei (Diff-Quik stain ×1000). (B) Photomicrograph of corneal cytology sample demonstrating a neutrophilic infiltrate. Neutrophils may be mixed with cellular debris, or seen as groups of individual cells on the slide (Diff-Quik stain ×1000). (C) Photomicrograph of corneal cytology sample demonstrating an eosinophilic infiltrate. Eosinophilic presence may be noted as individual cells with characteristic pink cytoplasmic granules, and/or as individual granules amidst cellular debris (Diff-Quik stain ×1000).

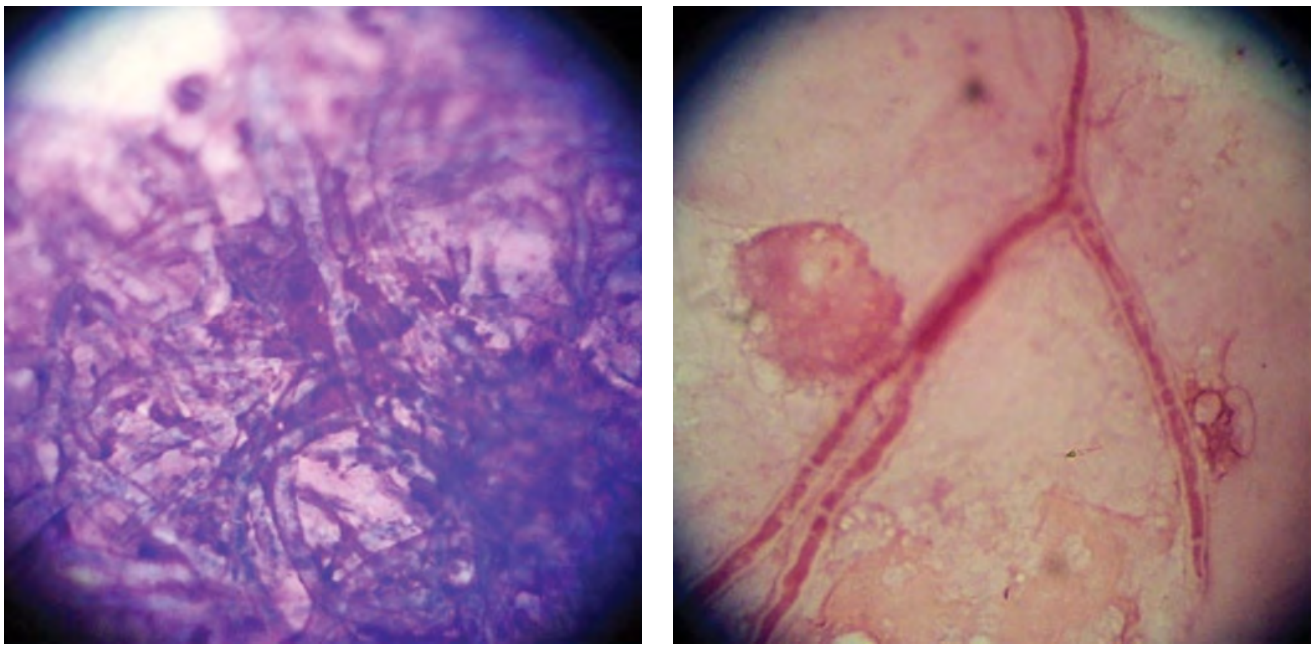
the sample site, particularly in samples taken from stromal abscesses.

Other noncellular elements that may be seen on corneal cytology include intracytoplasmic melanin granules (dark green to black granules found in cells scraped from the limbal region or from pigmented scars), vegetative foreign bodies, nonvegetative foreign bodies, parasites or parasitic body parts, and mineralized crystals. The latter may stain light blue with Diff-Quik and may correlate with deposits of calcium in the subepithelial layers of corneas from horses with stromal keratopathies (Figure 3.21A, B).



(A) (B)

Figure 3.18 (A) Photomicrograph of corneal cytology sample demonstrating intracellular bacteria. The cytoplasm of the epithelial cells is packed with small rod-shaped organisms (Diff-Quik stain ×1000). (B) Photomicrograph of corneal cytology sample demonstrating extracellular bacteria. Numerous cocci-shaped organisms are seen in short chains (Diff-Quik stain ×1000).



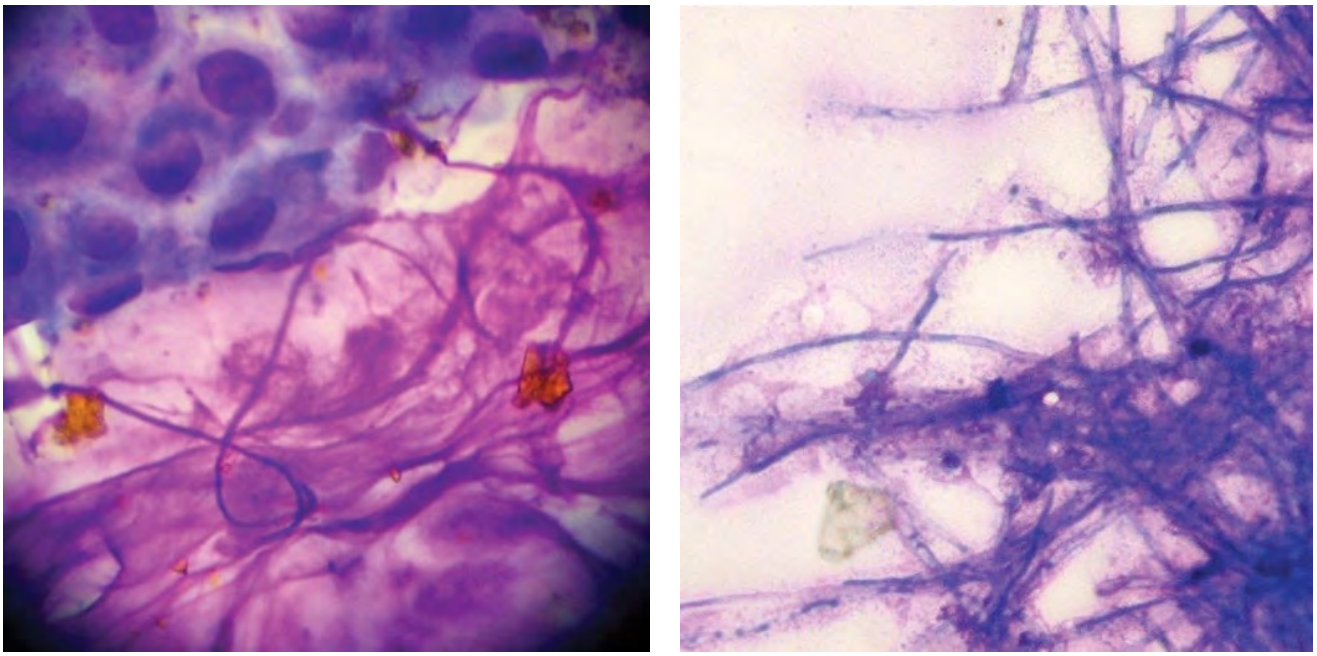
(A) (B)

Figure 3.19 (A) Photomicrograph of corneal cytology sample demonstrating fungal hyphae. Hyphae have parellel walls and are seen to branch (Diff-Quik stain ×1000). (B) Photomicrograph of corneal cytology sample demonstrating "negative staining" of hyphal walls paired with stain uptake in the hyphae luminal area. Septate partitions are easily seen (Gram stain ×1000).

Other ocular cytology indications

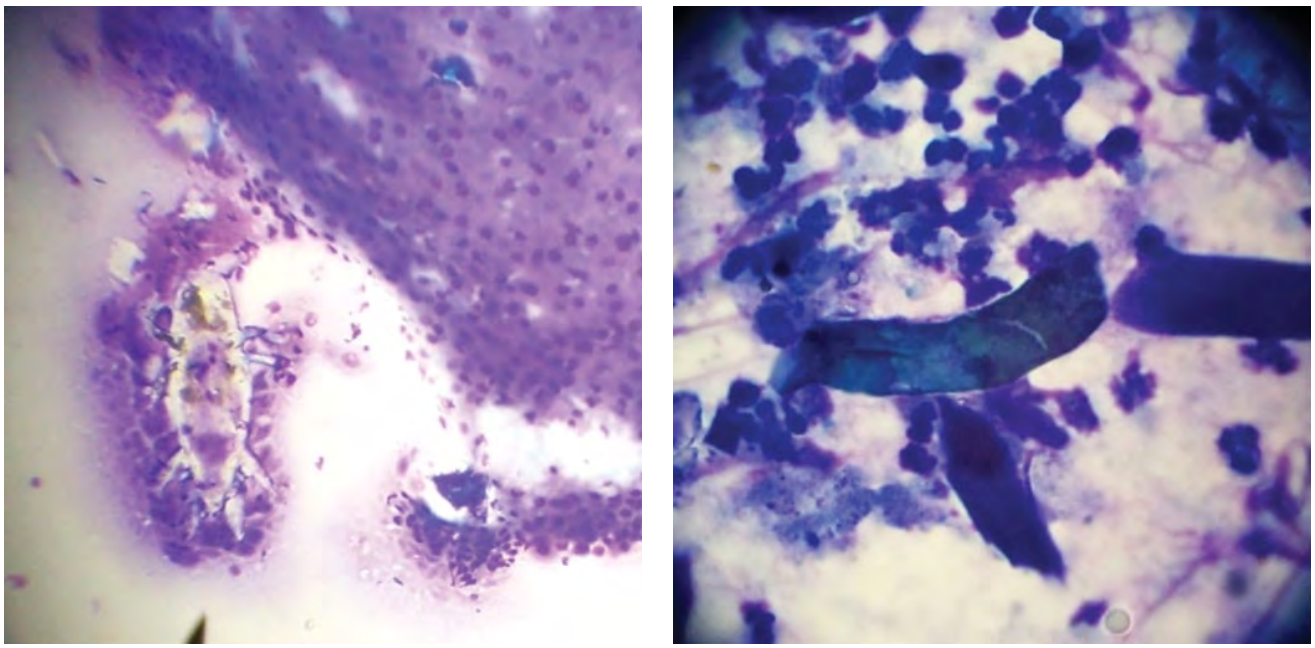
Cytology may be indicated in ocular tissues other than the cornea. Samples can be taken from bulbar, palpebral, or nictitans conjunctiva that is inflamed or abnormal in appearance, and analyzed as described in the section

Interpreting non-corneal cytology samples. Conjunctival samples will contain goblet cells in addition to the cellular and noncellular findings typically present in corneal samples. Goblet cells have eccentric nuclei and pale-blue cytoplasm (Figure 3.22).



(A) (B)

Figure 3.20 (A) Photomicrograph of corneal cytology specimen showing a raft of epithelial cells (**upper left**), and strand-like elements demonstating cytoplasmic streaming (**lower right**) that can easily be confused with fungal hyphae. The strands do not present in a branching morphology and are of variable thickness (Diff-Quik stain ×1000). (B) Photomicrograph of corneal specimen showing fungal hyphae that branch and are of uniform thickness (Diff-Quick stain ×1000).



(A) (B)

Figure 3.21 (A) Photomicrograph of corneal cytology sample that shows an intact mite (external parasite). Other areas of the sample contained additional mite body parts. This horse presented with severe pain and a small ulcer that had been present for several months. All signs resolved following debridement and administration of systemic ivermectin (Diff-Quik stain ×400). (B) Photomicrograph of corneal cytology sample taken from a horse with calcific keratopathy. Large blue structures represent mineralized crystals of calcium embedded among epithelial cells (Diff-Quik stain ×1000).

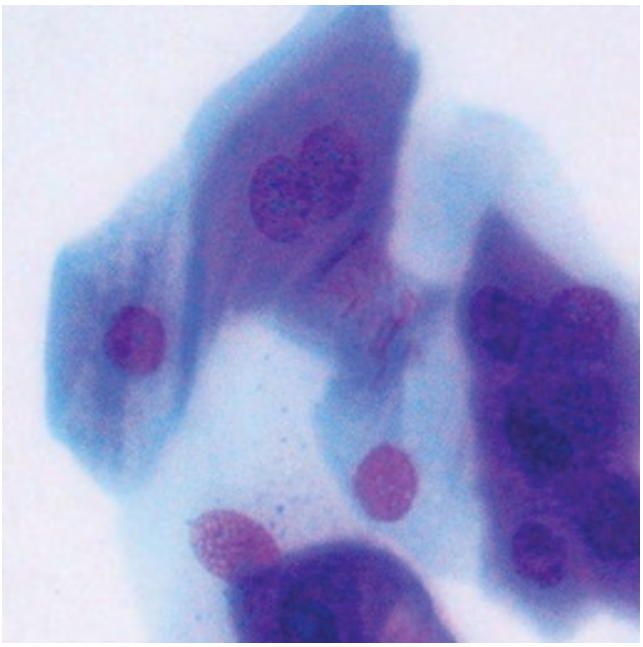


Figure 3.22 Photomicrograph of a normal conjunctival cytology sample (Diff-Quik stain ×1000).

A lymphocytic or eosinophilic infiltrate may be apparent in conjunctival samples from horses suffering from allergy. Material can be collected from the tarsal margin to analyze samples from horses that present with chalazion or meibomianitis. The conjunctiva bordering regions of suspected orbital fat prolapse should undergo fine-needle aspiration to check for adipocytes and fat elements and rule out neoplasia.

Lesions that are suspect for adnexal or corneal neoplasia can be analyzed by examining samples of cells that have been debrided from the lesion surface, collected by impression smear, or aspirated through a fine-needle puncture. These samples are best submitted to a reference laboratory as it is beyond the scope of most practice laboratories to interpret neoplastic samples. Most lesions suspicious for neoplasia should also be biopsied with the fixed tissue submitted for histopathology.

Ocular imaging

Ocular photography

A digital image provides accurate documentation of the observable problems, permits further study of the lesions as they relate to surrounding anatomy, and provides a baseline for monitoring subsequent progression or resolution of said lesions [56]. See online material for a detailed discussion of ocular photography.

Ultrasound of the ocular region

There are many clinical situations involving the eye or orbit in equine practice where valuable diagnostic information can be gleaned through ultrasound examination. Ultrasound is indicated for evaluation of any eye where the periorbit has an abnormal appearance without an obvious cause, and for any globe where the fundus and internal structures cannot be clearly inspected with a bright light and ophthalmoscope [57–61]. See Chapter 2 for more information on the technical aspects of ocular ultrasonography. The most common indications for field ultrasound are:

- Imaging the rim of the orbit and adjacent skull to screen for fractures or foreign bodies.
- Imaging of a swollen eyelid or periorbital enlargement to check for abscess, masses, or foreign body.
- Imaging of the globe to obtain detail on intraocular masses and cataracts, or to check for lens luxation, retinal detachment, or vitreal densities.
- Imaging of the globe and retrobulbar region to assess buphthalmos or exophthalmos.

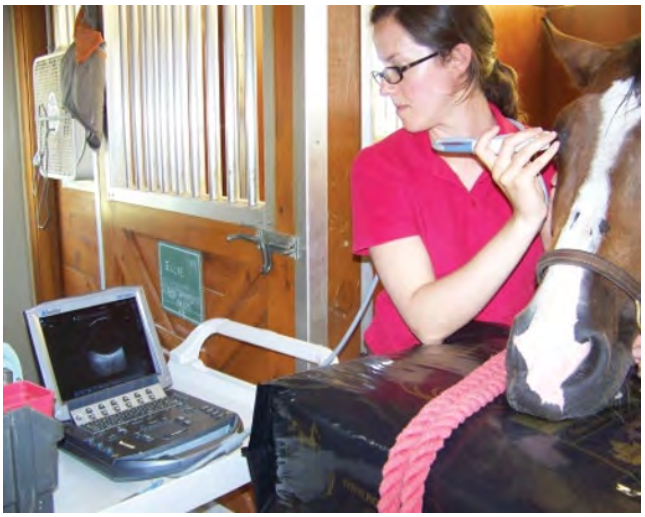


Figure 3.23 The equine globe can be examined using a transpalpebral approach with ultrasound machines used by ambulatory practitioners for orthopedic evaluations. This eye is being examined with a microconvex probe emitting a frequency of 10 MHz.

Ultrasound equipment used for routine orthopedic imaging is serviceable for field imaging of the eye for the above purposes. A 7.5- to 10-MHz probe will yield reasonable quality images. Probes with lower frequencies penetrate deeper into the orbit and may be useful for assessing the retrobulbar region. Probes with higher frequencies will yield the most detail of anterior structures but will be limited in depth of penetration. Convex, microconvex, or other probes with small scan heads that interface well with the curved surfaces around the eye usually produce images that are superior in detail to linear probes.

Imaging of the orbit, periorbit, or lids is done through the skin over the target area (Figure 3.23). Imaging of the globe and retrobulbar region can be done through the skin of the upper eyelid. It can also be done through a transcorneal approach if the cornea is desensitized with topical anesthetic. If the transcorneal approach is used, the ultrasound probe must be covered

with a sterile, watertight covering (e.g., surgical glove), and sterile packs of transmission gel should be applied to the corneal surface to promote sound wave transmission. See Chapter 2 for more information on the technique of ocular ultrasound and the normal appearance of the eye on ultrasound.

Radiographic imaging of the ocular region

There are fewer indications for radiographic imaging than ultrasound imaging in field situations, but radiography is helpful in cases of blunt trauma to the periorbit, suture line periostitis, sinus disease, or unexplained globe deviation. Radiographic imaging is also useful to check for radiodense foreign bodies or bony changes associated with periocular neoplasms [62].

Computed or digital radiology systems provide images that are superior to film radiography. Creative oblique angulation of the beam and imaging plate may be required to obtain the most useful orbital images, as standard lateral and dorsoventral projections will create an image where the orbit is superimposed over deeper structures. Contrast radiology may be helpful in cases of open sinus fractures, imaging of the nasolacrimal system, or evaluation of tracts that lead to skull fractures or foreign bodies [63–66].

Positioning for periocular radiography is aided by supporting the head of the horse on a bale table or other elevated surface. It may help to elevate the ventral mandible on a small block that rests on the table surface so that the base of the imaging plate can rest lower than the base of the mandible. Sedation of the horse will be necessary for optimal positioning, handler safety, and image quality. The imaging plate can be affixed to the head with a bungee cord or held by an assistant who is wearing appropriate protective shielding.

Additional information on radiography and advanced imaging of the periorbit and orbit is given in Chapter 2.

Common ocular conditions

Data describing the incidence and prevalence of ophthalmic disease in horses are sparse, but published reports indicate that ophthalmic abnormalities are a common finding in all populations of horses, particularly in geriatric horses and ponies in developed countries and in working equids in the developing regions of the world.

A survey of 102 neonatal Standardbred foals examined within 48 hours of birth found that 36.2% of these otherwise healthy foals showed ocular abnormalities. Most of the findings were judged to be acquired during parturition, and the majority of findings were minor lesions (ocular hemorrhages, entropion) that resolved with time or simple treatment [67]. Another survey of 70 foals of various breeds seen for nonophthalmic disease in a referral setting found that 56% of ill foals had one or more ophthalmic lesions, and 34% (24/70) had lesions that were considered vision threatening, including uveitis and severe corneal ulcers [68].

A survey of 204 Thoroughbreds done at a racetrack in Australia found that 67.6% of this young racehorse population (age range 2–9 years) had observable ophthalmic lesions. Potential vision-threatening disease (mature cataracts or extensive chorioretinitis) was recorded in 15 horses (7.4%). Findings considered nonvision threatening in the remaining 92.6% included a large number of horses with chorioretinal scars or depigmentation and several horses with eyelid scars, developmental cataracts, corneal scars, or other opacities. A minority exhibited unusual variants of ocular anatomy including colobomas, and either hypoplasia or hyperplasia of the granula iridica [69]. Another retrospective study analyzed the veterinary records of Thoroughbred horses racing in Japan and reported 2846 cases of ulcerative keratitis during a 9-year interval. The cases of corneal ulceration represented over 50% of the medical problems encountered. Most of the ulcers were healed in less than 10 days, but 24 (0.08%) took over 2 months to resolve, and 7 horses lost vision [70].

A paper describing ophthalmic findings in a closed herd of 267 Lippizzaner horses of varying ages in Austria reported that 203/267 (76%) had at least one ocular finding of note. Many of the horses were found to have lesions in more than one anatomic site. Of the entire group of horses, 44.6% had findings noted in the conjunctiva, 21.7% had lesions in the cornea, and 37.5% had lesions in the fundus. Cataract was noted in 8.9% of horses and eyelid lesions were discovered in 7.1% [71]. Another survey of 500 horses from the Indian Army of varying ages (range 3–23 years, with a mean of 11.4 years) found that 100 (20%) had one or more ocular disorders, many of them vision threatening or blinding. The most common finding was chronic interstitial keratitis (30%), followed by uveitis (24%), glaucoma (13%), conjunctivitis (12%), and corneal ulceration (8%) [72].

A recent survey in the UK of 200 geriatric horses aged 15 or older reported that 94% had one or more ocular findings of note. The most common finding was vitreal degeneration (66.0%), followed by cataract (58.5%) and senile retinopathy (33.7%) [73].

Data collected in the chapter author's practice confirms the reported high prevalence of ocular disease in horses in a general practice population [74]. Of 5790 unique patients who were examined for some kind of medical problem over a 6-year period (May 2009 to May 2015), 668 (or 11.5%) were recorded as having an abnormal ocular condition. The fifteen most common ocular diagnoses coded in the practice records are shown in Table 3.3. Corneal ulcer was the most common diagnosis, representing over half of the recorded "ocular problem codes" and 6.6% of all recorded medical problems of any system, followed by acute unilateral eyelid swelling, a common, and usually minor, seasonal complaint. Other ocular problems recorded included blindness, uveitis, significant cataracts, and eyelid lacerations. These diagnoses are serious conditions, and it is notable that each of these conditions accounted for over 10% of the collective ocular problems and over 1% of all noted medical problems involving any body system.

Table 3.3 Conditions commonly diagnosed in a general equine practice. Data were collected by querying the ocular "diagnosis codes" and comparing them to the total number of diagnosis codes entered for all body systems in the practice medical record system of Genesee Valley Equine Clinic from mid-2009 to mid-2015. The practice employs five veterinarians performing general ambulatory work on horses of a variety of breeds and disciplines.

Condition (unique patients for each code; some patients had more than one problem)	Number of unique patients	Percentage ocular diagnoses (total = 668)	Percentage of all recorded problems (total = 5790)
Corneal ulcer (more total ulcers were treated as many patients had more than one ulcer)	380	56.9	6.6
Unilateral eyelid swelling	120	17.9	2.1
Blind, one or two eyes	119	17.8	2.1
Uveitis (recurrent or insidious)	118	17.7	2.0
Conjunctivitis	77	11.5	1.3
Significant cataract	70	10.5	1.2
Eyelid laceration/trauma	57	8.8	1.0
Corneal opacity	41	6.1	0.7
Immune-mediated keratitis	41	6.1	0.7
Glaucoma	37	5.5	0.6
Chorioretinopathy—alar pattern of depigmentation around optic disc	25	3.7	0.4
Iris abnormality	22	3.3	0.4
Chorioretinopathy—major band lesion	19	2.8	0.3
Multiple congenital ocular anomaly syndrome	19	2.8	0.3
Lens luxation (mostly posterior)	18	2.7	0.3

Table 3.4 Common misdiagnoses.

Condition	Often diagnosed as	Aid to make correct diagnosis
Stromal abscess	Acute uveitis	Presence of focal nonstaining opacity within stroma. Asymmetric limbal vascularization
Fungal keratitis	Bacterial keratitis	Cytology of lesion demonstrates hyphae with septate, parallel, branching walls
Indolent ulcer	Infected ulcer	Cytology that shows no inflammatory response and no infectious elements. May need to be repeated to be sure
Eosinophilic keratitis	Primary bacterial keratitis	Cytology demonstrates numerous eosinophils
Calcific keratopathy	Corneal scar	Debridement reveals tiny gritty plaques within sites of corneal opacity. Cytology shows basophilic staining crystals. Concentrated ethylenediamine tetra-acetic acid (EDTA) will remove superficial deposits
Single corneal stria	Glaucoma	Measurement of normal IOP
Orbital fat prolapse	Neoplasia in conjunctiva	Fine needle aspiration; microscopic analysis reveals fat globules, acellular character
Immune-mediated keratitis	Corneal scar	Multifocal punctate character of some cases; swirly, smoke-like geographic character of others. Opacity changes over time. Vascularization of immune-mediated keratitis cases is common

The finding that 2% of the horses noted to have medical problems were blind in at least one eye and 2% were noted to have recurrent or insidious uveitis is noteworthy, as the literature contains scant data relating to the prevalence of uveitis and blindness in the equine population. These figures should not be taken as representing the incidence of disease in the entire practice population, as they simply reflect the positive cases found amidst all horses in the practice noted to have medical problems, which represented a subset of all the horses that the practice cared for during the survey interval. However, the numbers of cases of intraocular inflammation and/or blindness are significant; they demonstrate that vision-threatening disease is quite prevalent in a general practice population that is similar to many practices in the USA. Additional information on uveitis and management of blind horses can be found in Chapters 8 and 17.

Diagnosis of many equine ophthalmic problems is straightforward. However, some conditions with very different etiologies can present with similar clinical features, and thus may be misdiagnosed. Table 3.4 lists conditions that require close scrutiny or diagnostic testing to arrive at the appropriate diagnosis.

Field therapy

When a horse presents with a painful or abnormal ophthalmic condition, the practitioner must institute treatment on the farm. Once the horse has been examined and diagnostic tests and imaging procedures are completed, a plan will be formed. Many acute problems can be treated with medication administered by

owners. However, many chronic or severe conditions require the clinician to perform one or more therapeutic interventions during the farm call.

Topical medication

Topical medication is designed to mix with the ocular tear film [75] and thus bathe the cornea and conjunctiva with medication. Some products penetrate the cornea and reach therapeutic levels inside the eye; others have limited corneal penetration [76, 77]. Liquid forms of topical medication are administered in the form of eyedrops. Ointment forms of medication are packaged in small tubes containing 3–5 g of product and are administered in small strips squeezed out of the tube onto the ocular surface.

Chapters 7–11 present additional information on ophthalmic pharmaceuticals for problems of the equine globe, and information relating to therapy for the range of problems that will be encountered in horses is found throughout the text. Practitioners should prescribe or dispense commercially manufactured products that are approved by the FDA whenever available. Some medications may need to be prepared by a compounding pharmacy because they are not available in a strength or formulation that can be administered to horses, but such products should **only** be chosen when there is no comparable commercial product available.

Farm personnel can usually treat gentle horses diagnosed with a condition that is not causing severe pain with topical medication. Ointments are often prescribed because these formulations have a longer corneal contact time in the tear film than eyedrops. Ointments may be easier for laypersons to administer than drops. However, some products are only available in eyedrop form, and some conditions, particularly those requiring lifetime or long-term therapy, are best treated with topical solutions, not ointments. A step-by-step guide for instructing an owner in a technique that will facilitate topical application of both ointments and eyedrops is shown in Box 3.4 (Figure 3.24).

Frequently, an owner will not use an entire tube or bottle of medication to treat a problem. The unused portion will end up in the stable medicine cabinet. Horse owners must be warned of the risks of using an old ophthalmic medication (usually a mydriatic, antibiotic or steroid) on a painful eye that has not been examined. This practice may delay appropriate diagnosis of an infectious or inflammatory condition, or even potentiate development of a serious infection.

Horses with fractious temperaments, or those suffering from painful conditions, can be difficult to treat with either drops or ointments because they resent handling of the periocular or eyelid region. Resultant blepharospasm or head-shy behavior can make treatment challenging or dangerous and much of the medication may never reach the eye. Thus severe ocular conditions like infected or melting ulcers are usually managed with the aid of an SPL system.

Box 3.4 Steps for applying ophthalmic medication to the globe.

1. Place the index finger on the crease of the upper eyelid.
2. Lift the eyelid by gentle upward pressure of the index finger.
3. Roll the finger holding the eyelid under the superior rim of the orbit.
4. Use the thumb to slightly evert the skin of the lower eyelid.
5. Apply a ¼-inch strip of ointment onto the everted lower eyelid margin with the other hand OR apply two drops of liquid medication to the everted lower eyelid margin with the other hand.



Figure 3.24 The upper lid should be lifted by touching the crease of the lid skin with the index finger, then resting the tip of the digit under the orbital rim. Ointment can be spread along the inner margin of the lower eyelid.

SPL systems

SPL systems are specialized ophthalmic catheters that allow the administration of topical liquid medication through the lumen of a long tube that runs from the base of the neck into the eyelid. Medication is injected into a closed port near the withers and propelled towards the eye with a bolus of air. The tube discharges the drug through a flared silicone footplate that rests against the conjunctiva of the upper fornix or lower cul-de-sac. The injected solution then mixes with the tear film to medicate the cornea. SPL systems are a necessary treatment tool for several reasons:

- Horses with painful eye conditions are fractious to handle and difficult to treat.
- Severely traumatized globes are at risk for rupture and may not tolerate close handling for topical treatment.
- Many topical medications are only available in liquid format. It is difficult to administer a precise dosage into the tear film of horses without an SPL.
- The amount of effort required to treat serious cases round the clock is intense. SPL systems make the therapy as easy as possible for caretakers.

Corneal ulcers infected with fungus or bacteria, corneal lacerations or deep stromal wounds, melting ulcers, stromal abscesses, and cases of severe uveitis are examples of conditions that are best treated with SPL systems.

SPL systems are supplied with a sharp 12-G solid metal insertion trocar that is swaged into the silcone tubing. They are sold by MILA International (Florence, KY, www.milaint.com, tel. 1-888-645-2468) and by Jorgensen Labs (JorVet, Loveland, CO, www.jorvet.com). The MILA kits are sold in 36- and 60-inch lengths. Both size kits use 5-French-diameter silicone tubing and have identically sized footplates. The tubing from either size kit can be shortened to accommodate small patients and foals, but larger draft and Warmblood horses will require the longer length.

Systems that require passage of the silicone tubing through the lumen of a 12-G, 3-inch needle for insertion through the eyelid are also available (Jorgensen Labs). Most clinicians find that kits with swaged-on solid trocars are the easiest and safest to insert.

Choice of eyelid for insertion of an SPL system

SPL systems can be inserted in the fornix of the upper eyelid or the cul-de-sac of the lower lid, depending on clinician preference, patient temperament, degree of inflammation present in the eyelids, and the location of the lesion being treated [78]. Both sites have proven effective and well tolerated (Figure 3.25A, B). Some clinicians favor the lower eyelid site because the nictitans prevents migration of the footplate and subsequent complications from footplate contact with the cornea [79]. Others favor the upper eyelid because of ease of insertion and the simplicity of securing the tubing to the face in a straight line towards the forelock. Both sites accomplish the goal of delivering medication to the tear film that bathes the globe surface.

Insertion of an SPL system in the upper eyelid requires auriculopalpebral and supraorbital nerve blocks. The clinician must take care to puncture the skin with the trocar at the deepest part of the fornix, just adjacent to the orbital rim. The trocar should pierce the skin directly so that tunneling of the tubing in the subcutaneous tissue does not occur; the manufacturer's label on the tubing near the footplate should be visible about 2 cm above the outer skin exit site after the footplate is snugged to the palpebral conjunctiva.

Insertion of an SPL system into the lower eyelid will require local anesthesia of the skin of the lower eyelid that rests against the nictitans, and care must be taken to assure that the puncture site for the tubing is close enough to the nasal canthus that the nictitans protects the SPL footplate from rubbing against the cornea. Many clinicians tunnel the trocar through the subcutaneous tissues of the ventral periorbit towards the facial crest when they install a lower eyelid SPL system; if this is done the label that is close to the footplate will not be visible and the tubing will emerge from the skin a few centimeters ventral to the site where the tubing entered the palpebral conjunctiva.

Preparation for insertion of an SPL system

Items listed in Box 3.5 are assembled and placed on a clean, elevated surface. The forelock and mane are braided into seven to ten long braids secured with tape or rubber bands. As the system may remain in place for several weeks, it is helpful to



(A)



(B)

Figure 3.25 (A) SPL systems can be inserted into either the upper or the lower eyelid. SPL system inserted into the fornix of the superior lid. The tubing path runs to the poll region between the ears. (B) SPL system inserted into the cul-de-sac of the inferior lid. The tubing path follows the halter crown piece to the top mane braid.

Box 3.5 Items needed to install an SPL system in the field.

- Bale table or other head support
- Tuberculin syringes (box quantity will be dispensed for treatment)
- 25-G, ⅝-inch needles (box quantity will be dispensed for treatment)
- 3-mL syringes
- Detomidine for sedation
- Lidocaine or mepivicaine for local anesthesia
- Topical anesthetic
- 2% povidone iodine/saline solution for regional prep
- 4 × 4 gauze pads for regional prep and to build port
- SPL kit (MILA International)
- Sterile gloves
- Male catheter cap
- Wooden tongue depressor (may be part of kit)
- White adhesive tape roll
- Small rubber bands to secure mane braids
- Nonabsorbable 2-0 or 1-0 suture, cutting needle
- 5½-inch Olsen–Hegar needle holder
- Headlight or focal light source
- Colored tape to label treatment syringes
- Spreadsheet to outline treatment schedule



Figure 3.26 SPL systems can be used in foals. Due to bilateral corneal ulcers, this foal had two SPL systems inserted. The tubing was passed through "tufts" of the short neonatal mane isolated with loops of porous tape, and the left and right injection ports were sutured to the neck skin near the withers.

secure the portion of each braid closest to the crest with a wrap of tape so that the braided hair does not loosen over time. The tubing will be threaded through the base of the braids near the neck crest to prevent it from catching on obstacles. If the patient is a young foal or horse with a sparse mane, a number of tufts of mane hair can be gathered into short "pigtails" and secured with thin sections of adhesive tape (Figure 3.26). "Tube guides" will have to be fashioned out of tape butterfly wedges that are sewn to the skin near the crest of the neck if a horse with a roached (shaved) mane presents for SPL insertion.

Horses are heavily sedated with IV detomidine for insertion. Very young or fractious foals will require short-term general anesthesia for safe insertion, and the procedure is carried out with the foal in lateral recumbency. Barn personnel must be aware that a procedure involving the insertion of a sharp trocar close to the patient's globe is taking place. All disturbances must be minimized and local traffic of farm personnel and animals barred during the brief period when the trocar is inserted under the eyelid. Good lighting is essential; the veterinarian may choose to wear a strap-on headlamp or set up an auxiliary light source.

Box 3.6 Steps to install an SPL system.

1. Have assistant braid mane and forelock into a series of pigtail braids.
2. Sedate patient to a level where head rests on bale table.
3. Prep eyelids and periorbital region with 2% povidone iodine.
4. Administer auriculopalpebral block (if upper eyelid is used).
5. Infiltrate anesthetic over target site for trocar puncture.
6. Administer topical anesthetic to corneal surface/palpebral conjunctiva.
7. Test patient tolerance of eyelid manipulation.
8. Administer additional sedation with or without additional local anesthetic if uncooperative.
9. Advance trocar to target site, using gloved finger or kit tube as guide.
10. Puncture eyelid with trocar and pull tubing through skin.
11. Make two to three "butterfly wings" of adhesive tape to fix tubing to face.
12. Secure each wing with four simple interrupted sutures (two per side).
13. Use trocar as a guide to weave tubing through mane.
14. Trim tubing to a length a little shorter than anchor braid.
15. Thread a 20–G, 1¼-inch catheter (from kit) into tubing end.
16. Cap catheter hub with male catheter cap to complete injection port.
17. Affix injection port to tongue depressor using gauze and white tape.
18. Secure injection port splint to mane braid using tape and suture.

Inserting and securing an SPL system

The insertion process is summarized in Box 3.6 and depicted in Figure 3.27A–C. The periorbit is cleaned with a solution of 1:50 povidone iodine/physiologic saline and local anesthetic is administered over the intended target site in the eyelid. Several drops of topical anesthetic are instilled onto the corneal surface. Tolerance of lid manipulation should be tested by insertion of a gloved finger towards the chosen exit site, with a finger of the opposite hand applying pressure on the skin over the fingertip.

If sedation appears adequate, the SPL trocar is guided into the desired site by reinserting the finger to the test site, this time with the trocar lying in the space between the gloved digit and the lid, but not projecting beyond the tip of the digit. Alternatively, the operator can use the short plastic tube that is supplied with the SPL kit as a trocar guide—if this method is chosen, the guide tube is passed under the eyelid margin and pushed against the orbital rim. The trocar is then inserted through the lumen of the tube and advanced to the target site.

The trocar is carefully advanced to the conjunctiva adjacent to the orbit and then pushed completely through the lid skin. The

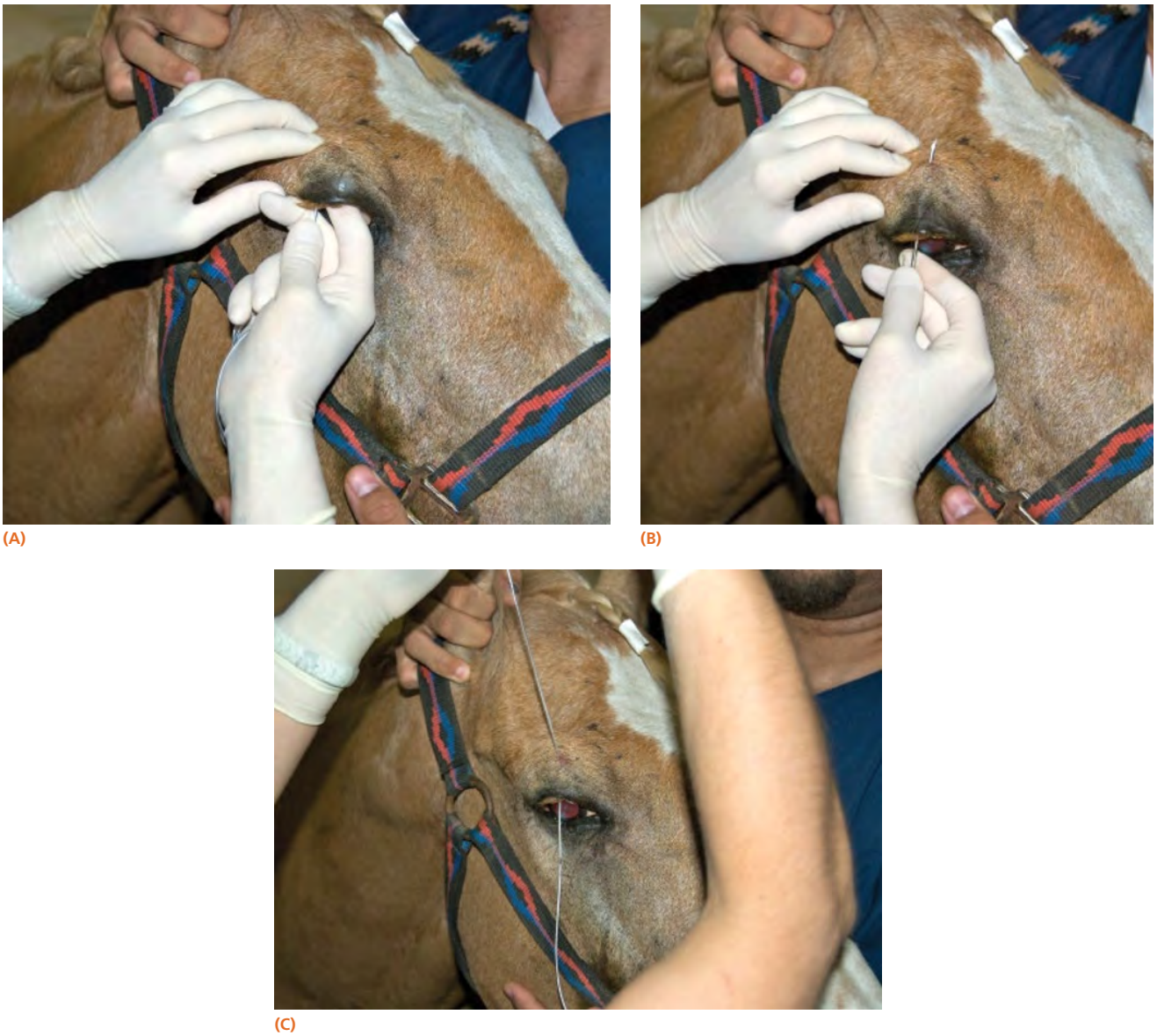


Figure 3.27 (A) The trocar must pierce the lid skin as deep into the fornix as possible. Prior to the skin piercing, the trocar is advanced to the intended exit site, with the surgeon using a gloved finger as a guide to prevent damage to the globe or lids. (B) The trocar is advanced to pierce the skin. (C) Once the lid is pierced, the trocar and the entire length of SPL tubing is pulled through the eyelid. Care is taken to assure that the slanted treatment footplate is snug with the oblique angle of the eyelid fornix.

trocar and attached tubing are then pulled through the pierced lid. Care is taken to assure that the slanted tube footplate is oriented parellel to, and snug with, the conjunctival surface of the oblique angle of the eyelid fornix or cul-de-sac. The sharp tip of the trocar should be capped with the plastic cover provided with the kit after it has been pulled through the eyelid for safety reasons.

The trocar will remain attached to the SPL tubing temporarily, to serve as a handy needle to thread the tubing through the braids or mane tufts along the neck. The trocar needle is uncapped and inserted under the forelock braid and the tubing is pulled though the parted hair of the braid base to emerge at the poll. The tubing is then threaded though the center of the most proximal braid next to the crest of the neck, then passed over the remainder of the braid, before being threaded "under" the next braid down the neck. As sequential braids are pierced, the trocar is used to pull the tubing through the braids. The tubing is woven through all the neck braids to the base of the neck. A stout braid near the withers is chosen for attachment of the injection port assembly. This braid will serve as an anchor for the injection port, and also as a "handle" for the owner to hold onto as medication is injected. Any excess length of tubing is then cut off and the extra tubing and trocar are discarded.

A 20-G, 1¼-inch IV catheter is carefully fed into the open tubing that remains next to the mane at the base of the neck to create the injection port assembly. A male catheter cap or similar injection port is threaded into the catheter hub to close the system.



(A)



(B)

Figure 3.28 (A) The trocar remains attached until the tubing has been threaded through preplaced mane braids or tufts. The tube is woven through successive braids until a secure braid is reached that has been chosen to anchor the injection port assembly. (B) The injection port is created by threading a 20-G, 1–1¼-inch catheter into the SPL tubing. The catheter is closed with a standard male injection cap. The catheter is then laid on a 3½-inch section of a wooden tongue depressor that was padded with gauze. The entire injection port is wrapped with porous tape and secured to the anchor braid with tape and suture.

The injection assembly (tubing, catheter, and cap) must then be protected and secured so that it will not come apart with repeated treatments or normal stable wear and tear (Figure 3.28A, B).

There are many ways to create a secure port system that will stand up to prolonged use. The following steps describe a method that has been used to create injection ports that have stayed in place for several months of field use:

1. Cut a wooden tongue depressor to a length of about 3½ inch. Wrap two or three 4 × 4 gauze squares around the flat surfaces of the wood. This will create a padded wooden splint for the injection port.
2. Lay the injection port (tubing, catheter, and cap) along the splint so that the cap lies on the splint about ½ inch from the distal end of the splint.
3. Wrap the entire splint plus injection port with porous tape to create a cocoon-like wrap that encloses the splint and tubing but exposes the injection cap.
4. Attach the splint to the anchoring braid with tape. Then take stout suture (embroidery thread or 1-0 or 2-0 suture) and sew the padded splint to the underlying braid with a few simple interrupted loops that pierce the tape and gauze on the underside of the splint, and affix the splint to a twist of the braided mane hair.

The length of tubing that runs from the eyelid to the forelock braid is then secured to the facial skin via a series of two or three "butterfly" stents made of short lengths of porous tape or duct tape that are folded over the tubing close to the eyelid and forelock (Figure 3.29A–C). As the tape "wings" may have to withstand stable wear and tear for several weeks it is recommended that each side of the tape wings be secured with two simple interrupted sutures of 1-0 or 1 nonabsorbable material, so that each wing is secured with a total of four sutures. Redundancy of the suture anchors will assure that the wings remain functional if one of the suture loops breaks between recheck visits.

Additional tips for secure placement of an SPL system that will hold up to repeated treatment and the field environment are shown in Box 3.7.

Medication delivery using an SPL system

The combined assembly of the mane braid and lavage injection port provides a convenient handle that can be gripped and steadied with one hand while the other hand is used for medication injection. Injection of medication is accomplished by infusing 0.1–0.2 mL of drug from a tuberculin syringe into the cap and catheter using a 25-G needle that is ⅝ inch long. The medication is then "chased" with approximately 1.5 mL of air that is injected **slowly** into the tube using a separate 3-mL syringe and 25-G needle (Figure 3.30). The air pressure delivers the drug into the tears. Delivery will usually be apparent when medication exits the tube, as the horse will react by tossing its head and the eye may tear slightly when the air bolus reaches the ocular surface. Tolerance of intensive SPL medication regimes can be improved by feeding the horse carrot bits or other palatable treats at each dosing session.

Treatment plans usually involve three to five medications per session, and most medications are clear in color. It is helpful to color-code syringes for the various medications with colored tape or label dots, and to keep each medication in a separate cup or bag so that the products do not become confused.



(A)



(B)



(C)

Figure 3.29 (A) Butterfly tape wings are fashioned from porous tape or duct tape to secure the tubing to the facial skin. The wing is closed around the tubing that exits the skin near the eyelid. (B) The first wing is sutured to the skin directly adjacent to the exit site, with four sutures placed for security. (C) Additional wings are sutured to the facial skin to secure the tubing as it traverses towards the mane.

A spreadsheet that provides check-off boxes for the administration of each medication, as well as detail of the time of administration, is essential for personnel treating the patient. Checking off boxes as treatments are completed will assure compliance and good communication between the team of treatment personnel. The sheet can also be used to clarify any storage requirements for medication, as some products may require refrigeration or protection from light.

Most horses with SPL tubes are treated with a number of drugs. The frequency of treatment varies with severity and chronicity of the problem but is generally from four to twelve times a day. Medication administration should be spaced 5–7 minutes apart for each bolus to minimize washout. The treatment schedule will involve a large number of tuberculin syringes and 25-G needles that are ⅝ inch in length. These items may be dispensed in box quantities for optimum compliance.

Box 3.7 Tips for managing an SPL system in the field.

- Cover horse's head with a fly mask or hood at all times.
- If horse goes outside, use "Sleazy" neck hood cover to protect tubing and port.
- Bind top of each mane braid with tape to keep braid tight.
- Fold tape wings over loops of tubing between mane braids to prevent drooping.
- Cover port with a plastic bag to keep it clean; replace as needed.
- Check tubing near insertion site often to assure that footplate is still snug.
- Check sutures on facial tape wings often; replace as needed.
- Go over medication process with owner; confirm dosage directions.
- Color-code medication syringes to avoid confusion of various products.
- Provide a daily spreadsheet with medication "check off" grid.
- Clarify storage precautions for all medications (refrigeration, protection from light).
- Observe patient tolerance of medication; coach owner as to restraint strategy.
- Encourage owner to use small treats to foster cooperative behavior.
- Check stall and/or paddock for hooks or objects that could snag SPL.
- Repair any breaks or leaks by splicing a 20-G catheter inside broken tubing ends.



Figure 3.30 The combined assembly of the mane braid and taped injection port provides a convenient handle that can be gripped with one hand while the other hand is used to inject medication. Note that the port assembly has been covered with a plastic bag for cleanliness; the bag is pierced to deliver medication into the cap.

Battery-powered, single-use medication pump devices (Infu-Disk (MILAInternational)) are available. These devices can be attached to the SPL tube singly, or several pumps can be hooked to the tube in parallel via "T ports" or "W adaptors" sold by the pump manufacturer. These devices infuse a small dose of a "cocktail" of medication through the tube at a continuous rate so that medication is constantly being mixed with the tear film. Eight different pumps are available that deliver solutions at rates ranging from 0.06 to 1 mL/hour. Depending on the rate of delivery, an individual pump will discharge its contents over an interval as short as 10 hours or as long as 7 days. Although the use of pumps is convenient, the cost of the devices, the lack of research demonstrating suitable drug combinations, and the propensity of horses to dislodge the pumps have resulted in their use only when traditional injections are not possible. Research has shown that such devices are not suitable for the delivery of voriconazole to treat horses with fungal keratitis, because the drug crystallizes within the silicone tube in conditions that approximate equine body temperature [80].

Protecting the SPL system

Quiet horses with SPL systems in place may tolerate solitary turnout in small paddocks if they wear a fly mask or other protective facial covering. Fly masks made of mesh screening are widely available from a variety of manufacturers, and recently a few goggle-type devices have become available for protection of the ocular region. The tubing that runs along the neck crest can be protected from snagging if the neck is covered with a common item of horse attire known as a "Sleazy." These stretchy, synthetic fabric articles are designed to protect the coats of show horses. They surround the neck and are held in place by a combination of a zipper that runs along the base of the neck and a strap that fastens around the axillary region (Figure 3.31A, B).

The injection port and splint assembly can be covered by a small plastic bag taped to the base of the assembly braid. The bag will protect the assembly parts if the horse rolls and will catch the injection cap if it becomes dislodged. Medication injections can be administered through the plastic bag by piercing it, and the bag can be replaced as needed.Alternatively, the splint assembly/injection port can be covered with a piece of aluminum foil that is unwrapped for treatment and replaced as needed.

Although rarely needed, hard cup hoods that cover the entire globe and orbit of the damaged eye are available in "left" and "right" models of various sizes (Eyesaver® (Jorgensen Labs)). Optimum air circulation will occur if the hard plastic ocular cup is perforated with several drilled 5- to 10-mm holes so it resembles a whiffle ball. The terrycloth "tear catchers" that snap into the inner aspect of the cup should be changed and washed daily, and a new gauze pad should be attached across the hood lumen.

Caution is advised when using hard cup hoods because severe periocular dermatitis can accompany their use (Figure 3.32A, B). Warm, humid environments may contribute to the development of ocular surface infections if the hood cups are not well maintained and properly ventilated. Hoods must be checked daily and discontinued or modified if dermatitis develops.

Management and repair of SPL systems

Properly managed SPL systems can remain in place for a month or more. While complications can occur [81–83], they can be minimized by daily inspection and simple management practices. The exterior of the catheter cap should be cleaned frequently with a wipe of 2% povidone iodine/physiologic saline



(A) (B)

Figure 3.31 (A) This horse's SPL system has been protected by a "Sleazy" neck cover and fly mask, facilitating safe solitary paddock turnout. (B) See-through ventilated goggle-like masks made of heavy-duty covers are a viable alternative to fly masks for protection of the SPL system and the ocular region. (*Source*: Mask in 3.31B an Equivizor™ mask courtesy of Protective Pet Solutions, Rocklin, CA, http://www.protectivepetsolutions.com/).



(A) (B)

Figure 3.32 (A) Clinicians who choose to use hard cup hoods as protective devices should drill holes in the hard plastic cups to improve air circulation. The hood must be cleaned and the "tear catchers" changed daily. (B) Severe periocular dermatitis can occur with hood use. The skin in contact with the hood should be checked at each change.

solution, and the cap should be replaced at 3- to 7-day intervals. The injection assembly can be retaped or re-assembled as necessary. The tape butterfly wings or plastic guides that secure the tubing to the face should be repaired and/or replaced if the sutures break. The SPL tube should be checked daily to assure that the footplate has not migrated. If the tube was inserted into the upper eyelid, the tubing that is visible above the exit hole in the eyelid should be checked to assure that the manufacturer's label is still visible.

The SPL tubing may occasionally develop small holes that leak fluid or the tubing may break if it becomes snagged on some item. As long as the hole or break occurs at least a few centimeters distal to the eyelid insertion site, these defects can be repaired by splicing a 20-G IV catheter into the lumen of the tubing at the break. The damaged tubing should be transected so that each end has a clean aperture with an intact margin. A 20-G, 1.25-inch catheter is threaded halfway into one end of the broken tubing. The catheter stylet is then removed and the plastic hub of the catheter is cut off. The other open end of the broken SPL tubing is then carefully slid around the remaining length of catheter and the tubing is sleeved onto the catheter tube until both broken ends meet. The spliced tubing section is then secured with tape around the center of the IV catheter, and sutured to the skin with a new tape butterfly that spans the spliced section (Figure 3.33A–D).

Removal of SPL systems

SPL systems should remain in place until the condition being treated is healed. If a clinician is uncertain about whether healing is complete, treatment may be stopped for several days with the tubing left in place. Findings noted at a subsequent recheck visit will reveal if the tubing can be removed, or if the treatment plan needs to be modified or medication needs to be resumed.

SPL tubes are easily removed in the standing, sedated horse by cutting the tube a few centimeters distal to the eyelid exit hole and removing all wings or guides that attach the cut section to the face. The tubing that remains attached to the footplate can be used as a "pole" to push the footplate away from the conjunctiva and into the fornix or cul-de-sac. Usually the footplate can be pushed enough that it will appear over the eyelid margin. From there it is easily removed (Figure 3.34). If the footplate does not emerge, a gloved finger can be inserted under the lid to "fish" for the loosened footplate. The remainder of the SPL tubing and the injection port assembly are easily removed from the mane by unthreading the woven sections, and cutting any connections that remain between the injection braid and the port assembly.

Occasionally the footplate will remain buried in the conjunctival tissues. In these instances, the exit site in the eyelid skin can be infiltrated with a small amount of local anesthetic, and a simple cut-down surgery can be performed around the tubing stump to remove the attached tubing remnant and footplate.

Subconjunctival injections

Subconjunctival injections are sometimes indicated to supply a concentrated dose of a therapeutic agent to the cornea or globe [84].

Horses requiring subconjunctival injections should be sedated. The procedure will be safest if the ventral mandible is supported on a bale table. The periocular region should be cleaned with 2% povidone iodine/physiologic saline, and topical anesthetic should be applied to the cornea and target sclera. Blepharospasm is prevented by the administration of an auriculopalpebral block. A sterile cotton-tipped applicator is used to apply additional topical anesthetic to the area chosen for injection (usually a patch of the bulbar conjunctiva over the dorsotemporal sclera). Access to the dorsal bulbar conjunctiva is facilitated by having the handler, who is standing on the opposite side of the horse, grasp the ear contralateral to the treated eye and gently roll the top of the head away from the clinician. The resultant oculovestibular motion will cause the globe to move ventrally within the orbit, exposing the dorsal sclera.

Subconjunctival injections are delivered in a volume that does not exceed 1 mL and are best administered with a 25- or 27-G, ⅝-inch needle attached to a tuberculin syringe. Prior to injection, a pair of Bishop-Harmon forceps is used to lift the target conjunctiva to test topical anesthesia and sedation. If no reaction occurs, the needle is then inserted under the conjunctiva with the bevel up, and the solution is injected (Figure 3.35). A proper subconjunctival injection slips the drug underneath Tenon's capsule just above the sclera, raising a bubble of conjunctiva containing the injected medication. Hemorrhage from the needle puncture is common, especially if the conjunctiva is inflamed. This complication (which can alarm observers) can be minimized by applying a sterile swab soaked with a few drops of 1:1000 epinephrine or 2.5% phenylephrine to the target conjunctiva prior to injection.

Standing surgery in the field

The majority of ocular problems treated surgically by ambulatory practitioners are done as standing procedures. Standing procedures can be separated into (1) simpler surgeries performed on the adnexa or cornea that require only sedation, subcutaneous regional anesthesia, and topical anesthesia (Box 3.8) and (2) more complex procedures of the nictitans, cornea, or globe that may require a very controlled surgical environment and/or retrobulbar nerve block to produce ocular immobility (Box 3.9).

The former set of procedures are readily performed in the field, but any condition that is anticipated to involve lengthy manipulation, sharp dissection, or very precise tissue handling is best performed in stocks in a clinic or hospital setting. The group of procedures that may require retrobulbar nerve block **must** be performed in stocks within a clinic setting that can provide optimal restraint, good lighting, and environmental control. Practitioners who do not have access to stocks should refer horses requiring more advanced standing surgery to

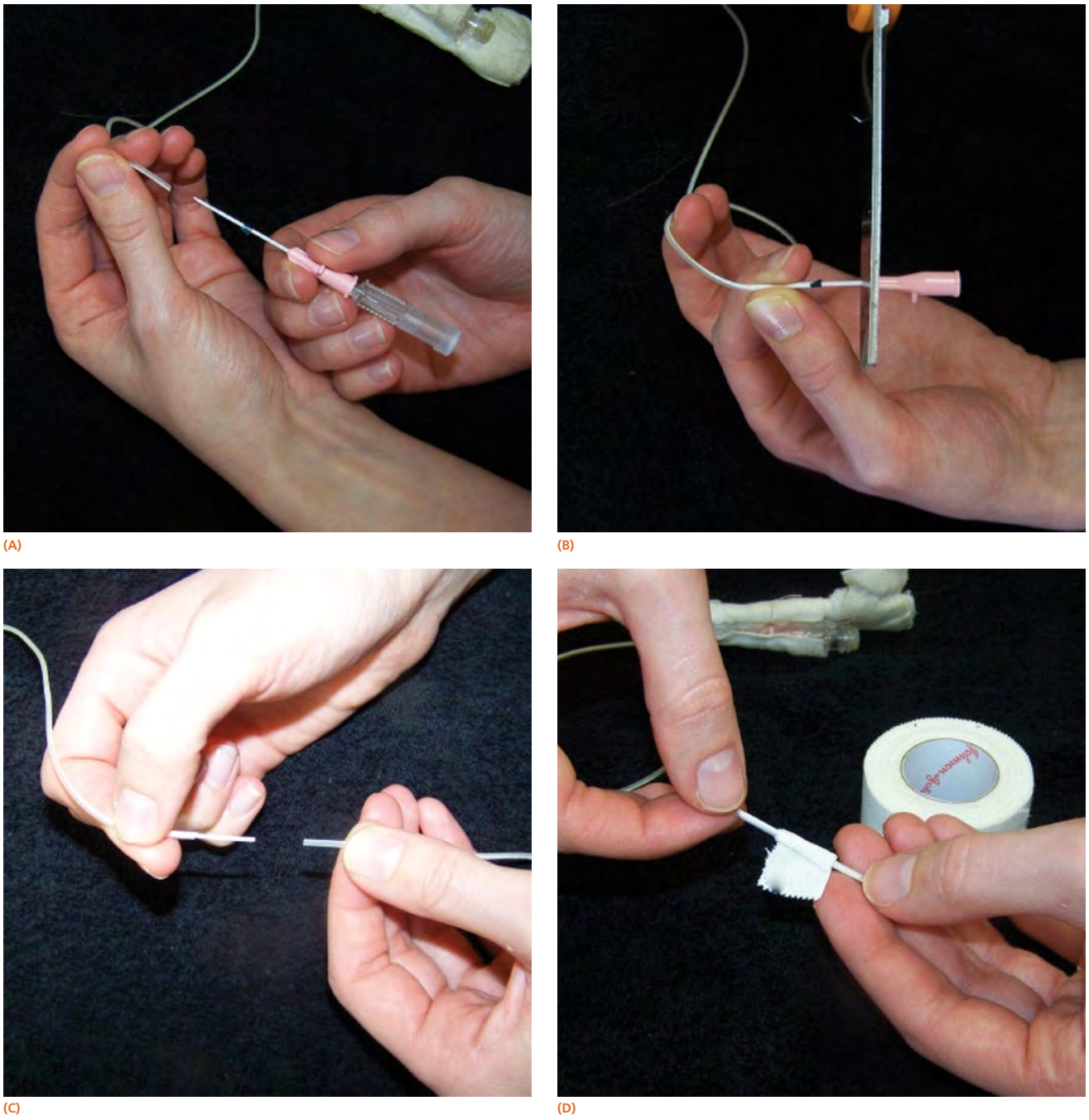


Figure 3.33 (A) Broken SPL tubing can be spliced. One end of the damaged tubing is threaded over half the length of a 20–G, 1¼-inch IV catheter. (B) The hub of the catheter is cut off. (C) The other end of the damaged tubing is carefully "sleeved" over the remaining section of the catheter until it meets the other transected end in the middle. (D) The spliced section is covered with adhesive tape. Additional tape wings are sutured to the face or neck skin adjacent to the spliced section to prevent the splice from being pulled apart.

appropriate facilities for safety and professional reasons. Box 3.10 provides a list of instruments that will be useful in many field procedures.

Recent review articles [85, 86] as well as material in various chapters of this text provide additional detail about common surgeries that are performed in the standing horse.

Retrobulbar nerve blocks

The horse has powerful retractor oculi muscles that retract the globe into the orbit in response to noxious stimuli. The retraction motion results in a sudden eversion of the nictitans across the nasal portion of the globe. Such globe and eyelid motion restricts surgical access to the nasal portion of the cornea and



Figure 3.34 SPL tubes are easily removed in the standing sedated horse. Once the tubing is cut a few centimeters away from the exit site, the remaining tube segment can be used as a "pole" to push the footplate away from the conjunctiva where it can easily be removed.

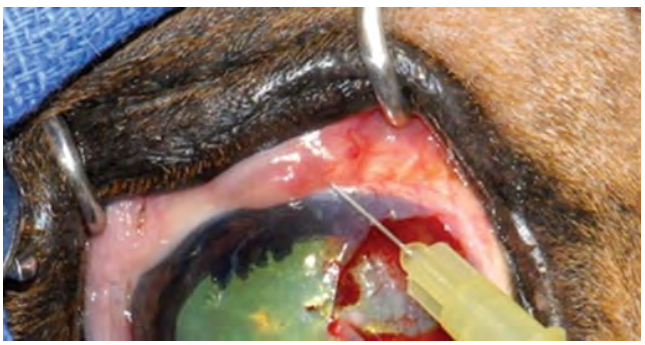


Figure 3.35 Subconjunctival injection in a horse after a superficial keratectomy. A 27-G needle is inserted under the dorsolateral bulbar conjunctiva. Up to 0.25 mL of fluid can be injected in one area, resulting in a balloon-like appearance to the bulbar conjunctiva.

Box 3.8 Standing surgical procedures that do not require retrobulbar block.

- Eyelid laceration repair
- Removal or biopsy of small eyelid masses
- Adjunctive therapy for adnexal neoplasia
- Conjunctival biopsy
- Corneal debridement
- Diamond burr debridement
- Superficial keratectomy

makes the globe unsafe to approach with sharp instruments. Consequently, certain standing procedures that stimulate globe retraction require the use of a retrobulbar block.

Box 3.9 Standing surgical procedures that may require retrobulbar block.

- Enucleation
- Third eyelid laceration repair
- Third eyelid removal
- Removal of superficial corneal foreign body
- Suture of small nonperforating corneal laceration
- Amputation of corneal flaps
- Aqueocentesis
- Intraocular injection
- Iris cyst laser ablation
- Laser cyclophotocoagulation for glaucoma
- Intraocular mass laser ablation

Box 3.10 Surgical instruments and sutures useful for standing field surgeries.

- Eyelid speculum
- Chalazion clamp
- Chalazion currettes
- Bishop-Harmon forceps
- Adson tissue forceps (rat tooth)
- Adson tissue forceps (smooth tooth)
- Curved Mayo scissors (small, medium)
- Curved Metzenbaum scissors (small, medium)
- Stevens tenotomy scissors
- 5½-inch Olsen–Hegar needle holder
- Castroviejo/Barraquer needle holder
- Scalpel handle (fits #10, #15 blades)
- Beaver scalpel handle (fits #64 blade)
- Small curved hemostats (mosquito)
- Small straight hemostats (mosquito)
- Large curved hemostats
- Absorbable suture (Vicryl), 5-0, 4-0, 3-0, 2-0
- Nonabsorbable suture (nylon), 5-0, 4-0, 3-0, 2-0

Retrobulbar blocks are described in detail in Chapter 1. They produce complete immobility of the globe by inducing paralysis of the retractor bulbi muscles. They also affect anesthesia of the optic nerve and the ophthalmic branch of the trigeminal nerve, so vision and tactile sensation are reduced. Horses that are restrained in stocks, sedated heavily, and subjected to both a retrobulbar block and various subcutaneous blocks that produce lid immobility and akinesia are good candidates for several ocular surgeries, including enucleation, removal of the third eyelid, selected microsurgical manipulations of the cornea, and a few of the simpler intraocular procedures. Standing ocular surgery may be desirable to reduce the risks of general anesthesia, especially in draft horses, geriatric patients, and horses with orthopedic disease. Standing surgery may also be chosen to treat selected conditions when the surgeon has access to stocks but not to an operating table.

Procedures that are done with retrobulbar blocks are aided by the topical application of a surface anesthetic (0.2–0.5 mL proparacaine HCl) and a surface vasoconstrictor (0.2 mL 2.5%

phenylephrine). These topical agents enhance surface anesthesia and aid in controlling hemorrhage from conjunctival blood vessels. If necessary, the agents may be reapplied in 15- to 20-minute intervals.

Head-mounted lighting and magnification aids

Any standing surgical procedure will be aided by focal illumination in the form of a headband-mounted lamp. Battery-powered headlamps containing multiple LED bulbs that strap on to the forehead with an elastic band produce very bright focal light that is helpful for procedures done at home stables. These inexpensive devices have very long battery life and can be purchased at outdoor stores. More costly examination headlights that emit xenon, solid-state, halogen, LED, or fiberoptic light are used in some clinic settings. These lights are powered by auxiliary electric sources or batteries, and can be purchased through a number of manufacturers and distributors.

Magnification is a helpful aid in many standing procedures. Practitioners choosing a head loupe should consider several factors when selecting a model, including resolution (the image should be clear from edge to edge), unit weight and comfort, field of view, degree of magnification, and depth of field. It is also important to choose a unit that is in focus at a comfortable working distance. Keeler binocular head loupes (www.keelerusa.com) are practical units equipped with frames that fit on the surgeon's head like a pair of eyeglasses. Models that deliver ×2.5 to ×5.5 magnification are available. A practical choice for field use is Keeler Model 2112-P-2012; it delivers ×2.5 magnification at a 46-cm working distance (Figure 3.35). Keeler Model 2113-P-2009 XL is a more powerful system suitable for more advanced microsurgical techniques; it delivers ×4.5 magnification within a 46-cm working distance. The K-LED model is equipped with 3-W LED lights that provide a light patch of up to 18,000 lux and is powered by a rechargeable battery. Additional head loupe units are made by a variety of manufacturers (Heine, Sheer Vision, Miltex, etc.) and are available through most veterinary distributors.

Preparation for standing procedures

Simple standing procedures done on the farm are facilitated by creative use of items at hand to fashion a "surgery room" within the barn. The site should be cleared of clutter, and available lighting should be optimized. Wind disturbance and local traffic of barn personnel and resident animals must be minimized. Head support of the patient at an efficient operating level is important. Creation of a "bale table" using four to six bales of hay, straw, or bedding covered by a clean cloth can make the difference between an "adequate" procedure and an excellent one. The surgeon should arrange the support so that the horse is comfortable, the head is stable, and a surface is available to use as an elbow rest if hand stability is needed. Depending on the height of the horse, the surgeon may perform the procedure standing on the ground, standing on a bale or stool, or sitting on a similar aid.

All items anticipated for the procedure(s) are assembled before the horse is presented for sedation and local anesthesia. A clean working table space for equipment should be created. Good lighting is critical for all standing procedures. Incandescent light sources do not provide sufficient illumination, so supplemental halogen or LED lighting is required. Many practitioners carry a small 250- to 750-W halogen work light (readily available at hardware stores) in their vehicles, and either hang the light on a nearby wall or raise it on a tripod base at a site where it will illuminate the operated eye.

Once the environment is readied for the procedure and all supplies are assembled, the horse is brought into the designated area for surgery. Sedation is administered and the periocular region is cleaned with 2% povidone iodine/physiologic saline solution. Choice of topical or regional anesthesia is dependent on the exact procedure planned, but most procedures require palpebral and supraorbital nerve blocks.

The following sections provide brief commentary on several conditions that are commonly handled in the field as standing surgeries (while other sections of this text provide additional detail on many of the procedures); the notes that follow are intended to provide perspective on how these conditions are dealt with in general practice.

Eyelid lacerations

Eyelid lacerations are a common field emergency, particularly in the summer months when insect irritation prompts horses to rub their faces on objects in the stall or pasture. The objects most commonly associated with eyelid tears are the metal handles of the 5-gallon water buckets that are ubiquitous in the stable environment. Horses who rub the periocular region on these thin metal bucket handles often get the eyelid margin trapped in the gap where the metal rod of the handle bends back in a "J" pattern to secure the handle to the bucket rim. When the eyelid is trapped in this small space, horses tend to pull back violently, tearing the eyelid margin.

Most eyelid lacerations are repaired on the farm, as emergency transport is rarely practical. Eyelid margin repair requires meticulous technique [87, 88], so all the aforementioned preparatory steps should be taken to stage an efficient operating space, and auxiliary lighting should be optimized. Solid head support is critical. Sedation may need to be heavy to assure patient cooperation. Local anesthesia will be required around the area that is damaged, but care should be taken not to overinflate the tissues that are torn. Excision of damaged lid tissue should be minimal, restricted mainly to removal of devitalized tags of skin and/or minor freshening of the skin margins that will be closed.

A two-layer closure is optimal. Sutures should be placed sparingly in the subconjunctival layer, and buried to assure that no portion of any knot or loop has the potential to abrade the cornea. Small-diameter suture is appropriate for both the subconjunctival and skin layers; a 4-0 to 5-0 diameter is practical in most field situations. Simple interrupted sutures are appropriate



(A) (B)

Figure 3.36 Eyelid lacerations are common field emergencies that are usually treated at the home stable. (A) This horse had a concurrent corneal ulcer; the SPL system was inserted in the intact lower eyelid at the same time the upper lid was repaired. (B) Cosmetic and functional results are excellent if meticulous technique is applied.

for both layers of the repair. The skin adjacent to the tarsal margin should be closed with a figure-of-eight pattern suture loop that apposes the torn tarsal margin exactly with no gap or step. Sutures should be removed from the sutured skin margins in 10–14 days. Post-operative treatment with systemic antibiotics and nonsteroidal medication for 5–7 days is advisable.

Cosmetic results of careful repairs of acute eyelid lacerations repaired promptly are usually very rewarding (Figure 3.36A, B). Horses that present with tears that are several days old can often be helped with a carefully planned revision surgery. More information on techniques of eyelid laceration repair can be found in Chapter 6.

Other field eyelid surgeries

Temporary correction of entropion

Temporary correction of entropion in neonatal foals is easily accomplished in the field as a short-term recumbent surgery. The foal should be sedated and placed in lateral recumbency with the affected eye up and the contralateral side of the face resting on a towel. The task of getting the foal to lie down may be facilitated by using the "thoracic squeeze" rope technique that has recently been shown to induce a state of somnolence in very young foals [89]. Local anesthetic is infiltrated below the lower lid tarsal margin, using a 25- or 22-G needle. Three to four vertical mattress sutures of 2-0 or 1-0 diameter are placed in the loose skin ventral and perpendicular to the tarsal margin to tighten the skin and evert the lower lid slightly. Care must be taken to assure that the suture tags do not have the potential to abrade the cornea. The tissue will usually gain enough subcutaneous fluid content and rigidity that entropion will not recur after the foal is about 10 days old, so the sutures can be removed at that time.

Temporary tarsorrhaphy

Temporary tarsorrhaphy is a procedure that is done in the field to achieve partial closure of the palpebral aperture by suturing the eyelid margins in apposition. The procedure is used to provide a mucosal surface to appose an indolent ulcer, to protect the cornea when a horse cannot blink due to facial nerve paralysis, or to reduce eyelid movement after a revision procedure. One to four horizontal mattress sutures of 3-0 to 5-0 nonabsorbable material are inserted along the eyelid margin, starting towards the lateral canthus. A gap is left at the nasal canthus to allow tears to drain. The sutures are pre-placed so as to split the eyelid, with the suture exiting the upper and lower eyelids at the level of the meibomian gland openings. Short stents made of rubber bands or IV tubing are threaded along the horizontal paths of the suture loop to stabilize the eyelid apposition.

Nictitans removal

Nictitans removal is often indicated for treatment of third eyelid neoplasia (Figure 3.37). The entire third eyelid can be removed in the standing patient by amputation of the gland and associated mucosa, including a wide section of mucosa that surrounds the central T-shaped cartilage [90].

Retrobulbar blocks are recommended for maximum restraint and patient comfort, but are not performed by every surgeon.



Figure 3.37 Neoplasia is the most common indication for removal of the nictitans. This horse suffered from a large squamous cell carcinoma of the leading edge of the third eyelid.

Patients who are not treated with retrobulbar block must receive complete regional anesthesia of the conjunctiva of the entire nictitans and adjacent palpebral conjunctiva. This is done by combining topical anesthesia (0.5% proparicaine sprayed onto the corneal and nictitans surface) with infiltration of the gland mucosa with 1–3 mL of lidocaine or mepivicaine. The patient should be well sedated to allow safe infiltration of local anesthetic into the target mucosa with a 25-G needle attached to a tuberculin syringe.

Amputation proceeds along the thin layers of mucosa that are closest to the globe, and may be facilitated if the conjunctiva that bridges the connection from the nictitans to the globe is clamped with curved hemostats that will aid hemostasis and serve as a guide for dissection. As the tissue sectioning proceeds, the gland is further everted so that the tissue is severed as far below the cartilage as possible. Closure of the conjunctival layers that remain in the fornix is desirable to prevent post-operative herniation of orbital fat. If the conjunctiva in the fornix is not closed, the orbital fat that is attached to the base of the gland tissue that can easily be accessed should be amputated. One study has been published comparing the outcome of cases that received general anesthesia versus standing surgery and those that had the conjunctiva sutured with those that did not. Complications were minimal in all groups and the outcomes were similar [91].

Repair of nictitans lacerations and resection of small tumors of the third eyelid are procedures that are facilitated by retrobulbar block when done in a standing patient. The block will render the gland immobile, enabling precise manipulation of the target tissues. These surgeries require suturing of the gland mucosa. Absorbable suture of fine diameter (5-0 to 7-0 Vicryl or Dexon) is used to repair the lid mucosa and great care is taken to assure that no suture tag abrades the cornea. Further description of surgical procedures involving the nictitans is found in Chapter 6.

Conjunctival biopsy

Conjunctival biopsy is indicated for investigation of masses or patches of conjunctiva with abnormal appearance [92]. The procedure can be performed in the standing, sedated horse with topical anesthetic. Hemorrhage can be minimized by applying a few drops of 2.5% phenylephrine to the site prior to tissue excision. Palpebral and frontal nerve blocks are helpful as they eliminate blepharospasm.

Surgical access to various sites on the bulbar conjunctiva can be aided by tipping the head of the horse to stimulate oculovestibular globe motion. Rolling the top of the horse's head away from the surgeon exposes the superior bulbar conjunctiva, and rolling the top of the head towards the surgeon exposes more of the inferior half of the globe. Suturing of the parent conjunctiva is rarely necessary as the mucosa heals well by second intention.

Corneal debridement

Corneal debridement is the most common standing ophthalmic procedure performed in the field. It is done for several reasons:

- to obtain diagnostic surface cellular samples of chronic or deep ulcers;
- to remove debris that is present within the ulcer bed;
- to stimulate epithelialization, and, in some cases, vascularization.

Debridement often begins with the procurement of culture and cytology samples; preparation for all these procedures is similar. Debridement tools that are also suitable for obtaining cytology samples include the blunt end of a sterile scalpel blade (the sharp end of the blade will remain encased in the foil wrapper; any size Bard Parker blade except a 22 blade is usable) and Kimura platinum spatulas. Cotton-tipped swabs are **not** used to obtain cytology samples, but are suitable for fine debridement of corneal defects.

Blunt-blade debridement is followed by lighter debridement of the lesion with a series of sterile cotton swabs (Figure 3.38A–D). Shallow lesions that are not being sampled for cytology may be simply debrided using swabs alone. Each dry swab is stroked in a firm but gentle "paintbrush" motion across the damaged region of the cornea, and the margin of the defect is then circled with the swab tip. The dry swab applies enough friction on the corneal surface to loosen poorly attached epithelium and roll it away from the underlying stroma. Swabs are replaced as they become soaked with tears and lose frictional action.

The size and character of the corneal defect will dictate the number of swabs that are used and the amount of corneal debris removed. Gentle debridement should proceed as long as epithelium peels away easily. Debridement of small superficial lesions surrounded by very loose epithelium will create a much larger defect than the original ulcer.

Corneal debridement with a motorized diamond burr

Recently, equine ophthalmologists have reported good clinical outcomes for selected cases that are debrided with a handheld, battery-operated tool known as the AlgerBrush II (The Alger

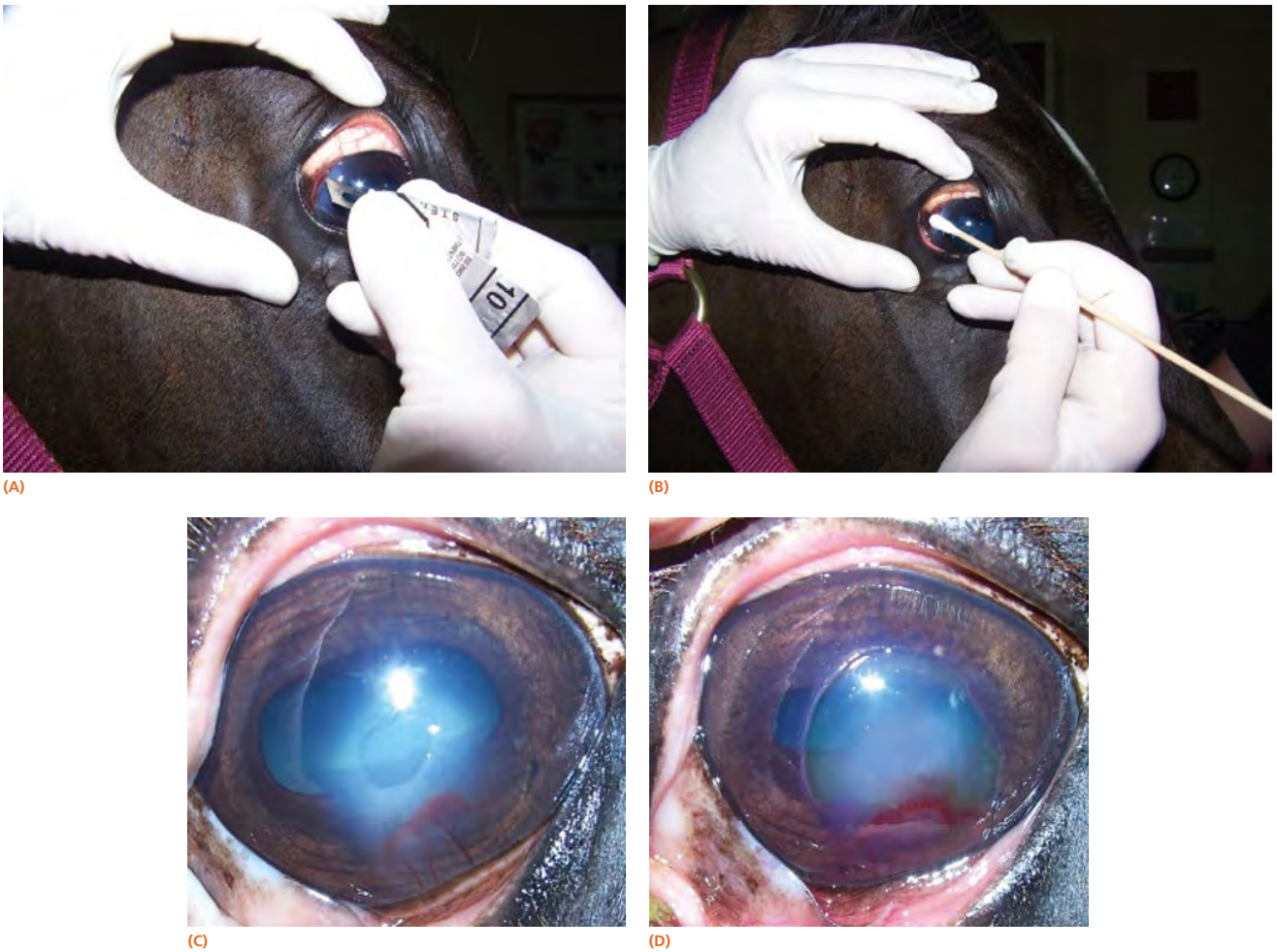


Figure 3.38 Debridement is a simple procedure that is often performed in the field. (A) Corneal debridement with a blunt metal blade is performed to obtain cytology samples, remove inflammatory debris and dead cells, and stimulate vascularization. (B) Finer debridement is performed with a series of sterile, dry, cotton-tipped swabs. (C) Pre-debridement image of an indolent corneal ulcer that had been present for 10 weeks. (D) A region of stroma more than five times the size of the original ulcer was exposed when the epithelium surrounding the ulcer was debrided. The ulcer went on to fully epithelialize within 3 weeks.

Company, Inc., Lago Vista, TX, www.algercompany.com). The machine motor is housed in a small cylinder the size of a miniature flashlight that is attached to a rotating chuck. The chuck shaft is attached to a spherical burr that is coated with fine-abrasive diamond-dust chips. The machine was originally developed to remove "rust rings" in the human cornea. The burr that is used in equine cases was developed to treat pterygium in people.

Diamond burr debridement is a simple, well-tolerated procedure that can be done under local and topical anesthesia in sedated horses (Figure 3.39). Debridement involves turning the motor that rotates the burr on and applying the revolving burr to the target region of the cornea. The procedure is completed in a matter of seconds.

At present the only indications for the procedure supported by published research are nonhealing corneal ulcers that have been present for a week or more that do not show any evidence of infection [93]. Cases of corneal calcific keratopathy and cases of eosinophilic keratitis have also been anecdotally reported to respond well to this therapy. It is important to perform cytology on cases under consideration for diamond burr debridement as the use of this tool in a case of primary infectious keratitis is contraindicated.

Burdock bristle keratopathy

Horses that live in temperate climates where burdock is a common pasture weed frequently present with burdock bristle keratopathy. The tiny microscopic pappus bristles (which provided the inspiration for the inventor of the adhesive hook and loop system known as Velcro) can become embedded in the cornea or conjunctiva, causing surface irritation, ulceration, and chronic discomfort. Horses suffering from this condition may also have multiple burdock thistles entangled in the mane or



Figure 3.39 Diamond burr debridement is a simple procedure that is indicated for indolent ulcers, eosinophilic keratitis, and calcific keratopathy.

tail, and inspection of the pasture will reveal weedy patches, often along the fence line, where the larger plant is established.

A typical case presents with a vascularized ulcer in the inferonasal cornea, surrounded by an opaque section of inflamed stroma. The nictitans mucosa apposing the corneal defect is usually swollen and inflamed. Atypical cases may present in other regions of the cornea as small focal regions of superficial vascularization with or without a staining epithelial defect. Discomfort is mild to moderate, and the horse may have been symptomatic for several days to weeks. The tiny plant barbs are rarely visible, even with slit-lamp magnification. However, the condition should be suspected if the mane is tangled with bristles or the conjunctiva on the nictitans mucosa facing the globe has a cobblestone appearance. Frequently, vessels on the nictitans will show focal hypertrophy, with the most intense vessel pattern pointing to the region where the bristles are probably embedded (Figure 3.40A–C).

Treatment involves removal of the embedded pappus bristles. Access to the surfaces that contain the bristles requires sedation, head support, and good topical anesthesia. If the nictitans is involved, it must be everted with a small hemostat so that the inner surface can be inspected and debrided.

Treatment is followed by topical application of a broad-spectrum antibiotic ointment and a mydriatic for several days. Resolution is confirmed when the ulcer bed heals, vascularization fades, and the horse becomes comfortable. A few cases require repeat treatment for full resolution.

Corneal foreign bodies

Horses occasionally present with a foreign body embedded in the cornea [94]. Each case must be assessed carefully to decide if it should be referred or if the horse can be treated in the field. Removal of a corneal foreign body can be attempted if the object appears to be lodged in the epithelium, or the upper third of the stroma. If the foreign body is lodged in the nasal quadrant of the eye, retrobulbar block may be required to avoid nictitans repulsion and allow full access to the damaged region of the cornea through globe immobilization.

A simple field technique that may dislodge a superficial foreign body is vigorous lavage of the entry site with sterile saline or eyewash using a spray device fashioned from a 12-mL syringe attached to the hub of a broken-off 25-G needle [95]. A Kimura platinum spatula, 20-G needle, or foreign body spud may also be used as an aid to remove the foreign body.

The surgeon must be aware that prolonged efforts at foreign body removal may actually drive the object deeper into the cornea. If simple manipulation fails to dislodge the object, the patient must be referred for removal under general anesthesia. Further information on corneal foreign body removal can be found in Chapter 7.

Corneal lacerations

Horses may present with corneal lacerations where some kind of trauma has incised a flap of epithelium attached to stroma (Figure 3.41A, B). Some superficial corneal flaps may be treatable in the field by amputation of the flap [96]. This will require heavy sedation, local anesthesia for eyelid akinesis, and topical anesthesia. A retrobulbar block may be needed for access to any part of the cornea that is close to the nictitans, and may also be desirable to immobilize the globe for safe and accurate amputation. The resultant defect is then treated with topical therapy appropriate for a deep ulcer.

Deep flaps that compromise more than 50% of the stromal thickness are best treated at referral facilities. Similarly, horses that present with deep lacerations that require suturing to close the corneal defect should be referred to a facility where the horse can be treated with appropriate microsurgical techniques under general anesthesia. See Chapter 7 for more information.

Aqueous paracentesis

Aqueous paracentesis is an advanced procedure that may be indicated for obtaining samples for culture and cytology, protein measurement, antibody titers, and polymerase chain reaction (PCR) in cases of intraocular inflammation or infection. It can also be used to instill doses of tissue plasminogen activator (TPA) into the anterior chamber to treat horses that present with excessive fibrin clots in the anterior segment.

The procedure is not without risk, so aqueous paracentesis is rarely performed in the field by general practitioners. If performed in the standing horse, the technique requires sedation, topical anesthesia, and, in most cases, a retrobulbar block. See Chapter 8 for more detail on the procedure and its risks.

Enucleation

Standing enucleation can be performed on selected patients with tractable temperaments [97, 98]. Standing surgery is the preferred option for very old patients, large draft horses, tiny



(A)

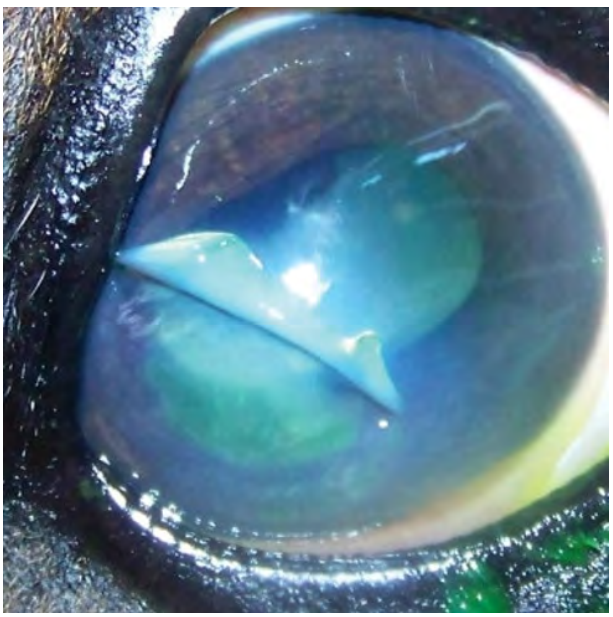


(B)

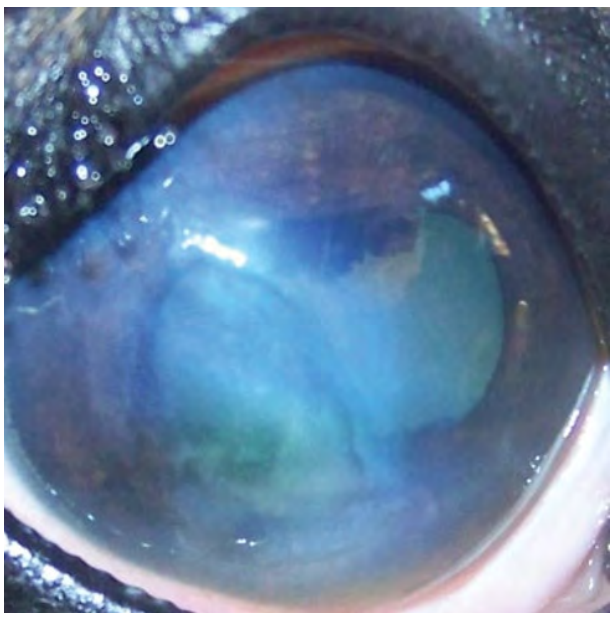


(C)

Figure 3.40 Tiny burdock pappus bristles can become embedded in the cornea or conjunctiva, causing ulceration and keratitis. (A) Burdock thistles are a common pasture weed in northern temperate regions. (B) Horses suffering from burdock bristle keratopathy often present with multiple thistles tangled in the mane or tail. (C) The prominent vessel suggests bristles are probably embedded in the nictitans and/or apposing corneal epithelium.



(A)



(B)

Figure 3.41 Corneal flaps involving less than 50% of the stroma may be amenable to amputation. (A) Acute corneal flap laceration in a 7-year-old gelding. (B) The flap was amputated with iris scissors and treated as a deep ulcer. It healed with a small region of fibrosis.

ponies, and other patients that are at risk for general anesthesia, but in recent years standing enucleation has been performed with increasing frequency at many institutions on other patients as well [99]. Safety concerns for both the surgeon and the patient dictate that standing enucleation be performed **only** when the patient is restrained in stocks. Standing enucleation is the most common indication for performing a retrobulbar block.

Referral

Practitioners who perform comprehensive examinations on all their patients, respond to ocular emergencies in a timely fashion, and master basic diagnostic tests, therapeutics, and a few simple standing surgeries can handle a large segment of the ophthalmic conditions that present in the average practice population. However, very serious or chronic ocular conditions will also present. These cases should be referred if there is a specialist who practices at a facility located within a reasonable distance. Examples of conditions that may benefit from referral include facial trauma that compromises eyelid function or globe position in the orbit, neoplasias affecting the ocular surface or adnexa, and corneal ulcers that are deep, melting, or chronic. Horses who suffer from recurrent uveitis, glaucoma, or immune-mediated keratitis may also be helped by evaluation at a referral institute.

In addition to delivering the horse to clinicians who are highly skilled in evaluating and treating ophthalmic problems, referral assures that the horse will have access to the advanced imaging, testing, and surgical options provided within the facility. Referral also sends the horse to a site where staffing is sufficient to deliver round-the-clock therapy. Success rates for referral cases are highest if the horse is referred early in its clinical course.

Unfortunately, clinicians are often presented with severe problems that would benefit from referral, but the owner of the horse declines due to economics or logistics of transporting the horse to a faraway facility. In such instances, clear communication about the severity of the problem must prevail, and the clinician is justified in presenting a guarded prognosis.

Ocular problems in working equids in the developing world

Please see the online material for further discussion on this topic.

Additional content

The book companion website at

www.wiley.com/go/gilger/ophthalmology

includes additional text and figures that are not in the printed book or E-book.

Please see the "**About the companion website**" page at the start of the book for details on how to access the website.

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CHAPTER 4

Ophthalmic diseases of foals

Marta Leiva and Teresa Peña

Introduction

The eye of the newborn foal is morphologically and functionally different from that of the weanling, yearling, or mature horse. Knowledge of the biological ocular anomalies at this early age is essential for recognition and understanding of different diseases in neonatal ophthalmology.

Ocular disorders of horses, although not as common as in dogs and cats, encompass a wide variety of conditions that may be congenital, inherited, or acquired. Whereas severe and vision-threatening congenital disorders are frequently diagnosed at sucklings, mild congenital conditions of the eye and adnexa may first be diagnosed after weaning or in adulthood. An understanding of the hereditary basis of ocular congenital abnormalities in foals is important for the equine practitioner in order to issue the most appropriate breeding advice. Acquired conditions that occur a few weeks after birth may be misinterpreted as congenital in origin if the examiner is unfamiliar with the normal neonatal eye, ocular development, or how other existing conditions may affect the eye. The purpose of this chapter is twofold: (1) to provide diagnostic tools to enable more accurate diagnoses of the eye disorders in foals, and (2) to review ocular disorders most commonly seen in foals with the aim of providing diagnostic and therapeutic approaches to treatment, as well as breeding advice, if applicable.

Vision in foals

Equine ophthalmologists may be asked to evaluate the visual capability of a newborn foal (less than 21 days of age). Many owners want to be sure that the investment in raising a foal will conclude with a horse that can be used for a specific purpose. Performing a complete ophthalmic examination is the first diagnostic step when evaluating a foal where visual impairment is suspected. Neurophthalmology has to be thoroughly evaluated as well as biomicroscopy, tonometry, and funduscopy in order to assess any primary ocular abnormality as the etiology of the visual impairment.

Vision is a complex mechanism in which the retinal stimuli are processed and interpreted by the brain, allowing visual perception. Although it has been well documented in small animals and to some extent in adult horses, specific reports on visual acuity in neonatal horses are lacking. Many different factors affect visual perception, which differs among species and individuals. Early maturation of the retina is considered one of the more important of those factors, showing differences between species that are mature and mobile at birth (precocial), and the ones that are incapable of moving around on their own after being born (altricial). In altricial species, such as man, postnatal retinal maturation is crucial for determining visual perception in pediatric patients, whereas in precocial species like the horse, the eye and vision is considered nearly mature at birth. Therefore the absence of specific studies regarding retinal and visual development in equine neonates leaves us no option but to consider that the eye and vision are mature in normal-term foals (see Chapter 12 for more details on equine vision).

In the dog and the cat, photoreceptors (rods and cones) continue their differentiation during the first weeks of life, but, unfortunately, although suspected, no similar data have been reported in foals [1, 2]. Consistent visual stimulation during neonatal life is required for proper development of the visual pathways. Deprivation amblyopia, described as reduced vision secondary to unexposed brain to visual stimulus early in life, although not documented in the horse, should be considered when treating with congenital cataracts and other anterior segment blinding disorders [3]. To avoid this possibility, cataract surgery prior to 6 months of age has been recommended in newborn foals with complete bilateral

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congenital cataracts. Chronic cycloplegia (i.e., topical atropine administration) has been suggested to cause deprivation amblyopia and result in poor vision, even if the eye is returned to a functional status [4, 5].

Special considerations for ocular examination in foals

The eye of the newborn foal (less than 21 days of age) is morphologically and functionally different from that of the mature horse. Knowledge of the biological ocular anomalies at this early age is essential for recognition and understanding of different diseases in neonatal ophthalmology. At birth, the foal's globe and adnexa are fully developed, showing open eyelids [6, 7].

Neonatal ophthalmic examination is very important to assess vision and any congenital or acquired abnormality that could alter the foal's performance. Healthy newborn foals should be examined within 12–36 hours of birth. Ophthalmic examination includes a thorough evaluation of the ocular and periocular structures in a quiet dark stall [7]. The examination is generally well tolerated if performed with an assistant cradling the foal's chest and tail, and the examiner steadying the head (Figure 4.1). Excessive foal restraint is not appropriate. Patient cooperation will be optimal if the foal and mare are close together and/or maintain visual contact. The foal should be positioned towards the mare's head to minimize her anxiety, with the mare restrained by an assistant or turned loose if only one assistant is available. Very restless foals can be better examined by placing them in a corner against the stable wall [8]. When examining sick postrated foals, a complete examination of one eye should be performed first before turning the foal body position for evaluating the second eye.

Neuro-ophthalmology

Although the normal timing for appearance of a positive menace response was reported to be 5 days of age in one study [9], the majority of studies agree that a menace response develops later, such as 14–16 days after birth [10–13]. This period can be even longer in foals with post-natal problems [6]. Furthermore, menace response, although present in 14- to 16-day-old foals, has been described as diminished until the foal is several weeks old [6, 14]. Dazzle reflex is present from birth, and, together with the observation of the foal ambulation, is useful in determining, to a certain degree, the visual status. A very bright light source is recommended to assess this reflex [7]. Newborn foals have sluggish and incomplete pupillary light reflexes (PLRs) for the first several days of life [13].

Whereas some authors believed that the palpebral reflex in newborn foals is slow and incomplete, yielding lagophthalmos [15], others found consistently normal palpebral reflexes (complete and fast) in 1-day-old healthy foals [13]. Healthy neonatal foals have reduced corneal sensitivity when compared to adults, and this reduction is even higher for sick newborn foals [16].

At short-distance examination, the globe has a mild ventromedial orientation at birth that gives neonates a slight downward gaze. This finding typically resolves after 2–4 weeks [7, 13].

Ocular adnexa

A healthy newborn foal may exhibit droopy eyelids and bilateral conjunctival congestion, the latter being maintained for the first 3 weeks of age [13]. Unilateral and bilateral conjunctival hemorrhages have been described in healthy newborn foals, showing a diffuse bright-red appearance, being dorsally located, and extending to the corneoscleral junction. Hemorrhages did not have any effect in the short-term vision, and resolved spontaneously and completely within 10–14 days [13, 17].



(A)



(B)

Figure 4.1 Ophthalmic examination in a newborn foal. (A) In healthy foals, the examination is performed with an assistant cradling the foal's chest and tail, if needed, and the examiner steadying the head. (B) Conversely, in sick foals, the examiner should adapt to the foal's decumbence position, while an assistant gently holds the head. Whenever possible, the foal should be examined near the mare to minimize their anxiety.

Anterior segment

The normal cornea of the newborn foal is clear, oval, and broader nasally, and its corneal thickness is thinnest at the center. The scleral shelf or overhang is more prominent dorsally and ventrally, which makes visualization of the angle more difficult. Bilateral perilimbal vascular ring, associated with diffuse corneal edema, has been reported in 1-day-old foals, without evidence of corneal ulceration, pain, or other intraocular abnormalities. Although physiological corneal neovascularization has been described in some species, in horses it has been rarely reported [13, 18]. The most probable etiology for this condition is the insult of the amniotic or allantoic fluid over the cornea during the last days of gestation. Clinical signs resolved completely within 10 days without topical treatment

The iris may be slightly gray in color and have a round pupil (Figure 4.2), acquiring its typical horizontal elliptical shape by the first month of age [8, 13, 14]. In addition, lens suture lines may be very prominent, and should not be mistaken for cataracts [13, 14, 19–21].

Tonometry

Tonometry in foals can be performed by means of rebound (TonoVet® (Icare Finland Oy, Helsinki) or applanation tonometry (Tono-Pen Vet® (Reichert Inc., NY) (Figure 4.3). Obtaining consistent and accurate reading with either instrument can be challenging in healthy foals with ocular conditions. The small disposable probe and reduced contact time of the rebound tonometry are desirable, especially when healthy naughty foals are examined (see Chapter 1). Conversely, in



(A) (B)

Figure 4.2 Appearance of the neonatal pupil is often round in contour (A) compared to the adult one (B).



(A) (B)

Figure 4.3 Tonometry in the foal. (A) Applanation tonometry (Tono-Pen XL®). (B) Rebound tonometry (Tonovet®). Note the smaller size of the probe touching the cornea.

sick foals, especially if they are recumbent, the use of the rebound tonometer may be challenging, as the probe has to be parallel to the ground and perpendicular to the ocular surface. Normal intraocular pressure (IOP) values reported for newborn foals are similar to those generally accepted for adults [13, 21].

Common funduscopic findings

The ocular fundus of the newborn foal is similar to the adult one, although some particularities need to be enlightened. The optic nerve head (ONH) usually appears rounded in shape and pale to deep pink in color. Bundles of axons traveling to the optic disc may be seen as light-gray streaks in the peripapillary area [10, 13, 22]. Mild to moderate bilateral **ONH congestion** has been reported in newborn foals aged 1–16 days [13, 23]. This biological anomaly has been associated also with an increase in intracranial pressure during delivery [23]. In addition, multifocal punctate to splash-like hemorrhages can be seen at the tapetal area during the first days of life. Bilateral presentation for this condition is more frequent. Both ONH congestion and retinal hemorrhages diminished with aging without treatment and were not associated with sequelae [13, 17]. Small punctual hemorrhages might also be seen on the ONH in some newborn foals. The etiology for these ocular fundus small hemorrhages has not been clarified yet, but birth trauma is suggested [23, 24].

Remnants of the **hyaloid artery** are a common finding in foals younger than 3–4 months of age, although complete hyaloid artery reabsorption may take longer in some foals (6–9 months) [13, 20, 21, 25, 26]. Remnants appear as a white or blood-filled line running from the central papilla through the central vitreous (Figure 4.4) [13, 14, 17].

Complementary test findings

Low tears secretion, reduced blinking rate, and increased corneal exposure have been reported in newborn foals, increasing the risk for corneal disease [11]. Therefore use of bilateral fluorescein dye application is indicated in both basic and complete ocular examinations in neonatal foals (see Chapter 1).

Eyelid disorders

Congenital eyelid diseases

Entropion

Prevalence

Entropion, or inversion of the eyelid margin, is one of the most common ocular congenital abnormalities in foals [14, 27], ranging from 4% in healthy foals [17] to 11.4% in sick foals [21]. It can occur both as a congenital defect and as an early acquired problem, with the latter far more frequent [28]. The inheritance of congenital entropion is unknown, although suspected in Thoroughbreds [24, 29] and Quarter horses [30].

Clinical appearance

Entropion can be unilateral or bilateral, and usually involves the lower eyelid, although the upper eyelid may be affected also [31]. Typically, clinical signs develop when facial hair contacts the cornea and conjunctiva, thereby stimulating the trigeminal nerve. The infolded eyelid margin may cause subsequent lacrimation and blepharospasm, inducing conjunctivitis, corneal ulceration, and keratitis (Figure 4.5). Conversely, corneal or conjunctival disease may incite a secondary spastic entropion that may worsen the clinical signs. The equine practitioner should be aware that clinical signs of ocular pain and

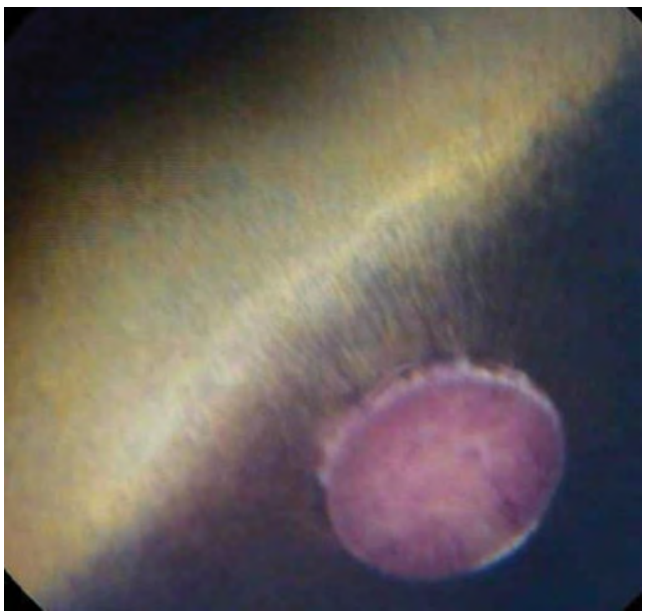


Figure 4.4 Funduscopic photograph of a 1-day-old foal. Note the remnant of the hyaloid artery hanging from the optic nerve head that is mildly congested.



Figure 4.5 Congenital entropion of the lower eyelid in a healthy neonatal foal. Note the corneal neovascularization and mucopurulent ocular discharge. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)

discomfort in foals will not be so evident as in adults, due to the foal's decreased corneal sensitivity [16].

Differential diagnosis

Although the diagnosis of entropion is straightforward, other congenital eyelid abnormalities such as ankyloblepharon, coloboma, dermoid, and cilia abnormalities may be considered. Congenital entropion in foals must be differentiated from acquired entropion secondary to systemic diseases, microphthalmia, eyelid trauma, cicatricial entropion, or any painful ocular disease causing blepharospasm [30, 32].

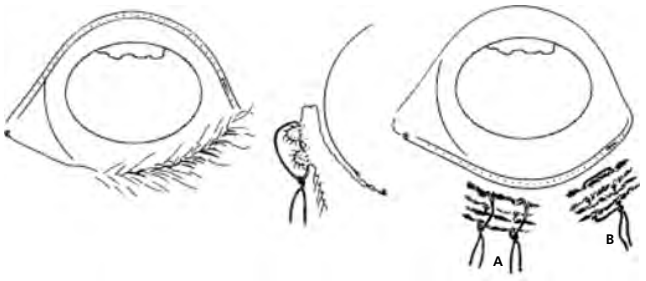
Treatment and prognosis

The goal treatment for entropion is to correct the abnormal inversion of the eyelid and facilitate healing of concurrent corneal or conjunctival disease, avoiding important sequels such as corneal fibrosis, corneal perforation, and corneal pigmentation. The treatment of choice depends on the cause, the severity, and the chronicity of the entropion. In congenital entropion, because the growing foal has a dynamic facial conformation, permanent surgical correction is not recommended until maturity is reached in order to avoid overcorrection and iatrogenic ectropion. The prognosis for vision is good if early diagnosis and treatment is performed.

Temporary repair Mild cases of congenital entropion may be resolved temporarily by manual eversion of the eyelids several times daily, followed by topical application of artificial tears and antibiotics during the first 2 weeks of life [20, 24, 25]. Although not particularly recommended by the authors, gentle squeezing of the affected eyelid between the thumb and forefinger has been reported as well, to temporarily correct mild congenital entropion by inducing subcutaneous edema [27]. In more severe cases, a temporary surgical repair is almost always needed to correct the anatomic and spastic components of the congenital entropion as soon as possible. Different techniques have been described for this purpose, such as subcutaneous injection of procaine penicillin G [24], liquid paraffin, silicone, hyaluronic acid, or other substances [33, 34], placement of temporary staples/vascular clips, and vertical mattress sutures [14, 25]. Although different injected material may be effective, the need for repeated injections, eyelid inflammation, and the potential for infection make this technique undesirable [28]. Undoubtedly, the surgical treatment of choice for congenital entropion is the vertical mattress suture. Temporary entropion repair is typically achieved under sedation in a mattress or Lembert pattern using 4-0 to 6-0 nonabsorbable monofilament suture material. The first bite should be located 1–2 mm away from the eyelid margin perpendicular to the eyelid. The distance between the first and the second suture bites will determine the amount of eyelid eversion achieved. A 2 = 1 = 1 knot securely ties the vertical mattress. The suture nearest to the cornea should be cut short, while the opposite end should be left longer to facilitate suture removal (Figure 4.6).

When placing temporary sutures, the "law of bisection" is recommended such that the first suture is passed in the center of the entropic eyelid, then additional sutures are placed in an identical fashion adjacent to the central suture, the number of sutures required being associated with the length of the entropion and the time the veterinarian is willing to maintain the rolling out effect. The use of a drop of cyanoacrylic adhesive to the knots has been described to secure suture knots [28]. Immediately after temporary tacking has been performed, palpebral reflex should be evaluated to ensure that the foal can blink normally. If the foal is lagophthalmic, one or two sutures may be removed to avoid exposure keratitis. Sutures typically remain in place for 2–4 weeks in most foals, with no need for eyecup or mask protection. Topical treatment depends on the secondary ocular findings; if ulcerative keratitis is present, appropriate management for corneal ulcer and secondary uveitis should be instituted. Ophthalmic preparations containing corticosteroids should be avoided.

Permanent surgical repair Rarely, nonresponsive congenital entropion in foals will need permanent surgical correction. The veterinarian should be aware that if definitive surgical repair is performed prematurely, the foal might be overcorrected, with an iatrogenic ectropion as a result. Many methods are available for correction, but the Hotz–Celsus procedure provides a



(A)



(B)

Figure 4.6 (A) Temporary entropion repair (tacking sutures) of the lower eyelid. (*Source*: Adapted from Stades FC and van der Woerdt A, 2013 [236]. © John Wiley & Sons.) (B) Tacking sutures to roll out the lower eyelid margin in a newborn Andalusian foal with entropion. Note how the suture near the cornea is cut shorter.

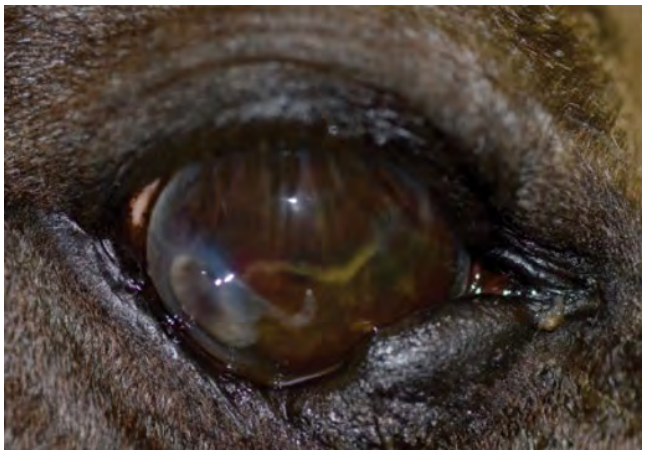


Figure 4.7 Clinical photograph of a 3-year-old Arabian mare. Note the absence of the majority of the lateral lower eyelid in association with corneal perforation and secondary anterior uveitis.

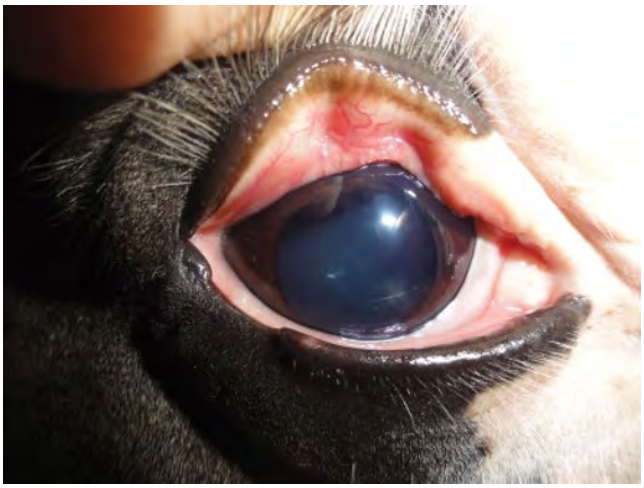


Figure 4.8 Lower eyelid coloboma. Note the short defect of the lateral lower eyelid in an otherwise normal eye. (*Source*: Reproduced with permission from Dr Fernando Malalana, Liverpool, UK.)

satisfactory result, dealing with most entropion conditions [30]. See Chapter 6 for detailed information on the surgical procedure and aftercare.

Other congenital diseases of the eyelid

Eyelid agenesis, coloboma, and ankyloblepharon are congenital conditions rarely reported in the horse [14, 24, 27, 29, 35, 36]. Upper eyelid agenesis (Figure 4.7) or absence of palpebra has been previously described and successfully treated by silicone subdermal implant in a Thoroughbred horse [36].

Coloboma or short full-thickness eyelid defects are common in the lower lid, sometimes being associated with multiple ocular defects [14]. The pathogenesis of this rare defect is unknown. Mild cases appear as a small notch in the eyelid and usually require little or no treatment (Figure 4.8). Cryodepilation of the eyelashes or eyelid hair causing any corneal irritations may be required, particularly if an erosion or corneal ulcers results. Larger defects need blepharoplastic procedures to prevent chronic corneal and conjunctival irritation [25].

Occasionally, the eyelids can be seen fused at birth, termed ankyloblepharon, with the nasal portion being slightly separated [27, 35]. Gentle traction is usually enough to part the lids, although, occasionally, surgery is needed to separate the eyelid margins [34]. A scissor blade can be used in a sliding motion to separate the lids; no cutting action is usually necessary [27]. Special care should be taken not to damage the cornea when surgically separating the eyelids. The ease in which the condition is commonly resolved suggests a thin avascular epithelial attachment between both eyelids [35]. Topical antibiotic and artificial tears ointments should be applied for 7 days.

Acquired eyelid diseases

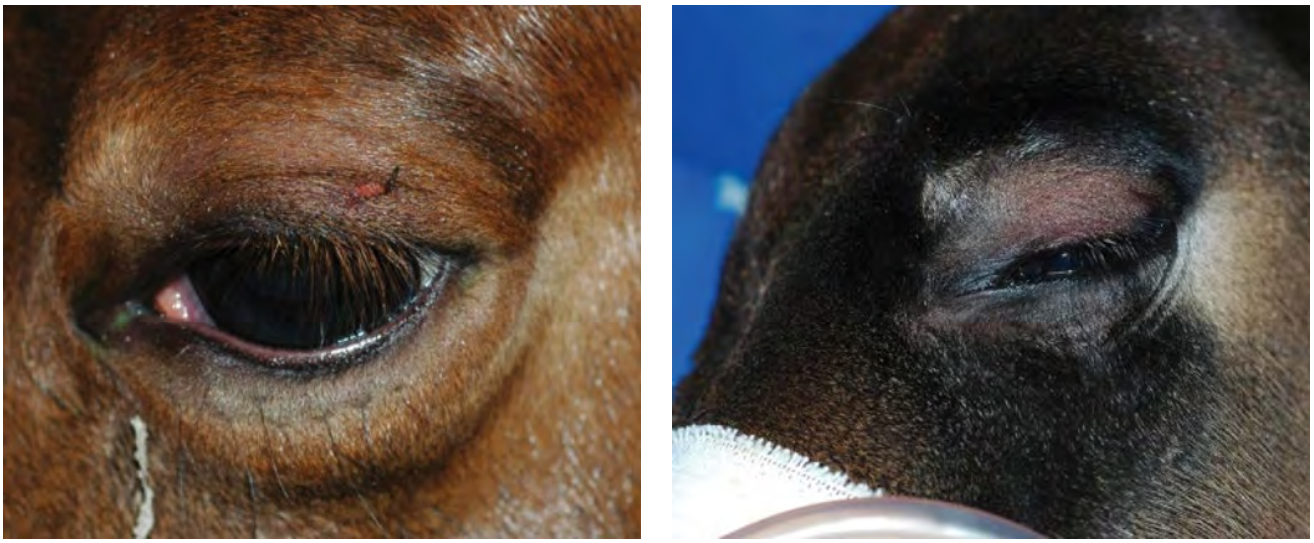
Despite the environment in which many foals are stabled and the prominent lateral positioning of their eyes, eyelid lacerations, contusions, abrasions, blepharedema, and blepharitis in healthy foals



Figure 4.9 Clinical photograph of a severe eyelid laceration, affecting upper and lower eyelids, in a newborn foal with complete congenital bilateral cataracts.

are rarely reported in the literature [14, 25]. Probably this lower incidence could be related to the innate maternal protectiveness of the mares and the natural behavior of the neonates. The veterinarian should be aware that intraocular blinding conditions, such as complete cataract, could predispose to an aberrant behavior and secondary eyelid contusions and lacerations (Figure 4.9).

The incidence of acquired eyelid disorders seems to be higher in systemically ill foals (Figure 4.10). Although the surgical and medical management for these conditions is similar to those



(A) (B)

Figure 4.10 Clinical photographs of septic newborn foals with blepharitis. (A) Note the marked blepharoedema, conjunctival hyperemia, and small epithelial ulcer in the upper eyelid. (B) Generalized blepharoedema and palpebral hyperemia.

described for adult horses (see Chapter 6), special considerations should be taken for recumbent ill foals, whose eyelids are in direct contact with the bedding. In order to minimize the development of secondary eyelid and corneal inflammatory conditions in these cases, supportive care should include maintenance of recumbent foals on clean dry bedding; maintenance in sternal recumbency as much as possible; and changing to the opposite recumbent side every 2 hours. A "donut" made from Soffban may also be helpful to prevent ocular trauma.

Third eyelid disorders

Congenital third eyelid disorders

Congenital abnormalities affecting the third eyelid are rare, with dermoid the most commonly reported condition [37, 38]. Dermoids, also known as benign choristomas, are congenital collections of normal tissue found in aberrant locations. Although present since birth, the condition has been recently described affecting the third eyelid in two nonrelated adult horses [37, 38]. In both cases, the clinical presentation consisted of recurrent corneal ulcers associated with the presence of aberrant long hairs growing along the margin of the third eyelid (Figure 4.11). Surgical excision is the treatment of choice for dermoids causing irritation to associated ocular structures.

The margin of the nictitans can present different degrees of pigmentation, being those associated with the conjunctival and limbal pigmentation. If the lack of margin pigmentation is unilateral it may induce an asymmetrical ocular/facial appearance, erroneously interpreted by the owner as being abnormally elevated [34]. Furthermore, nonpigmented margins may predispose to actinic inflammation or third eyelid tumors in adulthood (squamous cell carcinoma) [39].

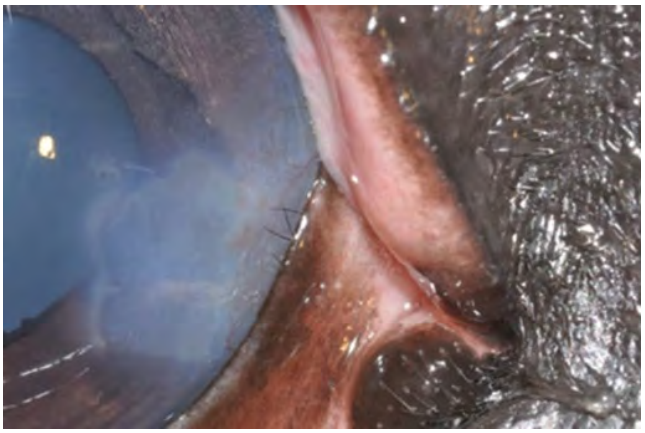


Figure 4.11 Appearance of a third eyelid dermoid with associated keratitis in an 8-year-old Gypsy Vanner gelding. (*Source*: Greenberg et al., 2012 [37]. Reproduced with permission from John Wiley & Sons.)

Acquired third eyelid disorders

Many of the acquired conditions of the third eyelid are secondary to other abnormalities of the globe and orbit. Foreign body and trauma are a common cause of third eyelid irritation and damage, and often are associated with concurrent conjunctival, eyelid, and corneal injuries (Figure 4.12). Due to the less corneal sensitivity of young horses, a foreign body may induce less evident clinical signs that may go unnoticed by the owner [16]. Examination of bulbar and palpebral conjunctiva of the nictitans following topical anesthetic administration is recommended if a ventromedial corneal lesion is diagnosed in a foal. Although third eyelid tumors are commonly seen in adults, the disorder has not been reported in foals.



Figure 4.12 Clinical photograph of a hemorrhage of the nictitating membrane after local blunt ocular trauma in a newborn foal.



Figure 4.13 Conjunctival dermoid in a 6-month-old Andalusian mare. (*Source*: Reproduced with permission from Dr Maya Caparrós, Manilva, Spain.)

Disorders of the nasolacrimal system

Imperforate nasal punctum and nasolacrimal duct atresia

Prevalence

Atresia or absence of the nasal punctum is the most common nasolacrimal congenital abnormality in the foal, which results in epiphora during the first months of age [14, 34, 40–42]. Additionally, a mild degree of distal nasolacrimal duct atresia can also be detected anywhere along its course [28, 34, 43]. To date, there is no evidence to support an inherited basis for these conditions in the horse. See Chapter 6 for detailed diagnosis and treatment of nasolacrimal disease in the foal.

Diseases of the conjunctiva

Congenital disorders

Congenital diseases of the equine conjunctiva are rare, with conjunctival dermoid being the most common (Figure 4.13).

Acquired disorders

Conjunctival hemorrhages

Prevalence

Conjunctival hemorrhages have been previously reported in neonatal healthy foals aged 1–4 days, ranging in incidence from 8.3% to 36% [13, 17, 44]. Despite being present at birth, this abnormality is not considered strictly congenital but likely acquired during parturition. Although no breed or gender predisposition has been described [44], only males were affected in the most recent retrospective study [13]. Unfortunately, the low number of affected newborn foals in this study does not support gender as an indirect indicator for conjunctival hemorrhage predisposition.

Pathogenesis

Although originally associated exclusively with maladjustment syndrome [45, 46], conjunctival hemorrhages have been recently reported in otherwise healthy foals [13, 44]. The pathogenesis for this condition in healthy foals has not been truly elucidated, but some hypotheses have been evaluated. A combination of perinatal factors, such as birth weight, fetal oversize, multiparity, and the speed and magnitude of delivery forces in the mare, might directly affect the incidence of subconjunctival hemorrhages [13, 44]. Oversized foals from uniparous mares have been described as the most commonly affected [44]. Such correlations suggest blunt trauma during delivery as the main cause of conjunctival hemorrhages in healthy foals [13, 25, 34, 44]. The thoracic compression during normal delivery, inducing secondary peaks of jugular venous and carotid arterial pressures [47], may cause conjunctival hemorrhages in foals [44].

Clinical appearance

Conjunctival hemorrhages are commonly diffuse, extending up to the corneoscleral junction of one or both eyes, and being mainly located in the dorsal or dorsolateral quadrants (Figure 4.14) [13, 44]. The location has been associated with a more exposed scleroconjunctival area in this region [44]. Affected eyes are visual and nonpainful [13, 44]. Although there may be some similarities in their etiology, no statistically significant relation has been established with corneal neovascularization or retinal hemorrhages [44].

Differential diagnosis

Subconjunctival hemorrhages can be seen in an otherwise neonatal healthy foal, but also in cases of maladjustment syndrome, trauma, coagulopathy, vasculitis, anemia, thrombocytopenia, disseminated intravascular coagulation, and a variety of systemic

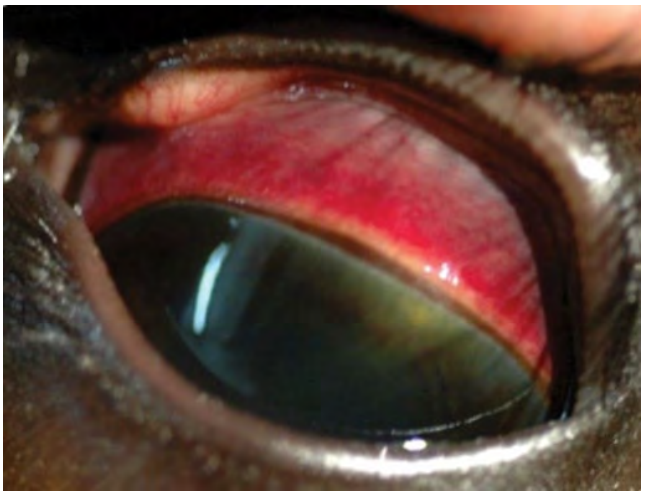


Figure 4.14 Diffuse conjunctival hemorrhage located in the dorsal quadrant in an otherwise healthy foal.

infections, including equine viral arteritis and equine infectious anemia [48]. In such cases, different systemic clinical signs, depending on the systemic illness, will accompany conjunctival signs. Complete physical and ophthalmic examination is strongly recommended in neonatal foals showing subconjunctival hemorrhages.

Treatment and prognosis

Subconjunctival hemorrhages do not affect vision and resolve spontaneously within 7 days [13, 44, 48]. In severe cases where a hematoma or chemosis is present, topical ophthalmic lubrication and mild anti-inflammatory topical drugs may be required. If associated with systemic illness, treatment of underlying active disease often results in resolution of the clinical signs. Subconjunctival hemorrhages have no effect on the foal's vision in the short and long term [13, 44].

Conjunctivitis/conjunctival congestion

Definition and prevalence

Conjunctivitis is common in healthy and systemic ill foals, being most often secondary to foreign bodies, environmental irritants (hay, sand, dirt, ammonia, and flying insects) or trauma. Sick foals that spend a lot of time lying down are especially at risk for developing conjunctivitis. Although less frequently diagnosed in neonatal foals, primary conjunctivitis has been reported in systemic bacterial or viral infections such as equine herpesvirus (EHV), rhinovirus, equine influenza, strangles, equine viral arteritis, *Actinobacillus* spp., and *Corynebacterium* spp. [14, 25]. The higher incidence of secondary conjunctivitis in newborn foals could be partially explained by two factors: their reduced tear production when compared to adult horses [16], thus lowering the available amount of tear lysozyme and lactoferrin and predisposing to secondary infections; and their low corneal sensitivity, which may prevent or delay the natural foreign body elimination (inducing less tearing and blepharospasm). One could hypothesize that the physiologic conjunctival defense mechanism in foals is not as efficient as in adult animals. Furthermore, immunodepressed foals, or those with congenital cellular and humoral immune deficiencies, appear to be at increased risk for conjunctivitis [14].

Clinical appearance

Clinical signs include unilateral or bilateral nonpainful conjunctival congestion and different degrees of ocular discharge (from serous to mucopurulent). The veterinarian should be aware that 1-day-old newborn foals are prompt to have conjunctival congestion without secondary mucopurulent discharge. The incidence of such conjunctival congestion in one study tapered progressively with age, being 71% in 1-day-old foals and 14% in foals aged 16–21 days [13]. This high incidence of unexplained conjunctival congestion has been related to the vascular compromise during delivery or to the direct contact between the amniotic liquid and conjunctiva in advanced gestational stages [44].

In foals with conjunctivitis, a thorough ocular and physical examination, especially of the respiratory tract, is recommended. Although conjunctivitis has commonly been classified as secondary in newborn foals, conjunctival cytologic study and culture may be helpful in some chronic cases [25].

Regardless of etiology, if mucopurulent discharge is present, locating and removal of the possible offending irritant by copious flushing of the conjunctival sacs, as well as topical wide-spectrum antibiotic, are indicated. Conversely, if no discharge is present, ocular tear replacement and daily-bedding reposition are recommended. Some foals may benefit from the use of topical nonsteroidal anti-inflamatory drugs once or twice daily.

Diseases of the cornea

Congenital diseases

Congenital corneal disease is uncommon in the horse, with megalocornea/cornea globosa and dermoid being most common.

Megalocornea/cornea globosa

Prevalence

Megalocornea and cornea globosa are two similar but different nonprogressive congenital corneal conditions that do not impair vision in the horse. Megalocornea is an enlargement of the corneal diameter with a short radius of curvature, while cornea globosa is a condition characterized by a normal corneal diameter with a long radius of curvature (Figure 4.15). Both diseases have been associated with normal IOP values in Rocky Mountain horses [49]. Although not reported in equine ophthalmology, megalocornea in human beings has a normal endothelial cell density. Future studies will be necessary to determine endothelial cell density of normal foals and those with megalocornea. Since the 1990s, these two ophthalmological terms have been somehow misused in equine ophthalmology, giving place to certain misunderstandings.



Figure 4.15 Abnormal corneal curvature of a horse with megalocornea/cornea globosa and MCOA.

Megalocornea has been reported to occur in two distinct patterns: as a **simple** unilateral isolated megalocornea, with no additional ocular or systemic manifestations [14], or as a component of a syndrome of multiple congenital ocular anomalies (MCOA), most commonly reported in Rocky Mountain horses, in which anterior macropalpebral fissure, anterior megalophthalmos, temporal iridal, ciliary and retinal cysts, iridal hypoplasia, cataracts, and retinal dysplasia may also be present [50, 51]. Cornea globosa has been reported only as a component of MCOA syndrome in foals, with no isolated cornea globosa cases described in the literature [50, 52–54]. Horses with the Silver coat color (also known as "chocolate") are the most commonly reported to be affected by megalocornea and cornea globosa [14, 50–52, 54, 55].

Pathogenesis

The physiopathology for megalocornea/cornea globosa in horses is poorly understood and may be related to lens induction during embryological development of the anterior segment. In humans, the optic cup growth is decreased due to a neuroectodermal abnormality, resulting in successive waves of migration of mesenchymal tissue over an excessively large, broad ciliary region, ultimately producing an enlarged corneal diameter [56].

Clinical appearance and diagnosis

Ocular findings of megalocornea include an excessively enlarged, clear cornea of normal thickness, whereas cornea globosa is seen as a dome-shaped cornea with globular contour and atypical and excessive protrusion. Although the disease can be suspected by the external appearance of the eye, objective diagnosis of megalocornea and cornea globosa is only made by comparing corneal diameter and radius of curvature measurements with the reference values for the breed and age of the patient. Unfortunately, there is no reported information on these parameters in foals, leaving the diagnosis of megalocornea and cornea globosa to a more subjective diagnosis.

Differential diagnosis

Simple isolated megalocornea should be differentiated from some conditions such as congenital glaucoma, exophthalmos, and cornea globosa. Hydrophthalmos secondary to congenital glaucoma differs from megalocornea in that the enlargement is not restricted to the cornea, affecting the complete fibrous layer. Furthermore, other findings such as diffuse corneal edema, Haab's striae, and high IOP may accompany the abnormal diffuse enlargement of the eye. Megalocornea and congenital glaucoma are clearly specific and separate entities. Exophthalmos, or cranial displacement of the globe due to a space-occupying retrobulbar mass, may appear similar to an abnormally large-appearing globe, but resistance to retropulsion will not be present with megalocornea. Finally, cornea globosa may resemble megalocornea, the main difference being the length of the radius of corneal curvature.

Treatment and prognosis

No treatment is necessary and both conditions have been described as nonprogressive. The corneal changes in affected animals do not determine the overall prognosis as much as the associated ocular anomalies, such as lens and retinal abnormalities [50–54].

Microcornea

Definition and prevalence

Microcornea, a congenitally small cornea in an otherwise normal-sized globe, is rarely reported in horses. The condition has been described as the only abnormal finding in a Thoroughbred Australian racehorse [57]. Historically, the term microcornea has been misused in cases of microphthalmic eyes, in which a "false" microcornea was associated with a small globe [26, 58].

Pathogenesis

A later developmental failure of normal growth and expansion of the optic cup with premature or delayed optic vesicle/ectoderm contact may produce microcornea [59].

Clinical appearance

The small size of the cornea in an otherwise normal globe will allow increased visualization of the sclera. Conversely, if the foal has micropalpebral fissure, a proportionally normal amount of sclera is visible [59]. Certainly, final diagnosis is based on corneal diameter measurement and comparison with normal reference values. Due to the lack of reference values for foals, comparison with the contralateral healthy eye is the common practice in unilateral cases.

Differential diagnosis

The main differential diagnosis for microcornea is phthisis bulbi and globe shrinkage, secondary to chronic inflammation. Although both presentations are associated with other inflammatory ocular anomalies, in some cases the distinction can be difficult to make without a complete examination. It is important to note that corneal size in eyes with microphthalmia is proportional to globe size, as well as to palpebral fissure length, and thus should not be considered as a true microcornea. Furthermore, foals that lack perilimbal conjunctival pigment may give the impression of microcornea because the white sclera will appear prominent.

Treatment and prognosis

No treatment is necessary for this congenital nonprogressive condition. The visual prognosis for microcornea alone is good; nevertheless, cases with corneal diameters less than 10 mm can be accompanied by marked visual impairment [60].

Corneal dermoids

Prevalence

Corneal dermoids or choristomas are nonprogressive, unilateral, or bilateral opacities of congenital origin, consisting of epithelial and dermis-like components found in an abnormal location. Although present at birth, they may become manifest later or even in adulthood [41]. Rarely reported in the literature, they have been described in a Standardbred colt, with no other ocular anomalies, and in a group of related Quarter horses in association with iridal hypoplasia and cataracts [61, 62].

Pathogenesis

Although the pathogenesis for this condition is unknown, and probably varies from case to case, a failure of surface ectoderm to differentiate into normal corneal epithelium has been suggested as the most probable cause. Alternatively, defective induction of surface ectoderm by the optic vesicle, producing skin rather than corneal epithelium, may be involved [2, 59].

Clinical appearance

A corneal dermoid is an aberrant piece of skin that is growing on the surface of the cornea and can show variable degrees of pigmentation [2]. Based on their clinical appearance, dermoids can be classified in two categories: typical hairy appearance and cobblestone appearance (Figure 4.16). The former, similar to dermoids in dogs [63], may have multiple visible hairs growing from the surface that can cause eye irritation. Conversely, the cobblestone or follicular dermoids do not present obvious surface hairs, being less commonly associated with secondary corneal lesions [61, 64]. The most common location for both presentations is at the dorsotemporal limbus; nevertheless, they may affect the eyelid or extend inferiorly, involving the lower and the third eyelids [24, 27, 62, 65]. If large dermoids are present, closure of the eyelid can be impeded, inducing different degrees of lagophthalmia.



Figure 4.16 Clinical photograph of a 6-month-old Andalusian mare with a dermoid located in the temporal corneal area associated with ASD. Note the cobblestone appearance, with no visible long hairs in the area. (*Source*: Reproduced with permission from Dr Maya Caparrós, Manilva, Spain.)

Although confined to the superficial layers of the cornea in other species, dermoids in the horse may extend to all corneal layers and may be associated with anterior segment malformations (Figure 4.16) [14, 20, 27]. Although biomicroscopy may help in establishing the depth of the lesion in the peripheral area, some more recently described imaging techniques, such as anterior segment optical coherence tomography (AS-OCT) and high-resolution ultrasound (HRU) biomicroscopy, may be of value for establishing their central depth [66, 67].

Differential diagnosis

Differential diagnosis depends on the appearance of the dermoid, its pigmentation, and the adnexal structures present. In cases of hairy dermoids, diagnosis is straightforward. In contrast, the cobblestone appearance has to be differentiated from corneal neoplasia, reactive lymphoid hyperplasia, nodular episcleritis, and foreign body or parasitic granulomas. Definitive diagnosis is based on clinical appearance and histopathologic evaluation. Histologically, dermoids typically contain a keratinized, variably pigmented, and stratified squamous epithelium [68]. They also include the regular presence of hair follicles, blood vessels, glandular tissue, adipose tissue, fibrous tissue, and nerves. Generally, the edges of ocular dermoids are indistinct and merge with the neighboring corneal and conjunctival epithelium and stroma [69].

Treatment and prognosis

Treatment of dermoids depends on the exact location, the size, and the presence of secondary ophthalmic problems. Small dermoids causing minimal irritation and not impairing vision can be left untreated or treated with periodic removal of irritating cilia, combined with topical lubrication [20, 25]. Conversely, larger dermoids, or those inducing secondary corneal or

conjunctival conditions, will benefit from surgical treatment. Surgery in those cases consists of removing the mass by keratectomy, sclerokeratectomy, or conjunctivectomy, if the cornea, sclera, or conjunctiva is affected, respectively. In most cases, corneal dermoids can be successfully treated by superficial keratectomy that has to extend 1–2 mm from the dermoid perimeter. Nevertheless, the surgeon must be aware that equine dermoids may extend into the deep corneal stroma, making it necessary to use surgical techniques to give tectonic support to the cornea, with risk of corneal perforation [14, 25, 27]. Thus an experienced surgeon under magnification and with appropriate instrumentation should perform surgical removal. Excision should be complete to avoid regrowth and histopathologic evaluation is highly recommended.

Based on the nonprogressive nature of this condition, if surgical removal is complete, the procedure is curative. Some degree of mild corneal opacity may remain following surgical removal.

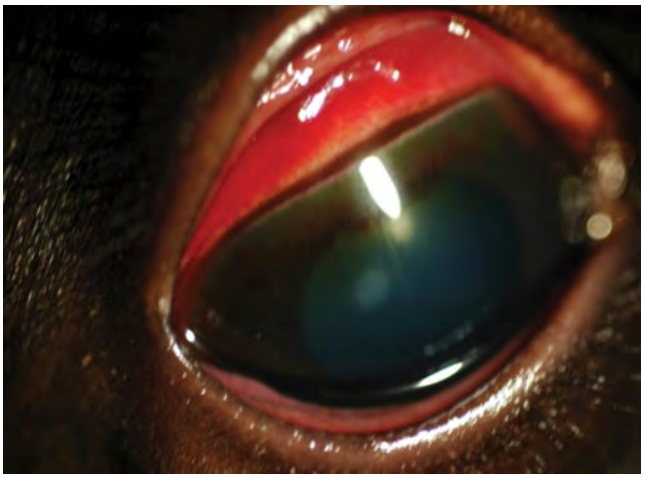


Figure 4.17 Corneal superficial neovascularization in a 1-day-old foal. Note the mild, short, straight, superficial vessels present along the whole length of the dorsal perilimbal region.

Corneal vascularization

Prevalence

Diffuse congenital corneal vascularization has been described bilaterally in 1-day-old healthy foals [13, 70–72].

Pathogenesis

The pathogenesis for this condition is unknown, although the presence of superficial bilateral corneal vessels in healthy 1-day-old neonatal foals suggests diffuse corneal irritation and inflammation by an external cause. The insult most probably occurred late in gestation when the palpebral fissure was opened, allowing superficial exposure of the cornea and conjunctiva to the amniotic fluid [13, 71]. A histopathologic study on newborn foals determined that the neo-vessels are superficial, located in the subepithelial stromal area [72]. These findings agree with the mild severity and no long-term corneal changes were seen some days after the first diagnosis of the condition [13, 71].

Clinical appearance

Corneal vessels are described as approximately 3 mm long, mild, short, and straight, and present most frequently along the entire length of the dorsal perilimbal region. The terminal portions of the vessels have an arborizing appearance, leading to a bright-red fringe within the dorsal cornea (Figure 4.17). These vessels have been seen in association with other clinical signs such as conjunctival hyperemia and vascular congestion [71], mild diffuse corneal edema, and subconjunctival hemorrhages [13]. Corneal neovascularization in foals has not been associated with corneal ulceration, ocular pain, discharge, or other intraocular abnormalities.

Differential diagnosis

Differential diagnosis for this congenital condition includes all the adnexal, corneal, and intraocular abnormalities able to induce corneal neovascularization. Thus a complete ophthalmic examination is recommended to rule out entropion, corneal ulceration, nonulcerative keratitis secondary to foreign bodies, anterior uveitis, and glaucoma.

Treatment and prognosis

In all reported cases, corneal vascularization resolved spontaneously in a centripetal direction within 10 days [13, 71].

Acquired diseases

Ulcerative keratitis

Prevalence

The incidence of corneal ulcerative disease has been historically described as high in sick foals [16], with incidences of 1% and 18.6% being reported in healthy and diseased foals, respectively [17, 21].

Etiology and pathogenic mechanism

Foals, especially systemically ill foals, have decreased corneal sensitivity [16]. This fact, combined with an absent menace response for the first couple of weeks of life, and a reduced STT I, may predispose the neonatal foal to corneal trauma. Corneal ulcers in the healthy neonatal foal are usually initiated by trauma, such as caused by stone injuries, feedstuffs, awns, or mare tail-swishing [25]. Conversely, in systemically ill foals, secondary entropion, reduced blinking, and, if recumbent, direct contact of the cornea with the bedding are the most common causes [73]. Viral ulcers are rarely diagnosed in foals, although equine herpesvirus-2 (EHV-2) should be considered if punctate ulcers or multiple punctate white corneal lesions are observed [24].

Independently of the underlying cause, once the corneal epithelium is disrupted, colonization and invasion of the stroma by environmental and normally nonpathogenic surface ocular bacteria or fungi may occur, establishing infection and prompting inflammatory cell influx [73, 74]. Specific inflammatory

responses that occur during infected corneal ulcers in foals are not known in detail, but it is likely that metalloproteinases, cytokines, growth factors, and polymorphonuclear leucocytes are major factors, as they are in the adult inflammatory response. There is general agreement on the high capacity of corneal ulcers in foals to melt, suggesting an immature balance of their proteolytic corneal activity when compared with adults. Unfortunately, no studies on metalloproteinase activity in foals are available at the moment.

An antidromic reflex is presumed to exist in the foal, as it does in adult horses [69], whereby corneal damage causes trigeminal nerve stimulation, subsequent stimulation of the ciliary and iris sphincter muscles, and iris capillary vasodilation and leucocyte chemotaxis [75]. Nevertheless, one might think that based on the reduced corneal sensitivity of the neonatal foal, the axonal reflex might be lower, and thus anterior uveitis secondary to uncomplicated corneal ulcers, if present, might go unnoticed.

Clinical signs

Ulcerative keratitis in the equine neonate often differs from adult horses in clinical signs and disease course. Nonspecific clinical signs of corneal ulceration in foals may be more difficult to detect than in adults, the level of discomfort being mild despite serious corneal disease. Foals may not show characteristic epiphora, blepharospasm, or conjunctival congestion, and the ulcers may be missed without daily fluorescein staining. The decreased corneal sensitivity may partially explain the lack of clinical signs often seen in sick neonates with corneal ulcers [16].

Based on clinical signs, corneal ulcers in foals can be classified into uncomplicated or complicated. Uncomplicated corneal ulcers are superficial, noninfected, and associated with minimal uveitis (Figure 4.18A). Close monitoring, daily if possible, is essential, as these superficial ulcers do have the potential to worsen [7, 14]. Complicated ulcers may show marked corneal edema, cellular infiltration, deepening of the ulcer bed, and potentially keratomalacia or "melting" (Figure 4.18B). As in adult horses, secondary anterior uveitis may be present, showing specific clinical signs such as aqueous flare, miosis, reduced IOP, hypopyon, or fibrin clot in the anterior chamber [76]. If the ulceration is chronic, corneal vascularization may appear. As in adults, corneal cytology and culture is mandatory in complicated corneal ulcers.

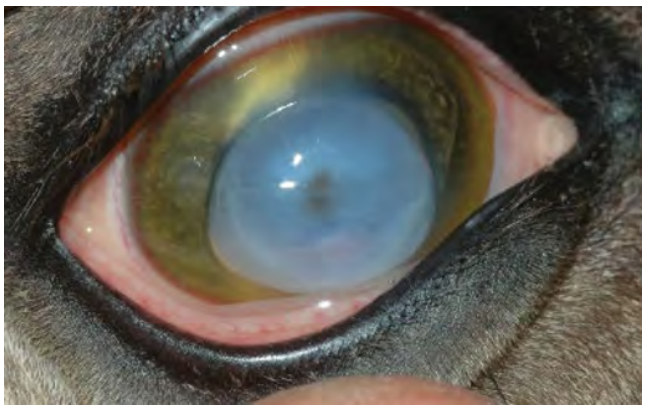
Treatment

Although corneal ulceration in foals might follow a mild early clinical course, early diagnosis and prompt therapy are strongly recommended if serious ocular complications are to be avoided. Furthermore, daily follow-up is important to ensure proper healing.

Medical therapy is almost always the major thrust to ulcer control in foals, albeit tempered by judicious use of surgical procedures. As in adults, the main goals of the topical treatment for a corneal ulcer are to control infection, inflammation, and pain, to decrease unregulated proteolysis, and to promote healing [69]—hence the similarity in treatment protocol between both age groups. The medical protocol to apply will differ depending on whether the ulcer is complicated or not. For further details see Chapter 7.



(A)



(B)

Figure 4.18 (A) Simple epithelial corneal ulcer in a newborn foal. (B) Melting ulcer in a newborn foal (*Source*: Photographs courtesy of Dr Riccardo Stoppini.)

Prognosis

The prognosis for retaining a visual, comfortable globe in foals with corneal ulceration depends upon controlling infection and corneal digestion, as well as simultaneous anterior uveitis. Prognosis is worse in complicated deep corneal ulcers. Although there are no studies reporting corneal wound healing in foals, in adults, experimentally induced corneal ulcers in which the epithelium, basement membrane, and anterior third of the stroma were surgically removed had a re-epithelization rate of 0.6 mm/day [77]. Due to the highly mitotic index of dividing cells in young individuals, one may expect that re-epithelization would be faster in foals [78]. Therefore a minimum of 0.6 mm/day re-epithelization rate should be expected in a noncomplicated corneal ulcer in foals.

Complications

Reported complications in corneal healing in foals include stromal abscess, severe secondary anterior uveitis, severe corneal scarring, corneal pigmentation, descemetocele, corneal perforation, endophthalmitis, and phthisis bulbi [25].

Corneal dystrophies

In strict ophthalmological terms, corneal dystrophies are defined as primary inherited biochemical abnormalities that are typically associated with bilateral, nonvascularized, central, and progressive opacities. The condition is not rare in adult horses [69, 79–81], but strangely has not been reported in foals.

Although some equine corneal dystrophies have defined causes, many are undefined and subject to theoretical or hypothetical discussion. Because of the dearth of confirmed causes, dystrophies are commonly divided by descriptive or anatomic means. Anatomic categories, such as endothelial dystrophy, relate to the portion of the cornea affected or damaged by the dystrophic changes. Descriptive categories, such as striate or multifocal punctate dystrophy, create a picture of the lesion [79]. In 1999, a system was established by the International Committee for the Classification of Corneal Dystrophies based on the underlying genetic mechanism, which demonstrates that corneal dystrophies represent more of a spectrum of disease [82]. Among those, the most commonly reported corneal dystrophy in horses is corneal endothelial dystrophy [79, 80, 83]. See Chapter 7 for details.

Nonulcerative keratopathies

Nonulcerative keratitis

Acquired nonulcerative keratitis is rarely reported in foals, being mostly secondary to corneal healing after a corneal ulcer (Figure 4.19). No cases of immune-mediated keratopathies have been reported in foals. When a nonulcerative keratitis is diagnosed in a foal, a thorough clinical history and ophthalmic examination should be obtained.

Irregular punctate corneal opacities

Irregular punctate corneal opacities of unknown onset located primarily in the epithelial layer have been observed in Thoroughbred foals. These opacities should be differentiated from punctate keratitis associated with EHV-2 in adult horses. The reported opacities resolved spontaneously over a 5-month period [19].

Linear keratopathy (Heusser's striae)

Dr Heusser first described linear keratopathy in foals in 1921 and named the condition as linear or striate dystrophy [84]. Since then, the abnormality has been better classified as linear keratopathy or Heusser's striae [85]. The condition consists of thin posterior refractile band or linear opacities with well-defined and parallel margins that most commonly transverse the horizontal meridian of the cornea in an otherwise normal foal's eye (Figure 4.20) [85]. They may be unilateral or bilateral, are nonedematous and nonprogressive, and have been shown to result from local thinning of the Descemet's membrane. Some affected horses have a single horizontal linear lesion and others have bifurcation of the lesion or two or more separate striae.

The cause remains unknown, although a transient periparturient rise in IOP may be responsible. Similar striate opacities can result from congenital glaucoma (Haab's striae) or blunt trauma to the globe. In these instances, the opacities are usually associated with other ocular signs. Glaucoma is clearly an important differential diagnosis for eyes with linear keratopathy, and a careful and thorough examination is necessary in all cases [80]. The cornea should also be stained with fluorescein to rule out corneal scratches. Some clinicians have expressed the concern that linear opacities occurring in otherwise normal eyes may have resulted from a transient postnatal elevation in IOP and may be indicative of incipient glaucoma. However, in the absence of more generalized ocular disease, it is reasonable at present to regard these opacities as a benign and incidental finding [80]. There is no treatment for the condition.

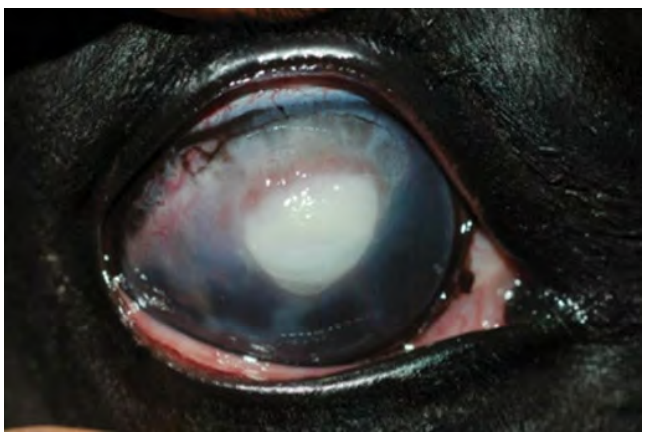


Figure 4.19 Clinical photograph of a 1-month-old Andalusian horse at initial presentation for evaluation of a corneal abscess. Note moderate corneal edema, corneal neovascularization, and severe corneal cellular infiltrate.



Figure 4.20 Heusser striae in an otherwise normal adult eye. (*Source*: Reproduced with permission from Dr Fernando Malalana, Liverpool, UK.)



Figure 4.21 Clinical photographs of a 7-month-old foal with ASD. Notice the PPMs located around the iris collarette, as well as the focal cornel opacification due to a DPM, and how the DPM is touching the corneal endothelium. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)

Dysplasic pupillary membranes

Dysplasic pupillary membranes (DPMs) are persistent remnants of the anterior tunica vasculosa lentis originating from the collarette of the iris extending into the anterior chamber to touch the lens or the cornea (Figure 4.21). Corneal opacities associated with DPMs attached to the corneal endothelium are rarely reported in foals. A complete ophthalmic examination is necessary, since DPMs can be associated with other congenital anomalies of the eye. Furthermore, DPMs should be differentiated from anterior synechia by observing the origin of a pupillary membrane at the iris collarette and the origin of a synechia at the pupillary margin. DPMs can be observed with transillumination examination. No treatment has been described for the condition.

Congenital corneal melanosis

Congenital corneal melanosis is a rare occurrence of unknown cause that affects a small area of corneal epithelium and anterior stroma [25]. Corneal vascularization is usually present, the condition being nonprogressive and nonpainful. The abnormality should be differentiated from dermoids. Treatment is generally not needed, but if vision is impaired a superficial keratectomy might be considered.

Hereditary equine regional dermal asthenia

Hereditary equine regional dermal asthenia (HERDA) is a connective tissue disorder observed in Quarter horses that has been associated with ocular findings such as mild corneal opacities, decreased corneal thickness, increased corneal curvature and corneal diameter, multifocal collagen fibers disorganization of the cornea, and increased incidence of corneal ulcers [86]. The disease is produced by an autosomal recessive missense mutation in the peptidylprolyl isomerase B (PPIB) gene. The homozygous PPIB mutation observed in HERDA-affected horses impairs collagen folding because of improper interactions between the proteins required for collagen biosynthesis [87]. The most common systemic signs include hyperextensibility, skin thinning and fragility, atrophic scars, tumor-like masses, ulcers, and swelling distributed along the dorsal areas. Although considered a congenital disease, the condition has not been reported in foals; therefore it is further discussed in Chapter 7.

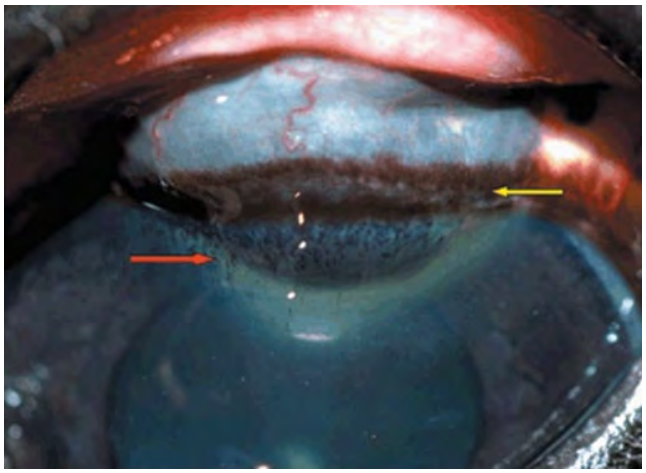


Figure 4.22 Darkly pigmented mass at the dorsal limbus (yellow arrow), extending 6 mm into the cornea within the stroma in a 6-month-old Hanoverian cross foal. A distinct crescent-shaped arc of corneal edema delineates the edge of the mass within the cornea (red arrow). (*Source*: From McMullen et al., 2008 [89].)

Corneal neoplasia in foals

Corneal congenital tumors are both rare and sporadic in horses [88]. An epibulbar melanoma with choroidal invasion was reported and confirmed by histopathology in a 6-month-old Hanoverian foal (Figure 4.22) [89]. However, although the mass had grown to considerable size, it was not compromising vision or ocular movements, making early detection difficult. The authors concluded that epibulbar melanoma should be considered a differential diagnosis for any pigmented ocular masses in foals.

Diseases of the anterior uvea

Congenital anterior uveal disorders

Congenital defects of the equine uvea are relatively uncommon and have included aniridia, iridal hypoplasia, anterior uveal cysts, anterior segment dysgenesis (ASD), persistent pupillary membrane (PPM), and DPM.

Developmental anomalies of the iris

Iridal hypoplasia

Prevalence

Iridal hypoplasia is an underdevelopment or incomplete development of the iris, historically interpreted as a cyst within the iris stroma [89, 90]. The condition has been documented as a sole clinical sign [91] or as one of the abnormalities in MCOA syndrome in Rocky Mountain horses, Exmoor ponies, Kentucky Mountain Saddle horses, Morgan horses, Belgian draft horses, Thoroughbreds, and Miniature breeds [50, 52–54, 92, 94]. Although seen in eyes with a variety of iris colors, iris hypoplasia

is seen predominantly in blue irides, being presented as a unilateral or bilateral condition [93]. There is no breed, age, or gender predisposition.

Pathogenesis

The developmental defect resulting in iridal hypoplasia arises early in embryonic life and may result from an incomplete forward migration of the optic cup after formation of the lens vesicle, or may be due to aberrant development of mesodermal tissue, which inhibits or misdirects normal forward ectodermal extension during iris formation [59]. Alternatively, maldevelopment of the capsulopupillary vessels or the tunica vasculosa lentis might prevent ingrowth of the iris [95]. The affected area shows iris stromal thinning that, due to aqueous humor pressure, is pressed forward, with the resulting protrusion.

Clinical appearance

Although iridal hypoplasia is a congenital disorder, affected horses may be diagnosed in adulthood, as the eyes are not painful and there is no discernable effect on vision [52, 91, 94]. Affected horses may present with dark and bulging areas of different sizes in the anterior surface of the iris that occasionally slightly distort the pupil and may be transilluminated (Figure 4.23). The location and size of the affected areas may vary, the dorsal iridal region being the most commonly affected. The condition is better visualized in bright light conditions (miotic pupil), by observing the retroillumination of the fundic reflection through the lesion. When the pupil is subsequently dilated, by the use of either mydriatic agents or dark adaptation, the bulging area disappears, taking on a wrinkled appearance.

Differential diagnosis

Differential diagnosis for the condition should include iris coloboma, iridal neoplasia, and iris atrophy. Careful examination under photopic and scotopic conditions should allow for an accurate diagnosis. It is highly unlikely that a neoplasm would allow for retroillumination of the fundic reflection or would deflate under conditions of pupillary dilation. However, should there be confusion, ocular ultrasonography may assist in making this differentiation. On the other hand, although iris atrophy is seen particularly in older horses, there are no reports in foals.

Treatment and prognosis

Iridal hypoplasia is a nonprogressive condition not associated per se with pain or vision impairment. Treatment is not needed, although historically the condition was successfully treated by removal of the anterior cyst wall [90].

Aniridia

Prevalence

Although true aniridia implies complete iridal absence, both histologically and gonioscopically, the term aniridia is used clinically in extreme forms of iris hypoplasia in which only a rudimentary, nonfunctional ridge of iridal tissue is present [96]. This bilateral condition has been rarely reported in the horse [62, 96–100], being described as an autosomal dominant trait in Belgian and Quarter horses [97, 98].

Pathogenesis

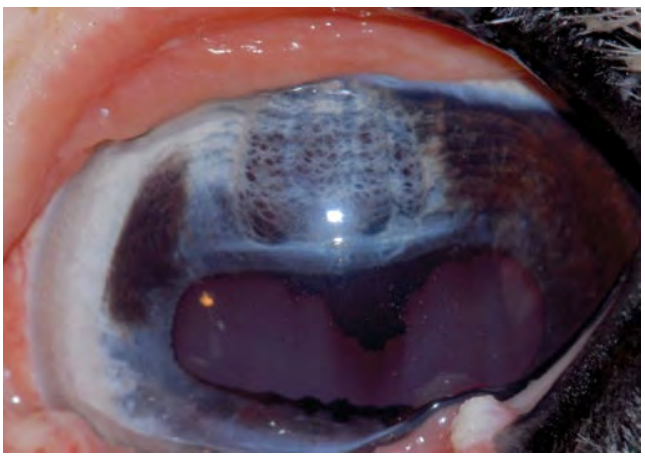
Iridal hypoplasia and aniridia share the same pathogenic mechanism, being more severe in aniridia [59].

Clinical appearance

Foals affected by aniridia are usually presented within the first few months of age with unusual appearance of both eyes, photophobia, and large pupils that do not respond to light [14, 20, 96, 100, 101]. The **corpora nigra** is usually absent and the rudimentary/absent iris allows visualization of the lens equator and ciliary processes (Figure 4.24). The condition can be associated with multiple ocular abnormalities, such as keratitis [96–98], limbal dermoids [97], nodular changes in the limbus [62, 96, 98, 100],



(A)



(B)

Figure 4.23 (A) Area of mild iridal hypoplasia. (*Source*: Reproduced with permission from Dr Fernando Malalana, Liverpool, UK.) (B) Area of marked iridal hypoplasia in a cross-bred gelding.



Figure 4.24 Aniridia in a horse. Notice the ciliary body processes and edge of the lens, which are not visible in normal horses. (*Source*: Photograph courtesy of Dr Michelle Willis.)



Figure 4.25 Typical iridal coloboma in a 5-year-old gelding. Notice the ventral distortion of the pupil. (*Source*: Reproduced with permission from Dr Fernando Malalana, Liverpool, UK.)

secondary focal cataracts [96, 97], presumed persistent pupillary membranes [96], microphthalmia, and aphakia [99]. Findings on posterior segment examination in affected horses have been uniformly unremarkable.

Differential diagnosis

Although the diagnosis of aniridia is straightforward and based on clinical signs, the condition should be differentiated from any cause of persistent mydriasis, such as ophthalmoplegia interna (oculomotor nerve lesion), in which the level of mydriasis can hinder visualization of the iris. The visualization of the lens equator and ciliary processes may be used as a key to differentiate between aniridia and iridal hypoplasia.

Treatment and prognosis

There is no specific treatment for aniridia in foals, except symptomatic supportive measures. Treatment of photophobia may include protective masks or specific tinted corneal lenses to reduce ambient illumination and increase patient comfort. Although no further anomalies have been reported to appear with time, lifelong regular follow-up care is recommended. Despite the degradation of photopic vision, many horses with aniridia have performed well in racing or other activities [96, 100].

Iris coloboma

Definition and prevalence

A notch, gap, hole, or fissure of the iris is described as a coloboma. Iris coloboma is an infrequent congenital anomaly, with no evidence of inheritance in the horse. It may occur as a sole defect or in eyes with other ocular defects and color dilution [91]. They may be classified as typical, when they appear in the midline, or atypical, occurring in another position.

Pathogenesis

Iridal colobomas arise early in gestation and are associated with defective closure of the optic fissure. Atypical colobomas are slightly more common than typical colobomas and arise later in gestation [91].

Clinical appearance

Affected foals may show different degrees of photophobia and lacrimation, depending on the size and location of the coloboma. The coloboma may resemble severe iridal hypoplasia, the geographic location of the condition being the main difference. Coloma involves the pupillary margin, changing the pupil's shape (Figure 4.25), whereas iridal hypoplasia is located in the thickest region of the iris (**iris collarette**), not affecting the pupillary margin. Iridal hypoplasia, if severe, may also distort the pupillary shape, though maintaining the pupillary margin. Colobomas provide an example of pseudopolycoria as there is no true sphincter muscle encircling the hole.

Treatment and prognosis

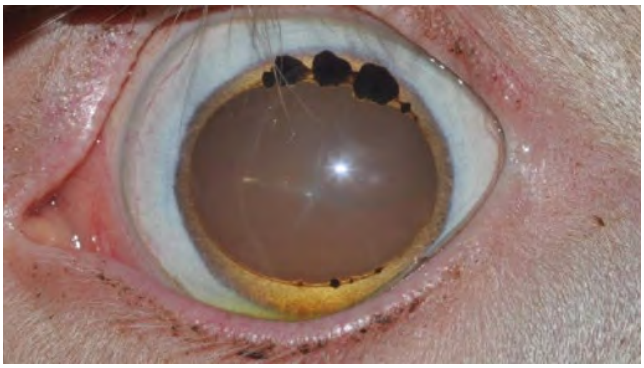
Iridal colobomas are a nonprogressive condition in foals. Although surgical treatment is commonly performed in humans with this condition [102], there are no reports of surgical repair in horses.

Other developmental iridal defects

Congenital miosis is a condition reported rarely in foals. When present, it has been associated with multiple ocular defects, including congenital glaucoma and MCOA syndrome (Figure 4.26A) [50, 52–54, 92]. As in humans, a bilateral rudimentary or absent dilator muscle has been observed on histopathology, causing pin-point pupils and severe visual impairment in scotopic light conditions [92, 103]. Although in foals no hereditary basis has been established, in humans the condition has been described as an autosomal dominant trait in association with megalocornea [103, 104]. No treatment has been described for this condition in foals. Other developmental iridal defects such as absent sphincter muscle, although not reported in the literature, may also be considered (Figure 4.26B).



(A)



(B)

Figure 4.26 (A) The eye of a Rocky Mountain horse with congenital miosis and megalocornea. Abnormalities include a miotic pupil, stromal hypoplasia with a flattened, circumferentially oriented granula iridica at the pupillary ruff, visible sphincter pupillae muscle, and absence of discernible collarette. Radially oriented deep stromal strands of iris tissue extend from the pupillary ruff toward the ciliary zone of the iris. (*Source*: From Ramsey DT et al: Congenital ocular abnormalities of Rocky Mountain Horses. *Vet Ophthalmol* 1999;2:47–59.) (B) Suspected iris sphincter hypoplasia in a foal. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)

Variations in iridal pigmentation

Heterochromia is a term used to describe iris color variation and is usually a normal variant; heterochromia iridum describes a situation where the iris of one eye has a different color from the iris of the other eye, while heterochromia iridis describes the situation where parts of the same iris, usually a sector, differ in color from the remainder [95].

In the horseman's lexicon, blue-eyed horses have lots of names, including "glass eyes," "wall eyes," and "china eyes." These eyes are characterized as showing some degree of photophobia when compared with the normal pigmented eyes. The condition is considered a normal variation.

In some foals, especially color-dilute animals, discrete superficial freckles or iridal nevus may be observed in the iris, consisting of clusters of melanocytes within the most anterior layers of the iris stroma [91]. Nevertheless, in the majority of cases, these asymptomatic conditions are diagnosed in adulthood [94].

A varying degree of deficiency of pigmentation (subalbinism) is seen in horses with MCOA syndrome [50] and as a normal iris variation in Welsh ponies and Welsh crosses in the UK [91]. Complete absence of iris pigment (albinism) is rare in foals [91]. Conversely to humans with oculocutaneous albinism, albinotic foals do not show strabismus or nystagmus [105].

Anterior segment dysgenesis

The term anterior segment dysgenesis (ASD) is a failure of the normal development of the tissues of the anterior segment of the eye [2]. In equine pediatrics, the term is used to describe several syndromes with different clinical presentations, including dysgenesis of the cornea, iridocorneal angle, iris, ciliary body, lens, and retina, as well as microphthalmos or hydrophthalmos [2, 50, 91, 92]. As the majority of the structures of the anterior segment derive from the optic crest, these conditions are also named neurocristopathies [2]. The severity of signs associated with ASD varies greatly. As a general rule, the more severe the abnormalities, the earlier in life the diagnosis will be pursued. Undoubtedly, the most commonly diagnosed ASDs in horses nowadays are PPMs, uveal cysts, and the clinically most severe MCOA syndrome.

Persistent pupillary membrane (PPM)

Definition and prevalence

The pupillary membrane is a primitive mesodermal tissue present during fetal development that forms a layer on the anterior face of the iris. This membrane consists of fine blood vessels and connective tissue and, in association with the hyaloid artery, is in charge of providing nutrition to the lens and anterior segment during its period of rapid differentiation [2]. Partial remnants of the pupillary membrane coming from the iris collarette are almost universal in neonatal foals, being seen as a sole clinical sign in an otherwise normal eye [19, 20, 24, 29], but also as part of more complex ASD syndromes (see Figure 4.21) [92, 94].

Pathogenesis

In normal ocular embryogenesis, posterior mesenchyme within the developing anterior chamber will form the iris peripherally and the pupillary membrane centrally. During development there is continuity between the hyaloid system-derived capsulopupillary vessels at the lens equator and the vascular arcades. This connection is broken as the eye grows so that the iris and pupillary membrane are independent of the hyaloid system, which forms most of the tunica vasculosa lentis. Near the end of the gestation period, the pupillary membrane begins to atrophy; the central arcades are first to disappear, followed by the remaining arcades and associated mesenchymal tissue [2].

Clinical appearance

Partial PPMs is a common finding in adults and young foals, usually noted as unilateral or bilateral delicate strands of pigmented tissue arising from the anterior surface of the iris collarette and extending a short distance into the aqueous, or

running circumferentially [91] (see Figure 4.21). Rarely, the remnants are more extensive and may bridge the pupil, or be adherent to the anterior lens capsule or the corneal endothelium, with associated lens or corneal opacities, respectively, at the point of contact. Such opacities would be present from birth and are better classified as DPMs than PPMs, as they acquire an abnormal distribution. Some DPMs may be observed as iridocorneal or iridolenticular adhesions and gonyosynechiae [50, 54].

Differential diagnosis

The diagnosis of PPMs is made on the basis of clinical appearance that is seen most easily when the pupil is constricted. Visualization of iris-to-iris PPMs that span the pupil is accomplished more easily with mydriasis, as the strands are pulled taut. Magnification may be required to appreciate small PPMs.

DPMs can be differentiated from anterior or posterior synechia by observing the origin of a pupillary membrane at the iris collarette, whereas the origin of a synechia is usually located at the pupillary margin.

Treatment and prognosis

In horses, opacities associated with PPMs are nonprogressive and rarely cause significant visual deficits. Treatment is not usually necessary.

Anterior uveal cysts

Definition and prevalence

Anterior uveal cysts are developmental cystic formations that may arise either from the posterior pigmented epithelium of the iris or from the inner ciliary body epithelium, and therefore are neuroectodermal in origin [2]. Despite their developmental origin, they are most commonly diagnosed in adulthood, this apparently late appearance being associated with sudden rapid dilatation. They are commonly seen as incidental findings in horses with otherwise normal eyes [50, 53, 54, 106], but also have been reported in association with other ASDs, such as MCOA syndrome [52–54, 107]. If these cysts are the only ocular anomalies in a Silver-diluted horse, the clinical findings are classified as the less severe MCOA phenotype, also known as cyst-phenotype. See Chapter 8 for more information.

Equine multiple congenital ocular anomalies syndrome

See Chapter 13 and online material for detailed information on MCOA syndrome.

Uveal congenital tumors

Primary intraocular neoplasms are uncommonly reported in the foal, the majority originating from melanocytic or neuroepithelial cells [74]. Primary intraocular neuroepithelial tumors are divided into tumors deriving from mature epithelium (adenoma and adenocarcinomas) and tumors deriving from primitive neuroectoderm (PNETs), such as medulloepithelioma and retinoblastoma [108]. Conversely to equine retinoblastoma that is seldom reported [109], medulloepithelioma has been more extensively described in the literature [110–118].

Medulloepithelioma

Prevalence

Unlike human ophthalmology, where medulloepitheliomas are commonly diagnosed at a young age [119, 120], equine medulloepitheliomas are mainly reported in adulthood [110–115, 117, 118], although descriptions in foals do exist (Table 4.1) [116]. The reason for this delayed presentation is not yet understood, but three main hypotheses should be considered. The first is related to the delayed complete differentiation of the ciliary body epithelium, predisposing though to embryonic neuroepithelium tumors [121]. The second is related to the adaptation capacity of horses for progressive, unilateral deteriorating vision. As they adapt well to unilateral blindness, medulloepithelioma could be easily overlooked by the owner or caretaker [122]. The last possible explanation for the late presentation of medulloepithelioma might be transformation of a benign version of the embryonic tumor into an aggressive, symptomatic neoplasm, in advance stages. Racial or hereditary predisposition has not been previously documented in the horse.

Table 4.1 Intraocular medulloepitheliomas reported in the horse.

Reference	Age	Sex	Diagnosis	Localization	Treatment	Follow-up	Recurrence
Folger (1919) [110]	2y	M	Malignant nonteratoid medulloepithelioma	ON	Enucleation	–	–
Blodi and Ramsay (1967) [126]	–	–	Malignant nonteratoid medulloepithelioma	ON	–	–	–
Bistner (1974) [111]	11y	M	Nonteratoid medulloepithelioma	Anterior uvea	Enucleation	–	–
Eagle RC et al. (1978) [112]	1.5y	F	Malignant nonteratoid medulloepithelioma	ON	Exenteration	–	–
Bistner et al.(1983) [113]	9y	M	Malignant nonteratoid neuroepithelioma	ON	Enucleation	2 m	Spread into calvarium
Szymanski (1987) [114]	5y	F	Malignant teratoid medulloepithelioma	CB	Enucleation	2y	No
Riis et al. (1990) [115]	4y	M	Nonteratoid medulloepithelioma	CB	Exenteration	–	–
Ueda et al. (1993) [116]	4 m	M	Malignant nonteratoid medulloepithelioma	ON	Euthanasia	No	–
Rebhun (1998) [117]	3y	F	Medulloepithelioma	–	Enucleation	–	–
Leiva (2013) [118]	11y	F	Benign teratoid medulloepithelioma	CB	Enucleation	6y	No

y, Years; m, months; ON, optic nerve; CB, ciliary body.

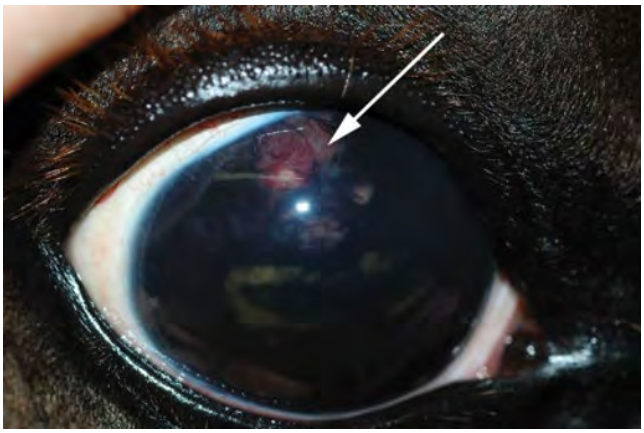


Figure 4.27 Clinical photograph of an 11-year-old Arabian mare with medulloepithelioma. Note the mild diffuse endothelial corneal edema and a pinkish mass in the dorsolateral iris region (**arrow**), coming from the posterior segment. (*Source*: Leiva et al., 2013 [118]. Reproduced with permission from John Wiley & Sons.)

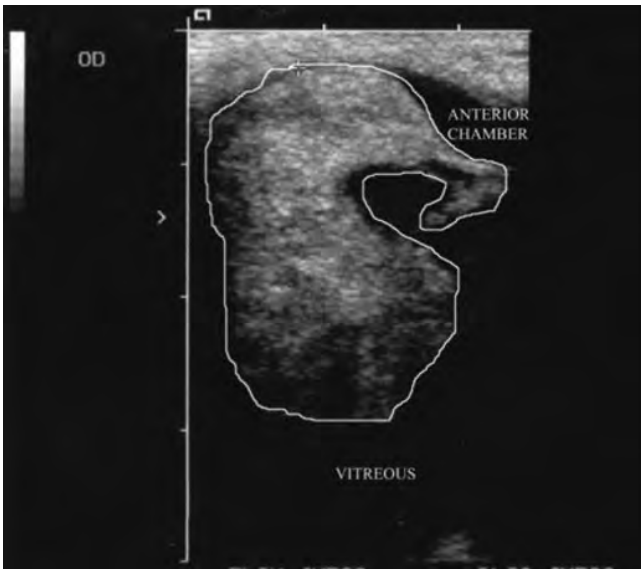


Figure 4.28 Ocular ultrasonography and gross section of a medulloepithelioma in an adult mare. (*Source*: Leiva et al., 2013 [118]. Reproduced with permission from John Wiley & Sons.)

Pathogenesis

Medulloepitheliomas are considered to be rare unilateral embryonal tumors that arise from the primitive neuroectoderm of the optic cup before differentiating into adult tissue [123, 124]. They can be classified as teratoid or nonteratoid. The less commonly described teratoid medulloepitheliomas may contain heteroplastic tissue such as hyaline cartilage, striated muscles, undifferentiated mesenchymal cells, and nervous tissue (Table 4.1) [114, 118].

Clinical appearance

Commonly affected horses present unilateral leukocoria or eye redness secondary to a nonpigmented unilateral mass, originating from the ciliary body, that occupies the posterior segment and part of the anterior (Figure 4.27). Medulloepithelioma, although less common, can also occur in other intraocular tissues, such as the optic nerve [112, 113]. These different locations could be related to the embryonic neuroectodermal origin of the tumor and its multipotentiality, which may allow it to differentiate into retina, ciliary epithelium, vitreous, or neuroglia [120].

Diagnosis

In human medicine, the diagnosis can be approached by means of ultrasound, fine-needle aspiration cytology, or histologic examination [120, 122]. Although there are no specific reported studies on the use of ultrasonography to diagnose equine medulloepithelioma, ultrasound can be considered a potentially helpful tool to establish the origin and intraocular extension [115] (Figure 4.28). Intraocular fine-needle aspiration, although being a relatively quick and simple procedure, is not regularly employed in horses due to its possible complications [125].

In many cases, the eyes are painful and already blind at first presentation; thus enucleation is the only rational course of action, without recourse to further investigation such as uveal biopsy or fine-needle aspiration. The definitive diagnosis is based on typical microscopic findings (Figure 4.29). The ultrastructural characterization of equine medulloepithelioma has been described elsewhere [118].

Treatment and prognosis

Enucleation or exenteration is the usual recommended treatment for medulloepithelioma in adult horses [110, 112–115, 117], while in foals, owners may request euthanasia [116]. Local resection by iridocyclectomy, although frequently applied in human ophthalmology, is not reported in horses, mainly because the majority of these tumors are in advanced stages when diagnosed.

Because long-term follow-up of horses with medulloepitheliomas has not been documented, long-term biologic behavior of these tumors is unknown. Like in humans, medulloepithelioma in horses generally tends to be locally aggressive neoplasm, but rarely results in distal metastasis [110]. In some cases the tumor may extend out of the eye and invade the optic nerve and the orbit, with occasional fatalities caused by intracranial extension [112, 126].

Acquired anterior uveal disorders

Reports on acquired anterior uveal disorders in foals are focused mainly on anterior uveitis.

Anterior uveitis

Anterior uveitis in foals has been reported secondary to ocular conditions, such as corneal ulcer or ocular trauma, as well as as an ocular manifestation of systemic diseases such as neonatal septicemia [14, 21, 127–130], *Rhodococcus equi* infection [131–134], strangles (*Streptococcus equi*) [14, 135, 136], adenoviral infection [137], equine viral arteritis [138], and equine herpesvirus-1 infection (EHV-1) infection [139]. In addition, individual reports on rib osteomyelitis [140] and hyphema secondary to neonatal isoerythrolysis [128] have been described.

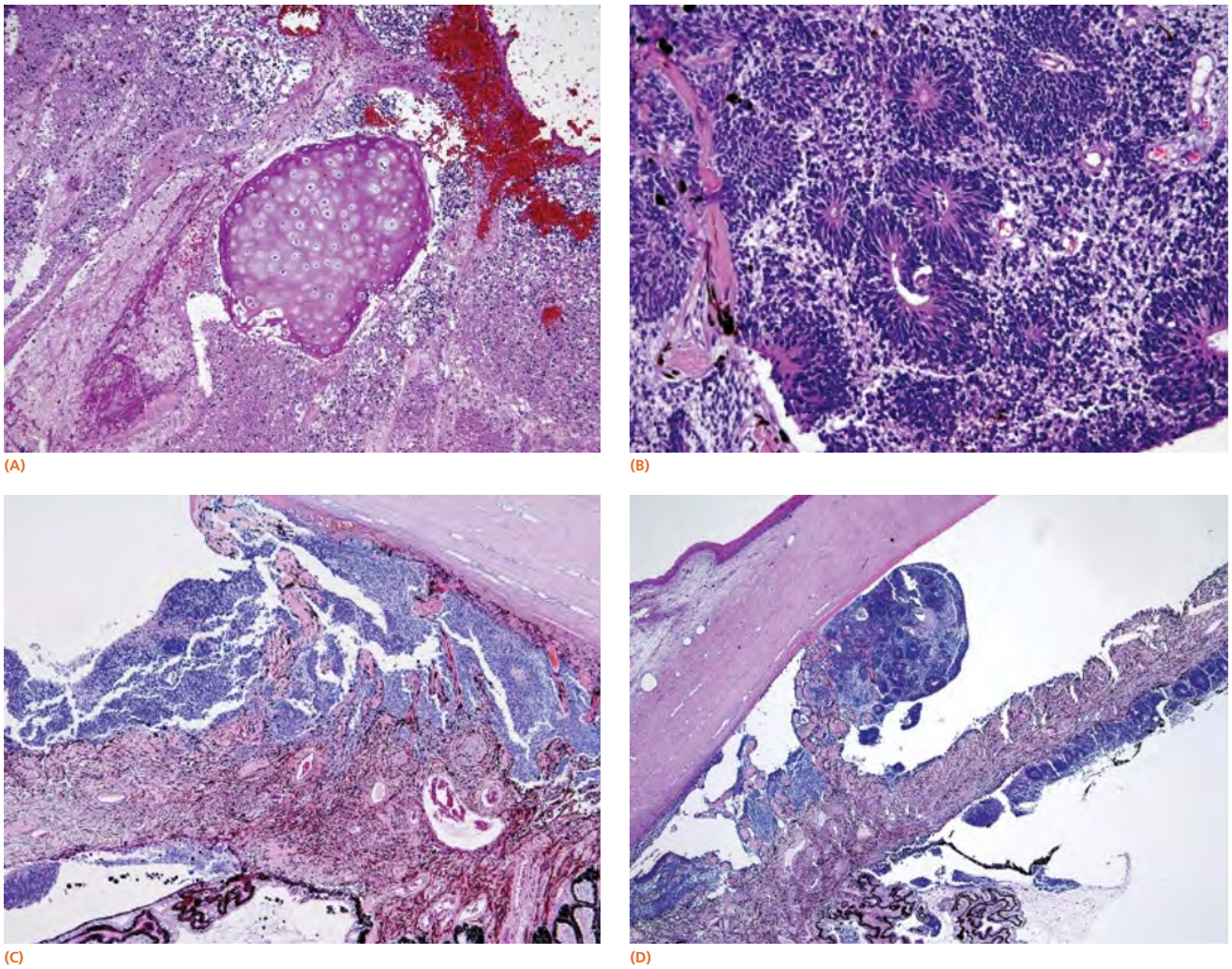


Figure 4.29 Histological aspects of the H&E-stained teratoid medulloepithelioma. **(A)** Isolated hyaline cartilage in a necrotic area (×40). **(B)** Flexner–Wintesteiner rosettes (×40). **(C)** Cords of neoplastic cells occupying the iridocorneal angle (×20). **(D)** Clusters of neoplastic cells associated with anterior and posterior iris (×20).

Signs of anterior uveitis are similar among the different systemic etiologies, without reported pathognomonic ocular signs. Very often, the severe degree of uveitis in newborn foals precludes posterior segment examination, and thus some posterior segment signs could go unnoticed.

Ocular therapy for the treatment of uveitis in these cases should include, apart from the specific systemic treatment for the triggering condition, frequent topical administration of corticosteroids and tropicamide or atropine. If untreated, the commonly seen aqueous flare and fibrin clots in the anterior chamber may induce corneal or lens sequelae, giving rise to different degrees of hemeralopia or even blindness.

Uveitis due to septicemia

Anterior uveitis in newborn foals is most commonly seen in septic animals, especially those that had failure of passive transfer of immunoglobulins or other immunodeficiencies [21, 130, 141–143]. In one clinical study, the incidence of anterior uveitis in septic newborn foals was 26% [130]. These septic animals were further classified based on the blood culture results and the sepsis score in bacteremic neonates (positive blood culture results) and nonbacteremic foals (negative blood culture but sepsis score ≥ 14). The higher incidence of uveitis seen in the former group (40%) when compared to the nonbacteremic group (19%) suggests an important role of bacteremia in triggering anterior uveitis in newborn foals; thus this proposes anterior uveitis as a component of the nonspecific inflammatory response syndrome (SIRS) [144].

Although ocular signs in septic horses have been described as both unilateral and bilateral [145], in a retrospective study on 74 septic newborn foals, only bilateral signs were displayed [130]. Asymmetrical presentation was frequently observed though. This finding might be related to the importance of the vascular endothelium in the pathogenesis of sepsis [143] and to the already known weakness of the equine blood–aqueous barrier (BAB) [146].



Figure 4.30 Clinical photograph of a septic eye in an Andalusian foal. Notice the amount of fibrin in the anterior chamber, as well as the mydriasis after 1 day of topical treatment.



Figure 4.31 Acute uveitis associated with *Rhodococcus* spp. infection in a 5-month-old gelding. Note the green hue to the iris (arrows) caused by fibrin seeping from the uveal vessels.

Reported cases of septic foals showed different degrees of ocular congestion, aqueous flare, miosis, and fibrin in the anterior chamber (Figure 4.30) [21, 130]. The fact that fibrin clots are most commonly seen in septic bacteremic foals [130] suggests a more severe damage of the BAB in these foals when compared to septic nonbacteremic or sick but nonseptic foals.

Theoretically, all microorganisms able to induce septicemia can enter the BAB and the blood–retinal barrier (BRB), inducing different degrees of intraocular signs in foals. These signs will depend mainly on the severity of BAB/BRB damage, the fenestrated BAB being more predisposed to endogenous damage than the nonfenestrated BRB [147]. Both Gram-positive and negative microorganisms have been previously related to anterior uveitis in newborn foals [25, 27, 130, 148]. Although a preliminary study on histopathologic findings in septic neonatal foals with uveitis failed to demonstrate intraocular microorganisms [72], further studies are needed to determine whether septicemia-resulting uveitis is a consequence of direct bacterial action or of immune-mediated injury driven by the microbial antigen.

A significant poor outcome for septic-uveitic foals was observed when compared to septic nonuveitic foals, suggesting anterior uveitis as a valuable survival prognosis factor for the affected animals [130]. This is an easily understandable fact if ocular signs are considered as one of the nonspecific inflammatory responses commonly related to the clinical condition.

A complete ocular examination should routinely be performed in sick foals with suspected sepsis in order to diagnose the inflammatory condition in early stages and apply the most appropriate treatment to guarantee visual soundness.

Uveitis due to Rhodococcus equi infection

Rhodococcus equi infection is one of the most important causes of disease in foals between 1 and 6 months of age, with most foals showing clinical signs before the age of 4 months. The most common manifestation of *R. equi* infections is a chronic suppurative bronchopneumonia with extensive abscessation and associated suppurative lymphadenitis [149]. Early clinical signs may only include a slight increase in respiratory rate and mild fever. These subtle clinical signs are usually missed or ignored, thus allowing the condition to progress and show an apparently acute onset. The most common reported clinical signs include decreased appetite, mild lethargy, fever, dyspnea, tachypnea, and immuno-mediated polyarthritis. Other less reported signs include cough and nasal discharge, septic arthritis, osteomyelitis, colic, diarrhea, keratouveitis, uveitis (Figure 4.31), and panophthalmitis [131–134, 150].

Diagnosis of *R. equi* infection is made based upon culture or polymerase chain reaction (PCR), vapA gene from fluid obtained from tracheobronchial aspirate (TBA) or aqueous paracentesis [131, 151]. Clinically, a suspected diagnosis may be based on the clinical signs, the radiographic findings, and the number of animals affected in a stud. A wide variety of antimicrobial agents are effective against *R. equi*, including erythromycin, azithromycin-rifampin, and clarithromycin [152–155]. The reader is referred to equine internal medicine books and journals for further information.

Uveitis due to strangles

Streptococcus equi subsp. *equi* infection (strangles) is an acute, contagious, upper respiratory tract disease of predominantly young horses, characterized by rhinopharyngitis and lymphadenitis of the submandibular and retropharyngeal lymph nodes. Yearlings and young adults are most at risk, followed by weanlings and then adults. Infection occurs by inhalation or ingestion of the organism, followed by attachment to the cells in the crypt of the tonsil and adjacent lymphoid nodules. Signs become apparent after an incubation period of 3–8 days, and the clinical course usually lasts 3–4 weeks. Affected foals and young horses typically become anorexic and depressed, and develop bilateral, serous to mucoid nasal discharge within 24 hours of onset of fever. In addition, lymph nodes will severely inflame, filling with pus. If the affected lymph nodes are behind the throat, the pressure on the pharynx from the pus-filled lymph nodes and throat inflammation can cause severe difficulty in breathing, hence the name

for the disease: "strangles." Rarely, *S. equi* may cause neonatal septicemia. Ocular reported findings include abscesses around the eyes, conjunctivitis, panophthalmitis, and chorioretinitis [135, 136, 156, 157].

Diagnosis of strangles is made based on characteristic clinical signs and positive culture of *S. equi* from abscesses [158]. Therapy is controversial, and the reader is referred to recent internal medicine textbooks.

Uveitis due to viral agents

Adenoviral infection is primary a problem in immunodeficient Arabian foals [137], in which affected animals develop fever, dyspnea, cough, diarrhea, leukopenia, panuveitis, and necrosis of the epithelium of the conjunctiva and lacrimal glands. The diagnosis is established on the basis of viral isolation results, serum antibody titers, and viral inclusion in the conjunctival exfoliated cells [159]. Therapy is supportive in nature and the mortality rate is considered high among foals with marked leucopenia

EHV-1 and equine viral arteritis, a disease caused by equine arteritis virus (EAV), have also been sporadically associated with anterior uveitis in foals [138, 139].

Disorders of the lens

Congenital disorders

Cataracts

Prevalence

Cataracts are the most commonly reported ocular defect in foals, representing approximately 35% of all congenital ocular defects [14, 20, 24, 27, 41, 160]. Most often, congenital cataracts occur as the sole ocular anomaly [5, 17, 25, 161–164], although they may be associated with other ocular congenital disorders such as microphthalmia, persistent pupillary membrane, iridal hypoplasia/aniridia, persistent hyaloid artery, megalocornea, corneal dermoid, and multiple ocular anomalies [50–54, 94, 96–98, 107, 165].

Congenital cataracts may be inherited or secondary to other developmental abnormalities, maternal influences, or environmental factors. Although heritability of cataracts in horses has not been widely studied, inheritance for this condition has been documented in Thoroughbred, Quarter, Morgan, and Belgian horses, and has been considered as a dominant trait in Belgian, Thoroughbred, and Quarter horses [22, 166–168]. Nevertheless, there have also been reported individual cases in different breeds whose hereditary basis has not been confirmed. In these cases, etiologies such as exposure to toxic substances, nutritional imbalance, ionizing radiation, infection and systemic diseases affecting the mare during pregnancy, and prenatal and birth trauma have been sporadically proposed [169]. In most instances, the cause of congenital cataracts remained unknown.

In all affected foals, a complete medical history should be obtained that includes information on previous affected offspring; ophthalmic status of the stallion, mare, and other close relatives; health and diet of the mare during gestation; and exposure of the mare to drugs, chemicals, disease, and radiation. No gender predisposition has been detected, although sex-linked genetic predisposition has been suggested in Exmoor ponies [94].

Pathogenesis

Very little is known about cataractogenesis in the foal. However, given the common phylogenic origin of mammals and interspecies similarity in anatomic organization of the mammalian lens, it is likely that much of the biochemical and physiochemical basis of cataract formation is common to all species. Developmental lens opacities arise from aberrant or interrupted evolution of the crystalline lens both *in utero* and postnatally, or from dysgenesis of the vascular framework surrounding the fetal lens. Their origins lie in abnormal differentiation and growth of derivatives of embryonic surface ectoderm, neural crest mesoectoderm and mesenchyme, or in disruption of the normal maturation and laying down of secondary fibers in the fetal and postnatal lens [170]. Most congenital cataracts can be morphologically related to a stage or process in the embryogenesis and growth of the lens or iris and anterior chamber. On this basis, some developmental cataracts can be predicted to be nonprogressive, while others, by far the minority, may be predicted to be potentially progressive. However, irrespective of the type of developmental cataract, any progression will be very slow. More than one form of developmental opacity may be present in a single eye [170].

Clinical appearance

Evident clinical signs may be present at birth or in early neonatal life. The affected foals show different degrees of leukocoria and vision impairment, depending on the location, density, and size of the cataract. Congenital cataracts may be unilateral or bilateral, and may be classified into four basic types (Figure 4.32): (1) complete cataract (most common), (2) lenticular or nuclear cataract, (3) capsulolenticular cataract, and (4) extralenticular cataract [17, 20, 96, 166, 170, 171].

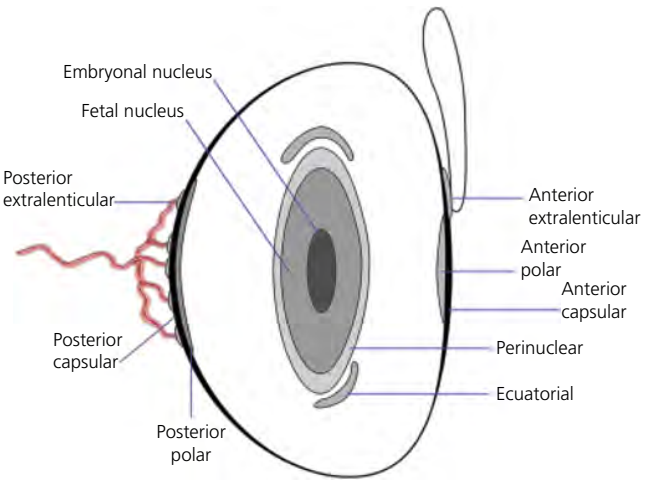
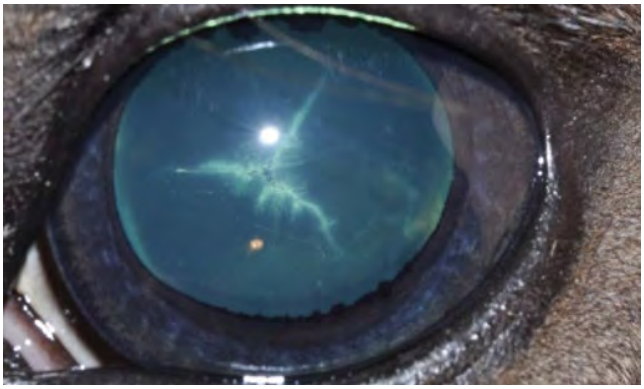


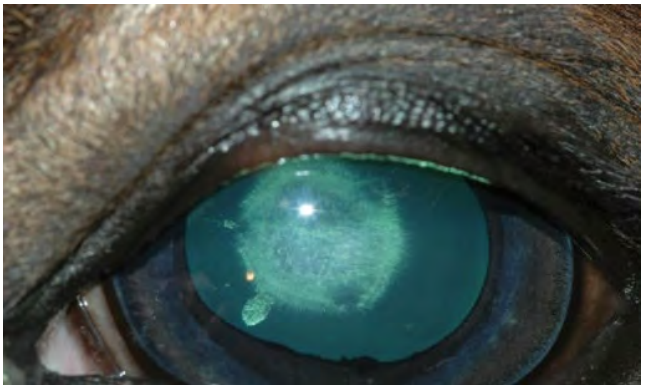
Figure 4.32 Classification scheme for congenital cataracts in foals according to their localization within the lens.



(A)



(B)



(C)

Figure 4.33 Clinical photographs of congenital cataracts in foals. (A) Complete mature cataract in a 4-day-old Andalusian horse. (B) Incipient posterior suture cataract. (C) Focal, axial, posterior cortical cataract in a newborn foal. (*Source*: Photographs courtesy of Dr Riccardo Stoppini.)

In the complete cataract the entire lens is cataractous, although some clearing of the cortex may be apparent near the zonular insertions [170] (Figure 4.33A). Lenticular cataracts are rarely associated with visual disability. This wide group includes zonal cataracts, embryonic nuclear cataracts, fetal nuclear cataract, perinuclear cataract, and equatorial, sutural (anterior or posterior sutural cataracts), and axial cataracts (floriform and elliptical cataracts) (Figure 4.33B). The ophthalmoscopic appearance of a nuclear cataract includes a ring-like opacity, a hollow sphere, or a solid opacity. With the exception of embryonic nuclear cataracts, these cataracts are usually bilateral but are not necessarily symmetrical. Capsulolenticular cataracts are seldom, if ever, associated with compromised vision, the most common ones being anterior capsular cataract, posterior capsular cataract, anterior polar cataract, and posterior polar cataract (Figure 4.33C). Extralenticular opacities evolve from the tunica vasculosa lentis and vascular framework of the iridopupillary membrane, and are likely to contain vascular, pigmentary, and connective tissue elements. The most common extralenticular opacities include retrolenticular fibroplasia, Mittendorf's dot, and persistent pupillary membranes (PPMs).

Differential diagnosis

Although the diagnosis of complete congenital cataracts is straightforward for an ophthalmologist, focal cataracts should be differentiated from prominent posterior Y-sutures commonly seen in newborn foals [13, 14, 19, 20]. Similarly, posterior polar cataracts should be differentiated from remnants of the hyaloid artery [13] and posterior segment opacification of different origins.

Prognosis and evolution

Although prognosis for cataract development can be made only on the basis of repeated ocular examinations, the veterinarian should be aware of the different progression of cataracts depending on the location and size. Focal extralenticular or capsulolenticular opacities are often nonprogressive [14, 20, 24, 160], while nuclear cataracts are rarely progressive. These latter cataracts often decrease in size when compared with the total lens size as new normal cortical fiber layers are produced throughout life [14, 24, 166, 172].

Treatment

Treatment of congenital cataracts in foals depends on the severity and intended use of the horse. Careful evaluation of the

eye with a congenital cataract is necessary to establish some prognosis and decide the most appropriate treatment plan. Although medical therapy that prevents cataract progression in clinical patients is not available, in cases of focal cataracts, mydriasis may improve vision in nuclear dense cataracts affecting the visual axis. Mydriasis may be achieved with 1% atropine ointment or solution applied topically twice daily until the pupil dilates, and then twice a week to maintain dilatation [14]. Nevertheless, the practitioner should be aware of the potential secondary gastrointestinal and intraocular effects of this topical drug [173–175].

One difficult question to answer is the optimal time to perform cataract surgery on foals affected by complete cataracts. Deprivation amblyopia, defined as decreased vision in one or both eyes subsequent to central fixation disuse caused by ocular opacities, is an important factor that may influence success rate following cataract surgery. Although this condition has not been ascertained in foals after the extraction of congenital cataracts, it occurs in children and laboratory animals [176–179]. Early return of vision may be paramount in foals for development of the higher visual centers. Most veterinary ophthalmologists recommend surgical removal of cataracts in foals once weaned; but only if the foal is healthy, no uveitis or other ocular problems are present, and the foal's personality tolerates the aggressive topical treatment.

Additionally, if untreated, some complete congenital cataracts may progress to hypermaturity, increasing the chances of lens-induced uveitis and post-operative complications [172]. The severity and duration of the intraocular inflammation may increase the likelihood of post-operative complications such as ocular hypertension and secondary glaucoma [172].

Special considerations Historically, congenital cataracts have been treated surgically by intracapsular lens extraction, aspiration, extracapsular lens extraction, and, most recently, phacoemulsification [5, 161–164, 168, 172, 178, 180–183].

Dr K.N. Gelatt initially described the main basic surgical considerations for cataract surgery in foals in 1969. Although surgical techniques have evolved since then, those basic considerations are still valid, including a strong attachment between lens posterior capsule and vitreous, lack of scleral rigidity, which may predispose to different degrees of ocular collapse proportional to corneal/limbal incision size, and a very thin and fragile posterior lens capsule rendering it prone to rupture and offering little impediment to vitreous prolapse [178]. Furthermore, cataracts in foals are notably softer than cataracts in middle-aged or adult animals [161]. Other considerations such as the very swallow anterior chamber peripherally, although not exclusive for foals, may hinder performing a corneal or episcleral incision without contacting the iris [183].

Phacoemulsification is the treatment of choice for complete congenital cataracts in foals [5, 162–164, 168, 183, 184]. See Chapter 9 for detailed information on cataract surgery in horses.

Post-surgical prognosis

A successful outcome post-operatively in foals undergoing phacoemulsification should include an assessment of the long-term visual capability. Horses can live for decades, and a successful visual outcome must be present for years to be considered a success. Unfortunately, the lack of long-term follow-up data in foals undergoing cataract surgery is particularly discouraging [162]. Horses are sold, their names changed, owners do not return the animals for examination, and thus they can be hard to find for follow-up. The most recent retrospective study with a higher number of foals and longest post-operative follow-up showed that 72.7% of the foals that underwent phacoemulsification were visual at ≤ 1 month post-operatively, 43.2% at 1–6 months post-operatively, 20.4% 6–12 months post-operatively, and 9.3% as young adults (more than 24 months post-operatively) [162]. Although the long-term outcome is not as good as veterinarian ophthalmologists would like, it seems to the authors that not removing the cataract and improving the vision status of these foals is also not satisfactory, and thus efforts should be made to improve the surgical results to restore and maintain sight in foals with cataracts.

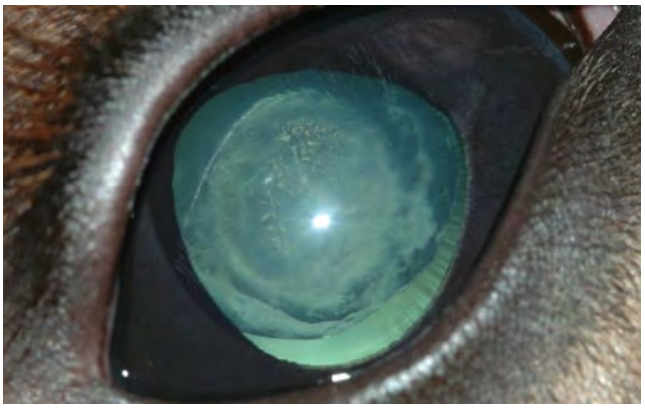
Other congenital abnormalities of the lens

Lens congenital abnormalities other than cataracts are uncommon in horses. They may be presented as the sole clinical sign or associated with other congenital ocular anomalies. Reported congenital lens conditions include aphakia, lens coloboma, microphakia, ectopia lentis, congenital lens luxation, spherophakia, lenticonus, and lentiglobus.

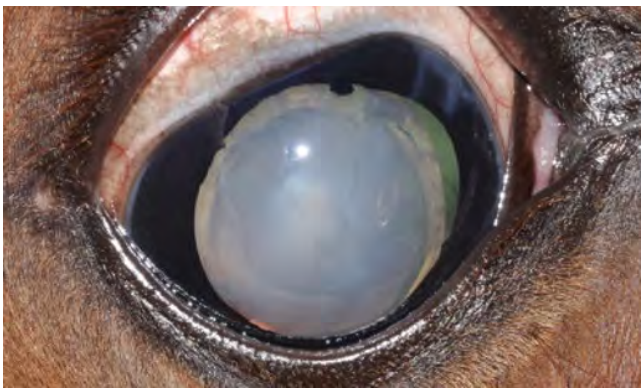
Congenital lens luxation and ectopia lentis

Congenital luxation, or dislocation of the lens, has been described secondary to a primary defect with abnormal zonules in form or number [2]. In comparison, ectopia lentis occurs when the lens vesicle fails to enter the optic cup, and the lens attempts to form in the anterior chamber [160]. These lenses may present with microphakia or spherophakia as well (Figure 4.34) [185]. Both situations, congenital luxation and ectopia lentis, are rare and, when present, they are often bilateral and associated with other ocular anomalies [14, 160, 186]. Lens luxation as part of MCOA syndrome has been described in ponies, accompanying other ocular anomalies such as iridal hypoplasia, cornea globosa, and iridocorneal angle abnormalities [54]. In both lenticular disorders the lens is often cataractous or spherophakic and may be located in the anterior chamber or in the vitreous cavity. In cases of congenital luxation in the anterior chamber, marked corneal edema and secondary glaucoma may be seen, whereas posterior luxated lens is commonly associated with iridodonesis, a deepened anterior chamber, and aphakic crescent.

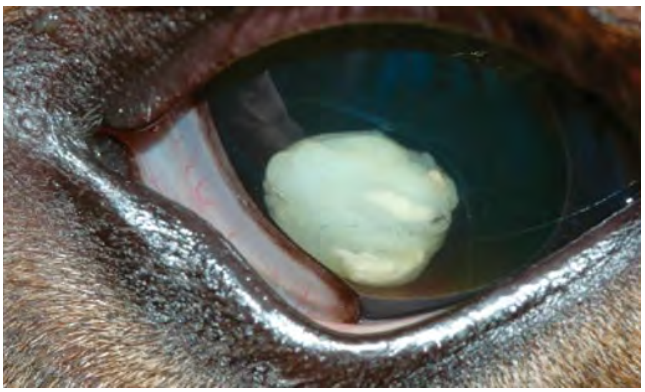
There are no reports on intracapsular lens extraction in foals, although a retrospective long-term evaluation in adults has revealed that the surgical intervention in these cases is associated with an extremely poor prognosis for both retention of vision and the globe [183, 187]. None of these anomalies, apart from MCOA, is thought to be hereditary [186].



(A)



(B)



(C)

Figure 4.34 (A) ASD in a 3-month-old foal. Notice the elongated zonules, immature cataract, iridal coloboma, and spherophakic lens. (B) Complete mature cataract, spherophakia, and vitreous prolapse in the medial pupillary margin in an ASD-affected foal. (C) ASD in a newborn foal showing ectopia lentis, lens resorption, and complete cataract. (*Source*: Photographs courtesy of Dr Riccardo Stoppini.)

Lens coloboma

Lens coloboma has been reported in foals as a notch-like defect at the equatorial lens [14, 57]. The condition is commonly associated with other congenital ocular defects such as iris and ciliary body colobomas [2, 14]. Embryogenesis of this defect is speculative, although a faulty development of the zonule is strongly suggested. The lens deprived of its normal pull in the defective region might be thicker and more spherical as if there were no loss of its substance. Like coloboma in other ocular locations, lens coloboma has been classified as typical or atypical, depending on its location. Lens colobomas do not impair vision significantly, but, if severe, may predispose to lens luxation [14].

Lenticonus and lentiglobus

Lenticonus and lentiglobus are defects in the lens shape in which the lens adopts a conical or globular contour, respectively. Altered shape can be located at the anterior or posterior aspects of the lens, but it has been more frequently described at the posterior lens pole. These defects have been sporadically reported in foals as unilateral lesions [188, 189]. Visual impairment is determined by the severity of the malformation, as well as the presence of associated cataract formation [14]. Because the lesion is usually unilateral, treatment will be an owner's option based on the foal's "performance" potential. Specific treatment has not been previously reported, but if vision is significantly impaired, phacoemulsification and IOL implantation will be the most indicated, according to the authors' criteria.

Microphakia

Microphakia or "small lens" may occur as an isolated defect, but it is almost always associated with other abnormalities such as microphthalmia and lens luxation. Unlike lens coloboma, microphakia is associated with elongated zonules and normal ciliary processes, visible when stretched (Figure 4.34) [14].

Acquired disorders

Acquired conditions of the lens are rare in foals. Similar to what happens in adults, these conditions may be associated with traumatic insults (coup-contrecoup or whiplash injuries) or other intraocular diseases, such as glaucoma and anterior uveitis [190].

Traumatic insults in the foal eye may induce lens luxation or subluxation if congenital anomalies of the zonules, chronic uveitis, or glaucoma are present. Furthermore, blunt and penetrating ocular trauma may rupture the elastic and thin anterior

lens capsule, leading to a severe intraocular inflammation of challenging management. Medical and surgical treatment of these conditions does not differ from the one recommended in adult horses (see Chapter 9).

Although not specifically reported in the literature, acquired cataracts in foals may represent sequelae of intraocular chronic inflammation secondary to systemic diseases, such as septicemia or *Rhodococcus* spp. infection. Early diagnosis and treatment of intraocular inflammation in foals is mandatory to reduce vision-threatening conditions. Other etiologies for cataract formation reported in adult horses, such as neoplasia, metabolic, or degenerative, are unlikely in foals.

Glaucoma

Glaucoma in foals

Equine glaucoma comprises a diverse group of vision-impairing intraocular disorders that have in common an elevation of IOP to a level incompatible with function of the retina and optic nerve, causing retinal ganglion cell death. Glaucoma can be congenital, primary or secondary.

Primary congenital glaucoma

Prevalence

Primary congenital glaucoma is uncommon and has been reported rarely in the horse, apart from in Thoroughbred, Arabian, and Standardbred horses [93, 190–192].

Pathogenesis

Pathogenesis is unknown, although the condition has been clinically and histopathologically reported in association with severe anterior chamber dysgenesis, and in some cases with lens luxation in foals [93, 190–195]. These findings raise the question of whether or not true primary congenital glaucoma exists in the horse [193, 195].

Clinical appearance

Clinical signs vary with the magnitude and duration of the IOP increase, as well as with the inciting cause of glaucoma [196]. Neonatal foals with glaucoma may show blindness, mild hydrophthalmos, opaque corneas, fixed and dilated pupils, corneal edema, corneal striae, retinal degeneration, and optic nerve cupping. In the reported cases, conditions such as lens luxation, lens coloboma, absent corpora nigra, and iridal hypoplasia were also described (Figure 4.35) [92, 190–192]. Diagnosis is based on clinical findings and tonometry readings.

Treatment and prognosis

Although enucleation in hydrophthalmic unilateral cases is a suitable surgical option, euthanasia is the more commonly requested treatment for unilateral as well as bilateral cases in foals [190, 192]. In general, prognosis for vision is poor, as eyes are already blind at first presentation.



Figure 4.35 Hydrophthalmos in a foal with congenital glaucoma. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)

Secondary congenital glaucoma

Secondary congenital glaucoma is extremely rare in foals. In the adult horse, it has been mostly associated with intraocular chronic inflammation, but this presentation has not been reported in foals. Other causes of secondary glaucoma such as ocular trauma and intraocular neoplasia may be found in young horses [196].

Diseases of the ocular posterior segment

Congenital posterior segment diseases

Congenital diseases in the posterior segment are uncommon in horses [20]. They may occur alone or in association with MCOA such as congenital megaloglobus, MCOA syndrome, or other ASD syndromes. The most commonly reported conditions in foals are retinal hemorrhages, colobomas, optic nerve hypoplasia, retinal dysplasia, retinal detachment, and congenital stationary night blindness (CSNB).

Retinal hemorrhages

Definition and prevalence

Retinal hemorrhage is a nonspecific lesion that may appear in different inflammatory diseases, but also in retinal detachment, trauma, clotting disorders, neoplasia, chorioretinitis, and other systemic conditions [14]. The condition has been described in both healthy and diseased foals, with incidences ranging from 11.4% to 29% in healthy newborn foals (within 96 hours of birth) [13, 17, 21, 23]. Hemorrhages can be seen as unilateral or bilateral findings [13, 23]. Although no gender predisposition has been generally seen [13, 17], female foals were significantly more affected in one study [23].

Pathogenesis

Retinal hemorrhages are seen more frequently in otherwise healthy foals [13, 17, 21, 23], casting doubts on their clinical significance. The etiology has not been clarified, but many clinicians consider that hemorrhages are due to the trauma of birth [13, 17, 23, 197], being associated in some studies with

large-sized foals or foals from uniparous mares [23, 197]. It has been suggested that a combination of anoxia/asphyxia and increased intraluminal pressure during birth may lead to vasodilation and vascular fragility, causing secondary retinal hemorrhages [23]. Fetal head compression with secondary vascular hypertension and capillary rupture during parturition has also been proposed [17, 23, 197].

Similarly, small retinal hemorrhages have been observed in foals suffering from neonatal maladjustment syndrome (hypoxic ischemic encephalopathy) at 1 or 2 days of age [197]. In addition, affected foals showed pupillary abnormalities, such as dilated and nonresponsive or miotic and asymmetric pupils. Apparent blindness accompanies a variety of neurologic and odd behavioral signs such as convulsions, opisthotonus, erection of the tail, hyperexcitability, coma, inability to stand, dog-sitting stance, frantic galloping movements, mouth breathing, teeth grinding, barking, sneezing, and loss of suck reflex. The syndrome was described primarily in Thoroughbreds and may result from circulatory disturbances induced in the foals at the time of birth [198].

Clinical appearance

Hemorrhages are mainly reported in the first 48 hours after birth, being observed mainly in the tapetal fundus and having a variable number (1–20 per eye) and shape [13, 17, 23]. While the majority of reported retrospective studies describe splash-like and small punctate hemorrhages [13, 21, 23], geographic hemorrhages have also been sporadically reported (Figure 4.36) [17]. Occasionally, punctual optic nerve hemorrhages have also been described [13, 23, 197].

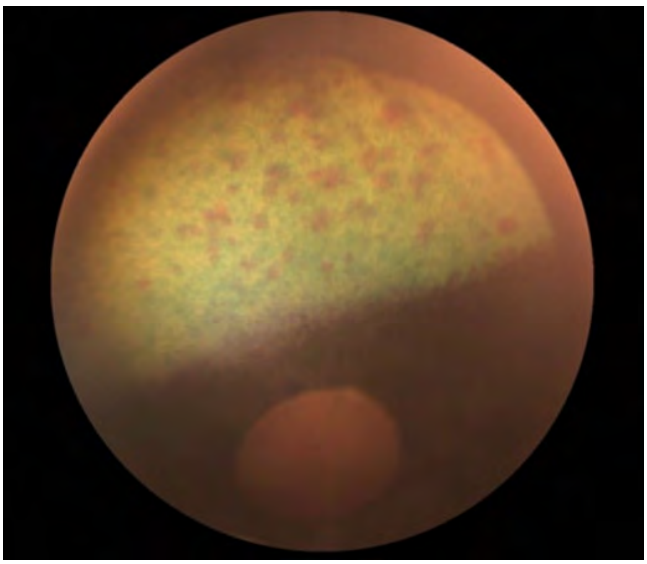


Figure 4.36 Funduscopic photograph of a 1-day old healthy foal. Note the bilateral punctate hemorrhages seen in the tapetal area.

Anatomic location

The anatomic location of the hemorrhages has not been elucidated; while some authors consider that they develop from the choroidal circulation [199], others suggest the subretinal space or the choriocapillaris as the most frequent locations [200, 201]. Conversely, bleeding from the optic discs has been suggested to be intraretinal in origin, as previously described in babies [13, 23]. In other nonpapillary areas of the fundus, because of the difference in blood supply, intraretinal lesions are unlikely.

Chronic subretinal lesions located between photoreceptors and retinal pigment epithelium (RPE) commonly cause RPE depigmentation and mechanical interference with the choriocapillaris. Based on the lack of RPE depigmentation seen after resolution of the reported retinal hemorrhages, the most probable location for these hemorrhages is the choriocapillaris. This anatomic location agrees with the tapetal clinical distribution observed in the reported cases, the nontapetal hemorrhages being hindered by the RPE pigmentation [23].

Treatment

Retinal hemorrhages resolve spontaneously within 7–10 days, resolution being faster in peripheral than in central hemorrhages [13, 17, 23]. Similarly, splash-like lesions took longer to reabsorb than punctate [23].

Colobomas of the posterior segment

Definition and prevalence

Colobomas refers to a congenital notch, gap, hole, or fissure of the ocular tissues [202]. Posterior segment colobomas may occur unilaterally as isolated entities or as part of complex malformation syndromes such as microphthalmia or MCOA [53, 94]. There is no breed or gender predisposition, although Appaloosa and Quarter horses have been suggested as being predisposed [197, 203].

Posterior segment colobomas may be seen affecting the optic nerve head (ONH) [94, 202, 204–206] or the RPE [53, 57]. ONH colobomas may be located in the region of the embryonic fissure, named typical colobomas (6 o´clock position) or in other locations (atypical colobomas). Atypical colobomas are most commonly seen in horses [57, 197]. Bilateral ONH colobomas in association with colobomas of the iris, ciliary body, lens, choroid, and retina have been described in a donkey [207].

Pathogenesis

Although the pathogenesis of typical coloboma is well known, the pathogenesis of atypical colobomas is still in debate. In typical coloboma, the inner layers of the optic cup, which should be approximated at the margin of the fissure, do not fuse to form a confluent neurosensory retina. The outer layer also fails to fuse, allowing the inner layer of the optic cup to evert through, resulting in a defect. The choroid and sclera, which are induced by developing RPE, fail to differentiate at the site. Instead, a membrane of undifferentiated retina covers poorly formed sclera. In colobomas

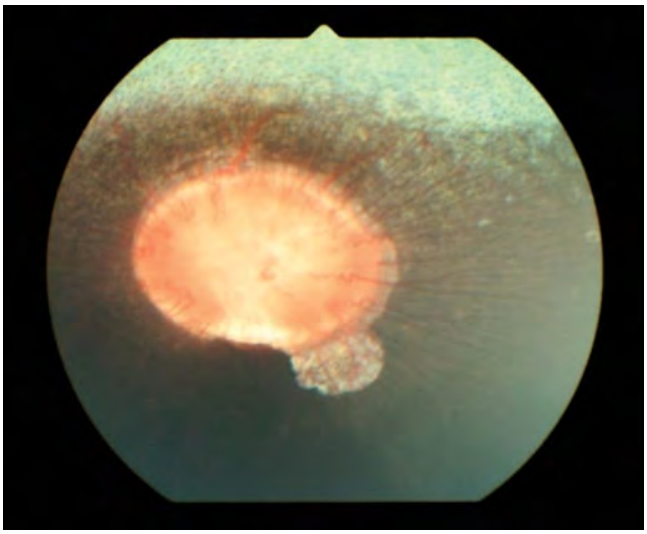


Figure 4.37 Small typical retinal pigmented epithelial coloboma adjacent to the optic nerve. This was an incidental finding without any clinical signs of vision deficits.

of the optic disc, the proximal portion of the optic stalk fails to close and the defect may extend into the choroid [197].

Clinical appearance

Despite most affected horses being asymptomatic and the lesions being found as incidental findings [208], others might present a history of blindness since birth [204–206]. Phenotypic expression of colobomatous defects in the posterior segment may vary from colobomatous ONHs to RPE colobomas or orbital cysts, the latter being clinically seen as anophthalmos.

In ONH colobomas, the size of the defect may vary from extensive, encompassing all ocular tissues derived from the embryonic retina, to partial, with defects that are barely noticeable, such as thinned choriocapillaris, pigment clumping, or small discrete chorioretinal defects along the fetal fissure (Figure 4.37). In the more severe presentations, the disc appears enlarged, vertically oval, and excavated, with the irregular floor bulging posteriorly and a membrane, derived from undifferentiated neurosensory retina, lining its surface or bridging the defect. Retinal tears or detachment may be present when pre-retinal fibrous tissue is visible in the coloboma. These conditions are usually associated with retinal dysplasia [197].

RPE colobomas, also known as "window defects," are seen most commonly in the nontapetal fundus surrounding the optic nerve as a well-demarcated, nonpigmented area with well-defined discrete border and no identifiable tissue depth. They are usually singular, but rarely occur as multiple lesions in a group [94, 208].

Diagnosis

For an experienced ophthalmologist the clinical diagnosis for both ONH and RPE colobomas is straightforward. The layers of the globe that are visible to the examiner can establish the depth of the coloboma: solid white lesions are typically associated with deep and severe colobomas, and orange or red lesions indicate choroidal vasculature, with a less severe coloboma. Small colobomas must be distinguished from the small 6-o'clock notch and peripapillary bright hyper-reflectivity that can be seen in some normal equine optic nerve heads [197].

Prognosis and heritability

The visual prognosis for affected horses depends on the severity of the coloboma, but also on the severity of the other associated ocular abnormalities, if present. While small ONH colobomas may be seen as an incidental finding [94, 197], severe ONH colobomas may be associated with different degrees of visual impairment [204–206].

RPE colobomas normally do not cause evident visual deficits [57], although, occasionally, large colobomas near the area centralis may have an impact on vision. However, as a general rule, the visual impact of an RPE coloboma seems to be less than that of an equally sized chorioretinal lesion.

Given the predisposition of colobomas in Quarter horses and Appaloosas, breeding of affected animals and their sires and dams should be avoided.

Optic nerve hypoplasia

Definition and prevalence

Optic nerve hypoplasia, or underdevelopment of the optic nerve, is a rare congenital abnormality in horses. It is of unknown origin, characterized by a reduced number or retinal ganglion cells. In one retrospective study its incidence accounted for 0.9% of all congenital anomalies [20].

Pathogenesis

Although difficult to document experimentally, optic nerve hypoplasia most likely results from a primary abnormality in the number or ultimate differentiation of the retinal ganglion cells [2].

Clinical appearance

Affected foals are likely to have a history of poor vision or blindness, with dilated pupils and reduced or absent pupillary light reflexes. In some cases, nystagmus may also be observed. The affected optic nerve appears pale and smaller than normal, and may be depressed or recessed [65, 209]. In some cases, retinal vessels are difficult to visualize, it being helpful to compare fellow eyes in unilateral or asymmetric cases. The ONH may be recessed away from the vitreous and will appear on focus with more negative diopter settings on the direct ophthalmoscope. The condition should be clinically differentiated from a reduction in the amount of the ONH myelinization that would lead to a small ONH in an otherwise normal and visual eye [2].

Treatment and heritability

There is no treatment for this condition and affected horses should not be used for breeding [203].

Retinal dysplasia

Definition and prevalence

Retinal dysplasia is a very rare developmental condition in horses, resulting in rosettes and multifocal retinal disorganization [2, 196]. Although mainly diagnosed as an incidental finding in MCOA-affected adult horses (cyst-phenotype) [50, 53], there are some individual reports in foals associated with other severe congenital conditions [65, 210]. Thoroughbreds appear to be predisposed, although no hereditary basis has been established [197]. Retinal dysplasia accounted for 3.5% of all congenital ocular anomalies in one study [20].

Pathogenesis

The cause is unknown. It has been classified as resulting from one of the following pathogenic mechanism: retinal nonattachment, defective RPE, or necrosis of the developing retina [2, 211]. *In utero* infections, although suggested [197, 203], have not been specifically associated with retinal dysplasia in the horse, leaving congenital noninfectious causes as the only confirmed etiology, so far.

Clinical appearance

On ophthalmic examination, affected foals may show bizarre single or multifocal, linear or geographic alterations in pigmentation, vascularity, tapetal color, and reflectivity (Figure 4.38). Retinal dysplasia has been identified in association with posterior segment cysts, suggesting enlargement of these retinal cysts as a possible cause [50, 53].

Diagnosis

The clinical diagnosis is straightforward. Nevertheless, the definitive diagnosis is based on histologic or OCT identification of the retinal rosette, a structure characterized by a central lumen surrounded by one or more layers or neuroblasts. Histopathologically, the neurosensory retina is folded upon itself, giving the appearance of a localized ring, termed a rosette.

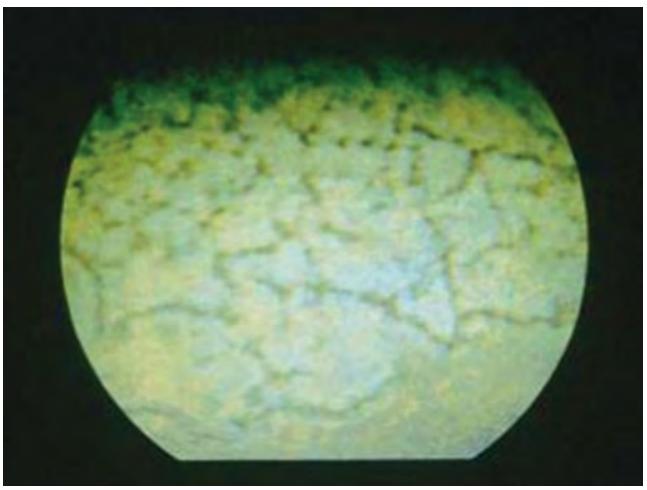


Figure 4.38 Retinal dysplasia is characterized by numerous pigmented folds in the superior peripapillary sensory retina. (*Source*: From Ramsey DT et al., 1999 [50].)

Treatment

There is no treatment for this nonprogressive congenital condition.

Prognosis and heritability

The lesion is nonprogressive and visual function depends upon the severity and extent of the maldevelopment, as well as the presence of other ocular abnormalities. The breeder should be aware that MCOA syndrome is a dominant trait with incomplete penetrance.

Retinal detachment

Definition and prevalence

Retinal detachment consists of the separation of the neuroretina from the underlying RPE, which implies a disruption of the intimate and essential (but structurally weak) association between the outer segments of the photoreceptors and the RPE. This loss of structural integrity is associated with a loss of function and secondary retinal degeneration in the affected area. The condition has been rarely reported in foals, although has been more frequently described in MCOA-affected adult horses [50–52, 107]. More frequently seen as a bilateral finding, unilateral cases may also occur [208]. Breed predisposition for the Standardbred and Thoroughbred has been suggested [197, 208].

Pathogenesis

The pathogenesis suggested is nonattachment of the neurosensory retina to the RPE secondary to incomplete invagination of the optic vesicle [2]. No infectious causes have been identified in the horse so far.

Clinical appearance

Affected animals show different degrees of visual deprivation, associated with nonresponsive mydriasis or slow pupillary light reflexes. Funduscopic examination in these foals may show anterior displacement of the retinal surface (seen as a grayish-colored veil) that, when severe, can be readily viewed directly through the pupil with a focal light source. In other less severe cases, the detached retina may be seen radiating from the ONH in translucent to opaque folds. In a complete retinal detachment with dialysis, the retina will be seen hanging in folds from the ONH. In addition, curvilinear streaks of hyperpigmented RPE, seen in association with uveal and retinal cysts, were suggested to mark the boundary of previous retinal detachments in MCOA-affected Rocky Mountain and Icelandic horses (Figure 4.39) [50, 107].

Diagnosis

Clinical diagnosis is straightforward for experienced ophthalmologists, although clinical differentiation with congenital retinoschisis is not feasible. Further imaging and histopathologic

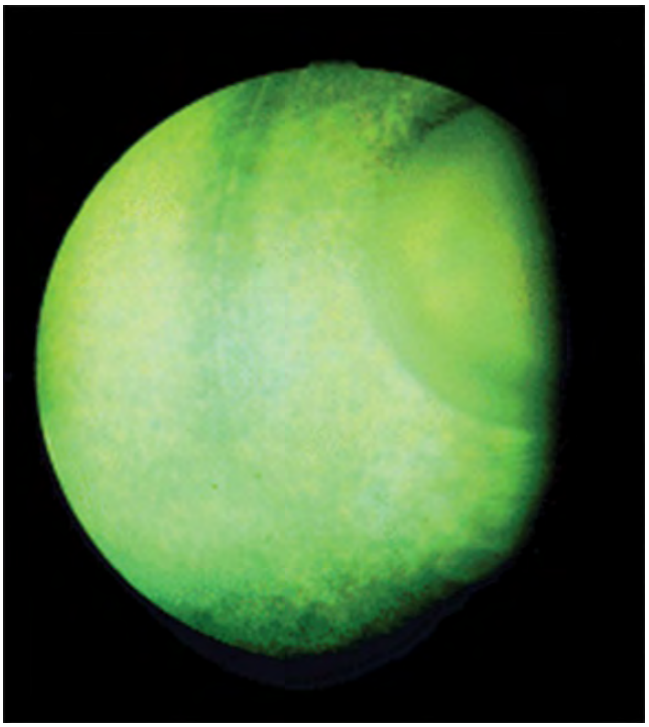


Figure 4.39 Detachment of the peripheral part of the temporal retina of the right eye of a Rocky Mountain horse with MCOA. A curvilinear pigmented line is present beyond the retinal detachment and signifies a demarcation line from a previous retinal detachment. (*Source*: From Ramsey DT et al., 1999 [50].)

studies are needed to distinguish between these two very close congenital retinal conditions.

Treatment

Although retinal detachment can be successfully treated in some animal species, there are no reports on treating this condition, when congenital, in foals. Possible intraretinal abnormalities and secondary retinal degeneration may be a concern when considering surgical treatment.

Prognosis and heritability

The visual impairment secondary to a congenital retinal detachment depends on its severity and location, focal retinal detachments being associated with clinically visual foals, and complete detachment with blindness. Although progression of the condition is rarely reported, focal retinal detachment may progress [197]. In general, the prognosis for return of vision is poor and owners may request euthanasia. Although heritability has not yet been established, affected horses should not be used for breeding.

Congenital stationary night blindness

Congenital stationary night blindness (CSNB) has been reported most commonly in the Appaloosa [212–216], although individual cases have been noted in Quarter horses [22], Thoroughbreds, Paso Fino, [217] and Standardbreds [208]. Similarly to CSNB in humans, it is characterized by impaired vision in dark conditions since birth [213]. While prevalence of CSNB in the horse has accounted for 3.5% of congenital ocular anomalies in one study [208], in the Appaloosa breed it has been reported as being 33% [216]. See Chapter 13 for a complete description.

Persistent hyaloid artery

Definition and prevalence

Persistent hyaloid artery (PHA) results from a failure of part of or the entire hyaloid artery to regress and is seldom reported in equine literature [94]. The hyaloid artery, also known as the posterior tunica vasculosa lentis (TVL), is the termination of the primitive ophthalmic artery that branches around the posterior lens capsule, and continues anteriorly to anastomose with the network of vessels in the pupillary membrane [2]. The complete TVL begins to regress before birth and reabsorption progresses, slowly, during the foal's life, and even into adulthood [13, 218]. Some authors describe complete reabsorption of the remnant by 3–4 months of age [20], while others establish 6–9 months as the maximum period for its physiologic reabsorption [13, 17, 24, 219, 220]. Due to the longer period of time needed for complete regression of the hyaloid artery in horses, both conditions, PHA and hyaloid remnants, appear together during the first 9 months of life. These terms have been misused for years in equine literature [14, 94, 220], inducing some controversial findings.

Pathogenesis

The pathogenic mechanism that prevents complete reabsorption of the hyaloid artery is unknown. Although proximal arteriolar vasoconstriction at birth has been suggested to precede vascular apoptosis and, later, necrosis, until complete reabsorption [2], there are no reports on the exact direction of the arterial reabsorption. While some studies describe vessel breakdown beginning in the middle of the artery, with the proximal and distal parts being the last to atrophy [187, 220], others suggest that detachment and atrophy might start close to the lens [13, 197].

Clinical appearence

In the few cases of PHA reported in sucklings, the condition has been described in association with other severe congenital abnormalities, such as cataracts and severe microphthalmia, precluding its direct observation [221, 222]. Similarly to what has been described in other species affected with this condition, if complete, PHA could hypothetically be recognized as a fine, white or red (depending on the degree of vascular perfusion), curving line traversing the vitreous from the center of the optic disc to the posterior aspect of the lens [169].

Differential diagnosis

PHA should be distinguished from the physiologic remnants of the hyaloid artery, commonly seen in newborn foals and considered as normal findings in foals until 9 months of age.

Although any presence of hyaloid artery in animals older than 9 months should be considered as PHA, the differentiation between both conditions is difficult at earlier ages. The scarce reports in newborn foals suggest that intraocular abnormalities should be expected in PHA-affected eyes [13, 74]. In foals older than 9 months, PHA may be observed as a small white linear tissue emerging from the center of the optic disc, also called Bergmeister's papilla.

In addition, PHA should also be differentiated from Mittendorf's dot, which is characterized by a small (1-mm) area of fibrosis, attached at the posterior lens capsule, and considered as a manifestation of incomplete regression of the hyaloid artery. Mittendorf's dot has been previously described in three adult Exmoor ponies and in a Thoroughbred horse [94, 202].

Treatment and prognosis

No treatment is indicated for the condition in horses. PHA is a nonprogressive condition that, in most cases, does not cause any visual impairment in horses [220, 222].

Aquired ocular fundus diseases

Acquired diseases of the ocular fundus have been rarely reported in foals. Although systemic diseases have been associated with posterior segment abnormalities, the reports considered in the literature are scarce and associated with anterior segment inflammatory processes.

Congenital diseases of the globe and orbit

Congenital abnormalities of the globe and the orbit have been sporadically described in foals, with microphthalmos the most commonly described disorder [20, 41].

Microphthalmos and anopthalmos

Definition and prevalence

Microphthalmos is a congenital or developmental anomaly in which the globe is abnormally small. Microphthalmia has been divided classically into three categories: (1) pure microphthalmia (nanophthalmia), where the eye is small but otherwise normal; (2) colobomatous microphthalmia, where the defect is associated with failure of involution of the optic vesicle or closure of the embryonic cleft; and (3) complicated microphthalmia, where anomalous development occurs, which is unrelated to fissure closure [223]. The presentation can be unilateral or bilateral and may be diagnosed as an isolated finding or, more frequently, it is associated with other systemic anomalies [65, 99, 224, 225]. Microphthalmia is considered one of the most reported congenital ocular abnormalities in the horse, ranging in incidence from 7% to 14.7% [20, 41]. An incidence of 4.6% was established in a retrospective study of equine congenital defects that result in death or euthanasia, being the fourth most commonly reported congenital anomaly [226].

Conversely, anophthalmia, or complete absence of ocular tissues, is extremely rare and normally associated with other severe malformations incompatible with life.

Pathogenesis

Embryologically, microphthalmos may result from different pathogenic mechanisms. Colobomatous microphthalmia has been associated with an incomplete closure of the optic fissure, preventing normal sealing and inflation of the globe, whereas complicated microphthalmia may be a consequence of a mistimed union of the migrating embryologic tissues. The severity of the microphthalmia depends on the gestational stage during which the insult occurs, being more severe when insult occurs early in the gestation, at the time of optic vesicle and lens formation [227]. The cause of this embryological dysfunction is unknown, although interaction between genetic and environmental factors is suggested [14]. A case of microphthalmia with brachygnathia has been reported in an older Friesian mare that received griseofulvin in the second month of gestation [228], and a case of bilateral microphthalmia was associated with strangles and the use of sulphadimethoxine during the sixth week of gestation [225]. Although all equine breeds may be affected, the Thoroughbred horse appears to have a higher incidence [229].

Clinical appearance

The condition is usually recognized in newborn foals [65, 224, 225, 228]. The main complaint is the reduced size of the globe and visual impairment. On examination, the size of the globe may vary considerably, from a near-normal structure with normal function, to a microscopic structure with only pigmented remnants (Figure 4.40). Furthermore, the microphthalmic eye may be associated with multiple intraocular and orbital malformations [65, 202, 224, 225, 228].



Figure 4.40 Clinical appearance of a complicated microphthalmic eye in a 3-month-old Andalusian horse.

Diagnosis

A complete ophthalmic examination should be performed in order to further classify the microphthalmia, and eventually make a visual prognosis. When severe, the condition may be differentiated from anophthalmia. Ocular/orbital ultrasound may help to evidence small remnants of the globe, thus allowing proper classification of the condition.

Treatment

The treatment protocols vary depending on the severity of the microphthalmia and the associated intraocular abnormalities. If the eye approaches normal size and is still visual, no treatment is recommended. When the nearly normal-sized eye is associated with complete cataracts, and has appropriate light responses and a normal ERG, it is often possible to restore useful vision with cataract surgery. If the affected eye is very small and blind, secondary conjunctivitis will lead to chronic discharge and require enucleation. For a more normal development of the orbit, stepwise increase in orbital conformer size may assist in the approximation of normal orbit size in the adult horse [229].

Prognosis and heritability

Visual impairment in foals with microphthalmia depends on its severity and on the intraocular associated signs. If severe and bilateral, the prognosis for vision is poor and euthanasia is the only course of action. In unilateral cases, however, the animal may manage well and adapt as it ages, although the owner may be aware of the abnormal development of the ipsilateral orbit and ipsilateral facial abnormality. Heritability for this condition has not been described in the foal, although affected animals should not be bred.

Strabismus

Strabismus, or deviation of the globe from its normal orientation in a non exophthalmic eye, may be noted alone or in combination with other congenital ocular abnormalities [220]. This is a rarely reported condition in horses, but has been reported in mules with an incidence of 0.5% [14]. There is a breed predisposition for Appaloosas, being affected by congenital hypertropia or dorsal deviation of the globe, as well as by dorsomedial strabismus in association with CSNB [214, 230]. This pathologic condition should be differentiated from the mild ventromedial strabismus commonly seen in newborn foals [13].

Other congenital diseases of the globe

Congenital conditions affecting the globe, other than microphthalmia, are seldom reported in equine ophthalmology. In contrast to that described in ancient mythology, no cases are viable, as those severe ocular abnormalities are always accompanied by other systemic deformities. A case of usual cyclopia, a rare form of holoprosencephaly characterized by the failure of the embryonic prosencephalon to properly divide the orbits of the eye into two cavities, was reported in a newborn foal [231]. In addition, a case of unusual cyclopia or synophthalmia, in which the two eyes were completely fused into one, has been noted in an Andalusian horse in the south of Spain [232] (Figure 4.41).

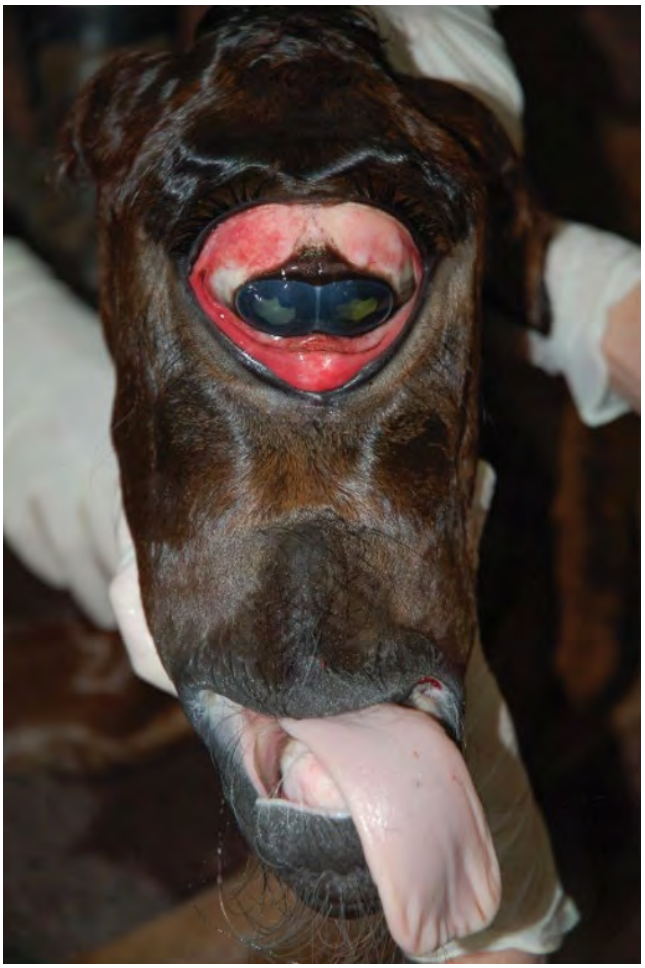


Figure 4.41 Synophthalmia in an Andalusian newborn foal. (*Source*: Reproduced with permission from Dr Alejandro Bayón, Murcia, Spain.)

Other congenital diseases of the orbit

Congenital diseases of the orbit are very rarely described in horses, with only two case reports [233–235]. If present in a foal, the diagnostic plan for exophthalmia is identical to that described in adults (see Chapter 5).

Orbital dermoids are particularly rare in horses, being reported just once [233]. A cystic dermoid causing unilateral exophthalmia by the age of 4 years was described in an Andalusian horse and successfully treated by dorsolateral orbitotomy through the supraorbital fossa. Prognosis depends on the size of the mass, extent of exophthalmos, and damage to the ocular surface, but, in general, the prognosis for saving the globe is good for small and moderately sized masses.

Vascular abnormalities of the globe and the orbit causing exophthalmia were observed in a 3-year-old horse with meningocerebral hemangiomatosis resembling Sturge–Weber disease [234]. In that individual, prominent arterioles affected the choroid plexus of the ventricles intracranially, together with milder vascular abnormalities in the orbit. This case presented with intermittent seizures and was euthanized; no ophthalmic ocular signs were reported. Venous sinus dilatations may be reduced surgically, but access is often limited.

Acquired diseases of the orbit

There are no specific reports on acquired diseases affecting the orbit in foals, although the same acquired diseases that affect adults may affect younger horses, with less tendency for neoplastic and degenerative conditions.

Additional content

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www.wiley.com/go/gilger/ophthalmology

includes additional text and figures that are not in the printed book or E-book.

Please see the "**About the companion website**" page at the start of the book for details on how to access the website.

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CHAPTER 5

Diseases and surgery of the globe and orbit

Claudia Hartley and Rachael A. Grundon*

Introduction

Diseases of the equine orbit may not be as common as diseases in other parts of the equine eye, but the impact of orbital disease is very high. Not only do diseases of the equine orbit result in profound cosmetic changes such as exophthalmos or strabismus, but also, in almost all cases, vision loss occurs. Unfortunately, these cosmetic changes and vision loss are commonly permanent, and prognosis of orbital disease in general is poor. The globe and orbit are subject to trauma, inflammation, neoplasia, congenital disease, and extension of disease into the orbit from adjacent cranial cavities, particularly the sinuses. Recent advances in imaging techniques and their wider availability have opened the door for more elaborate medical and surgical therapy. The desire for better cosmetic outcomes after serious ocular injury and trauma has resulted in better surgical repair of orbital fractures and a greater variety of surgical prostheses. In this chapter, diseases of the orbit and globe surgery are described, with emphasis on diagnostics, medical therapy, and surgical management.

Clinical anatomy and physiology

Skull and foramina

The horse is unusual in having a complete bony orbital rim (Figure 5.1). The orbit and globes are positioned laterally on the head and are ideally situated for a wide and panoramic visual field exceeding 340 degrees [1]. This seems appropriate for the horse's ecological niche as a grazer and consequently a prey animal, but perhaps it is less perfect for the activities it is commonly tasked with in today's society. The visual field is binocular, permitting stereoscopy, and the wide separation of the two globes provides greater depth perception than most other domestic species can attain. The main visual axis is approximately parallel with the long axis of the skull [2]. Equine vision is explored more thoroughly in Chapter 12.

The equine globe is among the largest in the mammalian kingdom, perhaps eclipsed in size only by the giraffe's eye. The axis of the globe in the horse is nearly perpendicular to that of the skull and angled with respect to the long axis of the orbit. The average dimensions of the adult horse globe are 43.68 mm anterior–posterior, 47.63 mm vertically, and 48.45 mm horizontally [3]. The globe of the mule is almost identical in size, measuring 43.0 mm, 47.5 mm, and 48.5 mm in the same orientation. The globe is not a sphere, but rather is compressed from anterior to posterior, with the ratios of the dimensions previously given being 1:1.09:1.10 for the horse and 1:1.10:1.12 for the mule [3]. The globe is located at the anterior border of the rather large orbit, which averages $62 \times 59 \times 98$ mm. The orbits are separated by 172 mm across the anterior surface of the frontal bone [3]. The remainder of the orbital cavity is filled largely by fat and muscle and is divided into pockets by layers of connective tissue that coordinate ocular mobility.

The orbital bones are the frontal, lacrimal, zygomatic, and temporal bones (clockwise for the right orbit), with the sphenoid and palatine bone forming the deeper internal wall of the orbit that separates it from the calvarium (see Figures 5.1 and 5.2C). The complete bony rim temporally and dorsally is composed of the frontal process of the zygomatic bone and zygomatic processes of the frontal and temporal bones. The supraorbital foramen is located in the anterior aspect of the frontal bone that forms the dorsal orbital rim. The lacrimal gland is closely adhered to the internal orbit near the dorsotemporal orbital rim. Inferiorly the zygomatic bone forms the lower rim, and nasally it is fused to the lacrimal bone, wherein embedded canals provide refuge to the nasolacrimal duct canaliculi (see Figures 5.1 and 5.2C). Beneath the globe, cushioning is provided by orbital fat that separates the globe from the palatine bone. Caudally the orbital floor is angled inferiorly until it is composed

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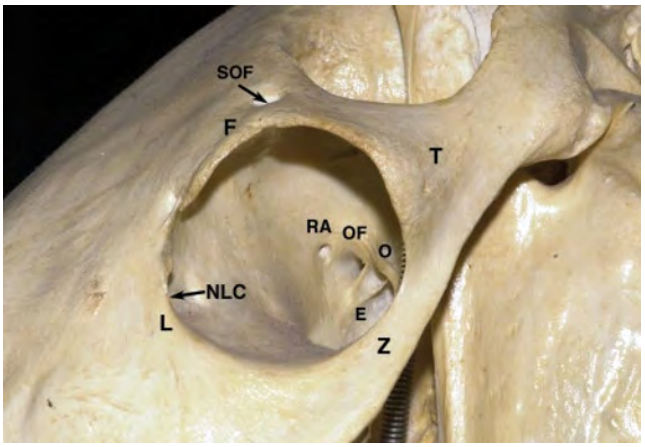


Figure 5.1 The horse has a complete bony orbital rim. The orbital bones include the frontal (F), lacrimal (L), zygomatic (Z), and temporal (T). The sphenoid and palatine bone forming the medial wall of the orbit separates the orbit from the calvarium. The nasolacrimal duct canaliculi (NLC) course through the lacrimal bone. The orbital foramina through the sphenoid bone includes, from anterior to posterior, the rostral alar (RA), orbital fissure (OF), optic (O), and ethmoidal (E) (see Table 5.1). The supraorbital foramen (SOF) exits through the frontal bone.

of soft tissues only, including the large pterygoid muscles that exert closing motion for the lower jaw. The bony floor of the orbit ends directly beneath the caudal aspect of the dorsal rim.

Various foramina provide conduits between the orbit and other compartments of the head, particularly through the calvarium to the brain. The efferent foramina are arranged curvilinearly along the sphenoid bone that forms the medial orbital wall. From anterior to posterior they are the rostral alar, orbital fissure, optic, and ethmoidal (Table 5.1) and are evident in Figure 5.1. The clinical significance of the location of the foramina lies in avoiding their contents during biopsy and exploratory procedures. The foramina appear to provide relatively minimal risk for extension of orbital infection or neoplasia, but they may be severely damaged during trauma to the calvarium, with serious consequences for vision. Fracture of the basisphenoid and basioccipital bones frequently occurs in blunt trauma to the poll. Afferent foramina are located in the extreme anteromedial portion of the orbit; they are the caudal palatine (major palatine artery and nerve), the maxillary (infraorbital artery, vein, and nerve), and sphenopalatine (sphenopalatine artery and vein and pterygopalatine nerve).

The **infraorbital foramen** is the point of egress of the infraorbital nerve, artery, and vein from the orbit, which can be palpated 1 cm rostral and 3 cm dorsal to the rostral edge of the facial crest, a third of the distance to the nostrils (Figure 5.2A, B). It may be partially obscured by the overlying muscular belly of the levator nasolabialis [4]. The infraorbital nerve arises from the maxillary branch of the trigeminal to provide sensory innervation to the upper lip, nostril, and cheek. Its major significance is in desensitization for laceration repair of those tissues, and infrequently for nerve blockade to evaluate the contribution of trigeminal summation in clinical head shakers [5]. The infraorbital canal bisects the maxillary sinus (see Figure 5.2D).

Periorbitum

The orbit is completely lined with a strong, multilayered periosteum/periorbitum. This dense fibrous connective tissue has surgical importance because it provides a formidable barrier to the extension of orbital disease beyond the soft-tissue contents into the bone architecture. Even moderately extensive stages of squamous cell carcinoma may be sufficiently contained by the periosteum, allowing successful and complete surgical removal of the neoplastic expansion. The periorbitum is retained in enucleation, and its anterior portion is preferably completely reapposed in closure. In the exenteration procedure, the entirety of the periorbitum is removed. In cases of orbital neoplasia that has broached the periorbita, the periosteum of the orbital bones should also be removed. If the periosteal surface overlying orbital bone has lost its thin glossy appearance, suggesting pathology, it should be elevated and removed; deeper lesions should be explored and treated appropriately.

Globe

The equine globe resides anteriorly within the orbit, supported by loosely packed retrobulbar tissues. Reflections of the periorbitum together with smooth muscle attach the globe to the orbital rim. The external wall of the globe is a trilayer, with the sclera and cornea forming the outer predominantly fibrous tunic, the highly vascular uvea forming the middle layer, and the neural layers of the retina being most internal. The thickness of the sclera is 1.05 mm where the optic nerve penetrates the posterior pole, 0.31 mm at the limbus, and 0.5 mm at the equator of the globe [6]. Consequently, during traumatic events, the sclera most frequently ruptures at the limbus, the potentially weakest area of the sclera [7]. The adult cornea measures 29.7–34.0 mm horizontally and 23.0–26.5 mm vertically [8]. When measured by ultrasonic pachymetry, the corneal thickness averages 0.793–0.893 mm, with no effect of gender or age but a tendency to be thicker in the dorsal and ventral quadrants [9, 10]. These values have also been reported for Miniature horses, where average corneal thickness was 0.785 mm, horizontal diameter was 25.8 mm, and vertical diameter was 19.4 mm [11]. Mean intraocular pressure (IOP) was 26.0 mm Hg [11]. The internal volume of the equine globe is large. In one study, the mean aqueous humor volume measured in six adult equine eyes was 3.04 ± 1.27 mL, and the mean vitreous humor volume was 26.15 ± 4.87 mL [6]. Total internal volume of the globe has been reported up to 45–50 mL with a weight of 100 g [6].

The multiple large bellies of the retractor bulbi muscle, which attach extensively around the posterior half of the sclera and are innervated by cranial nerve VI, dominate the extraocular muscles (Figure 5.3). The globe retraction reflex provides one of the major methods of evaluating this nerve's function. The other six muscles have typical attachments (Table 5.2) but more extensive bulk and insertion than is the case in many other species. Muscular attachments are seldom avulsed in orbital trauma (in contrast to the dog), but they may become entrapped and be unable to function after orbital fractures.

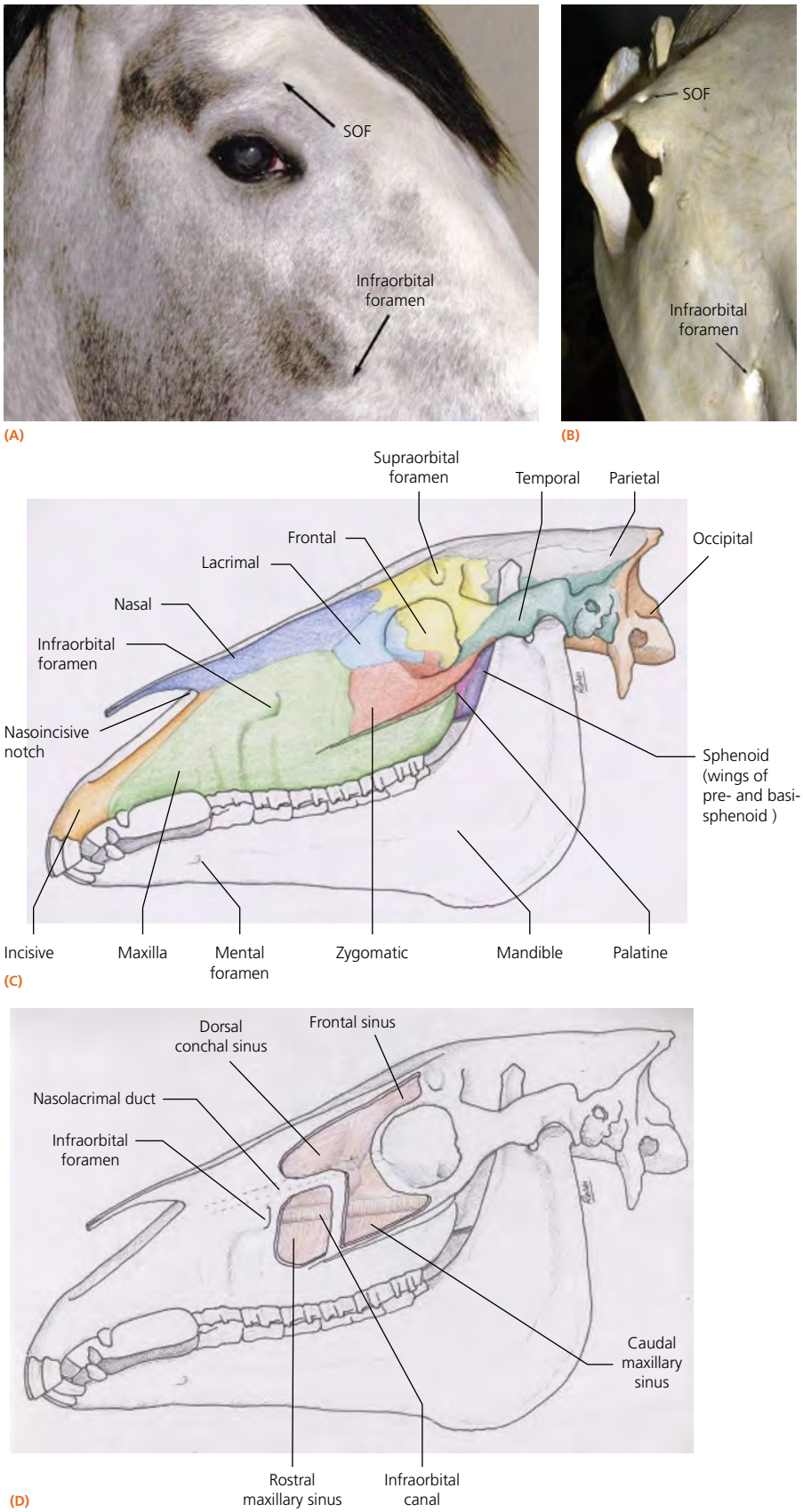


Figure 5.2 (A) The infraorbital foramen is the point of egress of the infraorbital nerve, artery, and vein from the orbit. It can be palpated 1 cm rostral and 3 cm dorsal to the rostral edge of the facial crest, a third of the distance to the nostrils (**arrows**). SOF, Supraorbital foramen. (B) Equine skull viewed from the front, demonstrating the right orbit and infraorbital foramen (**arrow**). (C) Equine skull illustrating the different skull bones. (D) Equine skull illustrating the paranasal sinuses. The infraorbital canal bisects the maxillary sinus. (*Source*: (C, D) Reproduced with permission from Roser Tetas Pont, Bedfordshire, UK.)

Orbital vascular supply

The vascular supply of the equine orbit has been described in detail, and the reader is referred to the excellent work of Simoens et al. and Ninomiya and Inomata [12, 13]. Most vessels cross through the orbit inferiorly and nasally and may be avoided by aspirating and biopsying the orbit only from the dorsal, lateral, or dorsomedial directions. The orbital branches of the external ophthalmic artery are variably derived from the internal maxillary artery deep within the orbit (Figure 5.4). Two functional groups, the ciliary arteries rostrally and the chorioretinal arteries caudally, perfuse the globe. Posterior ciliary arteries enter the sclera behind the equator in the cardinal positions to perfuse the choroid and continue forwards toward the anterior segment within the sclera. Anterior ciliary arteries enter superiorly and inferiorly caudal to the limbus. Multiple chorioretinal arteries (10–20) surround the optic nerve at its entry through the sclera, supplying retinal arteries and contributing to local choroidal perfusion [12].

The angular aqueous plexus drains into the veins of the choroidal venous system (anterior segments of the vortex veins) along with the venous drainage from the iris and ciliary processes. The choroidal venous drainage is via posterior segments of the vortex veins, which drain into circumferential veins known as the circle of Hovius. This is a complete venous circle located just anterior to the equator. The circle of Hovius is drained by four vortex veins (dorsal, ventral, lateral, and medial), which pass obliquely through the suprachoroidal space and exit the sclera just posterior to the equator. Additionally, several posterior ciliary veins also drain limited areas of the posterior choriocapillaris and perforate the sclera somewhat perpendicularly. It has been postulated that this duality may allow drainage via the posterior ciliary veins in the event of occlusion of the vortex veins, and vice versa [13].

Table 5.1 Structures perforating the orbit and contents.

Structure	Osteum
Maxillary artery and nerve	Rostral alar foramen
Ethmoidal artery, vein, nerve	Ethmoidal foramen
Optic nerve (II)	Optic foramen
Oculomotor nerve (III)	Orbital foramen
Trochlear nerve (IV)	Orbital foramen
Abducens nerve (VI)	Orbital foramen
Ophthalmic branch of trigeminal nerve (V)	Orbital foramen
Supraorbital artery, vein, nerve	Supraorbital foramen
Major palatine artery, vein, nerve	Caudal palatine foramen
Infraorbital vein, artery, nerve	Maxillary foramen
Sphenopalatine artery and vein and pterygopalatine nerve	Sphenopalatine foramen

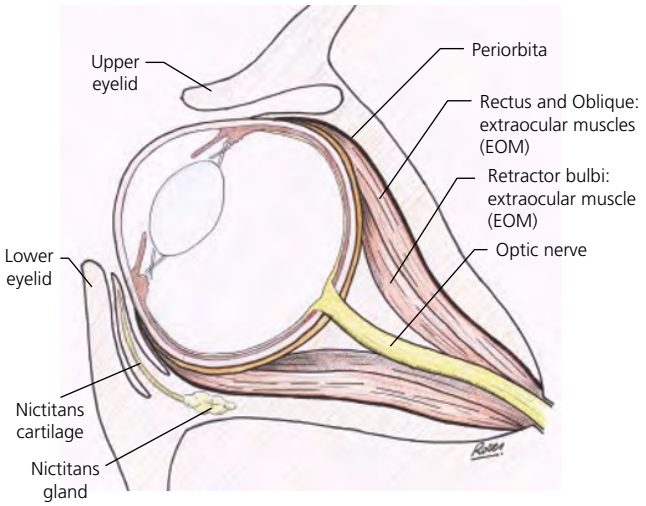


Figure 5.3 The extraocular muscles of the horse, revealing the multiple large bellies of the rectus (dorsal, ventral, lateral, and medial), obliques (dorsal and ventral), and retractor bulbi muscles, which attach extensively around the posterior half of the sclera. (*Source*: Reproduced with permission from Roser Tetas Pont, Bedfordshire, UK.)

Table 5.2 Orbital and ocular muscles: function and innervation.

	Function	Innervation
Extraocular muscle		
Dorsal rectus	Upward motion of globe	Oculomotor (III)
Ventral rectus	Downward motion	Oculomotor (III)
Medial rectus	Medial motion	Oculomotor (III)
Lateral rectus	Lateral motion	Abducens (VI)
Dorsal oblique	Rotation nasally and inferiorly	Trochlear (IV)
Ventral oblique	Rotation laterally and superiorly	Oculomotor (III)
Retractor bulbi	Posterior motion of globe	Abducens (VI)
Eyelid		
Levator palpebrae superioris	Elevates upper eyelid	Facial (VIII)
Levator angularis oculi	Elevates nasal eyelid/eyebrow	Oculomotor (III)
Malaris	Opens lower eyelid	Facial (VII)
Orbicularis oculi	Forceful closure of eyelids	Facial (VII)
Retractor angularis oculi	Retracts lateral canthus	Facial (VII)
Arrectores ciliorum	Elevates eyelashes	Sympathetic
Orbitalis (Müller's): superior and inferior tarsus and circular fibers	Retracts eyelid (smooth)	Sympathetic
Corrugator supercilii	Elevates upper eyelid	Facial (VII)

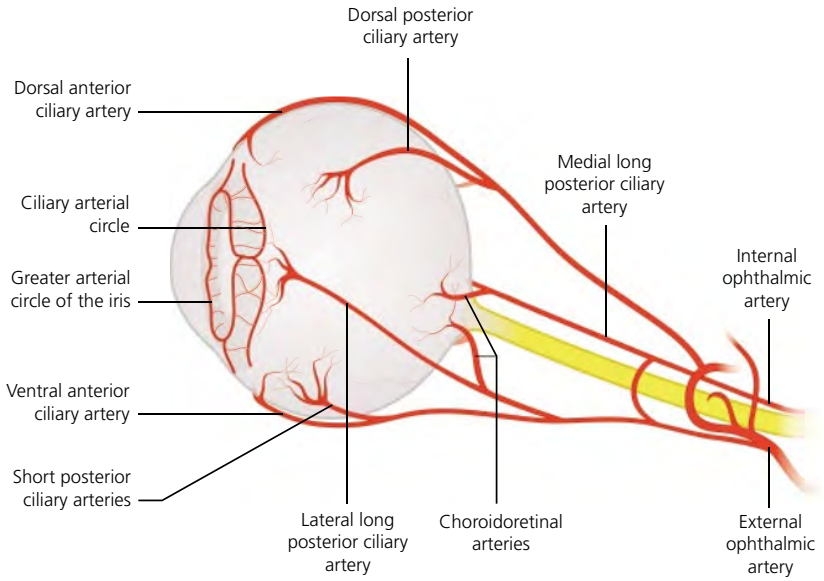


Figure 5.4 Arterial vascular supply to the equine orbit. (*Source*: Illustration by Samantha J Elmhurst BA Hons/LivingArt.)

The dorsal vortex, palpebral, and lacrimal veins course into the dorsal ophthalmic vein, before more caudal contributions from the anterior ciliary, supraorbital, muscularis, and infratrochlear veins join, and ultimately form the ophthalmic vein at the apex of the orbit. The ventral vortex vein anteriorly drains into the deep facial vein (former reflex vein), which also receives venous return from the muscular and palpebral veins, the great palatine, sphenopalatine, and infraorbital veins in the anterior orbit before entering the facial vein.

Structures adjacent to the orbit

Oral/buccal cavity

The buccal cavity is separated from the orbit in horses because of skull thickness and size and because of the complete bony orbit. Dental disease may still impact the orbit via the sinuses, but it must be substantial to do so. The last premolar and first three molars arise in the maxillary sinus, and the last molar abuts the sphenopalatine sinus. If oral disease is present or suspected, the buccal cavity should be opened and examined, and the horse's ability to prehend food should be further evaluated. Manipulation of the mandible on the maxilla will often elicit information about functional quality of apposition of the dental arcades. An oral speculum is necessary for more detailed analysis and should be performed if malodorous breath, evidence of food retention/packing, or chronic rhinorrhea or purulent discharge is present.

Guttural pouch

The guttural pouch is a diverticulum of the eustachian tube that occupies the area posterior to the mandible and is the site of multiple fragile structures. It extends anteriorly to closely approximate the orbit and enters the pharynx through a slit-like opening. Therefore disease of the guttural pouch may directly impact the orbit. More commonly, ocular disease may result from damage to the internal carotid artery that passes through the guttural pouch or to the cranial cervical ganglion of the autonomic nervous system. The most common diseases of the equine guttural pouches are bacterial or fungal infection, empyema, tympany, and temporohyoid osteoarthropathy. Many of these conditions require surgical intervention; however, the surgical approach is fraught with difficulty due to the proximity of important structures (e.g., the internal carotid artery). Rupture of the internal carotid artery is a life-threatening condition. See Chapter 15 for more information on guttural pouch disease.

Nasolacrimal duct

The nasolacrimal duct system originates proximally via large puncta in the upper and lower eyelids and is joined by canaliculi to the lacrimal sac, which is embedded in the lacrimal bone. Damage by fracture, direct blunt trauma, or infectious or inflammatory disease at this site may cause epiphora and chronic irritation. Treatment of nasolacrimal disease is described in Chapter 6. The nasolacrimal duct traverses the maxillary sinus, and sinusitis resulting in increased sinus pressure may functionally obstruct the duct, resulting in epiphora.

Periorbital sinuses

Periorbital sinuses, the frontal (conchofrontal), maxillary (caudal and rostral), and sphenopalatine, are in close anatomic proximity to the orbit (see Figure 5.2D). Primary sinus diseases may secondarily affect one or both orbits [14–19]. The **frontal sinus** is a shallow, wide sinus parallel with the frontal bone; it extends anteriorly from a line joining each temporomandibular joint forward almost to the dorsal turbinate bone that represents the conchofrontal sinus. The sinus system is lined with epithelium and is air filled; therefore an open fracture of any sinus is clinically relevant because it is considered a contaminated wound. The **maxillary sinus** extends ventrally from an imaginary line joining the medial canthus and the nasomaxillary notch, to just below the facial crest. The rostral border is the rostral extent of the facial crest, and the caudal border is the midline of the orbit.

Diminutive **ethmoidal and sphenopalatine sinuses** are present medial to the internal wall of the orbit and are more difficult to identify from external landmarks. Infection of the sphenopalatine sinuses may cause swelling and distention that can compress the optic nerve and chiasm, resulting in blindness [20]. Together with the frontal sinus, drainage is into the caudal maxillary sinus. Ultimately, drainage occurs from these sinuses into the nasal cavity.

When surgical drainage is indicated for sinus disease, trephination dorsal to a line between the infraorbital foramen and the medial canthus can result in nasolacrimal duct damage and must be avoided (see Figure 5.2D) [21]. Rostral and caudal trephine sites for the rostral maxillary sinus (RMS) have been described: 40% or 50% of the distance from the rostral end of the facial crest to the level of the medial canthus of the eye and 1 cm ventral to a line joining the infraorbital foramen and medial canthus, respectively. The rostral site was considered more reliable for entering the RMS. However, horses less than 5 years of age had a high risk of the trephine site overlying a cheek tooth and radiographic guidance was recommended for this group [135].

Ethmoid turbinates

The ethmoid turbinates are located axially and inferiorly to the orbit at the caudal end of the nasal cavity within the skull. This area receives a very rich vascular supply and may be the site of origin of ethmoidal hematomas (which cause chronic nasal disease) as well as aggressive carcinoma.

Orbital diagnostics

Oculokinetic reflexes

Although the horse typically does not display much independent globe motion, entrapment or compression of the globe within the orbit may be evaluated by taking advantage of the oculokinetic reflexes of the vestibular system. While standing at one side, the skull is grasped near the distal extremity, and gentle sweeping motions are made while observing for primary and secondary adjustments in globe position. Finally, a spiraling motion may be used to attempt to determine if tertiary motions are normal or not, although this maneuver may be more challenging for the examiner than the subject. For more information on neuro-ophthalmic examination see Chapter 14.

Forced duction tests

Passive forced duction testing requires desensitization (e.g., use of topical 0.5% proparacaine) and gentle retraction of the globe in the direction of interest (the motion is passive for the horse). Failure to achieve globe motion is regarded as a positive test result and indicates entrapment or disease of the muscle (restrictive muscle disease). **Active forced duction testing** requires participation of the patient, and the examiner observes and feels for attempted motion of the globe by muscle contraction in the direction of interest; it is difficult to undertake in equine patients.

Fine-needle aspiration

Fine-needle aspiration for cytology and biopsy for histopathology are highly desirable when attempting to make a diagnosis of the cause of an orbital mass lesion. Preferably, a thorough physical examination and imaging studies (e.g., computed tomography (CT), magnetic resonance imaging (MRI), and orbital ultrasound; see Chapter 2 for details) are performed prior to the aspiration or biopsy to specifically define the lesion location. Real-time, B-mode ultrasonography is recommended to guide sampling, permit observation of needle placement, and reduce the risk of iatrogenic trauma. Strabismus or globe displacement suggests the location of an intraorbital mass, which typically must be extensive to compress or decenter the globe. Intraconal masses displace the entire globe anteriorly, whereas extraconal masses cause strabismus and ocular displacement. Biopsy of orbital contents may be performed from the supraorbital fossa, from 1 cm lateral to the lateral canthus, and from the medial canthus parallel to the orbital wall, avoiding the inferior quadrant. Avoiding the major vessels and structures of the orbit is critical. Several samples may be acquired if the mass is firm, but hemorrhage may impede later sample acquisition.

Bacterial culture is indicated for samples acquired from any paranasal sinus, and potentially from orbital masses in younger animals where an abscess or septic cellulitis is suspected. Where generalized orbital cellulitis is present, microbial culture is desirable, but an appropriate sample is difficult to acquire, and the entire orbital contents appear homogenously expanded on ultrasonography; in such cases, a small biopsy may be preferable to an aspirate for culture purposes. Even when a systemic leucocytosis is demonstrated, blood cultures are highly unlikely to be useful unless a severe fever is present concurrently (>40.5°C, 105°F).

Orbital imaging

See Chapter 2 and online material for detailed information of imaging the orbit of a horse.

Impact of orbital diseases on the equine industry

Orbital disease is uncommon and of relatively low financial impact in general, although it is of very substantial and potentially life-threatening impact to the individual. Diseases of the equine orbit result in profound cosmetic changes, and, in almost all cases, vision loss occurs. Most treatable orbital diseases occur in juvenile and young horses and are predominantly traumatic or congenital, whereas the debilitating progressive orbital diseases that occur in older adult horses may be difficult to manage and often are impossible to cure. No epidemiologic studies are available to record the potential annual economic impact of orbital disease, but the major costs are likely be related to loss of use because of loss of vision, cosmetic defects, or possibly even loss of life. To minimize globe or orbital disease, preventive management strategies to reduce ocular trauma, cautious introduction of new

horses into group confinement, and early diagnosis, referral, and imaging of orbital disease are needed. It is possible that more routine use of advanced imaging, such as CT and MRI, and earlier surgical intervention may improve the prognosis or medical and surgical treatment of orbital disease.

There are no significant contagious or infectious diseases of the orbit that pose a threat to livestock in the USA and Europe. Among exotic diseases, African horse sickness, equine infectious anemia, and infectious diseases causing vasculitis may cause retrobulbar and supraorbital swelling and distension in multiple individuals (see Chapter 15). Quarantine, importation restrictions, and routine serologic testing are the major sources of protection against these diseases in the USA, Australia, and nonendemic areas of Europe.

Clinical signs of orbital disease

Abnormalities of globe position

Strabismus is deviation of the visual axis from the expected orientation, which is straight ahead in the horse. When both globes are focused forwards, there is an overlap of visual fields of 65 degrees of arc (see Chapter 12). This gives a good binocular field of view and good depth perception. The deviation induced by strabismus will disturb the collation and overlap of visual field information from each eye when it is interpreted in the midbrain and visual centers. In humans, misdirection of the visual axes results in diplopia or double vision.

Strabismus can be due to a space-occupying lesion within the orbit, distorting the globe from its resting position, or it can be the result of disturbance to the ocular muscle innervation or from muscular stricture, contracture, or mechanical entrapment. Strabismus in young stock is uncommon and likely to be congenital or breed related.

Neonatal foals often have a physiologic rotational strabismus (Figure 5.5A, B) that resolves to the adult orientation within the first 2–4 weeks of life. The horizontal pupil is rotated so that the nasal portion is ventral to the temporal portion, and the globe may also be rotated medially. The strabismus is considered physiologic and requires no therapy. Appaloosa foals with **congenital stationary night blindness** (CSNB) may also exhibit a dorsal strabismus (Figure 5.6). The relationship of the strabismus to CSNB is unclear [22, 23].

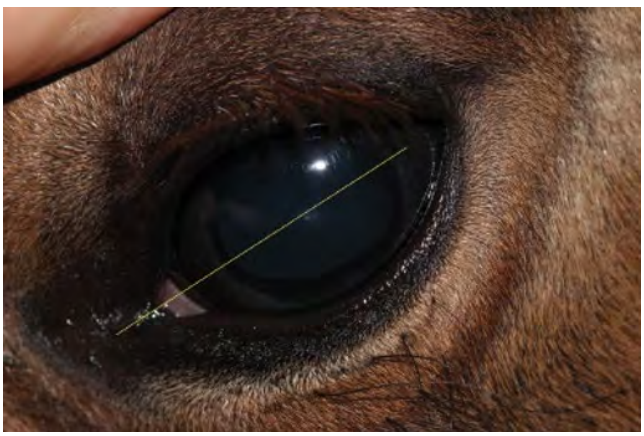
Acquired strabismus is often traumatic in origin due to muscle entrapment after an orbital fracture, or less commonly due to avulsion of a rectus muscle attachment. Muscle avulsion is seen much less frequently than in small animals. The most anterior rectus muscle attachments are for the ventral (8 mm from the limbus) and dorsal (9 mm from the limbus) rectus muscles, with a portion of the lateral rectus muscle attaching within 5 mm of the limbus [24].

Occasionally, central nervous system (CNS) infections may result in strabismus, most commonly **equine protozoal myeloencephalitis** (see Chapter 15) [25–27]. Midbrain (oculomotor nerve) lesions commonly result in a lateral strabismus [28]. Peripheral vestibular disease may result in strabismus, rather than nystagmus, and is often accentuated by elevation of the horse's head. Strabismus may be the only residual sign after recovery from vestibular disease [28].

Post-inflammatory stricture of an ocular muscle may result in moderate or severe strabismus but is uncommonly identified. If forced duction testing is used, the globe will be unable to rotate away from the strabismus. In contrast, muscle avulsion will permit a freely mobile globe (both towards and away from the strabismus). Over time, the opposing partner muscle will atrophy and fix the globe in position. This is occasionally recognized in horses after severe blunt trauma from the side or front.

Nystagmus

Nystagmus is an oscillatory movement of the globe, which may be horizontal, vertical, or rotational. Physiologic nystagmus is a normal compensatory reaction that occurs when the head turns,



(A)



(B)

Figure 5.5 (A) Four-day-old foal with the **line** demonstrating the physiologic rotational strabismus. (B) Adult ocular orientation for comparison. (*Source*: Photographs courtesy of Dr Rachael Grundon.)



Figure 5.6 Appaloosa affected with CSNB, demonstrating dorsomedial strabismus and an unusual gaze associated with head elevation (termed **star gazing**). The relationship of the strabismus to CSNB is unclear. (*Source*: Photograph courtesy of Dr David Wilkie.)

and is a direct response to differential stimuli within the inner ear and the vestibular system. This involuntary motion of the globe permits a more stable visual horizon and enhances stability of the visual field. Pathologic forms of nystagmus reflect damage to the vestibulocochlear apparatus (horizontal, rotatory) or CNS disease (vertical) [28]. Nystagmus most frequently accompanies CNS disease in the horse, which is most often due to an underlying infectious cause. Potential etiologies include equine protozoal myeloencephalitis (EPM); the viral encephalitides (Eastern equine encephalitis (EEE), Western equine encephalitis (WEE), Venezuelan equine encephalitis (VEE), West Nile Virus); aberrant parasite migration; and bacterial sepsis. Peripheral causes include EPM; trauma fracturing the petrous temporal, basisphenoid, or basioccipital bones; conditions affecting the guttural pouch (empyema, mycosis, chondroids); temporohyoid osteopathy (THO); and osteomyelitis adjacent to the inner ear and orbit. Evidence of concurrent depression substantially



Figure 5.7 Exophthalmos of the right eye due to an orbital mass. Note the prominence of the nictitans and mild dorsomedial strabismus, which suggests the mass is extraconal and nasal within the orbit.

worsens the prognosis. See Chapters 14 and 15 for details on the specific diseases and their treatment.

Abnormalities of globe location, size, and function

Exophthalmos

Exophthalmos describes the anterior displacement of a normal-sized globe within the orbit. The most common causes are retrobulbar masses, orbital cellulitis, and trauma that reduces the orbital space (Figure 5.7 and Table 5.3).

Exophthalmos is most easily identified by viewing the head from the front and comparing the angle of eyelashes, the relative prominence of the globe, and the size of the palpebral fissures of both eyes (Figure 5.9). In subtle exophthalmos, additional information may sometimes be obtained from viewing the head from behind (Figure 5.8). Palpation of the orbital rim and comparative assessment of the globes relative to that may also be helpful.

Any animal with exophthalmos should have the extent of globe retropulsion assessed. Gentle digital retropulsion (pushing the globes caudally through closed eyelids using the fingers) allows assessment of tissue pressure within the orbit. Both eyes can be retropulsed simultaneously to allow comparison. Typically, painful retropulsion suggests inflammatory disease (e.g., orbital cellulitis), whereas a nonpainful disease process would suggest neoplasia or cystic masses.

Enophthalmos

Enophthalmos is recession of the globe within the orbit and is usually secondary to loss of the orbital contents. Orbital fractures, especially of the ventral orbit, may create enophthalmos, as the bones no longer support the globe [29]. Enophthalmos in older horses may be due to resorption of orbital fat due to weight loss, but can also be exacerbated by reduction in bulk of the masticatory muscles secondary to poor dentistry. Poor dentistry will obviously contribute to any weight loss, and deeply sunken

Table 5.3 Literature review of causes of exophthalmos in the horse.

Primary location	Disease type	Number of animals affected	Reference
Periorbital sinus			
Cysts	Sinonasal cyst	1	Annear et al., 2008 [81]
	Hydatid cyst	1	Barnett et al., 1988 [60]
Inflammation	*Cryptococcus* granuloma	3	Roberts et al.,1981 [56] Scott et al., 1974 [15] Stewart et al, 2009 [16]
	Chronic bacterial sinusitis	1	Kanda et al., 2007 [77]
	Masseter muscle myonecrosis	1	Step et al., 1991 [68]
Neoplasia	Adenocarcinoma	3	Hill et al., 1989 [19] Dixon et al., 1999 [85] Davis et al., 2002 [37]
	Adenoma	2	Dixon et al., 1999 [85]
	Osteoma	2	Scotty et al., 2004 [89] Schaaf et al., 2007 [90]
	Squamous cell carcinoma	1	Dixon et al., 1999 [85]
	Fibrosarcoma	1	Dixon et al., 1999 [85]
	Undifferentiated sarcoma	1	Dixon et al., 1999 [85]
	Lymphosarcoma	1	Dixon et al., 1999 [85]
	Esthesioneuroblastoma	1	Dopke et al., 2005 [91]
Orbit			
Neoplasia	Neuroendocrine tumor	7	van Maanen et al., 1996 [14] Basher et al., 1997 [93] Matiasek et al., 2007 [94]
	Extra-adrenal paraganglioma	7	Goodhead et al., 1997 [95] Miesner et al., 2009 [137]
	Anaplastic sarcoma	5	Baptiste et al., 2000 [101]
	Squamous cell carcinoma	4	Dixon et al., 1999 [85] Baptiste et al., 2000 [101]
	Lymphosarcoma	2	Rebhun et al., 1998 [96]
	Malignant rhabdoid neoplasia	1	Hong et al., 1999 [112]
	Angiosarcoma	2	Bolton et al., 1990 [110] Bischofberger et al., 2008 [111]
	Fibroma	1	Colitz et al., 2000 [99]
	Adenocarcinoma	1	Baptiste et al., 2000 [101]
	Primitive neuroepithelium	1	Bistner et al., 1983 [100]
	Melanoma	1	Moore et al. 2000 [107]
Inflammation	Abscess	2	Hubert et al., 1996 [57] van den Top et al., 2007 [58]
	Granuloma caused by *Halicephalobus gingivalis*	1	Pearce et al., 2001 [62]
	Strongylus edentatus	1	Walde et al. 1976 [61]
Cysts	Dermoid cyst	1	Munoz et al., 2007 [43]
Other	Intradiploic hematoma	1	Kafarnik et al., 2014 [82]



(A) (B)

Figure 5.8 (A) Subtle exophthalmos in a 21-year-old cob mare, most obvious when viewed from the shoulder. (B) Contralateral normal eye for comparison. (*Source*: Photographs courtesy of the Animal Health Trust.)



Figure 5.9 Exophthalmos of the right eye due to orbital cellulitis. Note the distorted contour of the eyelids, mydriasis, supraorbital fossa swelling, and eyelash angle asymmetry of the right eye compared to the left.



Figure 5.10 Note pronounced sinkage of the supraorbital fossa. This can be masked in old horses with pituitary dysfunction and hirsutism.

supraorbital fossae may also be seen (Figure 5.10). Pars intermedia dysfunction in horses may accentuate resorption of fat and worsen the extent of enophthalmos, but this may be partly or completely masked by hirsutism. Chronically inflamed eyes may become phthisical over time and these can appear sunken but are not truly enophthalmic.

It has been suggested that fat mobilization occurs preferentially from sites with the greatest variation in individual fat-cell size. The orbital fat and supraorbital fossa fat cells are the smallest in the body, suggesting that fat resorption in this area occurs as a late outcome [30].

Neonatal foals may develop enophthalmia with secondary entropion when dehydrated. The enophthalmia is rapidly reversible (Figure 5.11) with hydration, although the entropion may require temporary tacking sutures while this is addressed (see Chapter 6). The normal globe position dictates the third eyelid position and gives lid support.

Enophthalmic eyes are normally visual, but this may be compromised by prominence of the nictitans, covering the cornea. Loss of eyelid support can lead to trichiasis, frank entropion, and chronic ocular discharge from misalignment of the tear punctae. A variety of treatment options are available to manage this issue (see Chapter 6). Primary entropion repair may create unwanted gaping between the globe and eyelid, allowing accumulation of mucus and debris. Cryosurgery can be performed on the offending hairs to decrease irritation, intradermal collagen fillers can be used to increase eyelid rigidity, or retrobulbar silicone devices may be tried to push the globe forward to a more normal position. Unfortunately, later migration and displacement of these silicone prostheses is likely to occur with recurrence of the primary problem.

Finally, enophthalmos may be associated with sympathetic denervation to the smooth muscle between the globe and orbital rim. This is often subtle in appearance but can be associated

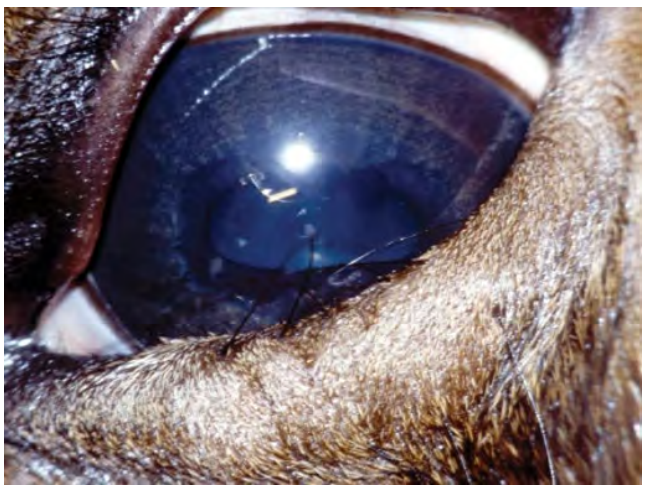


Figure 5.11 Dehydrated neonatal foal with enophthalmos and lower-eyelid entropion. Tacking sutures to roll out the lower eyelid and systemic support will allow the globes to rapidly return to their normal position. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)



(A)



(B)

Figure 5.12 (A) Phthisis bulbi of the horse's right eye, front view. (B) Phthisis bulbi, or shrunken globe, from chronic ocular inflammation associated with equine recurrent uveitis. (*Source*: Photograph courtesy of Dr Stacy Andrew.)

with prominence of the nictitans (see Chapters 6 and 14 for information on Horner's syndrome).

Phthisis bulbi

Phthisis bulbi is gradual shrinkage of the globe due to chronic inflammation and hypotony. Severe damage to the ciliary body epithelial cells results in reduced fluid production and eventual contraction in globe size (Figure 5.12). These eyes are no longer visual and thought should be given to enucleation to remove any possible discomfort. Globe shrinkage gives similar issues to enophthalmos relating to loss of lid support. Intrasceral prosthesis can be inserted into phthisical globes but will not expand globe size. This procedure will, however, prevent further shrinkage. A cosmetic shell, with or without enucleation and orbital prosthesis placement, may also improve the cosmetic outcome (see section **Cosmetic conformer and hydroxyapatite orbital implantation**) [31]. More information on treatment of intraocular inflammatory diseases can be found in Chapter 8.

Atrophia bulbi

Atrophia bulbi describes a small globe that is diminishing in size secondary to chronic inflammation, but is not yet a blind, end-stage globe of phthisis bulbi.

Hydrophthalmos (buphthalmos)

Hydrophthalmos refers to an unusually enlarged globe, associated with chronically increased IOP secondary to glaucoma. This is synonymous with the term buphthalmos, but as this term indicates that the globe is cow-sized, which is actually smaller than a horse globe, hydrophthalmos is the preferred term in equids. Hydrophthalmos suggests an enlarged globe, whatever the original size.

In adult horses, with glaucoma, globe size increases slowly and is associated with other clinical signs of glaucoma such as corneal edema and endothelial (Haab's) striae (Figure 5.13). Vision may be present, reduced, or absent at the time of diagnosis.



Figure 5.13 Hydrophthalmos (buphthalmos) in an adult horse with chronic glaucoma in the left eye. Note additional typical signs of chronic glaucoma such as corneal edema.

Vision may return if the increased IOP is controlled, even if mild globe enlargement remains.

Congenital glaucoma may also occur. Hydrophthalmos is more rapid in these cases due to the greater elasticity of young globes; however, vision is lost more rapidly and permanently. Hydrophthalmos must be differentiated from exophthalmos (displacement of a normal-sized globe), and in unilateral disease comparative ultrasound measurements can confirm this. See Chapter 10 for more information on the diagnosis and treatment of glaucoma in horses.

Megalophthalmos

Megalophthalmos refers to a distortion of the globe and has been used to describe the grouping of abnormalities found originally in Rocky Mountain horses with multiple congential ocular anomalies [32]. This disease has subsequently been described in Belgian Comtois and is associated with the silver dapple gene (see Chapter 13) [33]. Clinical signs include

increased corneal curvature (megalocornea), iris hypoplasia, congenital miosis, uveal cysts, cataracts, and retinal dysplasia. Persistent pupillary membranes may also be present [32].

Other signs of orbital disease

In addition to the clinical signs of orbital disease already described, other typical signs include a prominent nictitans, epiphora, subcutaneous emphysema, reduced airflow from the ipsilateral nostril, altered sinus percussion, episcleral vessel enlargement, bone deformation, keratoconjunctivitis sicca, and distention of the supraorbital fossa.

Prominent nictitans

The nictitans wraps around the globe within the ventromedial orbit and can be passively elevated by globe movement such as retropulsion or retraction. Small or sunken globes can also create a passive nictitans prominence. Space-occupying lesions within the orbit, especially extraconally, can displace the nictitans forward (Figure 5.14), creating prominence. Globe retropulsion should always be attempted when an elevated nictitans is present. A prominent nictitans can also be seen with nonorbital disease. Horner's syndrome can create this due to enophthalmos, although this is not always obvious in the horse. Horses with tetanus may show intermittent or spastic elevation of the nictitans. This can be induced by sudden stimulation such as clapping, touching the medial canthus, or attempting a menace response.

Epiphora

Epiphora is commonly associated with orbital disease, but this must be distinguished from epiphora due to eyelid swelling and distortion such as due to dacryocystitis, neoplasia, or infection (see Chapter 6).

In orbital and extraorbital disease, the nasolacrimal duct may be obstructed functionally or mechanically (e.g., by sinusitis, fracture, or neoplasia), or the eyelid puncta may become misaligned due to blepharoedema, blepharoconjunctivitis, exophthalmos, or enophthalmos. Normal tear flow through the nasolacrimal duct is not passive and depends in part upon vacuum development in the duct, created by the orbicularis oculi during eyelid closure, creating a "pumping" mechanism within the duct. Functional failure can be differentiated from mechanical obstruction by flushing of the nasolacrimal duct.

Emphysema

Accumulation of subcutaneous air is due to unidirectional aspiration of air and entrapment between the skin and calvarium (Figure 5.15). The most common cause is a sinus fracture, which should be considered an open contaminated wound. A depression or displaced fracture is almost always palpable, but radiography with skyline views or a CT scan should be performed if the fracture is not identified clinically. Air may also track up from air-filled mediastinal structures or the nasopharynx. Consideration could also be given to endoscopy of the nasopharynx, oesophagus, and trachea to look for evidence of damage. Infrequently, anaerobic bacterial sepsis may result in gas production, although this is uncommon in the equine head.



Figure 5.14 Elevated or prominent third eyelid in a horse with exophthalmos from an orbital neoplasm.

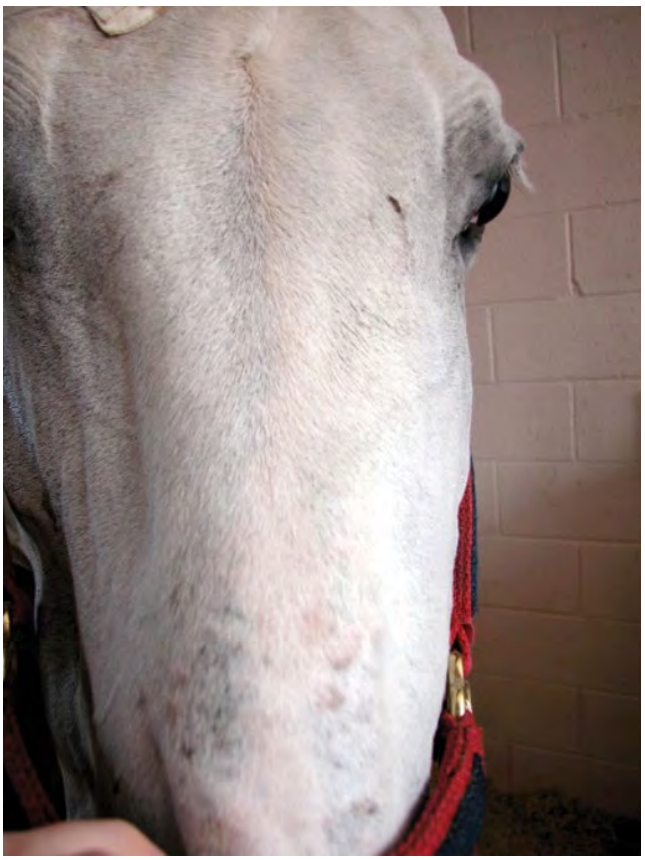


Figure 5.15 Subcutaneous emphysema from blunt trauma to the left frontal sinus. The accumulation of subcutaneous air is due to unidirectional aspiration of air and entrapment between the skin and calvarium.

Reduced airflow from the ipsilateral nostril

Reduced airflow from the ipsilateral nostril may be more subtle, but airflow may be detected by holding a piece of cotton in front of the nostril, or a cool glass slide to detect condensation of warm exhaled air. A large expanding mass impinging on the nasal cavity should be suspected if airflow is altered.

Sinus percussion

Tapping on the bony skull surrounding the sinuses can allow appreciation of differences in tone between air-filled areas or areas of increased density. Both sides should be percussed for comparison. Some horses do not appreciate this procedure, so care should be taken initially until the horse's response has been assessed. Opening the mandible reduces the mass of tissue being percussed and improves the sonic qualities.

Episcleral vessel enlargement

If direct compression of the retrobulbar optic cone occurs, venous stasis can cause the episcleral vessels to become quite prominent (Figure 5.16). The episcleral vessels are a significant cause of resistance in the generation of IOP via the conventional outflow. Thus increased IOP or glaucoma may develop secondary to this. This form of elevated IOP is often poorly responsive to treatment. Exophthalmos is variably observed. Retropulsion may not be abnormal because the functional obstruction surrounds the cone in the caudal orbit. Compression of the optic nerve causing vision loss is also possible.

Bone deformation

Sinus neoplasia or inflammation may cause deformation of the surrounding bone, as can haematoma. This may be uncomfortable on firm or deep palpation, especially at the edges were periosteal elevation may be occurring. Radiographic confirmation of the localized area is usually diagnostic and permits further sample acquisition. Periosteal reaction is less smooth and uniform than the normal bone margin and bone sutures.



Figure 5.16 Episcleral vascular congestion in a horse with a retrobulbar mass causing venous stasis.

Keratoconjunctivitis sicca

Keratoconjunctivitis sicca (KCS) together with ipsilateral facial nerve paralysis suggest trauma to the facial nerve proximal to the geniculate ganglion. Neuroparalytic keratitis results from more distal lesions. The vestibulocochlear nerve (VIII) should be critically evaluated if facial (VII) nerve disease is identified, because they are commonly injured together in proximity to the petrous temporal bone [28] or the ramus of the mandible [34].

Supraorbital fossa distension

Supraorbital fossa distension may accompany exophthalmos and space-occupying masses of the orbit (see Figure 5.7). It is a particularly prominent feature of African Horse Sickness, where hemorrhagic edema causes great distension. Equine viral arteritis results in a panvasculitis and secondary edema that appears similarly with edema and blepharoedema (see Chapter 15 for further details).

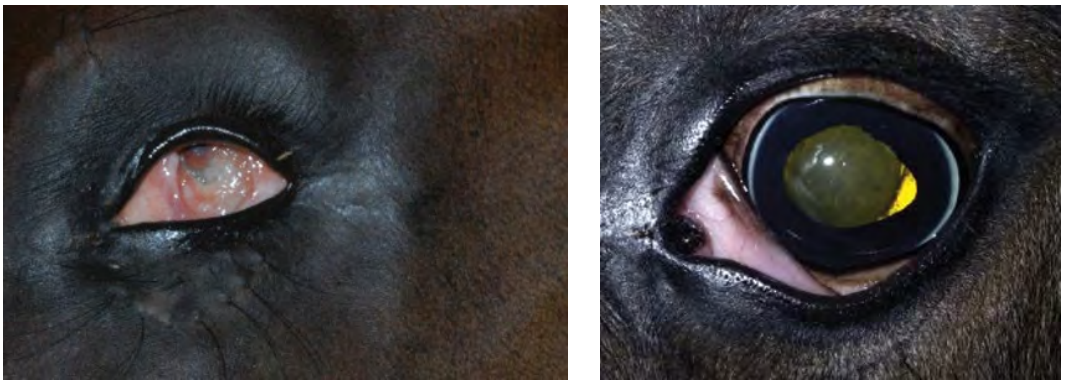
Congenital diseases

Microphthalmos

Microphthalmos is a congenital or developmentally small globe [22, 35–40]. Microphthalmos may be referred to as simple or complicated, depending on whether there are associated abnormalities. Embryologically, microphthalmos occurs due to incomplete closure of the optic fissure preventing normally scheduled establishment of IOP and globe expansion, or it may be the consequence of a mistimed union of the migrating embryologic tissues. Microphthalmia occurred in 14.7% of foals in one study [36] and 7% in another [41]. A single case of microphthalmia with brachygnathia has been reported in an older Friesian mare that received griseofulvin in the second month of gestation, similar to microphthalmia due to intoxication in other species [39]. Multiple ocular colobomas may accompany microphthalmia and result in severely debilitated and blind globes.

Clinical appearance and diagnosis

Microphthalmic eyes appear variably smaller than normal (Figure 5.17) and commonly have additional abnormalities including cataract and coloboma. **Nanophthalmos** refers to a globe that is smaller than normal but functional. **Anophthalmos**, that is complete absence of the globe, is exceedingly rare. More commonly, an excessively small globe remnant is present, appearing as a heavily pigmented spherical mass. In such cases, the predominant tissues identified are conjunctivae and nictitans. In an adult animal, distinguishing between microphthalmos and phthisis bulbi can be difficult, but lack of expansion of the orbit would suggest an early onset disease and histologically severe uveitis should be evident in phthisical globes (see Chapter 8).



(A) (B)

Figure 5.17 (A) Congenital microphthalmos, a developmental anomaly in which the eyeball is abnormally very small. The globe may not be visible, as seen in this foal. (B) In this foal, the globe is visible but small, and temporally there is a lens coloboma. (*Source*: Photograph courtesy of Dr David Wilkie.)

Treatment

If a microphthalmic globe is not exceedingly small, appears functional, and has a normal electroretinogram (ERG), then cataract surgery may be considered to restore vision. If performed early enough, a good outcome can be obtained (see Chapter 9).

If the condition is unilateral, and management of the complications difficult, surgical globe removal may be sensible. Orbital prostheses can be used to gain a better cosmetic outcome, and using sequentially larger orbital conformers may aid orbital enlargement and therefore further enhance cosmesis.

Prognosis and heritability

Prognosis for vision depends on severity of the microphthalmia, and the presence of accompanying ocular defects. It appears more common in the Thoroughbred and is often associated with cataract in this breed. Inheritance is suspected, but the mode is unknown. Conventional wisdom is to avoid repetition of the same mating.

Congenital glaucoma

Congenital glaucoma is rare but very dramatic, due to rapid globe enlargement. Secondary issues of exposure and ulceration may become a problem before vision is lost. These are typically poorly responsive to treatment. (For more information see Chapter 10.)

Orbital dermoids

Orbital dermoids are particularly rare in horses but may cause congenital or juvenile unilateral exophthalmos. Skin (haired or unhaired) within the orbit may result in a fluid-filled cystic mass that expands [38, 42, 43]. These may be slow to develop and may not present until a young adult [43]. Much more common are dermoids on the globe; usually unhaired, they are often on the dorsotemporal conjunctiva or limbus.

Clinical appearance and diagnosis

Orbital dermoids will present as any other space-occupying lesion within the orbit. As they enlarge, exophthalmos and distension of the supraorbital fossa may occur [43]. Fine-needle aspiration (FNA) of orbital dermoids may result in the collection of serous brown, discolored, poorly cellular fluid [43]. Complete diagnosis may rest with excisional biopsy at surgery, but suspicions can be raised with the history of a young horse and with appropriate imaging.

Treatment

An orbital dermoid requires surgical excision or orbital exenteration. Good pre-surgical imaging will allow planning of the approach. A dorsolateral approach through the supraorbital fossa with retraction of the temporalis muscle has been reportedly successful [43].

Prognosis

The prognosis would depend on the size of the mass, secondary damage to the globe, and the success of surgical removal. In general, the prognosis for saving the globe is good for small or moderately sized masses. Dermoids have no known heritability factor and dermoids of the globe carry an excellent prognosis if not full thickness. Surgical removal of a 5-cm retrobulbar dermoid cyst was successful and did not recur during 18 months of follow-up [43].

Vascular abnormalities of the orbit and globe

Orbital vascular anomalies occur uncommonly as a component of intracranial and extracranial congenital disease in humans. Pulsatile exophthalmos has been reported post exercise in several nonhorse species. A variety of neuroectodermal dysplasias have been reported in people, but specifically Sturge–Weber disease has been reported in a young horse [44]. In that individual, prominent arterioles affected the choroid plexus of the ventricles intracranially, together with milder vascular abnormalities in the orbit. The case presented with intermittent seizures and was euthanized. Orbital varices are often ascribed to traumatic origins.

Clinical appearance and diagnosis

Exophthalmos (intermittent or permanent) with a palpable or audible bruit diagnoses arterial abnormalities. External orbital vascular abnormalities are very obvious (Figure 5.18), but orbital



Figure 5.18 Juvenile Quarter horse filly with unilateral vascular anomalies of the left eyelids and orbit.

and intracranial arteriovenous anastomoses may be harder to identify. CT or MRI contrast studies may be helpful, along with 3D reconstruction. Recently, two suspected cases of superficial venous malformations have been described in the lower lids of horses, involving the medial angularis oculi vein and the lateral transverse facial vein [45].

Treatment

If nonessential arteriovenous anastomoses can be identified, an intravascular coil placement for embolization can be attempted. Venous sinus dilatations may be reduced surgically, but access is often limited.

Prognosis

Prognosis is unknown.

Acquired diseases

Clinical signs of nontraumatic orbital disease are gradual exophthalmos with local orbital distention or deformation. Additionally, signs may extend to deviate and involve the frontal or maxillary sinus, adjacent tooth roots (of the caudal upper cheek teeth), nasal cavity, ethmoid turbinate bones, or guttural pouch. Processes beginning in these structures that impinge on the orbit may present primarily because of exophthalmos, strabismus, or blindness. Direct extension of guttural pouch disease is more commonly due to secondary effects rather than direct mechanical extension.

Traumatic orbital disease

Traumatic damage to the orbit occurs more commonly in younger animals, males, and those with fractious personalities or subjected to group confinement. Athletic performance and transportation increase the risk of injury. In particular, rearing and panic-stricken behavior increase the likelihood of sudden blunt trauma, especially to the poll. The poll of the skull may transmit displacing forces to the sphenoid bones that form the internal orbital wall.

The dorsal orbital rim and zygomatic arch are at greatest risk of fracture because of their prominent location on the skull of the horse (Figure 5.19) [46, 47]. A retrospective study of equine orbital fractures demonstrated that horses with orbital fractures as result of a direct kick were more likely to sustain ocular trauma, experience vision loss, and undergo enucleation [46]. In this study, the causative incident (when witnessed) was rearing in a confined space (42%), a direct kick (33%), or colliding with a stationary object (25%).

Fractures of the orbit may be accompanied by displaced bony fragments, and these may impinge on orbital structures such as the globe, optic nerve, or extraocular muscles. Retrobulbar bony fragments have been reported to result in reduced ocular motility, signs of orbital pain, and exophthalmos depending on the location and size of the fragment.

Fracture of the frontal or maxillary bones may be further complicated by exposure of the extensive sinuses of the equine head and laceration of the profuse vasculature at the turbinate bones in close proximity to the orbit. Such fractures are considered open fractures. Equine orbital fractures are most commonly open fractures [47]. Traumatic injury to the ethmoid turbinates or sinuses can result in epistaxis, and entrapped hemorrhagic clots may become septic and possibly result in facial swelling.

Palpation and sinus percussion to compare both sides may be supplemented with radiography to localize fractures, hematomas, and fluid. The dental arcade should specifically be evaluated on radiographs to identify periapical tooth root abscesses, fractures of the roots or surrounding maxilla, or other lesion that may greatly affect the outcome. The thin periapical bone overlying the molars may be incomplete, predisposing that area to abscessation. The constant eruption of equine molar and premolar teeth contributes to the increasing size of the maxillary sinus and likely reduces the impact of dental disease inducing orbital disease.

Globe perforation

Introduction and clinical appearance

A soft, fluctuant ocular surface may indicate corneal or scleral perforation if the area is hemorrhagic or if a focal protrusion of tissue is present. Iris prolapse is typically darkly colored, but frequently fibrin and hyphema are also present, resulting in a tan-red surface (Figure 5.20). A dense red appearance to the entire anterior chamber indicates total hyphema or hemorrhage into the globe because of perforation or severe blunt trauma (Figure 5.21). Hyphema due to blunt trauma without an ocular perforation commonly develops into glaucoma and has a poor prognosis.

A perforation may initially reseal but remains mechanically unstable and may leak intermittently. Fluid leakage may be confirmed by the Seidel test (Figure 5.22). Rupture of the globe from blunt trauma most frequently occurs at or near the limbus. A scleral rupture site may be completely covered with conjunctiva



(A) (B)

Figure 5.19 (A) The dorsal orbital rim, especially laterally, has a prominence that is prone to trauma due to its lateral projection, as seen on a frontal view of this equine skull. (B) Traumatic fracture of the dorsal orbital rim associated with facial lacerations secondary to blunt trauma.

and therefore be difficult to visualize on ophthalmic examination. A scleral rupture is suspected if the globe is very soft despite complete hyphema, and no corneal defect is visible. Scleral perforation posterior to the equator is thankfully uncommon.

Extrusion of vitreous or the lens extraocularly indicates that severe trauma has occurred, vision will not return, and the perforation is likely too large to repair. Enucleation of the eye should be considered to avoid sepsis and continued severe pain. Keratomalacia, or melting ulcer, presents with a very soft gelatinous appearance, but the corneal surface bulges forward and is colored blue, gray, or tan, with an undulant but intact surface. Rupture of such an ulcer is recognized by a central brown-tan protrusion of iris, fibrin, and hyphema through the corneal perforation site (see Figure 5.20A). Corneal disease and rupture are discussed more extensively in Chapter 7.

Diagnosis

The globe's ability to transmit a pupillary light response (PLR) to the other eye (i.e., consensual PLR) implies that retinal function persists; this is a positive indication that vision may be saved. An absent consensual PLR may reflect severe intraocular disease or intense miosis of the pupil and opacity of the intraocular fluids. Other criteria should also be evaluated critically, such as a dazzle reflex and ocular ultrasound (see Chapters 1 and 2) to determine if surgical intervention should be aimed at preserving vision, a cosmetic globe, or enucleation.

With appropriate restraint, and if not contraindicated by lack of globe integrity, cautious transpalpebral ultrasonography permits evaluation of lens and retinal position (detachment), vitreal or subretinal hemorrhage, posterior globe rupture, and possibly intraocular foreign bodies. Caution is necessary to avoid complicating the injuries present. The probe position may be altered (e.g., placed laterally) to avoid complications, and even ultrasonography through the supraorbital fossa may be contributory.

Radiography, especially CT, is more useful to determine the extent of fractures and whether bone displacement is present. If the patient is ataxic, depressed, or somnolent, a neurologic



(A) (B)

Figure 5.20 (A) Red-tan material (fibrin, blood, iris) exiting a perforation of the cornea. The anterior chamber is collapsed, and the globe has hypotony and hyphema. (B) Dark uveal prolapse from a horizontal linear corneal laceration.



Figure 5.21 Limbal rupture and uveal prolapse following severe blunt trauma to the eye. Note the complete hyphema.

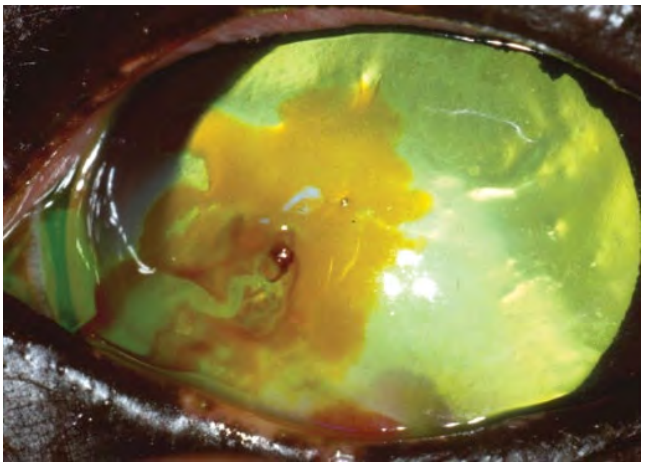


Figure 5.22 A Seidel test can be used to determine if a corneal wound is leaking aqueous humor. Concentrated, minimally diluted fluorescein is placed on the corneal surface such that the fluorescein has an orange appearance. Leaking aqueous humor will create a "river" of green, or diluted, fluorescein in the orange-concentrated fluorescein. (*Source*: Photograph courtesy of Dr Dennis Brooks.)

examination and head radiographs should be performed to confirm or refute fracture of the calvarium, which greatly impacts outcome. The advent of standing CT systems has greatly enhanced the diagnostic imaging capabilities for equine head trauma cases.

Treatment

Treatment for globe perforations depends on the severity and prognosis for vision. Globes with a chance to regain vision (e.g., normal posterior segment, dazzle reflex, and PLR) should have the perforation(s) repaired, usually by suturing the defect and covering it with a conjunctival flap. If corneal closure is excellent and the laceration not excessive, a conjunctival flap may be bypassed to reduce long-term fibrosis. If an ulcer perforates, a corneal transplant is the procedure of choice to avoid tissue distortion, and is usually supplemented by a conjunctival flap.

It is more difficult to close the surgical margins when they are caused by globe rupture rather than a surgical incision because of irregular directional changes (see Chapter 7). It is important to thoroughly evaluate the globe for other areas of rupture, including beneath the conjunctiva. It is not uncommon for multiple independent scleral tears to be present. A peritomy should be performed and the sclera examined in the vicinity of lacerations.

Eyes with retinal detachments, large corneal or scleral ruptures, substantial vitreal hemorrhage, or severe endophthalmitis have very poor visual prognosis and are painful. These horses should have an intraocular or hydroxyapatite prosthesis placed or have the globe enucleated. Unfortunately, globe removal is usually associated with the least complications and cost. Nonetheless, it is remarkable the degree of trauma the globe may sustain and yet retain/regain vision and comfort after meticulous surgical repair if performed early.

Prognosis

The prognosis for regaining sight after corneal perforation depends on the length of the prolapse (less than 10 mm), whether it arose from blunt trauma or ulcer perforation, the presence of a consensual PLR, and whether the limbus is involved [48]. Severe blunt trauma to the globe usually has a worse prognosis for vision and saving the eye than sharp penetrating injuries. Unrepaired globe lacerations have a poor prognosis for maintaining a comfortable eye.

Ocular injury associated with facial trauma

Facial trauma commonly involves ocular injury because of the prominent orbital location. The greatest risk is from lateral blunt impact. After trauma, the globe itself should be evaluated for normal motion and inflation, any possible mechanical entrapment of extraocular muscles, vision, and ocular discharge.

Concurrent clinical signs to be evaluated include presence of lagophthalmos, emphysema, displacement of skull sutures/bones resulting in an open fracture, appearance of facial asymmetry or deformity, presence or absence of air flow through the nostrils, and ability to masticate and swallow. The appearance of viscous yellow fluid in the external ear in tandem with a head tilt should be regarded as a particularly serious sign.

Clinical appearance and diagnosis

Globe examination should be sufficiently thorough to ensure that no serious injury is hidden by eyelid, nictitans, and any surface swelling. An auriculopalpebral nerve block and sedation will likely be necessary. Initial therapy may allow a better examination within 1 or 2 hours.

Diagnostics of value in determining the extent of facial trauma include palpation, oral examination, radiography with air as an inherent contrast agent, and more elaborate imaging techniques as required. Ocular ultrasonography is the alternative approach for determining whether the globe is inflated or a perforating injury has been sustained. Measurement of IOP may be of indirect value, but normal IOP does not exclude a perforating injury. Temporary closure may occur by dislodging intraocular contents into the void, and it is possible to sustain an IOP approaching normal despite slow leakage of aqueous humor, particularly if hemorrhage is extensive.

Orbital fractures in horses are commonly accompanied by facial asymmetry, blepharoedema, periocular lacerations, and conjunctival hyperemia or chemosis. Corneal ulceration and blepharospasm may also be present. Complications resulting in blindness or enucleation (retinal detachment or globe rupture) were infrequent in a retrospective study of 18 cases [47]. Euthanasia was recorded in two cases as a result of concomitant injuries. The majority of cases required some form of surgical intervention (reduction of displaced fractures, removal of small bony fragments or sequestra, sinus trephination, lavage, and drain placement).

The close proximity of the orbit to the frontal, maxillary, sphenopalatine, and ethmoidal sinuses, the nasal cavity, and tooth roots provides ample opportunity for extension of trauma to adjacent cavities. Communication of fractures with the paranasal sinuses are categorized as open fractures. Due to the presence of a normal bacterial and fungal flora within the sinuses, commonly in combination with trauma-induced hemorrhage, infection risk is higher for such injuries. Comminuted or open fractures may be associated with epistaxis or sinusitis and warrant more aggressive therapy.

Air may be introduced into the orbit and result in pneumophthalmos and subcutaneous emphysema. Aspiration occurs in a valved manner, entrapping air beneath the skin. Differentiation of anaerobic sepsis from air may be difficult, but if clinical signs are suggestive (febrile, leucocytosis, change in mentation, rapid progression), aspiration of fluid for cytologic examination and culture may be most useful. Metronidazole should be administered while test results are pending (Table 5.4).

Pneumocephalus has been reported in horses with head injuries and sinusitis [49]. Resolution of pneumocephalus was witnessed in this series with supportive treatment only. Development of a tension pneumocephalus has also been reported in the horse secondary to head trauma and warrants surgical intervention. Monitoring of gas accumulation within the calvarium, particularly with respect to effects of pressure on intracranial structures (e.g., midline shift or compression of ventricles seen on diagnostic imaging), and deteriorating neurological signs may assist in differentiating pneumocephalus from tension pneumocephalus.

Treatment

Therapy includes stabilizing the extent of damage to prevent further globe injury, ensuring adequate corneal protection and lubrication, and verifying vision or identifying the need to perform decompression. If eyelid lacerations or other open skin wounds are present, they should be cleaned, clipped, and apposed if appropriate. Eyelid margin defects should be realigned cautiously to ensure that no step defect is introduced, and to prevent any sutures from abrading the corneal surface. Specific examination of the tongue is worthwhile because even extensive lacerations may pass unnoticed in the horse. Deep lacerations may require suturing, and the results may be very rewarding because of the degree of vascular perfusion.

Minor orbital fractures may not require surgical treatment if facial asymmetry is minimal and there is no impact on adjacent structures. Many cases, including severe comminuted fractures, may require repositioning of fragments and interosseus wiring techniques or bone grafts. Some displaced bony fractures may be repositioned using a closed technique and digital palpation or a bone hook. Smaller bony fragments that lack a reliable vascular supply should be removed to prevent sequestrum formation. Open techniques may be required, particularly for extensive fractures involving the paranasal sinuses. Early surgical intervention is recommended due to fibrous fracture callus formation hampering reduction of displacements.

Table 5.4 Parenteral medications for orbital disease.

	Dose	Notes
IV antibiotic		
Penicillin-Na G	22,000–44,000 IU/kg IV q6h	
Gentamicin	6.6 mg/kg IV, IM q24h or 3.3 mg/kg IV, IM q12h	
Ampicillin sodium (trihydrate for IM use only)	20–50 mg/kg tid	Useful if penicillin-Na G is unavailable
Tetracycline	5–7.5 mg/kg IV q12h	Risk of anaphylaxis; recommend dilution, risk of diarrhea
Ceftiofur	2 mg/kg IV q12–24 h	Broad spectrum, good penetration
Enrofloxacin	5 mg/kg q24h	Off-label use, contraindicated in horses less than 3 years old (high risk of cartilage disorders)
Metronidazole	20 mg/kg q24h	Slow infusion
Oral antibiotic		
Trimethoprim sulfate	15–30 mg/kg PO q12h	Broad spectrum, well tolerated
Doxycycline	10 mg/kg PO q12h	
Enrofloxacin	7.5 mg/kg PO q24h	Off-label use; if indicated on sensitivity
Metronidazole	15 mg/kg PO	Occasionally indicated for anerobic infection
Anti-inflammatory		
Flunixin meglumine (Banamine)	1.1 mg/kg PO, IM, IV q12h 0.5 mg/kg q8h	
Phenylbutazone	2.2–4.4 mg/kg PO q12h	
Aspirin	15–30 mg/kg PO q24h	Least anti-inflammatory effect
Carprofen	0.7 mg/kg IV or PO q24h	Large animal formulation available; the small animal formulation should not be used
Meloxicam	0.6 mg/kg IV or PO q24h	
Gastric protectant		
Omeprazole	4 mg/kg PO qd 2 mg/kg PO qd (low dose)	For individuals on chronic NSAIDs. Low dose may be effective
Anthelmintic		
Ivermectin	0.3 mg/kg PO	Habronemiasis
Ivermectin	1.2 mg/kg PO	May repeat at 2- to 3-week intervals for halicephalobiasis, resistant habronemiasis
Fenbendazole (Panacur)	10 mg/kg PO × 5 days, or 50 mg/kg PO every third day	For aberrant strongyles and other nematodes

IM, Intramuscular; IU, international units; IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs; PO, by mouth; q6h, every 6 hours; q8h, every 8 hours; q12h, every 12 hours; q24h, every 24 hours; qd, daily; tid, three times daily.

Involvement of the facial nerve in head trauma may result in lagophthalmos and a poor or absent palpebral blink. Lacrimal function may also be affected, compounding potential corneal exposure and keratitis. Artificial tear replacements should be used to maintain corneal wetting and lubrication. A temporary tarsorrhaphy should be considered to protect the cornea during healing. A permanent partial lateral or medial tarsorrhaphy may be required where facial nerve damage is long-lasting and the threat of corneal exposure ongoing.

Initial medical therapy should include aggressive systemic anti-inflammatory agents (flunixin meglumine 1.1 mg/kg intravenously or orally (IV/PO)) and broad-spectrum systemic antibiotics if a skin break or sinus fracture is present (see Table 5.4). Surgical interventions to repair bony and soft-tissue trauma of the orbit are discussed in the section **Surgery of the orbit**.

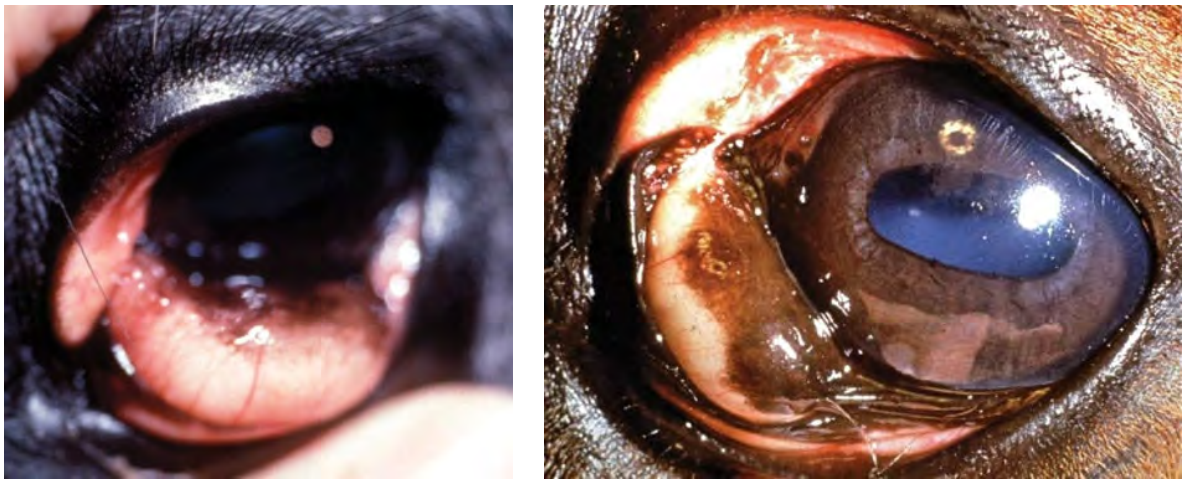
Penetrating orbital foreign bodies

Introduction and clinical appearance

Penetrating orbital foreign bodies such as gunshot that become lodged in the orbit may be identified by radiography, CT, and possibly ultrasonography. Standing sedation and CT may greatly facilitate identification of orbital foreign bodies and is useful in the case of metallic (ferrous) foreign bodies. Organic foreign bodies are more difficult to detect but may be identified on ultrasonographic evaluation if they cast an acoustic shadow. A penetrating tract may be apparent. Orbital cellulitis may occur as a delayed complication. General anesthesia and head MRI has been described in the identification of a wooden periorbital foreign body in a 14-year-old Rocky Mountain gelding [50].

Treatment

Metal fragments embedded in the globe may be surgically excised under general anesthesia if they are readily accessible. Masses embedded within orbital bones should be monitored and not excised unless they result in an unstable fracture, threaten vessels or other structures, or orbital cellulitis is present. Metal fragments within the orbital soft tissue should also be treated with benign neglect unless they are clinically unstable and present a risk of further damage. Gunshot is typically sterilized by the high temperature, whereas metal shards or organic materials that are lodged in the orbit should be treated with broad-spectrum systemic antibiotics as well as systemic anti-inflammatories.



(A) (B)

Figure 5.23 (A) Orbital and conjunctival swelling associated with fat prolapse. (*Source*: Photograph courtesy of Dr Mike Davidson.) (B) Pigmented mass from fat prolapse under the third eyelid.

Organic material should be removed as expeditiously as possible, and aggressive antimicrobial administration is warranted. MRI should not be performed where an intraocular foreign body may be magnetic.

Prognosis

The prognosis for vision is usually good unless the foreign bodies have penetrated the globe. Certain metal types may oxidize and discolor, inducing an inflammatory reaction.

Orbital fat prolapse

Orbital fat may herniate through weakened episcleral fascia or as a result of trauma to form a fluctuant subconjunctival mass (Figure 5.23) [51–53]. Aspiration or biopsy is recommended if the diagnosis is uncertain. Therapy is to resect the mass in toto and suture closed the conjunctival surface over the exposed area [54]. Future herniation of fat may be avoided by closure of a fascial layer (periorbita) beneath the conjunctiva if sufficient tissue is available [51–53]. A case series of 24 cases has been published suggesting the wound can be left to heal by secondary intention without encountering post-operative complications [55]. Iatrogenic fat prolapse may follow removal of the nictitans if the resulting conjunctival and fascial wounds are not sutured, but this is easily repaired by resecting and closing the herniation site.

Orbital proptosis

Introduction and clinical appearance

Proptosis is the physical displacement of the globe from the orbit (Figure 5.24). Although it is a devastating injury, fortunately proptosis is an uncommon incident in horses. If the eyelid margins become entrapped posterior to the equator of the globe, the prognosis for vision substantially worsens. Arterial flow and venous drainage are restricted, and the globe is completely exposed to mechanical trauma and corneal abrasion. Traumatic optic neuropathy results in blindness when the optic nerve is overstretched or suffers a severe whiplash or contrecoup injury, even if proptosis does not occur. It is diagnosed funduscopically as extrusions around the optic disc and subsequently by optic nerve head atrophy (see Chapter 11).



Figure 5.24 Displacement of the globe from the orbit, or proptosis, due to severe trauma. In this horse, the optic nerve and multiple extraocular muscles were transected, so the globe had to be enucleated.

Treatment

The earliest possible decompression (by performing a canthotomy if necessary) and return of the globe to the confines and protection of the orbit should be attempted. If the globe has been expelled from the orbit, sedation and extensive local anesthesia are given immediately, and a brief surgical preparation is performed. General anesthesia may be necessary for repair, but decompression of the proptosis should be performed urgently. Lidocaine 2% is administered at the lateral canthus and infiltrated along the eyelid margins. The globe should be vigorously cleansed and lubricated. A canthotomy may be performed. With adequate exposure, the fornices are examined for foreign bodies

Table 5.5 Topical medications for globe or orbital disease.

	Frequency	Notes
Lubrication		
Artificial tears ointment	q1h–tid as needed	If excessive exposure, may become desiccated
Refresh PM®	q1h–tid	More frequent administration necessary than ointment. Aids prevention of desiccation
Serum, autologous, homologous	q1h–tid	Refrigerate; viscous lubricant with anti-enzymatic properties
0.5% Hyaluronic acid	q2h–tid	Good viscosity
Hypertonic saline ointment 3% or 5%	bid–tid	If concurrent corneal edema or bullae at risk of ulceration
Antimicrobial		
Neomycin-polymyxin B-bacitracin ointment	tid–qid	Broad spectrum; rare drug-induced reaction to neomycin
Neomycin-polymyxin B-gramicidin solution		
Gentocin or tobramycin 0.3% solution or ointment	tid–qid	Moderate spectrum with minimal epithelial toxicity
Erythromycin ointment	tid–qid	Occasionally irritating, bacteriostatic
Chloramphenicol ointment or solution	tid–qid	Moderate spectrum, bacteriostatic
Fusidic acid carbomer gel	sid–bid	Mostly Gram-positive spectrum, bacteriocidal
Ciprofloxacin	qid	Moderate spectrum, bacteriocidal
Ofloxacin	qid	Moderate spectrum, bacteriocidal

sid, Once daily; bid, twice daily; tid, three times daily q1h, hourly; q2h, every 2 hours; qid, four times daily.

and other lacerations that require intervention. The orbital margin should be evaluated for fractures. A subpalpebral lavage system may be placed to permit medication delivery and complete tarsorrhaphy. If no other injuries are present, the globe is gradually retropulsed into the orbit using broadly applied pressure. Multiple broad tarsorrhaphy sutures are placed with stents and closed in steps to ensure complete apposition of the eyelids (see section **Tarsorrhaphy**). The canthotomy is closed routinely. Control of ocular and orbital inflammation by systemic anti-inflammatory medication is essential if vision is to be preserved (see Table 5.4). Oral corticosteroids have been advocated by some authors and may be more effective if no microbial contamination can be identified (dexamethasone 5–20 mg PO daily). Oral antibiotics are commonly administered. Use of topical therapy should be determined based on concurrent corneal ulceration (Table 5.5).

Prognosis

Prognosis for vision is poor if the globe is displaced from the orbit, and very guarded if the eyelids are entrapped behind the globe. If the optic nerve is transected or multiple extraocular muscles are ruptured (see Figure 5.24), enucleation or cosmetic implant should be considered.

Infectious orbital diseases

Orbital cellulitis

Perforation by a foreign body, direct trauma, and seeding by septic emboli are among the more common causes of orbital cellulitis. The globe is only at risk if therapy is delayed or when additional complications are present, for example, orbital fractures. The apparent rapid healing of facial wounds may disguise the severity of the situation. If a penetrating tract is present, sepsis may have a chance to establish before more obvious clinical signs are noted. Extension of inflammatory and infectious conditions from adjacent sinuses and cavities also occurs commonly. Uncontrolled septic endophthalmitis may progress to panuveitis and create orbital cellulitis. In these cases (Figure 5.25), enucleation should be considered to avoid bacterial or fungal invasion into the orbit. Conversely, orbital cellulitis rarely will induce uveitis.



Figure 5.25 Septic panophthalmitis may extend to the orbit, resulting in exophthalmos.

A more localized chronic process will result in the formation of a true abscess rather than generalized cellulitis, with the diminishment of a systemic response (leucocytosis, hyperfibrinogenemia, pyrexia). Granulomas resulting from *Actinomyces* spp. or *Habronema* nematodes have also been reported. *Cryptococcus* has been noted in the skull and rarely in the orbit. However, it should be considered as a differential diagnosis in nonresponsive

cellulitis [15]. Prolonged medical therapy in one case gave a survival time of 26 months until the expanding granuloma had come through the nasal cavity, and paranasal sinuses to the orbit [56]. *Cryptococcus* infection initiates through the respiratory or gastrointestinal tracts and travels via lymph nodes until it subsequently localizes in the orbit. Phycomycosis is rarely seen as orbital disease but may spread from the guttural pouches or nasopharynx, where its physical expansion may result in substantial obstruction to respiration. Such phycomycoses include *Conidiobolus* and *Basidiobolus* spp. These granulomas are very persistent, locally expansive, and may be difficult to control.

Clinical appearance and diagnosis

The orbital contents are distorted and swollen, bulging forwards through the orbital opening and restrained only by the eyelids. The supraorbital fossa may also become grossly distended. Severe exophthalmos can create lagophthalmos.

Blepharedema or blepharitis may be severe with accompanying conjunctival swelling, even to the point of overhanging the eyelids. The nictitans is often displaced from behind the globe, forcing it to prominence. Ocular discharge can be serous or mucoid but is often profuse. If the posterior segment can be visualized, small white exudates may be present overlying the optic nerve, where orbital cellulitis intimately involves the orbital cone. IOP will usually remain normal until sufficient swelling and inflammation is present to create vascular compromise, when retrobulbar tissue pressure begins to increase. This indicates a very severe condition.

Diagnostic tests to be considered include a complete blood count (CBC) to evaluate if any systemic effects are present (leucocytosis, hyperfibrinogenemia, hypergammaglobulinemia) and imaging to rule out retention of a foreign body. Pyrexia and general malaise can occur from orbital cellulitis or endophthalmitis alone; however, a thorough physical examination should be performed (including thoracic rebreathing) to identify primary or secondary disease elsewhere. Orbital ultrasonography (via the globe or the supraorbital fossa), CT or MRI, and FNA may also aid diagnosis [57, 58].

Treatment

Antimicrobial agents should be administered systemically at the highest tolerable doses based upon diagnostic findings. Aggressive systemic nonsteroidal anti-inflammatory drugs (NSAIDs) will aid reduction of high intraorbital tissue pressure and thus can help preserve globe health. Topical lubrication in the face of lagophthalmos, including any exposed and compromised conjunctiva, is vital. Cold compresses may help reduce local swelling and improve comfort levels.

Encapsulated abscesses are rare in the horse, but if identified can be drained surgically under general anesthesia [58]. Lavage of the area at surgery with broad-spectrum antibiotics may prove useful, for example, penicillin G. Debridement of malacic and necrotic tissue is ideal, but access is often poor, and due to the high concentration of important structures, iatrogenic damage should be avoided. Therapies proposed for pythiosis include direct intralesional injection of antifungal agents (such as amphotericin B) [59], IV sodium iodide and oral potassium iodide, and laser ablation. Prolonged therapy is required.

Prognosis

Prognosis depends on severity of disease, degree of vascular compromise and tissue damage, and response to treatment. Enucleation may be necessary to control pain from persistent endophthalmitis.

Parasitic orbital disease

Parasitic disease of the orbit presents as a space-occupying mass and exophthalmos. Hydatid cysts have been reported in the UK and Germany causing optic nerve atrophy and blindness [60]. Aberrant migration of other nematodes including *Strongylus vulgaris*, *Strongylus edentates*, *Halicephalobus gingivalis*, and *Draschia megastoma* are more common in the CNS but may be found in the orbit [61].

Halicephalobus gingivalis (syn. *H. deletrix*, syn. *Micronema deletrix*) is a ubiquitous saprophytic soil nematode that appears to enter the body through damaged mucosal barriers. This can cause orbital, neurologic, renal, and diffuse clinical signs, with CNS invasion a common and severe complication [62]. These may form granulomas, and successful removal from the orbital rim was reported in one case [63]. A fibrous lining surrounds the nematodes with macrophages and some eosinophils. Calcification can occur, visible radiographically. *Echinococcus granulosus equinus* has no public health significance and cycles between horses and canids. Habronemiasis (summer sores) may cause severe blepharoconjunctivitis, especially nasally, but rarely deeper structures (see Chapter 6).

Clinical appearance and diagnosis

Clinical appearance is typical of a retrobulbar mass. History of inadequate or infrequent deworming may be present. Concurrent systemic signs including hematuria, other renal signs, or neurologic signs carry a poor prognosis. *Halicephalobus deletrix* may cause uveitis and chorioretinitis, diagnosed with histopathologic evaluation [64]. Urine sediment should be examined for rhabditiform nematodes [65]. Ultrasonography or CT/MRI revealing a cystic structure should make one suspicious of hydatid disease of *Echinococcus* spp. Aspiration should be avoided to prevent dispersal of the organism.

Treatment

Administration of high doses of ivermectin (see Table 5.4) should be considered if parasitic orbital disease is suspected. For migrating strongyles, or where ivermectin has already been administered, a high dose of fenbendazole may be used orally but is not very effective. Orbital hydatid cysts are ideally removed surgically, with cautious dissection to avoid inadvertent puncture and dispersal of the contents. Percutaneous aspiration along with anthelmintic therapy has been reported [66]. *Halicephalobus*

gingivalis may be treated by ivermectin (1.2 mg/kg PO every 2 weeks for three or four treatments) [62]. If possible, the mass may also be surgically debulked.

Prognosis

Hydatid cysts are well tolerated unless so large as to create exophthalmos, and may be found elsewhere in the body as an incidental finding. Recurrence may accompany cyst rupture. Prognosis for halicephalobiasis depends on severity of disease and response to therapy. Large granulomas may cause blindness, especially if the optic nerve or retina is infiltrated. If signs of CNS involvement are apparent, the prognosis is very poor. Intraocular infection also carries a poor prognosis [64].

Noninfectious inflammatory diseases of the equine orbit

Inflammatory orbital disease is less common in horses than other domestic animals, due mostly to the greater bony demarcation of the orbit and the greater distance from the buccal cavity. Penetrating foreign bodies from the oral cavity are rare; however, sinusitis extending from the adjacent maxillary and frontal sinuses is more common. Ethmoidal masses may also induce orbital inflammation. Control of the primary disease process together with symptomatic orbital therapy is usually sufficient. If direct orbital involvement is present, the condition is managed as a primary orbital cellulitis.

Nutritional myopathy

Rarely, severe myonecrosis can result from inadequate dietary selenium and/or vitamin E. Cases localized to the muscles of mastication, specifically the masseter muscles, have been reported [28, 68]. A history of inadequate fresh forage and limited pasture access is typical. Box rest may protect other muscle groups and predispose the masticatory muscles. It is much less common than masticatory myositis in dogs but equally severe and is extremely painful, especially to palpation.

Clinical appearance

A reported case presented with acutely swollen masseter and temporalis muscles, exophthalmos, passive displacement of the nictitans, and severe chemosis resulting in herniation of the conjunctiva into the palpebral fissure. Supraorbital fossae were distended. Mouth opening was restricted (trismus), prehension was limited, and a distressed facial expression was apparent [68].

Diagnosis

The clinical presentation of this disease is very suggestive of masticatory myositis. Consideration should possibly be given to tetanus as a differential. All muscle groups should be evaluated, including the cardiac muscle. Dietary evaluation along with blood selenium and vitamin E levels will confirm the diagnosis; serum chemistry to evaluate the severity of the myositis is useful, and myoglobinuria may be present.

Treatment

Treatment of nutritional myopathy entails higher quality forage feeding, initial supplementation with selenium (25–50 mg), and subsequent daily selenium supplementation to reach 0.3 mcg/g of dietary intake per day. Daily oral supplementation of vitamin E (5000–10,000 IU PO daily) may also be considered. Supportive care to manage the myonecrosis includes NSAIDs, diuresis (possibly with IV fluid administration), and warm compresses of the affected muscles. Nutritional support may be required until normal feeding behavior is possible. In the reported case, oral dexamethasone and IV dimethyl sulfoxide (DMSO) were necessary to control the inflammation. The prognosis is poor if the animal is generally debilitated, and muscle atrophy may become profound on recovery.

Periostitis

Introduction and clinical appearance

Periostitis of the nasofrontal bone anastomoses/suture line is reasonably common in young horses, creating a swelling across the bridge of the face (Figure 5.26). In severe cases it can result in secondary periocular swelling and severe chemosis. Although predominantly of cosmetic interest [69], periostitis in the region of the nasolacrimal duct may result in partial or total obstruction and secondary overflow epiphora [70]. Clinical signs may be asymmetric or unilateral. Etiology has been suggested to be instability of the junctions of the frontal, nasal, and maxillary bones, although specific traumatic history is often not identifiable [69].

Diagnosis

Radiography is useful to confirm the extent of the condition and rule out any undiagnosed fractures. The age and history of the patient are important.

Treatment

Treatment involves the use of systemic NSAIDs to control clinical signs as necessary.

Prognosis

A permanent linear bony callus often results in a cosmetic blemish, but clinical signs resolve with time and maturity.

Other inflammatory orbital diseases

Other orbital diseases reported in other species may occur uncommonly in the horse (e.g., immune-mediated/eosinophilic myositis and pseudotumor), although they have yet to be reported in the literature. **Pseudotumor** is the term used to describe a particularly aggressive inflammatory condition of humans and cats that responds poorly or not at all to anti-inflammatory therapy [71–73]. The disease is progressive and affects both eyes. Reduced retropulsion and dramatic



Figure 5.26 Nasofrontal suture periostitis. This shows a latero-lateral oblique radiograph of a horse head. An increased bony density can be seen surrounding the nasofrontal suture creating a "bump" on the bony profile of the face. (*Source*: Image courtesy of Dr Rachael Grundon.)

exophthalmos with fixation of the globe may result, with enucleation required for control.

Periorbital nasal and sinus diseases

Sinusitis

Introduction and clinical appearance

Sinusitis or empyema (i.e., purulent material within the sinus) is one of the most common non-neoplastic diseases of the equine head. Clinical signs of sinus disease, other than possible exophthalmos, include unilateral nasal discharge, facial swelling, and decreased nasal airflow [74]. In a review of 277 cases seen at a referral equine hospital, 88% of cases presented with a nasal discharge and 46% with facial swelling [75].

Sinusitis was most commonly reported in the maxillary sinus, with 78% involving the caudal maxillary sinus and 61% involving the rostral maxillary sinus in one retrospective study of 200 referred equine paranasal sinus cases [76].

Equine sinusitis may have a variety of causes, including primary bacterial sinusitis, mycotic sinusitis, and dental disease-associated sinusitis, and secondary to sinus cysts, sinonasal neoplasia, progressive ethmoidal hematoma, and sinonasal trauma.

In one case, exophthalmos and protrusion of the maxillary bone was observed in a 12-year-old Thoroughbred for 6 months prior to clinical evaluation [77]. In another series, three horses presenting with unilateral or bilateral blindness were found to have infectious sphenopalatine sinusitis with subsequent distension and compression of adjacent optic nerve(s) and optic chiasm [20].

Diagnosis

Diagnosis is based on typical clinical signs of sinusitis. Definitive diagnosis is made based on skull radiographs or CT, endoscopy (via nasal cavity) and/or sinoscopy (via sinus trephination), and oral examination. A retrospective study of 200 cases of equine paranasal sinus disease found that sinoscopy was of great diagnostic value in 79% of cases, also helping to identify the presence of intrasinus progressive ethmoidal hematomas and mycotic plaques where present. Sinoscopy was reported as least helpful in identifying dental apical infections associated with sinusitis. This study did not include CT as a diagnostic modality [76].

In another study, radiographic abnormalities were identified in 81% of cases with sinonasal disease, but these resulted in a diagnosis in only 36% of cases [75]. Radiography for dental disease-associated sinusitis also has a reported low sensitivity due to superimposition of dental apices and radiopaque sinus contents [78]. CT and scintigraphy for evaluation of equine dental disease has been described, providing more sensitive, accurate, and earlier diagnosis of periapical infections in horses [79].

MRI of sinonasal lesions has been described in 14 horses [21]. Overall, MRI gave excellent information on location, nature, and origin of lesions, correlating well with intraoperative or post-mortem results. MRI was not useful in dental disease-associated sinusitis in two patients, where the affected tooth could not be, or was mistakenly, diagnosed.

Sinocentesis, or sampling of the sinus fluid, should be attempted for cytologic examination and culture [74]. MRI was the only antemortem diagnostic method used to diagnose sphenopalatine sinusitis in three horses with associated blindness [20].

Treatment

In primary infectious maxillary sinusitis, the fluid should be drained, the sinus lavaged, and appropriate systemic antimicrobial agents given. Standing sinusotomy and sinuscopic lavage via a maxillary sinuostomy approach for adult horses (note differences in trephination sites required for immature horses) has a reported good success rate [80]. In secondary infectious sinusitis, the primary underlying disease, which may include dental disease, facial fractures, granulomatous disease, or neoplasm, should be corrected if possible [74].

Prognosis

For primary sinusitis, clearing up the disease generally makes for a good prognosis. For secondary sinusitis, prognosis depends on the underlying cause. Excluding sinusitis secondary to sinus neoplasia, sinusitis cases have an excellent reported long-term response (91% cured, additional 7% improved) to appropriate treatment, with a median of one treatment [77]. Sinusitis secondary to sinus neoplasia had a reported cure rate of only 22%.

Nasal and sinus cysts

Introduction and clinical appearance

Maxillary sinus cysts may appear clinically similar to neoplastic masses (i.e., slow-growing, expansile) but are readily differentiated on imaging studies; they are more amenable to surgical control and removal. Cysts in the caudal maxillary sinus may result in exophthalmia [74, 80]. In one report of a horse with exophthalmos, CT revealed a large demarcated mass within the caudal maxillary and conchofrontal sinuses that resulted in lysis of the sphenoid and palatine bones and extension into the retrobulbar space [81]. **Dentigerous cysts**, or cysts from the dental arcade, occur uncommonly in the horse but may result in exophthalmos or deformation of the orbit. They typically are in close approximation to the petrous temporal bone, near the base of the external ear.

An intradiploic hematoma of the frontal bone causing exophthalmos in a mare has been reported that had imaging features (radiography and ultrasonography) reminiscent of a sinus cyst. CT with trephination, and cytology, were suggestive of an intradiploic bone mass, and a hematoma was confirmed on surgical exploration and histopathology [82].

Diagnosis

Diagnosis is based on clinical signs, radiology, and/or CT. Dentigerous cysts have a pathognomonic appearance on radiographs [83].

Treatment

Surgical resection is generally curative for sinus cysts. Surgical excision via a maxillary osteotomy has been reported under both general anesthesia and standing sedation. Cysts were firmly attached to the nasal concha in some cases, and these attached areas are generally left in situ to avoid marked epistaxis. Overall surgical success rate is reported as 92% in a long-term follow-up of 24 cases [80].

Sinus trephination, using a Steinmann pin and Jacobs chuck, resulted in the drainage of copious amounts of turbid, yellow fluid from the trephination site in one report [81]. A frontonasal osteoplastic flap [84] was performed, exposing a sinonasal cyst in the maxillary and conchofrontal sinuses. Removal of the cyst was possible (histology revealed ciliated pseudostratified columnar epithelium with mucus-producing goblet cells), and no recurrence was noted [81].

Sinus and nasal cavity neoplasia

Introduction and clinical appearance

Unilateral nasal discharge, facial swelling or deformation, and epistaxis are the most common clinical signs in cases of neoplasms of the sinonasal structures [85–87]. Exophthalmos occurs in approximately 20% of cases of sinus neoplasia [85–87]. The most common neoplasms of the periorbital sinuses that cause exophthalmos are, in order of frequency, adenocarcinoma, adenoma, osteoma, squamous cell carcinoma, fibrosarcoma, undifferentiated sarcoma, lymphosarcoma, and esthesioneuroblastoma (see Table 5.3) [80, 91]. Exophthalmos has also been reported from nasal neoplasia. In one case, a 9-year-old Trakehner gelding had exophthalmos associated with undifferentiated nasal adenocarcinoma affecting the orbit, with metastases to the right parotid gland, cranial cervical lymph nodes, fascial planes of the neck, and lungs [27].

In a retrospective study of 15 cases of equine sinonasal neoplasia examined by CT, the most commonly affected sinus was the conchofrontal sinus (100%), followed by the caudal maxillary sinus (67%) and the rostral maxillary sinus (60%) [92]. The authors included cases where tumors originated in the orbit and invaded the paranasal sinuses in this study. The most common apparent point of origin of the tumors was the retrobulbar area (27%), with involvement of the retrobulbar space in 67% of cases. Mass involvement of the retrobulbar space or sphenopalatine sinus was poorly identified using conventional radiography.

Diagnosis

Skull radiographs and CT are used to make a diagnosis of a sinus or nasal mass. Sinocentesis or biopsy is needed for definitive diagnosis. In one study of three sinus neoplasms, CT provided more information about the extent and severity of lesions than conventional radiography [87]. MRI has been recommended when exophthalmos or neurological signs are present as a better imaging modality than CT for evaluating orbital or intracranial disease [92].

Treatment

Surgical excision and adjunctive radiation therapy are generally recommended [85, 86].

Prognosis

The lesions are usually large and advanced, with much tissue destruction prior to definitive diagnosis [86]; therefore, in general, the prognosis for elimination of the neoplasm is poor. In one series, surgical treatment alone of seven malignant neoplasms resulted in recurrence within 6 months, but four out of five benign tumors did not recur [84]. In another large series of equine sinonasal disease referral cases, sinus neoplasia cases had the worst prognosis, with a cure rate of 22% [80].

Neoplasia of the orbit

Neoplasia of the equine orbit is reportedly much less common than in other domestic species. The most common tumors (cited in the literature) arising within the orbit are neuroendocrine tumors and extra-adrenal paraganglioma [14, 93–95, 137].

Anaplastic sarcoma, lymphosarcoma (Figure 5.27), and squamous cell carcinoma (Figure 5.28) are also common (see Table 5.3). These may be in fact common as a cause of exophthalmos in practice, but underreported in the literature. Squamous cell carcinoma (SCC) of the orbit arises as an extension of neoplasia from the globe or adnexa, especially the nictitans. Belgian and other draft breeds are at increased risk of developing SCC.

Lymphosarcoma is a generalized neoplasia, rarely limited to the orbit. It is often less obviously neoplastic, presenting as an insidious onset, gross blepharoedema with a reduced palpebral fissure. In one study, ocular lymphosarcoma was present in 21 of 79 cases [96]. Eyelid involvement was recorded in eleven cases, nonspecific uveitis in four, corneoscleral masses in two, and diffuse retrobulbar infiltration in two. Early diagnosis of lymphosarcoma will allow early therapy to be possible and improve short- to medium-term survival in these cases. Clinical suspicion should encourage early biopsy and a thorough systemic work-up for neoplastic staging. Lymphosarcoma can present as a solitary, rapidly enlarging orbital mass, leading to ocular proptosis [97].

Other less commonly reported neoplasias of the orbit include malignant rhabdoid neoplasia, fibroma, angiosarcoma, adenocarcinoma, and primitive neuroepithelium [28, 93, 98–103]. See the section **Specific orbital neoplasia** for more information on these individual neoplasm types.

Clinical appearance and diagnosis

Clinical signs of orbital neoplasia are those of a space-occupying lesion: exophthalmos, prominent displacement of the nictitans, orbital swelling, bone surface distortion (possibly with pain on palpation), strabismus if the mass is extraconal, anisocoria and/or blindness (if directly compressing the optic nerve), displacement of chemotic conjunctiva through the fissure, and, less commonly, epistaxis and signs referable to the involvement of adjacent cavities (Figures 5.27, 5.28, 5.29, and 5.30) [99, 103, 137].

Blindness may result from intracranial compression of the optic nerve by pars intermedia masses. Tissue infiltration by neoplastic tissue can be diffuse and severe, can be restricted to the orbit, or may involve other tissues. Clinical examination should include palpation of the orbital rim to identify evidence of periosteal reaction and bone infiltration. Local lymph nodes should be evaluated by palpation and aspiration for cytology if abnormalities are suspected. Exophthalmos may be pronounced, and distortion of the eyelids and palpebral conjunctivae may be profound (see Chapter 6 for more information on primary ocular adnexal neoplasia). These are not specific for primary orbital disease but can occur as the presenting sign for neoplasia arising elsewhere, such as the sinuses. In such cases, other



Figure 5.27 Bilateral exophthalmos in a yearling horse. Note the prominence of the nictitans, epiphora due to punctal misalignment, bulging of the supraorbital fossa, and distortion of the normal eyelid contour. Generalized lymphosarcoma was diagnosed at necropsy.



Figure 5.28 Exophthalmos from extensive medial canthus squamous cell carcinoma that has extended into the orbit.



Figure 5.29 Exophthalmos, elevation of the nictitans, periorbital swelling, and dorsal strabismus with a ventral orbital mass.



Figure 5.30 Transverse CT of a horse with exophthalmos. An adenocarcinoma arose from the maxillary, sphenoid, and frontal sinuses to occupy the orbit and subsequently invaded the calvarium.

clinical signs such as respiratory stridor, epistaxis, purulent discharge, or a fetid odor may be present and raise the index of suspicion. Three-dimensional imaging (CT or MRI) is the best method to determine the extent of the tumor and the most appropriate treatment [28, 104, 105, 137]. Orbital ultrasound, while easily performed, is generally less helpful, except to direct FNA for cytologic examination [106]. A biopsy is the only definitive method to confirm the presence of neoplasia.

Treatment

Treatment consists of surgical removal with or without adjunctive therapies (see section **Specific orbital neoplasia** and Chapter 6 for information on treatment of adnexal neoplasia). If it is desired to preserve the globe and eyelids, then early referral for imaging and surgery is to be encouraged, with histology acquired prior to starting therapy. Current medical control is relatively poor but improving, and some cases will respond well for weeks to months with aggressive use of corticosteroids and other anticancer therapy. Consultation with a specialist oncologist is recommended.

Prognosis

Unfortunately, orbital and paraorbital neoplasia is often relatively advanced before presentation and thus can appear to progress rapidly. Space is available for local expansion prior to obvious anatomic distortion and functional damage is often advanced. Thus ultimately the prognosis must be grave, but short-term palliation is sometimes possible, for example, to reach a foaling date.

Specific orbital neoplasia

Nasal and orbital adenocarcinoma

Extensive nasal and orbital adenocarcinoma can cause exophthalmos, strabismus, loss of physiologic nystagmus, and neurologic signs [27]. A grave prognosis should be attached to secondary metastases to the orbit that also induce neurologic signs and/or any paraneoplastic syndrome. In one reported case, the mass was noted to have arisen in the paranasal sinuses, trespassed across the orbit, and invaded the calvarium (see Figure 5.30) [27]. Imaging confirmed parenchymal brain involvement and allowed correct decision-making in that case. Especially significant were the metastases found in the parotid salivary gland, cranial cervical lymph nodes, and extending in fascial planes to the orbit, despite not being clinically apparent antemortem. The possibility of local extension and distant metastasis should always be considered and imaging performed, along with aspiration and cytology, even if only subtle changes are present. Thoracic radiography may be of value to identify masses, but negative findings do not exclude metastasis [26].

Adenocarcinoma of the frontal sinus in a 15-year-old horse expanded through the cribriform plate to enter the orbit and result in exophthalmos [19]. Adenocarcinomas of respiratory epithelium are typically very aggressive in horses. Unfortunately, neoplasia is often extensive on diagnosis (as previously discussed) and the prognosis is poorer when multiple structures are involved.

Neuroendocrine tumors, although uncommon, are the most common orbital tumor reported in the literature [75]. Neuroendocrine tumors, including extra-adrenal paragangliomas and undifferentiated neuroendocrine tumors, were the neoplasms identified in six of seven (86%) of horses evaluated for primary orbital disease in one study [137]. These horses exhibited nonpainful exophthalmia, and two had anisocoria and dilation of the pupil of the affected eye. Neuroendocrine tumors of the orbit grow slowly, and metastasis is rare, with exenteration giving a good cure rate [93, 137]. Care is advised at surgery, since reports of severe intraoperative haemorrhage and a decrease in mean arterial blood pressure have been published. This is believed to be due to handling of the neoplastic tissue at exenteration [93, 137]. The site of origin may be hard to define because the tumors often involve the orbit, nasal cavity, and paranasal sinus by the time of diagnosis [14].

Osteosarcoma occurs uncommonly and is typically associated with early distortion of the bony surface. It has been reported with dramatic distortion of the frontal bone, and radiographic studies are confirmatory [97].

Melanoma of ocular tissues is frequently benign, and primary excision is curative. However, a small percentage of these tumors are aggressively recurrent and may invade the orbit. A conjunctival

melanoma recurred twice, necessitating orbital exenteration that was curative for at least 5 years [107]. Specific typing of cell-surface receptors may permit identification of more aggressive tumors, allowing selective monitoring of suspicious tumors long term [108]. Melanomas have also been reported escaping from the globe into extraocular muscles [109] and also with the periorbital sinuses [85].

Angiosarcoma and hemangiosarcoma

Hemangiosarcomas most commonly arise from the temporal globe surface but can rapidly track caudally to penetrate the fascial tunics and invade the orbit. A case of medial canthal hemangiosarcoma progressed to invade the orbit and maxillary sinus in one individual [110]. An angiosarcoma of the eyelids in one report resulted in exophthalmos [111].

A single report of a malignant rhabdoid tumor treated with exenteration in a 2-year-old filly exists [112]. The tumor was present multifocally within the globe and orbit and had spread to the lymph nodes, salivary glands, and locally within the subcutaneous tissues of the head.

Medulloepitheioma and meningioma

Medulloepithelioma can arise in the orbit but also from the uvea and optic nerve. Exophthalmos and globe distortion may occur, but exenteration is curative [100, 102, 113].

Meningiomas can be seen as a rare cause of blindness in horses. It may become bilateral because the neoplasm often arises close to the optic chiasm. One report detailed a tumor that obliterated the maxillary, frontal, and sphenopalatine sinuses, but did not invade the calvarium [88]. The diagnosis in that horse was made histologically. Nervous-tissue tumors in horses are predominantly peripheral, and they risk reaching a peak at 4–6 years of age and remaining stable thereafter [114].

Iatrogenic orbital disease

Guttural pouch disease

Guttural pouch disease in the horse may be remarkably difficult to contain and resolve. Guttural pouch empyema, often associated with *Streptococcus equi*, is a challenging condition, with its treatment requiring mechanical as well as antimicrobial therapies. Formalin injection can result in control of clinical cases but cannot be recommended. One potential sequel to this treatment, of which the client should be advised, is thrombosis of the ophthalmic artery leading to blindness. Specific cases of occlusion of the internal carotid artery following formalin injection with resulting severe endophthalmitis have occurred (Figure 5.31). These have required enucleation to control the severe pain. Guttural pouch mycosis may erode into large vessels traversing the guttural pouch and cause hemorrhage. Surgical occlusion of the external and internal carotid and greater palatine arteries for the treatment of guttural pouch mycosis may cause ischemic optic neuropathy and blindness [115]. When transarterial coil embolization of the internal and external carotid arteries was used, rather than surgical ligation, no ocular complications were noted [115]. This may be the preferred method to control hemorrhage associated with guttural pouch infection [116].



Figure 5.31 Severe endophthalmitis following use of formalin injection for treatment of guttural pouch empyema.

Direct extension of guttural pouch disease is less common, but a case of guttural pouch mycosis resulted in blindness, due to expansion of the plaque to involve the optic nerve and optic chiasm within the calvarium, as well as the retina and orbit [117].

General treatment of orbital disease

Topical medications

Corneal complications of orbital disease are relatively common and may be addressed by frequent use of topical ophthalmic ointment or solutions (see Table 5.5). Exposure pathology secondary to lagophthalmos is the primary concern. The surface of the cornea must be protected from desiccation to avoid trauma, ulceration, stromal loss, and possibly globe perforation. Topical ointments are preferred for increased coatability and residence time. Petroleum-based lubricants are ideal; however, if the exposure is sufficient to result in desiccation of the ointment base between administration, then this should be supplemented with a gel-based lubricant. If lagophthalmos is significant, support such as a bandage contact lens or temporary tarsorrhaphy should be considered.

Systemic medications

The parenteral antibiotic of choice in horses with suspected or confirmed sepsis is injectable penicillin G (22,000–44,000 IU/kg IV every 6 hours) in combination with gentamicin (3.3 mg/kg IV every 12 hours or 6.6 mg/kg IV every 24 hours (see Table 5.4)).

This combination results in very broad-spectrum antimicrobial coverage with excellent distribution to the orbit and globe. These medications may also be used for emergency surgery, but penicillin G should be given as far in advance of anesthesia as possible, to avoid any complications with hypotension. Ampicillin sodium (20–50 mg/kg IV every 6–8 hours) can be used as a penicillin replacement. The trihydrate form of ampicillin should not be used intravenously. Procaine penicillin requires less frequent administration, but the typical volume of injection (30–35 mL) requires distribution over at least two sites and is generally a poor choice for long-term use. Gentamicin has broad effects against Gram-negative and some Gram-positive bacteria. This is a concentration-dependent antibiotic, so the high peak/low trough of once-daily dosing may be preferable in individuals with no contraindications such as renal disease. Enrofloxacin (7.5 mg/kg every 24 hours) has been reported to have good ocular and therefore presumably orbital penetration [118].

For prophylactic antimicrobial therapy, less intensive therapy is usually adequate. Oral antibiotics that achieve good tissue concentrations include trimethoprim sulfonamide (TMPS) (15–30 mg/kg PO every 12 hours), which is moderately broad spectrum, easily available in variable forms for dosing, and well tolerated, particularly for intermediate and long-term use. Oral doxycycline (10 mg/kg PO every 12 hours) is also well tolerated, but use should be confirmed by sensitivity testing. Doxycycline is not suitable for IV use. Tetracycline is more broad spectrum and can be used for cases of orbital cellulitis, especially if osteomyelitis is suspected. Caution should be used with IV use of tetracycline in horses to avoid anaphylaxis, and dilution in a moderate volume (100–500 mL) of saline has been recommended. All orally administered antibiotics in horses may result in diarrhea and bacterial overgrowth ("colitis X") that requires veterinary attention. Clients should be warned to look for this and report any incidence to allow treatment.

Antibiotics against anerobic bacteria are rather limited in horses, but metronidazole (15 mg/kg PO initial dose, then 7.5 mg/kg PO every 6 hours) is generally well tolerated orally. Use should be cases with confirmed anerobic infections, or where evidence of gas production is present. It may be used rectally in individuals with gastrointestinal intolerance.

Surgery of the orbit

Tarsorrhaphy

Indications for tarsorrhaphy are facial nerve trauma (temporary or permanent), neuroparalytic keratitis, exophthalmos, lagophthalmos, keratoconjunctivitis sicca, and post-ocular surgical intervention (i.e., protect the eye during recovery from general anesthesia). A variety of methods has been recommended, but multiple horizontal mattress sutures without the presence of a stent is preferred. The tarsorrhaphy suture enters the eyelid 3–5 mm from the margin, exits through the gray line of the meibomian gland orifices, or slightly anterior to it, and traverses the opposite eyelid in a symmetric manner (Figure 5.32). It is important that suture material does not contact the underlying cornea as ulceration may occur. Suture material of choice is a nonabsorbable 5.0 or 6-0, such as surgical nylon. If there is tension, a stent may be used on either side of the eyelid and may include use of rubber bands, sections of IV tubing, or a section of surgical drain material.

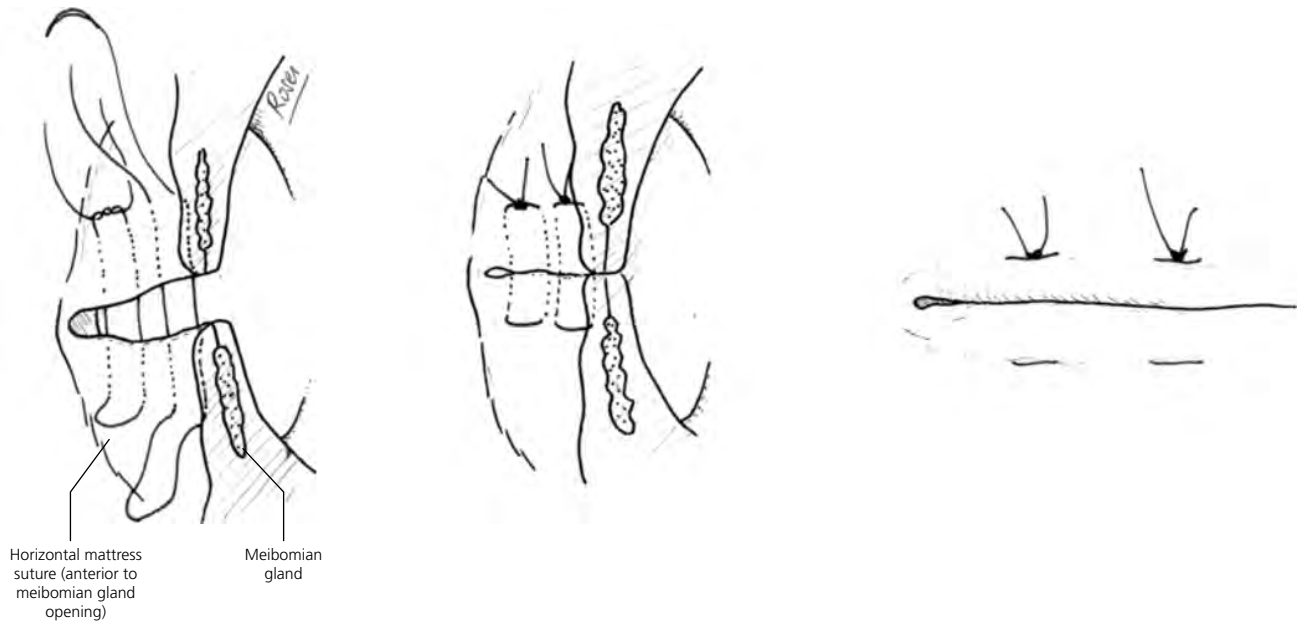


Figure 5.32 Temporary tarsorrhaphy for temporary protection of the cornea. The tarsorrhaphy horizontal mattress suture enters the eyelid 3–5 mm from the margin, exits through the gray line of the meibomian gland orifices, and traverses the opposite eyelid in a symmetric manner. Suture material of choice is nonabsorbable 5-0 or 6-0, such as surgical nylon. (*Source*: Reproduced with permission from Roser Tetas Pont, Bedfordshire, UK.)

Retrobulbar blockade

A retrobulbar block is highly recommended in any case of orbital surgery, especially where removal of the globe or evisceration is being performed. The block keeps the eye from moving during the procedure and provides analgesia during and after surgery. Retrobulbar nerve block has also been reported to ameliorate the oculocardiac reflex-mediated changes in heart rate during enucleation in horses under general anesthesia [119]. The procedure is outlined in detail in Chapter 1.

Orbital exploration

Orbital exploration is indicated to identify, sample, and/or remove masses of the equine orbit; to reduce fractures and reverse globe entrapment; to extract foreign bodies; and to investigate nonspecific causes of general orbital disease such as exophthalmos, nictitans prolapse, and generalized tissue displacement [29, 43, 99, 120]. The decision to perform an orbital exploratory should not be undertaken lightly. It behooves the surgeon to consider the potential lesions to be encountered and the surgical manipulations and skills that may be required, and to assimilate as many diagnostic results as are available before anesthesia induction. Surgery of the orbit for exploratory purposes may be challenging and requires advance planning and a surgical text for reference. Also of value are an anatomy atlas and a skull to aid in three-dimensional mental reconstruction of the lesion, its access routes, and its removal.

Three-dimensional (CT or MRI) imaging is strongly recommended prior to any orbital procedure in the horse to fully determine the extent of the lesion preoperatively [27, 104]. Minor procedures to remove an apparent anterior mass are seldom challenging, but resection and repositioning bone segments, restoring distorted anatomy, and extraction of embedded neoplastic masses while preserving a functional globe are challenging for any surgeon. Specific orthopedic instruments may be necessary to elevate the periosteum, to perform an orbitectomy, and to remove affected areas of bone. Ancillary equipment will frequently be necessary to control the pathology, for example, cryosurgery to limit the expansion or persistence of neoplastic cells. The most aggressive surgical resection is to elevate the periosteum in an attempt to remove the lesion in toto. This requires a meticulous surgical approach, careful dissection, and attention to preventing contamination of the surgical procedure. If the pathology has already breached the surgical containment, the risk of tumor recurrence or persisting infection is raised substantially.

Exploration of the equine orbit is rarely performed because of the complex nature of the anatomic structures, together with its infrequent indication. Typically, when exophthalmos is present in an older horse, suggesting an intraorbital mass, imaging reveals the mass to be sufficiently large that surgical debulking is either not reasonable or would also require concurrent removal of the globe. This procedure is described as **exenteration** and is considered a radical removal of the orbital contents in an effort to completely excise a lesion (with margins), or extend a comfortable life (see section **Exenteration**).

Orbital exploration would be indicated in a younger individual to identify, locate, and remove a mass. Examples of suitable lesions would be parasitic cysts or granulomas, encapsulated orbital abscesses, foreign bodies, circumscribed neoplasia, cystic dilation of the nasolacrimal or salivary apparatus such as the zygomatic gland, or a restrictive mass encircling the optic cone and resulting in secondary ocular disease, glaucoma, and possibly blindness.

The approach to the orbit for exploration depends on the expected location of the mass. Extraconal masses displace the globe and assist in localization. This area should then be subjected to advanced imaging techniques such as CT, MRI, or even contrast radiography with air or a radiopaque fluid. Ultrasonography rarely is diagnostic and does not allow determination of the extent of the lesion. Diagnostic orbitotomy is uncommon and risks extensive anesthesia and surgical time and dissection, but it may be necessary if more advanced imaging is unavailable. All tissues removed should be examined by histopathology, tissue imprints (cytology), and culture as appropriate.

Access to the deeper orbit is problematic because of the complete bony orbital rim. A dorsal orbitotomy approach [93] was reported to remove retrobulbar neuroendocrine tumors in three horses. A curvilinear skin incision is made just lateral to the sagittal crest of the frontal and parietal bones, traveling laterally beyond the zygomatic process of the frontal bone. Retraction of the temporalis muscle attachments exposes the extraocular muscle cone ventrally deep within the orbit. As an alternative, the zygomatic process of the frontal bone may be resected in section by an oscillating bone saw (or osteotome), with appropriate caution to avoid severing the neurovascular bundle within the supraorbital foramen [120]. This step exposes the dorsolateral globe and orbital contents, and the operating window may be further extended by performing a lateral canthotomy. The skin incision is made parallel to the zygomatic process of the frontal bone, cautiously incising to avoid sectioning nerve fibers that enter the orbicularis oculi laterally. The periosteum is incised anteriorly and reflected off, preserving it to permit its closure at the conclusion of the procedure. The zygomatic process is removed in an elongate section sufficient to expose the area of interest, after predrilling 20-gauge holes for its subsequent reattachment. Stay sutures may be placed around ocular muscles to permit gentle retraction and dissection of the globe and cone from the mass. Culture and biopsy for histopathologic examination may be obtained.

If the mass is to be removed in its entirety, cautious dissection should be performed to avoid inadvertent transection of the myriad vessels, nerves, and muscle attachments. Multiple layers of connective tissue are present in the orbit to maintain its precise alignment and function. Thus, prior to surgical intervention, it is worthwhile to precisely locate the mass within the orbit and determine whether it is intraconal, extraconal, or subperiosteal within the orbit. At the conclusion of the surgical procedure, the zygomatic process is repositioned and fixated with stainless steel surgical wire (20 gauge). Periosteal closure may be performed with simple interrupted absorbable suture

size 4-0 to 5-0. A subcutaneous closure is performed in like manner. The skin is reapposed with simple interrupted or cruciate nonabsorbable sutures. If a canthotomy was performed, it is closed, starting at the eyelid margin with a buried deep layer, and a skin layer that incorporates a figure-of-eight suture at the canthus. These sutures should be retained for 2–3 weeks to avoid subsequent dehiscence, because the site is mobile.

Orbital fracture

Fractures of the orbital rim are a potentially globe-threatening disease that may result in displacement, impingement, functional restriction, or laceration of the globe. Hemorrhage and increased tissue volume may compress the globe or its vascular channels. Most commonly, the dorsal orbital rim is fractured and is often diagnosed by observation and palpation (see Figures 5.33 and 5.19B). A retrospective study of 18 cases of equine orbital fractures revealed that fracture of the zygomatic process of the frontal bone was the most common (55.6%), followed by comminuted fractures of the zygomatic, frontal, and lacrimal bones (27.8%), and fractures of the zygomatic process of the temporal bone (16.7%) [121].

The fractured area may be quite painful, and care is indicated to avoid complicating the injury. Inferior orbital rim fractures may occur from blunt trauma due to polo balls or mallets, excessive disciplining, injuries in stalls, transportation, or pasture turnout. Fracture of the lacrimal bone may threaten the integrity of the nasolacrimal duct. Nasolacrimal duct obstruction may also result from the original fracture or attempts at fixation [122]. Fractures that are more extensive result from vehicular accidents and excess struggling in a panicked individual.

If the injury involved rearing or falling over backwards, damage to the poll may entail fractures to the basioccipital and consequently basisphenoid bone in the inner (floor) orbit. This can result in blindness if it involves the sphenoid foramina, and often epistaxis if the cranial fractures continue rostrally. Individuals less than 5 years old are most at risk of dissecting fracture, because the occipitosphenoid suture line remains incomplete until that time [83], and concussive force separates preferentially along that line. This area is particularly hard to diagnose and image with radiographs but is more easily investigated with CT. A complete neurologic examination may assist in determining the location of damage and identify neurological deficits that may accompany the fracture(s). When internal fractures are present, the demeanor and alertness of the patient are often reduced if the calvarium is traumatized and CNS damage occurs, which concurrently worsens the prognosis.

Imaging by radiography, and preferably CT, should be performed prior to initiating surgical intervention. Skyline views are helpful for the orbital rim but may be challenging to attain over the sinus. In fact, one study reported that digital palpation was better for diagnosis of orbital fractures than radiology [123]. Despite this, the extent of the fracture may be greater than anticipated from the imaged margins, and a complete evaluation of the injury is necessary before determining the ideal method of fixation. A CT scan is nearly always recommended when orbital fractures are present. The extent of the fractures and damage are readily visualized (Figure 5.34) [47].

When the ultimate cosmetic outcome is desired, closed fracture reduction is highly desirable. Under general anesthesia, zygomatic process fractures may be reduced by manipulation of the bone piece into position using a bone hook [123]. More complex fractures of the dorsal orbital rim may be reduced with a malleable plate or bone plate. If the fracture is repaired by open technique or if an implant is used, parenteral antibiotics are administered. Alignment of the orbital rim is attained more accurately if local tissue inflammation has been attenuated by systemic medications and local compression. Surgical intervention should be initiated early before callus formation becomes significant. Callus formation initiates very rapidly and may be well established at 7–10 days. Early stages of second-intention healing are typically advanced by 1 or 2 weeks [29, 123]. Fractures of the orbital margin may immediately result in



(A)



(B)

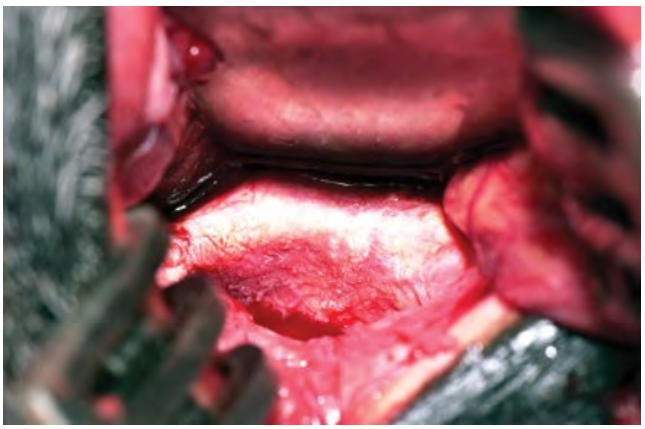
Figure 5.33 (A) Depressed dorsal orbital rim fracture resulting in a ventral displacement of the globe. (B) Dorsal orbital rim fracture with resulting exophthalmos, severe conjunctival swelling, and exposure keratitis.



Figure 5.34 Transverse CT of a horse with a displaced fracture of the dorsal orbital rim that is impinging on the globe. CT scans are the best imaging modality to determine the location of the fractures and extent of injury.



(A)



(B)

Figure 5.35 (A) Orbital fracture resulting in ventral strabismus from bone fragments impinging on the globe and extraocular muscles. (B) Ventral transconjunctival approach to the orbit for removal of bone fragments that are impinging on the extraocular muscles.

sequelae that require surgical intervention to prevent blinding and painful damage to the globe itself [124]. Entrapment of the ocular muscles, venous stasis, unstable fragment edges, and laceration of blood vessels may necessitate surgical intervention to stabilize the orbit and globe by decompressing the orbit and removing or repositioning the displaced bones (Figure 5.35).

Fractures of the skull's flat bones may be categorized as displaced or nondisplaced, and either open or closed. Closed nondisplaced fractures, together with some closed displaced fractures, are frequently permitted to heal by second intention [47]. Depressed fractures may be realigned by drilling a 2- to 3-mm hole in the bone fragment and inserting angled surgical wire or an instrument to elevate the bone fragment into position. Frequently, it is unnecessary to provide fixation when repositioned, but fixation with 20-gauge wire is appropriate if necessary. In most situations, cosmetic outcome is near perfect. Flat bones are likely to heal rapidly and pose little risk of complication if not exposed to further stress and extension of the fracture. Stall rest and limited athletic exercise are indicated, together with control of inflammation.

Commonly, emphysema occurs, which may be monitored for stabilization and treated with parenteral antibiotics because of the open sinus. Fracture pieces may alter position from day to day despite the large bulk of the equine skull. Such motion does not necessarily imply an unstable fracture, but it should be monitored to ensure that the fragment lines are not progressing. Fractures of the flat bones adjacent to the orbital rim seldom jeopardize the globe. However, if the zygomatic or palatine is fractured, the orbital floor may capsize at the time of fracture, and the globe becomes ventrally displaced.

When surgical repair is indicated or the fracture is open, it should be approached with a curvilinear skin incision to provide adequate exposure adjacent to the site, with careful dissection to

the location of the fracture. Acute open fractures should be clipped and surgically prepared and any necrotic or poorly viable skin and subcutaneous tissue removed. The exposed surfaces are flushed copiously with sterile saline or dilute povidone iodine, which may be administered via a pressure bag if desired, if appropriate measures to avoid further spread of contaminants are taken. Exposed bone should be debrided aggressively to ensure a healthy vascular supply.

Fractures that expose the periorbital sinuses may result in emphysema and epistaxis. Sinus fractures are considered open wounds and should be treated aggressively. If hemorrhage is substantial, prophylactic irrigation with saline (possibly with pressure bag) followed with antibiotic solution is appropriate. A drain may be placed if there is any evidence of infection (purulent exudate, cytologic evidence of bacteria or fungi). Alternatively, comprehensive parenteral antimicrobials and healing by second intention may be elected if displacement is minimal, because healing is typically rapid. Tetanus vaccination status should be evaluated, and tetanus antitoxin or toxoid administered as appropriate. The sinus egress should be verified, and if drainage is inadequate, the opening into the nasal cavity should be enhanced or an indwelling drain established. Microbial colonization of clotted hemorrhage within the sinus may lead to severe sinusitis.

Soft-tissue damage

Initial soft-tissue injuries should be treated aggressively with systemic anti-inflammatory agents together with antibiotics if an open wound is present (see Table 5.4). Cold compresses and compression bandages limit tissue volume expansion immediately post injury, which permits more accurate evaluation and reconstruction. Thorough cleansing and minor debridement are an important component of first-aid care, but if the orbit itself is open, caution is warranted to avoid introducing noxious fluids, cleansing agents, or petroleum-based products that may incite an aggressive inflammatory response.

Avulsion of ocular muscles may be repaired in the acute stages if local inflammation is adequately controlled. Alternatively, repair may be delayed by 1–2 weeks, during which anti-inflammatory therapy is administered. The muscle may be avulsed completely or be strained and lose its mechanical leverage. If the injury is very chronic, an avulsed muscle becomes fibrotic and is too short and mechanically ineffective to reattach. Reattachment of the muscle should be performed with a suture pattern designed to resist tearing or shearing. Sutures are placed adjacent to the original insertion with absorbable material such as 5-0 polyglactin 910. If the muscle and tendon are still inserted but are strained, it may only be necessary to imbricate the weakened tendinous attachment to achieve more normal globe position and restore function. It is often necessary to overcorrect the positional defect at surgery because of the tendency for the suture to loosen during resolution of the inflammation. Exposure of orbit contents, which are predominantly fat, may be resected and the fascial layers reapposed over the surface before closing the conjunctival layer.

Eyelid repair may also be necessary to restore a functional margin without step defect and to minimize cicatricial sequelae in the conjunctiva. Minor damage to the nictitans free margin is common in extensive trauma, and options are either repair with buried sutures or resection. Exposed cartilage poses a minor threat to corneal abrasion. Nasolacrimal duct laceration may be the most challenging to repair functionally. If stricture results, a new drainage conduit may be created into the adjacent sinus. Surgical intervention in the eyelid is reviewed in detail in Chapter 6.

Enucleation

Enucleation is indicated for the removal of a painful, blind, deformed, or traumatized eye, or where extensive neoplasia or infection renders survival of the globe unlikely or requires unreasonable duress for the patient. In some situations where only a single anesthesia is tolerable and the ipsilateral globe is visual, enucleation may be preferable to treatment of advanced disease. In individuals considered to be high-risk anesthesia candidates or who will not tolerate frequent medications, and for those where greater economic expenditure is not possible, removal of the globe is a rapid method to restore comfort and avoid further adverse sequelae. Enucleation may be the only humane intervention, but it is important to ensure that the anesthesia and post-operative recovery are not of greater risk than the discomfort of the presenting condition. Enucleation performed under general anesthesia carries risks associated with not only the surgery but also anesthesia and recovery [125]. Consideration should be given to enucleation using standing sedation, but should in either case be performed with appropriate pre-operative planning, aggressive analgesia, sedation, restraint, and appropriate counseling of the client and assisting staff [126, 127].

A brief candid discussion with the client about alternatives to enucleation is warranted before surgery. All alternatives to enucleation require ongoing maintenance care and have a greater incidence and spectrum of complications, as well as a larger initial and recurring financial investment. For the majority of horses, enucleation remains the most appropriate selection. Other surgeries available such as intrascleral prosthesis and cosmetic conformers offer potential cosmetic benefits but carry no benefit to the horse. The client may not initially contemplate cosmetic alternatives; however, they should be discussed to avoid the possibility later that another procedure would have been preferred if it had been made available. The only post-operative cosmetic alteration that can be performed is implantation of an orbital prosthesis beneath a closed palpebral fissure. Cosmetic alternatives to enucleation are detailed under the section **Evisceration and intrascleral prosthesis**.

The techniques for enucleation have varied little in recent years, and the major approaches reflect the reason for removing the globe. If neoplasia or severe infection is present, the preferred technique is a closed transpalpebral method (Figure 5.36). If the ocular disease is contained within the globe or does not threaten

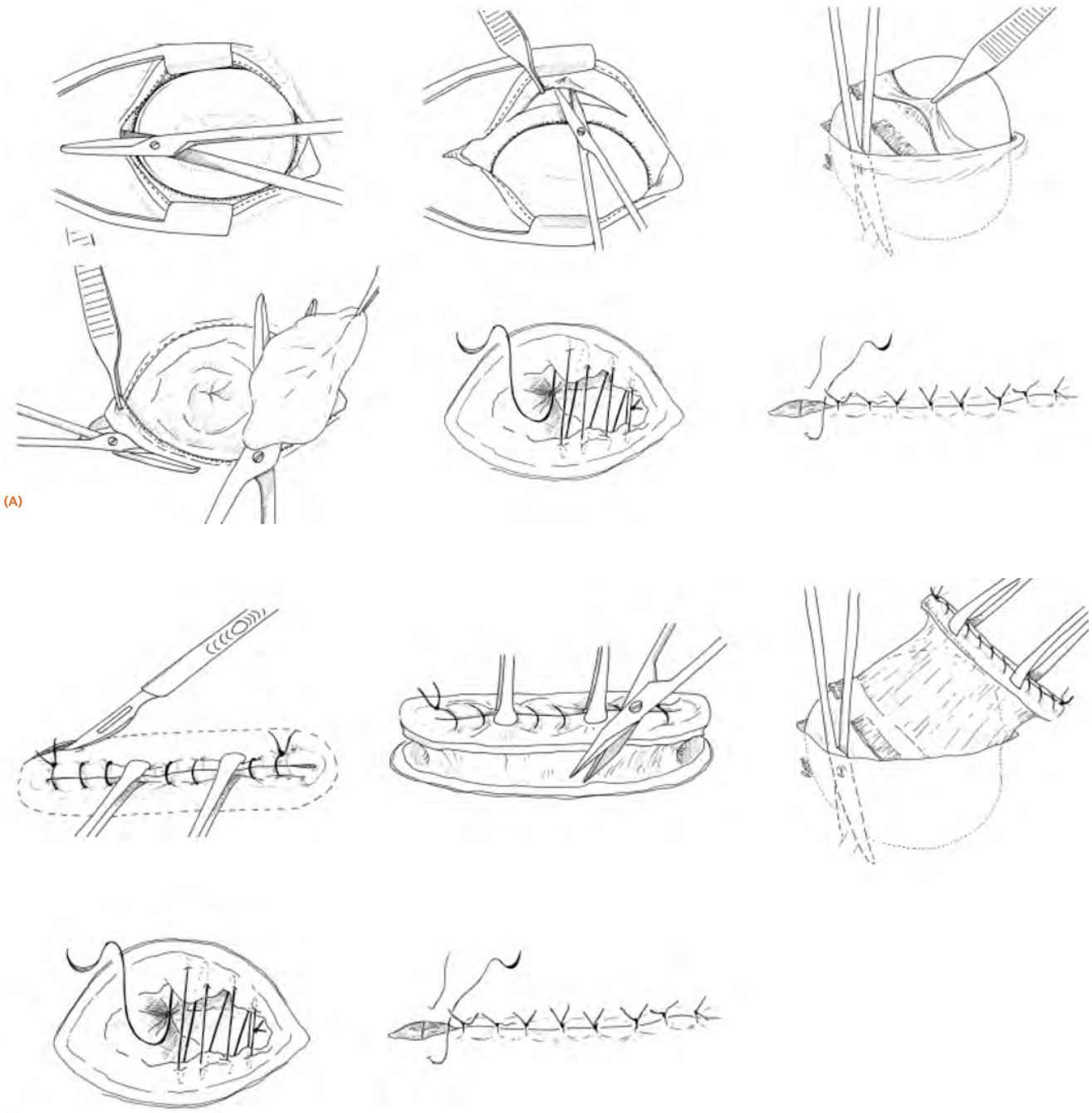


Figure 5.36 (A) Transconjunctival enucleation. A complete 360-degree conjunctival peritomy is completed adjacent to the limbus. Extraocular muscles are identified and resected at the globe, permitting its free rotation. The retrobulbar attachments of the retractor bulbi muscles are very extensive and are resected. The optic nerve is transected (but never clamped or ligated), and the globe is removed. The nictitans, eyelid margins, and conjunctiva are excised. The wound is closed in a minimum of two layers (see text). (B) Transpalpebral enucleation. The transpalpebral approach is preferred for removing septic globes and malignant neoplasia. Eyelid margins are temporarily tightly apposed with suture (2-0 nylon) in a continuous or interlocking pattern. An incision is made full thickness through the skin 5–7 mm from the eyelid margin to expose the subcutaneous tissues. The incision is extended to the periorbital margin, with care to avoid perforating the inner eyelid and contaminating the orbit with contents of the conjunctival fornix. Dissection is continued deeper to the fornix, and minor blunt dissection will rapidly free the globe from its surrounding tissue envelopes. The ocular muscles are resected, and the globe is removed. Closure is as described for transconjunctival enucleation. (*Source*: Reproduced with permission from Roser Tetas Pont, Bedfordshire, UK.)

the orbit, a transconjunctival approach is simpler, more easily performed, and results in less surgical trauma (Figure 5.36). Post-operative pain and inflammation are also reduced, because fewer tissue planes are interrupted. Routine preparation includes general cleansing of the face, surgical clipping of a 2.5- to 5-cm margin around the eyelids (in preference to shaving), removal of the eyelashes and possibly the vibrissae, and performing a surgical scrub of the skin with baby shampoo, chlorhexidine, or povidone iodine (Betadine®) scrub. Because of its epitheliotoxic effects, detergent is normally avoided on the globe, but it is not of concern in this procedure. The ocular surfaces may be cleansed with dilute povidone iodine and flushed with sterile saline. If under general anesthesia, the head is typically positioned laterally, preferably with the nose elevated to level the orbit, and the surgeon seated on the dorsal side. Routine draping is performed to establish a sterile field. A retrobulbar block is recommended (see Chapter 1) to improve anesthetic stability and reduce post-operative discomfort and intraoperative hemorrhage. This can be performed under ultrasound guidance to improve the success rate of the block if required [106]. Local auriculopalpebral and sensory nerve blocks may also be performed, together with topical proparacaine and phenylephrine. Local anesthesia greatly reduces reliance on general anesthesia and has a more profound effect on pain awareness, thus permitting a generally lighter anesthesia plane.

When performed under standing sedation it may be of benefit to perform all nerve blocks prior to the full surgical clipping and preparation to allow adequate time for the nerve blocks to work. A retrobulbar block, along with auriculopalpebral, supraorbital, lacrimal, zygomatic, and intratroclear nerve blocks, needs to be performed [126]. Topical proparacaine is also used on the cornea. The area that appears hardest to desensitize using regional nerve blocks is the dorsomedial lid and conjunctiva, and extra local anesthetic may be infiltrated there if desired. Extra local anesthetic may also be deposited at the site of the lateral canthotomy.

The transconjunctival enucleation is initiated with placement of an eyelid speculum, and a short lateral canthotomy is performed (see Figure 5.36). A complete peritomy is completed adjacent to the limbus. The extraocular muscles are identified and resected at the globe, permitting its free rotation. The retrobulbar attachments of the recti muscles are very extensive and are resected at their tendinous insertions to reduce hemorrhage. The optic nerve should never be clamped or ligated; instead, if necessary, the orbit may be temporarily packed with gauze and pressure applied to control bleeding. The nictitans may be removed concurrently with the globe or subsequently. To avoid subsequent dehiscence due to lacrimal secretions, it is imperative to remove the nictitans (including gland) and conjunctiva. In contrast, the lacrimal gland is rarely removed and typically somewhat difficult to identify. The orbital contents should always be inspected to ensure that no pathology remains. Capillary seepage is ubiquitous, but it should not preclude inspection of the orbit. Normal contents include moderate amounts of fat interspersed between fascial layers, the extraocular muscles, and periorbitum. The orbit may be flushed with saline and temporarily packed with sterile gauze. The conjunctiva is separated from the eyelid and Tenon's capsule, and the eyelid margin is resected from lateral to medial. Care is exercised to ensure the medial canthus is completely excised, while avoiding the angularis oculi vein just below.

An intraorbital prosthesis may be placed to limit sinkage of the orbital skin post surgery. Two forms of prosthesis are available: a round silicone ball and a hemiglobe attached to a flattened plate (available in two sizes) (Figures 5.37 and 5.38). Particular attention should be paid to removing any surgical powder on the prosthesis by rinsing or wiping it with saline or Betadine® solution. It is aseptically introduced into the orbit. The prosthesis size should be selected to occupy the orbit and approximate the size of the globe removed, typically ranging from 40 to 50 mm in size. The contralateral globe may be measured prior to anesthesia for size comparison. The prosthesis



(A)



(B)

Figure 5.37 (A) Intraorbital silicone prosthesis. (B) Intrascleral prosthesis that also may be placed in the orbit.

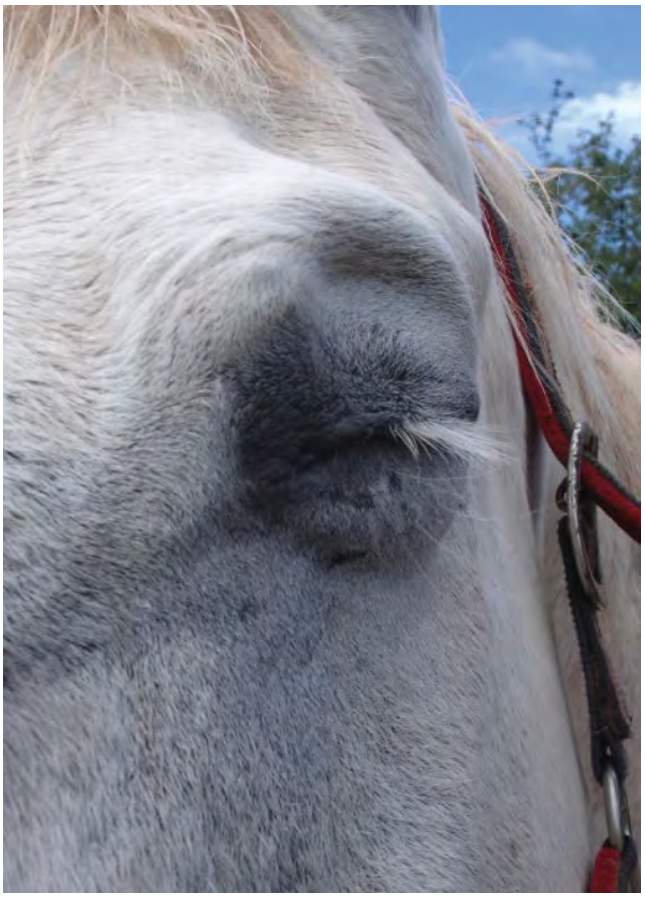


Figure 5.38 Intraorbital prosthesis 8 weeks post-operatively. (*Source*: Photograph courtesy of Dr Tim Knott.)

may be fixed in position if desired with 2-0 or 3-0 nylon suture attaching it to the periosteum, or by incorporating it into a surgical meshwork in an interlocking pattern, taking shallow bites in the prosthesis to maximize stabilization. Some previous surgical descriptions recommend cutting the anterior face to a flat surface to avoid a prominent anterior curvature under the eyelid. To avoid later migration of the prosthesis, dehiscence of the wound over the prosthesis, or expulsion of the prosthesis, closure of surgical margins should include complete apposition of a layer between the prosthesis and the eyelid skin.

Complications of using a prosthesis include wound dehiscence and draining tracts (Figure 5.39). Fewer complications may occur with an integrated orbital implant, as described with cosmetic prostheses under the section **Evisceration and intrascleral prosthesis**, but use of these integrated implants has not been described after enucleation.

Closure is performed in at least two layers. If desired, the periorbitum may be partially approximated with an interlocking layer of 0 to 2-0 nylon or polydioxanone in a continuous pattern. To ensure maximal apposition and closure, the surgical incision may need to be retracted to identify the incised margin of the periorbitum if it has recoiled. It is important to avoid combining the periorbital and subcutaneous layers; they should be closed separately, as a complete subcutaneous closure is required and this may not be achieved with the periorbitum. The subcutaneous layers are closed with an absorbable suture of the surgeon's preference. Either polydioxanone or polyglactin 910 are suitable, in sizes of 2-0 to 4-0. The pattern may be interrupted, continuous, interlocking, or cruciate as desired, with the former two being most commonly used. Continuous sutures have a greater risk of dehiscence, although this is rarely a practical problem. A watertight seal is desired in the subcutaneous layer. The skin layer is closed with nonabsorbable sutures in a cruciate or interrupted pattern, using 3-0 nylon or silk. As an alternative, if the patient is difficult to handle or to avoid suture removal, intradermal skin closure in a continuous pattern of 4-0 polyglactin 910 may be performed. Routine tetanus vaccine should be verified or be administered if the history is unknown. Tissue swelling is typically minimal at surgical conclusion but increases with recovery from anesthesia and increasing blood pressure. A small stent of swabs sutured over the wound to apply local pressure for 24 hours post surgery greatly reduces any postoperative swelling and is well tolerated.

The transpalpebral approach focuses on globe removal with constant separation of exposed surfaces from the orbital cavity. It is preferred for removing septic globes and malignant neoplasia. The eyelid margins are temporarily tightly apposed with suture (2-0 nylon) in a continuous or interlocking pattern. Allis tissue forceps may be placed on each knot end for identification and manipulation. An incision is made full thickness through the skin 5–7 mm from the eyelid margin to expose the subcutaneous tissues, which are bluntly dissected to divide the eyelid into dermal (retained) and tarsal (excised) layers. This is a potential space of embryologic derivation and readily separates. The division is extended to the periorbital margin, with care to avoid perforating the inner eyelid and contaminating the orbit with contents of the conjunctival fornix. The medial and lateral orbital ligaments are sharply severed with a surgical blade. Dissection through the reflections of the periorbitum/periosteum opens the orbital cavity deeper to the fornix, and minor blunt dissection will rapidly free the globe from its surrounding tissue envelopes. The ocular muscles are resected close to the globe, with limited visibility. The optic nerve should never be clamped or ligated; instead, if necessary, the orbit may be temporarily packed with gauze and pressure applied to control bleeding. The optic nerve is resected approximately1 cm posterior to the globe. Closure is as described for transconjunctival enucleation (see section **Enucleation**).

Enucleation has a low incidence of complications (less than 5%) [128]. It is imperative to remove the nictitans, the eyelid margins, and all of the conjunctiva; otherwise local or generalized dehiscence is likely to occur, with possible distension of the orbit with mucoid or mucoserous debris. Removal of the lacrimal gland from the dorsolateral orbit appears unnecessary. It is rarely entirely removed, even when intended, because of its protected location. Complete resection of the medial canthus



(A) (B)

Figure 5.39 (A) Intraorbital silicone prosthesis implanted into the orbit after enucleation of the left eye. (B) Central dehiscence and draining tract 5 years after placement of a silicone intraorbital prosthesis after enucleation.

ensures that dehiscence and drainage do not occur at the site of a persistent mucocutaneous junction after suture removal or absorption. If some retained tissue is present, a draining tract may occur. This may be surgically corrected by identifying and removing all of the tissue not removed previously. Orbital exploration should be performed before debridement, flushing, and closure. If the orbit may be septic, it should be debrided, extensively flushed with antibiotic solution, and a drain created through a stab wound ventral to the incision closure. The drain tubing is left in position until no further drainage occurs for 24 hours. Alternatively, gauze may be soaked in povidone iodine, rolled up, and placed in the orbit, passing through a stab incision and through a holding suture tied loosely in the skin. A section of gauze is removed (under sedation if needed) on a daily basis for 3–5 days or until the drainage becomes clear. The stab incision heals by second intention.

Evisceration and intrascleral prosthesis

The most common indications for evisceration are a cosmetic alternative to enucleation for blind, painful eyes or globes that are beginning the process of phthisis bulbi. In general, intraocular neoplasia and septic processes should be considered a contraindication to retaining the scleral/corneal shell with implant placement. However, intrascleral prostheses (ISPs) have been placed in such cases, and, with appropriate informed consent from the client, may not be an absolute contraindication [129]. Cosmetic alternatives that feature an artificial globe are available with the complete removal of the globe, but these require additional procedures to be performed at the time of first surgery (see section **Cosmetic conformer and hydroxyapatite orbital implantation**). All prostheses require routine maintenance and greater attention to cleanliness than enucleation. An ISP requires a single surgery but has a less cosmetic outcome and the potentially more serious complication of future corneal ulcers.

Consultation with a veterinary ophthalmologist should be carried out prior to surgery for potential candidates for cosmetic globes. Most owners find an ISP to be preferable to enucleation or retention of a phthisical globe, but it is important to discuss the fact that corneal ulceration may occur post-operatively and still requires therapy. More poignantly, if stromal loss occurs and is progressive, a conjunctival flap or intensive medication will be required. If perforation occurs and fails to granulate rapidly, enucleation is required, but a prosthetic hydroxyapatite implant remains a final alternative.

It is pertinent to consider that the cornea will still be at risk of ulceration unless vascularization occurs. Pre-existing corneal disease (traumatic or otherwise) increases the risk of complications post surgery, and an advancement conjunctival flap may be placed concurrently if the injury is near the limbus, such as a

corneoscleral laceration [130]. If anticipated management/lifestyle changes make daily observation unlikely, then evisceration is not an appropriate surgical choice. Corneal health is somewhat compromised with the removal of aqueous humor, and an adequate tear film and eyelid coverage is important to prevent future disease. Globes with pre-existing keratitis may also be regarded as high-risk candidates. Attempts to quantify tear production are warranted but may not be representative in light of concurrent trauma and pain.

Evisceration is the removal of the ocular contents with preservation of the ocular shell, comprising the cornea, sclera and its connective tissues, and conjunctiva. Surgical preparation is as for other intraocular surgery, with removal of eyelashes and fastidious surgical preparation of the skin. The cornea and conjunctival fornices are surgically prepared with dilute povidone iodine, which is adequately flushed with sterile saline. A brief sweep of the fornix may be performed with sterile cotton-tipped applicators to remove loose hairs, particularly from under the nictitans. Topical proparacaine and phenylephrine are applied several times. A self-adhesive drape is preferred to avoid any possible contamination of the intraocular space from the eyelid and skin hair.

The conjunctiva and Tenon's capsule are deeply incised over 160–180 degrees parallel and 6–8 mm posterior to the limbus to completely expose sclera [131]. If the eye has had chronic uveitis, Tenon's capsule may be remarkably thickened, requiring deep incision and blunt dissection to expose sclera. The sclera is incised full thickness in a position to permit easy closure. A shorter perpendicular incision traveling caudally (to complete a T shape) may be made for improved exposure. Dexterity permits the scleral incision to be entirely completed without perforating the uveal tract. The uveal tract and ocular contents may then be removed by rocking motions alternating between two nontoothed holding forceps. Alternatively, or if the tract ruptures, a lens loupe or probe may be used to undermine and remove the ocular contents. Caution is used to avoid damaging the corneal endothelium where possible. When the intraocular contents are removed and placed in formalin for histopathologic evaluation, the cavity is examined and debrided of remaining uvea. An intrascleral prosthesis is selected on the basis of corneal diameter, typically 1–2 mm larger than the corneal diameter of the ipsilateral or contralateral globe, approximately 36–40 mm for most adult horses. The prosthesis is cleaned of residual powder by rubbing it with a gauze moistened with dilute povidone iodine or sterile saline. The prosthesis is introduced, using caution to avoid touching the eyelids, and seated within the ocular tunics. Ability to appose the scleral margins is assessed, allowing accumulated hemorrhage to be expelled. The anterior surface of the prosthesis may be cut flat to reduce contact with the corneal endothelium, although this increases the likelihood of hemorrhage accumulating in this area, and its subsequent imbibition by the corneal stroma. At a later point, the heme breakdown products may result in a yellow-green corneal discoloration (Figure 5.40). Closure of the sclera is performed with interrupted sutures of absorbable material such as 4-0 to 6-0 polyglactin 910. The margins are apposed without excess tightness because the globe is no longer fluid filled. The conjunctiva and Tenon's capsule are closed in one layer with absorbable suture in a continuous or interrupted pattern, ensuring that complete coverage of the scleral incision and suture is achieved with Tenon's capsule to avoid later dehiscence.



Figure 5.40 Appearance of the cornea 5 days after evisceration of ocular contents and placement of an intraocular silicone prosthesis. There is corneal edema and ocular discoloration due to inflammation and resorbing blood products.

A partial temporary tarsorrhaphy is recommended postoperatively to reduce exposure and mechanical abrasion. The globe should be adequately lubricated, and routine postoperative therapy should include both topical and systemic antibiotics, and systemic anti-inflammatories. Increasing discharge or discomfort should prompt re-examination and fluorescein staining. Other than corneal ulceration, complications are uncommon but include endophthalmitis (septic or powder-induced); dehiscence of the surgical site if inadequately apposed, or if insufficient Tenon's capsule is incorporated; cellulitis from foreign-body response to surgical powder; and excessive periocular swelling if extensive dissection was performed. Histopathologic evidence of intraocular neoplasia or sepsis should prompt a discussion with the client about enucleation of the globe in toto with its prosthetic implant. Persistence of small amounts of uveal tissue does not appear to result in complications, but removal of the entire lens should be verified.

Most equine corneas vascularize and fibrose post surgery and may not be very cosmetic (Figure 5.41). If pigmentation occurs, the cornea appears very cosmetic. Corneal tattooing has been described, although it is not universally satisfactory [132]. A cosmetic shell or a black contact lens can be fitted over the prosthesis in some horses to achieve a more cosmetic appearance.

Exenteration

The most aggressive orbital diseases are preferably treated by exenteration, which is the removal of all the orbital contents together with the periosteal lining. The intent with this procedure



Figure 5.41 One year following evisceration of ocular contents and placement of an intraocular silicone prosthesis for treatment of chronic glaucoma. The cornea is extensively fibrotic and may become more cosmetic as the cornea pigments.

is to encapsulate the pathologic process within multiple natural tissue layers and remove them without contaminating the orbital cavity itself. Indications for exenteration are to control aggressive neoplasia, severe endophthalmitis, or orbital cellulitis, or as a palliative measure to control rapidly expanding neoplasia without an attempt to cure. Exenteration may be performed after the failure of enucleation or other local surgical intervention, or as the first procedure for aggressive disease. Enucleation procedures may be expanded into exenteration if unexpected orbital contamination is identified, but the advantage of closed tissue layers is usually lost in a converted procedure. A thorough pre-operative evaluation will permit the most appropriate procedure to be selected prior to commencing. In general, exenteration of the orbit is best undertaken under general anesthesia, particularly if periosteal elevation and resection is planned, as this is painful and frequently inadequately anesthetized in standing procedures [126].

Routine surgical preparation is performed, with a larger area of clipping and prepping. The procedure is performed similarly to transpalpebral enucleation, ensuring preservation of the intact tissue layers. Dissection is performed along the orbital margin to remove as many concentric tissue layers as possible. Neoplastic involvement of the eyelid should be incorporated in the surgical plan as wider surgical margins. When the incision is beyond the level of the conjunctival fornix, dissection is continued close to the orbital margin to remove the tissue layers intact. The periosteum is preferably removed with this procedure if the pathologic process has reached that tissue boundary. A periosteal elevator is necessary. If the periosteum itself is penetrated, adjunctive treatment of the bone margin should be considered by removal with Rongeurs or osteotome. Subsequent adjunctive treatment, either with cryotherapy or potentially with radiotherapy implants such as iridium beads, can follow. The orbit should be flushed with dilute povidone iodine to decontaminate it. If septic endophthalmitis was present and the tissue layers were compromised, the orbit may be flushed with broad-spectrum antibiotics (see Table 5.5). Orbital evaluation is greatly facilitated if a pre-operative retrobulbar block is placed with 1:100,000 epinephrine included. Ligation, hemostats, or cautery should be used as needed to permit a thorough evaluation.

A prosthetic implant is typically contraindicated by the pathology requiring the exenteration. However, if the globe and orbital contents are resected without contamination of the orbit, a meshwork of nonabsorbable suture material (2-0 or 3-0 nylon) may be placed across the orbit in an interlocking or continuous pattern to provide a flat surface for the dermis to rest upon, minimizing the tendency to exhibit a gaunt, hollow orbit post recovery. Often there is minimal periorbitum remaining, and the space is spanned with suture material only, which ultimately is likely to break down. Alternatively, a sheet of polypropylene (Prolene®) mesh can be sutured across the orbital rim. Subcutaneous and skin closure is routine.

After final closure of the skin layer, 10–20 mL of 0.5% bupivacaine may be aseptically injected transcutaneously to provide inexpensive short-term analgesia for up to 6 hours post recovery. This is useful in particular when a retrobulbar block was not performed prior to surgical exenteration.

If the orbit was contaminated during or prior to surgery, in addition to local lavage and antibiotics, a drain site should be created inferiorly; or less optimally, the incision should be maintained open post-operatively to permit drainage of exudate. The wound is managed to ensure drainage and granulation. The patient should be hospitalized and broad-spectrum systemic antibiotics administered. Granulation is typically well advanced by 7 days.

Complications of this procedure are predominantly incomplete removal of the neoplastic mass or infected tissue, allowing persistence of the pathologic process. Excessive swelling is common post exenteration because of the profound disturbance to the tissue layers and destruction of vascular beds. Every effort should be expended to ensure that inadvertent orbital contamination is avoided. More aggressive removal of blood clots and control of hemorrhage are necessary to identify the exact tissue boundaries.

Radical resection of eyelid skin and globe

A variation of these procedures has been described to permit closure of the orbit when large skin defects remain after neoplasm resection and globe removal [133]. In this procedure, the globe procedure is performed routinely, and any neoplastic mass is excised with a 5- to 10-mm margin. If the skin margins are too widely separated to be apposed, a 10-mm osteotome is used to remove up to 75% of the dorsal and lateral bony orbital rim (the zygomatic process) to reduce the prominence of this landmark and permit closer approximation of the skin wounds. Cruciate sutures are placed in the skin margins, and tension is



Figure 5.42 An inflatable device is placed under the skin and sequentially inflated with saline to stretch to overlying area (using the Radoran technique), giving more skin available for reconstruction. (*Source*: Photograph courtesy of Dr Cameron Whittaker.)



Figure 5.43 Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. A hydroxyapatite sphere is inserted into donor cadaver sclera and placed within the orbit following enucleation. Extraocular muscles are sutured to the donor sclera.

applied gradually at each site to close the defect. Releasing incisions 10 mm long are then positioned in a staggered pattern parallel and distant to the surgical wound to permit a mesh-like expansion of the surface area. In many situations, this permits a near-complete closure over the orbit. If sufficient time is available before surgery, skin expanders may be used to stretch the adjacent skin to allow a primary closure (Figure 5.42).

In the most extreme circumstances, the orbit may still remain open. In such cases, the skin is apposed in the most practical and complete method possible, using tension-bearing sutures such as vertical mattress and walking sutures; the remaining area is handled as a granulating open wound. Gauze packing of the orbit, protection of the surface, and topical disinfection are recommended. Systemic antibiotics are administered until a healthy granulation bed completely covers the internal orbit. Lavage is performed daily, initially with sterile saline, and after a healthy granulation bed is established in the orbit, continued with clean water. The authors reported excellent outcomes with diligent management and had no recurrences of the skin pathologies that were excised. Clients should be prepared for prolonged post-operative care and a gradual return to cosmetic appearance. Rotational skin flaps and grafts may be performed but are relatively high risk in the horse. Consultation with a specialist surgeon is recommended to determine the most practical and effective option for each individual case.

Cosmetic conformer and hydroxyapatite orbital implantation

An option for an improved cosmetic outcome when the globe must be removed is the use of ocular conformers placed over a prosthetic globe implant [31]. The primary candidates for such procedures are individuals for which the utmost cosmetic appearance is required. There is no benefit to the horse apart from cosmesis (and its secondary effect on treatment of the horse). The cosmetic appearance is superior to the implantation of an intrascleral prosthesis, and when the initial surgical intervention is healed, the risk of implant expulsion is extremely low. In contrast, the intrascleral prosthesis has risk of corneal ulceration, infection, and dehiscence via corneal trauma, and the potentially poor cosmetic appearance of an opaque and/or vascularized cornea.

The surgical procedure for hydroxyapatite-based conformers is performed similarly to the transconjunctival enucleation, but only the globe itself is removed. The extraocular muscles, conjunctival fornices, and other tissues within the orbit are carefully preserved. Cautious microsurgical techniques are necessary (general anesthesia is essential). Twenty-four hours prior to surgery, an immediately post-mortem globe is acquired, and the sclera is dissected free and submersed in 100% ethanol. Before anesthesia induction, a 40-mm hydroxyapatite sphere prosthesis is soaked in cefazolin for 1 hour, and the donor sclera is thoroughly lavaged in sterile saline. The sphere is inserted into the sclera using releasing incisions, which are closed with polyglactin 910 (Figure 5.43).

A stay suture through the eyelid skin and conjunctiva is useful to demarcate the levator muscle and the extent of the conjunctival fornix dorsally. A deep peritomy is performed to expose the sclera, and each extraocular muscle is identified and sutured with 5.0 polyglactin 910 and transected at the globe. The retractor bulbi muscles and optic nerve are severed, and the globe is removed. Full-thickness incisions, 2×4 mm in size, are made in the donor sclera 1 cm from the posterior pole. The sclera-clad prosthesis is inserted into the orbit with the exposed coral (at the site of the previous cornea) facing posteriorly. Each ocular muscle is inserted through the appropriate incision in apposition with the



Figure 5.44 Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. The conjunctiva is apposed over the orbital implant to create a single, large, conjunctiva-lined fornix.



Figure 5.45 Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. Antibiotic ointment is applied, and a generic plastic extrascleral conformer (prosthesis) is inserted between the eyelids and the conjunctival surface during the healing of the orbit to prevent contracture of the eyelids.

hydroxyapatite and sutured to the interior of the sclera. The oblique muscles are sutured to the sclera directly. Tenon's capsule and fascial layers are apposed across the anterior face of the implant, obscuring it. The peritomy edges are apposed to create a single large conjunctiva-lined fornix (Figure 5.44). Antibiotic ointment is applied, and a generic plastic extrascleral conformer (prosthesis) is inserted between the eyelids and the conjunctival surface (Figure 5.45). A compression bandage is placed and changed daily for 3 days. Routine post-operative antibiotics and anti-inflammatories are administered.

After the swelling has subsided, the tarsorrhaphy is removed, and the conjunctival fornix is lavaged and treated with topical antibiotics during extended hospitalization for 7 days. With appropriate healing, the patient may be discharged on topical antibiotics three times a day for 3 weeks and daily cleaning and repositioning of the conformer. At 4 weeks, the conformer is removed, and an impression is made to create a new device to correctly fill the fornix for the permanent conformer. This is usually done by an ocularist with experience of making equine prostheses. Typically, several black prostheses are used routinely, and one is painted by an ocularist to match the original globe (Figure 5.46A–C). The individually hand-painted conformers are used only for short periods because of cost ($3000–5000). At the final fitting, any further adjustments in the conformer can be made. Ocular mobility with this procedure may be moderate to excellent, depending on the positioning of the muscles, final prosthesis position, and the amount of tissue between the prosthesis and the conformer. The eyelid position and palpebral fissure size are determined at the time of surgery by the conformer, which should be placed continuously to ensure that no retraction occurs. If the conformer is cared for appropriately, the final outcome can be excellent (Figure 5.46C). Potential complications of expulsion of the implant or infection are less common with hydroxyapatite, because its porosity encourages vascular ingrowth and permanent tissue attachment. Potential candidates should be aware that the attempt to increase cosmesis also risks additional complications, and that ongoing care of the conformer is necessary [31].

Related surgical procedures

Trephination of sinuses

Standing sinus surgery is indicated in primary and secondary sinusitis, but may also be performed for diagnostic reasons. Sinus surgery can be divided into trephination surgeries and sinus flap surgeries (osteoplastic flaps). Trephination may be performed in the standing sedated or recumbent anesthetized horse, depending upon the indication and other procedures that must be performed. Standing sinus surgery results in reduced hemorrhage and therefore improved visualization, as well as avoiding the risks, costs, and facilities required for general anesthesia. General anesthesia is required for aggressive/invasive interventions and in fractious animals [134].

The maxillary sinus is most commonly involved, because it is the largest and the common exit for the air-filled spaces of the equine skull. Primary indications for trephination are exploration (sinuscopy), sample acquisition, flushing and drainage of sinusitis and solid masses, and repair of skull fractures. Trephination may be necessary to expose a fracture for repair, in which case it is considered an open contaminated site, because the sinuses communicate via the maxillary sinus to the nasal cavity. When sinusitis is diagnosed radiographically or clinically, samples are necessary for culture and cytology as well as to remove solid material, flush the sinus, and potentially establish drainage. Large volumes of hemorrhage should be flushed to prevent bacterial colonization [123]. Draining tracts, although rare, may develop through the orbit and skin. Inferior drainage should be established and the tract treated as a contaminated wound.

The major ocular significance of trephination of the maxillary sinus is the potential puncture and destruction of the nasolacrimal duct (NLD) or infraorbital nerve. The rostral maxillary



Figure 5.46 Hydroxyapatite orbital implant and cosmetic corneal-scleral prosthesis. The final corneal-scleral cosmetic prosthesis is made by an ocularist and can be made to appear like a normal eye (A), or can be black (B). With either cosmetic shell, the final appearance can be excellent (C).

sinus trephination site in mature horses should be performed 40% of the distance from the rostral end of the facial crest and the medial canthus of the eye, and 1 cm ventral to a line joining the infraorbital foramen and the medial canthus [135]. The caudal maxillary sinus trephination site is positioned 2 cm rostral and 2 cm ventral to the medial canthus of the eye. A frontal sinus trephination portal site is described at 0.5 cm caudal to a line drawn between the left end right medial canthi and halfway between the midline and the ipsilateral medial canthus. Trephination of the frontal sinus is of minor threat to the orbit unless a fracture line extends laterally. A bone flap centered on the midline between the orbits may be performed for greater access. This portal site is favored in young horses (5 years old or younger), whose cheek teeth occupy much of the maxillary sinuses and trephination risks damaging the reserve crowns of the cheek teeth [135].

Alternatively, if greater access is required, a skin and bone flap may be created under general anesthesia to flush the sinus and establish drainage [74, 84]. Standing sinus flap surgery has also been described, utilizing heavy sedation, analgesia, and instillation of local anesthetic at the surgical site and into the sinus lumen [134]. The flap is centered around the trephination sites and may be created with a bone saw and/or chisels to produce a three-sided rectangular bone flap (that can be replaced if periosteal and soft tissue attachments remain) or with a large trephine to create and remove a round disc of bone (which is discarded). Replacement of a bone flap has a better cosmetic result. In the absence of flap replacement, inclusion of periosteum in wound closure is considered helpful for sealing the sinus.

If the incision is made too dorsal, the nasolacrimal duct may be exposed or perforated; if damaged, it is likely to be difficult to repair. Attempts at repair may be made by cannulating the duct with a flexible retention stylette and realigning the sectioned area across the incision. Sutures should be placed parallel to the long axis of the duct. However, obstruction is likely, and if epiphora results, a canaliculorhinostomy may be required to establish internal drainage.

Dental surgery

Dental surgery has been traditionally performed under general anesthesia; however, more recently, standing equine dental surgery has gained popularity. An excellent review of standing dental surgical techniques has been recently published [136].

Dental disease seldom has direct impact on the equine orbit. The last premolar and first three molars arise in the maxillary sinus, and the last molar is adjacent to the sphenopalatine sinus. Dental disease may result in sinusitis that secondarily affects the orbit, and the caudal cheek teeth may establish tracts from infected tooth roots that abscessate. Spontaneous tracts and fistulas may be identified in the retrobulbar area. Extraction of molars may be challenging, and complications from that extraction may ultimately impact the orbit. Complicated surgical treatment of dental misalignment is attempted uncommonly but may place the orbit at risk of sequelae. Surgical correction of prognathism in older individuals has been performed by wiring the maxilla; the resulting tissue planes may induce cellulitis or sepsis that secondarily involves the orbit. Similarly, implantation of orthopedic plates and screws may result in secondary exophthalmos or lagophthalmos of the globe.

Future research

Advancement of imaging modalities will greatly improve our ability to identify, categorize, and diagnose equine orbital disease and, one hopes, concurrently result in retaining both the globe and vision. Advances in CT technology and use, for example, have made older imaging modalities such as routine radiology nearly obsolete for imaging orbital disease. New pathologic conditions of the equine orbit will likely be identified in the future as a result of advances in imaging, an increasing population of geriatric horses, and greater expectations of the horse-owning public. Improvements in medical, surgical, and radiotherapy for sinus and orbital neoplasia will ultimately improve the short and midterm outcome of such cases. Improved staging of orbital neoplasia may greatly enhance selecting cases for therapy and the number of visual and comfortable eyes that may be maintained. Further improvements in implant materials will generate new cosmetic procedures for individuals with painful or severely damaged globes.

Large, multicentered studies of orbital disease such as fractures, neoplasia, and infections are needed to better understand the causes, treatment, and outcome of orbital disease in the horse. Other than a few isolated examples, these studies are nonexistent in the literature.

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CHAPTER 6

Diseases of the adnexa and nasolacrimal system

Elizabeth A. Giuliano

Introduction

Equine ocular disease affecting the adnexa (i.e., appendages of the globe, including the superior, inferior, and third eyelid) and nasolacrimal (NL) system are commonly encountered in veterinary practice. When normal eyelid function is permanently damaged, the health of the globe is often compromised and vision may be lost. The importance of accurate, prompt diagnosis and treatment to restore/preserve normal anatomic function to both the eyelids and NL system should not be underestimated. This chapter reviews those diseases commonly affecting the equine adnexa and NL system, with the aim to provide diagnostic and therapeutic approaches to treatment.

Clinical anatomy and physiology

Eyelids

Equine eyelids conform to the same basic anatomy of other domestic animals. The three basic layers of the superior and inferior eyelids from external to internal are (1) the skin with its haired and associated sebaceous glands, (2) a musculofibrous layer consisting of muscle, connective tissue, and tarsal plate, and (3) the palpebral conjunctiva [1]. The eyelids are critical to ocular health in a number of ways. The blink reflex in response to tactile, chemical, or thermal stimuli of the skin, vibrissae, cilia, conjunctiva, or cornea serves to protect the eye. Reflex blinking (and tearing) also helps to remove any foreign particulate matter from the eye. The eyelids produce portions of the pre-ocular tear film (e.g., meibomian glands produce lipid and conjunctival goblet cells produce mucin) and facilitate tear distribution across, and clearance from, the corneal surface. Finally, the eyelids regulate the amount of light that enters the eye.

On the skin surface, the equine eye has three types of hair: vibrissae, cilia, and dermal hair (Figure 6.1). Typically, two to four vibrissae are present 2–3 cm dorsal to the medal canthus and eight to ten vibrissae emerge approximately 1 cm ventral to the inferior eyelid and run parallel to the interpalpebral fissure. The function of these relatively stiff hairs is to provide tactile stimuli via cranial nerve (CN) V; touching the vibrissae will usually prompt eyelid closure and therefore should be avoided during the ocular examination. Eyelid cilia originate just external to the opening of the meibomian glands on the palpebral margin and may be associated with other modified skin glands (e.g., glands similar to those of Zeis and Moll). Equine eyelid cilia are large and numerous on the superior eyelid, but few or absent on the inferior eyelid (Figure 6.1) [2]. Eyelid cilia primarily function to protect the cornea, shield the eye from light, and provide tactile sensory input. Fine, soft dermal hairs cover the eyelid surface in variable degrees of density. The area within 0.5 mm of the eyelid margin generally has few dermal hairs.

The tarsus or tarsal plate is a narrow dense layer of connective tissue located between the palpebral conjunctiva and the eyelid skin surface. Both superior and inferior eyelids possess a tarsal plate; however, it is more fully developed in the superior eyelid. The tarsi provide structure and rigidity to the eyelids [3]. Horses possess a well-defined orbitopalpebral sulcus, most evident in the superior eyelid (Figure 6.2) [1]. This sulcus forms a "fold" of skin that delineates the eyelid into an orbital portion and a tarsal portion; the orbital portion lies between the dorsal margin of the bony orbit and the globe, while the tarsal portion overlies the globe itself. Traumatic superior eyelid lacerations are often observed to "tear" along this sulcus and necessitate meticulous surgical repair [4].

The tarsal, or meibomian glands, are a row of well-developed sebaceous eyelid glands (Figure 6.3). Meibomian glands are arranged in a single row running parallel to the lid margins and are embedded within the tarsal plate. The glands open directly onto the eyelid margins in a row of evenly spaced orifices collectively known as the "gray line," an important surgical landmark. The meibomian glands secrete the lipid layer of the precorneal tear film. Other glandular structures in the equine eyelid include

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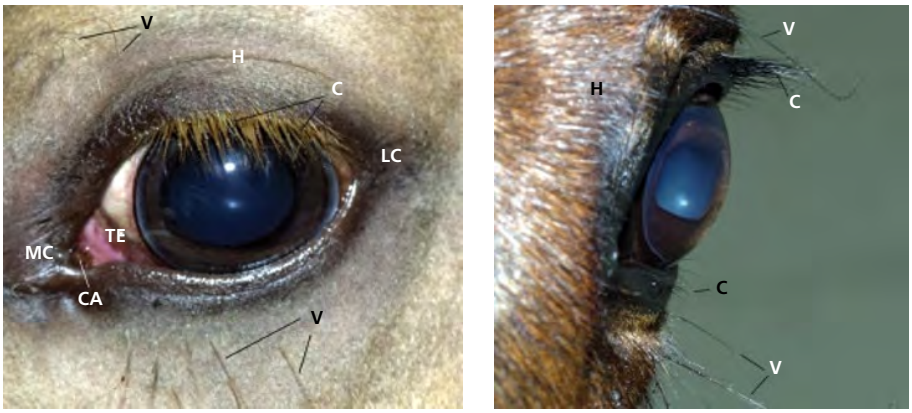


Figure 6.1 Equine eye as examined from the side (A) and front (B). Three types of hair are present on the equine eyelids, including vibrissae (V), cilia (C), and dermal hair (H). MC, Medial canthus; LC, lateral canthus; CA, lacrimal caruncle; TE, third eyelid.

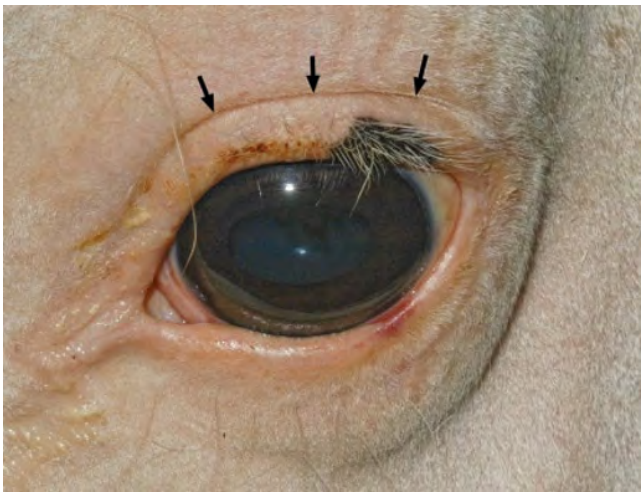


Figure 6.2 Prominent orbitopalpebral sulcus (skin fold) of the superior eyelid (**arrows**) delineating the orbital portion (above the skin fold) and tarsal portion (below the skin fold) of the eyelid.

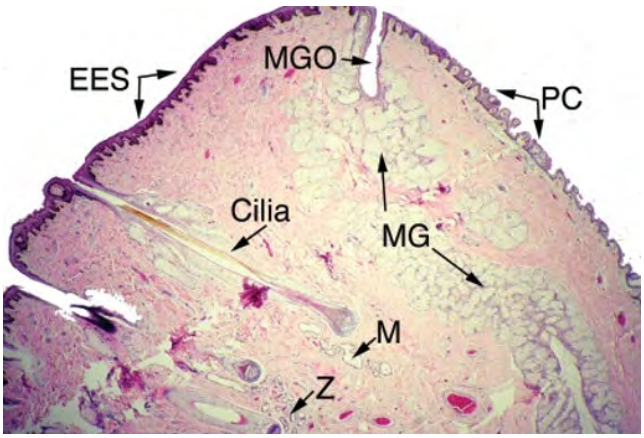


Figure 6.3 Histologic cross-section of the upper eyelid margin (40× magnification). The meibomian gland orifice (MGO) is the location of the mucocutaneous junction between the palpebral conjunctiva (PC) and external eyelid skin (EES). The meibomian gland (MG) is a large sebaceous gland. Sebaceous glands of Zeiss (Z) are adjacent to cilia, and apocrine glands of Moll (M) are deep to the cilia.

sebaceous glands associated with cilia (i.e., Zeis-like glands) and modified sweat glands (i.e., Moll-like or ciliary glands) (Figure 6.3) [3, 5, 6].

The eyelids are well vascularized via longitudinal vessels that run parallel to the eyelid margins and originate from the malar, superficial temporal, and ventral palpebral arteries [3, 5]. The excellent blood supply provides good healing of the eyelids after surgery or traumatic laceration. The eyelids have substantial lymphatic drainage, primarily to ipsilateral parotid and mandibular lymph nodes. This anatomic feature is of clinical significance in periocular neoplasia, especially squamous cell carcinoma (SCC), because the primary site of metastasis is to these draining lymph nodes [7].

Eyelid musculature, innervation, function, and clinical descriptions of periocular motor and sensory nerve blocks have been reviewed in Chapter 1. Briefly, motor innervation to the eyelids is from CN III (the oculomotor nerve) and CN VII (the facial nerve). Sensory innervation to all aspects of the equine eyelid is from CN V (the ophthalmic branch of the trigeminal nerve) (Figure 6.4).

The muscles of the eyelids consist of the levator anguli oculi medialis, levator palpebrae superioris, frontalis, orbicularis oculi, retractor anguli oculi, malaris, and Müller's muscle (Figure 6.5) [1]. The orbicularis oculi muscle, innervated by the palpebral branch of CN VII, surrounds the palpebral fissure to form a sphincter that closes the eyelids. The levator palpebrae superioris, innervated by CN III, originates in the posterior orbit, inserts into fibers of the orbicularis oculi muscle of the upper eyelid, and acts to elevate the upper eyelid. The malaris muscle, innervated by a branch of CN VII, attaches to the orbicularis oculi fibers of the lower eyelid and functions to lower the inferior eyelid. Müller's muscle is smooth muscle innervated by the sympathetic nervous system. It is oriented perpendicular to the eyelid margin and provides the "tone" to the tarsus. Loss of sympathetic tone to Müller's muscle occurs in Horner's syndrome and results in upper eyelid ptosis [8–10].

Other muscles that control equine eyelid movement include the retractor anguli muscle that retracts and anchors the lateral

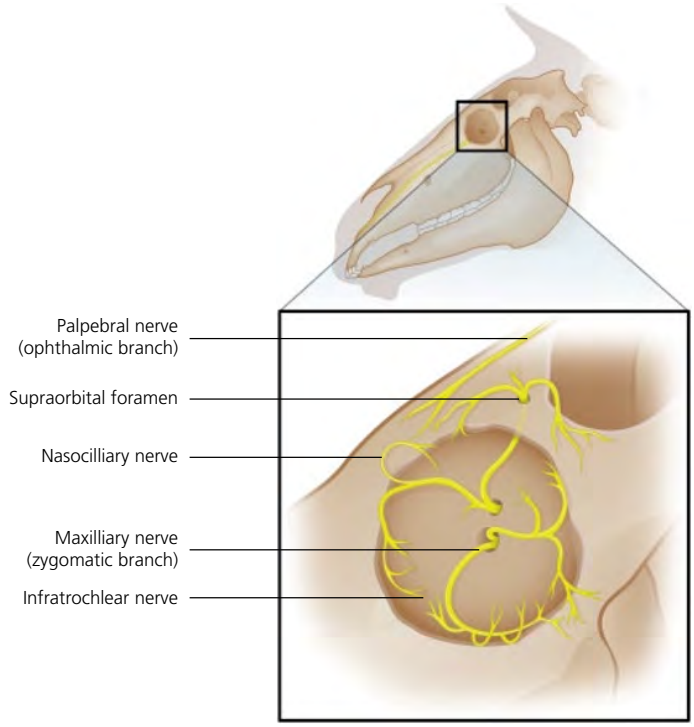


Figure 6.4 Schematic representation of equine eyelid innervation. Motor innervation to the eyelids is provided by CN III and CN VI. Sensory innervation to all equine periocular regions arises from CN V. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

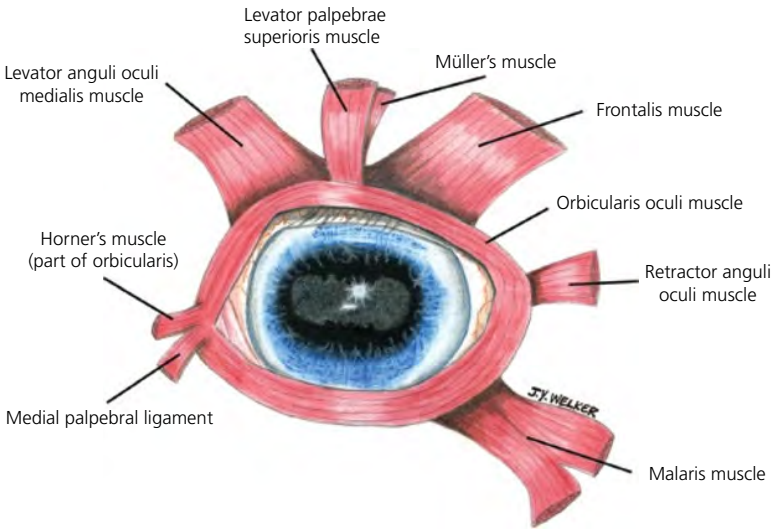


Figure 6.5 Muscles of the equine eyelid. (*Source*: Courtesy of Dr Jeanie Y. Welker.)

canthus and the levator anguli oculi medialis and frontalis muscles that provide slight elevation of the upper eyelid (Table 6.1).

In the adult healthy horse, the palpebral fissure is open approximately 36–51 mm (mean of 43.5 mm) in the horizontal plane (temporal to nasal) and approximately 25 mm at its widest vertical dimention [11]. The lateral canthus denotes the region where the superior and inferior eyelids adjoin temporally, while the medial canthus is where the superior and inferior eyelids meet nasally (see Figure 6.1). Structure of the equine eyelids is maintained not only by the palpebral muscles but also by palpebral ligaments. The medial canthal (palpebral) ligament is a

Table 6.1 Equine eyelid muscles, their innervation, and function.

Muscle	Innervation	Function
Orbicularis oculi	CN VII (facial)	Eyelid closure
Levator palpebrae superioris	CN III (oculomotor)	Elevate the superior eyelid
Malaris	CN VII (facial)	Depress the inferior eyelid
Müller's	Sympathetic	Elevate the superior eyelid
Retractor anguli oculi	CN VII (facial)	Lengthen palpebral fissure
Levator anguli oculi medialis	CN VII (facial)	Lengthen and elevate medial canthus
Frontalis	CN VII (facial)	Elevate the superior eyelid

firm, ligamentous band anchoring the medial canthus to the dense periorbital fascia and the periosteum of the medial orbital rim (Figure 6.5). The lacrimal sac lies just deep and ventral to this ligament. The anguli oculi vein runs just medial to the lacrimal sac. The lateral canthal (palpebral) ligament is formed by the junction of the temporal extremities of the superior and inferior eyelid tarsal plates and serves to anchor the lateral canthus to the lateral margin of the orbit. Normal eyelid position is necessary for adequate drainage of the tear film. Closure of the lids occurs from lateral (temporal) to medial (nasal). Normal eyelid closure distributes the pre-ocular tear film over the corneal surface and mechanically facilitates tear drainage out of the NL outflow tract. The lacrimal caruncle lies deep to the medial canthus and external to the third eyelid (see Figure 6.1). This structure varies somewhat in size among horses and may contain modified sebaceous and sweat glands. If enlarged, the lacrimal caruncle may protrude and prevent the eyelids from conforming as well to the medial aspect of the cornea compared to the lateral aspect [2]. Conjunctiva, a nonkeratinized squamous epithelium, lines the inner aspect of the superior and inferior eyelids (i.e., palpebral conjunctiva) (see Figure 6.3).

The third eyelid, or nictitating membrane (see Figure 6.1), originates in the ventromedial aspect of the orbit and moves passively in the dorsolateral direction with retropulsion of the globe or as the globe is retracted during blinking. The third eyelid is covered with conjunctiva that is richly endowed with goblet cells. A T-shaped cartilage lies within the body of the third eyelid and conforms to the corneal curvature of the globe. The cartilage provides structural support along the leading margin of the third eyelid via a horizontal "arm" and through the center of the third eyelid by its vertical component (Figure 6.6). The base of the third eyelid contains a lacrimal gland (tubuloacinar) that produces a portion of the aqueous component of the tear film (Figure 6.6) [12]. A large fat pad lies ventral to the gland of the third eyelid [5, 13].

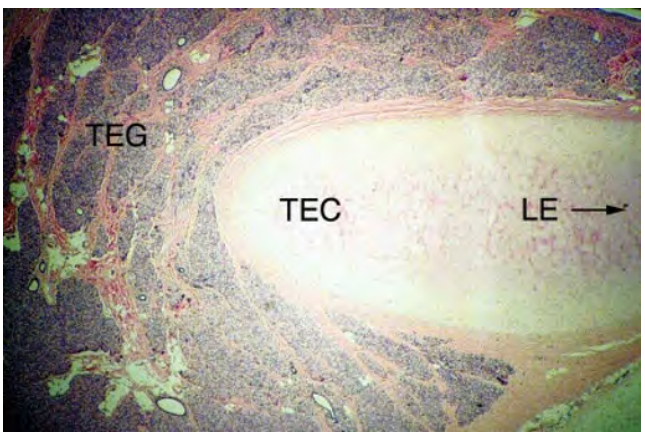


Figure 6.6 Cross-sectional anatomy of the base of the third eyelid (40× magnification). Third eyelid cartilage (TEC) runs through the center of the structure, with the third eyelid gland (TEG) surrounding the base of the third eyelid. The leading edge (LE) of the third eyelid is in the direction of the **arrow**.

Conjunctiva

Conjunctiva consists of nonkeratinized stratified columnar cells that are continuous with the corneal epithelium. The conjunctiva consists of three primary anatomic regions that are contiguous with each other and include the palpebral conjunctiva, the bulbar conjunctiva, and the fornix. The palpebral conjunctiva lines the superior and inferior eyelids (see Figure 6.3). The bulbar conjunctiva covers the anterior aspect of the globe to the limbus. The conjunctival fornix (superiorly) and cul-de-sac (inferiorly) are the junctions between those areas where the superior and inferior palpebral and bulbar conjunctiva meet, respectively [5, 14]. In the adult horse, the fornix (dorsally) is located approximately 3 cm from the limbus, while the cul-de-sac (ventrally) is approximately 2.5 cm from the limbus [5]. Conjunctiva also covers the anterior and posterior surfaces of the third eyelid. Conjunctiva is richly vascularized, variably pigmented (especially the bulbar conjunctiva), and has many goblet cells that contribute to the pre-ocular tear film [15]. In horses, it is common to visualize aggregates of lymphoid follicles located perilimbally (Figure 6.7). Likely, these lymphoid follicles represent part of the equine conjunctiva-associated lymphatic tissue (CALT) that has been shown to be integral to the ocular immune response in other species [16–19].

Nasolacrimal system

The NL system of the horse consists of both secretory and drainage portions. The lacrimal gland, a tubulo-acinar gland, is located dorsolateral to the globe and has three to five ductules that transport lacrimal fluid from the gland to the dorsal conjunctival fornix [3]. The gland of the third eyelid surrounds the base of the cartilage of the nictitans. The anatomic location of the distal NL orifice in the mule can be variable and is distinct from that described for horses and donkeys. A recent study found the most common location of the distal NL orifice in mules to be in the internal cutaneous tissue of the lateral wall of the external nares [20]. The percentage of aqueous tears produced by the gland of the third eyelid in horses is not known;

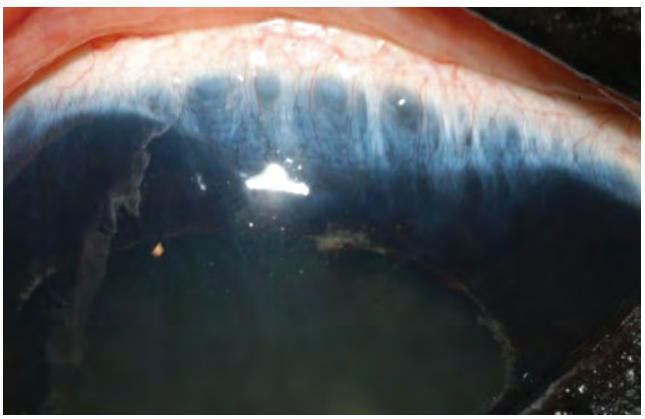


Figure 6.7 Prominent equine conjunctival lymphoid follicles visualized as rounded, relucent nodules at the superior limbus in this patient.

however, one study found that horses with surgically resected third eyelids did not have differences in basal (tested via Schirmer tear test (STT) II) or reflex (tested via STT I) tear production compared to normal horses [21]. In general, tear production in horses is robust, and copious reflex tearing can occur in response to ocular irritation or pain. Very few cases of keratoconjunctivitis sicca (KCS) in horses have been reported in the veterinary literature [22–25].

The NL drainage apparatus of the horse may become obstructed due to a foreign body, calcification, dentition abnormalities, inflammation/infection, or neoplastic processes [2, 26, 27]. The eyelid lacrimal puncta are oval openings, approximately 2 mm in diameter, and located 8–9 mm lateral to the medial canthus of the superior and inferior eyelids [28]. Through these puncta, lacrimal fluid enters the canaliculi, 3- to 4-mm-diameter tubes that join to form the main NL duct (Figure 6.8). The equine NL "sac" is much less developed than in human beings and anatomically represents only a slight dilation of the outflow tract where the two upper and lower canuliculi join [28]. The NL duct continues distally 7–8 cm within the osseous lacrimal canal of the lacrimal and maxillary bones (Figure 6.9) [28]. The duct narrows slightly immediately prior to its exit from the lacrimal canal of the maxilla bone (Figures 6.8 and 6.9).

Externally, the course of the nasolacrimal duct (NLD) through the maxillary bone follows a line from the medial canthus to the infratrochlear foramen [28]. The duct then courses in the submucosa along the nasal wall of the lateral aspect of the middle meatus, then dips ventrally as it courses in the ventral nasal fold. The duct curves laterally over the basal process of the incisive bone to open at a 3- to 4-mm, oval NL orifice on the ventral floor of the nasal vestibule (Figure 6.10) [28]. Two or more NL openings are very common in the nasal vestibule of horses. The total length of the NLD is approximately 24–30 cm long in the average adult horse [5].



Figure 6.8 Methyl methacrylate cast of the right NLD. A, Lacrimal canaliculus; B, lacrimal sac; C, narrowing of NLD at exit from lacrimal canal; D, flattening of duct by cartilage plate in sigmoid cartilage. (*Source*: Latimer et al., 1984 [28]. Reproduced with permission from American Veterinary Medical Association.)

Economic impact of ocular adnexal disease on the equine industry

Eyelid and NL diseases are among the most common ocular diseases in horses. According to a US Department of Agriculture (USDA) 1998 study, the overall prevalence rate for eye diseases was 7.4% in horses over 6 months of age [29]. Although this study did not differentiate among ocular problems, eyelid and

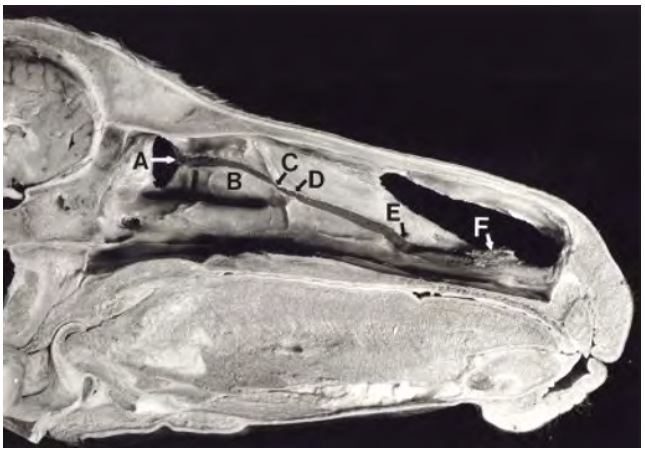


Figure 6.9 Methyl methacrylate cast of the left NLD with the medial bony orbit and medial wall of the lacrimal canal removed. A, Lacrimal sac; B, duct within lacrimal canal; C, narrowing of NLD at exit from lacrimal canal; D, exit of duct from lacrimal canal; E, duct pressed laterally by cartilaginous plate in alar fold; F, duct within basal fold. (*Source*: Latimer et al., 1984 [28]. Reproduced with permission from American Veterinary Medical Association.)



Figure 6.10 Nasal puncta of the NLD, a 3- to 4-mm, oval orifice on the ventral floor of the nasal vestubule.

NL diseases likely constitute the majority of these cases (e.g., eyelid disease is the second most common presenting complaint of horses presented to the Veterinary Health Center at the University of Missouri). It is reasonable to conclude that equine adnexal disease has a substantial economic impact on the equine industry in general.

Congenital ocular adnexal diseases

Entropion

Entropion, or turning in of the eyelid margins, is the most common ocular abnormality in foals (Figure 6.11) [30, 31]. Most commonly, the inferior temporal eyelid is affected, but both eyelids may be entropic. The most common cause of entropion in foals is secondary to loss of orbital fat (cachexia) or dehydration because of systemic illness or maladjustment. The loss of orbital contents results in globe retraction, thus allowing the eyelids to roll inward. The in-turned eyelids will result in corneal irritation and possibly ulceration from mechanical abrasion by the cilia and/or skin hair. The ocular discomfort from the "anatomic component" of entropion results in "spastic entropion" (e.g., the globe retracts secondary to pain, further exacerbating the degree of entropion already present).



Figure 6.11 Entropion secondary to enophthalmos in a foal with neonatal maladjustment syndrome. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)

Differential diagnosis

The most common cause in neonatal foals is systemic disease or maladjustment, as previously stated. However, some horses may be genetically predisposed, such as Thoroughbreds [32], Standardbreds [33], and Quarter horses [2]. The mode of inheritance or prevalence of this eyelid defect is not known. Other causes of entropion include microphthalmia, eyelid trauma, scarring (cicatricial entropion), and any disease causing prolonged blepharospasm [2, 34, 35]. Entropion in foals must be differentiated from other congenital eyelid abnormalities, such as ankyloblepharon, coloboma, dermoids, and cilia abnormalities (Table 6.2).

Treatment

The goal of treatment is to correct the abnormal inversion of the eyelids and to facilitate healing of concurrent conjunctivitis or keratitis. This therapeutic aim may be accomplished in a variety of ways. Most commonly, only a temporary tarsorrhaphy need be performed to correct the entropion while the foal is treated for any underlying systemic disease [36]. Once the foal recovers from systemic illness, normal orbital structures/content should re-establish eyelid support and position. In rare instances, the entropion persists and permanent surgical repair is required. In these foals, permanent repair of the eyelid should be delayed as long as possible, taking care to prevent corneal damage in the interim, because the rapid rate of head growth may result in facial changes (e.g., ectropion) and poor cosmetic results.

Medical therapy for entropion consists most commonly of corneal protection using frequent (every 4 hours) application of topical ophthalmic ointment on the affected eyes and appropriate therapy for any underlying systemic illness. Benign ophthalmic lubricating ointment (applied in conjunction with temporary tacking sutures—see section **Permanent surgical repair for entropion**) is often sufficient, providing no corneal ulceration is present. If ulcerative keratitis is present, appropriate management for corneal ulcer and secondary uveitis should be instituted. Systemic nonsteroidal medications and topical atropine should be used with caution in these sick foals. Ophthalmic preparations containing steroids should be avoided, as the recumbent nature of sick foals will predispose them to corneal ulceration even if fluorescein stain negative at initial presentation to the veterinarian. Various materials have been reported for use to correct entropion. Substances including saline, penicillin G, silicone, hyaluronic acid, and liquid paraffin

Table 6.2 Congenital eyelid abnormalities in horses [5, 30, 31, 34, 35, 37–39].

Abnormality	Appearance	Associated defects	Breeds
Ankyloblepharon	Adhesion of the eyelid margins (superior and/or inferior) after birth	Microphthalmos	
Eyelid coloboma	Full-thickness absence of the eyelid margin	Corneal or conjunctival defects or ocular colobomas	
Entropion	Turning in of the eyelid margin	Corneal ulceration, enophthalmos, neonatal maladjustment syndrome	Quarter horse Thoroughbred
Dermoid	Normal skin in an abnormal location	Conjunctival, corneal, or third eyelid dermoids	

have been injected into eyelid margins to cause temporary eversion [5]. Although these materials may be effective, the need for repeated injections, eyelid inflammation, and the potential for scarring make this technique undesirable.

Temporary surgical repair of the entropion is almost always needed to correct both the anatomic and spastic components of entropion (i.e., entropion → corneal irritation → blepharospasm and globe retraction → further exacerbation of entropion → etc.). Temporary surgical repair allows the cornea to heal without mechanical irritation and does not carry with it the risk of permanent eyelid disfigurement from overcorrection. Temporary entropion repair is typically achieved with the foal sedated, and placement of everting (tacking) sutures in a vertical mattress, simple interrupted pattern. Nonabsorbable, 4-0 to 5-0 monofilament suture is recommended. Silk has excellent knot security and can be used; however, it may result in mild to moderate eyelid tissue reaction. When placing temporary tacking sutures, the "law of bisection" is recommended, such that the first suture is passed in the center of the entropic eyelid, beginning 1–2 mm away from the eyelid margin perpendicular to the eyelid. The clinician should take care to avoid passing the suture through the eyelid margin, as sutures may be "torn out," resulting in a large eyelid defect. Next, an additional bite of skin ventral to the original bite is taken. The distance between the two suture bites will determine the amount of eyelid eversion achieved once the vertical mattress suture is securely tied. If, for example, a large eversion/imbrication is necessary to correct the entropic eyelid, a 1- to 2-cm distance between the dorsal and ventral bites of the vertical mattress suture may be required. Additional sutures are placed in an identical fashion adjacent (usually 5 mm between sutures) to the central suture (Figure 6.12). The number of sutures required will depend on the length of entropic eyelid. Knots should be secured with four throws, and the suture end nearest to the cornea should be cut short while the opposite end is left longer to facilitate suture removal. Applying a drop of cyanoacrylic adhesive to the knots will help ensure they will stay in place on the eyelid skin.

After temporary tacking has been performed, elicit a palpebral reflex to ensure that the foal can blink normally. If the foal is lagophthalmic (e.g., unable to close the eyelids completely) after temporary tacking, removal of one or more sutures may be necessary to prevent exposure keratitis. Sutures typically remain in place for 2–4 weeks in most foals.

Permanent surgical repair Permanent correction of entropion should only be performed after several attempts at temporary correction in foals. If the foal regains health and grows normally but entropion persists, permanent surgical repair is required. If definitive surgical repair is performed prematurely (i.e., with loss of orbital fat still present), the foal may be overcorrected and iatrogenic ectropion will result.

The most common surgical procedure for entropion involves an elliptical skin excision known as a Hotz–Celsus procedure (Figure 6.13). This surgical procedure permanently everts the eyelid margin by removing a segment of skin equal to the amount of skin that is entropic.

Some practical tips to help ensure success with a simple Hotz–Celsus include the following:

- The initial skin incision should be made close to the lid margin no more than 2–3 mm from the edge of the eyelid, at the haired–nonhaired junction, using a scalpel (e.g., #15 Bard-Parker blade).
- Use of a Jaeger lid plate (or a sterile tongue depressor coated with sterile lubricant ointment) will help support the eyelid and facilitate an accurate incision.



Figure 6.12 Temporary tacking sutures to roll out the eyelid margin in the foal with entropion in Figure 6.11. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)

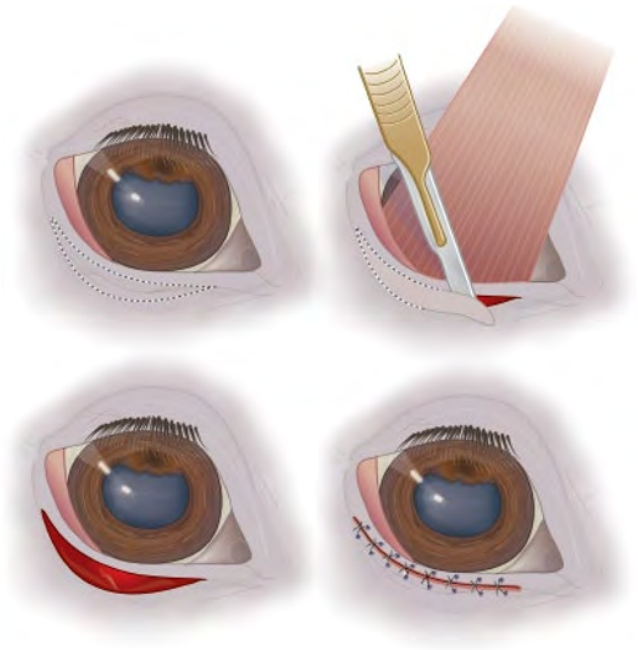


Figure 6.13 Holtz–Celsus entropion repair. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)



Figure 6.14 Horse undergoing Holtz–Celsus surgical repair for entropion.



Figure 6.15 Same patient as in Figure 6.14, 2 weeks post-operatively, at suture removal.



(A)



(B)

Figure 6.16 Inferior eyelid agenesis in a foal. (A) Right eye (OD). (B) Left eye (OS).

- Be certain to extend the incision parallel to the lid margin for the entire length of the affected area.
- The second incision should be made distal and relatively parallel to the first, tapering the ends to meet the first incision and incorporating enough eyelid tissue in the final ellipse to correct the entropion (Figure 6.13).
- Gently elevate one end of the incised tissue with fine-toothed forceps and excise the outlined skin and subcutaneous tissue with small scissors (e.g., Stevens tenotomy scissors) (Figure 6.14).
- Close the wound with 4-0 to 6-0 monofilament nonabsorbable suture in a simple interrupted pattern spaced at 2- to 3-mm intervals. To ensure an even closure without dog-ears, apply the "law of bisection."
- Cut the suture end nearer the lid margin close to the knot to avoid corneal irritation, but leave the distal end longer to aid removal.
- At the conclusion of surgery, be certain you can visualize the eyelid margin, without manipulating the lid, while the horse is still anesthetized.
- Post-operatively, an equine eye-cup may be used to prevent the horse rubbing at the eye if necessary. Appropriate medical management for any concurrent corneal ulceration should be instituted (see Chapter 7) and sutures should be removed in 10–14 days (Figure 6.15).

Other congenital diseases of the adnexa

Congenital adnexal diseases including ankyloblepharon, eyelid agenesis (Figure 6.16A, B), coloboma, dermoids (Figure 6.17), and cilia abnormalities have been reported [5, 30, 31, 34, 37–39]. Features of these conditions are listed in Table 6.2. Congenital ankyloblepharon, or fusion of the eyelids together after birth, is not normal in foals, since horses have fully developed adnexa at birth [5]. Separation of the eyelids should be attempted first manually, then using blunt dissection starting at the medial canthus [37]. Occasionally, foals will present blind with significant congenital ophthalmic disease that affects both the adnexa and the globe (Figure 6.18A, B) [40].

Congenital diseases of the nasolacrimal system

Epiphora

Epiphora, or overflow of tears, can occur from excessive lacrimation because of ocular irritation or because of an eyelid abnormality (e.g., entropion, distichia) or obstruction of the NLD [41]. Obstructions of the NLD occur as a result of, or develop secondary to, bacterial infections (i.e., dacryocystitis) and are associated with profound mucopurulent discharge (Figure 6.19). Additionally, suture exostosis has been reported to cause epiphora in horses [42, 43]. Congenital deficiency in tear production or KCS has not been reported in horses, but may occur. In fact, spontaneous development of KCS in horses, in general, is very uncommon, and the KCS that has been reported is typically secondary to trauma or other inflammatory disorders or endocrinopathies [22–25].

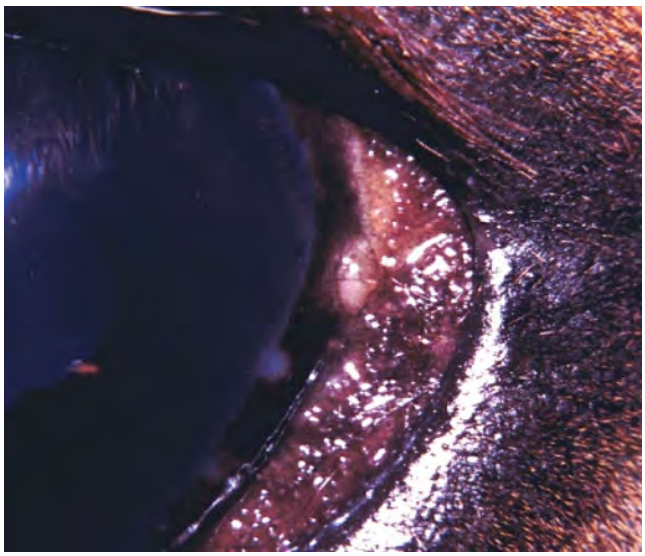


Figure 6.17 Conjunctival dermoid in a young horse. (*Source*: Photograph courtesy of Dr Riccardo Stoppini.)

Nasolacrimal duct atresia

The most common congenital defect of the NLD is NLD atresia [5, 30, 34, 37–39]. Bilateral supernumerary NL openings have also been reported to result in bilateral epiphora in a Morgan filly [44]. The most common defect is an imperforate nasal punctum, although eyelid punctal atresia or incomplete formation of the duct can occur anywhere along its course (see Figures 6.8 and 6.9). Mild to moderate, unilateral or bilateral epiphora is initially observed, but by 4–6 months of age the predominate clinical sign is severe mucopurulent ocular discharge (Figure 6.19) due to the development of secondary bacterial dacryocystitis. Diagnosis is made by direct observation of the nasal vestibule (i.e., lack of punctal openings) and inability to irrigate the NL system from the eyelid puncta. Swelling of the nasal epithelium distally, near the area of normal punctal opening, may also suggest atresia [5, 45, 46]. Rarely, eyelid punctal atresia may occur, resulting in failure of NL irrigation (retrograde) and conjunctival swelling [34].

Differential diagnosis

It is important to differentiate acquired obstructive diseases of the NLD from true atresia. Acquired obstructions generally have open, visible punctal openings (see Figure 6.10), but an inability to irrigate the NL system. Because nearly all cases of NL punctal atresia (either eyelid or nasal) have secondary dacryocystitis, bacterial culture and sensitivity should be submitted to appropriately manage concurrent infection. Contrast radiography (e.g., dacryocystorhinography (DCR)) can be very helpful in determining the exact location of the obstruction



(A)



(B)

Figure 6.18 Four-day-old foal euthanized due to blindness. Ophthalmic examination and histopathology revealed congenital bilateral microphthalmia and anterior segment dysgenesis (Peter's anomaly) with persistent hyperplasic primary vitreous. (A) Right eye. (B) Left eye.



Figure 6.19 **A** 2.5-year-old Quarter horse with a 20-month history of copious mucopurlent discharge from the left eye. Diagnostic testing confirmed imperforate left NLD punctum.



Figure 6.20 Contrast DCR of the horse in Figure 6.19 which revealed irregularities in NLD lumen diameter along the length of the lacrimal duct, with the greatest dilation at the distal end. These findings were consistent with permanent occlusion, chronic inflammation, and subsequent dilation of the NLD.

(see Chapter 1) (Figure 6.20). A diagnostic DCR may help determine the type of surgery that may be needed (i.e., incision of duct and stent placement v dacryocystorhinotomy/sinostomy) and the long-term prognosis [47]. Ultrasound, endoscopy, CT, MRI, and complementary radiographic projections (e.g., Wiener Schule) may also be helpful in the diagnosis and surgical planning of NL obstructive disease in horses [13, 48–50].

Treatment

Treatment consists of relieving the obstruction by creating a new opening, whether it be proximally or distally, treating the secondary bacterial infection, and preventing reobstruction [27, 51]. Topical and/or systemic antibiotics may result in a temporary improvement in clinical signs. However, unless the obstruction is relieved, the infection and clinical signs will quickly return; thus definitive surgical intervention is most frequently required for long-term successful resolution of epiphora or mucopurulent discharge. After surgery, topical ophthalmic drops are used to help address concurrent secondary dacryorhinocystitis. Drops are preferred over ointment as they will travel the length of the NLD much more effectively.

For optimal results, surgical opening of the obstructed or atretic puncta is always required, unless the NLD is agenic. Preoperative determination of the location(s) of the obstruction is critical for success. Usually, the obstruction is just at the opening to the nasal puncta, and creating a new opening at the site is curative. Pre-operatively determining the location of the obstruction(s) can be difficult, and careful physical examination (i.e., search carefully for submucosal swelling), DCR (Figure 6.20), and possibly advanced radiography (e.g., CT) can accurately delineate the specific obstructive location. With the horse heavily sedated or anesthetized, an attempt can be made manually to locate and open a presumed distal atretic puncta. A 5-French male silastic or plastic urinary catheter (with or without wire stent) is threaded normograde (from proximal to distal) through the dorsal cannaliculi into the NLD. The catheter is advanced until resistance is encountered. The catheter should not be forced ventrally if resistance is encountered, because severe hemorrhage may develop [52]. If it is only the nasal puncta that is occluded, the tip of the catheter will be palpable under the nasal mucosa. Occasionally, the duct terminates proximal to the normal puncta site, and careful palpation along



Figure 6.21 Horse in Figure 6.19, under general anesthesia. A 5-French closed-ended urinary catheter was threaded rostrally from the inferior lacrimal punctum to the blind end of the lacrimal duct. The cannula was digitally palpated through the wall of the nasal meatus and large curved scissors were used to create a distal NLD opening. The catheter was advanced through the NLD to exit through the newly created nasal punctum. Copious hemorrhage is to be expected with this surgery.

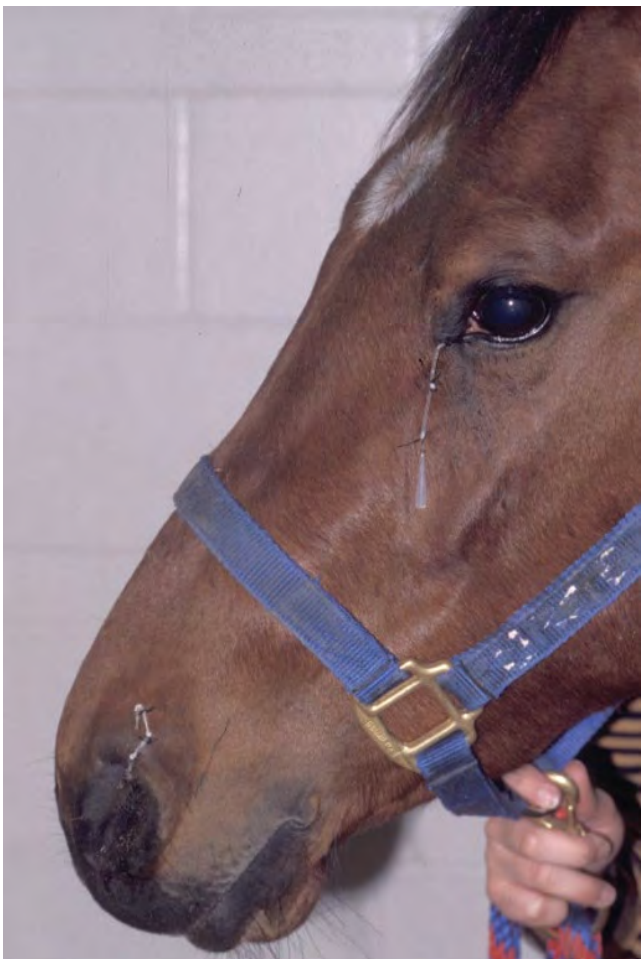


Figure 6.22 Horse in Figure 6.19, 5 days after undergoing surgery to correct distal NLD atresia. A 5-French closed-ended urinary catheter male urinary catheter is sutured to the skin at both the dorsal and ventral aspects of the NLD.

the course of the NLD is needed to locate the catheter tip. An incision is made over the catheter through the nasal mucosa and the catheter is pulled through the nares (Figure 6.21). Profound hemorrhage from the incision through the nasal mucosa is common; therefore only a single bold cut should be made, or the use of electrocautery on "cut mode" can be used to make the incision/opening. Diode laser photoablation has been reported to successfully create an NL orifice with less bleeding in the standing horse [51]. To recreate a punctal opening, the silastic tubing is sutured in place for 4–6 weeks (Figure 6.22).



Figure 6.23 Horse in Figure 6.19, 6 weeks after undergoing surgery to correct distal NLD atresia. Positive Jones test confirmed patency of the NL outflow tract.

After surgery, topical and systemic antibiotics should be given according to culture and antimicrobial susceptibility results; however, frequently the choice is topical triple antibiotic solution (every 8 hours). Oral antibiotic and anti-inflammatory therapy in horses should be used judiciously and for as minimal duration as possible (see section **General therapeutic considerations when treating horses for acquired adnexal or nasolacrimal disease**). Once the NL tube is removed after 4–6 weeks, a positive Jones test should be observed (i.e., fluorescein stain applied to the ocular surface on the affected side should be visualized at the nares, confirming patency of the NL outflow tract) (Figure 6.23).

General therapeutic considerations when treating horses for acquired adnexal or nasolacrimal disease

Overview

Whenever appropriate, specific medical or surgical therapies unique to particular equine adnexal or NL disease will be addressed in the discussion of those pathologic processes. Medical therapy for equine adnexal and NL diseases, regardless of whether or not surgery is part of the treatment regime, is frequently similar for a variety of infectious, inflammatory, and neoplastic diseases. For this reason, a brief review of medical therapy for these two ophthalmic anatomic regions in the horse merits discussion by way of a broad overview, to avoid redundancy throughout the remainder of this chapter.

It is worth noting that the majority of ocular pharmacokinetic ophthalmic drug studies have been performed in nonequine species, rendering much of the current clinical medical practice based on extrapolation from other species. This approach is problematic in that horses may be more prone to complications when systemic antimicrobial and anti-inflammatory agents are used than what is commonly observed using similar therapeutic strategies in other species. Additionally, there are no doubt significant differences in the pharmacokinetics of topical drugs, resulting from such factors as relative ocular size, tear production and flow dynamics, blink rate, and presence and motility of the third eyelid [5, 53].

The overall medical goal when treating horses with congenital or acquired adnexal or NL disease is to achieve therapeutically effective levels of an appropriate drug or combination of drugs at the affected site. Specifically, the clinician's goals are to: (1) decrease/control inflammation of the affected tissue, (2) prevent secondary infection, and (3) treat specific bacterial, fungal, or parasitic disease diagnosed by cytology, biopsy, and/or culture and sensitivity testing, which may be the primary cause of disease or secondary to some other primary pathologic process (e.g., neoplasia with secondary bacterial infection). As previously discussed, the adnexa of horses are richly vascularized, affording excellent blood supply to an infected (or potentially infected) area and thus greatly facilitating wound healing. However, the adnexa are also capable of a pronounced inflammatory response secondary to infectious, inflammatory, neoplastic, or traumatic processes (Figure 6.24). Considering the essential role of the adnexa and NL system in preserving corneal clarity and ocular comfort, therapeutic agents are frequently administered to address the aforementioned three primary treatment goals. Often, regardless of the primary etiologic process, adnexal and NL equine diseases are treated with a combination of systemic and topical medications. Detailed pharmacologic review of a wide variety of therapeutic agents currently used in horses is beyond the scope of this chapter and the reader is encouraged to seek additional information as needed [54, 55].



Figure 6.24 Horse with severe conjunctival chemosis and periocular swelling OD secondary to being struck by lightning.

Antimicrobial therapy

Systemic antimicrobial agents are frequently used in horses with eyelid or NL disease, but in many cases, their use is empirical and may not be necessary. Furthermore, the route and type of antimicrobial administered is frequently based on nonmedical directives such as cost, availability, or ease of administration. The gastrointestinal tract of horses is highly susceptible to the adverse effects of antimicrobial drugs due to disruption of normal intestinal microbial populations and proliferation of enteropathogens. Diarrhea, especially when accompanied by signs of endotoxemia, is the usual clinical manifestation of this potentially life-threatening complication of systemic antimicrobial use in horses. Consequently, judicious use of any systemic antimicrobial is recommended and careful consideration must be made as to whether or not a systemic antimicrobial is truly indicated in each individual case. This decision process is often in stark contrast to the more "general therapeutic approach" typical in small animal surgical ophthalmic patients where pre- and post-operative antimicrobial medications are routinely used. When deemed necessary due to obvious infection, antimicrobial selection is most appropriately made based on culture and sensitivity results of the affected area. Examples of systemic antibiotic usage, dose, and duration by the University of Missouri Veterinary Health Center are shown in Table 6.3.

Topical antimicrobial therapy for adnexal disease is dispensed commonly in ointment form to help "buffer" the cornea from any adnexal contour irregularities while the eyelid(s) is/are healing, and may be useful to prevent secondary corneal infection or abrasion. Ointments should not be used in cases where the cornea has already, or is at risk of, rupture(d). If NL infection

Table 6.3 Common systemic antibiotic agents currently used in horses with eyelid or NL disease when deemed necessary at the University of Missouri Veterinary Health Center.

Antibiotic	Dose and route	Frequency and duration
Ceftiofur	2.2 mg/kg IM	Twice daily for 5–7 days
Trimethoprim/ sulfamethoxazole	15–20 mg/kg orally	Twice daily for 5–7 days
Penicillin V potassium	22,000 IU/kg IV	Four times daily for 5–7 days, used together with gentamicin
Gentamicin	6.6 mg/kg IV	Once daily for 5–7 days, used together with penicillin V potassium

Table 6.4 Common systemic NSAIDs currently used in horses with eyelid or NL disease when deemed necessary at the University of Missouri Veterinary Health Center.

Anti-inflammatory	Dose and route	Frequency and duration
Phenylbutazone	4.4 mg/kg (high dose) IV or PO 2.2 mg/kg (low dose) IV or PO	High dose twice daily for 24–48 hours, then decrease to low dose twice daily for 5 days
Flunixin meglumine	1.1 mg/kg (high dose) IV or PO 0.5 mg/kg (low dose) IV or PO	High dose twice daily for 24–48 hours, then decrease to low dose twice daily for 5 days
Firocoxib	0.1 mg/kg orally	Once daily for 5–7 days
Meloxicam*	0.6 mg/kg orally	Once daily for 2 weeks

*Meloxicam is not used at MU-College of Veterinary Medicine because it is not readily available.

is present, then ophthalmic drops are preferred, as solutions or suspensions will more easily course down the NL outflow pathway than ointments to reach the affected target tissue. Perhaps the most common broad-spectrum topical antibiotic ointment routinely dispensed for eyelid trauma (including after surgical intervention) in the USA is triple antibiotic ointment (e.g., neomycin, bacitracin, polymyxin) or poly-bac (polymyxin and bacitracin) at a frequency of three to four times daily. Some clinicians may elect to use broad-spectrum ophthalmic antibiotic ointment preparations containing topical steroids as well; however, in areas where fungal keratitis is prevalent, caution is recommended due to the risk of keratomycosis [56]. Other relatively routine topical ophthalmic ointments dispensed in the face of adnexal disease include topical erythromycin, tetracycline, chloramphenicol, and nonophthalmic preparations of silver sulfadiazine ointment. Marked differences in normal ocular equine surface flora exist among individual horses and according to geographic location and seasonal variation [2, 56–59]. Due to this inherent variability of possible or primary infectious microbes to affect the equine adnexa or NL system, empirical treatment with standard antibiotics may be unsuccessful, especially if the horse has already been treated with topical or systemic antimicrobials prior to referral to a specialist. Whenever possible, further diagnostic testing is advisable. Even then, however, *in-vitro* sensitivity data may not necessarily reflect *in-vivo* clinical response, particularly if only topical medications are used to treat adnexal disease. Systemic routes of administration are more effective at reaching therapeutic drug levels in the adnexa.

Anti-inflammatory therapy

Veterinarians have long been familiar with the important role anti-inflammatory therapy plays in the treatment of periocular and ocular inflammation. Numerous systemic and topical corticosteroid and nonsteroidal anti-inflammatory drugs (NSAIDs) are commercially available. Again, the challenge clinicians are continually faced with when electing to treat a horse with periocular inflammation is to balance the potential therapeutic benefits of anti-inflammatory therapy against the occasional life-threatening risks of these drugs, especially when administered systemically. Systemic NSAID usage in horses is associated with the risk of both gastrointestinal disturbance and kidney damage [60–62]. For these reasons, the use of systemic NSAIDs should be restricted to the requirements of necessity and not provided beyond the recommended treatment period without further veterinary examination or consultation. If complications occur, horses typically manifest reduced appetite, lethargy, colic, poor performance, diarrhea, weakness, abnormal water consumption, and/or discolored urine. While uncommon, due to the severity of potential complications, owners should be advised to seek veterinary attention promptly if adverse side-effects are observed. Furthermore, risks of systemic NSAID toxicosis are increased if the horse fails to drink a normal quantity of water [62], so clients should be urged to ensure that their horse's water consumption be carefully scrutinized to ensure adequate intake.

Common systemic NSAIDs currently used in horses with adnexal or NL disease when deemed necessary to control inflammation and help alleviate periocular discomfort are listed in Table 6.4. Topical ophthalmic ointments, solutions, and suspensions of steroid and NSAIDs (e.g., dexamethasone, prednisolone acetate, flurbiprofen, diclofenac, suprofen) are also readily available or can be obtained through a licensed compounding pharmacy [63]. The same general principles discussed previously (see section **General therapeutic considerations when treating horses for acquired adnexal or nasolacrimal disease**) regarding topical therapy for adnexal or NL disease apply, and in most cases, if appropriate drug levels are to be reached in these two ophthalmic anatomic areas, systemic administration of anti-inflammatory therapy is more appropriate.

Equine ocular lavage systems

Horses may resent topical ophthalmic drug administration and can become dangerous to themselves and their owners or handlers when being medicated. Although more commonly



Figure 6.25 Horse with an ISPL in place. (*Source*: Schoster, 1992 [64].)

used in the treatment of ophthalmic diseases affecting the globe, equine ocular lavage systems may be useful in the treatment of adnexal or NL disease. Lavage tubes are typically categorized into two groups—indwelling NL and subpalpebral lavage (SPL) systems—and the latter may be further subcategorized as single or double entry systems [64]. Since 2000, an alternative single-entry SPL system for horses that is inserted in the medial aspect of the inferior eyelid has been described (the inferomedial subpalpebral lavage system (ISPL)) [65] and is now routinely used by many veterinary ophthalmologists (Figure 6.25).

Data from 86 horses demonstrated that the ISPL could be easily and safely placed in the lower medial eyelid, is well tolerated for periods of greater than a month, and can be used to successfully treat a wide variety of medical and surgical conditions, with a marked reduction in frequency and severity of complications compared with the more traditional superior eyelid SPL systems [65]. Regardless of the type of SPL system the clinician may prefer to use, instructions on the care and use of an indwelling lavage system are helpful to provide to owners/trainers. An example of such discharge instructions is provided in Box 6.1. See Chapter 3 for more information on the placement of SPL catheter systems.

Acquired adnexal diseases

Eyelid lacerations

Clinical appearance and diagnosis

The environment in which many horses are stabled, together with the prominent lateral positioning of their eyes, renders this species particularly susceptible to periocular trauma. Environmental and natural anatomic susceptibilities are compounded by the horse's acute "flight response," which causes most to react to stimuli by exaggerated and sometimes uncontrolled movements of their heads. Eyelid lacerations, as a result, are commonly encountered in horses. Generally, lacerations occur acutely and are easily noted by the horse's caretaker. Occasionally, if the horse is not monitored closely, presentation to a veterinarian may occur several days after the injury occurred, and secondary infection/inflammation will result in severe mucopurulent ocular discharge. In most cases, the severity of the appearance of the lesion does not correlate well with overall prognosis. Due to the excellent blood supply to the eyelids [14], most lacerations can be repaired to achieve a relatively well-functioning and cosmetic eyelid, even in the presence of significant secondary blepharitis. Therefore every attempt should be made to surgically repair all eyelid lacerations, taking care to avoid removing any hanging eyelid pedicles (Figures 6.26 and 6.27A, B). Despite the severity of the eyelid laceration (whether major or minor), a thorough ocular examination should be performed to identify and appropriately treat any associated ocular lesions (e.g., corneal ulcer or uveitis) [66].

Differential diagnosis

Severe ulcerative eyelid blepharitis or certain neoplasms (e.g., SCC) may appear as an eyelid laceration or trauma (Figure 6.28). Careful history will demonstrate that most of the former are chronic and progressive, unlike lacerations that occur acutely. If in doubt of the pathogenesis, biopsy and/or culture with sensitivity testing are warranted.

Pathogenesis

Lacerations likely occur in three ways: (1) blunt trauma from a crushing injury against the orbital rim, which may cause an irregular laceration and substantial eyelid swelling; (2) direct contact with sharp objects, such as a nail or metal edge, which can result in focal, relatively straight lacerations; and (3) ripping of the eyelid along its orbitopalpebral sulcus (see Figure 6.2), usually the result of when the eyelid margin is caught on a hook or sharp object and the horse suddenly moves away in reaction to the pain. Types 1 and 2 are frequently associated with underlying ocular damage, emphasizing the importance of a complete ocular examination. Wounds resulting from the third type of laceration (i.e., "ripping" lacerations) affect the superior eyelid more commonly than the inferior eyelid and extend parallel to the eyelid margin (see Figure 6.26). Often, the clinician can find evidence of a focal "nick," or skin wound, at the nasal or temporal canthus, likely representing

Box 6.1 Example of instructions that can be provided to equine owners on the use and maintenance of an SPL tube. (These instructions were specifically written for the ISPL [65]. used at the University of Missouri Veterinary Health Center.)

Use and Maintenance of the Equine SPL tube

Your horse has had an SPL tube placed in his/her eye(s). This should make medication administration much easier and safer for you and your horse. The tubes can be safely left in for several weeks and can be removed by your veterinarian when no longer needed. The following is an outline of how to use and care for these tubes.

1 Administration of medications: approximately 0.1 cc of the desired medication should be drawn up into a small (1-mL) syringe by inverting the eyedrop bottle and entering the dropper with a small (25-G) needle. The solution will be drawn up more easily if you squeeze the bottle slightly at the same time as drawing back on the syringe plunger. While the horse is well restrained, insert the needle into the rubber injection port on the end of the tube near the mane. Inject the solution (approximately 0.1 cc) and then inject approximately 1.0 mL of air into the tube in the same manner. This will expel the medication gently onto the eye's surface. If you stand on the same side as the eye to be treated, you should see a small amount of liquid bubble up inside the lower eyelid. It is critical that the air is injected very slowly so as not to cause pain for your horse. Because long-term medication is frequently needed in these cases, we must ensure that your horse does not begin to object to this technique.

- Only solutions thin enough to pass through the tube may be administered with this system. Please do not put any ointments through the tube.
- Keep the syringes and dropper bottles as clean as possible.
- Refrigerate any eye medications as directed.
- When administering more than one medication at the same time of the day, leave at least 5 minutes (preferably longer) between eye medications and begin with the least viscous medication. In your case, the preferred order would be:
  - i. _____
  - ii. _____
  - iii. _____
  - iv. _____

2 Care of the tube: there are three common sites at which the tube may require some maintenance, particularly if it is left in place for extended periods (i.e., weeks).

- The first is at the rubber injection port near the mane. You should have been provided with some spare parts for this. The modified (dull) needle is inserted into the end of the silicone lavage tube and pushed into the tubing until it is up against the hub. The rubber injection port is then screwed onto the modified needle hub. The needle should be retained on the silicon tube with some tape. Occasionally, a small leak in the silicon tube will occur at the end of the metal needle. In this case, the tube can be shortened, using clean scissors, as little as possible to remove the leaking section and the same or a new modified needle and injection port refitted.
- The second point at which leaks are sometimes seen is at the point of entry into the skin of the lower eyelid. This may be associated with some lower eyelid inflammation if the solutions leak into the subcutaneous tissues. This usually requires tube replacement. Please call your local veterinarian if you are concerned about leaks at this position.
- Finally, the sutures attaching the duct tape "wings" to the head may break free. If this occurs, they may be resutured by your veterinarian. Alternatively, you can reaffix them using a small drop of super glue (do not get super glue in the animal's eye), or with more adhesive tape.

3 Complications: complications with the inferonasal tube system are fortunately uncommon. Things to watch for are increasing levels of ocular discomfort (squinting, tearing, etc.); swelling, particularly at the point where the tube enters the lower lid; or movement of the tube, especially if the footplate migrates up out of the lower eyelid and could rub on the cornea. If the latter complication is seen, gently pull downward on the tube to reseat the footplate deeper in the eyelid and call your veterinarian.



Figure 6.26 Eyelid laceration, beginning medially and extending laterally. This tissue tag or hanging eyelid fragment should not be excised, but instead because of the excellent eyelid blood supply, this fragment can be replaced and usually it remains viable. (*Source*: Photograph courtesy of Dr Mike Davidson.)

the area of initial injury before the eyelid was subsequently torn as a result of the horse's rapid head movement (see Figure 6.27A). The globe is often spared additional injury in type 3 lacerations.

Treatment

Prompt surgical repair is the recommended treatment of all eyelid lacerations to avoid infection, reduce scarring and secondary corneal damage, and thereby optimize long-term outcome. Failure to repair an eyelid laceration (Figure 6.29), or amputation of a torn eyelid pedicle instead of primary repair, can result in chronic keratitis. Surgical repair can often be performed with sedation and local akinesia/anesthesia (motor block, ring block, and topical anesthetic), but may require general anesthesia [36, 67]. Minimal debridement is required due to the richly vascular nature of the lids and, as the eyelid margin cannot be recreated surgically, every attempt must be made to preserve it [5]. Meticulous repair of an eyelid laceration is crucial to avoid keratitis resulting from scar tissue formation and lid deformity (Figure 6.29). Horses should be vaccinated or boostered for tetanus following eyelid laceration due to the frequency with which



(A)



(B)

Figure 6.27 Upper eyelid laceration secondary to trauma. (A) The horse caught the temporal aspect of his upper eyelid on a foreign object, resulting in over half of the superior eyelid being torn. (B) Two-layer eyelid closure immediately following repair. Note that the horse was still under the effects of systemic sedation and regional eyelid akinesia.



Figure 6.28 This horse was affected with severe ulcerative lower eyelid SCC, which can sometimes mask as blepharitis or an eyelid laceration.



Figure 6.29 Chronic upper eyelid laceration that was never surgically repaired. The dorsal half of the torn eyelid pedicle has contracted to a small pedunculated remnant. Chronic mucopurulent ocular discharge and white corneal scarring are evident as a result of this traumatic eyelid laceration and secondary trichiasis. The horse also had an incidental lower eyelid coloboma. (*Source*: Photograph courtesy of Dr Marie Kerl.)

the injury is associated with metal objects. Judicious use of antimicrobial and anti-inflammatory therapy may be indicated (see section **General therapeutic considerations when treating horses for acquired adnexal or nasolacrimal disease**).

The wound edges should first be gently cleaned with a dilute (1:50) Betadine solution and the deep, subconjunctival layer should be closed initially. Two-layer closure is required to ensure that the conjunctival aspect of the eyelid does not gape during healing and induce scar formation, which may be irritating to the underlying cornea (Figure 6.30). Absorbable suture, such as 5-0 to 6-0 polyglatin 910, may be used in a simple interrupted pattern for the deep-layer wound closure. No suture material should contact the cornea. A useful surgical landmark to help avoid placing any sutures too close to the conjunctival surface is the "gray line," or the opening of the meibomian glands, which may be used as a "reference point" denoting the approximate mid-thickness plane of the eyelids. The surgeon should take care that the eyelid margin be meticulously reapposed with the first (i.e., deep) layer of sutures. Following completion of the deep layer closure, the eyelid skin is first closed at the margin with a figure-of-eight suture pattern or a mattress pattern of nonabsorbable 4-0 to 6-0 suture (see Figure 6.27B) [5, 68, 69]. Additional simple interrupted skin sutures are placed as needed every 2–3 mm until eyelid repair is complete. Incorrect closure of the eyelid margin or failure to use a two-layer closure may lead to chronic corneal

irritation (Figures 6.29 and 6.30). Skin sutures may be removed in 10–14 days and a protective eyecup may be needed to prevent the horse from rubbing at the repaired laceration site.

Prognosis

Prognosis after eyelid laceration repair is generally very good, providing that the surgery was performed accurately. Prognosis will be adversely affected based on the presence and severity of any concurrent ocular disease. A thorough ocular examination with careful search for possible retained foreign body material is indicated for all eyelid laceration cases. In rare cases, when eyelid trauma is so severe that repair is not possible, the horse may need to be exenterated and allowed to heal by second intention (Figure 6.31A, B).



Figure 6.30 A single-layer closure eyelid laceration repair with secondary corneal ulceration. Note that the eyelid margin is not apposed and there is gapping evident at the conjunctival aspect of the wound bed.

Blepharedema

The equine eyelid possesses a minimal amount of adipose tissue [5, 14]. This may be a contributing factor in the horse's ability to demonstrate profound chemosis in response to injury or infection (Figure 6.32). A swollen, drooping eyelid is referred to as pseudoptosis [5]. Differential diagnoses for unilateral and bilateral blepharedema are shown in Table 6.5. Treatment is directed at the underlying cause and protecting the cornea if eyelid function is compromised.

Blepharitis

Inflammation of the eyelids, or blepharitis, is not a common primary cause of eyelid disease in horses. The numerous causes for equine blepharitis typically arise secondary to trauma, bacterial or fungal infection, or parasitic infestation.

Infectious blepharitis

The most common cause of blepharitis in the horse is bacterial infection after penetrating trauma [2]. Blepharitis has been reported after blunt trauma associated with an orbital bone sequestrum [70]. Primary infectious causes of equine blepharitis have been reported due to *Moraxella* spp [71] and *Listeria monocytogenes* [72]. Fungal surface infections or granulomas can also cause blepharitis [2, 5]. Fungal organisms reported to cause blepharitis include *Trichophyton* spp., *Microsporum* spp., *Histoplasma farciminosus* (i.e., epizootic lymphangitis), *Cryptococcus mirandi*, *Aspergillus* spp., and *Rhinosporidium seeberi* [2, 5, 73, 74]. Parasites may also cause variable degrees of eyelid inflammation and include habronemiasis, *Thelazia lacrymalis*, and demodecosis [2, 38, 75–82]. Thelazia and demodex infestations are usually asymptomatic; however, a rare blepharitis characterized by meibomian gland inflammation, hair loss, and papulorpustular dermatitis has been reported secondary to demodex infestation [2]. With the widespread use



(A) (B)

Figure 6.31 (A) A 6-month-old foal that suffered total eyelid removal after being caught in a barbed-wire fence. Note that the entire cornea was fluorescein stain positive and there was complete eyelid avulsion, precluding any possibility of repair. (B) Exenteration was performed, and by 3 months post-operatively, a healthy bed of granulation tissue had filled the orbital space and wound closure was nearing completion.



Figure 6.32 Profound blepharedema with significant superior left eyelid chemosis and conjunctivitis secondary to an automobile accident. Several periocular skin lacerations are also evident.

Table 6.5 Causes of blepharedema of the equine eyelid [2, 5]

Unilateral	Bilateral
Blunt trauma	Self-trauma
Self trauma	Systemic diseases*
Insect bite	Equine viral arteritis
Snake bite	Babesiosis
Foreign body reaction	Lymphosarcoma
Abscess formation	Influenza
Orbital fat prolapse	Allergic/hypersensitivy
	Ocular parasites

* This list is not all-inclusive: see Chapter 15 for additional information.

of ivermectin in the 1990s, the prevalence of habronemiasis decreased; however, the development of resistant strains remains a distinct possibility.

Clinical appearance and diagnosis

Blepharitis, in general, appears as swelling and inflammation of the eyelid. Because of its prominence, the upper eyelid is more commonly affected than the lower eyelid. Bacterial infections following trauma have swelling surrounding an open wound with or without necrotic draining tracts (Figure 6.33). Dermal fungal infections may appear as bacterial infections or have an alopecic, scaling of the eyelid skin [2]. Habronemiasis

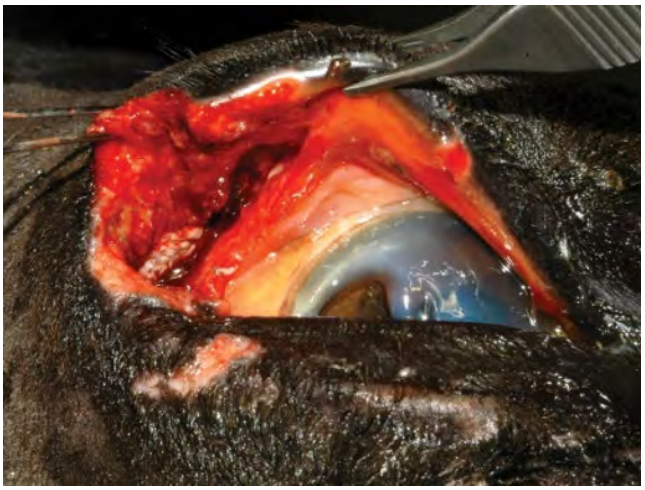


Figure 6.33 Eyelid trauma with secondary bacterial eyelid infection and caseous necrosis. A deep corneal ulcer is also present.



Figure 6.34 Equine habronemiasis often presents as raised, granulomatous, multifocal, white, nodular lesions, as seen in the medial canthal region of this horse's left inferior eyelid.

(*Habronema muscae*, *H. microstoma*, and *Draschia megastoma* are potential causative organisms) [5] appears as a raised, granulomatous, ulcerative lesion on the conjunctiva or mucocutaneous junction of the eyelid (Figure 6.34). This disease is also known as "summer sores," "swamp cancer," and granular dermatitis [75, 79, 82], because the condition appears during the hot and humid summer months when the main vectors, house and stable flies, are most severe.

Infection of the ocular tissue is by habronema larvae. Adult habronema organisms live in the equine stomach; larvae are passed in the feces, are ingested by fly larvae, become infective in the fly pupae, and are deposited near the eye (or other mucocutaneous junctions or wounds) [5, 82]. Dermal lesions may also develop on other areas on the body (Figure 6.35). The medial canthus and the caruncle area are the most common periocular areas affected, and the lesion



Figure 6.35 Habronemiasis infectious can occur at mucocutaneous junctions or at sites of injury. Here is habronemasis on a front leg. (*Source*: Photograph courtesy of Dr Mike Davidson.)

typically has discrete nodules or multilobulated masses (see Figure 6.34), with occasional mineral or "sulfur"-appearing nodules. Hypersensitivity to the organisms (especially dead organisms) results in pruritis, periocular alopecia, and occasionally secondary ocular disease such as corneal ulceration and uveitis.

Differential diagnosis and methods for definitive diagnosis

Blepharitis is often associated with conjunctivitis, and Table 6.6 lists the main causes of both diseases. In cases of infectious (bacterial or fungal) blepharitis, the definitive diagnosis is based on identifying the organism(s) on cytology and culture. Biopsy and histopathology are recommended if the lesion is chronic and nonresponsive to initial therapy. Habronemiasis is presumptively diagnosed based on the clinical appearance of the lesion (i.e., lesions typically occur during the fly season and have a raised, white to yellow, ulcerated appearance, sometimes with fistulous tracts and a yellow, casseous exudate with gritty foci of necrotic mineralized tissue) and response to therapy. Due to the numerous neutrophils, eosinophils, mast cells, and plasma cells in the cytology from habronemiasis lesions, one must differentiate it from mast cell tumors, phycomycetes, eosinophillic granulomas (nodular necrobiosis), and eosinophillic keratoconjunctivitis [2, 5, 75, 83–85]. Therefore if the organisms are not found on cytology, biopsy and histopathology are recommended for definitive diagnosis.

Treatment

Penetrating eyelid trauma with secondary infectious bacterial or fungal blepharitis usually heals rapidly with appropriate treatment because of the eyelid's excellent blood supply. The wound should be cultured (for bacterial and/or fungal culture and sensitivity) and a cytology sample collected; then it should be debrided and flushed with copious amounts of dilute (1:50) Betadine solution; finally, a careful search for and removal of any remaining foreign material should be performed. Judicious use of systemic and/or topical antimicrobial and anti-inflammatory therapy may be considered (see section **General therapeutic considerations when treating horses for acquired adnexal or nasolacrimal disease**). Warm compresses can be applied every 8–12 hours for the initial 5 days. Habronemiasis is treated by regular standard deworming recommendations (typically, ivermectin at a dose of 200 μg/kg PO, repeated in 30 days), debulking the affected lesion, controlling eyelid inflammation associated with larvae dying *in situ*, and educating owners about environmental strategies to control flies in an effort to decrease recurrence [86]. In one study, ivermectin alone caused marked improvement in habronemiasis lesions within 7 days in 87% of horses [87]. Topical therapies for habronemiasis lesions vary, and recommendations have included preparations of trichlorfon, nitrofurazone, and dimethylsulfoxide (DMSO) [79]; trichlorfon, nitrofurazone, dexamethasone, and DMSO [76]; and nitrofuratoin, ronnel solution, dexamethasone, and DMSO [75]—each applied every 12 hours to the lesion. Topical 0.03% echothiophate every 12 hours may be helpful as a larvacide [5], but it is not likely needed in addition to systemic ivermectin. Intralesional injections of triamcinolone or methylprednisolone may decrease inflammation in the affected areas [2, 5].

Surgical treatment For most blepharitis cases, wound management (as described previously) and judicious use of appropriate systemic antibiotics (based on culture and antimicrobial susceptibility testing) will help the lesion resolve. However, in cases of significant abscessation, the fluid and any caseous necrotic tissue should be removed, the wound flushed copiously with sterile saline, and comanagement of any ocular disease should be instituted (see Figure 6.33). If necessary, a drain may be placed for 3–7 days. In one study examining habronemiasis lesions, debulking or excising granulomatous lesions (to remove a source of chronic immune stimulation [5]), appropriate deworming, and administration of topical, intralesional, or systemic corticosteroids provided healing within a few weeks [86].

Table 6.6 Conjunctivitis and/or blepharitis in the horse.

Classification	Etiology	Predominant clinical signs
Secondary conjunctivitis (with/without blepharitis)	Corneal disease	Corneal ulcer, stromal abscess, blepharospasm, epiphora
	Uveitis	Epiphora, aqueous flare, miosis, conjunctival hyperemia
	Glaucoma	Elevated IOP, diffuse corneal edema
	Dacryocystitis	Purulent ocular discharge, negative Jones test
	Keratoconjunctivitis sicca [22–25, 99, 150]	Lackluster appearance to cornea, mucopurulent discharge
Primary conjunctivitis (with/without blepharitis)		
Immune-mediated	Follicular	Follicles on bulbar conjunctiva, epiphora
	Eosinophilic [23, 83, 84]	Thick, cheesy exudates, with/without corneal disease
	Allergic	Hyperemia, chemosis, serous discharge
	Nodular [309, 322]	"Conjunctival pseudotumor," nodular lymphocytic conjunctivitis
Bacterial	*Moraxella equi* [71, 323]	Mucocutaneous erosions, mucopurulent ocular discharge, blepharospasm
	Streptococcus equi [324]	Regional lymphadenitis (strangles), conjunctivitis, mucopurulent nasal discharge
	Listeria monocytogenes [72]	–
	Chlamydia and *Mycoplasma* [325]	Possible respiratory disease or polyarthritis
Fungal	Histoplasmosis [74]. and blastomycosis [5]	Conjunctivitis, lymph node involvement
	Aspergillus spp [5]	Granulomatous conjunctivitis
	Rhinosporidium seeberi [5]	Granulomatous conjunctivitis
Viral	Equine herpes type 2 [96, 326, 327]	Recurrent conjunctivitis, with/without corneal ulceration
	Equine herpes type 1 [328]	
	Equine herpes type 2 [103, 329]	
	Equine viral arteritis [330–332]	Conjunctivitis, blepharedema
	Adenovirus [333]	Keratouveitis, mucopurulent discharge
Parasitic	Onchocerchiasis [334]	Lateral limbal depigmentation, with/without uveitis
	Thelazia lacrymalis [81, 335]	Mild conjunctivitis, epiphora
	Ophthalmomyiasis externa [336]	
	Habronemiasis [75, 337]	Granuloma formation, mucopurulent exudate
	Trypanosoma evansi [338, 339]	Fever, anemia, conjunctivitis, edema of the legs and lower parts of the body, progressive weakness, loss of condition, loss of appetite
Trauma	Blunt trauma	Subconjunctival hemorrhage
	Foreign body	Severe blepharospasm, epiphora
Solar/actinic	UV radiation	Neoplastic precursor

Prognosis

With appropriate diagnosis and treatment, most of these lesions heal readily. Eyelid defects and other ocular damage as a result of the blepharitis depend on the extent and chronicity of the blepharitis.

Allergic, immune-mediated, and actinic blepharitis

Blepharitis can also be caused by local or systemic allergic diseases (see Chapter 15), immune-mediated diseases, and exposure to sunlight (with or without photosensitization) (Table 6.6). Local or systemic allergic diseases usually cause acute-onset bilateral belpharoedema, hyperemia, and pruritis. Chronically, allergic conditions can cause hyperpigmentation and scarring. Causes include chronic fly-bite irritation and environmental allergens such as molds, dust, sprays, and certain drugs. The eyelids can also be affected with immune-mediated diseases such as pemphigus foliaceus and bullous pemphigoid [2]. Typically, other mucocutaneous junctions on the body are also affected and these lesions are chronic, bilateral, and pruritic. Actinic blepharitis can occur in nonpigmented periocular tissues that have chronically been exposed to sunlight. The lesions appear hyperemic and ulcerated, typically at the eyelid margin (Figure 6.36). Actinic blepharitis may be a precursor lesion to SCC [7, 88]. Use of a high-ultraviolet (UV) radiation-blocking fly mask is encouraged for all horses that lack periocular pigmentation, to prevent actinic blepharitis and SCC.

Eyelash (ciliary) disorders

The three types of eyelash or ciliary disorders include trichiasis (normal eyelash hairs turned inward that rub on the conjunctiva/cornea), distichiasis (extra eyelashes, often seen exiting the meibomian gland openings, that may irritate the ocular surface), and ectopic cilia (an eyelash that exits through the conjunctiva, usually at the middle of the upper eyelid, and often results in blepharospasm, epiphora, and corneal ulceration). All three eyelash disorders are uncommon in horses, especially compared to other domestic species [89–91]. Trichiasis is the most common cilia abnormality and most frequently occurs after eyelid scarring following laceration or surgery [90] or secondary to entropion [35]. Distichia or ectopic cilia may be



Figure 6.36 Actinic blepharitis in the eyelids of an Appaloosa horse. Notice the hyperemic, ulcerated, and scarred eyelid and third eyelid margins. (*Source*: Photograph courtesy of Dr Mike Davidson.)

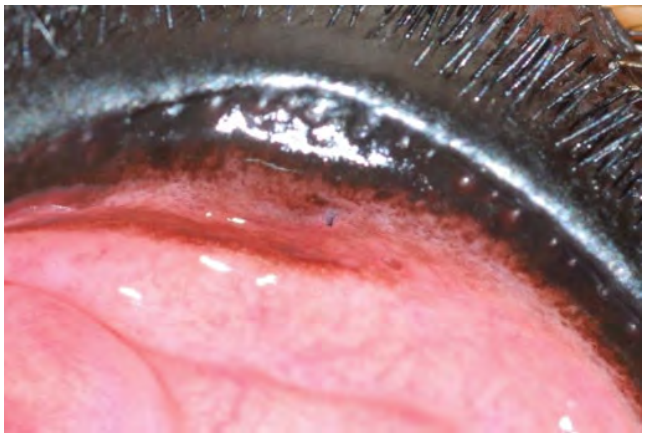


Figure 6.37 Ectopic cilia in the upper eyelid. Note the short dark cilia eroding through the palpebral conjunctiva.

congenital, but the clinical manifestations may not be evident for months to years [2, 41, 92, 93].

Clinical appearance and diagnosis

Any eyelash disorder has the potential to create chronic ocular irritation. As a result, presenting complaints include blepharospasm, epiphora, corneal ulceration, and/or corneal scarring. Careful evaluation using high magnification (usually via biomicroscopy) of the eyelid margin for any abnormal hairs touching the cornea during normal blink response is essential. Initially, examination without eyelid manipulation should be performed to evaluate for trichiasis. Eyelids should also be everted to search for distichia or ectopic cilia. Most commonly, distichia and ectopic cilia involve the upper eyelid in horses but may involve either eyelid (Figure 6.37). If secondary corneal scarring or ulceration result from an eyelash abnormality, the scar or ulcer will typically correspond anatomically with the offending eyelash problem (see Figure 6.29).

Differential diagnosis and methods for definitive diagnosis

The causes for chronic irritation to the surface of the eye should be considered in addition to cilia abnormalities. Differentials to be considered include burdock bristle keratitis (see Chapter 3) [94], other foreign bodies, infectious keratitis [95–98], keratoconjunctivitis sicca [22–25, 99], and other noninfectious keratopathies [83, 84, 98, 100].

Pathogenesis

Ectopic cilia and distichiasis are considered to be "extra" cilia that develop similarly to normal cilia but exit the eyelid at abnormal locations. For example, developing cilia may enter a meibomian gland and exit through its ductule, a path of least resistance, to then clinically manifest as distichiasis. Multiple distichia may exit a single meibominan gland orifice (districhiasis). Ectopic cilia exit directly through the palpebral conjunctiva instead of the eyelid margin (see Figure 6.37).

Treatment

The mainstay of therapy for any abnormal eyelash problem is removal of the abnormal or misdirected cilia (or eyelid hair) and correction of any eyelid scarring. Medical therapy alone (e.g., topical ophthalmic ointment), may help protect the cornea until surgery can be performed, but will not correct the underlying problem or alleviate the chronic irritation. The underlying cause for trichiasis (e.g., eyelid scarring, entropion, dermoid) should be surgically corrected. If eyelid scarring is the primary problem, the abnormal palpebral margin should be surgically excised and the margin reapposed with careful anatomic alignment using the principles discussed in eyelid laceration repair (Figures 6.38 and 6.39). Temporary tacking sutures or a permanent Hotz–Celsus procedure can be done to correct the entropion (see Figures 6.12, 6.13, 6.14, and 6.15) [5, 36, 90]. Distichia may be treated with cryotherapy (treatment of choice if numerous distichia are present or if they emerge from the eyelid margin in locations other than from the meibomian gland orifice) or electroepilation (for cases where only a few distichia are present and the cilia emerge from the meibomian gland orifices, thus allowing easy probe placement and less eyelid scarring secondary to electrocautery).

The goal with either modality is to destroy the base of the hair follicle such that the hair does not regrow. When cryotherapy is elected, the affected margin eyelid is held in a chalazion clamp which will enable the surgeon to both hold the eyelid in place and slow the blood supply to and from the affected site, ensuring a "slow thaw" secondary to the freezing cycle. Once the affected eyelid margin is secured in the chalazion clamp, a 4-mm cryoprobe is placed on the conjunctival surface of the eyelid centered over the base of the meibomian gland adjacent to the distichia that is to be removed. As the conjunctiva freezes, it will

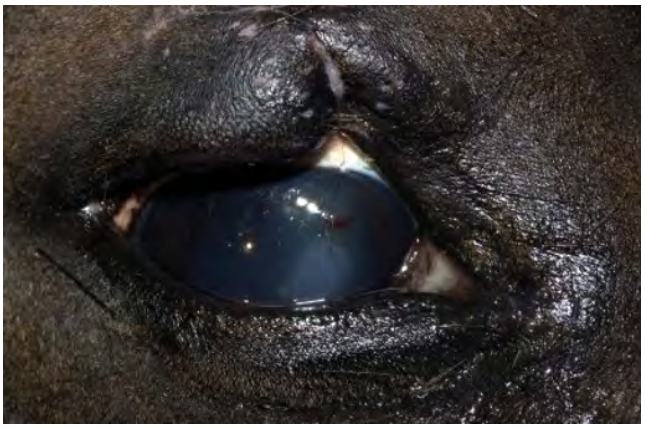


Figure 6.38 Eyelid scarring 2 months following a skin-only closure of a central upper eyelid laceration. Trichiasis is now present from the upper cilia resulting in a superficial cornea ulcer.

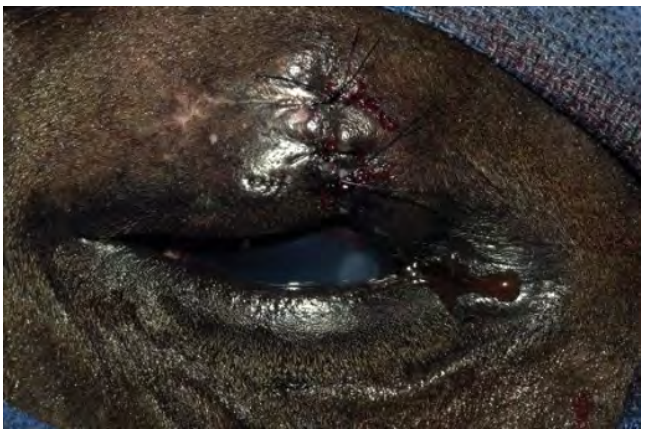


Figure 6.39 Repair of the cicatricial eyelid lesion in Figure 6.38. A V-plasty procedure was performed to remove the scarred portion of the eyelid, followed by a standard two-layer closure.

appear white. The probe should be held in a fixed location on the conjunctival surface until the tissue freezing is visualized to extend just beyond the distichia. If nitrous oxide cyro units are used, this cycle may be repeated two to three times in each location. Care must be taken not to cause tissue necrosis of the eyelid by overfreezing the eyelid margin. This risk is much greater when using liquid nitrogen units, as the freezing temperature is substantially colder (approximately –200°C) when compared to that obtained with nitrous oxide (approximately –80°C). Once the eyelid thaws, epilation of the distichia is attempted. Adequate cryotherapy is performed if there is no resistance to the epilation of the distichia. Partial tarsal plate excision or lid splitting has been attempted, but scarring and contracture may occur after surgery [91]. Ectopic cilia usually consist of a single hair or a focal group of hairs that should be removed by en-block excision and ancillary cryotherapy of the wound bed.



Figure 6.40 A 29-year-old horse with bilateral lateral eyelid entropion. The horse had mild enophthalmos from muscle atrophy, entropion (**arrows**), mild blepharospasm, and epiphora.

Prognosis

If all offending hairs can be located and removed, or the eyelid abnormality or scarring is minor and repairable, the long-term prognosis is excellent. Eyelash disorders are relatively uncommon in horses compared to dogs. Repeat treatment for new distichia or ectopic cilia is not frequently required.

Entropion in adult horses

Entropion, or inward turning of the eyelid, results in the eyelashes rubbing the cornea (as in trichiasis) and can cause significant ocular irritation and corneal damage. Conformational (or anatomic) entropion is rare in the horse [33], but typically occurs secondary to eyelid trauma (i.e., cicatricial entropion) or severe blepharospasm (i.e., spastic entropion) [5, 90]. Spastic entropion resulting from primary ocular inflammation may subside spontaneously once the inciting cause has been removed. Entropion can also occur with decrease in orbital support of the eyelids, such as with phthisis bulbi or enophthalmos from severe dehydration or loss of orbital fat, such as what is observed in young foals with neonatal maladjustment syndrome or elderly cachectic horses [53].

Clinical appearance and diagnosis

Entropion, whether present in a foal or adult horse, appears similarly. The eyelid margin is turned inward toward the cornea, with the cilia and eyelid hairs rubbing the surface of the cornea (see Figures 6.11 and 6.40). Associated conditions, such as corneal ulceration, enophthalmos, eyelid scarring, and/or phthisis bulbi may be present.

Differential diagnosis and pathogenesis

It is important to determine if the entropion is a primary or secondary ophthalmic problem. As previously discussed, the majority of horses affected have secondary entropion to some

other primary problem. Primary ocular problems that may result in secondary entropion in horses include blepharitis, enophthalmos, eyelid scarring, phthisis bulbi, and any cause of keratoconjunctivitis (e.g., burdock bristle keratitis [94], foreign bodies, infectious keratitis [95–98], keratoconjunctivitis sicca [22–24, 99], and other noninfectious keratopathies [83, 84, 97, 99]). Regardless of the cause, entropion will result in ocular irritation, which in turn will exacerbate the "spastic component" of any anatomic entropion (see section **Congenital ocular adnexal diseases**).

Treatment

To treat adult-onset entropion in horses adequately and to prevent recurrence, the primary underlying cause needs to be managed. Cicatricial entropion can be repaired surgically by removing the scarred eyelid [90]. Resolving the cause of ocular irritation, such as corneal ulceration or removal of a foreign body, will help the spastic entropion resolve. However, some conditions cannot be reversed, such as phthisis bulbi and enophthalmos from fat atrophy. Enucleation of a severely phthisical eye is recommended. Entropion repair can be considered for mild phthisis bulbi or enophthalmos. Treatment goals and strategies are the same in all ages of horses. Additional details regarding the medical and surgical management of entropion have been previously discussed (see **Entropion** in the section **Congenital ocular adnexal diseases** and Figures 6.13, 6.14, and 6.15).

Prognosis

Prognosis for entropion depends on the underlying cause. If the primary problem can be corrected while the eyelid margins are temporarily tacked (to address any spastic entropion that may be contributing to the primary ocular disease process), then the long-term prognosis is excellent. However, if the entropion is secondary to phthisis bulbi or enophthalmos that cannot be reversed by correcting an underlying systemic disease (e.g., emaciation/dehydration), then the prognosis is more guarded. In some cases, definitive surgical repair of the entropion may offer the horse improved ocular comfort even if the globe is nonvisual and blind (e.g., mild phthisis bulbi). In severe cases of entropion secondary to a blind shrunken (phthisical) or sunken (enophthalmic) globe, enucleation may offer the horse the most comfortable long-term outcome. Finally, if the horse has primary entropion, then properly performed definitive surgical repair carries a favorable prognosis.

Conjunctivitis

By definition, conjunctivitis implies inflammation of the palpebral and bulbar conjunctival tissues of the eye. The conjunctiva is richly vascularized and contains organized lymphoid tissue (also known as CALT [16, 17]; see Figure 6.7), which results in its innate ability to become easily inflamed in either primary or secondary conjunctivitis. When inflamed, the conjunctiva may demonstrate profound clinical changes, such as hyperemia (redness) and chemosis (edema). Common causes of conjunctivitis are listed in Table 6.6.



Figure 6.41 Significant conjunctival hyperemia, moderate chemosis, ciliary flush, and diffuse corneal edema are present in this horse with fungal keratitis.

Clinical appearance and diagnosis

One of the most common presenting complaints associated with the majority of ocular problems in most domestic animals is that of a "red eye." It is essential that the clinician determine if the conjunctivitis is a primary or secondary problem, as secondary conjunctivitides are frequently associated with vision-robbing diseases (Table 6.6) such as uveitis, glaucoma, and significant corneal disease (Figure 6.41). This differentiation is made based on careful external and internal ophthalmic examination as well as performing a minimum ophthalmic database (STT, fluorescein stain, IOP measurement, and, when indicated, cytology, culture, and sensitivity, or biopsy). Depending on the cause, the appearance of conjunctivitis will vary, from significant chemosis and hyperemia (see Figures 6.24 and 6.32) to more mild conjunctival changes but significant mucopurulent discharge (see Figure 6.19). A combination of both significant hyperemia and severe ocular discharge can be found in diseases such as eosinophilic keratoconjunctivitis (Figure 6.42).

Differential diagnosis and methods for definitive diagnosis

A complete and thorough ophthalmic examination should be done to rule out all ocular causes of secondary conjunctivitis. With rare exceptions (e.g., tonometry is not performed on globes at risk of corneal perforation), the minimum ophthalmic database (STT, fluorescein stain, IOP measurement) should be obtained prior to slit-lamp biomicroscopy and funduscopy being performed. Bacterial and/or fungal culture and antimicrobial susceptibility testing followed by cytologic examination of conjunctival scrapings should be performed on all eyes with a history of chronic conjunctivitis and eyes with mucopurulent ocular discharge. A thorough understanding of the normal

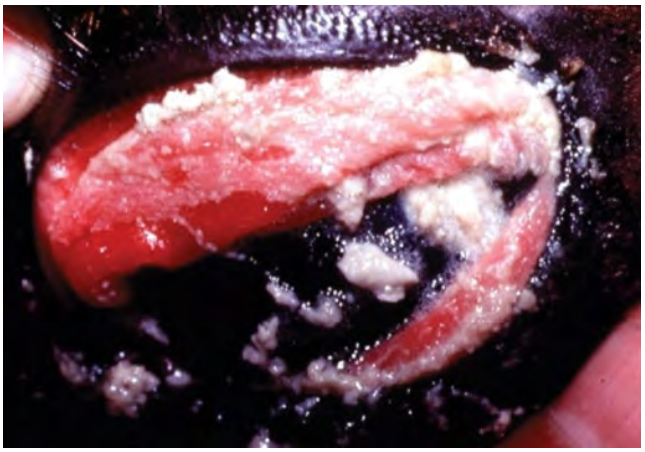


Figure 6.42 Severe caseous dicharge and conjunctivitis in a horse with eosinophillic keratoconjunctivitis. (*Source*: Photograph courtesy of Dr Mike Davidson.)

bacterial and fungal flora of the conjunctiva is essential when interpreting the results of diagnostic testing [15, 56, 58, 101–105]. A review of various studies of the normal equine corneal and conjunctival bacterial and fungal flora can be found in Chapter 7. If an infectious etiology (Table 6.6) is suspected, appropriate diagnostic testing is recommended and may necessitate that samples be sent to specialized laboratory facilities equipped to appropriately isolate and diagnose certain fungal or viral agents. Systemic disease must also be considered when evaluating a horse with conjunctivitis (see Chapter 15).

Treatment

Conjunctivitis is merely a clinical sign and not an etiologic diagnosis; therefore treatment should be directed at the primary or secondary cause for this ocular finding. Medical therapy for conjunctivitis is typically delivered via topical ophthalmic ointments administered three to four times per day. If more frequent application of medication is deemed necessary, then placement of an SPL tube with administration of ophthalmic solutions/suspensions may be a more convenient method of treatment (see section **General therapeutic considerations when treating horses for acquired adnexal or nasolacrimal disease**). Topical antibiotic therapy based on culture and antimicrobial susceptibility testing and cytology results is the mainstay of therapy. Topical broad-spectrum antibiotics, such as oxytetracycline and triple antibiotic ointment three to four times a day, are good initial therapeutic choices. If antiviral or antifungal agents are required for treatment, then formulations via a compounding pharmacy may be necessary (see Chapter 7). Clinicians should exercise caution in the use of topical anti-inflammatory therapy, particularly topical steroids, if treating equine patients in regions where fungal pathogens are endemic. No definitive surgical therapies exist for the treatment of conjunctivitis, with the possible exception of debulking a mass in the diagnosis and/or treatment of certain congenital (e.g., dermoid), infectious (e.g., parasitic), inflammatory (e.g., pseudotumor), and neoplastic lesions (e.g., SCC, melanoma) [106, 107]

Prognosis

The prognosis is usually good with primary infections, as most conjunctival infections respond well to topical therapy, generally within 5–7 days (Table 6.6). However, primary viral infections can be recurrent, and many systemic diseases that manifest with conjunctivitis as part of the horse's overall clinical findings can have serious and life-threatening complications (see Chapter 15).

Neurologic disorders of the eyelids

Several neurologic conditions may affect the eyelids and periocular structures. Neurologic conditions affecting the orbit and extraocular muscles are reviewed in Chapter 14. The two most common neurologic diseases of the ocular adnexa in the horse are Horner's syndrome and facial nerve paralysis.

Horner's syndrome

The autonomic nervous system (ANS) is an involuntary motor system composed of the parasympathetic and sympathetic divisions. It is known as the "involuntary," "visceral," or "vegetative" nervous system. Horner's syndrome results from loss of sympathetic innervation to the head, either unilaterally or bilaterally [10]. Knowledge of the sympathetic nerve pathway is essential to understanding the pathogenesis, diagnostic testing, treatment, and prognosis of a horse with Horner's syndrome. The sympathetic nervous system pathway begins in the hypothalamus and extends down the intermediolateral cell columns of the spinal cord to synapse at C8–T3. The axons from these cells exit the anterior nerve root of the spinal cord through the white ramus. The fibers (pre-ganglionic fibers) course through the brachial plexus and thoracic inlet, and ascend in the sympathetic trunk (with the jugular vein) to synapse at the cranial cervical ganglion. Post-ganglionic fibers then pass near the middle ear and through the orbital fissure, to form the sympathetic root of the ciliary ganglion. Short ciliary nerves (along with contributory fibers to the long ciliary nerves) extend to the dilator muscle of the iris. Therefore damage of the pathway from the hypothalamus to the short ciliary nerves may cause denervation, resulting in Horner's syndrome. Lesions that occur proximal to the ciliary ganglion are termed pre-ganglionic, while those distal to the ciliary ganglion are referred to as post-ganglionic.

Clinical appearance and diagnosis

The predominant clinical signs of Horner's syndrome in horses are ptosis, sweating on the head and neck, and increased cutaneous temperature in the denervated area (Figure 6.43) [8–10, 108–113]. Enophthalmos, miosis, elevated third eyelid, and increased lacrimation (which are common clinical signs in other animals) are



Figure 6.43 Right-sided Horner's syndrome. Note the predominant clinical signs of ipsilateral sweating above the eye and mild ptosis. Enophthalmos, miosis, and elevated third eyelid (which are common clinical signs in other animals) are not prominent in this horse. (*Source*: Photograph courtesy of Dr David A. Wilkie.)

variable, inconsistent, or mild in horses [8, 9, 108–112]. There are no vision deficits with sympathetic denervation and the diagnosis is based on recognition of clinical signs.

Differential diagnosis and methods for definitive diagnosis

Damage to the sympathetic trunk anywhere along its pathway may result in signs of Horner's syndrome (Box 6.2) (see Chapter 15). Trauma to the neck and spinal cord or vagosympathetic trunk (i.e., during jugular venepuncture) can also cause the disease [5, 111]. A case with Horner's syndrome associated with jugular venepuncture was mild and resolved within 14 hours [111]. Other possible causes in horses include idiopathic, guttural pouch infections, obstructive esophageal disorders [114]. Melanoma [8, 108, 109], anterior thoracic disorders [109], metastatic squamous cell carcinoma [109], and surgical procedures such as carotid artery catheterization [8] and cervicothoracic (stellate) ganglion blocks [115, 116]. Horner's syndrome may also be associated with concurrent laryngeal hemiplegia [9]. It has been experimentally induced by transection of the cervical sympathetic and vagosympathetic trunk [9, 112], and carotid artery catheterization [8]. The experimentally induced disease appeared nearly identical to naturally occurring clinical cases [9, 112].

Box 6.2 Causes of Horner's syndrome in the horse. [8–10, 108–117]

- Idiopathic
- Trauma to neck or spinal cord
- Jugular venapuncture or other trauma to vagosympathetic
- Gutteral pouch infections
- Obstructive esophageal disorders
- Anterior thoracic disorders
- Metastatic neoplasia (melanoma, SCC)
- Surgical procedures (carotid artery catheterization, cervicothoracic (stellate) ganglion blocks)

Diagnostic work-up for horses with unilateral or bilateral Horner's syndrome should consist of a complete ophthalmic and physical examination. Endoscopic examination of the ipsilateral guttural pouch, laryngeal function, and upper esophagus should be considered. Thoracic ultrasound or radiography may be useful to evaluate for anterior thoracic masses or infection.

Pharmacologic testing for Horner's syndrome consists of the application of certain topical medications to the eye and the response to treatment in an effort to localize the site of sympathetic nervous system damage [117, 118]. Such testing does not always reliably localize the lesion [9]. The law of denervation hypersensitivity provides the pharmacological basis for differentiating pre-ganglionic from post-ganglionic lesions in ANS disorders. Interruption of innervation to an organ results in loss of the degradative enzyme of the neurotransmitter, and, as a result, the synaptic receptor becomes extremely sensitive (known as "super-sensitive") to the neurohumoral agent. In other words, the receptors in the adjacent neuron (in the ganglion) or in the neuromuscular junction (effector organ) will be super-sensitive to their agonists when the preceding nerve or nerve ending is destroyed. Note that when pharmacologic testing for Horner's syndrome is performed, both eyes should receive identical amounts/concentrations of the pharmacologic agent used so that the denervated/affected side can be compared to the normal side for accurate test interpretation.

Topical drugs that have been used for pharmacologic testing for Horner's syndrome include cocaine (not commercially available), hydroxyamphetamine, and phenylephrine. Cocaine and hydroxyamphetamine are indirect-acting sympathomimetic drugs that do not bind adrenergic receptors directly but act to increase norepinephrine in the synaptic cleft. Cocaine (6%) blocks the reuptake of norepinephrine at the receptor sites of the iris dilator cells, which results in an accumulation of this neurotransmitter at the receptor site. There is no direct action on the receptor. Therefore a dilated pupil in response to topical cocaine would suggest a pre-ganglionic lesion. Hydroxyamphetamine (1%) stimulates endogenous release of norepinephrine from intact adrenergic nerve endings. It does not directly stimulate

the receptors. In central or pre-ganglionic neuron lesions, the post-ganglionic sympathetic neuron remains intact and hydroxyamphetamine stimulates release of stored norepinephrine, causing pupillary dilation. Lesions of the post-ganglionic neuron do not respond to hydroxyamphetamine, because there are no stores of norepinephrine to be released, and therefore no mydriasis results. Note that because the effects are unrelated to the phenomenon of denervation hypersensitivity (and thus are not dose-dependent), multiple drops of a 1% or use of a 5% solution may be necessary. Application of a sufficient amount of drug to both eyes to induce mydriasis in the control eye is necessary for accurate test interpretation.

Phenylephrine HCl (commercially available as a 2.5% or 10% solution) is a direct-acting sympathomimetic drug. Specifically, phenylephrine is an α1-adrenergic agonist with little effect on β-adrenergic receptors. Upregulation of adrenergic receptors on the denervated iris dilator muscle and hypersensitivity to phenylephrine occurs in lesions of the post-ganglionic sympathetic neuron. Thus dilation after topical application would suggest a post-ganglionic lesion. Pharmacologic testing with an indirect-acting sympathomimetic (hydroxyamphetamine) and a direct-acting sympathomimetic (phenylephrine) should be performed 24 hours apart.

Treatment

Treatment is based on eliminating the underlying cause if possible. Horner's syndrome from minor trauma to the sympathetic trunk will resolve spontaneously in hours to days. Idiopathic Horner's syndrome typically spontaneously resolves in weeks to months. Topical phenylephrine will temporarily resolve some of the clinical signs, but this is rarely used as a long-term therapy. Surgical treatment is indicated if needed to manage the underlying cause, such as guttural pouch infection or esophageal disorders.

Prognosis

Prognosis depends on the underlying cause and varies tremendously. Prognosis for resolution of clinical signs is excellent for Horner's syndrome associated with mild trauma [111]. Prognosis for resolution of the syndrome and overall life of the horse is poor if Horner's syndrome is the result of metastatic neoplasia [108–110].

Facial nerve paresis/paralysis

Facial nerve paralysis is the most common cranial nerve abnormality in horses [113, 119]. In one study, facial nerve paralysis represented the greatest number of all neurologic diseases in horses in Australia [119]. The facial nerve in the horse originates posterior to the pons, enters the internal acoustic meatus, travels through the facial canal of the petrous temporal bone, passes through the stylomastoid foramen, extends around the guttural pouch and under the parotid salivary gland, crosses the ramus of the mandible (externally) approximately 4 cm ventral to the temporomandibular joint, and then divides into dorsal and ventral buccal branches [5].

Clinical appearance and diagnosis

Clinical features of facial nerve paralysis include ptosis, lagophthalmos, ventral displacement and decreased motility of the ear pinna, decreased nostril function, flaccid lips, and deviation of the nose (either away from the lesion with acute facial nerve paralysis or toward the lesion with chronic paralysis) (Figure 6.44) [2, 5, 119–122]. Diagnosis is based on clinical signs and lack of facial nerve function (i.e., lagophthalmos and decreased or absent facial muscle function).



Figure 6.44 Acute left-sided facial nerve paralysis. Note the horse has ptosis, lagophthalmos, ventral displacement and decreased motility of the ear pinna, decreased nostril function, flaccid lips, and deviation of the nose away from the left-sided lesion. An upper eyelid SPL catheter has been placed to assist in the medical management of corneal disease. (*Source*: Photography courtesy of Dr Stacy Andrew.)

Differential diagnosis and methods for definitive diagnosis

Facial nerve paralysis should be differentiated from other causes of ptosis, such as Horner's syndrome. The normal anatomic pathway of the facial nerve requires that the clinician consider a variety of possible causes for facial nerve paralysis, including inflammation of the inner ear, guttural pouch, or salivary glands. Additionally, fractures to the stylohyoid bone, petrous temporal bone, or ramus of the mandible can damage the facial nerve [121]. Due to the external course of the nerve over the ramus of the mandible, trauma frequently affects this nerve, including prolonged recumbancy during disease or anesthesia [122]. A clinical sign of equine protozoal myeloencephalitis (EPM), a disease caused by *Sarcosystis neurona*, is facial nerve paralysis (see Chapter 15) [123–125]. There is a report of facial nerve paralysis associated with temporohyoid osteoarthropathy, diagnosed based on proliferation of the temporohyoid joints and stylohyoid bones on radiographs and guttural pouch endoscopy [120].

Treatment

Treatment is to provide protection for the cornea while addressing the underlying cause whenever possible. Topically applied artificial tear ointment should be given four to six times a day to keep the cornea moist and prevent ulceration. If a corneal ulcer is present, it should be treated with topical antibiotics to help prevent infection and manage any concurrent reflex uveitis (see Chapter 7). Surgical therapy is indicated if the primary problem necessitates surgical intervention (e.g., fractures or guttural pouch abnormalities). A partial temporary tarsorrhaphy is recommended using a single horizontal mattress suture of 4-0 nylon at the temporal aspect of the palpebral fissure. This will help protect the globe until facial nerve function returns.

Prognosis

Prognosis depends on the underlying cause. If improvement of the facial nerve paralysis does not occur in 3–4 weeks, then the prognosis is poor and the nerve damage is likely permanent. In cases of permanent facial nerve deficits, a permanent partial temporal tarsorrhaphy (i.e., closing the lateral one-fourth of the eyelid margins by removing the eyelid margins and closing the wound bed in a two-layer manner, as described in the section **Eyelid lacerations**) should be considered for increased corneal protection. Most horses with facial nerve paralysis maintain retractor bulbi function. The horse can retract the eye, elevate the third eyelid as a form of "blinking," and thus help distribute the tear film over the corneal surface. This action generally protects the medial two-thirds to three-quarters of the cornea, leaving the lateral cornea exposed. A permanent temporal tarsorrhaphy helps to protect the dorsolateral cornea.

Third eyelid disorders

The equine third eyelid, or nictitating membrane, originates in the ventromedial aspect of the rostral orbit and moves passively in the dorsolateral direction. The bulbar and palpebral surfaces of the third eyelid are covered with conjunctiva; therefore virtually all diseases reviewed previously in the **Conjunctivitis** section may also involve the third eyelid. The base of the third eyelid contains a lacrimal gland (tubuloacinar) that produces portions of the aqueous component of the tear film. Many of the conditions of the third eyelid are secondary to other abnormalities of the globe and orbit. The most common clinical disease affecting the equine nictitating membrane is SCC (Figure 6.45) [5, 126, 127].



Figure 6.45 Horse affected with SCC; the neoplasm is originating from the anterior ventrolateral aspect of the third eyelid and is easily visualized with ventral retraction of the lower eyelid and slight retropulsion of the globe.

Clinical appearance and diagnosis

The leading edge of the third eyelid is visible in the normal horse and it may or may not be pigmented (see Figure 6.1). Occasionally, a nonpigmented third eyelid may be more obvious and thus erroneously interpreted as being abnormally elevated [5]. An elevated third eyelid can be secondary to enophthalmos (i.e., from fat atrophy), retraction of the globe (e.g., with ocular discomfort such as corneal ulceration, uveitis, or other ocular disease), phthisis bulbi (Figure 6.46), an orbital space-occupying mass (e.g., a neoplasm, granuloma, or abscess) [128–132], or as a result of sympathetic denervation and Horner's syndrome [8, 9, 108–111, 113]. Bilateral third eyelid elevation has been associated with tetanus [133], ear tick (*Otobius megnini*) infestations [134], and possible other systemic disease in horses (see Chapter 15). Conjunctivitis, ulceration, swelling, and even erosion of the leading edge of the third eyelid are not uncommon in horses (see Figure 6.36), especially those that have pigmented eyelids but nonpigmented third eyelids [5]. Solar or actinic radiation and environmental irritants are usually the cause. These lesions may be precursors to SCC. Inflammation of the third eyelid has been associated with granuloma formation with habronemiasis [86].

Prolapsed gland of the nictitans has not been reported in horses. However, prolapsed orbital fat (specifically the anteromedial corpus adiposum) around the third eyelid can cause



Figure 6.46 An elevated third eyelid secondary to phthisis bulbi. The small size of the eye has allowed the third eyelid to passively extend anteriorly.

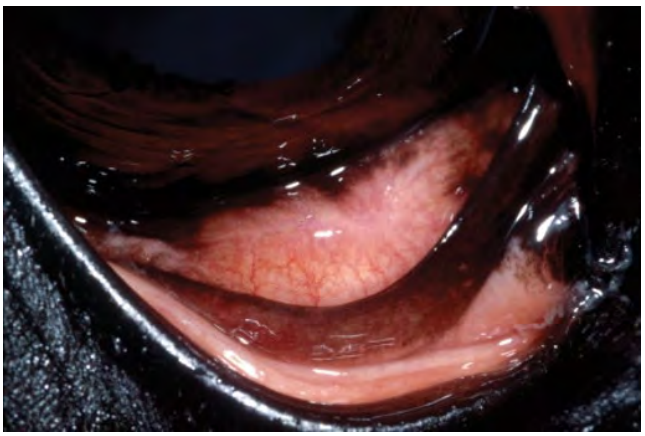


Figure 6.47 Prolapsed orbital fat near the base of the third eyelid. This condition in horses should not be mistaken for a prolapse of the gland of the third eyelid, as is commonly observed in some breeds of dogs but has never been reported in horses.

protrusion with a similar clinical appearance to a nictitating gland prolapse as is typically seen in some canine breeds (Figure 6.47) [135, 136].

Trauma to the third eyelid can result in lacerations of the conjunctiva and/or cartilage, hemorrhage, and swelling. In general, if the only abnormality is a conjunctival laceration, hemorrhage, or chemosis, the injury will rapidly heal without surgery. Topical antibiotics may be helpful to prevent further ocular irritation and to protect the surface of swollen tissue from desiccation. If substantial third eyelid chemosis results in lagophthalmos, a partial temporary tarsorrhaphy is recommended by way of a single horizontal mattress suture placed in the medial one-quarter of the eyelid [5]. The lateral palpebral fissure is allowed to remain open so that the horse can still maintain some vision and topical medications can be instilled on the ocular surface. If the cartilage is lacerated, surgical repair of the third eyelid should be attempted or, in severely damaged third eyelids, complete resection may be necessary.

Differential diagnosis and methods for definitive diagnosis

Third eyelid position abnormalities must be differentiated from primary ocular and orbital diseases (see Chapter 5), such as mass lesions in the orbit, enophthalmos, ocular discomfort, and phthisis bulbi (see Figure 6.46). Third eyelid inflammation should be differentiated from medial canthal habronemiasis (see Figure 6.34) and primary conjunctivitis. Lesions can be differentiated by culture, cytology, and biopsy. These tests are especially recommended in any chronic or nonreponsive inflammation or swelling. Evidence of primary orbital disease (i.e., exophthalmos or inability to retropulse the globe) or ocular disease (i.e., phthisis bulbi) would suggest the need for further diagnostic procedures to determine the cause of the clinical signs (see Chapter 5).

Treatment

Treatment should be directed at the underlying cause of the inflammation or swelling, with more targeted therapies aimed at addressing various types of neoplasia affecting the equine third eyelid [106, 107, 126, 127, 132, 137–142]. Topical antibiotics, with or without the addition of anti-inflammatories, are generally initially used; however, if the disease is unresponsive, then treatment should be guided by culture and antimicrobial susceptibility testing, cytology, and histopathology. Lacerations involving the cartilage of the third eyelid should be surgically repaired or the third eyelid removed entirely. Partial removal of the third eyelid is not recommended because exposed cartilage of the third eyelid can irritate the cornea. The overall goal of surgical therapy on the third eyelid is to remove the cause of ocular irritation (e.g., SCC—see Figure 6.45) without causing additional injury to the globe. To that end, all sutures and suture knots must be either buried under the conjunctiva or placed on the palpebral (i.e., "external") surface of the third eyelid. General anesthesia is recommended because the third eyelid and retractor bulbi muscles remain functioning even when the animal is tranquilized. Retrobulbar nerve block (RNB) may be a useful adjunct when performing surgery on the third eyelid [36, 143]; however, RNB and standing sedation may not provide sufficient immobility of the head when microsurgical techniques are required.

Removal of the third eyelid is a relatively common procedure that is performed when the third eyelid is affected by SCC (see Figure 6.45) or other neoplasia. Surgical removal occurs with the horse under general anesthesia or with standing sedation with or without retrobulbar nerve block [36, 126, 138]. If complete third eyelid resection is indicated, it is important that all of the cartilage, the gland of the third eyelid, and the dense fibrous tissue anchoring the third eyelid to the ventronasal aspect of the orbit are removed. Palpation of the third eyelid before and after excision is recommended. Commonly, if the third eyelid is removed due to a neoplastic lesion, ancillary

cryotherapy is then performed, taking care not to freeze the cornea. Many ophthalmic surgeons advocate suturing the conjunctival wound bed after third eyelid removal with a continuous pattern of 6-0 polyglactin 910 or similar suture to prevent subsequent orbital fat prolapse.

Prognosis

Assuming that further damage to the eye does not occur from chronic third eyelid abnormalities, poor placement of sutures during surgery of the third eyelid, or neoplastic processes that have extended beyond the surgical margins of resection, the prognosis for most third eyelid injuries is good.

Procedure for retrobulbar nerve block (RNB)

Certain minor ocular surgical procedures, such as biopsies and third eyelid removal, can be performed in horses using standing sedation protocols and RNB [143]. When performed correctly, the RNB will paralyze the retractor bulbi muscle and thus help to keep the eye immobile. See Chapters 1 and 2 for more information.

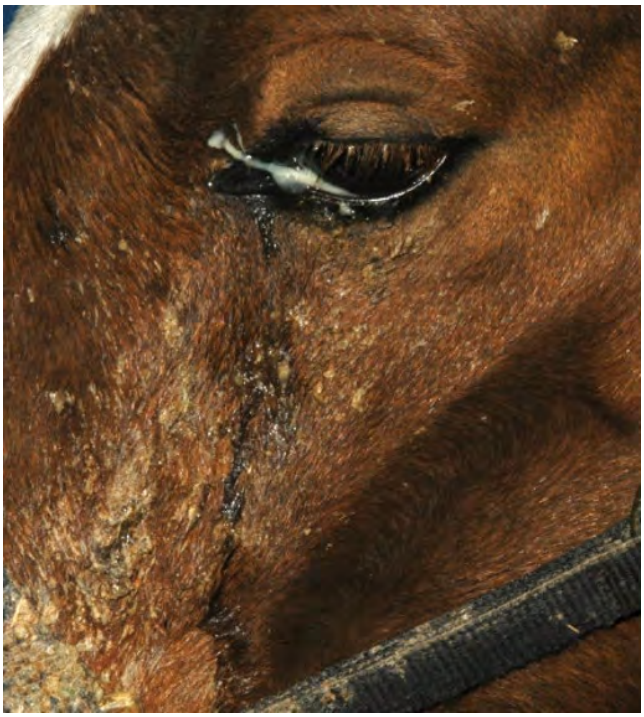


Figure 6.48 A 3-month-old foal with significant mucopurulant ocular discharge secondary to NLD obstruction.

Acquired nasolacrimal disorders

Nasolacrimal duct obstruction

Congenital NL atresia is one of the most common congenital ocular diseases in horses and usually causes clinical signs of copious ocular discharge in foals between 2 and 6 months of age (see section **Congenital diseases of the nasolacrimal system**). Acquired NL disorders include obstructions from inflammation (dacryocystitis), strictures, foreign bodies, dental disease [144], and trauma [2, 26, 27, 145–148].

Clinical appearance and diagnosis

Obstruction of the NLD occurs most commonly secondary to intraluminal foreign material, and clinical signs include epiphora, conjunctivitis, and often significant mucopurulent discharge (Figure 6.48). Foreign material can sometimes be successfully removed by retrograde saline flush (see section **Nasolacrimal duct atresia**) [5, 147]. Initial diagnosis is made by inability of topical fluorescein dye to exit the ventral NL puncta (a negative Jones test). Inflammation or trauma to the NLD may cause hemorrhage to emanate from the ventral NL meatus, a condition called dacryohemorrhea [149].

Differential diagnosis and methods for definitive diagnosis

In all cases of epiphora, the clinician needs to differentiate between causes of increased lacrimation versus obstruction of tear outflow (Figure 6.49). The most common cause of increased lacrimation is ocular pain, indicative of either surface (e.g., conjunctivitis, keratitis) or intraocular (e.g. uveitis, glaucoma) disease. Some horses have seasonal epiphora or dacryocystitis and present typically with bilateral disease. This may be caused by environmental changes (e.g., increase in dry, dusty environment), allergies, or insects.

The diagnostic approach to any horse with epiphora is to begin with a complete ophthalmic examination and acquisition of the minimum ophthalmic database, including specific evaluation for a positive Jones test (i.e., presence of fluorescein stain at the nasal punctum indicative of normal tear flow down the NL system—see Figure 6.23). If mucopurulent discharge is present, antimicrobial susceptibility testing should be performed as well as cytology of the discharge. Following these tests, retrograde and normograde NL irrigation should be attempted with the horse tranquilized. If irrigation is successful at clearing an obstruction, copious irrigation of the NLD should then be performed to ensure all debris has been cleared. Excessive force when irrigating the NLD should be avoided to prevent rupture or other damage to the NLD. Unsuccessful irrigation attempts at NLD irrigation with the horse under standing sedation warrant additional diagnostic testing, such as DCR (see Figure 6.20), ultrasound, or endoscopy, to better delineate the site of obstruction and determine if there are any surrounding bony abnormalities [20, 28, 48–52, 146, 147]. CT [13, 148] and video endoscopy [27] have also been used to image defects in the NLD.

Pathogenesis

Dacryocystitis, or inflammation of the NLD, is generally the result of a complete or partial obstruction, secondary retention of tears in the duct, and bacterial proliferation in the stagnant

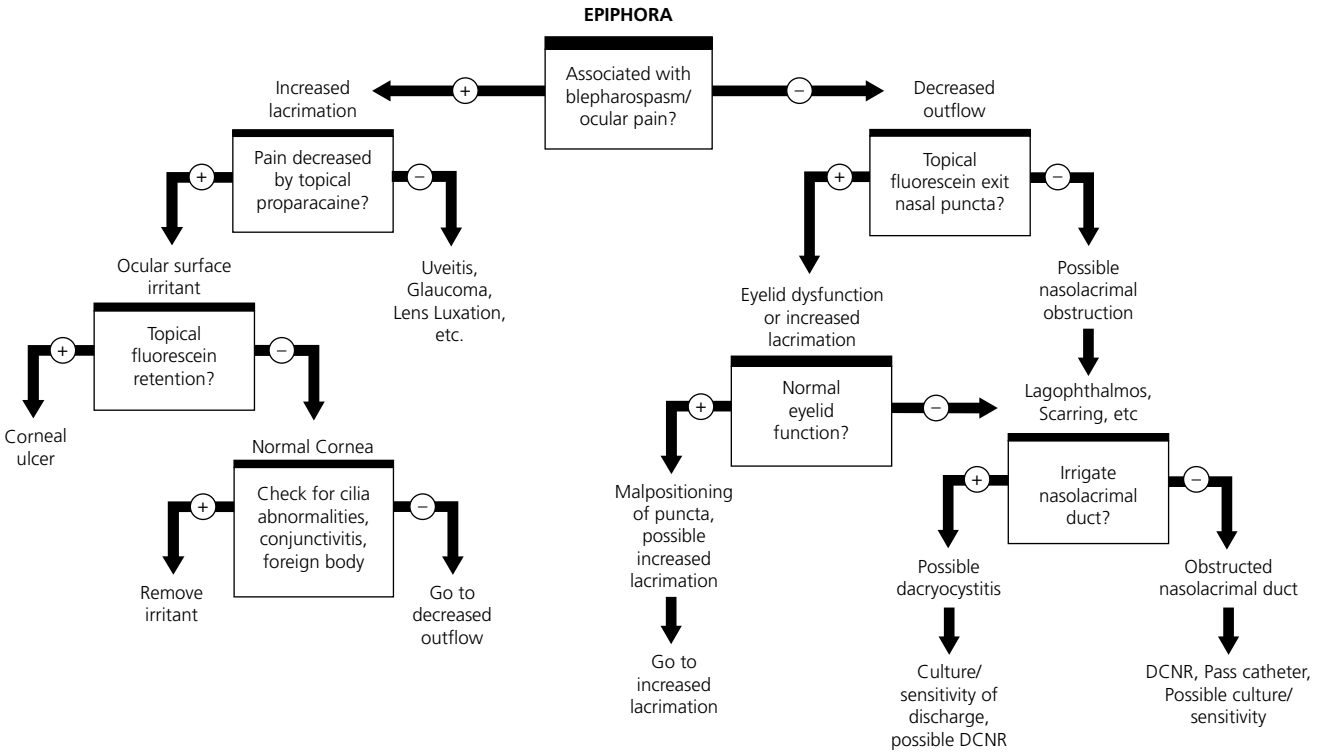


Figure 6.49 Flow chart for diagnosis and treatment of epiphora. (*Source*: Gilger, 2011 [343]. Reproduced with permission from Elsevier.)

tear fluid. Obstructions can occur from environmental debris accumulating in the NLD, especially at areas of normal narrowing of the duct such as immediately prior to its exit from the lacrimal canal of the maxilla bone [52]. Damage to the lacrimal canal of the maxillary bone from external trauma, sinus infections, or upper arcade dental disease may cause strictures of the NLD [2, 26, 50, 145, 146].

Treatment

NLD obstructions should be treated medically; however, surgical intervention may also be required [43]. Topical broad-spectrum antibiotic solution (type based on antimicrobial susceptibility results) should be used every 6 hours once the NLD obstruction has been relieved. Solutions are preferred over ointments because they will pass through the NLD more readily. Antibiotic solutions containing a topical corticosteroid may be beneficial to decrease swelling in the NLD, providing there are no ocular surface contraindications (e.g., a corneal ulcer). Treatment should be continued for at least 2 weeks. If there has been repeated obstruction or episodes of dacryocystitis, if the obstruction was difficult to resolve, or if there was stricture of the duct visualized by DCR or other imaging modalities, then a surgical stent or catheter should be placed for 4–6 weeks. A 5-French male silastic or plastic canine urinary catheter (with or without wire stent) is threaded normograde (from proximal to distal) or retrograde. The catheter is advanced until resistance is encountered. The catheter should not be forced if resistance is encountered, because severe hemorrhage may develop [52]. Once passed, the silastic tubing is sutured in place for 4–6 weeks (see Figure 6.22). Judicious use of oral anti-inflammatory and oral antibiotic medication may be considered in these cases (see section **General therapeutic considerations when treating horses for acquired adnexal or nasolacrimal disease**).

Surgery to correct NLD obstruction is sometimes required [51]. If there is any abnormality that is compressing the NLD it should be alleviated. This would include surgery to relieve swelling from sinusitis or dental disease, or to repair facial fractures or canaliculi lacerations [2, 26, 144, 145]. If, by contrast, the NLD cannot be opened or is permanently destroyed, creating a new tear outflow pathway is needed. Creating a pathway from the canaliculi to the nasal cavity (canaliculorhinostomy) [147] or from the ventral medial conjunctival surface to the maxillary sinus (conjunctivosinostomy) [47] can successfully establish this goal. These procedures involve drilling a hole using a Steinmann pin or drill through the lacrimal bone into the maxillary sinus or nasal cavity, then placing a stent for 4–6 weeks to allow the incisions to heal and epithelialize the new outflow pathway. Although successful, these procedures can be challenging due to extensive hemorrhage, the density of equine facial bones, and the propensity of the newly created outflow pathway to stricture and close over time.

Prognosis

In general, the prognosis for NLD obstructions (typically with secondary dacryocystitis) that can be relatively easily unblocked and without repeat occurrence is good. It is essential to

determine the location, extent, and cause of the obstruction to adequately treat it. Some horses can tolerate mild epiphora if the owners can keep the periocular area ventral to the eye clean and prevent fly infestation. Environmental control efforts aimed at decreasing particulate debris, allergens, and insect infestation can help to decrease the clinical severity and/or recurrence of NL disease in horses. Horses with severe and recurrent NLD obstructions requiring more aggressive surgical intervention (e.g., canaliculorhinostomy or conjunctivosinostomy) have a more guarded successful long-term prognosis, but there are few published reports of these more advanced surgical techniques [47, 147].

Keratoconjunctivitis sicca

Keratoconjunctivitis sicca (KCS) or dry eye is very uncommon in horses [22–24, 99, 150, 151]. Nearly all cases of KCS in horses have been associated with trauma [22, 24] and, to date, there has not been a definitive case of immune-mediated lacrimal gland adenitis, which is the most common cause of KCS in dogs [152–154]. A case report of equine KCS attributable to hypothyroidism has been reported [25]. Some authors have subdivided KCS into tear-deficient dry eye and evaporative dry eye, which is desiccation of the ocular surface secondary to facial nerve paralysis (or other eyelid dysfunction), loss of corneal sensation, and other primary ocular surfaces diseases [151].

Clinical appearance and diagnosis

Dry eye in horses may present with a variety of possible clinical signs, including blepharospasm, mucopurulent ocular discharge, a dry, lusterless appearance to the cornea, and keratitis. Definitive diagnosis should be confirmed by assessment of clinical signs together with STT values. The STT should be performed before manipulation of the periocular or ocular structures and at the onset of complete ophthalmic examination to minimize reflex tearing (see Chapter 1). Normal horses have been reported to have STT I (measurement of tears without the use of a topical anesthetic) values between 11 and greater than 30 mm of wetting per minute and 15–20 mm/30 seconds [21, 155, 156]. One study evaluating tear testing in horses found no differences in values obtained between STT I and STT II (i.e., with topical anesthetic) and no significant differences based on age, season, environment, gender, time of day, or location of placement of strips [156]. Tranquilization does not affect STT values; however, general inhalant anesthesia with halothane does affect the STT for up to 3 hours [155]. STT measurements of 10–15 mm/min or less with clinical signs of dry eye would be suggestive of the clinical diagnosis of KCS in horses.

Differential diagnosis and methods for definitive diagnosis

Although it is most appropriate to perform the minimum ophthalmic database (STT, fluorescein stain, and IOP measurement) on any animal presenting with ocular disease, frequently even veterinary ophthalmologists do not routinely perform tear testing on horses. This is likely due to the fact that KCS is a rare disease in this species and that many horses present with an ocular disease that results in an overabundance of tears (known as epiphora). An STT is indicated if evidence of CN VII dysfunction (i.e., following trauma, facial paralysis, etc.) is observed, if the cornea and/or conjunctiva appear dry, if tenacious mucoid ocular discharge is present, whenever corneal vascularization and/or ulceration is present that is persisting beyond the anticipated time for wound healing to have occurred, or if the ocular problem remains of undetermined etiology. KCS is most commonly the result of CN V or VII trauma, but has also been reported in cases of fractures of the mandible and stylohyoid bone, locoweed poisoning, eosinophilic dacryadenitis, hypothyroidism, and in association with corneal stromal sequestration [2, 5, 22–25, 150]. The clinician must differentiate KCS from other much more common diseases, especially primary keratitis and NLD obstruction.

Treatment

Medical therapy is the mainstay of treatment. Initial therapy should consist of topical broad-spectrum antibiotic ointment to help reduce the secondary bacterial infections that commonly develop. Topical artificial tear ointments, used three to four times daily, will help keep the cornea of most horses healthy. However, it must be stressed to the owners the importance of the continued use of the medication. Use of topical 0.25% pilocarpine, vitamin A, and acetylcysteine used once a day have been recommended for treatment of horses with KCS [5]; however, their efficacy has not been reported. Topical cyclosporine A (CsA) has also been recommended in equine KCS with reports of improvement of clinical signs [150]. However, because horses have never been documented to have primary lacrimal adenitis as an etiology for their KCS, the pathophysiology by which topical CsA may improve clinical signs is not completely understood. Use of topical corticosteroids may also initially improve clinical signs of KCS, but should be used with extreme caution because of the risk of development of corneal ulceration in KCS eyes. Occlusion of the NL puncta by cauterization has been recommended for mild cases [5], but the efficacy of this technique is unknown. In horses with facial nerve deficits, loss of corneal sensation, or chronic unrelenting KCS, a temporary or permanent lateral tarsorrhaphy may help protect the cornea. A parotid duct transposition (to provide salivary secretion to the corneal surface) has been attempted in a horse, but long-term results were not reported [157]. In severe cases of dry eye that do not respond to therapy and are persistently painful, enucleation of the eye should be considered.

Prognosis

Acute KCS associated with trauma, anesthesia, or systemic disease generally will resolve as the horse recovers from its primary disease. KCS associated with increased evaporation of tears due to lagophthalmos or loss of corneal sensation will resolve if, and when, the neurologic disease resolves. Generally, neurologic causes of KCS resolve in 3–4 weeks. Regardless of the cause or

duration, it is imperative that the cornea be kept moist and well protected, or chronic keratitis/conjunctivitis will result. In chronic cases of equine KCS, most horses will develop progressive corneal edema, vascularization, corneal ulceration, and/or fibrosis with resultant decreased vision. Enucleation may be indicated to restore comfort to chronically painful, blind horses affected by KCS.

Adnexal neoplasia

Approximately 10% of equine neoplasms affect the eye or periocular structures [158, 159]. Neoplastic adnexal disease represents the most common, and certainly often the most frustrating, of all equine eyelid diseases [126, 127, 132, 137, 139–142, 160–164]. The most common periocular masses include sarcoid, SCC, papilloma, lymphosarcoma (LSA), and melanoma [2, 5, 26, 128, 158, 159, 165]. Identical treatments administered to similarly appearing tumor types can have different clinical outcomes. Why one horse responds well to therapy and another does not warrants further study. Variability in clinical response is likely one important reason why a myriad of different treatment options exist for any given equine neoplasm [160]. It is difficult to draw definitive conclusions regarding biologic behavior or response to treatment from reviewing the veterinary literature. Study design varies widely and may be limited to isolated case reports [166, 167]. Very few reports exist with greater than 100 horses included and containing at least a year (or longer) follow-up time after specific therapy for a particular tumor type has been used [168]. This is in stark contrast to the studies that are routinely published in physician ophthalmology [169]. Treatment efficacy is challenging to critically assess because some studies are not designed with a control population for adequate comparison purposes and are often based on a subset of cases referred to specialty/teaching hospitals. Referral cases are frequently those that are refractory to "conventional" treatment modalities and may have already undergone treatment prior to being included in the study; therefore the population of horses examined is skewed. Methods of data reporting (i.e., recurrence rate versus disease-free interval) also vary among publications. The reader should be aware of these limitations when reviewing the literature.

Sarcoids

Sarcoids, cutaneous tumors of fibroblastic origin, are the most common neoplasm of horses [165, 170, 171]. They often have proliferative and hyperplastic epithelial components, and while metastasis is rare, recurrence is common, especially with the more invasive lesions. Size and location dictate their clinical significance. Periocular/eyelid sarcoids are common and may result in significant pathology to the eye, either by disrupting normal eyelid function or by directly rubbing on the eye (i.e., "mass" effect) [172–174]. In one series, periocular sarcoids represented 14% of total sarcoids [175]. Due to the close proximity of periocular structures to the globe, some treatments reported for use on sarcoids elsewhere on the body cannot be used on eyelids without risking significant damage to the globe [168].

Clinical appearance and diagnosis

The clinical appearance of sarcoids varies and they are most commonly classified into five broad categories: occult, verrucose, nodular (A and B), fibroblastic (A and B), and mixed equine sarcoids. [168, 176]. Occult sarcoid appears as an alopecic area with fine epidermal nodules. Verrucose sarcoids are thickened and hyperkeratotic with extensive flaking of the skin. Nodular type A sarcoids (Figure 6.50) are well defined, ovoid, and entirely subcutaneous, while type B sarcoids are similar but involve the epidermis (Figure 6.51). Fibroblastic sarcoids appear fleshy and ulcerated and can be pedunculated (type A) or have a broad base (type B) (Figure 6.52). Mixed sarcoids have one or more of the features of the other types of sarcoids (Figure 6.53). Periocular sarcoids are most commonly nodular, fibroblastic, or mixed. Sarcoids usually develop in young horses between 3 and



Figure 6.50 A nodular type A sarcoid in the upper medial eyelid. Nodular type A sarcoids are well defined, ovoid, and entirely subcutaneous.



Figure 6.51 A nodular type B sarcoid in the upper medial eyelid and medial canthus. Nodular type B sarcoids are well defined, ovoid, and involve the epidermis.



Figure 6.52 Fibroblastic sarcoids appear fleshy and ulcerated and can have a pedunculated (type A) or a broad base (type B). Here is a type A fibroblastic sarcoid.



Figure 6.53 An extensive mixed type (i.e., features of one or more types of sarcoids) of the medial upper eyelid and medial canthus of a horse with significant facial involvement.

6 years of age; however, horses as young as yearlings have developed sarcoids [175]. Nearly all breeds have been reported to develop sarcoids. Quarterhorses, Appaloosas, and Abrabians may be at increased risk, while Standardbreds may be at decreased risk [177, 178].

Differential diagnosis and methods for definitive diagnosis

A surgical biopsy is always required for definitive diagnosis. Exuberant granulation tissue may be present and difficult to distinguish clinically from sarcoid [175]. Histopathology should be used to rule out other eyelid mass lesions such as habronemiasis, melanoma, SCC, papilloma, and orbital fat prolapse. Histologically, all clinical types of sarcoids have increased density of dermal fibroblasts (i.e., fibroblastic proliferation). Epidermal hyperplasia, hyperkeratosis, and rete peg formation were only found consistently in the verrucous and mixed types but not consistently in occult and nodular sarcoids in one study [176]. Sarcoids commonly invade the subcutis and the deeper muscular structures around the eye [168, 179].

Pathogenesis

The pathological features are generally considered to be well established; however, debate remains over possible etiologies. Sarcoids have long been thought to have a viral origin. This infectious origin was supported by the fact that epizootics have occurred in individual herds [175, 180]. Numerous studies have associated bovine papilloma virus (BPV) with equine sarcoids [175, 176, 181–190]. Intradermal inoculation of horses with cell-free extracts from bovine skin tumors caused by BPV resulted in lesions that clinically and histologically resembled equine sarcoids [181, 183, 191]. BPV has not been found in natural cases of equine sarcoid by electron microscopy [175], but DNA sequences of BPV (types 1 and 2) have been found in equine sarcoid by southern blotting and PCR techniques [185–190, 192–194]. Equine sarcoids appear to contain detectable viral DNA and RNA; they are also known to express the BPV types 1 and 2 major transforming protein E5, but appear not to produce infectious virions [175, 186–190, 193]. In one study, no mutations of the tumor-suppressor gene p53 were identified in equine sarcoids, suggesting that p53 mutations do not have a primary role in the pathogenesis of this tumor [195]. However, the authors speculated that the high BPV infection in equine sarcoids may indicate the functional inactivation of p53 by BPV-encoded E6 protein [195]. Another study found that no telomerase activity could be detected in equine sarcoids, suggesting that telomerase does not play a major role in pathogenesis [196].

Genetic predisposition has been reported. Sarcoid occurrence was associated with the major histocompatibility complex (MHC) encoded class I equine leucocyte antigen (ELA) W3 B1 haplotype in Irish, Swiss, and French-bred Warmbloods [197]. An association between sarcoid susceptibility and the MHC encoded class II allele ELA W13 has also been found in several breeds [175, 198]. An association between early-onset sarcoids and A5 ELA increased recurrence rates after surgery and W13 ELA, and increased prevalence of sarcoid and A3W13 ELA has been reported [199]. Another study demonstrated correlation between the development of sarcoids and heterozygosity for the equine severe combined immunodeficiency (SCID) allele [200].

Treatment

Various therapies have been reported (Table 6.7) and are summarized in the following sections.

Table 6.7 Literature review of treatment for periocular sarcoids in horses.

Medical therapy

Type of therapy	Drug	Dose	Number of cases	Percentage of nonrecurrence
Topical therapy	AW4-LUDES ointment [168]	Once daily for 5 days	146	35
	5% 5-Fluorouracil [168]	Bid × 5 days, then qd for 5 days, then QOD for five applications	9	67
Immunotherapy	BCG [173]	1.0 mL/cm^2 of tumor surface every 2–4 weeks	26	100
	BCG [168]			
	Ocult, verrucose, mixed	1.0 mL/cm^2 every 2–4 weeks	52	0
	Nodular or fibroblastic	1.0 mL/cm^2 every 2–4 weeks	300	69
Chemotherapy	Cisplatin [209]	1 mg/cm^3 every 2 weeks for four treatments	19	95
	Cisplatin [168]	1 mg/cm^3 every 2 weeks for four treatments	18	33

Surgical therapy

Type of therapy	Description	Number of cases	Percentage of nonrecurrence
Surgical excision [170]	Excision	–	50
Surgical excision [168]	Excision	28	18
Cryotherapy [219]	Double or triple freeze–thaw to –25°C	–	–
Cryotherapy [168]	Double or triple freeze–thaw to –25°C	23	9
Hyperthermia [168]	Tissue temperatures between 41°C and 45°C	2	0

Brachytherapy

Radioisotope	Dose	Number of cases	Percentage of nonrecurrence
^{222}Radon seeds [228]	6000 cGy	19	92
^{198}Gold seeds [230]	7000 cGy	19	90
^{192}Iridium seeds [174, 227]	60 Gy	115	87, 100
^{192}Iridium pins [168]	7000–9000 cGy	53	98

BCG, Bacille Calmette-Guérin; bid, twice daily; qd, every day; QOD, every other day.

Topical medical treatment Several topical substances (e.g., oil of rosemary, arsenic powder, engine grease, tea tree oil), mostly irritants, have been used for treatment of sarcoids [5, 168]. A popular topical product, XXTERRA™ (Larson Laboratories, CO) has Bloodroot (*Sanguineria canadensis*) as the active ingredient. The topical herbal substance irritates the sarcoid, which stimulates the immune system to mount a response to the tumor. Anecdotally, there has been a 95% response rate. Because these substances are irritating, they induce severe keratitis and should not be used on or near the eye. AW4 ointment, which consists of 10% 5-fluorouracil and oil of rosemary (once daily for 5 days) was used in 146 periocular sarcoids in one study and resulted in a nonrecurrence rate of 35% [168].

Immunotherapy Immunotherapy (e.g., *Mycobacterium* cell wall extracts, live whole-cell bacille Calmette-Guérin (BCG), proprionibacterial cell wall extracts) has been successfully used to treat equine sacroids. [168, 172, 173, 175, 201–206]. These products are believed to stimulate the immune system to recognize tumor cell-specific antigens, thereby enhancing tumor cell destruction. The most common immunotherapy for periocular sarcoids has been the injection of BCG [168, 173, 202–204, 206]. The administration technique is to saturate the tumor with BCG typically at a dose of 1.0 mL/cm^2 of tumor surface (Figure 6.54) [173]. The injection is repeated at variable intervals (most commonly every 2–4 weeks) until complete regression of the tumor occurs. In one study, complete regression was observed in 100% of periocular tumors in 31 horses, with an average of 11.7 mL per treatment, 3.2 treatments per tumor, and a range of 14 to 252 days to achieve remission [173]. Local and systemic anaphylaxis has been noted especially after the second injection [203]. Pre-treatment with flunixin meglumine, antihistamines, and/or corticosteroids may be required.

Other substances have been used for immunotherapy in the treatment of sarcoids and include autogenous tumor vaccines, other mycobacterial cell-wall fragments, recombinant human



Figure 6.54 Pre-placed needles for infiltration with BCG or cisplatin of a nodular sarcoid.



Figure 6.55 Post-operative after surgical excision of a large medial periocular sarcoid.



Figure 6.56 Same horse as shown in Figure 6.55 after excision of a large mixed sarcoid and three intralesional cisplatin treatments.

tumor necrosis factor (TNF alpha), and xanthate compounds [172, 203, 207]. In a large review of periocular sarcoids [168], immunotherapy with intralesional BCG had poor results with verrucose, occult, and mixed sarcoids, while BCG immunomodulation therapy for fibroblastic and nodular lesions had a good overall response of 69% (Table 6.7). Side-effects observed included sinus tracts in 15% of cases and transient swelling after injections [168].

Chemotherapy Intralesional cisplatin has been the most common type of chemotherapy used for sarcoids. [174, 208–210]. Use of topical 5-flurouracil (5-FU) has also been reported, with six of nine verrucose and occult sarcoids demonstrating good response [211]. However, only those sarcoids away from the eye and eyelid margins should be treated with 5-FU because of the irritating qualities of the drug. Injection with an oily emulsion of cisplatin consisted of four treatments at 2-week intervals at a dose of 1 mg cisplatin/cm^3 of tumor tissue [209]. Cisplatin injections are performed in a manner similar to the technique described for BCG injection (Figures 6.54, 6.55, and 6.56). Complete regression was observed in 95% of the sarcoids, with a 1-year relapse-free rate of 87% [209]. Side-effects or toxicity associated with the chemotherapy were deemed minimal [209]. Electrochemical stimulation may enhance the effectiveness of cisplatin chemotherapy of sarcoids [208]. Following cisplatin injection, an electropulsator was used to deliver pulses of 0.1 ms at a 1-Hz frequency with a 1.3-kV voltage to the sarcoid. Although an excellent regression of the tumors was noted, the effect on the eye and the tolerance of a horse to the electrostimulation of the sensitive periocular tissues was not reported. In a review of 18 periocular sarcoids, use of intralesional chemotherapy resulted in nonrecurrence in 33% [168]. Cisplatin beads have also been reported for use in equine cutaneous tumors, including sarcoids and SCC [212].

Surgical excision In general, surgical excision (Figures 6.55 and 6.56) without adjunctive therapies (e.g., cryotherapy, interstitial irradiation, immunotherapy, cryotherapy) is not recommended and has an approximately 50% recurrence rate by 1 year [170]. In a review of 28 periocular sarcoids treated by surgical excision alone, a recurrence rate of 92% was found [168]. Split-thickness autogenous skin grafts improved cosmetic results after excision of sarcoids and there were no recurrences

in the three horses in one study [213]. Carbon dioxide laser ablation of sarcoids has a lower recurrence rate than surgical excision alone; however, unless the skin is closed primarily, exuberant granulation may develop [175, 214]. Early onset, long duration, and large size all appeared to increase risk of recurrence [199] and there may be a greater likelihood for local recurrence when sarcoids have a surgical margin that is positive for BPV DNA [193]. Surgical resection and photodynamic therapy has also been used to treat periocular sarcoids in a limited number of cases with favorable results [215].

Cryotherapy Cryotherapy is a commonly used surgical treatment for sarcoids, either alone or following surgical debulking of the tumor. [5, 168, 216–218]. The sarcoid is destroyed and the ensuing eschar separates from the underlying granulation bed. Healing following cryotherapy always occurs by second intention. Principles of cryotherapy to ensure proper freezing include a double or triple freeze–thaw cycle with a rapid freeze and slow thaw. Second, tissues must be frozen to at least −25°C, and the frozen area should encompass a margin of 0.5 cm around the tumor periphery [219]. Use of thermocouple temperature needles is recommended to ensure that the desired tissue temperature is achieved. Two commonly used types of cryotherapy are nitrous oxide and liquid nitrogen. Delivery of cryotherapy for equine sarcoids is recommended via a probe. If nitrous oxide is used, increased time and overlapping of the sites must be allowed for to compensate for the slow freezing and lack of penetration [219]. Liquid nitrogen provides a faster freeze and can achieve tissue temperatures that are substantially lower (approximately −200°C) than those obtained with nitrous oxide (approximately −80°C). Care must be taken to not cause tissue necrosis of the eyelid by overfreezing the eyelid margin. Sloughing of tissue will occur 2–4 weeks after cryotherapy and tissue depigmentation may remain for 6 months or more. Repeated treatments may be required for large or recurrent lesions [220].

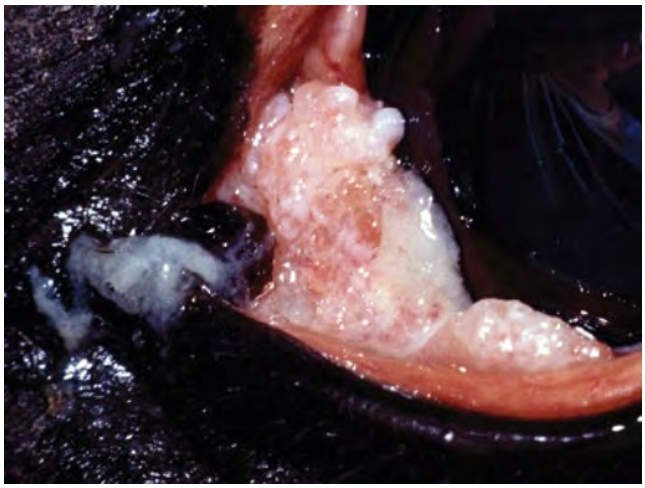
Hyperthermia Neoplastic tissues are more sensitive to elevated temperatures than normal cells, and temperatures between 41 °C and 45°C will preferentially destroy neoplastic tissue but not normal cells [219]. Minimal changes were seen on the normal equine eye from hyperthermia [221]. There have been several studies evaluating hyperthermia in the treatment of equine SCC [2, 5, 222, 223], but only a few with treatment of sarcoids. In a review of periocular sarcoids, two were treated by hyperthermia and both of them recurred [168]. In another case series, 10/11 sarcoids demonstrated no evidence of tumor regrowth after final hyperthermia treatment, and the authors recommended initial surgical debulking with a minimum of five hyperthermia treatments at 2- to 4-week intervals, with the first hyperthermia treatment to be performed prior to wound bed closure [224].



Figure 6.57 Iridium implants for treatment of a lower eyelid sarcoid. The plastic tubes are pre-placed and then the iridium inserted. Total treatment time is typically 7 days and then the tubes are removed.

Brachytherapy Brachytherapy uses small gamma radioactive sources that are placed on or within neoplasms, allowing a high dose of radiation to be delivered to the tissue and minimal radiation exposure to surrounding tissues [174, 219, 225–227]. The radioactive sources are usually removed once the desired dose is delivered to the tissue. The length of time that is required depends on the isotope used. Isotopes that have been used include ^{198}gold, ^{192}iridium, ^{222}radon, ^{137}cesium, and tantalum [219, 228]. ^{192}Iridium is most commonly used and the isotope is contained within stainless-steel rods at 1-cm intervals in a plastic coating or within needles which are placed in the tumor in parallel rows approximately 1 cm apart (Figure 6.57) [174, 226, 229]. ^{192}Iridium has a half-life of 74.2 days and typical doses of 5000–9000 cGy take approximately 7–14 days of implantation prior to removal [229].

A 94% tumor-free incidence at 1 year in 16 sarcoids was found in one study [229]. In a study of periocular sarcoids treated by ^{192}iridium brachytherapy at a dose of 60 Gy (minimum dose), the 1- and 5-year progression-free survival rates for sarcoids were 86.6% and 74.0%, respectively [174]. In another study of periocular sarcoids that received ^{192}iridium brachytherapy (n=53) a nonrecurrence rate of 98% was found [168]. In a more recent study, eight horses with periocular sarcoids were successfully treated with ^{192}iridium interstitial brachytherapy [227]. Use of other brachytherapy modalities in sarcoids have had similar results (Table 6.7) [174, 225, 226, 228–231]. Side-effects of the radiation therapy are uncommon, but some chronic ocular effects such palpebral fibrosis, cataract, keratitis, corneal edema, bone sequestrum, and corneal ulceration have been reported [168, 174, 232]. Special licensure, isolation requirements, possibility of human radiation exposure, overall cost, and availability make this treatment option more challenging in some cases.



(A)



(B)

Figure 6.58 (A) An infiltrating third eyelid SCC. (B) Four weeks after total excision the third eyelid and simple continuous closure of the conjunctiva. (*Source*: Photographs courtesy of Dr Riccardo Stoppini.)

Prognosis

Failure to induce complete regression of periocular sarcoids will frequently result in regrowth of the tumor and recurrence may be more aggressive (i.e., extensive local infiltration and faster growth). Therefore, if treatment is pursued, potent and aggressive therapy is recommended from the outset of treatment to more quickly destroy the tissue and prevent recurrences [168]. Patients should be closely monitored with regular follow-up examinations and retreatment promptly initiated if recurrence is noted [139]. However, the clinician must be aware that the extensive debulking around the eye is not possible due to the horse's facial anatomy/lack of skin-flap surgical options. Certain treatment methods, such as surface irritants, should be used with great caution in the vicinity of the eye, lest the globe be secondarily damaged and vision compromised [168].



Figure 6.59 Large proliferative lateral limbal SCC.

Squamous cell carcinoma

SCC is the most common neoplasm of the equine eye and ocular adnexa [128, 233], and the second most common tumor of the horse overall [158]. At one institution, ocular SCC represented approximately 10% of all equine ocular disease [7].

SCC may involve the corneoconjunctiva, bulbar conjunctiva, third eyelid, and eyelids [128, 232]. Biological behavior of ocular SCC is reported to differ depending on location [235], with the prognosis for eyelid SCC worse compared to the other sites of the eye [236]. Typically, SCC is locally invasive and slow to metastasize [165]. Metastasis to local lymph nodes, salivary glands, olfactory regions, and lungs can occur [164, 237, 238].

Clinical appearance and diagnosis

Increased prevalence of SCC is associated with various environmental factors, including geographic influences of increased longitude, decreased latitude, increased altitude, and increased mean annual solar radiation exposure [88]. An increased prevalence of ocular SCC may occur with age, and a breed predilection for draft breeds and Appaloosas has been reported [7, 88]. Horses with light hair and minimal skin pigmentation have higher prevalence of ocular SCC [7, 88]. Mean equine age at diagnosis with ocular/periocular SCC has been reported to be 9.8 years [237], 11 years [239], 11.8 years [7], and 11.1 years [88], with a range of 3–26 years [240]. Gender predisposition of ocular SCC is unknown. One study noted a high prevalence of SCC in geldings, double the rate of mares and five times that of stallions affected, suggesting the possibility that endogenous sex hormone levels may be associated with ocular SCC development in the horse [88]. However, this finding may simply reflect gender distribution of the general client-owned equine population. Other studies have found no gender predisposition differences [223, 241]. Unilateral involvement is most common, but in one study bilateral ocular SCC was observed in 16% of horses [236]. The most common ocular locations for SCC are the nictitating membrane and medial canthus (approximately 28%) (Figure 6.58), limbus (approximately 28%) (Figure 6.59), lower



Figure 6.60 Lower eyelid SCC in a Paint horse. Notice how the neoplastic tissue involves only the nonpigmented eyelid margin and stops where the pigmentation begins.



Figure 6.61 Focal, proliferative, papillomatous inferior eyelid SCC.

eyelid (approximately 23%) (Figures 6.60 and 6.61), and other locations (21%) (i.e., cornea, conjunctiva, orbit) [7, 128, 236, 242].

Actinic solar keratitis may transform to carcinoma *in-situ* SCC (see Figure 6.36) that often appears as hyperemic eyelid erosive plaques with dark-staining crusts. These lesions frequently undergo further cellular change to become papillomatous SCC (see Figure 6.61); alternatively, SCC may appear as a raised mass with a pink, cobblestone appearance (see Figure 6.59) and may progress to large, fleshy masses, with variable degrees of ulceration, necrosis, and inflammation that can infiltrate the orbit (Figure 6.62) [5, 235, 243–245]

Differential diagnosis and methods for definitive diagnosis

SCC should be suspected with any erosive, erythematous, or raised ocular mass [139, 243]. Atypical, pigmented SCC has been reported [246], emphasizing the need for histologic confirmation of all abnormal periocular and ocular lesions. Differential diagnosis for SCC includes other tumors (papilloma, melanoma, mastocytoma, basal cell carcinoma, schwannoma, adenoma and adenocarcinoma, hemangioma and hemangiosarcoma, lymphoma and LSA), conjunctivitis (lymphoid hyperplasia, follicular conjunctivitis), inflammatory lesions (abscesses, granulation tissue, foreign body reaction, solar-induced inflammation), and parasites (*Habronema*, *Onchocerca*, *Thelazia*) [5, 75, 128, 129, 135, 136, 139, 168, 243, 247–251].



Figure 6.62 Belgian horse affected by an extensive third eyelid SCC with orbital invasion.

Histologically, SCC has been subdivided into four basic types: plaque (i.e., carcinoma *in situ*), papillomatous, noninvasive SCC, and invasive SCC [252]. Plaque formation involves primarily the proliferation of the stratum spinosum; however, all layers of the epithelium can be proliferative. Papilloma formation will occur when underlying connective tissue invades hyperkeratotic epithelium. Noninvasive SCC exhibits malignant transformation of the basilar layer of the epithelium with development of hyperchromatic nuclei, increased mitotic figures, pleomorphism, and loss of polarity. Invasive SCC extends past the basal epithelium into the subepithelial tissue and can have variable degrees of differentiation. Well-differentiated neoplasms are characterized by whorl formation, keratinized foci (i.e., "keratin pearls"), and intercellular bridges (Figure 6.63). In poorly differentiated SCC, neoplastic cells are frequently arranged in cords or nests, but have minimal cellular keratinization [252]. An inflammatory infiltrate composed mostly of $CD3^+$ T lymphocytes, $CD79^+$ B cells, macrophages, and numerous immunoglobulin (IgG) plasma cells is commonly associated with SCCs [253]. In one study, no significant correlation was found between the nature of the inflammatory infiltrate and the SCC histological grade or degree of invasion [253]. However, expression of MHC class II by neoplastic epithelial cells may induce an improved local antitumor immune response [253].

Pathogenesis

Any chronic irritation may promote neoplastic transformation of epithelium into SCC, especially at mucocutaneous junctions. Unlike sarcoids, equine SCC has not been shown to exhibit viral antigens [254], though some evidence suggests that a viral

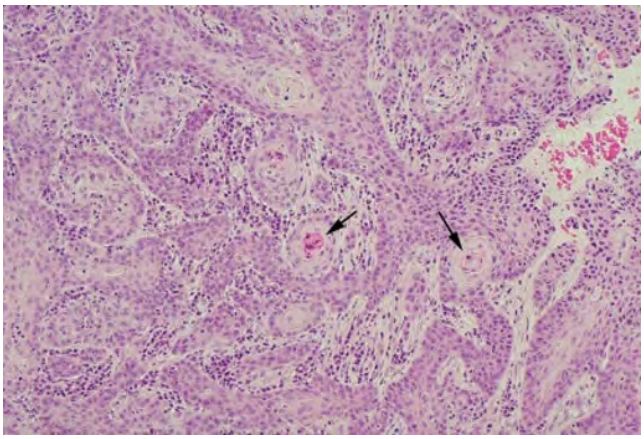


Figure 6.63 Histologic section of an eyelid SCC (H&E stain, 400× magnification). This well-differentiated neoplasm is characterized by whorl formation, keratinized foci (i.e., "keratin pearls" (**arrows**)), and intercellular bridges.

etiology may play a role in SCC pathogenesis [255]. Irritation from actinic and/or UV radiation has been thought to promote the development of SCC. Clinically, horses living at higher elevations with increased sunlight exposure have a higher incidence of SCC [88]. Overexpression of the tumor suppressor protein p53, possibly mutated due to UV radiation, plays an important role in SCC development in many animals [34, 195, 256, 257]. The p53 antigen has been detected immunohistochemically in formalin-fixed tissues of SCCs of domestic animals [195, 256, 257]. In two separate studies, 100% of equine ocular SCCs overexpressed p53 [34, 257].

The role of cyclo-oxygenase (COX) in the pathogenesis of equine SCC is still undetermined. COX are a family of enzymes responsible for conversion of arachidonic acid to prostaglandins, and multiple isoforms exist, with COX-1 and COX-2 being the most biologically active [258]. High levels of COX-2 expression have been detected in many human and veterinary neoplasms, including SCC of the head and neck [259]. Correlations have been made in humans with head and neck SCC between overexpression of COX-2 in neoplastic tissues and poor prognostic factors [259]. A limited number of investigations specifically examining the role of COX in naturally occurring equine ocular and periocular SCC have been conducted to date [60, 258, 261] and interest in this area appears to have arisen largely from a single case report [166]. One report examined three equine conjunctival SCC, as well as specimens from other affected regions, and from normal horses [261]. In that study, all tissues, both nonneoplastic and SCC tissues, expressed both COX-1 and COX-2 proteins [261]. A second study found weak positive immunostaining of COX-2 expression in 6 of 22 ocular SCC and all positive samples were from corneal specimens [258]. A third immunohistochemical study examined 15 SCC-affected tissues (five corneal, five eyelid, and five third eyelid) against site-matched controls and found immunoreactivity for both COX-1 and COX-2 to be significantly greater in affected equine corneas compared to control corneas, but no significant differences were detected in COX-1 or COX-2 reactivity in the eyelid or third eyelid SCC compared with site-matched controls [260].

Treatment

Treatment is variable, and commonly reported therapies are summarized in Table 6.8 and described in more detail in the following paragraphs. Eyelid tattooing in horses with little to no eyelid pigmentation may afford some protection against the development of periocular SCC; however, more research is needed [262].

Immunotherapy Historically, immunotherapy for ocular SCC has not been employed as commonly as for equine sarcoids. [236, 242, 263]. Immunotherapy, when used, should be limited to SCC affecting the eyelid only, to avoid globe injury. The most common immunotherapy for ocular SCC has been injection of BCG, although other "vaccines" have been used [236, 242, 263]. The goal of treatment for eyelid SCC using BCG is identical to that described for equine sarcoids (see section **Sarcoids**) [173].

Chemotherapy Intralesional cisplatin has been the most common type of chemotherapy used for treatment of ocular SCC [210, 264]. Treatment with an oily emulsion of cisplatin for SCC is identical to what is described for equine sarcoids (see section **Sarcoids**). Complete regression was observed in five of seven cases (71%), with a 1-year relapse-free rate of 65% (Table 6.8) [209]. Side-effects and toxicity associated with the chemotherapy were deemed minimal [209]. Another study found no difference in outcome between tumors that were injected immediately after cytoreductive surgery versus those treated after the skin had healed, except in aggressive tumors that had cellular regrowth within the post-operative period [210]. Therefore it is recommended that cisplatin treatment immediately follow surgery when tumor proliferation index is not known [210].

Other chemotherapeutic agents for equine SCC include 5-FU, mitomycin C, and piroxicam [160]. Use of topical 5-FU has also been successfully used on SCC of the external genitalia [211], but there are no published reports of the use of 5-FU on ocular tissues with SCC. Recently, a study examining the effectiveness of mitomycin C as an adjunctive therapy to CO_2 laser ablation treatment of ocular SCC in eight horses reported a success rate of 70%, with follow-up times ranging from 11 to 24 months [265]. To the author's knowledge, mitomycin C use in the treatment of adnexal SCC had not been reported to date. A single case of successful treatment (i.e., no recurrence 5 years following therapy) of metastatic SCC (i.e., from the primary site at the lip to the submandibular lymph nodes) with oral piroxicam (80 mg orally every 24 hours) has been reported [166]. After 90 days of treatment, the primary and metastatic SCC had resolved. Several bouts of colic occurred and the piroxicam was

Table 6.8 Literature review of treatment for ocular SCC in horses.

Medical therapy

Type of therapy	Drug	Dose	Number of cases	Percentage of nonrecurrence
Immunotherapy	BCG [263]	1.0 mL/cm^2 of tumor surface every 2–4 weeks	1	100
	Noncommercial vaccine [236]	–	2	–
Chemotherapy	Cisplatin [209]	1 mg/cm^3 every 2 weeks for four treatments	7	71

Surgical therapy

Type of therapy	Description	Number of cases	Percentage of nonrecurrence
Surgical excision [223]	Excision	18	56
Cryotherapy [223]	Double or triple freeze–thaw to –25°C	6	33
Cryotherapy [274]	Double or triple freeze–thaw to –25°C	5	100
Cryotherapy [272]	Double or triple freeze–thaw to –25°C	3	67
Hyperthermia [223]	Tissue temperatures between 41°C and 45°C	1	100
Hyperthermia [222]	Tissue temperatures between 41°C and 45°C	8	75
CO_2 laser ablation [269]	Ablate tissue	4	100
Photodynamic therapy [241]	Match PDT agent to laser of appropriate wavelength	10	100

Brachytherapy

Radioisotope	Dose (cGy)	Number of cases	Percentage of nonrecurrence
^{60}Cobalt or ^{137}cesium [276]	5000	19	73.6
^{198}Gold seeds [230]	7000	3	100
^{192}Iridium pins [340]	7000	21	100
^{222}Radon, ^{125}iodine, or ^{192}iridium [240]	5000–10,000	10	80
^{192}Iridium [223]	–	10	75
^{192}Iridium [174]	6000	52	81.8
^{90}Strongium [341]	25,000	27	89
^{90}Strongium [240]	10,000	8	88
^{90}Strongium [342]	–	24	76
^{90}Strongium [223]	–	7	100

reduced to a maintenance dose of 80 mg orally every 48 hours indefinitely, without further gastrointestinal difficulties [166]. The usefulness of NSAIDs as inhibitors of COX in the treatment of periocular and ocular equine SCC is not known (see **Pathogenesis of disease process and progression** under section **Squamous cell carcinoma**).

Surgical treatment Surgical excision is almost always indicated to obtain definitive histologic diagnosis of any periocular/eyelid mass and to debulk total tumor size prior to administration of ancillary therapy [139, 142]. Surgical excision can be curative if the surgeon removes a 2-cm tumor-free margin on all sides of the mass. This degree of surgical margin is nearly impossible to achieve on any ocular or periocular SCC. Preservation of eyelid function is essential to ocular comfort and vision. Extensive blepharoplastic procedures, commonly used in canine patients affected by eyelid masses that involve more than one-third of the total eyelid margin, are fraught with complications in horses due to their facial anatomy. The equine facial skin is firmly attached to the underlying connective tissue and has poor superficial blood supply; thus blepharoplastic procedures (i.e., advancement flaps, rhomboidal flaps) are rarely successful and some portion of the flap will often necrose (Figure 6.64) [5, 266].

Depending on the primary ophthalmic site of SCC, tumor-free margins can be obtained with enucleation/exenteration or complete excision of a third eyelid (for focal SCC affecting the leading edge of the nictitans) [126, 138, 267]. In most cases of equine eyelid, limbal, or corneal SCC, surgical excision using sharp dissection (i.e., debulking all grossly affected neoplastic tissue) and adjunctive therapy (e.g., chemotherapy, cyrotherapy, hyperthermia, radiation, or photodynamic therapy) are recommended for optimal long-term prognosis [160, 243]. CO_2 laser ablation has been reported for use on corneal/conjunctival SCC, but not with adnexal SCC (Figure 6.65) [265, 268, 269]. If used, the surgeon must be cautious to ensure that deep corneal penetration from the laser does not occur by taking care to use the laser on a defocused setting. Corneal scarring or corneal



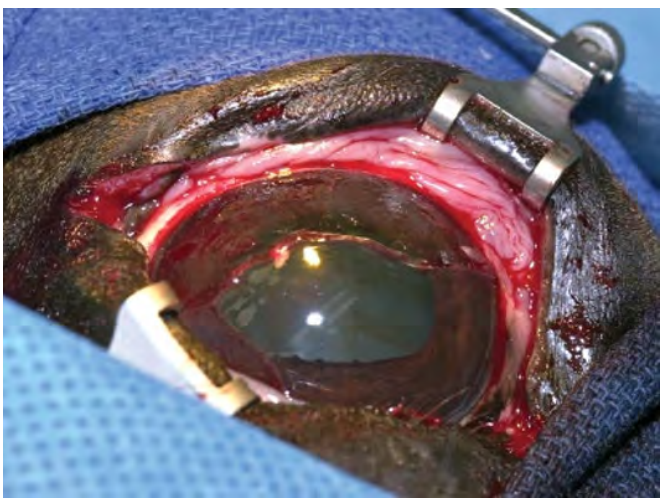
Figure 6.64 H-plasty or advancement eyelid flap for reconstruction after excision of a lower eyelid SCC. The leading edge of the flap has become necrotic, which is common after blepharoplastic procedures in the horse. (*Source*: Photograph courtesy of Dr Mike Davidson.)

perforation can occur with CO_2 laser ablation if the surgeon is not experienced with this modality. With extensive, invasive SCC, partial orbital rim resection, mesh skin expansion, and second intention healing can be used to close the large skin wounds [270]. In one study, surgical excision alone (without ancillary therapy) of the third eyelid had an SCC recurrence rate of 33% (6 of 14 cases), while 66% (two of three) of limbal SCC recurred with surgical excision alone (Table 6.8) [223].

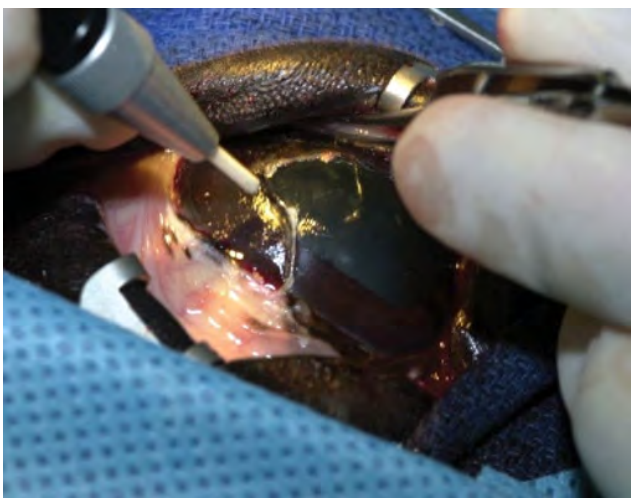
Cryotherapy Cryotherapy is a commonly used surgical treatment for ocular SCC, usually following surgical debulking of the tumor [216, 220, 223, 236, 271–273]. The technique for use of cyrotherapy for adnexal SCC is identical to that described for sarcoids using a double or triple freeze–thaw cycle (–25°C) with a rapid freeze and slow thaw (Figure 6.66) (see **Cryotherapy** under section **Sarcoids**) [219]. When treating eyelid SCC with cyrotherapy (or sarcoids), care must be taken to protect the



(A)

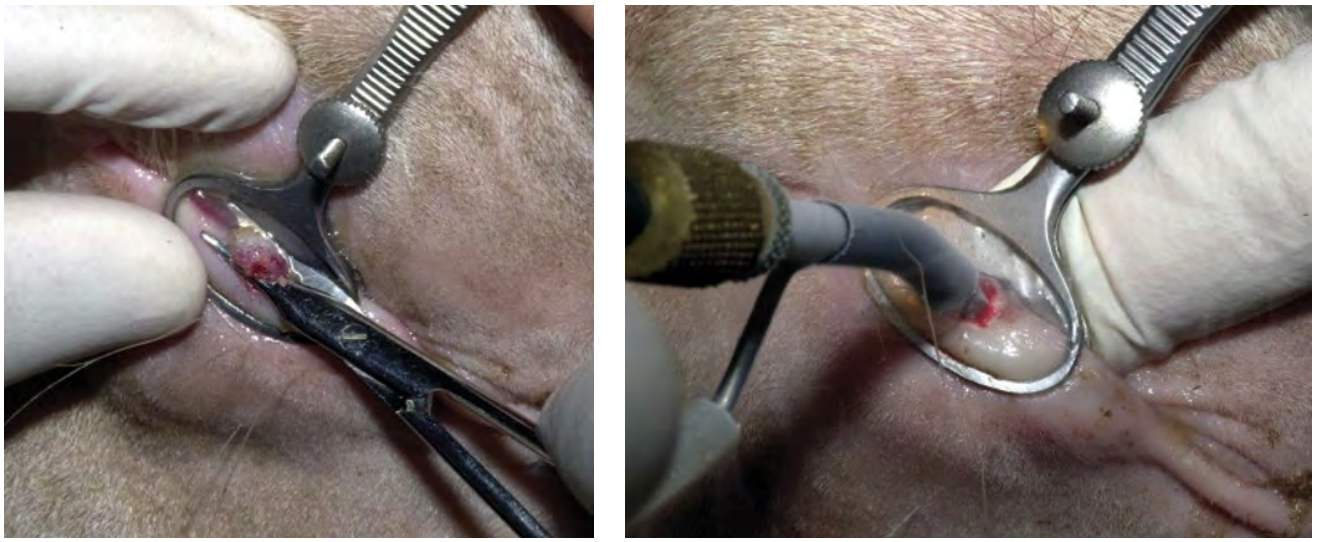


(B)



(C)

Figure 6.65 (A) Extensive lateral corneal SCC that had extended from the lateral limbus. (B) Superficial keratectomy has been performed to remove the corneal and limbal SCC. (C) CO_2 laser ablation is being performed on the surgical bed to destroy remaining SCC cells.



(A) (B)

Figure 6.66 (A) Surgical debulking of a papillomatous lower eyelid SCC using a chalazion clamp and Stevens tenotomy scissors. (B) Following surgical debulking, the tumor bed is treated with cryotherapy (double freeze–thaw cycle).

underlying cornea. Often, corneal protective devices are crudely fashioned using sections of a styrofoam cup and a liberal amount of sterile lubrication. Repeated treatments may be required for large or recurrent lesions [220]. In three small studies of ocular SCC treated with cryotherapy, one of three (33%) [272], one of six (17%) [223], and none of five [274] cases had recurrence (Table 6.8).

Hyperthermia Hyperthermia has been used as an adjunctive therapy for equine sarcoids and bovine and equine SCC [224]. It has been recommended for eyelid, conjunctival, and limbal SCC, but not for SCC with deep penetration [222]. Temperatures between 41°C and 45°C will preferentially destroy neoplastic tissue but not normal cells [219]. Typically, a radiofrequency hyperthermia device is placed against the tissue and it is heated to 50°C for 30 seconds. Minimal changes were seen on the normal equine eye from hyperthermia [221]. There have been several studies evaluating hyperthermia in the treatment of equine SCC [5, 222, 223, 236]. In one study, ocular SCC in eight horses was treated by radiofrequency hyperthermia, resulting in 75% complete regression and 25% partial regression. Complete regression occurred in 66% of tumors given a second hyperthermia treatment (Table 6.8) [222].

Brachytherapy Brachytherapy uses small gamma radioactive sources that are placed on or within neoplasms, allowing a high dose of radiation to be delivered to the tissue and minimal radiation to surrounding tissues (see Figure 6.57) [219, 275]. Brachytherapy is recommended for eyelid and conjunctival SCC, but not for limbal and orbital SCC. The type of radioactive sources, surgical technique, and complications of brachytherapy for use with ocular SCC are identical to those described for sarcoids [174, 225, 230, 240, 276–278]. Brachytherapy has been successful and often has some of the highest non-recurrence rates of any ancillary therapy for equine ocular SCC (Table 6.8). However, the high cost, limited availability, licensure issues, and human radiation exposure risks make this mode of therapy less desirable or not a viable option in many cases.

Photodynamic therapy Photodynamic therapy (PDT) is a modality for the treatment of a variety of ailments, including solid tumors, age-related macular degeneration, and atherosclerotic plaques [279–281]. PDT involves the use of photochemical reactions mediated through the interaction of photosensitizing agents, light, and oxygen [282]. Selective uptake and retention of a photosensitizer by the target cells and microvascular endothelial cells, followed by irradiation with light of a specific wavelength, initiates necrosis and apoptosis of the target cells, vascular shutdown, and inflammation through formation of toxic singlet oxygen and free radicals [282]. Tumor selectivity in treatment occurs through a combination of selective retention of the photoactive chemical by neoplastic cells and delivery of light to a highly specific area [282].

Photosensitizers are typically administered to the patient by IV injection. However, IV injection of a photoactive drug to a horse is not deemed feasible at this time. Recent studies have investigated the use of local PDT in the treatment of equine periocular tumors in both clinical patients and a murine model [239, 241, 283–286]. In these clinical investigations, a photoactive agent is injected locally into the wound bed immediately after surgical resection of the tumor and followed by light irradiation (Figures 6.67, 6.68, and 6.69). Results of surgical resection and local PDT to date have been favorable for naïve equine periocular



Figure 6.67 Extensive lower right eyelid SCC in a 6-year-old Quarter horse.

SCC [239, 241], sarcoids [215], and in one case of eyelid melanoma [287]. However, more research is needed before PDT can be adequately compared to other more established treatment modalities for equine periocular tumors. Importantly, when one considers the photochemistry of PDT and its method of tumor cell killing, this author would not recommend PDT be used as a "rescue modality" for periocular tumors that have already undergone other forms of treatment [282].

Prognosis

Recurrence rates within a year of treatment have been reported between 50% and 66.7% with surgery alone, and range from 25% to 67% with surgery and ancillary irradiation or cryotherapy [223, 275]. A 42.4% recurrence rate for ocular SCC with surgical excision, radiofrequency hyperthermia, or both has also been reported [7]. In another study, treatments included surgical excision, surgical excision with ^{90}Sr beta irradiation, surgical excision with cryotherapy, surgical excision with radiofrequency, surgical excision with ^{137}cesium interstitial radiotherapy, and/or immunotherapy, and the overall recurrence rate was 30.4% [236]. Poorer prognosis is associated with SCC originating at the eyelid, compared to the third eyelid, nasal canthus, or limbus in one study [236]. Larger sized masses, orbital extension, and recurrent SCC were associated with lower survival times [236]. Metastasis of ocular SCC to local lymph nodes, salivary glands, and lungs can occur and has been reported in isolated cases or case series [164, 238], 6% of cases in one study [7], and 15.4% in another [237]. Metastasis occurs most commonly to the regional (submandibular) lymph nodes, salivary glands, and thorax, and as extension into the orbit, sinus, and calvarium. Local invasion of the tumor often accompanies ulcerative necrosis and inflammation, resulting in significant ocular discomfort. No single treatment modality has proven to be effective, and either the SCC itself or treatment complications may threaten both visual outcome and long-term survival.

Melanoma

Melanoma is a relatively uncommon tumor of the horse involving between 3.8% and 4.8% of total neoplasms [158, 159, 165]. In one study reviewing 84 melanomas in horses, the most common sites of occurrence were under the tail (93.9%), the perianal region (43.0%), the lips (33.0%), and the eyelids (24.0%) [288]. Melanoma is most common in horses with gray or white hair [5, 242]. A slowly progressive, cutaneous, partially alopecic, pigmented mass of the eyelids is the typical clinical appearance of most equine adnexal melanoma (Figure 6.70). The size and location of the mass will dictate the clinical signs, varying from no ocular irritation to blepharospasm and corneal irritation. Older horses are predisposed to the development of melanoma, possibly because proliferation of melanocytes is a manifestation of aging [242, 289]. Fleury et al. [290] found that melanoma development, size of mass, and number of masses were significantly correlated with older Camargue-type gray-skinned horses (a prevalence of 67% at ages greater than 15 years). Development of melanoma was not associated with gender or sun exposure [290]. In a study of 296 gray Lipizzaner horses, dermal melanomas were present in 148 horses (50%), with higher incidence in older horses [291]. A genetic predisposition for dermal melanoma was also suggested [291]. A malignant conjunctival melanoma of a horse has been described [292].

Differential diagnosis and methods for definitive diagnosis

Differential diagnoses include all other causes of eyelid tumors and swellings such as sarcoid, habronemiasis, SCC, papilloma, LSA, and orbital fat prolapse. Biopsy and histopathology are recommended for definitive diagnosis.

Equine melanomas have highly variable histologic and cytologic patterns that can make definitive diagnosis difficult. Four clinical syndromes of dermal melanomas have been described in horses: melanocytic nevus, dermal melanoma, dermal melanomatosis, and anaplastic malignant melanoma [293]. Epithelioid, round, and spindle cellular morphology occur in equine melanomas with variable and inconsistent tumor pigmentation. The site of the tumor, the depth of invasion, and the number of mitotic figures per high-power field are used histologically to predict biologic behavior. However, in one study, histologic characteristics of dermal melanomas were not predictive of malignancy in most horses [294]. Special stains may help confirm the diagnosis. Melanoma cells are usually positive for vimentin, S100, neuron-specific enolase, and Melan-A, and negative for cytokeratin [295]. Currently, there is no single definitive diagnostic test capable of differentiating between benign and malignant melanocytic neoplasms or that would serve as a predictor for survival time. In one study, most metastatic melanomas showed overexpression of p53 and demonstrated apoptosis, but no differences were observed between

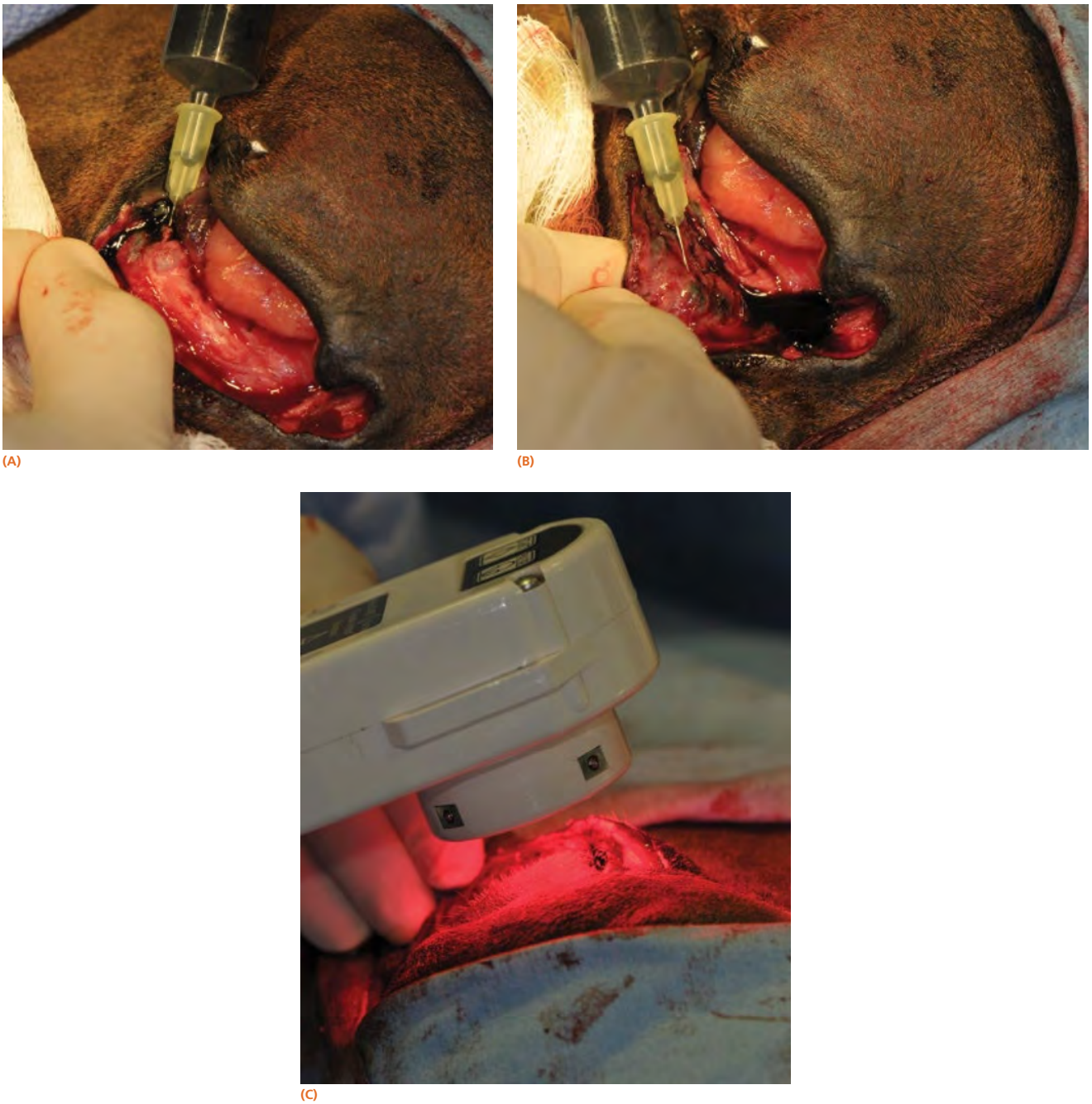


Figure 6.68 (A) After surgical debulking with sharp dissection of the SCC of the horse in Figure 6.67, Visudyne, a commercially available photoactive agent, is being carefully injected into the tumor bed using a 27-G needle to minimize extravasation of the drug during subcutaneous injection. (B) Visudyne is meticulously and thoroughly injected into the tumor bed using a 27 guage needle to minimize extravasation of the drug during subcutaneous injection. (C) Immediately following Visudyne injection, laser irradiation is performed with an LED device emitting a wavelength of 690 nm which activates the photoactive agent. It is critical to match the laser source with the photoactive agent being used, as several different photoactive agents are currently commercially available.

malignant and benign dermal melanomas in growth fraction, S-phase index, or DNA configuration [296]. It was concluded that equine melanomas had substantially different phenotypic characteristics in comparison with melanocytic tumors in dogs, cats, and humans [296].

Treatment

There are few reports of the treatment of equine adnexal melanomas, so success rates of various treatments are not known. Prior to initiating therapy, careful evaluation of the entire horse is recommended to rule out metastatic disease. Examination of



Figure 6.69 Horse from Figures 6.67 and 6.68, first day post-operative PDT therapy. Note that extensive eyelid swelling is to be expected immediately after PDT for approximately 5–7 days. Here, a Q-tip is being used to elevate the upper lid and evaluate the cornea and underlying structures.

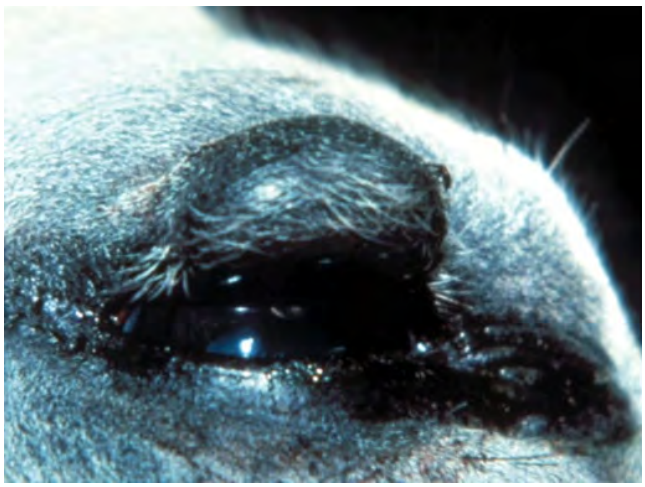


Figure 6.70 Large upper eyelid melanoma. (*Source*: Photograph courtesy of Dr Mike Davidson.)

affected horses should include a thorough skin evaluation, with particular attention to the area under the tail and perianal area, oral inspection, chest radiography and/or ultrasonography, and rectal palpation. There are no known studies on the effectiveness of intralesional chemotherapy or immunotherapy on melanomas. Oral cimetadine (dose 2.5 mg/kg of body weight orally every 8 hours) has been used to shrink nonocular melanomas in horses [297], but no studies have been published on this treatment modality for adnexal melanomas. Surgical excision, CO_2 laser ablation, cryotherapy, and PDT have been used. Success rates have not been published; however, one study described the successful removal of a nonocular dermal melanoma in a horse by CO_2 laser ablation [298]. Surgical resection and local photodynamic therapy for a lower eyelid melanoma has also been performed [287], resulting in a disease-free interval of 5 years. Excision of an eyelid melanoma is usually curative, because most of the masses are benign. However, a case report of a conjunctival melanoma described recurrence and metastasis [292].



Figure 6.71 Inferotemporal eyelid and conjunctival LSA.

Prognosis

Malignant melanoma occurs in horses 108, 109, 288, 291, 292, 294–296, 299–301], but the overall rate of malignancy is unknown. In one study, the most common sites for metastases were the lymph nodes, liver, spleen, skeletal muscle, lungs, and vascular beds [294]. Horses may have dermal melanomas for years (range 1–6 years) before developing metastatic disease [294].

Lymphosarcoma

LSA is a relatively uncommon neoplasm in the horse, especially when compared to other domestic animals, such as cows, dogs, and cats. Isolated case reports of equine adnexal LSA have been published [302–304]. LSA represented 1.3% and 4.8% of all tumors in the horse in two separate studies, respectively [158, 159]. Unilateral and bilateral ocular lesions have been reported with equine LSA [249, 250, 305, 306]. More recently, a study in which extraocular lymphoma involving the eyelid, third eyelid, cornea, sclera, and/or conjunctiva was diagnosed in 26 horses examined clinical features of this disease and prognosis [162]. Prognosis for clinical remission in horses with extraocular lymphoma was deemed fair to good, providing the affected tissues were able to be completely excised and horses did not have eyelid or cutaneous involvement [162].

Differential diagnosis and methods for definitive diagnosis

Ocular lesions occurred in 27% of horses with systemic LSA in one study [249]. Infiltration of the eyelids and conjunctiva are the most common ocular manifestation (Figure 6.71) [249, 305, 306].



Figure 6.72 Yearling Paint horse with systemic LSA with ocular and orbital invasion.

Orbital and/or third eyelid involvement can also occur (Figure 6.72) [249, 304, 306]. In a recent study, horses with extraocular lymphoma and any cutaneous or eyelid involvement had a 13 times greater chance of having a poor outcome than horses with no cutaneous or eyelid involvement [162]. Lesions to the third eyelid, corneosclera, and conjunctiva were either nodular or diffuse in nature, and nodular lesions when compared to diffuse lesions were associated with a higher chance of a positive outcome [162]. Adnexal LSA need to be differentiated from other causes of eyelid tumors and swelling such as sarcoid, habronemiasis, SCC, papilloma, melanoma, and orbital fat prolapse. Biopsy and histopathology are required for definitive diagnosis.

Pathogenesis

Immunohistochemical classification of equine malignant LSA has been reported in one study and revealed that equine LSA was composed of a heterogeneous cell population, with most tumors containing B and T lymphocytes [307]. In this study, 42% of tumors contained primarily neoplastic B lymphocytes, 35% had diffuse large B-cell lymphoma with 40–80% nonneoplastic T lymphocytes (called "T-cell-rich, large B-cell lymphomas"), and 19% had primarily neoplastic T lymphocytes [307]. Equine lymphoma, while traditionally thought of as an incurable disease, may carry a more favorable prognosis if a horse is diagnosed with conjunctival lymphoma or the disease manifests early as a solitary extraocular mass that is able to be completely excised [162]

Treatment

Treatment for horses affected with diffuse adnexal manifestations of LSA are limited. In one report with bilateral eyelid involvement, treatment with oral prednisolone (400 mg orally once daily) had no effect, but intramuscular injection of dexamethasone (30 mg every other day) resulted in marked reduction of eyelid swelling attributed to LSA during the limited time the horse received follow-up examinations [305]. In a second case report of primary bilateral third eyelid LSA, the horse underwent complete third eyelid removal and remained disease free for 3 years [304]. Localized nodular LSA that are able to be completely excised appear to carry a more favorable long-term prognosis than horses with diffuse eyelid and cutaneous involvement [162]. Further study is needed.

Prognosis

In general, the long-term prognosis for survival is poor if the disease is multicentric or disseminated [5]. The prognosis for clinical remission in horses with extraocular lymphoma in which the affected tissues are completely excised and there is no eyelid or cutaneous involvement is considered, in one study, to be fair to good [162].

Conjunctival pseudotumors or bilateral nodular lymphocytic conjunctivitis

Conjunctival pseudotumors or nodular lymphocytic conjunctivitis (NLC) appears as a unilateral or bilateral, nodular or smooth, pink, nonulcerated conjunctival mass (Figure 6.73) [308, 309]. In one study of five horses, the masses were nodular in two cases and relatively flat and more diffuse in three cases [309]. The third eyelid was involved in three cases and bulbar conjunctival and cornea in two cases [309].

Differential diagnosis and methods for definitive diagnosis

Conjunctival pseudotumors need to be differentiated from other causes of eyelid masses and swellings such as sarcoid, habronemiasis, neoplasia (e.g., SCC, LSA, papilloma, and melanoma), and orbital fat prolapse. Biopsy and histopathology are required for definitive diagnosis. Histopathologically, these lesions are characterized by nodular lymphoid components and presence of lymphocytes, plasma cells, and histiocytes [308]. The bulbar conjunctiva may be infiltrated by small nodular masses composed of dense aggregates of primarily small mature lymphocytes admixed with less mature, usually intermediate-sized, lymphoblasts, histiocytes, and rare neutrophils (Figure 6.73C). The cellular infiltrate can form follicles of lymphocytic hyperplasia. Etiologic agents should be ruled out using special stains [308, 309]. Immunohistochemical characterization of lesions in one report detected B and T lymphocytes, macrophages, and other histiocytes [308].

Pathogenesis

Equine conjunctival inflammatory pseudotumor is suspected to have an immune-mediated pathogenesis based on the characterization of inflammatory cell infiltrate and the absence of infectious agents (bacterial, fungal, or parasitic) or foreign bodies [308, 309].

Treatment

Surgical debulking and local administration of anti-inflammatory agents (i.e., intralesional corticosteriod with or without topical corticosteroids) are the mainstays of therapy. [308, 309].

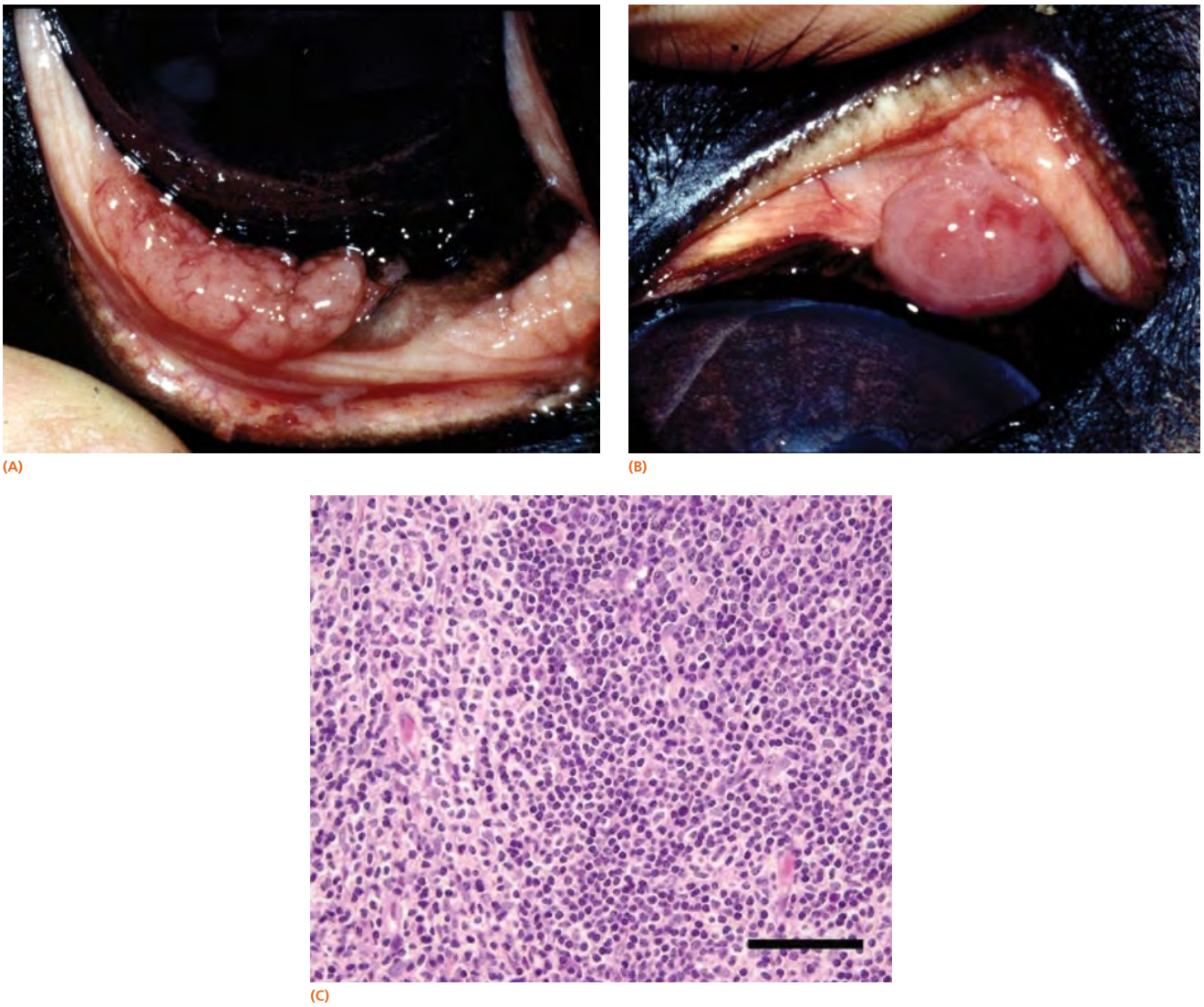


Figure 6.73 (A) Conjunctival proliferative lobulated mass at the basal portion of the third eyelid, diagnosed on histopathology as a nodular lymphocytic conjunctivitis or conjunctival pseudotumor. (B) Another proliferative conjunctival mass located at the dorsal limbus, also confirmed on histopathology as nodular lymphocytic conjunctivitis or conjunctival pseudotumor. (C) Histologically, both masses had similar findings of a heterogeneous population of mononuclear cells, with predominantly small mature lymphocytes on the right half of the field and larger histiocytes on the left half (bar = 50 mm). (*Source*: Photographs courtesy of Dr Riccardo Stoppini.)

Prognosis

The prognosis appears to be good when lesions are treated as described above [309]. Rapid recurrence is possible, requiring repeated treatment [308].

Other adnexal neoplasms

Various other equine adnexal and/or conjunctival tumors have been reported, including angiomas, angiosarcomas, hemangiosarcoma,[140, 310–315]. fibroma, fibrosarcoma, [231, 316]. adenoma, adenocarcinoma [317], lacrimal gland carcinoma [132, 158], epithelioma [163], basal cell carcinoma [318], melanoma [137], and mast cell tumors [141, 162, 235]. Similar to other mass lesions of the eyelid or conjunctiva, histopathology is required for definitive diagnosis and to rule out all previously discussed mass lesions affecting this region of the equine eye. Immunohistochemical staining can be helpful to further characterize a tumor, such as staining with factor-VIII-related antigen to confirm whether or not the mass has a vascular endothelial origin (e.g., angiomas, angiosarcomas, hemangiosarcoma) [313, 319]. Vascular neoplasms must be differentiated from intravascular papillary endothelial hyperplasia, a benign proliferative lesion [320], and venous orbital malformations [321]. Treatment varies depending on the neoplasm; however, excision with an adjunctive therapy such as cryotherapy is generally recommended.

Future research

Additional research is warranted for a wide variety of diseases affecting the equine eyelid, conjunctiva, and NL system. For example, very little is known regarding the specific genetic defect and mode of inheritance for many equine adnexal diseases, especially entropion and NLD atresia. Pharmacokinetic and ocular distribution of most systemically administered antibiotics has yet to be determined for horses. Enhanced imaging techniques represent an exciting new area of potential development in the diagnosis and treatment of many equine ocular diseases. Finally, well-designed, prospective clinical trials with adequate case numbers and appropriate case follow-up are lacking for equine adnexal neoplastic disease. The further study of equine ocular adnexal and NL disease will only improve our ability to better restore and preserve ocular comfort and vision.

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CHAPTER 7

Diseases of the cornea

Dennis E. Brooks, Andrew Matthews, and Alison B. Clode*

Introduction

The ocular surface, comprising the precorneal tear film (PCTF), conjunctiva, limbus, and cornea, and the associated adnexal structures form an integrated and optically specialized functional unit [1], and at over 2000 mm^2 in the adult horse is one of the most anatomically extensive of terrestrial mammals (Figures 7.1, 7.2, 7.3, and 7.4).

The cornea and tear film represent the interface of the visual system with the external environment, and are responsible for 70–80% of the refractive power of the adult mammalian eye. Unrestrained injury or insult typically results in loss of transparency, frequently permanently or for protracted periods, which will compromise or disable function in the affected eye. The large and exposed equine cornea is vulnerable to direct traumatic, toxic, or infectious insult, and the typically overt nature of corneal disease in the horse (namely pain and discoloration) means that corneal disease is the most common reason for elective ophthalmic examination in first-opinion equine clinical practice. Inflammation can compromise corneal function by destroying its structural integrity or by distorting and disturbing its optical properties, engendering opacification and the creation of irregular astigmatism [2]. Fibrosis, neovascularization, and edema at any or all levels within the cornea will jeopardize its optical function to a greater or lesser degree [2].

The relative simplicity of the cornea's anatomical architecture belies the complexity of the physiological processes directed towards the critical goal of maintaining its transparency and geometric profile, and the pathological process to which it becomes subject. Defenses against pathogen incursion are based around maintaining the anatomic integrity of the ocular surface and the delicate balance of local inflammation–counterinflammation mediated primarily by innate immune responses. This latter is integral to the elimination of potential pathogens while maintaining the commensal microbial population, and to regulation of the normal turnover of damaged or effete epithelial cells. Much of the acute corneal disease encountered in clinical practice is associated with imbalance of this inflammation–counterinflammation process towards overexpression of keratolytic neutrophil responses in the face of aggressively pathogenic microorganisms, or from uncontrolled repair responses or dysregulated adaptive immune responses.

The precorneal tear film

The PCTF is a specific geographic component of the preocular tear film. It is classically described as a trilaminar structure adherent to and covering the external cornea, forming an integral and important physicochemical component of the surface defense mechanism of the external eye. The PCTF forms a physical barrier to microbial colonization of the cornea, and has a janitorial role in collecting microbial, cellular, and environmental debris for flushing from the ocular surface by the coordinated mechanisms of basal and reflex tear replenishment and blinking. The PCTF acts to lubricate the corneal surface to facilitate eyelid movement, has potent antimicrobial and immunomodulating properties, and is integral to corneal repair.

The adult horse tear film has an average volume of 234 μL. The PCTF is some 93 μm in thickness, is replaced approximately every 7 minutes [3], and has a pH of 8.33 ± 0.15 [4]. Very little is known specifically about the biology of the equine PCTF; however, the tear film phenotype is highly conserved across species and it is likely that the equine PCTF is largely similar in structure and function to other species. An exception to this is the change occurring in the closed eye PCTF phenotype in primates during sleep, where the microenvironment appears to adopt a subclinical proinflammatory profile [5], believed to be necessary to protect against pathogens trapped under the closed lid. The

* Dr Clode was the author of the cornea chapter in the second edition of *Equine Ophthalmology*. Approximately 70% of this previous chapter has been updated for the third edition of *Equine Ophthalmology*.

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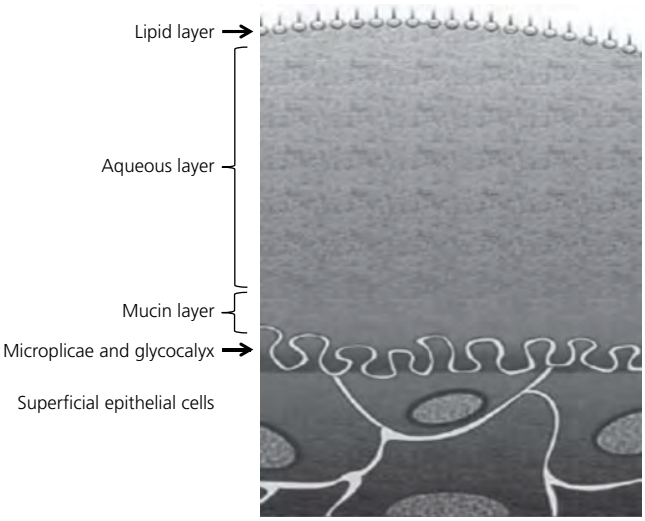


Figure 7.1 Diagrammatic representation of PCTF.

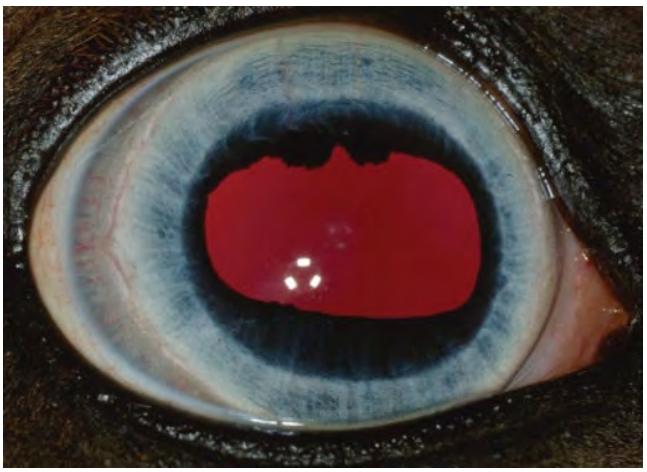


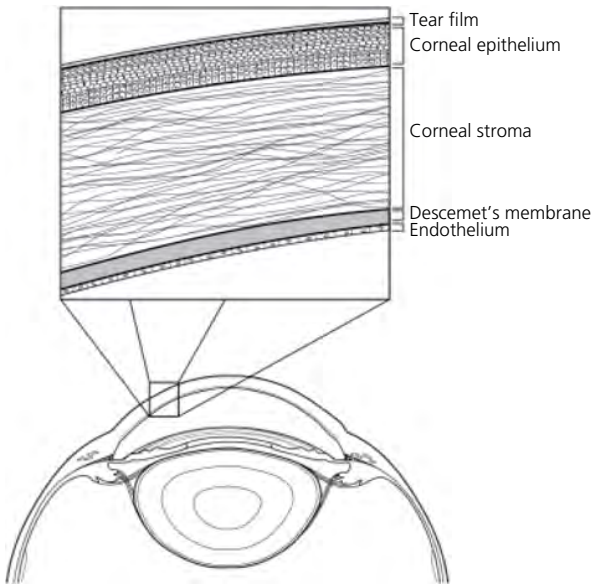
Figure 7.2 The normal clear cornea in a horse with a heterochromic iris.

significance of this phenomenon in equidae, with a diurnal and arrhythmically photic lifestyle incorporating only brief periods of sleep, is unknown; however, the closed eye PCTF may be of great clinical importance in the horse with painful keratitis and persistent blepharospasm.

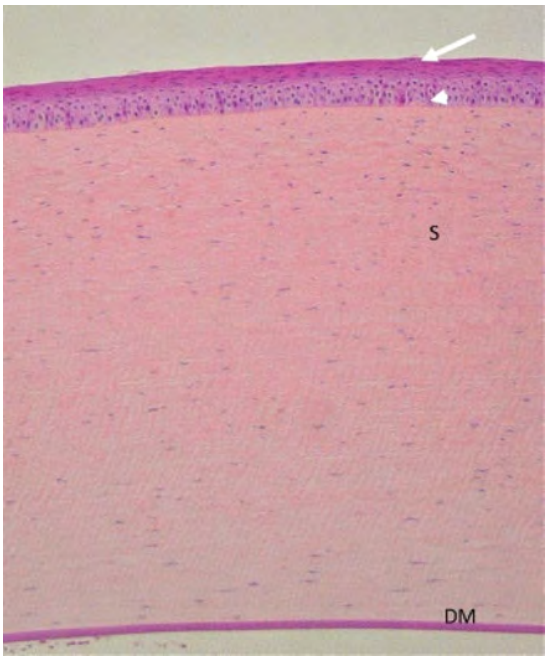
PCTF anatomy and function

The PCTF has three layers [6]. (Figure 7.1):

- The outermost **lipid layer** is derived from the meibomian glands of the eyelid margins, forming a smooth optical surface and retarding evaporation of aqueous tears. It interacts with lipid-binding proteins in the aqueous layer (e.g., lipocalin) to maintain the low surface tension and surfactant effect essential to maintain PCTF stability, thickness, and blink-driven even spread, and to maintain the PCTF within the confines of the palpebral aperture [7, 8].
- The middle **aqueous layer** is the major component of the PCTF, comprising a solution of salts, proteins, and secreted mucins



(A)



(B)

Figure 7.3 (A) Diagram of equine cornea. Enlarged inset demonstrates relative proportions of corneal epithelium, stroma and Descemet's membrane/endothelium. (B) Histologic image of a normal equine cornea (H&E ×400). Note columnar basal epithelial cell layer (**arrow**) with nonkeratinized stratified squamous surface cells (**arrowhead**). Also note the sparse, scattered stromal cells (keratocytes) among the collagen lamellae comprising the stroma (S). The eosinophilic posterior layer is Descemet's membrane (DM), with a few associated endothelial cells (the remaining cells were artifactually lost during tissue processing).

along with redundant cells, and is derived primarily from the lacrimal glands and corneal and conjunctival epithelial cells. In the horse it has been shown to contain the immunoglobulins (Ig) G, M, A, and G(T) [9, 10], along with urea [11],

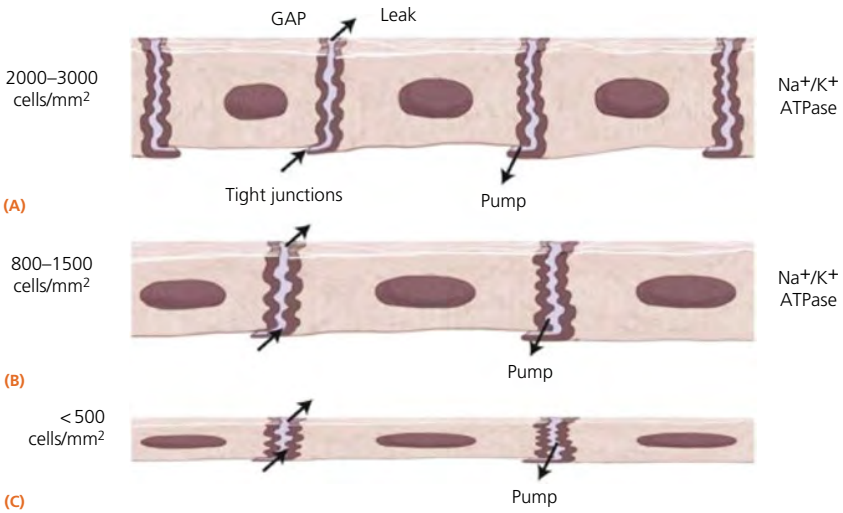


Figure 7.4 Corneal endothelium, a single layer of closely interdigitating hexagonal cells that forms a physical barrier between the cornea and aqueous humor, utilizes an active pumping mechanism to keep water and solutes out of the cornea. This diagram of corneal endothelial cells demonstrates location of the Na^+/K^+-ATPase pump and tight junction locations. (A) Normal concentration of endothelial cells. (B) Reduced concentration of endothelial cells. (C) Low concentration of endothelial cells and resulting leakage of aqueous humor into the corneal stroma.

cortisol [12], and connective tissue growth factor (CTGF) [13]. The aqueous tear film is rich in antimicrobial proteins (AMPs), forming a passive component of the innate immune system of the ocular surface. These AMPs act synergistically and are typically constitutively expressed, often at low concentrations which can be upregulated in response to insult, and include:

Lysozyme: this makes up 20–40% of the protein composition of the aqueous layer and kills primarily Gram-positive bacteria and some fungi by a direct disabling action on the microbial cell wall, causing osmotic lysis of the organism.

Lactoferrin: this makes up some 20% of aqueous layer protein and both inhibits microbial growth by binding bivalent cations, including iron, essential for microbial nutrition, and, as a cationic detergent, directly kills some bacteria by its lytic action on the cell wall.

Lipocalin: this makes up some 25% of the aqueous layer proteins, and inhibits bacterial and fungal growth by binding to and blocking microbial siderophores used to transport iron into the organism.

Secretory phospholipase A_2: this is a minor protein component, but one that has very potent activity against Gram-positive bacteria, based on its ability to hydrolyze the phospholipids abundant in the bacterial cell membrane.

Cationic antimicrobial peptides: these include **α defensins** produced by neutrophils and which bind to the negatively charged microbial cell membrane, causing disruption, leakage, and death. **Betalysins** and **secretory leucocyte protease inhibitor (SLPI)** are other directly acting cation antimicrobial peptides, the latter being also a potent inhibitor of neutrophil elastase (NE) capable of protecting host cells against the damaging effects of the enzyme.

Surfactant proteins (SP) A and D: these are C-type lectins produced by the lacrimal gland and by corneal and conjunctival epithelial cells which bind to the surface carbohydrate moieties on both phagocytic cells and bacteria, promoting phagocytosis and inhibiting both the growth of Gram-negative bacteria and their adhesion to target cells. SP-D inhibits corneal invasion by *Pseudomonas aeruginosa.*

Secretory IgA (sIgA): IgA is produced by plasma cells in the lacrimal gland and conjunctiva-associated lymphoid tissue (CALT) and is released into the tear film in a dimeric form (sIgA) by a process of epithelial transcytosis during which the IgA monomer is attached to a secretory component derived from epithelial cell IgA receptor. IgA is a poor activator of complement and a relatively poor opsonin, and appears to act by neutralizing the attachment of a microorganism to the host cell and by binding to adhesion molecules on microbial pathogens to cause their aggregation and physical entrapment in the tear film. IgA and CALT form major components of a mucosal immune defense system for the cornea.

Complement and complement regulatory proteins: these appear constitutively in small amounts in the normal tear film, derived from plasma and from neutrophils and surface epithelial cells. Activation is principally via the alternative pathway, resulting in the generation of membrane attack complexes capable of lysing pathogens and host cells. Local complement regulatory proteins, such as lactoferrin and epithelial cell membrane-bound CD55 and CD59, control unnecessary activation to prevent bystander tissue damage. Complement expression is significantly increased in the closed eye phenotype.

In addition to these antimicrobial proteins, the aqueous component of the PCTF contains a plethora of soluble pro- and anti-inflammatory and vasoactive cytokines and chemokines, along with neutrophil and epithelial cell-derived proteases and plasma-derived protease inhibitors [5, 14]. These reflect the dynamic inflammatory–counterinflammatory-driven immune surveillance necessary to maintain the health of the ocular surface microenvironment, to prevent the overgrowth and colonization of potential pathogens, and to prevent corneal angiogenesis.

- The inner **mucus layer** is in immediate apposition to the superficial epithelial cells and is formed from, predominantly, the gel-forming secreted mucin MUC 5AC produced by conjunctival goblet cells under parasympathetic stimulation. The separation between the middle aqueous tear layer and the posterior mucin layer is not precisely distinct, making definitive thickness measurements of the two tear components difficult. It is highly likely that these two components form a graded mixture, with the anterior mucin component gradually blending into the posterior aqueous lacrimal tear component [1, 15]. The mucin blanket interacts with the membrane-bound mucins of the glycocalyx on the apical membranes of the superficial epithelial cells in such a way as to allow shearing at the interface during blinking, and the hydrophilic properties of the mucus layer effectively tether the PTF to the epithelial surface [16, 17]. The mucus layer of the PTF functions to physically trap and promote the clearance of debris, pathogens, and allergens from the ocular surface, to lubricate the corneal surface, and to provide a reservoir of AMPs which accumulate in the mucin blanket [6].

  The mucins of the epithelial glycocalyx, which include MUC 1, MUC 4, and MUC 16, are produced by the epithelial cells and are attached to the microplicae of the apical surface of the superficial epithelial cells. These apical membrane mucins are held together by the carbohydrate-binding protein galectin-3 to create a continuous protective biophysical barrier protecting the epithelial surface. There is evidence that the transmembrane mucins and glycans of the glycocalyx prevent adhesion of pathogens, including *Staphylococcus aureus*, and that microbial proteases are able to compromise the glycocalyx barrier to allow access to the epithelium [16]. Galectin-3, while fundamental to the physical integrity of the glycocalyx barrier, appears able to bind to some viral and microbial pathogens, enhancing their infectivity, and glycocalyx compromise and enhanced galectin-3 expression during repair of corneal abrasions may promote pathogen adhesion [16].

Consequences of PCTF disruption or loss

PCTF abnormality will have a major impact on the health of the corneal surface, yet in the horse, little is known about the circumstances and consequences of PCTF dysfunction.

In addition to the blood–retinal barrier and blood–aqueous barrier, the existence of a blood–tear barrier can be inferred because of the marked differences between protein concentrations in tear fluid and plasma, and because of the similar magnitude of this concentration differential for various proteins https://www.dropbox.com/s/uz59pdx7xkh2klr/9781471865275_Print%20Pdf.pdf?dl=018). Breakdown of the blood–tear barrier is a significant component of ocular surface failure in inflammatory disease, changing the character of the tear film towards that of an exudate and accelerating the extravasation of inflammatory cells on to the ocular surface [18].

Reduction of secretion of the aqueous component is infrequently reported in the horse as a sequel to head trauma, inner ear disease, and dacryoadenitis, and increased evaporation and disrupted spread and blink-driven clearance is associated with exophthalmos, ptosis, and geographic loss or deformation of the eyelid margin. However, the consequences of disruption of PCTF adhesion to the epithelium resulting from superficial cell injury, dysplastic change, or depolarization, particularly during repair, are largely unknown but are likely to be of considerable importance, yet are frequently unaccounted for in therapy.

Inflammatory conjunctival and eyelid disease, such as meibomianitis, will have a significant impact on PCFT composition, increasing evaporative loss as the lipid layer production decreases and potentially resulting in upregulated expression of angiogenic factors, corneal vascularization, and compromise of immune privilege. Impairment of the PCTF antimicrobial and immune surveillance function will result in imbalance of the resident microbial population of the ocular surface, favoring growth of potential keratopathogens, and compromise of the physical barrier created by the PCTF allows access of potential pathogens to the epithelial surface.

Assessing the tear film

Several means of assessing the tear film are available for use in the horse in a clinical setting. These tests are relatively crude and the results in general poorly reproducible. However, used with circumspection and together, they are likely to give a broadly useful assessment of the PCTF in the diagnostic work-up of ocular surface disease. These techniques are described in detail in Chapter 1.

- **Schirmer tear test (STT)**: this assesses production of the aqueous component of the tear film.
- **Rose bengal stain**: in laboratory models, this stain is quickly taken up in a dose-dependent manner by viable corneal epithelial cells, but is subsequently rapidly toxic to these cells. Staining is blocked by the membrane-bound mucins of the glycocalyx, and stain uptake is likely to indicate compromise or loss of the mucin layer of the tear film and/or the presence of abnormal or depolarized superficial epithelial cells [19–21].
- **Lissamine green stain**: this works in the same fashion as rose bengal, but is markedly less toxic to epithelial cells.
- **Fluorescein stain:** fluorescein is soluble in the aqueous layer of the tear film and is distributed across the corneal surface on initial instillation. It is rapidly flushed from the ocular surface by blinking. It is retained on the corneal surface in areas where the squamous cells are absent or where there is disruption of the intercellular tight junctions between the epithelial cells, allowing uptake of the dye by both viable and compromised epithelial cells. As such, it has low specificity for PCTF disruption.
- **Tear film breakup time (TFBUT)** (see Chapter 1): this is a crude test of the qualitative and quantitative integrity of the tear film, but gives no diagnostic information of the cause of tear film compromise [19, 20]. A TFBUT of less than 10 seconds is probably abnormal in the horse [22, 23].

Corneal anatomy, physiology, and embryology

Grossly, the normal cornea measures 29.7–34.0 mm horizontally and 23.0 to–26.5 mm vertically in an adult horse [24, 25], and 20.5–26.6 mm horizontally and 19.5–24.0 mm vertically in younger horses [25, 26]. In Miniature horses, mean horizontal and vertical diameters measure 25.8 mm and 19.4 mm, respectively, and increase with age up to 7 and 5 years, respectively [27]. Corneal diameter also increases with age in normal Rocky Mountain horses [25]. Compared to other mammals, the equine cornea is relatively flat, with a mean corneal curvature in Rocky Mountain horses measured at 20.59 ± 1.72 D versus a curvature of 16.46 ± 1.5 D calculated for normal adult horses of other breeds [25, 28].

In vivo corneal thickness measurements in normal horses, obtained via ultrasonic pachymetry, are greater peripherally than centrally [29], with the mean central cornea measured at 770 μm and 814.6 μm [25, 29] and the peripheral cornea at a mean of 793 μm [27] and range of 887–917.3 μm [29]. The peripheral cornea is thicker dorsally [29]. In Warmbloods, mean central corneal thickness was 818 μm, measured using high-frequency ultrasound [30]. Measured using confocal microscopy, median central corneal thickness in normal adult eyes was 835 μm (725–920 μm) [31]. Using spectral-domain optical coherence tomography (SD-OCT), a mean central corneal thickness of 812 μm has been reported [32]. Following enucleation, the mean central corneal thickness of normal adult horses measured 893 μm, being significantly thicker dorsally and ventrally relative to centrally, medially, and laterally [33]. Mean central corneal thickness in normal Miniature horses was 785.6 μm [27]. In healthy Rocky Mountain horses and Warmbloods the corneal thickness increases with age [25, 30], whereas no variation in corneal thickness has been noted with age or gender in adult Miniature horses or horses of other breeds [27, 31].

Histologically, the equine cornea comprises three primary layers of alternating lipophilicity: the superficial epithelium (lipophilic), central stroma (hydrophilic), and deep endothelium (lipophilic) (Figure 7.2). The stratified squamous epithelium is continuous with the conjunctival epithelium, and consists of 8–12 layers of nonkeratinized squamous cells, wing cells, and basal cells. It has been reported to have a thickness centrally of 117–141 μm and 175 μm measured using confocal microscopy and SD-OCT, respectively [31, 32]. Basal cells are progenitor cells and undergo mitosis at a rate of 10–15% per day, with cells progressively differentiating, migrating anteriorly, and desquamating. Epithelial cells at the basal or suprabasal layers move centripetally in mice at an average rate of 26 μm/day [34]. In the human cornea, the epithelial cell turnover interval is 7 days [35]. In horses, experimentally induced corneal ulcers in which the epithelium, basement membrane (BM), and anterior third of the stroma were surgically removed had a median time to re-epithelialization of 11 days, equivalent to an epithelial cell migration rate of 0.6 mm/day [36].

Epithelial transparency is largely determined by the presence of soluble intracellular crystallins [37]. The epithelial cells are spatially polarized with the apical and basolateral plasma membrane domains adapted to specific functions: for example, the attachment of membrane-bound glcyocalyx mucins to microplicae on the apical membrane of the superficial squamous cells. Epithelial glycocalyx acts to physically trap particulate and microbial debris, and has a direct anti-inflammatory action via the downregulation of Toll-like receptor activation on epithelial cells [38]. Tight intercellular junctions (**zonulae occludens**) are present on the basolateral surfaces of the superficial cells, and form the primary barrier to molecular diffusion through the cornea. Desmosomes, adherent junctions, and gap junctions occur between squamous, wing, and basal cells, anchoring the cytoskeletons of adjoining cells and permitting intercellular communication. Basal cell hemidesmosomes linked to laminin–collagen complexes in the BM bridge the BM and extend into the anterior stroma to create an "anchor complex" firmly attaching the basal epithelial cells to the stroma [39]. The BM is a complex arrangement of collagen (predominantly type IV), laminins, heparan sulfate PGs, nidogens (sulfated glycoproteins acting as link proteins), fibronectin, and other protein moieties. The composition shows some variation between the central and limbal cornea, probably reflecting the role of the BM and extracellular matrix (ECM) in the regulation of limbal stem cell responses to injury [40]. In addition to its role in epithelial cell growth, proliferation, and differentiation, the BM has a regulatory role in the normal cornea to modulate the transfer of epithelial transforming growth factor beta 1 (TGF-β1) and other growth factors into the anterior stroma, limiting TGF-β1-dependent myofibroblast differentiation and growth. Myofibroblast proliferation following BM injury results in the local production of abnormal ECM, consequently delaying BM regeneration and causing protracted anterior corneal haze. Only with the ultimate regeneration of normal BM will myofibroblast apoptosis occur, allowing restoration of a normal keratocyte population and the return of transparency [39]. Recurrent epithelial erosions arise where the disrupted BM fragments interfere with basal cell division and differentiation, resulting in poorly adherent dysplastic epithelium, believed to be in part a consequence of disrupted expression of the integrin transmembrane-linking proteins of the hemidesmosome component of the anchor complex [39].

In the mammalian cornea, a population of multipotent stem cells capable of self-renewal through asymmetric division is resident in the basal epithelial layer at the limbus, the transition zone between the cornea and conjunctiva, and is a major source of progenitor cells for the replenishment of the continually differentiating and desquamating corneal epithelium throughout life. Basal epithelial limbal stem cells have been identified in the horse cornea [41]. Limbal stem cells are triggered to proliferate and stratify as they migrate centripetally, ultimately becoming terminally differentiated epithelial cells. Stem cell turnover in the normal cornea is relatively slow, but is upregulated eight- to ninefold in the 36- to 48-hour period following corneal injury in laboratory animals. Stem cell division and amplification is controlled by limbal BM and ECM-derived growth factors, adhesion molecules, and cytokines. In addition to the limbal stem

cell population, there is some evidence of the existence of stem cell reservoirs among the basal epithelial cells of the central cornea [40, 42]. Langerhans cells, a subset of dendritic cells (DC), and, like DCs, a professional antigen-presenting cell (APC), are found in the basal epithelial layer and decrease in number from the limbus centrally [31]. Melanocytes are found in the basal epithelial layer at the limbus in some horses [31].

Epithelial cells are the source of a variety of pro- and anti-inflammatory cytokines and chemokines present in the tear film, and which are in part responsible for regulation of the dynamic inflammatory–counterinflammatory-driven immune surveillance fundamental to the health of the ocular surface. Additionally, epithelial cells express molecular factors responsible for both constitutive replacement and post-injury repair of epithelial cells, including adhesion molecules (e.g., intercellular adhesion molecule-1 (ICAM-1) and vascular adhesion molecule 1 (VCAM-1) and thymosin-β4 [35].

The stroma, which is 90% of the corneal thickness, is largely an ECM composed of water (75–80%), collagen fibers, a proteoglycan (PG) matrix made up of core proteins linked to glycosaminoglycan (GAG) side chains, primarily dermatan sulfate, chondroitin sulfate, and keratin sulfate, and small amounts of fibronectin and laminin isotypes [37]. The PG component of the stroma is intensely hydophillic and is responsible for the compressive and expansive material properties of the cornea. The horse stroma has unique regional biochemical differences in the relative content of PGs chondroitin 6 sulfate (C6S) and chondroitin 4 sulfate (C4S), with higher levels of C6S in the superficial layers and more C4S in the deeper layers both centrally and peripherally [43]. C4S has less water-holding capacity than the C6S, such that corneal edema tends to clinically become more prominent in the superficial horse cornea [43]. The swelling properties of the superficial anterior stroma affect epithelial function and tear film stability and adhesion in the horse with marked corneal edema [44].

Stromal collagen comprises a lamellar arrangement of heterotypic type I and V fibrils of uniform diameter aligned in parallel arrays tangentially to the corneal surface. Type III collagen, although not detected in the cornea, is present in the loose connective tissue of the limbus and sclera. The monodisperse distribution and uniform spacing of the corneal fibrils at an interval less than the wavelength of light is largely responsible for normal stromal transparency, and is maintained by the physicochemical properties and state of relative dehydration of the PG matrix [37, 45, 46]. Increased hydration of the PG matrix, resulting from the ingress of water from the tear film or aqueous humor following breakdown of the epithelial or endothelial barriers, or from defective molecular composition of the PG matrix, causes swelling of the stroma and spatial disruption of the collagen array, causing scatter of transmitted light and loss of transparency (corneal edema). In addition, stromal edema results in loss of the PG matrix and lysis of keratocytes [47]. Edema can range in gross presentation from vague corneal haze to frank opacity. The corneal stroma is relatively acellular, with small numbers of fibrocyte-like mesenchymal cells, keratocytes, being present mainly in the anterior stroma. These cells exhibit a flattened stellate morphology and connect horizontally with one another to form a keratocyte network. The network is highly organized and intercellular communication occurs through gap junctions. Vertical interconnections between keratocytes in adjacent layers are not frequent but also exist [48].

Due to this microanatomical arrangement, keratocyte networks are positioned ideally to interact with migrating neutrophils traveling between (but not through) the collagen layers [48]. Postnatally, keratocytes become relatively inert and undergo only limited division or apoptosis in normal circumstances. Keratinocyte cytosol comprises mainly soluble crystallins, contributing to maintenance of stromal transparency. Following corneal injury, keratinocytes distal to the wound divide and differentiate into wound fibroblasts and myofibroblasts. Both are repair phenotypes and are capable of synthesizing and remodeling collagen and the PG ECM through a process of synthesis of matrix components and secretion of matrix-degrading proteins. Myofibroblasts are probably primarily responsible for wound contraction and reorganization in the later stages of repair [37]. Small numbers of neural crest-derived stem cells are present in the anterior stroma at the limbus and probably replenish the keratinocyte population after injury [49]. The stroma has a small resident population of macrophages and APCs (Langerhans cells and DCs), with greater numbers towards the limbus [31].

Deep to the stroma is Descemet's membrane (Figure 7.2). This is the specialized BM of the endothelial layer. It averages 30–38 μm in thickness in the adult horse [32, 50], and, as it is formed throughout life, thickness increases with age at a rate of 2 μm/year [32]. Descemet's membrane is acellular and comprises a stratified arrangement of mainly types III, IV, and VIII collagen in a PG matrix, the precise collagen composition varying with depth. It is only loosely intermeshed with the overlying stromal collagen. Although entirely collagenous, Descemet's membrane in the horse can be observed to exhibit elastic properties (e.g., retraction of severed margins), and appears relatively resistant to hydrolysis by endogenous proteases.

The endothelium is a monolayer comprising a regular mosaic of metabolically active hexagonal cells some 20–25 μm in diameter. Mean endothelial cell density (ECD) in normal horses is 3155 cells/mm^2 [25] and ranges from 2473–3581 cells/mm^2 [31]. ECD shows no variation with gender [31, 33] but declines with increasing age [33]. In most mammals, ECD increases towards the limbus [47, 51]. The endothelium has a barrier function and is responsible for maintaining the steady-state osmotic gradient between the hydrophilic stroma and anterior chamber aqueous necessary for corneal transparency (Figure 7.3).

Endothelial cells are derived from the neural crest, and are joined at their apical margins by "leaky" junctional complexes which retard but do not block the osmotic transfer of water, solutes, macromolecules, and nutrients into the stroma. The individual cells incorporate an active ion–water transfer function, based on an Na^+/K^+-ATPase-dependent transmembrane pump, which moves water from the stroma to the aqueous against the

osmotic and hydrostatic gradients, and can ultimately result in movement of 6–8 mL/hour of water from the stroma to the aqueous humor [52]. The efficiency of the barrier and ion–water transfer function is determined by ECD and the presence of certain cofactors (i.e., calcium, glutathione, bicarbonate) in the aqueous humor. The endothelium has a significant functional reserve, and cell density is required to fall below 400–700 cells/mm^2 before stromal hydration ensues (Figure 7.3) [47]. Endothelial cells in the adult have a very limited capacity to divide, and cell loss with age is balanced by migration and spread of existing cells, along with a decrease in the permeability of the junctional complexes and an increase in the number of transmembrane pumps [47]. Endothelial cells are sensitive to chemical and microbial toxins and to local changes in pH. Proinflammatory cytokines, in particular TNFα, adversely affect endothelial function by mechanisms independent of apoptosis, possibly by disrupting the cells' cytoskeleton to physically loosen and dehisce the junctional complexes [51, 53]. This is to a degree reversible [53]. Clinical observation indicates that equine corneal endothelial cells appear to be relatively resilient, and able to restore and maintain corneal deturgescence in spite of protracted inflammatory insult. Following sharp transection of the endothelial layer, cells from the wound margins bridge the defect to form an irregular array of polygonal cells, which, initially, forms an ineffective barrier to water ingress. These cells progressively remodel to hexagonal cells and recover their transmembrane pump function and junctional complexes, potentially returning the stroma to normal transparency. There is evidence of a population of stem cells in the limbal endothelium and trabecular meshwork, although their role in regeneration after injury is unknown [54].

Nutrition

Oxygen is supplied to the cornea by the external atmosphere and PCTF, with lesser amounts provided by the aqueous humor and limbal blood vessels [47]. When the eyelids are closed, the palpebral conjunctiva provides smaller amounts of oxygen [47]. Glucose, amino acids, and vitamins are predominantly obtained from the aqueous humor, with smaller amounts from the PCTF and limbal blood vessels [47]. Additional glucose may be obtained from subepithelial glycogen stores in times of increased demand such as wound healing, via either aerobic or anaerobic (glycolysis) metabolism [47].

Innervation

The mammalian cornea receives most of its innervation from the terminal branches of the ciliary nerves, derived from the ophthalmic division of the trigeminal nerve. Nonmyelinated sensory nerve fibers enter the peripheral mid stroma from the limbus and run centripetally and anteriorly to form subepithelial (anterior stromal) plexuses, from where nerves penetrate the BM to form sub-basal plexuses. From the latter, branching leashes extend vertically and horizontally to terminate within the epithelial cell architecture [31, 55, 56]. There is an increasing density of nerve fibers from the posterior to the anterior cornea, with the more posterior cornea, adjacent to Descemet's membrane, being effectively devoid of nerve fibers. The anterior cornea is the most sensitive structure in the mammalian body, and is highly responsive to minor stimuli, with some 300–500 times the number of nerve endings present than are found in skin. Thermal, mechanical, chemical, and polymodal nocioreceptors are present in the cornea [57]. Corneal innervation has several functions: it is the afferent arm of both the tearing and blink reflexes which are principally responsible for mechanical protection of the ocular surfaces, and it has a trophic role in epithelial regeneration and repair. The neurotransmitters substance P, calcitonin gene-related peptide, vasoactive intestinal peptide-1 (VIP-1), and acetylcholine are present in the cornea. Substance P is a neurotrophic peptide which is functionally synergistic with insulin-like growth factor-1 (IGF-1) in enhancing epithelial cell migration and attachment by upregulating basal cell integrin expression. This is mediated principally through neurokinin 1 (NK1) receptors, which also mediate the role substance P plays in the genesis of neurogenic inflammation and the innate immune response on the ocular surface [58]. Corneal nerves are involved in the antidromic axon reflex, resulting in transient uveitis (miosis and aqueous flare) associated with painful corneal disease.

Loss or depletion of corneal innervation is associated with reduced epithelial cell division, increased epithelial permeability, and retarded wound closure, and, potentially, reduced tear production and depletion of limbal stem cells [58, 59], resulting in a range of epithelial disorders collectively known as neurotrophic keratopathies. This can follow trigeminal or more peripheral nerve injury, corneal surgeries, and chemical or thermal injury.

In normal adult horses, corneal sensitivity, quantified using the corneal touch threshold measured by Cochet–Bonnet esthesiometry, is greatest in the central, ventral, and lateral quadrants relative to the nasal and dorsal quadrants [60, 61]. In sick foals, corneal sensitivity is significantly decreased in all quadrants relative to normal foals and adults [60]. Decreased corneal sensitivity is found in horses over 15 years old and in older horses with pituitary pars intermedia dysfunction (PPID), and may be in part responsible for the increased incidence of nonhealing superficial ulcers in these groups [62].

Autonomic sensory fibers are found in the cornea, though their function is unknown [56].

Embryology [63]

Corneal epithelium derives from the surface ectoderm of the optic cup, and has a common origin with skin. In later gestation, epithelial cells acquire the phenotypic components typical of secretory or absorptive epithelium found at other body sites.

Corneal stroma develops primarily from centripetally migrating neural crest-derived neuroectodermal cells undergoing *in-situ* mesenchymal transformation as they occupy the space between the primordial epithelium and anterior lens following completion of invagination of the optic cup. Descemet's membrane and endothelium subsequently develop from the neural crest-derived mesenchymal cells of the posterior stroma.

The structures involved in the production and drainage of aqueous humor evolve contemporaneously with the formation

of the anterior chamber and regression of the vascular tunic of the fetal lens. Hydrodynamic forces created by the aqueous assist with molding of the corneal curvature.

Corneal immunobiology

See online material.

Ocular surface microflora

The normal corneal and conjunctival surface microflora are primarily Gram-positive bacteria and fungal organisms, but Gram-negative organisms are also typically present (Tables 7.1–7.3). Consistent with earlier reports [64–66] more recent evaluations of horses in the USA identified *Staphylococcus* spp. (22–50%) [67, 68], *Bacillus* spp. (17–32%) [67, 68], and *Corynebacterium* spp. (29%) [67] as common isolates, in addition to an apparently increasing prevalence of *Streptomyces* spp. (66%) [68]. The most common Gram-negative isolates from horses in the USA are *Moraxella* spp. (28%), *Escherichia* spp. (24%), *Acinetobacter* spp. (18%), and *Enterobacter* spp. (14%) [68]. In the UK, bacteria, most frequently *Acinetobacter* spp. (17%) and *Staphylococcus* spp. (14%), were isolated from 52% of normal eyes [69]. In Italy, the most common isolates from the normal eyes of healthy donkeys were *Staphylcoccus* spp. (65%) and Enterobacteriaceae (10%) [70].

Fungal organisms isolated from normal horses in the greatest frequency in the USA include *Aspergillus* spp., *Cladosporium* spp., *Alternaria* spp., and *Penicillium* spp (Table 7.3) [66–68, 71]. In the UK, the most commonly isolated fungi were *Mucor* spp. 6.67% (4/60) and *Aspergillus* spp. 5% (3/60) [69]. In Brazil,

Table 7.1 Gram-positive bacterial isolates from conjunctival/corneal samples from healthy horses (2003–2005).

Reference Country (state)	Andrew et al. [67] USA (FL)	Gemensky et al. [68] USA (OH)
Organism	**Percentage (number/total)**	
Actinomyces	6 (135/137)	
Bacillus	17 (398/2357)	32
Corynebacterium	29 (689/2357)	4
Dermatophilus	<1 (3/2357)	
Diphtheroid		10
Enterococcus		2
Lactobacillus	<1 (1/2357)	
Micrococcus	2 (53/2357)	8
Rhodococcus	<1 (5/2357)	
Staphylococcus	22 (513/2357)	52
Streptococcus	4 (87/2357)	36
Streptomyces	<1 (19/2357)	66
Unidentified	<1 (6/2357)	

Table 7.2 Gram-negative bacterial isolates from conjunctival/corneal samples from healthy horses (2003–2005).

Reference Country (state)	Andrew et al. [67] USA (FL)	Gemensky et al. [68] USA (OH)
Organism	**Percentage (number/total)**	
Acinetobacter		18
Actinobacillus		2
Alcaligenes	<1 (2/2357)	
Citrobacter		8
Enterobacter		14
Escherichia	<1 (1/2357)	24
Klebsiella	<1 (5/2357)	
Moraxella	10 (225/2357)	28
Pasteurella	<1 (4/2357)	
Proteus	<1 (1/2357)	
Pseudomonas	<1 (1/2357)	8
Sphingomonas	<1 (1/2357)	
Stenotrophomonas	<1 (2/2357)	

Table 7.3 Fungal isolates from conjunctival/corneal samples from healthy horses (2003–2005).

Reference Country (state)	Rosa et al. [72] Brazil	Andrew et al. [67] USA (FL)	Gemensky et al. [68] USA (OH)
Organism	**Percentage of isolate (number/total)**		
Acremonium		5 (25/541)	
Alternaria		2 (11/541)	6
Aspergillus	37 (75/204)	6 (30/541)	78
Candida		<1 (3/541)	
Cephalosporium			2
Cladosporium	6 (13/204)	8 (44/541)	32
Chrysosporium		8 (44/541)	
Curvularia		<1 (3/541)	2
Drechslera		1 (7/541)	
Epicoccum		1 (6/541)	
Eurotium	2 (4/204)		
Fonsecaea		<1 (1/541)	
Fusarium	<1 (1/204)	1 (8/541)	2
Geotrichum	1 (2/204)	<1 (2/541)	
Gliocladium		<1 (1/541)	
Gliomastix	<1 (1/204)		
Mucor	2 (5/204)		4
Nigrospora		<1 (2/541)	
Paecilomyces		1 (6/541)	
Papulaspora		<1 (1/541)	
Penicillium	29 (60/204)	5 (29/541)	2
Phialophora		<1 (2/541)	
Pseudallescheria		<1 (1/541)	
Rhizopus	1 (2/204)	5 (25/541)	
Scedosporium		<1 (2/541)	2
Scopulariopsis	18 (37/204)	2 (10/541)	6
Sporothrix		<1 (2/541)	
Stemphylium			4
Syncephalastrum	2 (5/204)		
Torulopsis		<1 (2/541)	
Trichcladium		<1 (2/541)	
Trichoderma	21 (43/204)		
Trichophyton		<1 (2/541)	
Trichosporon		<1 (2/541)	
Tripospermum		<1 (1/541)	
Verticillium	<1 (1/204)	<1 (1/541)	
Wallemia		<1 (1/541)	
Wangiella		<1 (2/541)	
Unidentified	11 (23/204)	49 (263/541)	

Aspergillus spp. and *Penicillium* spp. were isolated from 37% (75/204) and 29% (60/204) of normal eyes, respectively [72]. In Switzerland, fungi were isolated from at least one eye of 92% of horses sampled, with *Alternaria* spp. being isolated from 72% (46/64) of horses, and *Aspergillus* spp. and *Penicillium* spp. being isolated from 8% (5/64) and 6% (4/64) of horses, respectively [73]. In Iran, *Aspergillus* spp. and *Penicillium* spp. were isolated from 19% and 15% of horses, respectively [74].

Corneal pathophysiology: corneal wound healing and repair of the ocular surface

General concepts

Wound healing cascade

The epithelium, stroma, endothelium, corneal nerves, tear-producing glands, and the PTF contribute to the maintenance of ocular surface smoothness and integrity that is critically important to the function of the eye. Following injury, these ocular surface components participate in an orchestrated and coordinated response that attempts to efficiently restore corneal structure and function. Many cytokines and receptors modulate the process. Activation of these systems also attracts immune and inflammatory cells that function to eliminate debris and any microbes which may breach the injured PCTF and epithelial surface and gain entry to the corneal stroma [75].

Corneal wound healing is a complex and interdependent process of transformation of fibroblasts, vascular incursion, intercellular signaling involving cytokines, neuropeptides, growth factors, and chemokines, keratolytic activity of serine proteases and matrix metalloproteinases, and the protection of corneal tissue from free radical damage (online Figure 7.63) [76]. The healing of the cornea is also unique relative to other soft tissues because it is avascular. Healing of corneal wounds such as ulcers depends on the mitosis and centripetal migration of healthy corneal and conjunctival epithelial cells to cover the ulcer site, and their subsequent attachment to the injured corneal stroma [75]. Epithelial mitosis and migration, stromal cell necrosis, keratocyte proliferation, myofibroblast generation, collagen deposition, and inflammatory cell infiltration all contribute to the wound healing cascade and are also likely modulated by cytokines derived from corneal cells, the lacrimal gland, and inflammatory cells [75].

The cascade of responses to injury to the cornea is initiated very rapidly regardless of the type of injury, although there appear to be a few key cytokine modulators that act as "master regulators" of the response. Some of these master regulators and their receptors are likely to be constitutively produced and, therefore, constantly available to initiate the wound healing response. These initiators are likely to be masked until needed so that their activity is not unleashed unduly, at least in the normal cornea. Thus these master regulators serve as ever-vigilant guardians, silently waiting and ready to trigger the inflammatory and repair cascade at the first sign of injury [75].

Interleukin-1 (IL-1) appears to be a master modulator of many of the events involved in the corneal healing response cascade. Keratocyte apoptosis is the earliest stromal event noted following epithelial cell injury and remains a likely target for modulation of the overall wound healing response. IL-1 upregulates the expression of collagenases and metalloproteinases by keratocytes. These enzymes have an important role in remodeling collagen during corneal wound healing. IL-1 and TNFα also upregulate the expression of monocyte chemotactic protein-1 (MCP-1) from keratocytes and corneal epithelial cells. IL-1 also potentiates the chemotactic effect of platelet-derived growth factor (PDGF) on corneal fibroblasts [75].

Leucocytes, cell migration, and the corneal injury response

Corneal injury initiates an acute inflammatory response. Leucocyte–endothelial adhesion molecules regulate neutrophil extravasation from the limbal and conjunctival vessels [77]. Once in corneal contact via the tear film, neutrophils form adhesion molecule-dependent contacts with collagen of the stromal ECM, and keratocytes provide contact guidance by serving as an adhesive substrate and a source of neutrophil chemoattractants (chemokines) [78]. Beginning approximately 12–24 hours after injury to the cornea, there is an influx of inflammatory cells into the corneal stroma. Once in the stroma, these inflammatory cells can migrate at a rate of 11–43 mm/day in laboratory models [79].

Vascular endothelial cells in the inflamed limbus change their cell membrane characteristics from "cytophobic" to "cytophilic" and become adhesive to intraluminal leucocytes. Adherent leucocytes migrate between endothelial cells (diapedesis) through spaces created by endothelial cell contraction. Once through the endothelial cell BM, leucocytes migrate along chemoattractant concentration gradients in contact with keratocyte networks to the site of injury. This neutrophil locomotion may be integrin dependent [79]. At the site of injury these leucocytes liberate proteases to break down damaged tissue in an accelerating fashion and subsequently phagocytize cellular and noncellular debris. Macrophages arrive later to remove more debris and liberate the cytokines required to begin the reparative phase [80].

Polymorphonuclear cells (PMN), predominantly neutrophils, are fundamental drivers of the cellular events necessary to heal corneal wounds [78, 81]. However, excessive numbers of PMN are associated with catastrophic increases in tear and stromal protease levels (online Figures 7.91–7.98, 7.236, 7.249, 7.250, and 7.251) [14, 78, 81]. The signals that draw these inflammatory cells into the corneal stroma following the corneal injury are most likely soluble cytokines or chemokines released following injury. Corneal keratocytes and fibroblasts produce monocyte chemotactic protein-1 (MCP-1), also called monocyte chemotactic and activating factor (MCAF) when stimulated by IL-1 or TNFα [75]. It seems likely that one important function of stromal neutrophils in the uninjured eye is the scavenging of cellular components released from keratocytes that undergo programed cell death [75]. Macrophages are also found in acute ocular surface disease

to cause release of inflammatory and angiogenic mediators, and to aid the killing and degradation of pathogenic microbes [75].

Fibronectin

Fibronectin is a high molecular weight plasma glycoprotein which functions in the promotion of cell adhesion, migration, and differentiation, and enhances the phagocytic activity by leucocytes and macrophages [78, 82]. On the ocular surface, fibronectin plays an important role in corneal wound healing. Early in the ocular surface repair process, fibronectin and fibrin are deposited on the exposed corneal epithelial BM and/or stroma to create a temporary matrix for epithelial cell migration, and then disappear as the epithelial cells cover the defect [18, 82]. Fibronectin fragments are potent chemoattractants for leucocytes, and fibronectin, together with immunoglobulin, enhances phagocytosis of bacteria by leucocytes [18]. The source of fibronectin is tear fluid: leakage from dilated conjunctival blood vessels, secretion from the lacrimal gland, or secretion from the ocular surface epithelium (corneal or conjunctival) and stromal keratocytes [18, 82].

Proteases of the ocular surface

Both maintenance of corneal health and repair during disease or wound healing depend on proteolytic enzymes and their inhibitors for regulating tissue turnover [83–87]. In normal corneas, enzyme inhibition balances degradative activity to promote corneal tissue homeostasis. Disease may result in excessive proteolytic activity by enzymes derived from the PCTF, corneal epithelial cells, keratocytes, infiltrating inflammatory cells, and infectious organisms [14, 84, 85, 88–91]. This excess proteolytic activity manifests as corneal stromal "melting," or keratomalacia, which is the basic biomechanical driver of corneal ulceration.

The two most extensively studied groups of corneal proteinases are the matrix metalloproteinases (MMPs) and the serine proteases, specifically NE [83]. NE, produced by leucocytes, digests collagen types III and IV, laminin, fibronectin, and heparan sulfate [14, 92–94], and has been identified at significantly higher levels in the preocular tear film of horses with ulcerative keratitis than in normal controls [14]. MMP-2 and MMP-9 are both gelatinases but appear to play different roles in corneal physiology. Using immunohistochemistry, MMP-2 was found to be constitutively present in healthy equine cornea, primarily in the epithelium and to lesser degrees in the stroma and endothelium, while MMP-9 was not identified in healthy equine cornea [83]. In diseased equine cornea, MMP-2 expression was increased throughout the equine cornea, along with concurrent MMP-9 expression [83]. The use of gelatin zymography to identify proteolytic activity of MMP-2 and MMP-9 documented an increase in total tear film proteolytic activity in ulcerated equine eyes relative to the contralateral healthy eye, with a decrease in activity compared with that of the contralateral healthy eye by the day of ulcer healing [95]. These findings support the role of MMP-2 in corneal homeostasis, becoming locally activated in times of minor wound repair [84, 85, 91], whereas MMP-9 is expressed by epithelial cells and PMNs following more extensive corneal wounding [85, 85, 96, 97]. Control of this proteolytic activity therefore constitutes a significant component of therapy in such conditions.

Growth factors of the ocular surface

As in other tissues, healing of corneal wounds is enhanced by peptide growth factors, which, following local and systemic production, reach the avascular cornea via aqueous humor, tears, and limbal blood vessels. Epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), connective tissue growth factor (CTGF), keratinocyte growth factor (KGF), insulin-like growth factor (IGF), and hepatocyte growth factor (HGF) perform varied functions, such as promotion or inhibition of corneal epithelial cell proliferation or migration, keratocyte proliferation, and inflammatory cell influx [98]. The complex and incompletely understood interactions and potential species differences among growth factors make definitive statements about their functions difficult. In laboratory models, EGF has been documented to increase normal cell turnover, promote vascularization, and stimulate healing of epithelial and endothelial wounds [99]. PDGF enhances tissue repair by influencing inflammatory reactions, vascularization, proliferation, chemotaxis, and ECM production [100]. TGF-β increases collagen synthesis, possibly due to increasing production of CTGF, which stimulates fibroblast and collagen production [101, 102]; however, it also inhibits epithelial cell proliferation and keratocyte migration [98], producing varied effects on overall corneal wound healing.

Evaluation of growth factors in horses has been more limited. Using cultured equine epithelial cells and keratocytes, increased proliferation of epithelial cells and keratocytes in response to EGF and PDGF was noted, while TGF-β decreased proliferation of both [36]. Use of high-dose (50 mcg/mL) and low-dose (5 mcg/mL) EGF in horses with experimentally induced corneal ulcers identified a trend toward more rapid healing in the high-dose group. However, both doses of EGF were associated with increased corneal edema, vascularization, melanosis, and scarring, side-effects that likely negate any potential benefit of administration of EGF as performed in that study [36]. Additionally, CTGF has been identified in the tear fluid of both normal and ulcerated equine eyes, with lower levels in ulcerated eyes postulated to be associated with exhausted production of CTGF by lacrimal and third eyelid glands, and/or increased utilization of CTGF by ocular surface receptors [13]. Vascular endothelial growth factor (VEGF) and pigment epithelium-derived factor (PEDF) are involved in equine stromal abscessation [103, 104].

Corneal wound healing—in depth

See online material.

Clinically important sequelae to corneal wounding in the horse

See online material.

Congenital abnormalities

Congenital corneal abnormalities in foals are rare [105–108]. They are predominantly developmental fetopathies rather than acquired disease, and are typically sporadic and may be unilateral. They are frequently associated with more generalized ocular abnormalities. The heritability of most congenital corneal abnormalities is unknown.

Dermoids

Corneal dermoids, or choristomas, are nonprogressive, unilateral or bilateral, congenital lesions consisting of epithelial and dermis-like components found in an abnormal location (Figure 7.5). There is no breed predilection, and they have been recorded in Standardbreds [109] and Thoroughbreds. They usually occur in isolation, but have been recorded in Quarter horses [154] and in other breeds in association with aniridia (iris hypoplasia) and cataracts (online Figure 7.36) [110, 111].

Although the pathogenesis is unknown, abnormal differentiation of a group of ectodermal-derived cells early in development may be involved. Alternately, defective induction of surface ectoderm by the optic vesicle, producing skin rather than corneal epithelium, may be involved [63]. Histologically, keratinized stratified squamous epithelium (versus the nonkeratinized epithelium of the cornea) overlies an irregular dermis which may contain hair follicles, sweat glands, and sebaceous glands [112]. At the axial margin, collagen within the dermis blends with that of the corneal stroma, and the epidermis becomes contiguous with the corneal epithelium. The presence of cartilage or bone within the dermoid is rare.

Corneal dermoids are generally noticed shortly after birth, and will vary in geographic extent. They most frequently arise at the dorsal limbus and present as typically superficial, variably pigmented, and potentially haired, discrete elevated masses. Irritation may be caused if large lesions impede eyelid closure or if hairs from the lesion contact the corneal surface. Clinical appearance is diagnostic in most cases; however, definitive diagnosis and differentiation from other reactive or neoplastic masses is by excisional biopsy and histopathology.

Small dermoids can be managed conservatively. However, since most corneal dermoids are superficial, removal by keratectomy provides complete resolution. Post-operative care is as for an uncomplicated superficial ulcer, and includes prophylactic topical antibiotic administration until the keratectomy site has re-epithelialized, and topical atropine and systemic analgesics (nonsteroidal anti-inflammatory drugs (NSAIDs)) if reflex anterior uveitis is present. Dermoids rarely can extend into the stroma. In these instances thorough evaluation prior to removal, using appropriate instrumentation and magnification, is necessary.



Figure 7.5 Congenital dermoid at dorsal limbus in an otherwise normal eye.

Microcornea

The appearance of relative corneal undersize in an otherwise normal and visual globe is not uncommon [113], and this appearance may appear exaggerated in the absence of bulbar conjunctival pigment. Microcornea may be associated with anterior segment dysgenesis (ASD) (Figure 7.6).

Corneas of diameters of less than 10 mm are usually associated with complex microphthalmos and blindness.

Megalocornea and cornea globosa

Megalocornea (enlarged cornea) and cornea globosa (abnormally shaped cornea) have been observed in 43 of 71 phenotypically homozygous multiple congenital ocular abnormalities (MCOA) horses (online Figure 7.37) [25, 114]. This is a complex ocular developmental syndrome seen in several breeds of horse and pony, and is associated with silver dapple coat color [115]. Haplotypic linkage of MCOA with a missense mutation of the pre-melanosomal protein 17 (PMEL17) gene on chromosome 6 has been established [116]. Homozygous phenotypes typically present a spectrum of ocular abnormalities in addition to megalocornea/cornea globosa, including iris hypoplasia, shallow anterior chamber, goniosynechae, cataracts, and retinal dysplasia and detachment.

Affected horses have a clear cornea with normal central topography, grossly observable increased corneal diameter, a



Figure 7.6 Congenital microcornea in association with ASD.

shortened radius of corneal curvature, and a globular protruding corneal contour (online Figure 7.37).

There is no treatment and the condition is nonprogressive. However, affected foals may have problems with exposure keratopathy and increased risk of ulceration. In these cases, topical lubricant therapy is required. Megalocornea/cornea globosa must be differentiated from primary or congenital glaucoma, these having a very poor prognosis.

Sclerocornea

Sclerocornea describes diffuse, abnormal collagenization of the cornea causing the cornea to blend with the sclera, obliterating the limbus. It is likely to be associated with more extensive ocular fetopathies or with complex microphthalmos syndrome (online Figure 7.38).

Leucoma

Leucoma describes any focal opacity of the cornea. In the neonate, leucomas may occur in otherwise normal eyes and can vary in location, extent, and corneal depth, and do not progress (Figure 7.7).

Congenital leucoma can be associated with ASD syndrome and with persistent pupillary membranes (online Figures 7.39 and 7.40). In the former, pigmented mesenchymal tissue remnants typically extend from the iris or pupillary margin to insert onto the posterior cornea, resulting in dense stromal opacities. These opacities are typically axial, and isolated blood vessels may extend into the opacity from the limbus. In the former, the leucoma may be confined to the posterior stroma. The corneal opacities are typically vascularized and superficial pigmentation may be present.

In neither case does the leucoma progress.

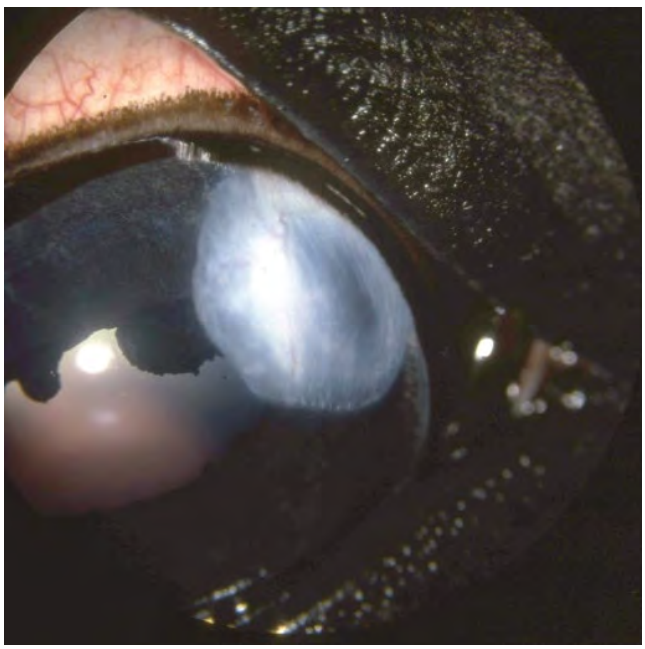


Figure 7.7 Congenital leucoma in a yearling Highland pony, present since birth. The well-defined opacity infiltrates the posterior stroma. The eye is otherwise normal.

Ectasia

Congenital corneal ectasia, or thinning, is a rare finding. The thinned area of cornea may be lined with iris tissue, where the lesion is more correctly referred to as congenital staphyloma (online Figure 7.41). It is nonprogressive, and where this is the sole abnormality, affected eyes are likely to be normally visual.

Congenital vascularization and pigmentation

Congenital corneal vascularization has been reported in a Thoroughbred foal examined at 16 hours of age [117] and in a foal associated with congenital corneal melanosis [118]. In the reported cases, the pathogenesis is unknown but believed to be associated with late-term intrauterine influences (such as placentitis, or possibly trauma). Late in gestation, the eyelids are no longer attached to each other, allowing exposure of the corneas and conjunctiva to amniotic fluid and any irritants within it.

Clinical signs include bulbar and palpebral conjunctivitis, hyperemia, and vascular congestion (online Figure 7.42) [117]. Short, straight, superficial perilimbal vessels extended from the conjunctiva onto the dorsal cornea [117], and no other ocular abnormalities or signs of ocular pain were present. Pigment, where present, is typically superficial.

Differential diagnoses include post-natally acquired keratitis associated with trauma, entropion, foreign bodies, keratoconjunctivitis sicca (KCS), congenital anterior uveitis, and congenital glaucoma.

In the reported cases, no treatment was necessary and the vascularization resolved spontaneously within 7 days. Thorough evaluation is required to rule out other causes of keratitis, where specific treatment is likely to be required.

Primary epithelial disease

Primary, nonerosive, epithelial disease represents a group of pathologies characterized by disruption of the normal epithelial cell architecture and surface contour, and identified principally by epithelial uptake of fluorescein or rose bengal dyes. These diseases are poorly described in the horse.

Epithelial disruption and loss is a primary presenting sign of putative epitheliotropic viral infection, and is described later in the section **Putative viral keratitis**. An irregularly proliferative epitheliopathy, referred to as "epithelial keratopathy," has been described in the horse [119] (see section **Immune-mediated keratitis**).

Primary epithelial disease should be differentiated from secondary disease, which is a consistent finding in tear-deficient or evaporative keratopathies (see section **Evaporative and tear-deficient keratopathies**). Epithelial disease can arise secondary to eyelid or conjunctival disease (e.g., allergic blepharoconjunctivitis, meibomianitis). These present as geographic areas of superficial perilimbal vascularization, stromal haze, and, in some instances, fluorescein-negative epithelial swelling and edema, confined to an area in contiguity with abnormal or inflamed palpebral conjunctiva or the eyelid margin (Figure 7.8). The epithelial changes are presumably a consequence of proinflammatory and vasculogenic cytokine

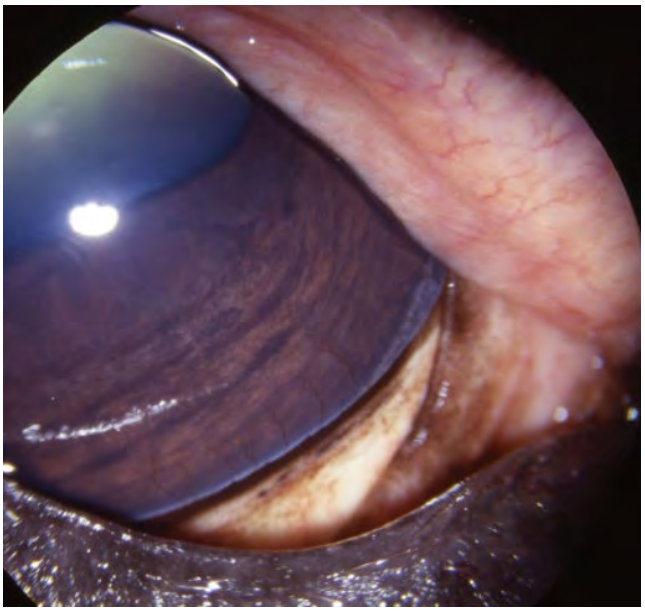


Figure 7.8 Superficial vascularization and mild superficial keratitis secondary to chronic conjunctivitis.

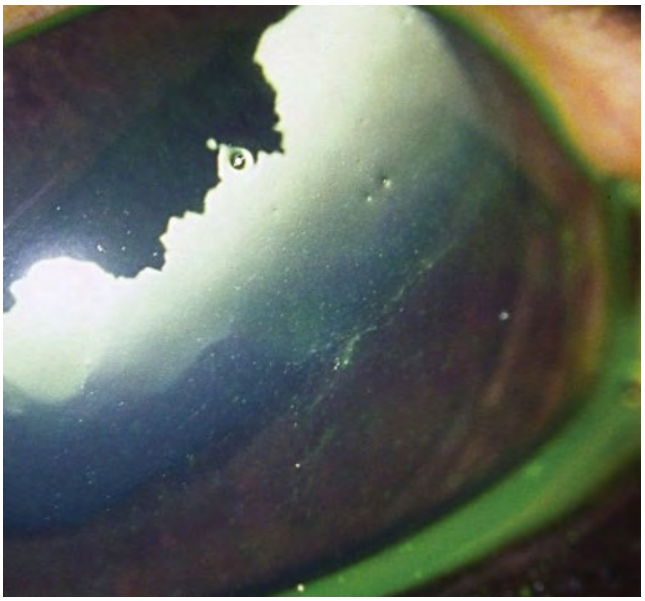


Figure 7.9 Linear anatomic disruption of epithelial contour in the central cornea in a case of suspected primary epithelial disease. The epithelial lesion does not retain fluorescein.

and chemokine release into the tear film from inflamed contiguous tissue. Treatment in these cases is directed against the primary clinical problem.

Chronic nonhealing epithelial erosions are described in the section **Ocular surface disruption and corneal ulceration**.

Prevalence

Primary epithelial disease has been recorded only in adult horses, and there is no obvious breed or sex predisposition.

Pathogenesis

The primary pathological event in these diseases appears to be the appearance of abnormal or dysplastic epithelial cells, variably causing accelerated loss or exaggerated accumulation of superficial cells, and disruption of intercellular linkages. The BM appears intact. The etiological drivers of these pathologies are poorly understood and likely to be complex, but may involve qualitative tear film abnormalities, molecular anomalies within the BM and anterior stroma, and infectious agents, these possibly acting in some instances as epitopic triggers of deviant innate immunoresponsiveness rather than as replicating cytodestructive pathogens. Epithelial keratomycosis, presenting as punctate epithelial lesions (online Figure 7.103), has been described as a specific disease entity in the USA (Figures 7.73, 7.75, and 7.76) (see section **Fungal corneal ulceration: the biological continuum of equine ulcerative keratomycosis**) [120–123].

Diagnosis

Diagnosis is based on clinical signs. The diseases are typically unilateral and are associated with slight to moderate ocular pain. The exception to this is putative viral disease which can present with severe ocular pain. Geographic anterior stromal haze is usually present, and superficial vascularization can appear with chronicity. Most typically, on biomicroscopy there are geographic areas of abnormal epithelial transparency and contour. The eye is otherwise normal. The area of epithelial disruption may be fluorescein negative (Figure 7.9 and online Figure 7.43).

However, where present, the pattern of epithelial fluorescein retention may be punctate, dendritic, or diffuse, presumably reflecting the anatomic configuration of the epithelial cell response to insult (Figures 7.10 and 7.11, and online Figure 7.44). Some eyes may be correspondingly rose bengal positive; however, individual cases may be fluorescein positive but rose bengal negative. TFBUT may identify abnormal tear adhesion and distribution within the affected areas, but gives no indicator of specific etiology.

Cytology is typically unrewarding, but may differentiate rare instances of early *in-situ* carcinoma. PCRs on epithelial samples can help identify the presence of an infectious agent, although some circumspection in interpretation of the results is necessary where commensal or nonpathogenic organisms or ubiquitous agents, for example, equine herpesvirus-2 (EHV-2), are identified. Quantitative PCRs may be more helpful where they are available. Histopathology on superficial keratectomy (SK) samples may provide information on the nature of the underlying pathology.

Treatment

Treatment in all cases is difficult to rationalize and is frequently frustrating, often with several therapies being introduced sequentially in the hope of some improvement. Any initial

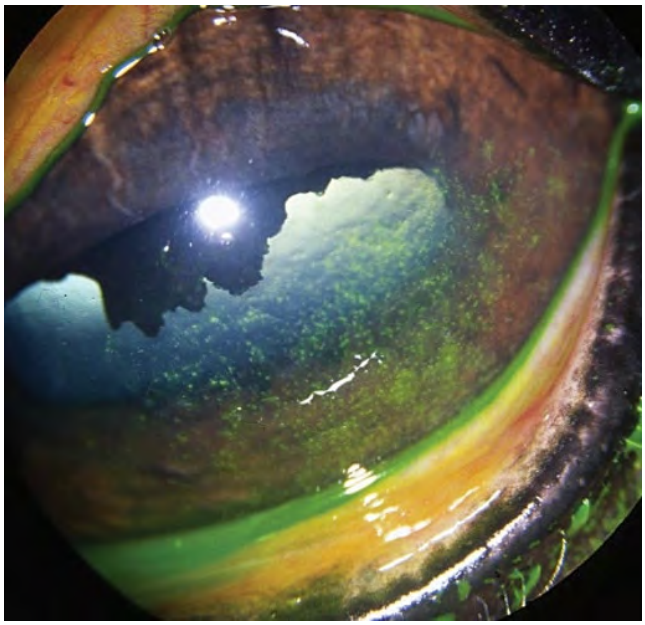


Figure 7.10 Punctate epithelial fluorescein retention in suspected primary epithelial disease.

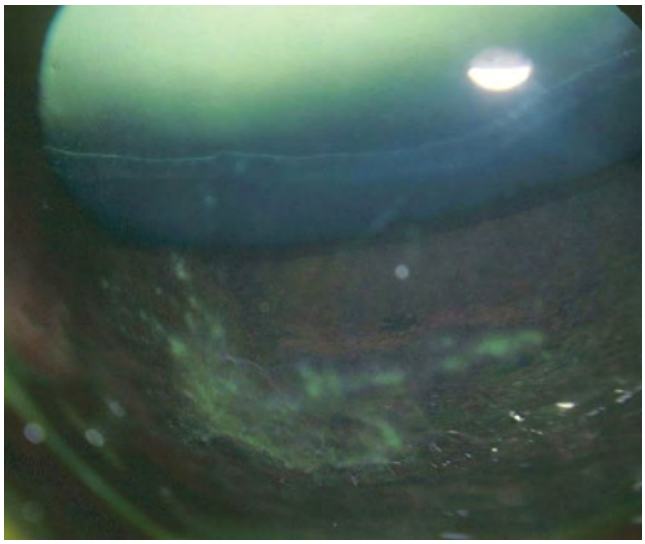


Figure 7.11 Dendritic epithelial fluorescein retention in suspected primary epithelial disease.

improvement may not be sustained, and long-term topical therapy is often required. Options include:

- Tear film replacement or support. Topical serum can be helpful
- Topical antibiotics, antifungals, or antivirals according to PCR results
- Steroidal or nonsteroidal anti-inflammatories
- Immunosupressants: cyclosporine A (CsA), oral, and topical doxycycline or minocycline
- Debridement of the area of affected epithelium. Diamond burr debridement is typically very useful
- SK.

Prognosis

In all cases, the prognosis is guarded, and, with time, affected eyes become increasingly refractory to treatment. Spontaneous recovery is possible; however, recurrence at some time distant cannot be excluded in any one case.

Evaporative and tear-deficient keratopathies

Evaporative and tear-deficient keratopathies are two categories of "dry eye" syndrome recognized in horses [124], both presenting as a superficial keratitis of varying severity, with recurring or epithelial sloughing, vascularization, and, in some cases, pigmentation [124]. They are a consequence of abnormal production, composition, distribution, breakup, or loss of the preocular tear film [124].

Evaporative keratopathies

Prevalence

Evaporative keratopathies are synonymous with exposure keratopathies, and can affect any age or breed. They are frequently associated with lagophthalmos and anatomic disruption of the lid margin resulting from primary adnexal diseases such as large colobomas, and secondary lid problems such as neoplasia, unrepaired lid injury, chronic conjunctivitis, chronic blepharitis, and parasitic granuloma. In relatively rare instances of meibomianitis and chelazion in the horse, impaired production of the lipid layer of the tear film is likely to exacerbate evaporative loss of the aqueous component [124]. Evaporative dry eye is also a complication of exophthalmos, resulting from expansive retrobulbar pathology including neoplasia, abscess, or hydatid cyst, or in megalophthalmic foals. Ptosis, causing blink mechanism disruption, and resulting from facial nerve paresis, Horner's syndrome, equine dysautonomia, or botulism, is only rarely associated with evaporative dry eye. Protracted general anesthesia can be associated with evaporative dry eye, and topical ocular lubricants should be routinely used to protect the ocular surface. Similarly, the corneal hypoasthesia present in sick neonatal foals can predispose to evaporative dry eye problems [60]. Extreme environmental conditions can potentially result in evaporative keratopathies.

Diagnosis

Evaporative keratopathy should be presumed to be potentially present in all of the clinical situations described above (online Figure 7.28).

Treatment

In all cases of evaporative keratopathy, the primary cause should be identified and where possible corrected. Regular application of ocular lubricants or artificial tears will mitigate the effect of tear film loss, and temporary tarsorrhaphy or bandage contact lenses may be helpful in protecting the cornea in some cases.

Tear-deficient keratopathies

Tear-deficient keratopathies may be qualitative or quantitative [124]. KCS is the result of a quantitative deficiency in the aqueous portion of the preocular tear film. Qualitative abnormalities of the aqueous constituent composition or of the mucin layer–epithelial glycocalyx structure and stability have not been described in the horse. However, if present, they are likely to impact on ocular surface health and cause disruption of epithelial cell turnover and repair, and to predispose the ocular surface to infectious injury (see section **Fungal-induced precorneal tear film instability**). Following recovery from ocular surface or corneal disease or injury, most typically ulceration, some horses may show persistent mild blepharospasm in the absence of any overt clinical abnormality of the ocular surface. STT I times are normal; however, TFBUT may be decreased and the corneal surface may retain rose bengal and lissamine green stain in an irregular or geographic pattern, possibly reflecting mildly dysplastic or abnormally polarized repair epithelium (online Figure 7.45). Some corneal scars will retain Rose Bengal, as will neoplastic epithelial cells.

Prevalence

KCS is rare and has been reported in mainly younger horses. There is a single report of idiopathic KCS in a 19-year-old Shetland pony [125].

Pathogenesis

KCS is most frequently the result of disruption of the parasympathetic nerve supply to the lacrimal gland. The anatomy of the autonomic supply to the lacrimal gland in the horse is unresolved. However, the model is that the preganglionic parasympathetic fibers arising in the lacrimal nucleus within the pons combine with sensory fibers from the facial nucleus as far as the geniculate ganglion lying within the facial canal. Here the preganglionic and sensory fibers to the lacrimal gland leave the facial nerve trunk to form the major petrosal branch of the facial nerve, these nerves exiting the skull via the closely proximate petrosal and stylomastoid foramina, respectively. The parasympathetic preganglionic neurones synapse with postganglionic fibers in the pterygopaplatine ganglion located in the ventral floor of the orbit. The postganglionic fibers reach the gland via the zygomatic branch of the maxillary division of the trigeminal nerve. Sensory fibers travel to the gland in the lacrimal nerve of the ophthalmic division of the trigeminal nerve.

Because of the exposed anatomic location of these nerves in the temporal part of the skull, KCS is associated with fractures of the stylohyoid bone [126] and the proximal vertical ramus of the mandible [127]. KCS is reported in cases of temporohyoid osteoarthropathy (middle ear disease) [128]. Because of the anatomic proximity of the facial nerve, concurrent facial palsy may be present in these cases. KCS may also be present along with facial nerve paralysis in vestibular disease if the lesion is proximal to the geniculate ganglion [124]. Bilateral KCS has been reported associated with suspected basilar skull fracture [129]. KCS has only infrequently been reported in association with the systemic debility and generalized neurotoxicity associated with locoweed (genera *Astragulus* and *Oxytropis*) poisoning of horses in the USA [130], apparently resulting from direct toxicity to the lacrimal gland. Putatively immune-mediated dacryoadenitis causing bilateral KCS has been reported in horses, in one case aberrant *Thelazia lacrimalis* migration being suspected as a cause [131–133]. KCS thought to be due to peripheral parasympathetic neuropathy has been reported in a 6-year-old Warmblood with hypothyroidism [134]. Dacryoadenitis and KCS are recorded in association with eosinophilic keratitis [135]. Congenital KCS does occur, although the condition is rare and the cause is unknown [136]. Unlike in the dog, oral trimethoprim-sulfa (30 mg/kg once a day) does not reduce tear production in the horse [137]. Cases of KCS in the horse are frequently idiopathic [124, 125, 138]. Acute dacryoadenitis or lacrimal gland abscessation are not reported to be associated with reduced aqueous tear production [139, 140], and surgical removal of the lacrimal gland does not result in absolute KCS [140].

Diagnosis

Diagnosis of KCS is based upon presenting clinical signs, which include blepharospasm, mucopurulent discharge, a dull and lackluster cornea, and overt keratoconjunctivitis (Figure 7.12). Depending on the cause, other signs such as ptosis and periocular swelling may be present. Diagnosis is confirmed by STT. STT I assesses basal and reflex aqueous tear production results. Results in normal horses vary widely and mean values from 12.7 to 26.2mm/min are reported [141–143]. No horses with STT I results of less than 10 mm/min were found in a population of normal horses [141], and, in general, STT I results of 0–10 mm/min or less are considered diagnostic of KCS [144]. Comparison with tear production in the contralateral eye may be useful in field cases. However, caution should be exercised since some normal horses show significant variation in STT I results between both



Figure 7.12 Keratoconjunctivitis sicca, showing mucoid discharge, epithelial erosion, stromal haze, and lackluster corneal surface. STT I was less than 4 mm/min in this eye.

eyes [141]. Aqueous tear production in horses shows circadian variation [142], and sequential testing should take account of this. STT II measures basal aqueous tear production, and no variation between STT I and STT II was reported in one study [141].

Tear film instability can lead to poor healing of infected and noninfected corneal ulcers in the horse. The normal tear film is continuous over the cornea, with blinking maintaining this continuity. If the tear film is abnormal and cannot provide nutrition to the injured cornea, corneal healing can be delayed. The TFBUT test is another use of fluorescein dye that can assess the stability of the tear film. Fluorescein dye is placed on the cornea and not flushed off. The lid is manually blinked three times and held open to expose the tear film to evaporation. Dark, dry spots will appear under cobalt-blue-filtered light as part of normal evaporation of tears. The time required for a dry spot to appear on the corneal surface after blinking in the TFBUT in a normal healthy horse eye is approximately 20 seconds. A TFBUT of less than 10 seconds is abnormal and associated with instability of the mucin layer of the tear film in horses [22, 23]. Abnormal TFBUT values in nonhealing ulcers can indicate a reason and mechanism for the failure of an ulcer to heal.

Treatment

Where possible, a primary cause should be identified and treated. Local medical treatment generally involves the long-term use of corneal lubricants and sodium-hyaluronate-based tear replacement products every 2–6 hours. CsA appears to have some lacrimogenic effect in dogs when applied topically [143], and twice daily topical use of 2% CsA in two horses may have effected short-term improvement in aqueous tear production [129, 131]. The use of topical CsA in the longer term management of KCS in horses has not been extensively investigated; however, twice daily use of topical 2% CsA over a 26-month period helped restore and maintain adequate aqueous tear production (15 mm/min) in a 7-year-old Conemarra stallion where surgical parotid duct transposition had failed [133]. Where topical CsA has been shown to have a beneficial effect, an episclerally placed, sustained release CsA implant could be considered and may reduce the frequency of topical medication. Lacrimostimulation using topical pilocarpine in concentrations from 0.124% to 4% has produced mixed short-term results in horses with KCS [126, 129, 131, 132]. Any concurrent corneal ulceration should be treated as required.

Parotid duct transposition, using salivary gland secretions to lubricate the ocular surface, has been successfully performed in two horses [133, 138]. In one case where bilateral transposition was performed, failure in the left eye resulted from avascular necrosis of the distal duct [133]. Enucleation is an option where treatment is not feasible.

Prognosis

In all cases of tear-deficient keratopathies the prognosis is guarded. Aqueous tear production does not return to normal in most cases, and lifelong medication with tear substitutes is required.

Trauma, wounds, and foreign bodies

Traumatic cornea injury, including foreign bodies, partial- and full-thickness lacerations, and iris prolapse, is encountered relatively frequently in horses because of the prominence of their globe and the presence of unavoidable hazards in their environment [145–147].

Prevalence

A study of corneal lacerations in horses identified blunt trauma as the cause in 46.5% (20/43 eyes) versus sharp trauma in 23.3% (10/43 eyes) and undetermined causes in 30.2% (13/43 eyes) [145]. Iris prolapse developed in 46.9% of perforations from infected corneal ulcers and from trauma-induced full-thickness corneal lacerations (15/32 eyes each). Iris prolapse occurred in 6.2% (2/32 eyes) with ruptured deep stromal abscesses (DSA) [146].

Pathogenesis

Potential corneal and conjunctival foreign bodies may be readily encountered in the immediate environment of most horses, and specific geographic problems do occur, notably burdock pappus bristles in the northeastern USA during the the fall [148]. If lodged within the conjunctiva or fornices, foreign bodies may cause persistent corneal irritation, resulting in erosion, superficial ulceration, and vascularization, and will predispose corneal infection. If lodged within the cornea, they can cause anything from mild local irritation and vascularization to a more extensive local inflammatory response, stromal abscess (SA), and anterior uveitis.

Traumatic injury of the cornea can be classified according to the depth of cornea involved.

- **Superficial**: typically epithelial injury with minimal anterior stromal loss
- **Penetrating**: the stroma is involved to a varying depth up to Descemet's membrane
- **Perforating**: the cornea has been penetrated and the anterior chamber entered, becoming directly involved.

Penetrating and perforating lacerations may result both from blunt trauma (i.e., collision with stationary objects, whiplash injury from branches or riding crops, or kicks from other horses) and from sharp trauma (i.e., nails, sticks). Owing to the distribution of forces within the eye, blunt trauma may also be associated with more extensive intraocular injury, including lens luxation, retinal detachment, choroidal rupture, and intraocular hemorrhage (Figure 7.13).

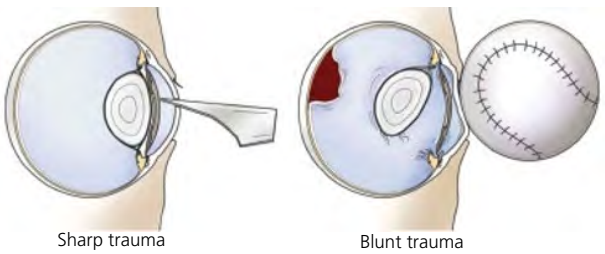


Figure 7.13 Diagram showing effects of sharp versus blunt ocular trauma. Sharp trauma is more likely to severely affect the cornea, anterior chamber and lens. Blunt trauma is more likely to produce severe posterior segment damage.

Circumferential corneoscleral rupture at the limbus can result from blunt trauma [149], and partial or total evisceration of the ocular contents can follow (Figure 7.14 and online Figure 7.46). Sharp trauma may penetrate the cornea, iris, and lens (Figures 7.13, 7.16, 7.17, and 7.18).

Iris prolapse results from corneal perforation caused by both sharp trauma and rupture of a deep corneal ulcer or SA. Iris prolapse appears to be an innate protective mechanism causing rapid sealing of the corneal wound (Figure 7.15 and online Figures 7.13, 7.14, 7.15, 7.16, and 7.46).

Corneal foreign bodies

Diagnosis

The primary presenting clinical signs of corneal foreign bodies are epiphora, blepharospasm, and corneal opacity and vascularization, the extent of each being determined by the size, depth, nature of, and duration of the foreign body. Foreign bodies lodged in the conjunctival fornices or under the third eyelid, and, less commonly, superficial foreign bodies retained



Figure 7.14 A ruptured cornea with iris prolapse and lens expulsion. The globe was enucleated.



Figure 7.15 A 13-year-old Quarter horse gelding with corneal perforation and iris prolapse, with associated miosis, anterior uveitis, and shallow anterior chamber. Note the perilimbal corneal vascularization indicative of a chronic process.

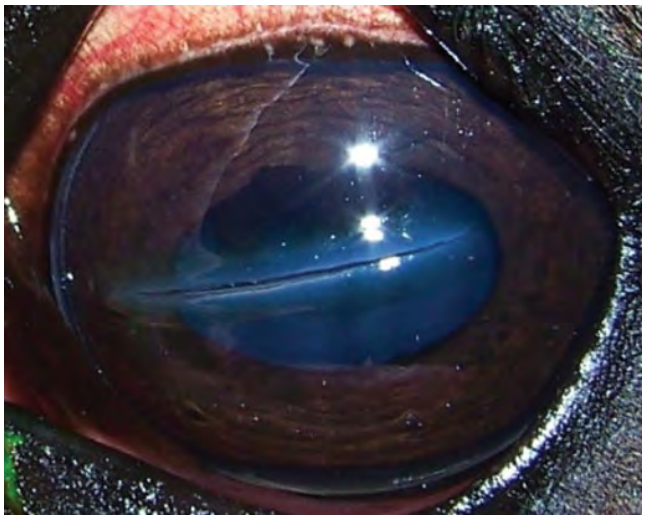


Figure 7.16 A sharp laceration of the central cornea from a tree branch was treated medically and healed well, but could have also been sutured. (*Source*: Image courtesy of Dr Ann Dwyer.)

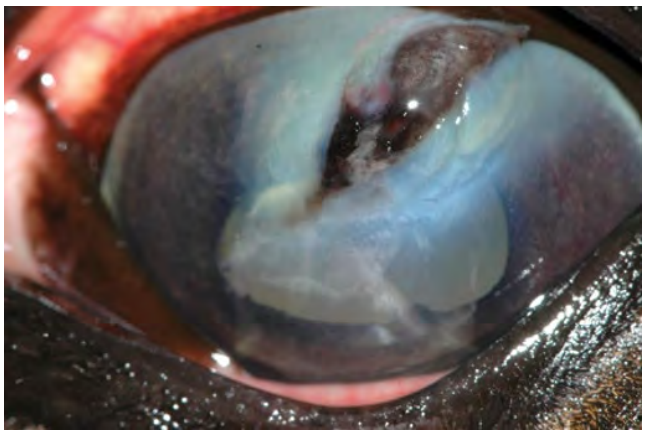


Figure 7.17 A long linear corneal laceration with iris prolapse is treated with corneal suturing and a conjunctival pedical graft.



Figure 7.18 Three weeks post-operatively the eye in Figure 7.17 has some conjunctival graft retraction evident. The eye is visual.

on the corneal surface by the surface tension of the tear film, will rapidly abrade the corneal epithelium as they are moved across the corneal surface by lid action (Figure 7.19). This may result in local erosion and ulceration corresponding to the area of contact of the foreign body or more extensive geographic erosion.

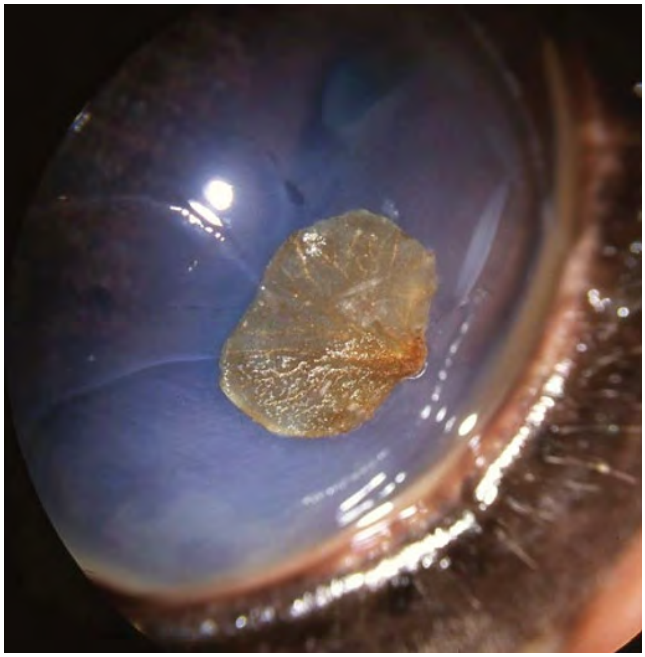


Figure 7.19 Superficial foreign body in Miniature Shetland pony. A leaf segment is trapped in the tear film and causing extensive epithelial abrasion as it moves freely with blinking.



Figure 7.20 Superficial foreign body in an old pony. A grain ear is embedded in the superficial stroma, causing a marked vascular response and extensive edema.

Solitary foreign bodies, typically forage or grain debris, can penetrate and lodge in the anterior stroma (Figure 7.20), rapidly resulting in increasing local edema and inflammatory cell infiltrate. In the case of shallow-angled penetrating wounds, dirt and particulate debris can be inoculated into the anterior stroma (online Figure 7.20), becoming trapped under increasingly edematous epithelium. Deep stromal lodgment of particularly organic foreign bodies will provoke an aggressive local inflammatory response, which may obscure the presence of the foreign body (Figure 7.21). The presence of multiple foreign bodies, as in the case of burdock bristles, may result in geographically extensive edema and disruption of the corneal contour (online Figure 7.21).

Penetrating foreign bodies extending into or becoming lodged in the anterior chamber are typically associated with some degree of hyphema or anterior uveitis. The severity of the uveitis increases if infection becomes established or there is lens capsule penetration causing leakage of uveitogenic lens material into the anterior chamber. The resulting corneal edema will impede visualization of a foreign body, and ultrasonography may be necessary to identify the presence of a foreign body in the anterior chamber (online Figures 7.22 and 7.23).

Rarely, small inert foreign bodies (e.g., glass) in the cornea or anterior chamber will provoke minimal response.

Diagnosis is based on clinical signs and identifying the presence of the foreign body. Conjunctival foreign bodies should be suspected in all cases of geographically discrete erosion or superficial ulceration, and a thorough examination of the fornices carried out under sedation and local anesthesia. Frequently, a foreign body will provoke extensive chemosis, causing the conjunctiva to envelop and obscure the foreign body, and in these cases the lid should be fully everted and the conjunctiva flushed with saline under gentle pressure to identify and dislodge the foreign body. Corneal foreign bodies are usually obvious;

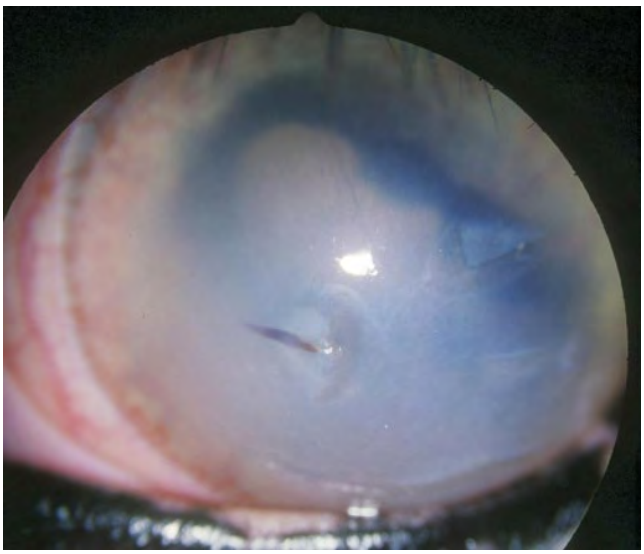


Figure 7.21 Penetrating foreign body: a thorn fragment deeply embedded in the corneal stroma and partly obscured by extensive edema. Adjacent superficial laceration areas and anterior uveitis are present.

however, magnification or biomicroscopy may be necessary to locate and assess the depth of smaller objects. Slit-lamp biomicroscopy is helpful in locating very small and deeply located foreign material, but its use can be limited by the extent of corneal edema and cell infiltration present. *In vivo* confocal microscopy has been used to identify embedded microscopic corneal foreign bodies, including burdock pappus bristle fragments and surgical glove powder [150]. Ultrasound biomicroscopy has the potential to identify some small corneal foreign bodies [151], although there are no reports describing its use in the horse.

Burdock pappus bristles or their fragments are difficult to identify, even with magnification, and may be associated with only mild discomfort [148]. In some instances, affected horses are symptomatic for several days to weeks before being presented for examination. Commonly, the bristles become lodged under the third eyelid, resulting in superficial excoriation of the cornea contiguous to the third eyelid (see Figure 3.40). Where embedded bristles cannot specifically be identified, presumptive diagnosis is based on clinical presentation, time of year, and probability of exposure to the plant (affected horses commonly have thistles entangled in the mane, forelock, or tail). Atypical cases can present as small areas of limbal vascularization, with or without an epithelial defect, distant from the third eyelid [148].

Treatment

The primary aim in all cases is removal of the foreign body as atraumatically as possible, followed by treatment of the site as an infected abrasion or ulcer. Removal of superficial foreign bodies can usually be achieved in the standing sedated horse using a palpebral nerve block and topical anesthesia. The foreign body can be removed using a dry cotton swab, a Kimura platinum spatula, or by hydropulsion with sterile saline or buffered salt solution using a 5-mL syringe and 25-G needle with the tip removed [152]. Deeper and embedded stromal foreign bodies may require removal under general anesthesia. In these instances, the foreign body can be removed using a foreign body spud, fine corneal forceps, or a blunted 25-G needle. Where possible, the foreign body should be grasped and removed by reversal of its entry pathway. However, in some instances it is necessary to incise down onto the foreign body to facilitate extraction.

Removal of particulate debris locally dispersed under detached epithelium or in the anterior stroma requires removal of the overlying epithelium and stroma before removal of the debris by hydropulsion or gentle debridement, or by SK. Scattered superficial speculate and debris such as burdock bristles should be removed by gentle debridement using the blunt end of a scalpel blade or the open jaw of a small hemostat, followed by copious lavage of the site using sterile saline. In the case of burdock bristles, following debridement, a final "sweep" of the site using a dry surgical swab wrapped round a gloved finger is recommended, before final lavage [148].

Close monitoring of the eye for potential complications such as progressive ulceration, infection, or abscess is required in all instances.

Penetrating corneal foreign bodies can be associated with loss of aqueous humor alone or with additional damage to intraocular structures. Hypotony and hyphema can be present. Small corneal perforations can be sutured after removal of the foreign body and therapy for infection and uveitis is initiated. Fibrin and hyphema clear relatively quickly from the anterior chamber in the horse once the primary insult is removed; however, clearance can be accelerated by intracameral injection of tissue plasminogen activator (TPA) (50–150 mcg in 0.1 mL balanced salt solution (BSS)) 48 hours after bleeding has stopped. If the globe is so damaged that there is severe hypotony, globe collapse, cataract, and retinal detachment, the eye should be enucleated.

Small inorganic intraocular foreign bodies (e.g., glass shard) can be tolerated in the horse, causing minimal problems once the initial traumatic uveitis has resolved. However, these eyes should be closely monitored and the foreign body removed where the potential for debilitating sequelae exceeds the risk of iatrogenic injury associated with surgery. Organic material retained within the anterior chamber will inevitably cause endophthalmitis and, ultimately, phthisis bulbi, and where the material cannot be safely removed or where the existing injury is irreparably extensive, then enucleation should be considered.

Prognosis

Where the foreign body is removed shortly after entry, the prognosis is, in general, excellent. However, in some instances, a permanent corneal facet may form (Figure 7.22). Although some degree of astigmatism will be present, this is of no consequence in most instances. Delay in removal or incomplete removal increase the risk of infection, including mycosis. Penetrating foreign bodies typically cause some degree of anterior uveitis, and even after successful removal and aggressive

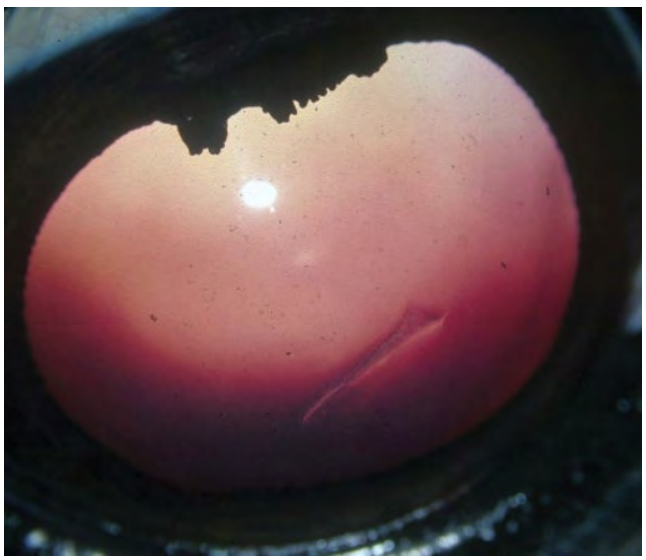


Figure 7.22 Epithelialized corneal facet as a consequence of superficial foreign body lodgment.

post-surgical management, sequelae such as synechae and cataract are likely. Phthisis is inevitable in some instances.

Lens capsule perforation can be associated with cataract formation, and where there is leakage of lens material into the eye, frequently intractable phacoclastic uveitis occurs and will markedly compromise clinical outcome.

Nonlacerating blunt trauma

Diagnosis

Diagnosis is based on clinical presentation. Frequently, there is no definitive history of trauma, and a traumatic incident is presumptive. Signs highly suggestive of blunt trauma, such as orbital fracture, may be present. Nonpenetrating blunt trauma, direct to the globe or through closed lids, results in a pressure wave traversing the fluid ocular media and can result in a number of specific corneal pathologies in both the short and long term. Several of these pathologies may be present in any one eye, and they include:

- Geographic or generalized edema, arising from endothelial dysfunction secondary to traumatic anterior uveitis (Figure 7.23), or, possibly, from Descemet's membrane detachment (online Figure 7.8).
- Rupture of Descemet's membrane. These appear as typically linear refractile opacities, and may be discontinuous (Figure 7.24), bridge the horizontal or parasagittal vertical meridian, or extend in a branching pattern across the cornea (Figure 7.25). In the early stages these may be accompanied by locally contiguous or more generalized stromal edema (online Figure 7.24).
- Dense retrocorneal fibrotic membranes (RCFMs) (also called posterior collagenous zones) may form in some cases where there is extensive anterior segment injury (Figure 7.26). See section **Uncommon Keratopathies** in online version.
- Local tearing and dehiscence of the pectinate ligaments (online Figure 7.25).
- Corneal folding (Figure 7.27) is a very rare consequence of periorbital trauma.

Deep corneal pathologies, and intraocular injury, may be obscured at initial examination by extensive stromal edema, and become evident only several days to weeks after injury as corneal clearing progresses. Ultrasound examination in the presence of generalized corneal opacity can be extremely useful to identify major intraocular injury, including hyphema, lens luxation or subluxation, intravitreal hemorrhage, and vitreoretinal detachment. Infrared photography facilitates examination of the anterior chamber and iris through an edematous cornea [153].

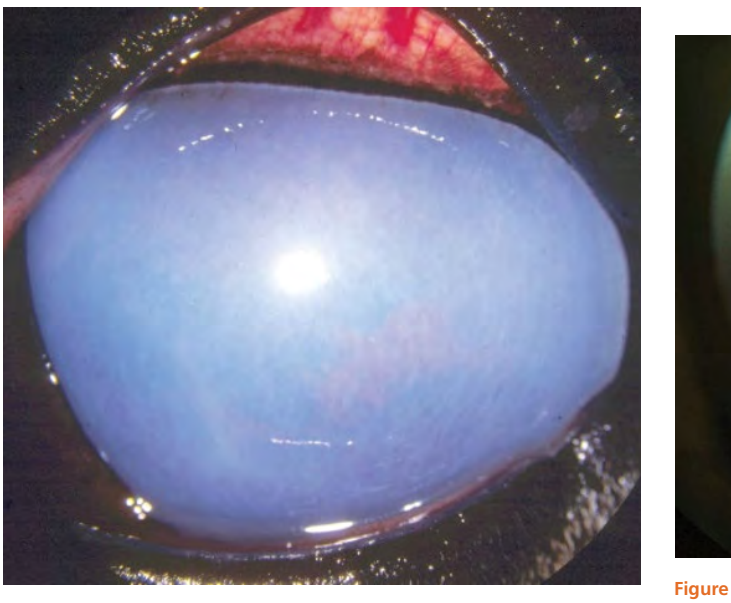


Figure 7.23 Generalized corneal edema following blunt trauma to the globe. Hyphema is present.



Figure 7.24 Discontinuous rupture in Descemet's membrane resulting from direct blunt ocular trauma. The lesion appears as linear and slightly refractile deep opacity in the axial cornea.

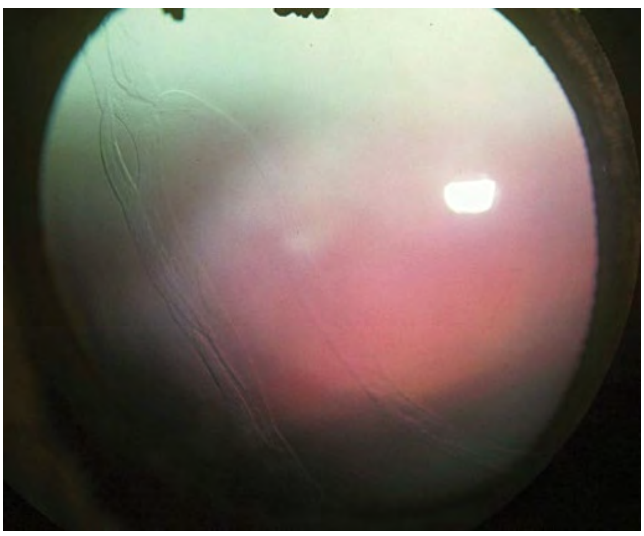


Figure 7.25 Branching refractile striae associated with rupture of Descemet's membrane following blunt ocular trauma. There is extensive vitreal and chorioretinal degeneration in this blind eye.

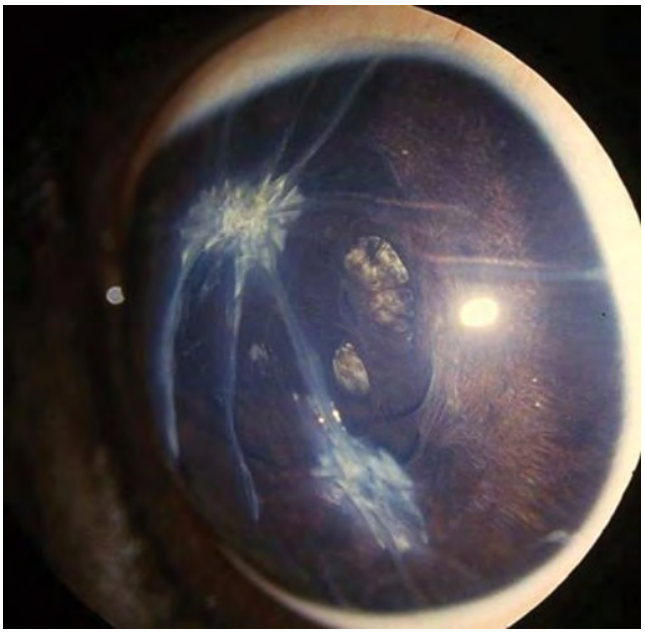


Figure 7.26 Dense linear retrocorneal fibrous membranes (RCFMs) (posterior collagenous zones) radiate from the dorsal axial cornea following severe focal blunt trauma. Linear refractile opacities more typical of Descemet's membrane ruptures are also present in the dorsolateral corneal quadrant. There is extensive intraocular injury and the eye is slightly phthisical.

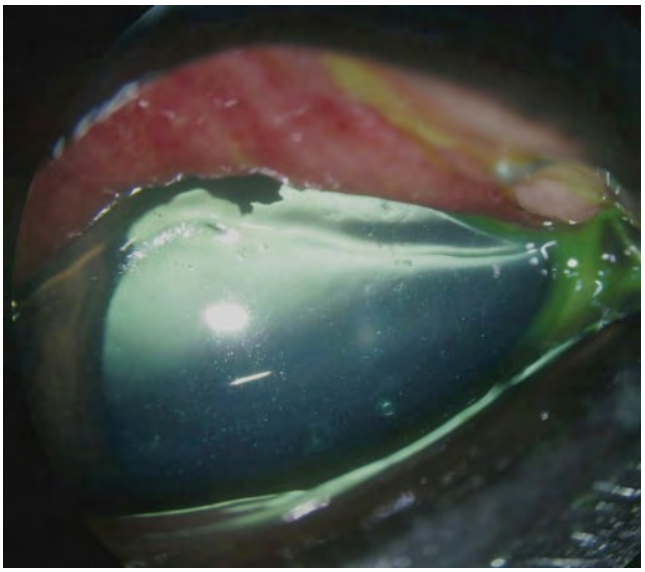


Figure 7.27 Folding of the cornea near the horizontal meridian following blunt periorbital trauma. The eye is blind but otherwise normal, and extensive periorbital fractures were present.

Treatment

Initial treatment is directed at controlling anterior uveitis, and is instituted as for noninfectious uveitis arising from any cause, including local and systemic corticosteroids, systemic NSAIDs, and topical atropine. In the case of hyphema, Injection of recombinant TPA into the anterior chamber 48 hours after bleeding has stopped may accelerate clot dispersal and prevent RCFM formation, promoting corneal clarity. However, recombinant TPA has a dose-dependent toxic effect on cultured corneal endothelial cells [154], and the recommended dose (50–150 mcg in 0.1 mL BSS) should not be exceeded.

In all instances, the globe and periorbital area must be carefully examined for the presence of foreign bodies or fractures, including rare orbital "blow–out" fractures, involving primarily the lacrimal bone [155].

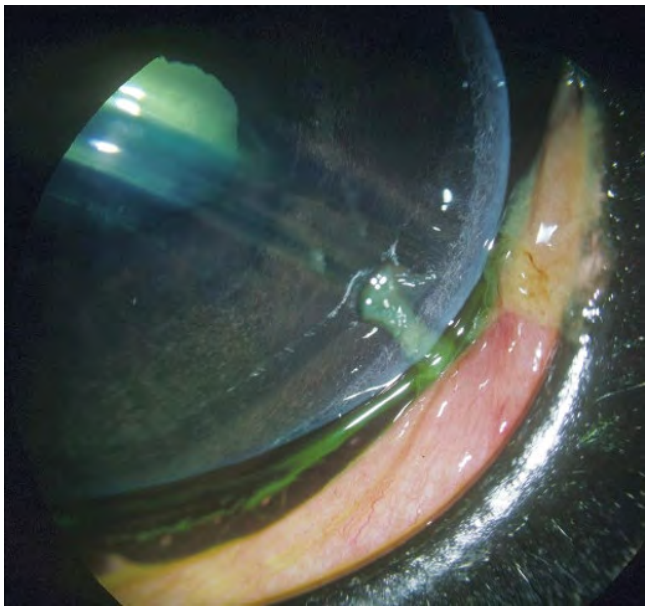


Figure 7.28 Superficial laceration. The superficial epithelium has been neatly excised from the deeper layers and remains attached at the limbus. The resulting abrasion shows only very muted fluorescein retention.

Prognosis

The prognosis in all cases is initially guarded, and ultimately becomes dependent on the extent, severity, and permanency of any intraocular injury, in particular cataracts, peripapillary or generalized chorioretinopathy, and neuroretinopathy. Injuries to Descemet's membrane, pectinate ligament avulsions, and RCFMs result in permanent corneal opacities to a greater or lesser degree.

Corneal lacerations

Diagnosis

All corneal lacerations are initially associated with overt pain, blepharospasm, and epiphora. Sedation and palpebral nerve block is required to facilitate examination in most cases. Until the depth of any laceration is established, forced manual opening of the eyelids must be avoided to prevent iatrogenic rupture of the globe. Diagnosis is based on visual assessment of the extent and depth of the laceration. Direct magnification or slit-lamp biomicroscopy is invariably helpful. Superficial lacerations involve the epithelium and anterior stroma to a varying depth. In cases where the epithelium alone is involved, the injury may be classed as a simple abrasion (Figure 7.28). Penetrating

lacerations involve the epithelium and stroma to the depth of Descemet's membrane, and can have any extent, configuration, and angle of penetration. In the case of deep penetrating lacerations, local stromal edema will cause the edges of the wound to bulge, extending the apparent width of the wound (Figure 7.29).

All deep penetrating lacerations should be subject to Seidel's test for aqueous leakage, that is, to identify the presence of corneal perforation, which will significantly affect the management of the injury (Figure 7.30). Larger perforating lacerations typically are rapidly sealed with anteriorly prolapsed iris and fibrin, presenting a characteristic grayish-red to black mass within the depth of the injury (Figure 7.17 and online Figure 7.26) (see section **Corneal perforation: iris prolapse**). This represents an innate protective response in instances of perforating injury, aimed at preserving ocular contents. Exceptionally, small penetrating lacerations may seal with fibrin alone (Figure 7.31). All penetrating and perforating lacerations are at high risk of infection, resulting in stromal lysis and expansion of the edges of the laceration, and, in the case of perforating lacerations, infectious anterior uveitis and endophthalmitis.

Geographically extensive penetrating lacerations can result in expulsion of ocular contents along with widespread corneal opacity, intra- and extraocular fibrin accumulation (online Figure 7.27), and eyelid swelling. In these instances, careful transpalpebral B-mode ultrasonography, carried out using minimal probe pressure, can be used to determine the extent of intraocular injury, which critically influences both management and prognosis. Circumferential corneoscleral lacerations at the limbus, typically resulting from violent blunt trauma, are at a very high risk of loss of ocular contents and/or chorioretinal tearing, markedly affecting the subsequent management. Careful transpalpebral B-mode ultrasonography is helpful in assessing the extent of injury in these cases.

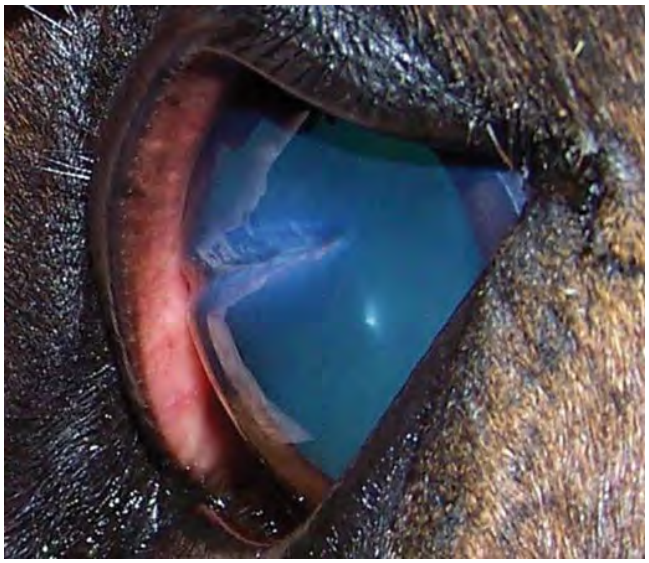


Figure 7.29 Deep penetrating laceration 3 days after injury. Stromal hydration edges cause swelling and bulging of the wound margins, causing the wound to gape and precluding primary closure. (*Source*: Image courtesy of Dr Ann Dwyer.)

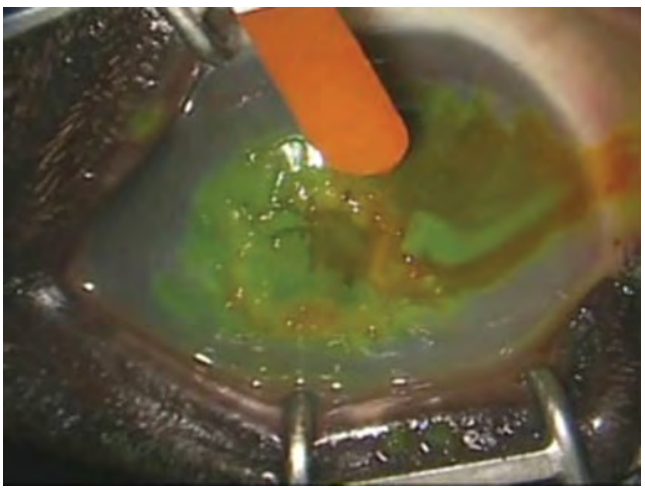


Figure 7.30 A positive Seidel's test evidenced by a change in fluorescein color indicates a leaking suture following a PK.

Treatment

Superficial lacerations are managed by debridement of any loose or detached epithelium and stroma, with the exposed stroma subsequently treated as a simple superficial ulcer. In uncomplicated cases, rapid re-epithelialization of the defect within 2–7 days depending on its geographic extent is expected.

In all cases of penetrating and perforating lacerations, prompt intervention will markedly improve outcome. More superficial penetrating lacerations, where ragged or detached stromal edges are presented, can be effectively managed by sharp excision of

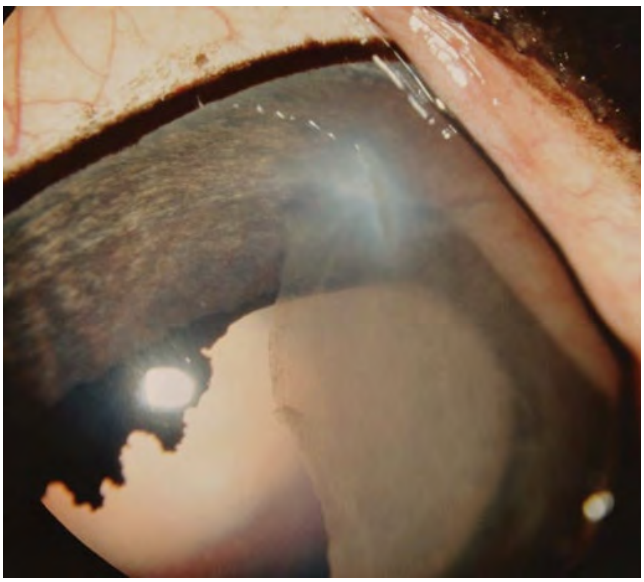


Figure 7.31 This small perforating laceration, occurring 24 hours previously, has been sealed by fibrin, which can be seen attached to the inner aspect of the laceration. There is no evidence of active uveitis and Seidel's test showed no aqueous leakage.

redundant detached stroma and epithelium, and subsequently managed as for an ulcer. Deeper or more extensive penetrating lacerations with intact and overtly healthy wound margins should be managed where possible by primary surgical closure of the corneal wound (see section **Corneal surgery**). Where there is marked edematous swelling of otherwise healthy wound margins, causing gaping of the wound, conservative management, as for ulceration, may achieve a better optical outcome than will result from suturing. Where the wound margins are devitalized, debridement followed by conservative management, or, in the case of large wounds, a grafting procedure, should be undertaken (see section **Corneal surgery**).

Perforating lacerations will invariably be associated with loss of aqueous humor. The horse eye is not tolerant of sustained hypotony and, left uncorrected, phthisis bulbi is the likely outcome. Small perforating wounds sealed with anterior chamber fibrin and with minimal uveitis may do well with minimal medical intervention, namely providing antibiotic, antiprotease, and anti-inflammatory cover; however, such wounds should be closely monitored. In general, perforating wounds, in particular those with iris prolapse where a visual globe is the goal, are optimally managed by iris resection and/or repositioning followed by surgical closure of the corneal wound, with or without conjunctival grafting or placement of a biological dressing (for details of surgical options and procedures see section **Corneal perforation: iris prolapse**). Where there are financial constraints and the wound and prolapse are relatively small, conservative medical management, using topical and systemic antibiotics, systemic NSAIDs, and topical 1% atropine to dilate the pupil, can preserve the globe. However, there is a high but not inevitable risk of complications such as endophthalmitis, atrophy of the globe, phthisis bulbi, and blindness. In eyes with no dazzle reflex, extensive corneolimbal or scleral wounds, and loss of ocular content, enucleation is the best option.

Prognosis

The prognosis in the case of more superficial, uncomplicated, and conservatively managed lacerations is good. Some degree of corneal haze is likely to occur where there has been stromal involvement. In some instances, residual corneal sensitivity to nonspecific irritants such as draughts remains, possibly as a consequence of poor tear film adhesion to the repair epithelium. Regular use of topical ocular lubricants can be helpful in these eyes.

Sutured penetrating lacerations typically heal well, but require careful post-surgical monitoring for infection, suture reaction, and wound breakdown. In the event of wound breakdown, the sutures should be removed and the wound treated as an infected ulcer. Corneal sutures typically result in local stromal scarring, which will diminish over several months to years.

The prognosis for preservation of a visual globe in cases of penetrating lacerations depends on the extent and geographic location of the injury, with limbal or scleral involvement being a poor prognostic indicator. Central lacerations with iris prolapse have a reasonable chance of maintaining vision where intervention is prompt and aggressive, and where the extent of intraocular injury, hyphema, or ocular content loss is limited (see section **Corneal perforation: iris prolapse**) [147].

Chemical and thermal injury

Prevalence

Chemical injuries are infrequently reported in horses, but considering environmental, stabling, and handling variables, they are likely to be under-reported in the literature. Thermal injury can result from stable fires, lightning strike [156], and improper use of thermokeratoplasty or surgical lasers. Case reports in the literature include a mare with presumed organophosphate fly-wipe contact [157] and a gelding with suspected lightning strike [156].

Pathogenesis

Acidic (pH < 7.0) chemical burns coagulate epithelial surface proteins, creating a barrier to further penetration of the agent into the cornea or intraocular environment [158]. In contrast, alkali (pH > 7.0) burns denature epithelial surface proteins, severely impairing barrier function and allowing penetration into the deeper cornea, potentially causing rapidly progressing and extensive keratolysis [159]. Additional factors pertinent to the agent play a role in ocular damage, including its concentration and temperature and the force with which it contacts the cornea [158]. The neutrophil recruitment and consequent elevation in protease inflammatory response which drives the keratomalacic response in alkali injury occurs initially 12–24 hours after injury and then again at 21 days [160].

Corneal epithelium will regenerate after thermal injury if limbal stem cells are present. Stromal collagen response varies with the severity of direct thermal contact, from transient and reversible fibril contraction to irreversible breakdown of interfibrillar covalent bonds and keratomalacia [161].

Diagnosis

There is typically a history of exposure to a chemical or thermal hazard. As in any species, clinical signs of chemical and thermal burns are nonspecific, consisting primarily of varying degrees of blepharospasm, epiphora, chemosis, and conjunctival hyperemia (Figure 7.32) [158, 159]. Corneal opacification is frequent, due to either edema associated with ulceration or keratomalacia associated with an aggressive neutrophil response.

Acid injury is more common and results in geographically well-demarcated and frequently extensive superficial ulceration (Figure 7.33). Alkali injury is relatively rare, and causes rapidly progressive cornea liquefaction. Depending on causal circumstances, injuries can involve the adnexa and periocular area.

Because of the protective blink response, direct thermal injury to the cornea is likely to be superficial even where there is extensive eyelid injury. High-powered laser burns are associated with rapid stromal breakdown and progressive keratomalacia

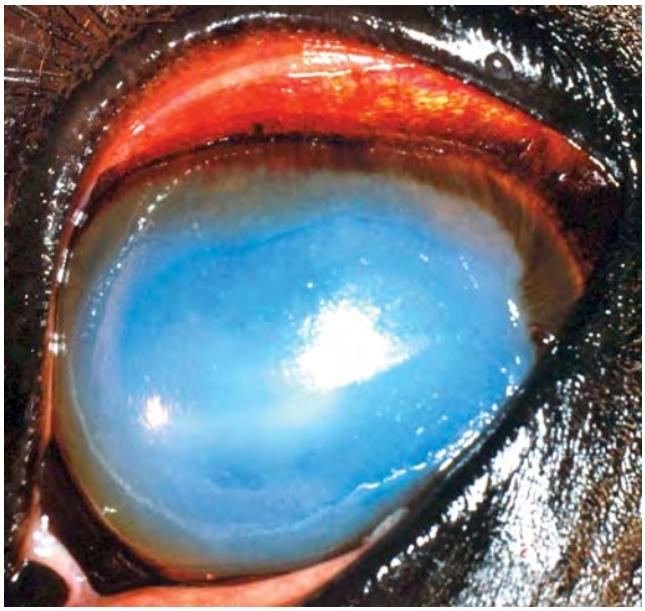


Figure 7.32 Chemical keratitis resulting from accidental contact with formalin. There is extensive superficial ulceration, corneal vascularization, blepharedema, and conjunctival hyperemia.

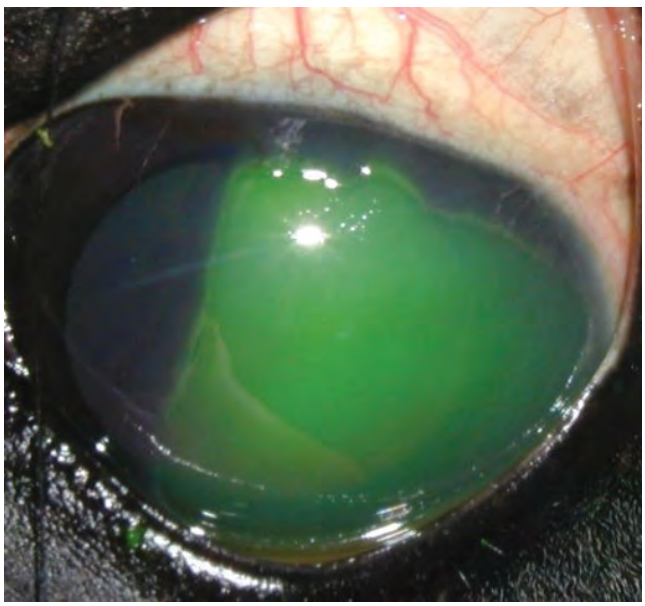


Figure 7.33 Acid burn keratitis, showing an extensive and well-demarcated superficial ulcer.

(Figure 7.34). Corneal edema, vascularization, and hydrops without ulceration were associated with suspected lightning strike, and attributed to short-duration "flashover" contact [156].

Differential diagnosis

The history and possible collateral injury (e.g., periocular damage) will usually help rule out certain diagnoses. In the case of superficial injury, differential diagnoses include sterile nonhealing ulcers and trauma. In cases of more extensive ulceration



Figure 7.34 Keratomalacia and deep corneal ulceration from *Pseudomonas* infection following overzealous use of a surgical laser. There is simultaneous injury to the conjunctiva and eyelid. Secondary infection is highly probable in such cases.

and keratomalacia, differential diagnoses should include infected (bacterial, fungal) and sterile melting ulcers.

Treatment

The most important aspect of treatment of corneal chemical contact and injury is immediate, copious, and prolonged irrigation [158]. Specific solutions able to neutralize both acid and alkali burns have been formulated [159], but time is critical, and readily available eyewash, lactated Ringer's solution (LRS), or even tap water are more clinically useful. Care should be taken to ensure that all quadrants of the cornea, as well as all aspects of the conjunctiva and fornix, are irrigated. Following irrigation, a prophylactic topical antibiotic, topical mydriatic/cycloplegic, and oral NSAID should be administered to prevent infection and provide analgesia to the compromised ocular surface [158, 159]. Antiprotease agents, such as tetracyclines, serum, and ethylenediamine tetra-acetic acid (EDTA), should be administered topically to minimize collagenolysis. Citrate and ascorbic acid have been shown to be useful in humans with alkali burns as free-radical scavengers and inhibitors of proteolysis [158]. A mainstay of therapy in human patients with ocular burns is the very early use of topical corticosteroids [158, 159], but this is not recommended in equine patients, considering the potential for secondary infection and the typical time delay in instigating therapy.

In the case of extensive injury refractory to medical therapy alone, surgical stabilization or reconstruction of the ocular surface may be necessary. Removal of necrotic tissue and placement of conjunctival pedicle grafts, amniotic membrane transplants (AMTs), or full-thickness corneal grafts (penetrating keratoplasty (PK)) may be indicated [113, 162].

Prognosis
The prognosis for recovery from a chemical corneal burn depends upon the degree of damage of limbal epithelial cells [158]. These serve as the source for regenerating epithelial cells. Treatment may be prolonged, and scarring may be pronounced.

Dystrophic diseases

Dystrophies are primary biochemical abnormalities of the cornea leading to its physiological dysfunction, typically causing opacification and loss of contour. In humans, multiple forms of corneal dystrophy are described, and have been traditionally classified according to their clinical phenotype and primary anatomic location [163]. More recently, they have been classified according to their genetic mechanisms [164]. In humans, the disease processes are typically, but not invariably, bilateral and symmetrical, and begin axially, then spread peripherally. They are without any relationship to environmental or systemic factors, and most are heritable [163, 165]. In the horse, diseases falling broadly under these defining criteria of corneal dystrophy have been only infrequently described.

Progressive paracentral edema
This is an unreported disease.

Prevalence
The disease affects adult horses, with no apparent sex predisposition. Warmblood and Warmblood crosses were over-represented in six cases. In five of six cases the disease was unilateral.

Pathogenesis
The pathogenesis is unknown, although primary endothelial dysfunction is likely.

Diagnosis
Diagnosis is based on clinical presentation. There is a demarcated geographic paracentral area of stromal edema, typically in the ventral quadrants, surrounded by a zone of mid to deep stromal cleft or vesicle formation (Figure 7.35). The corneal surface contour over the edematous area bulges anteriorly. There is no vascularization and no uptake of fluorescein or rose bengal dyes. The eyes are otherwise normal and affected eyes are not painful. Intraocular pressure (IOP) is normal. The disease is very slowly progressive over several years, with the area of edema expanding centripetally to potentially involve over half the geographic corneal area.

Treatment
Medical treatment involving anti-inflammatory, antimicrobial, and immunomodulatory therapy has been uniformly unsuccessful. Surgical treatment has not been attempted.

Prognosis
Prognosis for corneal clearing is, in general, poor. However, in the one horse with bilateral disease there was spontaneous resolution of the long-standing opacities at the age of 23 years.

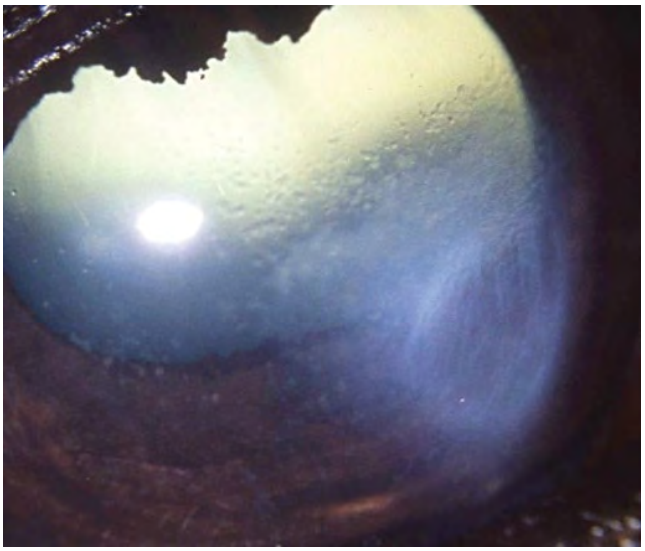


Figure 7.35 Progressive paracentral edema, present for 1 year in this eye of a 7-year-old Warmblood gelding. There is a defined circular area of stromal edema surrounded by multiple satellite stromal vesicles. There is no vascularization.

Idiopathic primary edema (bullous keratopathy)
Idiopathic primary edema is a rare, usually unilateral, condition believed to arise from a functional abnormality in the endothelium, resulting in the net ingress of water from the anterior chamber and consequent stromal overhydration [166–168].

Prevalence
This is a disease reported in adult horses. There is no known sex or breed predisposition.

Pathogenesis
A specific etiopathogenesis has not been identified in the horse, although primary dystrophic endothelial disease or immune-mediated endothelial degeneration has been suggested [82, 168]. Histology of enucleate eyes suggests that endothelial cell dehiscence and loss may be involved in some instances [168]. Once ECD falls below a critical level, stromal hydration rapidly ensues [47]. Stromal overhydration can cause physiological hydrodissection of the epithelial–stromal interface, resulting in epithelial detachment and bullae formation.

Diagnosis
Clinically, there is dense and nonpainful stromal edema and swelling, generally of rapid onset and beginning in the mid-ventral cornea and progressing to involve the entire cornea (Figure 7.36). Subepithelial bullae (bullous keratopathy) may form and may subsequently rupture or be abraided by lid action, resulting in shallow erosions which cause low-grade ocular discomfort [97, 215]. Uptake of fluorescein and rose bengal dyes is variable (Figure 7.36). Perilimbal mid-stromal neovascularization may develop with time. IOP is within normal limits, and should be measured over anatomically normal cornea where possible. IOP measurements should be repeated as the edema

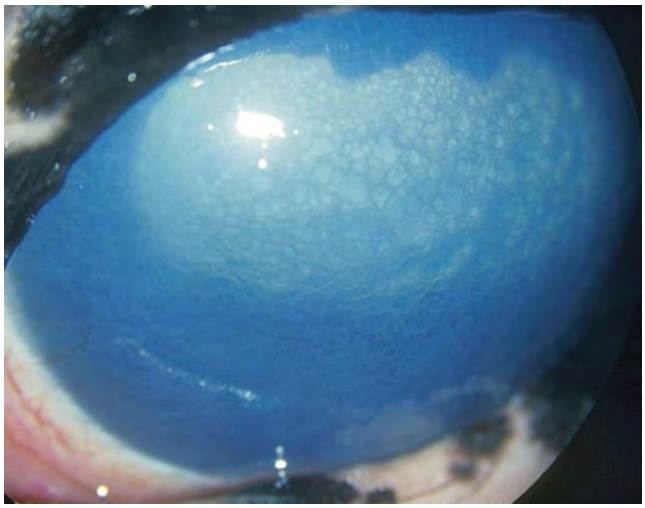


Figure 7.36 Idiopathic primary edema (bullous keratopathy) in a 12-year-old Thoroughbred mare. There is extensive stromal edema with epithelial bulla formation. IOP is normal.



Figure 7.37 Pellucid dystrophy in a Friesian horse. There is a small, progressive, and well-defined deep ulcer in the ventrolateral cornea. There is no vascularization present. (*Source*: Image courtesy of Mary Lassaline-Utter.)

progresses. No other ocular abnormality is evident. If available, *in vivo* confocal microscopy may be helpful in identifying anatomic disruption or loss of endothelial cells [31, 169].

Differential diagnosis

Diffuse corneal edema can result from blunt trauma, detachment of Descemet's membrane, anterior uveitis, anterior lens luxation, space-occupying lesions in the anterior chamber, and putative immune-mediated keratitis (IMMK). Critically, idiopathic primary edema must be differentiated from glaucoma. In cases of acute glaucoma in adult horses, resulting in rapidly progressive diffuse stromal edema and bullous keratopathy, the affected eyes are generally painful and IOP is consistently elevated.

Treatment

Conventional treatment relies upon the use of topical nonproprietary hyperosmotic preparations such as 7.5% saline, 10% glycerine, or 5% hypertonic saline ointment. These, at best, will achieve transient clearing of the cornea in most cases, and frequent instillation, up to six times daily, is necessary. Topical 0.2% CsA is reported anecdotally to have been of clinical benefit. Topical corticosteroids are conventionally used and may have some rationale, along with CsA, where an immune-mediated etiology is suspected. However, corticosteroids should be avoided where epithelial erosions are present. Erosions and superficial ulcers resulting from ruptured bullae may be managed using topical serum or chondroitin sulfate-containing ocular lubricants [113]. The latter may provide some improvement in comfort level [113].

In general, definitive treatment for endothelial disease involves full-thickness transplantation of fresh, healthy donor cornea with an intact endothelial layer. Due to the current impracticality of that procedure in equine veterinary medicine [170–172], surgical treatment is primarily directed toward minimizing the effect of painful bullae. When corneal bullae develop, thermal keratoplasty, as reported in dogs with endothelial degeneration [173] and in dogs and horses with nonhealing superficial ulcers [174], may be performed to induce a fibrotic reaction between epithelium surrounding an ulcer and the anterior stroma, ideally minimizing bullae recurrence. This procedure has not been reported in horses with endothelial disease, but, anecdotally, it has met with some success.

Prognosis

The prognosis in all cases of endothelial degeneration/dystrophy is very guarded to poor. Medical treatment is typically ineffective, and even where some corneal clearing is achieved, it typically does not continue to completion.

Corneal dystrophy in Friesian horses

Progressive, typically bilateral, and geographically symmetrical focal stromal thinning, in some cases leading to corneal perforation, has been described in a group of related Friesian horses (Figure 7.37) [175].

Prevalence

Nine horses were included in the case series. Ages ranged from 2 to 19 years, with an average age of 10.7 years. Eight of the nine affected horses were males. All affected horses shared a common ancestor within six generations. In the nine affected horses included in the cases series, the lesions were bilateral. Unilateral lesions were noted in four other horses at the time of examination, and these horses were excluded from the cases series [175].

Pathogenesis

The mechanisms underlying the progressive stromal loss in the affected horses were not identified; however, connective tissue dystrophy was suspected on the basis of the bilateral and symmetric nature of the lesions, and the genetic closeness of the subjects identified by pedigree mapping.

There is some similarity to pellucid marginal degeneration (PMD) in humans [175]. This is a rare, adult-onset, noninflammatory, nonhereditary, and usually bilateral cause of corneal ectasia, with clear crescentic peripheral corneal thinning in the inferior quadrants [176, 177]. PMD is more common in males. Histopathologically, in PMD the affected cornea shows a replacement of the subepithelial Bowman's layer with a collagenous pannus. The anterior stroma contains degenerated collagen fibrils, the lamellae are fused, and keratocytes appear like fibroblasts, suggesting that PMD may be a disorder of collagen synthesis [176].

Diagnosis

Diagnosis is based on the breed and clinical presentation [176]. Pain levels vary at presentation, and depend on the depth of the stromal lesion. Only single lesions are reported to occur in any one eye, and where the lesions are bilateral at the time of presentation they are geographically symmetric but can vary in depth. The lesions appear as well-defined circular defects in the inferior corneal contour, more typically involving the inferotemporal quadrant. The depth of the lesion at time of presentation can extend from a shallow epithelialized facet through to fluorescein-positive epithelial erosion and ulceration, and can variably involve increasing tissue loss up to descemetocele. Without appropriate treatment there appears to be a high risk of corneal perforation, which was reported to have occurred in 9 of 16 eyes. The average diameter of the lesions at presentation is 5 mm. Vascularization of the lesion is not prominent during the initial ulcerative phases of the disease. The rate of progression to perforation is not recorded. Uveitis is not present unless the cornea has perforated. In cases presenting with an overt lesion in only one eye, the cornea in the opposite eye should be carefully examined for the presence of pathology.

Cytology and culture of the lesion is unlikely to be diagnostic but may exclude a primary infectious etiology. However, concurrent and coincidental infection of the lesion is possible [222].

Differential diagnosis

Differential diagnoses include trauma, infectious ulceration, and iris prolapse.

Treatment

Because of the potential for progression to corneal perforation, treatment should be implemented in all cases and at all stages [176]. Choice of treatment depends on the depth of the lesion at the time of presentation, but surgical intervention is necessary and appropriate, and should follow the general guidelines for surgical management of corneal ulcers (see section Corneal surgery). Shallow facets and superficial erosions respond well to diamond burr debridement. Deeper ulcers and descemetoceles should be managed by keratectomy followed by conjunctival grafting or amnion transplant. Perforation and iris prolapse should be managed using support grafting techniques and systemic medical therapy.

Prognosis

Most cases appear to respond well to surgical treatment, and visual outcomes are excellent where perforation has not occurred. Although recurrence following treatment has not been observed, affected horses should be closely monitored. Where perforation and iris prolapse has occurred, corneal scarring and leucoma will be present over the long term.

Hyperelastosis cutis (hereditary equine regional dermal asthenia)

Hyperelastosis cutis (HC), also known as hereditary equine regional dermal asthenia (HERDA), is an autosomal recessive skin fragility syndrome observed in American Quarter horses and related breeds [178, 179]. Affected horses appear normal at birth, but by 2 years of age most present a progressive picture of dermal seroma or hematoma formation, ulceration, and poorly resolving wounds with skin sloughing. The G6R mutation in the cytosolic protein cyclophilin B found in the Quarter horse impedes the biosynthesis of type I collagen in affected horse fibroblasts. This is the result of a delay in folding and secretion of the protein consequent upon decreased production of hydroxylysine and glucosyl-galactosyl hydroxylysine [178].

HERDA-affected horses show significant thinning of their central and dorsal corneas, increased corneal curvature and diameter, and increased tear production. Zones of disrupted stromal collagen alignment are present, and most affected corneas exhibit mild stromal haze and are more liable to ulcerative disease [180, 181].

Degenerative diseases

Degenerative diseases represent a series of corneal pathologies arising secondarily to anterior segment injury or disease, including trauma and endogenous inflammatory disease.

Corneal mineralization

Superficial (subepithelial) or stromal corneal mineralization is a relatively common spontaneous form of dystrophic calcification usually associated with anterior segment inflammatory disease. Deposition is frequently defined geographically by the interpalpebral fissure (Figure 7.35 and online Figure 7.72), and in the case of subepithelial deposition has been described as "calcific band keratopathy" [113].

Prevalence

Any age, sex, or breed of horse may be affected. Mineralization has been recorded in 6% of cases of endogenous uveitis in the northeastern USA [182].

Pathogenesis

The mechanism of corneal deposition of calcium salts, presumed to be calcium-phosphate or calcium-hydroxyapatite, in cases of keratitis and uveitis is unknown. In humans, calcium and

phosphate ions exist in tears, aqueous humor, and interstitial fluids at concentrations close to their solubility products. Precipitation of calcium salts is thought to occur as a result of inflammation-driven increase in tear film or corneal microenvironment pH, along with concurrent local increase in calcium or phosphate ion concentration and increased evaporation of tears [183, 184]. The use of phosphate buffer in topical anti-inflammatory medications has been implicated in calcium salt precipitation, particularly in cases where there is stromal involvement [184]. Once present, the mineralized deposits themselves may result in a self-perpetuating low-grade inflammatory response [185].

Diagnosis

Diagnosis is based on clinical appearance and the presence of anterior segment inflammatory changes. Superficial (subepithelial) mineralization arises at the interface of the stroma and epithelial BM, and occurs in both endogenous uveitis and nonulcerative keratitis (Figure 7.38 and online Figure 7.29). The mineralized area typically, although not invariably, adopts an oblate or linear configuration, geographically defined by the palpebral aperture. In these cases, the peripheral cornea often remains free of mineralized deposit. The deposits are variably dense and small lucent areas may be present within the lesion, possibly corresponding to the points of penetration of corneal nerves through the BM. Thicker deposits may elevate the corneal surface, resulting in excoriation of the epithelium and shallow ulceration.

Mineralization of the central or anterior stroma can occur as a sequel to chronic or recurrent keratitis and recurrent uveitis [136, 186]. It appears as dense, crystalloid, or semirefractile opacities, typically within the interpalpebral fissure in the case of uveitis (online Figure 7.31) or geographically related to the zone of inflammatory insult in the case of keratitis (online Figure 7.30).

Mineralization of superficial ulcers can occur but is uncommon (online Figure 7.32) [187]. Tectonic or plate-like superficial corneal mineralization has been observed in a yearling Thoroughbred colt with no history of ocular disease (Figure 7.39).

Treatment

In all cases, the primary focus is the control of the underlying inflammatory disease, and small superficial and stromal calcified deposits may resolve spontaneously following resolution of the primary keratitis or uveitis. In the case of persisting subepithelial mineralization, topical 0.4–1.5% sodium EDTA in a neutral solution can be used to promote dispersal of the deposit [185]. It can be administered to effect by continuous infusion via a subpalpebral lavage (SPL) tube, or applied after topical anesthesia by using cotton microbial sampling swabs soaked in the solution. The latter method has the advantage of the clinician being able to gently debride the overlying epithelium to promote dispersal of the deposit. Similarly, diamond burr debridement can be used in conjunction with EDTA soaks and is the recommended therapy for this condition. More concentrated sodium EDTA solutions of up to 5% can be used [188], but generalized epithelial dehiscence and superficial ulceration may be a problem. In long-standing or refractory lesions, SK may be attempted, but significant scarring is likely to result [188]. Stromal mineralization can be similarly managed, but mid to deep stromal deposits are likely to be refractory to medical treatment.

Prognosis

Prognosis is generally good in the case of subepithelial mineralization. However, in general, mineralization reflects the duration and severity of the underlying inflammatory pathology which is the major determinant of prognosis.

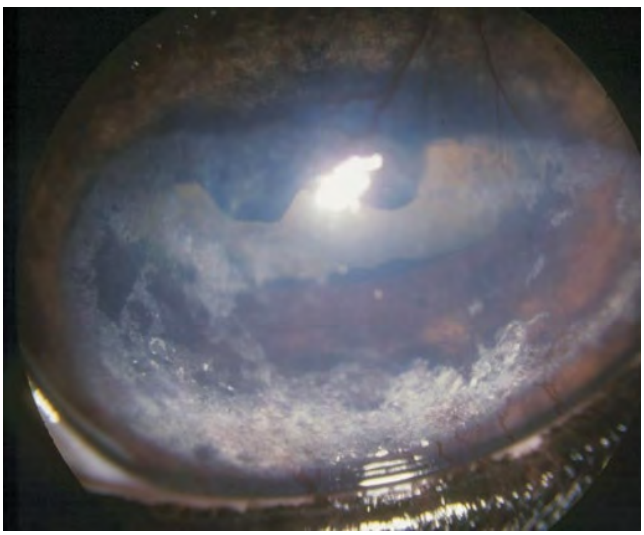


Figure 7.38 Subepithelial mineralization in endogenous uveitis. The demarcation of the mineralized area by the palpebral fissure has led to the lesion being described as "calcific band keratopathy."

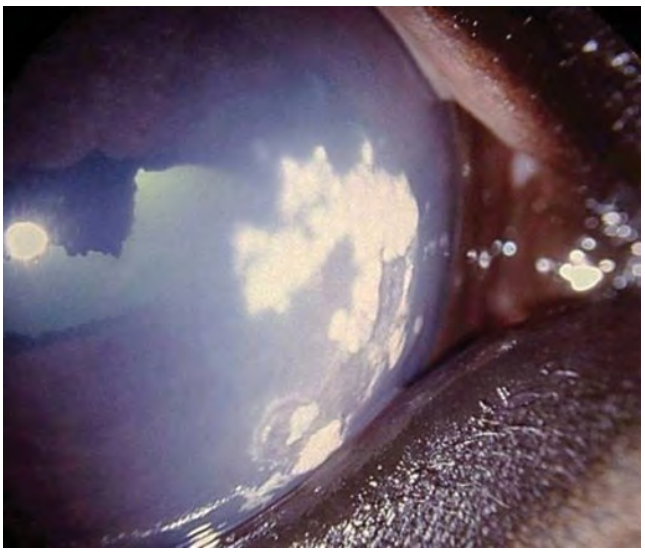


Figure 7.39 Tectonic superficial mineralization in the otherwise normal eye in a yearling Thoroughbred colt. The cause of the mineralization was not established. Segments of mineralized cornea have been sloughed from the ventral area of the lesion.



Figure 7.40 Linear keratopathy, showing the typical deep striate refractile opacity traversing the horizontal corneal meridian in an otherwise normal eye.

Linear keratopathy

Single linear refractile corneal opacities, typically bridging the cornea, are an incidental finding in otherwise normal eyes (Figures 7.40 and online Figure 7.33) [166, 168, 188–192].

Prevalence

Linear keratopathy has been observed only in adult horses, and has not been reported in foals. There is no known sex [192] or breed predilection. The lesions were observed in 4% of Lipizzaner horses and in 1% of Australian Throughbreds [193].

Pathogenesis

The lesions represent marked thinning of Descemet's membrane with normal contiguous endothelium. Histologically the lesions are similar to the striate discontinuities in Descemet's membrane seen in horses' eyes with glaucoma and trauma (Figure 7.41) [194]. They do not show the curling, recoiled edges typical of Haab's striae in glaucomatous eyes in other species, possibly reflecting specific biomechanical properties of equine Descemet's membrane [195]. The cause is unknown, although congenital dysplasia has been suggested [191, 196]. However the similarity of the lesions with those seen in glaucoma suggests the lesions arise as a consequence of an abrupt and transient rise in IOP, possibly acting along a plane of potential mechanical weakness at the horizontal meridian of Descemet's membrane (online Figure 7.34). At a gross and histological level there is some morphological similarity with the striate tears in Descemet's membrane associated with birth trauma in human infants, thought to be a consequence of acute elevation in IOP exceeding the elastic limit of the neonatal Descemet's membrane [197].

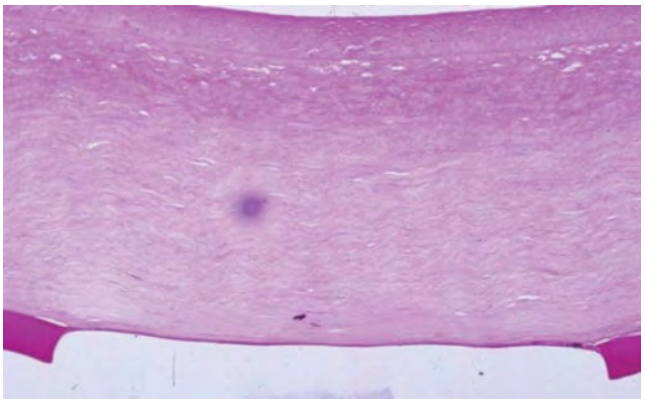


Figure 7.41 Linear keratopathy. Histological section showing a well-demarcated area of thinning or discontinuity in Descemet's membrane. The edges of the lesion do not show the recoil or curling typical of Haab's striae in glaucomatous eyes in other species.

Diagnosis

Diagnosis is based on clinical presentation. The lesions are present in otherwise clinically normal, normotensive eyes. The opacities are non-edematous and are uniformly less than 1–2 mm in width and only very infrequently branch. Typically, the lesions bridge the horizontal meridian of the cornea (Figure 7.40), but can be found vertically or obliquely bridging the parasagittal cornea (online Figure 7.33). Rarely, the lesions bridge the perilimbal cornea.

Differential diagnosis

Similar refractile corneal opacities are seen in eyes with glaucoma and following direct blunt trauma to the globe. However, in these instances, the opacities are usually multiple and branching and are associated with other ocular abnormalities, including elevated IOP, corneal stromal edema and fibrosis, cataracts, and vitreoretinal abnormalities. Isolated and often multiple linear discontinuities in Descemet's membrane are found in some eyes after blunt trauma.

Treatment

There is no treatment.

Prognosis

The prognosis is good in all cases. These opacities do not progress in their normal course, and do not indicate predisposition to glaucoma.

Immune-mediated keratitis

IMMK is a generic term used to describe a heterogeneous group of idiopathic nonulcerative corneal inflammatory diseases, linked in that their origins are presumed to lie in the expression of dysregulated, primarily adaptive, immune responses [168, 198–204]. The clinical spectrum of IMMK is very wide, suggesting

that several different disease processes are likely to be involved, and identifying IMMK as a syndrome rather than as a specific or definitive diagnosis.

The largest constituent subgroups of IMMKs are unique to the horse, and represent nonspecific inflammatory pathologies classified according to clinical presentation and progression, depth of inflammation within the cornea, and response to anti-inflammatory or immunomodulatory therapy [168, 198–204]. The precise etiogeneses are unknown, but it is likely that most if not all are driven to some degree by aberration or derangement of the normally inert immunoresponsiveness of the healthy cornea, based around the anterior ocular segment's immune and angiogenic privilege, as previously described (see online version **Corneal Immunobiology**).

Classed among the IMMKs are relatively rarely recognized entities, such as pannus and episclerokeratitis, which show some clinical similarity to the diseases in other species [168]. Also included in the broad IMMK group of diseases are eosinophilic keratitis [205] and the subepithelial punctate keratitis putatively attributed to persistent EHV-2 or EHV-5 infection, along with the poorly defined group of inflammatory diseases characterized principally by rapid and reversible pigment infiltration of the basal epithelial layer or stroma [268].

Nonulcerative corneal disease is reported in pinnipeds on the western seaboard of the USA, and while these primarily represent chronic degenerative pathologies believed to be associated with excess ultraviolet (UV) exposure [206], some commonality in etiogenesis with the equine IMMKs may exist.

Prevalence

IMMKs have a worldwide occurrence, although geographic differences both in clinical presentation and incidence within the local horse populations seems to occur. In some locations they are a common reason for first-opinion ophthalmic examination. IMMKs have been reported to date only in mature horses.

Pathogenesis

Only limited information on the immunopathogenic background of IMMK has been published. In superficial or mid-stromal IMMK, the predominant type of cellular reaction was lymphocytic–plasmacytic inflammation, with variable degrees of histiocytic and polymorphonuclear cell infiltrate, stromal necrosis, and epithelial hyperplasia [200, 203]. The presence of CD4+ T helper cells and CD8+ cytotoxic T cells in keratectomy samples taken from clinical cases of superficial stromal IMMK has been demonstrated [204]. However, it is probable that the molecular events determining the clinical expression of IMMKs involve a complex and interdependent cytokine cascade, triggered primarily by antigen-primed APC–T-cell interaction in the immunologically compromised cornea driving an amplifying proinflammatory response promoting angiogenesis and immunocyte chemoattraction.

Corneal injury, including surgery, and consequent vascularization is likely to be a major factor in compromise or downregulation of normal immune privilege in the cornea and anterior ocular segment. However, only relatively few horses develop IMMK subsequent to ocular injury. This, along with the highly variable clinical presentation of suspected IMMK where there is no history of injury, suggests that a significant complexity of molecular and cellular events occurs in the cornea in any one case. Factors influencing the clinical expression of the immunoinflammatory response in cases of suspected IMMK are likely to include:

- The nature of the antigen involved. This may be sequestered microbial or viral heteroantigens or their epitopes acting directly or through molecular mimicry of corneal proteins. Immunological cross-reaction of corneal proteins with leptospiral organisms or DNA fragment epitopes is well documented [207–210]. Unmasking of corneal autoantigens, such as has been demonstrated in experimental autoimmune keratitis in mice [211], and subsequent epitope spreading may be involved in some instances.
- The dose and route of presentation of the putative antigen.
- The immunophenotype of the patient, in particular the T-cell phenotype, may influence the expression and aggressiveness of the immunoinflammatory response [212].
- The immune environment in the cornea at the time of antigen presentation. The extent of angiogenic and immune privilege compromise and potential immunoreactivity in the cornea will relate to the degree of vascularization, the cytokine profile of the ocular surface microenvironment, the corneal ECM, and the aqueous humor, and the efficiency of the normal apoptosis mechanisms controlling T-cell exclusion from the cornea.

A primary clinical feature of IMMK is the absence of anterior uveitis, even in the presence of apparently aggressive deep keratitis. This is likely to be a consequence of anterior chamber-associated immune deviation (ACAID) being maintained in the affected eye, protecting the intraocular structures of the anterior segment from involvement in the immunoinflammatory response.

Diagnosis

Diagnosis is based on clinical presentation and exclusion of differential diagnoses such as acute trauma, uveitis, and glaucoma. The IMMKs are typically unilateral, and because IMMK may be outwardly an innocuous disease, in many cases corneal abnormalities have been present for some time prior to presentation.

Cardinal presenting features of the disease are corneal opacity in the absence of uveitis and the absence of overt ocular discomfort. The clinical presentation is very variable; however, in any one case, typically all the following are consistently present to a varying degree.

- Corneal vascularization. Blood vessels enter the cornea from the limbus at different anatomic levels, the level apparently determined by the location of the inflammatory response.
- Corneal edema. This relates to the location of the inflammatory response, and can vary from epithelial edema through to anterior stromal edema and panstromal edema. Focal stromal lacunae or corneal hydrops can be present.

- Cell infiltration at different anatomic levels.

Other signs that can be variably present include:

- Epithelial hyperplasia and disruption of corneal surface contour.
- Transient epithelial bullae. Their presence is usually accompanied by ocular discomfort.
- Conjunctival hyperemia.
- Superficial and stromal pigmentation.
- Subepithelial and stromal mineralization.
- Stromal fibrosis in long-standing stromal disease.
- Intrastromal hemorrhage.
- Presence of corneal "ghost" vessels.

Broadly, IMMKs have been grouped according to the anatomic level of the primary inflammatory response. This classification can be applied in the majority of cases; however, the near-unique clinical appearance of a significant minority of cases excludes them from this anatomic classification.

Chronic superficial IMMK

Chronic superficial IMMK, initially unilateral but potentially becoming bilateral, is characterized by an insidious onset with only slight to moderate discomfort. The lesion may be initially restricted to the area under the upper eyelid or, less frequently, the third eyelid or paracentral cornea [199–202]. There is prominent subepithelial branching vascularization from the limbus, often with perivascular epithelial edema and mild cell infiltration of the superficial stroma, although the latter is not a common feature of the disease (Figure 7.42 and online Figure 7.47). Tear production is normal, and no fluorescein uptake occurs. The apposing palpebral conjunctiva is typically moderately hyperemic. It is probable that in some cases the keratitis reflects primary conjunctival pathology, with proinflammatory and vasculogenic cytokines originating in the conjunctiva entering the tear film to target the apposing cornea.

In the USA, the superficial keratitis is accompanied by a yellowish-white anterior stromal cell infiltrate (Figure 7.43) [201]. Corneal abrasions may occur adjacent to the corneal edema or in other non-edematous corneal regions.

Chronic deep/mid-stromal IMMK

In the UK, this is reported to recur at irregular intervals of up to several years [201, 202], and there is frequently a history of ocular trauma or active phase of the disease, an extensive, dense, mid- to deep-stromal edema, and fibrovascular response (Figure 7.44 and online Figure 7.49). The intensity of the stromal changes varies among cases and episodes, but despite the

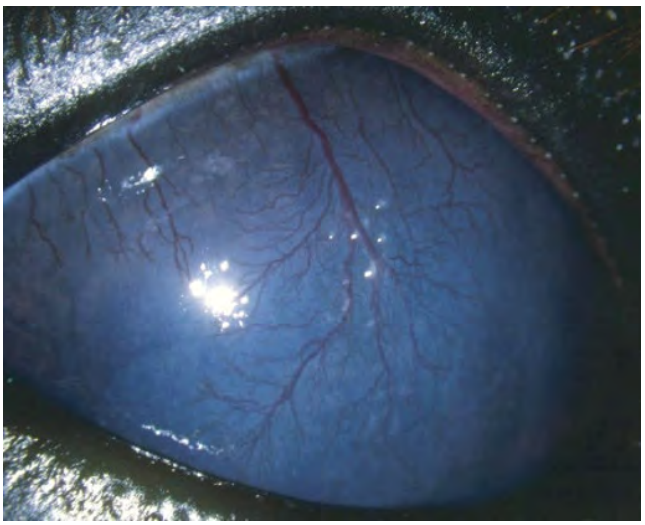


Figure 7.42 UK superficial IMMK, showing superficial vascularization of the dorsal corneal quadrants and epithelial edema and bullae forming. This is a long-standing (10 months) and untreated case, refractory to medical treatment.

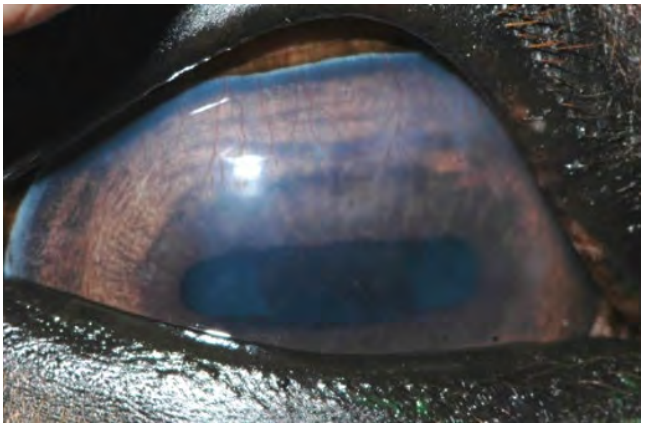


Figure 7.43 US superficial IMMK, showing superficial vascularization in the dorsal corneal quadrants with mild cell infiltration of the anterior stroma at the distal end of the blood vessels.

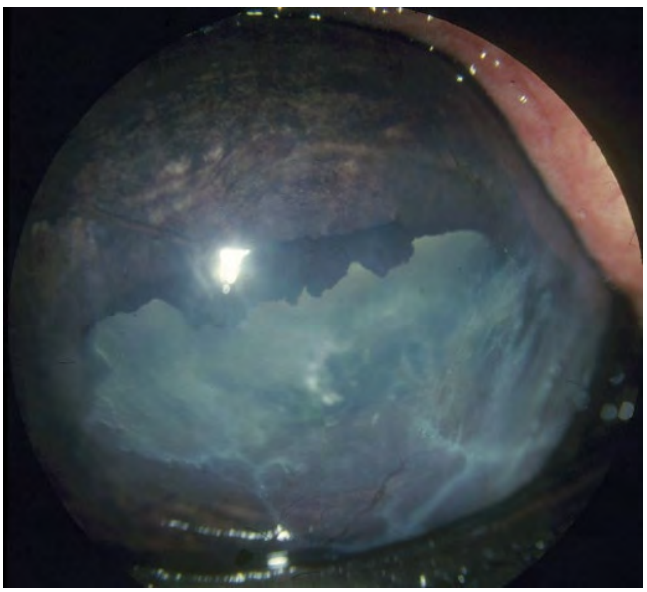


Figure 7.44 Chronic deep (mid-stromal) IMMK, showing extensive vascularization, deep corneal edema, greenish lacunae, and diffuse cell infiltration in the central cornea.

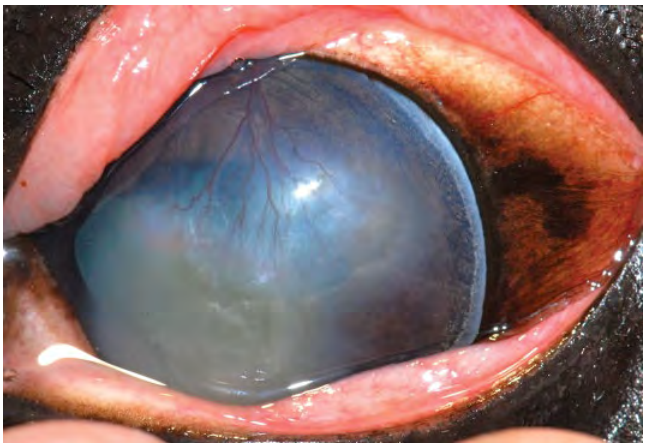


Figure 7.45 Clinical photograph of a horse with chronic active deep keratitis, demonstrating prominent corneal vascularization, edema, and cellular infiltration.

dramatic appearance of affected corneas, ocular pain is minimal. Subepithelial bullae may form and rupture, causing superficial erosions. In some eyes, lacunae of greenish/orange-tinged fluid may collect within the central and paracentral mid-stromal cornea (Figure 7.44 and online Figure 7.48). Transient subepithelial calcium deposition may occur in some eyes. During the quiescent or inactive phase of the disease, there is modest diffuse stromal fibrosis and scattered anterior stromal vascularization. Ghost blood vessels, empty of blood, may be evident.

In the quiescent stages of the recurrent disease in the USA, cellular infiltration may be more prominent in mid-stromal IMMK, and the lateral paracentral, ventral, or central cornea is most commonly affected (Figures 7.45 and online Figure 7.50) [201, 202]. Recurrence can be a feature of the disease.

Endotheliitis

In the UK, this disease has an acute onset and is characterized by pronounced central edema and, in some instances, corneal hydrops (Figure 7.46). Prominent isolated arborizing blood vessels encroach upon the affected area at the level of the posterior stroma or Descemet's membrane, and dense clumps of cells are frequently noted adhering to the endothelium in the region of the terminal blood vessels (online Figure 7.51). In long-standing cases, stromal mineralization can occur (online Figure 7.30). Despite the endothelial involvement, the anterior chamber is otherwise normal.

In the USA, this disease takes a more chronic and insidious course, with the extent of the corneal edema and vascularization less pronounced (Figure 7.47). The disease may be bilateral, and ocular pain and uveitis are frequently evident, suggesting this represents a different disease from that described typically in the UK.

Treatment

The broad management protocol in all cases involves initially aggressive use of glucocorticoids, NSAIDs, and immunosuppressive agents, alone or in combination, and with varying outcomes.



Figure 7.46 UK endotheliitis, showing typical central corneal edema and corneal hydrops.



Figure 7.47 US endotheliitis. The edema and deep vascularization present are less prominent than seen in the typical UK presentation shown in Figure 7.46. Unlike the UK, the disease in the USA is typically refractory to medical treatment, suggesting that, along with differences in clinical presentation, these are different disease entities.

Surgical keratectomy has been used successfully, in some cases refractory to medical therapy. Therapy is often complex and frustrating, and is governed by the following paradigm:

- Early intervention is appropriate. In general, these diseases become both increasingly refractory to medical therapy and increasingly liable to recurrence with time.
- Broad guidelines for medical therapy based on clinical experience apply in the case of the IMMKs described above, and these are listed below. However, in reality, IMMK therapy is largely empirical and at the discretion of the individual clinician.

- Trial and failure protocols involving the sequential or concurrent use of medications listed below (in section **Medical treatment**) are typical.
- Therapy is often required for protracted periods to control recrudescence of the disease. Usually this involves tapering the frequency of topical administration of the medication to the minimum required to control the expression of the disease. Lifetime maintenance therapy may be required, and costs and owner compliance can become a significant problem.
- Spontaneous resolution of the disease may occur after several months to years, in particular in deep and mid-stromal keratitis. This makes objective assessment of therapy difficult. However, recurrence at some time distant from the initial episode is unpredictable. In the case of chronic deep keratitis in the UK, it appears inevitable.

Medical treatment Medical therapy to date has been based upon attempts to directly suppress the inflammatory response and modulate the presumptive immune events driving that response. The inherent complexity of these events, where individual antigen–immunophenotype interactions are likely to determine the expression of inflammatory pathways, makes it likely that any response to therapy will vary between individual cases. However, empirical modulation of the broad immunoinflammatory response using available chemotherapeutic agents permits some degree of rationally targeted therapy.

Glucocorticoids Drugs in the glucocorticoid (GC) class have diverse anti-inflammatory, immunosuppressive, and antiangiogenic effects and are a primary empirical therapy in equine IMMK. Through activation of the pleiotropic glucocorticoid receptor (GR) and inhibition of the central transcription factors nuclear factor κB (NF-κB) and AP-1, T-cell activation and expression of proinflammatory cytokines are downregulated [213, 214]. GCs also reduce local expression of chemotactic proteins and cell adhesion molecules, restricting migration of inflammatory cells to sites of tissue injury.

Dexamethasone induces T-cell suppression and impairs T-cell receptor signaling in a nongenomic fashion [215], in part by blocking maturation of the immune synapse (IS) at the T-cell/APC contact site [216]. Acting via the GR, glucocorticoids interfere with toll-like receptor (TLR) signaling to downregulate the expression of innate immunity on the ocular surface [217].

Glucocorticoids inhibit corneal angiogenesis via decreased gene expression of VEGF and inhibition of the macrophage precursors of corneal vascular endothelium, and as such potentially are of therapeutic value in limiting local vascular responses that are important in the downregulation of corneal immune privilege.

Nonsteroidal anti-inflammatories Topical and oral NSAIDs can be used as glucocorticoid-sparing therapy. Their effectiveness is likely to be less than that of glucocorticoids.

Cyclosporine A and tacrolimus CsA and tacrolimus are potent immunosuppressive agents in the calcineurin inhibitor class. They act to downregulate immunocyte activity via suppressing transcription of proinflammatory cytokines, principally IL-2. Calcineurin is responsible for the induction of a family of nuclear transcription factors known as nuclear factors of activated T lymphocytes (NFATs), which define the expression of proinflammatory peptides. CsA is a cyclic nonribosomal peptide that binds the cytosolic immunophilin cyclophilin in activated T cells, forming a complex that inhibits the cytoplasmic phosphatase calcineurin. Tacrolimus (FK506) is a macrolide lactone that forms a calcineurin-inhibiting complex with the cytosolic FK506 binding cyclophilin of T cells. Additionally, both CsA and tacrolimus selectively prevent T-cell receptor conjugation with APCs at the immune synapse (IS) [216]. Calcineurin inhibitors have been used as glucocorticoid-sparing drugs in human ophthalmic medicine [218, 219]. In the horse, the IMMKs appear to be variably responsive to both classes of drug in single use, and their combined topical use at full therapeutic doses is often employed.

In January 2015, CsA was removed from the Fédération Equestre Internationale (FEI) list of prohibited substances. The FEI website should be consulted for the current forensic status of the drug.

Sirolimus (rapamycin) Sirolimus is a macrolide immunosuppressive agent that binds to the cytosolic FK-binding protein 12 (FKBP12) of T cells, forming a complex that inhibits the mammalian target of rapamycin (mTOR) and blocking the cytoproliferative response to IL-2. In addition, unlike the calcineurin inhibitors, rapamycin promotes the expansion of regulatory T-cell clones *in vivo*, suggesting a possible tolerance-inducing role for the drug in the management of immunoinflammatory disease [220]. Its use as a corticosteroid-sparing agent in human ophthalmic medicine is being investigated [219]. There are as yet no reports of its topical use in the management of corneal disease in the horse, but the intravitreal use of sirolimus in a horse with ERU quickly reduced the inflammation but also caused a cataract.

Doxycycline and minocycline In addition to the antibiotic properties of doxycycline and minocycline, these pleiotropic synthetic tetracyclines have specific anti-inflammatory and immunosuppressive actions based principally on suppression of T-cell co-stimulation via downregulation of IL-1β expression by macrophages and DCs [221]. In addition, inhibition of TGF-β1-induced expression of MMP-9 may give the drugs some antiangiogenic and anticytoproliferative properties [222]. The drugs' immunosuppressive action also derives in part from increasing Fas-L expression on ocular parenchymal and endothelial cells, enhancing local apoptosis of immunocytes and sprouting vascular endothelial cells. This reduction in the neovascularization potential of injured ocular tissue may have the effect of preserving immune privilege and ocular function [223].

Doxycycline and minocycline concentrate at sites of inflammation, and their anti-inflammatory effects appear to be dose dependent. In the horse, doxycycline is rapidly absorbed after oral administration at doses ranging from of 5 mg/kg to

20 mg/kg [70, 224, 225], and reaches readily detectable levels in the tear film and aqueous of normal eyes after daily oral administration of 20 mg/kg [70, 226]. However, topical rather than systemic administration may be appropriate in the case of doxycycline to avoid the potential side-effects of systemic use. Minocycline is rapidly absorbed after twice daily oral administration of 4 mg/kg, and reaches levels in excess of 90% of minimal inhibitory concentration (MIC(90)) for many Gram-positive pathogens in the tear film in normal eyes, but not in aqueous humor in normal eyes or where the blood–aqueous barrier was disrupted [227, 228].

To date, there is anecdotal evidence only to support topical or systemic use of these drugs to manage equine IMMKs.

Guidelines for the use of medical therapy in IMMK

Chronic superficial IMMK: in the UK, this disease is refractory to topical glucocorticoids alone, but most cases will respond to two to three times daily application of topical 0.2–2% CsA. In the USA, glucocorticoids in combination with CsA is recommended, with the glucocorticoids being tapered off and the CsA reduced to once daily administration according to the clinical response.

Chronic deep/mid-stromal IMMK: in both the UK and USA, this disease is relatively refractory to medical treatment. In the UK, topical glucocorticoids and CsA are used in combination two to three times daily. This may result in rapid improvement in the clinical signs in a few cases, but is unlikely to result in complete resolution. In most cases, treatment needs to be continued and the doses altered according to response for up to several months. Oral doxycycline 10 mg/kg twice daily can be used speculatively on its own or to supplement topical therapy. This dose should be maintained for 10 days, before gradually reducing the dose over a further 20 days according to response. The absence of clinical improvement after 10 days suggests failure of this modality. Where doxycycline appears to be effective in controlling the disease, repeated treatment should be implemented if the disease recurs. All horses receiving oral doxycycline must be monitored for side-effects, in particular entercolitis.

Endotheliitis: in the UK, most cases of this disease will respond favorably and rapidly to two to three times daily administration of topical glucocorticoids. With early intervention, complete resolution without recurrence is usual.

In the USA, this disease is poorly responsive to all therapy, although there are anecdotal reports of successful use of topical NSAIDs (e.g., bromfenac) in reducing the corneal response [201, 202]. The differences in clinical presentation and therapeutic response between the disease in the USA and UK suggest these are separate disease entities.

Oral doxycycline may be tried on a speculative basis where other therapies fail.

Surgical treatment There are anecdotal reports of the successful use of keratectomy to remove affected corneal tissue in cases of superficial or deep/mid-stromal IMMK [201, 202]. The rationale is based on the removal of the antigen load, damping the immunoinflammatory response, and driving re-epithialization and repair. Surgical intervention will also alter the local corneal immune environment, possible favoring immunosuppression. Some degree of permanent fibrosis at the keratectomy site should be expected.

Episcleral surgical implantation of silicone matrix CsA delivery devices targets the cornea with the drug. The procedure, carried out standing or under general anesthesia, is well tolerated and is associated with a favorable therapeutic response in cases of superficial IMMK and, particularly, endotheliitis in the USA and in Europe [229]. The implant is not successful in cases of mid-stromal IMMK, although this may be dose related [229]. Where successful, CsA implantation reduces or eliminates the need for topical medication and the compliance problems associated with long-term topical medication. Implantation should only be undertaken following indication of a favorable response to topically administered CsA. The implant is designed to result in drug release for 12–18 months, with some horses likely to require multiple implants over their lifetime [229].

Autologous bone-marrow-derived mesenchymal stem cells administered by subconjunctival injection is reported to have been successful in controlling otherwise refractory superficial IMMK in one horse [230].

Other presumptively immune-mediated keratopathies

Epithelial keratopathy

Epithelial keratopathy is a sporadic unilateral disease affecting adult horses of any age. There is a diffuse, central, superficial corneal opacity, usually associated with slight blepharospasm, and in some instances with mild conjunctival hyperemia (Figure 7.48). Vascularization is not a feature of the disease, but

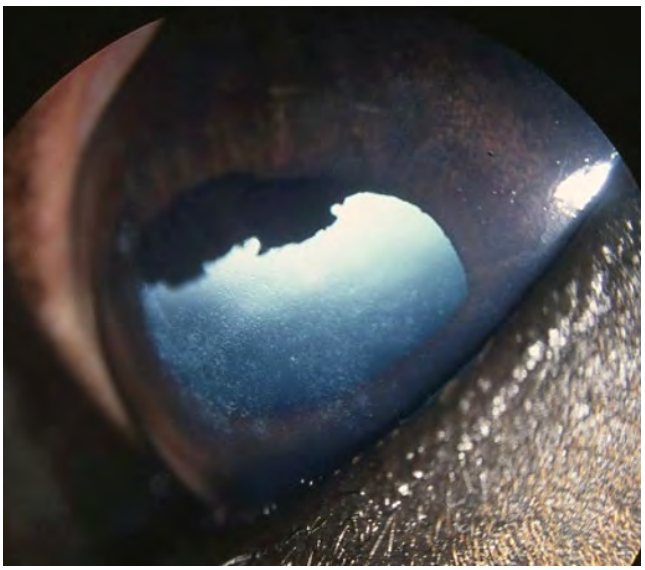


Figure 7.48 Epithelial keratopathy. Irregular clumps of epithelial cells disrupt the corneal contour in the area defined by the interpalpebral fissure. Localized anterior stromal haze is evident, but there is no associated vascularization.

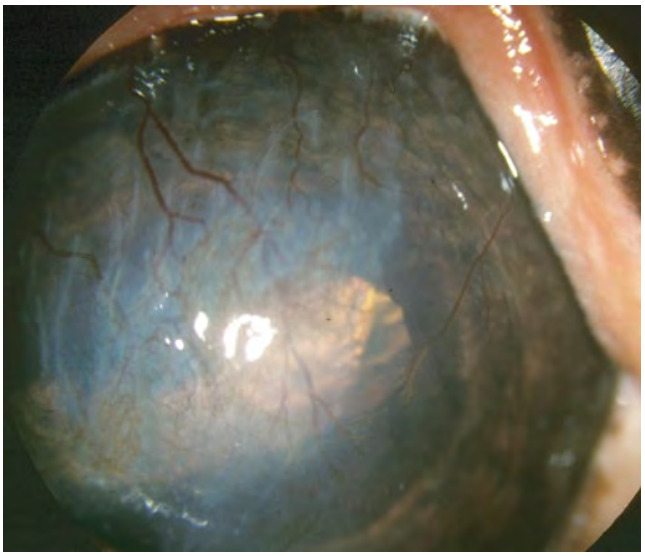


Figure 7.49 Pannus in the left eye of a 14-year-old part-bred mare. There is marked epithelial and subepithelial fibrocellular infiltrate and vascularization from the limbus, extensively disrupting the corneal surface contour. The other eye was similarly though less extensively affected. There is no uveitis and the eyes are comfortable.



Figure 7.50 Episclerokeratitis in the left eye of a 9-year-old Warmblood gelding. There is episcleral congestion and conjunctival pigment dispersal at the dorsolateral limbus, along with perilimbal corneal edema, cell infiltration, and anterior stromal vascularization. (*Source*: Image courtesy of Ben Chilvers.)

may be present in long-standing cases. The superficial opacity represents irregular, occasionally coalescing clumps or islands of abnormal epithelium disrupting the corneal surface contour. Localized anterior stromal haze may be present, and the lesions are typically defined by the interpalpebral fissure. Unaffected areas of cornea appear normal. Fluorescein and rose bengal stains are retained in the interstices between the islands of abnormal epithelium. STTs are normal.

This disease typically responds favorably to topical glucocorticoids. However, long-standing cases are refractory to treatment.

Pannus

This is a relatively rare bilateral disease. The cause is unknown. Affected corneas present with a superficial fibrovascular infiltrate extending from the limbus for a variable distance onto the corneal surface. Whitish epithelial and subepithelial infiltrates and subepithelial edema are present, and the corneal surface contour is extensively disrupted (Figure 7.49). There is no uveitis present. Topical glucocorticoids result in significant clinical improvement, but this may not be sustained. One case went on to develop severe bilateral uveitis.

Episclerokeratitis

This is a rare unilateral condition involving mainly the dorsolateral quadrant of the cornea. The cause is unknown. An arc of well-defined stromal edema and extends into the cornea from the limbus, and short superficial blood vessels extend into the edematous area from the limbus (Figure 7.50). There is local conjunctival hyperemia and pigment dispersal, and typically marked episcleral congestion. The disease is responsive to topical glucocorticoids.

Pigmentary keratopathies

This is a heterogeneous group of relatively rare nonulcerative diseases presenting with obvious superficial or stromal pigment infiltration from the limbus along with vascularization and edema (online Figure 7.52). Affected eyes are otherwise normal. The diseases may have an acute onset and some are associated with significant ocular pain. Typically, affected eyes respond to topical glucocorticoids.

Superficial punctate keratopathy

This is a relatively common and usually benign but frequently frustrating disease. The disease is characterized by multifocal punctate opacities in the central, paracentral, or ventral cornea (Figure 7.51). The opacities are located in the subepithelial stroma and may have a faint surrounding cell infiltrate. There is typically no vascularization and the horse has minimal or no signs of discomfort. Affected corneas are fluorescein and rose bengal negative. In some eyes there are transient episodic increases in the density of the lesions, and this may be associated with obvious discomfort. The cause is unknown, and it may be difficult to differentiate this disease from punctate primary epithelial disease, epithelial nonulcerative keratomycosis, or the punctate keratopathy attributed to EHV-2 and EHV-5 (online Figure 7.54) [201, 202].

Treatment is usually unrewarding, although topical glucocorticoids may result in some transient clearing of the cornea during episodes of increasing density and discomfort.

Prognosis

Because of the poor understanding of the underlying etiopathogeneses in cases of presumptively IMMK, and the individual variation in presentation and response to therapy, the prognosis in all cases is guarded pending treatment. Even with a favorable

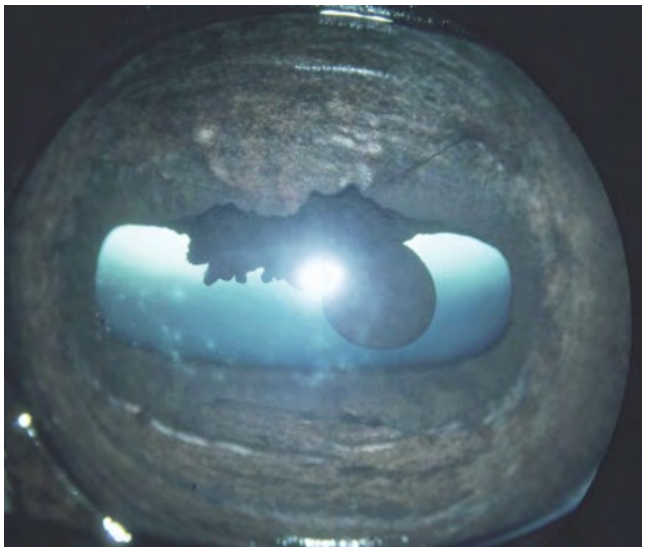


Figure 7.51 Superficial punctate keratopathy in the right eye of a 13-year-old part-Thoroughbred gelding. There are multiple faint anterior stromal opacities in the central cornea. The eye is slightly uncomfortable but is otherwise normal.

response to treatment, recurrence is unpredictable and some horses will require long-term if not lifelong medication.

Eosinophillic keratitis

Eosinophillic keratitis/keratoconjunctivitis (EK) comes under the broad classification of immune-mediated corneal disease, and may represent a hypersensitivity response to environmental or parasitic allergens [205].

Prevalence

EK is increasingly recognized worldwide, though geographic variation in the incidence of the disease within each country does occur [205]. There is no obvious breed predisposition [205], although the disease appears rare in ponies. It has been reported in a donkey [231]. The disease predominantly affects young and middle-aged animals [135, 205], and has a seasonal incidence in the northern hemisphere, with most cases occurring in summer and fall [205, 232].

Pathogenesis

Although eosinophils are identified with the response to allergic or parasitic stimuli, the pathogenesis of EK remains unknown. Environmental irritants or allergens, fomites, organisms, improper management practices, and seasonal changes have been suggested as being able to initiate EK [135, 233]. Mild eosinophilic infiltration has been inconsistently identified in cases of parasitic keratoconjunctivitis [234], suggesting a possible association with parasite infestation in some but not all EK-affected individuals. It has been proposed that an allergic or inflammatory reaction involving long-term use of macrocyclic lactone anthelmintics may also be involved [135]. Mast cell degranulation induced by any of the above factors may recruit eosinophils to the cornea [135], where

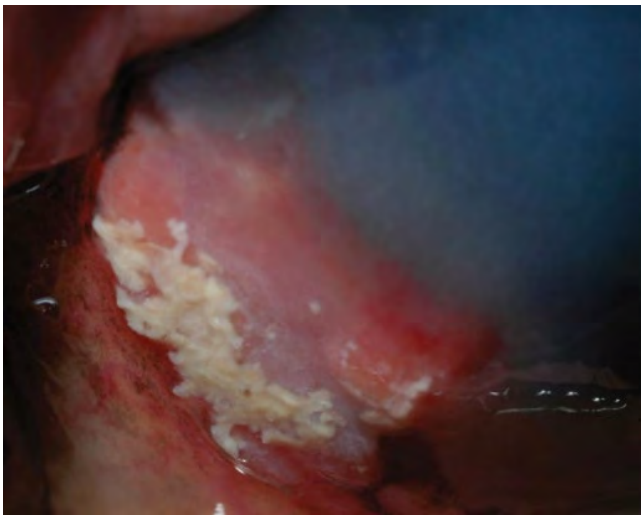


Figure 7.52 Eosinophilic keratitis, showing a white superficial caseous plaque and underlying densely vascularized cornea in the ventronasal quadrant.

eosinophil granule proteins may perpetuate inflammation and inhibit wound healing via cytotoxicity, further mast cell degranulation, and neutrophil activation, as well as by deleteriously affecting epithelial cell morphology and viability [235]. Feline herpesvirus-1 is detected with greater frequency in cats with eosinophilic keratitis than in cats without (76% versus 5.9% polymerase chain reaction (PCR)-positive, respectively) [236], but evaluation of a possible role of EHV in equine EK has not been performed.

Diagnosis

The disease is more usually bilateral [135, 205], and horses with EK may present initially with nonspecific signs of mild to severe blepharospasm, chemosis, conjunctival hyperemia, epiphora, and caseous mucoid discharge, although the degree of discomfort may be variable [135, 185, 237]. The corneal lesions appear as gray of whitish-pink necrotic and variably caseous plaques, frequently overlying superficial corneal ulceration and typically beginning in the ventronasal or ventral peripheral limbal cornea before extending onto the axial cornea (Figure 7.52). Yellow excretions (sulfur granules) may be present. Small lesions may be obscured by the overlying third eyelid, and may be difficult to identify (Figure 7.53).

Other, less usual presentations of EK are discrete multiple superficial caseous foci extending across the corneal surface (Figure 7.54) or dense, well-defined, deep stromal yellow-white cellular infiltration (Figure 7.55). Corneal vascularization is variable, but may be locally very intense. Concurrent infectious ulceration, KCS, and lacrimal adenitis may be present [205, 233]. Affected corneas are at risk of secondary bacterial and fungal infection [205], and any sudden deterioration of the cornea should alert the clinician to this possibility.

Recurrence in subsequent years is reported in 33% of cases [205], although this may reflect failure of complete resolution of the disease in some cases [205].



Figure 7.53 Eosinophilic keratitis, showing a small ulcerated lesion with sloughing necrotic epithelium under the third eyelid. (*Source*: Image courtesy of Brian Paterson.)

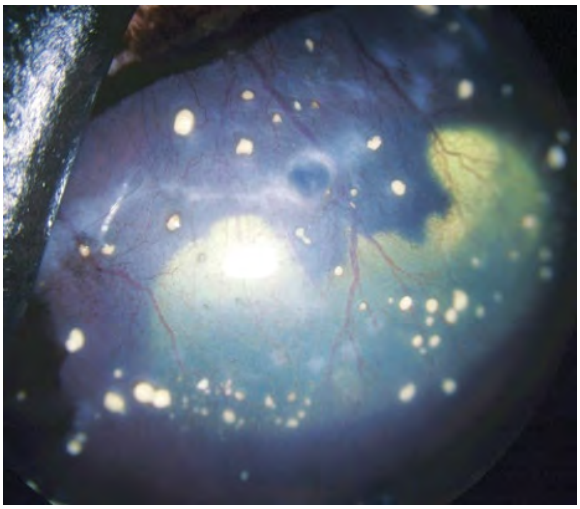


Figure 7.54 Eosinophilic keratitis. Multiple focal caseous plaques are present in the dorsal corneal quadrants. There is extensive anterior stromal vascularization and local anterior stromal fibrosis marks the sites of already sloughed plaques.



Figure 7.55 Eosinophilic keratitis. There is a well-defined zone of dense yellow-white cellular infiltrate in the perilimbal lateral cornea. (*Source*: Image courtesy of Brian Gilger.)

Confirmation of a clinical diagnosis is based on corneal cytology which demonstrates abundant eosinophils accompanied by smaller numbers of mast cells, lymphocytes, plasma cells, and neutrophils (Figure 7.56) [135, 237]. Histopathologic evaluation of the plaques reveals subepithelial foci of fragmented and degenerated collagen fibers infiltrated by eosinophils and neutrophils, with smaller numbers of lymphocytes, plasma cells, and macrophages. The epithelial basement is thickened (Figure 7.57) [237]. A brightly eosinophilic,

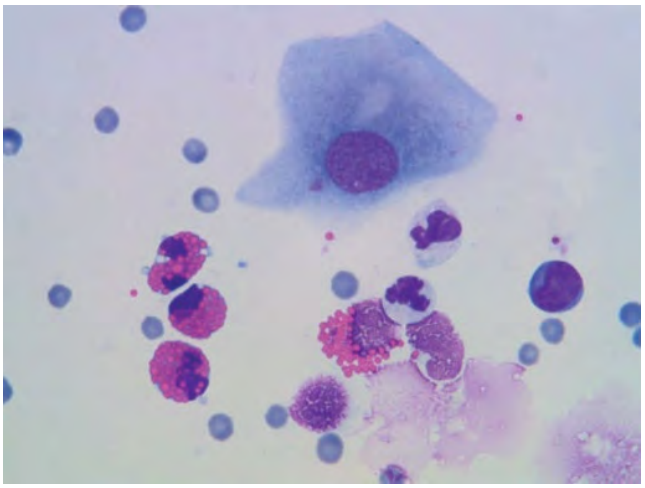


Figure 7.56 Cytology of a scraping sample obtained from a case of eosinophillic keratitis, showing eosinophils along with epithelial and inflammatory cells (Diff-Quik, ×100).

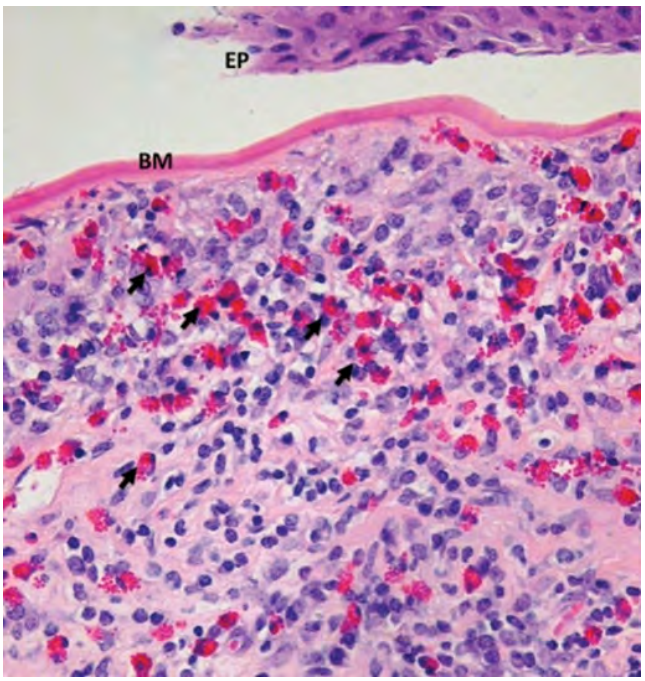


Figure 7.57 Histological image of an SK sample obtained from a horse with eosinophillic keratitis. There are numerous eosinophils interspersed with mixed inflammatory cells. The basement membrane (BM) appears thickened and overlying epithelium (EP) is nonadherent.

acellular, granular material may surround the plaques [237]. Parasitic microfilaria have not been reported in any affected eyes [113, 135].

Differential diagnosis

Differential diagnoses for EK include other infiltrative, potentially ulcerative corneal diseases: fungal, bacterial, parasitic (*Onchocerca cervicalis*), and immune-mediated (lymphoplasmacytic) keratitis; neoplasia (squamous cell carcinoma (SCC), *in-situ* carcinoma, mastocytoma); mineral deposition; and fibrosis.

Treatment

Medical treatment Targeted treatment of the underlying immune component of EK is necessary to achieve resolution, with topical glucocorticoids being the primary therapy (Table 7.4). Corticosteroid use in the presence of concurrent corneal ulceration increases the risk of secondary infection, and prophylactic antibiotics can be administered in conjunction with topical steroids at the discretion of the treating clinician. Topical NSAIDs have been observed to increase the severity of EK in some cases, possibly by NSAID-induced potentiation of inflammation mediated by leukotriene B4, a major regulator of eosinophilic disease in the horse [238]. Systemic NSAIDs and corticosteroids may be indicated to both control the disease process and provide analgesia. In consideration of the frequent detection of mast cells with eosinophilic disease, topical mast cell stabilizers (e.g., sodium chromoglycate) may also be indicated, although their pharmacokinetics and efficacy in the horse have not been assessed. Topical CsA 1.5% solution has been evaluated in cats with eosinophilic keratitis and resulted in improvement of lesions within 3 weeks in 31 of 35 cats [239]. No similar evaluation of CsA or related immunomodulating drugs has been performed in horses; their use should therefore be subject to caution. On suspicion or confirmation of secondary bacterial or fungal infection, therapeutic topical antibiotics and antifungals should be introduced as required.

Concurrent treatment with the antihistamine cetirizine, a selective H1 receptor antagonist, at a dose of 0.4 mg/kg twice daily significantly reduces the likelihood of recurrence in subsequent years [205].

Medical treatment is typically protracted [135], and an average time to resolution of 3.7 months is reported [205].

Surgical treatment Gentle blunt debridement of the caseous material is likely to improve the therapeutic response. Diamond burr debridement of any superficial ulcerated areas will shorten the course of the disease, possibly owing to removal of degenerate BM and any residual intracellular eosinophil granule major basic protein, which are both likely to impede epithelial repair [240].

Prognosis

EK typically requires long-term therapy to achieve complete resolution, but has an overall good prognosis. However, recurrence in subsequent years is possible.

Putative viral keratitis

An etiological role for a replicating epitheliotropic virus in primary corneal disease in the horse is unresolved. However, EHV, especially EHV-2 and EHV-5, are frequently cited as primary corneal pathogens. In humans, herpes simplex virus (HSV) is widespread, and infection and replication in corneal epithelial cells is well recognized. Although HSV is readily removed from epithelial cells, largely by the innate immune system, the virus can establish latent infection in the trigeminal ganglion, resulting in recurrent epithelial infection [241]. Herpes stromal keratitis (HSK) is a deep keratitis of varying severity arising subsequent and consequent to epithelial disease. The immunopathogenesis of HSK is not fully understood, but may involve: (1) reactivity of HSV-specific CD4+ T cells to HSV antigen present in the cornea; (2) autoimmunity to corneal tissue resulting from molecular mimicry by HSV proteins; or (3) bystander activation of CD4+ T cells by the cytokine milieu present in the cornea [241]. Whether similar mechanisms can

Table 7.4 Medical therapy for eosinophilic keratitis/keratoconjunctivitis.

Drug class	Example(s)	Formulation	Dosage	Other points
Topical corticosteroid	Neomycin/polymyxin/dexamethasone 0.1%; prednisolone acetate 1%	Ointment Solution Suspension	¼-inch strip q6–8h 0.1–0.2 mL q6–8h	Slowly (over weeks) decrease frequency as lesions improve
Topical therapeutic mydriatic cycloplegic	Atropine	Ointment Solution	¼-inch strip q12–48h 0.1–0.2 mL q12–48h	Frequency depends upon degree of mydriasis achieved between doses
Topical mast cell stabilizers	Olopatadine	Solution	0.1–0.2 mL q6–8h	Slowly decrease frequency as lesions improve
Topical prophylactic antibiotic	See Table 7.5			Used in presence of corneal ulcer
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h	
Systemic corticosteroid	Prednisolone	Tablet	0.5–1.0 mg/kg PO q12–24h, taper	

give rise to disease following exposure to herpes virus in the horse cornea is unknown.

Prevalence

In the UK, cases of a sporadic, acutely painful superficial keratitis, which resolved within 24–48 hours after topical administration of the anti-DNA virus drug idoxuridine, have been described, although no specific virus has been identified [242]. EHV-1 is reported to have been isolated from the corneal epithelium of a horse with superficial punctate keratitis [243]. In Germany, six of eight cases of superficial punctuate keratitis resolved after treatment with topical acyclovir and CsA for more than 14 days, and EHV-2 DNA was isolated from two of three affected eyes, but also from one of three normal contralateral eyes [244]. A dexamethasone-treated pony was intranasally infected with EHV-2 isolated from a foal with superficial keratitis and subsequently developed conjunctivitis and upper respiratory disease. Three months later, dexamethasone treatment resulted in detection of virus on the ocular surface, and at post-mortem EHV-2 virus was detected in conjunctival samples [245]. In the USA, EHV-2 was isolated from conjunctival scrapings taken from a mare presenting with a moderately painful, unilateral ventral corneal edema and superficial vascularization, and which subsequently responded rapidly to topical trifluridine [246]. Equine adenovirus types 1 and 2 were not identified in swabs taken from the conjunctival sacs of 43 horses with primary keratopathies or keratitis [247].

In Europe, EHV-2 was isolated from corneal biopsies taken from 3- to 6-week-old foals involved in a herd outbreak of focal superficial keratitis and conjunctivitis [248], and in Australia EHV-2 was isolated from the eyes of three of five weanling foals sampled from a group of 35 involved in a herd outbreak of keratoconjunctivitis and respiratory disease [249]. In Germany, EHV-2 was identified using nested PCRs from conjunctival swabs taken from 12 of 27 horses presented to a veterinary clinic with either "superficial, punctuate, macular and deep keratoconjunctivitis, or bullous keratopathy," and also from 2 of 21 normal controls [250]. EHV-2 viral genome or antigen was detected using PCR in conjunctival swabs of 28.6% of normal eyes and from 8.3% of eyes with keratoconjunctivitis [251], and the viral genome was shown to be present in histiocyte-like cells co-localized with Langerhans cells in the conjunctival submucosa [251]. A study of Lipizzaner horses showed that EHV-2 and EHV-5 were detected in 62.8% and 51.1%, respectively, of at least one of peripheral blood leucocytes, nasal swab, and conjunctival swab. Both viruses were detected in 39.5% of horses tested [252]. However, data analysis was unable to demonstrate any association of EHV-2 or EHV-5 with ocular disease [252, 253]. In the USA, using quantitative PCR (qPCR), EHV-2 was found in conjunctival swabs of 2 of 12 horses with idiopathic keratoconjunctivitis and in zero of six controls, and EHV-5 was found equally in case and control horses [254], and the authors concluded that qPCR was not useful for the etiologic diagnosis of idiopathic keratoconjunctivitis.

The high seroprevalence of EHV-2 and EHV-5 antibodies in the general horse population indicates that exposure is widespread, particularly in young animals, and that association of the viral genome or antigen with ocular disease cannot easily be established in any one case.

Pathogenesis

The putative viral disease in the UK is associated with locally destructive epithelial changes, usually accompanied by exposure of anterior stroma.

Any specific keratopathogenic mechanisms of EHV-2 and EHV-5 are unknown. EHV-2 and EHV-5 are gammaherpesviruses. Gammaherpesviruses can result in lifelong infections characterized by variable periods of disease recrudescence and latency. Gammaherpesviruses establish latency in lymphocytes, and EHV-2 has also been identified as latent in the trigeminal and ciliary ganglia [245, 251, 255]. Latency within the trigeminal ganglia may be associated with shedding of the virus onto the ocular surface and other disease processes in which EHV-2 has been implicated (e.g., rhinitis, bronchiolitis, tracheitis, and pneumonia), inasmuch as the ocular and nasal mucosa are both innervated by branches of the trigeminal nerve [249, 255]. Reactivation is most likely during periods of stress, such as breeding and transport.

Diagnosis

In the UK, putative viral disease is typically unilateral and associated with severe ocular pain, epiphora, conjunctival hyperemia, and reflex miosis. There is no systemic disease, and it is not contagious to in-contact horses. Two types of the disease are described [82, 136]. In the first the lesions appear as fine, irregular, fluorescein-positive epithelial fissures with contiguous anterior stromal haze. Rarely, these fissures may coalesce, resulting in a dendritic-like lesion (online Figure 7.53), and in some instances may form a shallow geographic ulcer. In the second, the lesions appear as multiple focal, fluorescein-positive, epithelial erosions or superficial ulcers, less than 0.5 mm in diameter, with perilesional anterior stromal edema (Figure 7.58). Some ulcers will heal spontaneously, leaving a combination of ulcerated and nonulcerated anterior stromal opacities. Scattered superficial vascularization occurs with chronicity in some cases.

The most common manifestation of the keratitis usually attributed to EHV-2 or EHV-5 in adult horses is multifocal basal epithelial and subepithelial opacities, usually in the central cornea (online Figure 7.54) [185, 188]. These stain variably with fluorescein and rose bengal. Superficial vascularization is associated with the opacities in some instances. Affected horses exhibit varying but usually mild ocular discomfort. The results of PCRs on conjunctival swabs taken to support a diagnosis, including qPCR, are often equivocal for viral infection [254].

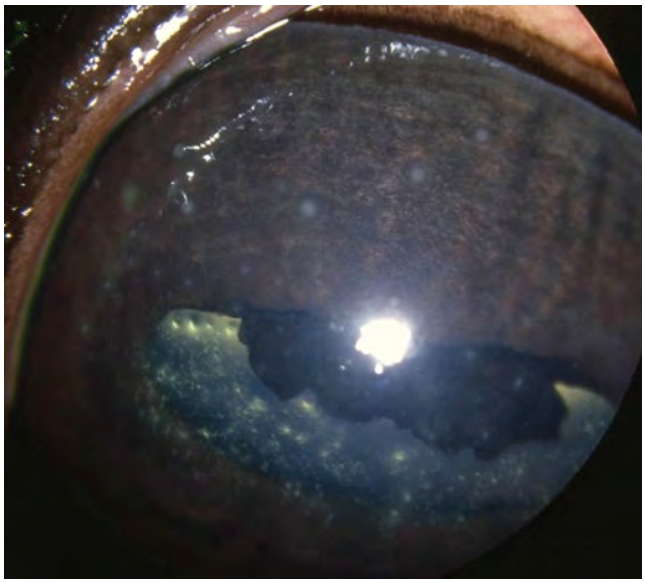


Figure 7.58 Putative viral keratitis. Small, discrete epithelial erosions and superficial ulcers in the dorsal and central cornea of an acutely painful eye.

Reflex uveitis is a feature of the acute putative viral keratitis seen in the UK. However, viral-like epithelial lesions may be associated with aggressive and refractory anterior uveitis in a small number of cases (online Figure 7.55). These latter cases may involve other, possibly secondary, corneal or uveal pathogens, including fungi.

Clinical manifestations of disease caused by EHV-1 are distinctly different and demonstrate nervous system involvement (blindness, strabismus, optic neuritis, exposure keratitis, etc.) [113].

Treatment

In the UK, both types of the disease respond to topical 0.5–1% idoxuridine solution or 1% trifluorothymidine applied every 2–4 hours until the eye is comfortable and re-epithelialization is evident. Both drugs are thymidine analogs converted into the active triphosphate form for incorporation into viral DNA by a viral-encoded kinase. Drugs such as acyclovir, ganciclovir, and pencyclovir, used in treating HSV in humans, require to be converted into the active phosphate form by a kinase encoded by HSV or other human herpesviruses, and although *in-vitro* efficacy against EHV-1 is demonstrable [256], their efficacy in ocular disease in the horse is unpredictable. Anecdotal reports indicate that both topical human recombinant interferon alpha (3000 IU/mL in artificial tears) and CsA, the latter used over a relatively long period, may be useful in managing some cases of the disease [82]. Topical glucocorticoids should not be used during the acute stages of the disease. They are likely to provide symptomatic relief, but may be associated with latency and subsequent recurrence of the disease.

Topical NSAID administration may be useful in controlling inflammation associated with putative viral keratitis [233]. Oral L-lysine supplementation is recommended in other species to control recrudescence of herpetic diseases; it acts by competitively inhibiting the incorporation of arginine into the viral genome, thereby decreasing viral replication. L-lysine supplementation as therapy for possible herpesvirus infection has not been evaluated in horses. However, anecdotal evidence suggests that clinical signs may be decreased in horses receiving 10–30 g of L-lysine orally once daily [233]. In the presence of corneal ulceration, prophylactic topical antibiotic and oral analgesic therapy (NSAID) is indicated, along with a topical therapeutic mydriatic/cycloplegic agent if reflex anterior uveitis is also present.

Treatment of the relatively mild multifocal subepithelial keratitis attributed to EHV-2 and EHV-5 is along broadly similar lines to those described above.

Prognosis

Considering the recrudescing nature of herpesvirus infections in other species, the prognosis for complete resolution of presumptive herpetic keratitis/keratoconjunctivitis is variable. However, clinical signs are usually successfully managed, and an overall comfortable and visually functional globe is maintained.

Parasitic keratitis

Parasitic keratitis has become increasingly rare with the widespread use of macrocyclic lactone anthelminthics.

Prevalence

Onchocerca cervicalis is a parasite that can infect equine ocular tissues, particularly the cornea, conjunctiva, and dermal tissues. Correlation of dermal and ocular infections is inconsistent, with reports documenting both the presence and absence of dermal and/or ocular microfilariae, with or without consistent ocular lesions [257, 258]. A 1987 report from the southeastern USA identified dermal microfilariae in nearly 53% (153/292) of horses examined at a slaughterhouse; of these, 40% (60/153) had ocular changes consistent with onchocerciasis, while over 40% without dermal microfilariae (58/138) had similar ocular lesions [259]. Prevalence rates may vary by geographic locale. In 1995, microfilariae were detected in only 1.1% (4/368) of horses in France, none of which had ocular lesions [260]. Overall, a decreasing prevalence of *Onchocerca* worldwide is probably attributable to increasing use of oral ivermectin in particular as a deworming agent. Both moxidectin and ivermectin are effective against the microfilariae; their efficacy against adult worms residing in the nuchal ligament appears limited [261].

Adults and larvae of *Thelazia lacrymalis* reside in the conjunctival sacs and lacrimal gland ducts of horses worldwide. Infection rates of between 3% and 30% have been documented in horses in Europe [260, 262, 263] and 43–50% in horses in Kentucky [264], although these are likely to have fallen with the increasing use of macrocyclic lactones.

The larvae of *Habronema muscae* and *Draschia megastoma* can be found in the conjunctivae, proximal lacrimal system, and periocular skin of horses worldwide. The adults live in the gastric mucosa and infection rates for *Habronema* spp. of between 1% and 25% have been found in horses in Europe [262, 265]. In horses in Kentucky in the mid-1980s, infection rates for *Habronema* spp. and *Draschia* spp. were 65% and 29%, respectively [266].

The larvae of the oestrid fly *Gedoelstia* in South Africa can penetrate the conjunctiva of the third eyelid of horses to cause severe conjunctivitis and nonhealing corneal erosions and ulcers [267, 268].

Pathogenesis

Adult *Onchocerca* nematodes live in the nuchal ligament of horses and produce microfilaria which migrate through adjacent subcutaneous tissues and are then ingested by *Simulium* spp. flies or *Culicoides* spp. midges. Following development into their infective stage within the intermediate host, microfilariae are transmitted to another horse through the insects' bite, where they subsequently develop into an adult. Aberrant migration of noninfective microfilariae to the ocular region results in clinical signs and lesions of ocular onchocerciasis, which are thought to be more severe in conjunction with microfilarial death [258].

The intermediate host and vector of *Thelazia lacrymalis* larvae are nonbiting *Muscid* (house) and *Stomoxyid* (stable) flies which feed on ocular secretions [263]. Infestation is usually asymptomatic or presents as a mild conjunctivitis, but the parasite has been implicated as a cause of ulcerative keratitis [263].

The intermediate host and vector of *Habronema* spp. and *Draschia* spp. are *Muscid* and *Stomoxyid* flies, respectively, and their location in periocular tissues is accidental. Dead larvae elicit a local granulomatous inflammatory response, which in the palpebral conjunctiva can result in erosion, ulceration, and abscessation of the apposing cornea (Figure 7.59).

The horse is an opportunist rather than definitive host of the *Gedoelstia* larvae. First instar larvae are deposited on the ocular surface, where they cause nonspecific local irritation [267, 268].

Diagnosis

Acute and chronic presentations of ocular onchocerciasis have been defined [258], but they actually represent a continuum of clinical disease. The most consistent finding in all cases is conjunctivitis, manifesting most distinctly as dorsolateral limbal nodules and focal vitiligo (Figure 7.60) [257, 258, 269], although these lesions may not be specific for *Onchocerca*. Corneal lesions in acute keratitis cases may include multifocal feathery, whitish superficial stromal opacities located in close proximity to the lateral limbus, along with diffuse corneal edema, and vascularization (online Figure 7.56) [258]. Corneal ulceration appears to be an infrequent finding. With chronicity, corneal fibrosis and vascularization may develop [258, 269]. Anterior uveitis may also be present, and affected individuals appear most likely to present with signs of ocular pain (blepharospasm, epiphora, photophobia), with or without keratitis [258]. Active (subretinal infiltrates, retinal detachment) and inactive (depigmentation, hyper-reflectivity) posterior uveitis has also been documented [258, 269]. Definitive diagnosis is made by identifying microfilariae via conjunctival snip biopsies and ruling out other possible diagnoses as appropriate (i.e., ocular surface cytology, cultures).

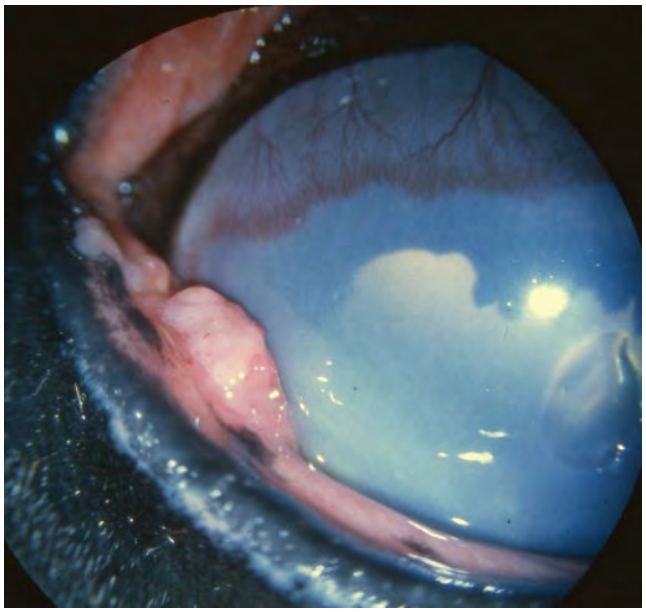


Figure 7.59 Habronemiasis. Corneal excoriation and abscessation secondary to *Habronema* spp. larval granuloma in the apposing ventrolateral palpebral conjunctiva.



Figure 7.60 Dorsolateral conjunctival depigmentation associated with *Onchocerca cervicalis* filarial infestation.



Figure 7.61 *Thelazia lacrymalis* adults free swimming in the tear film. There is an associated mild conjunctivitis. (*Source*: Image courtesy of Deborah Walker.)

Free-swimming adult *Thelazia lacrymalis* are usually visible in the PCTF (Figure 7.61). Larval stages may be identified in conjunctival washes. Their presence in ulcerated eyes may be coincidental.

Habronema spp. infestation presents as irregular pink conjunctival masses (Figure 7.59). These masses may be solitary or multiple, and typically contain characteristic mineralized foci ("sulfur granules") which can result in corneal excoriation. Definitive diagnosis is based on histopathology, showing an intense eosinophil response and mast cell infiltrate, mineralized deposits, and larval fragments.

Gedoelstia larvae buried within the conjunctiva cause severe chemosis, conjunctivitis, and superficial ulceration in horses in southern Africa (online Figure 7.57).

Differential diagnosis

Differential diagnoses for ocular onchocerciasis include other causes of nonulcerative keratoconjunctivitis (SA, IMMK, eosinophilic keratoconjunctivitis, nonulcerative keratouveitis (NUKU), neoplasia (particularly SCC)), and other causes of uveitis (e.g., trauma, ERU).

Differential diagnoses of habronemiasis include neoplasia (particularly SCC) and infectious granuloma. The presence of large numbers of mast cells in biopsy sections of the granuloma can lead to a misdiagnosis of mast cell tumor.

Treatment

Ivermectin (0.2 mg/kg IM or PO) and moxidectin (0.4 mg/kg PO) are effective at reducing numbers of onchocercal microfilaria but have no effect on the adult worms. Minimizing the development of an adult worm burden is best achieved by following a regular deworming protocol, which will ideally decrease development of clinical disease. Individuals who have current or previous signs consistent with ocular onchocerciasis can be pretreated with a systemic NSAID prior to administration of a parasiticide. Therapy for ocular lesions is symptomatic: keratitis without ulceration and anterior uveitis are treated with topical corticosteroids, topical atropine, and oral NSAIDs.

Thelazia lacrymalis adults and larvae are removed from the ocular surface by repeated saline lavage and oral moxidectin should be administered.

Debulking of the granuloma along with local corticosteroids application and oral moxidectin is effective in cases of larval habronemiasis. Corticosteroids should not be used where corneal ulceration is present. Any concurrent corneal ulcer or abscess should be managed routinely.

Geodoelstia larvae must be flushed and mechanically removed from the fornices. Later stages of the larvae are sensitive to ivermectin. Larvae within the conjunctiva must be physically removed.

Prognosis

Considering the prevalence of the vectors in the environment, and in the case of *Onchocerca* the inability to treat the adult worms, routine deworming is the most important and effective method of preventing disease.

Conjunctival depigmentation generally remains following removal of *Onchocerca* microfilaria and resolution of the clinical signs.

Ocular surface disruption and corneal ulceration

Recurrent erosion (chronic nonhealing corneal erosion)

Indolent or nonhealing superficial erosions are characterized by decreased adhesion of migrating corneal epithelial cells to the intact epithelial BM, variable contiguous stromal cellular infiltrate, and absence of stromal loss. These erosions are frequently recurrent, with cyclical repair and re-injury occurring at a varying interval, often for several episodes. In the majority of histologic samples from horses with recurrent erosions, dysmature epithelial cells adjacent to the lesion were nonadherent to the BM. Intraepithelial inflammatory cell infiltration was uncommon; however, an anterior stromal hyaline zone, intrastromal inflammation, fibrosis, and vascularization were variably present [270]. Recurrent erosions are relatively common in the horse [270–280]. Both adults and foals may be affected [273–276]. Typically, the lesions are sterile and there is no contributing abnormality of the eyelids or palpebral conjunctiva. The etiology is poorly understood in all species, but is likely to involve a complex process of failure of normal BM regeneration and absent or delayed hemidesmosome attachment following minor superficial insult [270, 273]. Over-expression of matrix metalloproteinases by abnormal basal epithelial cells in combination with anomalous expression of adhesion macromolecules such as fibronectin and laminin may be contributing

factors. A hyaline membrane covering the lesion may hinder communication between epithelial and stromal cells to prevent healing. In some cases the disease may represent a primary epithelial BM disease [270, 273]. Rarely a focal endothelial abnormality, for example, in association with anterior synechia, may compromise stromal and epithelial repair, contributing to a nonhealing epithelial erosion.

Clinical appearance

Owing to the extensive sensory innervation of the superficial cornea, horses with erosions are generally in some degree of discomfort. Blepharospasm, blepharedema, epiphora, and conjunctival hyperemia are common, along with mild to pronounced anterior stromal haze [273]. Fluorescein retention within the erosion bed is typically muted. Nonadherent epithelial edges, identified by leakage of fluorescein underneath the epithelium surrounding the erosion, are a consistent finding (Figures 7.62, 7.63, 7.64, and 7.65 and online Figures 7.58, 7.59, 7.60, 7.61, 7.62, 7.64, 7.73, 7.74, 7.75, and 7.81) [273]. Some degree of vascularization occurs [273]. Anterior stromal cellular infiltrate, visible as yellowish opacification of the lesion, is only infrequently noted in uncomplicated erosions, even where present at a histological level. In isolated cases, erosions can be associated with mild secondary anterior uveitis manifesting as miosis, low-grade aqueous flare, and/or hypotony.

Differential diagnosis

As with any ocular surface discontinuity, it is important to identify and eliminate the underlying cause, as well as rule out infection. Underlying causes to consider include eyelid abnormalities (entropion, ectropion, trichiasis), qualitative or quantitative tear film abnormalities, and pre-existing corneal disease (degeneration, dystrophic disease, bullous keratopathy, primary epithelial disease). Cytology and bacterial (aerobic, anerobic) and fungal cultures should be performed to rule out infection. Histopathology may be performed on corneal biopsy



Figure 7.62 Superficial, noninfected, indolent ulcer with corneal edema is present. Superficial corneal vascularization is beginning.

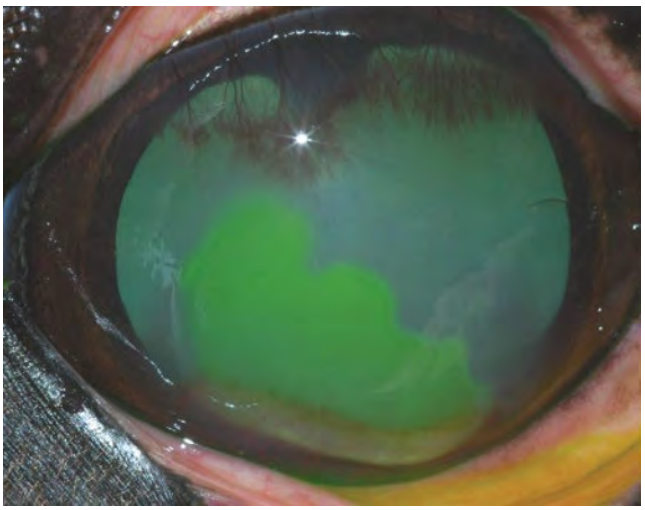


Figure 7.63 The ulcer in Figure 7.58 is stained with fluorescein dye.

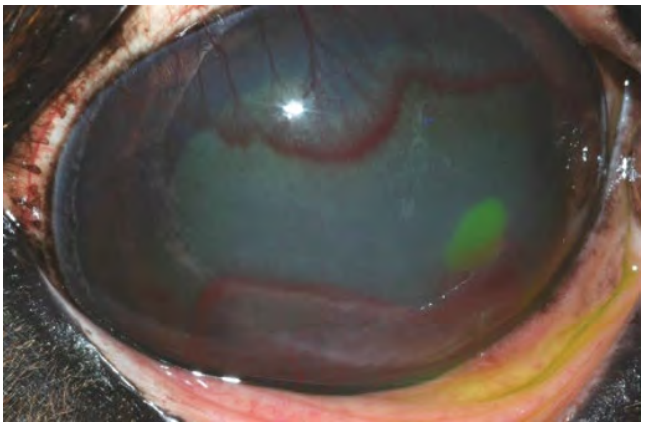


Figure 7.64 Thirteen days later the ulcer in Figure 7.58 has reduced in size.

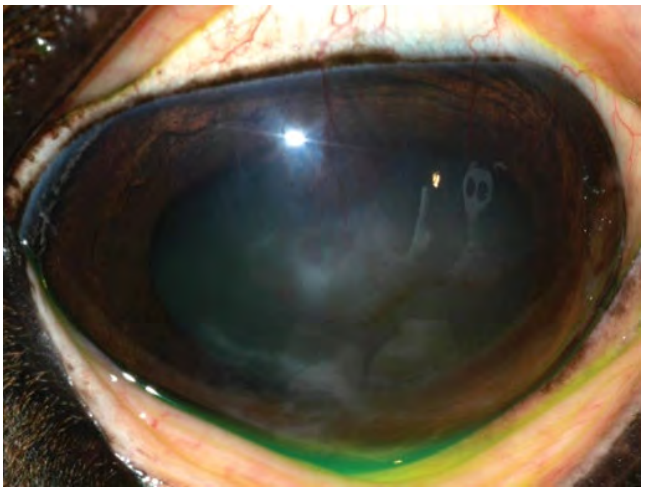


Figure 7.65 Thirty-five days since the image shown in Figure 7.58 was taken, the ulcer healed, with faint subepithelial scarring fibrosis causing a corneal haze. The ulcer recurred 2 weeks later.

Table 7.5 Appropriate medical therapy for an uncomplicated, superficial corneal ulcer.

Drug class	Example(s)	Formulation(s)	Dose/frequency
Prophylactic antibiotic	Neomycin/polymyxin B/ gramicidin; oxytetracycline; erythromycin; chloramphenicol	Ointment Solution	¼-inch strip q6–8h 0.1–0.2 mL q6–8h
Therapeutic mydriatic cycloplegic	Atropine	Ointment Solution	¼-inch strip q24–48h 0.1–0.2 mL q24–48h
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h
Antiprotease	Serum	0.1–0.2 ml	q6–8h

specimens of horses with recurrent erosions. These show discontinuous, disorganized, dysplastic epithelium, increased numbers of stromal fibroblasts, variable vascularization, and variable presence of inflammatory cells [270, 273]. Considering the risk of undetected bacterial and fungal infections, it is important to rule out infectious ulcerative diseases prior to arriving at a diagnosis of an uncomplicated nonhealing erosion.

Treatment

Primary therapy for an uncomplicated erosion includes topical antibiotics as prophylaxis for infection, a topical antiprotease such as serum to reduce tear film protease activity, topical mydriatic/cycloplegic (1% atropine), and systemic NSAID to treat the secondary reflex uveitis where necessary (Table 7.5). An appropriate topical antibiotic should be broad spectrum and minimally epitheliotoxic: for example, neomycin/polymyxin B/bacitracin, erythromycin, or oxytetracycline ointments. Tetracyclines have anti-MMP activity, which may help stabilize the protein matrix involved in healing an epithelial wound, and therefore may have added benefit in treatment of erosions beyond their antibacterial effect [221, 281, 282]. Topical prophylactic antibiotics are administered every 6–8 hours, while the mydriatic/cycloplegic is generally needed once every 24–48 hours to effect.

Horses will re-epithelialize noninfected erosions at an average rate of 0.6 mm/day [104]. In humans, this process is completed at a rate of 60–80 μm/hour, corresponding to healing a 6-mm defect within 48 hours. If the BM is damaged, complete healing may be prolonged as re-establishment of BM and associated adhesion complexes must occur. Debridement of the redundant epithelial margins of nonhealing erosions is essential to remove nonadherent epithelial cells and speed healing [82, 273, 280]. Generally debridement is done only once and can be used in conjunction with a therapeutic soft contact lens (An Vision (Salt Lake City, UT)) and temporary tarsorrhaphy to physically protect the regenerating basal epithelium. Diamond burr debridement has the advantage of effectively removing both redundant peripheral epithelium and any hyaline zone lining the base of the lesion, and is a first line therapeutic intervention [280].

Additional therapies, carried out where medical treatment and debridement fail, include thermal cautery, grid keratotomy, and SK to address any underlying anterior stromal abnormality [82]. Thermal cautery involves the creation of multifocal superficial stromal burns throughout the erosion bed and within the surrounding 1 mm of normal epithelium. These are intended to alter the abnormal anterior stromal hyalinized zone [271]. A grid keratotomy, performed by creating a hatched grid across the entire erosion bed through the BM, exposes epithelial cells to stromal collagen type I, which is believed to promote more effective basal cell attachment [275, 282–285]. However, grid keratotomy may promote extension and entrapment of subclinical infection into the anterior stroma, and should be performed with circumspection in geographic regions with a high prevalence of bacterial and fungal keratitis. SK involves removal of the entire abnormal BM and anterior stroma associated with the defect, allowing the resulting wound to heal by second intention (see section **Corneal surgery**) [286, 287]. Soft contact lenses have also been found to be effective in treating superficial noninfected ulcers in horses [288]. Following each of these procedures, medical therapy is indicated.

Prognosis

With appropriate medical and/or surgical therapy, the prognosis for nonhealing erosions is good. In a study involving 23 horses, those treated with debridement alone healed in a mean of 15.3 days, those treated with a grid keratotomy healed in a mean of 16 days, and those receiving SK healed in 23 days [273]. It is important to note, however, that only 63% of those treated with debridement alone healed, while 78–80% of those treated with grid keratotomy or SK healed. In a study of ten horses receiving grid keratotomy, the mean healing time for seven of the patients was just over 8 days [275]. These horses healed with minimal corneal vascularization or edema, which reportedly resolved. Two of the horses experienced complications attributed to "viral" keratitis, but no other problems were noted. Thermal cautery resulted in healing of chronic erosions within 2 weeks in two horses with unilateral disease, with no reports of complications [271]

Bacterial corneal ulceration

The environment of the horse is such that the ocular surface is constantly exposed to potentially pathogenic bacteria. The microbial flora of the horse varies depending on the age of the

horse, season of year, housing conditions, and the geographic area [67, 68, 71, 72, 82, 289–292]. The normal equine eye has an ocular surface bacterial flora that consists primarily of Gram-positive, nonpathogenic bacteria [68, 285, 287]. The presence of a few Gram-negative rods is normal. Nonpathogenic commensal bacteria compete for nutrients with potentially pathogenic bacteria to suppress the opportunity for colonization by the latter [76]. Potentially pathogenic *Staphylococcus* spp., *Listeria* spp., *Streptococcus* spp., and other Gram-positive bacteria can cause infectious keratitis in horses [67, 68, 71, 72, 82, 282]. Young horses appear at greater risk of Gram-negative infections [67]. Gram-negative bacteria known to be associated with equine corneal ulcers include *Pseudomonas* spp. and assorted coliform bacteria [68, 185, 289, 290, 293]. Mixed bacterial and fungal infections can also be present [144, 293]. The microbial population of a horse with an ulcer can change during antimicrobial treatment [68].

The healthy corneal epithelium and tear film of the horse represent formidable physical barriers to epithelial and stromal invasion of potential pathogens, but injuries to the ocular surface of horses are common [82]. Ocular surface defense mechanisms, including tear washout mechanisms, are highly effective in protecting the cornea against incursion by opportunist keratopathogens [82]. If bacteria are able to evade the innate corneal defense mechanisms suppressing microbial growth and colonization, they have the opportunity to invade the cornea. At all stages of ulcer formation, the damage control and repair mechanisms of the ocular surface attempt to control and reverse stromal breakdown. Early failure of repair of epithelial cell damage is a primary conduit into the ulcerative process [76, 80, 82].

An organism's virulence (i.e., ability to rapidly cause serious disease) relates to its ability to adhere to an epithelial surface, and to induce inflammation and the consequent activation of locally destructive microbial and host-derived proteases. *Pseudomonas aeruginosa* and *Staphylococcus aureus* are able to adhere to injured epithelium at the edge of a superficial corneal defect, but do not adhere well to intact corneal epithelium or to stroma [82]. The process of bacterial adherence generally involves a chemical or structural interaction between microbial cell wall adhesins and receptors on the target epithelial or other cell. *Pseudomonas aeruginosa* has evolved filamentous cell wall appendages termed fimbriae which interact and adhere to corneal epithelial cell membrane, and excavations in the corneal epithelial cell membrane subsequently form around the adherent bacterium. The bacteria enter the cell at these sites, and once within the cell are no longer accessible to the host's innate defenses and to most antibiotics. The *Pseudomonas* organisms can then replicate within the epithelial cell, or, migrating through the epithelial cell mass, can enter the anterior stroma. Entry of *Pseudomonas* into the corneal epithelial cell involves active metabolic processes, and the entire process from adherence to early stromal penetration in the rabbit eye model occurs in 1 hour [82].

Once pathogenic organisms enter the stroma, they replicate and spread radially and deeply, migrating between the stromal collagen lamellae [82]. The intrastromal spread of the bacteria is facilitated by the release of potent proteoglycanases, including serine proteases and matrix metalloproteinases, by both the pathogen and reactive keratocytes, rapidly lysing stromal ECM [76, 80, 82]. Significant elevations in these proteases are found in horses with infectious keratitis [82]. *Staphylococcus aureus* is able to resist phagocytosis by macrophages during the early stages of corneal invasion and produces the cytodestructive toxins hyaluronidase, alpha toxin, and leukocidins [82]. *Pseudomonas aeruginosa* produces exotoxins, endotoxins, and proteases [82]. β-hemolytic *Streptococcus* spp. produces a specific exotoxin which drives rapid corneal destruction, and is particularly pathogenic in the horse [76].

Corneal microbial invasion is immediately followed by infiltration of the corneal stroma by neutrophils chemotactically attracted into the cornea from the eyelid and limbal blood vessels, both directly and via the PCTF [76]. Chemoattractants attached to or released from capillary endothelial cells tether and arrest circulating leucocytes, and, using integrins for traction, these then cross the capillary wall by diapedesis, before following directional cues created by a chemoattractant concentration gradient to enter and progress through the cornea [76]. Leucocytes attracted into the anterior chamber attach to the corneal endothelium, and can aggregate to form keratic precipitates (KPs).

Following entry of microbes and PMNs into the cornea, a progressive destructive process involving necrosis of stromal keratocytes and their phagocytosis by PMNs and recruited macrophages then occurs [76]. This process does not appear to be associated with increased bacterial MMP production [82]. Prostaglandins, leucotrienes, proteases, and cytokines are released from epithelial cells and subepithelial keratocytes in response to corneal injury [76, 80, 82].

As PMNs migrate centrifugally from the injury site in the anterior stroma, the overlying epithelial BM is lysed, leading to progressive sloughing of this perilesional tissue. The enlarged epithelial defect attracts further migration of PMNs into the corneal stroma [76]. Collagenolysis accompanying this accelerating sequestration and degranulation of PMNs exponentially increases the cycle of stromal lysis and consequent PMN recruitment (Figures 7.66 and 7.67) [76]. If the replication and spread of microbes is not halted by the host's innate defenses or by therapeutic intervention and the PMN-derived protease-driven stromal necrosis cannot be controlled, the cyclical process of PMN recruitment and stromal degradation will ultimately lead to total loss of stromal tissue and corneal perforation [76].

Leucocyte infiltration of ulcerated stroma results in a change in color of the cornea from clear to turbid white to yellow. Neutrophils eliminate bacteria by phagocytosis, but are unable to phagocytize fungi. However, degradative proteases, superoxide radicals, and peroxides released from sequestrated neutrophils, while an integral part of the damage control and repair process,

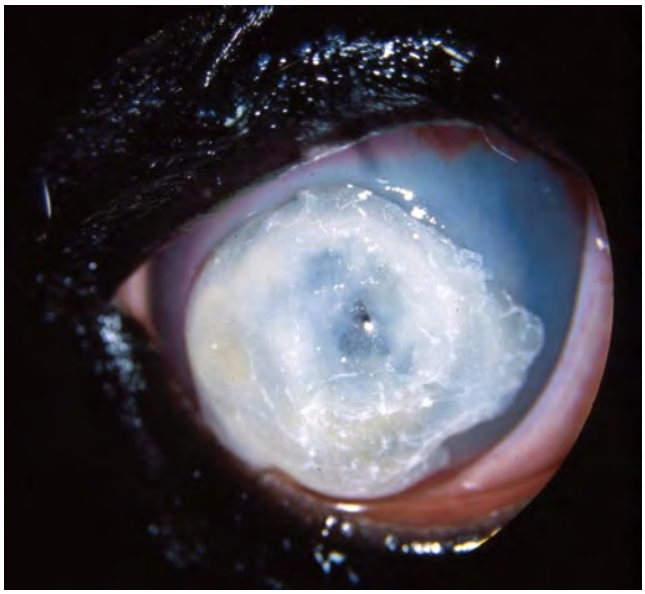


Figure 7.66 A large-diameter melting ulcer with a prominent cellular infiltrate and a very thin center caused by *Staphylococcus* spp. The dark spot in the center ruptured to cause an iris prolapse, which was repaired with a large conjunctival graft.

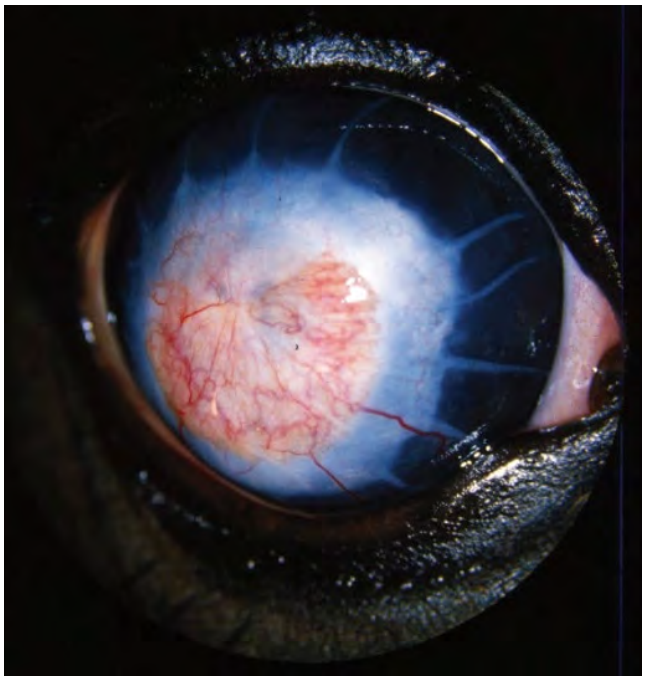


Figure 7.67 The eye in Figure 7.66 is scarred axially 1 month post-operatively. The owner thought the horse had some peripheral vision in this eye.

once they have exceeded the innate inhibitory capacity on the ocular surface have the potential to rapidly accelerate stromal collagen and ECM breakdown to the stage of keratomalacia or corneal "melting." [76, 80, 82]. Appropriate antibacterial therapy can rapidly sterilize corneal ulcers; however, the large numbers of neutrophils present can be responsible for progressive stromal

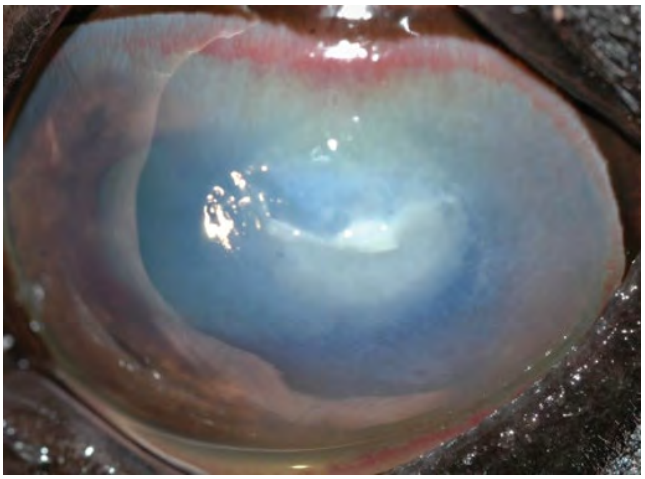


Figure 7.68 An ulcer with cellular infiltrate and early limbal vascularization is present. Fungi were found on cytology.

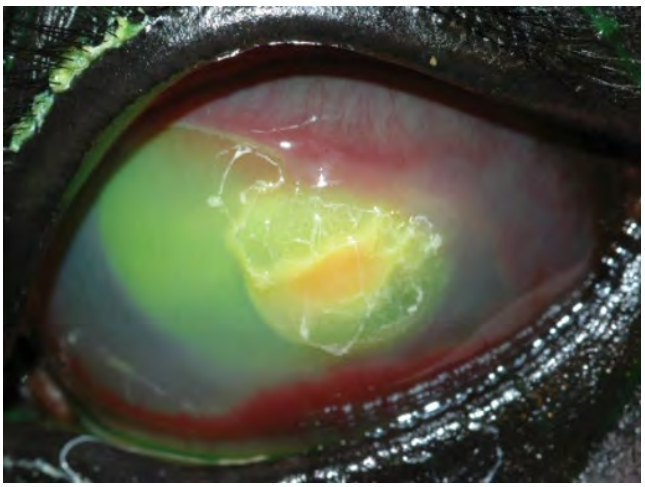


Figure 7.69 Two weeks later, a fungal plaque has formed in the eye shown in Figure 7.68, and corneal neovascularization progressed dramatically.

lysis. Thus ulceration can progress in the absence of significant infection, driven by the host's own neutrophil response.

Once the destructive ulcerative process is controlled, repair progresses and induces extensive fibroblastic collagen deposition from reactive keratocytes that ultimately cause corneal haze and scarring [76, 80, 82]. The injured horse cornea does, however, have the often unrecognized and remarkable ability to slowly remodel, significantly reducing the extent and density of initially large corneal scars (Figures 7.68, 7.69, 7.70, 7.71, and 7.72).

Prevalence

Bacterial ulceration is frequently encountered in horses. In one evaluation of 38 eyes from 37 horses with ulcerative keratitis, only six had no bacterial growth [289]. Isolation of either bacteria and/or fungal organisms from horses with undefined extraocular disease identified positive cultures in 98/123 eyes (79.7%), with *Streptococcus* spp. (43.9%), *Staphylococcus* spp.

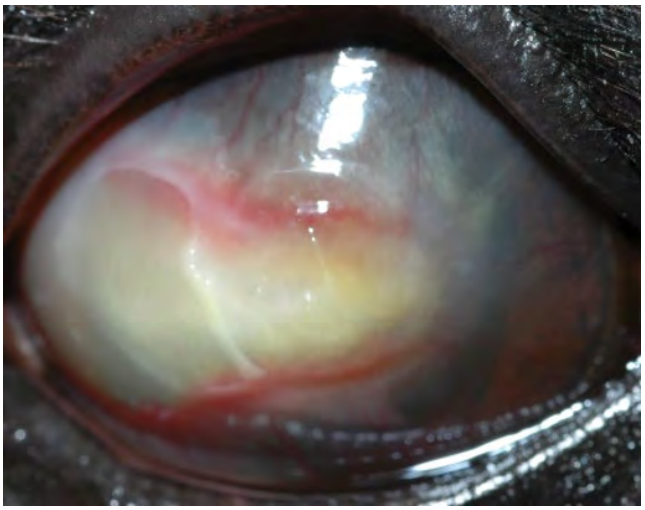
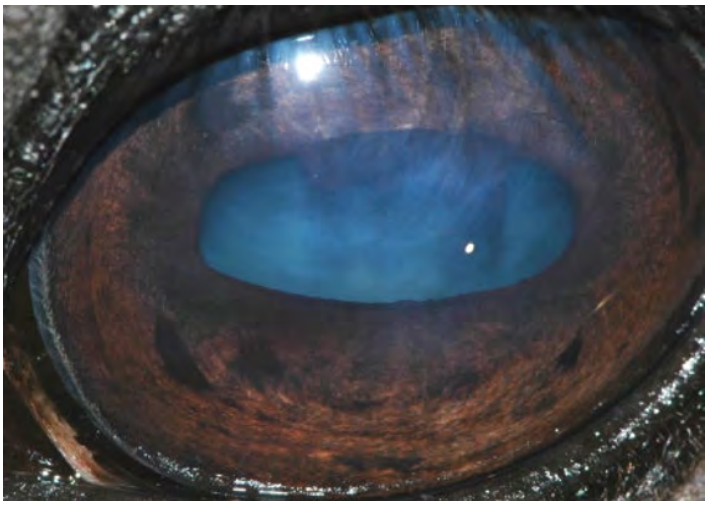


Figure 7.70 One week later, the fungal plaque in Figure 7.65 is absent, revealing a cellular infiltrate, with further progression of the corneal vascularization.



Figure 7.71 Two weeks later, the affected area (shown in online Figure 7.67) is healed, leaving stromal granulation tissue and some pigment.



(A)



(B)

Figure 7.72 (A) Five years later, the eye in Figures 7.68, 7.69, 7.70, 7.71 has remodeled, leaving a mild corneal haze from subepithelial fibrosis. (B) Slit-lamp finding of opacities found in horse corneas following healing of corneal ulcers, SA, and corneas that have had lamellar keratoplasties. The **arrows** point at the linear opacity and the **arrowhead** at the endothelium in the eye in Figures 7.68, 7.69, 7.70, 7.71, 7.72A. This opacity may be fibrosis and responsible for the haze following corneal healing.

(24.2%), and *Pseudomonas* spp. (13.8%) most frequently identified [290]. In 41 eyes of horses with ulcerative keratitis in the northeast USA, bacteria or fungal organisms were identified on cytology samples from 23/36 eyes (64%) and cultured from 22/39 eyes (56%), eight of which were *Pseudomonas* spp [291]. While *Staphylococcus*, *Streptococcus*, and *Pseudomonas* spp. are the most common isolates, numerous other organisms have been reported as either known or presumed pathogenic bacteria (Tables 7.6 and 7.7) [289–305], including anerobic bacteria, frequently *Clostridium* spp., in 18/140 horses (12.9%) with corneal ulcers, often with coinciding aerobic bacterial growth [306].

Clinical appearance

Bacterial keratitis typically presents with nonspecific clinical signs such as blepharospasm, epiphora, ocular discharge, photophobia, and corneal opacification [307, 308], and may be overtly indistinguishable from other ocular diseases. However, bacterial ulcerative keratitis can initially present as minor corneal epithelial abrasions or superficial ulcers with slight outward signs of ocular pain or discomfort [82, 294]. Small corneal abrasions and superficial ulcers are detected through oblique transillumination and fluorescein dye retention. Anterior uveitis and corneal vascularization may not be clinically pronounced in acute bacterial

Table 7.6 Number of presumed pathogenic, Gram-negative bacterial isolates identified in horses with ulcerative bacterial keratitis.

Reference	Utter et al., 2009 [377]	Ledbetter and Scarlett, 2008 [306]	Keller and Hendrix, 2005 [292]	Lassaline et al., 2005 [407]	Sauer et al., 2003 [298]	Rebhun et al., 1999 [299]	Sweeney and Irby, 1996 [309]	Moore et al., 1995 [291]
Organism genus (respiration, morphology)								
Acinetobacter (A, bacilli)	6		3		2			3
Actinobacillus (FA, rod)			1					2
Aeromonas (FA, bacilli)						1		
Burkholderia (A, rod)					1			
Enterobacter (FA, rod)	3				2			
Escherichia (FA, rod)			1		5			4
Flavobacterium (FA, rod)					2			
Fusobacterium (AN, rod)		1						
Klebsiella (FA, rod)			1					1
Moraxella (A, diplococci)					1			3
Neisseria (A, diplococci)			1					
Ochrobactrum (A, coccobacillus)					1			
Pantoea (FA, rod)			1					
Pasteurella (FA, pleomorphic)					2			1
Proteus (FA, rod)			1					
Providencia (FA, rod)								2
Pseudomonas (A, rod)	5		6	3	15		70	14
Salmonella (FA, rod)								
Serratia (FA, rod)			2		3			
Nonfermenting rods			4					

Reference	Adamson and Jang, 1985 [300]	McLaughlin et al., 1983 [290]	Moore et al., 1983 [289]	Divers and George, 1982 [301]	Rebhun, 1981 [302]	Gelatt, 1974 [303]
Organism genus (respiration, morphology)						
Acinetobacter (A, bacilli)		1	6			
Actinobacillus (FA, rod)						
Aeromonas (FA, bacilli)						
Burkholderia (A, rod)						
Enterobacter (FA, rod)		8	9		1	
Escherichia (FA, rod)		5	2		1	
Flavobacterium (FA, rod)		1				
Fusobacterium (AN, rod)						
Klebsiella (FA, rod)		3	4			
Moraxella (A, diplococci)		3				
Neisseria (A, diplococci)		1				
Ochrobactrum (A, coccobacillus)						
Pantoea (FA, rod)						
Pasteurella (FA, pleomorphic)		3	1			
Proteus (FA, rod)		4	1			
Providencia (FA, rod)			1			
Pseudomonas (A, rod)		17	10	1		1
Salmonella (FA, rod)	1					
Serratia (FA, rod)						
Nonfermenting rods						

A, Aerobe; AN, anerobe; FA, facultative anerobe.

Table 7.7 Number of presumed pathogenic, Gram-positive bacterial isolates identified in horses with ulcerative bacterial keratitis.

References	Utter et al., 2009 [377]	Ledbetter and Scarlett, 2008 [306]	Keller and Hendrix, 2005 [292]	Sauer et al., 2003 [298]	Sanchez et al., 2001 [296]	Brooks et al., 2000 [305]	Cullen and Grahn, 2000 [304]
Organism genus (respiration, morphology)							
Actinomyces (FA, rod)		2					
Bacillus (A, rod)					13		
Clostridium (AN, rod)	2	16					
Corynebacterium (FA, rod)	3	5	2	1	4	1	
Diplococcus					1		
Enterococcus (FA, cocci/diplo)				1			
Eubacterium (AN, rod)		1					
Listeria (FA, rod/bacilli)					1		
Micrococcus (A, cocci)				1			
Nocardia (A, rod)				1	1		
Peptostreptococcus (AN, cocci)		1					
Propionibacterium (AN, rod)		1					
Staphylococcus spp. (FA, cocci)		16		2	17	5	
Coagulase-positive *Staphylococcus* (i.e., *S. aureus*) (cocci)	2		3	4			
Coagulase-negative *Staphylococcus* (i.e., *S. epidermidis*)			3	1			
Streptococcus spp. (FA, cocci)				1	22		
α-Hemolytic *Streptococcus* spp. (i.e., *S. pneumoniae*)	1	6	1				
β-Hemolytic *Streptococcus* spp. (i.e., *S. equi zooepidemicus*)	5	10	18	15	32	11	1
Nonhemolytic *Streptococcus* spp.			2				
Nutritionally variant streptococci			35		24		
Macrococcus			1				

A, Aerobe; AN, anerobe; FA, facultative aerobe.

abrasions and superficial ulcers, and a slowly progressive or indolent course often belies the potential seriousness of the condition. Extensive intrastromal bacterial invasion accompanied by vascularization, conjunctival injection, and corneal edema may eventually become evident, with progression from acute superficial ulcers/abrasions (online Figures 7.65–7.71, 7.82, 7.83, 7.84, 7.85, 7.26, and 7.27). Both superficial and deep corneal vascularization and overt reflex uveitis are typically present. Keratomalacia or stromal "melting" appears as a gelatinous, often dependent, gray coagulum adherent to the margins or central regions (or both) of an ulcer. Deep penetration of the stroma to Descemet's membrane (descemetocoele) with corneal perforation is a possible sequela in all cases of bacterial corneal ulcers in the horse [82, 294]. Critically, it should be recognized that descemetoceles are not painful, and an abrupt increase in comfort in any ulcerative lesion should alert the clinician to their possible presence.

Definitive correlation of clinical appearance with individual pathogens is not possible, but reports of ulcerative keratitis associated with β-hemolytic *Streptococcus equi* documented severe keratomalacia in 11/11 eyes and marked uveitis in 8/11 eyes [305], marking this organism as a very serious keratopathogen in the horse. *Pseudomonas* spp. ulcers are also frequently rapidly progressive and are associated with marked uveitis [82, 113, 289, 309]. In humans, anerobic bacterial infections of the cornea are associated with a characteristic clinical appearance of gaseous stromal bubbles and a frothy coagulum in the ulcer bed [310, 311]. These characteristics were not consistently noted in horses with anerobic infections, but in one study all anerobe-infected ulcers were stromal, and most had keratomalacia [306].

Differential diagnoses

Differential diagnoses for bacterial keratitis include other infectious infiltrative ulcerative diseases (e.g., fungal keratitis, "viral" keratitis, foreign body) and noninfectious infiltrative ulcerative diseases (sterile keratitis, eosinophilic keratoconjunctivitis). Nonulcerative conditions should also be considered in the differential for bacterial keratitis in the horse (e.g., IMMK, SA, calcific band keratopathy, and corneal neoplasia). Marked ocular discomfort, the clinical appearance of cellular infiltrate (whitish-yellowish corneal opacification), corneal edema, and pronounced anterior uveitis typically distinguish infected infiltrative ulcerative diseases from noninfected ulcerative disease (e.g., simple superficial ulcer, indolent ulcer, chronic erosion).

Diagnostic techniques for ulcerative keratitis

Definitive diagnosis is based on a combination of corneal cytology and bacterial culture and sensitivity. See Chapters 1 and 2 for a full description of the technique of collecting and interpreting corneal cultures and cytology.

Table 7.8 Medical therapy for an infected corneal ulcer: bacterial.

Drug class	Example(s)	Formulation(s)	Dose	Notes
Topical therapeutic antibiotic	Gram-positive: moxifloxacin, chloramphenicol, neomycin, bacitracin Gram-negative: ciprofloxacin, ofloxacin, aminoglycosides, chloramphenicol,* neomycin, polymyxin B	Ointment† Solution	¼-inch strip q2–4h 0.1–0.2 mL q2–4h	
Topical therapeutic mydriatic/cycloplegic	Atropine	Ointment† Solution	¼-inch strip q12–24h 0.1–0.2 mL q12–24h	Frequency is based on degree of mydriasis achieved between doses
Topical antiprotease	See Table 7.9			
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h	
Systemic antibiotic	Trimethoprim sulfamethoxazole (T) Doxycycline (D) Potassium penicillin (P) Gentamicin (G)	Varies with drug	20–30 mg/kg PO q12h (T) 10–20 mg/kg PO q12h (D) 20,000 U/kg IV q6h (P) 4–6.6 mg/kg IM or IV q24h (G)	

* Not effective versus *Pseudomonas* spp.
† Avoid administering a topical ointment if a full-thickness corneal wound is present or may occur.

It is important to approach each case of ulcerative corneal disease in the horse in a systematic manner. Most cases can be diagnosed on the basis of standard laboratory techniques. Fluorescein stain must be used. Cytologic examination and microbiologic cultures of deep or rapidly progressing ulcers are very beneficial in determining the proper antimicrobial therapy [82, 294, 312]. Corneal cultures should be obtained first, followed by corneal scrapings for cytology [82, 294]. Vigorous corneal scrapings at the edge and base of the lesion to detect bacteria can be obtained with the handle end of a sterile scalpel blade and topical anesthesia. Superficial swabbing cannot be expected to yield the organism (or organisms) in a high percentage of cases, as any pathogens are generally deep within the ulcer [82, 294].

Staining with fluorescein dye for detection of an abrasion and ulcer is critical in the horse [82, 294]. The hydrophilic fluorescein dye moves rapidly into the stroma when the corneal epithelium is absent. Corneal erosions, where the BM is intact, stain only faintly with fluorescein, whereas ulcers stain very brightly. Critically, it should be recognized that descemetoceles do not retain fluorescein dye, and a descemetocele can be recognized as a dark, nonstaining clearing at the bottom of a deep ulcer. However, deep ulcers with a thin layer of overlying stroma ("predescemetoceles") will stain with fluorescein.

Seidel's test is utilized in horses for detecting corneal rupture and aqueous humor leakage. Touching a moistened fluorescein strip to a suspected full-thickness corneal defect will result in a color change in the dye as the aqueous humor dilutes the fluorescein. The orange color will turn green (see Figure 7.30) or become clear depending on the amount of aqueous leakage.

Treatment

Medical treatment Medical therapy always comprises a major thrust of ulcer control, tempered by judicious use of adjunctive surgical intervention (Table 7.8) [82, 294]. An aggressive pharmacologic attack should satisfy the therapeutic objectives of reducing microbial activity, decreasing uveitis, and reducing tear film concentrations of MMPs. Reduced MMP activity is associated with improvement of the clinical signs of ulcerative keratitis in horses. Treatment frequently needs to be sustained for weeks. Repopulation of potentially or actually pathogenic bacteria and fungi can occur during and after the administration of topical antibiotics in the horse [67]. This is especially true for Gram-positive bacteria such as *Streptococcus* spp [67].

Corneal ulcers in horses are typically painful, and topical treatment is usually difficult. In a fractious horse or one with a painful eye needing frequent therapy, SPL treatment systems are employed [82, 294]. The dorsal or ventral palpebral fornix can be used for lavage tubing placement [313, 314], but the increased exposure to and absorption of medications instilled into the dorsal fornix achieved higher concentrations of the medications in the cornea and anterior chamber [315].

Continuous rate infusion (CRI) pump systems can be used attached to SPL systems for aggressive topical therapy, and combinations of drugs or "cocktails" have been utilized in these continuous perfusion pumps for therapy of catastrophic corneal problems [316]. A single-useCRI delivery pump (Infu-Disc (Medical-e-Cell, San Diego, CA)) has been developed, which can be attached to an SPL system and secured to the halter at eye level for continuous delivery of topical ophthalmic medications. The device continuously releases fluid at a predetermined rate (0.02–4.0 mL/hour) for up to 7 days. There are currently only

limited data on the effect of both continuous infusion systems and drug combinations on individual drug bioavailability, stability, and interactions, and on solution sterility. In general, care is needed in compounding multiple drug solutions, and medications will inevitably be diluted when this format is used. When fluorescein was applied at a rate of 0.14 mL/hour for 72 hours, the overall mean tear film fluorescein concentration was approximately 20% of the applied concentration of fluorescein [317]. One cocktail of equal volumes of natamycin 3.33%, tobramycin 0.3%, cefazolin 5.5%, and equine serum has been studied [316]. This drug combination was at least as effective as each medication separately for inhibiting microbial growth of all pathogens tested and was significantly more effective against B-hemolytic *Streptococcus* spp., *Aspergillus* spp., and *Fusarium* spp. than the relevant medications separately. Blockage of the CRI pump by the drugs can occur [318]. Some drugs, such as voriconazole, can become unstable in the pumps at high temperatures [318], and voriconazole 1% solution is not suitable for use in a CRI-SPL unit. Several pumps were subjectively delivering less volume of medication than specified, suggesting pump failure or blockage of the SPL [318]. The dilution of serum with other drugs reduces its antiprotease activity. Antiproteinase activity of serum was a concentration-dependent event, which enabled serum alone to achieve significantly greater activity than in the drug combination [316]. Continuous infusion of any drug, alone or in combination, may have the undesired effect of dilution or disruption of the tear film, compromising healing and repair.

Ulcer sterilization Increasing antimicrobial resistance has been reported in several common bacterial pathogens, emphasizing the importance of sensitivity testing in each case. A study of bacteria isolated from horses with ulcerative keratitis in Tennessee from 1993 to 2004 documented susceptibility to ciprofloxacin (5/5) and chloramphenicol (17/17) for *Streptococcus equi* subsp. *zooepidemicus*; however, resistance was documented to the components of common triple antibiotic preparations (neomycin, polymyxin B, bacitracin) and other aminoglycosides, particularly tobramycin (12 of 13) [292]. A similar pattern was reported in two evaluations of *Streptococcus* isolates from Florida [298], although susceptibility to enrofloxacin was lower [305]. All *Pseudomonas aeruginosa* isolates from Tennessee were sensitive to aminoglycosides (11/11) and fluoroquinolones (6/6) [292]; these results were similar to those in previous reports documenting susceptibilities of *Pseudomonas* spp. to aminoglycosides ranging from 85% to 93% [291, 309]. In contrast, a study of isolates from horses in Florida from 1991 to 2000 found a significant increase in resistance of *Pseudomonas* isolates to gentamicin [298]. *Pseudomonas aeruginosa* isolates from human ocular disease have lower *in vitro* susceptibility to moxifloxacin than ciprofloxacin [319, 320]. Considering this accumulated information, identification of Gram-positive organisms may indicate topical chloramphenicol or fluoroquinolones as appropriate empirical therapy, while identification of Gram-negative organisms may provide indication for aminoglycosides or fluoroquinolones. In the presence of increasing resistance patterns, however, the importance of determining susceptibility patterns for individual isolates cannot be overemphasized. For example, in the two decades since the introduction of the fluoroquinolone ciprofloxacin, increasing *in vitro* resistance to ciprofloxacin has been identified among Gram-positive bacterial isolates from cases of ocular disease in humans [321–323].

The ulcer must be sterilized, although sterility does not necessarily equate with rapid or complete healing [82, 294]. Infection initiates and complicates ulcerative disease processes, but it is the proteinase activity in the PTF and stroma that drives and perpetuates it. Appropriate antibiotics, such as gentamicin, ciprofloxacin, or tobramicin ophthalmic solutions or ointments, may be used topically to treat Gram-negative bacterial ulcers [82, 289, 294]. Topical ocular administration of 0.3% ciprofloxacin and 0.5% moxifloxacin reach therapeutic concentrations in tears and corneal tissue of horses, even when there is an intact epithelium [324]. Amikacin (10 mg/mL) may also be used topically for Gram-negative bacteria. Chloramphenicol may penetrate the cornea but is a bacteriostatic drug that should be used carefully. Cefazolin (55 mg/mL) is best for treatment of equine ulcers with Gram-positive bacterial infections, and can be proportionally combined in a therapeutic cocktail with ophthalmic tobramycin, serum, and ophthalmic natamycin [82]. Antibiotic solutions suitable for topical ophthalmic use can be prepared using BSS and parenteral powder preparations designed for IV use. These solutions are inherently unstable and should not be stored for more than 24 hours. An increasing resistance to tobramycin and gentamicin by *Pseudomonas* and *Streptococcus* spp. in horses has been noticed in Florida [298]. These tobramycin- and gentamicin-resistant *Pseudomonas* spp., however, remain sensitive to ciprofloxacin.

Oral or parenteral antibiotics may also be administered to horses with bacterial keratitis, but the penetration of most systemic antibiotics into the horse cornea, anterior chamber, and preocular tear film is unknown. Drugs able to penetrate to either the intraocular environment or the preocular tear film may be in direct contact with infected corneal tissue, potentially increasing their therapeutic efficacy. In cases of corneal vascularization and intraocular inflammation, as present in horses with significant ocular surface disease, it may be necessary to increase drug levels. In addition to its antimicrobial effect, doxycycline has anticollagenolytic and anti-inflammatory activity and has been advocated for treatment of ocular surface disease as well as enhancement of corneal repair [325]. Oral administration of doxycycline to horses with uninflamed eyes at a dose of 10 mg/kg twice daily for 5 days did not result in appreciable aqueous or vitreous humor levels in one study [326], while another study in which normal horses were given 20 mg/kg every 12 hours for five doses did find measurable intraocular levels [327]. A third study in which normal horses were administered 20 mg/kg doxycycline once daily found measurable drug levels in the preocular tear film [328]. Other antibiotics (e.g., trimethoprim sulfa, fluoroquinolones) at appropriate doses may also be administered to horses with bacterial keratitis.

Table 7.9 Antiproteases commonly used as therapy for infectious equine keratitis.

Antiprotease	Mechanism of action	Target	Administration
EDTA 0.2%	Zinc and calcium chelation	MMPs	Topical
Autologous serum	Entrapment of protease	Serine proteases and MMPs	Topical
α2-macroglobulin		Serine proteases	
Prealbumin antiprotease			
Tetracyclines	Zinc and calcium chelation	MMPs	Topical (0.1%) Oral
N-acetylcysteine 5–10%	Zinc and calcium chelation	MMPs	Topical
Ilomastat 0.1%	Zinc and calcium chelation	MMPs	Topical

Control of uveitis In the horse, as in other species, iridocyclitis to some degree is the usual and expected sequela to ulcerative keratitis. Uveal inflammation is incited through an axon reflex mediated by the ophthalmic branch of the trigeminal nerve, which is sensory for the cornea, conjunctiva, and uvea [82, 294]. The horse is particularly sensitive to this corneal ulcer-associated axon reflex uveitis. Miosis, aqueous flare, hypopyon, and hypotony are present to some degree in all eyes with ulcers. In some cases, controlling the uveitis may be as therapeutically challenging as healing the cornea. The horse does have an ability to compartmentalize the intraocular inflammation such that severe iridocyclitis may not be associated with posterior segment inflammation. Topically applied anticholinergics (e.g., 1% atropine) are effective cycloplegics, causing pupillary dilatation, and will also stabilize the blood–aqueous barrier to reduce aqueous flare. Relaxation of the ciliary muscles also eliminates ciliary spasm, a major cause of ocular pain. Pupillary dilatation protects the visual axis from occlusion, and it may minimize development of synechiae [82, 294]. Synechiae are adhesions between the iris and lens. They can occur very quickly in the horse, and have the potential to compromise vision in the healed eye by preventing dilatation of the pupil. Topical atropine (1%) and phenylephrine (2.5%) in combination can dilate some pupils when synechiae are present. Tissue plasminogen activator (TPA) (50 μg/0.1 mL BSS intracamerally) can also aid synechia breakdown in some cases [82, 294]. Horses on topical atropine more than four times per day should be watched closely for symptoms of reduced gut motility and, in rare cases, colic [82, 294, 329].

Oral or parenteral anti-inflammatory medications are administered to reduce iridocyclitis with NSAIDs, a safer choice than systemic steroids in horses with bacterial keratitis. No studies comparing relative efficacy of various NSAIDs (e.g., phenylbutazone, flunixin meglumine, firocoxib) in reducing signs of uveitis in horses with ulcers have been performed, but, subjectively, flunixin seems to have the best effect on reducing intraocular inflammation.

Collagenolysis prevention Corneal bacterial infection (especially *Streptococcus* and *Pseudomonas* spp.) triggers a dramatic host response, resulting in sudden, rapid corneal liquefaction, progressing to perforation as a consequence of elevation of PTF and stromal proteases [14, 82, 95, 294, 330–336]. Inhibition of PTF proteases such as MMP-9 and NE is critical to healing of all diseases involving ocular surface disruption and corneal ulceration in the horse. MMPs are inhibited by innate tissue inhibitors of metalloproteinases (TIMPS), serum, EDTA, tetracyclines, including doxycycline, ilomostat, and acetylcysteine. Serine proteases such as NE are inhibited by serum, primarily by the prealbumin protease inhibitor and alpha-2 macroglobulin. NE does not appear to directly cause collagenolysis in the horse, but it reduces the inhibitory activity of TIMPS against MMPs. Further, MMPs inhibit the serum prealbumin inhibitor present in serum (Table 7.9), paradoxically increasing local NE concentration, and promoting collagenolysis through increased local MMP activity [95, 294, 330, 331].

EDTA, tetracyclines, and N-acetylcysteine inhibit MMPs by chelating calcium and zinc, ionic cofactors necessary for enzymatic stability and function [330]. Tetracyclines also inhibit expression of other inflammatory mediators (e.g., IL-1, B cells, macrophages) [83, 221, 281, 282, 337–339]. Ilomastat is a synthetic MMP inhibitor [340]. Comparison of relative efficacy of available anticollagenase substances demonstrates consistently strong antiproteolytic activity for equine serum, EDTA, N-acetylcysteine, and tetracyclines. In an *in vitro* study of tear film from horses with ulcerative keratitis, equine serum and N-acetylcysteine decreased total proteolytic activity by 90% and 99%, respectively [330], and *in vitro* collagenase activity on corneal tissue samples was decreased by approximately 50% [14]. EDTA and doxycycline decreased total *in vitro* proteolytic activity by 99% and 96%, respectively [330].

Serum and other antiproteases have been successfully used in the treatment of severe dry eye, persistent epithelial defects, and other severe ocular surface disorders (see Table 7.5) [1, 95, 330, 331, 336, 341–344]. It is proposed that growth factors, fibronectin, and vitamins in serum support the proliferation of corneal epithelial cells [344]. Serum rather than fresh frozen plasma (FFP) was significantly superior in stimulating cell growth, migration, and differentiation. The superior epitheliotropic capacity of serum might be due to the higher concentration of proliferation mediators such as EGF and PDGF and its higher content of vitamin A [344]. A long clotting time (>/= 120 minutes), a sharp centrifugation (3000 xg for 15 minutes), and dilution

with BSS improve the ability of serum eyedrops to support proliferation, migration, and differentiation of corneal epithelial cells [342]. Serum eyedrops may be produced as an unpreserved blood preparation. They are by nature nonallergenic and their biomechanical and biochemical properties are similar to normal tears [343]. Topically administered autogenous serum should be used in equine ulcers with evidence of collagenolysis, infection, or chronicity [95, 294, 330, 331, 335, 336]. Serum can be administered topically as frequent pulse medication or by continuous infusion, and should be administered at room temperature. It can be stored frozen or in a refridgerator [262, 336, 345, 346], and has an anticipated shelf life of 8 days. Contamination of the serum is unlikely, but the serum should be closely monitored for changes in turbidity. Mixing serum with other pharmaceuticals such as antibiotics reduces its antiprotease effects [316].

There is evidence that EDTA and serum have a synergistic antiprotease action, and can be advantageously used in combination in instances of severe keratomalacia or melting [95, 330, 331, 334, 336, 345, 346]. Caution is advised in using acetylcysteine, as its mucinolytic action will disrupt and destabilize the tear film. It should be noted that any cornea treated with acetylcysteine will inevitably become rose bengal positive. Topical and/or oral doxycycline can also reduce tear film protease activity in equine corneal ulcers [328, 336].

Antiprotease therapy should be administered until stromal liquefaction and ulcer progression ceases and early evidence of healing is present [82, 95, 330, 331, 334, 336, 345]. Since MMPs are fundamental to epithelial and stromal repair and regenerative processes, their use should be restricted or curtailed once restorative healing is underway. An exception to this is serum.

A new method of accelerating healing of corneal ulcers is corneal collagen cross-linking (CXL). CXL is induced by illumination of the corneal stroma with ultraviolet light (UVA) after instillation of riboflavin (vitamin B2) eyedrops. This is hypothesized to induce changes in the collagen which stabilizes stromal breakdown, and has been used successfully to treat infectious ulcerative keratitis in horses [347].

When to discontinue medical therapy of a corneal ulcer All topically applied medications are likely to impede corneal repair to some extent, and therapy of a corneal ulcer in a horse can be reduced in stages. The frequency of topically administered antibiotics can be reduced once fluorescein dye retention is absent, indicating epithelialization of the ulcer. Topically administered antiproteases, with the exception of serum, can be reduced in frequency when there is evidence of reduction in extent of the ulcerated area, and discontinued once fluorescein dye retention is absent. Serum can be discontinued completely when the clinician is confident that the PTF over any corneal scar is stable. Topically administered mydriatic/cycloplegics such as atropine can be reduced in frequency when uveitis is controlled, indicated by spontaneous pupil dilation and absence of aqueous flare. Systemically administered NSAIDs may be reduced as the ulcer heals and according to the amount of ocular pain present.

Inappropriate therapy for ocular surface failure associated with infection Corticosteroid therapy by all routes is contraindicated in the treatment of active corneal infections in the horse. Topical corticosteroids may have the potential to cause abscessation where viable bacteria or fungi are trapped in the stroma as the corneal epithelium migrates into the ulcer. Topical corticosteroids should also be avoided if the tear film remains unstable over the roughened surface of a corneal scar [82, 294].

Topical corticosteroid use in the later stages of healing to reduce the size of a post-ulcer corneal scar or speed withdrawal of blood vessels should be used with circumspection, particularly in regions where keratomycosis is a significant problem.

Surgical treatment If medical therapy is delayed or ineffective, surgical therapy may be used to provide an immediate vascular supply, with the intent of provision of fibroblasts, growth factors, and protease inhibitors, and, in some cases, structural support. Indications for surgery include ulcers with greater than 50% loss of depth of corneal thickness, ulcers with less than 50% loss of corneal thickness but worsening despite appropriate therapy, descemetoceles, and perforated ulcers [82, 291, 294, 307]. In addition to overt appearance of the ulcer, the severity of anterior uveitis present is a guide to the degree of control of the ulcerative process; for example, a relatively superficial bacterial ulcer associated with moderate to severe uveitis suggests worsening or lack of control.

Surgical procedures include conjunctival grafts (pedicle, bipedicle, hood, bridge, free island, tarsopalpebral, 360-degree), lamellar corneal grafts (corneoconjunctival transposition, corneoscleral transposition), and grafts with natural (autologous cornea, amnion) or synthetic/biosynthetic (biosist, A-cell) tissues. Details of surgical procedures are described in the sections **Surgical treatment**. Following surgical intervention, medical therapy should continue as before, unless a change in antimicrobial selection is indicated.

Prognosis

The prognosis for retaining a visual, comfortable globe in horses with bacterial keratitis depends upon rapid control of infection and corneal digestion, as well as coinciding anterior uveitis. If the infection and stromal breakdown can be halted, the ocular surface then undergoes a process of repair and restoration, which includes vascularization, GAG synthesis, collagen synthesis and realignment (i.e., scar formation), and re-epithelialization [83]. A positive visual outcome resulted in 8/11 eyes with β-hemolytic *Streptococcus equi* infection following combination medical and surgical therapy [305]. Of 33 eyes infected with nutritionally variant *Streptococci* spp., 22 healed with vision and one healed without vision following medical therapy, and three healed with vision following surgical therapy [295]. Of 70 eyes with *Pseudomonas* spp. infected ulcers, 53/70 (76%) retained vision with medical and/or surgical therapy, and the remaining were blind or enucleated [309].

Surgical intervention, in particular conjunctival grafts, can be anticipated to result in more extensive corneal scarring than where medical therapy alone resolves the ulcer.

Table 7.10 Potentially pathogenic fungal organisms isolated from horses with ulcerative keratitis.

Organism	Number of isolates 2000–2009	References 2000–2009	Number of isolates 1990–1999	References 1990–1999	Number of isolates prior to 1990	References prior to 1990
Alternaria			1	291	5	349, 357
Aspergillus	72	123, 305, 348, 376, 377, 391, 418, 550	65	291, 350, 359–364	22	109, 349, 354–356
Candida	8	550	10	291, 359, 361, 363, 365	1	357
Cephalosporium					1	348
Chrysosporium	1	391	1	350		
Cladorrhinum			1	367		
Cladosporium			1	361		
Cryptococcus					2	349
Curunlara			1	350		
Curvularia	2	305, 391	1	360		
Cylindrocarpon			6	360, 362, 366		
Cystodendron			1	360		
Drechslera					1	349
Fusarium	15	348, 391, 418, 550	23	291, 359–363	8	109, 349, 352, 353, 355, 357
Geotrichum			1	291	1	356
Hanseniaspora			1	361		
Histoplasma	1	369				
Microsporum	3	348, 550				
Mucor	2	550	5	361, 363	5	349, 354, 357
Paecilomyces	2	368			2	349
Penicillium	2	348, 391	6	291, 360–362	6	109, 349, 357
Pichia	1	550				
Pseudallescheria	1	550	1	361	1	358
Rhizoctonia					1	349
Rhizopus					1	109
Rhodotorula					1	349
Saccharomyces					1	349
Scedosporium	1	550	2	359		
Scopulariopsis	1	391	1	291		
Scytalidium			1	362		
Stemphylium	1	550	1	359		
Torulopsis			2	361, 362		
Trichoderma					1	349
Trichophyton			1	350		
Trichosporon	1	550	2	359, 363	1	109
Verticillium	1	550				
Unidentified yeast	3	348, 550	4	360, 362		

FUNGAL CORNEAL ULCERATION: the biological continuum of equine ulcerative keratomycosis

Several forms of keratomycosis are frequently reported in horses, particularly in warm months and in geographic areas with warm, humid climates (see online Figures 7.99–7.151, 7.171, 7.172, 7.173, 7.174, and 175) [82, 120, 122, 348–350]. A fungus defines any member of the broad group of eukaryotic organisms which includes mushrooms, molds, and yeasts. They are heterotrophic organisms that are typically filamentous and multicellular, and are characterized by the absence of chlorophyll [82, 351]. Fungal filaments are also called hyphae, and can be interrupted or divided by cross-walls or septa [351]. Several fungi, including yeasts, have been implicated as keratopathogens (Table 7.10) [289–291, 350–369], including septate filamentous fungi commonly found in microbial flora of the normal equine ocular surface (e.g., *Fusarium*, *Aspergillus*, *Penicillium* spp.) [71, 82, 185]. Individual hypha have a surrounding, definitive cell wall made up of chitins, glucans, and mannans [351]. Chitin, which is a structural polysaccharide, is a cell wall component of fungal hyphae that is absent in vertebrate systems. The plasma membrane of fungal hyphae, interior to the cell wall, contains ergosterol, which is a cell membrane sterol frequently targeted by antifungal agents [81].

Fungal organisms are ubiquitous in the equine environment, and are considered normal inhabitants of the equine ocular surface microflora, although many have a significant keratopathogenic potential [64, 65, 67, 68, 72, 82, 185, 293, 360, 370, 371]. In the semitropical environment of Florida, the conjunctiva in 95% of normal horses was found to have a fungal flora that included *Aspergillus*, *Penicillium*, *Alternaria*, and *Cladosporium* spp., or some combination of the four [71]. Geographic environmental differences undoubtedly exist to account for variation among particular fungal species and their pathologic capability (see Table 7.3) [103, 120, 371, 372].

Aspergillus and *Fusarium* are common causes of very destructive fungal infections in the horse in the USA [66, 82, 289, 292]. *Aspergillus flavus*, *Aspergillus niger*, *Fusarium solani*, *and Mortierella wolfii* were found in horses with keratomycosis in Japan [289]. *Aspergillus* was also reported in horses with keratomycosis in Switzerland [73].

Pathogenesis

Pathogenesis commonly begins with ocular surface disruption and tear film instability, leading to an epithelial defect and stromal invasion by the commensal fungal organism [120, 121, 294, 349]. Seeding of fungi from a foreign body of plant origin may also occur [185, 293]. Potentially keratopathogenic fungi in horses appear to be able to adhere to healthy corneal epithelial cells in the presence of an unstable PCTF [123]. In the case of highly pathogenic fungi, stromal penetration and vertical posterior movement results from the release of proteases and other enzymes from the fungi, chemoattracted leucocytes, and reactive keratocytes [14, 138, 188, 331, 373]. Fungi of low pathogenicity adhere poorly, attract only limited numbers of PMNs, resulting in lower local concentrations of proteases, and move laterally or horizontally in the corneal stroma [374]. The conidia (asexual spores) of *Aspergillus* spp. are smaller than those of *Fusarium* spp. and can penetrate deeper into the cornea [373]. Some fungi, such as *Fusarium* spp., form biofilms, making them particularly difficult to kill and eliminate [373].

The more pathogenic fungi infecting the horse cornea appear to have specific affinity for the posterior stroma and Descemet's membrane, with hyphae frequently being found associated with PMN infiltration deep in the equine cornea [14, 138, 185, 294]. This deep corneal invasion to the level of Descemet's membrane can progress further and lead to liberation of fungi into the anterior chamber, iris, and lens, in some cases causing aggressive endophthalmitis [14, 103, 104, 137, 185, 294, 366, 370].

Most reports have indicated an increased incidence of ulcerative and nonulcerative fungal keratitis in the summer and fall months [82, 349, 350], although other reports contradict this [67, 371, 372]. Any seasonality may result from temperature and humidity factors favoring fungal replication, or it may simply reflect an increase in the amount of time that horses spend indoors [66]. In the southern USA, ulcerative keratomycosis occurs throughout the year, with most cases occurring in the late fall to winter months (i.e., October through January) [360].

Use of topical corticosteroids has been implicated in enhancing fungal replication as well as in predisposing the cornea to fungal infection and decreasing the efficacy of antifungal agents [66, 375]. One report stated that 10 (62.5%) of 16 horses with ulcerative keratomycosis had been previously treated with topical or subconjunctival corticosteroids [289]. In another study, only 6 (15.4%) of 39 horses had been previously treated with topical corticosteroids [360], but topical antibiotics had been used in 32 (82.1%) of these 39 horses before referral and diagnosis [360]. These results suggest that previous treatment with topical antibiotics may have as great an influence as previous topical corticosteroid treatment on the occurrence of equine ulcerative keratomycosis [294, 360]. Topical antibiotic therapy will suppress susceptible saprophytic and commensal bacterial microbiota, altering the overall population balance [82], and potentially creating a microenvironment favorable for fungal replication. A prospective study comparing ocular microflora populations in normal horses following experimental administration of antibiotic and antibiotic–corticosteroid combination medications identified no treatment effect, but did document an initial decrease in positive fungal cultures in both treated and untreated control eyes [68], suggesting that factors in addition to topical medications are involved in establishment of fungal infection.

It has been hypothesized that corneal trauma was necessary for fungal invasion and infection of the horse cornea. However, clinical observation indicates that some fungi can induce primary disease of the tear film and cornea in horses in the absence of predisposing corneal injury [122, 123]. A further reason why the incidence of keratomycosis in the horse exceeds that in the dog, cat, and cow may be that the PRR/TLR phenotype-determined innate proinflammatory immunoresponsiveness to fungal challenge on the ocular surface of susceptible horses is of a magnitude to readily overwhelm the local control mechanisms, resulting in an accelerating cycle of rapid stromal lysis, fungal penetration, and neutrophil recruitment. Horses may also be inherently predisposed to keratomycosis due to local downregulation of the angiogenic response to fungal exposure, determined by factors specific to the pathogen, to the host, or to both.

Variant forms of equine keratomycosis

Fungal-induced precorneal tear film instability

Fungal-induced "PCTF instability" can be a precursor to ulcerative keratomycosis, and may be the earliest form of equine keratomycosis. The cause is not known at this time, although environmental irritants, such as wind, causing increased PTF evaporation and disruption, may play a role in the pathogenesis and persistence of fungal-induced PTF instability (Figures 7.73 and 7.74 and online Figure 7.79) [82, 123, 371]. Fungal-induced PCTF instability appears to represent a qualitative form of tear-deficiency keratitis. The corneal surface appears dry and roughened from compromised adherence of the tear film to corneal epithelial cells, although the quantitative PTF, measured by STT, is normal. These eyes are mildly uncomfortable, diffusely or focally rose bengal positive, and fluorescein negative in the early stages. Slit-lamp biomicroscopy reveals generalized or multifocal whitish epithelial and subepithelial opacities. Examination of histologic and cytologic specimens from these lesions found fungal hyphae in the PTF and hyphae attached to the epithelium. With time, weak focal fluorescein staining may accompany the rose bengal staining. Small foci of fluorescein retention in fungal-induced PCTF instability are microerosions, indicating

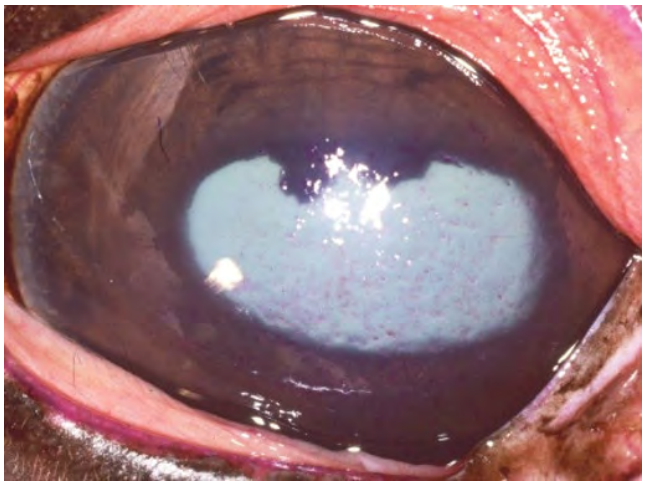


Figure 7.73 *Aspergillus* is associated with this rose-bengal-positive, fluorescein-negative keratopathy interpreted to be the PTF form of keratomycosis. This condition eventually develops to a melting ulcer (see Figure 7.74).

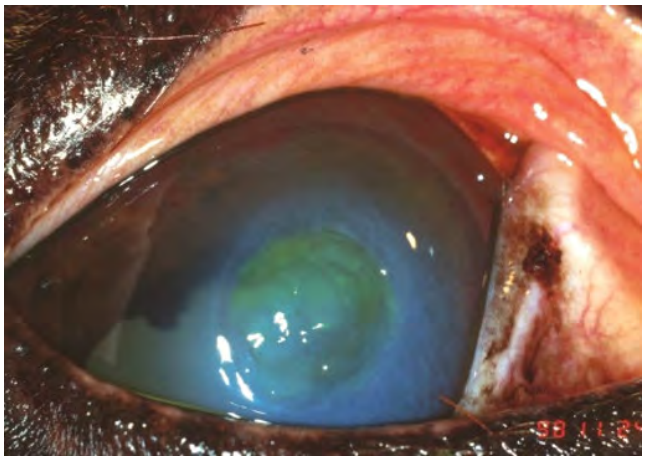


Figure 7.74 The keratopathy in Figure 7.73 subsequently progresses to the more typically recognized ulcerative form of keratomycosis.

partial loss of epithelial cell layering. Rose bengal staining indicates tear film instability and superficial epithelial cell devitalization or depolarization [82, 123]. Treatment is topical serum and antifungals, and fly masks are used to mitigate environmental effects on the PTF. Affected eyes can subsequently develop overt ulcerative keratomycosis.

Epithelial nonulcerative keratomycosis

Epithelial nonulcerative keratomycosis is now recognized as a form of equine keratomycosis. The fungi are diffusely located over the entire cornea in the superficial layers of the corneal epithelium. There is mild ocular pain, extremely subtle corneal haze, and the cornea is gritty to the touch. Very faint fluorescein retention is indicative of corneal abrasion (Figures 7.75 and 7.76 and online Figures 7.100, 7.101, 7.102, 7.103, and 7.104). There may also be very slight to negative rose bengal staining. Slit-lamp

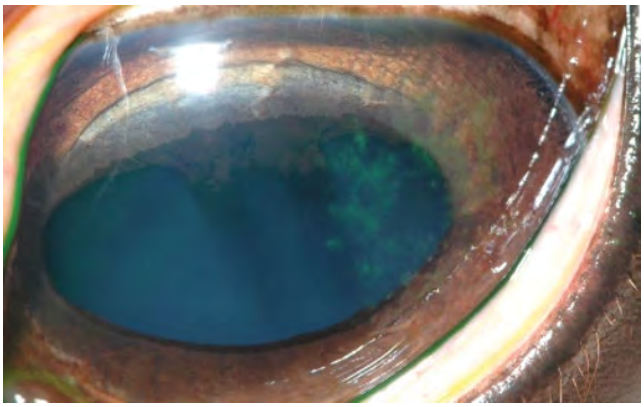


Figure 7.75 The corneal abrasions found in this horse eye were caused by *Aspergillus*. Pain was slight and there was no detectable anterior uveitis. Slit-lamp examination found epithelial opacity only.

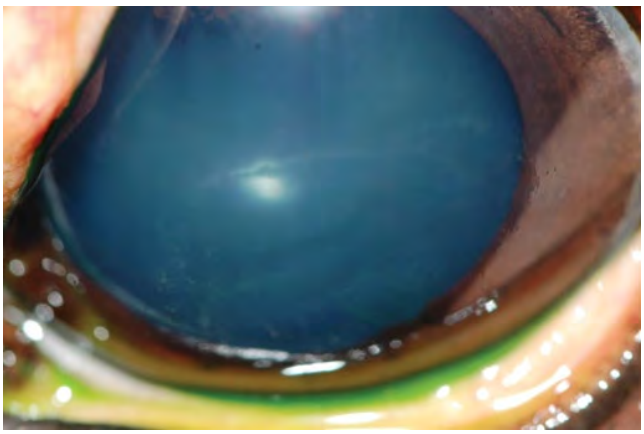


Figure 7.76 Slight fluorescein retention is found in an eye with the epithelial form of keratomycosis.

biomicroscopy reveals focal or generalized epithelial opacities. Hyphae are identified on cytology and culture, and the condition is in general responsive to topical imidazoles. The clinical appearance of this form of superficial keratomycosis may not be specific, and can mimic some forms of IMMK.

Subepithelial keratomycosis

Subepithelial keratomycosis represents another type of early-stage equine keratomycosis, and is difficult to recognize without slit-lamp biomicroscopy [121, 122]. The corneal lesions are present as either punctate (Figure 7.77) or diffuse (Figure 7.78 and online Figures 7.105 and 7.106) subepithelial opacities. The opacities are weakly fluorescein positive in some cases, suggesting epithelial cell involvement. A few cases are rose bengal positive. The subepithelial form of keratomycosis may be a sequela of epithelial nonulcerative keratomycosis. Other differential diagnoses for subepithelial keratomycosis are IMMK, "viral" keratitis, KCS, anterior stromal haze associated with primary epithelial disease, and subepithelial corneal fibrosis, specifically that following healing of a corneal ulcer.



Figure 7.77 No fluorescein or rose bengal dye retention is present in the central area of this horse's eye with subepithelial keratomycosis.



Figure 7.78 Subepithelial keratomycosis is manifest as subepithelial opacity (**arrow**) with the slit-lamp. This slit-lamp appearance is also present with a healed corneal scar and superficial IMMK.

Ulcerative keratomycosis

Superficial corneal ulcers, mid-stromal ulcers, and deep melting ulcers are the classic and most common forms of ulcerative keratomycosis (see figures in section **Surgical treatment**). These comprise between 50% and 80% of keratomycosis cases in various retrospective studies [82, 113]. Fungal-induced PCTF instability, epithelial nonulcerative keratomycosis, and subepithelial keratomycosis in the horse may represent preliminary phases of a continuum of clinical conditions that ultimately progress to ulcerative keratomycosis. The depth of the ulcerative changes in any one case is likely to reflect both the keratopathogenicity of the fungus involved and the intensity of the host response to infection [374].



Figure 7.79 The dry appearance to this superficial corneal ulcer is associated with PTF disruption from keratomycosis. This may be the earliest form of keratomycosis and preceeds ulceration.

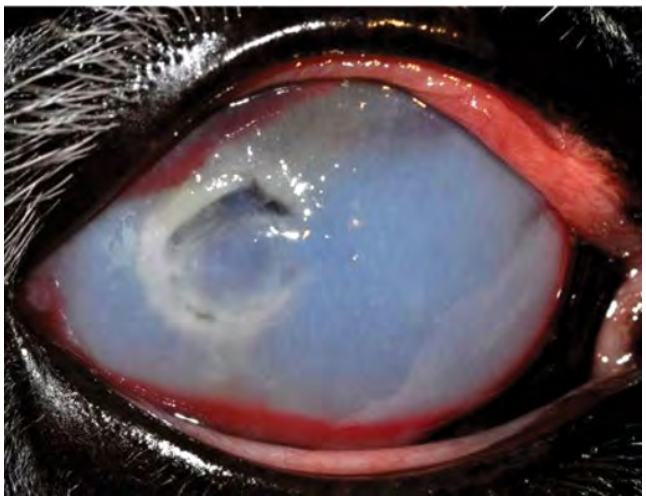


Figure 7.80 A deep stromal groove is forming dorsally in this large-diameter ulcer with an encircling cellular infiltrate. The ulcer perforated and was enucleated.

Ulcerative keratitis refers to the disruption and loss of the corneal epithelium with varying amounts of stromal loss, and may have concurrent bacterial or fungal infection (or both) (Figure 7.79). Ulcerative keratomycosis presents in two recognizable forms: either as an area of relatively superficial ulceration and infiltration surrounded by a curvilinear region of stromal loss, known as a groove or furrow (Figure 7.80 and online Figures 7.107, 7.159, 7.160, 7.161, 7.162, 7.176, 7.177, 7.178, and 7.179), or as overt deep ulceration (i.e., melting ulcer, descemetocele, or perforated ulcer), with or without iris prolapse [82, 359, 376]. The groove can develop at any point in the disease process, but typically occurs rapidly (i.e., over 24–48 hours), and generally does not extend around the entire circumference of the infiltrated area. Groove formation appears to be a mechanism by which the horse's innate defense mechanisms attempt to slough or

eliminate infected and degenerate stromal tissue. Severe keratomalacia, descemetocele formation, or corneal perforation may follow groove formation, or these may occur without obvious groove or furrow formation [82, 359, 376, 377]. Due to the intensity of the inflammatory reaction occurring in ulcerative keratomycosis in the horse, ocular pain and anterior uveitis are typically very pronounced.

Ulcerative keratomycosis is a serious, sight-threatening disease in the horse, and the veterinary literature is replete with cases of poor visual outcome in the various types of equine keratomycosis [82, 185, 293]. Clinical signs associated with it include fluorescein dye retention, keratomalacia, miosis, hypopyon, anterior chamber fibrin formation, blepharospasm, epiphora, and photophobia [82]. Corneal vascularization from the limbus occurs at several levels, determined by the depth of the stromal pathology, and may be very pronounced. However, many pathogenic fungi release antiangiogenic factors (e.g., PEDF), during replication and growth, and vascular ingress may be halted several millimeters distant from the periphery of the lesion. A high diagnostic suspicion of keratomycosis is associated with halting of vascular ingress distant from the lesion. Definitive diagnosis of ulcerative keratomycosis is made on the basis of finding fungal hyphae, molds, or yeasts during cytologic or PCR examination of a corneal scraping, culture of the corneal lesion, and/or histologic examination of a surgical keratectomy specimen [82].

Combined medical and surgical therapy is indicated if fungal ulcers are extremely deep, are not responding to medical treatment, or worsen despite medical treatment. Early surgical intervention can markedly improve outcome. Surgeries for keratomycosis include conjunctival pedicle grafts, bridge grafts, hood grafts and island grafts, AMTs, and full-thickness penetrating or lamellar keratoplasty (LK) (Figures 7.97, 7.101, 7.104, 7.109 and online Figures 7.180–7.219, 7.242–7.348, 7.152, 7.153, 7.154, 7.155, 7.163–7.170) [82, 185, 293, 294].

Aggressive medical and surgical therapy for ulcerative keratomycosis in horses should result in a positive visual outcome and ocular survival in more than 90% of eyes [82, 360]. Despite this, ulcerative keratomycosis therapy in the horse is typically prolonged, and end-stage scarring of the cornea may be prominent.

Thick pigmented fungal plaques

Some horse eyes with keratomycosis develop thick (over 1-mm), brown pigmented plaques on the corneal surface (Figures 7.81 and 7.82). Suppurative keratitis is found beneath the plaques. The plaques are generally surrounded by intense corneal vascularization. Surgical removal of the plaque by keratectomy is necessary to speed healing. The tear film is generally unstable near the plaques [82, 294, 378].

Superficial fungal stromal abscesses

Superficial SA may be caused initially by superficial corneal ulcers (Figures 7.83, 7.84, 7.85, and 7.86). The ulcers then rapidly heal, resulting in intact epithelium covering infected stroma, forming a superficial SA. Both bacteria and fungi may be involved. Most



Figure 7.81 A brown fungal plaque is present with a yellow cellular infiltrate beneath the plaque and red vascularization at the edge of the plaque.

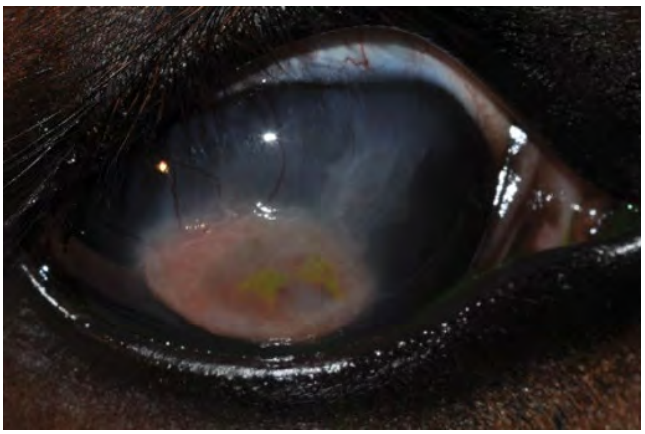


Figure 7.82 Thirteen days later, the plaque in Figure 7.81 is absent, with granulation tissue present at the previous location of the fungal plaque. Two areas of fluorescein dye retention are still present.



Figure 7.83 A superficial SA is forming a white fungal plaque with a groove. Edema and anterior uveitis are present. Limbal vessels are approaching the lateral edge of the groove.

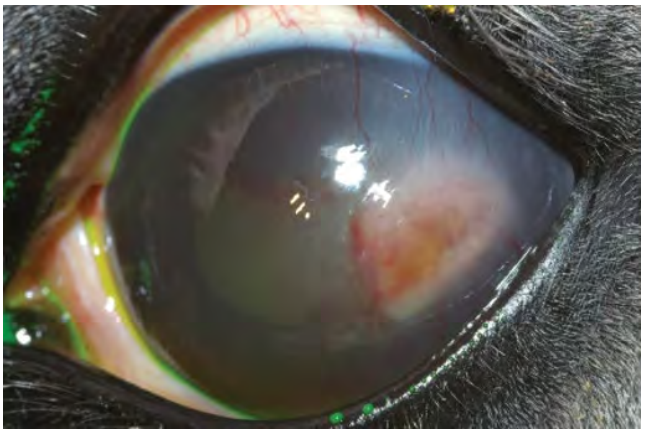


Figure 7.84 Three weeks later, the plaque in Figure 7.83 has sloughed and the lesion site vascularized. The pupil is only mid-dilated from topical atropine, suggesting some degree of anterior uveitis is still present.

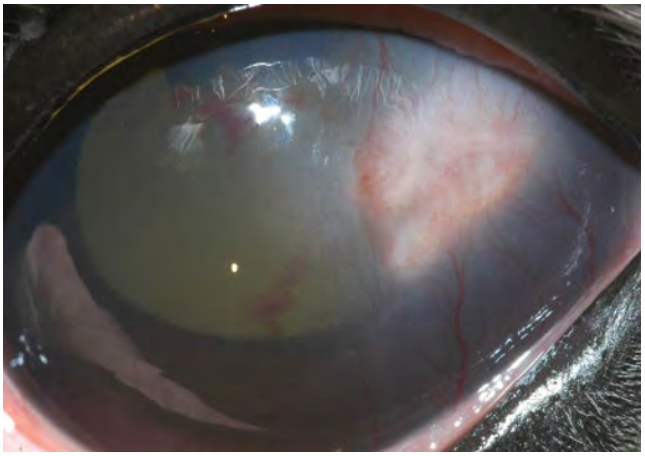


Figure 7.85 Four weeks since medical therapy was initiated, the eye in Figures 7.83 and 7.84 has more remodeling of the lesion site, with some stromal hemorrhages present from regressing blood vessels.

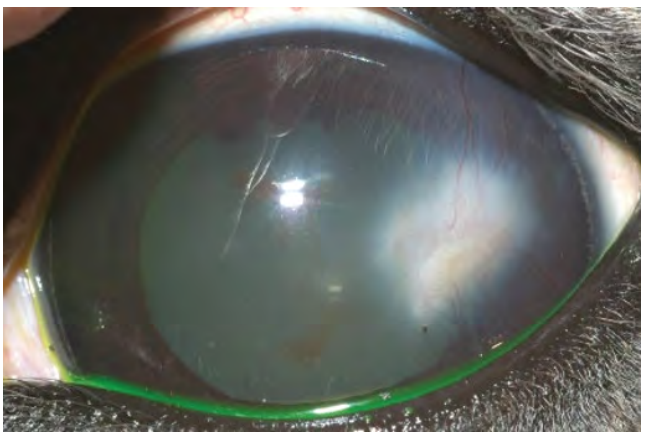


Figure 7.86 Seven weeks since medical therapy was initiated, the eye in Figures 7.83, 7.84, 7.85 has complete resolution of the fungal plaque, leaving a small anterior stromal scar.

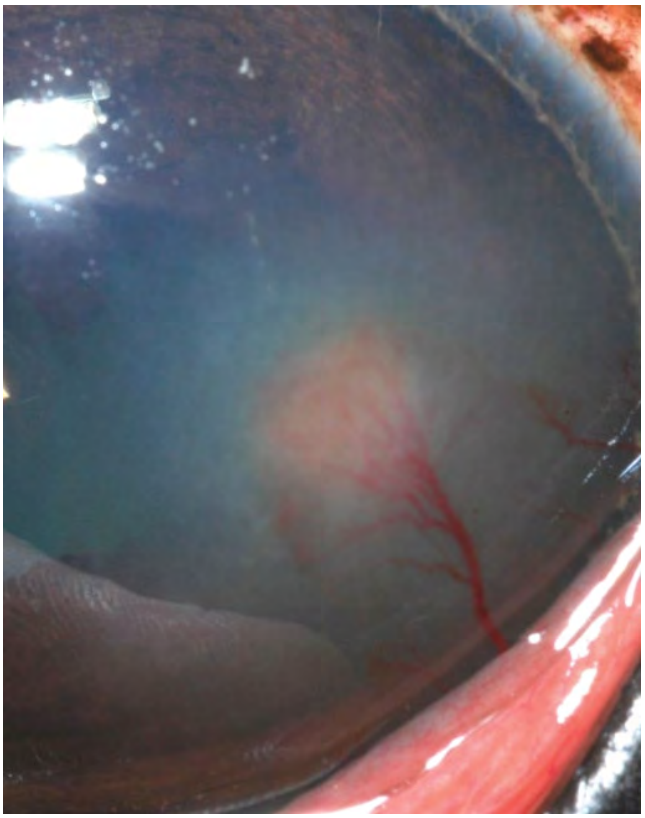


Figure 7.87 A deep stromal abscess (DSA) is obscured by a tuft of stromal vessels located anterior to the abscess.

superficial SA respond to aggressive topical medical therapy with antibiotics and antifungals [294].

Full-thickness fungal stromal abscesses

Fungal SA may be superficial initially and then move vertically. All layers of the cornea can be affected. Iridocyclitis is generally very intense with full-thickness fungal SA. PK is necessary for successful resolution in many cases [294].

Deep fungal stromal abscesses

An SA can result from stromal inoculation of fungi through a small corneal epithelial cell defect (Figures 7.87, 7.88, 7.89, 7.90, and 7.91) [294]. It may also arise hematogenously from the iris vasculature, with extravasated hyphae attaching to the corneal endothelium and lens capsule [379]. Fungi become encapsulated in the deep corneal stroma after penetration from the anterior chamber or following re-epithelialization of a corneal ulcer over the inoculation site. Yellow-white opacities at the level of the posterior stroma, Descemet's membrane, and endothelium are present, with the possibility of rupture of the abscess into the anterior chamber. Corneal edema is present and vascularization of the stroma anterior to the abscess occurs in many cases. Vascularization may be asymmetrical and fail to reach the abscess site at sectors on the abscess periphery. The majority of DSA are due to fungi [294]. Anterior uveitis can be intense, and untreated DSA is a

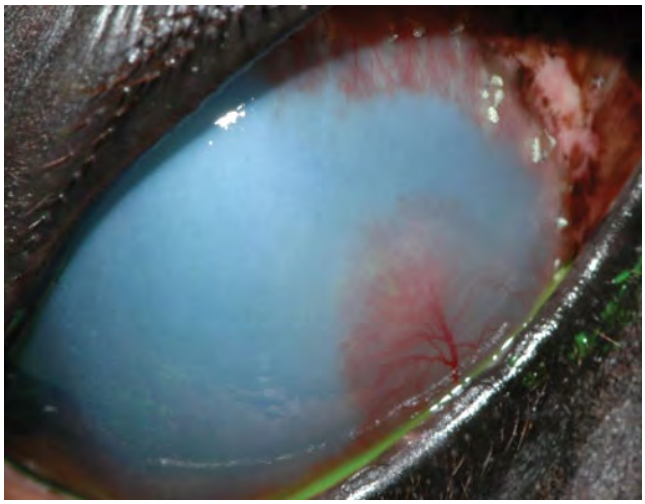


Figure 7.88 Twelve days post DLEK surgery, the eye in Figure 7.87 has generalized edema, vessels passed the incision, and some donor graft opacification.

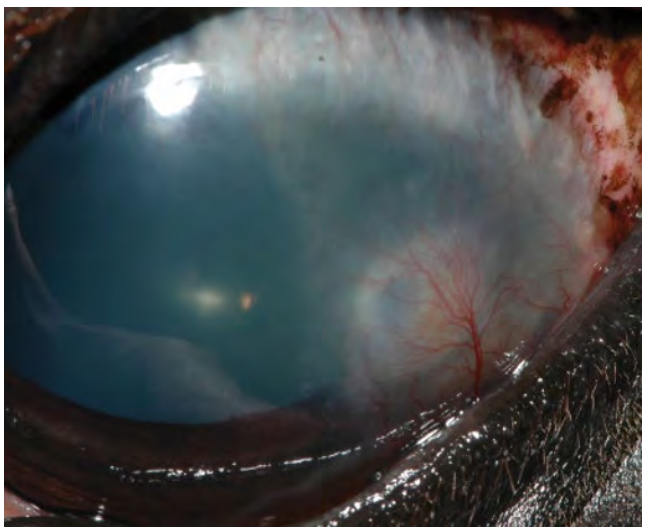


Figure 7.89 One month post DLEK surgery, the eye in Figures 7.87 and 7.88 has dramatic corneal clearing, with no evidence of uveitis, opacification of the donor graft, and linear opacities at the limbus from the sutures.

sight-threatening disease. LK and aggressive medical therapy are the preferred treatment for most DSA.

Iris prolapse

Iris prolapse is defined as corneal, limbal, or scleral perforation (or some combination of the three), with iris protrusion through the wound after trauma or deep ulceration. The iris moves anteriorly to seal the damaged cornea. Iris prolapse may be associated with destructive keratomycosis. Surgical repair with PK and intensive medical therapy are the standard of care in these cases where the eye is to be saved, with approximately 68% of treated cases visual post treatment [146, 147].



Figure 7.90 Two years post-operatively, the eye in Figures 7.87, 7.88, 7.89 has an endothelial scar at the DLEK site.

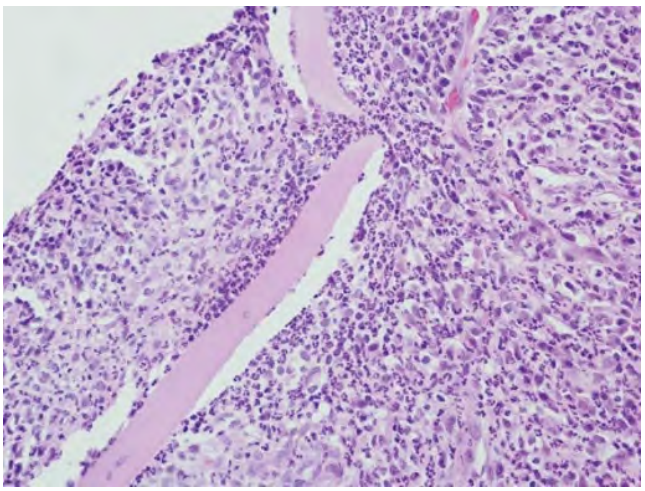


Figure 7.91 Histologic section of a DSA, with tremendous numbers of neutrophils on both sides of a rupture in Descemet's membrane.

Lens and fungi

Descemet's membrane and the lens capsule are both type IV collagen. Fungi can be associated with iris abscesses and lens capsule colonization in the horse. A persistent and typically severe uveitis is present, but the condition is difficult to successfully treat if the lens is involved [379]. *Fusarium* spp. and *Cladosporium* spp. have been cultured from eyes with lens capsule invasion [379]. The success rate for therapy of intraocular keratomycosis with lens invasion is low [379].

Equine keratomycosis: diagnostic techniques and therapy

Diagnosis

Equine keratomycosis is represented clinically and pathologically as a continuum of clinical lesions and presentations. One form of keratomycosis may proceed to the next or even revert to the previous clinical form. There appear to be several clinical

variations of keratomycosis in the horse, as described in the section **Ulcerative keratomycosis**.

Clinical suspicion for fungal involvement and response to antifungal therapy can also aid in making the diagnosis. In one report, cytology (86.1% positive) and culture (84.6% positive) were effective means of making the diagnosis of keratomycosis [360]. Because of the propensity for deep invasion by fungal organisms, however, false negative cytologic or culture results may be obtained from superficial cytology specimens, and it is imperative that samples are taken from the base and posterior wall of deep ulcerative lesions [294]. Histopathologic examination of keratectomy specimens can also be highly effective for obtaining evidence of fungi, but these specimens must be obtained after keratectomy and, thus, are less frequently available for diagnostic purposes [82, 360]. Nested polymerase chain reaction (PCR) results confirmed all cytologically positive cases of fungal keratitis in one study. Nested PCR identified a greater spectrum of organisms than either culture or qualitative PCR [380], leading to difficulty in differentiation of commensal or nonpathogenic from pathogenic fungi in any one sample, or where multiple identifications are made [381, 382]. Quantitative PCR may overcome this to some extent, if available.

In vivo corneal confocal microscopy is a rapid and noninvasive method of diagnosing fungal keratitis in the horse. This imaging technique is useful for both ulcerative and nonulcerative fungal keratitis, and is particularly advantageous for confirming the presence of fungi in deep stromal lesions [150, 383]. Linear, branching, hyper-reflective structures that were 2–6 μm in width and 200 to > 400 μm in length were detected in all horses with filamentous fungal keratitis (Figure 7.92). Round to oval hyper-reflective structures that were 2–8 μm in diameter were detected in a horse with yeast keratitis [383].

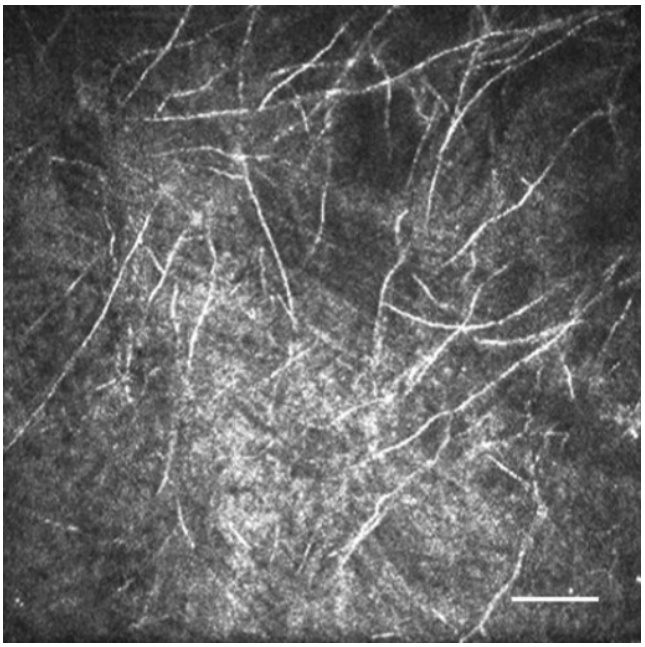


Figure 7.92 Confocal microscopy reveals linear hyphae in a horse with keratomycosis. (Bar =50 μm.) (*Source*: Image courtesy of Dr Eric Ledbetter.)

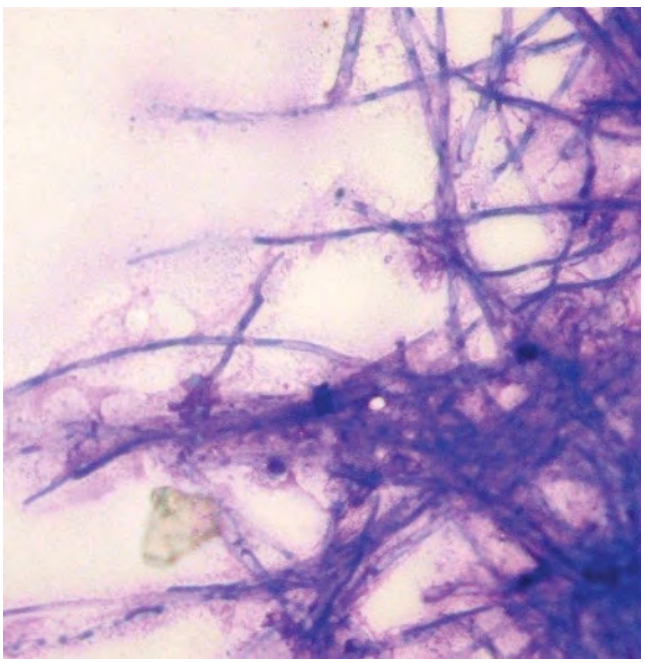


Figure 7.93 Cytologic sample from the cornea of a horse with keratomycosis. Parallel cell walls are faintly visible demarcating the edge of individual hyphae (Diff-Quik stain).

Differential diagnosis

Differential diagnoses for ulcerative fungal keratitis include other infiltrative ulcerative diseases (bacterial keratitis, eosinophilic keratoconjunctivitis, IMMK, herpesvirus keratitis), trauma, corneal degeneration, calcific band keratopathy, and corneal neoplasia. The high degree of variability among clinical presentations mandates a high index of suspicion for fungal keratitis in predisposed geographic regions. In addition, mixed bacterial and fungal infections may be present in as many as 20–33% of cases [348, 360, 361]. Initial diagnosis is by corneal cytology (Figure 7.93) and bacterial and fungal cultures, with histopathology and molecular-based techniques (PCR) providing additional confirmation. A study of 48 animals with corneal ulcers receiving cytology and bacterial and fungal cultures identified infection in 35 eyes using cytology, cultures, or both, versus 26 and 29 eyes by cytology or culture alone, respectively [312]. Of 10 eyes with keratomycosis, infection was diagnosed by cytology in 4/9 eyes and by culture in 8/10 [348]. Histopathologic evaluation of specimens collected at the time of surgical therapy for fungal keratitis may identify fungal hyphae (Figure 7.94) [360], but speciation is not possible by this method alone.

Treatment

Medical treatment Treatment must be directed against both the fungi and the corneal and intraocular inflammatory responses occurring as a consequence after fungal replication and hyphal death (Tables 7.11–7.13) Clinical impressions are that it is not

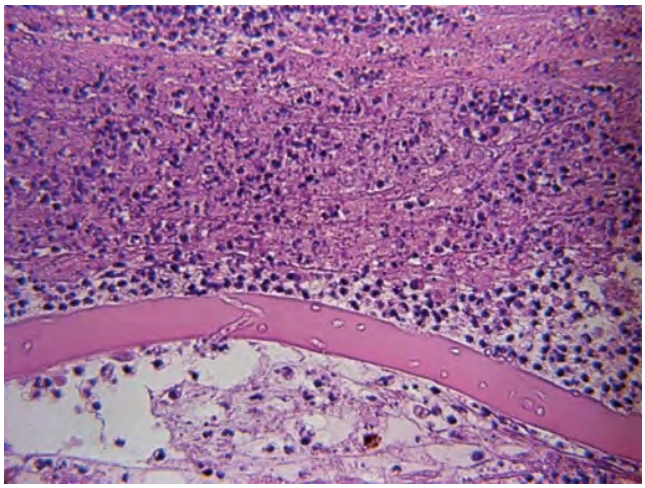


Figure 7.94 H&E-stained corneal surgical biopsy specimen, showing numerous fungal hyphae in corneal stroma and infiltrating Descemet's membrane.

particularly difficult to kill fungi, but that the dead hyphae are only slowly removed by the innate ocular defense mechanisms. This delay results in protracted inflammation and slow healing [82, 120, 185, 293, 294]. Dead hyphae attract leucocytes, primarily PMNs which are too small to phagocytize hyphae. Macrophages are capable of phagocytosing hyphae, but are present in insufficient numbers to effect rapid removal of the hyphae [103].

Fungicidal activity of most antifungal drugs is concentration dependent. However, the high fungicidal concentrations of these drugs in the horse cornea are difficult to reliably achieve in practice, and many agents, including miconazole, are generally considered to exhibit fungistatic activity only. Loss of corneal epithelium results in increased intracorneal and aqueous drug penetration, and will increase their fungicidal potential [82, 120, 185, 293, 294]. Long duration of antifungal drug exposure has been recommended to achieve complete fungal destruction and resolution of clinical signs, but this has not been experimentally

Table 7.11 Systemically administered antifungal agents.

Class	Mechanism of action	Example(s)	Dosage	Notes
Azoles	Inhibit ergosterol synthesis; intracellular accumulation of toxic metabolites; cell membrane damage	Fluconazole	14 mg/kg PO once, then 5 mg/kg PO q24h	Good intraocular penetration, with or without inflammation; spectrum more limited than other azoles
		Itraconazole	1.5 mg/kg IV q24h 5 mg/kg PO q24h	Poor intraocular penetration; if PO administration, use IV solution, as capsules have highly variable absorption
		Voriconazole	3 mg/kg PO q12h	Good intraocular penetration, with or without inflammation; spectrum more limited than other azoles

Table 7.12 Topical ophthalmic antifungal agents.

Class	Mechanism of action	Example(s)	Formulation and storage	Frequency*	Notes
Polyenes	Cell membrane permeability and leakage; oxidative damage	Natamycin	5% suspension	q2–4h	Only commercially available ophthalmic antifungal; best for ulcerative disease
		Amphotericin B	0.075–0.20% solution in sterile water, dark bottle, refrigerate	q2–4h	Best for ulcerative disease; increased epithelial toxicity relative to natamycin
Triazoles	Inhibit ergosterol synthesis; intracellular accumulation of toxic metabolites; cell membrane damage	Fluconazole	0.2% solution	q2–4h	Poorer efficacy versus both yeast and filamentous agents than other azoles
		Itraconazole	1% in 30% DMSO	q2–4h	Good penetration through intact epithelium
		Voriconazole	1% solution in sterile water, refrigerate	q2–4h	Good penetration through intact epithelium
Imidazoles	Inhibit ergosterol synthesis; intracellular accumulation of toxic metabolites; cell membrane damage	Ketoconazole	1%	q2–4h	Best for ulcerative disease; poorer efficacy than other azoles
		Miconazole	1%	q2–4h	Good penetration through intact epithelium
Other	Metal ions bind microbial DNA and inhibit synthesis	Silver sulfadiazine	1% ointment	q12–24h	
	Germicide	Povidone iodine	2% solution	q24h	

* Suggested initial frequency, depending upon severity of infection and inflammatory response; may be decreased or increased as appropriate for individual case.

Table 7.13 Combination therapy for infectious ulcerative keratitis: fungal.

Drug class	Example(s)	Formulation	Dose/frequency	Notes
Topical antifungal	Natamycin 5%, voriconazole 1%, miconazole 1%, itraconazole 1%/DMSO 30%	Solution Suspension	0.1– 0.2 mL q2–4h	
Topical prophylactic or therapeutic antibiotic*	See Tables 7.5 and 7.8			
Topical therapeutic mydriatic/cycloplegic	Atropine	Ointment Solution	¼-inch strip q12–24h 0.1–0.2 mL q12–24h	Frequency depends on degree of mydriasis achieved between doses
Topical antiprotease	See Table 7.9			
Systemic antifungal	Fluconazole (F) Voriconazole (V)	Tablets Tablets Suspension Solution	14 mg/kg PO once, then 5 mg/kg PO q24h (F) 3 mg/kg PO q12h (V)	Good intraocular penetration but poor spectrum relative to other azoles (F); good intraocular penetration and good spectrum of activity (V)
Systemic NSAID	Flunixin meglumine	Paste Solution	1.1 mg/kg PO or IV q12h	
Systemic antibiotic	Trimethoprim sulfamethoxazole (T) Doxycycline (D) Potassium penicillin (P) Gentamicin (G)	Varies with drug	20–30 mg/kg PO q12h (T) 10–20 mg/kg PO q12h (D) 20,000 U/kg IV q6h (P) 4 – 6.6 mg/kg IM or IV q24h (G)	

* Prophylactic antibiotic therapy is indicated as for ulcerative keratitis, with therapeutic antibiotics administered if coinciding bacterial infection is suspected or confirmed.

verified [82, 120, 185, 293, 294]. Antifungal susceptibility testing on fungal isolates from horses is recommended, but it can take several weeks to obtain results, and it is not always consistent with clinical outcomes.

Three general classes of antifungals are currently available: polyenes, azoles, and nucleoside analogs. Polyenes (natamycin, amphotericin B) preferentially bind ergosterol, the cell membrane sterol unique to fungi, increasing cell membrane permeability [82, 384–386]. They are also able to bind cholesterol, the sterol present in all mammalian cell membranes, potentially creating their toxicity [82, 144, 448, 449]. Azoles (miconazole, ketoconazole, fluconazole, itraconazole, voriconazole) preferentially bind to a fungal-specific enzyme in the cytochrome P450 system, inhibiting ergosterol synthesis, increasing membrane permeability, and altering fungal cell enzyme systems [386]. The nucleoside analog flucytosine is enzymatically altered within the fungal cell to the cytotoxic principal fluorouracil [384].

Polyenes (natamycin and amphotericin B) are broad spectrum, with generally good efficacy against filamentous fungi and yeasts [384]. Natamycin (5%) is the only approved topical ophthalmic antifungal agent currently commercially available in the USA. It is generally believed that natamycin has only limited epithelial penetration [387], although one study has indicated that it may penetrate an intact corneal epithelium [388]. Natamycin is used topically in the horse [82, 293, 294], and is reported as being very effective against *Fusarium* spp., less so against *Aspergillus* spp., and least effective against yeasts [82, 185, 293, 294]. However, one study in the horse showed that in contrast to variable results against filamentous fungi, natamycin has consistently good *in vitro* efficacy against yeast isolates [389]. Natamycin is produced by the bacteria *Streptomyces natalensi*s, which is part of the normal corneal microflora of the horse and which may produce endogenous tear film levels of natamycin, possibly contributing to suppression of the commensal fungal populations on the ocular surface. A lack of efficacy of natamycin against *Aspergillus* spp. has been recorded in Florida, and natamycin is very irritating *in vitro* to healthy corneal cells [390]. *In vitro* analysis of efficacy of natamycin against isolates from equine keratomycosis reveals variable results relative to azoles [349, 362, 389] and to silver sulfadiazine [391]. However, the minimum inhibitory concentrations (MICs) of natamycin in combination with tobramycin, cefazolin, and equine serum against *Aspergillus* and *Fusarium* isolates *in vitro* were significantly lower than calculated MICs for natamycin alone [293]. In human keratomycosis, topical natamycin treatment was associated with significantly better clinical and microbiological outcomes than voriconazole, with much of the difference attributable to improved outcomes in *Fusarium* cases [392]. This study concluded that voriconazole should not be used as monotherapy in filamentous keratitis [392]. In human keratomycosis, decreased *in vitro* susceptibility to natamycin has been associated with increased infiltrate or scar size and an increased chance of perforation. There was no association between *in vitro* susceptibility to voriconazole and outcome [393].

Amphotericin B is often used topically in horses, despite poor epithelial penetration following topical administration, and at higher concentrations appearing potentially toxic to the corneal epithelium [394]. In the presence of a corneal ulcer, topical administration may result in therapeutic stromal levels, but the comparative safety and better spectrum [389] of natamycin make it a preferable drug. Subconjunctival administration of

amphotericin B, which may provide sustained high drug levels, may be performed in cases of refractory keratomycosis, but concern exists regarding potential for local toxic effects [386]. A treatment regimen of 0.2 mL of a 5 mg/mL solution administered subconjunctivally every 48 hours, generally for three doses, has been utilized on several horses, with overall favorable results. Systemic administration of amphotericin B for corneal disease is generally not recommended because of the high risk of systemic toxicity.

Azoles are available for topical, oral, and intravenous administration. Common agents include fluconazole, miconazole, itraconazole, and voriconazole [82, 289, 291, 395]. Miconazole, administered either topically or subconjunctivally (5–10 mg every 24–48 hours), has good to excellent intraocular penetration, as evaluated in other species [61, 384]. Miconazole (1%) has been used successfully and frequently as a topical antifungal agent in the horse, [82, 185, 293, 294] and is effective against *Aspergillus* spp. It is an imidazole antifungal drug with excellent corneal penetration, especially in those corneas with denuded epithelium [82, 185, 293, 294]. The 1% solution also does not retard corneal healing or cause pathologic changes during corneal epithelial regeneration [82, 185, 293, 294]. In Florida, microbial resistance to miconazole has been noted, with a reduction in efficacy against *Fusarium* spp [362]. The gynecologic cream preparation of miconazole is no longer recommended for topical use in the horse as it can be very irritating to the eye. Topical administration of 1% voriconazole solution is well tolerated and penetrates the cornea in normal eyes at therapeutic levels, and is effective against *Fusarium* spp. and *Aspergillus* spp [395]. Topically administered itraconazole 1% in 30% dimethyl sulfoxide (DMSO) has good intraocular penetration, as measured by corneal tissue levels in horses with normal corneas, and produced no signs of ocular irritation [362]. Systemic administration of imidazoles can aid treatment of keratomycosis. Oral and intravenous administration of a single 4 mg/kg dose of voriconazole resulted in detectable aqueous humor levels in the absence of intraocular inflammation [395], while repeated oral dosing of 3 mg/kg every 12 hours maintained potentially therapeutic plasma levels [396]. Itraconazole may also be administered orally or intravenously, but it was not detectable experimentally in the aqueous humor of uninflamed equine eyes [397]. Fluconazole, administered intravenously or orally at 10 mg/kg, demonstrated low aqueous humor levels in horses without intraocular inflammation [398]. Both breakdown of the blood–ocular barrier associated with uveitis and the presence of significant corneal vascularization may result in therapeutic intraocular and corneal levels of fluconazole, although this has not been evaluated in the horse. Intrastromal injection of voriconazole, intralesionally and/or perilesionally, can aid therapy of SA. However, the efficacy and safety of this route has not been assessed objectively.

Studies of the relative *in vitro* efficacy of the agents against equine keratomycosis isolates have consistently identified a broader spectrum for miconazole and itraconazole relative to fluconazole [362, 389], but comparison with voriconazole and other newer azoles, such as posaconazole and ravuconazole, with expanded spectra of actions [399, 400], has not been performed in horses.

Silver sulfadiazine is a topical antimicrobial agent with both antifungal and antibacterial activity and has been used in equine eyes, but cannot be generally recommended [82, 185, 293, 294]. Dilute (1:50) povidone iodine is effective against bacteria, fungi, viruses, and protozoa, and it has been used therapeutically for corneal ulcers in the horse [82, 185, 293, 294]. It may have particular efficacy against *Fusarium* isolates [82, 185, 293, 294].

Terbinafine is an allylamine antifungal agent that inhibits ergosterol synthesis and leads to toxic intracellular accumulation of the precursor squalene. Topical ocular administration of compounded 0.2% terbinafine solution does not result in detectable aqueous humor or plasma levels following administration to normal equine eyes, suggesting that its use for deep corneal or intraocular fungal infections in equine ophthalmology may be limited [401].

Frequency of treatment is another important aspect to consider with antifungal agents. A current therapeutic protocol for equine keratomycosis using topical voriconazole is to apply the drug initially four times per day for the first week [82, 185, 293, 294]. This treatment frequency was determined empirically because the intensity of iridocyclitis was often noted to be magnified dramatically on the day after topical antifungal administration at treatment frequencies higher than this. Sudden death of stromal fungi can result in acute iridocyclitis in some eyes. Topical antifungal medications can subsequently be increased to more often if necessary [82, 185, 293, 294]. Excessive protease activity in eyes with ulcerative keratomycosis is reduced with topically administered serum, EDTA, and emulsified or "flowable" amniotic membrane [1]. These products can be administered alone or combined in the same eye. Importantly, EDTA also breaks down biofilms and can potentiate the antifungal effects of miconazole, ketoconazole, itraconazole, and natamycin [402]. Systemically administered doxycycline can also aid in reducing tear film and stromal protease activity [328].

Iridocyclitis is a frequent finding in horses with ulcerative keratomycosis, and can temporarily escalate in intensity after hyphal death. It must be aggressively treated and controlled [82, 185, 293, 294, 360]. Flunixin meglumine is the most frequently used NSAID in practice and is efficacious for systemic treatment of keratomycosis-associated uveitis, but has the drawback of reducing the speed of vascularization of the corneal ulcers. Phenylbutazone does not appear to have an effect on corneal vascularization but is not as effective as flunixin at controlling ocular pain. One percent atropine sulfate is used in all cases for its mydriatic and cycloplegic effects (i.e., to dilate the pupil, stabilize the iris blood vessels, and diminish ciliary muscle spasm) [82, 185, 293, 294, 360]. Topical 2.5% phenylephrine (every 8 hours) in conjunction with atropine may be necessary to achieve mydriasis in uveitic eyes with synechia.

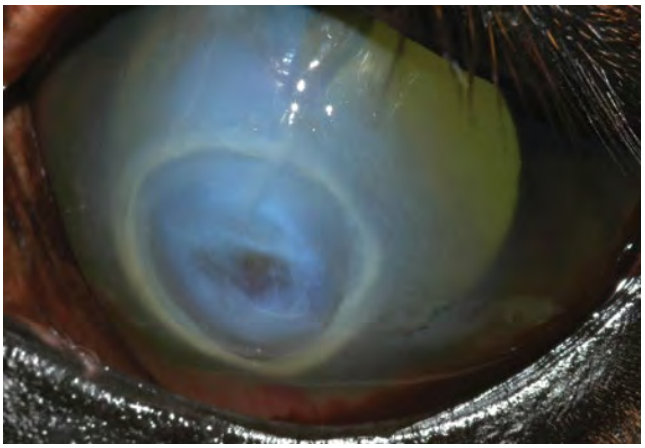


Figure 7.95 A melting ulcer with groove and thin center is present and caused by a beta-hemolytic *Streptococcus*.

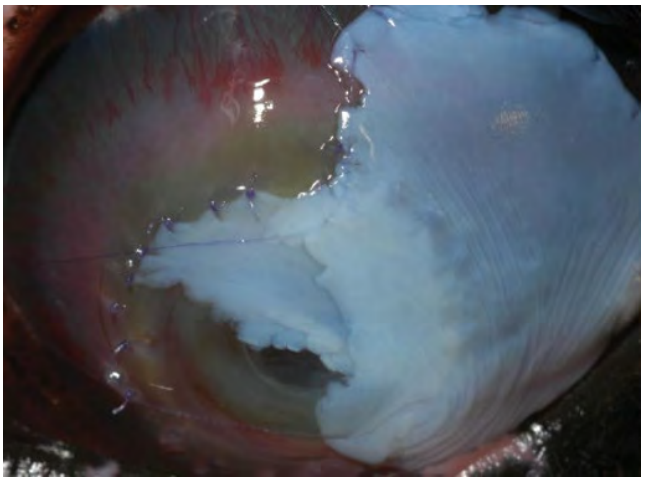


Figure 7.97 The eye in Figures 7.95 and 7.96, 2 weeks post-operatively has partial amnion retraction of both the inner and outer amnion layers.

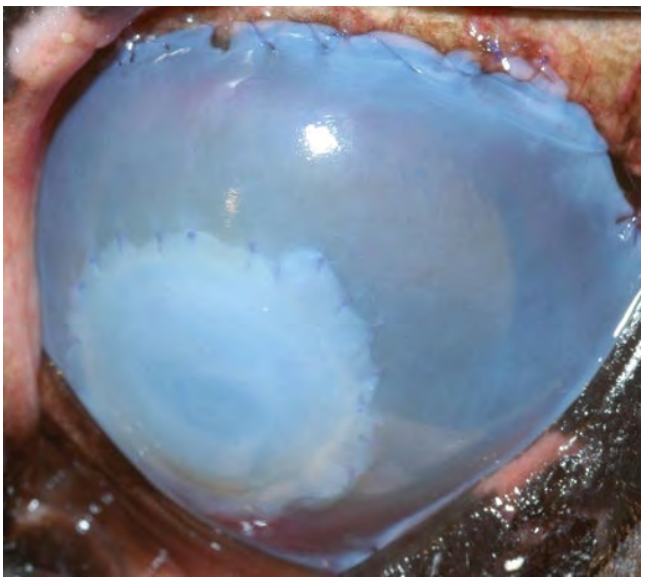


Figure 7.96 The eye in Figure 7.95 is treated with a double amnion transplant.

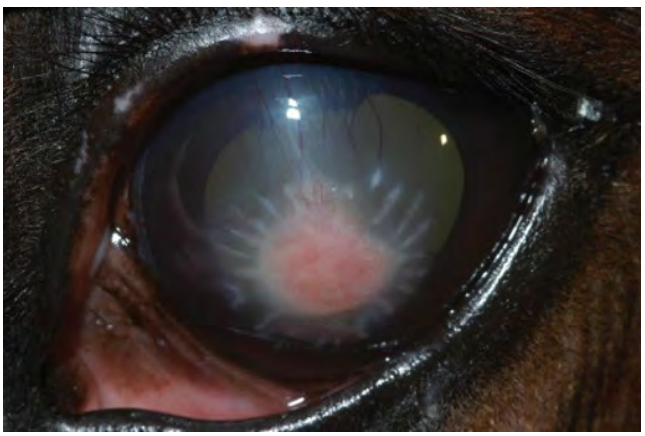


Figure 7.98 The eye in Figures 7.95, 7.96, 7.97 is healed, with a central area of granulation tissue.

Surgical treatment Surgical therapy is performed to remove infectious organisms and inflammatory cells and to stabilize weakened cornea. Specific indications for therapy include stromal loss of greater than one-third corneal thickness [including deep ulcers with grooves and descemetocele, corneal perforation, uncontrolled anterior uveitis, or in cases limited to no response to medical therapy) [124, 307, 403, 404]. Surgical options include direct suturing and superficial or lamellar keratectomy with or without conjunctival grafting [82, 113, 131, 307, 403, 405]; amnion [406–408] or biosynthetic material [409] grafting (Figures 7.95, 7.96, 7.97, and 7.98); corneoconjunctival transposition [410] (Figures 7.99, 7.100, 7.101, and 7.102); posterior lamellar or deep lamellar endothelial keratoplasty (PLK and DLEK, respectively) (Figures 7.103–7.109) [82, 113, 170, 294, 403]; and PK with or without coverage by a conjunctival graft [82,



Figure 7.99 An iris prolapse secondary to a melting fungal ulcer is present.

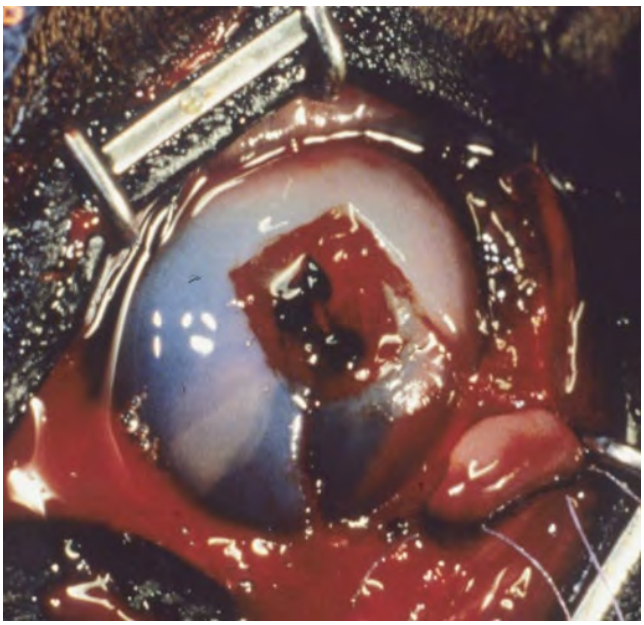


Figure 7.100 The eye in Figure 7.99 is repaired with a corneoconjunctival transposition (intraoperative image).



Figure 7.101 One week post-operatively in the eye in Figures 7.99 and 7.100 the transposition is swollen and corneal edema is present.

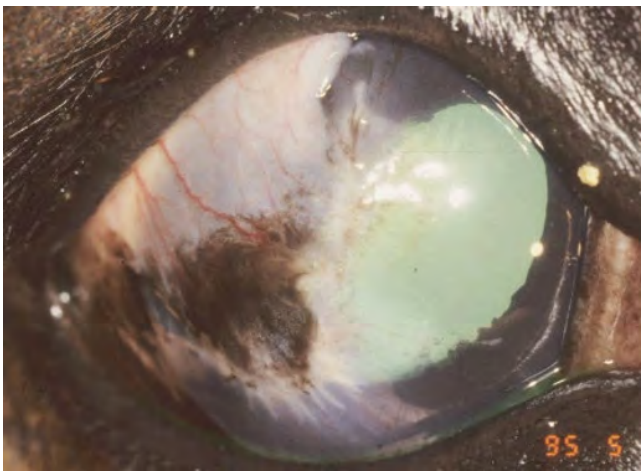


Figure 7.102 One month post-operatively the eye in Figures 7.99, 7.100, 7.101 has a healed surgical site. The eye is visual.

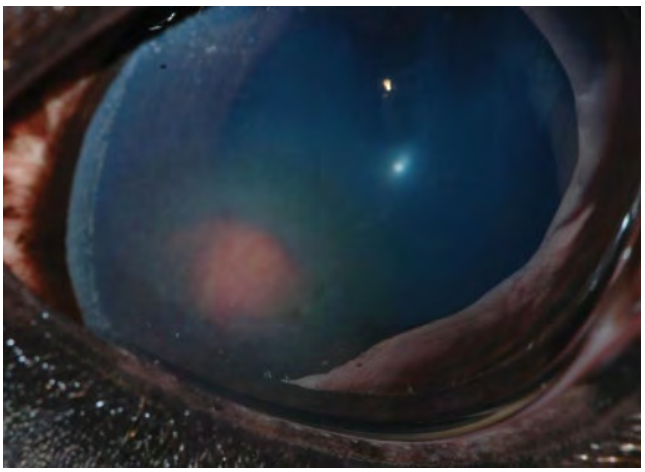


Figure 7.103 A DSA has small vessel infiltration anterior to the abscess. There is uveitis and discomfort. A DLEK was performed to remove the DSA.

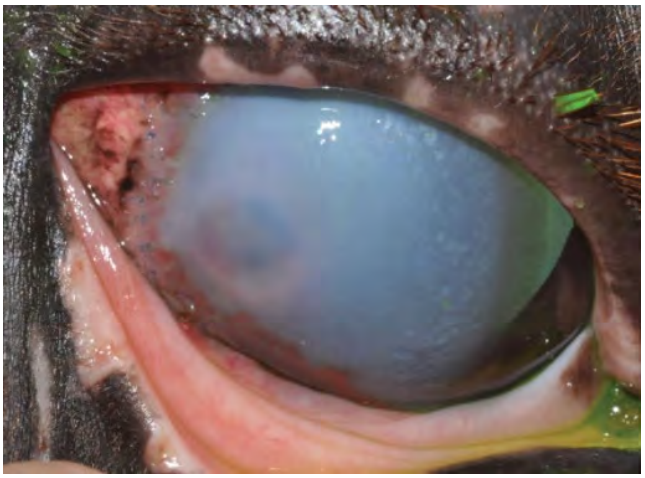


Figure 7.104 One week post-operatively, the eye in Figure 7.99 has more corneal edema from the stromal dissection, corneal bullae, vascularization of the incision, and a transparent donor graft.

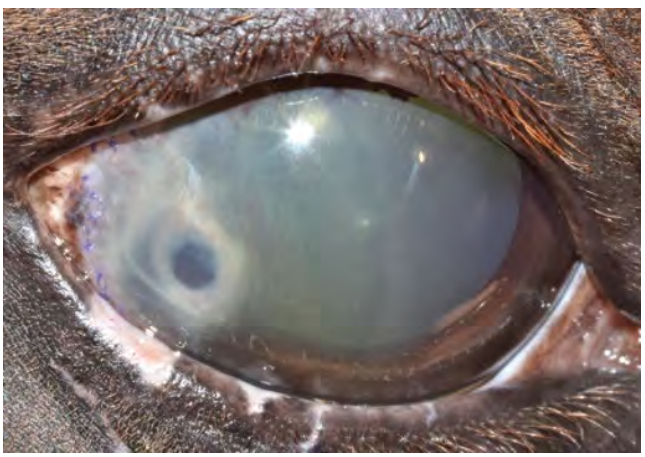


Figure 7.105 Three weeks post-operatively, the eye in Figure 7.103 has reduction in vascularization and fibrosis of the surgical site, although the donor graft remains clear.

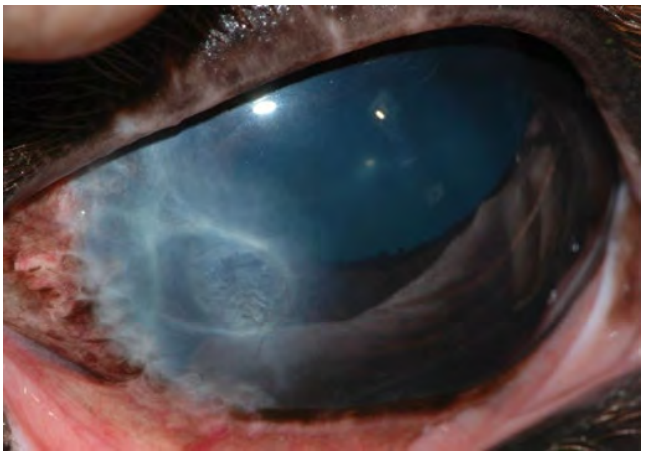


Figure 7.106 Thirty-one days post-operatively, the eye in Figure 7.103 has healed, with stromal fibrosis and donor graft opacification.

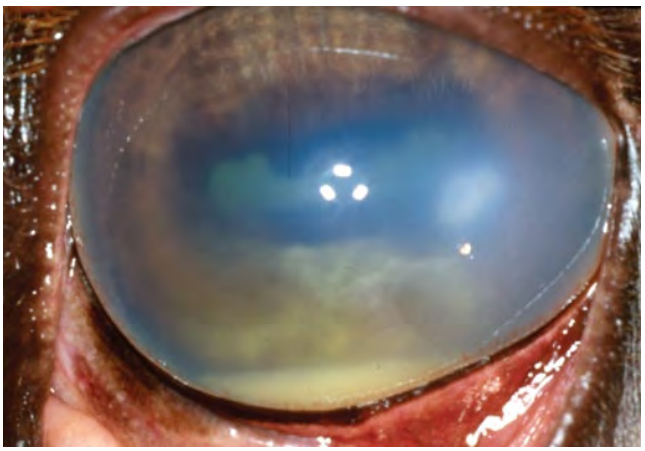


Figure 7.107 This DSA with hypopyon and fibrin in the anterior chamber was surgically treated with a PLK.

113, 170, 294, 403] for a detailed review of procedures see the section **Corneal surgery**.

Prognosis

The prognosis depends upon aggressive, appropriate therapeutic intervention. In a series of nine horses with keratomycosis, mean treatment duration was 35 days (range 16–53 days), resulting in excellent vision in six and globe retention in eight [363]. A favorable visual outcome and globe retention were reported in over 90% and 95%, respectively, of 39 cases of ulcerative keratomycosis receiving either medical or medical and surgical therapy, treated for a mean duration of 48 days (range 31–192 days) [360]. Ten cases treated for a median of 73 days (range 45–120 days) had a favorable visual outcome in 50% and globe retention in 70% [348]. In cases with corneal disease other than ulcerative keratomycosis, PK, PLK, and DLEK resulted in a favorable visual outcome in 77.9%, 98.1%, and 89.9% of 206 eyes, respectively [170].

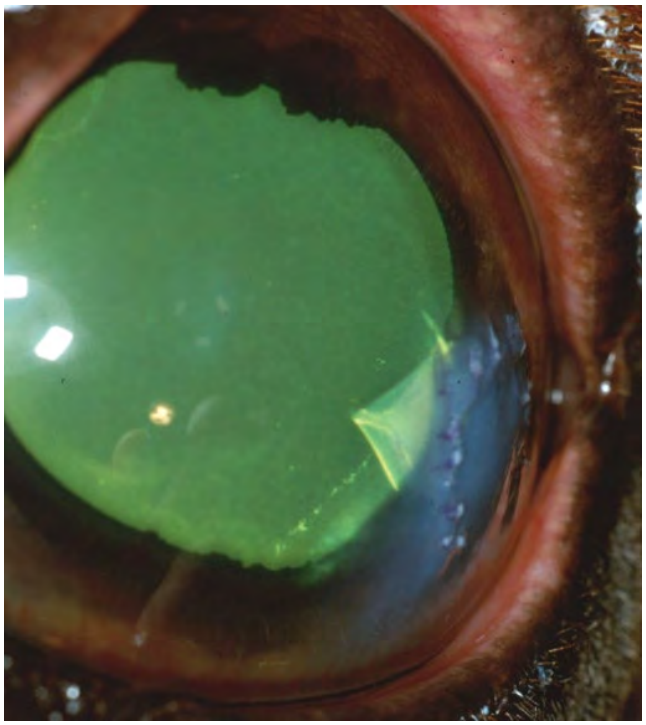


Figure 7.108 Four days post-operatively, the PLK site in Figure 7.107 has partial donor graft dislocation.



Figure 7.109 Nine days post-operatively, the PLK site in Figures 7.107 and 7.108 exhibits slight edema but is progressing nicely. There is little evidence of uveitis.

Stromal abscesses: focal chemoattraction of neutrophils to the equine ocular surface and cornea

Introduction and pathogenesis

SA may be superficial, deep, or full thickness. The etiology of stromal abscessation is complex, not totally understood in the

horse, and probably involves multiple causes. Most corneal SA appear to develop after epithelial cells adjacent to an epithelial micropuncture divide and migrate over the wound, sealing infectious agents or foreign bodies in the anterior to deep stroma [82, 113, 170, 370, 399, 411–416]. Soluble microbial antigens, stromal collagen fragments, and cytokines, such as IL-1 released from epithelial cells, may diffuse to the limbus for exposure to the lymphatic system and enter the bloodstream via perilimbal vessels, or diffuse into the tears and aqueous humor to attract rapid migration of neutrophils into the cornea through stromal keratocyte networks [82, 113, 170, 370, 399, 411–416]. These neutrophils then release proteolytic enzymes into the stroma to cause further local collagen degeneration and exacerbate the initial chemoattraction for neutrophil migration [82]. The immune-privileged state of the cornea may contribute to a delayed recognition of pathogens or other heteroantigens inoculated directly into the corneal stroma by the adaptive immune system, tempering the later stages of the neutrophil response and confining local sequestration of effete neutrophils to result in an abscess.

The re-epithelialization of the micropuncture forms a barrier that can protect the bacteria or fungi from topically administered antimicrobial medications, and can interfere with both diagnosis and treatment. A specific stimulus capable of promoting epithelialization or the absence of an inhibitor of epithelialization, not found in other types of equine ulcerative keratitis, may aid the formation of SA [82, 113, 170, 370, 399, 411–413]. Corneal SA in the horse can be a vision-threatening sequela to an apparently minor initial superficial corneal ulceration [82, 113, 170, 370, 399, 411–414].

The micropuncture hypothesis of sporadic abscessation does not, however, explain the clustering of cases of SA to a specific farm or location, where groups of horses develop SA after environmental changes such as new bedding or after moving to pastures with excessive plant growth. Nor does it explain an increased frequency of SA at certain times of the year [82, 294], or SA occurring in related animals. The latter suggests a familial or genetic predisposition to stromal abscessation in some horses. Some DSA, at the level of Descemet's membrane, appear to be a consequence of endothelial penetration by pathogens emanating from the anterior uvea [379], possibly secondary to a systemic infectious process. Corneal SA can involve bacteria or fungi, or they can be sterile. In general, superficial SA tend to be associated with bacteria and DSA with fungi. The keratopathogenicity of fungi may determine the depth of an SA, with fungi of low pathogenicity staying relatively superficial and moving horizontally within the stroma, and more aggressive fungi moving deeper vertically within the stroma [374].

Many cytologic, microbiologic, and histopathologic samples fail to yield diagnostic evidence of infection [82, 113, 170, 370, 399, 411–414]. Representative pre-operative cultures are difficult, if not impossible, to obtain because of both the intact, epithelialized surface of the abscess and the deep location of the lesions in the cornea. The epithelium and stroma over DSA generally are relatively healthy, and may be difficult to remove to access the abscess for diagnostic sampling [82, 113, 170, 370, 399, 411–414]. One study of ten SA yielded 60% positive bacterial cultures for *Streptococcus* spp. or *Staphylococcus* spp [412]. In another study, histopathologic evaluation of 13 biopsy specimens identified cocci in only one sample versus fungal hyphae in 5/13 (38%) and no etiologic agent in 7/13 (54%) [371]. Microbiology samples were taken from surgical biopsies in another series of 51 DSA, with 9 out of the 51 samples positive for growth of bacteria (17.6%). Bacteria found on the microbiology samples were either Gram-positive (α-hemolytic *Streptococcus*, *Corynebacterium* spp., *Streptococcus dysgalactiae* subsp. *equisimilis*, *Staphylococcus* spp., *Staphylococcus aureus*, nonhemolytic *Staphylococcus)* or Gram-negative (*Acinetobacter* spp., *Alcaligenes faecalis*, *Enterobacter aerogenes*) [103, 372]. Three out of the 51 samples had fungal growth (5.9%, 3/51). Fungal species were identified as *Fusarium* spp., *Aspergillus* spp., and an unidentified mold. Two of the cases with fungal growth were also culture positive for bacteria (3.9%, 2/51) [103, 372]. Fungal hyphae were found histologically in 47.1% (n=24) of the DSA cases. Histopathologically, most fungal DSA showed suppurative keratitis (n=34; 66.7%) and little to no stromal vascularization infiltrating the abscess (negative association, $P = 0.005$) [103, 372]. Fungal hyphae have been identified in 50% and 70% of surgical biopsy specimens, frequently localized near or in Descemet's membrane [415, 416]. Similar results were obtained in another study of 11 biopsy specimens, with fungal hyphae identified in 36% (4/11) and no infectious agent in 64% (7/11) [417]. Histopathologic recognition of fungal organisms adjacent to and within Descemet's membrane suggests a possible tropism for fungi to the GAGs located in the deeper stroma [82].

Corneal vascularization in response to insult is a complex process reflecting the balance between angiogenic and antiangiogenic factors in the normal avascular cornea [82]. A normal cornea will have little to no expression of angiogenic factors and a high normal or constitutive expression of antiangiogenic factors [103, 372]. Injury to the cornea will stimulate proinflammatory cytokines such as IL-1 (IL-1α and IL-1β) to induce infiltration of leucocytes to the injured corneal tissue. This will initiate vascularization of the cornea by the secretion of angiogenic factors such as VEGF-A [103, 372] PEDF is an antiangiogenic and anti-inflammatory cytokine that has a stronger antiangiogenic activity in the cornea than any of the other known angiogenic inhibitors [103, 372]. The balance between VEGF-A and PEDF may be disturbed during inflammatory and infectious keratitis, resulting in corneal vascularization [103, 372]. In the case of fungi, vascularization necessary for healing an SA may be mild and slow to develop in intensity relative to the degree of infection and inflammation, possibly exacerbated by antiangiogenic factors inherent to the fungi. *Fusarium* spp. and *Aspergillus* spp. isolates from equine keratomycosis have demonstrated inhibition of vascular growth *in vitro* [418]. Three angiogenesis-related factors were expressed in DSA tissue of horses. A negative association between VEGF-A and PEDF

when compared to the presence of fungal hyphae indicated that abscesses positive for these two factors will most likely not have fungal hyphae present [103]. The presence of monocytes in a DSA correlates with the absence of fungal hyphae, and the majority of exclusively neutrophil DSA typically have hyphae present [103].

Prevalence

Since the 1980s, there have been radical changes in the understanding of the pathogenesis and treatment of equine SA. SA were formerly considered a problem related to equine recurrent uveitis, or caused by corneal microtrauma, corneal foreign bodies, or corneal bacterial infection. Corneal SA in horses were in the past most commonly diagnosed in subtropical climatic areas of the world [413].

Reports of equine corneal SA suggest that the prevalence of diagnosis is increasing, but whether this is due to increased recognition, variations in climate, or a true increase in occurrence is unknown [359, 370, 371, 376, 413]. The total number of equine patients diagnosed with DSA at the University of Florida between 1991 and 2013 was 390, with more cases seen in 2003–2005 than other years [371]. DSA represented 14% of the horse cases presenting to the University of Florida from 1991 to 1993 [416]. There was an apparent seasonal effect, with more of the equine DSA presented in the less hot and humid spring and winter months that the summer months [372].

Clinical appearance

SA may occur at any location in the cornea (i.e., axial, paraxial, peripheral) and at any depth (i.e., superficial stromal, midstromal, endothelial, or full thickness). They are characterized by focal whitish to yellow cellular infiltrate, which may be clearly demarcated within the stroma or may have diffuse, hazy edges with feathery extensions into adjacent stroma [82, 113, 170, 294, 370, 411–414]. In the early stages, some eyes with SA may present clinical signs suggestive of minor corneal trauma and slight anterior uveitis, creating a false impression of a benign disease. However, as the abscess progresses, mild-to-fulminating secondary iridocyclitis occurs [82, 113, 170, 294, 370, 411–414]. Single or multiple abscesses may be present. Fluorescein staining is generally negative, but focal dye uptake may be present where an epithelial micropuncture is patent [82, 113, 170, 294, 370, 411–414]. A characteristic feature of some SA is a waxing and waning clinical course, manifested by periods of severe ocular pain, corneal opacification, and mild to fulminating anterior uveitis alternating with periods of relatively mild clinical signs [416]. Recurrence of SA is possible and may be related to failure to kill fungi or the inability of the immune system to remove dead hyphae. The recurring lesions tend to be orange in color. Abscesses located adjacent to the endothelium may rupture into the anterior chamber, producing more consistent signs of pain and anterior uveitis, commonly with attachment of inflammatory detritus (fibrin, cells) to the posterior aspect of the abscess. Vascularization may vary in its anatomic level and its intensity, but is typically deep and most prominent in the limbal sector adjacent to the abscess. Superficial corneal vascularization may obscure the view of a DSA. Corneal neovascularization to a central corneal ulcer typically involves vessel ingrowth from the entire limbus, whereas neovascularization of a central SA may be localized to a limbal sector and can obscure a view of the abscess [82, 113, 170, 294, 370, 411–414].

Quiescent SA are an occasional finding in an otherwise quiet eye, probably resulting from endogenous suppression of earlier acute disease. Because of the possibility of recrudescence of acute disease in these eyes, attempts should be made to eliminate any infectious focus suspected of being present.

Differential diagnosis

Any condition causing corneal opacification should be considered as a differential diagnosis for an SA: inflammatory conditions (e.g., IMMK, eosinophilic keratitis, nonulcerative keratouveitis, corneal foreign body, granulation tissue, parasitic keratitis), noninflammatory conditions (e.g., calcific band keratopathy, mineral or lipid deposition, corneal dystrophies, corneal fibrosis), and neoplastic conditions (e.g., SCC, angiosarcoma, amelanotic melanoma) should all be considered. For diagnosis of SA, an intact epithelium will interfere with effective collection of samples, but these can be obtained if the SA is surgically removed. Evaluation of biopsy specimens and cultures obtained at the time of surgery provide a more certain diagnosis as to the role of infection in the SA. Routine hematoxylin–eosin (H&E) staining can identify fungal hyphae and/or bacteria. Special stains (periodic acid–Schiff (PAS), Gomori's methenamine silver (GMS)) may be necessary to more definitively identify hyphae [417]. Cellular infiltrate is predominantly neutrophilic in most fungal SA with variable lymphocyte, plasma cell, and macrophage involvement, and vascularization and fibroblastic cells may be present. It is unusual to find hyphae in SA with a predominance of macrophages [82, 113, 170, 294, 370, 411–414, 417]. Molecular techniques such as PCR to detect DNA from infectious organisms can be used, if available, in the rapid diagnosis of fungi causing SA [381].

A chronic SA with secondary uveitis obscured by corneal vascularization may be difficult to differentiate from eyes with equine recurrent uveitis. Topical epinephrine or phenylephrine can blanch the superficial blood vessels to expose a DSA. Melting and infected ulcers of horses are also associated with severe anterior uveitis, but each is distinct in general appearance from an SA, with ulcers invariably retaining fluorescein stain [82, 113, 170, 294, 370, 411–414].

Treatment

Medical treatment Early and aggressive medical therapy can be reliably successful in many superficial and anterior SA, particularly bacterial abscesses [412]. However, both medical therapy and surgical intervention are usually necessary in mid to deep SA, particularly fungal abscesses, or where medical therapy fails to quickly stall the progress of the disease. Therapy

is directed towards elimination of infection and stromal degeneration, and iridocyclitis suppression, and, importantly, to promote vascularization of the lesion necessary to drive expedient and effective healing of the lesion [413].

Medical treatment will be a combination of antimicrobial medications, mydriatic/cycloplegic drugs, and anti-inflammatory medications. SPL systems are imperative and will expedite aggressive medical therapy. The antimicrobial medication will normally be a combination of an antibiotic and an antifungal drug [82, 113]. Topical antimicrobial medications should be administrated between four and six times daily for 4–6 weeks according to response, and longer therapy is likely with fungal involvement [82, 113, 360].

Because the location of SA may preclude identification of a specific etiologic agent, empiric antimicrobial therapy is targeted toward presumptive bacterial or fungal pathogens. Selection of individual drugs must take into consideration that biphasic drugs, or those with both hydrophobic and hydrophilic properties, are best able to penetrate the intact corneal epithelium and stroma to reach the site of infection. Bioavailability of topical drugs will vary between species, and the limited data available in the horse mean that clinical protocols for many pharmaceuticals represent "best practice," based largely on collective clinical experience. For antibiotic selection, chloramphenicol and some fluoroquinolones penetrate the corneal epithelium in other species, while aminoglycosides generally do not. In normal equine eyes, 0.5% moxifloxacin has been demonstrated to reach greater intraocular concentrations following topical administration than 0.3% ciprofloxacin [419]. Ciprofloxacin was shown to have a long half-life of elimination from the equine tear film, potentially indicating a stromal reservoir following topical application [420]. For antifungal selection, topical 5% natamycin is generally believed to minimally penetrate the corneal epithelium, but topical 1% voriconazole has been demonstrated to have good intraocular penetration in normal equine eyes [120, 395, 413]. It is important to note that increased intracorneal drug concentrations can be achieved with more frequent application, as is possible topically, and with removal of the epithelial barrier. The latter is achieved by therapeutic debridement of the overlying corneal epithelium, and should be incorporated into the therapeutic protocol in most cases. This is of particular significance when using antifungal agents, most of which are fungicidal only at high local concentrations.

Intralesional and perilesional injection of antifungal medications into human and equine DSA has recently been described [421, 422]. This procedure specifically aims to kill fungi within the cornea and is only likely to be effective when a fungal agent is present. Intrastromal injection of 1% voriconazole solution appeared to contribute to rapid resolution of clinical disease without significant complications in one horse study [318]. Treatment with intracorneal and subconjunctival administration of 1% voriconazole was successful in two other horses with SA, resolving the corneal SA and the secondary uveitis. In DSA with only limited or no vascularization it might be possible to induce vascularization and accelerate resolution by intracorneal injection of an angiogenic factor such as VEGF-A, alone or in combination with an antifungal drug. There are currently no objective reports on the efficacy or safety of these procedures, and corneal stromal lamellar fracture, conjunctival hyperemia/chemosis, and mild–moderate corneal stromal fibrosis are potential complications of this technique [422].

Oral antibiotics and antifungal agents, as indicated for treatment of bacterial and fungal keratitis (Tables 7.8 and 7.13), can be used with significant benefit in SA, particularly given the potential damaging consequences of failure to eliminate infection [82, 113, 170, 294, 370, 411–414]. With the exception of oral tetracyclines (doxycycline), use of anticollagenase agents is generally not indicated, owing to their uncertain penetration and the anticipated increased presence of blood-derived protease inhibitors associated with advancing perilesional vascularization.

A mydriatic/cycloplegic drug such as atropine 1% ophthalmic solution instilled topically between one and four times daily is used to achieve pupil dilatation and cycloplegia, and is essential to manage the often severe secondary inflammation in the anterior segment [82].

Systemic NSAIDs are critical in the medical treatment of SA, with flunixin meglumine or phenylbutazone being the NSAIDs of choice. However, the cyclo-oxygenase and lipoxygenase inflammatory pathways are critical drivers of corneal angiogenesis, and use of flunixin meglumine, a potent cyclo-oxygenase inhibitor, at higher doses, will decrease the speed of corneal vascularization, and will impede or delay healing. Vascular perfusion and formation of corneal vessels increases when flunixin meglumine is changed to phenylbutazone during therapy, or when the dose is reduced. There is a critical balance when using flunixin meglumine between reducing the iridocyclitis, which can potentially blind the horse, and not inhibiting the vascular ingress necessary to resolve the stromal keratitis [82, 113, 170, 294, 370, 411–414]. A recommended protocol is a starting dose of 1.1 mg/kg flunixin meglumine every 12 hours IV or PO until the anterior segment inflammation is resolving, subsequently decreasing and tapering the dose to effect. It is recommended, however, that an SA patient be kept on low-dose systemic NSAIDs throughout the treatment period [82]. The patient should be monitored for systemic toxicity, in particular renal and alimentary effects, throughout.

Signs of healing of an SA are neovascularization extending throughout the abscessed area, although this may be difficult to identify in the case of DSA. The whitish-yellow cellular infiltrate of the abscess will be replaced with beige- or gray-tinged fibrotic tissue, and anterior segment inflammation (uveitis) will diminish and be more easily controlled using reduced doses of systemic NSAIDs [411, 415, 416]. "Flare-up" of uveitis at any point during treatment is an indicator that the infection remains present and the corneal pathology active, and should prompt further aggressive medical treatment or surgical intervention [82, 113].

Specific considerations for medical therapy of deep stromal and full-thickness abscesses SA do not completely heal until they become vascularized, either indirectly from a conjunctival graft or directly from corneal vascular ingrowth [82, 113, 170, 294, 370, 411–414]. Both deep and superficial corneal vascularization must occur in DSA for the lesion to resolve. Abscess material projecting into the anterior chamber does not vascularize and will continue to stimulate iridocyclitis. Corneal vascularization is generally present to some degree in DSA, but ingress is generally slower than the 1–2 mm per day reported in the horse and may be due to imbalance between angiogenic and antiangiogenic factors influenced by fungi in the DSA [82, 113, 170, 294, 370, 411–414]. Vascularization of DSA may only occur superficial to the abscess, or to the abscess margin, but not vascularize the deeper lesion itself. The inherent capability of the horse eye to vascularize the stroma near Descemet's membrane in eyes with DSA is very poor. Superficial stromal vessels do not move vertically into the deeper cornea where a DSA is found. Deeper vessels from the limbus may do this over a long period of time, although DSA with anterior chamber entry will not vascularize.

DSA generally have a poor therapeutic outcome with medical therapy alone as they vascularize poorly or not at all [82, 113, 170, 294, 370, 411–414]. This is particularly the case with DSA involving Descemet's membrane, which are predominantly fungal infections. Although vascularization may ultimately heal any abscess, the process in DSA is slow and risks extensive and visually compromising damage to the eye; removal of the abscess is the most expedient means of reliably resolving the condition and minimizing collateral ocular injury. If significant improvement in the signs associated with a DSA does not occur within the first 48–72 hours of intensive and appropriate medical therapy, surgical intervention will significantly improve outcome and reduce the duration of therapy. Delaying surgery in these cases is likely to adversely affect outcome [82, 113, 170, 294, 370, 411–414].

Surgical treatment In general, aggressive surgical intervention to excise sequestered organisms and necrotic debris, along with metabolites, and toxins from the degenerating leucocytes will significantly improve outcomes. Surgery will also provide tissue for definitive etiologic diagnosis via culture, histology, or PCR, allowing institution of targeted antimicrobial therapy.

The following surgical techniques have been described for treatment of equine SA: an SK may aid penetration of drugs to the abscess [412]; SK with conjunctival graft [423]; PK [170, 403, 404, 414]; posterior lamellar keratoplasty (PLK) [404, 415]; deep lamellar endothelial keratoplasty (DLEK) [404, 416]; deep anterior lamellar keratoplasty (DALK) [424]; carbon dioxide laser keratectomy (CDLK) with conjunctival graft [425]; and enucleation for intractable cases (Figures 7.96, 7.100, 7.104, 7.108, online Figures 7.180–7.219, 7.242–248, 7.152, 7.153, 7.154, 7.155, 7.163–170) [82]. These techniques are described in detail in the section **Corneal surgery**.

Most DSA are of a solid, inspissated nature, cannot be surgically "drained," and require to be excised. A very few SA are liquified in the early stages of formation and can be removed by drainage by cannulation. Deep lamellar and penetrating keratoplasties [82, 113, 170, 294, 370, 411–414]. are used in eyes with abscesses near Descemet's membrane and in eyes with rupture of the abscess into the anterior chamber. Placing a conjunctival pedicle graft over an LK site rapidly restores the physical integrity of the cornea, supplying fibrovascular tissue to fill in the stromal defect, and delivering an indirect blood supply to promote vascularization. In addition, conjunctival grafts allow plasma, monocytes, antibodies, and systemically administered antibiotics to reach the diseased cornea [426, 427].

PK is full-thickness microsurgical transplantation of the corneal epithelium, stroma, and Descemet's membrane/endothelium, [170, 190]. and may be performed for therapeutic and tectonic reasons in horses with full-thickness SA. With appropriate surgical experience, PK is a viable, routine, and successful surgical technique in horses with full-thickness SA or DSA, resulting in very good visual outcome in most cases (approximately 80%) [170, 190, 404].

The concept of LK is to target and replace only diseased corneal tissue while retaining the normal healthy corneal tissue [428–431]. This targeted replacement of individual diseased components of the cornea is suitable for treatment of equine SA [404]. DLEK and PLK are split-thickness LK performed to only replace diseased endothelium and Descemet's membrane in DSA and abscesses projecting into the anterior chamber [170, 190]. The epithelium and stroma of horses with DSA may be edematous or vascularized but is left intact with DLEK and PLK. The overall success rates for rapid return to visual function for surgical therapy of DSA by DLEK and PLK in horses are higher than for PK [170, 190, 404].

Prognosis

Visual outcome for both medical and surgical treatment of stromal abscesses As with ulcerative keratomycosis, the prognosis depends upon aggressive, appropriate therapeutic intervention. The visual outcome for SA depends to a large extent on the depth and extent of the abscess at the time of diagnosis, and whether the healing process has been achieved medically or with adjunctive surgical intervention. It is also determined by the skill and experience of the surgical team involved. Less scarring of the cornea results with medical treatment alone, and small DSA successfully treated medically frequently have minimal scarring. Surgical intervention will increase the probability of significant scarring and compromise of the visual axis [82, 170], but is frequently necessary to preserve the eye.

One report [170] showed that a positive visual outcome from PK surgeries in 86 horses was 77.9%, from PLK surgeries in 54 horses was 98.1%, and from DLEK surgeries on 66 horses was 89.4%. A series of case reports describing laser treatment for SA under the name of CDLK surgery comparing DLEK/PLK and PK surgeries with the CDLK method found few complications but did not report visual outcomes [425].

Corneal neoplasia: corneal squamous cell carcinoma

Prevalence

SCC is the most common tumor of the equine cornea [432, 433]. Horses with minimal ocular and periocular pigmentation, as found frequently in breeds with two or more coat colors such as Appaloosas, Quarter horses, and Paints, are at increased risk of developing SCC [433–439]. Thoroughbreds [437–439], Haflingers [440, 441], and draft horses (Belgians, Shires, Clydesdales) also demonstrate an increased prevalence, even with adequate ocular pigmentation [432, 435, 437, 439, 442, 443]. Prevalence increases with age, with the mean age of affected individuals between 9 and 13 years [433–437, 439, 442–444]. No clear sex predilection has been identified, although some studies show a higher occurrence in geldings [435, 436]. Bilateral involvement can be as high as 20% [435–438, 442, 443]. Other factors associated with increased prevalence include heredity, high levels of solar radiation and UV light exposure, increasing longitude and altitude, and decreasing latitude [435].

Pathogenesis

SCC can be considered a continuum of epithelial transformation, beginning with non-neoplastic epithelial dysplasia and progressing to neoplastic changes (Figure 7.110). The underlying pathogenesis of ocular SCC in all species is incompletely understood; however, UV light [435], p53 gene mutations [445, 446], viral infection [447], genetics [448], hormonal [449], and immune factors [448] may contribute [435, 439]. One study detected expression of a p53 mutant in all six samples of equine SCC from unspecified ocular locations, which may result from UV radiation-induced damage [445]. An additional pathophysiologic mechanism may involve cyclo-oxygenase 2 (COX-2) enzyme overexpression, which has been detected in precancerous and cancerous skin lesions in humans, dogs, and cats [450–453]. COX-2 activity results in production of prostaglandins, which increase cell proliferation, inhibit apoptosis, promote angiogenesis, alter cellular adhesion, inhibit immune surveillance, and activate xenobiotics into reactive carcinogenic substances [454]. Results vary with study methodology, but immunohistochemistry (IHC) evaluation has identified increased COX-2 expression in equine corneas with SCC versus normal equine corneas [405, 442, 455].

Corneal SCC can arise in isolation, but is more typically contiguous with limbal and conjunctival SCC. There is no grading system of equine ocular SCC, but the majority of cases are described as low-grade malignancy on the basis of their nuclear morphology and mitotic index [436]. However, if invasion of the BM and extension of the tumor into the corneal stroma has occurred, the tumor is considered to be invasive [434]. Invasion through Descemet's membrane has not been reported; however, rare, highly aggressive tumors may invade the anterior chamber by growing around Descemet's membrane and penetrating the iridocorneal angle [456, 457]. Histopathologic evaluation of biopsy specimens shows the characteristic features of sheets, cords, and whorls of malignantly transformed epithelial cells exhibiting pleomorphism, nuclear hyperchromasia, prominent nucleoli, mitotic figures, and keratin pearl formation (Figure 7.111, online Figures 7.220–7.229) [458]. Histologically, most corneal tumors tend to remain within the anterior stroma, and are associated with varying degrees of lymphoplasmocytic inflammation.

Carcinoma *in situ* (intraepithelial carcinoma) refers to the growth of dysplastic or neoplastic cells within the anatomic confines of the epithelium, and which does not extend beyond the BM to involve the corneal stroma. It is not known whether carcinoma *in situ* can progress to SCC in the horse, but it is likely that significant potential for progression exists.

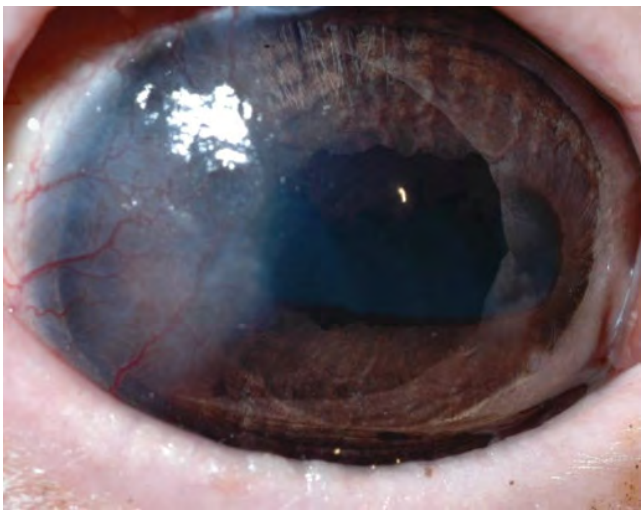


Figure 7.110 Corneal epithelial dysplasia is a precursor to SCC.

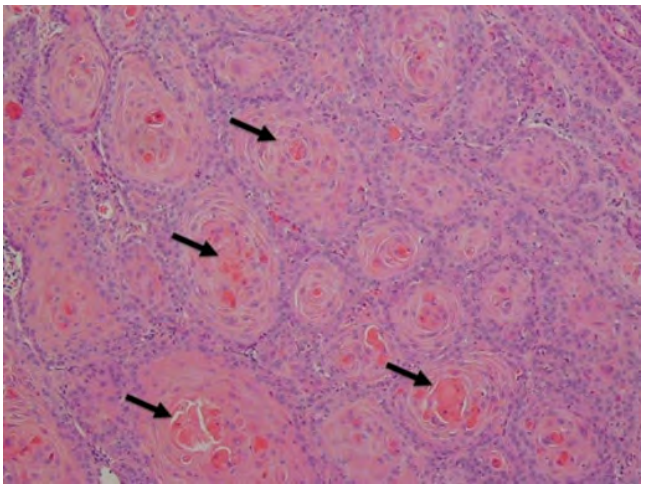


Figure 7.111 Histologic image of corneal sample obtained from a horse with extensive invasive corneal SCC. Neoplastic cells are arranged in whorls surrounding brightly eosinophilic keratin pearls (**arrows**), a hallmark of SCC. Neoplastic cells exhibit moderate anisocytosis and anisokaryosis, with few mitotic figures (H&E ×100).

Corneal stromal invasive SCC (CSI-SCC) is an SCC variant with a distinctive growth pattern of intrastromal islands of neoplastic tissue extending to the limbus in the presence of normal or mildly dysplastic epithelium and normal Descemet's membrane [436]. Although not strictly falling within the definition of SCC, corneal keratosis refers to a squamous papilloma-like lesion arising from the perilimbal epithelium and extending into the anterior stroma. The lesions have a marked inflammatory core and may have a pre-neoplastic potential (online Figure 7.230).

Clinical appearance

Corneal SCC originates from the cornea, conjunctiva, or limbus. The lateral limbus is the most frequent location, with lesions commonly appearing nodular, variably elevated, white-pink, and fleshy (Figures 7.112, 7.113, 7.114, 7.115, and 7.116) [434, 459–462]. Secondary infection or necrosis may be present, making some individual tumors more friable. Affected horses generally have no to only mild signs of discomfort (i.e., blepharospasm, epiphora) and minimal to no accompanying anterior uveitis [440, 459, 461, 462].

Carcinoma *in situ* of the conjunctiva, cornea, or limbus is often asymptomatic in the early stages, the only visible sign of the tumor being a small white to light pink irregular mass. The lesion typically stains with rose bengal, which can be used to demarcate the zone of abnormal tissue which may extend beyond the obvious margins of the lesion. As the corneal lesions extend, they present as thickened, superficial, vascularized, granular, grayish–white, plaque-like lesions, often with a well-defined leading edge.

CSI-SCC presents a grayish-white irregular stromal opacity within a thickened, edematous, and vascularized cornea. The epithelium is intact and relatively smooth. The tumor is easily misdiagnosed as an intractable deep keratitis, and definitive diagnosis is reached only on histopathology after keratectomy or enucleation [436].

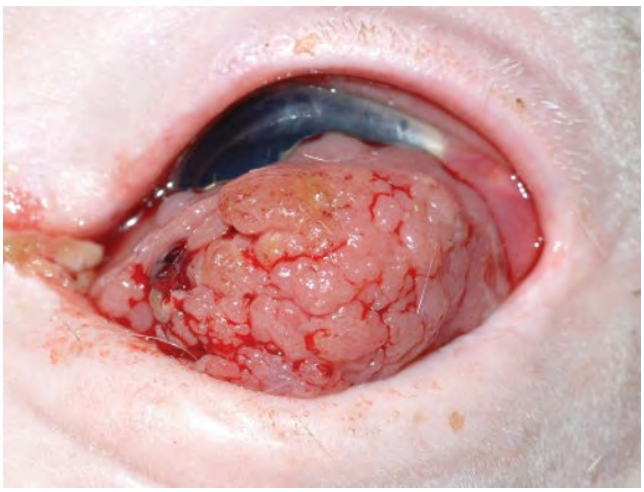


Figure 7.112 Proliferative SCC in this white pony was treated with keratectomy, beta radiation, and an amnion membrane transplant.

Corneal keratosis presents as a florid cauliflower-like lesion, being multilobulated and compacted. Generally, the lesions are light pink in color, and begin at the lateral limbus and extend into the cornea and less so onto the conjunctiva.

Diagnosis

In most cases a provisional diagnosis can be based on clinical appearance. However, definitive diagnosis in all cases is based on histopathology of excisional biopsy.

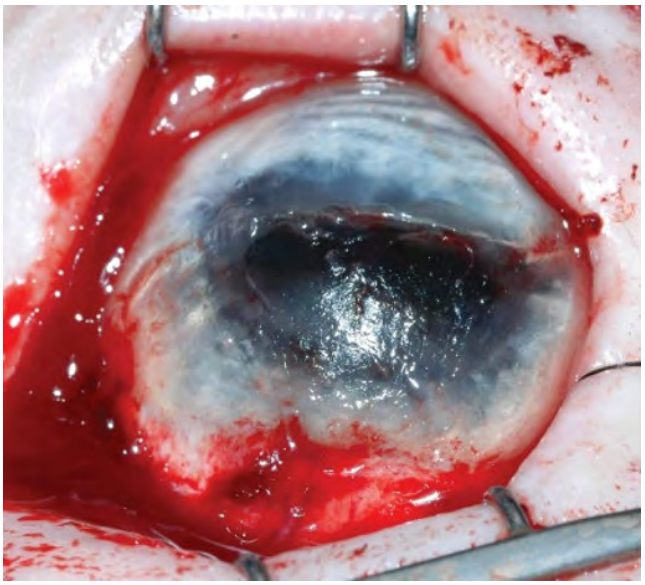


Figure 7.113 The tumor has been surgically removed by keratectomy prior to irradiation (intraoperative image) in the eye in Figure 7.112.



Figure 7.114 Nine days post-operatively, the eye in Figures 7.112 and 7.113 has swelling and plasma discoloration of the amnion.

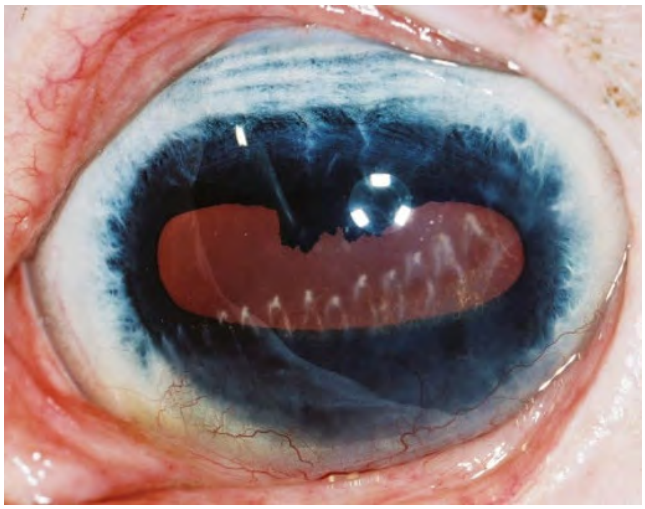


Figure 7.115 Two months post-operatively, the eye in Figures 7.112, 7.113, 7.114 has resolution of the surgery, with linear tracks from the sutures still present.

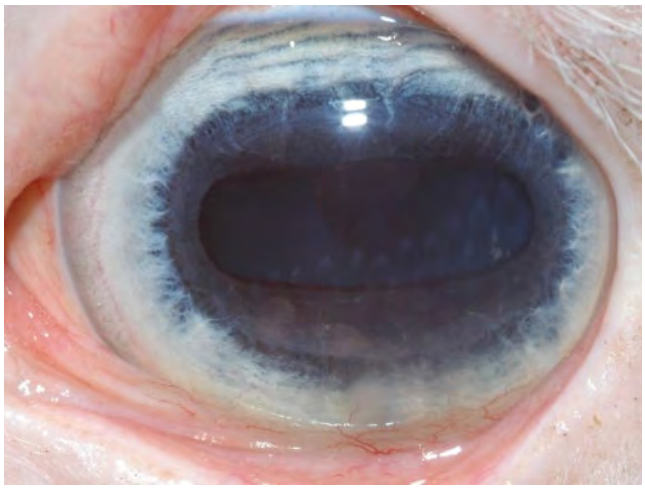


Figure 7.116 Two years post-operatively, the eye in Figures 7.112, 7.113, 7.114, 7.115 has a slight haze present but no recurrence of the SCC.

Differential diagnosis

Corneal fibrosis and other neoplastic (i.e., mastocytosis, lymphosarcoma (LSA) (online Figures 7.230, 7.231, 7.232, and 7.233), amelanotic melanoma (Figure 7.123), histiocytic sarcoma, angiosarcoma) and infiltrative (SA, immune-mediated, eosinophilic keratitis, corneal degeneration, granulation tissue e.g., habronema) diseases should be considered as differential diagnoses for SCC. Limbal conjunctival lymphocytic hyperplasia (pseudotumour) also resembles early SCC (online Figures 7.231, 7.232, and 7.233).

Treatment

Medical treatment Many treatment modalities for corneal and limbal SCC have been described and include excision, cryotherapy, radiofrequency hyperthermia, radiotherapy, topical and intralesional chemotherapy, bacille Calmette–Guérin (BCG) cell wall extract, and carbon dioxide laser ablation [13–42]. Untreated corneal and limbal SCC can invade local soft tissues [433, 463, 464]. Medical therapy alone is ineffective as sole treatment for corneal SCC but may constitute an effective adjunctive therapeutic measure.

Use of mitomycin, a DNA-crosslinking chemotherapeutic agent, has been described for treatment of corneolimbal SCC in horses. One protocol describes either a 1- or 5-minute application of 0.4 mg/mL mitomycin solution at the time of surgical removal [444]. It can be used topically as a 0.04% solution applied four times daily on a 7 days on, 7 days off regime. Resolution rates of 70–80% have been reported anecdotally, and it may be useful as a primary therapy in small corneal carcinomas *in situ*. There are no reports on the safety of this regime, and operator exposure issues are likely to be a problem.

Although it has not been evaluated as therapy for corneal SCC, topical 5-fluorouracil (5-FU) has shown efficacy in treatment of cutaneous SCC in horses [465]. One percent 5-FU ointment is applied to the ocular surface once daily for 4 days every two weeks until the tumor has regressed, and may be a useful primary therapy for small corneal carcinomas *in situ* [466, 467]. However, this may cause local necrosis and be poorly tolerated by some horses.

Based on identification of increased COX-2 expression in some equine ocular SCC, and pending further clinical evaluation, systemic administration of COX-2-specific inhibitors (e.g., piroxicam 80 mg once daily PO) may be empirically useful in some horses [468]. Treatment is likely to be required for several months before its effect can be evaluated.

Surgical treatment Early surgical resection alone of SCC can be curative where clean margins can be obtained. However, consideration must be given to the extent of tumor growth, including depth, surface area, and involvement of the adjacent eyelid or third eyelid [459–462]. In some cases, tumor invasion may be significant enough to necessitate enucleation or exenteration, rather than simple tumor resection [437, 438, 443, 459, 460]. Small corneal tumors or carcinoma *in situ* of the corneolimbus may be effectively treated with simple keratectomy. Unfortunately, many SCC are not diagnosed until it is difficult to obtain clean surgical margins without compromising the globe. Therefore, it is recommended that corneolimbal and corneal SCC receive adjunctive treatment (including radiation therapy, cryotherapy, radiofrequency hyperthermia, or topical and systemic chemotherapy) without or in combination with excision by keratectomy.

It is not unusual for granulation tissue to develop at the site 7–14 days post surgically. This can be indistinguishable from tumor recurrence without biopsy (Figure 7.117), but responds rapidly to topical or intralesional corticosteroids.

PK for corneal SCC has also been described. This is not a typical therapy for SCC, since most corneal lesions are limbal and rarely extend beyond the anterior stroma. The case described had a tumor located just dorsal to axial that arose from the margin of a previously resected lateral limbal SCC. Slit-lamp

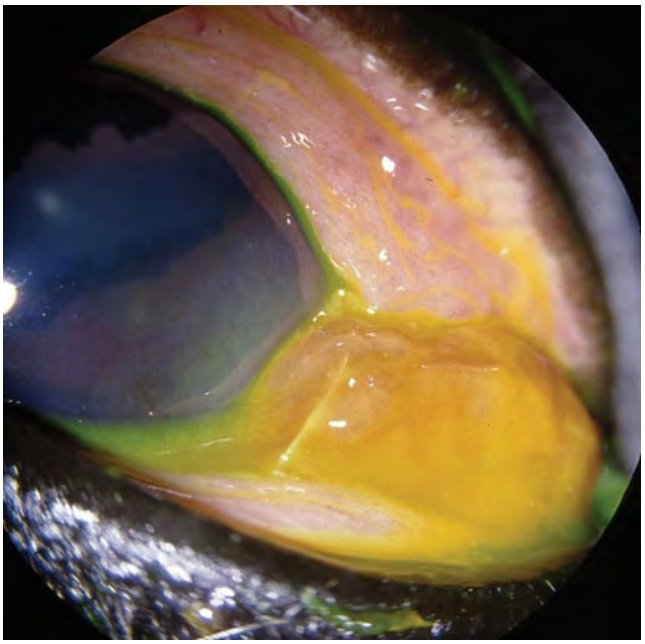


Figure 7.117 Granuloma 12 days following excision of a corneoconjunctival SCC.

biomicroscopy revealed that this tumor extended unusually deep into the stroma. A full-thickness PK with corneal transplantation was deemed the only effective therapy [469].

Cryotherapy Following surgical removal of the tumor, or for tumors less than 2 cm^2 [440], cryosurgery may be performed using compressed nitrous oxide or liquid nitrogen cryosurgical units [460]. Cryotherapy with liquid nitrogen or nitrous oxide can be effective, with optimal cryonecrosis of malignant cells being achieved between –20° and –40°C using a double freeze–thaw technique [435, 470]. Either a closed probe or spray can be used. The closed probe gives better application accuracy, while the spray is faster, but collateral tissue damage and runoff distant to the site are potential complications [468]. Cryosurgery is affordable and easily attainable. It can be used for eyelid, nictitans, conjunctival, and corneal tumors [470, 471]. Cryotherapy is especially useful when treatment of a limbal tumor cannot be done with a strontium probe due to lack of availability or when the time required to treat a very large tumor is prohibitive due to exposure and anesthetic time. The skin and cornea that is not to be frozen can be protected using a heavy layer of petrolatum. A rounded piece of styrofoam, as from a cup, covered in petrolatum works well to protect the cornea when freezing the conjunctiva/limbus. Small superficial tumors should be frozen until the iceball extends 3–5 mm beyond the visible tumor margin [435, 470]. Keratectomy sites that have been frozen seem to heal exceptionally slowly. The ulcers after keratectomy are treated with a broad-spectrum ophthalmic antibiotic and atropine as needed post operatively. Post cryotherapy, eyelids may be extremely erythemic and edematous for several days.

Radiation therapy Beta irradiation using 90Sr, with a tissue penetration of 1–2 mm, is a good option for treating corneal lesions while minimizing potential lens or retinal damage [459, 472]. Following tumor removal with keratectomy, a handheld probe is used to deliver 80–120 Gy [438, 439] or 200 Gy [408, 434] of radiation per site, generally for one to six sites in total. It is strongly recommended to cover the keratectomy site with amnion following irradiation to prevent an aggressive keratolytic response. Topical prophylactic antibiotics, serum, and a therapeutic mydriatic/cycloplegic, as well as an oral NSAID for analgesia, are administered until the surgically induced ulcer heals [459, 469]. Eighty to ninety percent of horses with corneal SCC that undergo keratectomy and beta radiation are cured after one treatment [439, 473]. Re-epithelialization may be delayed [459], and transient corneal clouding [439] may occur post-operatively. Beta irradiation has been implicated in the development of progressive corneal edema, bullous keratopathy [474], and more severe corneal damage in humans [475]. Recurrent tumors are often cured with a second treatment [473]. Most strontium units are portable and easy to use and maintain. Their primary disadvantage is availability and the need for a radiation-handling license.

Hyperthermia Radiofrequency hyperthermia utilizes the greater sensitivity of malignant cells (compared to normal cells) to temperatures between 41°C and 45°C to enable selective destruction of tumor cells, with or without initial surgical removal [437, 472]. Using a portable unit, small (less than 4 cm diameter), superficial ocular surface, tumors are heated to 50°C for 30 seconds [472]. Post-operatively, topical prophylactic antibiotics, a therapeutic mydriatic/cycloplegic agent, and oral NSAIDs are administered as needed [472]. Healing is evidenced by visible color changes and sloughing of the lesion, generally within 3 days following treatment, with formation of granulation tissue that resolves to a leucoma [472]. Advantages of radiofrequency hyperthermia include availability of portable units and comparatively easier technical application [472]. Hyperthermia should not be used in large tumors of 4–5 cm diameter that penetrate deeply into the conjunctiva.

Carbon dioxide laser The carbon dioxide (CO_2) laser emits radiation in the infrared spectrum (10,600 nm), which is absorbed by water molecules [461]. Flash boiling and vaporization of cells results, leading to tissue ablation when applied at a lower energy with a defocused beam [461]. Tumor removal can be performed with the CO_2 laser itself, or laser energy can be applied to the tumor bed following resection by SK [461]. Excision followed by laser therapy is preferred, as this provides a tissue sample of the lesion for histopathologic evaluation. Post-operative care includes topical prophylactic antibiotic and therapeutic mydriatic/cycloplegic application, as well as systemic NSAID administration [461]. Minimal chemosis, corneal edema, or signs of ocular pain are evident post-operatively, and most surgical wounds re-epithelialize

within 14 days, resolving to a corneal leucoma over subsequent weeks to months [461]. Advantages of the CO_2 laser include rapid tumor removal with a zone of cellular destruction in adjacent remaining tissue, effective hemostasis, and maintenance of a dry surgical field for maximal visualization. Sealing of nerve endings and vessels by the laser reduces post-operative edema, exudation, patient discomfort, and the potential for metastatic spread and infection [461]. Disadvantages include delayed re-epithelialization, as well as availability, cost, and use of equipment [461].

The technique involves using a CO_2 laser with an articulated arm. The laser is operated in the continuous mode with a power setting of 3–6 on the low scale, which corresponds to an average output of 3–8 W. A defocused beam is used to provide ablation rather than cutting. Depending on the size of the tumor, a keratectomy may be done prior to laser ablation. The tumors are vaporized *in situ*, until all visible tumor is gone. The bed is then lasered until it is covered with a brown char extending 5 mm into normal tissue. Topical broad-spectrum antibiotics are used until the cornea is fluorescein negative.

Topical and systemic chemotherapy This is described in the section **Medical treatment**.

Prognosis

Early, appropriate, and aggressive intervention, typically involving resection and adjunctive therapy where required, is curative in most cases of corneal or corneolimbal SCC. Published reports on the prognosis of ocular SCC are mainly derived from the databases of secondary and tertiary referral clinics, and are likely to reflect the inherent bias of dealing with clinically advanced or already recurring cases.

The prognosis for globe retention in horses with corneal/limbal/conjunctival SCC is dependent largely upon tumor size and selection of adjunctive treatment (Table 7.14). The risk of metastasis with ocular SCC in general is reported to be low (0.3–18.6%) [432, 433, 437, 443, 462, 475], but the tumors are frequently locally invasive with a potentially high risk of recurrence [437, 438]. A study of ten eyes treated with topical 0.4 mg/mL mitomycin C following surgical resection and CO_2 laser ablation of the tumor showed 11-month 60% and 80% nonrecurrence rates following an application duration of 1 and 5 minutes, respectively [444].

SK combined with cryosurgery for limbal neoplasia resulted in a 71% success rate over a mean follow-up period of 4.5 years (range 12 months to 18 years), with a significantly greater chance of recurrence when lesions had a surface area greater than 2 cm^2 [440]. Of five corneal lesions treated with beta irradiation following surgical cytoreduction, none recurred over the 2-year duration of follow-up, with transient corneal clouding being the most common side-effect [439]. Another study found 35.2% (12/34) of corneal lesions treated with surgery alone recurred, versus 0% (0/9) of those treated with adjunctive beta irradiation [438]. The same study found 51.5% (17/33) of limbal or bulbar conjunctival lesions recurred when treated with surgery alone, versus 30.8% (4/13) of those also treated with beta irradiation [438]. Twelve eyes treated with SK (with or without 90Sr-irradiation or cryotherapy) followed by placement of amnion or bulbar conjunctival grafts had no tumor recurrence for the 21–1163 (mean 226) days of follow-up [408]. Due to the small number of horses receiving bulbar conjunctival grafts (n=3), no comparison could be made regarding relative nonrecurrence between the two graft types. A larger study of 38 eyes treated with SK, 90Sr-irradation, and bulbar conjunctival grafts identified that 63% (24/38 eyes) were tumor free for the length of follow-up, which increased to 83% (24/29 eyes) when evaluating only horses followed longer than 2 weeks [434]. The mean duration until recurrence was 1754 days, with 40% recurring within 3 months, and mean days to recurrence of 709 for the remaining 60%. Two horses in that study experienced significant corneal damage (melting ulcer and iris prolapse), although no speculation was made regarding whether the damage resulted from any portion of the therapeutic intervention.

PK for treatment of corneal SCC which recurred following surgical excision, beta irradiation, and radiofrequency hyperthermia maintained a visual eye in the affected horse [469].

Vascular tumors

Prevalence

Benign and malignant blood vascular tumors (hemangioma and hemangiosarcoma, respectively) and lymph vascular tumors (lymphangioma and lymphangiosarcoma [476], respectively), as well as benign and malignant vascular tumors of undetermined origin (angioma and angiosarcoma, respectively) are rarely reported to involve the equine cornea. Limbal hemangiomas, hemangiosarcomas, and angiosarcomas have been described in the eyes of middle-aged horses. All three described cases in one series were Thoroughbreds [477], and other reported breeds include Appaloosa, Quarter horse, and Arabian [423, 478, 479].

Pathogenesis

The pathogenesis of vascular tumors is currently unknown. Ultraviolet light and decreased periocular pigmentation may play a role [423, 478, 480]. Most vascular tumors with conjunctival involvement arise from the limbal conjunctiva. Hemangiomas are typically well circumscribed and composed of variably sized vascular spaces lined with a single layer of uniform endothelial cells with rare mitotic figures [481]. Hemangiosarcomas have a combination of well-defined rudimentary vascular channels, with or without red blood cells, lined by pleomorphic endothelial cells with bulging nuclei and frequent mitotic figures; they may be locally invasive as well as metastatic [423, 480]. Considering the variable presence of red blood cells in blood vascular tumors, distinction between

Table 7.14 Success rates for adjunctive therapies following surgical resection of corneolimbal squamous cell carcinoma in horses.

Treatment modality	References	Number of eyes	Protocol	Nonrecurrence	Side-effects
Topical mitomycin C	Rayner and Van Zyl, 2006 [444]	10	CO_2 laser ablation of lesion; 1 (n=5) or 5 (n=5) minutes of intraoperative topical application of 0.4 mg/mL mitomycin C	60% nonrecurrence (1 minute) and 80% nonrecurrence (5 minutes) for minimum of 11 months	Epiphora Localized corneal edema
Cryotherapy	Bosch and Klein, 2005 [440]	14	Solid, closed-tip probe; liquid nitrogen; 2–3 mm overlap between successive sites; double freeze–thaw for 1 mm around tip	71% nonrecurrence, with mean follow-up 4.5 years; all with tumor surface area > 2 cm^2 failed; all with tumor surface area < 1 cm^2 succeeded	Post-operative discomfort Transient focal corneal edema
	Mosunic et al., 2004 [438]	34	As above	45% nonrecurrence (11/34 lost to follow-up)	Temporary bullous keratopathy
	Schoster, 1992 [460]	3	As above	No recurrence over length of follow-up (21–36 months)	Granulation tissue
Cryotherapy + bulbar conjunctival graft	Ollivier et al., 2006 [408]	1	Double freeze–thaw	No recurrence over length of follow-up (1 year)	Post-operative discomfort Mild persistent corneal opacification
Radiofrequency hyperthermia	Grier et al., 1980 [472]	45 tumors, location not specified, cattle and horses	Minimal surgical debulking; contact electrodes in place for 30 seconds after tissue temperature of 50°C reached	75% (6/8) horses tumor free at 2–10 months	Post-operative discomfort Visible tumor sloughing over 1 week Subsequent leucoma Uveitis
CO_2 laser	English et al., 1990 [461]	4	Continuous mode, power setting 3–6 on low scale (3–8 W output); defocused beam SK performed in 2 eyes prior to laser application Tumor removed via laser ablation in 2 eyes	No recurrence for length of follow-up (7–20 months) Recurrence in one eye at 4 months	Minimal post-operative discomfort Ocular discharge Re-epithelialization in 7–14 days Single linear laser burn
Beta irradiation	Walker et al., 1986 [439]	5	100 Gy 90Sr irradiation	No recurrence of length of follow-up (2 years)	Swelling Cloudiness
	Rebhun, 1990 [459]	24 eyes	8000–10,000 rad 90Sr per tumor immediately following keratectomy	No recurrence in 25 eyes over length of follow-up (1–9 years)	Re-epithelialization in 3–4 weeks
	Mosunic et al., 2004 [438]	23, surgery only; 22, surgery and 90Sr	Single dose of 80–120 Gy 90Sr (22 eyes)	Surgery only: 15% nonrecurrence (3/23 lost to follow-up) Surgery and 90Sr: 65% nonrecurrence (11/23 lost to follow-up)	
Beta irradiation + bulbar conjunctival graft	Plummer et al., 2008 [416]	38	90Sr probe; 1–6 sites; 20 Gy (20,000 β-rad) per site	9 lost to follow-up Mean duration of nonrecurrence for 24/29 was 1754 ± 1319 days Mean duration to recurrence for 5/29 was 449 ± 339 days	Melting ulcer Iris prolapse
	Ollivier et al., 2006 [408]	2	90Sr probe; 1–4 sites; 20 Gy (20,000 β-rad) per site; conjunctival (versus amnion) graft selected if small or single keratectomy site	No recurrence over length of follow-up (range 225–1163 days)	Post-operative discomfort Mild persistent corneal opacification
Beta irradiation + equine amnion graft	Ollivier et al., 2006 [408]	7	90Sr probe; 1–4 sites; 20 Gy (20,000 β-rad) per site; amnion placed over large or multiple keratectomy sites	No recurrence over length of follow-up (range 21–223 days)	Post-operative discomfort Mild persistent corneal opacification
Equine amnion graft	Ollivier et al., 2006 [408]	2	Amnion graft placed over SK site	No recurrence over length of follow-up (range 230–778 days)	Post-operative discomfort Mild persistent corneal opacification

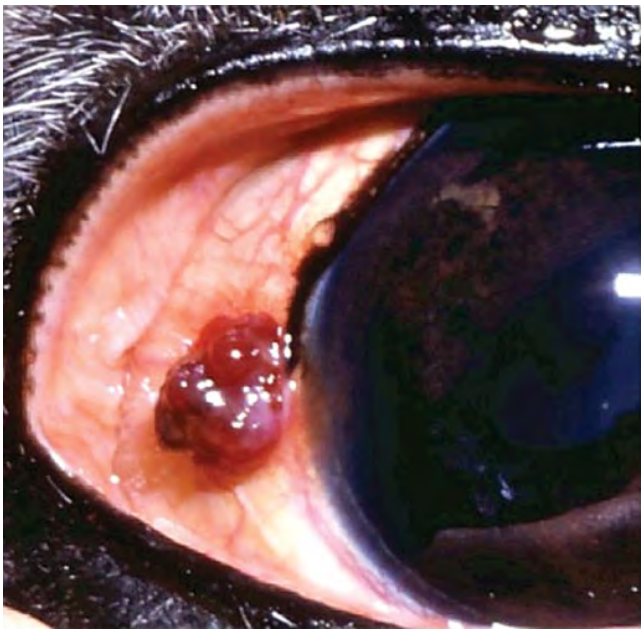


Figure 7.118 A limbal hemangioma, characterized by focal distension of conjunctival blood vessels and vascular extension into the limbal cornea.



Figure 7.119 Limbal hemangiosarcoma, with invasive extension into the cornea.

blood and lymph vascular tumors can be difficult. Immunohistochemical evaluation with factor VIII-related antigen (FVIII-RAg), a marker strongly expressed by blood vascular endothelial cells [423], may aid in the distinction; however, tumors of both tissue types may be immunohistochemically positive [423].

Diagnosis

The clinical appearance of ocular surface vascular tumors is highly variable. They may appear as enlarged limbal blood vessels, focal corneal vascularization and edema, red cystic limbal masses, or solid pink corneoconjunctival masses, with or without invasion into deeper corneal layers (Figures 7.118 and 7.119) [423–480, 482]. They may also be accompanied by significant serosanguinous ocular discharge, with variable clinical signs of pain or intraocular inflammation [423–480, 482]. Definitive diagnosis is by histopathology.

Differential diagnoses

Other corneoscleral neoplastic diseases (SCC, LSA, mastocytoma, histiocytic sarcoma), as well as inflammatory lesions (granuloma, SA) are differential diagnoses for vascular tumors.

Treatment

Ocular hemangiomas have been successfully treated with surgical removal with adjunctive beta irradiation or cryotherapy [477, 479, 483]. Enucleation was performed in one horse with a large lesion that had no evidence of metastatic disease [423]. Malignant tumors are more aggressive clinically, invading the orbit and periorbital sinuses and metastasizing through mandibular and cervical lymph nodes [423, 479, 480]. A Miniature horse with corneal lymphangiosarcoma demonstrated pulmonary metastasis [476].

In contrast to ocular hemangiomas, angiosarcomas do not appear to be radiosensitive [477, 480].

Prognosis

The prognosis for benign vascular tumors of the cornea appears favorable, provided detection is early [479]. The prognosis for malignant vascular tumors is guarded, with early and aggressive recognition and treatment necessary. Of four horses with histologically confirmed angiosarcoma, all died within 18 months, due to either confirmed metastasis or extensive local recurrence [480]. Early and aggressive surgical debulking, including orbital exenteration, was performed on several horses, only one of which was alive 18 months post-operatively [423, 477]. A histologically "low-grade" hemangiosarcoma responded to keratectomy/conjunctivectomy alone [482].

Melanoma

Prevalence

Melanomas of the cornea and sclera, termed limbal or epibulbar melanomas, are rare in horses. A benign epibulbar melanoma was reported in a 7-year-old Miniature Argentine horse [483], and a low-grade malignant epibulbar melanoma was reported in a 6-month-old Hanoverian [484]. A nonpigmented corneal melanoma occurring in conjunction with a pigmented conjunctival melanoma was reported in a 20-year-old Tennessee Walking horse [485].

Pathogenesis

The inciting cause for proliferation of melanocytes at the corneoscleral limbus is unknown, but UV radiation, chemical exposure, trauma, chronic irritation, coexistence of cutaneous

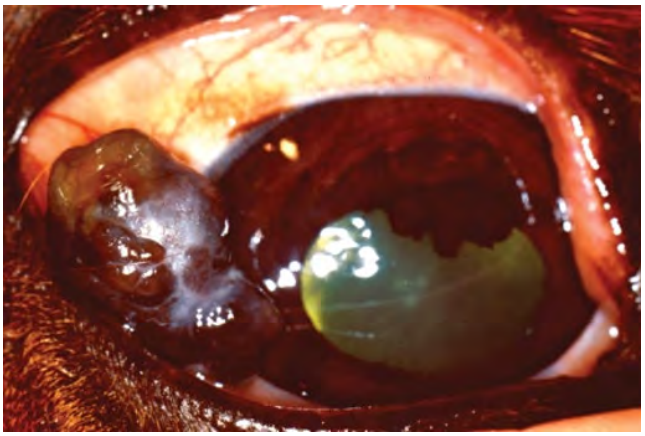


Figure 7.120 A lateral limbal melanoma.

melanomas, and genetic variables have been considered as potential factors in animals and humans [485–487]. While equine dermal melanomas and melanomatosis occur in gray horses [488], no predisposing factors for the occurrence of corneal or scleral melanomas have been identified.

Histopathologic evaluation of samples from previous cases identified packets and bundles of spindyloid to polygonal cells with indistinct borders, and eosinophilic cytoplasm separated by a fine fibrovascular stroma [482]. Pigmentation was variable, and mitotic figures were absent [482, 484] or infrequent [485]. Depending upon the degree of pigmentation, bleaching may be necessary [484]. If the neoplastic cell type is difficult to identify, such as may occur in amelanotic or poorly pigmented masses, special stains (Fontana-Masson) or immunohistochemical markers (S-100, melanin A, tyrosinase, HMSA 45) may be utilized [458].

Diagnosis

Signs of ocular pain or irritation may be absent or very mild in affected horses [485, 488, 489]. The mass may be present at any location on the limbus and is frequently raised, firm, and fixed to the underlying limbus [485], visibly infiltrating the adjacent corneal stroma (Figure 7.120, online Figures 7.234 and 7.235) [484]. The mass itself may be heavily pigmented [484] or unpigmented [485], and the overlying conjunctiva may be heavily pigmented [482], or unpigmented [484]. One horse had an unpigmented corneal lesion adjacent to a pigmented conjunctival lesion [484]. Procedures that may be helpful for complete clinical evaluation include gonioscopy and ocular ultrasound, but definitive diagnosis requires a biopsy.

Differential diagnosis

Differential diagnoses for epibulbar or limbal melanomas include non-neoplastic proliferative diseases (eosinophilic keratoconjunctivitis, parasitic keratoconjunctivitis, bacterial or fungal keratitis, granulation tissue), and neoplastic diseases (SCC, angiosarcoma, mastocytoma). Additionally, nonproliferative diseases such as subconjunctival fat prolapse, staphyloma, orbital cyst, and dermoid should be considered.

Treatment

Medical treatment Protracted systemic administration of the histamine H2 antagonist cimetidine has been reported in horses with cutaneous melanoma, with variable ability to effect tumor regression [490–492]. Additional nonsurgical treatments reported for cutaneous melanoma include autogenous vaccination with select tumor anticipated to promote immune recognition and elimination of the tumor [489], and intratumoral vaccination with a viral-derived suicide gene that sensitizes tumor cells to antiviral medication [493]. Each of these treatments may be combined with surgical excision if indicated, but none has been evaluated specifically as treatment for epibulbar melanoma.

Surgical treatment As reported in horses or other species, surgical resection of epibulbar melanomas may be performed via lamellar corneosclerectomy or full-thickness resection with reconstruction by homologous corneoscleral, third eyelid, or synthetic grafting procedures [113, 485, 489]. Adjunctive procedures may include cryotherapy, beta irradiation, or laser photocoagulation [82, 113]. In cases with significant extension or local invasion, enucleation may be indicated [484].

Prognosis

In consideration of the few reported cases in the veterinary literature, the prognosis for limbal melanoma in horses is difficult to determine. Of the reported cases, one was histopathologically diagnosed as low-grade malignant melanoma and was particularly locally aggressive, with marked proliferation within days of partial resection necessitating enucleation 8 days later [82, 113, 484]. Systemic metastases were absent, and no local recurrence was noted 14 months later. The two other cases were diagnosed as benign, and affected horses were free of recurrence for 10 months and 2 years, respectively, following excision [483, 485].

Mast cell tumor/mastocytosis

Prevalence

Proliferative mast cell lesions involving the eye have been rarely reported in the horse. The terms mast cell tumor and mastocytoma are used to describe growths with neoplastic tendencies, while mastocytosis describes mast cell lesions without neoplastic characteristics [487].

Mastocytomas have been reported in a 12-year-old Quarter horse [494], a 12-year-old Dutch Warmblood, a 23-year-old New Forest horse [440], and a 3-year-old Marwari mare [495]. Mastocytosis has been reported in a 9-month-old Arabian colt [490] and a 5-year-old pony [491].

Pathogenesis

The underlying cause of mastocytosis/mastocytoma is unknown, and it is unknown whether the accumulation of mast cells is a reactive or a neoplastic change [491]. One report of generalized

mastocytosis in a foal detailed 1 year of the appearance of multiple skin nodules followed by spontaneous regression, but the underlying stimulus was not identified [492].

In the horse, the ocular lesions may have a conjunctival or scleral origin, although it may be difficult to establish the origin in any one case. Histologic evaluation of biopsy specimens identifies sheets of large, well-differentiated round cells with hyperchromatic nuclei and granular eosinophilic cytoplasm. The granules stain metachromatically with toluidine blue, confirming them to be mast cells. Eosinophilic inflammation is common, and mitotic figures are rare. Differentiation between mastocytosis and mastocytoma (mast cell tumor) may be contentious, and ocular mast cell lesions in the horse are reported to fit a histological diagnosis of both [490].

Diagnosis

With the exception of ocular discharge, minimal signs of pain are present in affected animals [440, 490, 491]. However, where there is conjunctival involvement, fluctuating chemosis and lid swelling may be evident, presumed to be a consequence of local vasoactive amine release. Reported lesions have all arisen at the limbus and extended into the cornea, and have varied in color from grayish-white to tan to pinkish-white [440, 490, 491]. They may be flat or irregular, and the surface may be roughened or smooth [440, 490, 491]. In one case, the mass appeared under the third eyelid [495]. Lesions may be rapidly progressive, and arise at multiple sites in the one eye (Figure 7.121). Given the small number of reported cases, no conclusions can be drawn regarding clinically differentiating mastocytosis from mastocytoma.

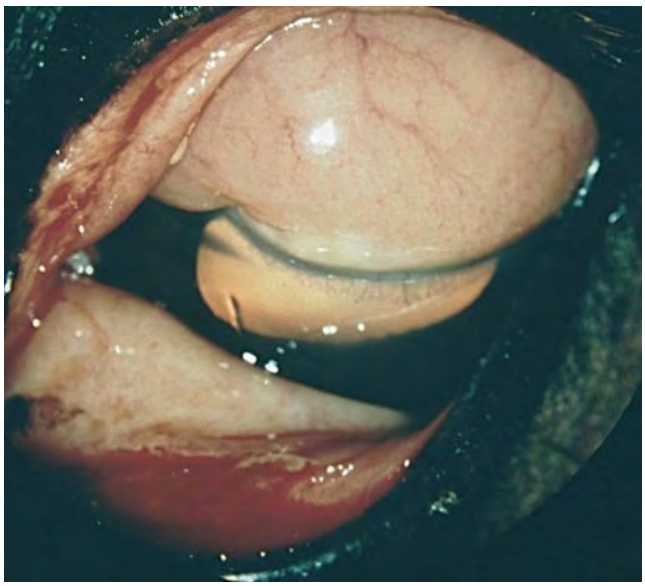


Figure 7.121 Mast cell tumors in the left eye of a 26-year-old Arab-cross gelding. Tumors are present in the corneosclera dorsally and within the ventronasal lower eyelid.

Differential diagnosis

Other neoplastic lesions (SCC, LSA, melanoma), as well as non-neoplastic lesions (nodular conjunctivitis, eosinophilic keratitis, granulation tissue, parasitic granuloma, orbital fat prolapse, corneal abscess, subconjunctival cyst) should be considered as differential diagnoses for mast cell lesions. Cytology and histopathology provide definitive diagnosis.

Treatment

Surgical excision via lamellar sclerectomy or corneosclerectomy was performed in five cases [440, 490, 491], with one of those cases receiving adjunctive strontium-90 therapy [494]. and two others receiving cryotherapy [556] at the time of surgery. In one case, the mass was surgically removed by lamellar keratectomy, and a defocused CO_2 laser used as adjunctive therapy [495].

Prognosis

Cutaneous mastocytosis may undergo spontaneous remission [492], which may also occur with ocular lesions. If the tumor is large and interfering with appropriate eyelid function, surgical excision is recommended to avoid secondary complications such as exposure keratopathy.

Although few cases have been reported, the prognosis following surgical intervention is likely to be favorable in most instances. Surgical excision alone in one case resulted in no recurrence for the duration of follow-up of 45 months [490]. However, excision alone resulted in recurrence and elective euthanasia at 3 months in another case [491]. The cases receiving adjunctive cryotherapy, radiotherapy, or CO_2 laser therapy had no reported recurrence, the last at 32 months after surgery [440, 494, 495]. Rapidly progressive lesions or lesions arising at multiple sites are likely to have a poor prognosis.

Lymphoma/lymphosarcoma

Prevalence

Corneoscleral LSA is rare in the horse, with 2 of 21 cases of ocular LSA presenting with corneal masses, one bilaterally affected and one unilaterally (Figure 7.122) [496]. In another study, 5 of 26 horses (19%) with ocular lymphoma had corneoscleral involvement [497]. A case of primary corneal lymphoma in the horse has been reported to develop following chronic IMMK and long-term topical anti-inflammatory therapy [498].

Pathogenesis

The pathogenesis of LSA is unknown [499], but ocular LSA is generally considered to be a local manifestation of the multicentric form of systemic LSA, which frequently involves peripheral lymph nodes and skin [496, 499]. However, ocular lymphoma may occur in isolation, or may be the first area of the body noted to be affected in multicentric lymphoma/LSA of the horse [497].

Since immunocytes are excluded from the normal cornea, primary corneal lymphoma is likely to be a consequence of

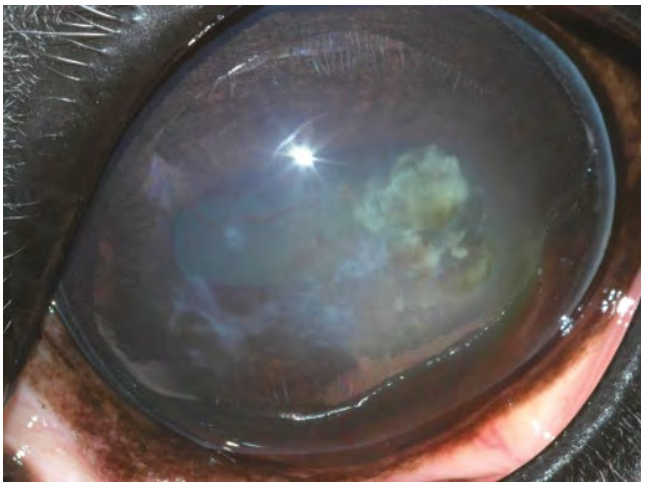


Figure 7.122 Corneal B-cell lymphoma was misdiagnosed initially as IMMK.

neoplastic transformation of lymphocytes involved in corneal immunoinflammatory disease. Concerns have been raised over lymphoid malignancy associated with calcineurin inhibitors used in immunosuppressive therapy in humans; however, evidence supporting this is very limited [500].

Diagnosis

Corneoscleral LSA was located in the temporal or ventrotemporal quadrants, crossing the limbus to include both cornea and sclera [496]. The masses were raised, smooth, firm, nonulcerated, pink to pink-white, and well vascularized. The presence of ocular pain or secondary uveitis was not reported. Corneoscleral involvement in ocular lymphoma presented as nodular or diffuse white-pink lesions [497]. In all cases, diagnosis is by biopsy.

Primary intracorneal lymphoma presents as intractable stromal keratitis. Diagnosis is on histopathology after keratectomy or enucleation.

Differential diagnosis

Other neoplastic lesions (SCC, hemangioma, angiosarcoma, melanoma, MCT), IMMK, eosinophilic keratitis, granulation tissue, and corneoscleral foreign bodies should be considered as possible differential diagnoses for corneoscleral LSA.

Differential diagnoses for primary intracorneal lymphoma are IMMK, corneal fibrosis, and CSI-SCC.

Treatment

Surgical excision with adjunctive therapy using mitomycin C and electronic surface brachytherapy was well tolerated and considered curative at 16 months post therapy in one case secondary to IMMK [498]. As a manifestation of systemic LSA, treatment for ocular LSA involves staging the overall disease state in the patient and treating accordingly. In the case of isolated ocular lymphoma with corneoscleral involvement, surgical excision of discrete lesions may be attempted, and

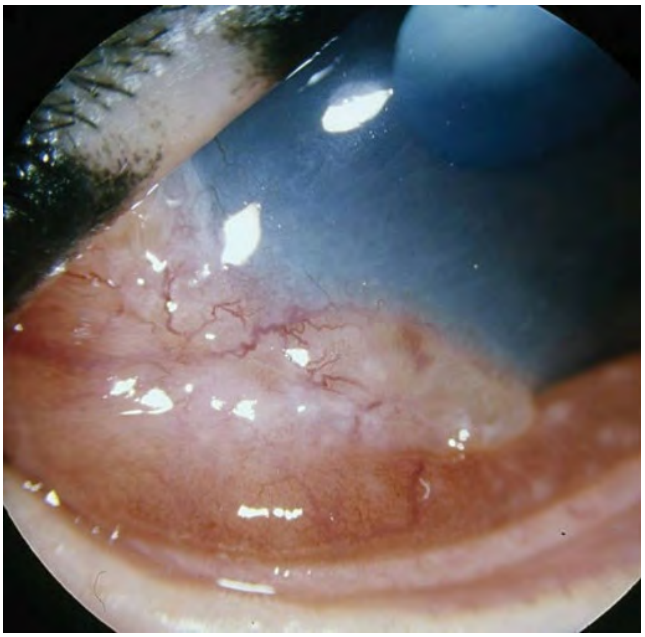


Figure 7.123 Corneoscleral histiocytic sarcoma in the right eye of a 12-year-old Cob gelding.

adjunctive therapy instituted at the discretion of the surgeon [497]. Eyes with extensive and diffuse ocular lesions or with primary corneal lymphoma should be enucleated.

Prognosis

The prognosis is grave if detection is delayed or there is peripheral lymph node or visceral organ involvement. Twenty of 21 horses with ocular LSA (eyelid, orbital, third eyelid, intraocular, and corneal) died or were euthanized within 6 months due to systemic disease associated with LSA lesions [496]. However, in a more recent report, four of five horses diagnosed with corneoscleral LSA experienced a favorable outcome (no evidence of recurrence or systemic involvement) following surgical resection or enucleation, and, in general, nodular lesions when compared to diffuse lesions were associated with a higher chance of a positive outcome [497].

Recognition of ocular lesions may precede identification of systemic signs, potentially enabling more rapid diagnosis and aggressive treatment of the latter [497].

Histiocytic sarcoma

Corneoscleral histiocytic sarcoma is a rare lesion in the horse, and it has been reported in a 12-year-old Cob-type gelding [501]. The lesion presents as a slowly progressive nodular limbal pink mass (Figure 7.123), superficially like SCC. Diagnosis is by biopsy and immunophenotyping of the round to spindle-shaped neoplastic cells. As in other species, the lesion may be one of a continuum of mesenchymal fibrous tumors, which includes

inflammatory lesions, for example, nodular fasciitis or episcleritis.

In the cases described, the mass extended posteriorly beyond the equator and the eye was enucleated. However, early or smaller lesions may respond to local corticosteroids or local excision.

Corneal surgery

Equipment

Appropriate equipment is vital to the ability to successfully perform corneal surgery. A focal light source and magnification, provided by either surgical loupes or an operating microscope, are essential. The specific instruments utilized for each procedure will vary, but a standard intraocular pack is generally sufficient (Table 7.14) [113].

Appropriate suture selection is equally important. Absorbable suture types are most common in veterinary ophthalmology, since removal is not necessary, whereas removal of nonabsorbable sutures may require a repeat general anesthetic episode. Absorbable sutures incite a greater local inflammatory response, however, which may be detrimental to maintenance of corneal clarity. All sutures indicated for use in the cornea are attached to a spatula needle (Figure 7.124) which splits the corneal lamellae and enables placement of sutures at the appropriate depth.

Patient preparation

Depending upon the surgical procedure, facility, patient condition and temperament, and comfort level of the surgeon, corneal procedures may be performed either under standing sedation with local anesthesia or under general anesthesia [113]. When performing procedures under standing sedation, local anesthetic blocks should be utilized to minimize eyelid movement (auriculopalpebral block), provide ocular surface anesthesia (frontal block, topical anesthetic administration), and minimize globe movement (retrobulbar block (see Chapter 1)). These same blocks are also appropriately used when the patient is under general anesthesia. Neuromuscular blocking agents may be used to fix the eye position under general anesthesia, provided mechanical ventilation is available.

Preparation of the surgical site begins with careful trimming of eyelashes and periocular hair. Dilute povidone iodine solution (Betadine) (1:50), baby shampoo, and sterile eyewash should be used to clean the ocular and periocular area [113]. Chlorhexidine, alcohol, and other surgical preparation solutions should not be used around the eye. Careful cleaning of the conjunctival fornices with cotton swabs soaked in dilute Betadine should be performed, with care taken to avoid damaging potentially compromised cornea. Topical local anesthetic should be administered prior to and following following surgical preparation in the standing sedated horse. Ointments should not be administered prior to or during corneal or intraocular surgery, as they are potentially damaging to intraocular tissues, can become entrapped in a sutured wound, and may interfere with proper surgical technique [502].

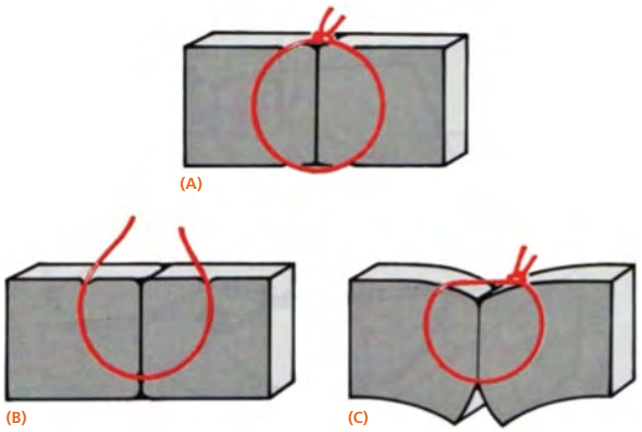


Figure 7.124 Proper suture depth placement during corneal surgery. (A) Full-thickness suture placement may result in leakage, seeding of bacteria into anterior chamber, or epithelial downgrowth. (B) Appropriate deep stromal placement of corneal sutures. (C) Too shallow placement of corneal sutures results in posterior wound gaping and increased possibility of wound dehiscence and scar formation.

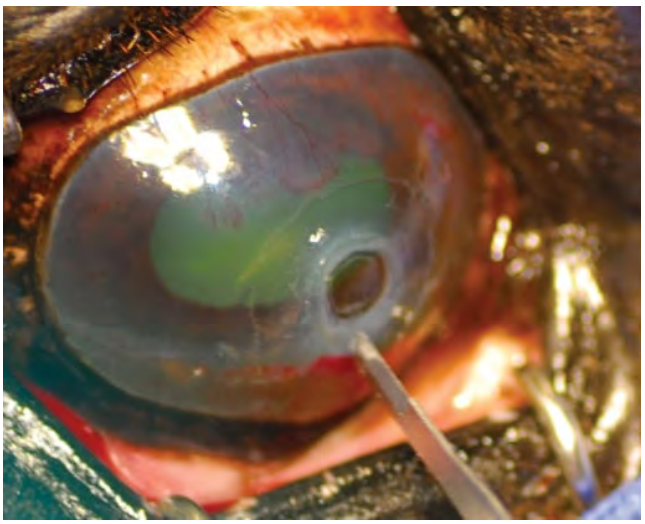


Figure 7.125 Debriding of the epithelium around a corneal ulcer with a microsurgical blade during surgery.

Surgical procedures

General considerations

Epithelial debridement

Even if healthy, the epithelium surrounding corneal wounds should be debrided with sterile cotton-tipped applicators, cellulose swabs, or a Beaver #64 microsurgical blade (Figure 7.125). This helps to prevent down-growth of the epithelium into the wound margins, which can lead to wound leakage and dehiscence and stimulates vascular ingrowth. It also aids adhesion between the conjunctival stroma and an ulcer bed during a conjunctival graft surgery. Frequent irrigation

(i.e., every 20–30 seconds) of the epithelium with a sterile ocular-specific irrigating solution, such as BSS, throughout the procedure is essential to prevent surface drying and epithelial devitalization [113].

Suture placement

When placing sutures in the cornea, sutures should be placed 1–2 mm apart at a depth of 75–90% of the corneal stroma [403, 410]. If sutures are placed too superficially, the internal aspect of the wound will not be apposed and the healing rate inhibited. If placed too deep such that the needle and suture penetrate the endothelium, wound leakage, ocular hypotony, and intraocular infection may occur. When suturing a conjunctival or amnion graft over a corneal wound, the first bite should be through the grafting material and the second bite into the cornea. Initial cardinal sutures should be placed through the distal end of the conjunctival or amnion graft. Sutures at the edge of a keratectomy wound can be placed more superficially (i.e., half to two-thirds thickness of the stroma). Surgeon's knots are recommended in corneal surgery.

Anterior chamber maintenance

When full-thickness corneal wounds are present preoperatively or will be made intraoperatively, formation and maintenance of the anterior chamber is critical for the health of the eye and for accurate surgical correction of the corneal defect. Sterile viscoelastic materials are used, because they possess balanced viscosity, cohesiveness, coatability, pseudoplasticity, and the elasticity necessary to maintain the shape of the globe and protect the endothelium during the surgery [113, 503]. In theory, viscoelastics are removed from the anterior chamber at the conclusion of surgery [503], but clinical experience is that leaving viscoelastics in the anterior chamber of horses seems to have more benefits than disadvantages, and they can be left *in situ.*

Hemostasis

Topical administration of dilute (1:10,000) epinephrine is helpful for maintaining hemostasis by vasoconstricting conjunctival and corneal vessels during manipulation of the conjunctiva and cornea. This results in a bloodless surgical field and prevents hemorrhage within the anterior chamber. Wet-field low-voltage cautery may also be used to cauterize conjunctival vessels, "erase" the cornea prior to making an incision, and cauterize iris hemorrhage during iris prolapse repair.

Direct corneal suturing

Indications

Direct corneal suturing may be performed to repair wounds where the margins can be accurately apposed with minimal tension and there is no tissue loss—such as partial- or full-thickness corneal, corneal, scleral limbal lacerations, or very small (less than 1 mm) corneal perforations [113, 145, 146]. If tissue at the margins of a corneal wound is necrotic, infected, malacic, or appears devitalized in any way, this abnormal tissue should be removed and a grafting procedure considered.

Procedure

Epithelium surrounding the wound should be debrided with a blade. Full-thickness wound edges may be apposed with absorbable 7-0 to 9-0 suture in a simple interrupted, simple continuous, or double saw-toothed pattern with sutures placed at 75–90% depth [113, 399, 403]. A conjunctival graft can be placed over the site of corneal, scleral, or limbal repair if a vascular supply, physical support, and antiproteases are desired, but this is not always necessary. To ensure that watertight wound closure has been achieved, a Seidel's test should be performed by applying concentrated fluorescein stain, which will appear yellow-orange, to the corneal surface. Aqueous humor leakage will dilute the fluorescein, causing a focal change in color from yellow-orange to green. If a suture is responsible for the aqueous leak, then that suture must be replaced.

Post-operative care

Medical therapy with topical antibiotics, a therapeutic mydriatic/cycloplegic agent, and a systemic NSAID are indicated. If the wound is partial thickness, fresh, and has no signs of infection, prophylactic antibiotics alone may be appropriate, but it is generally recommended to also utilize topical mydriatic/cycloplegics and antiproteases such as serum when the corneal condition requires suturing. Full-thickness wounds or perforations should be treated with a therapeutic topical antibiotic with good intraocular penetration to provide greater protection against endophthalmitis. Supplementary systemic antibiotic administration may be indicated.

Complications

Complications that may follow direct suturing of a partial-thickness corneal wound include infection, dehiscence, excessive scar formation, and altered corneal curvature (astigmatism). Additional complications that may be encountered following repair of a full-thickness corneal wound include reperforation with subsequent aqueous humor leakage, iris prolapse, or globe collapse, and complications secondary to severe anterior uveitis (synechiae, cataract, and ultimately phthisis bulbi) [145, 146].

Superficial keratectomy

Indications

SK is the surgical removal of the corneal epithelium, BM, and anterior stroma, and is indicated to remove neoplastic [113], dysplastic (dermoid) [109], or infected corneal tissue [307, 417]. to promote healing in some instances of IMMK [200], or in managing nonhealing erosion [373]. The resulting wound bed may be left to heal by second intention as a sterile ulcer. However, this is not generally recommended if the keratectomy site received irradiation as part of the therapy. A conjunctival or amnion graft may be performed over the keratectomy site if the depth of the keratectomy is greater than half the corneal

thickness, if the diseased tissue cannot be entirely removed, or if other concerns regarding ability of the wound to heal are present (e.g., deficient tear production or keratomalacia) [403]. Conjunctival grafting will increase the likelihood of scarring slightly more than an amnion graft.

Complete incisional keratectomy The profile of the area of cornea to be removed is outlined to the required depth with a dermal biopsy punch, corneal trephine, diamond knife, or microsurgical blade in a round, square, or triangular shape [113]. Fixed-depth corneal knives can be useful for this. The edge of the cornea to be removed is grasped with microsurgical (e.g., Colibri) forceps, and lamellar dissection of the entire incised area is performed with either a Martinez lamellar corneal dissector, a crescent blade, or a Beaver #64 microsurgical blade angled parallel to the stromal lamellae. The excised tissue can then be submitted for histopathology and, if appropriate, bacterial and fungal cultures.

Partial incision keratectomy A small corneal incision is made to the appropriate depth, adjacent to the involved portion of cornea that is to be removed [113]. The width of the incision should allow a microsurgical blade, a crescent blade, or lamellar corneal dissector to be inserted between the underlying corneal lamellae, following which complete lamellar dissection of the involved corneal tissue is performed. Corneal section scissors are then inserted through the initial incision and underrun cornea to excise and complete the keratectomy.

General anesthesia is frequently preferred for surgical procedures of the equine cornea, but SK can be performed by experienced microsurgeons with the horse standing under heavy sedation (e.g., detomidine 0.01 mg/kg) [113]. Because the partial incision keratectomy requires only a single perpendicular corneal incision, it is the procedure of choice in the standing horse. Use of regional anesthetic (topical ocular anesthetic; auriculopalpebral, frontal, and retrobulbar nerve blocks; see Chapter 1) and other methods of restraint (e.g., humane twitch) greatly facilitate the procedure.

Post-operative care

Topical antibiotics should be administered as for a corneal ulceration, with selection depending upon disease process (i.e., prophylactic versus therapeutic antibiotics, with or without antifungal medications). Topical mydriatic/cycloplegic agents, topical antiproteases, and systemic NSAID administration are also necessary. If treating corneal neoplasia, adjunctive therapies may be indicated, such as beta irradiation, CO_2 laser, or topical chemotherapy.

Complications

Depending upon the underlying disease process for which an SK is performed, complications are generally minimal. Such complications include delayed healing, infection and deep stromal involvement, keratomalacia, perforation, recurrence of the original lesion, and increased corneal opacification in the formation of excessive scarring, pigmentation, or granulation tissue formation.

Thermal keratoplasty

Low-voltage electrocautery can be effective for treating corneas with pronounced corneal edema and bullous keratopathy (Figures 7.126 and 7.127) [271, 504]. A handheld thermal cautery unit is used to make multiple, small (</= 1 mm in diameter), superficial burns throughout the affected area. The cautery unit is applied just until the slightest degree of contraction of the collagen fibrils is observed [271]. This technique alters the epithelium and stroma to reduce corneal edema [504]. Thermal keratoplasty seems to be more effective in the horse at reducing corneal edema when the edema is secondary to endothelial



Figure 7.126 Corneal edema is present in an eye that has uveitis and had recent phacoemulsification cataract surgery 2 weeks earlier.

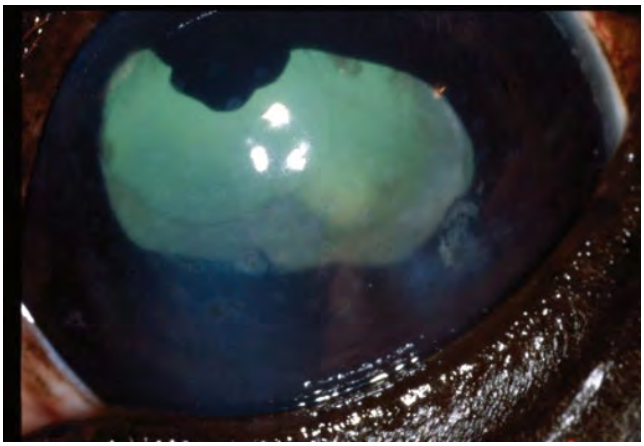


Figure 7.127 Two weeks post thermal keratoplasty, the edema in the eye in Figure 7.126 is clearing.

disease caused by uveitis than edema secondary to endothelial disease caused by glaucoma.

Diamond burr debridement

The diamond burr jewelry cleaning tool is useful for debriding abnormal epithelium in noninfected corneal erosions in horses, removing the degenerate anterior stroma in eosinophilic keratitis, and removing subepithelial calcium in superficial mineralization (calcific band keratopathy). It can be easily accomplished in the standing sedated horse using topical anesthesia. The round 3.5-mm-diameter pterygium burr is best for removing epithelium and devitalized tissue, where BM or anterior stroma is not to be removed. Healing time post burr debridement averaged 15.5 ± 9.3 days in one study of 60 horses with nonhealing erosions with no evidence of corneal infection on cytology [280]. Complications of diamond burr debridement are rare.

Conjunctival grafts

Indications

Conjunctival grafts are indicated for corneal diseases such as keratectomy sites, deep ulcers [505], melting ulcers, and descemetoceles [82, 113, 403], as well as putatively immune-mediated [200]. and superficial nonhealing ulcers [273] in which the underlying pathogenesis may not be definitively known prior to surgery.

Conjunctival grafts or transplants can be transposed and sutured onto the cornea to provide sufficient tissue to strengthen weakened corneas, but they are not as strong as corneal grafts, and both procedures may be combined in some horses. Conjunctival autografts contain limbal stem cells, blood vessels, and lymphatics, thus offering significant antibacterial, antifungal, antiviral, antiprotease, and anticollagenase effects. With conjunctival grafts, PMNs, antibodies, plasma, and α-2-macroglobulins are immediately placed directly in the corneal ulcer bed [82, 95, 294]. Systemic antibiotics can enter the ulcer site at higher levels through leakage from the conjunctival graft vasculature. The fibrovascular or deeper stromal layer of the conjunctival transplant (Tenon's capsule) offers fibroblasts and some collagen with which to begin rebuilding the corneal stroma. Conjunctival grafts will result in various sizes and degrees of corneal scars [82, 294]. Scarring can be minimized, however, by removal of necrotic cornea with keratectomy prior to graft placement, and may respond to topical medical therapy when corneal healing is complete. Pigment at the limbus will be transposed to the corneal surface if the conjunctiva used for the graft is pigmented.

Conjunctival autografts are more difficult to perform than nictitating membrane flaps, but they are simpler than corneoconjunctival and corneoscleral transpositions, and PK surgeries [82, 95, 294]. They are also easier to perform in the horse than in other species, because the horse has an extensive reserve of very mobile bulbar conjunctiva. Conjunctival autografts from either bulbar or palpebral conjunctiva should be thin, and they should not include Tenon's capsule or the bulbar fascia [82, 95, 294]. Any Tenon's capsule present should be stripped or cut from the graft so that the graft easily lies over the corneal defect before suture placement. Inclusion of Tenon's capsule may contribute to surgical failure by increasing post-operative traction on the transplanted conjunctival tissue. Conjunctival grafts should have tension-relieving sutures placed at the limbus to prevent the graft pulling away from the ulcer bed prematurely [82, 95, 294]. Melting ulcers should always be stabilized with medical therapy, if possible, before graft placement to prevent protease digestion of any absorbable sutures to avoid premature graft release [82, 95, 294]. Leakage of aqueous humor through a corneal perforation must be identified with a Seidel's test and corrected with a biomaterial such as Biosist, Acell, amnion, or cornea prior to conjunctival graft placement, or the graft may leak and retract prematurely.

Variations of conjunctival grafts include pedicle, bipedicle, bridge, hood, 360-degree, island, and tarsopalpebral grafts, with the type selected depending upon the extent and location of the disease process. Gundersen flaps are conjunctival pedicle grafts placed over severely edematous cornea to aid resolution of edema by absorption of edema fluid into conjunctival graft vessels [82].

Pedicle grafts are most commonly performed in the horse. They are dissected from conjunctiva between the limbus and fornix, and rotated out on the cornea, with the proximal end of the graft having the conjunctival blood vessels that perfuse the graft [82, 95, 294]. Minimal healthy cornea is covered by pedicle grafts, which allows evaluation of uninvolved cornea and intraocular structures. Both centrally and peripherally located cornea lesions may be effectively treated. Bipedicle and bridge conjunctival grafts are used for larger central or linear corneal ulcers lesions with a greater proportion of diseased and uninvolved cornea covered. Hood grafts effectively cover smaller peripheral corneal and limbal lesions, and generally only slightly affect the ability to visualize the remainder of the cornea or intraocular structures. In contrast, 360-degree grafts utilized for extensive corneal disease cover the entire corneal surface, blinding the patient during the recovery period and eliminating the ability to evaluate intraocular structures [82, 95, 294]. Free island grafts are used as a source of collagen, as they lack a blood supply, but are therefore rarely indicated in the management of serious equine corneal disease. Tarsopalpebral grafts are harvested from the palpebral conjunctiva, making them more susceptible to tension from eyelid movement and compromised blood supply from the frequently extensive length of the graft. In the absence of sufficient viable bulbar conjunctiva, however, they may be useful. Overall, graft selection is based upon the location and size of the lesion, ease of access to prepare the graft site, proximity to the limbus, and presence of conjunctival pigmentation [82, 95, 294, 410]. The ideal orientation for grafts is in a dorsal-ventral direction so as to decrease drag associated with eyelid movement, with the pedicle(s) as short as possible.

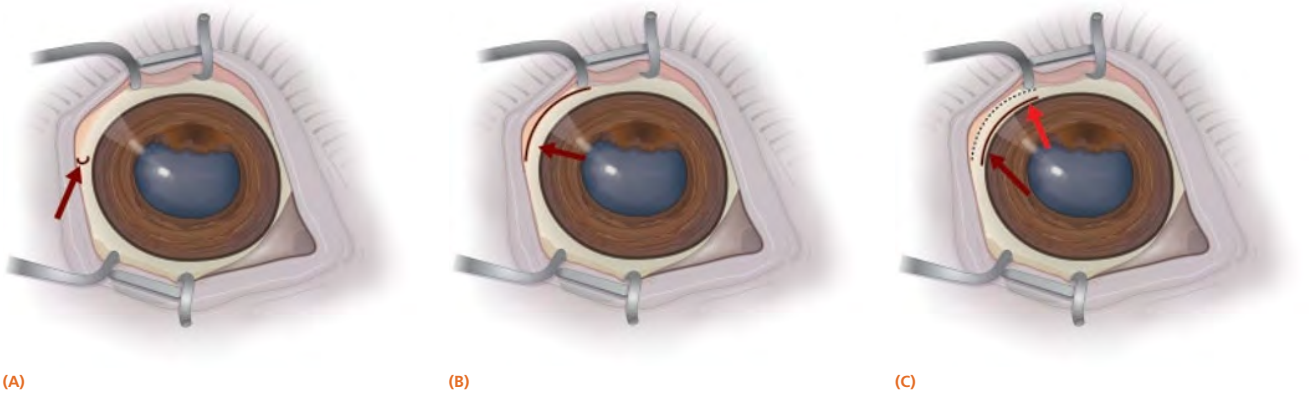


Figure 7.128 Surgical steps for performing a conjunctival pedicle graft. **(A)** Location of starting incision for conjunctival graft. The bulbar conjunctiva is grasped 1 mm posterior to the limbus with Colibri forceps, and a snip incision is made with scissors. **(B)** Once blunt dissection of the entire graft is complete, tenotomy scissors are used to make a cut parallel and 1 mm posterior to the limbus. **(C)** For a pedicle graft, a cut 1–2 mm wider than the wound to be covered is made at the tip of the incision, directed toward the fornix. A third cut parallel to the initial limbal cut and directed from the tip toward the base of the graft is made, completing the rotational pedicle graft. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

Procedure

The epithelium surrounding the corneal ulcer wound edges is debrided, and necrotic or infected tissue removed with a blade and corneal scissors (online Figures 7.87, 7.88, 7.89, and 7.90, 7.114, 7.115, 7.116, 7.117, 7.144, 7.145, 7.146, 7.147, 7.152, 7.153, 7.154, 7.159, 7.160, 7.161, and 7.162) [113]. Where indicated, any missing cornea is replaced with a larger diameter frozen corneal donor graft and sutured in place prior to conjunctival graft mobilization. Once the appropriate conjunctival graft type and harvesting location are selected, the selected bulbar conjunctiva is grasped 1 mm posterior to the limbus with 0.12- to 0.3-mm Colibri forceps, and a snip incision is made at the limbus, with curved, blunt-tipped Westcott tenotomy scissors (Figure 7.128A). The tip of the scissors is inserted through the incision between the conjunctiva and the deeper, closely adherent fibrous connective tissue, Tenon's capsule. Tenon's capsule is separated from the conjunctiva by blunt dissection along the graft length. Once blunt dissection of the entire graft length is complete, and without regrasping with the Colibri forceps, Westcott tenotomy scissors are used to make a cut parallel to and 1 mm posterior to the limbus along the graft length (Figure 7.128B, C). For a pedicle graft, a cut is then made at the distal tip of the incision, perpendicular to the limbus and directed toward the fornix. This second cut should extend 1–2 mm wider than the wound to be covered. A third cut parallel to the initial limbal incision and directed from the tip toward the base of the graft is made, completing the rotational pedicle graft (Figure 7.128D). Given the single source of blood supply, the base of a pedicle graft should be wider than the tip, and the graft should not be rotated more than 45 degrees to prevent a reduction in vascular perfusion of the graft [82, 95, 113, 294, 410].

A bipedicle graft is created by harvesting a graft in a similar manner, so the base of the second graft is located 180 degrees to the base of the first and the tips of the graft meet over the lesion (Figure 7.129).

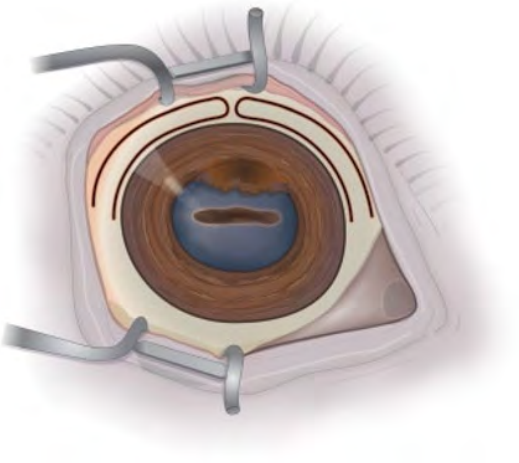


Figure 7.129 A bipedicle graft is created by harvesting a graft in a similar manner, so the base of the second graft is located 180 degrees to the base of the first and the tips of the graft meet over the lesion. (*Source*: Illustration by Samantha J Elmhurst BA Hons/LivingArt.)

A bridge graft is created by an initial cut parallel to the limbus extending 180 degrees around the limbus, with a second parallel cut near the fornix creating a graft that is 1–2 mm wider than the lesion (Figure 7.130).

To create a hood or advancement graft, an incision parallel to the limbus on either side of a peripheral lesion is made, and incisions perpendicular to the limbus are made extending posteriorly on either side to enable the graft to be slid over and sutured to the corneal defect (Figure 7.131).

Island grafts are harvested from any available conjunctiva, whereas tarsopalpebral grafts are harvested in a manner similar to pedicle grafts, with the base anchored near the eyelid margin and the tip of the graft originating from the conjunctival fornix (Figure 7.132). Regardless of graft configuration, 7-0 to 9-0 absorbable (polyglactin 910, polyglycolic acid) or nonabsorbable

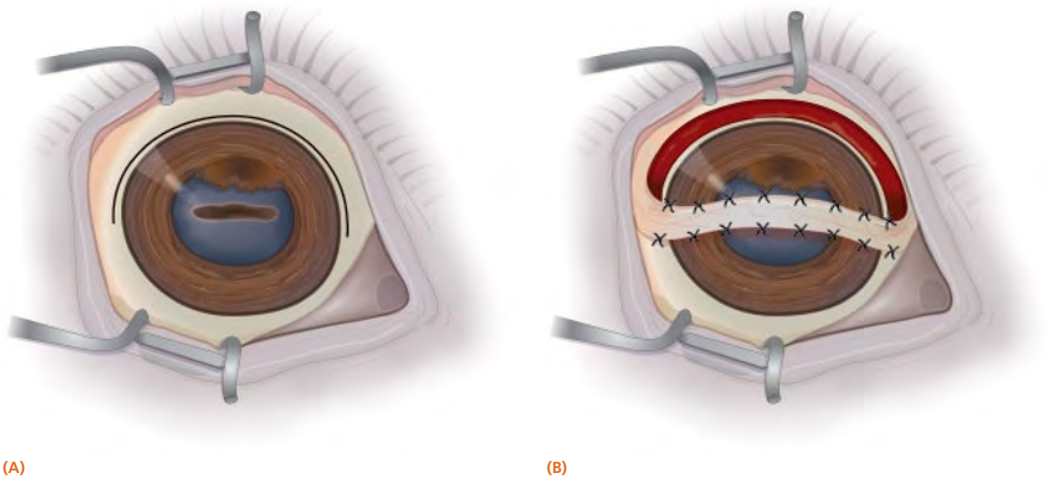


Figure 7.130 A bridge graft is created by an initial cut parallel to the limbus, extending 180 degrees around the limbus, with a second parallel cut near the fornix, creating a graft that is 1–2 mm wider than the lesion (A), then extending the entire "bridge" to cover the lesion (B). (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

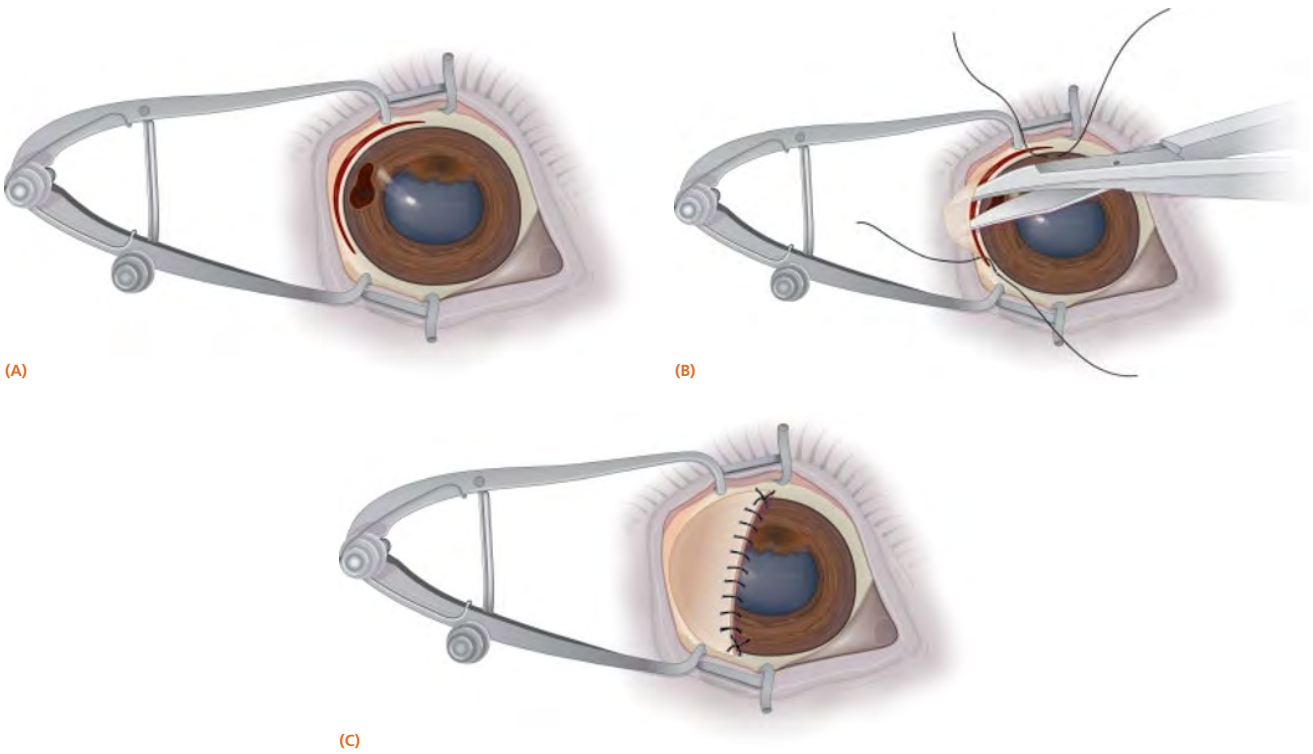
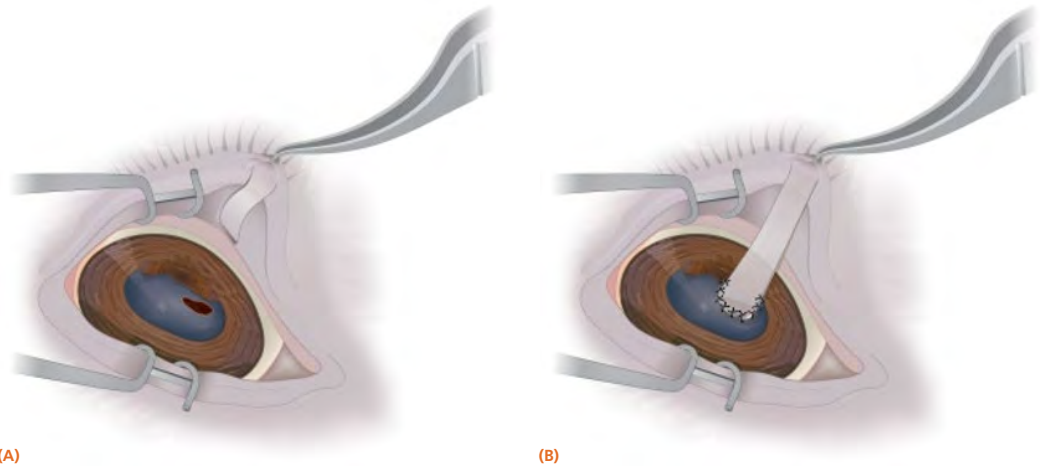


Figure 7.131 A hood or advancement graft is created by making an incision parallel to the limbus on either side of a peripheral lesion (A, B); then a perpendicular incision extending posteriorly is made on either side to enable the graft to be slid over the defect (C). (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

(monofilament nylon) suture material in a simple interrupted, simple continuous, or double saw-toothed continuous pattern is used to anchor the graft to the cornea in horses [113]. As the proteases in the PTF can digest the absorbable sutures used in conjunctival graft surgery, larger diameter suture may be best for the horse.

Specific comments on conjunctival graft procedures in the horse

The conjunctival graft should be made thin but not so thin it is white on placement [82, 95, 113, 294, 410]. The conjunctival epithelium is very sensitive to mechanical trauma such that when manipulating or holding conjunctival tissue during conjunctival



(A) (B)

Figure 7.132 Tarsopalpebral grafts are harvested in a manner similar to pedicle grafts, but with the base anchored near the eyelid margin (A) and the tip of the graft originating from the conjunctival fornix instead of the bulbar conjunctiva (B). (*Source*: Illustrations by Samantha J Elmhurst BA Hons/ LivingArt.)

graft creation, only the stroma should be gently held with the corneal forceps. Tears in the flap should be sutured. Conjunctival graft fibrosis and failure may be associated with iris prolapse under the flap if there is a corneal perforation with leakage of aqueous humor. Perform a Seidel's test on every deep ulcer prior to graft placement. Aqueous humor leakage induces fibroplasia of the corneal side of the graft such that this surface becomes thickened and fibrotic and will not completely adhere to the wound. The graft may still partially adhere, but vascularization of the cornea may fail if there is a corneal leak. Graft bruising manifesting as purple areas of the graft may indicate flap ischemia [82, 95, 113, 294, 410]. A white graft has become avascular and may prematurely retract. Graft bulging may indicate iris prolapse under the flap and can be monitored by assessing IOP and Seidel's test. Continue antiproteinases after graft placement, or absorbable sutures may be dissolved prematurely. *Streptococcus* spp. and *Aspergillus* spp. can melt a flap due to the induction of an aggressive horse proteolytic response, and sudden changes in conjunctival graft integrity should alert the clinician to possible infection [82]. The conjunctiva surrounding the donor site may be sutured in a simple continuous pattern. A partial temporary tarsorrhaphy should be placed to protect the ocular surface from injury during recovery from general anesthesia.

Post-operative care

Factors increasing the risk for failure include improper debridement of the surrounding cornea, which may allow epithelium to grow under the graft and compromise attachment; inadequate removal of any Tenon's capsule; inadequate size of the graft, which may increase tension and dehiscence; failure to identify an aqueous humor microleak; improper suture placement; and failure to control infection. It should be noted that excessive removal of Tenon's capsule may render the graft avascular and ineffective [410]. Topical antibiotics, antifungals, and a therapeutic mydriatic/cycloplegic, as well as systemic antibiotics, antifungals, and NSAIDs should be administered as appropriate for the disease condition being treated. Topical antiprotease medications should be continued, despite the direct supply of plasma from the graft to the cornea, in order to prevent degeneration of the absorbable sutures by tear film proteases. In the first days post-operatively, the graft should be well vascularized and apposed, because the risk of dehiscence is greatest within the first week following surgery. As the disease process resolves, most consistently indicated by increased comfort and decreased anterior uveitis and often accompanied by decreased vascularization of the graft, medications may be reduced. A minimum of 8–10 weeks post-operatively, the pedicle portion of the graft is trimmed, allowing incorporation of the graft into the cornea and minimizing scar formation [144]. Trimming of the graft is accomplished with or without sedation, utilizing topical ocular anesthetic and topical phenylephrine or dilute (1:10,000) epinephrine for vasoconstriction.

Where a temporary tarsorrhaphy is in place, the perfusion and viability of the graft can be assessed using transpalpebral Doppler ultrasongraphy.

Corneoconjunctival/corneoscleral transposition

Indications

Corneoconjunctival (and corneoscleral) transpositions are autologous, partial-thickness (lamellar) corneal grafts in which the peripheral cornea is grafted into the axial cornea, maintaining its conjunctival (or conjunctival and scleral) vascular attachments (Figures 7.100 and 7.101). Transposition of adjacent sclera increases the tectonic strength of the peripheral cornea, but the tectonic strength of the remaining scleral bed is decreased and scarring of the peripheral cornea is increased, making corneoconjunctival transpositions the more commonly performed procedure. A corneoconjunctival transposition is

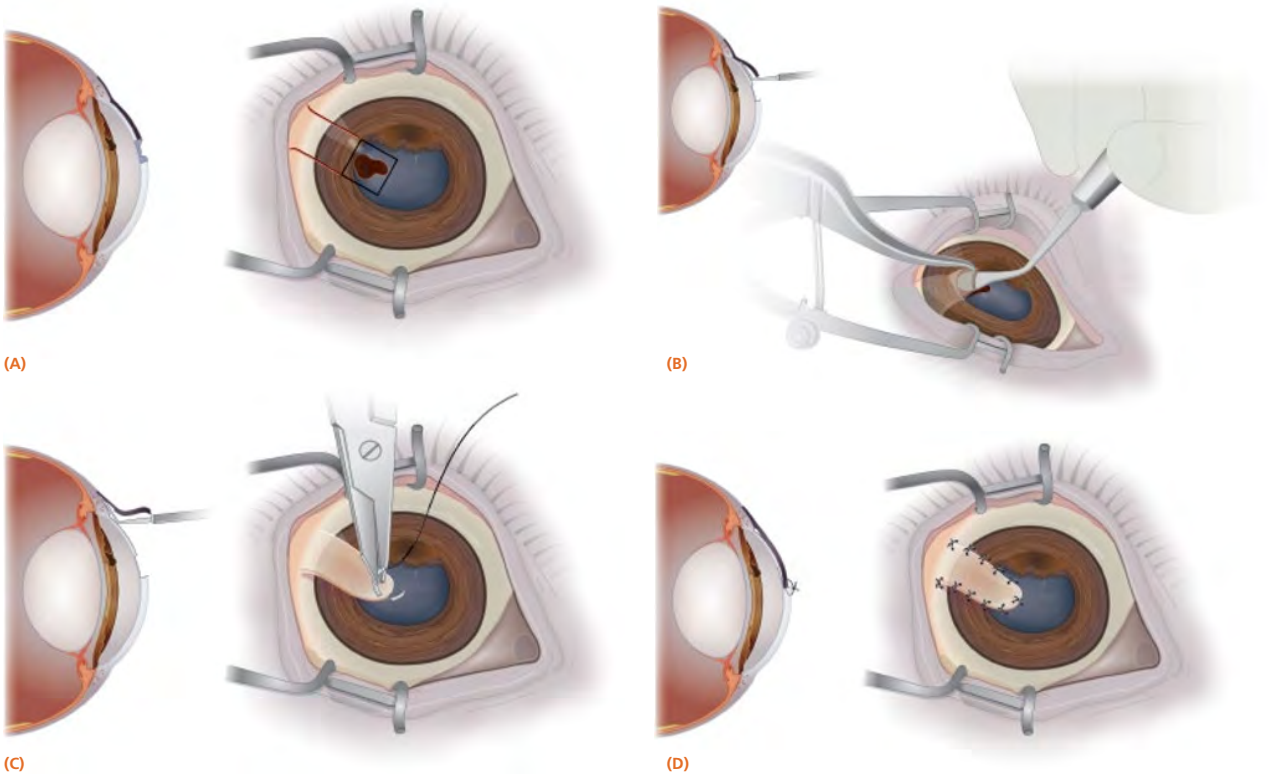


Figure 7.133 Surgical steps for performing corneoconjunctival transposition. **(A)** A #64 microsurgical blade is used to create two diverging, half-thickness incisions from the medial and lateral edges of the wound toward the limbus. **(B)** A #64 microsurgical blade or a Martinez lamellar corneal dissector is used to separate the corneal lamellae toward the limbus, at half thickness of the cornea. **(C)** Underlying Tenon's capsule is dissected from the conjunctiva, and the conjunctiva is separated from the superficial sclera, which allows sliding of a flap of cornea and conjunctiva (with or without sclera) axially to cover the defect. **(D)** Sutured corneoconjunctival transposition. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

indicated for axial stromal defects less than 30% of the corneal diameter [294, 410], with the goal of producing less scarring than occurs with a homologous corneal graft. While maintenance of a healthy vascular supply is one of the advantages of this type of sliding graft, the inability to sever the vascular pedicle, as is done with conjunctival grafts, can lead to increased scarring. Relative to a full-thickness homologous corneal graft, corneoconjunctival grafts provide less structural support, since they can only be partial thickness. Furthermore, corneoconjunctival transposition procedures damage normal peripheral cornea, which can be an additional disadvantage.

Procedure

The recipient site is prepared by debridement of the epithelium and necrotic or infected tissue. Ideally, the graft will be anchored dorsally and is created by using a Beaver #64 blade to score two diverging, half-thickness incisions from the medial and lateral edges of the wound toward the limbus (Figure 7.133) [113]. The incisions are extended at least 1 mm into the conjunctiva (or sclera if performing a corneoscleral transposition). Colibri forceps are used to grasp the axial edge of the defect (tip of the graft), and a Beaver #64 microsurgical blade or a Martinez lamellar corneal dissector is used to separate the corneal lamellae toward the limbus, at half thickness of the cornea (Figure 7.133A, B). Westcott tenotomy scissors are used to bluntly dissect underlying Tenon's capsule from the conjunctiva and to separate the conjunctiva from the limbus (or superficial sclera from deeper sclera at the limbus), allowing sliding of a flap of cornea and conjunctiva (with or without sclera) axially to cover the defect (Figure 7.133C). Simple interrupted sutures of 8-0 or 9-0 polyglactin 910 (or 9-0 to 10-0 nylon) are placed from the donor cornea to the recipient wound bed, starting at the distal tip of the graft, and either simple interrupted, simple continuous, or double saw-toothed suture patterns are placed between the conjunctiva and cornea, extending toward the limbus (Figure 7.133D).

Post-operative care

Post-operative care is similar to that for conjunctival grafts, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic/cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are still necessary post-operatively, although blood-derived antiproteases are reaching the graft through direct vascular supply. As the disease process resolves, most consistently indicated by

increased comfort and decreased anterior uveitis, medications can be reduced, and corneal clarity will gradually be restored. In contrast to conjunctival grafts, trimming of the vascular supply to the graft is not possible, because it is incorporated into the peripheral cornea.

Complications

Complications associated with corneoconjunctival (corneoscleral) transposition include dehiscence, scar formation, and uncontrolled infection. Few reports on use of these grafts in horses exist, and of two horses receiving this surgery for ulcerative iris prolapse, one became phthisical and one was blind [193].

Amniotic membrane transplants: the "self-sacrificing or disposable dressing"

AMT is an effective therapy for many ocular surface pathologies in the horse. It facilitates the migration and differentiation of epithelial cells and the reinforcement of cellular adhesion of those same cells, and will modulate stromal scarring and decrease ocular surface inflammation [1, 406–480, 506–512]. It has also been shown to have antiangiogenic and antimicrobial effects [406, 408]. This relatively acellular material is very strong and has become a widely used tissue for ocular surface reconstruction in human ophthalmology [406–408]. Its uses and indications are constantly evolving and expanding in both human and veterinary ophthalmology. For example, it can be used in severe melting disease of the ocular surface in horses, where traditional conjunctival grafting would render a sighted or a potentially sighted globe blind due to extensive post-operative fibrosis. AMT should be considered as a primary surgical option for horses with destructive keratitis.

AMTs should be thought of as "disposable dressings" which allow tear film proteases and corneal microbes to attack the amnion to ameliorate their direct effects on the horse cornea. The AMT then "sacrifices" itself and retracts on its own, or can be surgically removed 7–10 days post-operatively, to be "disposed" of to allow the inherent corneal healing of the horse to continue. Additionally, AMT can be used as a substrate for the growth or expansion of epithelial cells for transplantation [406, 506–509]. It can be used to cover the surgical site following SK, for example, for SCC, to avoid infection, minimize pain, and limit scarring and symblepharon formation [408].

Other biological and biosynthetic materials, such as porcine small-intestinal submucosa and A-cell, may also be used for disease processes in which amnion is indicated [82, 406], although no comparative study of the benefits of these against amnion exist at this time.

Principles of use

Amniotic membrane consists of three basic layers: an epithelial monolayer, a BM, and a thick, avascular, and sparsely cellular stromal matrix. The epithelium is usually damaged and rendered nonviable by the preparation and storage procedures, so it is not usually a consideration in its therapeutic use [406]. Amniotic BM has a network of compacted reticular fibers, giving it considerable tensile strength, good structural integrity, transparency, and elasticity, and which is known to promote epithelial cell migration, adhesion, and differentiation. Like the BMs of normal cornea and conjunctiva, that of amnion consists primarily of types IV, V, and VII collagen, and fibronectin. Laminins 1 and 5 present in amnion BM facilitate corneal epithelial cell adhesion and anchorage to the stroma [1, 406–408, 506–509]. Amnion is a superior substrate for the growth and proliferation of epithelial cells and their progenitors, as it allows them to maintain their normal morphology and differentiation, prevents epithelial cell apoptosis, prolongs their lifespan, and, in the case of progenitor cells, maintains their clonogenicity [406]. These properties allow amnion to be placed surgically onto recipient corneas to replace limbal stem cell deficiencies, facilitate epithelialization of long-standing ulcerations, and repair corneas damaged from a variety of insults [406].

The stromal side of amniotic membrane consists of a loose matrix of fibroblasts, PGs, glycoproteins, and collagen, and is rich in fetal hyaluronic acid [406]. Several growth factors have been identified in this stromal matrix, including hepatocyte growth factor, TGF-β, EGF, and KGF, all of which may contribute to scar reduction. Amnion has been shown to suppress TGF-β signaling, and the proliferation and myofibroblastic differentiation of corneal, limbal, and conjunctival fibroblasts [406]. This action is a principal driver of scar reduction after ocular surface reconstruction and injury. Several amnion stromal growth factors may also support re-epithelialization following AMT [406]. The amnion stromal matrix also has the ability to suppress the expression and activity of proinflammatory and other cytokines originating from the ocular surface epithelia, and which are major drivers of ocular surface disease. These include IL-1α, IL-2, IL-8, interferon λ, tumor necrosis factors (TNF) α and β, basic fibroblast growth factor, and PDGF [406]. The stromal matrix also decreases ocular inflammation by attracting and sequestering inflammatory cells on the diseased ocular surface, which then undergo rapid apoptosis. Additionally, natural inhibitors of MMP-2 and MMP-9, nitric oxide synthase, and potent anti-inflammatory cytokines including IL-10 and IL-1 receptor antagonists have been found in amniotic stroma [406]. Various antiangiogenic substances have also been recognized in amnion [406–408].

There is evidence that amniotic membrane has diverse nonspecific antimicrobial and antiviral properties [406, 509]. The chorioamnion is an effective barrier to the spread of bacteria from the mare to the fetus [1, 406]. Additionally, various compounds promoting antimicrobial immunity can be found in amnion, including various interleukins, interferons, TNF-α, activin A, inhibin A, pre-B cell colony-enhancing factor, and leukemia inhibitory factor [406].

A reference identification map of the equine AMPs has been produced and 149 different proteins were identified [513]. Equine amnion contains lumican and dermatopontin which

may influence corneal healing [513]. Lumican has been found in migrating corneal epithelial cells during wound healing. It may play a role in epithelial cell migration and adhesion and also can modulate inflammation during wound healing. Lumican-deficient animals develop bilateral cornea opacity.

Dermatopontin has multiple potential actions in the cornea. It induces fibroblast cell adhesion, probably via integrin-type receptors. Dermatopontin accelerates collagen fibrillogenesis and modifies newly formed collagen fibrils. It is present in the developing wound matrix, and is the first nonintegrin protein that has been shown to activate fibronectin [513]. Dermatopontin also enhances the hyaluronic acid accumulation in the stromal ECM [513].

Indications

AMTs have protective functions in corneas that have been functionally and structurally compromised by disease or following surgery. The anti-inflammatory and antiangiogenic properties of amnion make it an ideal substance to mitigate the destructive forces at work in several types of equine keratopathy [406, 510]. By decreasing the concentration of inflammatory cytokines, AMT can reduce the severity of corneal melting and corneal neovascularization, and improve the likelihood of functional repair of both epithelial and stromal defects. By modulating corneal fibroblasts, it can decrease scarring and improve corneal clarity [406, 510]. AMT therapy in human ophthalmology is considered superior to the placement of conjunctival grafts and tarsorrhaphy as it provides a more optically and cosmetically acceptable outcome. There is some evidence in the horse that AMT can also provide superior cosmetic and visual outcomes in cases of destructive keratitis [406].

In horses, AMT has been successfully used in cases of ulcerative keratitis and keratomalacia to preserve globe integrity and a clear visual axis, and as an adjunct in the reconstruction of the cornea and conjunctiva following excision of surface neoplasms [406–408]. It has also been used successfully in clinical cases of keratomalacia, ankyloblepharon, and following resection of corneal neoplasia in dogs and cats [511, 512]. Amniotic membrane transplantation is a versatile surgical technique in both human and veterinary ophthalmology, with a constantly expanding list of potential indications [406].

Harvesting and storage

It is, in general, not deemed necessary to screen donor mares for specific diseases or infections, but care should be taken to aseptically harvest and process amnion-healthy placentas from healthy mares with no known history of transmissible disease. Amnion may be harvested at Caesarian section surgeries. The fetal component of the placenta which consists of the inner amnion and the outer chorion forms the limits of the sac that encloses the fetus [406]. The amniotic epithelial monolayer is adjacent to the fetus, while the spongy stromal matrix sits adjacent to the chorion. The amnion is relatively easily separated from the chorion by blunt dissection as the amniotic stroma is only loosely connected to the chorion [406]. The amnion is recognized as the avascular portion. The amnion is placed in 2 L of phosphate-buffered saline (PBS) (Fischer Scientific, Hampton, NH) with 5 mg EDTA for 30 minutes, and then washed completely three times in PBS. It is then cut to a manageable size (5 × 5 cm squares), and placed epithelial side up on nitrocellulose laboratory paper (Biorad Laboratories, Richmond, CA). The amnion is then placed in a 1:1 mixture of glycerol and Hanks BSS (Fischer Scientific, Hampton, NH), and frozen at –80°C until further use. Amnion may also be freeze-dried or lyophilized for storage [406].

Application methods

There are three basic methods for the application of AMT upon which the surgical technique chosen for an individual case is based [406].

Inlay or graft technique: in this procedure, the amnion is tailored to the size of the defect and is meant to act as a scaffold for epithelial cell migration. This graft then becomes integrated into the host tissue. The amnion is secured with sutures, with its BM orientated superficially to allow migration of surrounding epithelial cells onto the membrane [406].

Overlay or patch technique: this utilizes amnion as a form of biological contact lens in order to protect the healing surface of the underlying defect. The patch may also reduce inflammation by its barrier effect blocking chemical mediators in the tear fluid. When used as a patch, the amnion is sutured with the BM orientated to oppose and contact the cornea. This prevents adhesion and incorporation of the patch, which ultimately sloughs. Experience shows that sloughing 7–10 days post-operatively yields the least corneal scarring and provides the most therapeutic benefit in the horse [406].

Filling-in or layering technique: an initial piece of amnion is trimmed to the size of the defect and placed within the depth of the ulcer crater. A second, larger graft is then secured to the edges of the defect in an inlay fashion. A further additional larger patch may then be placed as an overlay and protects the two deeper layers [406].

Transplant technique

In preparation for surgical placement of amniotic membrane, the eye should be prepped routinely with an antimicrobial wash, usually dilute Betadine, and a topical anesthetic agent applied. Loose epithelium surrounding an epithelial or stromal defect, or over an area of bullous keratopathy, should be debrided with forceps, microsurgical sponges, and a microsurgical blade [406]. Any diseased or fibrotic conjunctiva or cornea should be completely resected prior to placement of the patch. Once the wound or defect is adequately prepared, the amnion should be trimmed to the desired size (usually 1 mm larger than the defect) and sutured over the lesion. For visual orientation of the amnion patch, the epithelial side amnion is shiny and the stromal surface can be identified by the presence of vitreous-like strands [406]. Typically, simple interrupted or continuous sutures will

be used on any graft-type applications [406] using 7-0 to 8-0 Vicryl or other absorbable suture material.

Sutureless techniques are in development in an attempt to improve the ease of application, decrease the time required for application and anesthesia, and improve patient comfort [406]. Fibrin tissue glues have shown significant promise, but their cost at present is prohibitive [406]. Some success has been achieved using minute quantities of surgical tissue adhesive (Tissuemend II) (Veterinary Product Labs, Phoenix, AZ)) to apply both amniotic membrane and synthetic corneal replacement material in veterinary patients [406].

Post-operative care

Post-operative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in keratomycosis cases, and a topical therapeutic mydriatic/cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are administered post-operatively to protect the cornea and prevent absorbable suture breakdown. If orientated with the BM side down, the layers of amnion visibly slough, generally within 3–4 weeks of surgery [407], whereas there is less chance of sloughing and more chance of incorporation if the amnion is orientated with the stromal surface opposing the cornea [408].

Complications

Complications associated with placement of an amnion graft include premature sloughing or dehiscence, failure to control melting or infection, and post-operative corneal haze or scarring.

Outcomes

Subjectively, amnion grafts have been reported to produce less corneal scarring than conjunctival grafts when used to cover SK beds following removal of corneolimbal SCC and beta radiation therapy [408]. Of nine horses receiving amnion grafts in addition to SK, and in some cases strontium-90 irradiation, for corneolimbal SCC, all had subjectively less scarring than those treated with conjunctival grafts (online Figures 7.168–7.179, 7.189, 7.190, 7,191, and 7.192) [408]. Three horses with severe *Pseudomonas* keratomalacia treated with amnion grafts were sighted and comfortable at last follow-up [407]. In a report of 58 horses treated using AMT, 31 were treated for melting ulcers or bullous keratopathy, 13 had AMT performed in conjunction with PK, 12 received AMT following keratectomy for a superficial neoplasm, and two received AMT following keratectomy for biopsy and treatment of an IMMK [406]. At the final post-operative examination, visual status was assessed and 53 affected eyes (91%) were determined to be sighted [406]. The five eyes that were not sighted had either severe corneal scarring, secondary intraocular damage resulting in phthisis bulbi with cataract formation and extensive posterior synechia, or were enucleated because of endophthalmitis. Mild corneal scarring was present in 40 eyes (69%) [406]. Moderate corneal scarring with acceptable cosmesis was present in 14 eyes (24%). Unacceptable cosmesis with severe scarring occurred in four eyes (7.0%). The eyes ultimately characterized with moderate or severe scarring were those most severely affected by primary disease [406].

Targeted lamellar keratoplasty and full-thickness corneal transplantation for inflammatory keratopathies in the horse

General concepts of corneal transplantation

Corneal transplantation is the most widely practised form of organ transplantation in humans, with nearly 60,000 surgeries performed worldwide every year [514–517]. Due to the immunologic privilege of the cornea, corneal transplantation in humans with noninflammatory dystrophic keratopathies has a success rate approaching 75% 5 years post-operatively. Keratitis, infection, corneal vascularization, and/or the need for reoperations dramatically reduce the success rate of corneal transplantation in human patients [516–519].

Corneal transplantation can be performed for optical, therapeutic, tectonic, and cosmetic reasons in horses [170, 403, 404, 414, 521]. Optical transplants restore or improve vision in cases of corneal edema. Therapeutic transplants attempt to control medically refractory corneal disease by reducing antigenic stimulation and removing infectious and necrotic debris and toxins from degenerating neutrophils and microbes. Tectonic transplants are done to preserve or restore the structural integrity of the eye when corneal tissue is missing, and cosmetic grafts improve the appearance of the eye without necessarily improving vision [82, 170].

Four basic corneal transplantation surgical procedures have been described in the horse. PK is used for full-thickness SA or deep ulcers/iris prolapses [170, 403, 404, 414, 521]. Three split-thickness forms of corneal transplantation are used: PLK for DSA with a clear overlying anterior stroma in the axial cornea [170, 403, 404, 414–416, 521], DLEK for limbal DSA where the superficial cornea may be vascularized or edematous but is otherwise normal [82, 170, 294, 416], and DALK for severe melting ulcers [424].

Penetrating keratoplasty

Principles

PK is full-thickness microsurgical transplantation of the corneal epithelium, stroma, and Descemet's membrane/endothelium [170, 294, 521–523]. PK has long been the standard procedure for treating irreversible opacification of the human cornea from various infectious and noninfectious keratopathies [522]. The terms penetrating and perforating can be confusing. The term PK is defined by its reference point of the incision in the globe; therefore when a full-thickness PK graft is performed, the incision penetrates or enters the globe but perforates or enters and exits the cornea.

The success rate of PK in noninflamed human corneas is high compared with those in other human organ transplants because of the low rate of immunologic rejection of corneal tissue. Graft

rejection manifested as graft opacification does, however, occur in human patients with vascularized, infected corneas, and subsequent repeat PK procedures in these eyes are inevitably less successful [523]. Severe keratitis causing total destruction of limbal stem-cell-bearing tissue is also considered a risk factor for PK failure in humans [522].

PK in all species suffers from the inherent problem of creating a weak vertical stromal wound that requires surface corneal sutures [514, 515]. Vertical incisions are more prone to leak at low IOP levels [524]. The incised stroma at the PK site never regains the structural integrity and strength of normal stroma. Topographic distortion of the cornea due to corneal sutures results in refractive instability in humans following PK [514, 515].

Corneal sutures must provide a great compressive force to create a watertight seal of the junction between the donor and recipient corneal tissue [524]. The sutures loosen as corneal edema following PK resolves, and the corneal tissue contracts to allow tissue separation and aqueous leakage in some eyes [514, 515]. Sutures are a leading cause of graft infection and vascularization [514, 515]. Corneal sensory denervation is also a problem following PK in humans and may take a year or more post-operatively to resolve [525].

Indications and surgical procedure

Corneal transplantation for treatment of severe inflammatory nonulcerative and ulcerative keratopathies with corneal vascularization, infection, and keratomalacia ("melting") has been performed successfully in horses since the early 1980s (Figures 7.88, 7.89, 7.90, 7.104, 7.105, 7.106, 7.107, 7.108, 7.109, 7.134, 7.135, 7.136, 7.137, 7.138, 7.139, online Figures 7.86, 7.87, 7.88, 7.89, and 7.90) [82, 170, 294, 414–416]. Some clinicians may, however, favor the term "corneal grafting" rather than "corneal transplantation" for horse patients, as the use of frozen corneal tissue without tissue matching is more a grafting procedure than a substitute for missing or damaged cornea.

Full-thickness PK may be performed in horses for therapeutic and tectonic reasons for melting ulcers with extensive stromal

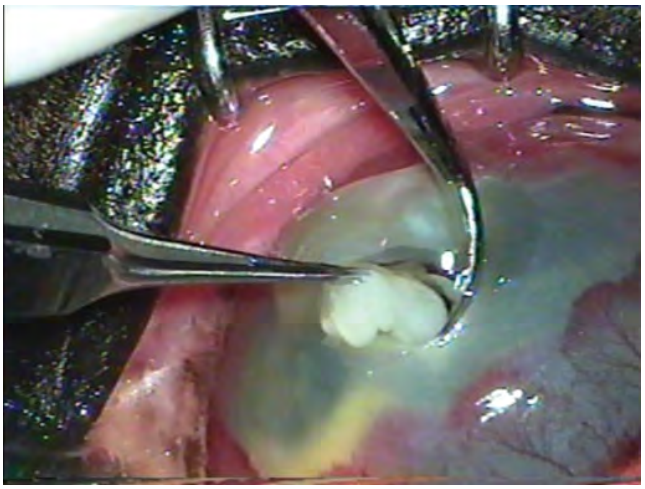


Figure 7.135 After half-thickness trephination, corneal scissors are used to remove the diseased cornea.

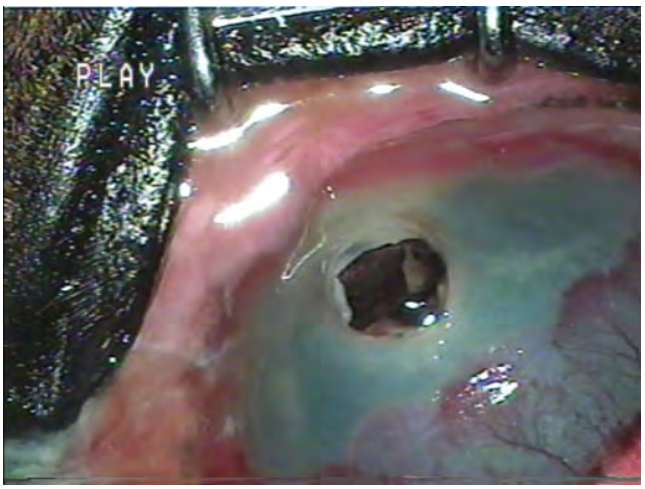


Figure 7.136 Iris plugs the surgical site.



Figure 7.134 A full-thickness SA is to receive a PK and conjunctival graft.

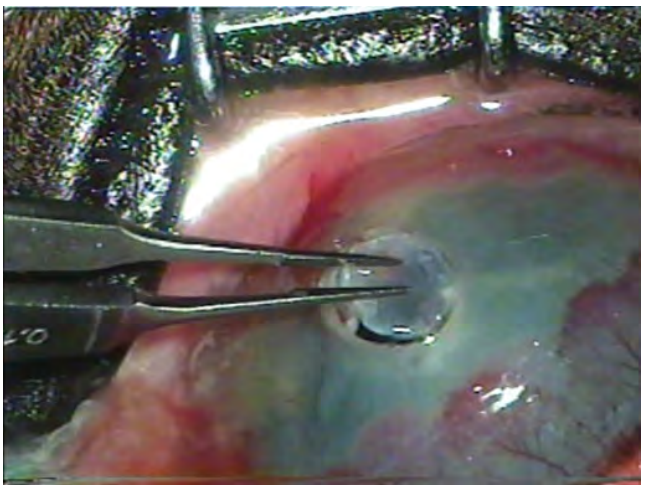


Figure 7.137 The corneal donor graft is placed in position.

loss, iris prolapse/descemetoceles, and full-thickness SA. PK has become a viable, routine, and successful surgical technique in horses with severe keratitis [82, 113, 521], and is associated with a very good visual outcome in the majority of cases (approximately 80%). This is true despite the fact that nearly all the corneal transplant donor tissue grafts in horses having PK vascularize post-operatively and exhibit significant degrees of full-thickness corneal opacification at the surgical site (Figures 7.128, 7.129, 7.130, 7.131, 7.132, and 7.133) [82, 113, 521]. Corneal transplantation for optical reasons is not possible at this time in the horse.

While grafts as large as 25 mm in diameter have been reported, the most common sizes, and those with the best chance of surgical success in horses, are between 6 and 8 mm [113, 170]. Placement of a conjunctival graft over a PK may be indicated to provide physical support to the incision, prevent aqueous microleaks, and provide a plasma lavage to the ocular surface and incision. The disadvantage of adding the conjunctival graft is there being increased corneal scarring [113, 170].

Donor cornea preservation

Fresh homologous tissue can be used to perform PK providing structural support to the globe and improved likelihood of corneal clarity due to transplantation of viable endothelium, but the logistical difficulty of acquiring fresh tissue at the time it is needed makes fresh corneal grafts rare in veterinary ophthalmology. Frozen donor cornea is most often used in horses, and is obtained within 24 hours of death from horses with normal eyes euthanized for noninfectious diseases. The corneas from these horses are then hemisected and stored frozen at –20°C in a broad-spectrum antibiotic solution, or in corneal storage media (Optisol) (Chiron Ophthalmics, Irvine, CA)). Frozen homologous grafts are thus most frequently available for corneal transplantation in the horse.

Surgical technique

All PK, PLK, DALK, and DLEK procedures are performed under general anesthesia and muscular paralysis. An operating microscope is utilized for each procedure.

The surgical approach for PK in horses has been previously described in other published findings. See Figures 7.134–7.140 [170, 414, 521]. The size of the corneal lesion is determined with calipers. The recipient globe is stabilized with scleral fixation sutures of 5-0 nylon. Hemorrhage of vascularized cornea can be minimized using topical phenylephrine (2.5%), pressure, and/or electrocautery. A corneal trephine of appropriate size is centered over the diseased area and then rotated with minimal downward pressure to obtain a clearcut, round incision with vertical sides. The incision with the trephine approaches to just near, but should not penetrate Descemet's membrane. Several trephines of different diameter can be used to create multiple levels of tissue incision to reduce aqueous humor leakage. Large-diameter trephines are used superficially, and smaller diameter trephines used in the deep stroma. The remaining intact deep stromal tissue is vertically incised with a Beaver #65 blade to enter the anterior chamber, being careful to avoid the iris, granulae iridicae, and lens. The button of diseased host tissue is then removed with corneal section scissors. The keratectomy buttons from DSA cases are processed for aerobic and fungal culture and sensitivity, cytology, and histopathology.

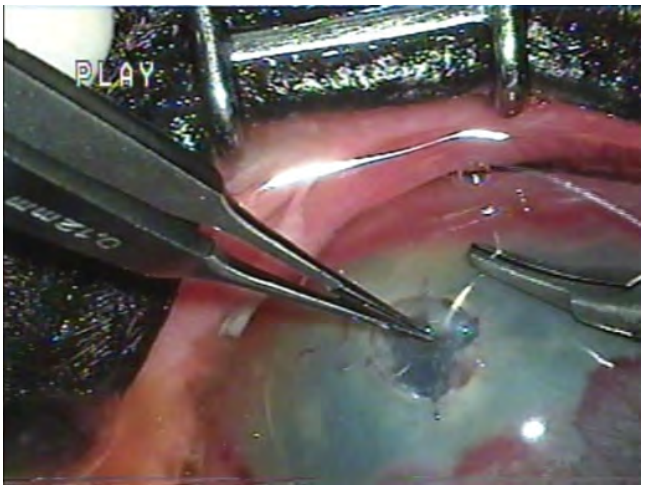


Figure 7.138 The donor graft is sutured into position.

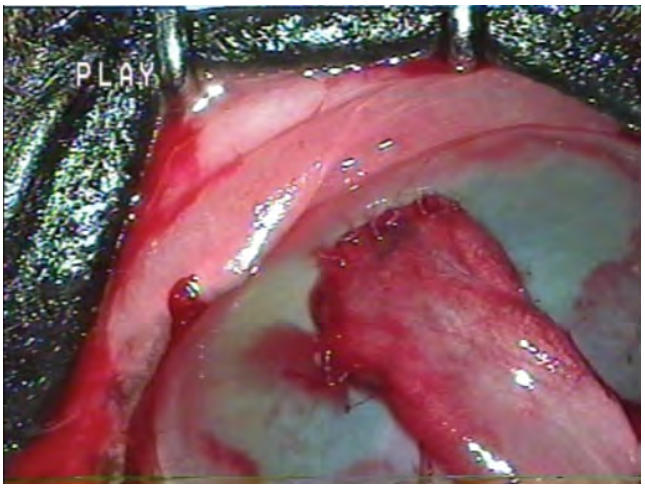


Figure 7.139 A conjunctival pedicle graft is placed over the PK site to support the graft and minimize the occurrence of microleaks.

The anterior chamber is reformed by injecting viscoelastic solution (hyaluronate sodium, 10 mg/mL, Hylartin V™ (Pfizer Animal Health, New York, NY)) into the anterior chamber. The viscoelastic solution also moves the iris posteriorly, breaks down any adhesions between the cornea and the iris, and prevents direct contact with the lens capsule [170, 414, 521]. A full-thickness donor button, 1-mm-diameter larger than the recipient bed, is then trephined from the endothelial to the epithelial side of the donor cornea. The donor cornea is most easily handled when slightly, but not completely, thawed. The donor button is grasped with fine-toothed forceps, while paying particular attention to the orientation of the epithelium/endothelium, placed on a

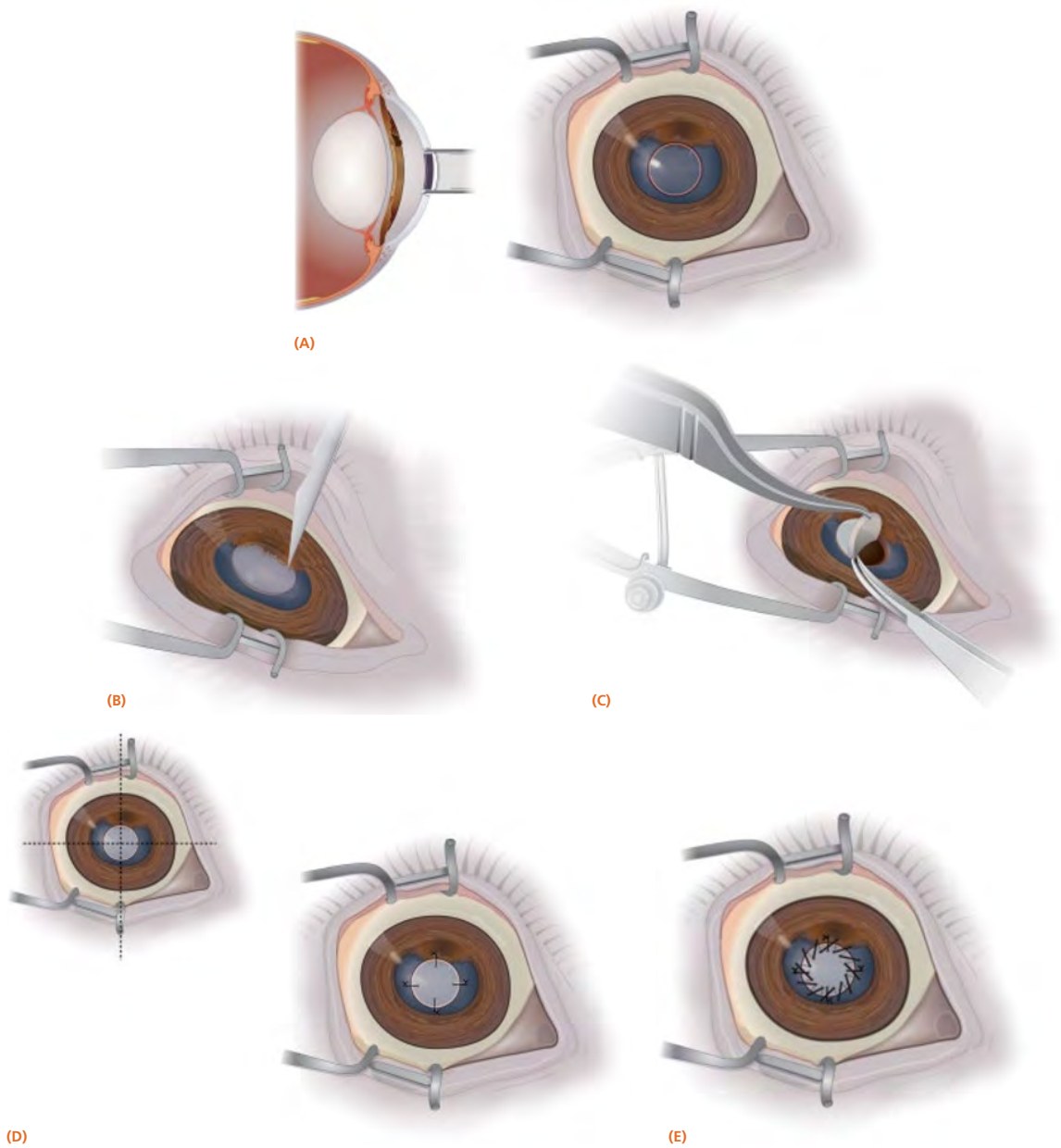


Figure 7.140 Surgical steps for performing penetrating keratopathy. (A) A corneal trephine is used to create a perpendicular corneal incision to approximately 75% depth. (B) A Beaver #65 blade or other sharp blade is used to enter the anterior chamber at one aspect of the trephine incision, taking care to avoid puncturing the iris or lens. (C) Right- and left-handed corneal section scissors are used to complete the incision and allow removal of the lesion. (D) The donor button is placed in the surgical site, endothelium side down, with care taken to grasp the button at the epithelial/stromal junction, avoiding contact with the endothelium. Four cardinal simple interrupted sutures are placed from the donor button to the recipient cornea at the 12-, 3-, 6-, and 9-o'clock positions. (E) The remainder of the graft is sutured with either simple interrupted, simple continuous, or double-continuous sutures of preferably 9-0 absorbable suture. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

gauze swab, and kept moistened with LRS. The epithelium is not removed from the corneal donor button.

The donor cornea is placed in the recipient bed, and four cardinal sutures of 8-0 Vicryl (Ethicon, Somerville, NJ) or 9-0 nylon (Ethilon (Ethicon)) placed at the 12-, 6-, 9-, and 3-o'clock positions [170, 414, 521]. Simple interrupted sutures are placed to fill in the remaining sectors in each quadrant; alternatively, a simple continuous suture pattern is placed to hold the graft. The corneal epithelium is very sensitive to mechanical trauma such that when manipulating or holding corneal tissue, only the

stroma should be held with the corneal forceps. Once the donor cornea is sutured into place, viscoelastic solution is again injected at the limbus with a 20- to 22-G needle to completely reform the anterior chamber. The viscoelastic solution is not removed from the anterior chamber. A Seidel's test is performed to check for incisional or sutural microleaks.

A conjunctival pedicle or amniotic membrane graft can then be sutured over the keratectomy/graft site in eyes with evidence of infection, melting, or vascularization to achieve more rapid assimilation of the graft into the cornea [170, 414, 521]. This also helps in reducing the chance of an aqueous microleak occurring when graft rejection causes swelling of the donor tissue. A temporary lateral tarsorrhaphy is performed to minimize eyelid trauma to the PK. Autogenous serum to decrease tear film proteinases attacking the graft and sutures and CsA to reduce graft rejection are added to the other medications post-operatively.

Post-operative care

Post-operative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic/cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are still necessary even if a conjunctival graft is also placed.

Outcomes

The medical records of 86 horses that had PK have been reviewed [170]. The PK procedure was performed for iris prolapse (n=32), medically nonresponsive full-thickness SA (n=31), melting fungal ulcers (n=14), descemetoceles (n=7), corneal foreign body (n=1), and severe keratoconus (n=1) (online Figures 7.87, 7.88, 7.89, 7.90, 7.128, 7.196, 7.197, 7.198, 7.199, 7.200, 7.213, 7.214, 7.215, 7.216, 7.217, 7.218, and 7.219). The visual outcome was positive in 67/86 eyes (77.9%) that had PK. The average time for complete healing in PK cases with a successful visual outcome was 46.7 ± 23.1 days.

Marked edema and swelling of the recipient corneal tissue may be present over the first few days but should resolve, provided dehiscence does not occur. The donor cornea begins to swell and lose transparency 3–7 days post-operatively. As the disease process resolves, most consistently indicated by increased comfort and decreased anterior uveitis, medications can be reduced. Trimming of the overlying conjunctival graft may be performed a minimum of 4–6 weeks post-operatively.

Complications

Complications included graft failure (i.e., infection, malacia) requiring surgical repair or replacement, aqueous leakage from wound dehiscence or suture microleaks, focal nonprogressive cataract formation, and hyphema. The graft epithelium sloughed 3–5 days post-operatively in most PK eyes. The corneal grafts in most horses do vascularize, and all have some degree of graft opacity post-operatively that reduces with time. Suture site scarring will be present in the cornea.

Component lamellar keratoplasty: targeted transplantation of ocular surface layers

The concept of LK is to target and replace only diseased corneal tissue while retaining normal healthy corneal tissue, and it is quite suited for several keratopathies of the horse [404, 428–431]. The various transplantable "components" of the cornea include the epithelium, epithelial stem cells, stroma, and DM/endothelium [404]. Corneal components can be transplanted as lamellar sections of donor cornea, or as *ex vivo* expanded cell sheets with or without biologic carriers [1, 170, 422, 430]. LK is utilized for tectonic reasons to replace damaged stroma in melting corneal ulcers, as it provides enhanced donor graft survival and improved visual outcomes compared to PK [431]. DLEK and PLK are split-thickness LKs utilized to replace diseased endothelium from Fuch's endothelial dystrophy and bullous keratopathy in humans, and DSA in horses. The remaining healthy corneal layers are preserved in DLEK and PLK [404]. The overall success rates for rapid return to visual function for surgical therapy of DSA by DLEK and PLK in horses are higher than for PK [170, 415, 416].

Targeted epithelial layer lamellar transplantation

Severe ocular surface diseases caused by total limbal stem-cell deficiency in humans can be treated by epithelial layer lamellar transplantation [1, 404]. The transplantation of epithelial cells restores epithelial stratification and barrier function, and stabilizes and reduces the existing keratitis. Targeted replacement of corneal epithelium can be accomplished by limbal transplantation of intact limbal epithelial stem cells attached to AMTs [1, 404, 430], or transplantation of sheets of cultivated epithelial stem cells [1, 430]. Viable equine limbal stem cells have been attached to equine amniotic membrane for targeted epithelial layer transplantation, and this technique is available for use in the horse.

Targeted anterior stromal lamellar transplantation

ALK replaces the stroma, stromal keratocytes, and the epithelial layer with its transient amplifying cells [430]. The healthy endothelium and Descemet's membrane are retained in order to reduce the risk of endothelial allograft reaction [428, 429, 431]. Preservation of Descemet's membrane and endothelium slows corneal graft rejection and speeds corneal healing [428, 429, 431]. Indications for ALK include anterior stromal scars, corneal melting disorders, predescemetoceles, descemetoceles that have small perforations, large-diameter descemetoceles, stromal corneal tumors, corneal melting and infection, and corneal ulcers with grooves [428, 429, 431].

The purpose of ALK is to attempt to surgically create a descemetocele. The traditional technique of ALK is to manually dissect the stromal host tissue layer by layer with the use of corneal lamellar dissectors until DM is exposed. There is reported to be a weak adhesion between the deep stroma and adjacent DM in humans, and the goal of ALK is to use this transition zone to more easily manually dissect the stroma from Descemet's

membrane [428]. It is still difficult to manually obtain a precise and perfectly smooth lamellar dissection, and to venture deep enough to remove the majority of deep diseased stroma without causing perforation. The visual outcomes in humans following manual ALK are generally relatively poor [428, 429, 431].

Deep anterior lamellar keratoplasty

DALK is a new surgical technique to safely remove the entire corneal stroma down to bare DM. It has the ability to remove all diseased stroma in order to lead to better visual outcomes [428], and lowers the risk of endothelial cell allograft rejection that would occur with PK [431]. Indications for DALK in humans include keratoconus, chemical and thermal corneal burns, patients with vascularized corneas who are at high risk of rejection, and corneal perforations [428, 429, 431]. Segmental removal of the diseased host stroma is performed in DALK by manual peeling of the anterior portion of the diseased stroma, and then deep intrastromal injection of an "air bubble," or a viscoelastic solution, into a tissue plane between Descemet's membrane and the remaining diseased posterior stroma to dissect and cause clean separation within this potential space [428, 429, 431]. The donor Descemet's membrane and endothelium is simply peeled off the donor tissue such that lamellar dissection of the donor cornea is unnecessary. The continuous layer of host Descemet's membrane and endothelium present after DALK improves post-operative refraction, reduces astigmatism, and follows a more benign wound healing process, compared with PK where scarring of the donor cornea is observed both in the superficial corneal stroma and endothelium [428, 429, 431, 522]. Microperforation of Descemet's membrane during DALK occurs in 10–39% of human cases [428].

DALK is indicated in horses for rapidly progressive, large-diameter, catastrophic, melting corneal ulcers with and without exposure of Descemet's membrane and corneal ulcers with groove formation (Figures 7.141, 7.142, 7.143, and 7.144, online Figures 7.65–7.71, 7.109–7.113, 7.185, 7.186, 7.187, and 7.188) [404]. This procedure essentially attempts to create a descemetocele and then replaces all diseased corneal tissues anterior to Descemet's membrane, and has been carried out successfully in horses with melting ulcers, descemetoceles, and corneal perforations with iris prolapse [404].

Achieving a "true" DALK procedure down to bare Descemet's membrane is difficult in the horse [404, 424]. as there does not appear to be a potential "space" or "loose adhesion" between the equine Descemet's membrane and posterior stroma [428, 429, 431, 522]. Hydrodissection, viscodissection, and corneal dissectors are used to bluntly dissect most of the diseased stroma from the equine Descemet's membrane. Pressure in the deep stromal lamellae by injecting air or a viscoelastic though a 30-G needle into the deep stroma can then be used to further dissect and detach the remaining diseased stroma from Descemet's membrane. This pressure-associated microdissection produces a dome-shaped detachment of the stroma from Descemet's membrane that allows the remaining diseased stroma to be removed to expose the smooth and refractile Descemet's membrane.

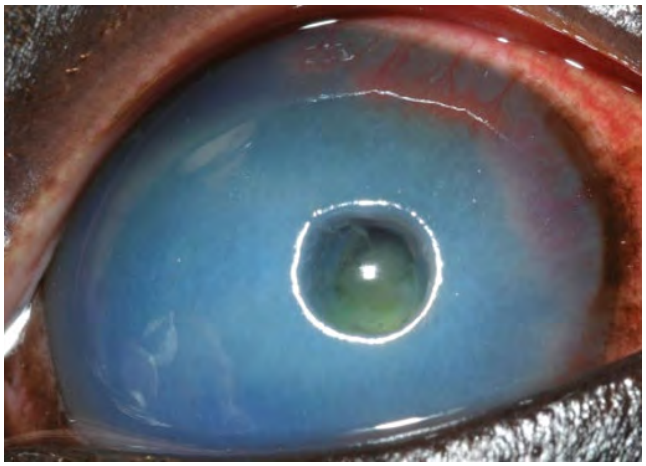


Figure 7.141 Descemetocele is present with corneal edema and neovascularization.

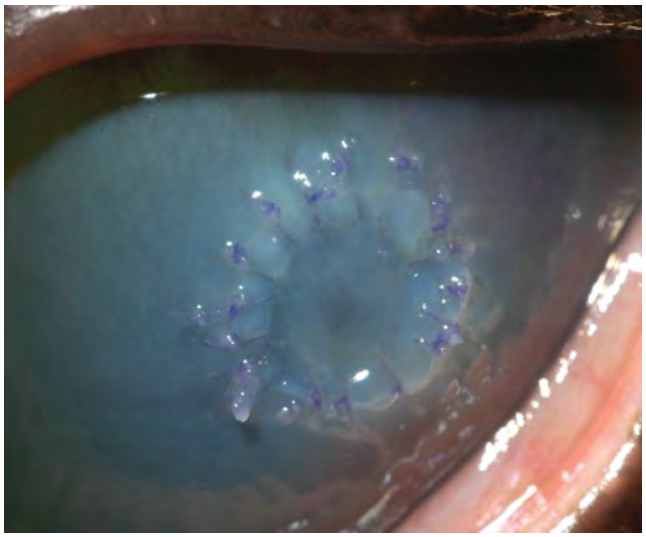


Figure 7.142 The eye in Figure 7.141 is treated with a DALK.



Figure 7.143 Twelve days post-operatively, the corneal graft in Figure 7.142 is vascularizing.



Figure 7.144 Twenty-one days post-operatively, the graft in Figures 7.142 and 7.143 is vascularized and healed.

Cases of microperforation of Descemet's membrane during this part of the surgery can be resolved by injecting air into the anterior chamber [428, 429, 431, 522]. A study in enucleated horse globes found that using viscoelastic to dissect the stroma resulted in perforations in 18% of the eyes during surgery and exposure of Descemet's membrane in 28% of the eyes, with mean thickness of the remaining stroma being 70.4 μm. Perforations occurred in 42% of the eyes using air for dissection, with exposure of Descemet's membrane in 60% of the eyes and a mean thickness of the remaining stroma being 23.3 μm [424].

Targeted posterior stroma and Descemet's membrane transplantation

The inherent philosophy of split-thickness or lamellar corneal surgery is to replace only the diseased portion of the cornea, leaving the normal tissue intact [428, 431, 514, 515, 521, 522]. PLK and DLEK are both split-thickness LKs that replace diseased posterior corneal stroma, Descemet's membrane, and endothelium with donor tissue, while retaining the epithelium and anterior corneal stroma [428, 431, 514, 515, 521, 522, 526]. DSA of horses are regions of focal neutrophilic and fungal invasion of the posterior stroma, Descemet's membrane, and endothelium [82, 113]. Many DSA have extension into the anterior chamber [82]. The superficial cornea may be vascularized and edematous to some degree but is otherwise normal [82, 170]. DLEK and PLK are important surgical methods for resolving medically nonresponsive DSA with anterior chamber invasion in horses.

Posterior lamellar keratoplasty

PLK in horses is recommended for DSA in axial corneas that are 10 mm or less in diameter. The overlying epithelium may be edematous but is intact, and the anterior stroma may be vascularized but should not have a cellular infiltrate [170, 415, 521]. The PLK procedure involves less surgical time and heals faster than full-thickness keratoplasty (PK).

Surgical technique

The surgical approach (Figure 7.145) has been described in other published findings [170, 415, 521]. A three-sided, rectangular, anterior lamellar corneal flap, hinged on one side, is constructed by hand dissection to two-thirds stromal thickness over the SA [170, 415, 521]. The superficial flap of epithelium and anterior stroma is made at least 1 mm larger on each side than the diameter of the DSA. A Martinez corneal dissector is used to undermine and elevate the superficial corneal layers to expose the abscess. The flap is gently raised, the abscess measured with calipers, and then a trephine, Beaver #65 blade, and corneal transplant scissors are used to remove the posterior SA, Descemet's membrane, and endothelium. The deep keratectomy button is then processed for aerobic bacterial and fungal culture and sensitivity, cytology, and histopathology.

The anterior chamber is reformed by injection of viscoelastic [170, 415, 521]. A circular donor graft of posterior stroma, Descemet's membrane, and endothelium 1 mm larger than the defect is cut from donor tissue using a trephine. The graft is placed in the corneal defect, and sutured every 2 mm using 8-0 absorbable suture material in a simple interrupted pattern. The three-sided superficial flap is then sutured in place using 8-0 absorbable suture material. The viscoelastic is not removed from the anterior chamber. Partial temporary tarsorrhaphies are placed in all eyes to protect the graft during recovery.

Post-operative care

Post-operative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic/cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases such as serum are administered to reduce tear film protease activity caused by the keratotomy and corneal suture placement.

Outcomes

The medical records of 54 horses receiving PLK were reviewed [170]. The PLK procedure was performed for single (n=49) and multiple (n=5) medically nonresponsive DSA of the axial cornea. The visual outcome was positive in 53/54 eyes (98.1%) that had PLK. The average time for complete healing when defined as being off all medications in PLK cases with a successful visual outcome was 30.8 ± 9.5 days. The donor graft remained transparent for up to 7 days and then opacified. Subepithelial opacification and graft opacification can be seen with a slit-lamp. Suture marks were present in the cornea [170].

Complications

Complications include flap ulcers, aqueous leakage from wound dehiscence or suture microleaks, and suture abscesses [170].

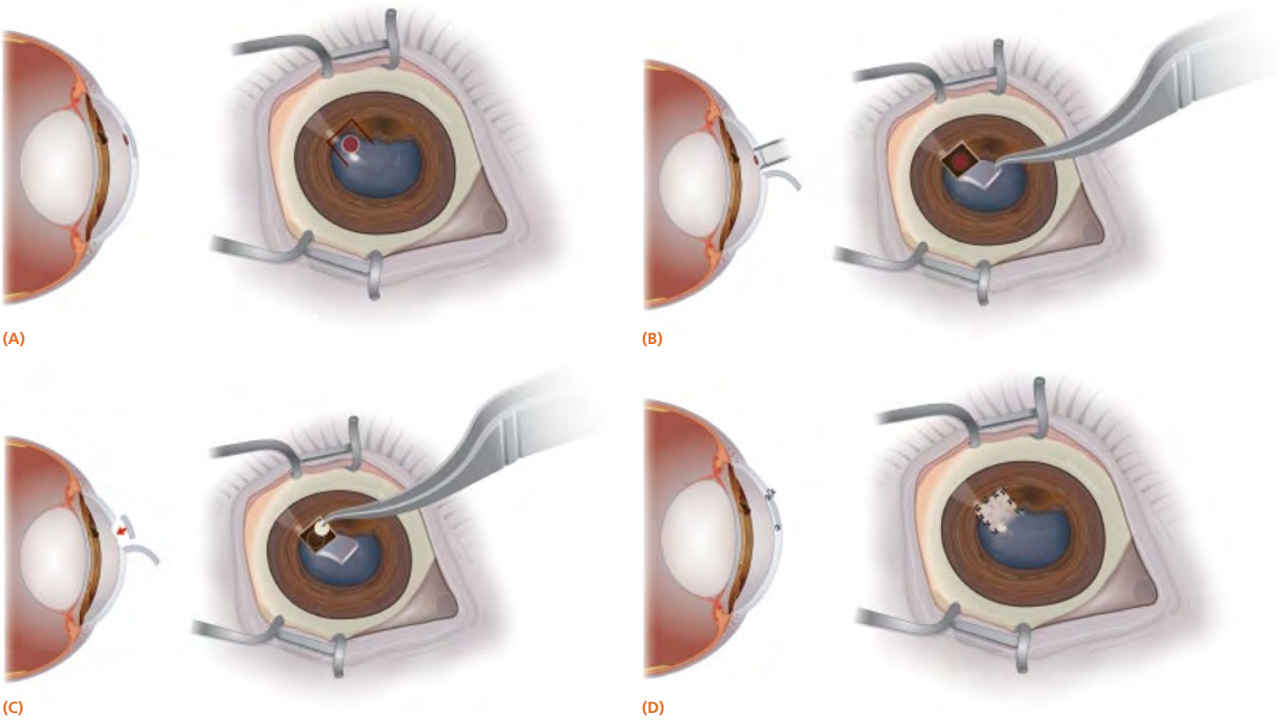


Figure 7.145 Surgical steps for performing PLK. (A) A #64 microsurgical blade is used to create a three-sided (rectangular), half- to three-quarters thickness incision over the deep lesion, with each incision extending 1 mm beyond the edge of the lesion. (B) A Martinez lamellar corneal dissector or #64 microsurgical blade is used for lamellar dissection of the flap, allowing reflection of the flap and exposure of the underlying deep lesion. A corneal trephine or dermal biopsy punch is used to score an incision in the posterior stroma surrounding the deep lesion, and a #65 microsurgical blade is used to enter the anterior chamber. (C) The donor corneal button is placed in the recipient site and four cardinal simple interrupted sutures, at 12-, 3-, 6-, and 9-o'clock, are placed from the graft to the recipient cornea, using 8-0 or 9-0 absorbable suture. (D) The anterior stromal flap is replaced over the donor cornea and sutured in place with simple interrupted or simple continuous sutures. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

Deep lamellar endothelial keratoplasty

Surgical technique

DLEK is recommended for medically nonresponsive DSA in the peripheral cornea that are 10 mm or less in diameter, and have moderate vascularization and edema of the overlying epithelium and anterior stroma with no stromal cellular infiltrate (Figures 7.87, 7.88, 7.89, 7.90, 7.103, 7.104, 7.105, and 7.106) DLEK may also be useful for therapy of endotheliopathy such as immune-mediated endotheliitis. DLEK transfers healthy Descemet's membrane and endothelium while preserving the corneal surface and topography. It is faster to perform than PK, less often associated with aqueous microleaks, and leaves a fully intact epithelium, with limbal sutures only present post-operatively in the limbal cornea (online Figures 7.193, 7.194, and 7.195) [170, 415, 521].

A limbal incision up to 25 mm in length is made to two-thirds stromal depth (Figure 7.146) [170, 415, 521]. A stromal pocket is formed manually over the DSA with a Martinez corneal dissector or crescent blade. The superficial flap of normal epithelium and vascularized stroma is gently retracted and Descemet's membrane and endothelium with the abscess are removed with a trephine and corneal scissors. The anterior two-thirds of the donor corneal tissue is removed by manual dissection and discarded, and a trephine 1 mm larger in diameter than the recipient site is used to obtain the circular lamellar donor graft of normal Descemet's membrane and endothelium. The superficial corneal flap is partially sutured at the limbus, the endothelial donor graft gently inserted into place with Utrata forceps, and the limbal incision then sutured closed. The graft self-adheres to the recipient stroma by action of the endothelial pump, but may need to be repositioned by a needle inserted at the limbus. The graft is supported during the immediate post-operative period by viscoelastic injected into the anterior chamber [170, 415, 521].

Post-operative care

Post-operative care is similar to that for other grafting procedures, consisting of topical therapeutic antibiotics, topical antifungals in the presence of keratomycosis, and a topical therapeutic mydriatic/cycloplegic. Systemic antibiotics and antifungals may be indicated, as well as systemic NSAIDs. Topical antiproteases are generally used to protect the sutures and incision from tear film proteases elevated from surgical manipulation [416]. CsA can be administered topically post-operatively to control graft rejection [416].

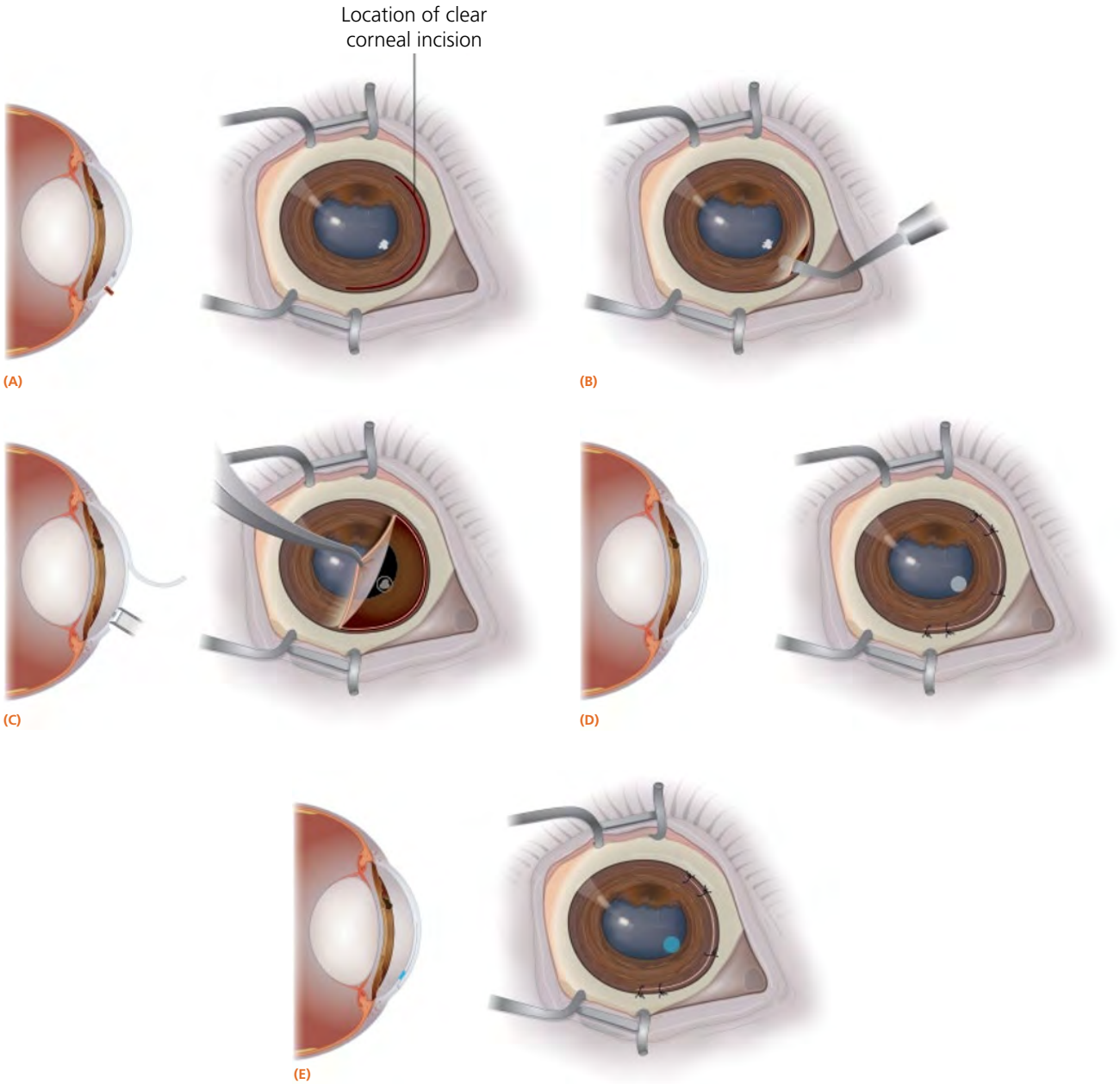


Figure 7.146 Surgical steps for performing DLEK. **(A)** A #64 microsurgical blade is used to create a half- to two-thirds-depth clear corneal incision along the limbus adjacent to the lesion. **(B)** A corneal dissector is used to separate the corneal lamellae surrounding and overlying the lesion. **(C)** A corneal trephine or dermal biopsy punch is used to create an incision around the lesion. **(D)** The recipient anterior corneal flap is replaced and partially sutured closed with simple interrupted sutures of 8-0 or 9-0 absorbable or nonabsorbable suture. **(E)** Prior to complete closure of the incision, the donor cornea button is inserted into the hole where recipient cornea was removed, endothelial side down. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

Outcomes

The medical records of 66 horses receiving DLEK were reviewed [170]. The DLEK procedure was performed for medically non-responsive DSA of the peripheral cornea (n=66). The visual outcome was positive in 59/66 eyes (89.4%) that had DLEK. The average time for complete healing when defined as being off all medications in DLEK cases with a successful visual outcome was 35.8 ± 14.7 days. The superficial epithelium and stroma remain transparent in DLEK. The donor graft remains transparent for up to 7 days and then vascularizes and opacifies [170]. The endothelial scar is typically vascularized and eventually becomes opaque, and is similar between PLK and DLEK but much better than with PK.

Complications

Complications of DLEK in the horse include suture abscesses, suture incision microleaks, incision edema, and graft misalignment. Corneal edema associated with the extensive corneal

dissection is typically pronounced immediately post-operatively with bullae formation in some eyes, and then will nearly completely resolve over several weeks in DLEK cases [170]. Subepithelial opacification anterior to the graft and graft opacification due to presumed graft rejection can be seen using slit-lamp biomicroscopy after healing of DLEK in all cases [170].

Corneal transplantation in horses

Technical observations

The ability to perform corneal transplantation in the horse is increasing and the capability of achieving a positive visual outcome improving dramatically The following observations are based on the results of over 350 corneal transplants of all types performed at the University of Florida up till 2015. The corneal epithelium is very sensitive to mechanical trauma such that when manipulating or holding corneal tissue, especially at the edge of an incision, only the stroma should be held with the corneal forceps. Frozen corneas were utilized in 95% of the procedures with satisfactory results. It is easiest to handle the frozen cornea when it is partially rather than completely thawed. Corneas could be stored at –20°C for 6 months and still used satisfactorily. In spite of the damage freezing does to the endothelium, many equine donor grafts that were initially opaque while frozen became transparent in the cornea for several days. The majority eventually developed some degree of opacity, but a few PLK and DLEK grafts again regained their transparency in the long term, suggesting that the horse endothelial cells are capable of expansion and migration to cover the endothelial deficit [170].

Early rejection is manifested by graft swelling beginning 3–7 days post-operatively in all types of transplants. Progressive graft rejection is manifested by loss of transparency, and occurs in all horse eyes in the short term. Graft opacification is less apparent in DLEK than PK. However, eyes selected for PK were overall more severely diseased, with more pre-operative corneal destruction and stromal loss and more aggressive uveitis 170].

PLK and DLEK comments specific for DSA

Eyes with DSA generally have relatively normal anterior stroma contiguous to the lesions. Simply removing the DSA and not replacing the tissue with a transplant results in generalized corneal edema that takes months to resolve [170]. Adhesions or synechia between the abscess and iris are often present, and thick fibrin membranes were often noted intraoperatively on the posterior cornea, anterior iris face, and lens. The pupil was often partially occluded by these membranes. Hypopyon was allowed to drain from the anterior chamber intraoperatively. Iris membranes were removed with caution or not at all due to the risk of hemorrhage. Retrocorneal membranes could be gently dissected from the cornea with viscodissection, but vigorous traction can cause serious hyphema. Suture tracks in the recipient cornea were often present at DLEK and PLK surgical sites [170]. The absorbable suture Vicryl was used in all cases despite its reputation for inducing vascularization, and rarely caused overt inflammation in the horse corneas.

Graft rejection

The cornea is an immune-privileged tissue due primarily to its avascular nature and the presence of immunosuppressive and antiangiogenic peptides in its immediate aqueous environment. The homeostasis of the afferent and efferent responses of ocular immunity is undermined in corneal transplant rejection to cause selective injury to donor corneal cells. Inflammation and consequent vascularization of the host cornea further increases the risk of rejection of the avascular donor tissue [527].

Acute transplant rejection is mediated by macrophages and T lymphocytes and begins in the first week after surgery. Following corneal transplantation, recipient APCs enter the graft and endocytose exogenous donor alloantigen of the minor or major histocompatibility complex (MHC) types. The APCs then migrate to a local lymph node where the alloantigen is presented on MHC class II molecules to naïve CD4 cells and on MHC class I molecules to naïve CD8 cells. Once a T cell is activated in a lymph node there is rapid expansion of alloantigen-specific T cells which enter the circulation. Vascular cornea permits relatively easy exposure of these cells to graft antigens. CD4+ and CD8+ T lymphocytes, macrophages, and natural killer (NK) cells infiltrate the graft. Both CD4+ and CD8+ T lymphocytes may mediate rejection, but neither is essential to the process [527]. Donor APCs transplanted in the graft or passenger leucocytes can also directly mediate graft rejection and may constitute the majority of the alloreactive T cells in acute graft rejection [527].

Infection, vascularization, and previous surgery increase the chance of graft failure [527]. Epithelial rejection is often asymptomatic but manifests as epithelial opacity. This can lead to rejection of deeper corneal layers. Subepithelial infiltrates and opacities are noted in early stromal rejection, but this can progress to spreading graft opacification and reduced vision. Endothelial rejection is uncomfortable, and is indicated by a line of leucocyte migration into the donor tissue, followed by local or diffuse edema and keratic precipitates. Iridocyclitis will also be found in eyes with endothelial cell rejection [527]. Intensive topical corticosteroid therapy is the main therapy for rejection in humans [527].

Corneal graft procedures for noninflammatory dystrophic conditions are the most successful of clinical transplants in humans [516, 518]. All eyes in horses that have corneal transplants would be considered high risk for failure or rejection based on the human criteria, as the grafts are placed in inflamed, infected, and vascularized cornea. Vascularization downregulates the immune privilege of the cornea, allowing antigens to leave the graft via blood vessels and lymphatics and permitting host APCs into the graft [528]. Placing a conjunctival flap, as is done in many horse PK patients, probably guarantees graft rejection but is frequently necessary to support the weakened tissue surrounding the graft site [170].

The location and size of the transplant sites in the cornea may influence corneal rejection. Graft sites closer to the limbus, presumably because of their proximity to limbal blood vessels, and

keratoplasties greater than 8.0 mm in diameter are associated with increased rejection rates in humans [518–520]. Large grafts in the horse (more than 10 mm in diameter) also seemed to have a more dramatic scarring effect, but these were generally also the most severe cases pre-operatively. Paradoxically, vascularization provides tectonic and nutritional support to the horse corneal transplant graft, and a donor graft is not considered to have healed until it vascularizes [82, 170]. Grafts closer to the limbus are considered more desirable for transplant in horses with DSA due to their proximity to limbal blood vessels, yet this proximity to the limbus undoubtedly increases the rejection rate [518–520].

General discussion

Surgical procedures for corneal transplantation in the horse are still evolving, but corneal transplantation is a tectonically viable surgery with an overall vision retention success rate of 88.5% in treating vascularized and infected equine corneal disease [170]. It is not possible at present to achieve corneal clarity for purely optical reasons following corneal transplantation in the horse. The donor graft rejection process in the horse is persistent, overwhelming, and cannot be stopped at the present time [170]. Prevention of corneal graft rejection lies with the reduction of the donor antigen tissue load, tissue matching, and suppressing the host immune response [517]. Partial graft rejection and scar formation have to date been unavoidable with PK, PLK, and DLEK procedures in high-risk horse patients. In corneal transplantation in the horse, it appears important to use the minimal graft size necessary to achieve the therapeutic goal.

Better techniques of donor graft preservation and an understanding of both the triggers for rejection and the rejection process itself in corneal transplantation in the horse are critical to overcoming the rapid donor graft rejection process noted in the horse. It is unlikely that we will ever achieve the high level of transparency in the corneal transplants in our horse patients that physicians do in human patients receiving corneal transplants [529]. A small corneal scar is considered a satisfactory outcome in the horse. Corneal transplants in humans with corneal vascularization and/or infection are rejected and scar similarly to our horse patients, and are considered failures needing reoperation.

Descemetocele: near rupture of the ocular surface

Descemet's membrane is the BM of the corneal endothelium, and is located between the most posterior aspect of the stroma and the corneal endothelium. It is elastic and consists mainly of collagen type IV. Descemet's membrane of the horse is approximately 38–40 μm thick and is produced throughout life [32, 82].

Enzymatic dissolution of the corneal epithelium and stroma with exposure of Descemet's membrane in the horse is termed a descemetocele. A stromal groove or furrow is a precursor to descemetocele formation as neutrophilic dissection of the corneal lamellae within a melting ulcer occurs in order to slough degenerate stromal collagen, inflammatory cells, and microbes from the ocular surface. The problem in melting ulcers is that Descemet's membrane can also be affected by proteases. A descemetocele is manifested clinically as a clearing of the cornea, and may appear dark or shiny depending on pupil dilation permitting light reflection from the tapetum. The IOP may cause anterior bulging of Descemet's membrane. Fluorescein dye is not retained by exposed Descemet's membrane, although the exposed bare stromal walls of the descemetocele will stain positive. Because of the absence of sensory innervation in the posterior cornea, descemetocele affected eyes may appear overtly comfortable, and any apparent sudden improvement in pain levels in cases of deep stromal ulceration should prompt urgent re-examination for the presence of a descemetocole.

A descemetocele is an area of structural weakness, and is associated with a high risk of corneal perforation with iris prolapse. Epithelial cells can migrate over the edge of a descemetocele to attempt to cover the exposed stromal collagen and bare Descemet's membrane. This is manifest clinically as a smooth appearance to the edge of the descemetocele, and the walls of the descemetocele then do not retain fluorescein dye (online Figure 7.249). In some cases, the descemetocele can remain in this indolent and high-risk state for protected periods (online Figure 7.249).

Medical therapy for a descemetocele is similar to that for a melting ulcer, with topical antimicrobials, antiproteases, and mydriatic/cycloplegics, and systemic antibiotics and NSAIDs. It is possible to heal small descemetoceles with medical therapy alone (online Figures 7.250 and 7.251). However, there is a high risk of corneal perforation throughout the treatment period, and surgical intervention using DALK or PK procedures is the recommended standard of care.

Corneal perforation: iris prolapse

In the event of corneal perforation, the iris moves anteriorly to prevent aqueous humor leakage, or can partially prolapse through the corneal perforation. Fibrin leaking from iris blood vessels attempts to seal the perforation and restore the integrity of the ocular surface. This process is a normal protective mechanism.

Iris prolapse in the horse can occur after acute ocular trauma, particularly sharp and perforating corneal injuries causing rupture of the cornea, limbus, or sclera [82, 146, 147, 170]. Corneal perforation with iris prolapse in the horse also occurs secondary to enzymatic degradation of stromal collagen and ground substance caused by infectious and noninfectious ulcerative keratitis [82, 146, 147, 170].

The prognosis for horses with perforating corneal lacerations is generally considered to be guarded, depending on the size of the corneal lesion, location of the corneal perforation, the degree of iridocyclitis prior to perforation, the length of time iris

prolapse is present, and the mechanism for the iris prolapse. Perforating lacerations caused by sharp injuries are generally associated with a better prognosis than those caused by blunt or missile injuries [82, 145, 170, 530, 531]. High-energy, blunt ocular trauma may result in hyphema or globe rupture (or both) at the limbus or equator where the sclera is thinnest [530, 531]. The prognosis of iris prolapse with corneal lacerations and mild hyphema is slightly more favorable, albeit still guarded, compared with that for horses having corneal lacerations and total hyphema [82, 145, 170, 530, 531]. In one study in horses, iris prolapse and hyphema comprising greater than an estimated 10% of the anterior chamber resulted in blindness, phthisis bulbi, or enucleation [146, 147].

Perforating lacerations confined to the cornea and measuring 15 mm or less in length tend to have a favorable visual outcome after surgical repair. Iridectomy does not generally exacerbate post-operative uveitis or adversely affect visual outcome, and it may facilitate post-operative mydriasis and prevent septic endophthalmitis [146, 147]. Conversely, perforating corneal lacerations measuring 15 mm or more in length and extending to, along, or beyond the limbus are inclined to a poor visual outcome and enucleation. Chances of retaining vision may also be substantially reduced in perforating corneal wounds accompanied by hyphema [82, 146, 147]. Endogenous tissue plasminogen activator (TPA) on the equine iris surface can digest small amounts of anterior chamber fibrin and small blood clots. Large amounts of anterior chamber fibrin and large blood clots will disappear faster following the injection into the anterior chamber of TPA (50–150 μg in 0.1 mL via intracameral injection). Vigorous mechanical lavage of anterior chamber fibrin and blood can exacerbate hemorrhaging.

Eyes with perforating corneal ulcers and iris prolapse of longer than 15 days duration, as well as eyes with iris prolapse from melting ulcers, and iris prolapse with ulcers with concomitant fungal and bacterial infections (or both) tend to have a poor visual outcome [146, 147, 170]. Eyes with iris prolapse and bacterial or fungal corneal ulcers of long duration may have substantially more pre-operative iridocyclitis and be at a greater risk of developing aggressive endophthalmitis post-operatively than ulcers of short duration, thus predisposing to more extensive development of anterior and posterior synechiae, cataract, glaucoma, and retinal detachment [146, 147].

Surgical technique (online Figures 7.155, 7.156, 7.157, 7.163, 7.164, 7.165, 7.166, 7.167, 7.180, 7.181, 7.182, 7.183, 7.184, 7.202–7.212)

Several concepts are important in the microsurgery of iris prolapse repair [82, 170]. If an iris prolapse is fresh, an attempt can be made to replace the protruding iris. If the iris tissue is damaged or necrotic, the protruding iris is excised with electrocautery [82, 170]. Hemorrhage is always a risk if the vascular iris is transected. Conjunctival grafts alone [146] and PK plus a conjunctival graft [147]. have been used to surgically treat iris prolapse. A Seidel's test is used to test for suture line integrity post-operatively. Blood and fibrin clots in the anterior chamber are carefully digested with TPA (50–150 μg in 0.1 mL via intracameral injection). TPA can successfully digest blood clots in the anterior chamber that have been present for 2 weeks in horses [82, 170].

In horses with iris prolapse where surgical repair is not an option, attempts to reduce aqueous humor leakage can be attempted with tissue or surgical glues [532]. Amnion, Biosyst, or Acell can be "glued" to the corneal defect with glues such as Tissuemend II. The area of the cornea that is to be "glued" must be completely dried for the glue to adhere. A hair dryer set on warm (not hot!) is useful for this purpose. If the amnion or other biomaterial adheres, the cornea will epithelialize under the glue to plug the leak. The glue will then dehisce.

Outcomes

In a review of 32 horses, iris prolapse was found secondary to a melting corneal ulcer in 15 horses (47%), following rupture of an SA in two horses (6%), and associated with a full-thickness corneal laceration in 15 horses (47%) [146, 147]. Twenty-one of the horses underwent medical therapy and surgical repair with direct closure alone or a conjunctival graft. Four months post-operatively, 40% of the eyes that had iris prolapse from a melting ulcer were visual and 33% of the eyes that had iris prolapse from a corneal laceration were visual [146, 147].

In a later study, 37 horses with iris prolapses caused by corneal ulcers with keratomalacia were treated surgically with either PK alone ($n=9$) or PK with either a conjunctival pedicle flap ($n=22$), AMT ($n=5$), or amnion membrane and conjunctival pedicle flap ($n=1$) [147]. The eyes were visual post-operatively in the majority of the cases ($n=24$; 64.9%) that had missing corneal tissue replaced with donor cornea. Limited vision was noted in six eyes (16.2%), three eyes became phthisical (8.1%), and four globes were enucleated (10.8%). The addition of the corneal button was thought to increase the visual outcomes by replacing the missing collagen and preventing leakage of aqueous humor during the post-operative period [147].

Post-surgical corneal scarring

Healing and subsequent remodeling of the horse cornea with ulcerative and nonulcerative keratopathy generally results in some degree of subepithelial and deeper stromal opacification and haze, and corneal vascularization. Subepithelial and deeper stromal PG and reparative collagen production associated with healing are responsible for slight to severe corneal haze (see Figure 7.69B). Corneal neovascularization also contributes to this problem as it causes irregularities of the ocular surface that interferes with light refraction, and increases the vulnerability of the ocular surface to immunological attack.

During the months to years following corneal injury and wound healing, there is a return to normalcy with elimination of inflammatory and myofibroblast/fibroblast cells and restoration of the quiescent state of the keratocytes. This process is associated with remodeling of any disordered collagen that may be laid down during the wound healing process [75]. This stromal remodeling process can continue for years and result in at least partial clearing of even the most severe stromal scar in the horse.

There is pressure on clinicians working with horses with clinical scarring to ameliorate the corneal opacification following successful treatment of a severe keratopathy. Topically administered corticosteroids, CsA, and mitomycin C have been used to reduce corneal haze and vascularization in the horse [82]. Topical corticosteroid use after a serious corneal infection carries an unquantifiable risk of reinfection and abscessation and should be used with caution. Some clinicians, particularly those in geographic locations with a high incidence of keratomycosis, will avoid their use completely in these circumstances. CsA is safe to use and can aid fibroblast and pigment removal, but this does not occur quickly in the horse. Mitomycin C effectively downregulated the scarring potential of equine corneal fibroblasts *in vitro* by reducing the degree of transdifferentiation of corneal fibroblasts to myofibroblasts, and has some promise for clinical use [533]. New products such as hyaluronic acid substitutes (e.g., EquitrX (Bayer, Shawnee Mission, KS)) may encourage corneal stromal ECM changes and could have some potential to induce scar reduction in the horse.

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CHAPTER 8

Diseases of the uvea, uveitis, and recurrent uveitis

Brian C. Gilger and Steven R. Hollingsworth*

Anatomy and physiology of the uveal tract

The uveal tract is comprised of the iris, ciliary body, and choroid and is anatomically similar to the uveal tract of other species in most clinically relevant aspects. As in most herbivores, the adult equine pupil is horizontally oval.

Iris

The iris functions as a shutter that responds to prevailing light conditions by modulating the size of the pupil. The anterior surface of the iris is without a contiguous epithelial layer and is composed of connective tissue interspersed with fibroblasts and melanocytes. Beneath this surface layer is the iris stroma, which consists of chromatophores, fibroblasts, and collagen fibers that cradle a plexus of blood vessels. Within the central stroma and circumferentially oriented along the pupillary margin is the parasympathetically innervated iris sphincter muscle. Immediately posterior to the iris stroma is the iris dilator muscle, which is radially oriented and sympathetically innervated. The posterior aspect of the iris is lined with a double layer of densely melanotic epithelial cells (Figure 8.1). The dorsal aspect of the pupillary margin is capped with a cystic extension of the posterior epithelium, the corpora nigra (or granula iridica) (Figure 8.2).

Ciliary body

The ciliary body produces aqueous humor through active secretion and ultrafiltration of plasma. The ciliary body is posterior to the base of the iris and is approximately triangular in cross-section. As viewed from the vitreous cavity, the ciliary body is divided into the anteriorly positioned pars plicata and the posteriorly positioned pars plana. As the name suggests, the pars plicata is characterized by a folded or pleated appearance, although the number, prominence, and shape of the ciliary processes vary among species. In general, species with large anterior chambers, such as horses, have more processes than those with small anterior chambers. Carnivores' ciliary processes tend to be long and thin, whereas those of herbivores, including the horse, resemble blunted ridges [1]. From the ciliary processes, zonular fibers extend and connect to the equatorial region of the lens. The pars plana is a relatively smooth, flat portion that extends from the pars plicata to the most peripheral extension of the retina (the ora ciliaris retinae). The width of the pars plana varies and is widest dorsolaterally [2].

The entire inner surface of the ciliary body (the surface in contact with the vitreous body) is lined with a double row of epithelial cells. The innermost epithelial cell layer (from the perspective of the vitreous cavity) is nonpigmented and referred to as the **nonpigmented epithelium** (NPE) of the ciliary body. The NPE is confluent at the ora ciliaris retinae with the sensory retina, and at the posterior base of the iris with the innermost layer of the posterior iris epithelium. The second epithelial cell layer is heavily melanotic and is referred to as the **pigmented epithelium** of the ciliary body. The pigmented epithelium lies immediately under the NPE and is contiguous with the retinal epithelium at the ora ciliaris retinae and at the posterior base of the iris with the outermost layer of the posterior iris epithelium. Tight junctions between NPE cells are thought to represent the epithelial portion of the blood–aqueous barrier [3]. Deep to the two-layer ciliary body epithelium, each ciliary process has a central portion of connective tissue and a vascular plexus which is fenestrated, allowing leakage of plasma into the ciliary body stroma (Figure 8.3). The epithelial portion of the blood–aqueous barrier filters this plasma, removing virtually all protein and cells.

*Dr Hollingsworth was the author of the uvea chapter in the second edition of *Equine Ophthalmology*. Only approximately 20–30% of this previous chapter has been updated and combined with the equine uveitis chapter for the third edition of *Equine Ophthalmology*.

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Thus the aqueous humor represents an ultrafiltrate of plasma. In addition to this filtration function, the NPE contains carbonic anhydrase, which catalyzes the active transport-mediated portion of aqueous humor production (Figure 8.4) [1]. Beneath the ciliary processes, lying on the internal surface of the sclera and forming the base of the ciliary body triangle, is the ciliary body musculature. Virtually all mammals have circumferentially oriented, parasympathetically innervated, smooth ciliary body muscles. When these muscles are contracted, the zonular fibers are relaxed, which in turn allows the lens to passively thicken. This mechanism is responsible for accommodation in mammals. However, most nonprimate mammals have poorly developed ciliary body musculature and therefore poor accommodative ability.

Anterior to the ciliary body musculature and visible at the juncture of the base of the anterior face of the iris and the limbus is the ciliary cleft. Spanning the opening of this cleft are strands of connective tissue called **pectinate ligaments**, which extend from the base of the iris to insert on the inner aspect of the limbus. The ciliary cleft is posterior to the pectinate ligaments and filled with a sponge-like network of connective tissue beams, the trabecular meshwork. In the horse, these beams are completely lined with endothelial cells called **trabecular cells**



Figure 8.1 Photomicrograph of a normal equine iris. IDM, Iris dilator muscle; IS, iris stroma; ISM, iris sphincter muscle; PIE, posterior iris epithelium (×4).

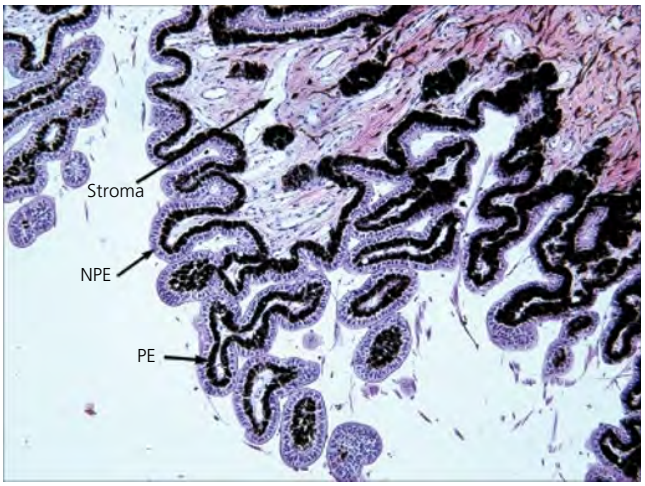
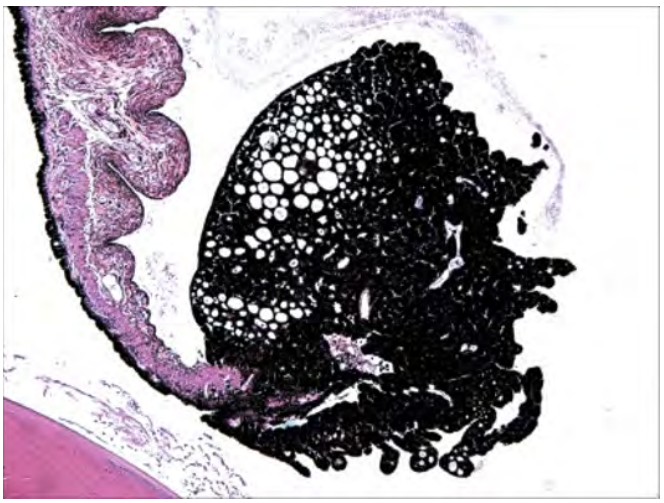


Figure 8.3 Photomicrograph of normal equine ciliary body. NPE, Nonpigmented ciliary body epithelium; PE, pigmented ciliary body epithelium (×4).



(A)



(B)

Figure 8.2 (A) Infrared clinical photograph of the normal equine eye with normal large dorsal corpora nigra. (B) Photomicrograph of normal equine corpora nigra as a cystic extension of the posterior iris epithelium (×2).

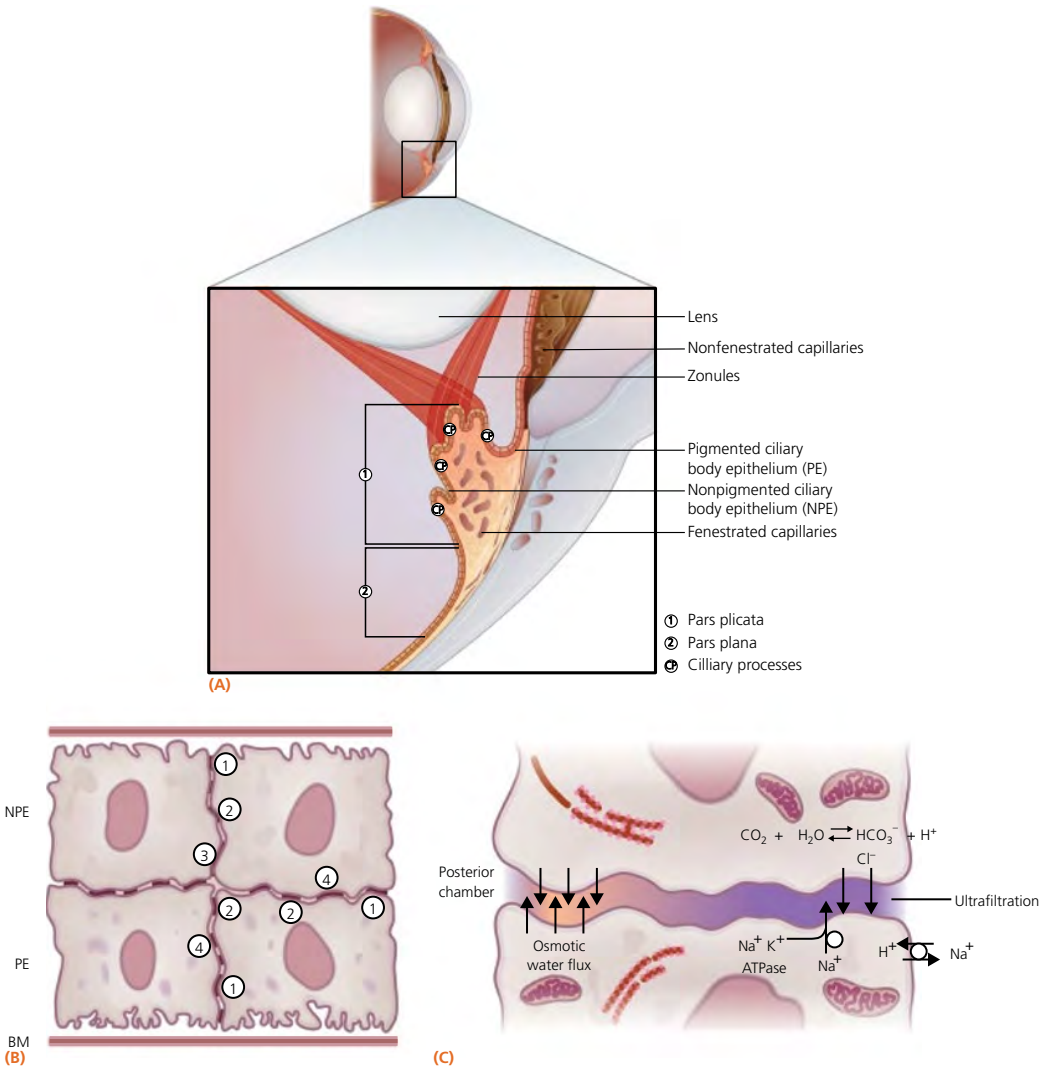


Figure 8.4 (A) Ciliary body anatomy. (B) Note the tight junctions (located at #1–4) between the lateral borders of the nonpigmented ciliary body epithelium (NPE), which represents the epithelial portion of the blood–aqueous barrier. PE, Pigmented ciliary body epithelium; BM, basement membrane. (C) There is active transport of sodium and bicarbonate ions (by the action of the enzyme carbonic anhydrase), which contributes to production of aqueous humor. These enzyme systems are located in the lateral wall of the ciliary body NPE. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

[1]. The ciliary cleft is the location of aqueous humor outflow. Any process that interferes with normal outflow can lead to increased intraocular pressure (IOP) (see the discussion of equine glaucoma in Chapter 10).

Choroid

The choroid is the posterior aspect of the uveal layer and has two main components. Covering the inner surface of the sclera is a thick plexus of vessels embedded in densely melanotic connective tissue that radiate out from the area of the optic disk. Most of these vessels are veins that unite to form the vortex veins near the equator. View of the choroidal vessels is usually obscured ventrally by melanin in the retinal epithelium and dorsally by the tapetum, but may be seen in lightly pigmented individuals (Figure 8.5) [4–6]. The tapetum occupies roughly the dorsal half of the fundus and is located immediately interior to the choroidal vasculature. The tapetum varies in color but is usually blue-green to yellow, and is often associated with iris and coat color. While cellular in carnivores, the tapetum in herbivores is made up of highly organized collagenous fibers. In the tapetal area, capillaries from the choroidal arteries run through the tapetal fibers to provide nutrition to the retina. When viewed end-on ophthalmoscopically, these vessels appear as multiple small dots throughout the tapetal area and are called the **stars of Winslow** (Figure 8.6). Because the horse has a paurangiotic retinal vascular pattern, the choroid is responsible for supplying nutrition to the entire retina, with the exception of the peripapillar area.

The uveal tract contains most of the blood supply of the eye and is in direct contact with peripheral vasculature. Therefore diseases of the systemic circulation (e.g, septicemia, bacteremia) will also affect the uveal blood circulation. There is a barrier between this blood circulation and the internal aspects of the eye, termed the **blood–ocular barrier** (Figure 8.8). The blood–ocular barrier consists of the blood–aqueous barrier (i.e, tight junctions between the NPE cells of the ciliary body and nonfenestrated iridal blood vessels) and the blood–retinal barrier (i.e, tight junctions between the cells of the retinal pigmented epithelium and nonfenestrated retinal vessels). These semipermeable barriers normally prevent large molecules and cells from entering the eye and help the intraocular fluids remain clear. The blood–ocular barrier also limits the immune response to the internal aspects of the eye, causing the eye to be considered an immune-privileged site. With trauma or inflammation, these barriers can be disrupted, allowing blood products and cells to enter the eye. Flare, cell accumulation, or haze in the aqueous or vitreous are clinically observable signs of the disruption of the blood–ocular barrier that occurs in uveitis. Disruption of the barrier enables activation of various host immune responses, including antibody production to self-antigens that are not normally recognized by the horse's own immune system, as well as antibody production to foreign antigens inside the eye.

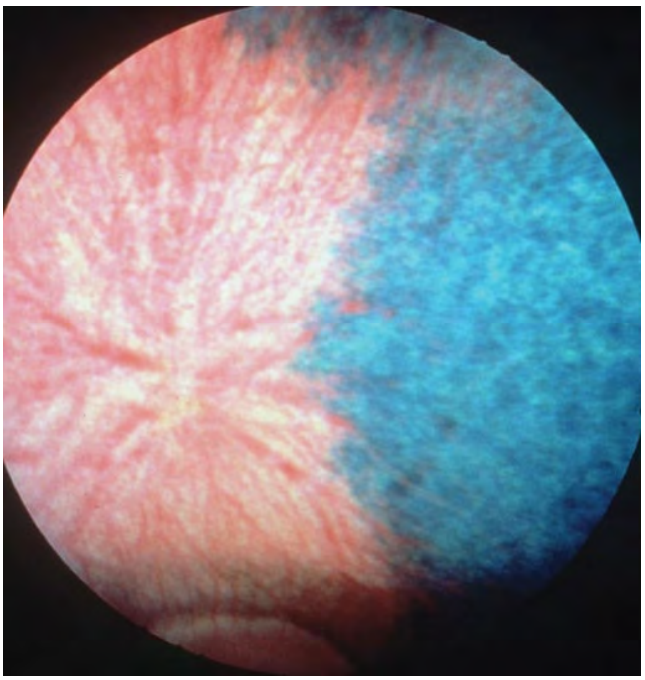


Figure 8.5 Geographic absence of the tapetum dorsal to the optic disc, allowing for visualization of the choroidal vasculature and vortex vein area.

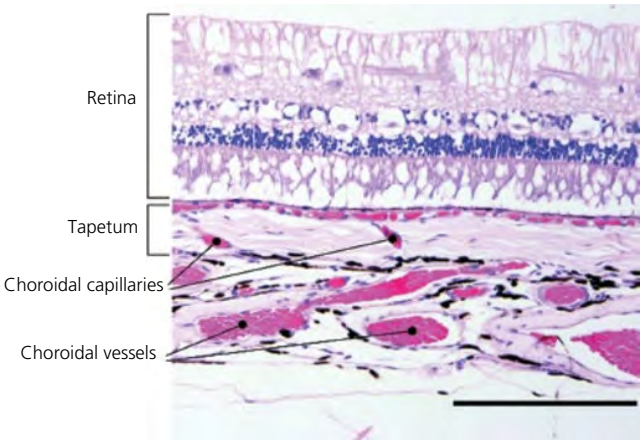


Figure 8.6 Photomicrograph of normal equine choroid (bar = 200 μm; ×100). (*Source*: Photomicrograph courtesy of Dr Christopher M. Reilly.)

Congenital diseases of the uvea

Aniridia

Although the term aniridia implies complete absence of an iris, it has been applied to a clinical condition reported in horses in which only a rudimentary, nonfunctional ridge of iridal tissue is present (Figure 8.7). Aniridia was first reported in 1955 in a Belgian draft stallion and 65 of his offspring who were similarly affected [7]. The author concluded that aniridia was a heritable defect passed via an autosomal-dominant mode. Subsequently, aniridia was described in a Quarter Horse stallion [8]. In an ensuing study, eight offspring of that stallion were followed, and seven demonstrated aniridia [9]. The authors concluded the mode of inheritance was similar to that of the Belgian draft stallion. Since then, aniridia has been observed sporadically, being specifically reported in a Thoroughbred colt [10] and a Welsh/Thoroughbred-cross filly [11].

Horses affected with aniridia are usually presented within the first few months of age because the client has noticed such signs as an unusual appearance of both eyes, excessive squinting in bright sunlight, and/or overreacting to flashes of light. On ophthalmic examination, the pupils are widely dilated and nonresponsive. The



Figure 8.7 Aniridia. Notice the ciliary body processes and edge of the lens, which are not visible in normal horses. (*Source*: Photograph courtesy of Dr Michelle Willis.)

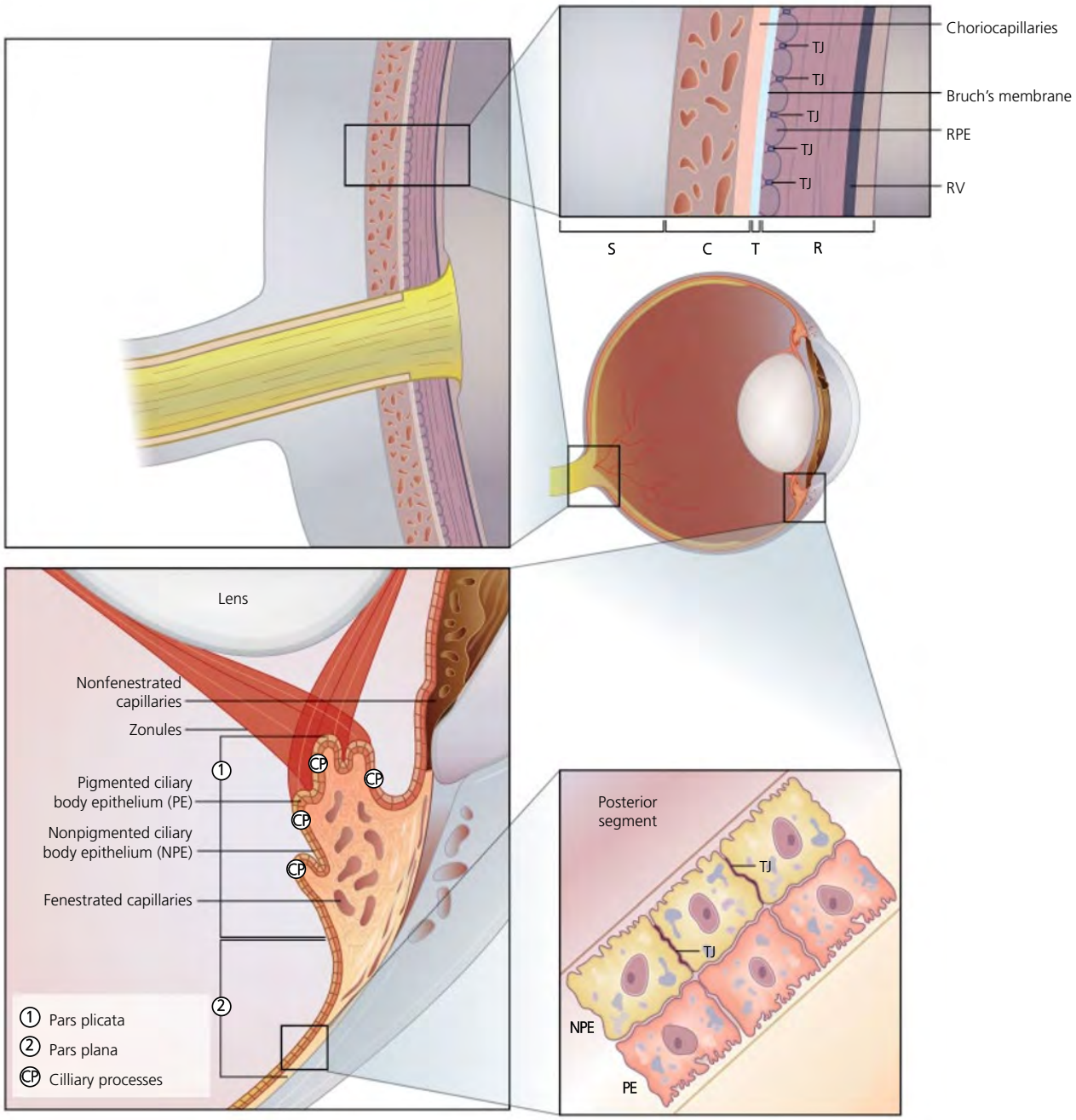


Figure 8.8 The barrier between blood circulation and internal aspects of the eye is called the blood–ocular barrier and consists of the blood–aqueous and blood–retinal barriers, which normally prevent large molecules and cells from entering the eye. TJ, Tight junctions; RPE, retinal pigmented epithelium; RV, retinal vessels; T, tapetum; S, sclera; C, choroid; R, retina. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

extent of the pupillary dilation is so marked that the lens equator and ciliary body processes are visible. The corpora nigra is absent. Virtually every reported case of aniridia has been accompanied by what is described as corneal vascularization and nodular changes along the dorsal and sometimes the ventral aspect of the limbus [8–11]. When affected globes have been available for histopathologic examination, fine hairs have been found growing from the corneal nodules. These have been identified as dermoids. Cataractous changes are also a frequent accompanying sign with aniridia. The cataracts are usually focal and found in the anterior cortex. They are sometimes present at the time of initial examination, but may not arise until later and tend to be slowly progressive.

Persistent pupillary membrane (PPM) was reported in one patient [11]. Findings on posterior segment examinations in horses with aniridia have been uniformly unremarkable. The diagnosis of aniridia is straightforward and based on clinical signs alone (Figure 8.8). No treatment is available. Many horses with aniridia have performed well in racing or other activities [10, 11].

Anterior segment dysgenesis/persistent pupillary membrane

The terms anterior segment dysgenesis and multiple congenital ocular anomalies (MCOA) are used to describe several syndromes with different clinical presentations. See Chapter 5 for more information on MCOA. Ophthalmic structures potentially affected by anterior segment dysgenesis include the cornea, iridocorneal angle, iris, ciliary body, lens, and retina, as well as the globe itself as manifested by microphthalmos or hydrophthalmos (i.e, enlarged eye) [12–15]. The severity of signs associated with anterior segment dysgenesis varies greatly.

Because most of the structures of the anterior segment are derived from the neural crest, alterations in the differentiation and migration of this layer lead to the signs associated with anterior segment dysgenesis [14]. Specific reported malformations involving the anterior uvea include miosis, iris hypoplasia, iris and ciliary body cysts, and PPMs. Of these, the most common clinical manifestation of anterior segment dysgenesis in domestic species, including the horse, is PPMs [14]. During embryonic development, a vascular plexus called the **pupillary membrane** covers the anterior surface of the iris and the pupillary aperture. This membrane rarifies near the end of gestation, but remnants can often be found in neonatal foals [15]. When such strands persist into adulthood, they are called PPMs. In adult horses, it is not uncommon to find small PPMs that originate from the collarette region of the iris and extend a few millimeters. Usually these strands either terminate as a free end in the aqueous or attach to the anterior surface of the iris (Figure 8.9). Occasionally, PPMs attach to the anterior lens capsule or posterior surface of the cornea. In such instances, opacification is usually seen where the PPMs attach. Such opacities would be present from birth. However, in most equine patients, the distal ends of the PPMs are free floating or attached to adjacent iris. In such instances, no secondary signs are found.

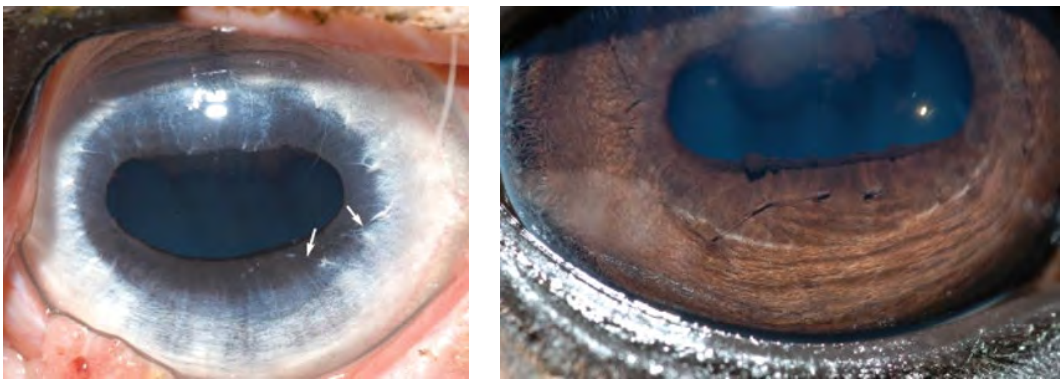
The diagnosis of PPMs is made on the basis of clinical appearance. In horses, opacities associated with PPMs rarely cause significant visual deficits, and treatment is not usually indicated.

Anterior uveal cysts

Uveal cysts may or may not be congenital in origin, but are included in this section because they have been noted in horses of many different ages, including young horses, and may be present as very small cysts at birth, only to enlarge and become apparent later in life. Anterior uveal cysts may be found in four locations: (1) the corpora nigra, (2) along the margin of the pupil or free floating in the anterior chamber, (3) attached to the ciliary body, and (4) within the iris stroma. The corpora nigra normally protrudes from the dorsal aspect of the pupillary margin and to a lesser degree from the ventral margin. It is a vacuolated extension of the posterior iris epithelium. Because many horses that have cystic corpora nigra are middle aged or older, it is possible that the condition is not congenital. The cause (or causes) of cystic corpora nigra is not known, but it does not seem to be related to past or present intraocular inflammation [16].

When the corpora nigra becomes cystic, its normally roughened appearance becomes smooth and spherical (Figure 8.10). The condition is usually unilateral, but can be bilateral, and the size of the cysts can vary markedly. Most are sufficiently small that they do not cause significant interference with vision. However, depending on the specific location, even moderate-sized cysts can partially inhibit the visual field, especially when the horse is in bright light and the pupil is miotic. For this reason, horses with cystic corpora nigra should be initially evaluated without pharmacologic dilation and under conditions of bright illumination so the extent of pupillary aperture blockage can be accurately assessed.

Differential diagnoses of corpora nigral cysts include inflammatory or neoplastic changes to the iris in the area of the corpora nigra. Although ultrasonography could be used to



(A) (B)

Figure 8.9 (A) Iris to iris PPMs (**arrows**) in an adult horse. (B) Pigmented iris with PPMs.

differentiate cystic corpora nigra from inflammatory or neoplastic infiltrates, this is rarely necessary because the clinical appearance is usually sufficiently characteristic.

Although treatment is not ordinarily necessary, the most effective and noninvasive treatment is deflation of the cystic corpora nigra with a laser. In a series of eight horses with signs including loss of vision, being startled when approached from the affected side, head shaking, and poor jumping performance, treatment with an ophthalmic neodymium-yttrium aluminum garnet (Nd:YAG) laser was effective in resolving the vision problems in all horses [16]. To perform this procedure, only sedation and an auriculopalpebral nerve block is required. After surgery, some horses required a short course of topical antiinflammatory and mydriatic medication, but most of the horses were comfortable without treatment. An 810-nm diode laser delivered through an indirect ophthalmoscope headset has also been used successfully to shrink cysts in dogs, cats, and horses [17].

Iridal cysts may be found distinctly separate from the corpora nigra along the margin of the pupil or free floating in the anterior chamber. These cysts are believed to develop in a manner similar to iridal cysts in dogs and represent a failure of the two layers of neuroectoderm to completely fuse, thus allowing fluid to accumulate in areas between the two-layered posterior iris epithelium. Because iridal cysts can enlarge, it has been theorized that some of the posterior iridal epithelial cells that compose the lining of the cyst retain secretory ability [18, 19]. The clinical appearance of these cysts is spherical to oval and smooth. Although they can occasionally be transilluminated, most appear opaque (Figure 8.11). Sometimes the cysts will spontaneously rupture and leave a circular area of pigmentation on the anterior lens capsule or the posterior surface of the cornea.

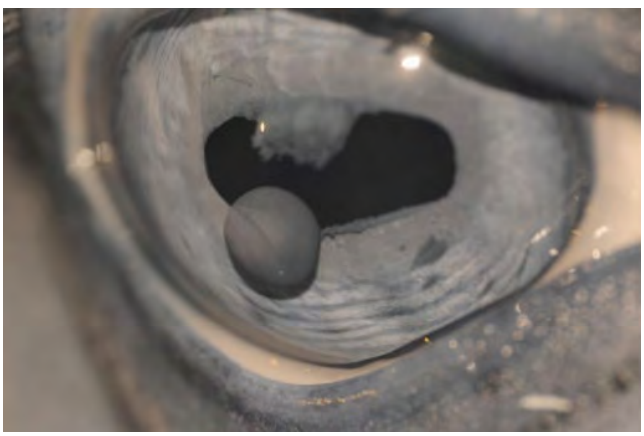
As with cysts of the corpora nigra, these must be differentiated from inflammatory or neoplastic masses, but this is rarely a problem because of the characteristic clinical appearance. Treatment is not commonly indicated because these iridal cysts seldom cause pain or visual impairment. Should removal be deemed necessary, they can be deflated with an Nd:YAG laser, as described for cysts of the corpora nigra (Figure 8.12) [16]. Alternatively, a 27- to 30-G needle attached to a tuberculin syringe can be introduced into the anterior chamber at the limbus. The needle is used



Figure 8.10 Infrared image of a dorsal corpora nigra cyst.



Figure 8.11 Iris cyst along the ventral pupillary margin.



(A)



(B)

Figure 8.12 (A) Infrared image of an iris cyst in the lower leaf of the iris immediately before application of an ophthalmic Nd:YAG laser. (B) Infrared image of an iris cyst in the lower leaf of the iris immediately after application of an ophthalmic Nd:YAG laser, demonstrating deflation of the cyst.

to perforate the cyst wall while gentle pressure from the syringe collapses the cyst [18]. This procedure is invasive and requires post-operative treatment with topical anti-inflammatory and mydriatic medications for the resultant uveitis.

Ciliary body cysts are believed to originate in a manner similar to that of iridal cysts, except in this instance, the failure of the two layers of the neuroectoderm to fuse is in the area of the ciliary body, so these cyst walls are made up of NPE (Figure 8.13) [12, 19]. Ciliary body cysts are a manifestation of the MCOA syndrome in Rocky Mountain horses and other horse breeds [12]. Other potential causes of ciliary body cysts include inflammatory processes, traction from zonules, and age. Because the walls of these cysts are usually lined with NPE, they can be transilluminated. They tend to be oval and relatively large, often extending from the pars plicata to the ora ciliaris retinae (Figure 8.14). Ciliary body cysts are most commonly located ventrolaterally, and they can be difficult to detect without pharmacologic mydriasis [12].



Figure 8.13 Photomicrograph of ciliary body cyst (×10).



Figure 8.14 Temporal ciliary body cyst visible through dilated pupil.

As with the other anterior uveal cysts, differential diagnoses include inflammatory and neoplastic disease, such as uveal melanoma. Although ocular ultrasonography can be used to confirm the diagnosis of ciliary body cyst, the shape, contour, and ability to transilluminate make this differentiation straightforward on the basis of clinical signs alone. These cysts do not routinely cause pain or visual impairment, and treatment is not necessary.

Uveal coloboma

Uveal coloboma, such as iris coloboma, are rare in horses, but can manifest as typical (ventral or 6 o'clock position) or atypical notch or gap of the iris [15]. These full-thickness, notch-like defects of the pupillary margin (Figure 8.15) can be unilateral or bilateral, and are not associated with detectable vision deficits. Iris coloboma has been associated with the multiple congenital ocular anomaly syndrome in Rocky Mountain horses [12] and reported as a congenital anomaly in Miniature horses [20]. Typical colobomas arise early in gestation and are associated with defective closure of the optic fissure and may be associated with additional ocular defects, so it is important to evaluate the remainder of the globe carefully. Atypical colobomas have been reported to be more common than typical ones and arise later in gestation [15]. These lesions may be isolated iris defects or associated with other ocular abnormalities. A full-thickness atypical coloboma may result in an iris defect called "pseudopolycorea," which is a hole in the iris without a true sphincter muscle encircling the defect [15]. There is no treatment for this condition and coloboma should be differentiated from synechia, iris hypoplasia (Figure 8.16), and iris atrophy.

Iris hypoplasia

Iris hypoplasia commonly manifest in horses with blue irides as dark, bulging areas observed predominately in the dorsal region iris, although they can be present in the ventral aspect of the iris and in eyes with brown irides. Previously, these areas in the



Figure 8.15 Ventral notch-like defect of the iris characteristic of a "typical" iris coloboma. (*Source*: Image courtesy of Dr Riccardo Stoppini.)

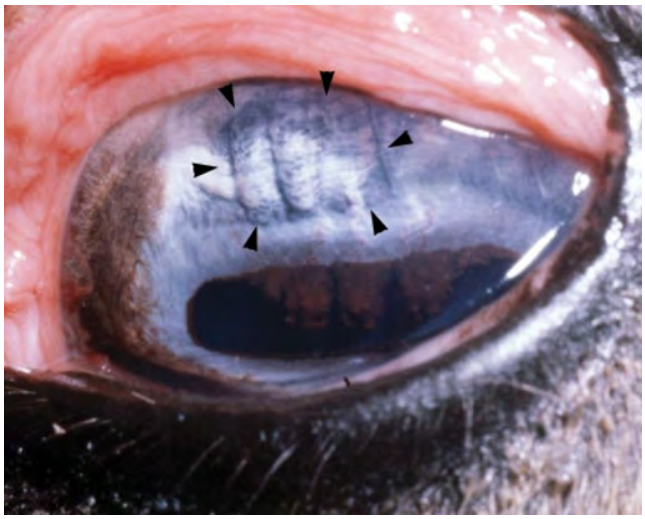


Figure 8.16 Area of iris hypoplasia (outlined by **arrowheads**).

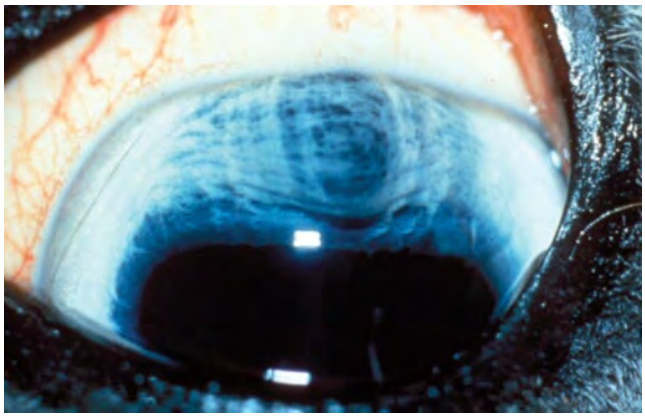


Figure 8.17 Iris hypoplasia with bulging dark area. (*Source*: Courtesy of Dr Mike Davidson.)

anterior surface of the iris have been interpreted as cysts within the iris stroma [21]. However, histopathologically, these lesions represent areas of iridal stromal hypoplasia; the iris protrusion, or bulging, was the result of aqueous humor pressure in the posterior chamber pushing the relatively weaker portion of iris forward [22].

The classic clinical picture of iris hypoplasia is a dark area, usually within the dorsal portion of the iris, that bulges forward (Figure 8.17). The condition can be unilateral or bilateral. Age, breed, and sex predispositions do not seem to exist [22]. The affected eyes are not painful, and there is no discernable effect on vision, although some horses may have increased sensitivity to light. The dark, bulging areas are most evident when examined in bright light with a motic pupil. The fact that these protruding areas actually represent thinning of the iris stroma is confirmed by passing a bright, focal beam of light through the pupil and observing the retroillumination of the fundic reflection through the lesion. To confirm the diagnosis of iris hypoplasia, the pupil can be pharmacologically dilated. With the pupil mydriatic, the bulging area disappears, taking on a wrinkled appearance. The most important condition to be ruled out for this clinical presentation is iridal neoplasia, specifically melanoma. Ocular ultrasonography can assist in making this differentiation, but careful examination under conditions of both miosis and mydriasis, as described in Chapter 1, should allow for an accurate diagnosis. It is highly unlikely that a neoplasm or inflammatory cell accumulation would allow for retroillumination of the fundic reflection or would "deflate" under conditions of pupillary dilation. However, should there be confusion after careful ophthalmic examination, ocular ultrasonography would be indicated. No treatment is required for iris hypoplasia.

Primary neuroectodermal intraocular tumors

Most primary neuroectodermal intraocular neoplasms are congenital, deriving from the primitive neuroectoderm of the optic cup. Medulloepithelioma of the anterior uvea is infrequently reported in the horse [23–30]. These tumors arise from undifferentiated medullary epithelial cells that line the inner portion of the embryonic optic cup [27, 31]. Normally, these cells differentiate into numerous epithelial cell lines in the adult eye, including the posterior iris epithelium, the ciliary body NPE, and the retinal epithelium. In horses with this tumor, a portion of these cells fail to differentiate. In the horse, medulloepitheliomas most frequently arise from the ciliary body region. On histologic examination, medulloepitheliomas usually demonstrate nonpigmented neuroepithelial cells arranged in tubules and rosettes. They are classified as either teratoid [27] or nonteratoid [24, 25], depending on whether the neoplastic cell population is characterized by relatively homogeneous, undifferentiated primitive neuroepithelium or contains tissues not normally found in the eye, such as cartilage, muscle, and brain tissue [32].

Medulloepitheliomas are most frequently diagnosed in young adult horses presented because of a fleshy mass noted within the pupil [25] or anterior chamber [24, 26]. However, this neoplasm should be on the differential list for older horses also, as evidenced by a a medulloepithelioma diagnosed in an 11-year-old Arabian mare [26] and a case of a meduloepithelioma/retinoblastoma diagnosed in a 14-year-old gelding. Differential diagnoses include other intraocular neoplasms, such as melanoma, and cystic changes of the iris or ciliary body. The clinical characteristics of anterior uveal cysts have been described in the section **Anterior uveal cysts**. Confirmation that an intraocular mass is solid tissue (as opposed to a cystic structure) and delineation of the specific location of the mass can be readily accomplished with ocular ultrasonography. Distinction between medulloepithelioma and intraocular melanoma is possible on the basis of clinical appearance. Melanomas are usually darkly pigmented and arise from the anterior surface of the iris, whereas medulloepitheliomas are most often fleshy masses apparent within the pupil.

Although it is usually not necessary for determining appropriate clinical action, biopsy of a ciliary body medulloepithelioma has been described [25].

It has been suggested that there may be two subtypes of medulloepithelioma in the horse: one is the more common mass derived from the ciliary body that has a more benign nature, while masses from the retinal or optic nerve tissue may be more aggressive in growth [29]. Ophthalmic changes associated with growth of the mass include corneal vascularization, corneal edema, corneal fibrosis, anterior uveitis, glaucoma, and buphthalmos (Figure 8.18) [23]. Metastasis of intraocular medulloepitheliomas are thought to be a rare and a late event. Extension into the orbit has been described in one horse [30]. The treatment of choice is enucleation or exenteration if there is evidence that scleral integrity has been compromised.



Figure 8.18 Medulloepithelioma causing corneal vascularization, corneal fibrosis, and buphthalmos and completely filling the intraocular space. (*Source*: Photograph courtesy of Dr Carol M. Szymanski.)

Acquired diseases of the uvea

Uveitis

Uveitis, by definition, is the inflammation of the uveal tract of the eye. The inflammation may involve primarily the iris and ciliary body (anterior uveitis) or the choroid and retina (posterior uveitis), but most commonly in horses, all anatomic areas of the uveal tract are inflamed (pan-uveitis). In the horse, the inflammation can be acute in onset, chronic, or recurrent. Further, equine recurrent uveitis (ERU) can be active (inflammatory episode occurring) or quiescent (no active inflammation). It is important that the equine clinician differentiates between acute uveitis, which has many underlying causes, and ERU, which is an immune-mediated disorder (as discussed in the section **Equine recurrent uveitis**). Therefore when the clinician examines a horse with suspected uveitis, he/she should answer three important questions to best diagnose and manage the case:

1. Does the horse have signs of active or quiescent uveitis?
2. Is the uveitis acute in onset, chronic (unresolved), or recurrent?
3. Is the uveitis primary (endogenous) or secondary to an ocular or systemic abnormality?

To answer these questions, a thorough history with recording of all ophthalmic abnormalities (time of onset of disease, duration of disease, treatments, sequelae) should be performed first, followed by a complete ophthalmic and physical examination. If the internal structures of the eye cannot be visualized because of opaque ocular media or other abnormality, then an ocular ultrasound should be performed to evaluate for ocular masses, lens luxation, or other primary ocular disease.

Acute active uveitis

Typical clinical signs associated with acute uveitis are all due to damage of the anterior uvea and subsequent compromise of the blood–aqueous barrier. Box 8.1 summarizes these signs (Figure 8.19). The initial diagnosis of uveitis is based on clinical signs. The common denominator of all the proposed causes of

Box 8.1 Signs associated with acute anterior uveitis.

- Blepharospasm
- Epiphora
- Conjunctival hyperemia
- Episcleral injection
- Diffuse corneal edema
- Corneal vascularization
- Keratic precipitates
- Aqueous flare
- Fibrin clots in anterior chamber
- Hypopyon
- Hyphema
- Change in iris color
- Rubeosis iridis
- Miosis
- Inflammatory deposits on posterior lens capsule
- Hazy appearance to anterior vitreous



Figure 8.19 Acute episode of anterior uveitis with a fibrin clot in the anterior chamber.

anterior uveitis is damage to the uveal tract. This leads to the release of the mediators of inflammation such as prostaglandins, leukotrienes, and histamines [33]. Although the specific roles of the different mediators are still unclear and may vary between species, the overall effects of their release are iris sphincter and ciliary body muscle spasm, increased vascular permeability, and breakdown of the blood–ocular barriers. This is followed by leakage of protein, fibrin, and potentially cells into the aqueous humor, which accounts for the clinical signs most commonly associated with acute anterior uveitis: blepharospasm, epiphora, aqueous flare, fibrin clots in the anterior chamber, miosis, and vitreous cellular infiltrate.

Because all the uveal tissues are abundantly populated with blood vessels, the physiology of early inflammation involves vascular congestion. This congestion causes dilation of the overlying episcleral blood vessels, resulting in episcleral vascular hyperemia that causes the characteristic "red eye" appearance of uveitis. Congestion and inflammation of the uveal vessels causes leakage of protein and fluid into the surrounding connective tissues as the blood–ocular barrier is disrupted. Infiltration of mononuclear cells into the uveal perivascular space is facilitated by vascular permeability, particularly in the ciliary body. Iris sphincter muscle spasm causes miosis and blocks the ability of the iris to adjust to prevailing light conditions. Accumulation of inflammatory cells and byproducts in the aqueous humor may obstruct the trabecular meshwork or uveoscleral region, resulting in secondary glaucoma. Chronically, glaucoma may occur from synechia, vascular overgrowth of the iridocorneal angle, or fibrosis of the uveal tissue.

Transparency of the cornea is compromised when inflammatory mediators in the aqueous humor cause altered function of the corneal endothelium. Disruption of the endothelial sodium/potassium–adenosine triphosphatase (Na+/K+-ATPase) pump, which normally keeps the cornea relatively dehydrated, contributes to development of corneal edema. Edema can become permanent if endothelial dysfunction is severe. Corneal cellular infiltrate or extensive vascularization is **not** a primary feature of uveitis; if present, the clinician should rule out primary corneal diseases such as stromal abscessation, immune-mediated keratitis, abd heterochromic iridocyclitis [34–36].

Function of the retina is disrupted if the photoreceptors are deprived of oxygen and other nutrients normally supplied by the choriocapillaris, if inflammatory toxins from the vitreous damage cellular components, or if the retina detaches as a result of subretinal exudates and cellular infiltrate from the inner choroid.

The posterior segment of the eye may have altered clarity from leakage of blood cells, macromolecules, and plasma components from the choroid and ciliary body into the vitreous. Infiltrating mononuclear cells and inflammatory cytokines can alter waste removal and contribute to liquefaction of the normally gel-like framework of the vitreous. Loss of the viscoelastic properties, combined with traction from the collapsing collagen network of the vitreous, may exert pull on the sparsely anchored retina and contribute to detachments and vision loss.

Box 8.2 Possible causes of acute uveitis.

Any injury to a horse's eye may result in uveitis and possible development of the syndrome of ERU. Some examples include:

Trauma

Blunt or penetrating injury

Bacterial organisms

Leptospira
Brucella
Streptococcus
Rhodococcus equi
Borrelia burgdorferi (Lyme disease)

Viral organisms

Equine influenza
Equine viral arteritis
Parainfluenza type 3
Equine herpesvirus types 1 and 2

Parasites

Onchocerca
Strongylus
Toxoplasma

Miscellaneous

Endotoxemia
Septicemia
Tooth root abscesses
Neoplasia

Causes

Because there is an almost endless list of proposed causes of anterior uveitis (Box 8.2) [37–42], a number of laboratory tests have been proposed to augment the complete ophthalmic and

physical examination and help determine the underlying cause of a specific episode of acute anterior uveitis (see discussion of systemic diseases in Chapter 15). These would include complete blood count, serum chemistry profiles, serologic tests for specific infectious causes such as leptospirosis and borreliosis, and conjunctival biopsies for detection of *Onchocerca* microfilaria. Although tests for specific infectious agents can assist in ascertaining the underlying cause, the results must be interpreted with caution because horses without uveitis can often have positive test results for many of these agents.

If a specific underlying cause can be identified, treatment centers on addressing that cause. Concomitant with treatment of the cause, or if no specific cause is found, the eye is treated symptomatically to reduce pain and minimize the intraocular damage associated with anterior uveitis. A list of common therapeutic agents with rationales for use, usual frequency and dosage, and adverse effects is shown in Table 8.1.

The initial therapeutic approach for an acute episode of anterior uveitis is aggressive treatment in an attempt to rapidly counteract the inflammation. As the signs of acute uveitis begin to lessen, the frequency of medication can be slowly reduced. However, complete cessation of treatment is not advised until all clinical signs have resolved for at least 1 month. Most horses that are presented with acute uveitis initially respond well to symptomatic treatment. The long-term prognosis can often be problematic because recurrence is common and each inflammatory episode causes further intraocular damage. Long-term adverse sequelae for uveitis include corneal scarring, cataract formation, glaucoma, and retinal degeneration.

Chronic and end-stage uveitis

Chronic uveitis may develop after a few days of unrelenting severe inflammation or following multiple recurrent episodes of uveitis. Common signs of chronic uveitis include corneal edema, keratic precipitates, iris fibrosis and hyperpigmentation, posterior synechia, corpora nigra degeneration (smooth edges), miosis, cataract formation, vitreous degeneration and discoloration, and peripapillary retinal degeneration (Figure 8.20).

End-stage uveitis is an advanced stage of chronic uveitis when the eye has developed phthisis bulbi, a small and shrunken eye (Figure 8.21).

Equine recurrent uveitis

Equine recurrent uveitis (ERU), also known as **moon blindness**, **iridocyclitis**, and **periodic ophthalmia**, has often been cited as the most common cause of blindness in horses [43–48]. This immune-mediated, panuveitis syndrome has a reported prevalence of 2–25% in horses in the USA [44, 47, 48]. However, field observations suggest that 1–2% of American horses suffer clinical disease serious enough to threaten vision [45].

ERU is characterized by recurrent episodes of intraocular inflammation separated, in most horses, by periods of remission ("quiescence") in which there are no signs of active intraocular



Figure 8.20 Common signs of chronic uveitis, including posterior synechia and cataract formation.

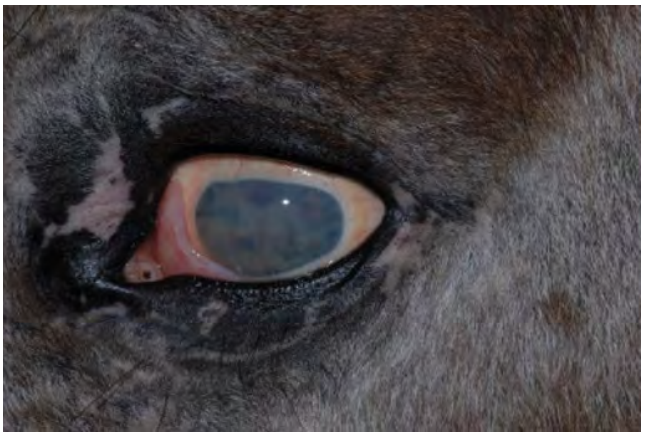
Table 8.1 Medical therapy for uveal diseases.

Topical medications	Frequency	Adverse effects
Prednisolone acetate, 1%	q1h–bid	Can compromise ocular surface immunity
Dexamethasone, 0.1%	q1h–bid	Can compromise ocular surface immunity
Flurbiprofen, 0.03%	q1h–bid	May prolong corneal ulcer healing
Diclofenac, 0.1%	q1h–bid	May prolong corneal ulcer healing
Bromfenac, 0.1%	q1h–bid	May prolong corneal ulcer healing
Cyclosporine A, 0.2–2%	q1h–bid	None
Atropine, 1%	q8h–q48h	May decrease gut motility
Systemic medications	**Dose**	**Adverse effects**
Flunixin meglumine	0.6 mg/kg IV, IM, PO initially, then 0.26 mg/kg PO	Long-term use can lead to gastric and renal problems
Phenylbutazone	4.4 mg/kg IV or PO q24h, or 1 g IV or 1 g PO bid	Long-term use can lead to gastric and renal problems
Aspirin	Mature horses: two to four 240-grain boluses PO or 10–26 mg/kg PO q24h–bid	Long-term use can lead to gastric problems
Dexamethasone	6–10 mg/day PO or 2.6–6 mg IM q24h	Laminitis, must use with caution
Prednisolone	100–300 mg/day IM, PO	Laminitis, must use with caution
Triamcinolone	1–2 mg subconjunctival or 2.5–5 mg intravitreal	Can compromise ocular surface immunity

bid, Twice a day; hr, hour; IM, intramuscularly; IV, intravenously; PO, orally; q, every.



(A)



(B)

Figure 8.21 (A) Bilateral phthisis bulbi in both eyes in a horse with chronic end-stage uveitis. (B) Eye with phthisis bulbi demonstrating a shrunken globe and cloudy cornea.

inflammation. These "bouts" of inflammation are separated by weeks to sometimes years. ERU generally develops after an initial bout of primary uveitis [45, 47–51], but not every case of initial equine uveitis will develop into ERU (see section **Diagnosis**). Cause of the primary uveitis, environmental factors, and genetic makeup of the horse all play a role in the development of ERU, and each horse that develops signs of uveitis is considered at risk for ERU until several years have passed without relapse after the primary uveitis.

History

ERU-like diseases have been described in horses since Vegetius wrote of recurrent eye inflammation in the fourth century AD [43]. Initially the syndrome was thought to be caused by the changes in the moon, hence the descriptive term **moon blindness**, still prevalent today. Much speculation occurred in the eighteenth, nineteenth, and early twentieth centuries as to the cause(s) of ERU. Before 1940, prevailing theories included various infectious causes, hereditary predisposition, thyroid deficiency, riboflavin deficiency, climate, toxin hypersensitivity, and parasites [43, 52, 53]. Early reviews describing the clinical examination and pathologic findings of ERU [43, 52, 53]. speculated further on infectious causes, and subsequent research was directed toward investigating bacterial etiologies. In 1947, Rimpau [54] presented evidence connecting some cases of the syndrome with leptospirosis, and in the following year, Heusser published data linking positive serum agglutinin titers to *Leptospira interrogans* serogroups Grippotyphosa, Pomona, and Australis in German horses [55]. Although prevalence has varied with the geographic region, leptospirosis has been linked to initiation of spontaneous ERU around the world [45, 54–73].

Other bacterial, viral, protozoan, and parasitic, as well as noninfectious etiologies have been associated with the syndrome [44, 74, 75]. The pathophysiology of ERU is far more complex than a simple systemic infection or traumatic episode. Research in horses, humans, and laboratory and domestic animals has shown that recurrent intraocular inflammation is multifactorial in origin, related to the genetic makeup of the individual and strongly immune mediated. Numerous investigations have described the variety of changes that accompany the syndrome in the anterior and posterior segment at the cellular level [49, 76–84]. Studies probing immune mechanisms responsible for triggering inflammatory episodes and tissue destruction, and relationships between genetics, equine major histocompatibility complex (MHC), and ERU susceptibility are ongoing [49, 77, 85–87]. ERU is an intricate disease complex, and defining the pathogenesis and risk factors will continue to challenge scientists and clinicians as research continues for effective therapies.

Classification

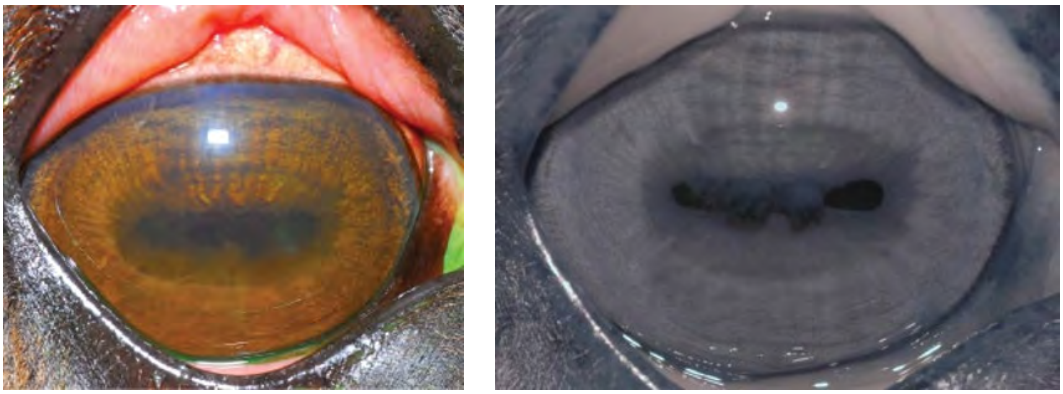
The syndrome of ERU must be differentiated from primary uveitis, which is a different disease pathophysiologically. Any cause of breakdown of the blood–ocular barrier may result in clinical signs associated with a clinical diagnosis of uveitis; however, ERU is a separate disease characterized by chronic recurrent bouts of uveitis. See later discussion regarding the diagnosis of ERU and pathophysiology of the development of this syndrome. Horses experiencing an initial episode of uveitis from any cause are at risk for ERU but are not classified as ERU cases until two or more episodes of inflammation have been observed. If several (i.e, two or more) years have passed without occurrence of a second episode of uveitis, the risk of development of ERU in that horse is diminished.

ERU is further characterized into three main clinical syndromes in horses: classic, insidious, and posterior ERU (Table 8.2). Because ERU most commonly involves all areas of the uveal tract (i.e, panuveitis), the human anatomic classification of uveitis (i.e, anterior, intermediate, and posterior uveitis) is not particularly distinguishing in horses.

Classic ERU is most common and is characterized by active inflammatory episodes in the eye, followed by periods of minimal observable ocular inflammation. The acute active

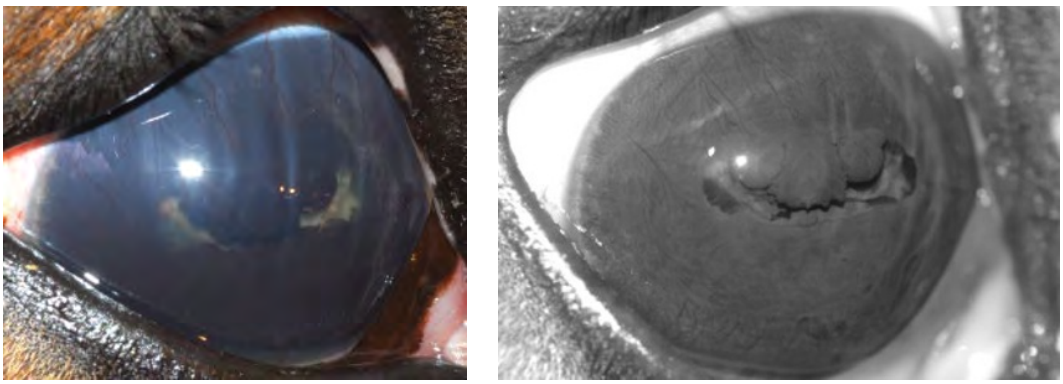
Table 8.2 Clinical classification and stage of chronicity of equine uveitis.

		Description
Clinical classification	Classic recurrent	Active inflammatory episodes followed by periods of minimal ocular inflammation
	Insidious	Persistent low-grade intraocular inflammation without overt signs of discomfort
	Primary posterior	Recurrent inflammation primarily in the vitreous, retina, and choroid
Stage of chronicity	Active/acute	Actively inflamed eye with signs of intraocular inflammation
	Quiescent	No clinical evidence of active internal inflammation and a comfortable eye
	End-stage	Blind eyes with phthisis bulbi with possibly dense cataract, luxated lens, detached retina, and/or loss of normal pupillary architecture



(A) (B)

Figure 8.22 Active bout of anterior uveitis. (A) Inflammation is observed primarily in the anterior segment, with conjunctival hyperemia, iris hyperemia/swelling, intense miosis, and fibrin in the anterior chamber. (B) Infrared photograph of the same eye as in **(A)** demonstrating intense miosis and iris swelling.



(A) (B)

Figure 8.23 Chronic ocular changes in an eye with multiple recurrent episodes of uveitis. (A) Mild corneal edema, multifocal posterior synechia, corpora nigra atrophy, iris hyperpigmentation, and dense cataract are visible and are all signs typical of chronic ERU. (B) Infrared photograph of the same eye as in **(A)** showing iris detail.

phase of ERU predominantly involves inflammation of the iris, ciliary body, and choroid, with concurrent involvement of the cornea, anterior chamber, lens, retina, and vitreous (Figure 8.22). After variable periods of time, the quiescent phase is generally followed by further and increasingly severe attacks of uveitis. In many horses, the repeated episodes of inflammation cause development of cataract, intraocular adhesions, phthisis bulbi, and vision loss (Figure 8.23) [47, 52, 74, 75].

Insidious ERU is characterized by a low-grade intraocular inflammation that does not manifest as outwardly painful episodes but has a gradual and cumulative destructive effect, which leads to degeneration of ocular structures and chronic clinical signs of ERU (Figure 8.24). This type of ERU is most commonly seen in Appaloosa and Draft breed horses.

Posterior ERU is inflammation predominantly in the vitreous, retina, and choroid (although mild anterior segment inflammation is commonly present). Clinical signs include bouts of vitreal inflammation, cloudiness, retinal detachment, and vision loss (Figure 8.25). Chronically, these horses may develop cataracts, retinal detachments, vitreal degeneration

(with or without fibrous strands), and retinal degeneration. This syndrome is most common in Warmbloods and draft breeds.

ERU may be further separated according to stage of chronicity, with cases labeled as "active or acute," "quiescent," or "end-stage" (see Table 8.2).

Acute or active cases show active pain and observable internal inflammation manifested as blepharospasm, mild to moderate corneal edema, aqueous flare, aqueous cells, hypopyon, iris hyperemia, miosis, hypotony, vitreal cellular infiltrate, and possibly retinal inflammation and detachment (Figure 8.26).

Quiescent cases are outwardly comfortable and show little active acute internal inflammation on clinical examination. However, they may have chronic inflammatory sequelae such as synechiae, corpora nigra atrophy, iris hyperpigmentation, cataract, or vitreous degeneration (Figure 8.27).

End-stage cases are usually eyes with chronic ERU with severe and often blinding changes such as phthisis bulbi, dense



Figure 8.26 A horse experiencing a classic acute inflammatory episode of ERU. Periocular swelling, lacrimation, and corneal edema are visible.



Figure 8.24 An Appaloosa horse with insidious uveitis. These horses do not show overt signs of discomfort, but ocular examination reveals chronic inflammatory changes. In this eye there is corneal edema, iris hyperpigmentation, dyscoria, corpora nigra atrophy, miosis, and cataract formation.

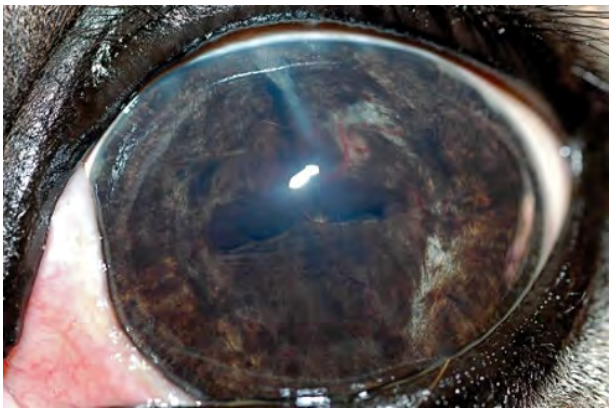


Figure 8.27 Clinical signs of chronic ERU. Corpora nigra atrophy, iris hyperpigmentation, miosi,s, and possibly cataract formation are present.



(A)



(B)

Figure 8.25 (A) Dense vitreous opacities and yellow discoloration of the vitreous in an eye with primarily posterior uveitis. (B) Vitreal debris in another horse with primary posterior uvetis.

cataract, luxated lens, detached retina, and/or loss of normal pupillary architecture (Figure 8.28).

Clinical appearance

Signalment No age or gender predilections have been reported for ERU; however, in a recent study of 224 horses (338 eyes) with ERU, affected horses included 140 geldings (62.5%), 82 mares (36.6%), and 2 stallions (0.9%), and breeds included 54 Appaloosas (24.1%), 37 Quarter horses (16.5%), 35 Thoroughbreds (15.6%), 13 Warmbloods (5.8%), 11 Hanoverians (5.0%), 11 Paint horses (5.0%), and 26 other breeds [73]. Age of the horses at time of presentation for ERU ranged from 2 to 30 years (mean 11.7 years, standard deviation (SD) 5.6 years, median 11 years) [73]. Another study of 160 horses with ERU found that half presented before 12 years of age, a time when horses are in their prime performance years [45].

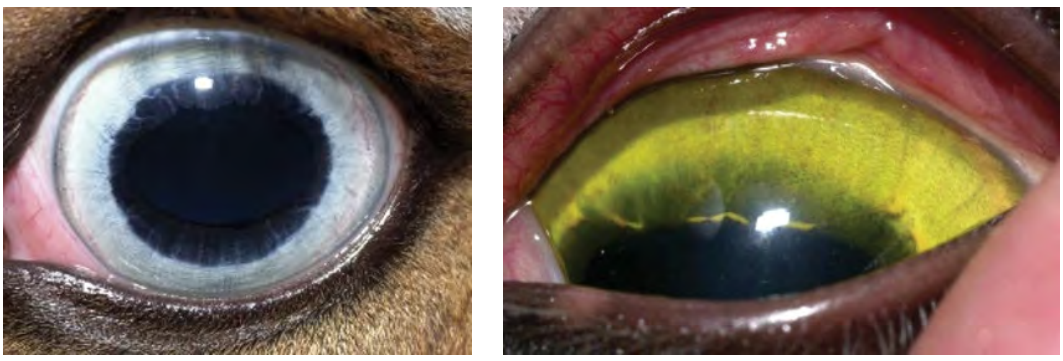
Ocular signs: anterior segment Clinical signs of ERU are variable and depend on the stage of the episode, pre-existing chronic ocular changes, the nature of the inflammation, and the anatomic location of the majority of the inflammation. A horse experiencing a classic acute inflammatory episode presents with pain, lacrimation, and blepharospasm (see Figure 8.26). The cornea can be slightly edematous, with the resultant opacity being most marked at the periphery. Corneal cellular infiltrate (i.e, white or yellow corneal infiltrate) or extensive corneal vascularization are not common in ERU, and their presence may suggest primary corneal disease instead of ERU. Short, deep, circumlimbal vascularization is frequent, however, and the length of the vessels are proportional to the duration of the episode. Fluorescein dye uptake will be negative, unless the horse has suffered a secondary ulcer from self-trauma. The anterior chamber may appear cloudy or hazy due to aqueous flare, and hypopyon or hyphema may be present in the ventral anterior chamber. Keratic precipitates may be visible as focal white spots on the endothelium of the cornea.



Figure 8.28 End-stage chronic uveitis with corpora nigra atrophy, posterior synechia, dyscoria, iris hyperpigmentation, and posterior lens luxation.

A cardinal sign of active uveitis is miosis (see Figure 8.22) [75], always present in an acute episode unless mydriatics have been administered or synechiae distort the pupil. The iris may be dull in color, show mottled pigmentation or depigmentation, or have changes in color or fibrosis (Figure 8.29). Corpora nigra degeneration with thinning and depigmentation of the iris margin is very characteristic of ERU and may develop after several inflammatory episodes (see Figures 8.23–8.29).

A horse with insidious ERU may not appear to be in pain, but examination of the eyes often shows inflammatory changes suggestive of chronic inflammation. Commonly, the conjunctiva and episclera are hyperemic and mild to moderate blepharitis is often observed (see Figure 8.24). The cornea may be mildly edematous, dull, or hazy. Corneal cellular infiltrate or extensive vascularization is not a feature of insidious ERU, although focal limbal vascularization may be discernible. Fluorescein dye uptake will usually be negative. Aqueous flare (1–2+) is usually visible on slit-lamp biomicroscopy. The iris is discolored and hyperpigmented. Degeneration of the corpora nigrans is a hallmark clinical sign of insidious ERU and is commonly associated with iris atrophy and fibrosis (see Figure 8.24). The pupil is usually miotic with a sluggish pupillary light reflex.



(A) (B)

Figure 8.29 Iris color changes in ERU. In acute uveitis, the iris can change to a yellow or even green color as a result of infiltration or inflammatory cells and serum. This color change is most prominent in blue or light-colored irises. (A) Noninflamed right eye of a light-colored horse. (B) Left eye of the same horse with a discolored iris due to active uveitis. Note peripheral corneal vascularization and miosis.

Inflammatory sequelae and scarring are often apparent in the anterior segment of both classic and insidious ERU cases. Posterior synechia, pigment on the anterior lens capsule, or pupillary occlusion are common manifestations of past damage in both classic and insidious ERU (see Figure 8.23). Focal or diffuse cataracts may be apparent (Figures 8.30 and 8.31). Dense cataracts may obscure visualization of the posterior segment, and lens luxation or subluxation are observed occasionally (see Figure 8.28).

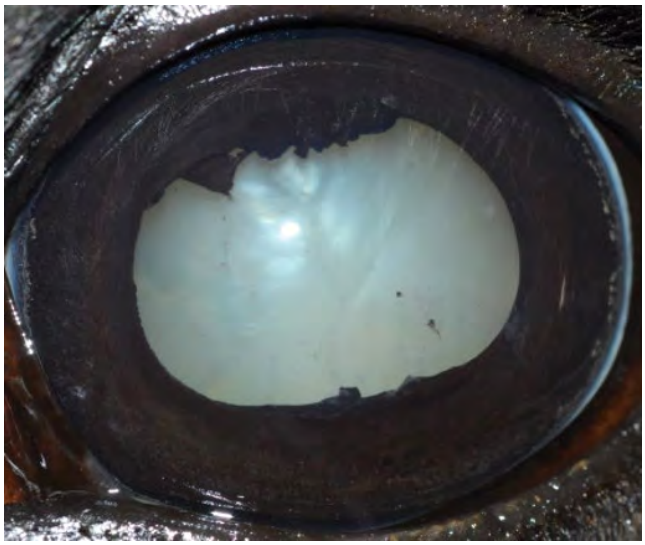


Figure 8.30 Mature, complete cataract formation in a horse with chronic ERU. Note iris hyperpigmentation, corpora nigra degeneration, and pigment on the anterior lens capsule—all typical signs of multiple recurrent episodes of uveitis.

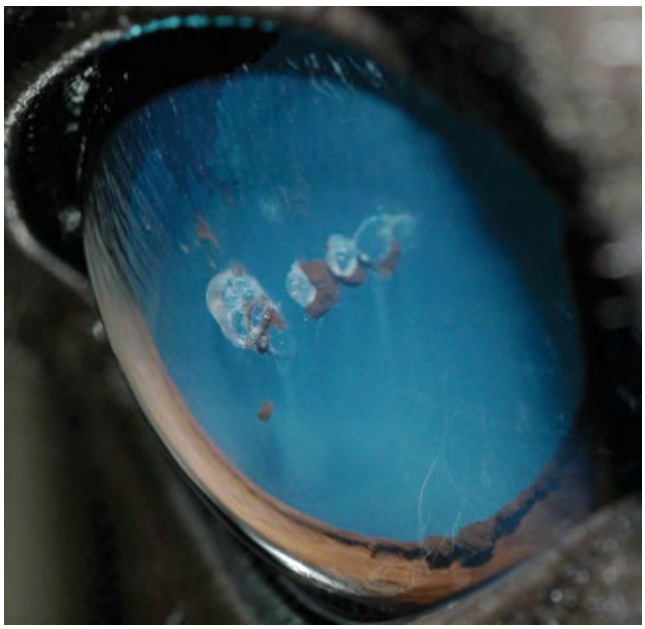


Figure 8.31 Pigment deposits ("rests") on the anterior lens capsule are common with ERU. These are likely the result of temporary posterior synechia. Capsular and/or anterior cortical cataract and subcapsular cysts are common and visible adjacent to the pigment in this photograph.

Most eyes with acute uveitis are hypotensive, with IOPs of 5–12 mm Hg, and commonly the anterior chamber is shallow. Glaucoma is a common sequela to all types of ERU, and this secondary glaucoma may be the most common underlying cause of glaucoma in horses (see Chapter 10). Horses that develop secondary glaucoma will have diffuse corneal edema that does not respond to anti-inflammatory medications, or at least does not respond as well as observed in previous bouts. IOPs typically range from 35 to 80 mm Hg in these eyes. Enlarged eyes and development of cornea striae secondary to glaucoma occur with chronic ERU (Figure 8.32). Horses with ERU that develop secondary glaucoma have a particularly poor prognosis for vision [73].

Ocular signs: posterior segment In acute classic or insidious ERU, the posterior segment of the eye is usually not visible because of anterior segment cloudiness of ocular media and miosis. When these eyes are quiescent and pupils are dilated, the chronic sequelae of ERU may be observed. Posterior segment lesions are more easily observed in horses with posterior ERU because the anterior segment is relatively normal, especially early in the disease. With chronicity, however, posterior synechia, cataract, and vitreal debris will limit the view of the posterior segment even in eyes with predominantly posterior ERU.

Some horses have no observable vitritis but show chorioretinal scarring of the peripapillary region or other evidence of retinal degeneration. The most common patterns of chorioretinal scarring are seen in the nontapetal area near the disc and present as either multiple, small, circular focal areas of depigmentation with a central area of hyperpigmentation ("bullet-hole" scarring) (Figure 8.33) or wing-shaped areas of depigmentation nasal and temporal to the optic disc ("butterfly" lesions (Figure 8.34)). Although once thought to be pathognomonic for ERU, other inflammatory conditions, such as blunt ocular trauma, may also result in peripapillary depigmentation.

Some horses with posterior uveitis demonstrate severe vitritis, where detail of the fundus is obscured and the optic disc

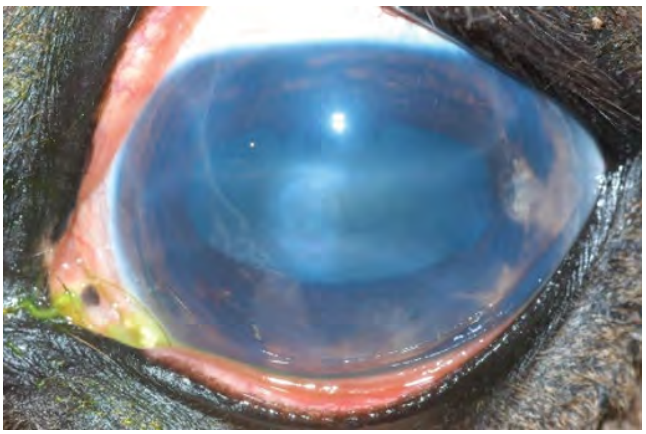


Figure 8.32 Enlarged eye secondary to glaucoma that developed as a result of chronic ERU. Note the mild diffuse corneal edema, fibrosis, and horizontal corneal striae.

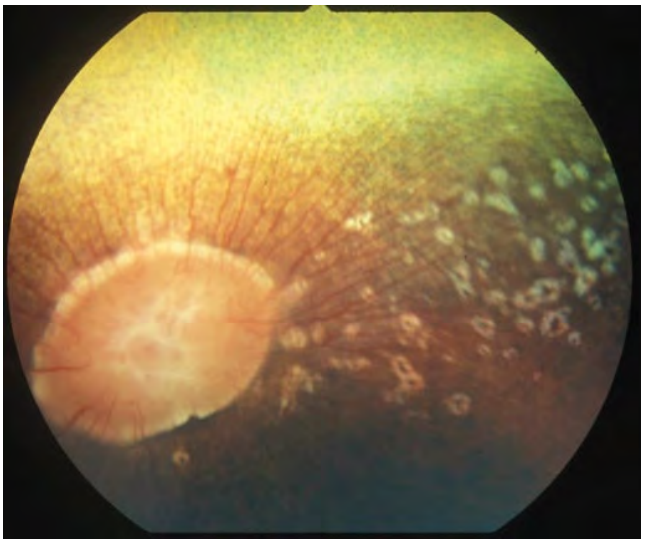


Figure 8.33 Chorioretinal scarring is in the nontapetal area near the disc and appears as multiple, small, circular focal areas of depigmentation with a central area of hyperpigmentation ("bullet-hole" scarring). These lesions are suggestive of previous inflammation but not specifically ERU.

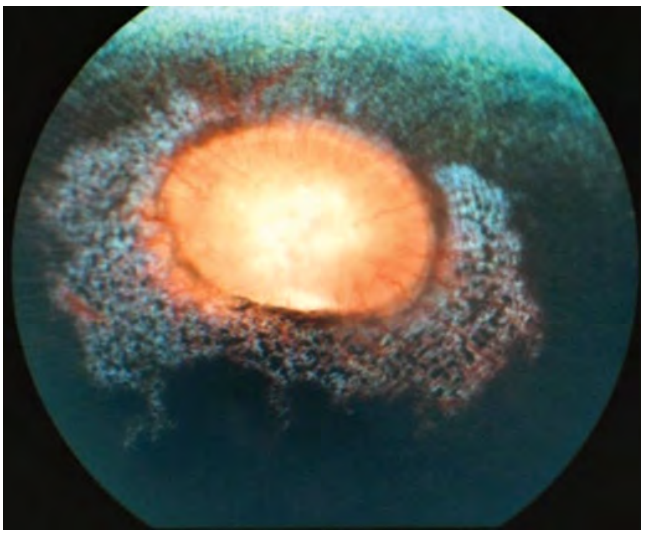


Figure 8.34 Wing-shaped areas of hypopigmentation nasal and temporal to the optic disc ("butterfly" lesions). These lesions are suggestive of previous inflammation but not specifically ERU.

appears orange-red owing to the vitreal inflammation and haze. Liquefaction of the vitreous is common, as are visible strands of clumped infiltrating mononuclear cells and inflammatory products ("floaters") (Figure 8.35). These opacities appear to float and move easily in the vitreous in response to eye movements. Fibrinous traction bands may be apparent as white spike-like structures that radiate from the perimeter of the optic disc (Figure 8.36). Retinal detachments may be present and appear as a veil-like transparency that obscures fundic detail. In fact, ERU is one of the most common causes of retinal detachment in horses (Figure 8.37) [88].



Figure 8.35 Vitreal degeneration and cellular infiltrate in the vitreous. Liquefaction of the vitreous is common in ERU, as are visible strands of clumped, infiltrating mononuclear cells and inflammatory products.

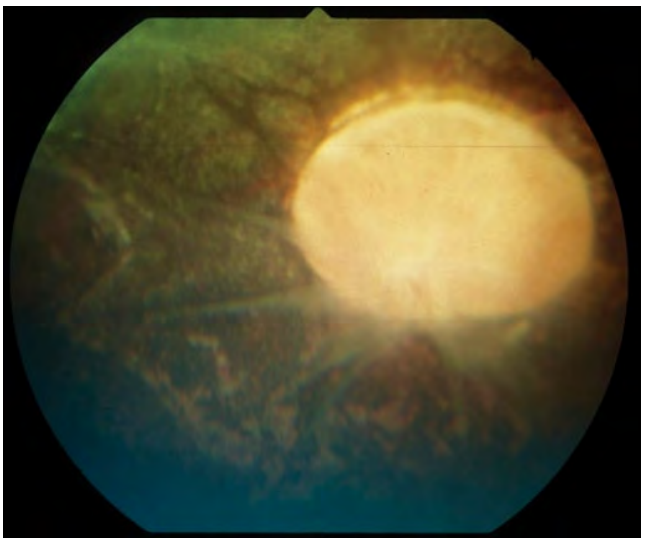


Figure 8.36 Fibrinous traction bands that radiate from the perimeter of the optic disc.

Chronic end-stage ERU

Horses with chronic end-stage ERU show variable degrees of discomfort and inflammatory sequelae. Recurrent episodes of inflammation may subside but may be replaced by constant low-grade discomfort from blepharitis, mucopurulent lacrimation, conjunctivitis, and ocular irritation. Some horses appear comfortable and do not have signs of recurrent episodes of inflammation. Ocular structures often become severely scarred if eyes undergo phthisis bulbi. In these eyes, corneal scarring may be dense and develop folding and anterior synechiae (see Figure 8.21). Iris architecture may be lost or indistinct. Cataracts and lens luxations are common, and the color of the lens may become yellow. Complete retinal detachment

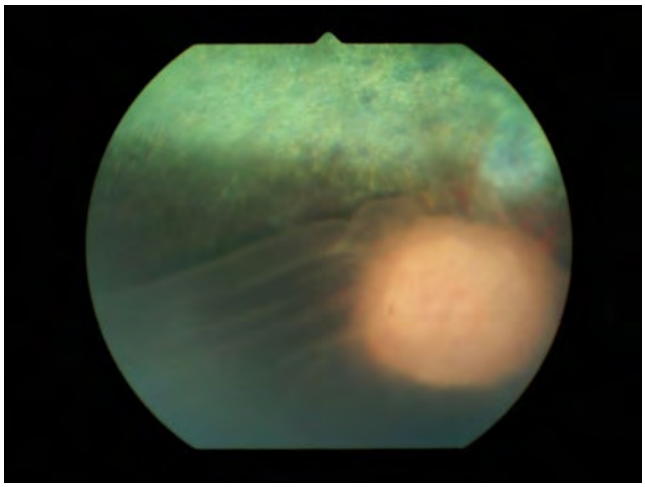


Figure 8.37 Complete retina detachment in a horse with chronic ERU. The retina has disinserted dorsally and has folded down over the optic disc.



Figure 8.38 A head tilt or "star-gazing" head posture is sometimes observed in blind horses with end-stage ERU and must be differentiated from congenital stationary night blindness. (*Source*: Photograph courtesy of Dr Ann Dwyer.)

is also common. The nictitans may become elevated or prolapse as the globe becomes phthisical, and the mucosa may show chronic inflammation. A head tilt or "star-gazing" head posture is sometimes observed in blind horses with end-stage ERU (Figure 8.38).

Bilateral versus unilateral ocular involvement

The initial episode of uveitis may be bilateral or unilateral. Recurrences may occur in one or both eyes. Sometimes one eye suffers initial inflammation, and then the other eye becomes inflamed at a later interval. In other instances, inflammation remains in just one eye. The majority of cases of insidious ERU are bilateral, but one eye may be more severely affected than the other.

One study found that approximately 50% of eyes with leptospiral-induced ERU were bilateral [89]. In this same study, 81% of Appaloosa horses with ERU had bilateral involvement [89]. Of a small series of 32 horses that were seronegative to *L. interrogans* serogroup Pomona and were of non-Appaloosa breeding, 38% had bilateral involvement (Table 8.3) [89]. In a recent study evaluating the long-term prognosis of ERU, 66% of horses were affected bilaterally (338 eyes affected in 224 horses) [73].

Immunologic aspects

Pathogenesis of ERU is immune mediated and it is generally agreed that a dysregulated immune response causes the disease [49]. It explains the recurrences of inflammation, the positive effect of corticosteroids (or other more selective immunosuppressive agents), and the insufficient therapeutic success of antibiotics. The relevance of the inflammatory reaction is underscored by the successful therapeutic strategy of immunosuppression, the gold standard therapy to control ERU for decades [90, 91].

General features of ocular immunology and ERU

Physiologically, the inner eye is devoid of immune cells, and the eye maintains an immunosuppressive environment through, for example, factors expressed in the vitreous such as transforming growth factor β (TGF-β). The eye has long been recognized as an immune-privileged organ. Immune privilege in the eye was originally ascribed to its separation from the systemic immune system by the blood–ocular barrier, lack of lymphatics, and the presence of limited numbers of resident leucocytes. However, extensive detailed work has demonstrated that privilege is in fact a far more active process than this. The blood–ocular barrier is a specialized endothelium with tight junctions that control cell traffic in a highly regulated fashion. Naïve T cells cannot cross the normal blood–retinal barrier because of the high shear stress in the retinal vessels and the lack of appropriate adhesion molecules. Expression of chemokines such as RANTES in the ciliary epithelium may play a role in recruitment and activation of leucocytes in diseased eyes [80]. Furthermore, inner and outer blood–retinal barriers keep cells from the healthy inner eye [92]. Retinal blood vessels that are similar to cerebral blood vessels maintain the inner blood–ocular barrier. This physiologic barrier comprises a single layer of nonfenestrated endothelial cells that have tight junctions. The retinal pigment epithelium maintains the outer blood–retinal barrier [92]. Because the horse retina is mainly avascular, the outer blood–retinal

Table 8.3 Outcome, chronic ocular changes, and concurrent ocular problems in Appaloosa and non-Appaloosa horses that are seropositive or seronegative for *L.* Pomona.

	Appaloosa horses				Non-Appaloosa horses				Total	
Serology to *L.* Pomona	**Positive**		**Negative**		**Positive**		**Negative**		**Total**	**Percentage**
Total number with uveitis	14		28		86		32		160	100
Unilateral ERU	5	36%	3	11%	48	56%	20	62%	76	48
Bilateral ERU	9	64%	25	89%	38	44%	12	38%	84	52
Vision loss (1 or 2 eyes)	14	100%	20	72%	44	51%	11	34%	89	56
Bilateral vision loss	7	50%	8	29%	15	17%	2	6%	32	20
Chronic ocular changes										
Corneal striae	2	14%	5	18%	4	5%	2	6%	13	8
Corneal scars	4	29%	10	36%	22	26%	6	7%	42	26
Corneal calcium deposits	1	7%	1	4%	8	9%	0		10	6
Corneal streaks	6	43%	4	14%	5	19%	0		15	9
Corneal opacity, other	0		0		3		0		3	8
Corpora nigrans excess	0		4	14%	5	19%	3	9%	12	2
Iris atrophy	7	50%	16	67%	16	19%	2	6%	41	26
Iris color change	5	36%	12	43%	13	22%	3	9%	33	21
Anterior synechiae	1	7%	0		3	3%	0		4	3
Posterior synechiae	6	43%	11	39%	23	27%	5	16%	45	28
Lens luxation	4	29%	8	29%	6	7%	4	13%	22	14
Diffuse cataract	10	71%	21	75%	26	30%	9	28%	66	41
Focal cataract	5	36%	4	14%	16	19%	3	9%	23	14
Vitritis	0		6	21%	23	27%	7	22%	41	26
Vitreal traction bands	0		2	7%	7	8%	2	6%	11	7
Detached retina	0		2	7%	9	10%	0		11	7
Peripapillary alar depigment	1	7%	5	18%	5	19%	8	25%	19	12
Peripapillary focal depigment	3	21%	1	4%	11	13%	9	28%	24	15
Glaucoma	1	7%	8	29%	6	7%	3	9%	18	11
Phthisis bulbi	7	7%	3	11%	13	15%	1	3%	24	15
Concurrent problems										
Corneal ulcers	4	29%	12	42%	19	22%	8	25%	43	27
COPD (heaves)	1	7%	6	21%	0		1	3%	8	5
Laminitis	2	14%	3	11%	2	2%	0		7	4
Abortion	0		0		2	2%	0		2	1
Fever in past	0		0		7	8%	0		7	4
Night blindness	0		3	11%	0		0		3	2
Neoplasia	1	7%	1	4%	2	2%	3	9%	7	4
Cushing's	0		1	4%	0		0		1	0
Enucleations	0		3	11%	2	2%	1	3%	6	4
Injuries secondary to blindness	1	7%	3	11%	6	7%	4	13%	14	9
Died or euthanized due to blindness	2	14%	6	22%	7	8%	0		15	9

COPD, Chronic destructive pulmonary disease.

barrier (retinal pigment epithelium) mainly keeps the immune effector cell-free environment in equine eyes [93].

In ERU, large amounts of leucocytes are able to enter the inner eye and cause damage to the inner ocular tissues [77]. Analysis of the infiltrating cells revealed that the majority of cells are lymphocytes in most ERU cases [77]. These cells are predominantly CD4-positive T cells that secrete proinflammatory cytokines such as interleukin 2 (IL-2) and interferon γ (IFN-γ) [79]. The IFN-γ-producing phenotype is named TH1 helper cell. TH cells are involved in activating and directing other immune cells and are particularly important in the immune system. They are essential in determining B-cell antibody class switching, in the activation and growth of cytotoxic T cells, and in maximizing activity of macrophages [94]. It is this diversity in function and their role in influencing other cells that gives helper T cells their name.

TH17 cells are a newly identified subset of CD4+ T-helper cells producing IL-17 [95]. They are found at interfaces between the external environment and the internal environment, such as the skin and lining of the gastrointestinal (GI) tract. Numerous immune regulatory functions have been reported for the IL-17 family of cytokines, presumably due to their induction of many immune signaling molecules. Most notably, IL-17 is involved in inducing and mediating proinflammatory responses [95]. IL-17

induces the production of many other cytokines, chemokines, and prostaglandins from many cell types. The increased expression of chemokines attracts other cells, including neutrophils but not eosinophils. TH17 lymphocytes are implicated in a variety of immune-related diseases, including rheumatoid arthritis [96]. Novel data from experimental uveitis models in rodents also point to a significant role of IL-17 in uveitis [97, 98]. It is interesting to note that whereas the TH17 line typically recruited a mostly granulocytic inflammatory infiltrate into the eye, the TH1 line recruited a predominantly mononuclear infiltrate. In ERU eyes, strong immunoreactivity for IL-17 in the nonpigmented ciliary epithelium and in mononuclear cells infiltrating the iris and ciliary body suggested that IL-17-secreting TH17 cells play a role in the pathogenesis of ERU [99].

Autoantigens and ERU

Uveitis is a clinically heterogeneous disease and initiating events of the immunopathology in ERU remain obscure. In many autoimmune disorders, infections have been discussed as triggering events, either by antigenic mimicry with a pathogen's antigen or as a bystander effect due to the general systemic or local immune stimulation by the pathogen. The historical association between leptospiral infection and development of ERU suggests this pathogen is a potent activator of the immunopathology in ERU (see section **Leptospirosis and ERU**).

Although the antigenic triggers of autoimmune uveitis are still under discussion, there is a large body of evidence implicating responses to retinal antigens in the etiology and/or progression of the disease. One of the explanations that has been offered for the clinical heterogeneity of uveitis cases is a difference in the antigens being recognized. Many, though certainly not all, ERU cases have detectable immunologic responses to retinal antigens, most often to interstitial retinol-binding protein (IRBP) [78]. IRBP is a large glycoprotein (140 kDa) known to bind retinoids and found primarily in the interphotoreceptor matrix of the retina between the retinal pigment epithelium and the photoreceptor cells. It is thought to transport retinoids between the retinal pigment epithelium and the photoreceptors, a critical role in the visual process. Further, immune reactions of diseased horses are additionally directed against S-antigen (S-Ag) [100, 101], a photoreceptor protein found in rods and in the pineal gland, exerting an inhibitory function in the light transduction cascade. In almost all ERU cases, serum and vitreal autoantibodies against both autoantigens are detectable. Since antiretinal antibodies do not seem to be essential for the induction of uveitis, as shown in several experimental autoimmune uveoretinitis (EAU) models [102], and the predominating infiltrates in eyes of ERU horses are T-helper cells, the T-cell specificity is even more interesting and important in the pathogenesis of ERU.

An immune response to cellular retinaldehyde-binding protein (CRALBP) was detectable in a large percentage of ERU cases [103]. CRALBP was determined as a novel uveitis autoantigen and was subsequently tested with samples of human autoimmune uveitis patients [104]. Fifty-four percent of tested patients were CRALBP autoantibody positive, thereby underscoring the relevance of ERU as a model for human autoimmune uveitis. Considerable evidence indicates that CRALBP is a component of the rod and cone visual cycles, the sequences of reactions responsible for the regeneration of 11-*cis*-retinal after photoisomerization. The protein is abundant in RPE cells, where many of the reactions of the rod visual cycle take place, and in Müller cells, which have been implicated in cone visual pigment regeneration.

Synaptotagmin-1 is protein integral to synaptic vesicle membranes. It has recently been identified as the first cell membrane-associated autoantigen in ERU and may play a role in dysregulation of retinal neurotransmitter release in uveitis. This autoantigen showed a downregulation in the majority of ERU-affected retinas [105].

Although retinal autoantigen-specific Th1 cells have been demonstrated to trigger ERU progression and relapses (see section **Pathogenesis**), the molecular processes leading to retinal and tissue degeneration and consequently blindness remain as yet unknown. Systematic exploration of the intraocular proteomes of spontaneous uveitis and healthy controls has made it possible to identify several differentially regulated proteins that belong to pathways involved in immune response and the maintenance of the blood–retinal barrier [106, 107]. One upregulated candidate in the retina in ERU is, amongst others, complement component 3 (C3) [108]. Novel data indicate an activated complement system also in sera of ERU cases [108]. This is interesting, because intraocular complement activation, specifically engagement of complement receptor 3, had a significant impact on disease activity in experimental autoimmune uveitis in rats [109, 110]. The role of complement system activation in ERU merits further exploration in the pathogenesis of ERU.

Another candidate is pigment epithelium-derived factor (PEDF), a neurotrophic factor and potent inhibitor of angiogenesis [111]. PEDF is produced by the retinal pigment epithelial (RPE) cells and retinal Müller glial cells (RMG) and is significantly downregulated intraocularly in uveitis to around 20% of the normal expression level [112]. PEDF is a regulator of inflammatory factors and suppresses endothelial permeability by protecting tight junction proteins [113]. In ERU, a direct link between downregulation of PEDF and concomitant appearance of vascular endothelial growth factor (VEGF) and IFN-γ in the retina has been demonstrated [106]. Additionally, uveitic changes in the retina were accompanied by upregulation of glial fibrillary acidic protein (GFAP) and vimentin, as well as downregulation of glutamine synthetase [106, 112]. These expression patterns point to an activated state of RMG in the disease process [114]. The activated RMG downregulate the expression of PEDF and begin expressing IFN-γ, a proinflammatory cytokine typical for TH1 cells [106]. Therefore RMG may play a fatal role in uveitic disease progression by directly triggering inflammation processes through the expression and secretion of IFN-γ. Most interesting, a significant downregulation of PEDF could

also be demonstrated in sera of ERU cases, consistent with earlier observations in ERU vitreous [112] and retina [106]. This suggests that the downregulation of PEDF under inflammatory conditions is not only limited to the eye. The findings of a significantly lower PEDF expression in ERU cases, in not only the target organ but also the serum, suggests PEDF as a promising uveitis biomarker.

Recent studies have demonstrated a decreased talin and septin 7 expression in peripheral blood-derived granulocytes of ERU horses [115, 116]. Talin 1 plays an important role in the activation of integrins and therefore is crucial for adhesion, migration, and survival of cells; while septin 7 plays a role in regulation of cell shape, motility, and migration of cells. Together, the downregulation of talin 1 and septin 7 suggests a role of the innate immune system in the pathogenesis of ERU [115, 116].

Immunologic pathogenesis

Current concepts to explain the origin and perpetuation of autoimmune diseases include molecular mimicry [117], bystander activation [118], and epitope spreading [119, 120]. These mechanisms do not exclude each other but could appear together and even interact. **Epitope spreading** is defined as the diversification of epitope specificity from the initial focused, dominant, epitope-specific immune response, directed against a self or foreign protein, to cryptic epitopes on that protein (intramolecular spreading) or other proteins (intermolecular spreading).

The immune response consists of an initial magnification phase and a later downregulatory phase to return the immune system to homeostasis. In most autoimmune diseases, several autoantigens participate in the pathogenesis, as mentioned above [121], and epitope spreading is most likely accountable for disease induction, progression, and inflammatory relapses [122–126]. The shifts in immunoreactivity could account for the remitting/relapsing character of ERU.

Different target antigens may be important for a given individual, depending on their genetic background. Genetic background and antigens encountered influence the direction and extent of epitope reactivity and probably play an important role in the heterogeneous clinical manifestations of disease [127]. In many autoimmune diseases, epitope spreading is suspected to occur as a result of an immune response against endogenous target antigens primary and secondary to the release of self-antigen during the chronic autoimmune response [127]. The formation of new antibodies may determine a different clinical picture. For example, the transformation of anterior uveitis to posterior uveitis may be an excellent example of the effects of epitope spreading. Through tissue damage, cryptic or hidden epitopes on the same molecule will be suddenly presented to the immune system. The end result is that every target antigen generally contains several epitopes, each of which reacts with a T cell or antibody response of different specificity and affinity. Thus epitope spreading in autoimmune diseases results in the detection of an increasing array of autoantibodies against various target antigens. Studies have confirmed epitope spreading in a high percentage of cases of ERU [76]. In a more recent study, vitreous-based immunoglobulin (Ig) M responses to the retinal proteome were demonstrated in 34 of 50 ERU specimens, whereas no retinal-specific IgM antibodies were detectable in healthy vitreous [128]. The IgM reacted to highly diverse and numerous retinal proteins in the ERU-diseased samples. As vitreous samples were derived from horses with different ERU stages, the diversity may indicate changing immune reactions during the course of disease, accounting for the remitting/relapsing character of the disease and could be the basis for the epitope spreading pathogenesis of ERU [128].

Analyses of autoantigen and epitope specificity of autoaggressive T cells from ERU cases revealed evidence for inter- and intramolecular epitope spreading [76]. Epitope spreading is only pathogenesis-associated if the targeted epitope has pathogenic potential. Therefore it was essential to evaluate the uveitogenic potential of all involved autoantigens directly in the horse. Surprisingly, S-Ag, which is seen as the major uveitis autoantigen in human autoimmune uveitis and is used by many researchers as autoantigen to experimentally induce uveitis in Lewis rats for uveitis research, widely failed to induce uveitis in horses [129]. S-Ag-induced uveitis is monophasic in rats [100] and was also monophasic in one horse that developed uveitis after S-Ag injection [129]. In contrast, CRALBP and IRBP proved their uveitogenicity in the horse with an incidence of 100% [103]. Further, both CRALBP and IRBP autoantigens were capable of reinducing uveitis in the horse [103], closely resembling the clinical course of spontaneous ERU. Equine experimental uveitis induced with CRALBP or IRBP is the only animal model where relapses of an autoimmune disease can be reinduced in a well-defined and predictable manner.

Uveitic relapses are notable even in phthisical and blind eyes [130]. Histopathologic examination of ERU eyes and eyes from experimentally induced uveitides revealed an almost complete loss of the photoreceptor outer segments in advanced stages of disease [78, 100]. In other autoimmune diseases, such as Hashimoto's thyroiditis, a termination of autoimmune attacks is notable after depletion of autoantigens [131, 132]. Because the photoreceptor outer segments host two major autoantigens, retinal S-Ag (arrestin) and IRBP [133], the ongoing immune pathology after destruction of the physiologic expression sites of these proteins was difficult to explain. Therefore autoantigen expression levels of IRBP, S-Ag, and CRALBP in uveitic retinas at several clinical stages were compared to healthy control retinas. IRBP, S-Ag, and CRALBP were clearly detectable in proteomes of normal equine retina and in retinas with different stages of uveitis. Although the composition of retinal proteomes differed considerably between healthy and diseased state [120], IRBP, S-Ag, and CRALBP amounts remained unchanged despite photoreceptor rhodopsin expression levels that reduced to 27% of original expression, indicating extensive retinal damage [107]. The unchanged total amount of these major retinal autoantigens

indicates that the autoantigenic target protein is present despite considerable destruction of its hosting structures and can thus trigger unabated relapses in patients with blind eyes.

Leptospirosis and ERU

The initial association of leptospirosis with ERU reported in Germany in the 1940s by Rimpau [54] and Heussler [55] was followed by case reports of an outbreak of acute leptospirosis on two horse farms in Ithaca, New York [51, 65, 134–136]. Analysis of events on one of the Ithaca farms showed that in the spring of 1952, 6 of 15 resident horses developed acute systemic disease confirmed as infection with *L. interrogans* serogroup Pomona [135]. All horses recovered, but one of the six developed intraocular inflammation during acute disease that later become recurrent [65]. The majority of the remaining horses developed ERU 18–24 months after the initial infection. This pattern is typical of leptospiral-associated ERU—ocular signs at the time of acute infection are generally subclinical or mild, but overt ocular inflammation develops months to years later. Recurrence of uveitis is typical, with subsequent episodes of inflammation often increasing in severity and threatening vision.

Experimental work to try to reproduce this unusual pattern ensued in the 1960s at Purdue University, Indiana. Morter et al. [137] succeeded in inducing leptospiral-associated uveitis by subcutaneously injecting guinea pig blood containing live *L. interrogans* serogroup Pomona organisms into a group of ponies. All the ponies developed systemic leptospiral infections that resolved but were followed by the development of ocular inflammation in the ensuing 15 months post exposure [137–139]. The ponies had ERU that varied in intensity but resulted in blinding sequelae in many cases. Subsequent analysis of the ocular tissues of this same set of ponies in recent studies has shown that the pathology and immunohistopathology of the experimental disease were quite similar to that of spontaneous cases of leptospiral-induced ERU [81, 140].

A large body of research has been stimulated by the early reports of clinical and experimental leptospiral-related ERU, but the precise pathogenesis of induction of uveitis and the role of the organism in recurrent disease is poorly understood, although much progress has been made recently. In 1985, clinicians at the University of Florida used enzyme-linked immunosorbent assay (ELISA) to detect antibodies specific to *L. interrogans* serogroup Pomona in the sera, aqueous, and vitreous humor of horses with ERU. Their data suggest that antibodies in the ocular media may be synthesized in the eye rather than just leaking across the blood–ocular barrier [61, 141]. Further analyses of aqueous and vitreous humor samples from horses support the concept that some horses with ERU have intraocular antibody synthesis to *Leptospira* [57–59, 72, 73, 78, 142].

In 1985, Argentinean researchers demonstrated an antigenic relationship between *Leptospira* and the equine cornea, suggesting that molecular mimicry occurs between the bacteria and host tissues [143]. Subsequent work has demonstrated that tears and aqueous humor from horses inoculated with *Leptospira* contain antibodies that bind to the cornea [144] and that the antigenic relationship between the bacteria and ocular tissues includes the lens as well and involves a peptide fragment [145]. A leptospiral DNA fragment was found to encode cross-reacting epitopes toward equine cornea. This fragment was found in several pathogenic *L. interrogans* subgroups but not in the nonpathogenic *L. biflexa* [63]. Furthermore, in aqueous and vitreous humor from equine eyes with uveitis, IgA and IgG to *L. interrogans* lipoproteins LruA and LruB were significantly higher than in companion sera, indicating intraocular antibody production.90 Also, LruA- and LruB-specific antisera cross-reacted to normal equine lens, ciliary body, and retina, suggesting an immunopathogenic role in leptospiral-induced ERU [84, 146]. In humans with both leptospiral-associated and known autoimmune uveitis (i.e, Fuchs uveitis or Behçet's syndrome), serum antibodies cross-reacted with LruA and LruB lipoproteins, suggesting similarities in the disease pathogenesis [147]. Recently, antibodies against LruC, a leptospiral lipoprotein located in the inner leaflet of the leptospiral outer membrane, were significantly higher in eye fluids and sera of uveitic horses compared to normal horses, suggesting that LruC may play a role in equine leptospiral uveitis [148]. These studies support the idea that leptospiral infections are potent initiators of autoimmune disease in the eye through a "molecular mimicry" pathogenesis.

Isolation of *L. interrogans* serogroup Pomona from the aqueous humor of horses affected with ERU was reported in 1977 [149]. Leptospiral organisms have been cultured from equine eyes with uveitis in California [60], Germany [68], and Louisiana [72], and in these studies there were some instances where leptospiral DNA was detected in samples that were culture negative [58, 60, 72]. The precise role the organisms play in mediating recurrences remains to be clarified; however, the presence of leptospiral organisms, organism fragments, or DNA would likely heighten the chance of development of autoimmune disease.

Leptospirosis is a bacterial disease affecting domestic animals, wildlife, and humans. Leptospirae are the smallest spirochete bacteria, measuring less than 0.3 μm in width and 6–30 μm in length. They have a tightly wound spiral shape with a distinctive hook on one or both ends. Other genera of related pathogenic spirochetes include *Treponema* (agents of syphilis and swine dysentery) and *Borrelia* (agents of relapsing fever and Lyme disease). It does not stain with conventional pathology stains, requiring special silver impregnation stains for identification. Clinical tests available to diagnose leptospiral infections include direct culture of infected organs or body fluids, microscopic agglutination testing of sera or ocular fluids, polymerase chain reaction (PCR) analysis of ocular fluids, and fluorescent antibody testing of urine samples.

Leptospirae are aquatic unicellular organisms found in river and lake waters and in sewage. *Leptospira interrogans* is host adapted, and infective strains are maintained in a variety of mammalian species. The principal reservoirs for the serogroups associated with ERU are deer, cattle, swine, and rats. The organisms

multiply in the kidneys of adapted hosts and are shed in the urine. Pathogenic leptospires can only survive for short periods in soil outside a host but are able to live for up to 6 weeks in ground water if environmental conditions include slightly alkaline conditions (pH 6.2–8), low salinity, and moderate temperatures above 22 °C.

Exposure to the organism occurs when horses drink contaminated ground water or food that contains urine shed from a host-adapted species. Horses pastured next to unvaccinated cattle or pigs, and horses that live on farms frequented by deer or infested with rats are at increased risk for exposure. Ponds on the property, the use of pond water as drinking water, and close proximity to a river are other frequently observed risk factors (Figure 8.39) [45]. Clinical infections are thought to be most prevalent during rainy periods in the spring and fall. The inciting organisms enter the body through mechanical penetration of mucous membranes or abraded skin and rapidly gain access to the vascular space. Bacteremia persists for about 8 days. Invasion of many internal organs occurs, and infection induces a strong host antibody response that is first detectable in the serum 4–8 days post exposure [137]. Organisms are eliminated rapidly from the blood and most organs by host mechanisms. However, localization of organisms in the genital tract and renal tubules [150, 151] may occur, and the infected horse may shed pathogenic leptospires in the urine for up to 3 months [137].

Acute signs of leptospirosis in the horse include transient depression, fever, icterus, anemia, and anorexia. Sporadic reports of severe disease in neonates or adult horses exist [152, 153], and the disease has been associated with many equine abortions in Kentucky [154, 155], but most infections are outwardly

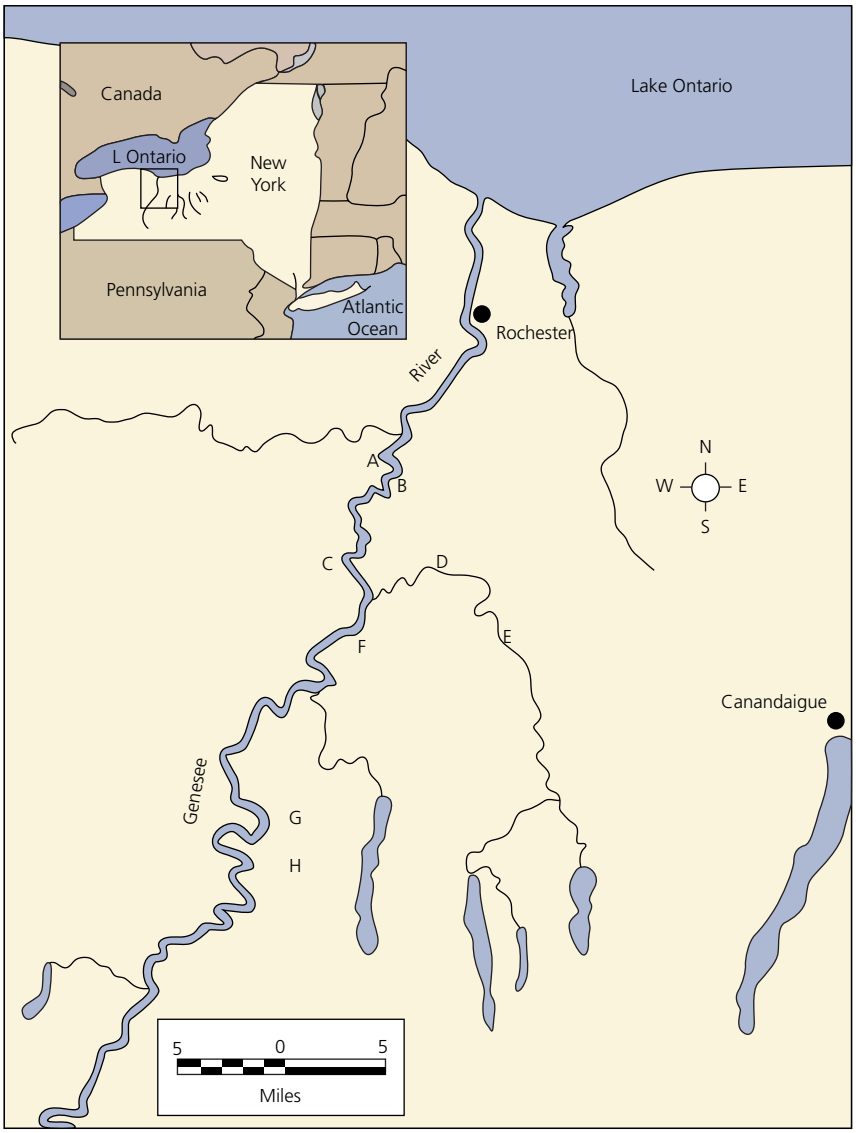


Figure 8.39 Map of farms that had multiple cases of *Leptospira* Pomona-associated ERU, showing proximity to the Genesee River of New York State. (*Source*: Gilger, 2011 [235]. Reproduced with permisison from Elsevier.)

self-limiting. Clinical diagnostics that would confirm acute infection in the horse are rarely performed, because observable initial illness is generally mild, brief, and likely subclinical [156]. Serologic surveys in horses have shown that exposure to leptospires is common, but variable according to geographic region and climate. Seropositivity rates tend to be highest in tropical climates [72, 150], wet environments [157], and river valleys in temperate climates, especially in the Ohio, Delaware [158, 159], Genesee [45], and Mississippi [66]. River valleys in North America. These regions also have high rates of ERU in resident horse populations [45, 66]. However, leptospiral seroprevalence is much less in dry environments around the world [160].

Classification and clinical testing

Biologically, leptospirae are classified into two large species: *L. biflexa*, the nonpathogenic, free-living, and saprophytic complex, and *L. interrogans*, the parasitic species complex that causes disease. *Leptospira interrogans* is further classified into over 20 serogroups. Diagnostic laboratories distinguish exposure to these serogroups by performing serial microagglutination titers (MAT) on equine sera or ocular fluids, looking for antibodies to leptospiral surface antigens. The *L. interrogans* serogroups most often incriminated in equine disease are Pomona and Grippotyphosa [45, 55, 58, 60, 65–68, 72, 73, 153–155, 161]. In some studies, the serogroup most often associated with ERU in North and South America was Pomona [45, 60, 66, 161], while in other studies, the serogroup Grippotyphosa predominated [58, 68, 73, 142]. Sporadic reports have also associated serogroups Autumnalis [47], Icterohemmorrhagiae [66, 142], Australis, Sejroe, and Javanica [62] with ERU.

Most public diagnostic laboratories perform MAT for five to seven serogroups (Pomona, Icterohaemorrhagiae, Grippotyphosa, Canicola, Hardjo, and sometimes Bratislava and Autumnalis). Interpreting serology for leptospiral reactivity can be confusing. A large number of horses that live in temperate or tropical climates demonstrate low titers to one or more serogroups, and exposure analysis is often not performed until years after episodes of ERU have begun, when titer levels in these animals are usually low.

Acute infections are characterized by high titer seroreactivity to at least one serogroup by the eighth day after infection [137]. Cross-reactivity to one or more other serogroups is common due to surface antigen overlap, and is usually detectable at the same time but at reduced titer levels. Over time, the titer to the predominant serogroup falls to lower dilution levels, but positive seroreactivity to the original panel of serogroups persists for many years and probably for life. Usually the predominant serogroup titer will be elevated above the cross-reacting serogroups for several years after infection. For example, seroreactivity to serogroup Pomona is often associated with seroreactivity to serogroup Icterohemmorrhagiae [45, 66, 162]. The horse has been shown to be an adapted host that can maintain the Bratislava serogroup [151], but, to date, this serogroup has not been associated with ERU.

One study has shown that 56% of horses with ERU from an upstate New York river valley were seropositive for *Leptospira* Pomona, while only 9% of normal horses were seropositive.3 In recent studies in North Carolina and Louisiana, approximately 45% of ERU horses were seropositive for leptospira [72, 73]. Other studies have demonstrated leptospiral seroreactivity [55, 66] or evidence of *Leptospira* in ocular media [55, 58, 60, 66, 68] in a majority of their affected study populations. These data imply that any positive Pomona titer in a horse (i.e, ≥ 1:400) should be considered a risk factor for ERU. In some studies, analysis of the ocular fluids or tissues of affected horses has shown that leptospiral organisms or leptospiral DNA can be isolated but in other studies no evidence of *Leptospira* could be found [142, 163]. This means that although positive seroreactivity to pathogenic groups of leptospires, particularly Pomona and Grippotyphosa, is often linked to ERU etiology, positive or negative seroreactivity does not rule in or out leptospirosis as a contributing factor to the disease.

Therefore, to more definitively determine if ERU is leptospiral associated, it is recommended that analysis of intraocular antibody production (i.e, calculating the Goldmann–Witmer coefficient (C-value)) combined with real-time PCR analysis for organismal DNA in the eye (aqueous or vitreous humor) should be done [164]. This is considered the most sensitive method for comprehensive diagnosis of the role of or ganisms in the pathogenesis of uveitis. The C-value is determined by calculating the aqueous:serum leptospiral MAT ratio for each serovar. A C-value of more than 1 is considered positive to suggest intraocular antibody production. However, studies [164–168] suggest a more stringent C-value of more than 3 or 4 to definitively demonstrate intraocular antibody production a study of active leptospiral uveitis in humans [168]. In a study of active human leptospiral uveitis, 72% had positive aqueous humor MAT results, and 80% were positive for leptospiral DNA by PCR analysis. However, results of that study also revealed that a combination of MAT and PCR improves diagnosis of the disease [168]. Recommendations for interpretation of leptospiral testing in horses are shown in Table 8.4.

The exact interaction that occurs between bacterial infection and the host immune system in ERU is a subject of debate. Strong evidence of antibodies against *Leptospira* in the eye, coupled with demonstration of molecular mimicry between leptospiral DNA fragments and equine cornea and lens, supports an autoimmune component, as does the existence

Table 8.4 Interpretation of leptospiral testing for uveitis.

Leptospiral tests	Serum titer	Aqueous humor/serum titer (C value) > 4	Aqueous or vitreous humor leptospiral PCR
Uveitis not likely leptospiral associated	–	–	–
	+	–	–
	–	–	+ (false +)
Uveitis likely leptospiral associated	+	+	+
	–	+	+
	+	+	– (false –)

+, Positive; –, negative.

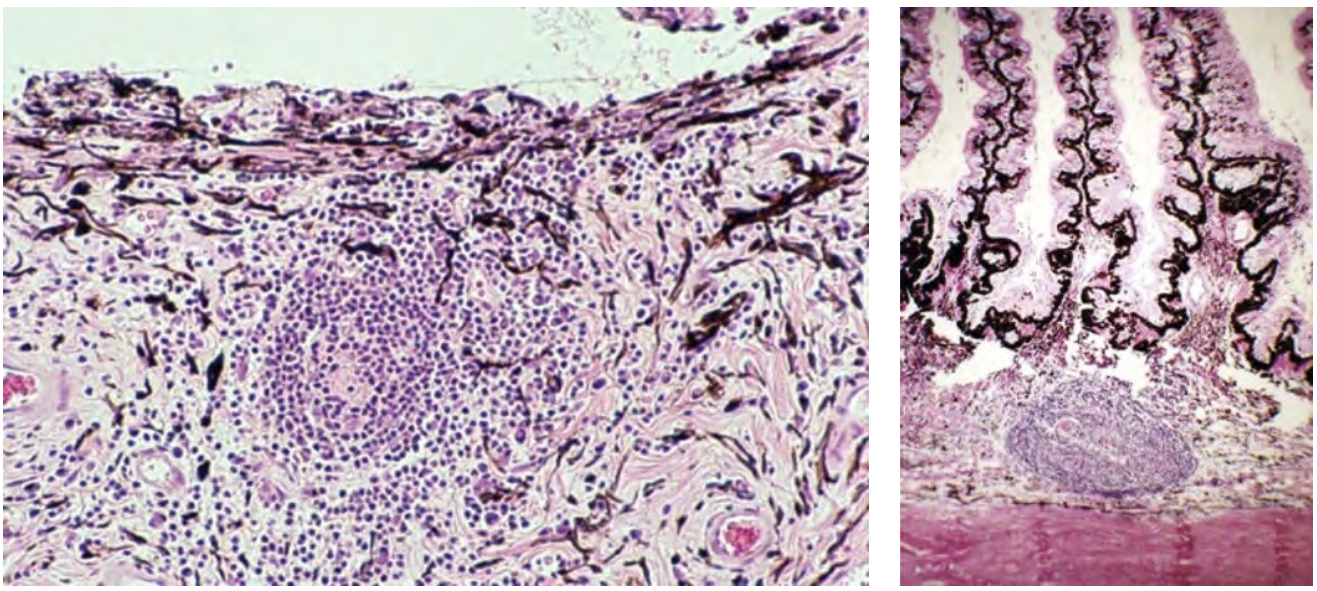
of antiretinal seroreactivity in leptospiral-related ERU horses. The presence of MHC class II expression and Ig deposition on resident and infiltrating cells in the eyes and pineal glands of these horses suggests that leptospiral infection may modulate the immune response of the eye. Because the disease has an immune pathogenesis, it is likely the genetic makeup of the individual, specifically the MHC, also plays a role in determining both susceptibility to leptospirosis as an inciting trigger and severity of subsequent inflammatory episodes.

A likely scenario regarding the pathogenesis of the immune-mediated leptospiral-associated ERU is as follows. When the inflammatory and uveitis process has been initiated, possibly by leptospiral infection (or other ocular disease), there is a general loss of ocular immune tolerance. In this environment, activated antigen-presenting cells in the uveal tract will effectively present autoantigens to the adaptive immune system, and cross-reaction between infectious agents and self-antigens can occur. *Leptospira* organisms (lipoprotein fragments and DNA) have been demonstrated to be particularly cross-reactive with equine ocular tissues [58, 60, 84, 143, 144, 147]. When cross-reactivity occurs and self-antigens are recognized and processed, the specific subcellular site, or epitope, is processed within cytoplasmic endosomes to ultimately present to T cells. Autoantigen cleavage in these endosomes can create neoepitopes, from either novel conformations or realignment of protein sequences [76]. This process can lead to intramolecular epitope spreading, which is the development of autoantibodies against additional components of the autoantigen [76]. Similarly, autoantibodies specific for one antigen may bind to apoptotic bodies or other similar autoantigens produced or recognized during inflammatory processes, leading to activated antigen-presenting cell uptake of this material and reamplification of inflammatory response (i.e, intermolecular epitope spreading) [76]. This reamplification of the inflammatory response to these neoepitopes likely explains the recurring nature of the inflammation characteristic of ERU [76].

Pathology

Anterior uvea The pathology of early ERU involves congestion of the vessels of the anterior uvea and infiltration of the uveal tract with inflammatory cells. The iris and ciliary body are infiltrated first by neutrophils. The neutrophils, which may escape into the anterior chamber to cause visible hypopyon, are soon replaced by large numbers of lymphocytes as well as some plasma cells and macrophages. Exudates of fibrin, serum proteins, and other substances are a predominant feature. Gross or histopathologic examination of eyes acutely affected with ERU show notable exudates on the surface of the iris, ciliary body, and ciliary processes and over the lenticular capsule. Serous and cellular exudates are also noted in the iridic stroma, in trabecular meshwork, and in the aqueous and vitreous humors. Simultaneous congestion and infiltration occurs in the conjunctiva. The retina is relatively unaffected in the first few attacks of inflammation.

With chronicity and further recurrences, organization of the lymphocyte infiltrate is evident. The ciliary body and base of the iris regularly demonstrate prominent lymphocytic nodules (Figure 8.40). The lymphocytes in the center of the nodules are B lymphocytes, whereas those on the periphery of the nodules, and most of the diffuse infiltrating population, are T lymphocytes [81, 83]. Lymphocyte follicles may also be seen in the conjunctiva adjacent to the limbus. The function of these lymphoid follicles is very interesting and could account for the relapses, since immunologically primed cells remain directly in the eye after the uveitic attack. Although T cells dominate the inflammation



(A) (B)

Figure 8.40 (A) Lymphocytic follicle or nodule formation at the base of **(A)** the iris and (B) the ciliary body, a common feature in eyes with ERU (H&E ×400).

in ERU, autoantibodies are also detectable in sera and ocular tissues and can be used to detect autoantigen specificity.

As pathologic damage continues, the epithelium of the ciliary processes and uveal blood vessel walls thickens. Exudates occur in the uvea and are easily seen occupying space over the ciliary processes and on the posterior epithelium of the iris. Histopathology of the ciliary body [147, 178] of spontaneous ERU has demonstrated three characteristic features: (1) presence of a thick, noncellular hyaline membrane (amyloid-like) tightly adherent to the inner aspect of the nonpigmented ciliary epithelial cells (NPE), (2) eosinophilic linear inclusions in the cytoplasm of the NPE, and (3) accumulation of clusters of lymphocytes and plasma cells directly within the NPE layer of the posterior iris and ciliary body.

The finding of the hyaline membrane adjacent to the posterior aspect of the iris (Figure 8.41) (characteristically staining orange-red with Congo red stain), coupled with the presence of the linear cytoplasmic inclusion bodies in the adjacent NPE (Figure 8.42) is highly suggestive of the presence of ERU [147, 178]. The characteristic hyaline membrane lining the nonpigmented ciliary epithelium of horses has been recently identified as amyloid A; however, the significance of this finding is unknown [170].

The lens often shows thick exudates adherent to the capsule, particularly on the posterior aspect, in early ERU and syncheia of the anterior capsule in chronic ERU. With adherence, lens capsule proliferates and cataracts develop (Figure 8.43). Luxation of the lens is common as deterioration of the zonules occurs. Wrinkling of the lens capsule (secondary to a hypermature, resorbing cataract) or lens calcification may occur.

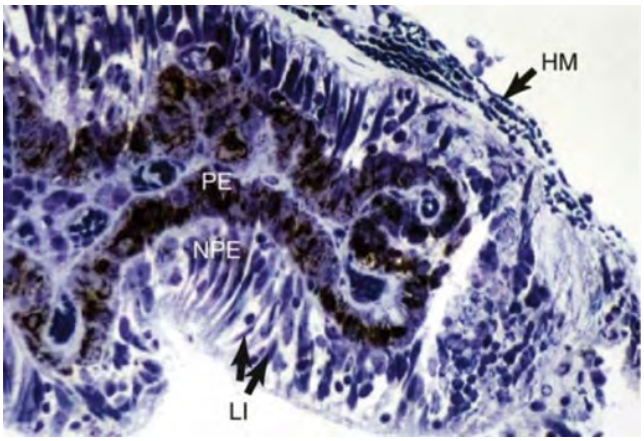


Figure 8.41 Ciliary process from an eye with chronic ERU. HM, Hyaline membrane; LI, linear cytoplasmic inclusions in the NPE; NPE, nonpigmented epithelium; PE, pigmented epithelium (H&E ×400). (*Source*: Photograph courtesy of Dr Penny Coolie.)

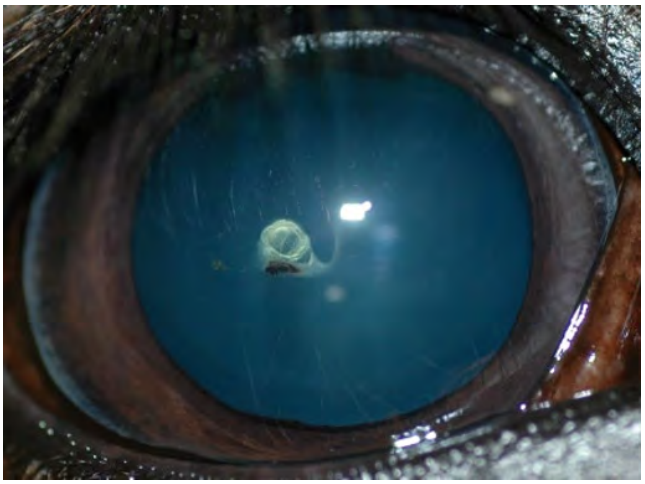
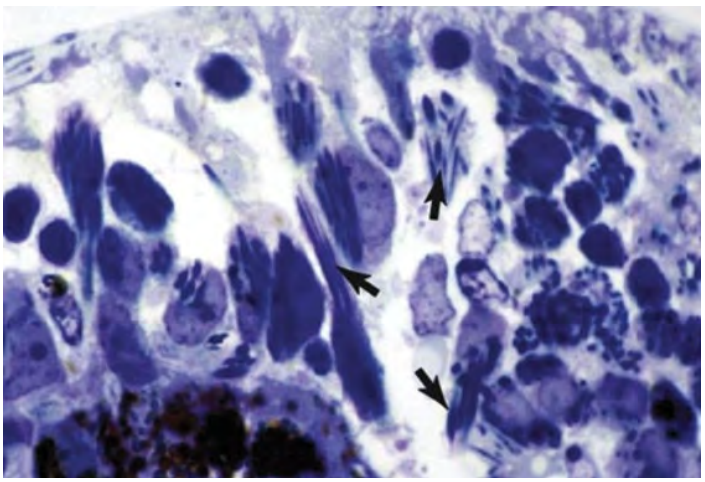
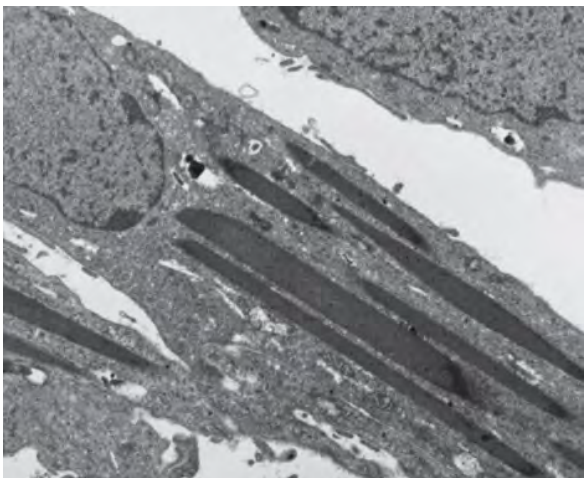


Figure 8.43 Anterior capsule proliferation, cystic formation, pigment adherence from the iris, and cataract formation in chronic ERU.



(A)



(B)

Figure 8.42 (A) Linear cytoplasmic inclusions (**arrows**) in the NPE from an eye with chronic ERU (H&E ×1000). (B) Transmission electron microscope image of the NPE linear cytoplasmic inclusions (×5000). (*Source*: Photographs courtesy of Dr Penny Coolie.)

Posterior segment Although acute cases of ERU show pathology that is most distinct in the anterior uvea, recurrence and chronicity of inflammation bring many changes to the retina and adjacent choroid. Scattered foci of T-lymphocytic infiltration are seen, particularly near the ora ciliaris retinae and optic nerve head. The RPE may undergo focal hypertrophy or degeneration. Serofibrinous exudate is commonly seen between the RPE and the photoreceptors and can be so extensive that it replaces the vitreous in a portion of the posterior chamber (Figure 8.44). Loss of rods and cones secondary to macrophage activity, destruction of the inner nuclear layer [77], and detachment of the retina may follow, with the RPE remaining attached to Bruch's membrane of the choroid, and the rest of the retina collapsing into the posterior chamber. Furthermore, recent studies have shown that there is a significant reduction of fibronectin and osteopontin production from Müller cells in ERU, which provides less neuroprotection, contributing to retinal damage [171].

Pathologic changes observed around the optic nerve head of horses with ERU include surface infiltrate (Figure 8.45), occasional lymphocyte nodule formation, and retinal traction folds around the margin of the nerve. Infiltrating cells in the perivascular and parenchymal space of the nerve are immunoreactive.

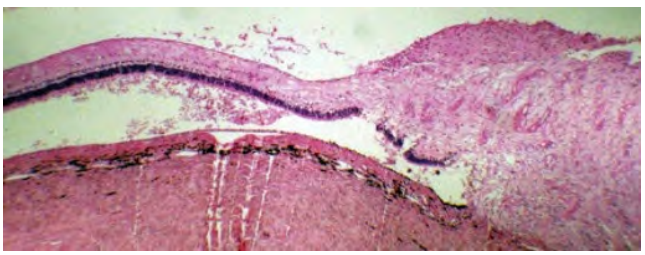


Figure 8.44 Serofibrinous exudate is commonly seen between the retinal pigmented epithelium and photoreceptors in horses with ERU. This image shows optic nerve involvement and retinal detachment with exudates (H&E ×31.25). (*Source*: Photograph courtesy of Dr Carolyn Kalsow.)

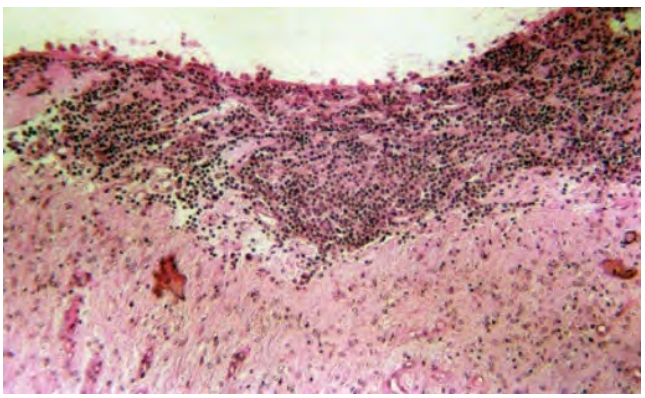


Figure 8.45 Pathologic changes observed around the optic nerve head in horses with ERU include surface infiltrate, occasional lymphocyte nodule formation, and retinal traction folds around the margin of the nerve. This image shows optic nerve infiltrate. This is the same horse as shown in Figure 8.44 (H&E ×31.25). (*Source*: Photograph courtesy of Dr Carolyn Kalsow.)

The optic nerve itself can show swelling or may be cupped or atrophied if secondary glaucoma is present [81].

The pineal gland and ERU Several studies have shown that ERU is accompanied by inflammation in the pineal gland of the brain. Earlier studies showed that experimental uveitis induced in guinea pigs with soluble retinal proteins also led to involvement of the pineal gland in the inflammatory process [172]. Pineal glands were infiltrated by lymphocytes and observable before retinal involvement [172]. Interestingly, the same group later also demonstrated pinealitis in ERU cases [82, 173, 174]. Septal areas of pineal glands from horses with uveitis had clusters of MHC class II antigen-expressing cells and T lymphocytes [173].

ERU in Appaloosa horses

Early ERU literature claimed that there was no breed predilection. However, in 1988, clinicians at Cornell University, New York, analyzed admission records of 16,242 cases and found that the Appaloosa breed had a significantly higher risk of developing uveitis relative to Thoroughbreds, and that Standardbreds had a reduced risk for the syndrome [175]. This study supported the observations of many equine practitioners who had diagnosed insidious uveitis in a large number of their Appaloosa patients, many of whom developed blindness or other secondary complications. A field study of a large number of cases in New York confirmed the breed predilection and reported that the odds of finding uveitis were 8.3 times greater in Appaloosas than in all other breeds combined [45].

Uveitis in the Appaloosa breed is often clinically distinct from classic ERU reported in other breeds. Many affected horses show an insidious course of disease without overt recurrent episodes of pain, so lumping these cases with horses that exhibit classic recurrences may be misleading. In fact, uveitis in the Appaloosa horse may have a different disease cause and pathogenesis than classic ERU, and further study is needed. Age of onset is variable and often difficult to determine, because the owner of an affected horse may be unaware of a problem until a veterinary examination is done or the horse shows overt vision loss.

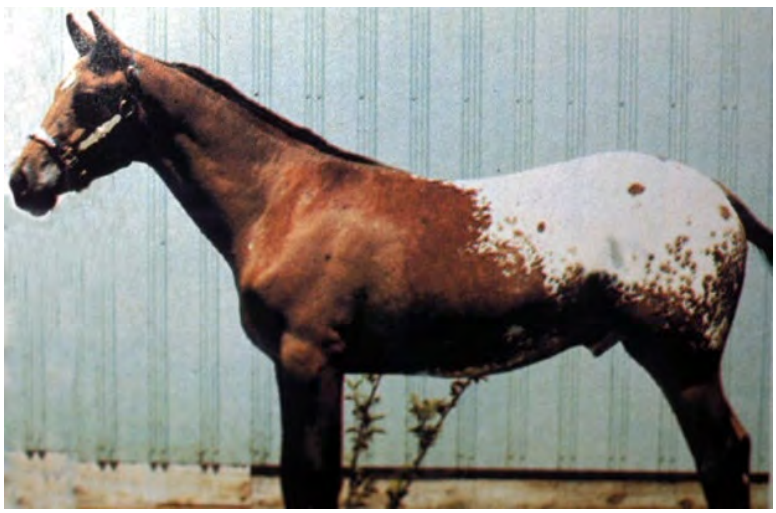
Secondary complications and severe degeneration of ocular tissues are common sequelae of uveitis in Appaloosas. Analysis of records of 160 cases of horses with uveitis in New York showed that 25%, or 42, of these cases occurred in Appaloosas, and that this subset of 42 horses had many characteristic chronic ocular changes and concurrent medical problems (see Table 8.3) [89]. Over 80% of cases were bilateral. During an 11-year period of observation, 38% of the afflicted horses were treated for acute corneal ulcers, and corneal scars indicating previous ulcers were apparent in a third of the cases. Glaucoma signs were present in 21%. Over half of the Appaloosas followed showed iris atrophy, and slightly less than half had developed or presented with posterior synechiae. Diffuse cataract developed in nearly three-quarters of the group, and a third of them experienced lens luxation or subluxation. Posterior changes like vitritis,

chorioretinitis, or detached retina were common but hard to quantify, because many of the horses developed cataracts that obscured visualization of these structures. Nearly a quarter of the cases went on to develop phthisis bulbi in one or both eyes (see Table 8.2) [89]. In a recent study, Appaloosa horses represented over 24% of all horses with ERU and were significantly more likely to be assessed as blind in one or both eyes after ERU than all other breeds. Additionally, of the 54 Appaloosas with ERU included in this study, 87% were affected bilaterally [73].

Coat color pattern of affected horses trended towards horses with overall light base coats and focal darker spots ("Foundation-type" or "Leopard" Appaloosas). Appaloosas that had dark basic coat patterns with a light "blanket" over the rump were less likely to develop ERU. Affected horses often showed annual coat color changes, with their base coat becoming lighter as they aged (Figure 8.46). Night blindness was only rarely associated with uveitis, being confirmed in just 3 of 42 cases, which is much less frequent than recently reported [176]. Interestingly,



(A)



(B)

Figure 8.46 (A) Example of an Appaloosa horse with an annual coat color that changes with its base coat and becomes lighter as the horse ages. This type of Appaloosa horse may be more likely to have ERU. (B) Example of an Appaloosa horse with a dark basic coat pattern with a light "blanket" over the rump. This type of Appaloosa horse is less likely to have ERU.

17% of affected Appaloosas showed signs of recurrent obstructive airway disease (heaves), often severe in nature [89].

Appaloosas that live in river valleys or other temperate areas may become infected with leptospirosis because of environmental risks. One study showed that Appaloosa horses seropositive to *L. interrogans* serogroup Pomona have a particularly severe clinical course and a nearly 100% incidence of blindness in one or both eyes [45]. These cases often showed clinical disease that was a hybrid between classic and insidious forms of uveitis—the horses would experience recurrent episodes of fulminant ocular inflammation and severe pain and also show signs of progressive deterioration in the interludes between episodes.

Any disease that has a breed proclivity likely has a genetic basis. Recent studies in Appaloosas have demonstrated that markers at both the Leopard complex spotting (LP) locus on equine chromosome 1 (ECA1) and within the major histopathology complex (MHC) on equine chromosome 20 are associated with insidious ERU risk in Appaloosa horses [87]. In addition, ERU is strongly associated with the MHC class I haplotype ELA-A9 in a population of German Warmblood horses [85, 86].

Differential diagnosis and methods for definitive diagnosis

The clinical diagnosis of ERU is based on the presence of characteristic clinical signs and history of documented recurrent or, in the case of insidious ERU, persistent episodes of uveitis. Both features are required to make this clinical diagnosis, especially to differentiate ERU from non-ERU uveitis (i.e, primary uveitis) and other causes of recurrent or persistent ocular cloudiness and/or inflammation, such as herpesvirus keratitis, immune-mediated keratitis, glaucoma, and stromal abscessation. These and many other primary conditions of the eye result in ocular clinical signs typical of ERU, particularly pain, blepharospasm, photophobia, miosis, and altered corneal transparency. If the eye has clinical signs consistent with uveitis, it is critical that the clinician differentiate between primary uveitis and ERU. These are two separate diseases.

It is also particularly important to differentiate primary corneal disease from ERU. Deep nonulcerative infectious keratitis (i.e, stromal abscesses), such as that associated with fungal infections, is commonly misdiagnosed as ERU. Deep stromal abscesses wax and wane in severity (although they are generally progressive) and are associated with severe pain, aqueous flare, miosis, corneal edema, and hypopyon. Treatment of infectious keratitis with topical corticosteroids, a common treatment of ERU, can result in substantial worsening of the stromal abscess. Use of topical corticosteroids is contraindicated for most primary corneal problems, and failure to properly treat ulcers or other problems (e.g, corneal ulcer or foreign body, stromal abscess, unusual keratitis, glaucoma, corneal or intraocular neoplasia) may have disastrous consequences. These diseases are referred to as "masquerading syndromes" of ERU (Table 8.5).

A thorough ocular examination is needed, with careful inspection of the eyelids and cornea to rule out primary corneal disease. If palpebral and conjunctival swelling obstructs a portion of the cornea, a repeat examination may be needed after nonsteroidal anti-inflammatory drug (NSAID) therapy has reduced pain and swelling. Scrutiny for other differentials requires a careful inspection of all accessory anatomic structures of the eye, looking for masses, pigment changes, scars, opacities, accumulation of fluid in the ocular media, and changes of the fundus, particularly the peripapillary region. The clinician should perform a complete ophthalmic examination in both eyes of the animal, even if only one eye has active inflammation. Tonometry is recommended in all cases to rule out glaucoma or document hypotony that often accompanies ERU. A complete ophthalmic examination is also important in quiet, comfortable (i.e, quiescent) eyes to document clinical signs consistent with past uveitis (synechiae, pigment on the anterior lens capsule, diffuse cataract, peripapillary scarring, etc.).

A careful history of previous episodes of inflammation should be obtained, including a description of the signs observed by the owner. If the owner reports that the horse has had brief or protracted episodes of ocular pain or swelling in the past, the scenario is strongly suggestive of ERU. However, if owners report that the horse has had no observable eye inflammation or do not know the history of the animal, these horses may have the insidious form of ERU (especially if the horse is an Appaloosa or draft breed), or horses may have classic ERU but have not had

Table 8.5 Differentiating ERU from other causes of ocular inflammation*.

Syndrome	Comment	Diagnostic aid
Non-ERU uveitis	Anterior or posterior uveitis	History of no recurrence of uveitis
Corneal ulcer	Self-trauma, corticosteroids contraindicated	Fluorescein dye positive, focal opacity or defect
Stromal abscess	Past trauma, corticosteroids contraindicated	Fluorescein dye negative, focal yellow-white opacity
Immune-mediated keratitis	Appearance may change often, severity varies, recurrent inflammation possible	Fluorescein dye negative, multiple opacities, variable pattern
Herpes keratitis	Variable pain, may retain rose bengal	Fluorescein dye variable, multiple punctate or linear opacities
Corneal foreign body	May be vascularized focally, may be visible	Fluorescein dye variable
Corneal neoplasia	Squamous cell carcinoma, melanoma	Mass or cellular infiltrate visible on corneal surface or through epithelium
Intraocular neoplasia	Melanoma, medulloepithelioma, anterior or posterior segments	Ocular ultrasonography, or may visualize in anterior chamber
Glaucoma	Often secondary to ERU, persistent corneal edema	Tonometry

* "Masquerading syndromes" of ERU.

an episode that has been witnessed by the owner. In cases where the history is unknown but ERU is suspected, at least three signs of disease (corpora nigra atrophy, pigment on anterior lens capsule, synechiae, iris fibrosis or color change, cataract, lens luxation or subluxation, vitreal opacities, retinal detachment or traction bands, peripapillary scarring in a focal or alar pattern) **and** a history of recurrent ocular disease are needed before making a presumptive diagnosis of previous ERU [47].

Other tests that may be used in assessing the horse that presents with acute primary uveitis or signs compatible with previous disease include complete blood count and blood chemistry. Leptospiral titers of the serum and eye fluids is useful for testing previous exposure to this well-known risk factor, but may not be particularly helpful in determining treatment. See additional information in the section **Classification and clinical testing**. In addition to leptospiral MAT serology, blood may be submitted to test for exposure to Lyme disease (serum titer and Western blot analysis) and/or equine viral arteritis. Fecal parasite analysis is indicated, as well as a full physical examination of other body systems to check for concurrent problems (see Box 8.2 and Table 8.5).

Owner education and counseling is indicated whenever signs of ERU are detected during a routine ophthalmic examination. The owner should be educated about the disease syndrome, and a frank discussion of visual prognosis should occur. It is best to stress the possible scenarios early and prepare owners for the expense, treatment effort, and progression associated with overt future attacks. Frequent veterinary follow-up examinations should be recommended. In cases where the veterinarian suspects either insidious or classic ERU that has been unobserved by the current owner, biannual examination coupled with immediate evaluation if the horse suffers pain in one or both eyes should help sort out the diagnosis. Referral to a board-certified veterinary ophthalmologist may be helpful in providing a complete examination of cases of uncertain etiology.

Prognosis

Visual prognosis of 112 cases of ERU that were followed for a 7-year period in the Genesee River Valley (USA) were reviewed [45], and the visual outcome, chronic ocular changes, and concurrent medical problems in a group of 160 cases (including the original 112) were followed over 11 years [89]. The horses were segregated by breed and seroreactivity to *L. interrogans* serogroup Pomona. Of the total group of 160 horses, 20% (32) had no known risk factor for ERU—that is, they were seronegative and nonAppaloosas. Of the remaining 128 horses, 86 were leptospiral seropositive nonAppaloosa horses, 28 were Appaloosa horses with insidious uveitis, and 14 were horses that were both Appaloosas and seropositive to *L.* Pomona. Table 8.3 summarizes the chronic ocular changes observed in these four groups, concurrent medical problems observed, and the eventual visual outcome. Common ocular sequelae seen in these ERU horses included corneal focal scars, calcium deposits, and other corneal opacities. Leptospiral-seropositive horses experienced a high rate of calcific band keratopathy. Striae and dense corneal streaks were common in Appaloosas, and their presence was associated with blindness. Iris atrophy and color change were common, especially in Appaloosas and seropositive horses. Anterior synechia were rare unless phthisis bulbi was present, but posterior synechia occurred in nearly a third of all cases and 40% of Appaloosas. Diffuse cataract(s) developed in 41% of all cases, and nearly three-fourths of the Appaloosas. These were a common cause of blindness. Lens luxation was common in Appaloosas (29%). Severe vitreal opacity (vitritis) was observed in nearly a third of the cases. Peripapillary scarring (focal or alar) was also present in about a third of the horses. Cataracts and synechiae often obstructed posterior segment evaluation, so inflammatory changes were probably under-reported. Appaloosas had the highest rate of glaucoma (21%). Phthisical eyes developed most often in Appaloosas and leptospiral-seropositive horses.

Owners are often concerned that horses with ERU will have to be enucleated. In the described series, only 4% (6/160) were enucleated for complications from corneal infection or glaucoma. Of more concern is the fact that 43 of the 160 horses (27%) were treated for corneal ulcers over the observation period. Risk of corneal ulcers in ERU horses should be stressed, as owners often choose to medicate horses with painful eyes themselves, and they may potentiate serious infections by applying corticosteroids and delaying proper diagnosis. Additionally, in this study, ten horses suffered from calcific band keratopathy.

The overall prognosis for sight in horses with uveitis has been described as poor.10 Limited data have been published regarding actual rates of vision loss in horses with ERU. In the New York study, complete blindness was noted in 20% (32/160) of all the horses followed long term. Unilateral blindness occurred in 36% (57/160). Overall, 56% of all horses experienced blindness in one or both eyes [89].

Appaloosas and seropositive horses were at increased risk for blindness. Seropositive Appaloosas had the worst visual prognosis: all lost vision in at least one eye, and 50% became completely blind. Appaloosas that had never been exposed to *L.* Pomona and who suffered insidious disease fared a little better. The rate of vision loss in one or both eyes was 72%, with 29% experiencing total blindness. Horses that had been exposed to *L.* Pomona but were not Appaloosas lost vision in one or both eyes 49% of the time and had a total blindness rate of 17%. Horses that were seronegative to *L.* Pomona and were not Appaloosas had the best visual prognosis; 34% became blind in one or both eyes, and total blindness occurred in only 6% [89].

These results were supported by a recent study of the long-term prognosis of 224 horses (338 eyes) with ERU in which it was shown that ERU had a tremendous negative impact on horses and their owners as a result of vision loss, decrease in function, change in ownership, expense of diagnostics and treatment, GI and orthopedic disease, and death (euthanasia) of the horse as a direct result of ERU [73]. Of these horses, loss of the eye occurred in 41 horses (12.1% of total) and 46.9% were reported blind in the affected eye(s), including 28.9% bilaterally

blind horses. Fifty-seven horses (29.4%) did not return to their previous role, while 61 (31.4%) performed at a reduced level. ERU decreased the monetary value of 164 horses. Thirty-seven (19.1%) horses changed ownership as a direct result of ERU [73]. The impact of ERU in this study was particularly severe in horses of the Appaloosa breed and in horses having positive titers (serum and/or aqueous humor titers) to leptospirosis serovars, especially *L.* Pomona and *L.* Grippotyphosa. Furthermore, horses with cataracts, elevated IOP, and/or hyalitis had poor prognosis for vision. Appaloosa horses were significantly over-represented in this study compared to the study population; 87.0% had bilateral disease, and after ERU on follow-up, 58.0% of Appaloosa horses were assessed as blind [73].

Treatment

The main goals of therapy for ERU are to preserve vision, reduce and control ocular inflammation in an attempt to limit permanent damage to the eye, control pain, and prevent recurrence. In horses where a definite inciting cause has been identified, treatment is directed at eliminating the primary problem, and initial tests to isolate an inciting agent are performed (see section **Diagnosis**). Usually, however, due to the immune-mediated pathogenesis of ERU, a particular cause cannot be isolated. In these instances, therapy is directed at treatment of symptoms and reducing ocular inflammation.

Practical and stable-management practices to decrease ERU Practices that decrease ocular injury or minimize the inflammatory stimuli may decrease or eliminate the development of recurrent episodes of uveitis in ERU (Box 8.3). It may be possible to eliminate environmental triggers (e.g, allergens, antigens.) of the recurrent episodes of uveitis by changing the horse's pasture, pasture mates, or stable, increasing insect and rodent control, decreasing sun exposure, or changing bedding type. Trauma to the eye(s) can also be decreased by eliminating sharp edges, nails, and hooks in the stable, taping up exposed handles on feed and water buckets, removing low tree branches in the pasture, reducing the training and show schedule, minimizing trailering, and implementing the constant use of a quality fly mask. Ensuring that the horse has proper hoof care, an optimal anthelmintic schedule, and proper diet may also reduce uveitis episodes by minimizing infectious disease occurrence and optimizing systemic health.

Anecdotal reports have suggested that vaccination with multivalent vaccines or administration of a number of different individual vaccines on the same day is sometimes associated with a relapse of signs of ocular inflammation. For this reason, it is recommended that horses with ERU be given their annual vaccinations in at least two sessions spaced a week or more apart, rather than all at once. Alternatively, pretreating with a systemic NSAID 24 hours prior to vaccination and repeating the NSAID at the time of vaccination may prevent a flare-up. The attending veterinarian should determine the appropriate immunizations and the route and frequency of administration of the products.

Vaccination of horses against leptospirosis Vaccination of horses with a leptospiral bacterin has been proposed as a preventive measure for leptospiral-associated ERU [134]. Several bovine vaccines that contain bacterins of pathogenic leptospiral serogroups are available commercially and all are labeled solely for use in the bovine or porcine species. Insofar as ERU has been shown to have a strong immune-mediated component, and research has demonstrated molecular homology between equine ocular tissues and leptospiral proteins, it is not known if vaccination carries any risk of exacerbating the immune response or precipitating inflammation.

Anecdotal reports suggest that selective use of a bacterin on farms with demonstrated risk of exposure to *Leptospira* has reduced incidence of eye disease [134]. However, acute uveitis signs have also been observed shortly after vaccine administration in a few horses who had unknown past exposure to the bacteria. A study of the effect of an inactivated bovine vaccine against six serovars of *L. interrogans* in a small number of ERU horses demonstrated no significant increase or decrease in recurrent episodes of inflammation after vaccination compared to control groups receiving adjuvant only [177].

In October 2015, an equine *L.* Pomona monovalent vaccine (Lepto Eq Innovator (Zoetis Inc, Florham Park, NJ)) was approved and marketed for the prevention of leptospiral-associated uveitis and abortion. The recommendation is to vaccinate at-risk horses that did not have signs of ERU. Vaccination of ERU-affected horses is not recommended. Vaccination may be considered on farms in the known geographic risk zones that have had multiple cases of ERU in the past, assuming the clinician and horse owner have discussed the possible risks versus benefits of the

Box 8.3 Practical and stable-management practices to decrease ERU.

Environmental

- Change pasture/stable/pasture mates
- Increase insect and rodent control
- Decrease dust
- Decrease sun exposure
- Change bedding type

Health maintenance

- Proper hoof and dental care
- Optimal anthelmintic and vaccination schedule
- Avoid large multivalent vaccines; split up immunizations
- Proper diet; minimize weeds in pasture

Decrease ocular trauma

- "Soften" stable (eliminate sharp objects), tape up bucket handle hooks
- Eliminate low tree branches and burdock plants in pasture
- Decrease training and show schedule
- Minimize trailering
- Do not feed from hay nets
- Use quality fly mask

vaccination. Before any decision is made to immunize, it would be best to perform leptospiral serology tests on all horses on those farms. Vaccine administration should be limited to horses that are seronegative to *L. interrogans* and have normal eyes. What effect vaccination will have on intraocular fluid MAT testing and whether or not this monovalent vaccine will actually reduce the incidence of ERU is unknown.

Medical treatment Because vision loss is a common long-term manifestation of ERU, initial therapy must be aggressive (see Table 8.1). The two main goals of therapy are to reduce discomfort, which is achieved through mydriatic/cycloplegics (e.g, topical atropine), and to reduce inflammation with systemic medications (e.g, corticosteroids and NSAIDs). Topical atropine 1% is generally given to effect and then continued as required to maintain pupil dilation, usually once a day. If the pupil does not dilate after topical atropine use, addition of 10% phenylephrine HCl topically (every 6 hours) for 24–48 hours may help achieve mydriasis. Phenylephrine is an alpha agonist but has poor mydriatic/cycloplegic effect in horses [178]. When used in combination with topical atropine, there may be a slightly improved mydriatic effect than that observed with atropine alone. Poor response to mydriatics in general suggests that severe intraocular inflammation is present; therefore control of the inflammation is required to allow the mydriatics to function. Increasing frequency of topical atropine (e.g, greater than every 8 hours) or increased concentrations of atropine (e.g, 2–4%) is rarely indicated and could predispose the horse to colic [179].

Topical corticosteroids are used to decrease inflammation. Prednisolone acetate 1% and dexamethasone HCl 0.1% are the most commonly used topical corticosteroids. Both medications have excellent ocular penetration. Frequency of therapy varies according to the severity of the disease, and ranges from hourly topical application to once-daily application. Dexamethasone is used most often in clinical situations because it is available in an ointment form and inexpensive. Topical corticosteroids have side-effects, including the ability to potentiate infections and collagenase enzymes (melting of the cornea), delaying epithelialization of corneal ulcers, and possibly potentiation of the development of calcific band keratopathy.

Topical NSAIDS (e.g, 0.03% flurbiprofen, 0.09% bromfenac sodium, or 0.1% diclofenac sodium) can also be used. Their main advantages are that they can be administered without concern for potentiating infections, but they do delay epithelialization of corneal ulcers. Although bromfenac is a very potent NSAID compared to the others, in general, the anti-inflammatory effect of topical NSAIDs is much less than topical dexamethasone and prednisolone.

Systemic therapy is the most potent therapy for management of ERU. Oral, intramuscular, or intravenous (IV) flunixin meglumine is one of the most potent anti-inflammatory medications for the eye (see Table 8.1). Phenylbutazone and aspirin are much less effective. Systemic dexamethasone or prednisolone are also effective, but generally are only recommended in severe cases that will not respond to other anti-inflammatory medication (see Table 8.1).

Initial therapy is instituted for at least 1–2 weeks and should be tapered off at minimum over an additional 2 weeks after the resolution of clinical signs. Tapering of medication is **very** important to prevent a rebound bout of inflammation from sudden withdrawal of medications. Owners should be warned about this and told not to discontinue medications despite resolution of clinical signs.

In severe cases of ERU, local subconjunctival injections of corticosteroids may be indicated as an adjunct to therapy. The steroid of choice subconjunctivally is 2 mg of triamcinolone acetamide (0.2 mL of 10 mg/mL solution). Triamcinolone injections will deliver medication for 7–10 days and will not result in granuloma or abscess formation that other steroids, such as methylprednisolone acetate, will cause. However, once the injections are given, the steroid treatment cannot be withdrawn. Additionally, intravitreal injections of triamcinolone (2.5–10 mg) could be considered [180]. The chronic presence of corticosteroids may delay healing of corneal ulcers and substantially predispose the eye to fungal keratitis. Therefore subconjunctival and intravitreal injection of corticosteroids should be used with extreme caution. See Chapter 3 for more information and the technique for subconjunctival and intravitreal injections.

Response to medical treatment Response to treatment of clinical cases of ERU is variable and difficult to predict. Acute attacks of inflammation may last a few days or several weeks. Some recurrences are mild and respond quickly to simple treatment with mydriatics, topical corticosteroids, and systemic NSAIDs, while other episodes are severe and highly refractive to treatment. Subsequent bouts of inflammation may not show the same response to therapy as the initial episode. If a subsequent bout of uveitis does not respond to therapy as in previous episodes and the cornea is edematous, secondary glaucoma (see Figure 8.32) may have developed and should be diagnosed and monitored by tonometry.

Repeat episodes of ocular inflammation may be progressively more severe and refractive to therapy in some horses. These horses usually go blind in the affected eye(s) despite therapy. Other horses experience a few mild relapses, then never suffer another episode. Still others (primarily Appaloosas and horses of draft breeding) experience insidious disease that progresses quietly but relentlessly regardless of treatment. The multiple factors that contribute to the onset of the syndrome in a particular horse (inciting etiology, the specific immune system, and genetics of the host) probably play a key role in determining susceptibility to recurrence, response to therapy, and eventual visual outcome.

Antibiotic therapies Traditional treatments used for ERU (i.e, corticosteroids, mydriatics, and NSAIDs) are aimed at reducing inflammation and minimizing permanent ocular damage at each active episode. These treatments are not likely to be effective in preventing recurrence of disease. Other medications used to

prevent or decrease severity of recurrent episodes, such as aspirin, phenylbutazone, and various herbal treatments, have limited efficacy and potential detrimental effects on the GI and hematologic systems when used chronically in the horse.

However, several anecdotal reports of benefit using antibiotics as a primary treatment of ERU have emerged. In cases of suspected leptospiral infections (e.g, an elevated leptospiral serum or ocular fluid titer), a 4-week course of oral doxycycline (12 mg/kg PO every 12 hours) or enrofloxacin (7.5 mg/kg PO every 24 hours) [181] is proposed to minimize or eliminate recurrent episodes of uveitis. It is thought that these therapies may kill residual organisms that may be responsible for ERU episodes, but no studies have been done to determine if this is the mode of action or if these medications are having another effect. Furthermore, with the strong evidence that ERU is an immune-mediated disease, the use of antibiotics is unlikely to be successful [76–79, 103, 107, 112] and in fact there are no reports of their success in treatment of ERU with or without a leptospiral association. Additionally, in one study, oral administration of doxycycline failed to achieve therapeutic drug concentration in the aqueous or vitreous humor of normal horses [182]. Single injections of 4 mg of gentamicin into the vitreous cavity have also been reported anecdotally to help minimize or eliminate recurrent episodes of uveitis in cases of leptospiral-associated ERU. However, the effectiveness of these treatments has not been reported, and the mode of action, complications, and long-term results of these therapies have not been determined. Until studies are reported, it is recommended that these treatments be used with caution and only as a last resort. Acupuncture, herbal, methylsulfonylmethane (MSM), and holistic therapies may be worth an attempt as long as their use is concurrent with traditional medications or in cases where traditional medication is poorly effective.

Autologous mesenchymal stem cell therapy Mesenchymal stem cells (MSCs) have been demonstrated to be immunomodulatory through the mechanisms of secretion of soluble immunosuppressvie factors, induction of T-cell anergy, apoptosis, activation of regulatory T cells, and inducing tolerogenic dendritic cells. It is clear that MSCs modulate both innate and adaptive immune responses, and evidence is now emerging that the local microenvironment is key in the activation of MSCs to become immunosuppressive [183].

Several studies have demonstrated the therapeutic effect of MSCs on EAU in rats [184, 185]. In one study, IV MSC therapy reduced the severity of interphotoreceptor binding protein-induced EAU when administered before disease creation, and it delayed the onset of the disease if administered preventively [184]. In another study, IV administration of MSCs in EAU rats decreased the production of TH1 and TH17 cytokines, while the production of TH2 and regulatory T-cell (Treg) cytokines IL-10 and TGF-β) was elevated during the entire course of EAU. These results were interpreted by the authors to demonstrate that MSCs can regulate negatively both TH1 and TH17 responses and restore the balance of TH17/Tregs in the course of EAU, which is important for the regression of the disease [185].

These experimental results showing the immunomodulatory effects and therapeutic benefit of the use of MSCs for therapy of experimental autoimmune uveitis strongly suggest that there may be benefit of autologous MSC therapy in ERU. A recent clinical trial has been initiated at the University of California, Davis, evaluating the use of fat-derived autologous MSC injected intravenously for treatment of ERU. The results of this study are not yet available. Local ocular injections of MSCs may also be beneficial, but location of injection, number of cells to inject, adverse effects, long-term complications, and long-term efficacy are some of the many questions that need to be answered before this therapy can be used routinely for the treatment of ERU.

Suprachoroidal cyclosporine sustained-release devices Ocular sustained-release medication devices or implants have many advantages over more traditional methods of drug administration to the eye [186]. These advantages include delivery of constant therapeutic levels of drug directly to the site of action, bypassing some of the blood–ocular barriers, and eliminating the need to rely on owners to treat their horse. Release rates are typically well below toxic levels of the drug; therefore higher concentrations of the drug are achieved in the eye without any systemic side-effects. Devices also have the benefit of being more convenient for the patient and reducing the risk involved with frequent intravitreal injections [186].

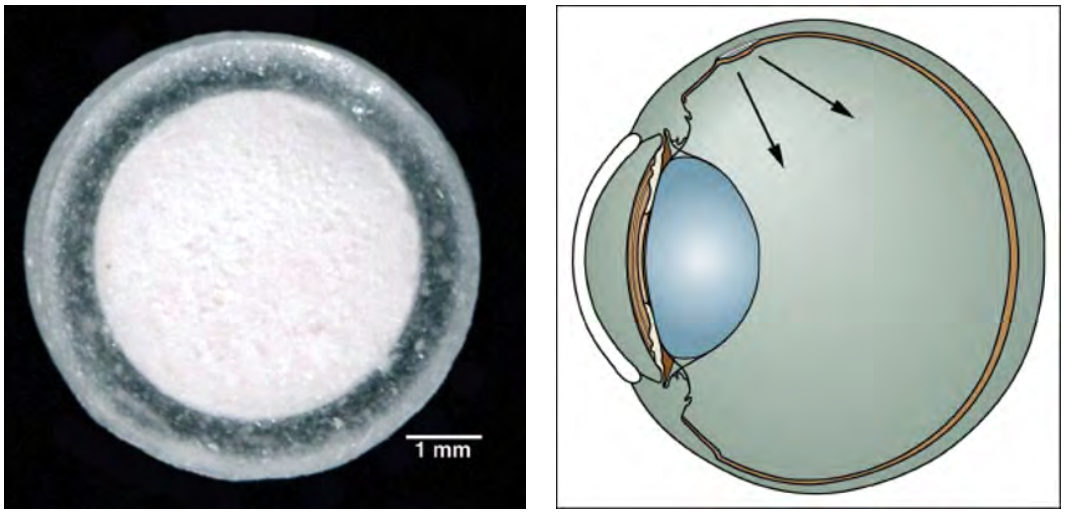
Cyclosporine A (CsA) is a 1.2-kDa cyclic peptide that blocks the transcription of IL-2 production and the responsiveness of the T cell [187, 188]; it may be the ideal drug to prevent the activation of T lymphocytes and recurrence of uveitis. However, CsA is hydrophobic and does not penetrate into the eye when applied topically [189–191], and systemic treatment may promote serious side-effects such as renal, hepatic, and neurologic toxicity [192]. CsA is also very costly to administer to a horse, and its safety, pharmacokinetics, and toxicity have not been evaluated.

Originally, a polyvinyl alcohol silicone-coated intravitreal CsA sustained-delivery device that had been shown previously to produce a sustained level of CsA in rabbit ocular tissues [193, 194] was evaluated for use in horses. A CsA device was implanted into normal horse eyes for up to 1 year and was not associated with ocular inflammation or complications [195]. In equine eyes with experimentally induced uveitis, the CsA decreased the duration and severity of inflammation, cellular infiltration, tissue destruction, and level of transcription of proinflammatory cytokines [196]. In a study using CsA devices in horses with naturally occurring ERU [197], horses with frequent recurrence of uveitis without vision-threatening ocular changes (i.e, cataracts, retinal degeneration) or systemic illnesses were selected to receive the device. Although the device prevented the development of recurrent episodes in 81% of horses, complications were noted after surgery that included intraocular hemorrhage, progression of cataract, and retinal detachment [197]. The surgical intervention

in fragile ERU eyes was thought to be the source of the observed complications, so less-invasive methods were evaluated for the constant release of CsA.

A device (Figure 8.47) was developed to be inserted into the suprachoroidal space and allow constant release of CsA (or other selected immunosuppressive medications) directly to the ciliary body. Horses with chronic documented ERU (as determined after complete ophthalmic examination) that have little or no active inflammation but are experiencing frequent recurrences or early relapse of active ERU after stopping medications are appropriate candidates for surgical placement of a CsA implant. Horses with active inflamed eyes that cannot be controlled with anti-inflammatory medications are **not** candidates for CsA implantation because CsA has poor anti-inflammatory properties (its immunosuppressive properties help prevent new recurrent episodes), and inflamed eyes are prone to post-surgical complications. Control of active inflammation with traditional anti-inflammatory medications is critical for success of the CsA implantation technique. Evidence of significant cataract formation or other ocular condition (e.g, glaucoma) makes the animal a poor candidate for surgery.

The suprachoroidal implant surgical technique requires usually that the horse be placed under general anesthesia. A 1-cm conjunctival incision is made in the dorsolateral bulbar conjunctiva. A 7-mm-wide scleral flap is made, exposing the uveal tract (the black uvea is just visible through the sclera) approximately 8 mm posterior to the limbus and just lateral to the insertion of the dorsal rectus muscle (Figure 8.48A). The CsA-containing device is placed in the incision, in contact with the uveal tract (Figure 8.48B). The scleral flap and incision are closed with 6-0 Vicryl (Figure 8.48C). Post-operative medications include flunixin meglumine (500 mg PO every 24 hours) for 5 days, topical triple antibiotic ophthalmic ointment every 12 hours for 10 days, and topical atropine ointment every 24 hours



(A) (B)

Figure 8.47 (A) A reservoir/matrix device designed for long-term release of CsA to the eye. (*Source*: Courtesy of Dr Mike Robinson.) (B) Schematic of the placement of a suprachoroidal drug-delivery device. Drug delivery is in the direction of the **arrows**.



(A) (B) (C)

Figure 8.48 Suprachoroidal CsA-releasing device implantation. (A) A 7-mm-wide scleral flap is made, exposing the uveal tract (the black uvea is just visible through the sclera) approximately 8 mm posterior to the limbus and just lateral to the insertion of the dorsal rectus muscle. (B) The CsA-containing device is placed into the incision, in contact with the uveal tract. (C) The scleral flap and conjunctival incision are closed with 6-0 polyglactin 910 sutures.

for 7 days. Some horses have had a mild flare-up following discontinuation of the flunixin meglumine.

Data from clinical patients suggest that it takes 30–45 days after implantation of the device to get adequate ocular levels of CsA. If recurrent episodes occur, traditional treatment with systemic NSAIDs, topical steroids, and atropine is recommended. Horses have been reported to have recurrent episodes after surgery, but, subjectively, less medication is required to control the active inflammation, and the duration of the inflammatory episodes are shorter. More importantly, the suprachoroidal implant is not associated with any vision-threatening complications such as retinal detachment. The duration of delivery of medication from the current devices is approximately 36 months.

Use of suprachoroidal placement of a CsA device for the treatment of clinical cases of ERU has been reported [55]. Using this device, mean vitreous CsA concentrations were 0.20 ± 0.14 µg/mL at 4 weeks and 0.14 ± 0.04 µg/mL at 9 weeks. CsA was not detected in the cornea, aqueous humor, or peripheral blood at either 4 or 9 weeks after implantation.

Sixty-seven horses received implants in one or both eyes in a 2006 study [91] and mean follow-up was 14.2 months. The number of uveitis flare-ups was significantly decreased after surgery ($P < 0.0001$). The percentage of eyes with vision at 6 months after surgery was 98% (68/69), after 12 months was 93% (43/46), after 18 months was 90% (28/31), and after 24 months was 96% (22/23). Overall, 85% (68/80) of eyes had vision after surgery [91].

Data from 186 eyes of 156 horses that had CsA devices implanted for ERU were reviewed [90]. Horses with ERU from six centers in the USA and two in Europe had the CsA device implanted. Mean follow-up was 29 months (1–7 years). Horses with implants had significantly fewer flare-ups after surgery (mean 0.05 flare-ups/month) than prior to implantation. Overall, 79.9% were visual at the last follow-up time. Only three eyes required a repeat implant, all 4 years or longer after the first implant. These results suggested that the suprachoroidal placement of the CsA device resulted in excellent long-term control of ERU [90]. Because recurrences of inflammation did not increase after the theoretical depletion of the CsA (approximately 3–4 years), it is possible that autoreactive T cells may undergo anergy after a period of time in the presence of CsA, after which recurrence of disease will not occur.

*Pars plana vitrectomy** Since the 1980s, pars plana vitrectomy (PPV) has been used in the management of chronic endogenous uveitis in humans [198–202]. The main goal was to improve vision by clearing the media or removing membranes. However, PPV in eyes with chronic uveitis also altered or diminished the severity as well as the frequency of uveitis relapses [200]. There is evidence that PPV has a beneficial effect on the clinical course of chronic endogenous posterior uveitis in humans, possibly by physically removing any resident inflammatory cells with the vitreous [200]. Despite the reported complications (i.e, vitreal hemorrhage, cataract formation, retinal detachment) following PPV, the majority of the patients were able to switch from rigorous systemic pre-operative medication to simple eyedrops or no treatment at all [199].

In 1991, PPV was described in the management of ERU [203]. PPV has since been used in the treatment of ERU primarily in Europe [130, 204, 205]. Similar to the human counterpart, the most common complications reported in horses are transient hypopyon, vitreal and/or retinal hemorrhage, retinal detachment, and cataract formation [204].

Patient selection Because of the possible serious complications of PPV, patient selection is of great importance. All patients are examined by slit-lamp biomicroscopy, indirect and direct ophthalmoscopy, and applanation tonometry. Ultrasonography is performed in cases with opaque media. The diagnosis of ERU must be confirmed and is based on the description in the section **Differential diagnosis and methods for definitive diagnosis**; there must be characteristic signs of acute or chronic uveitis and a documented history of recurrent episodes of acute uveitis. Horses with dense vitreal opacity may benefit most from vitrectomy, not only by decreasing recurrent episodes, but also from improving vision by removal of vitreal debris.

Horses ideally are operated on when in the quiescent stage of the disease. Because of the transpupillary visualization of the vitrectomy probe during the procedure, the optical media (i.e, cornea, anterior chamber, lens) should be as transparent as possible. The pupil should dilate maximally with no or few posterior synechiae. Pre-existing focal cataracts are likely to progress following PPV and should be taken into consideration when selecting patients. In patients with secondary glaucoma, phthisis bulbi, or pre-existing retinal detachment, PPV should not be recommended. Owners should be carefully informed of the surgery, as well as the possible intra- and post-operative complications.

Pre-operative and post-operative medication Topical 0.1% dexamethasone drops in combination with neomycin and polymyxin B are administered four times daily beginning 1 week prior to surgery. Systemic NSAIDs (i.e, flunixin meglumine) are administered beginning 3 days pre-operatively. The pupil is dilated with 1% atropine drops on the day of surgery. Post-operatively, topical dexamethasone/neomycin/polymyxin B eyedrops are continued three times daily for 2 weeks, and then tapered over another 4 weeks. Systemic NSAIDs are continued for 1 week.

Surgical technique A standard two-port PPV is performed in lateral recumbence under general inhalation anesthesia. The eye is prepared for intraocular surgery. After draping, an eyelid speculum is inserted. A lateral canthotomy may improve

* *Contribution written by Dr Bernhard Spiess*

exposure of the globe, but this is usually not necessary. A limbal stay-suture in the 12 o'clock position is placed for globe manipulation. A limbal-based conjunctival flap is prepared and the sclera exposed medially and laterally to the dorsal rectus muscle. Using a CO_2 laser, a first sclerotomy is performed 10 mm posterior to the limbus. A right-handed surgeon will place this first entry to the left of the rectus muscle. A double-ended lacrimal dilator may be used to enlarge the sclerotomy if necessary. The irrigation port is inserted and its footplate secured to the sclera with two sutures (4-0 polyglactin 910 (Figure 8.49)). With the vitrectomy unit in continuous irrigation mode and the fluid-containing bottle positioned 85 cm higher than the surgical site, the IOP will be around 40 mm Hg. Balanced salt solution with 40 mg of gentamicin added per 500 mL is used as irrigation fluid.

A second laser sclerotomy is performed, again 10 mm posterior to the limbus and to the right of the rectus muscle. The vitrectomy probe is carefully inserted and advanced in the direction of the center of the vitreous (see Figure 8.49). Again, the sclerotomy may be enlarged with a lacrimal dilator if necessary. Both sclerotomies should be tight enough to prevent leakage of irrigation fluid, which would make maintenance of IOP difficult. The vitrectomy probe should be held at an approximately 70-degree angle and passed toward the optic nerve, taking care to avoid touching the lens when inserting the probe. The probe tip should be held with the aspiration port facing the surgeon. The central and anterior parts of the vitreous can be removed by direct visualization through the dilated pupil. Indirect ophthalmoscopy using a 20-D lens is used to visualize posterior and peripheral parts of the vitreous.

Alternatively, a custom-made equine vitrectomy contact lens (Acrivet, Berlin, Germany) can be used to visualize the posterior segment through the operating microscope (Figure 8.50). Aspiration of vitreous can easily be observed, especially if there are inflammatory materials. Estimating the distance between the probe and its shadow cast onto the retina will help the surgeon to avoid touching the retina. Throughout the entire procedure, the IOP should be maintained at approximately 40 mm Hg. Slight wrinkling of the retina, seen with the aid of the ophthalmoscope, indicates that the IOP may be too low. Vitrectomy should be interrupted until a normal IOP is restored. The procedure is continued until all turbid vitreal material has been removed. Under continuous irrigation, the vitrectomy probe is removed and the sclerotomy closed with one or two single interrupted sutures using 4-0 polyglactin 910. Subsequently, the irrigation port is removed. Remaining peripheral vitreous will usually prevent fluid from escaping through this sclerotomy, which is closed with 4-0 polyglactin 910. The conjunctiva is closed with polyglactin 910 in a continuous pattern. A canthotomy is closed with a figure-of-eight suture using 4-0 nonabsorbable suture material. At the end of surgery, 20 mg of methylprednisolone may be injected subconjunctivally in the inferior bulbar conjunctiva.

Some differences in performing this procedure in the horse have been established. To avoid uveal hemorrhage, both sclerotomies are performed using a CO_2 laser in continuous mode at 50 W. Commercially available standard vitrectomy probes are too short for use in horses. A 55-mm oscillating vitrectomy with a guillotine-like chopping blade probe is used at 12 Hz, an aspiration vacuum of 400 mm Hg, and a flow rate of 15 mL/min. High oscillation frequency, moderate suction, and low flow are used to minimize vitreoretinal traction and decrease the incidence of iatrogenic retinal breaks.

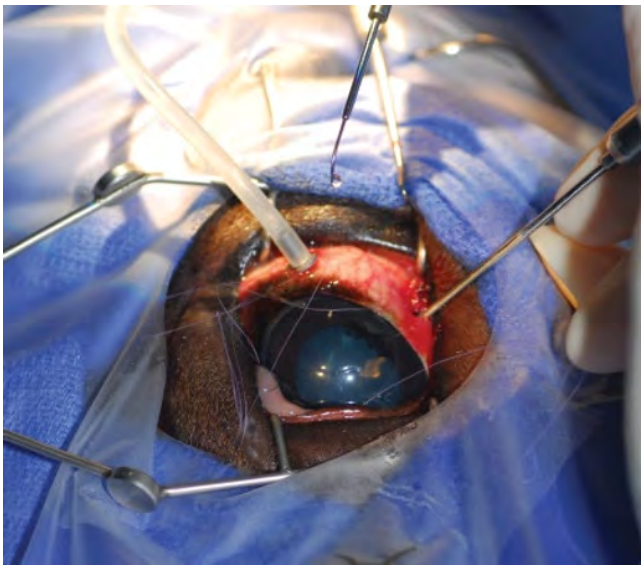


Figure 8.49 Surgeon's view during vitrectomy surgery. The infusion tip is fixed in the sclera at the 11-o'clock position; the cutter is introduced at the 1-o'clock position and observed through the pupil. (*Source*: Photograph courtesy of Hartmut Gerhards and Bettina Wollanke.)

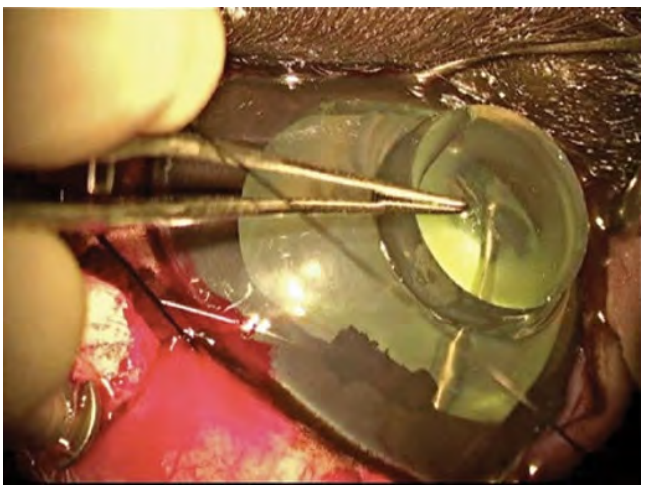


Figure 8.50 A custom-made equine vitrectomy contact lens can be used to visualize the posterior segment through the operating microscope and make vitrectomy more precise by improving visualization. The vitrectomy needle is visualized through the lens.

Complications Intraoperative complications include lens trauma, vitreal/retinal hemorrhage, and retinal detachment. Maintaining IOP at around 40 mm Hg and using a CO2 laser instead of surgical blades for the sclerotomies can avoid hemorrhage. Touching the retina should also be avoided as it results in immediate hemorrhage and subsequent detachment [203, 204]. Early post-operative complications (less than 3 months) include cataract formation and retinal detachment. Late complications occurring after 3 months include cataract formation and recurrence of active uveitis [202, 204].

Prognosis Seventy-three percent of horses that underwent PPV showed no further recurrence of uveitis [206]. Twenty-two continued to suffer from recurrent episodes of uveitis. The remaining horses were reported to have experienced only one more episode of uveitis, which was easily controlled with topical anti-inflammatory therapy [206].

Vitreous samples of every horse were submitted, and 78% were positive for *Leptospira* spp. MAT serology. Of the *Leptospira*-positive horses, 81% showed no further recurrences after vitrectomy, while of the *Leptospira*-negative patients, 83% had further recurrences [206]. This suggests that PPV represents a successful surgical therapy for horses suffering from *Leptospira*-related ERU, whereas patients testing negative for *Leptospira* spp. are poorer candidates for this surgery [206]. They may, however, be more suitable candidates for the implantation of cyclosporin-releasing devices [90, 91].

Clinical experience would suggest that aqueous humor and/or vitreous samples of horses suffering from ERU should be tested for *Leptospira* spp, and that the decision to perform PPV should be based on these results. In another study of 38 cases, five eyes showed recurrence of uveitis between 10 days and 3 years post-operatively [204]. Thirty-three eyes showed no recurrence during a follow-up period of up to 5 years. Vision remained stable in 28 eyes and improved in one eye. The remaining eyes showed marked vision loss as a result of cataracts, phthisis bulbi, or unknown cause. Of the five eyes with ERU, two demonstrated marked loss of vision, while three maintained pre-operative vision [204].

In an earlier study of 43 eyes post PPV, 42 remained free of ERU during a follow-up period of 67 months [207]. Seventy percent of these eyes retained some vision. The most common complication was cataract formation in 19/43 eyes, followed by phthisis bulbi in 6 eyes, and retinal detachment in 4 eyes [207].

In selected patients with consenting owners, PPV offers a promising alternative to conventional therapy. With few exceptions, eyes show no recurrence of uveitis after PPV. However, a significant number of post-operative complications cause visual impairment or blindness. The most common long-term post-operative complication appears to be cataract formation (Figure 8.51). It is unclear whether pre-existing lenticular opacities progress despite PPV or if the progression is caused by the procedure. Touching the posterior lens capsule during PPV invariably leads to focal cataracts, which very often progress. Retinal and vitreal hemorrhage is the most common intraoperative complication. Maintaining a high-normal IOP, careful manipulation of the vitrectomy probe, and avoidance of touching the retina usually prevent such complications. Choroidal hemorrhage can be avoided with the use of a CO2 laser instead of a surgical blade. Despite these complications, PPV appears to be a promising method for long-term control of leptospiral-induced ERU.

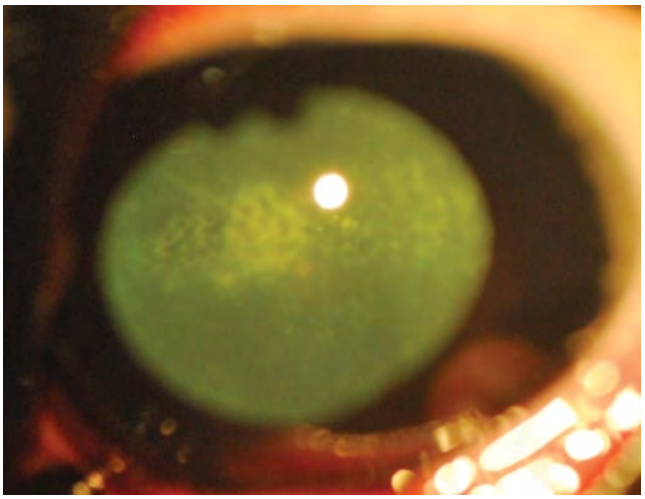


Figure 8.51 Cataract formation after vitrectomy for ERU. (*Source*: Photograph courtesy of Hartmut Gerhards and Bettina Wollanke.)

Ocular neoplasia

Melanoma

Although melanoma is relatively rare in horses, the literature contains numerous case reports of equine intraocular melanoma [208–215]. A review of these cases reveals some interesting trends. In older gray horses, cutaneous melanoma is a common finding. Most reported that intraocular melanoma cases also occurred in gray or partially gray horses, but most of the horses were young adults, between 5 and 10 years of age. Only one of these horses also had skin lesions, which were described as "inguinal nodules." These nodules were not removed and did not change during the 6-month period during which the horse was followed up, and therefore cannot be assumed to be melanomas [214]. Although none of the reported cases documented metastasis, and the neoplasms were generally not judged to be malignant on histopathologic examination, rapid growth within the eye was common. One patient may have had a primary intraocular uveal melanoma extend through the cornea, but the originating tissue of that neoplasm could not be determined [215]. The most common site of origin was the iris, but melanomas arising from the ciliary body were also reported.

The initial clinical appearance of anterior uveal melanomas differs according to whether the ciliary body or the iris is the tissue of origin, how rapidly the neoplasm is growing, and the length of time before a medical evaluation is sought. When a horse with melanoma is presented early in the course of the disease, common clinical signs include focal corneal edema with a dark mass filling the anterior chamber, which is often in contact with the posterior surface of the cornea (Figures 8.52 and 8.53).

Depending on the location and extent of the mass, dyscoria may be present. It should be noted that melanomas in horses with lightly pigmented irises may appear pink and fleshy (Figure 8.54) [213]. The rest of the cornea in these patients is usually clear, and there is no aqueous flare. Evidence of pain is usually absent. As the neoplasm gets larger, common clinical signs include blindness, blepharospasm, epiphora, buphthalmos, diffuse corneal edema, aqueous flare, and anterior chamber masses that often obliterate any normal architecture and prevent visualization of deeper structures. When structures deep to the iris can be seen, the lens is usually cataractous. If the tissue of origin is the ciliary body, a dark mass may be seen on the posterior surface of the lens, extending into the vitreous cavity [211].

Differential diagnoses for a mass in the anterior chamber include uveal cyst, iris hypoplasia, or extension of a mass from the posterior segment (Figure 8.55) [24, 38, 45]. This determination is usually not difficult to make. Cysts of the ciliary body, iris, and corpora nigra are all smooth and oval to spherical. Additionally, cysts can occasionally be transilluminated. This clinical presentation would be contrasted to that of melanoma, which most frequently appears as an irregularly shaped mass arising from the anterior aspect of the iris and filling most if not all of the anterior chamber. On those occasions when there is doubt on the basis of clinical presentation, ocular ultrasonography

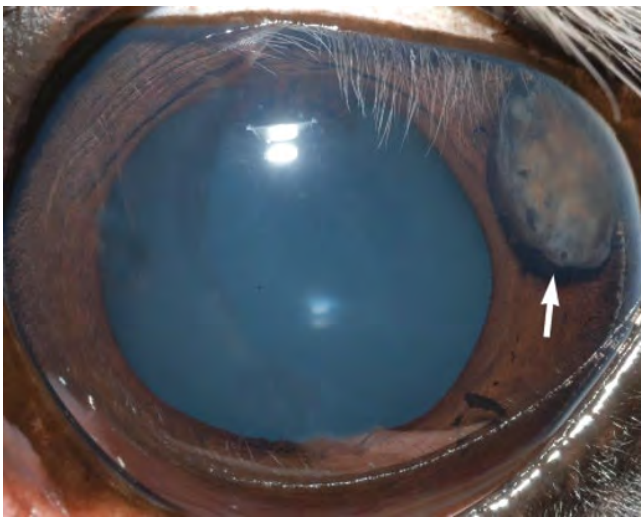


Figure 8.52 Intraocular melanoma (**arrow**) arising from the anterior surface of the iris and in contact with the posterior surface of the cornea.

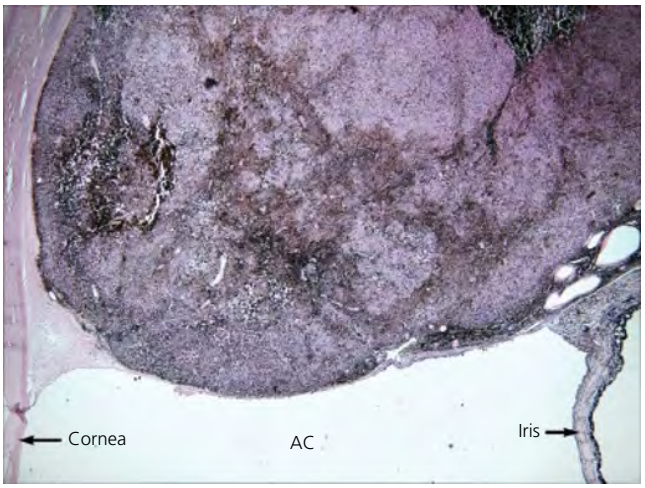


Figure 8.53 Photomicrograph of intraocular melanoma arising from the anterior surface of the iris, filling the anterior chamber (AC), and in contact with the posterior surface of the cornea (×2).



(A) (B)

Figure 8.54 **(A)** Iris melanoma in a gray pony arising from the temoral iris and in contact with the posterior surface of the cornea. **(B)** B-mode corneal optical coherence tomography demonstrating invasion of the mass (M) through Descemet's membrane (DM) and into the corneal stroma (S). CE, Corneal epithelium.



(A) (B)

Figure 8.55 (A) Fleshy mass apparently originating from the iris. (B) Gross histopathologic section demonstrating the anterior chamber mass to be an extension of a neoplasm arising from the posterior segment. (*Source*: Photograph courtesy of Dr Derek C. Knottenbelt.)

can be used to differentiate cystic structures from solid masses [208]. As discussed previously, horses with iris hypoplasia usually either have completely blue irides or exhibit heterochromic irides. Although the bulging forward of dark tissue characteristic of iris hypoplasia can mimic a melanoma, a number of characteristics allow for differentiation between the two conditions. These include ability to transilluminate, deflation of the bulging area with mydriasis, and absence of significant enlargement over time [21, 22]. In the case of the tumor extension from the posterior segment, careful examination will reveal a large mass present in the vitreous cavity, making primary intraocular melanoma less likely [216].

The pathogenesis of melanoma has been debated for years in both human and veterinary medicine [217–219]. Although differences exist in regard to intraocular melanoma among species, many believe that melanomas in general arise from pre-existing nevi [208, 211, 220]. This theory is based in part on the fact that histopathologic examination of anterior uveal melanomas commonly reveals two cell types: (1) plump, spherical cells with abundant melanin granules, and (2) smaller, pleomorphic, spindle-shaped cells, which may have a relatively higher nucleus-to-cytoplasm ratio (Figure 8.56) [208, 210, 212]. Mitotic figures are rare. One theory is that the plump, spherical cells represent a melanocytoma or nevus, which is the precursor of the melanoma portion of the mass represented by the spindle-shaped cells [208, 211, 220].

Among equine patients, sector iridectomy has been successful in the treatment of intraocular melanoma (Figure 8.57) [212, 213]. In one report, a diode laser was used to treat 23 dogs with isolated masses believed to represent iridal melanoma [221]. The results of that study were encouraging in that the dogs were able to maintain comfortable, visual eyes as long as 4 years after treatment. Surgical Nd:YAG laser treatment of uveal melanomas in equine eyes has caused shrinkage of the masses; however, corneal edema and secondary uveitis are common adverse effects of laser therapy (Figure 8.58). Oral cimetidine (dose 2.5 mg/kg body

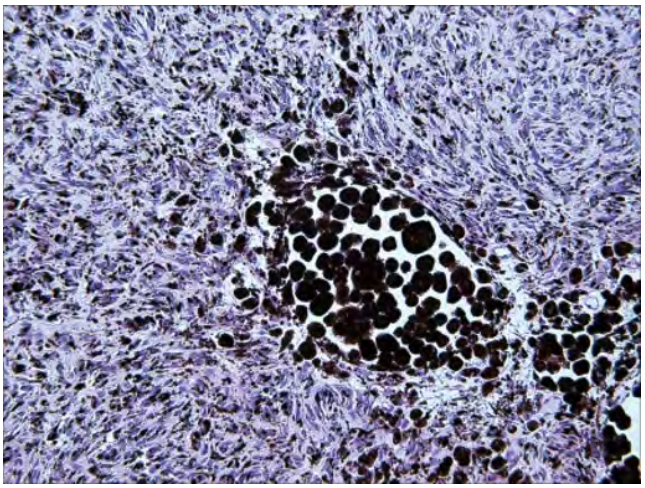


Figure 8.56 Photomicrograph of intraocular melanoma. Note the central area of plump, spherical, highly melanotic cells surrounded by pleomorphic, spindle-shaped cells (×10).



Figure 8.57 Four months after sector iridectomy on the patient in Figure 8.54.



Figure 8.58 Surgical Nd:YAG laser treatment of a uveal melanoma in an equine eye.

weight, administered orally (PO) every 8 hours) has been used to shrink nonocular melanomas in horses, but no studies have been done to determine the effect of cimetidine on uveal masses [222]. Additionally, there are several clinical trials ongoing evaluating an equine-specific (http://research.vetmed.ufl.edu/clinical-trials/large-animal/vaccine-study-for-gray-horses-with-melanoma/) or canine-specific melanoma vaccine for the management of cutaneous melanoma. To date, there have been no results reported on the efficacy of these vaccines on ocular melanomas.

Generally, when masses grow large and result in ocular discomfort, intraocular melanoma in horses has been treated by enucleation or exenteration. Success with these procedures has been high, and metastasis has not been reported [208, 211, 214, 215].

Lymphoma

Lymphoma is the most common systemic neoplastic disease with an ocular manifestation in the horse [223, 224]. Ocular manifestation of lymphoma has been documented in many species, but the specific ophthalmic structure most commonly affected varies among species. In cattle, exophthalmos caused by orbital masses is the most common ocular manifestation of lymphoma [225], whereas in dogs and cats with systemic lymphoma, anterior uveal involvement is the most common ocular sign [226, 227]. In one study of 79 horses with confirmed systemic lymphoma, 21 had ocular lesions. In these horses, eyelid swelling and inflammation were the most common ocular signs (11/21), with anterior uveal involvement being the next most common sign (4/21) [228].

The signs associated with anterior uveal manifestation of systemic lymphoma are nonspecific and include blepharospasm, episcleral injection, corneal edema and vascularization, aqueous flare, hypopyon, hyphema, iridal congestion, and swelling. Frequently these nonspecific signs are accompanied by a history of chronicity and poor response to anti-inflammatory medication. In addition, the ophthalmic signs are usually accompanied by nonspecific signs of systemic disease such as fever, respiratory disorders, weight loss, peripheral lymphadenopathy, and anemia [229, 230].

Intraocular lymphoma cannot usually be differentiated from other potential causes of anterior uveitis on the basis of ocular signs alone (see Box 8.2). The diagnosis of systemic lymphoma should be considered in any horse with anterior uveitis, especially when it is accompanied by systemic signs of illness such as fever, weight loss, lethargy, and swollen lymph nodes. The diagnosis of lymphoma can be confirmed by identification of neoplastic lymphocytes from samples of solid tissues such as the spleen, lymph nodes, or skin nodules or by centesis of affected body cavities (thoracic or abdominal). In spite of this, diagnosis can be challenging, and confirmation occurs in less than 60% of cases [223].

The pathogenesis of systemic equine lymphoma remains obscure. There are currently no known risk factors. Most affected horses are young adults between 4 and 10 years of age. No breed or sex predisposition has been demonstrated [223]. The systemic treatment of lymphoma is outlined in equine medicine texts [223]. In general, success rates have been low for systemic lymphoma. The ocular portion of the treatment regimen would be the same as that previously described in the section **Treatment** for anterior uveitis.

Other metastatic neoplasia

Multiple myeloma has been described to metastasize into the eye and induce uveitis, intraocular and scleral hemorrhage, retinal detachment, and blindness in combination with signs of systemic illness [231]. There is a case report of multiple-site metastasis of a thyroid carcinoma to the uveal tract of a horse with persistent uveitis [232]. Recently there was a description of a 10-year-old German Warmblood that presented with a depigmented iris mass that also had raised retinal lesions, fever, and enlarged submandibular lymph nodes. On workup, the horse was found to have splenomegaly and severe pulmonary nodules and consolidated lung associated with primary pulmonary adenocarcinoma. The iris and retinal lesions were metastatic adenocarcinoma [233].

Future research

Future understanding of ERU in all species will revolve around the investigation of several key questions [234].

- What genetic makeup predisposes individuals to develop disease?
- If the disease is autoimmune, which autoantigens participate in the initiation and perpetuation of inflammation?
- What immune mechanisms initiate the immune response and mediate tissue destruction?

In horses, other questions can be added:

- Is ERU one disease or a symptom/syndrome with many causes?
- Is the insidious form of ERU a different disease with different etiology and pathogenesis than classic ERU?

Further studies are needed to determine the genetic predisposition for ERU. It is not likely to be a monogenetic disease, but research is needed to identify susceptibility factors for ERU.

New immunomodulatory therapies, such as autologous MSCs, may offer hope in the medical management. Perfecting new and practical sustained-release drug delivery devices or injections are also needed.

Studies need to be undertaken to determine what effect a new equine leptospiral vaccine has on the incidence of ERU, in addition to the effect on the diagnosis of leptospiral uveitis.

Blindness or reduced vision is a common outcome for people and horses, and uveitis is a cause of large economic and humanitarian losses worldwide. Continued research on ERU should provide deeper understanding of the clinicopathologic features of uveitis in all species, and new therapies under development for horses may lead to improved therapy for people, with subsequent reduction in the incidence of blindness in both species worldwide [234].

Acknowledgments

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CHAPTER 9

Diseases and surgery of the lens

Richard J. McMullen Jr and Brian C. Gilger

Introduction

Diseases of the lens in horses are not common, but when present and significant, render the animal devalued, dangerous for some uses, and predisposed to self-injury. This may possibly lead to euthanasia because of the horse's inability to work or produce. The most common lens disease in all species is cataract—opacity of the lens and/or its capsule. Cataracts can occur congenitally or be acquired postnatally. It is estimated that cataracts are present in 5–7% of all horses with otherwise normal eyes [1]. These range from incipient opacities to larger visually disturbing cataracts. Other less commonly recognized lens diseases include abnormal shape and abnormal position of the lens. Diagnosis and treatment of these diseases of the lens are described in detail in this chapter.

Clinical anatomy and physiology

Aside from the cornea, the crystalline lens is the most important refractive structure of the eye. Its role is to focus incoming light onto the area centralis. The lens is unique as it is transparent and devoid of innervation and vascular structures, yet it grows throughout embryological development and continues until death of the horse. Lens embryology, anatomy, physiology, and function differ little between terrestrial species [2]. Lens epithelial cells (LECs) line the anterior aspect of the lens in a monolayer and perform the majority of the metabolic functions for this structure (Figure 9.1). They transport solutes between the lens and the aqueous humor, are important for enzymatic activity, secrete capsular material, and their metabolism maintains lens transparency [3]. Any imbalance in enzymatic activity or lens metabolism due to DNA or protein damage to the anterior LEC can lead to cataractogenesis [3].

The remainder of the lens is made up of terminally differentiating and differentiated lens fiber cells. The process of terminal differentiation begins in the equatorial (or lens bow) (Figure 9.1) region and entails elongation, loss of cellular structures, post-translational modification of proteins, and gradual migration into the cortex. During this migration, lens fiber cells lose their nuclei through an apoptosis-like mechanism [4]. Losing cellular structures ensures the clarity of the lens by removing potentially light-scattering elements from the incoming light pathway. The region immediately inside the area of organelle loss is called the organelle-free zone (OFZ)[5] and begins in the nucleus.

Clinically, the lens has three major regions of importance: the nucleus, the cortex, and the lens capsule. Beginning from the center and moving towards the outside, the nucleus is the oldest section of the lens. There are three subdivisions of the nucleus based on the age of the animal (Figure 9.1). The central, innermost nucleus is the embryonic nucleus that is formed from primary lens fibers at the earliest time of lens development. The region that then surrounds the embryonic nucleus is the fetal nucleus. These are the first secondary lens fibers and they form until the animal is born. Therefore, at birth, the lens is only made up of the embryonic and fetal nuclei surrounded by the lens capsule. The lens capsule is continuously produced, throughout development and post-natal life, by the anterior lens epithelial cells. Post-natally, the secondary lens fibers create the cortical region and begin to form the future adult nucleus. As a young adult (approximately 5–7 years of age), the lens will have an obvious area between the lens capsule and the outermost nucleus that is the cortical region. The cortical region is comprised of the newest cells that are continually being moved inward; therefore any random elongating cortical fiber cell is surrounded on the inner aspect by an older fiber cell, on each side by similar-aged fiber cells, and at its outer aspect by a newer fiber cell. At approximately 15–20 years of age, the entire nucleus is more obvious due to the layers of cells that have been compressed over time that begin to refract light. This is termed nuclear sclerosis and is a typical aging change in all eyes (Figure 9.2).

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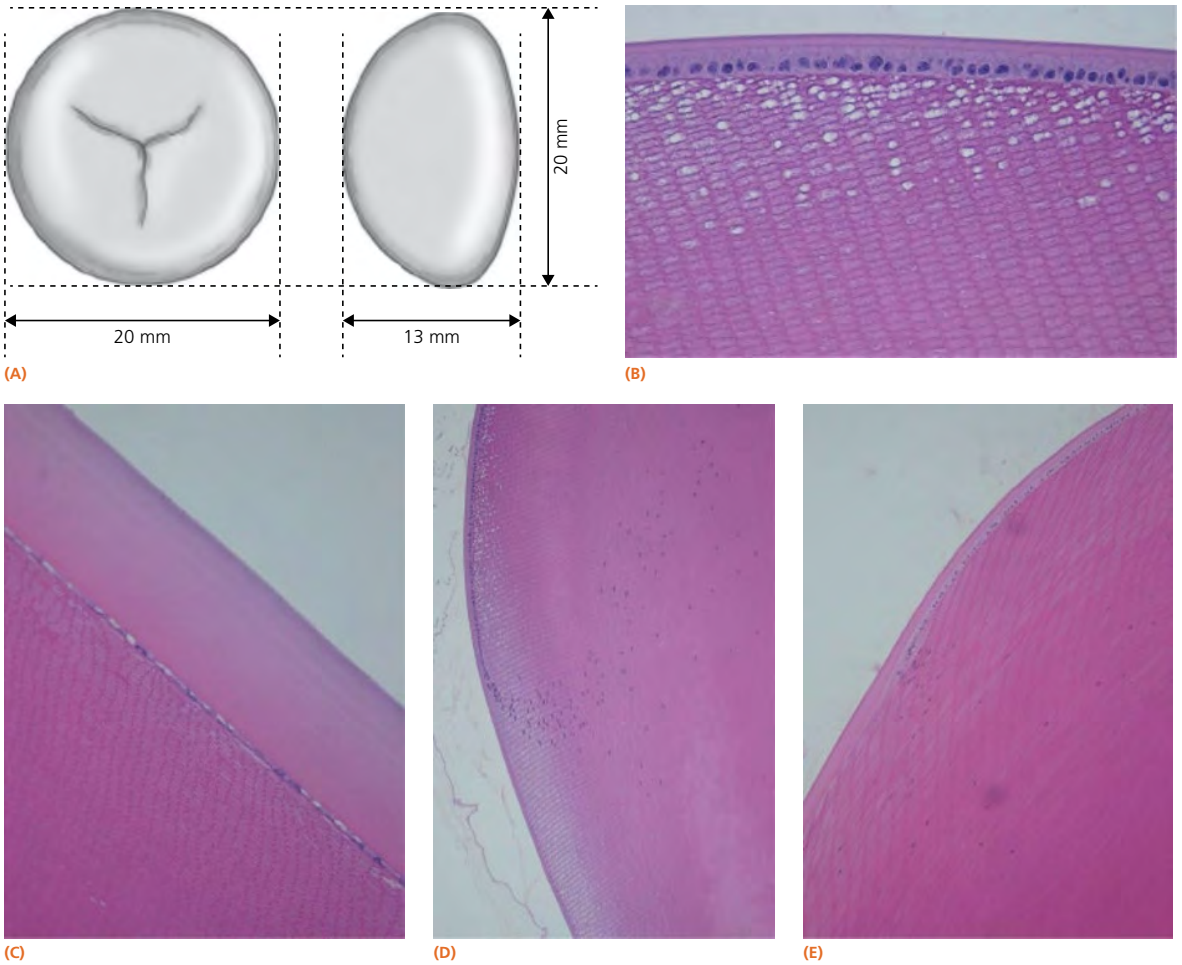


Figure 9.1 (A) Schematic cross-section of the adult equine lens. (B) Photomicrograph of the anterior lens capsule from a 2-day-old Thoroughbred (TB) foal. Note the prominent lens epithelial cells and thin anterior capsule compared with Figure 9.1C (H&E, ×400). (C) Photomicrograph of the anterior lens capsule from a 10-year-old Quarter horse (QH) gelding (H&E, ×400). (D) Photomicrograph of the lens bow in the foal from Figure 9.1B (H&E, ×100). (E) Photomicrograph of the lens bow from the QH gelding in Figure 9.1C (H&E, ×100).

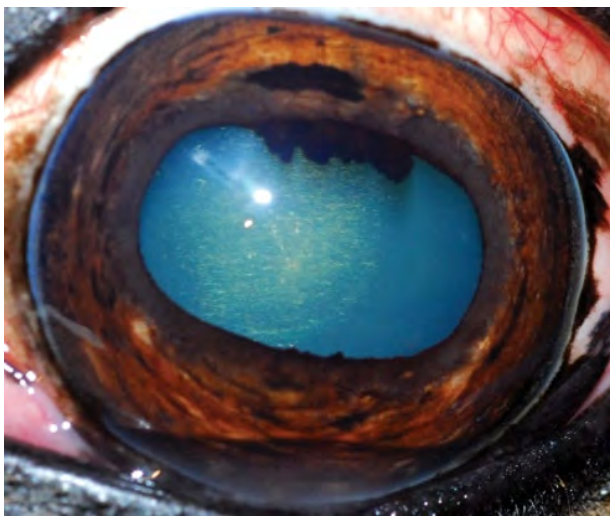


Figure 9.2 Nuclear sclerosis in a middle-aged Quarter horse gelding. Note the lens changes appear as yellow "scratches" resembling steel wool.

Economic impact of lens disease on the equine industry

The impact of lens disease on the equine industry has not been critically evaluated. However, if the estimate of 8% incidence of equine recurrent uveitis (ERU) in all horses holds true, then it is safe to estimate that all of those horses have some cataract formation. The cataract may not be clinically relevant, as some only have small cataracts, but any opacity of the lens could possibly diminish the horse's capacity to work, resulting in loss of income for the owner [6].

Congenital diseases

Ocular abnormalities of the neonatal foal may be congenital, inherited, or acquired. Congenital defects may be due to genetic causes/inheritance, toxins, nutritional imbalance, ionizing

radiation, or other idiopathic causes [7, 8]. Cataracts are the most common congenital abnormality present in foals, with a 33.6–35.3% incidence in cases of congenital ocular defects [8–10]. Other lens anomalies include spherophakia, lenticonus, and coloboma.

Congenital cataracts

Congenital cataracts are the largest group of developmental lens opacities in horses. Inherited congenital cataracts have been documented in Thoroughbreds, Quarter horses, and Morgans [10–15]. Rocky Mountain horses can also develop congenital nuclear cataracts but have concurrent multiple anterior segment anomalies [16]. Depending on when the cataract originated, it can sometimes be possible to estimate the time it originated and also determine whether it will progress. Nuclear cataracts involving the embryonic or fetal nuclei do not progress and usually become smaller, relative to the rest of the lens, as the animal ages. Perinuclear cataracts, by nature of when the cortex begins to develop relative to the date of birth, occur just after the animal is born. The nucleus and the inner nuclei are usually clear. This type of cataract, or nuclear cataracts, are inherited in the Morgan horse [11]. Cataracts are often seen in equine eyes with other anomalies such as microphakia and anterior segment dysgenesis (Figure 9.3) in Rocky Mountain Spotted horses, Comtois horses, Icelandic horses, and ponies with multiple congenital ocular anomalies (MCOA) [17–24]. However, in a survey of 53 Miniature horses, an epinuclear cataract was identified in only one horse with MCOA [18]. Congenital cataracts can occur with persistent pupillary membranes and aniridia [25, 26].

Clinical and pedigree evaluation of a herd of 28 Exmoor ponies in Canada favored a sex-linked mode of inheritance for cataracts [23].

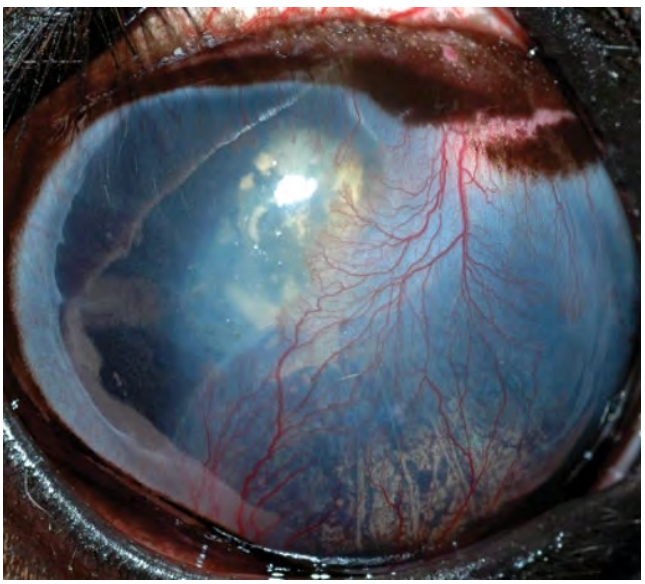


Figure 9.3 Axial view of anterior segment dysgenesis in a young Thoroughbred yearling.

Primary aphakia, microphakia, and coloboma

Primary aphakia and microphakia (Figure 9.4) are extremely rare and occur with other anomalies in the eye, including coloboma (Figure 9.5), due to inadequate insertion of zonules at the lens equator [27, 28]. In cases of presumed aphakia or microphakia, without other ocular anomalies, it is possible that the lens developed a cataract *in utero* and it was resorbed prior to birth or soon after. Lens colobomas may go undetected when examination is carried out without induction of pharmacological mydriasis, or they may be misinterpreted as a lens subluxation (Figure 9.6). A distinctive "notch" or "step" along the lens perimeter, which is devoid of lens zonules, is characteristic for a lens coloboma (see Figure 9.5).

Ectopia lentis

Ectopia lentis, also rare, occurs when the lens vesicle fails to enter the optic cup and the lens attempts to form in the anterior chamber. In one case, the lens was also microphakic and spherophakic [28]. Congenitally displaced lenses are often abnormal in shape (spherophakia) and smaller than normal. The early contact between the optic vesicle and the surface ectoderm, and its subsequent appropriate changes, results in a normally positioned, a normally shaped, and a transparent lens. If anything interferes with any of these steps, the lens will be abnormal in position, shape, and opacity. The most severe anomaly occurs when the initial contact does not separate appropriately, resulting in anterior segment dysgenesis, anterior lenticonus, and anterior capsular cataracts [24, 29]. Anterior segment dysgenesis often occurs with microphakia [27, 30–32].

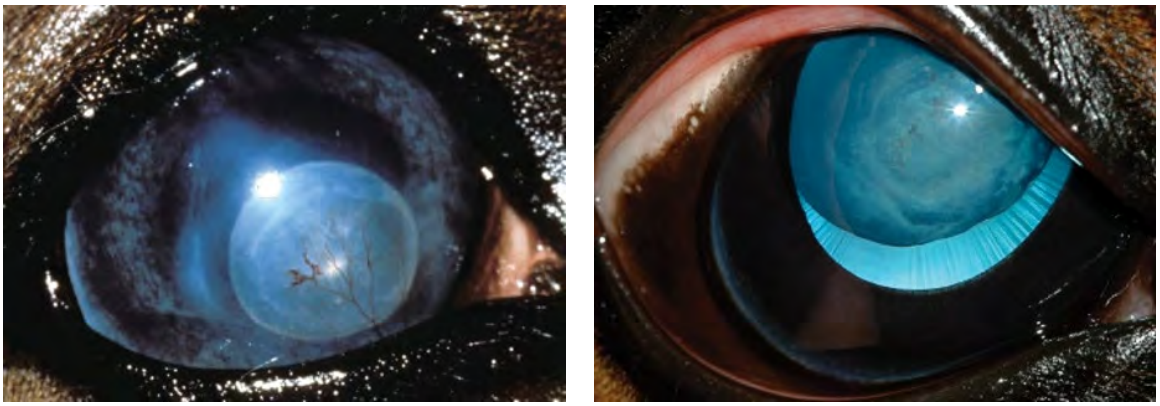
Lentiglobus and lenticonus

Lentiglobus is also a malformation of the lens and occurs when the anterior or posterior aspect of the lens is prominent and spheroid in shape. This is in contrast to lenticonus, which is a conical projection of the anterior or posterior aspect of the lens. Both conditions are rare.

Congenital anomalies that may be associated with cataracts

Examples of congenital anomalies that may be associated with cataracts include persistent pupillary membranes, persistent hyaloid artery, persistent hyperplastic primary vitreous/tunica vasculosa lentis (PHPV/PHTVL) (Figure 9.7), posterior lenticonus, microphakia, microphthalmos and lens coloboma. The hyaloid artery system is typically resorbed within the first few weeks post-natally. However, complete regression of the hyaloid system, including its remnants, occurs by 6–9 months of age in horses [33].

Persistent pupillary membranes (PPMs) in horses are often seen in clinically normal horses. One study including 169 neonatal Thoroughbred foals found PPMs in 28% of left eyes and 25% of right eyes, and 23% of the foals had bilateral involvement.34 However, PPMs that arise from the iris collarette and attach to the anterior lens capsule are rare [26]. The same study



(A) (B)



(C)

Figure 9.4 (A) Anterior lens luxation, mild corneal edema and keratitis, and microphakia in a foal. (*Source*: Photograph courtesy of Dr David Wilkie.) (B) Lens resorption (possible microphakia) in a 4-day-old Thoroughbred foal. (C) Left eye of the foal in **(B)**, with further lens resorption and cataract density. Note the lack of zonular attachment. (*Source*: Photographs B and C courtesy of Dr Riccardo Stoppini.)

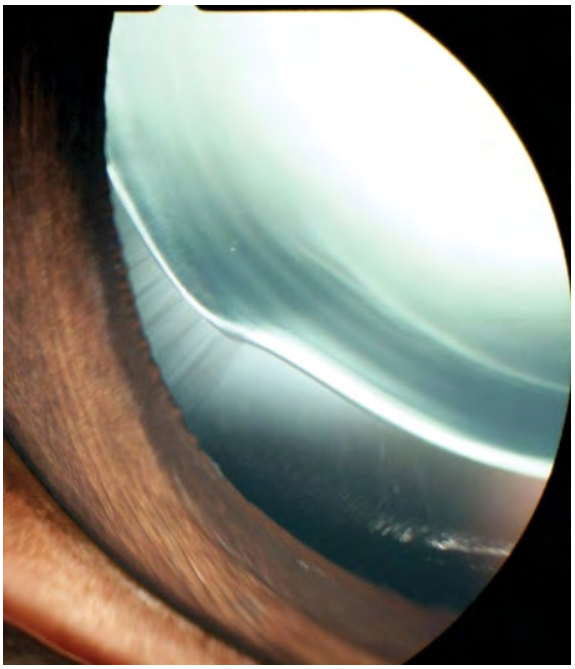
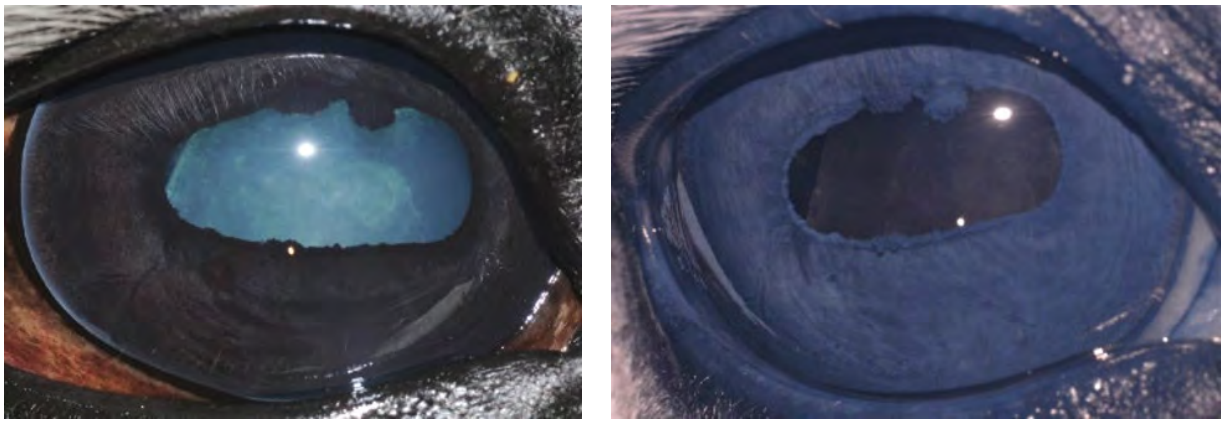


Figure 9.5 Ventral lens coloboma in a young Warmblood stallion. Note the notch along the ventral lens equator just beyond the last visible lens zonules.

of neonatal foals found the hyaloid artery or its remnants present in 83% of left eyes and 87.5% of right eyes, and 80% were bilateral [34]. One horse in this survey had bilateral capsular cataracts related to the hyaloid remnant [34]. In a survey of Thoroughbred racehorses in Australia, one horse, from a total of 204, was found to have a hyaloid remnant [35]. In a recent study in which 102 neonatal foals were evaluated, 100% of the foals showed various degrees of remnants of the hyaloid system, whereas only 1/102 foals was diagnosed with a unilateral congenital nuclear cataract [36]. PHPV/PHTVL (see Figure 9.7) has not been described in the equine literature. Mittendorf's dot, the anterior attachment of the hyaloid artery to the posterior lens pole, has been documented and can occur in a triradiate configuration [26]. Bergmeister's papillae, a remnant of the hyaloid artery seen protruding from the optic nerve head, is rare in horses.

Acquired diseases

Acquired diseases of the lens in mature horses include subluxation, luxation, puncture or laceration, expansion, rupture, and opacity of the lens or lens capsule (cataract). Although several of the lesions discussed in this section may also be encountered in



(A) (B)

Figure 9.6 (A) Through a relatively miotic pupil, only the bright, hyper-reflective edge of the temporal lens equator can be visualized. Without considering the gradual curvature of the peripheral lens, this lens coloboma may be misinterpreted as lens subluxation. Note shadows on the ventrotemporal iris caused by Haab's striae extending axially from the limbus at approximately 7 and 8 o'clock positions. (B) Transition between the temporal peripheral lens and edge of the pupil is more readily visible in this infrared image due to the jet-black appearance of the aphakic cresent. Additionally, multiple Haab's striae are more easily recognized against the blue-gray background of the iris.

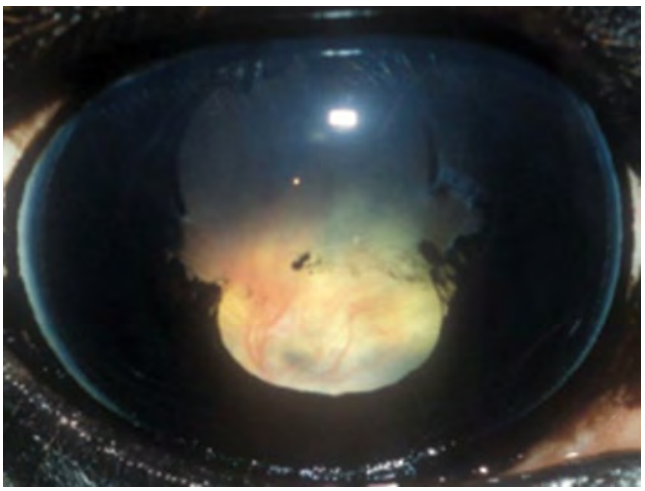
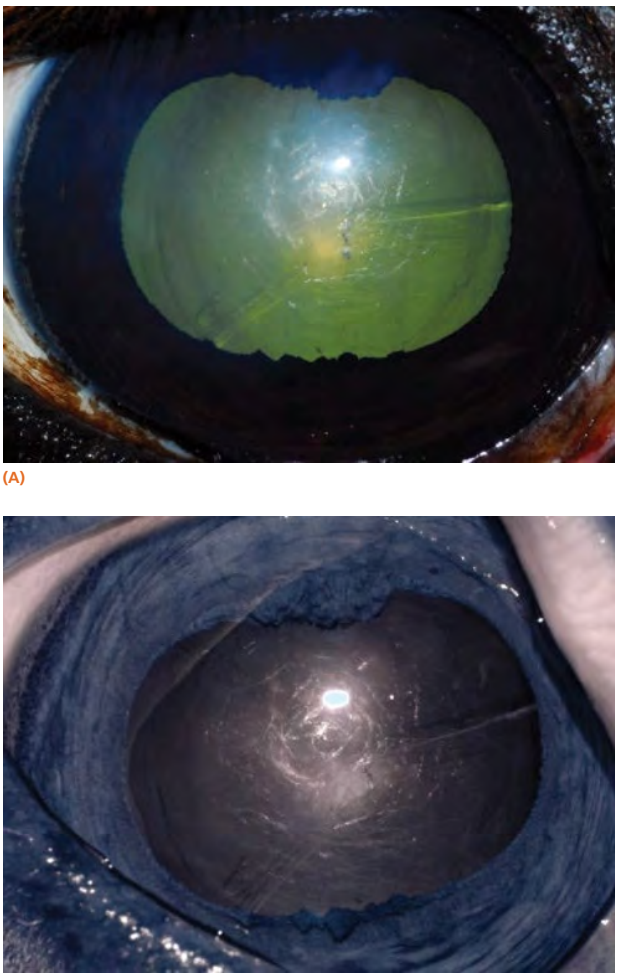


Figure 9.7 PHPV/PHTVL in a young Warmblood mare. Note the narrow, vertically oval pupil with multifocal posterior synechiae and anterior lens capsule pigment deposition.

foals, they are most commonly identified during ophthalmic examination of the adult horse. A recent description of lens opacities with representative photographs proposes an extensive classification system based on etiology [1]. Most cataracts in horses develop secondary to intraocular disease such as uveitis (ERU and other forms of anterior and/or posterior uveitis), retinal detachment, neoplasia, coup-contrecoup or whiplash injury to the globe, advanced age, metabolic diseases or toxins, intraocular surgery, and radiation therapy [1, 37–41]. Senile cataracts (Figure 9.8) can be frequently encountered in horses greater than 15 years of age, and may interfere with vision [1, 42]. Many geriatric horse lenses show increased nuclear delineation, or nuclear sclerosis (see Figure 9.2), which may be associated with the development of senile cataracts. Recently, in a survey of 200 geriatric horses (defined as 15 years of age or older),



(A) (B)

Figure 9.8 (A) Senile cataract in a geriatric Quarter horse gelding. A circular zone of discontinuity can be seen at the junction between the lens nucleus and lens cortex. (B) Infrared digital image provides an enhanced view of the cataract.

cataracts were identified in 58.5% of the horses evaluated [31]. Occasionally, increased brunescence (Figure 9.9) of the lens nucleus can be seen in such instances [1].

Cataracts

As in other animal species and humans, cataract development is a common sequelae of uveitis (Figure 9.10) and trauma (Figure 9.11). The rate of cataract progression is dependent upon the underlying cause. ERU and other forms of uveitis are associated with an accelerated rate of cataract progression, and it is still generally accepted that inflammation of the anterior uvea (e.g., ERU) is the most common cause of acquired cataracts in horses [1, 14, 26, 43–63].

Clinical appearance

The classification of adult cataracts can follow several different schemas. Briefly, cataracts can be described by their age of onset (congenital, juvenile, or senile/geriatric), cause (e.g., hereditary,

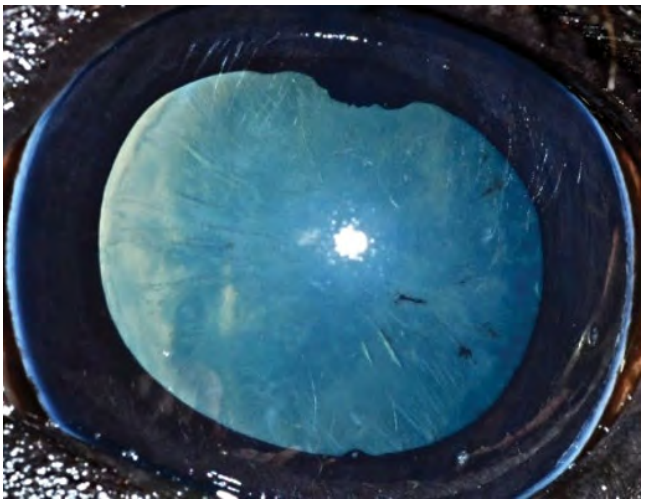
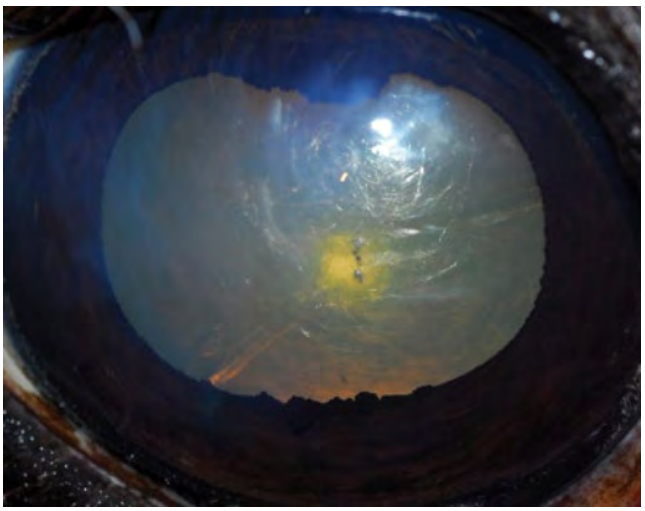


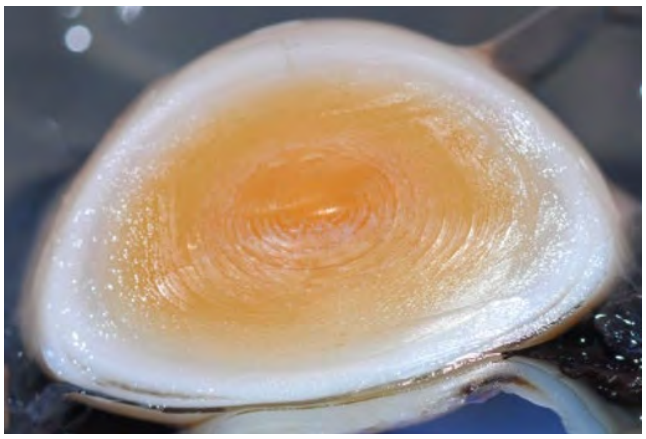
Figure 9.10 Diffuse, immature, anterior and posterior cortical cataract associated with ERU in a 7-year-old Rocky Mountain horse mare.



(A)

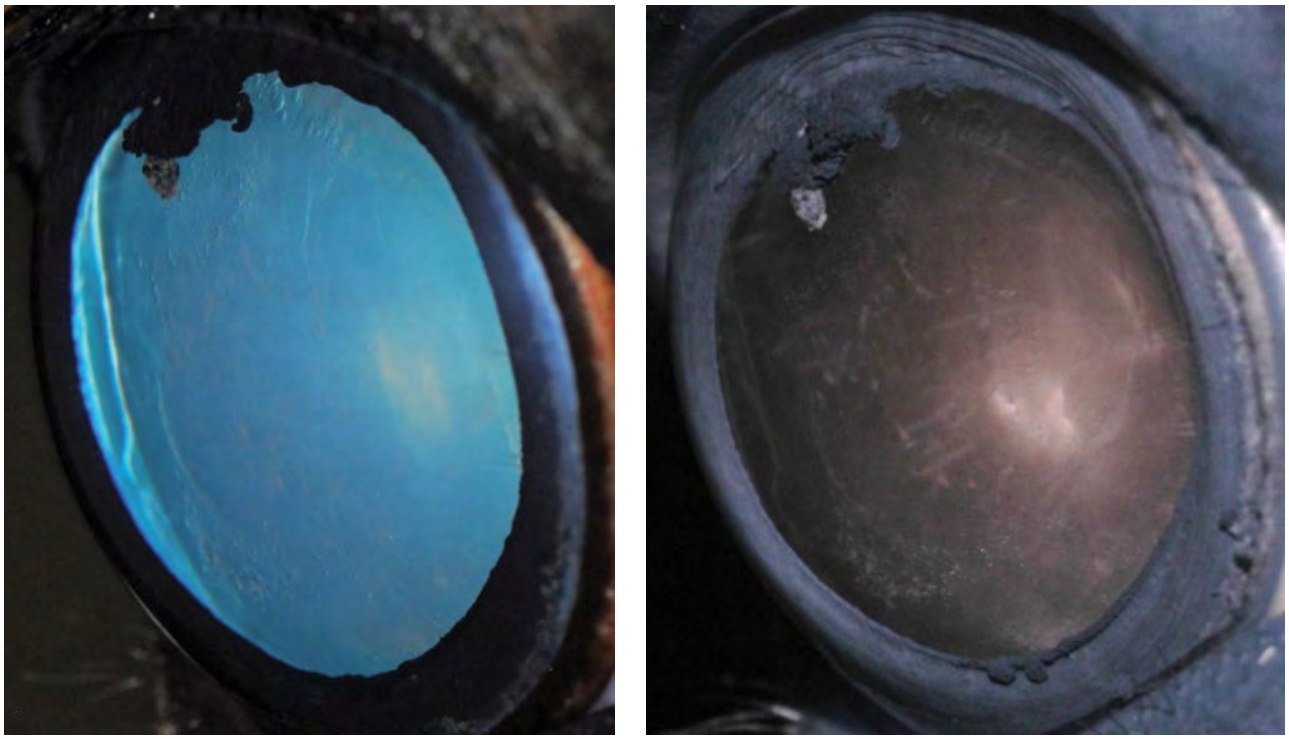


(B)



(C)

Figure 9.9 (A) Brunescence (increased yellow discolorization) of the lens occurs as a normal part of aging. (B) Central, nuclear brunescence associated with a senile cataract in an aging Quarter horse. (C) Gross pathologic section of a lens from a 22-year-old Quarter horse gelding (not the same eye as in B). Note how the brunescence is most intense within the nucleus.



(A) (B)

Figure 9.11 (A) Diffuse, immature, anterior and posterior cortical and nuclear cataract that developed following blunt force trauma in an 11-year-old Quarter horse gelding. (B) View of the cataract is enhanced in infrared.

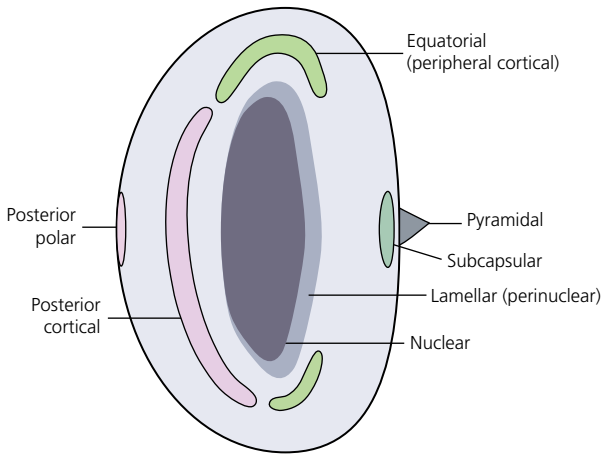


Figure 9.12 Sketch of the lens. Classification scheme for cataracts according to their location within the lens.

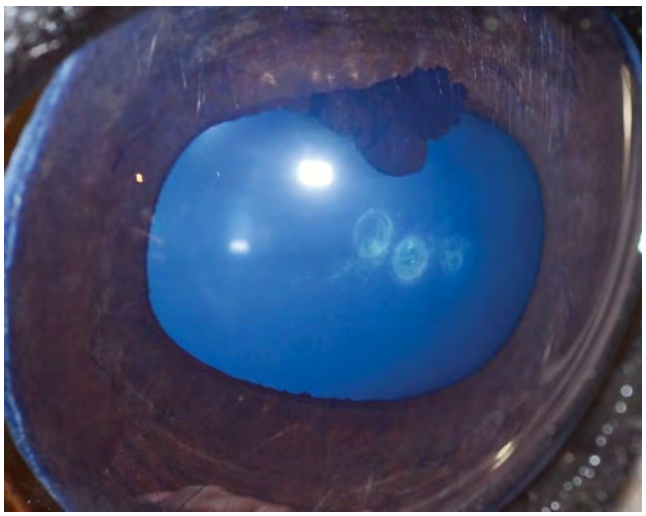


Figure 9.13 Focal, incipient, anterior polar cataract.

secondary to uveitis, trauma, toxin, nutritional, or metabolic disease), or location within the lens (anterior polar, anterior subcapsular, anterior cortical, lamellar/perinuclear, equatorial, peripheral cortical, posterior cortical, posterior subcapsular, or posterior polar) (Figures 9.12–9.19). Several characteristics of a cataract, including location, density, size of a focal cataract, and blockage of the fundic reflex, help to determine its effect on vision [14, 64].

Differential diagnosis

Acquired cataracts in horses are often caused by uveitis (Figure 9.20) or trauma (Figure 9.21) [37–45, 48, 50, 52, 53, 55–59, 61–63, 65–67]. In a recent survey in a closed herd of Lipizzaners, cataracts were diagnosed in 24 of the 267 horses (8.9%) examined [68]. Juvenile cataracts, common in many canine breeds, are uncommonly reported in horses [14, 66, 67].

Cystic lesions associated with the anterior lens capsule and/or anterior subcapsular cortex (Figure 9.22) are being identified more frequently and appear to precede anterior uveitis and are independent of ocular trauma [14, 26, 51]. Senile cataracts significant enough to interfere with vision are also uncommon in horses [69]. Nuclear sclerosis is a relatively common finding among aged horses, but vision generally remains clinically unaffected [51, 70].

Lens suture lines (Y sutures) can be visualized in most foals and adult horses during routine ophthalmic examination, and it is important to differentiate these opacities from cataracts [7, 8, 70, 71]. In a group of 144 foals, ranging in age from 5 days to 19.5 weeks (mean age 9.4 weeks), lens sutures were visible in 137 animals [7].



Figure 9.14 Diffuse, incipient, anterior subcapsular cataract in the right eye of a 19-year-old Morgan gelding.

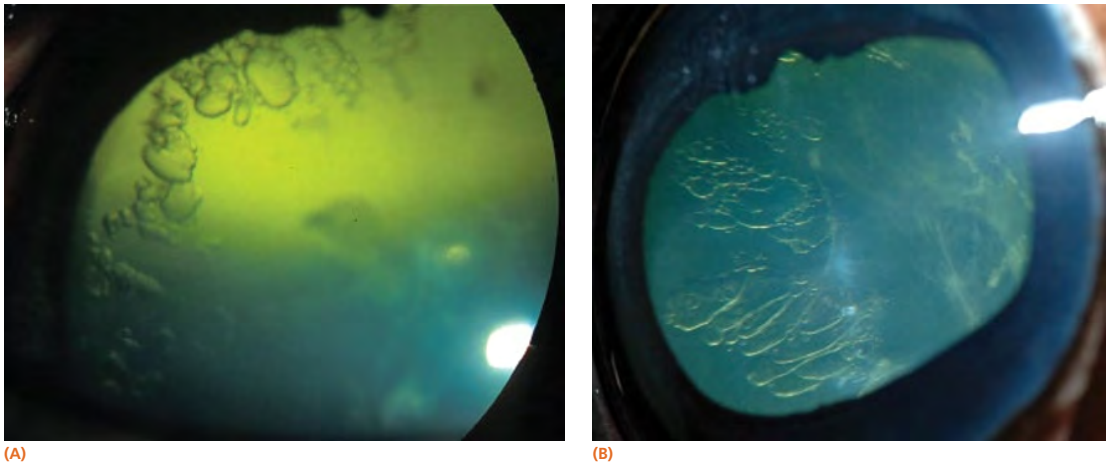


Figure 9.15 Focal, incipient, anterior cortical cataract in the left eye of a 12-year-old Thoroughbred gelding.

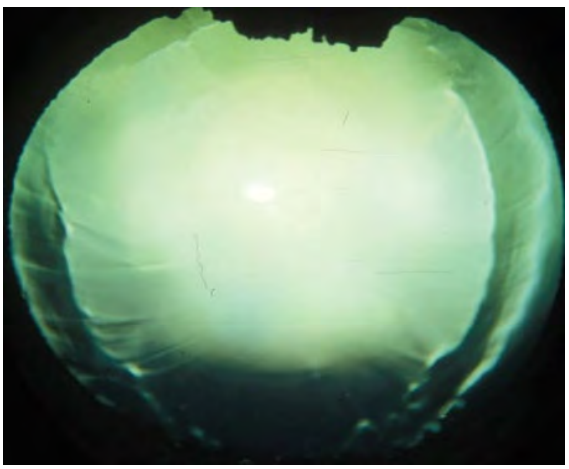


(A) (B)

Figure 9.16 (A) Lamellar (perinuclear) cataract with a small, focal, anterior cortical cataract in the right eye of a 19-year-old Percheron mare. This clinical presentation can be easily mistaken for subluxation of the lens if careful examination is not performed. (B) In infrared, note the abrupt transition from a slight gray color (cataractous area of the lens) to jet black which represents the clear cortical aspect of the lens.

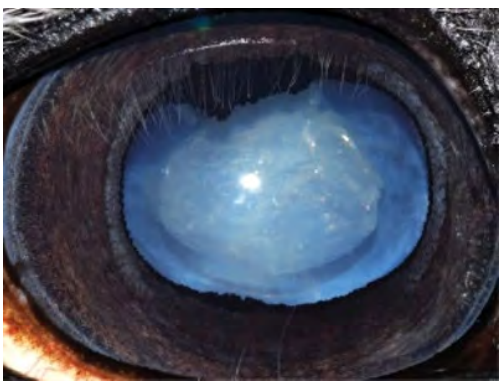


(A) (B)

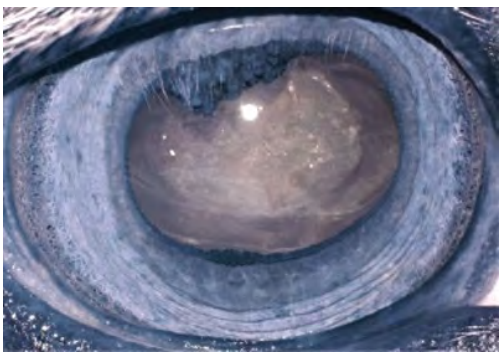


(C)

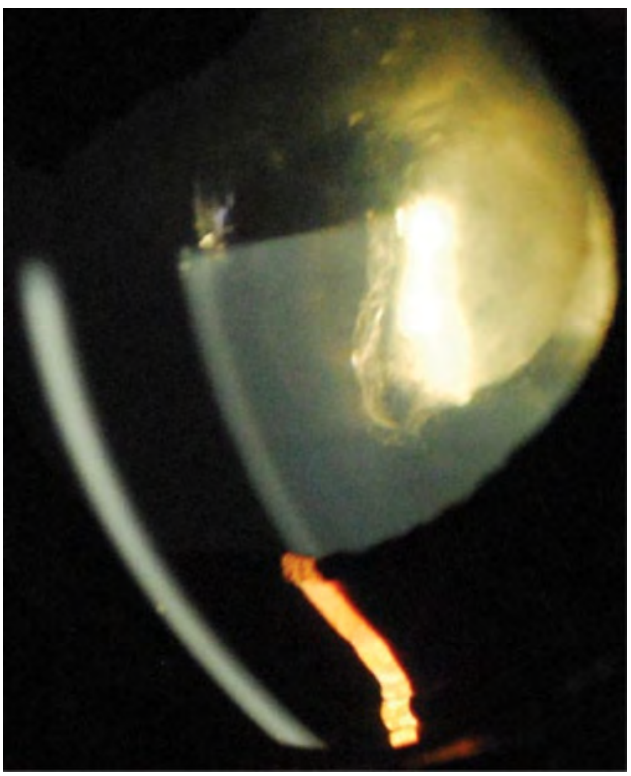
Figure 9.17 (A) Vesicles within the peripheral, equatorial cortex associated with early ERU in a 7-year-old Warmblood mare. (B) Vesicles within the peripheral, equator of the lens associated with early ERU. (C) Equatorial, cortical cataract in a young Warmblood gelding. This type of cataract can be easily missed if the pupil is not dilated.



(A)



(B)



(C)

Figure 9.18 (A) Nuclear and posterior cortical cataract in a 12-year-old Pony gelding. (B) Infrared. (C) Slit-lamp photograph. Note presence of a small, focal anterior cortical cataract above the upper portion of beam of light associated with the anterior lens capsule.

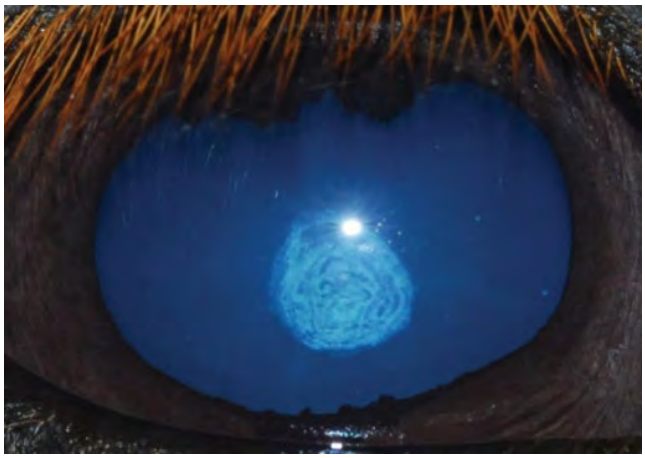


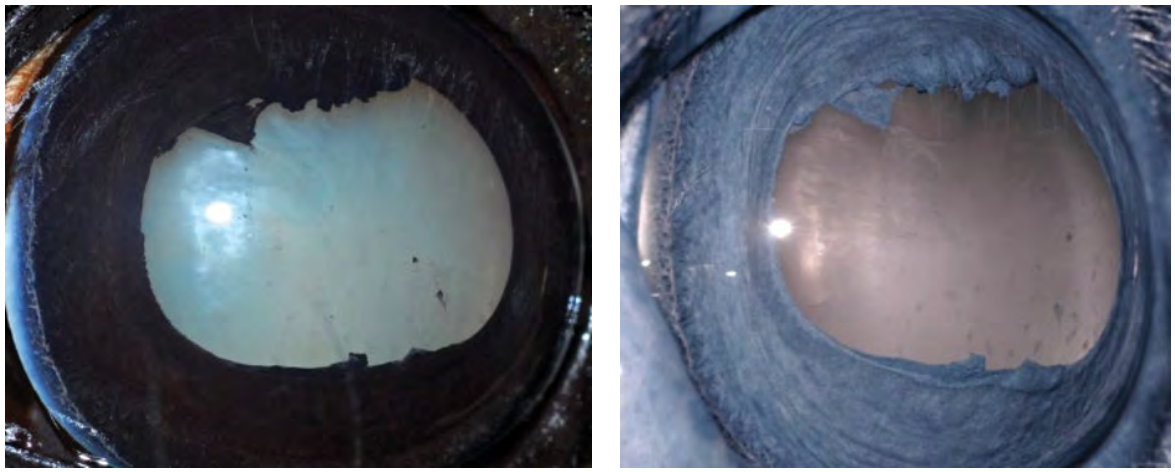
Figure 9.19 Focal, axial, posterior cortical cataract. Axial location of this axial posterior cortical cataract is demonstrated.

Treatment

Historically, horses with cataracts associated with ERU were not considered appropriate candidates for cataract surgery. Concurrent pathologic ocular changes in the eye and the high rate of post-operative complications resulted in very low surgical success rates [64, 72]. Two recent retrospective studies provide data emphasizing the increased risk of post-cataract surgery complications in horses with cataracts associated with ERU [61, 62]. However, cataract surgery in horses with well-controlled uveitis may be considered as a means of increasing quality of life by restoring vision [48, 63, 73–75].

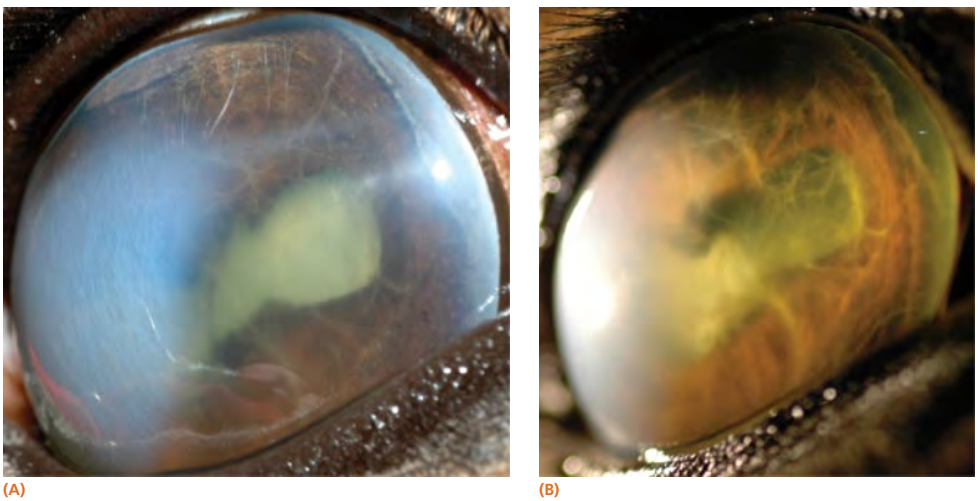
Lens luxation

Lens luxation or subluxation may be caused by congenital anomalies of the zonules, chronic uveitis, or glaucoma, and may be exacerbated by trauma [52, 53, 57, 59, 65, 76]. A luxated lens



(A) (B)

Figure 9.20 (A) Complete, mature cataract associated with chronic ERU. (B) Note the bluish-gray color of the pupil in infrared, consistent with cataractous changes, or opacifications, of the lens. (*Source*: McMullen et al., 2009 [98]. Reproduced with permission from John Wiley & Sons.)



(A) (B)

Figure 9.21 (A) Mature cataract developed as a result of significant blunt force trauma. Also note the medial corneal edema and fibrin accumulation in the anterior chamber. (B) Tangential lighting allows direct visualization of the temporal iris disinsertion.

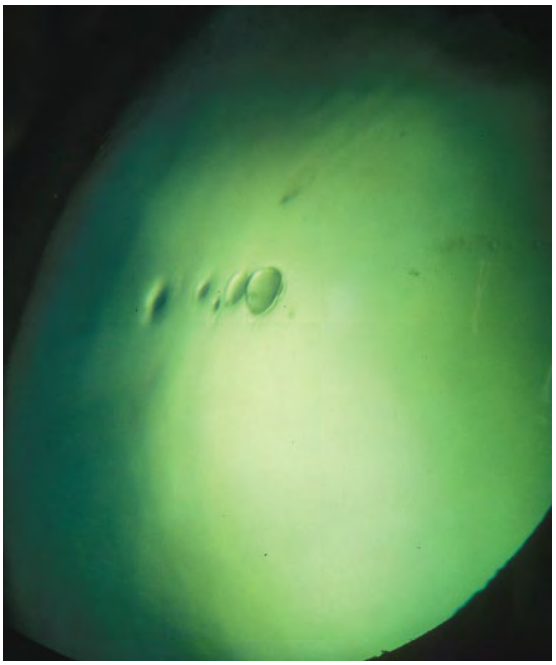


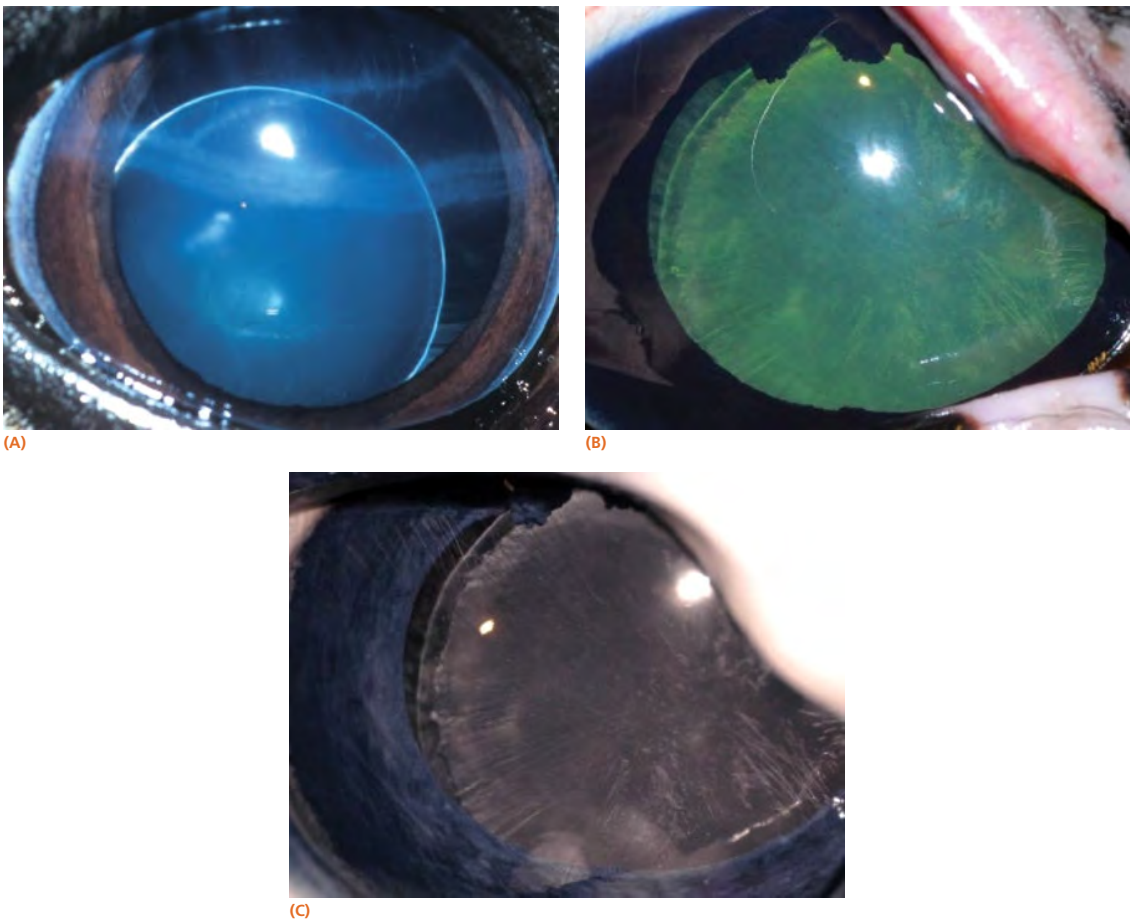
Figure 9.22 Multiple, small, anterior subcapsular cysts.

will usually become cataractous, with focal or diffuse opacification appearing immediately or weeks following a traumatic incident as a result of the disruption in the protein exchange between the aqueous humor and the lens [57, 77, 78].

Clinical appearance

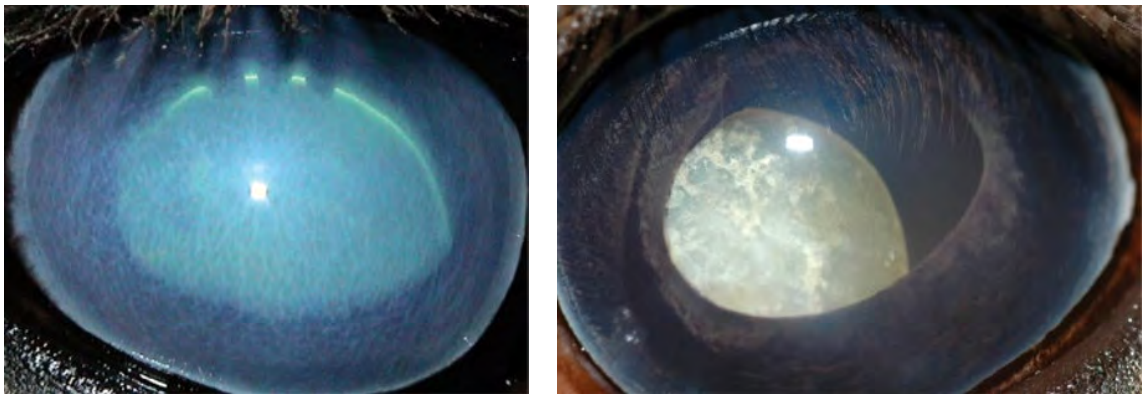
Lens luxation and subluxation, in general, are rare in horses [75]. A subluxated lens is one that has partially broken free from its zonular attachments; however, the lens remains within its normal position behind the iris and within the patellar fossa (Figure 9.23). Slight displacement of the lens, however, allows the edge of the lens to be visible within the pupil, producing the appearance of an aphakic crescent (Figure 9.24). Complete luxation manifests as displacement of the lens into either the anterior chamber (i.e., anterior lens luxtion) (Figure 9.25) or the vitreous body (i.e., posterior lens luxation) (Figure 9.26) [17].

Because of the lack of physical contact between the posterior iris surface and the anterior surface of the lens in cases of significant subluxation or luxation of the lens, iridal instability manifests as a slight vibration of the iris (iridodenesis) that can be visualized during ophthalmic examination. Primary (hereditary) lens luxation has not been documented in the adult horse;



(A) (B) (C)

Figure 9.23 (A) Lens subluxation associated with primary glaucoma in a 12-year-old Icelandic Pony mare. (B) Early lens subluxation associated with chronic ERU. Note the refractile edge of the lens just axial to the temporal edge of the pupil. (C) Space between the pupil and edge of the lens is more readily identified in infrared.



(A) (B)

Figure 9.24 (A) Superior subluxation associated with chronic ERU and secondary glaucoma. Although the cornea is diffusely edematous, the edge of the lens is readily identified during direct retroillumination. (B) Subluxation and mature cataract in a young Warmblood gelding. Note the large aphakic crescent within the temporal aspect of the pupil.



Figure 9.25 Due to the refractile nature of the lens perimeter, the luxated lens is readily identifiable within the anterior chamber of this 18-year-old Icelandic horse stallion. Note the multiple Haab's striae lined with pigment and the mild axial corneal edema. This horse was diagnosed with secondary glaucoma associated with lens instability.



Figure 9.26 Posterior lens luxation in a 14-year-old Appaloosa mare.



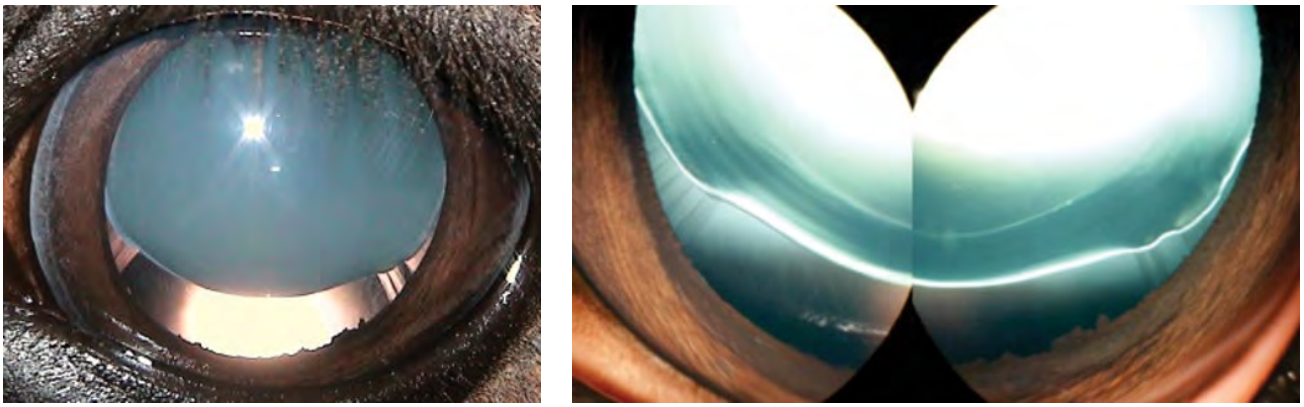
Figure 9.27 Medial lens coloboma as seen during direct retroillumination in a 12-year-old Haflinger gelding.

however, congenital bilateral lens subluxation in an Arab-cross foal [79] and subluxation and cataract formation associated with the MCOA syndrome described in Rocky Mountain Spotted horses [17, 18], Comtois horses [19], ponies [20, 22], Icelandic horses [21], and Exmoor ponies [23] have been reported. The prognosis for vision and globe retention is dependent upon the nature and severity of the primary ocular disease [75, 80].

Differential diagnosis

It is imperative that the primary underlying condition be identified when a horse with either a lens subluxation or luxation is being evaluated.

A rare, presumably congenital anomaly, which must be differentiated from a lens subluxation, is a lens coloboma (Figure 9.27) [28]. Faulty lens zonule formation, and therefore lack of insertion at



(A) (B)

Figure 9.28 (A) Overview of ventral lens coloboma in a young Warmblood stallion. (B) This photomontage demonstrates, in greater detail, the lens coloboma depicted in **(A)**. Note the lack of zonular attachments along the inferior border of the lens. Distinct notches in the inferior lens can be seen at the 4 and 8 o'clock positions, and represent transition from an area of zonular attachment to an area devoid of those attachments.



Figure 9.29 Medial lens subluxation in a horse with chronic ERU and secondary glaucoma. Note the multiple, focal posterior synechiae, the complete, mature cataract, and the vitreal adhesions along the medial lens border.

the lens equator, results in an area where the lens equator is not stabilized and held in its normal position. This results in a focal flattening or notch in the peripheral lens equator associated with the missing zonules. An aphakic crescent can usually be identified (Figure 9.28), but signs of ocular inflammation (e.g., aqueous flare, miosis) are not generally associated with lens colobomas, and should be differentiated from a subluxation of the lens secondary to anterior uveitis or glaucoma (Figure 9.29).

Treatment

A lens that is partially (subluxation) or completely displaced into the vitreous body (posterior lens luxation) may not require surgical intervention as long as the eye remains comfortable and the inflammation associated with the primary insult can be controlled with topical and systemic anti-inflammatory medications. The horse should be continually monitored for signs of ocular discomfort (blepharospasm and epiphora) or discoloration (corneal edema), which may indicate inflammation, glaucoma, or anterior lens luxation.

Intracapsular lens extraction has historically been recommended in cases of lens luxation in an attempt to preserve vision [11, 14, 81, 82]. Recent, retrospective, long-term evaluation in such cases has revealed that surgical intervention is coupled with an extremely poor prognosis for both retention of vision and the globe [80]. However, prior to surgical intervention being considered, an attempt should be made to determine the underlying cause for the lens displacement. Because extensive uveal tissue damage may be incurred as a result of the underlying uveitis or trauma precluding lens luxation, phthisis bulbi or blindness associated with retinal degeneration may result, especially in cases involving posterior lens luxation [75, 83]. As an alternative to lens removal in uncomfortable blind eyes with secondary lens luxation, enucleation or evisceration with insertion of intrascleral silicone prosthesis may be considered [84–88].

Lens capsule rupture

Blunt or penetrating ocular trauma is relatively common in the horse, and lens capsule rupture may be incurred as a result. Lens capsule ruptures may be associated with rupture, laceration, or puncture of the cornea or sclera, but may also occur as a result of blunt force trauma. Uveal or retinal tissue exposure as well as herniated lens material may lead to the development of severe uveitis or blindness (Figure 9.30) [15, 81, 89].

Clinical appearance

Any penetrating ocular injury has the potential to cause damage to the lens capsule, and corneal lacerations are relatively common in the horse [65, 90–93]. Thorough evaluation of the lens capsule is required following any case involving penetrating or perforating corneal injuries. Due to the inherent nature of such injuries, it is often difficult, if not impossible, to adequately evaluate the lens capsule simply using only direct ophthalmoscopy



Figure 9.30 Lens capsule rupture following blunt force trauma in a young Warmblood mare. Lens cortex can be seen protruding into the anterior chamber ventrally.

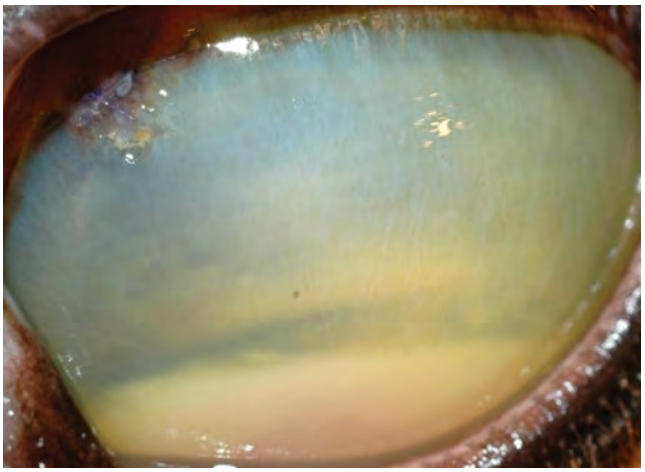


Figure 9.31 Severe endophthalmitis that developed approximately 3 weeks post phacoemulsification. This eye did not receive an IOL.

or slit-lamp biomicroscopy. Ocular ultrasonography, high-resolution ocular ultrasonography, and infrared digital photography may increase the probability of identifying a disruption of the anterior lens capsule [24, 94–98].

In severe cases, the anterior chamber may be collapsed, uveal prolapse may be present, and lens material may be extruding from the lens capsule or corneal wound. Even in cases without full-thickness corneal defects, signs of anterior uveitis will usually be present, and include fibrin formation or hyphema, and miosis, making ophthalmoscopic examination of the lens nearly impossible. Clinical evaluation of the lens can be facilitated by removal of the intraocular fibrin, irrigating the anterior chamber, and dilating the pupil with dilute (1:10,000) intracameral epinephrine, with the horse in lateral recumbancy under general anesthesia, prior to surgical correction of the corneal defect [75]. It is important to have the animal paralyzed or have performed a retrobulbar block in order to fully manipulate the globe and to minimize tension from the extraocular muscles when performing these procedures.



Figure 9.32 Small, focal subepithelial anterior lens capsule cyst. Pigment deposition inferior to the cyst is suggestive of a previous rupture of the cyst resulting in a bout of lens-induced anterior uveitis.

Differential diagnosis

Chronic and insidious intraocular inflammation may torment a horse following a penetrating ocular injury. Endophthalmitis may be caused by intraocular sequestration of bacterial or fungal organisms, deposition of foreign material (i.e., plant material), the release of lens proteins, and/or an unrelenting inflammatory response to these insults (Figure 9.31). Thorough ocular examination, aerobic and anaerobic bacterial and fungal culture, and sensitivity of corneal scrapings and intraocular fluids, as well as ocular ultrasonography are often necessary to identify the underlying cause of the ocular inflammation prior to deciding which medical or surgical approach is most appropriate.

Anterior subepithelial cysts (Figure 9.32) are an additional, poorly characterized ocular disease that appears to involve the anterior subcapsular epithelium and/or subepithelial anterior cortex (Figure 9.33), and they should be considered when

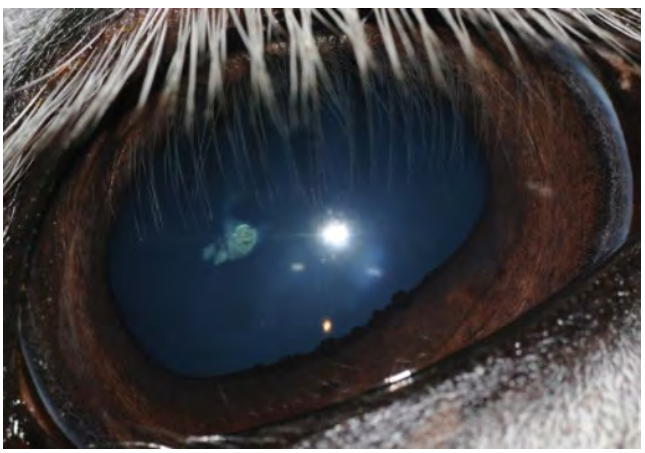


Figure 9.33 A small, subcapsular anterior lens cyst with associated incipient cortical opacification and slight protrusion of the anterior lens capsule into the anterior chamber.



Figure 9.34 Focal pigment adhesion on the temporal anterior lens capsule covering a previously identified anterior lens capsule cyst. This eye had suffered multiple bouts of inflammation that have ceased following occlusion of the cyst with pigment.



Figure 9.35 A geographic posterior cortical cataract developed in this horse following blunt force trauma. Note the hyphema in the ventral aspect of the anterior chamber and focal pigment adhesion to the anterior lens capsule at the 4 o'clock position within the pupil. The granulation tissue visible developed secondary to wound dehiscence following lateral canthal laceration repair.



Figure 9.36 Focal, axial, pyramidal, subcapsular, anterior cortical cataract.

evaluating a case of recurrent anterior uveitis or ocular trauma with anterior lens involvement. Although very little information exists on this presumably congenital abnormality, it is being identified with increasing frequency.

Usually, horses present with a history and/or clinical signs of chronic ERU (i.e., blepharospasm, epiphora, and miosis with mild aqueous flare) that are associated with active and quiescent periods of inflammation. In general, these lesions respond rapidly to topical and systemic anti-inflammatory medications and topical mydriatics, with signs completely subsiding within 1–2 weeks. However, as with chronic ERU, they tend to go through a vaguely predictable period of quiescence prior to additional phases of acute inflammation. With the exception of pigment deposition surrounding the cystic lesion on the anterior lens capsule (Figure 9.34), the iris itself does not usually show signs of chronic inflammation (i.e., corpora nigra degeneration, iridal hyperpigmentation). Cases that prove more resistant to medical therapy alone may benefit from surgical implantation of a suprachoroidal cyclosporine implant [63, 99, 100] for long-term suppression of inflammation, or lens extraction with intraocular lens (IOL) implantation, if the lesion is large enough that it is also affecting vision [14, 26].

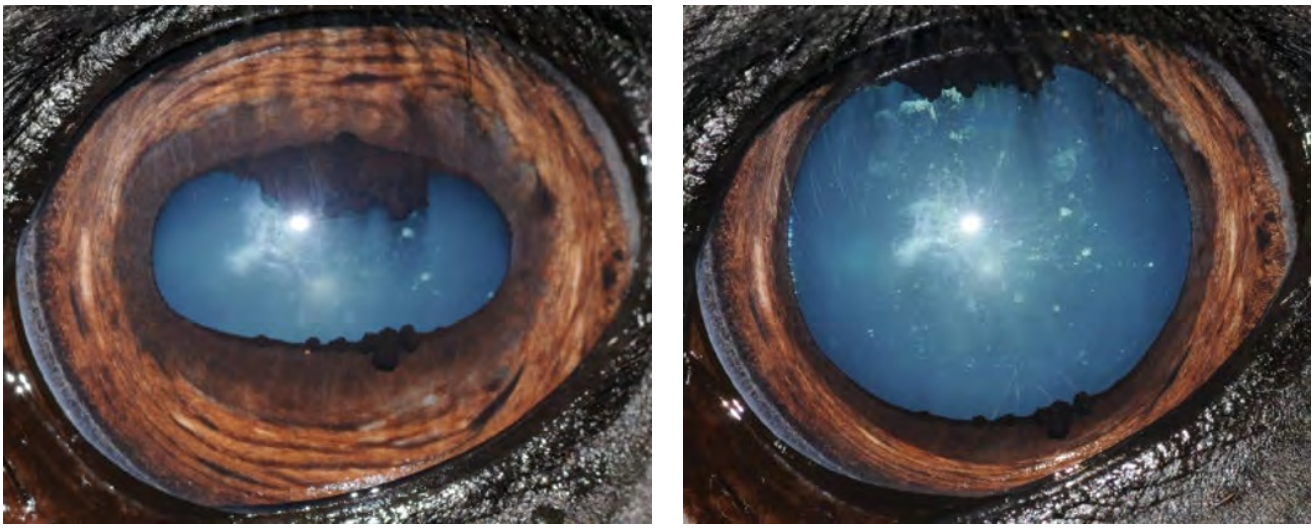
Treatment

Surgical lens removal is the treatment of choice in dogs following capsule rupture, and should be performed at the same time as the surgical correction of the corneoscleral injuries [86, 89, 101]. Although little information pertaining to this manifestation of lens disease in the horse has been published, phacoemulsification following acute anterior lens capsule rupture has been successfully performed [102]. Prognosis for vision is poor following blunt trauma, as it can result in cataract development (Figure 9.35), lens capsule rupture (see Figure 9.30), staphylomas at the limbus [86], and, potentially, subsequent retinal detachment. It has been suggested that evisceration with intrascleral silicone prosthesis or enucleation may be indicated [84, 87, 88, 103]. However, some anecdotal success has been achieved with early surgical intervention (lens removal).

Evaluation and treatment of cataracts

Evaluation

A complete ophthalmic examination should be a routine part of any pre-purchase or insurance examination, and should be conducted during the initial physical examination on all newborn foals [37, 82, 104]. Prompt and complete pupillary light responses (PLRs) and a blink response to bright light (dazzle) are generally indicative of adequate retinal function [82]. A focal light source, such as a penlight or Finoff transilluminator, generally allow for identification of diffuse or focal axial cataracts (Figure 9.36); however, complete evaluation of the lens requires pharmacological mydriasis (Figure 9.37) [81].



(A) (B)

Figure 9.37 (A) Diffuse, anterior, subcapsular anterior cortical cataract as seen through a mid-sized pupil. (B) Same eye as in Figure 9.37A following application of topical 1% tropicamide to facilitate mydriasis. Anterior cortical lens opacifications extend well into the periphery of the lens.



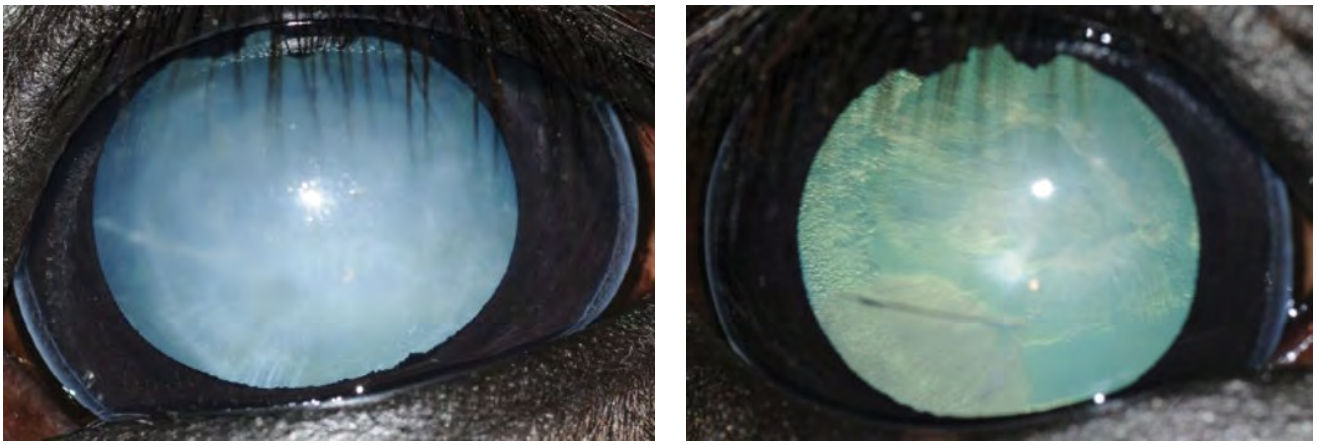
(A) (B)

Figure 9.38 (A) Diffuse immature anterior cortical cataract of the right eye in a young German riding pony. (B) Less significant immature anterior cortical cataract of the left eye in the same horse. Both lens opacifications were incidental findings not associated with behavioral or visual changes noted by the owner.

Two doses of topical 1% tropicamide, 0.1–0.2 mL topically at 5-minute intervals, will generally provide adequate mydriasis of the equine pupil to facilitate ophthalmic examination within 15–30 minutes. Focal incipient cataracts (Figure 9.38) do not prevent evaluation of the equine ocular fundus. However, if diffuse cataracts are present (Figure 9.39), both ocular ultrasonography [24] and electroretinography [105–108] should be performed (see Chapter 1 for more details) to evaluate retinal integrity and function [14, 75, 81].

Medical treatment

Medical therapy that prevents cataract progression in clinical patients is not available [109, 110]. Continued progression of cataracts to the stage of hypermaturity is commonly associated with chronic, low-grade, persistent lens-induced uveitis (LIU). The effects of LIU on the overall health of the eye have yet to be determined. However, it may contribute to the reduced success rate following phacoemulsification in horses with chronic LIU [61, 62, 81, 111]. Pharmacologic mydriasis has been used in an attempt to increase the visual potential in horses with focal axial or nuclear cataracts. One percent atropine ointment or solution is applied topically, once daily, until complete mydriasis is achieved, at which time the frequency of administration is reduced to a frequency necessary to maintain the pupil in a dilated state [11, 37, 71]. Photophobia may be associated with prolonged mydriasis and is commonly manifested by lacrimation and blepharospasm when the eye is exposed to light [75]. Horses that develop photophobia as a result of the previously



(A) (B)

Figure 9.39 (A) Diffuse, immature cortical cataract of the left eye in an Arabian filly. (B) Less significant, diffuse, immature posterior cortical and equatorial cataract in the right eye in the same filly.

described treatment should have the administration of atropine stopped, and should be sheltered from bright light until the effects of atropinization have subsided. The effects can take more than 14 days to subside in the normal equine eye [112].

Selection of patients for surgery

The decision to treat cataracts in the horse is one wrought with both philosophical and ethical concerns. The question of liability is one that must be addressed, especially in the context of injury to a rider following lens extraction surgery that leaves the horse with less than optimal vision. Vision in every horse that has had cataract surgery should be considered compromised, even those horses receiving an IOL implant. Cataract surgery in horses, as well as the pre-and post-operative treatment periods, represents a challenge to the clinician. Both the size of the eye and the animal's mass provide certain obstacles that must first be overcome prior to surgical intervention being considered successful. The horse's potential for return to function must also be considered thoroughly.

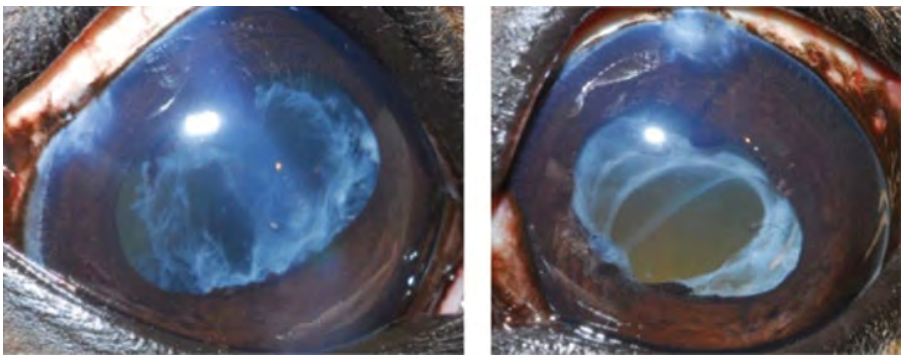
Although post-operative vision in the aphakic horse has recently been reported as functionally normal [47, 66, 113–115], aphakia has historically been considered to cause the horse to be visually impaired [11, 14, 46, 114]. Current methods routinely used to evaluate vision in the horse are very crude and, consequently, provide only a subjective and rudimentary assessment of a horse's ability to see [47]. The aphakic equine globe (Figure 9.40) is markedly hyperopic [66, 114]. The average refractive error of the aphakic adult equine globe is +9.5 D ($n = 14$, range +7.5 to +10 D) [66, 114, 116, 117].

Despite this marked degree of ametropia, and the limited number of cases with long-term follow-up, horses were considered to have no visual difficulties, and in some, vision was considered to be as good as it was prior to the development of cataracts [113, 114]. Fife et al. reported favorable short-term visual results following equine cataract surgery over a 10-year period; however, long-term follow-up (1 year or more) was only available for 13 of the eyes originally undergoing phacoemulsification [47]. None of the horses received an IOL implant, nor were they refracted post-operatively. Visual function was assessed using standard diagnostic tests (i.e., PLR, menace, dazzle, and behavioral testing), and relied to a large extent on responses from owners or referring veterinarians [47]. Two recent retrospective studies and a case report have attempted to shed some light on the degree of long-term vision retention in horses and foals undergoing phacoemulsification [61, 62, 118]. Brooks et al. found that 25/95 horses (26.3%) remained visual at 12 to > 24 months post-operatively, while the percentage of foals remaining visual at 12 to > 24 months post-operatively was 9.3% (4/44 foals). Only one of the nine horses receiving an IOL implant in this study remained visual at 12 to > 24 months post-operatively. Of the 24 horses with ERU undergoing phacoemulsification, 9 were visual at 12 to > 24 months (37.5%) [61]. Edelman et al [62] retrospectively evaluated the records from 41 horses (46 eyes), with 21 of the 46 eyes receiving an IOL implant. Chronic uveitis was present in 12 of the 46 eyes prior to phacoemulsification. The majority (14/21 eyes) of the pseudophakic and almost half (11/25 eyes) of the aphakic eyes remained visual at the last follow-up examination. Chronic uveitis present prior to phacoemulsification (3/12 eyes) resulted in a greater risk of blindness following surgery than in the eyes without chronic uveitis (22/34 eyes) present [62]. Implantation of an IOL has resulted in refractive results within ± 1.00–1.50 D following surgery in both adults and foals [62, 118, 119], which corresponds well to the refractive state of equine eyes free from signs of ophthalmic disease [120–123]. The majority of horses receiving IOL implants have remained visual post-operatively [61, 62, 118, 119].

The age of the horse at the time of surgery has historically been an important variable associated with a successful outcome following lens extraction in horses. Recently, most of the publications pertaining to equine cataract surgery have represented a wide age range, with cataract surgery in adult



(A)



(B)

Figure 9.40 (A) Bilateral aphakia following phacoemulsification in a 13-year-old Pony mare. (B) Magnified view of both eyes from **(A)**. Note the anterior and posterior capsular fibrosis and corneal fibrosis associated with corneal incisions; these are to be expected, to some degree, following cataract surgery in horses.

horses receiving increasingly more attention [47, 61, 62, 73, 83, 113, 114, 119, 124–126].

The age of the equine patient at the time of surgery may also influence the post-operative success rate [75]. A condition known as deprivation amblyopia has been described in children with congenital cataracts and in laboratory animals deprived of early vision [75, 127–130]. Vision is decreased in one or both eyes subsequent to central fixation disuse as a result of ocular opacities [128]. The potential for deprivation amblyopia should be considered in foals presenting for cataract surgery. This would dictate that early surgical intervention should be recommended for foals with congenital cataracts [14, 46, 128, 130]. The incidence of deprivation amblyopia has not been ascertained in older foals following extraction of congenital cataracts [75, 118]. Congenital cataracts, if left untreated, may progress to hypermature cataracts as the animal ages, and LIU may develop. Early surgical intervention is recommended, as the severity and duration of the intraocular inflammation may increase the likelihood of post-operative complications such as ocular hypertension and secondary glaucoma (Figure 9.41) [14, 82].

In the past, it has been suggested that younger foals were more suitable for cataract surgery because their smaller size made them easier to restrain, thus facilitating post-operative ocular medication. The temperament of the foal should be such that it allows for frequent handling and treatment [14, 67, 79, 118, 131]. Foals that are accustomed to frequent handling and that are halter-trained are preferred candidates for cataract surgery, as they are more likely to tolerate post-operative treatments with minimal risk to themselves and to the personnel administering the medication [14, 46, 67, 79, 86, 113, 115, 118, 131]. Previous studies evaluating the results of cataract surgery in foals demonstrated that foals younger than 6 months of age were more likely to have a positive outcome following cataract surgery [67, 132, 132]. Foals older than 6 months of age were found to be more difficult to medicate topically following surgery, and were more likely to have hypermature cataracts. Therefore the best post-operative prognosis was reserved for halter-trained foals amenable to regular handling and possessing a docile demeanor [67, 113, 132]. Since then, several reports describing successful cataract surgery in the adult horse have been published [47, 61, 62, 66, 83, 114, 119, 124–126]. Available literature pertaining to cataract surgery and IOL placement in foals remains limited [118, 131, 132].

Concomitant systemic problems or additional ocular anomalies may justify postponement or denial of cataract surgery. In foals, thoracic radiographs, in addition to routine pre-operative

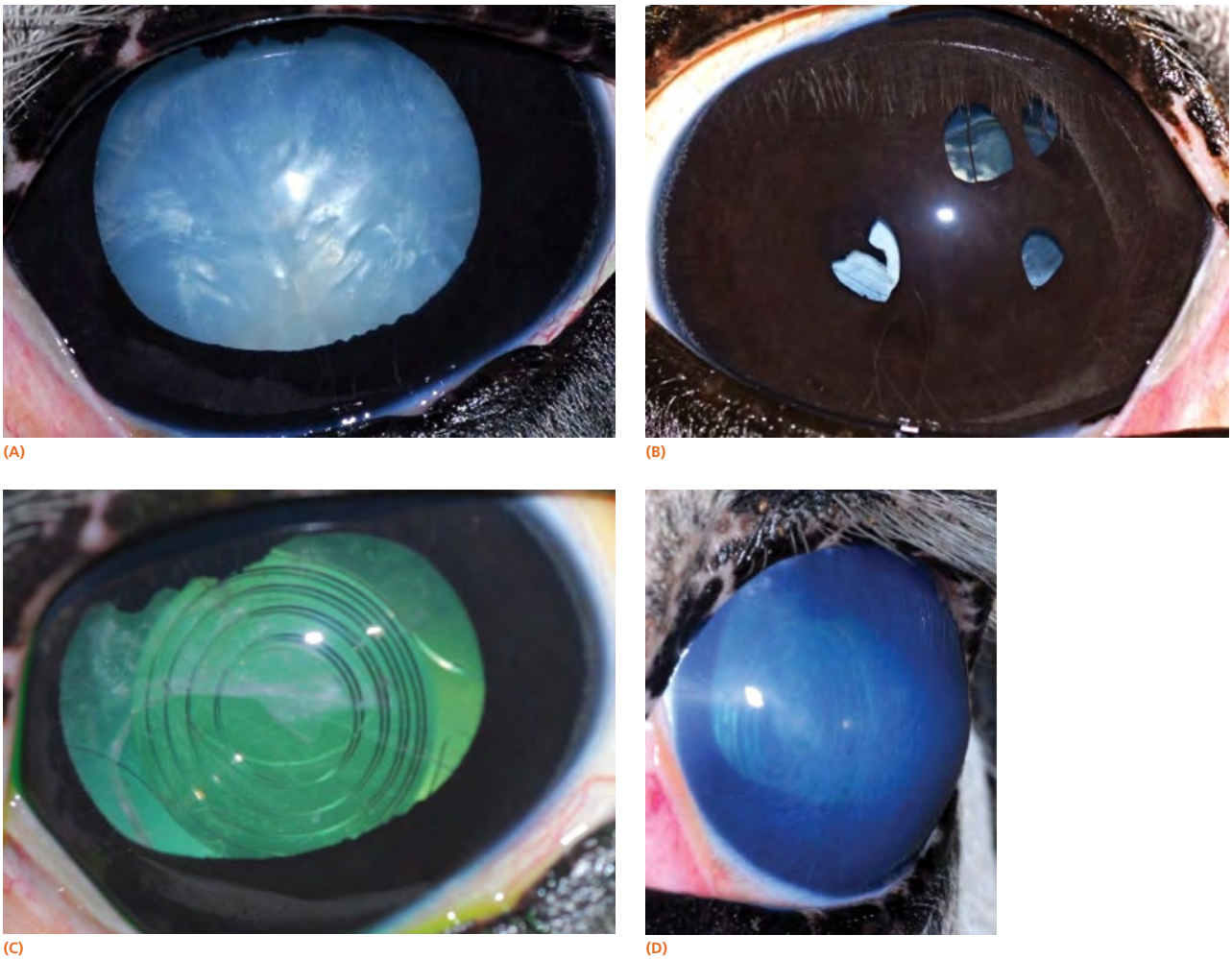


Figure 9.41 (A) Mature cataract in the left eye of a 3-year-old Thoroughbred gelding. (B) Right eye from the horse in **(A)**. Seclusio pupillae and hypermature, resorptive cataract associated with chronic lens-induced uveitis. (C) Same eye as in Figure 9.42A 1 week after phacoemulsification and implantation of a 25-D IOL. (D) Same eye 8 weeks post cataract surgery. Note the diffuse corneal edema and buphthalmic appearance of the globe. This globe developed uncontrollable secondary glaucoma which led to the horse being euthanized.

blood screening, will help to rule out *Rhodococcus* spp. infection or other infections [75, 133].

Once it has been determined that a cataract is present, complete examination of the ocular and adnexal structures should be carried out in order to identify any additional congenital or acquired abnormalities. Foals with complete congenital cataracts associated with blindness or progressive immature cataracts influencing behavior are potential candidates for surgery. Careful evaluation of the eyelids, conjunctiva, and cornea should reveal any concomitant congenital or acquired diseases present requiring treatment prior to cataract surgery [14, 67, 82]. Retinal function can be confirmed with the presence of brisk PLRs and a blink response to bright light (dazzle), and an electroretinogram (ERG) [14, 82, 104–108, 134].

Congenital stationary night blindness has been reported in the Appaloosa, Thoroughbred, and Paso Fino breeds [135–139]. A pre-operative ERG should be considered mandatory in the aforementioned breeds and is recommended in any potential equine cataract surgery candidate. Other congenital ocular anomalies with the potential to cause blindness, regardless of the condition of the lens, are generally considered a contraindication to cataract surgery, and include retinal detachment and optic nerve hypoplasia [14, 46]. Microphakia is also generally considered a contraindication to cataract surgery, but mild cases have undergone lens extraction surgery with favorable results [14, 46, 113].

Use of subpalpebral lavage systems allows post-operative medication protocols to be more easily followed because they increase the ease in topical medication application (Figure 9.42) [140, 141]. Commercially available subpalpebral lavage kits are now available. As a result, a potential surgical candidate's attitude and demeanor play a less-important role in the pre-operative decision-making process.



Figure 9.42 Bilateral, superior eyelid subpalpebral lavage systems (SPL) in two horses prior to bilateral phacoemulsification and subsequent IOL implantation. The SPLs greatly facilitate pre- and post-operative ophthalmic medications.

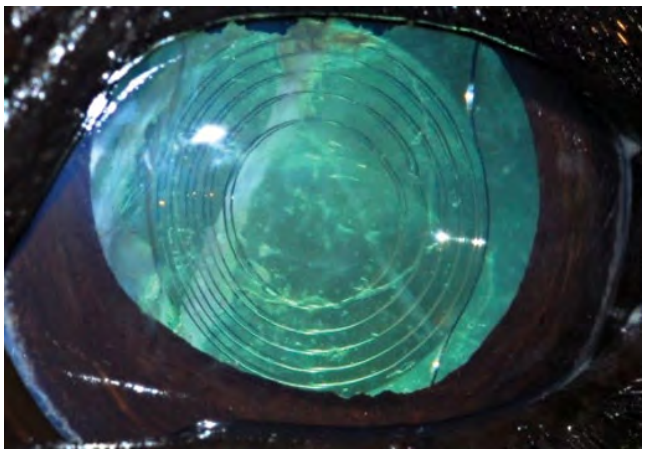


Figure 9.43 Post-operative photograph of an 18-D, foldable, equine IOL implant in a 23-year-old Walking horse gelding. The haptics are in a vertical position because of pre-existing posterior and medial capsular tears that prevented horizontal positioning.

Much progress has been made over the past few years in the development of an appropriate equine IOL implant [83, 126, 142–144]. Although much work remains to be performed before a universal equine IOL can be recommended, our current recommendation is that an IOL should be placed in any equine globe that undergoes lens extraction unless pre-existing (i.e., large lens capsule tear) or intraoperative complications prevent its placement (Figure 9.43). Post-operatively, horses that have received an IOL subjectively appear to have much better vision than aphakic horses, even those horses with a marked myopic refractive error [73, 118, 119, 126].

Extensive owner education is needed prior to equine cataract surgery. The owner should be informed that his or her horse will require prolonged aftercare for at least 3 months post-operatively, even with no immediate, short-, or long-term complications associated with the surgery. Also, owners should be cautioned that vision in the eye(s) undergoing lens extraction, with or without IOL implantation, will be compromised following surgery. Currently, it is not possible to accurately predict how well a horse will see following cataract surgery, and post-operative assessment of vision will rely on reports from the owner and referring veterinarian, and follow-up ophthalmic examinations and visual testing; which should also include ocular ultrasonography and streak retinoscopy.

Pre-surgical diagnostic testing

Any horse, regardless of age, that is a potential candidate for cataract surgery should be otherwise healthy and amenable to prolonged medical therapy. Any concurrent health problems and ophthalmic disease or abnormalities should be addressed and, if necessary, treated prior to scheduling elective cataract surgery.

In foals, special attention should be paid to the respiratory tract, and a thorough pulmonary examination including auscultation and thoracic radiographs and ultrasonography are recommended to rule out subclinical or insidious pulmonary diseases. Additionally, a complete pre-operative evaluation of the potential surgical candidate should be performed, and should include a complete history (including current and previous medical therapy) and physical and ophthalmic examination. Pre-anesthetic evaluation should also include a complete blood count (CBC) and serum chemistry profile (Chem) with fibrinogen.

If the cataracts are determined or suspected to be congenital, the animal should be closely examined for evidence of additional general or ophthalmic congenital defects. Similar precautions should be taken if trauma or uveitis is suspected. In these cases, complete and thorough evaluation of the uveal tract, vitreous, and retina is of prime importance.

A thorough and detailed history should reveal when the owner or handler initially noticed visual deficits, and if they can be associated with any specific time of day. If the animal's vision is more severely affected under normal daylight conditions, cataracts may likely be the reason. However, if vision is adversely affected in poor- or dim-lighting conditions, retinal degeneration may be responsible. Some foals or horses with visual deficits may be presented to the veterinarian with a history of repeated cuts and abrasions to the face, chest, and forelimbs, or may be suspected of having neurologic or gait abnormalities. In addition to a thorough physical and ocular examination, including streak retinoscopy, additional diagnostic testing in the form of an ERG is indicated (Figure 9.44).

A complete ophthalmic examination is an essential part of the pre-operative evaluation of the potential cataract surgery candidate. Evaluation of vision is performed as part of this examination and may include observation of the animal in an obstacle-course setting, alternately blindfolding each of the eyes in order to observe subtle changes in performance, as well as more standard



Figure 9.44 An ERG is being performed in a 12-year-old Warmblood gelding.

tests including menace, dazzle, and direct and consensual PLRs. This should be followed by thorough examination of the orbit and eyelids, the nictitating membrane, conjunctiva, cornea, anterior chamber, iris, lens, and if visualization is possible, the vitreous, retina, and optic disc. Ocular examination is facilitated if performed in a semidark and quiet examination room, stall, or isolated area of the barn. A focal light source, such as a transilluminator or portable hand-held slit-lamp, is used to perform the examination. Additional instrumentation includes a direct ophthalmoscope, head-mounted indirect ophthalmoscope, and condensing lenses (14 D, 20 D, and 28 D). For details regarding their use see Chapter 1. PLRs, Schirmer tear tests, and intraocular pressure (IOP) measurements with an applanation (TonoPen) or rebound (TonoVet) tonometer should be performed prior to the pupils being dilated.

Tropicamide 1%, a short-acting mydriatic agent, is applied topically to facilitate dilation of the pupil, allowing complete evaluation of the lens (grading and staging of the cataract), vitreous, retina, and optic disc. Two-tenths of a milliliter of tropicamide is applied to the cornea via a 1-mL syringe with a 25-G needle hub attached or with an insulin syringe with a swaged-on 30-G needle (needle broken off at the tip of the hub or syringe, respectively). Application may be repeated at 5- to 10-minute intervals, and maximal dilation can be expected after 20–30 minutes. One or two applications are typically sufficient.

Various concomitant ocular diseases may be a contraindication for elective lens removal or may increase the risk of intra- or post-operative complications. Examples of diseases that can potentially complicate surgical intervention if not eliminated prior to lens removal are distichiasis, entropion, keratoconjunctivitis sicca, and corneal ulceration. Examples of more serious ocular diseases that may not only complicate surgical intervention but also serve as a contraindication include immune-mediated keratitis, ERU, lens subluxation with or without vitreal presentation into the anterior chamber, and retinal diseases (retinal degeneration or retinal detachment). However, advances in the treatment of ERU and improvements in equine phacoemulsification techniques and instrumentation have recently led to favorable results in several cases that would have been previously deemed unsuitable for surgery [73, 83, 126].

Additional diagnostic testing in the form of an ERG and ocular ultrasonography should be routinely performed as part of the pre-surgical equine cataract patient work-up. Both of these tests reveal information about the posterior segment that cannot be obtained, or which may be missed, during routine ophthalmic examination. Cataract formation is a common complication associated with ERU, and, as a result, concomitant retinal involvement must be ruled out prior to recommending the horse for surgery. Both ERG and ocular ultrasonography are standard pre-operative diagnostic tests used routinely in small-animal ophthalmology. As both of these procedures can adequately be performed on the standing, sedated horse, every effort should be made to make them routine procedures in equine ophthalmology as well [24, 95, 105, 126, 142–144]. Ocular ultrasonography is an important tool used to identify pre-existing lens or vitreal abnormalities and to rule out retinal diseases as part of the pre-operative cataract patient evaluation [24, 95, 97, 126, 132, 145–147]. Additionally, the data generated, collected, and evaluated on the various globe dimensions (i.e., anterior chamber depth (ACD), crystalline lens thickness (CLT), vitreal chamber depth (VCD), and axial globe length (AGL)) via ultrasonography are invaluable in the quest to develop an appropriate IOL for the horse [119, 126, 142–144].

Pre-operative care

The pre-operative treatment protocol that has been used to successfully manage equine cataract patients at North Carolina State University and the Equine Clinic Munich-Riem in Munich, Germany, is shown in Table 9.1. Placement of a subpalpebral lavage system the day prior to cataract surgery greatly facilitates the application of topical ophthalmic medications [140, 141]. Pre-operative medical management is extremely important, and greatly influences the overall success rate in equine cataract patients undergoing surgical lens removal and subsequent lens replacement. Pre-operative mydriasis is essential to ensure visualization of the lens during phacoemulsification, as well as inhibiting post-operative adhesions between the iris and anterior lens capsule (posterior synechia) and/or the cornea (anterior synechia). Mydriasis is facilitated with the topical application of 1% atropine sulfate ophthalmic solution. Several ocular diseases (ERU, uveitis secondary to trauma or severe corneal disease) can lead to the formation of posterior or anterior synechiae that may prevent complete mydriasis.

Secondary infection of the globe following cataract surgery is a well-recognized and devastating complication in this species [47, 61, 62, 66, 111]. As a consequence, rigid pre- and post-operative antibiotic treatment protocols have been established to minimize the risk of this complication. Horses undergoing cataract surgery at North Carolina State University and the

Table 9.1 Pre-operative treatment protocol for equine cataract surgery patients.

Drug	Dose and route of administration	Frequency	Duration
Systemic medications			
Penicillin§	22,000 IU/kg IV	q6h	24–48 hours
Gentamicin§	6.6 mg/kg IV	q24h	24–48 hours
Cefquinom*	1 mg/kg IV, IM	q24h	24 hours
Flunixin meglumine	1.1 mg/kg IV, PO	q12–24 h	10–14 days
	0.55 mg/kg IV, PO	q12–q24h	10–14 days
Omeprazole	2 mg/kg PO	q24h	14–28 days
Topical ophthalmic medications			
Corticosteroids			
Neomycin-polymyxin B sulfates Dexamethasone§	0.1 mL SPL	q6h	24 hours before surgery
		q30min	2 hours before surgery
Prenisolone acetate*	0.1 mL SPL	q6h	24 hours before surgery
		q30min	2 hours before surgery
Antibiotics			
Neomycin-polymyxin B sulfates	0.1 mL SPL	q6h	24 hours before surgery
Dexamethasone§		q30min	2 hours before surgery
Moxifloxacin§	0.1 mL SPL	q2h	24 hours before surgery
Cefquinom (fortified)*	0.1 mL SPL	q6h	24 hours before surgery
		q30min	2 hours before surgery
Nonsteroidal anti-inflammatories (NSAIDs)			
Bromfenac	0.1 mL SPL	q12h	24 hours before surgery
		q30min	2 hours before surgery
Mydriatics			
Atropine sulfate 0.5–1%	0.1 mL SPL	q30min	2 hours before surgery

IU, International Units; IV, intravenous; IM, intramuscular; kg, kilogram of body weight; PO, per os (oral); SPL, through subpalpebral lavage catheter.
* Equine Clinic Munich-Riem.
§ North Carolina State University.

Equine Clinic Munich-Riem routinely receive systemic antibiotics to minimize the risk of post-operative endophthalmitis.

Topical and systemic anti-inflammatory medications are key in preventing or minimizing both pre- and post-operative ocular inflammation (uveitis). Systemic nonsteroidal anti-inflammatory medications (NSAIDs) in combination with topical NSAIDs or glucocorticoids are very effective at preventing and controlling ocular inflammation in the horse.

Anesthesia

General anesthesia is required for horses undergoing cataract surgery. Following induction, inhalant anesthetics are used for maintenance. The horse is positioned in lateral or dorsal recumbency, with the head supported with pads, sandbags, and/or inflatable ring-shaped cushions (small, thick inner-tubes) (Figure 9.45). It is essential that the head be positioned so that the iris is on a parallel plane with the ground. Any deviation from this parallel plane will result in difficulties in visualization during all aspects of the surgical procedure.

To facilitate proper globe position and to minimize anterior vitreous presentation, either systemic paralytic muscle relaxants (e.g., atracurium, vecuronium, and pancuronium) or a retrobulbar block (see Chapter 1 for a description of this technique) should be utilized to facilitate a motionless, slightly anteriorly displaced globe during phacoemulsification. Systemic paralyzation or a retrobulbar block also decrease the potential for the oculocardiac reflex and limit forward movement of the posterior lens



Figure 9.45 The horse's head is elevated using multiple pads and a small rubber innertube. Elastic tape is used to secure the horse's head to the table.

capsule and vitreous during surgery by decreasing tension on the globe from extraocular muscles [66].

Surgery, preparation, draping, and equipment

Clipping of the periocular hair followed by aseptic preparation using 1:50 Betadine solution diluted in sterile saline solution is performed. The type of drape used at the surgical site is at the discretion of the surgeon and commonly includes three or four Huck towels covered with a complete surgical drape (covering the head and neck, with the eye shape cut out), or a special adhesive ophthalmic aperture drape (Figure 9.46).

Many equine-specific intraocular instruments are available to facilitate phacoemulsification and irrigation/aspiration surgery in the larger equine eye. There are many phacoemulsification machines to choose from, including human or veterinary-specific machines. The phacoemulsification needles used in horses are typically longer than those used in canine or feline patients, and additional choices include flared tips as well as Kelman tips with or without a flare. These flared or angled tips are designed to engage the cataract better and emulsify the lens fragments more efficiently than the traditional needles; however, there are only a limited number of different needle tips available for use with the equine-specific handpieces. At present, three different (based on overall and optic dimensions) foldable equine-specific acrylic IOLs are commercially available. The different IOLs can be categorized by dioptric strength, as well as by total (haptic to haptic length) or optic diameter. The 14-D IOL comes in two sizes, with an optic diameter of 12 mm and a total length of 21 mm or an optic diameter of 13 mm and a total length of 22 mm; these IOLs are generally recommended for implantation in foals following phacoemulsification of congenital cataracts or in small ponies, respectively. The other IOLs have a dioptric strength of 21 D and 18 D and a total length of 24 mm. The 21-D, 18-D, and 14-D IOLs have been implanted in adult equine globes following phacoemulsification, with variable post-operative refractive results [61, 62, 73, 119]. The 18-D and 14-D IOLs both result in post-operative refraction within ± 1.00–1.50 D of emmetropia [73, 119, 123]. Based on the small number of horses with IOLs evaluated to date, the ideal IOL refractive power for adult horses appears to be between 18 D and 14 D [73, 119, 126].

Special lens-holding forceps and implantation forceps, specifically designed for the horse, facilitate introduction of the IOL into the capsular bag following phacoemulsification. An equine eyelid speculum prototype is being tested that provides both uniform opening of the palpebral fissure and elevation of the eyelids, decreasing or eliminating tension on the globe during surgery (Figure 9.47).

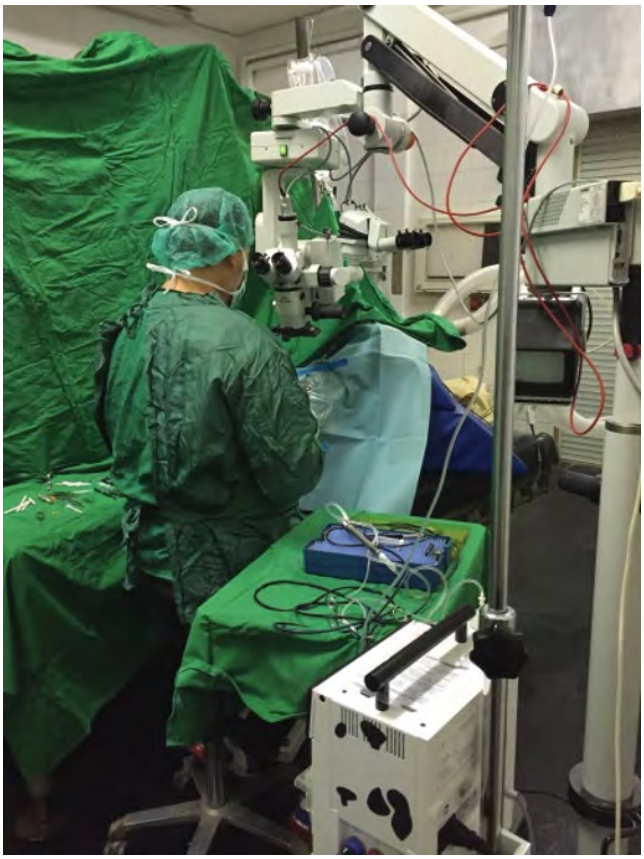


Figure 9.46 A fully draped horse during phacoemulsification.

Surgical techniques

Four different surgical techniques have been previously described for the removal of equine cataracts: aspiration, extracapsular lens extraction, intracapsular lens extraction, and phacofragmentation (phacoemulsification) with aspiration [14, 66, 67, 124, 132, 148, 153]. Of these four, only phacoemulsification with aspiration can be recommended for modern routine cataract surgery. Although certain indications for both intra- and extracapsular lens extractions exist, they are infrequently encountered in most species. Clear corneal incisions (CCIs) or limbal-based incisions beneath a conjunctival flap serve as the surgical approach for the techniques listed above. In young foals, it is often possible to

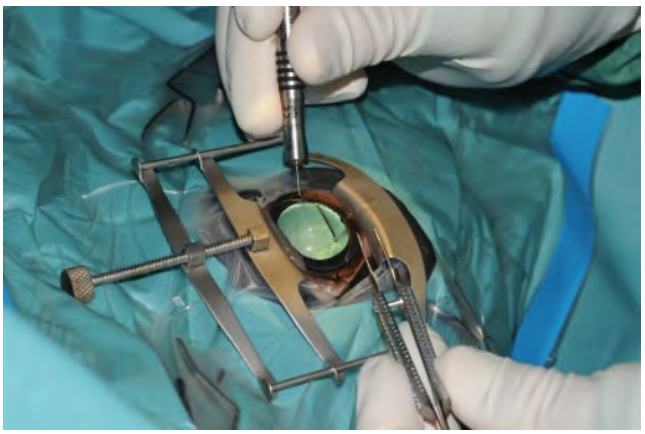


Figure 9.47 An equine-specific eyelid speculum prototype is shown in place during the initial stage of high-frequency diathermy anterior capsulotomy. The prototype provides uniform opening of the palpebral fissure and elevates the eyelids away from the cornea, thus minimizing pressure on the globe.

aspirate the entire lens because of their soft, liquid state, and aspiration with or without phacoemulsification is recommended.

Phacoemulsification with aspiration

Small-incision phacoemulsification with aspiration utilizing instrumentation specifically modified for the equine eye is the current standard of care for cataract surgery in the horse [47, 61, 62, 66, 73, 124–127, 131, 143, 150].

Following positioning, sterile preparation of the surgical site, and draping of the surgical field, an eyelid speculum is placed to maintain adequate exposure of the globe during surgery. Either a subconjunctival, scleral-based incision [124] or a CCI can be made to allow access to the anterior chamber; choice is based on surgeon preference. The scleral-based approach has the advantage of positioning the incision further away from the pupillary margin, reducing the risk of intraoperative iris/corpora nigra prolapse, and is potentially associated with less astigmatism. This type of incision is also covered by conjunctiva following primary closure [14, 124]. A disadvantage of the scleral-based incision is hemorrhage that may gain access to the anterior chamber and obstruct the surgeon's view during the procedure.

Commonly, a two-step (bilaminar) CCI is made approximately 1–2 mm axial and parallel to the limbus at approximately the 2 o'clock position medial or lateral to the corpora nigra. An initial 4-mm corneal groove (approximately 90% corneal depth) is made using a #64 microsurgical blade (Beaver blade), followed by penetration of the remaining 10% corneal depth at an approximately 45-degree angle through the center of the initial groove incision using a tapered, beveled keratome (2.8 mm). The advantages of a CCI are lack of hemorrhage in the surgical field and ease of access to the lens due to the angle of approach. Disadvantages of the CCI are possible scarring at the incision site (cosmetic) and potential corneal astigmatism induced by creation and closure of the incision. CCIs are routinely closed with simple interrupted or continuous suture patterns using absorbable microsurgical suture material (8-0 or 9.0 polyglactin 910, Vicryl or Catgut GmbH), with or without placement of a small conjunctival hood graft over the incision.

A modification to the CCI described above is the creation of a trilaminar (three-step) corneal incision that is truly self-sealing [151, 152]. The initial groove is made as described above for the bilaminar CCI, and is followed by a 2-mm tunnel incision that is initiated at a depth of approximately 50% of the initial incision. The 2-mm tunnel is created by inserting a #64 microsurgical blade through the initial groove incision (depth of approximately 50%) and extending the blade axially, angling slightly toward the corneal endothelial surface. A small amount of viscoelastic material can then be injected through the initial groove and into the 2-mm tunnel to ensure that the correct plane is followed with the beveled keratome for final entry into the anterior chamber. Finally, a beveled keratome is inserted through the initial groove and tunnel incisions, and the remaining deep layers of the cornea are penetrated at an approximately 45-degree angle, allowing access to the anterior chamber (Figure 9.48) [153].

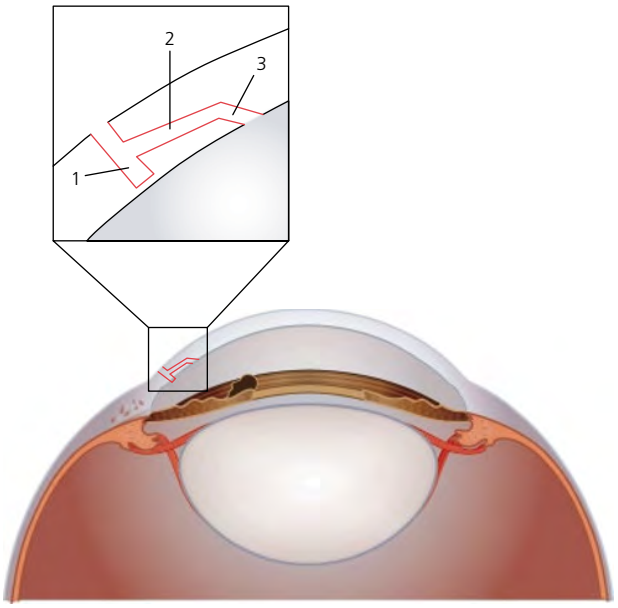


Figure 9.48 A trilaminar CCI [155, 156]. 1, Initial groove made to a depth of approximately 90% corneal thickness. 2, Stromal tunnel initiated from the initial groove at a depth of approximately 50%. This tunnel should have a length of 2 mm and is angled slightly toward the posterior aspect of the cornea. 3, Penetration of the posterior cornea (remainder of corneal stroma, Descemet's membrane, and corneal endothelium) is achieved by inserting a beveled keratome through the initial incision (1) and stromal tunnel (2) and entering the anterior chamber at an approximately 45-degree angle. A small amount of viscoelastic can be injected into the stromal tunnel (2) prior to insertion of the keratome to ensure placement into the original tissue plane [156] (*Source*: Modified from Langerman 1994 [152]).

By performing the CCI in this manner, a proximal hinge is created at the base of the incision, which prevents the incision from leaking. This is especially advantageous in the horse, as it prevents the iris/corpora nigra from migrating to the corneal incision during phacoemulsification of the lens and aspiration of the cortex, as well as during insertion of the IOL following extension of the CCI. This technique allows for a completely formed anterior chamber throughout the surgical procedure, and additionally helps to decrease the amount of viscoelastic utilized throughout the surgery (Figures 9.49 and 9.50).

An anterior capsulotomy is performed to provide an opening through which the lens nucleus and cortex can be emulsified and aspirated. The capsulotomy can be performed traditionally as a capsulorhexis or alternatively with the assistance of high-frequency diathermy (Figures 9.47 and 9.51).

A traditional capsulorhexis is performed following penetration of the anterior lens capsule with either the tip of the beveled keratome immediately following penetration of the anterior chamber, or multiple interconnecting stab incisions with a small-gauge needle (27 G), to form a small curvilinear opening to allow insertion of Utrata forceps. The circular capsulorhexis is made by grasping the leading edge of the anterior lens capsule flap at the site of the initial incision and tearing the capsule in a clockwise manner, regrasping periodically to prevent radial

tears, until the opposite side of the initial incision is reached. Once it has been ensured that the circular capsulotomy is no longer attached to the anterior lens capsule, it is removed from the anterior chamber. The capsulotomy should be approximately 1 mm smaller in diameter than the optic diameter of the IOL that will be inserted following phacoemulsification and aspiration of the lens. Use of a high-frequency diathermy tip to perform the capsulotomy greatly reduces the risk of radial tears, and allows for a more accurately sized opening and consistently axial placement of the anterior lens capsule [73, 154].

As mentioned, phacoemulsification with aspiration is the technique of choice for routine cataract surgery in the horse [14, 47, 73, 74, 118, 119, 124–126]. It involves the use of high-frequency ultrasonic vibrations to break down, or emulsify, the lens, and aspiration of the cortex and nucleus through a single needle. Phacoemulsification and aspiration are most commonly performed through a single incision, via a single needle which infuses irrigating solution, aspirates, and provides ultrasonic phacoemulsification [75]. Several fluid types have been used to irrigate and maintain the anterior chamber during cataract surgery in the horse [66, 67, 155]. Balanced saline solution and lactated Ringer's solution, warmed to 37 °C (98.6 °F), are most commonly used. Heparin, epinephrine, and sodium bicarbonate have also been added to the irrigation fluids during intraocular

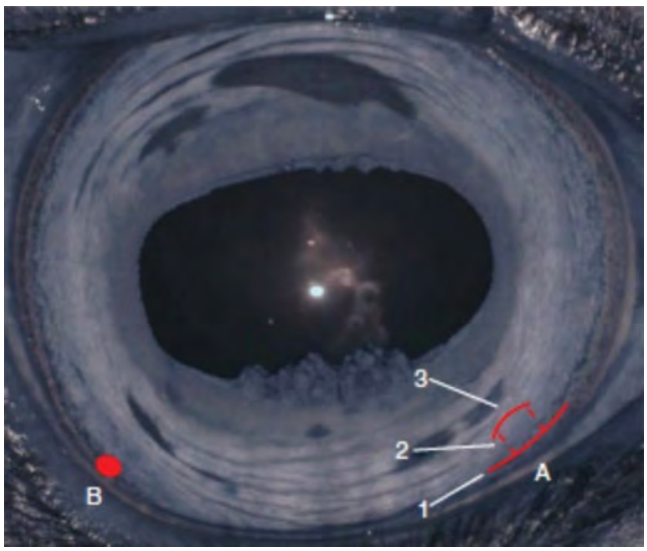


Figure 9.49 Infrared image of an equine globe demonstrating trilaminar CCI construction and placement of a second incision for a planned two-handed phacoemulsification procedure. A, Suggested position, temporal or medial to the corpora nigra, for construction of a trilaminar CCI. A1–3, Placement of a second incision, approximately 3 to 4 o'clock position away from the CCI. Incision is created using a 20-G needle to tunnel through the cornea, beginning just posterior to the limbus. A second instrument, used to assist with phacoemulsification of the lens or manipulation of the IOL implant can be introduced through this incision. B, Site of accessory port access for lens manipulator.

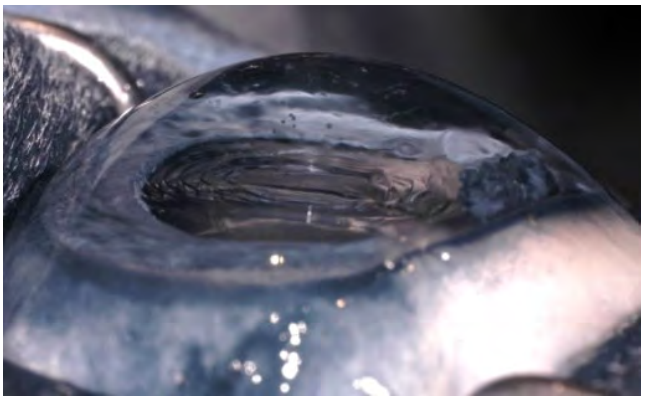
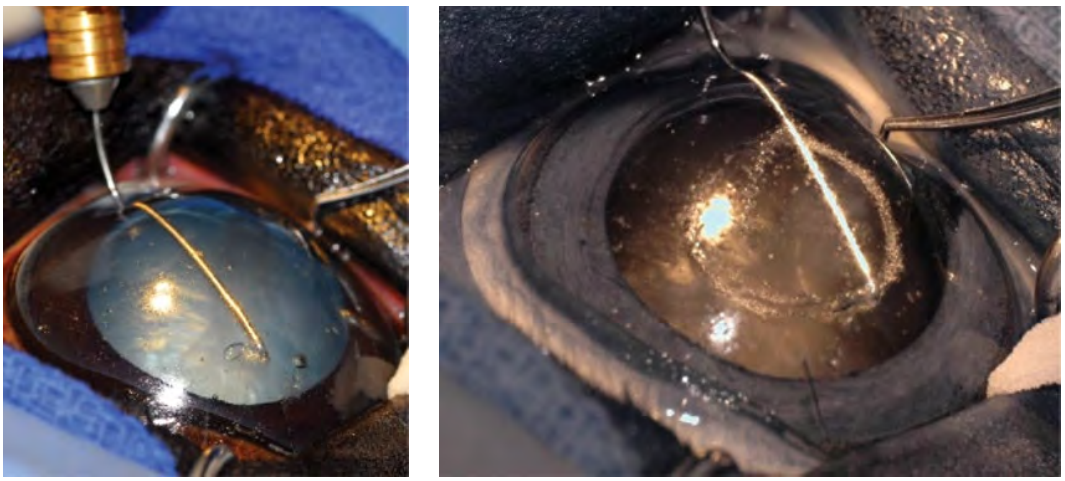


Figure 9.50 Infrared image demonstrating a formed anterior chamber (AC) and immediate post-implantation view of an 18–D, foldable, equine-specific IOL implant. Note the formed AC and IOL position. Small air bubbles suspended in the viscoelastic substance within the AC appear as small, dark, punctate areas, in contrast to the lighter iridal background.



(A) (B)

Figure 9.51 Intraoperative color (A) and infrared (B) images of high-frequency (HF) diathermy-assisted anterior capsulotomy being performed. Target capsulotomy size is 12 mm in diameter (equine IOL optic diameter is 13 mm). HF diathermy allows for a precise, axial capsulotomy. The risk of radial tears, which can make IOL insertion difficult or impossible, is minimized with this technique.

surgery in horses [75]. During phacoemulsification, a viscoelastic substance is introduced into the anterior chamber to maintain its shape and to protect the corneal endothelium from injury [156, 159]. If a single incision or one-handed technique is used, the phacoemulsification needle is introduced through the opening in the anterior lens capsule (Figure 9.52). The lens cortex and nucleus are emulsified and aspirated, with great care taken to avoid penetrating the posterior lens capsule, which is extremely thin and highly mobile within the globe following removal of the lens material [75, 124].

A second stab incision can be made by introducing a 20-G needle or 1-mm keratome into the anterior chamber at a point approximately 4 o'clock position away from the initial CCI, on the opposite side of the superior corpora nigra (Figure 9.53). A second instrument (e.g., nucleus rotator) can be introduced through this incision, and can be used to assist in phacoemulsification by increasing stabilization and/or manipulating or breaking up of the lens (i.e., two-handed phacoemulsification) (Figure 9.54).

Following emulsification of the cortex and nucleus, the phacoemulsification needle is removed. It is then replaced with an irrigation/aspiration tip (0.5 mm diameter) that is used to remove all remaining lens cortex from the equatorial region of the capsular bag (Figure 9.55). For complete removal of the peripheral cortex from the lens capsule, a longer, equine-specific irrigation/aspiration needle is essential.

Once the cataract has been successfully emulsified and the remaining cortex has been aspirated, the lens capsule and anterior chamber are re-inflated with a viscoelastic substance if an IOL is to be implanted into the eye (Figure 9.56). If pre-existing or intraoperative complications prevent IOL implantation, the corneal incision(s) are closed using 8-0 or 9.0 polyglactin 910 using the surgeon's preferred suture pattern. If an IOL can be implanted, the CCI is extended to allow for introduction of the lens. Currently, equine IOLs must be manually implanted using lens-folding forceps to maintain the lens in a folded position

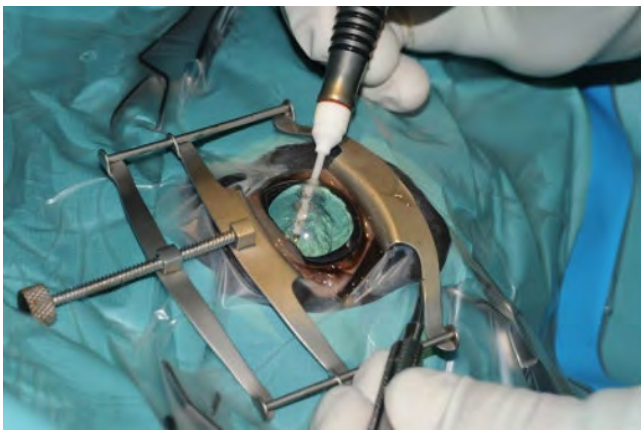


Figure 9.52 Initial stage of the phacoemulsification process. The needle tip forms the initial groove within the anterior lens cortex.

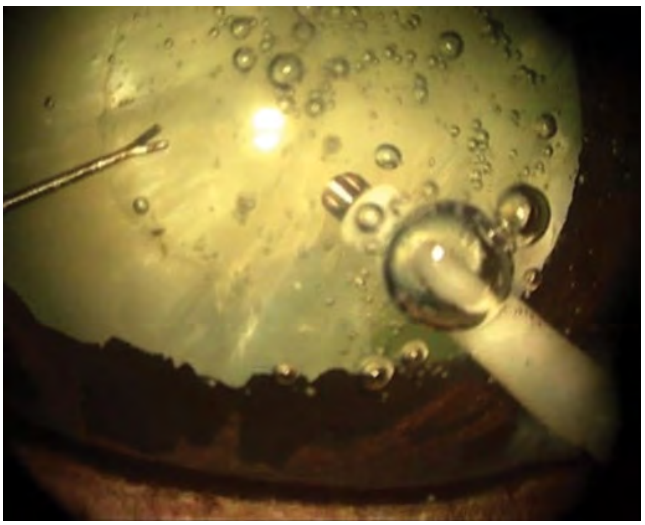


Figure 9.54 Intraoperative digital image demonstrating two-handed phacoemulsification being performed. The phacoemulsification needle is on the right and an equine-specific nucleus rotator can be seen to the left.



Figure 9.53 A 20-G needle creates a second incision at the 2 o'clock position, which provides access to the anterior chamber for a second instrument. The trilaminar CCI can be seen at the 10 o'clock position (relative to the globe's normal position).

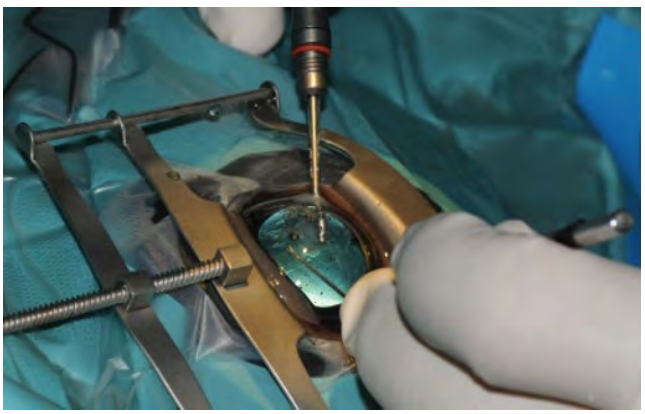


Figure 9.55 Irrigation/aspiration of the lens capsule follows phacoemulsification of the lens nucleus and cortex. Note, a two-handed technique is being used, with the non-dominant hand (links) utilizing a second instrument (nucleus rotator) to help direct cortical lens material towards the irrigation/aspiration tip.

while being introduced into the lens capsule through the extended CCI (Figure 9.57). A lens rotator inserted through the initial or second incision can be useful in ensuring proper IOL introduction and positioning of the haptics (Figure 9.58).

The IOL haptics are commonly placed in a horizontal (3 to 9 o'clock) position (Figure 9.59), as opposed to a vertical (12 to 6 o'clock) position, if possible, to allow for a more aesthetic appearance within the horizontally elongated equine pupil. Following introduction and positioning of the IOL, the corneal incision(s) is/are closed using 8-0 to 9.0 polyglactin 910 using the surgeon's preferred suture pattern. We do not routinely remove the viscoelastic from the anterior chamber via irrigation/aspiration in our equine patients. If one chooses to remove the viscoelastic substance, this should be performed prior to final closure of the incision. Once the incision is closed, the globe is reinflated to an IOP of approximately 15–20 mm Hg (this may be confirmed via tonometry) and the incision is examined, via fluorescein (e.g., Seidel test) (Figure 9.60), to ensure that a watertight seal has been established.



Figure 9.58 Infrared image of a lens rotator placed through the original, extended trilaminar CCI, being used to reposition the IOL implant within the capsular bag.

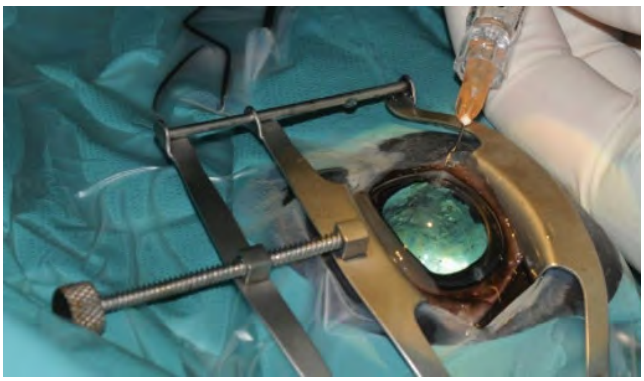
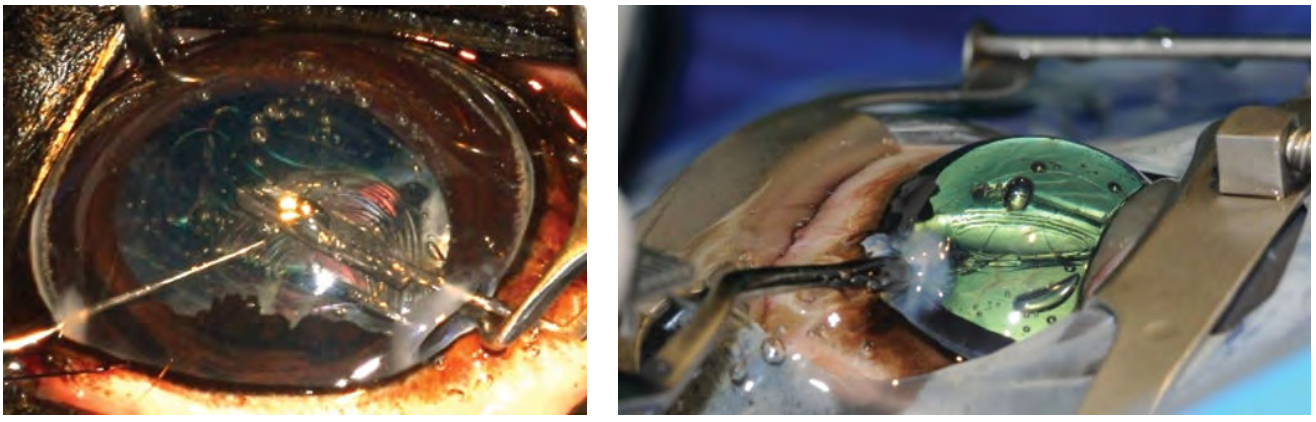


Figure 9.56 Injection of viscoelastic substance into the anterior chamber and capsular bag following phacoemulsification and irrigation/aspiration to facilitate implantation of an IOL.



Figure 9.59 IOL haptics have been placed horizontally to allow for a more aesthetic appearance within the horizontally elongated equine pupil. Due to the large size of the equine lens, posterior capsular folds (as can be seen spanning the pupil from approximately 9:30 to 3:30 o'clock positions) are relatively common.



(A) (B)

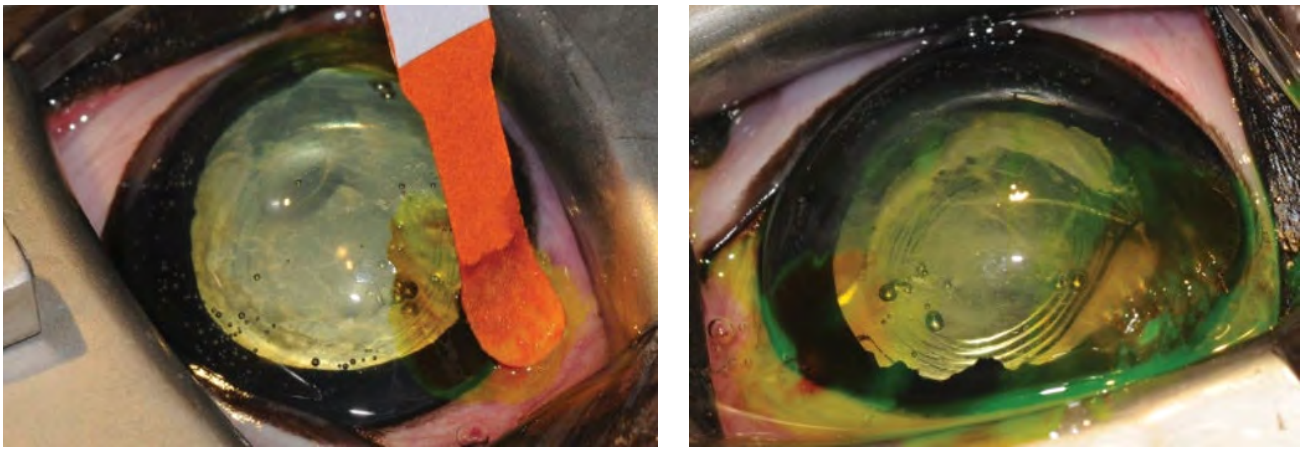
Figure 9.57 (A) Manual insertion of a foldable, equine-specific, 18-D IOL through a trilaminar CCI. A two-handed technique is being used, with an equine-specific nucleus rotator inserted through the second incision to assist with proper IOL placement. (B) An 18-D IOL is being inserted through an extended trilaminar CCI using IOL insertion forceps.

Extracapsular and intracapsular lens extraction

Both extracapsular and intracapsular lens extractions require larger incisions than with phacoemulsification. Larger incisions increase the risk of complications including extrusion of the iris and corpora nigra, vitreous herniation, secondary glaucoma, and retinal detachment [80, 158]. Lens luxation in horses is rare and newer phacoemulsification units are powerful enough to emulsify most lenses, even those with compromised support.

Post-operative management

Typical post-operative management of equine cataract patients includes topical and systemic anti-inflammatory medications and antibiotics (Table 9.2). If a corneal ulcer is not present, then topical corticosteroids are used every 4–6 hours. Some surgeons also use topical NSAIDs (e.g., flurbiprofen, diclofenac, nepafenac, bromfenac). All patients receive broad-spectrum antibiotic medications. Systemic NSAIDs (e.g., flunixin-meglumine) are used in all patients at a tapering dose over 2–4 weeks. Systemic



(A) (B)

Figure 9.60 (A) A Seidel test, using concentrated fluorescein, is being applied to the trilaminar CCI after closure following phacoemulsification and implantation of a +14-D IOL in a 6-month-old Swedish Warmblood foal. Failure to achieve a watertight corneal incision allows aqueous humor to leak from the anterior chamber, resulting in a hyperfluorescent line of fluid continuously running through the applied ring of fluorescein applied to the suture line. (B) This is the same CCI as in **(A)**, shown from a different angle. The Seidel test was negative, confirming a watertight incision.

Table 9.2 Post-operative treatment protocol for equine cataract surgery patients.

Drug	Dose and route of administration	Frequency	Duration
Systemic medications			
Trimethoprim sulfa (TMS)§	20 mg/kg PO	q12h	7–14 days
Cefquinom*	1 mg/kg IV, IM	q24h	7 –10 days
Flunixin meglumine	1.1 mg/kg IV, PO	q12–24 h	10–14 days
	0.55 mg/kg IV, PO	q12–24 h	10–14 days
Omeprazole	2 mg/kg PO	q24h	14–28 days
Topical ophthalmic medications			
Corticosteroids			
Neomycin-polymyxin B sulfates Dexamethasone§	0.1 mL SPL	q6h	Tapering dose over 3-month period
Prenisolone acetate*	0.1 mL SPL	q6h	Tapering dose over 3-month period
Antibiotics			
Neomycin-polymyxin B sulfates Dexamethasone§	0.1 mL SPL	q6h	Tapering dose over 3-month period
Moxifloxacin§	0.1 mL SPL	q6h	5–7 days
Cefquinom (fortified)*	0.1 mL SPL	q6h	30–60 days
Nonsteroidal anti-inflammatories (NSAIDs)			
Bromfenac	0.1 mL SPL	q12h	Tapering dose over 3-month period
Mydriatics			
Atropine sulfate 0.5–1%	0.1 mL SPL	q12h, reduce to q24–48 h following maximum mydriasis	28 days

IV, Intravenous; IM, intramuscular; kg, kilogram of body weight; PO, per os (oral); SPL, through subpalpebral lavage catheter.
* Equine Clinic Munich-Riem.
§ North Carolina State University.

antibiotics are typically used perioperatively and continued for 5–7 days post-operatively. If a corneal ulcer develops, topical corticosteroids are discontinued and only topical NSAIDs are used in their place. Newer generation NSAID drops (i.e., nepafenac and bromfenac) are almost, if not as effective as topical corticosteroids and have been shown to effectively control inflammation and decrease long-term secondary capsular opacification [159, 160].

Specific post-operative diagnostic tests should be performed following cataract surgery in all equine patients. Serial post-operative ophthalmic examinations and tonometry will help the clinician to recognize early signs of post-operative complications that may necessitate changes in medical management. Streak retinoscopy and ocular ultrasonography provide important data on the refractive state of the globe and the post-operative IOL position (Figure 9.61), respectively. These data are extremely important for the development and refinement of equine IOLs, and ocular ultrasonography also allows the clinician to evaluate the posterior segment of the eye in those cases in which post-operative inflammation or infection preclude direct visualization [24, 95, 116, 118, 119, 123, 126, 142].

Complications and sequelae

Potential issues present prior to surgery

Some cataractous lenses can have problems that will complicate the intraoperative procedure as well as increase the incidence of post-operative complications. These include lens capsule rupture, active uncontrolled uveitis, lens instability, posterior or anterior synechia, pre-existing lens capsule fibrosis, and vitreal herniation into the anterior chamber. Pre-operative identification of any of these findings allows for proper surgical planning.

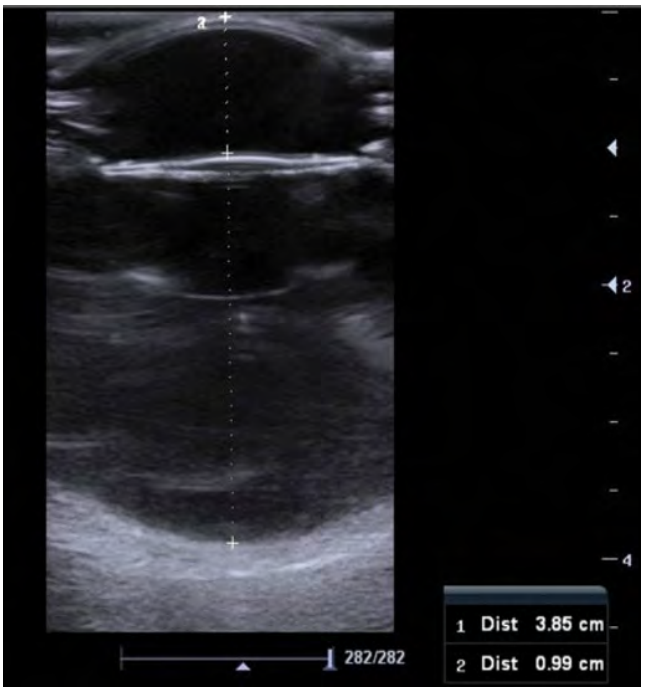


Figure 9.61 Post-operative ocular ultrasound image from a 1.5-year-old Arabian filly. 1, Axial globe length (AxL). 2, Post-operative anterior chamber depth (PACD). PACD represents the IOL distance from the cornea following implantation, and has a significant effect on the post-operative refractive state of the globe.

Potential issues during surgery

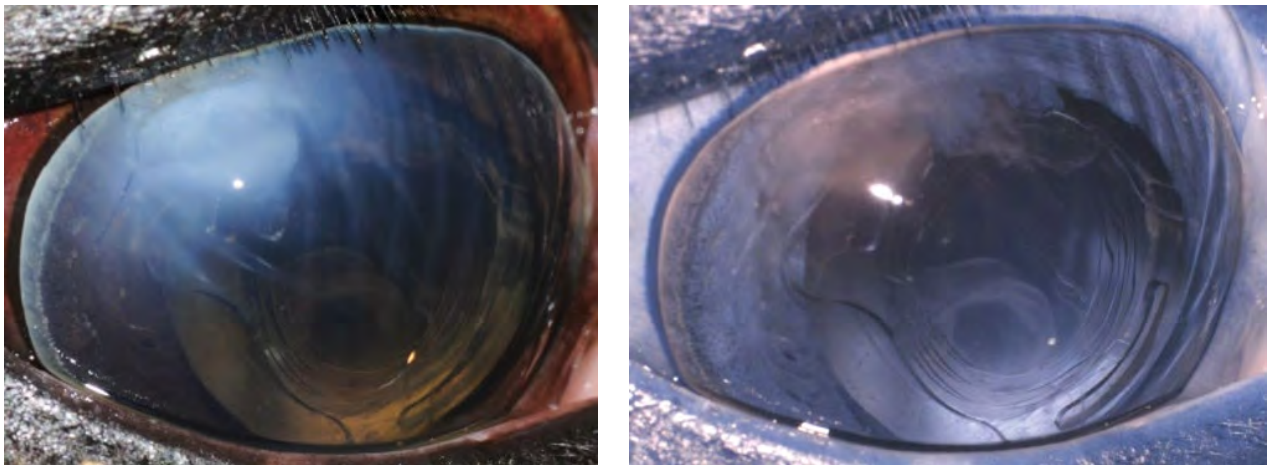
Intraoperative complications include posterior lens capsule tears, vitreal presentation through the posterior lens capsular tear, and loss of lens material into the vitreous through a lens capsule rupture. The risk of posterior capsular tears can be minimized, if not avoided, with careful technique, proper use of viscoelastic material, surgical experience, and patience. If they do occur, cohesive viscoelastic material is used to tamponade the vitreous and avoid its herniation into the lens capsule [158]. Even small posterior capsule tears can enlarge due to vitreous bulging anteriorly through the capsular tear [66]. Loss of small fragments of lens material into the vitreous slowly resorb and usually do not cause excessive inflammation [161]. However, larger fragments of cortical material are very inflammatory and efforts should be made to remove them from the vitreous either using viscoelastic material to float them anteriorly or with the use of a vitrector.

Other complications include hemorrhage and iris or corpora nigra herniation through the incision, and miosis [161]. Uncontrolled hemorrhage may be difficult to contain, depending upon where it originates. Some can be stopped by injecting 1:10,000 epinephrine at the site of hemorrhage [162], and viscoelastic material can also be used to stop bleeding. Hemorrhage that has leaked into the vitreous resolves very slowly and predisposes to retinal detachments.

Prolapse of the iris or corpora nigra in horses frequently occurs during cataract surgery. One major cause is injection of an excessive amount of viscoelastic material into the anterior chamber. The viscoelastic material then gains access to the posterior chamber beneath the iris adjacent to the incision, causing the iris and corpora nigra to migrate towards the incision. Iris or corpora nigra prolapse can also occur upon removal of the phacoemulsification needle from the anterior chamber. Careful repositioning of the prolapsed iris is performed, though the iris may be prone to hemorrhage when manipulated.66 The risk of iris and/or corpora nigra prolapse can be minimized by construction of a trilaminar CCI [151–153].

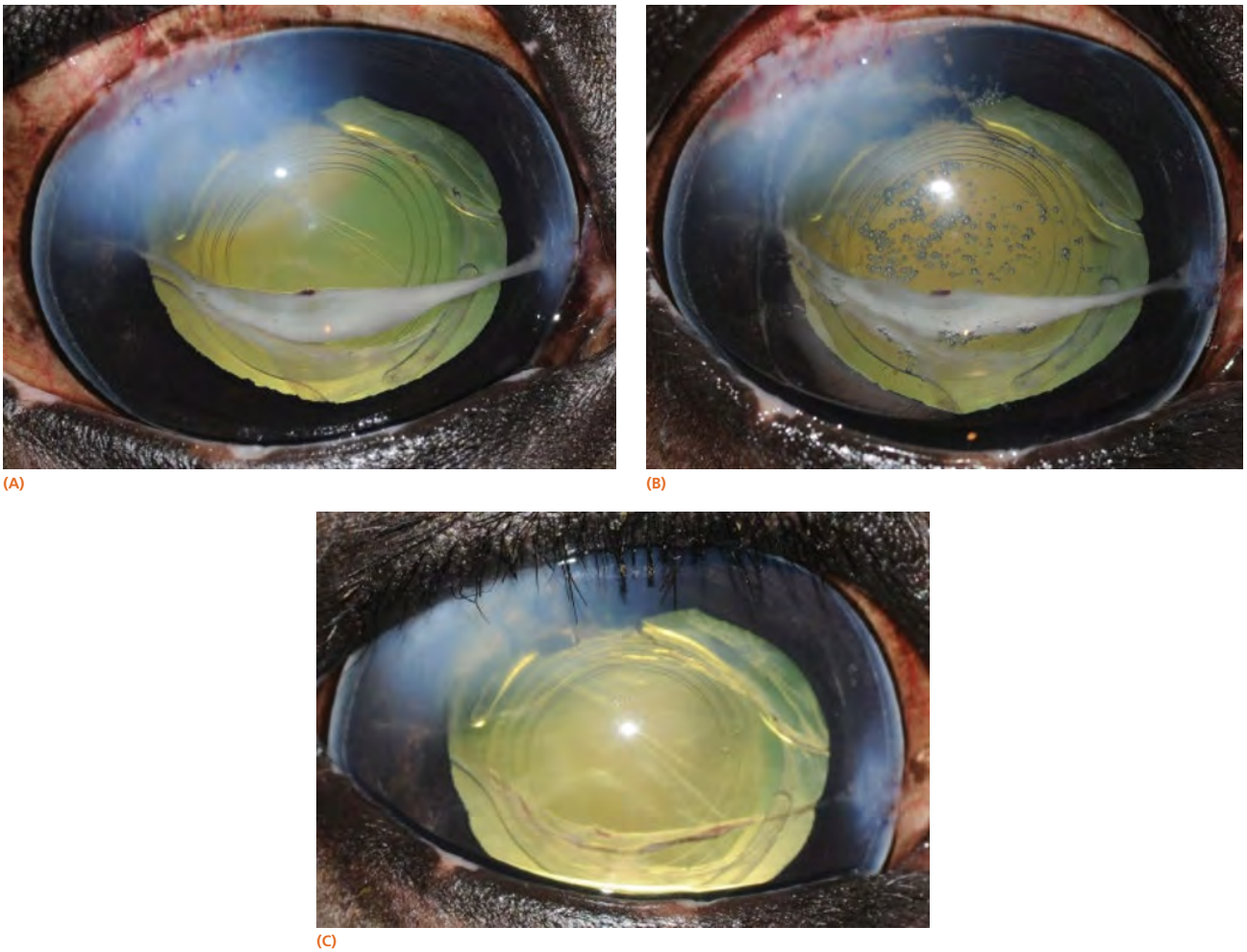
Potential issues following surgery

Post-operative complications include those that occur immediately (within hours) following surgery and those that occur days later. Common post-operative complications that occur immediately after or soon after cataract surgery in horses include fibrin formation in the anterior chamber, hyphema, decreased menace response, vitreal prolapse into the anterior chamber, corneal incision suture rupture, anterior IOL displacement (Figure 9.62), and dislocation of a concurrently implanted cyclosporine implant [47]. Persistent fibrin and contracted blood clots can be dissolved using intracameral tissue plasminogen activator (TPA) (Figure 9.63). Other complications a corneal



(A) (B)

Figure 9.62 (A) Subtle corneal folds (seen as vertical opacifications in the cornea extending from the dorsal limbus) indicate a hypotonic globe. CCI closure has ruptured (note the suture tag on the surface of the dorsotemporal cornea) and only a small amount of aqueous humor remains in the anterior chamber (AC). The IOL has prolapsed through the anterior capsulotomy and into the AC. (B) View of the IOL haptic anterior to the iris is enhanced in infrared.



(A) (B) (C)

Figure 9.63 (A) A thick band of fibrin can be seen spanning the anterior chamber (AC) from the 10 to 3 o'clock positions and appears to be associated with the primary and secondary corneal incisions approximately 6 days following repositioning of the IOL within the capsular bag. (B) Immediately following intracameral TPA injection. Note the air bubbles in the anterior chamber. They were introduced at the end of the TPA injection and were completely resolved by 20 hours post TPA injection (see C). (C) Approximately 20 hours post TPA injection. Only a small band of fibrin remains within the AC, and completely resolved within the following 72 hours.

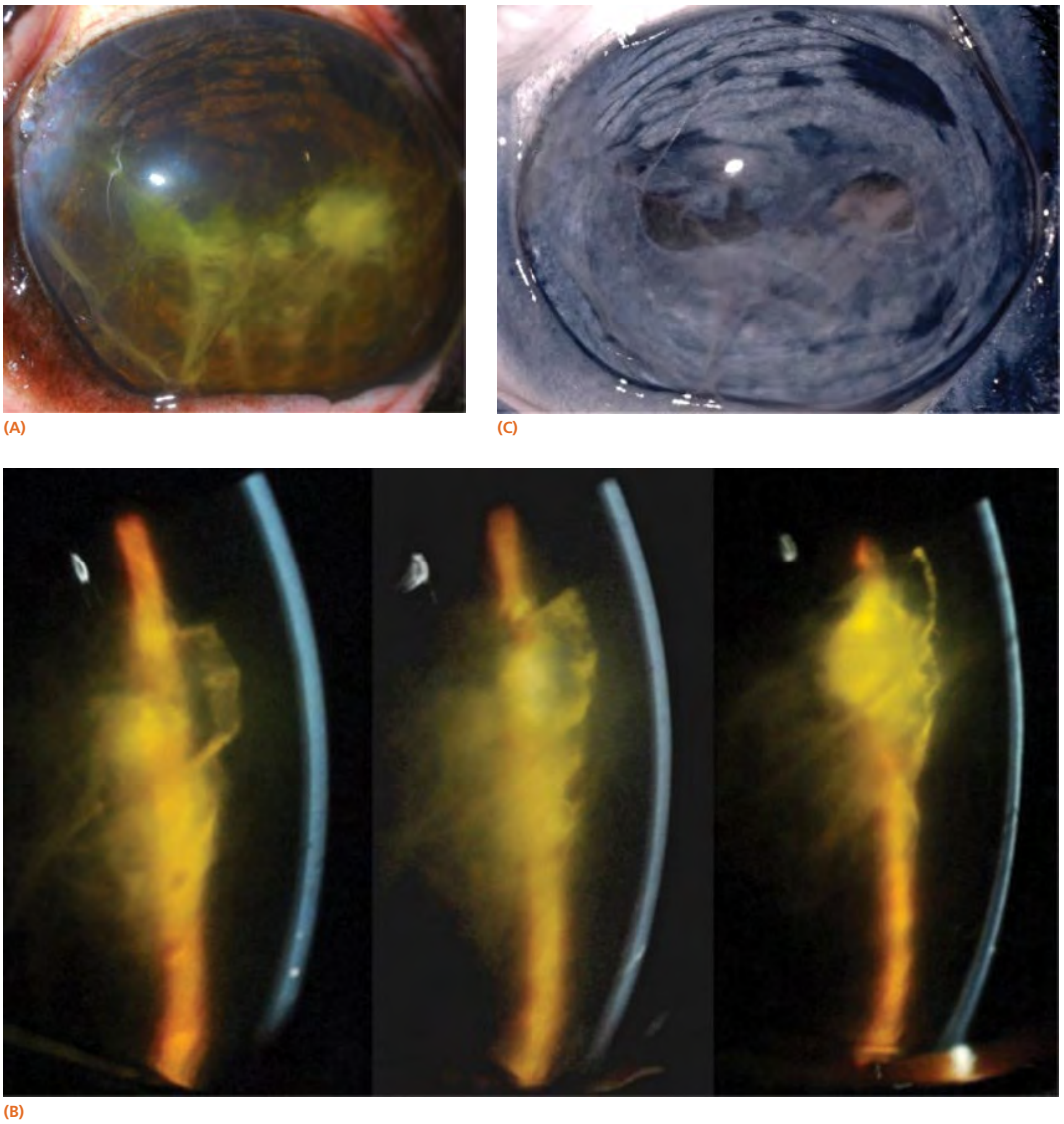


Figure 9.64 (A) Severe, uncontrollable panuveitis that developed approximately 3 weeks following phacoemulsification and implantation of an 18-D, foldable, equine-specific IOL. (B) Slit-lamp images highlighting fibrin accumulation within the anterior chamber (AC). Note consolidation of inflammatory debris within the posterior aspect of the AC and the relatively clear zone closer to the cornea. (C) Clearer infrared view of the anterior iridal surface and pupillary margin. Note that fibrin within the AC is not as readily visible as in the color image **(A)**, but the infrared image provides an unobstructed view of the focal posterior synechia located at the 6 o'clock position of the pupil.

edema, post-operative ocular hypertension, and corneal ulceration [47, 61, 66]. Due to the use of topical corticosteroids during the post-operative treatment period, any corneal ulcer that develops must be closely monitored for signs of fungal keratitis and treated aggressively immediately upon detection.

Complications occurring beyond the immediate post-operative period include chronic uncontrollable uveitis (Figure 9.64), posterior synechia and resulting dyscoria (Figure 9.65) or iris bombe, retinal detachment, and endophthalmitis (Figures 9.31 and 9.66) [47, 61, 66]. Endophthalmitis is the most serious sight-threatening complication that can occur in the relative immediate post-operative period. *Streptococcus* spp. and *Staphylococcus* spp. were the most common bacterial organisms cultured in one study [66]. Chronic, unrelenting uveitis can occur due to pre-existing ERU [47, 61, 62].

Other long-term complications following cataract surgery include fibropupillary membranes and endothelial degeneration resulting in diffuse corneal edema [61, 164]. In foals that had undergone phacoemulsification, the trainers or owners thought the animals had visual impairment at night or in dim light, though their day vision was good [67]. The most common long-term post-operative complication was posterior capsular opacification (Figures 9.40 and 9.67) [47, 61, 66, 67, 73, 82]. This is also the most common post-operative complication in all species evaluated,that is, dog and human, that undergo extracapsular cataract surgery [163–165]. In addition to using

cyclo-oxygenase (COX)-2 inhibitors post-operatively to reduce long-term posterior capsule opacification [162, 163], irrigation of the capsule with distilled deionized water or trypan blue, as well as implantation of IOLs, has been shown to reduce posterior capsule opacification in humans, and may be beneficial in horses as well [166–168].

Only one horse in a retrospective study of 36 horses (51 eyes) had glaucoma as a post-operative complication, though five horses developed post-operative hypertension that resolved with anti-inflammatory and antiglaucoma medications [47]. Two recent retrospective studies both reported three eyes each that resulted in enucleation due to secondary glaucoma [61, 62]. Although devastating when it occurs, glaucoma does not appear to be a major post-operative complication, though this may be due to aggressive anti-inflammatory therapy in the pre-operative and post-operative stages (see Figure 9.41).

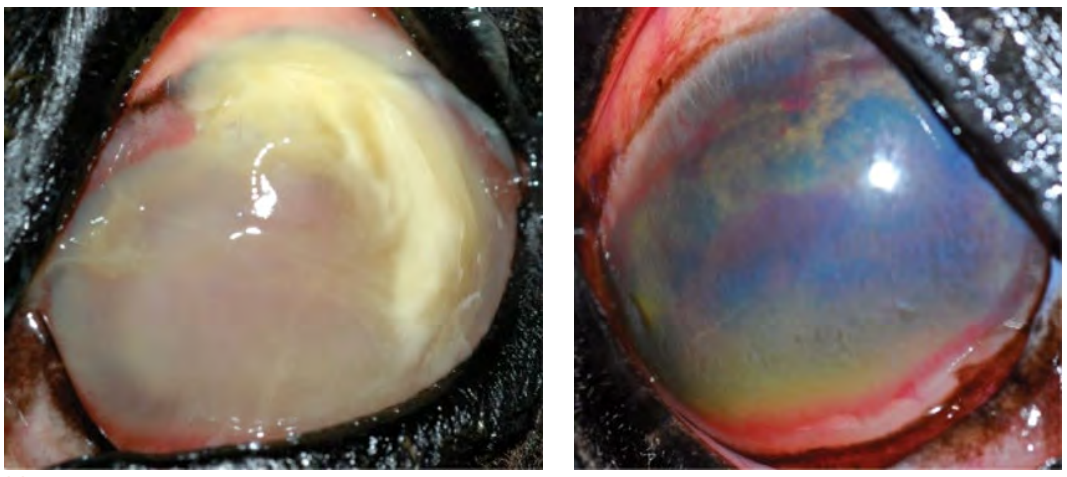
A study from 1983 involving foals reported that 10 of 13 eyes had vision 6 months following surgery, though five of these had reduced night vision and three had severe keratouveitis leaving



Figure 9.65 Intraoperative iris prolapse through the CCI resulted in this moderately misshapen pupil (dyscoria). This photograph was taken during the 6-month follow-up. Note the small, dense, white opacification within the central area of the IOL optic. This is a small posterior capsular plaque that was identified during surgery, following removal of the cataractous lens. It has remained unchanged throughout the post-operative follow-up period.



Figure 9.67 Mild posterior capsular opacification approximately 1 month following phacoemulsification and implantation of a 25–D, foldable, equine-specific IOL. Note the irregulary shaped (dyscoric) pupil that has resulted from intraoperative iridal prolapse through the CCI, and the small focal area of posterior synechia at the 4 o'clock position of the pupillary margin.



(A) (B)

Figure 9.66 **(A)** Severe endophthalmitis in a geriatric Quarter horse following extracapsular lens extraction through a large corneal incision ("open sky" technique). **(B)** Endophthalmitis in a 24-year-old Welsh Pony mare that developed between days 14 and 21 following phacoemulsification with subsequent IOL placement.

them with only light perception [67]. With improved surgical instruments and techniques and UV-protective IOLs, these complications should diminish. Overall, long-term visual outcome reported in the literature is good. However, loss to long-term follow-up continues to be a problem in the horse [47, 61, 62, 118, 119]. The increased use of IOLs in horses will presumably improve post-operative visual function and allow more horses to return to their prior level of performance following surgery.

Future research

Much progress has been made regarding the development and validation of an appropriate equine IOL since the first edition of this textbook was published. Although three different sized, commercially available, foldable, equine-specific IOLs, with different refractive powers, are currently available, substantial data supporting the use of one strength over another is lacking. Much work remains to be done before a universal equine IOL can be recommended. Ocular ultrasonography should be performed in every horse that presents for evaluation for cataract surgery, and pre-operative globe measurements should be obtained and recorded in a standardized manner. Following lens removal and IOL implantation, post-operative ultrasound data should again be collected. These data can be pooled nationally, or even globally, and regression analysis performed to help determine the most appropriate dioptric strength for an equine IOL.

Streak retinoscopy is a simple, but underutilized, diagnostic test that should be used regularly in pre- and post-operative cataract patients [116, 120–123]. Granted, if a horse presents with bilateral cataracts, it may not be possible to obtain reliable pre-operative refractive data. However, in horses with unilateral cataracts, the refractive state of the contralateral eye can be used to represent the pre-operative refractive state of the affected eye. The post-operative refractive state of the eye following IOL implantation via streak retinoscopy, along with the post-operative anterior chamber depth obtained with ocular ultrasonography, are the only objective means currently available to evaluate the ability of the eye to function visually following lens removal. The more widely used both of these diagnostic tests become, the more the reliability of the data will increase.

Electroretinography, although sporadically utilized as part of the pre-cataract surgery evaluation, is another underused diagnostic test in equine ophthalmology. In order to enhance our understanding of vision in horses, it is necessary to obtain more detailed information elucidating equine retinal function.

Current existing methods of the clinical evaluation of vision are both crude and inadequate. Efforts are being made to develop simple reproducible methods of visual field testing that will greatly benefit our ability to assess post-operative evaluation of cataract patients.

Improved surgical technique and instrumentation has continued to improve the success of cataract surgery in horses. Small-incision phacoemulsification and aspiration has greatly improved the surgical outcomes in all equine cataract patients. However, there is still much room for improvement with regards to corneal entry incisions to minimize the risk of intraoperative iris prolapse, anterior and posterior capsulotomy techniques, IOL design, appropriate dioptric strength, and insertion techniques. Additionally, in order to continue to improve long-term success of cataract surgery, especially concerning vision, appropriate and effective intraoperative and post-operative protocols to prevent posterior capsular opacification and which minimize vision-threatening complications must be continually refined.

Additional content

The book companion website at

www.wiley.com/go/gilger/ophthalmology

includes additional text and figures that are not in the printed book or E-book.

Please see the "**About the companion website**" page at the start of the book for details on how to access the website.

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CHAPTER 10

Glaucoma

David A. Wilkie, Anne J. Gemensky-Metzler, Mary Lassaline*, and Dennis E. Brooks*

Introduction

Glaucoma is a diverse group of ocular conditions that results in the loss of retinal ganglion cells (RGCs), degeneration of the optic nerve, and a loss of vision. This is most commonly a disorder of aqueous humor outflow resulting in an elevated intraocular pressure (IOP). It can occur as a congenital, primary, or secondary disorder, and secondary glaucoma is most common in the horse. In this chapter, the anatomy, physiology, etiologies, clinical signs, pathogenesis, and medical and surgical therapy of equine glaucoma are discussed.

Clinical anatomy and physiology

Aqueous humor production and outflow

To understand and treat glaucoma, it is first essential to understand the anatomy and physiology of the equine anterior uvea (iris and ciliary body). The ciliary body is divided into the anterior pars plicata and posterior pars plana. In the horse, the pars plicata consists of approximately 102 processes which are comprised of a stroma and vascular core covered by pigmented and nonpigmented epithelial cell layers [1, 2]. These processes produce the aqueous humor. The pars plana is bordered by the pars plicata anteriorly and the retina posteriorly. The equine ciliary body is asymmetrical, being wider anterior to posterior in the dorso- and ventrotemporal regions and narrower nasally [3]. (Figure 10.1) The internal length of the normal equine pars plicata ranges from 5.33 to 10.67 mm and the pars plana from 0.33 to 3.17 mm [3].

Understanding of the ciliary body anatomy and the changes in this anatomy as a consequence of chronic glaucoma are essential for the surgical treatment of glaucoma by either transcleral or endolaser cyclophotoablation [4]. At the anteriormost aspect of the ciliary body is the iris root, ciliary cleft, and iridocorneal angle (ICA). The ICA or ciliary cleft is bordered anteriorly by the peripheral cornea and perilimbal sclera and posteriorly by the peripheral iris and ciliary body (Figures 10.2 and 10.3). Extending from the base of the anterior iris to the inner limbus are broad pectinate ligaments that span the ciliary cleft, and in the horse, these are clinically visible at the nasal and temporal limbus. Within the ciliary cleft is the trabecular meshwork through which aqueous humor drains [5–8].

Knowledge of aqueous humor formation and the structure of the aqueous humor drainage apparatus is critical to understanding glaucoma in horses. The aqueous humor is continuously produced by the ciliary body to supply the metabolic needs of several avascular intraocular structures (cornea, lens, trabecular meshwork). Aqueous humor is formed primarily by active secretion by the ciliary processes of the pars plicata, utilizing energy and the enzyme carbonic anhydrase. This enzymatic production can be inhibited pharmacologically through the administration of carbonic anhydrase inhibitors. A small portion of aqueous humor production also arises from passive diffusion and ultrafiltration of blood in the ciliary body circulation. To maintain a steady state, aqueous fluid circulates and then drains through the ICA (conventional) and uveoscleral (unconventional) outflow pathways (Figure 10.4) [7].

Once formed, aqueous humor flows from the posterior chamber, through the pupil into the anterior chamber to the ICA and finally exits through the trabecular meshwork, the intrascleral plexus and into the vortex veins. Aqueous humor flows between the pectinate ligaments into and through the cell-lined trabecular beams of the uveal trabecular meshwork (UTM), the corneoscleral trabecular meshwork (CSTM), the angular aqueous plexus (AAP), and then into the intrascleral plexus (ISP) in the conventional outflow pathway. The aqueous humor then drains from the ISP into the vortex veins that empty into the choroid. The UTM, CSTM, and AAP compose 74.3%, 21.5%, and 4.2% of the equine ICA area, respectively [5, 7, 8]. In addition, aqueous humor drains via the iris, ciliary body, and

*Drs Lassaline and Brooks were the authors of the glaucoma chapter in the second edition of *Equine Ophthalmology*. Approximately 20–30% of this previous chapter has been updated for the third edition of *Equine Ophthalmology*.

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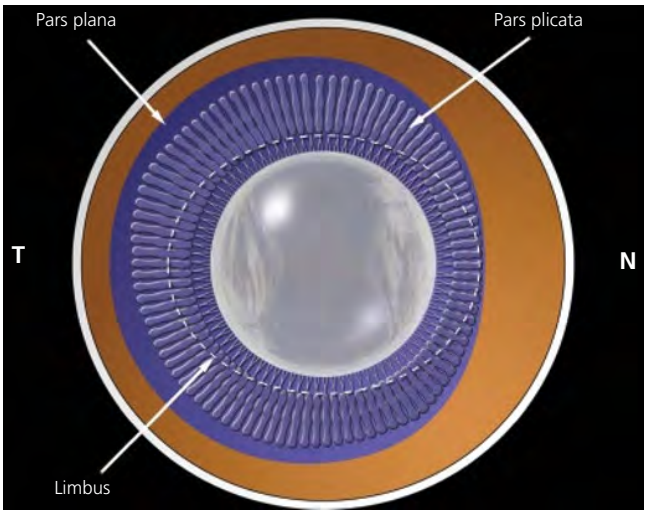


Figure 10.1 Schematic of the equine ciliary body as viewed posteriorly, demonstrating asymmetry of nasal (N) and temporal (T) aspects.

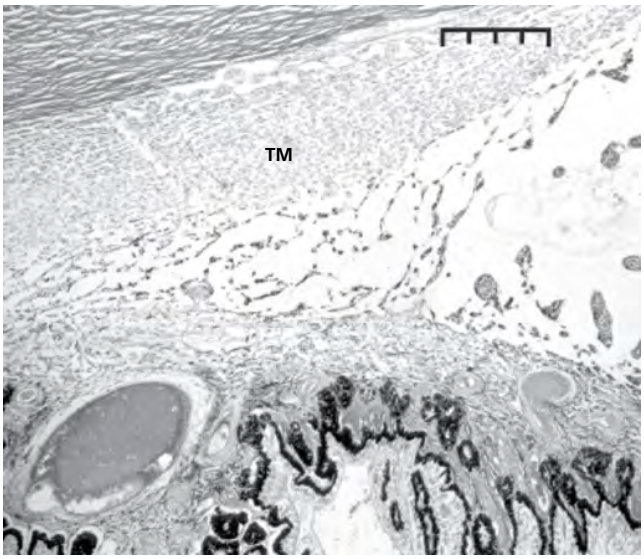


Figure 10.2 Trabecular meshworks (TM) of the ICA of the horse are very large, wide, and open for the conventional outflow of aqueous humor (periodic acid-Schiff stain; bar = 70 mm).

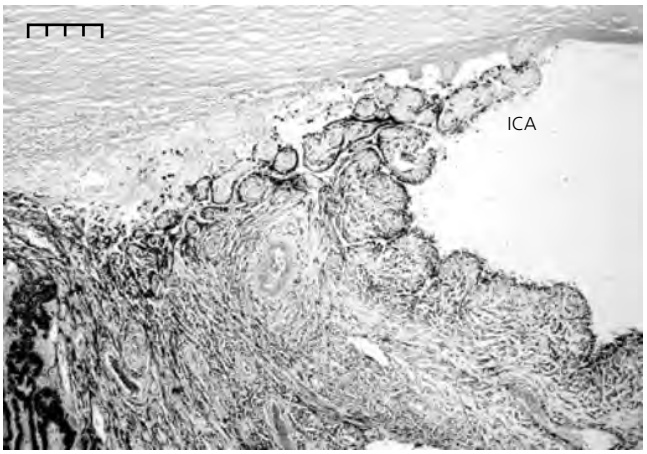


Figure 10.3 The ICA and trabecular meshworks of this horse with glaucoma have collapsed (periodic acid-Schiff stain; bar = 80 mm).

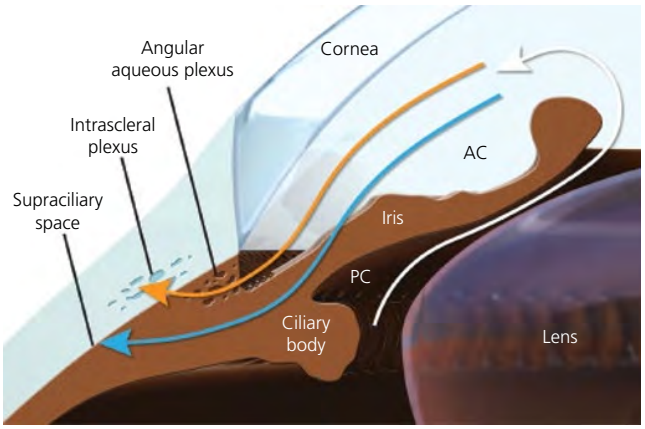


Figure 10.4 Equine aqueous humor outflow pathways. Aqueous humor moves through the trabecular meshwork, to the angular aqueous plexus, to the intrascleral plexus, and then drains into the vortex veins (conventional outflow) and in addition through the supraciliary space (uveoscleral outflow). AC, Anterior chamber; PC, posterior chamber. The **white arrow** indicates aqueous humor flow from the ciliary body through the pupil into the AC. The **orange arrow** indicates conventional and **blue arrow** uveoscleral aqueous humor outflow. (*Source*: Reproduced by permission of Ohio State University.)

suprachoroidal and supraciliary spaces, termed the unconventional or uveoscleral outflow pathway [8].

Resistance to outflow is focused at the AAP and ISP in the conventional outflow system of the horse. The intertrabecular spaces of the UTM are very wide, and the spaces of the CSTM are very narrow. The CSTM acts as a sieve or filter for large particles, but it may or may not restrict aqueous flow directly. The AAP is a plexus of radially oriented, narrow-diameter vessels. The ISP consists of an extensive network of anastomosing circumferential channels that drain aqueous humor to the vortex venous system. The ISP and vortex venous systems have a rich collateralization. Aqueous humor thus follows a path of low resistance in the UTM and CSTM, high resistance to outflow in the narrow tributaries of the AAP and ISP, and low resistance to outflow again in the vortex venous systems [5–8]. It is the balance between aqueous humor production, circulation, drainage, and resistance to outflow that results in the normal IOP.

Microsphere perfusion studies have shown that the suprachoroidal and supraciliary spaces provide an extensive unconventional outflow pathway to the sclera and choroid in the horse [8]. The intertrabecular spaces of the equine ICA provide a large area of aqueous humor contact with the iris and ciliary body. Aqueous humor can enter the anterior iris face to drain into the vortex veins, and it also leaves the UTM through the interstitial spaces of the ciliary body musculature to drain into the supraciliary and suprachoroidal spaces and choroid [1–3]. It is noted that uveoscleral outflow appears to be extensive in the horse, but the exact proportion of conventional versus unconventional outflow is not reported for the equine eye [5, 9]. (see Chapter 8 for more information).

Retinal ganglion cells and optic nerve

The horse has a very large retinal sensory surface area, vast numbers of photoreceptors, a massive population of RGCs with large cell bodies, a large optic disc area and optic nerve cross-sectional area (15.7 mm^2 versus 5.17 mm^2 in humans), high total optic nerve axon counts (1.076 × 106 versus 1.159 × 106 in humans), large mean individual optic nerve axon cross-sectional areas (3.11 mm^2 versus 1.75 mm^2 in humans), and 4.4 times the percentage of optic nerve axons larger than 2 mm in diameter compared with humans (35.5% in horses versus 8% in humans) [10]. The comparatively low density of axons in the horse optic nerve (62,800 axons/mm^2 in horses versus 175,000 axons/mm^2 in humans) undoubtedly reflects a low tissue density of RGCs, because the ratio of ganglion cells to optic nerve axons is 1:1. The marked proportion of large-diameter ganglion cells in the horse retina may be an adaptation to cover a large retinal sensory surface area with a relatively low population density of ganglion cells [10].

RGC axons of the retinal nerve fiber layer become arranged into optic nerve fiber bundles by astrocytes in the choroidal lamina cribrosa. The scleral lamina cribrosa is a specialized extracellular matrix of the central nervous system that spans the scleral canal as a complex, multilayered set of collagenous plates (Figure 10.5) [5]. The multiple plates of the scleral lamina cribrosa contain a hydrodynamic extracellular matrix of elastic and collagen fibers (types I, III, and VI), astrocytes, and capillaries.

The prelaminar optic nerve is known as the optic disc, optic nerve head (ONH), or optic papilla and is surrounded by the white peripapillary scleral ring of Elschnig noted at the 6 o'clock position in the horse ONH. Myelin extends anterior to the equine lamina cribrosa to cover the surface of the optic disc. The myelinated axons generally stop at the edge of the scleral canal, although myelinated axons in the retinal nerve fiber layer are noted in the horizontal retinal quadrants of some horses. Scanning laser ophthalmoscopy of the equine ONH indicates that the neuroretinal rim area is smallest at the superior and inferior rims of the horse optic disc and larger at the nasal and temporal rims (Figure 10.6). The intrapapillary region of the ONH is the area inside Bruch's membrane at the scleral canal and consists of the neuroretinal rim and the optic cup (Figure 10.7).

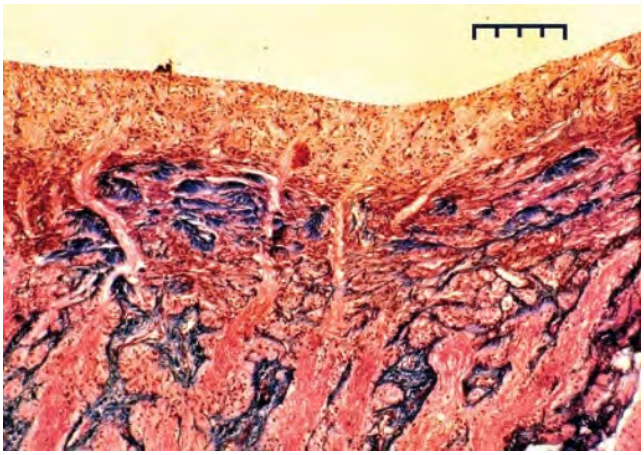
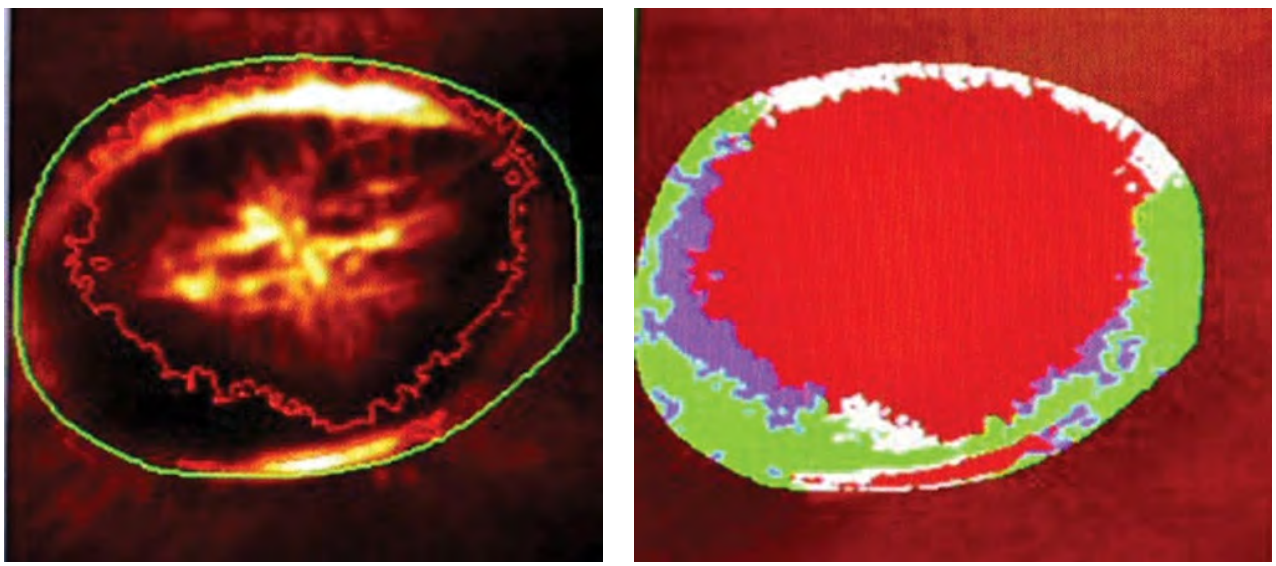


Figure 10.5 This histologic section of a normal equine optic nerve has the neural axon bundles (**pink**) passing through plates of the scleral lamina cribrosa (collagen is **blue**) (Gomori's trichrome stain; bar = 2.3 mm).



(A) (B)

Figure 10.6 (A) Scanning laser tomography of the oval ONH of this healthy horse consists of a confocal laser tomographic, extended focus, reflectance/intensity image. (B) A stereometric topography analysis image in pseudocolor. **Red** indicates areas below the retinal surface, and **green** areas above the retinal surface. **White** areas are caused by irregularities in the disc surface. Note posterior excavation of neuroretinal rim at the 6 o'clock position. Scanning laser tomographic measurements indicate that the equine neuroretinal rim area is smallest at the superior and inferior rims and largest at the nasal and temporal rims. Disc area is 17.6 mm^2, cup area is 14.6 mm^2, and cup-to-disc area ratio is 0.83 in this horse.

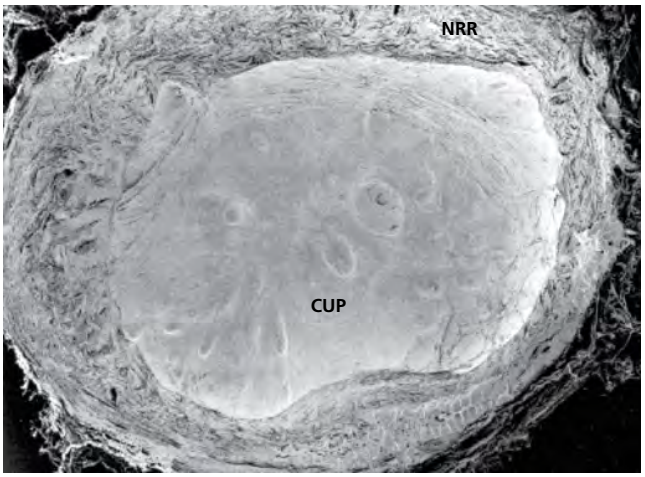


Figure 10.7 The prelaminar optic nerve is known as the optic disc, optic nerve head (ONH), or optic papilla. The equine ONH is oval, with the horizontal axis longer. The intrapapillary region of the ONH consists of the narrow neuroretinal rim (NRR) and the large central optic cup (CUP). This scanning electron micrograph illustrates the NRR and CUP.

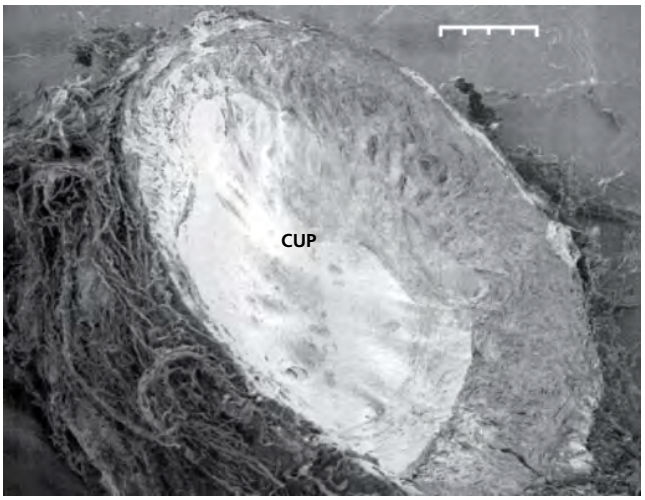


Figure 10.8 This scanning electron micrograph demonstrates optic nerve head cup (CUP) enlargement associated with advanced glaucoma in the horse. Optic nerve "cupping" occurs as a result of axonal loss, laminar plate compression, and posterior bowing of the lamina cribrosa. The neuroretinal rim narrows because RGCs and axons are lost in glaucoma. The ratio of the cup-to-disc area is used to evaluate progression of glaucomatous optic nerve damage (bar = 690 mm).

ONH atrophy or "cupping" is associated with chronic glaucoma (Figure 10.8) and occurs as a result of axonal loss, laminar plate compression (Figure 10.9), rotation of the scleral insertion zone posteriorly, outward bowing of the lamina cribrosa, and a widening of the scleral canal behind Bruch's membrane. The associated enlargement of the ONH cup with these laminar and axonal changes is unique to glaucoma and not found in other optic neuropathies. The ratio of the cup-to-disc area is used to evaluate progression of glaucomatous optic nerve damage in humans. Enlargement of the cup-to-disc



Figure 10.9 Glaucoma causes compression of the anterior laminar beams of the lamina cribrosa (LC) in this trypsin digest of the ONH of a horse with glaucoma (bar = 500 mm).

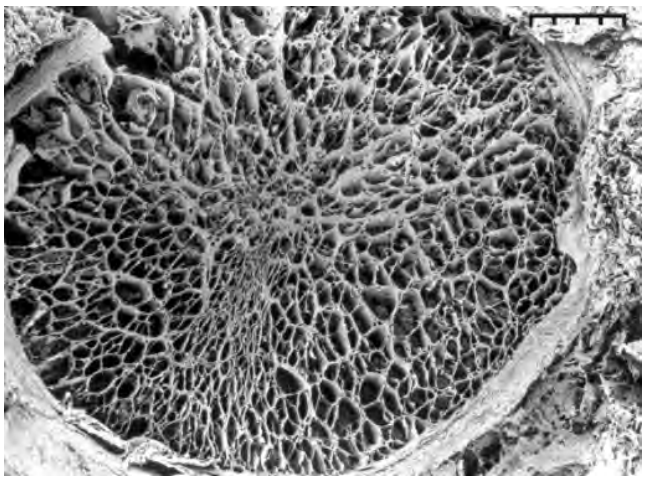


Figure 10.10 This trypsin digest of the scleral lamina cribrosa of a horse reveals the many laminar pores through which optic nerve axon bundles exit the eye to go to the brain (bar = 690 mm).

ratio indicates optic nerve axonal loss and is associated with deterioration in visual fields.

The intralaminar optic nerve of horses with glaucoma contains a significantly larger total number of laminar pores, pores of significantly smaller individual area, and pores that are rounder than those in the intralaminar optic nerve of healthy horses (Figure 10.10) [5]. The intralaminar optic nerves of horses with glaucoma contain a higher percentage of connective tissue (74%) than the optic nerves of healthy horses (67%). These differences may represent an anatomic variation found in horses predisposed to develop glaucoma, as well as changes resulting from IOP-induced radial stress forces causing stretching of the scleral lamina cribrosa.

The scleral lamina cribrosa is a transition zone of high to low hydrostatic tissue pressure caused by the prominent pressure gradient formed by the IOP and intraorbital pressure. The axoplasmic flow in the optic nerve axons is subjected to this abrupt change in tissue pressure [6]. The elevated IOP found in glaucoma exacerbates this pressure gradient and is associated

with posterior displacement of the lamina cribrosa and disruption of optic nerve axon axoplasmic flow (see Figure 10.9). Disruption of axoplasmic flow may be exacerbated by the sharp edge of Bruch's membrane at the edge of the scleral canal. The lamina cribrosa is thus an active and compliant structure in the horse; its movement during normal and abnormal fluctuations in IOP can both protect and obstruct optic nerve axoplasmic flow [5].

Intraocular pressure

The balance between aqueous humor production, circulation, drainage, and resistance to outflow results in normal IOP. Obstruction to the outflow of aqueous humor results in an elevation in IOP, and a persistent IOP elevation reduces vascular perfusion and induces degeneration of the retina and optic nerve.

In a clinical setting, IOP in the horse may be measured using either a Tono-Pen® (Reichert Inc., Depew, NY) or a TonoVet® (Icare Finland OY, Helsinki, Finland). In normal horses, using the Tono-Pen applanation tonometer, mean IOP was 23.3 ± 6.9 mm Hg, with a range from 7 to 37 mm Hg [11–15]. See Chapter 1 for more information regarding tonometry in the horse.

Pathophysiology

Pathologic elevation of IOP is always the result of a decrease in aqueous humor outflow. Physical obstruction of the aqueous humor outflow pathways can occur as a result of pre-iridal post-inflammatory membranes, obstruction of the ICA with inflammatory debris and fibrosis, synechia causing pupillary block, iris bombe or ICA obstruction, and trabecular compression and angle closure [14]. Anterior lens luxation and vitreal prolapse, more common in Appaloosas and Rocky Mountain-type horses, may obstruct the pupil or the ICA. ICA obstruction by melanoma or other neoplastic cells can also result in an elevation in IOP [7].

A chronic elevation in IOP results in compressive conformational distortion within the scleral lamina cribrosa, resulting in rotation, misalignment, and collapse of the laminar pores and laminar channels such that optic nerve axoplasmic flow is reduced and eventually blocked, leading to RGC death. Glaucoma in the horse results in extensive and diffuse optic nerve damage, and the optic nerve axon density in horses with glaucoma is reduced by 65% [10]. Gliosis is dramatic, with glial cells predominating in glaucoma-induced optic nerve atrophy. The median individual optic nerve axon cross-sectional areas are smaller in glaucomatous equine eyes than in normal eyes (1.60 mm^2 versus 1.35 mm^2), indicating that horses with glaucoma lose optic nerve axons of large individual cross-sectional area more rapidly than medium- and small-sized axons [10]. Axons of all sizes are eventually injured by chronically elevated IOP, but some RGCs and their axons appear to be IOP resistant and vision can often be retained for substantial periods in horses, despite extreme elevations in IOP. As such, horses appear more tolerant of ocular hypertension than other species, with some anecdotal reports indicating that IOP can remain high (more than 50 mm Hg) for several days and horses can retain vision, unlike dogs and other species.

Diagnosis and clinical signs

Etiology

Glaucoma has a variety of etiologies, but ultimately all result in a common path—a reduction in aqueous humor outflow, resulting in an increase in IOP that is incompatible with normal retinal and optic nerve function. All glaucomas consist of five stages: (1) an initial event or series of events that progressively reduces function of the aqueous humor outflow system, (2) morphologic alterations of the aqueous humor outflow system that eventually lead to outflow obstruction and IOP elevation, (3) elevated IOP that is too high for normal RGC and optic nerve axon function, (4) RGC and optic nerve axon degeneration, and (5) progressive visual deterioration that eventually leads to blindness [18].

Equine glaucoma can be categorized as congenital, primary, or secondary. Congenital equine glaucoma is associated with developmental abnormalities of the ICA and in many cases with the more severe anterior segment dysgenesis (Figure 10.11) [19–25]. Congenital glaucoma has been reported in Thoroughbred, Arabian, and Standardbred foals [21, 22, 26].

While primary glaucoma has been described in the horse, it is uncommon, and it remains controversial as to whether true primary glaucoma exists in the horse [19, 24]. Equine glaucoma most commonly occurs secondary to a predisposing cause, typically chronic intraocular inflammation as seen with equine recurrent uveitis (ERU) [24, 26–29]. In two retrospective studies and a histologic study, clinical signs and histologic signs compatible with ERU were observed in 85–91% of horses with glaucoma [26–28]. A histologic study of equine glaucoma suggests that

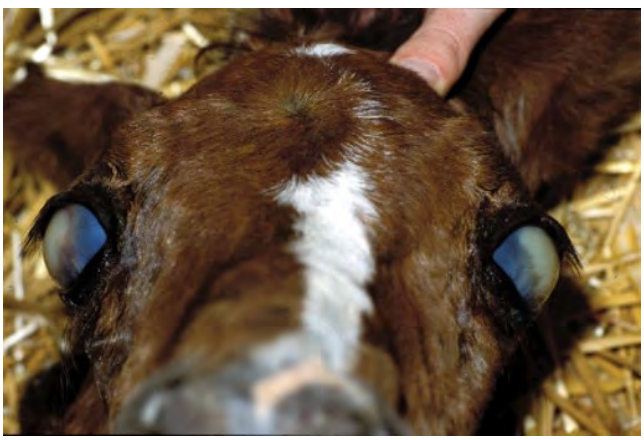


Figure 10.11 Bilateral, congenital glaucoma in a newborn foal. Buphthalmia (megaloglobus), diffuse corneal edema, corneal vascularization, and axial corneal opacity are present. The foal is blind.

Appaloosa and older horses may be predisposed [28]. While elevated IOP is clearly the primary risk factor for rapid progression of optic nerve damage and blindness in the horse, ERU is the primary risk factor for development of glaucoma. The mechanisms by which ERU may result in secondary glaucoma include pre-iridal fibrovascular membrane formation, anterior or posterior synechiae, and inflammatory debris, cells, and blood obstructing the outflow pathways. Secondary glaucoma can also result from other intraocular diseases such as ocular trauma and intraocular neoplasia [30].

The reported prevalence of glaucoma in the horse is low (0.07%) compared to dogs (1.7%) and humans (1–2%) [31–33]. This may be explained by the prominent role of uveoscleral aqueous humor outflow in the horse, which may be higher than that in other species, and by microanatomic differences in the aqueous humor outflow pathways in horses compared with those in other species [5, 7, 8]. Glaucoma has been reported in the following horses: American Paint, Standardbred, Morgan, Trakehner, Percheron, mule, Paso Fino, Quarter, Tennessee Walking, Thoroughbred, Arabian, Pony (Americas, Connemara, Shetland), American Saddlebred, and Warmbloods [10, 12, 17, 21, 24, 27]. In one study, Ponies and the Appaloosa, independent of its breed-related predisposition to uveitis, were at increased risk for developing glaucoma [20]. The Appaloosa is also at increased risk for ERU [34, 35]. Multiple studies have found that horses older than 15 years are at increased risk for glaucoma [20, 26–28].

Diagnosis

The diagnosis of glaucoma is based on the history, clinical signs (Table 10.1), and documentation of elevated IOP. Since most equine glaucoma is secondary to ERU, clinical signs associated with concurrent active or inactive intraocular inflammation are often present. These include chemosis, blepharospasm, photophobia, miosis, aqueous flare, cataract, synechia, keratic precipitates, atrophy of the corpora nigra, retinal and optic nerve atrophy, vitreous degeneration, and retinal detachment (Figure 10.12). A lack of any post-inflammatory changes or other predisposing conditions of the anterior or posterior segment in a horse with elevated IOP may lead to a diagnosis of primary glaucoma.

The IOP in horses with glaucoma often does not remain consistently elevated. Significant, asynchronous, diurnal fluctuations in IOP can occur in diseased globes, resulting in a waxing and waning of clinical signs such as diffuse corneal edema [20, 36]. Frequent tonometric IOP measurements during a day or at the time clinical signs are most apparent may be necessary to initially detect transient acute IOP elevation. This wide variation in IOP not only interferes with the diagnosis of glaucoma but also complicates the monitoring of response to therapy.

Equine glaucoma may not be easily recognized in the early stages of the disease because of the subtle initial clinical signs. This is further complicated by the fact that equine veterinarians often have a low index of suspicion of glaucoma in horses with eye problems. The predominant clinical sign of equine glaucoma may be partial or complete corneal edema. Acute glaucoma is less commonly observed in the horse as clinical signs are subtle and often missed. Acute glaucoma may result in pain (photophobia, blepharospasm, lacrimation), blepharedema, episcleral injection, focal or diffuse corneal edema, mydriasis (provided uveitis or posterior synechiae are not present), and



Figure 10.12 Iris hyperpigmentation, corpora nigra polishing, a fixed dilated pupil associated with extensive posterior synechia, hypermature cataract, anterior lens capsular pigmentation, and pre-iridal fibrovascular membrane extending across the anterior lens capsule are noted in this eye diagnosed with chronic ERU and early secondary glaucoma.

Table 10.1 Clinical signs of glaucoma.

Sign	Acute/active glaucoma	Chronic glaucoma
Corneal edema	May be transient-diffuse	May be permanent-diffuse
Corneal band opacities	May be present	Often present
Aqueous flare	May be present	Inconsistent
Pupil	Mydriasis (unless synechia present)	Fixed, dilated pupil (unless synechia present)
Uveitis	Often concurrent	May be present
Lens	May see subluxation	May see subluxation or luxation, often posterior, with/without cataract
Posterior segment changes	Not typical	Optic nerve atrophy, lamina cribrosa exposed
Blepharospasm	Mild to severe	Not typical
Buphthalmos	Not typical	Typical
Blindness	Not typical	Typical



Figure 10.13 Acute equine glaucoma with diffuse corneal edema and mydriasis. IOP was 60 mmHg



Figure 10.14 Vertical corneal edema is an early warning sign of glaucoma in the horse. This may result from a significant break in Descemet's membrane.

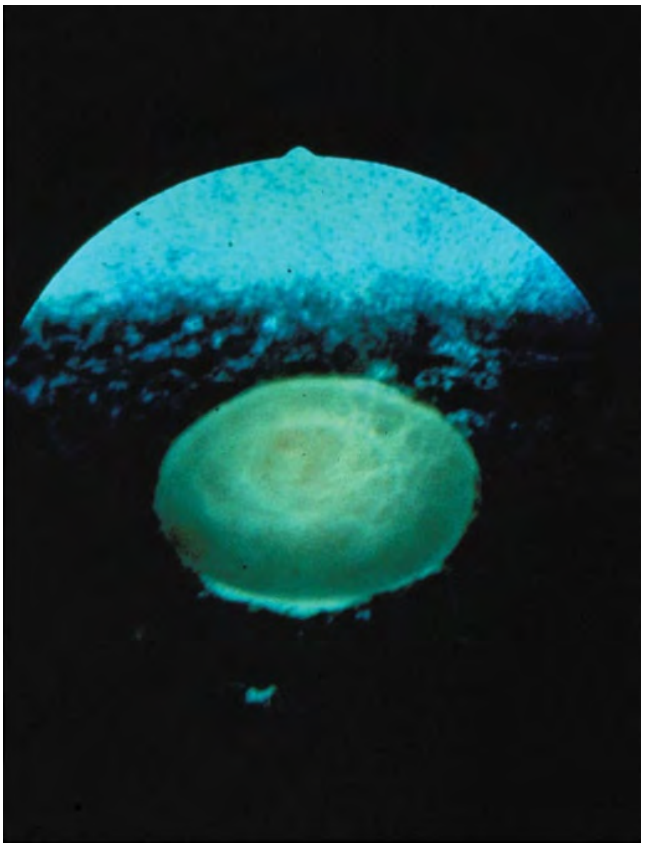


Figure 10.15 This fundus photograph shows optic nerve atrophy caused by glaucoma. The anterior lamina cribrosa is seen as reticulated lines caused by loss of myelin and axons.



Figure 10.16 Diffuse corneal edema and buphthalmos are present in the right eye of this Appaloosa with chronic glaucoma.

decreased menace (Figure 10.13). In acute or subacute cases of glaucoma with severe elevations of IOP, acute breaks in Descemet's membrane may manifest clinically as wide bands of corneal edema (Figure 10.14).

With more chronic disease, corneal edema, enlargement of the globe (buphthalmos/hydrophthalmos), decreased vision, fixed and dilated pupil, corneal striae, lens subluxation or luxation, cataract, and retinal and optic nerve degeneration and cupping are observed (Figures 10.15, 10.16, 10.17, 10.18, and 10.19). In addition, exposure keratitis may result from severe buphthalmos. Blindness typically occurs late in the course of equine glaucoma.

While fixed and dilated pupils are commonly observed in horses with glaucoma, positive dazzle and menace reflexes may remain in many eyes with chronic glaucoma. In a retrospective study of 42 glaucomatous equine eyes, 41 eyes were sighted at presentation [27]. The large number of axons in the optic nerve of the horse may act as an anatomic reservoir of axons that provide some protection against total loss of vision despite very high IOP. Some RGCs may actually be IOP resistant. Horses with glaucoma also appear to lose large optic nerve axons more rapidly than medium and small axons. Large RGCs are involved in motion detection, stereopsis, and sensitivity to dim light, but the consequences of the loss of such axons to the visual capabilities of the horse in early glaucoma are not known. Despite the apparent relative resistance of equine ganglion cells and axons



Figure 10.17 Chronic glaucoma with buphthalmos, numerous corneal striae, diffuse corneal edema, and mydriasis.



Figure 10.19 Anterior lens luxation, cataract, and secondary glaucoma in a 21-year-old Arabian mare.

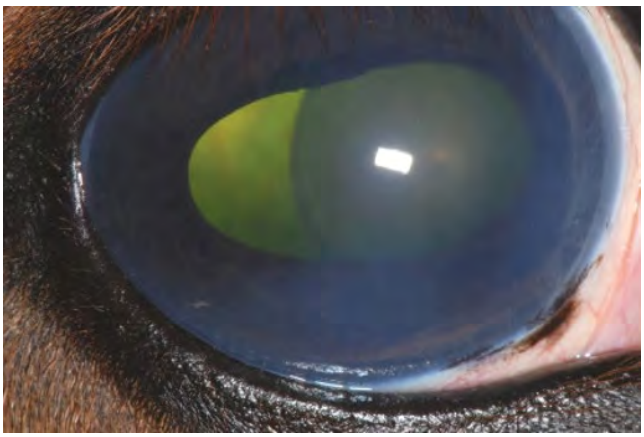


Figure 10.18 Chronic glaucoma with buphthalmos, diffuse corneal edema, corneal vascularization, and lens subluxation.



Figure 10.20 Equine corneal band opacities or band keratopathy. Multiple, thin linear opacities at the level of Descemet's membrane are present. The IOP of this horse is normal and there is no history or clinical evidence of previous inflammation or glaucoma.

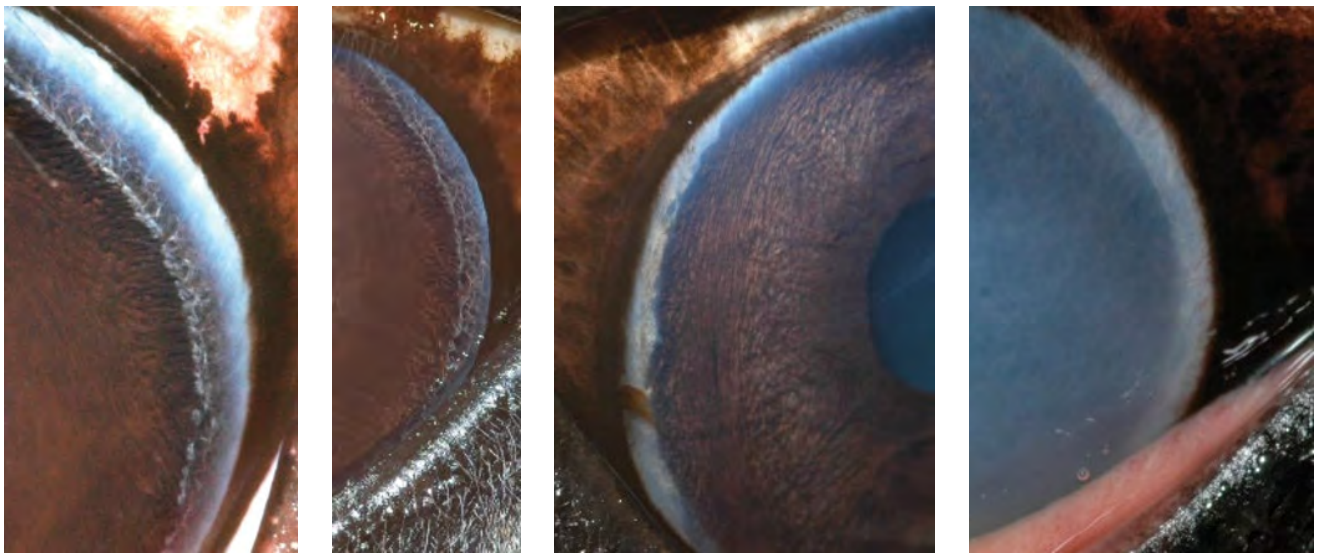
compared to other species, the progressive sustained elevation in IOP found in equine glaucoma is ultimately associated with optic nerve atrophy and cupping, retinal degeneration, and blindness. In horses, buphthalmos may partially or fully resolve and globe size may return to normal with reduction of IOP to a normal level. This may be a function of greater elasticity of the equine fibrous tunic. This differs from canine glaucoma where buphthalmia is permanent and is typically associated with blindness.

The linear opacities (corneal stria) seen in chronic equine glaucoma often extend from limbus to limbus and are areas of fibrosis at sites of thinning or breaks in Descemet's membrane [37, 38]. Similar linear opacities seen in normal horses have been termed band keratopathy (band opacities), and may not be significant (Figure 10.20). When linear deep corneal opacities are observed, a complete ophthalmic examination should be performed to look for evidence of prior inflammation or glaucoma, vision should be assessed, and IOP determined. With suspicion of glaucoma, ICAs should be routinely examined for alterations in width and degree of obstruction (Figure 10.21).

Treatment

Medical treatment

Treatment of equine glaucoma includes both medical and surgical management. Medical management follows the same general guidelines as that for glaucoma in other species, with the aim of therapy being the reduction of IOP, often combined with the concurrent suppression of iridocyclitis. The initial response to IOP-reducing medical therapy in early cases of equine glaucoma is often favorable, but the long-term prognosis for maintaining vision with medical therapy alone is guarded. Unfortunately, many horses with glaucoma are presented late in



(A) (B) (C) (D)

Figure 10.21 (A) Normal ICA is easily viewed in the horse. Pectinate ligaments from the iris insert in clear cornea near the limbus. (B) Aqueous humor percolates through spaces between pectinate ligaments to enter the ICA. (C) The ICA is more solid and narrowed, causing aqueous humor outflow obstruction in this eye with glaucoma. (D) It is difficult to visualize the ICA in this Paso Fino with glaucoma.

the course of the disease. However, despite dramatically high IOP, partial vision may be retained for extended periods in some horses. It is the authors' opinion that glaucoma is particularly aggressive and difficult to control in the Appaloosa.

The goals of therapy in glaucoma are to reduce IOP to levels compatible with the health of the retina and optic nerve by decreasing production of aqueous humor by the ciliary body and increasing outflow of aqueous humor through both the conventional and unconventional outflow systems. Uveitis must be concurrently suppressed if present. Various combinations of drugs and surgery may be needed to reduce IOP to selected target levels. A target IOP of less than 20 mm Hg is a reasonable goal in the glaucomatous equine eye. Control of IOP can improve vision in horses with decreased vision through resolution of marked corneal edema and improvement of retinal and optic nerve vascular perfusion. The size of the horse generally makes systemic medication less desirable, so medical therapy using topical agents is most common.

Prior to choosing a course of therapy, essential questions to consider are: (1) presence or absence of vision, (2) concurrent ocular disease, (3) age and purpose of the horse, (4) economic factors, and (5) ease of treatment and ability of the owner to treat at the appropriate frequency. In some instances, such as irreversible blindness, an aged/retired horse, or inability of the client to medicate appropriately, enucleation, prosthesis, or in some instances pharmacologic ablation may be the treatment of choice.

Topical β-adrenergic blocker

The β-adrenergic blocker timolol maleate (0.5%) was shown to decrease IOP in normal horses by 17% (4.2 mm Hg) with twice-daily topical administration [39] β-Blockers interfere with the production of cyclic adenosine monophosphate by the enzyme adenylcyclase to reduce aqueous humor production. The maximum effect was in the afternoon and occurred 4.5 days after administration. A decrease in pupil size was observed in another study with normal horses, but there were no other adverse effects [39].

Topical or oral carbonic anhydrase inhibitor

Aqueous humor production can be reduced if 99% of the carbonic anhydrase enzyme in the ciliary body is inhibited. The carbonic anhydrase inhibitor dorzolamide (2%), alone or in combination with timolol maleate, was effective in lowering IOP by 10% (2 mm Hg) when administered topically twice a day in normal horses [40]. Once-a-day use increased IOP in normal horses in another study [39]. Brinzolamide, a carbonic anhydrase inhibitor associated with fewer side-effects in people, most likely due to a physiologic pH (relative to dorzolamide, which is acidic), has been shown to decrease IOP following once- and twice-daily topical administration of a 1% solution in normal horses [41]. Of all the topical glaucoma agents, timolol maleate and dorzolamide administered every 8 hours are most effective in the horse and their combination is more effective than when the two drugs are administered concomitantly [42].

Acetazolamide, dichlorphenamide, and methazolamide are systemically administered carbonic anhydrase inhibitors that have been used to reduce IOP in other species, but the pharmacokinetics have been studied only for acetazolamide in horses. In horses, when acetazolamide is given orally, it is absorbed rapidly and has somewhat low bioavailability, but it is eliminated more slowly than when it is administered intravenously [43]. Acetazolamide has been shown to reduce clinical signs of hyperkalemia in horses with hyperkalemic periodic paralysis when given at 4.4 mg/kg twice daily, but no studies have evaluated

the effect of acetazolamide on IOP in either normal or glaucomatous horses. Administration of systemic carbonic anhydrase inhibitors should be accompanied by electrolyte supplementation because of expected potassium loss.

Topical direct- and indirect-acting parasympathomimetic drugs

Direct- and indirect-acting parasympathomimetic drugs increase the facility of aqueous outflow in many mammals by constricting the ciliary muscles to open the trabecular meshwork. These drugs also inhibit unconventional outflow. In a study with normal horses, pilocarpine did not decrease IOP, and actually trended toward increasing IOP after multiple twice-daily applications. It also decreased vertical pupil size [13]. Acetylcholinesterase inhibitors such as demecarium bromide have effects similar to those of pilocarpine. Demecarium bromide has been used in dogs with glaucoma to reduce IOP [44], as well as to delay the onset of glaucoma in the second eye of dogs with primary closed-angle glaucoma [45]. The use of these drugs in horses with glaucoma is not recommended.

Topical prostaglandin analogs

Prostaglandin analogs have revolutionized the treatment of glaucoma in dogs [45, 46], but have not proven as promising for horses. Latanoprost (0.005%) is an analog of prostaglandin F2a that increases uveoscleral outflow and induces miosis. In one study, latanoprost had no effect on IOP or pupil size in the normal equine eye when administered once a day [47]. In another study, latanoprost lowered IOP by 1 mm Hg in geldings (5%) and 3 mm Hg in mares (17%), but administration was associated with a high frequency of prostaglandin-induced adverse effects that included conjunctival hyperemia, epiphora, and blepharospasm [4850]. Synthetic prostaglandins may potentiate the clinical signs of uveitis and therefore should be used cautiously, if at all, in horses with glaucoma.

Topical mydriatics/atropine

Atropine has been recommended as possible therapy for equine glaucoma [8]. It was once thought to reduce the incidence of glaucoma in horses with uveitis. However, atropine should be used cautiously in horses with glaucoma because it may cause acute IOP elevations and does not appear to have the benefit of lowering IOP as once proposed. Atropine administered once a day had no effect on IOP but caused mydriasis in one study [49]. In another study, atropine administered twice a day caused an 11% reduction in IOP in treated eyes of ten horses and an increase in IOP in one horse [50]. Use of topically administered atropine for the specific purpose of IOP reduction is not recommended unless daily tonometric IOP measuring is available. However, judicious administration of atropine may be warranted in eyes with concurrent active uveitis and glaucoma.

Anti-inflammatory therapy

Anti-inflammatory therapy consisting of topically administered corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs), and/or systemically administered NSAIDs, such as phenylbutazone and flunixin meglumine, is beneficial in the control of uveitis that may be contributing to the elevation of IOP. Chronic use of systemic NSAIDs can be associated with complications such as kidney disease and right dorsal colitis; cautious use and close monitoring for clinical signs associated with these complications are essential. In horses with glaucoma and ERU, where surgical management of glaucoma is performed, concurrent implantation of a suprachoroidal, sustained-release delivery device to administer cyclosporine may be of benefit [51].

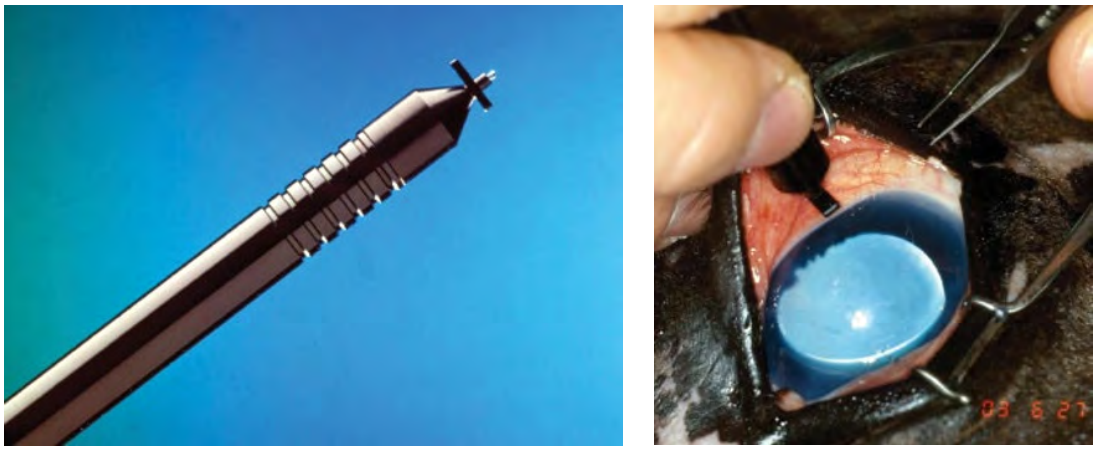
Surgical treatment

When medical therapy is inadequate, surgery can be performed to control IOP, preserve vision, and provide comfort in the horse with glaucoma. Currently available surgical options for horses with a glaucomatous but visual eye include laser cyclophotoablation and placement of gonioimplant device. Historically, cyclocrosurgery was performed [52], but given the significant side-effects, its use has been largely replaced by laser cyclophotocoagulation. Chemical ciliary body ablation, placement of an intrascleral prostheses, and enucleation are indicated for blind, chronically painful, and buphthalmic eyes.

Laser cyclophotocoagulation

When IOP cannot be controlled with medical therapy, transscleral diode or neodymium-yttrium aluminum garnet (Nd:YAG) laser cyclophotocoagulation (TSCP) or ablation may be a viable alternative for long-term IOP control. Laser TSCP involves the use of laser energy to preferentially destroy the ciliary body epithelium and stroma of the pars plicata, thereby reducing aqueous humor production. Of the various laser sources available, the semiconductor diode laser has been used most commonly for TSCP in veterinary ophthalmology (Figure 10.22). The diode laser emits light with a wavelength of 810 nm, which interacts with melanin in pigmented tissues.

Contact TSCP has been shown to be effective in controlling IOP and maintaining vision in the horse [4]. After Nd:YAG laser TSCP in the glaucomatous equine eye, a mean drop of 17 mm Hg was documented during the first few days, with a mean decrease of 25 mm Hg at 20 weeks post-operatively. The recommended settings for the Nd:YAG laser are 10 W, 0.4 seconds [53]. Using a diode laser to perform TSCP in normal horses, a 20% reduction in IOP was noted 6 months following treatment [54]. After diode laser TSCP, the IOP-lowering effects occur within 2–4 weeks. At least 40–60 sites in the dorsolateral and ventrolateral quadrants, 4–6 mm posterior to the limbus should be targeted with the laser in a nonbuphthalmic equine globe. In the buphthalmic equine globe, the external landmarks to perform TSCP have been revised, with the current recommendation of 6–8 mm dorsally, 5–6 mm dorsotemporally, and 4–5 mm ventrally and ventrotemporally (Figure 10.23) [4].4 Accurate anatomic positioning of TSCP optimizes therapeutic outcomes. The settings for the diode laser are 1500 mW power, 1500 milliseconds duration (2.25 J/site) [3, 55]. Too



(A) (B)

Figure 10.22 (A, B) Diode laser TSCP being performed for glaucoma. The probe is positioned 4–6 mm posterior to the limbus in the dorsal and ventral temporal quadrants.

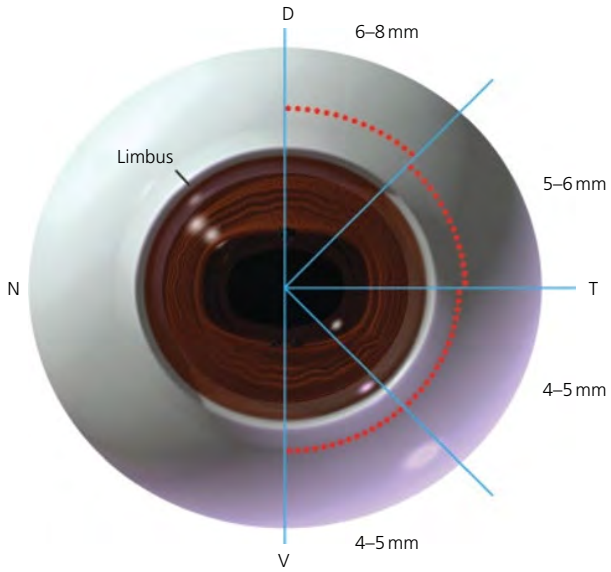


Figure 10.23 External landmarks to perform TSCP in a buphthalmic equine globe. **Red dots** indicate sites of laser application. N, Nasal; D, dorsal; T, temporal; V, ventral. (*Source*: Gemensky-Metzler AJ, et al., 2014 [4]. Reproduced with permission from John Wiley & Sons.)



Figure 10.24 Endocyclophotocoagulation of the ciliary processes is utilized to deliver laser energy directly to the ciliary processes. The white areas were just photocoagulated with the red aiming beam of the laser.

little laser energy (0.75 J/site) does not cause sufficient coagulative necrosis to the pars plicata, whereas too much laser energy (4 J/site) will cause too much collateral damage to normal tissue [55]. The glaucomatous equine eye is very responsive to TSCP treatment, and this is the therapy of choice for long-term IOP control. This procedure can be combined with the concurrent implantation of a suprachoroidal, sustained-release delivery device to administer cyclosporine [51].

Uveitis and corneal edema may initially increase after TSCP. In addition, IOP may increase immediately following completion of the procedure, so IOP should be determined prior to and immediately following TSCP. If elevated, a passive aqueocentesis is performed using a 30-G needle to lower the IOP to less than 20 mmHg. Medical therapy must be maintained until postoperative uveitis is reduced and IOP controlled. Superficial corneal ulcers may develop as a result of corneal desensitization from the TSCP or exposure during the procedure. Corneal ulceration is most common when the TSCP is performed 360 degrees around the globe and is avoidable if TSCP is restricted to the lateral aspect of the globe.

Endoscopic cyclophotocoagulation (ECP) using a diode laser has been used with increasing success to control refractory glaucoma in humans [56], dogs, and cats [57]. The use of ECP has been described in normal horses (Figures 10.24 and 10.25) [58]. With this procedure, an endoscopic system is used to provide a direct view of the ciliary processes, the target of cyclophotocoagulation, thereby minimizing the risk of collateral tissue damage.

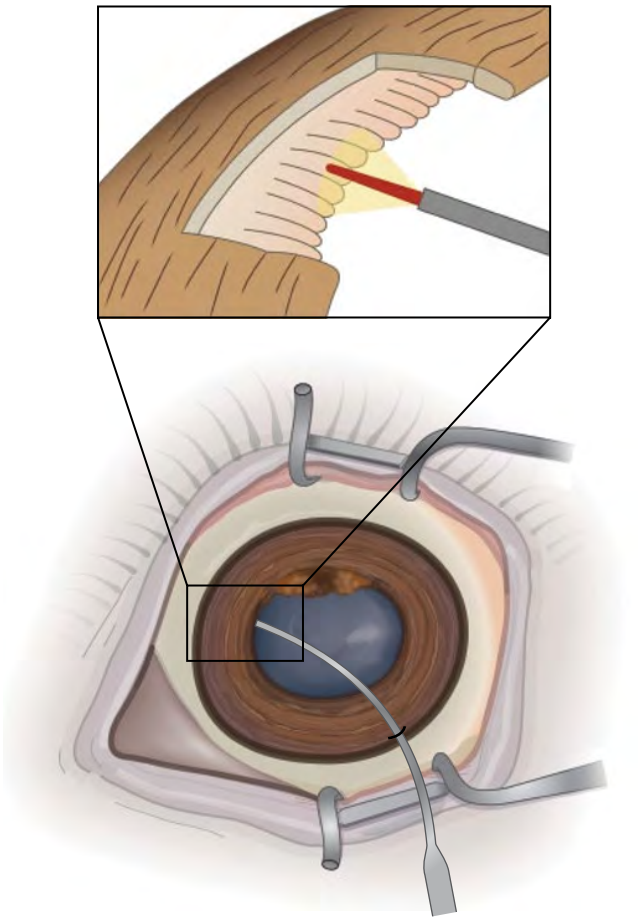


Figure 10.25 An equine globe with the curved equine-specific endolaser probe inserted through a ventrolateral 3-mm trilaminar clear corneal incision. The **expanded box** represents the dorsomedial section of the globe, with the ciliary processes exposed behind the iris. The tip of the endolaser probe is visible, with the red beam representing laser energy and the yellow-color fan indicates the number of ciliary processes visible endoscopically during laser application. (*Source*: Gilger 2011 [66]. Original drawing courtesy of Dr Richard McMullen.)

Reported efficacy for lowering IOP and preserving vision in dogs is 80–90% [57, 59]. When compared to TSCP, ECP requires general anesthesia and intraocular placement of the laser. In a study using normal equine cadaver globes and normal horses, endoscopic laser energy delivery through a 50-mm modified probe in a range between 0.90 and 1 [14]. J resulted in the desired coagulative tissue effects on the ciliary body without excessive collateral tissue damage [58]. This study utilized an anterior chamber approach as is most commonly used in the canine eye; however, this approach may result in development of iatrogenic cataract in phakic horses, suggesting that a pars plana approach should be evaluated [58]. No studies to date have been published to demonstrate efficacy in horses with glaucoma, and therefore further studies are needed prior to routine use of the modality in horses.

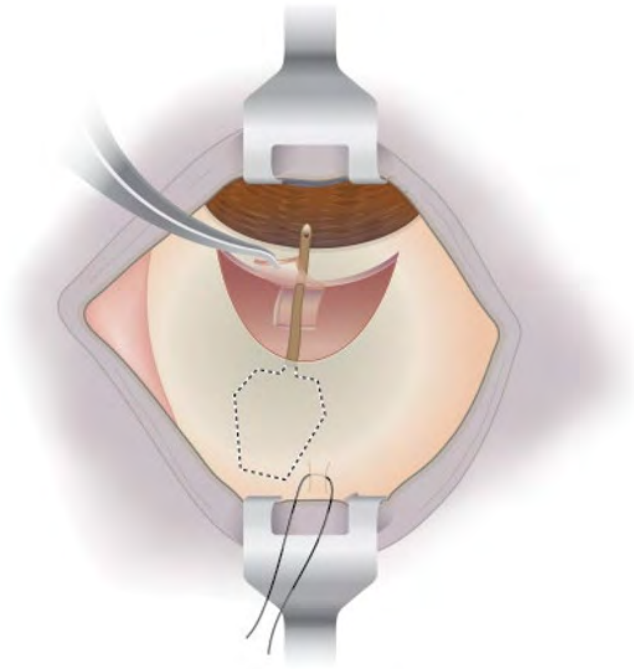


Figure 10.26 Schematic of gonioimplant. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

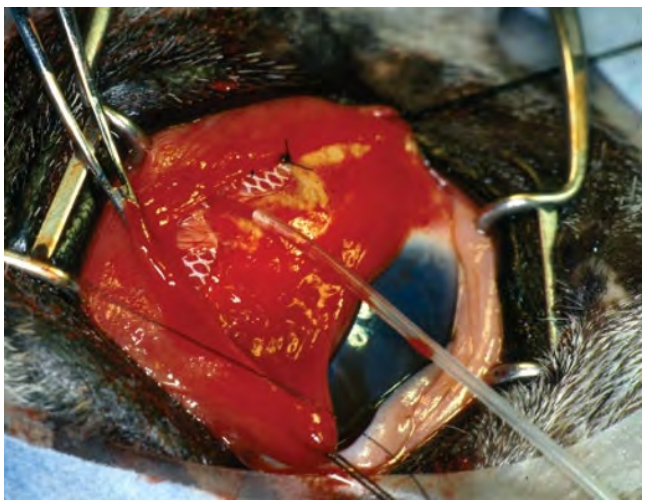


Figure 10.27 A gonioimplant is placed in the eye of an Appaloosa with glaucoma unresponsive to medical therapy.

Gonioimplants

Gonioimplant filtration surgeries to bypass the obstructed ICA and direct the outflow of aqueous humor to the subconjunctival spaces can be used to reduce IOP in patients with glaucoma. These implants may have a short lifespan due to fibrosis of the drainage tube and filtration bleb, but they can be particularly effective when combined with laser cycloablation. IOP is controlled in the short term by the implant and long term by the laser effects. These implants are experimental in the horse (Figures 10.26 and 10.27) but have been successful in dogs,

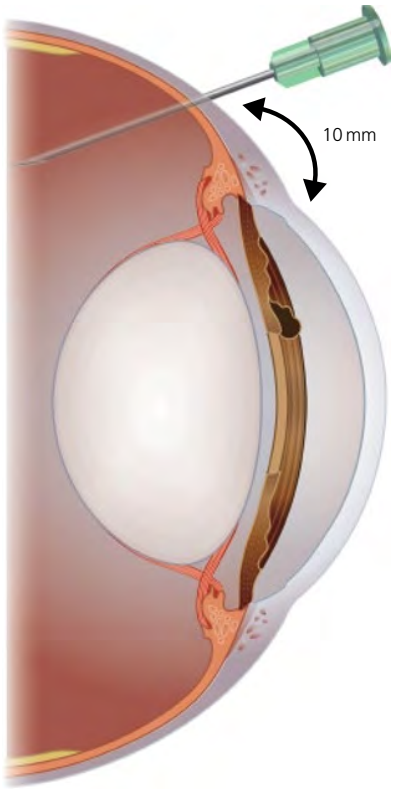


Figure 10.28 Schematic of gentamicin injection. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

controlling IOP in 74–76% and preserving vision in 41–58% of dogs after 12 months [60, 61].

Recently, a Baerveldt® gonioimplant was reported to control IOP and preserve vision for 402 days in a glaucomatous horse that was refractory to standard medical and surgical therapy [62]. Additionally, a feasibility study evaluating Ahmed® aqueous shunts in normal horses demonstrated a significant reduction in IOP up to postoperative day 28 [63]. Significant complications included fibrosis around the implant, a shallow anterior chamber, and varying degrees of keratitis [63].

Chemical ciliary body ablation

Intravitreal injection of intravenous gentamicin (50 mg with 1 mg of dexamethasone) can ablate the ciliary body and induce phthisis bulbi in a blind equine eye to reduce or eliminate pain and progressive buphthalmos. A single injection is typically sufficient for pain reduction, but a second may be necessary in some cases. Prior to the injection, sedation, frontal nerve block, instillation of topical anesthetic, and phenylephrine (2.5%) for vasoconstriction of the conjunctival vessels are performed. With appropriate restraint of the patient, the intravitreal injection is performed with a 22- to 20-G needle attached to a 3-mL syringe (Figure 10.28). The needle is positioned dorsolaterally, approximately 10 mm posterior to the limbus at a 45-degree angle, toward the optic nerve and away from the lens (Figure 10.29).

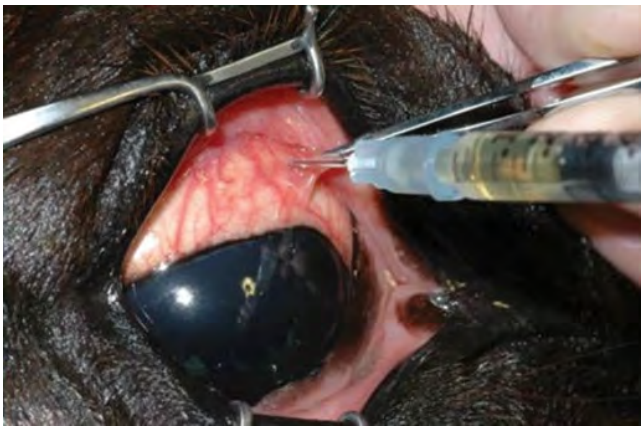


Figure 10.29 Gentamicin injection being performed.

Before the gentamicin/dexamethasone is injected, an equal volume (or greater) of vitreous is aspirated. If no vitreous can be aspirated, an aqueous paracentesis can be performed to decrease the intraocular volume and thereby temporarily decrease IOP. Equal volumes of dexamethasone may minimize discomfort from the injection. Flunixin meglumine administered prior to and for several days following injection may lessen discomfort and uveitis. Complications may include pain, uveitis, hyphema, cataract, and phthisis bulbi (expected). In canine chronic glaucoma, intravitreal cidofovir has been used in place of gentamicin with effective reduction in IOP and decreased side-effects [64]. The use of intravitreal cidofovir has not been evaluated in chronic equine glaucoma.

Enucleation and intrascleral prosthesis

For eyes with glaucoma secondary to intraocular infection or intraocular neoplasia and blind glaucomatous eyes with chronic pain associated with ERU, anterior lens luxation or ulcerative keratitis enucleation should be considered. Chronically painful and blind eyes and severely buphthalmic globes should be enucleated or have an intrascleral prosthesis implanted. A 34- to 44-mm-diameter intrascleral silicone implant can provide a cosmetic alternative to enucleation (Figure 10.30) [29, 65]. An intrascleral prosthesis should only be considered if the corneal and adnexal tissues are healthy and intraocular neoplasia is not suspected [29]. Intraorbital silicone implants can minimize the sinking of the skin into the orbital space after enucleation. The benefits of these cosmetic salvage procedures to the owner must be weighed against the increased risk of post-operative complications to the horse. Corneal necrosis and perforation may occur following an intrascleral prosthesis during the short-term post-operative period. Infection of the orbit and/or extrusion of intraorbital implants months to years following surgery are potential significant complications of using intraorbital implants. See Chapter 5 for more information on these procedures.



Figure 10.30 An intraocular silicone prosthesis after evisceration of the globe due to chronic glaucoma. Although the cornea was scarred, the horse appeared comfortable and received no therapy.

Future research

Equine glaucoma remains a poorly understood and frustrating chronic equine ocular disease that may require long-term medical therapy, often combined with surgical intervention. The prevalence of equine glaucoma is likely significantly higher than what is currently published, given the lack of awareness and availability of tonometry in general equine practice. Many of the topical glaucoma therapies effective in human and canine eyes are ineffective or even contraindicated in equine glaucoma. Further studies to evaluate and perfect newer surgical therapies such as gonioimplantation and endocyclophotocoagulation need to be performed in horses with glaucoma. It will only be through increased awareness in equine practice, increased availability of tonometry, early diagnosis, and further evaluation of medical and surgical therapies that progress will be made in the management of equine glaucoma and ultimately the preservation of vision in affected horses.

Additional content

The book companion website at

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includes additional text and figures that are not in the printed book or E-book.

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CHAPTER 11

Diseases of the equine vitreous and retina

Rachel A. Allbaugh, Wendy M. Townsend, and David A. Wilkie*

Introduction

Evaluation of the posterior segment of the equine eye is an essential part of an ophthalmic, pre-purchase, and general physical examination. Initial examination includes a history with respect to vision, determination of menace response and pupillary light reflex (PLR), and evaluation of clarity of transmitting media (cornea, aqueous, lens, vitreous). The resting pupil size and direct and consensual PLRs are assessed. Menace response should be evaluated in various visual fields: anterior, central, and posterior. Although it is possible to examine portions of the fundus without dilation, for proper examination of the posterior segment of the equine eye, mydriasis, a darkened environment, and proper equipment are essential. It should be noted on a pre-purchase examination if the pupil was or was not dilated for the ophthalmic examination.

Diagnostic mydriasis is achieved by using topical 1% tropicamide ophthalmic solution, which has an onset of action of 25 minutes and a duration of action of up to 12 hours [1]. As a solution, 0.2 mL of tropicamide is easily sprayed on the cornea with a tuberculin syringe and the hub of a 25-G needle. If required, sedation and nerve blocks can be performed to facilitate examination. Blocking of the auriculopalpebral nerve will facilitate examination by allowing the clinician to more easily open the eyelids. See Chapter 1 for additional information on complete ophthalmic examination in the horse.

Ocular posterior segment abnormalities can be congenital or acquired and include both primary ophthalmic and systemic diseases. When present, posterior segment abnormalities must be assessed with respect to current and future visual impact, and importance with respect to usefulness and safety of the horse. The clinician should remember that much of what is examined by ophthalmoscopy is a direct extension of the brain and central nervous system (CNS). In addition, it is the only area where small blood vessels can be viewed directly. This is, in reality, clinical histopathology. Lesions adjacent to the optic nerve or involving the area centralis will have a greater impact on vision than those that are more peripheral. The menace response in various visual fields and obstacle-course testing can be used to assess visual ability. In addition, evidence of anterior segment disease or inflammation and the possibility of progression and future inflammatory episodes should be discussed. Use of the animal must also be considered, because a barrel horse or competitive jumper requires greater vision than a brood mare or halter show horse. The possibility that a lesion is inherited or breed-related should also be addressed if the animal is to be used for breeding.

The significance of posterior segment disease to an individual horse and the equine industry is difficult to quantitate. Equine recurrent uveitis (ERU) affects 2–25% of the equine population and is the most common cause of posterior segment abnormalities. As a result of ERU, secondary glaucoma, hyalitis, retinal detachment, and retinal and optic nerve degeneration may affect vision and, thus, horse function. These changes are generally observed by owners and can be quantitated. However, more subtle lesions may go unnoticed, resulting in poor performance and affecting use without the owner being aware of the reason. In addition, posterior segment abnormalities noted on a pre-purchase examination may result in a loss of value. Finally, horses with posterior segment lesions significant enough to result in visual disturbance may present a safety concern for the owner with respect to riding, driving, or behavior.

The impact of posterior segment disease is significantly greater than has been appreciated, and veterinarians are strongly encouraged to make examination of the posterior segment a routine part of a physical and pre-purchase examination. In a survey of 204 racing Thoroughbred horses in Australia, ocular abnormalities were observed in 138 (67.6%) of the horses examined [2]. Of these findings, potential vision-threatening abnormalities were noted in 15 (7.4%) and nonvision-threatening abnormalities in 117 (57.4%) of the horses examined [2]. The most frequent abnormalities involved the retina and lens, with abnormalities of the retina noted in over half of the horses examined [2].

* Dr Wilkie was the author of the Retinal chapter in the second edition of *Equine Ophthalmology*. Only approximately 20–30% of this previous chapter has been updated for the third edition of *Equine Ophthalmology*.

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Clinical anatomy and physiology

The posterior segment of the eye includes the vitreous, retina, choroid, sclera, and optic nerve. The anterior-most extent of the posterior segment is the ora ciliaris retinae where the retina attaches to the pars plana of the ciliary body. The anterior extension of the ora ciliaris varies by quadrant of the eye and is important because it has significance for glaucoma and vitreoretinal surgery [3]. The ora is located more anteriorly in the nasal and ventral quadrants and further posterior in the dorsal and temporal quadrants [3]. This makes the dorsal and temporal locations the areas of choice for surgical approaches to the posterior segment and for trans-scleral and endocyclophotocoagulation.

The vitreous body is predominately composed of type II collagen fibrils, hyaluronic acid, and water. It is divided into cortical, intermediate, and central zones and has a volume of approximately 28 mL in the adult horse [4, 5]. Normally, the vitreous is transparent and uniform in appearance. Abnormalities of the vitreous generally result in loss of uniformity, with debris, membranes, and collagen fibrils appearing to float and swirl in a liquid medium. In addition, changes in vitreous color are often noted as a result of inflammation with the vitreous and the lens appearing yellow-green in color as a result of chronic inflammation. On ultrasonography, the vitreous is normally anechoic, with increased vitreous echogenicity indicating degeneration, inflammation, hemorrhage, mass lesions, or retinal detachment. There is evidence that the vitreous may have a role as an effector in some instances of ERU, and pars plana vitrectomy has been advocated to control recurrent inflammation in ERU [6].

The retina consists of the neurosensory retina (NSR) and retinal pigment epithelium (RPE). The photoreceptors, rods and cones, are located in the sensory retina. The rods predominate and are responsible for achromatic low-light vision, whereas the cones are responsible for vision in bright light and color vision. The horse lacks a fovea but has a **visual streak**, which serves as the area of maximum visual acuity and has an increased density of retinal ganglion cells. The temporal end of the visual streak has the highest cell density, the **area centralis**, and is responsible for binocular vision [7–9]. The equine visual streak is a horizontal band 1×22 mm and is located approximately 3 mm dorsotemporal to the optic nerve [8, 10]. The concentration of ganglion cells in the visual streak is 4000–6000 cells/mm^2, compared with less than 500 cells/mm^2 in the dorsal and ventral retina [7, 11]. In addition to regional differences in ganglion cell density, it has been shown that variation in ganglion cell density within the area centralis also occurs according to breed of horse and skull conformation [12]. Evaluation of the equine inner retina has demonstrated the presence of bipolar, amacrine, horizontal, and Müller cells in percentages of 44%, 24%, 1%, and 29%, respectively [13]. Specific markers for these and other retinal cells have been identified for the equine retina [14]. The horse has dichromatic vision with a short wavelength cone (spectral peak of 425 nm) and a middle wavelength cone (spectral peak of 540 nm) [15]. This translates into a blue-gray and yellow-green visual spectrum. The horse has been shown to be able to discriminate color from grays and to demonstrate color discrimination performance behavior [16]. The visual field of the horse is approximately 350 degrees, with a small area, 65–80 degrees, of binocular overlap [9, 17]. See Chapter 12 for more information on equine vision.

The equine optic disc is normally oval, salmon-pink, and situated ventral and slightly temporal in the nontapetal fundus (Figure 11.1). The optic nerve will fill the view of a direct ophthalmoscope (Figure 11.2); it measures 3–5 mm vertically and has a horizontal diameter of 5–8 mm [18]. The optic nerve in foals may appear more round.

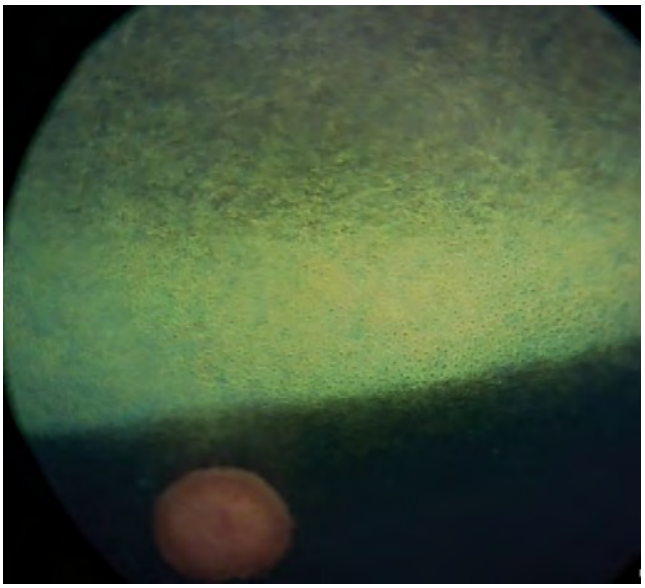


Figure 11.1 Normal equine fundus with stars of Winslow visible as black dots within the tapetum.

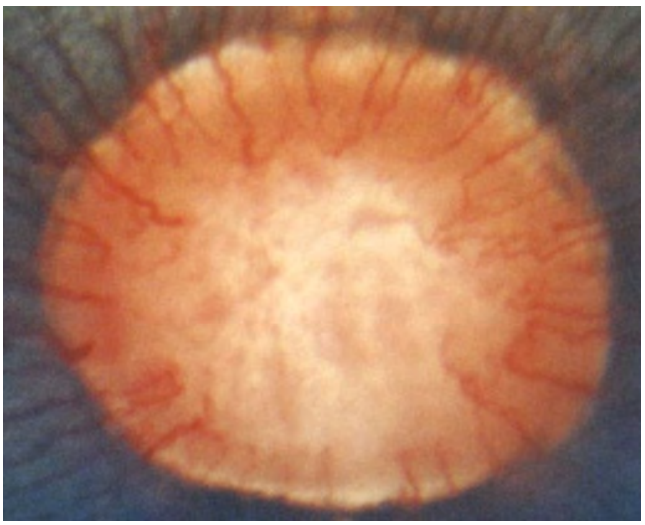


Figure 11.2 An equine optic nerve as seen by direct examination.

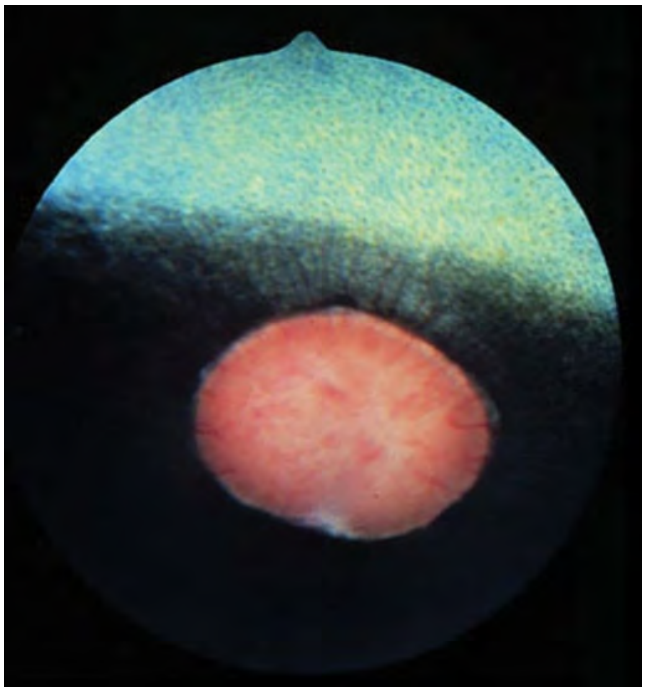


Figure 11.3 Normal optic nerve and peripapillary fundus. Note the normal notch at the 6 o'clock position of the optic nerve and decrease in number of retinal vessels in this region.

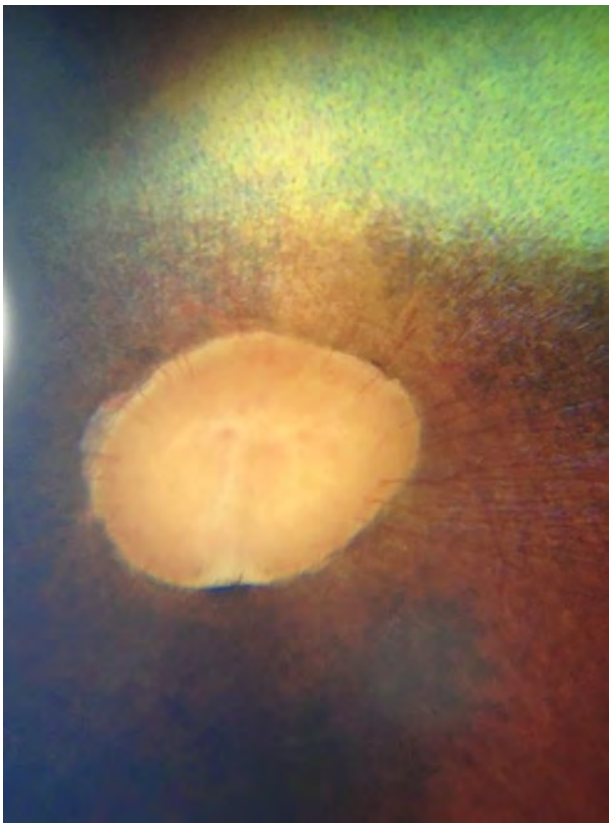


Figure 11.4 An equine optic nerve with the normal notch at the 6 o'clock position and extra myelin visible extending beyond the margin at 10 o'clock, a variation of normal. (*Source*: Photograph courtesy of Dr Tim Knott, United Kingdom.)

The surface of the optic nerve is often irregular and honeycombed as a result of the axons exiting at the fibrous lamina cribrosa. Ventrally, the optic nerve may appear notched (Figures 11.3 and 11.4). It is composed of approximately 1 million axons, with larger axons found at the periphery of the optic nerve as compared with the central portion [10, 19]. These large axons are lost first in equine glaucoma [19].

Although the optic nerve is myelinated, myelin does not typically extend to the intraocular portion of the nerve. If myelin does extend into the eye, it is most often associated with retinal vessels. Myelin extending along the nerve fiber layer axons appears as light-gray striations and is more common in aged horses (Figures 11.5 and 11.6).

The margin of the optic nerve may have a peripapillary ring associated with changes in thickness of the tapetum or pigmentation of the RPE or choroid. This circumpapillary ring can be dark or hypopigmented. This is a normal variation, provided that the overlying retinal vessels do not deviate or attenuate while crossing this region (Figure 11.7). Changes in vessel direction or thickness suggest a coloboma or degeneration. The axons of the retinal ganglion cells exit the eye through the scleral lamina cribrosa. The adult equine lamina cribrosa is a complex, multilayered structure comprised of myelinated optic nerve axons, capillaries, astrocytes, and an extracellular matrix [20]. The macromolecular structure of the equine lamina cribrosa may make it resistant to changes associated with elevations of intraocular pressure (IOP) and offer protection to the optic nerve axons [20]. This is supported

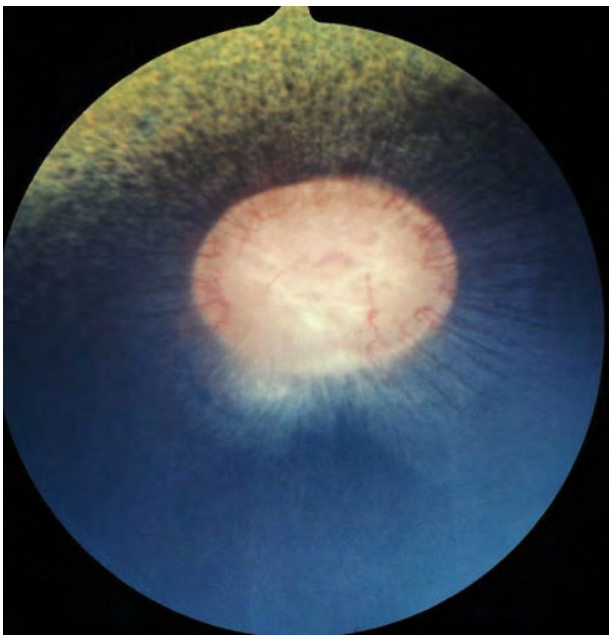


Figure 11.5 Myelin is seen radiating from the optic nerve along the nerve fiber layer axons in this aged horse. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

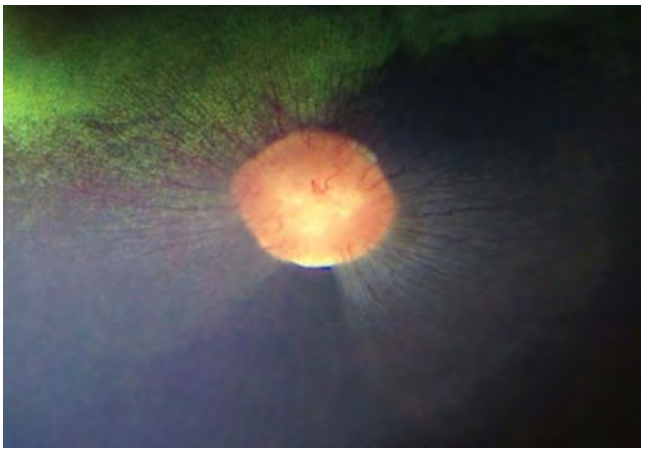


Figure 11.6 A small blood vessel is visible emerging from the center of the optic disc and myelin is visible radiating from the optic nerve along with the retinal blood vessels in the nerve fiber layer. These are normal variations. (*Source*: Photograph courtesy of Dr Tim Knott, United Kingdom.)

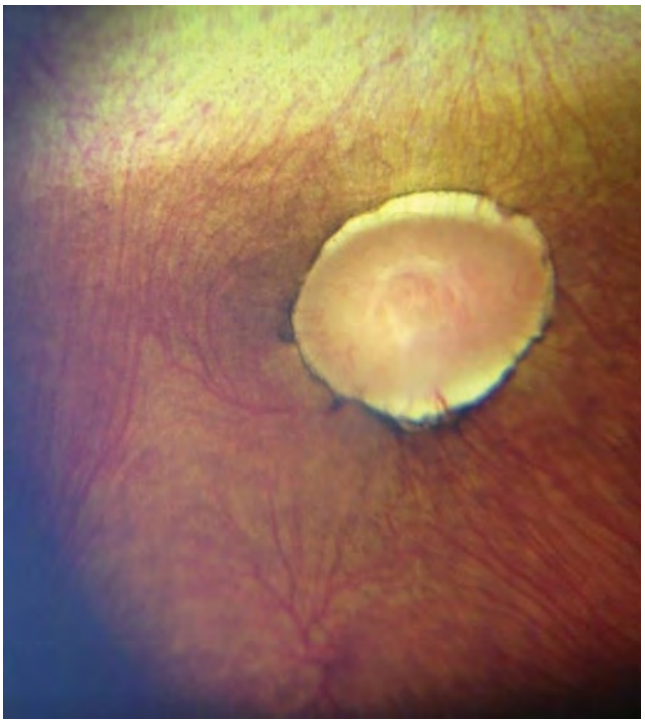


Figure 11.7 Subalbinotic fundus with a thin area of pigment visible just outside the lamina cribrosa and not covered with optic nerve myelination. This is a normal variation. (*Source*: Photograph courtesy of Dr Tim Knott, United Kingdom.)

clinically by the preservation of vision in horses despite often chronic elevations in IOP.

The horse has a paurangiotic (partially vascularized) retina with 30–60 small retinal vessels radiating from the margin of the optic disc. Arterioles and venules cannot be distinguished from one another and may be absent at the 6 o'clock region of the nerve (Figure 11.8). These vessels are visible for a distance of

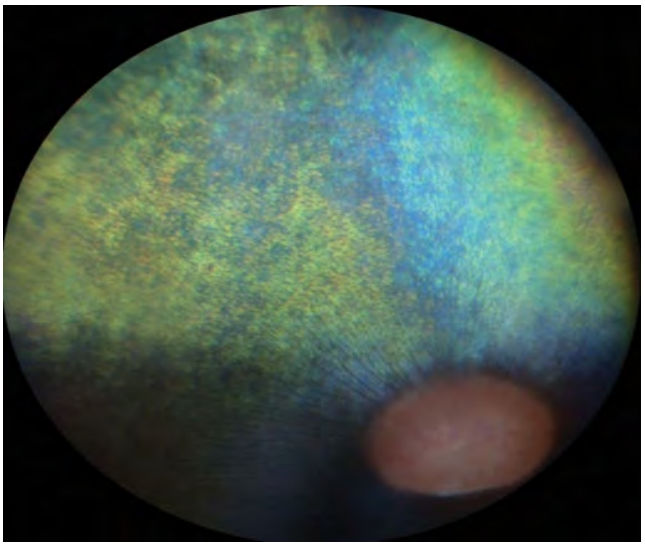


Figure 11.8 Normal optic nerve, retinal blood vessels, and tapetal fundus in a mule.

1–2 disc diameters but are less prominent dorsal and ventral to the optic nerve. Occasionally, a small vessel may be seen to emerge from the central optic nerve and course across its surface (see Figure 11.6). The remainder of the equine retina is avascular. The thickness of the NSR varies from 250 μm medial to the optic disc to 80 μm at the ora ciliaris, yet the majority is less than 130 μm in thickness to allow for oxygen diffusion from the underlying choroid [21]. The choroid, or vascular tunic, is external to the NSR and is composed of the larger choroidal vessels, the tapetum, choriocapillaris, and melanocytes.

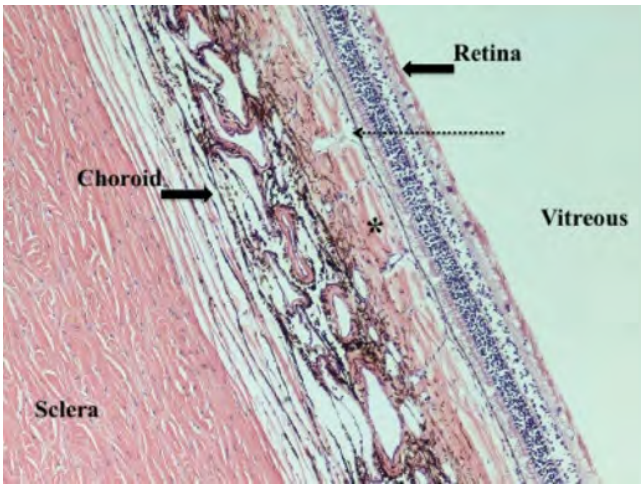
Horses have a fibrous tapetum within the dorsal choroid (Figure 11.9). The wavelength of the light reflected by the equine tapetum, 468 nm, is usable by rod photopigment and increases the sensitivity of vision in low-light conditions [22]. Although the tapetum improves the threshold of light detection, there has been concern that it may also cause glare and thereby decreases visual acuity in bright light [18]. However, a recent study demonstrated that the wavelength of light reflected from the tapetum is far from the spectral peak of the cones responsible for bright light visual resolution, and therefore is unlikely to seriously degrade the visual resolution achieved in bright light [22].

Examination of the posterior segment

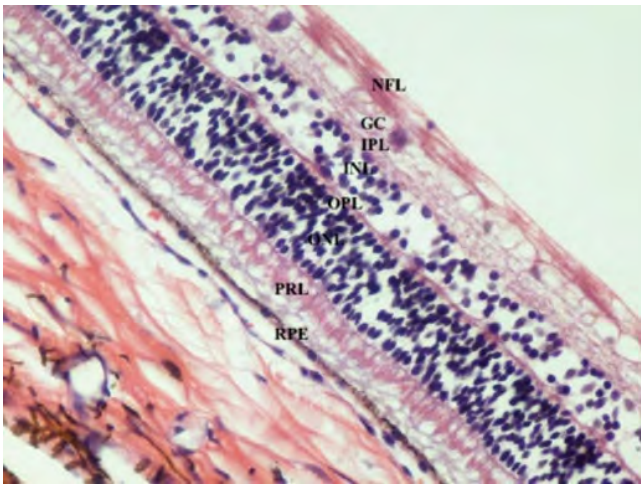
Clinical examination

Biomicroscopy

Biomicroscopy should be used for examination of not only the anterior segment but also the anterior third of the vitreous for vitreous syneresis, asteroid hyalosis, debris, membranes, vascular remnants, and hyalitis. See Chapter 1 for more information. A yellow-green discoloration of the vitreous may be observed in uveitis cases and is indicative of serum staining due to intraocular inflammation.



(A)



(B)

Figure 11.9 (A) Histologic section of the posterior segment of the equine eye (H&E × 100). **Asterisk**, tapetum; **dotted arrow**, star of Winslow (H&E × 100). (B) Histologic section through the nontapetal equine retina (H&E × 200). NFL, Nerve fiber layer; GC, ganglion cell; IPL, inner plexiform layer; INL, inner nuclear layer; OPL, outer plexiform layer; ONL, outer nuclear layer; PRL, photoreceptor layer; RPE, retinal pigment epithelium (H&E × 200).



Figure 11.10 Indirect ophthalmoscopic examination using a Finnoff transilluminator as the light source and a 20-D lens. This technique is used when an indirect headset is not available.

Direct and indirect ophthalmoscopy

Both direct and indirect ophthalmoscopy should be used for examination of the equine posterior segment. Indirect examination is performed initially for an overview of the fundus, and direct ophthalmoscopy is preferred for detailed examination of the optic nerve and retinal blood vessels. Indirect examination with a 20-diopter (D) condensing lens and a Finoff transilluminator (Figure 11.10) will provide a more panoramic but less magnified view of the fundus with lateral and axial magnifications of 0.79× and 0.84×, respectively [23]. Use of a 14-D condensing lens provides greater magnication with lateral and axial magnifications of 1.18× and 1.86×, respectively [23].

Indirect examination offers better visualization of the peripheral retina. Also it can be performed by using an indirect headset that affords stereopsis and illumination, and leaves the examiner with a free hand to elevate the superior eyelid (Figure 11.11). It allows visualization of the fundus through cloudy transmitting media, such as aqueous flare or lenticular sclerosis, which is more challenging with direct examination. A virtual, upside-down, reversed image is visualized (Figure 11.12).

An intermediate option for fundus examination is the PanOptic ophthalmoscope (Welch Allyn, Skaneateles Falls, NY). The PanOptic ophthalmoscope is a wide-view, direct ophthalmoscope that provides an erect image with a five-times greater field of view, but less magnification than that provided by standard direct ophthalmoscopy (Figure 11.13).

Direct examination provides the greatest magnification, with lateral and axial magnifications of 7.9× and 8.4×, respectively [23].



Figure 11.11 Indirect ophthalmoscopic examination with a 20-D condensing lens and a binocular headset. (*Source*: Reproduced with permission from Andy Matthews, Angus, Scotland.)



Figure 11.12 The equine posterior segment as seen through a 20-D indirect lens. The image is upside down and reversed. (*Source*: Reproduced with permission from Andy Matthews, Angus, Scotland.)



Figure 11.13 Examination of the posterior segment using the Welch Allyn PanOptic® wide-view, direct ophthalmoscope.

Direct ophthalmoscopy should be used for detailed examination of the optic nerve, retinal blood vessels, and peripapillary region. For examination of the posterior segment, the direct ophthalmoscope is set to 0 D and the ophthalmoscope is held less than 2 cm from the horse's eye (Figure 11.14). The optic nerve should be in focus for most examiners at this setting. Changing the diopter settings positively or negatively will allow the clinician to focus more anterior (vitread) or more posterior to determine whether an abnormality is elevated or depressed, respectively. The image obtained with a direct ophthalmoscope is upright and magnified (see Figure 11.2). Abnormalities of the cornea, aqueous, lens, and vitreous can



Figure 11.14 Technique of direct ophthalmoscopy in the horse using a Welch Allyn direct ophthalmoscope.

make direct examination difficult. In such instances, indirect examination should be attempted. See Chapter 1 for more information on ophthalmoscopy.

Interpretation

During examination of the fundus, what the clinician sees is dependent on the color and thickness of the three concentric tunics—the retina, choroid, and sclera—that comprise the posterior eye wall. The NSR has the optical consistency of wax or tissue paper, rendering tissues below it less reflective and dull. A loss of retinal tissue will therefore increase the reflectivity and brightness of the underlying tissue. This is called **hyper-reflectivity** in the tapetal fundus. Alternately, thickening of the retina (e.g., edema, inflammatory or neoplastic cells, dysplasia) will obscure and dull the underlying tissue, resulting in tapetal **hyporeflectivity**. The outermost layer of the retina is the monolayer RPE, which is normally pigmented in the ventral nontapetal retina and nonpigmented over the tapetum in most horses. The choroid or vascular tunic is composed of melanin-containing cells, blood vessels, and, dorsally, the fibrous tapetum. The outermost fibrous tunic, the sclera, appears white. The coat color of the horse, amount of melanin, and thickness of the tapetum all influence the normal appearance on fundic examination. Variations in the normal equine fundus are common, and familiarity with these variations is essential before one can interpret and understand abnormalities [24–30].

The fundus is divided into the dorsal tapetal and ventral nontapetal regions. The fibrous tapetum is situated in the dorsal choroid and is responsible for the characteristic yellow-green color of this portion of the fundus. Variations in tapetal color are related to iris and coat color and include yellow, orange, and blue-green [25, 26, 29]. Dark bay and brown horses usually have a blue-green tapetum with a dark nontapetal region (Figures 11.15 and 11.16). Lighter chestnuts and palominos may have a yellow tapetum with a less pigmented nontapetal region

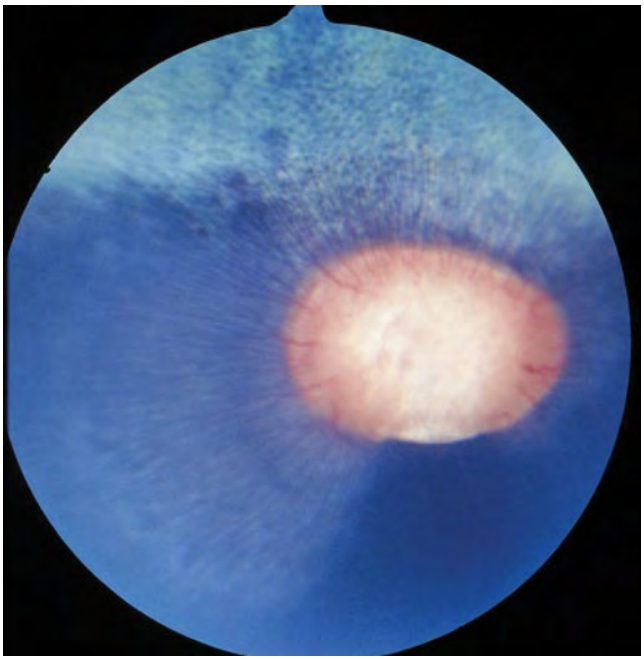


Figure 11.15 Normal fundus of a dark-bay horse with a blue tapetum. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

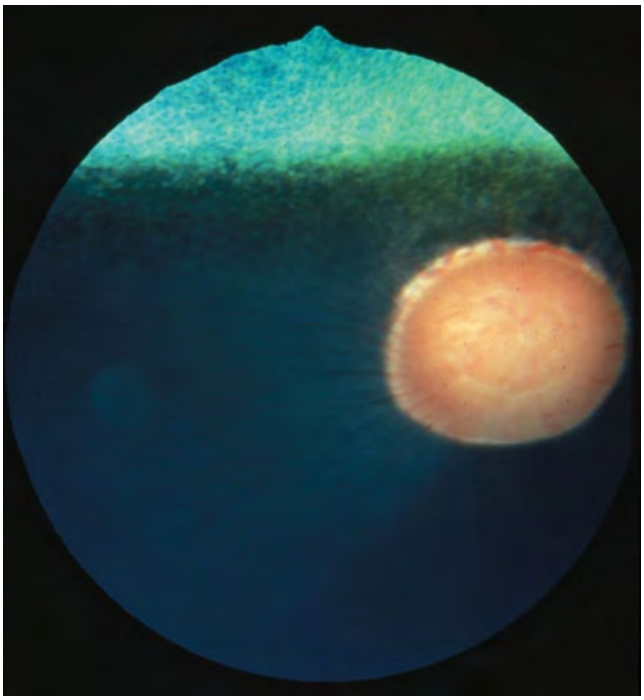


Figure 11.16 Normal fundus with a green tapetum.

(Figures 11.17 and 11.18). Gray and white horses generally have a yellow tapetum with a lightly pigmented or nonpigmented nontapetal fundus. This may allow visualization of the choroidal vasculature and sclera.

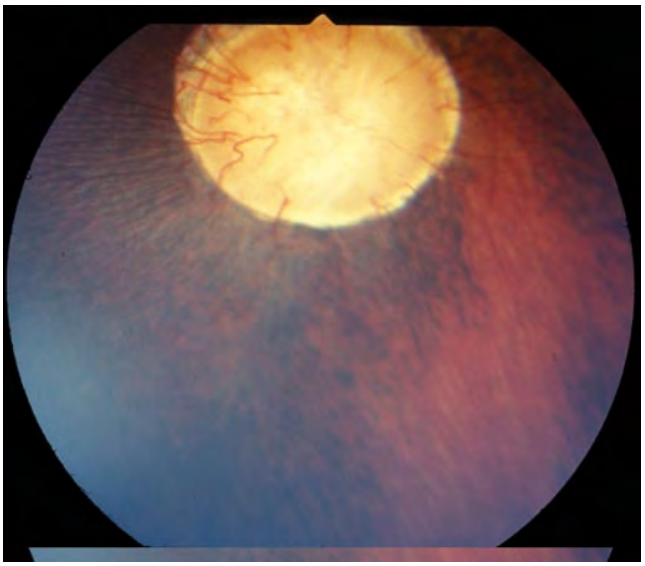


Figure 11.17 Nontapetal fundus of a light-colored horse. An area of choroidal hypopigmentation is present, allowing visualization of the choroidal vasculature.

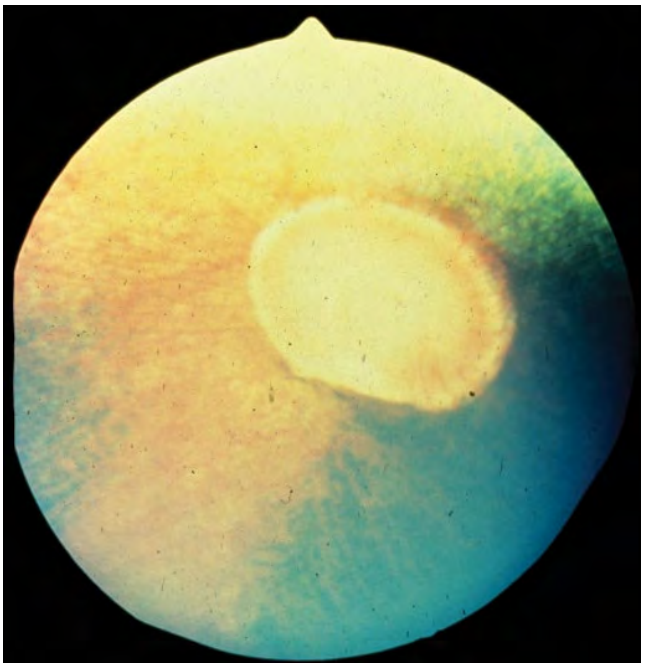
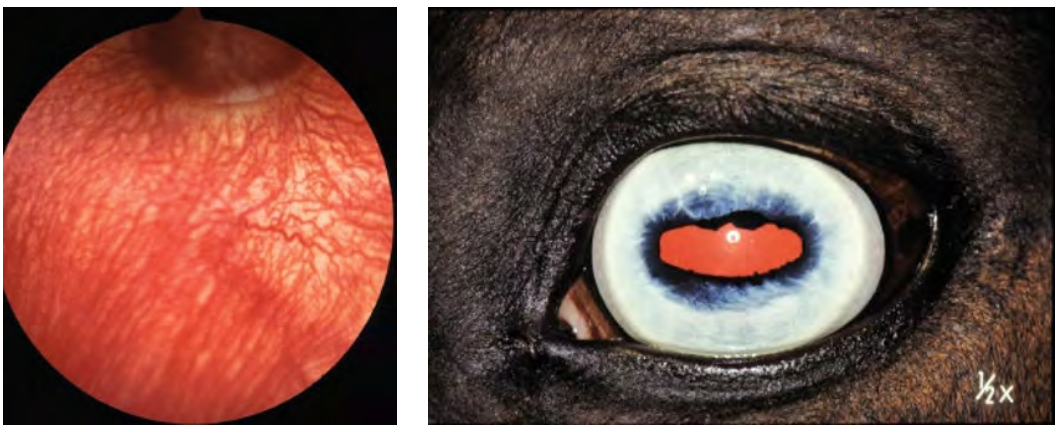


Figure 11.18 Normal fundus of a palomino horse, demonstrating a yellow tapetum and area of choroidal hypopigmentation.



(A) (B)

Figure 11.19 (A) Normal fundus of an albinotic eye. This photo was taken in the ventral, nontapetal fundus. (B) Gross external photograph of the same horse, showing a red fundic reflex and blue iris. (*Source*: Photographs courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

Finally, in color-dilute horses, the tapetum may be hypoplastic or absent [31, 32]. Tapetal hypoplasia can be generalized or confined to a portion of the tapetum, most often immediately dorsal to the optic disc (Figures 11.19 and 11.20). Color and thickness of the tapetum and choroidal pigment vary not only between horses but also within horses from right to left eye.

Near the periphery of the tapetum, it is not unusual to see focal areas of RPE pigmentation obscuring the underlying tapetum (Figure 11.21). In addition, random foci of RPE pigmented freckles or nevi may appear throughout the tapetum (Figure 11.22). These must be differentiated from post-inflammatory hyperpigmentation or choroidal melanoma. Uniformly distributed dark dots are typically seen throughout the tapetum and are end-on small choroidal arterioles called the **stars of Winslow**, which serve to supply the retina via the choriocapillaris (Figure 11.23).

The ventral, nontapetal fundus is generally dark brown or black but can appear lighter or nonpigmented, depending on coat color [25, 26]. In color-dilute horses the tapetum may be hypoplastic or absent, and the choroid and RPE may demonstrate partial or complete albinism. This can affect one or both eyes and can even be observed to vary within an eye. Choroidal vasculature and vortex veins may be visible, especially in

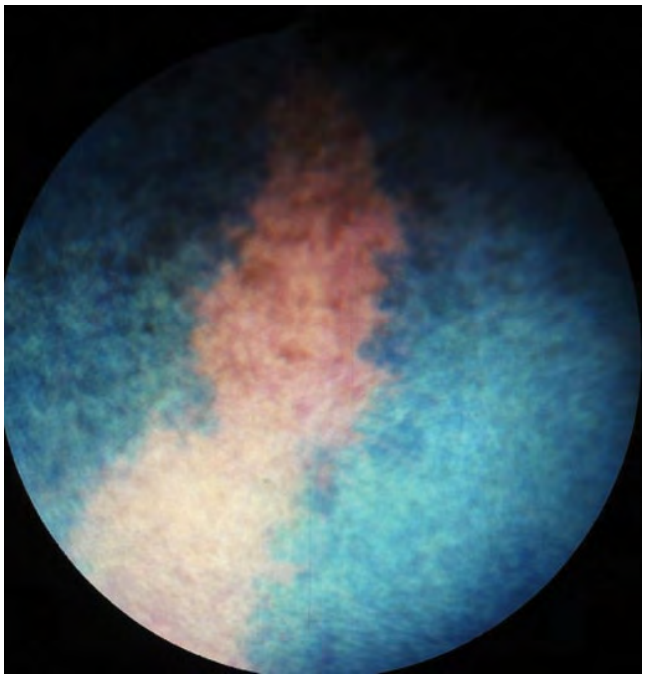


Figure 11.20 Normal fundus with a linear area of tapetal hypoplasia. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

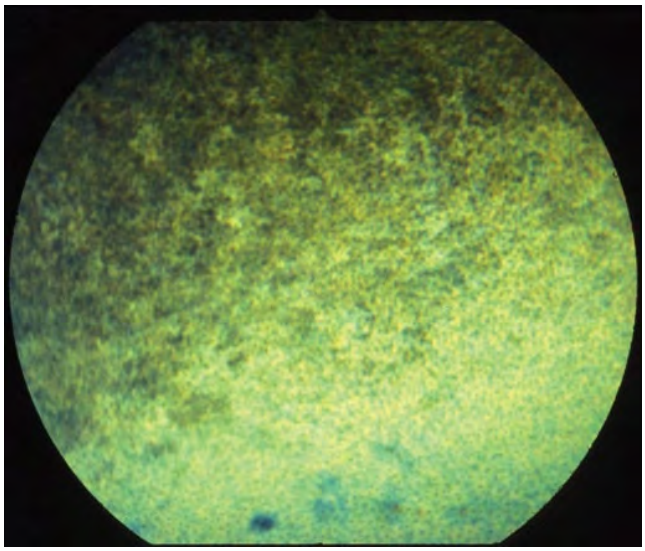


Figure 11.21 Dorsal tapetum with areas of RPE pigmentation obscuring the underlying green tapetum. This is a normal variation.

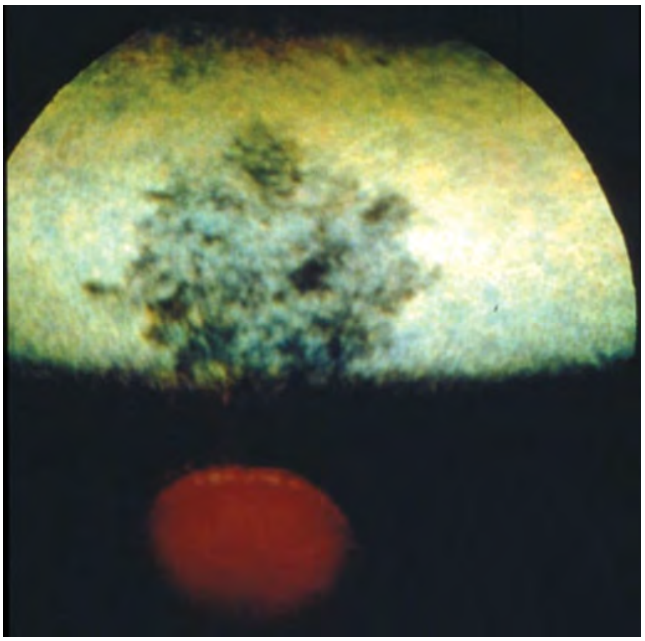


Figure 11.22 RPE pigmentation over the tapetal retina dorsal to the optic nerve. This is a normal variation.

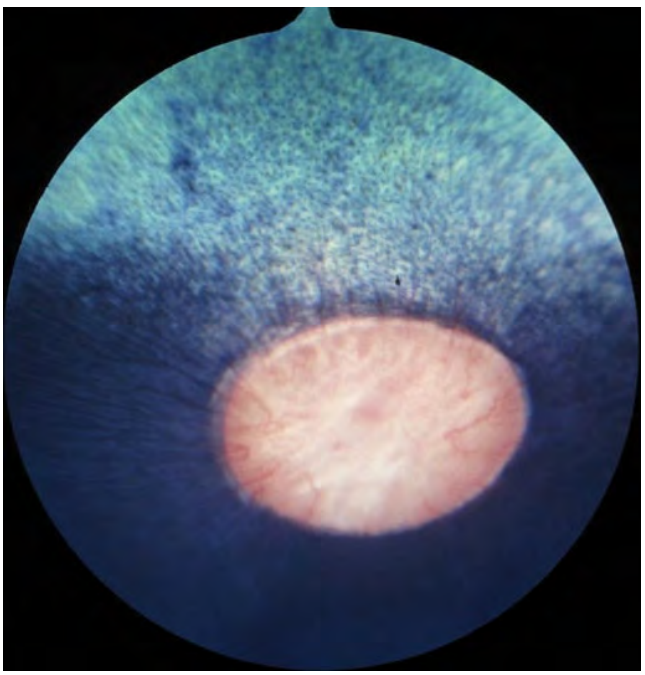


Figure 11.23 Normal equine fundus. Stars of Winslow are apparent dorsal to the optic nerve as multifocal, uniform black dots in the tapetal fundus. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

association with tapetal hypoplasia and ocular albinism (Figures 11.24 and 11.25). These vessels may appear as radiating, dark striae seen through a normal tapetum or as red vessels in a subalbinotic to albinotic eye.

The peripapillary region should be examined closely as most abnormalities are identified in this area. Peripapillary lesions can be of greater visual significance because of the high concentration of retinal axons. However, one must be careful in interpretation as several variations of normal may also be present that could be misconstrued as lesions. Focal areas of nontapetal fundus nonpigmentation or depigmentation (Figure 11.26) are often normal variations, but previous intraocular inflammation can also result in depigmentation. For example, infection with

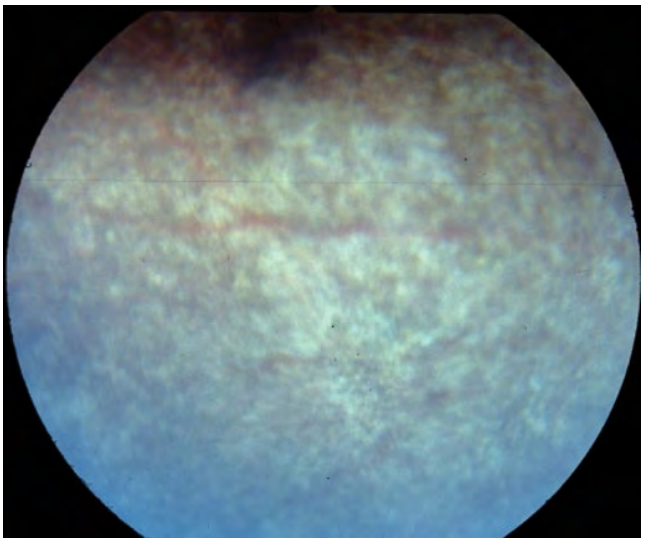


Figure 11.24 Normal nontapetal fundus of a color-dilute horse. The underlying choroidal vasculature can be seen.

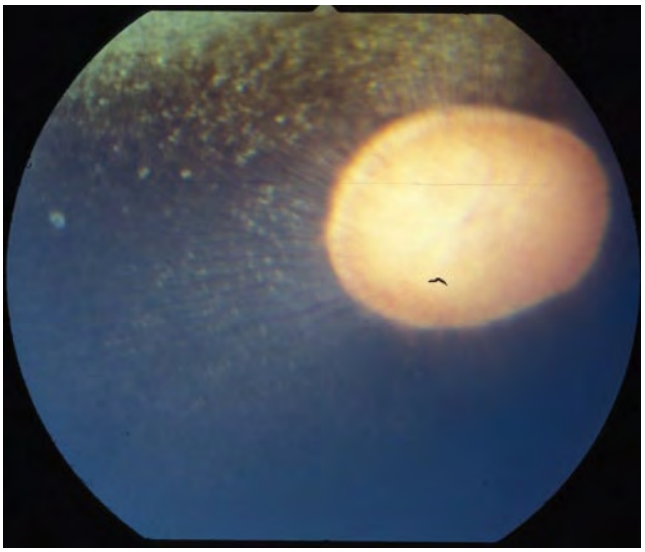


Figure 11.26 Peripapillary pigment variation. Multifocal areas of hypopigmentation are noted. The overlying retinal vessels are normal.

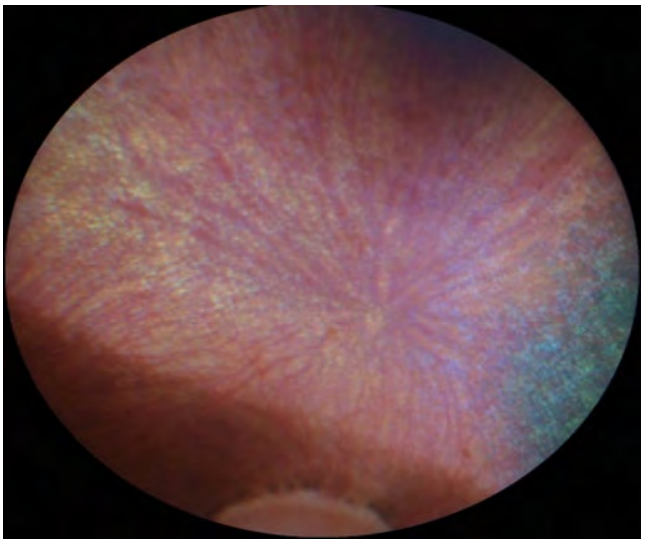


Figure 11.25 Normal fundus of a color-dilute and mostly atapetal horse, with the choroidal vortex vein visible dorsal to the optic nerve head.

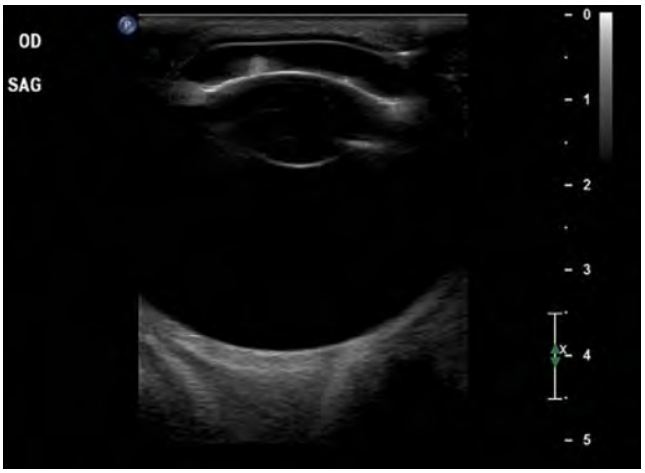


Figure 11.27 Ultrasound examination of a normal eye, with corpora nigra visible anterior to the clear lens and no opacities present in the vitreous.

equine herpesvirus-1 (EHV-1) has been reported to result in focal white chorioretinal lesions in the nontapetal fundus (see section **Chorioretinitis**) [33].

Posterior segment examination should include clinical evaluation of the vitreous, tapetal and nontapetal fundus, retina, retinal blood vessels, and optic nerve. Additional posterior segment diagnostic tests may include ocular ultrasonography [34], optical coherence tomography (OCT) [35], electroretinography (ERG) [36], visual evoked potential (VEP) [37], fluorescein angiography [38], computed tomography (CT), and magnetic resonance imaging (MRI). See Chapters 1 and 2 for more information.

Advanced diagnostics

Ultrasonography

Ultrasonography is indicated when opacities of the transmitting media prevent examination of the posterior segment. Ultrasonography allows visualization of the cornea, anterior chamber, iris leaflets, ciliary body, lens, vitreous body, optic nerve, and the retina, choroid, and sclera in combination (Figure 11.27) [34]. Typically, cataracts and hyphema are the most common indications for ultrasound examination of the posterior aspect of the globe [34]. Conditions such as hyalitis, vitreal opacities, retinal detachment, and choroiditis can be visualized with ultrasonography (Figure 11.28) [34]. A 5- to 20-MHz ultrasound probe will provide diagnostic images of the posterior globe, with 7.5 or 10-MHz probes preferred. The 5-MHz probe provides less

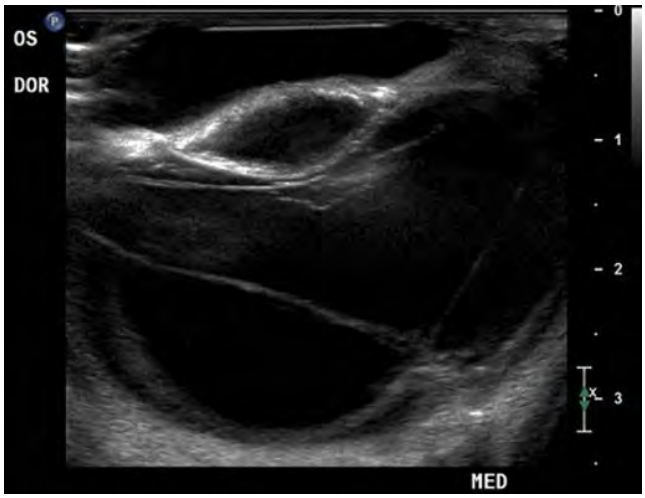


Figure 11.28 Ultrasonic appearance of an eye presented for cataract evaluation, showing a complete retinal detachment with hyperechoic lines present in the vitreous, depicted by a classic "seagull" sign.

near-field resolution and greater penetration of the orbit, whereas the 20-MHz probe provides excellent resolution of the anterior segment, but the posterior eye wall is the limit of its penetration in the equine eye. Direct corneal contact with the use of methylcellulose gel is the technique of choice, provided that the cornea is intact. Imaging can be performed through the eyelid if the cornea is compromised. See Chapter 2 for more information.

Optical computed tomography

A handheld spectral-domain optical coherence tomography (SD-OCT) instrument has been used to image the retina and optic nerve head in standing, sedated horses [35]. Using OCT, the highest total retinal and nerve fiber layer thickness was found nasally at the level of the optic nerve head (459 and 377 μm, respectively), followed by the temporal (449 and 357 μm), dorsal (336 and 229 μm), and ventral (231 and 128 μm) quadrants [35]. Common equine fundus lesions have also been imaged using SD-OCT (Figures 11.29, 11.30, 11.31, 11.32, 11.33, and 11.34) [39]. See Chapter 2 for more information.

Electroretinography

While ERG has traditionally been performed using general anesthesia, a technique for obtaining a flash photopic and scotopic ERG in a standing sedated horse has been described, making this test more easily obtained and associated with less risk and expense [36]. An ERG is indicated to evaluate retinal function prior to cataract surgery and to assess retinal health and aid in diagnosis of congenital stationary night blindness (CSNB), glaucoma, equine motor neuron disease, chorioretinitis, optic neuritis, and ocular trauma. See Chapter 1 for more information.

Visual evoked potentials

Visual evoked potentials (VEPs) have been recorded in horses [37, 40, 41]. The highest amplitudes are obtained when the active electrode is placed 6–9 cm rostral to the nuchal crest [40].

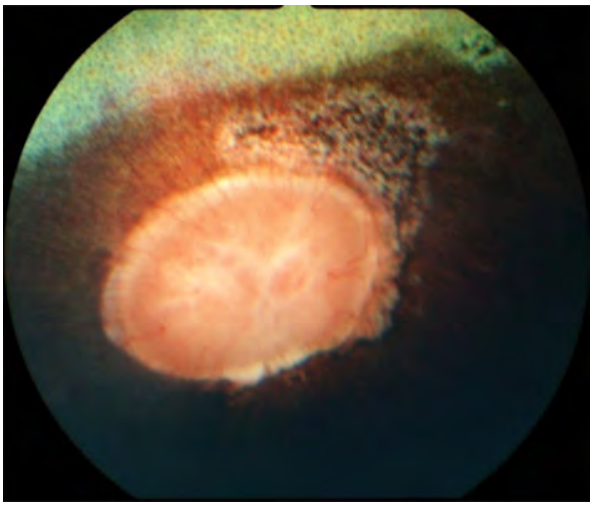


Figure 11.29 Color ocular fundus of the left eye of a 12-year-old, Hanoverian gelding. There is a depigmented lesion dorsotemporal to the optic disc.

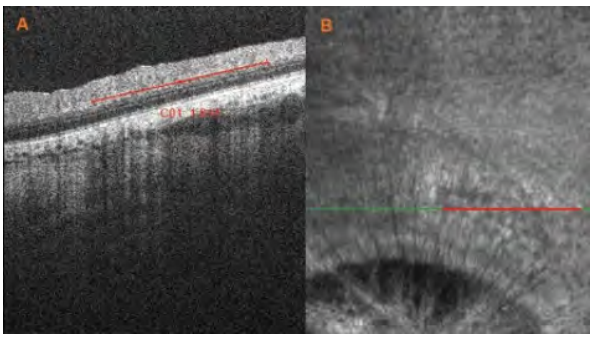


Figure 11.30 B-scan (A) and en-face view (B) OCT image of the lesion seen in Figure 11.29. The green and red horizontal line in B represents the area for the B-scan in A. The red line on both images indicates the area of the lesion. This study suggests that there is depigmentation but not degeneration of the retina since the retinal structure appears normal at the site of the lesion.

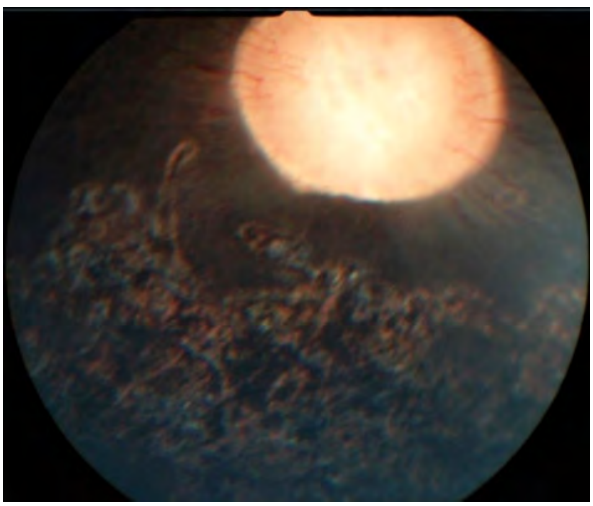


Figure 11.31 Color ocular fundus photograph of the left eye of a 3 year old, Quarter horse gelding which had flipped over backwards and sustained pterygoid skull fractures.

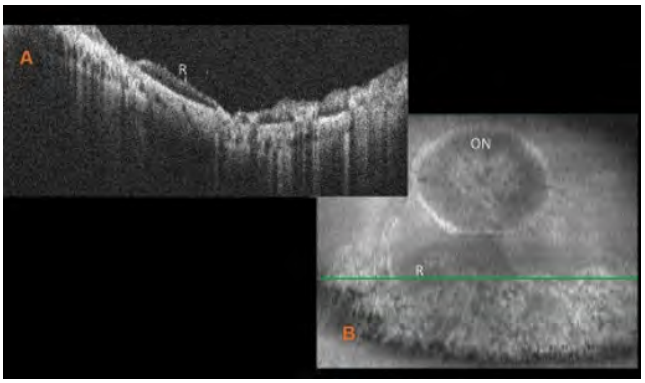


Figure 11.32 B-scan (A) and en-face view (B) OCT image of the lesion seen in Figure 11.31. There are multiple areas of retinal thinning visible on the B-scan, suggesting retinal degeneration. The section labeled R on both images corresponds to normal-appearing retina. ON, Optic nerve. This study suggests that there is degeneration of the retina and not just depigmentation.

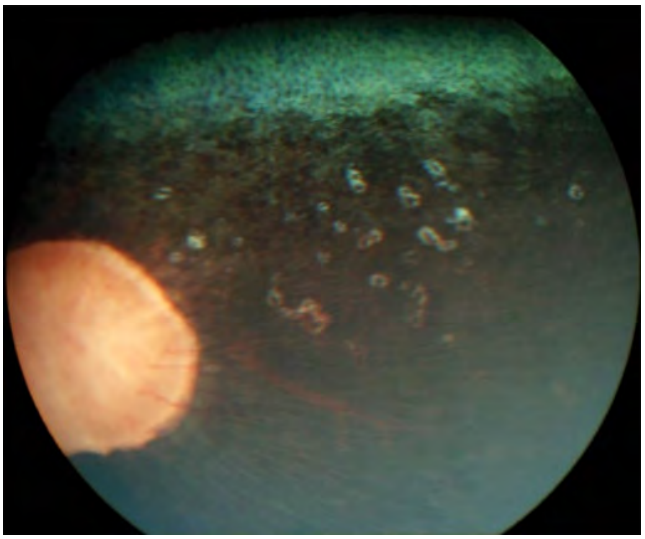


Figure 11.33 Color ocular fundus photograph of a 25-year-old Warmblood mare with multifocal retinopathy, or "bullet-hole" lesions, in the nontapetal ocular fundus.

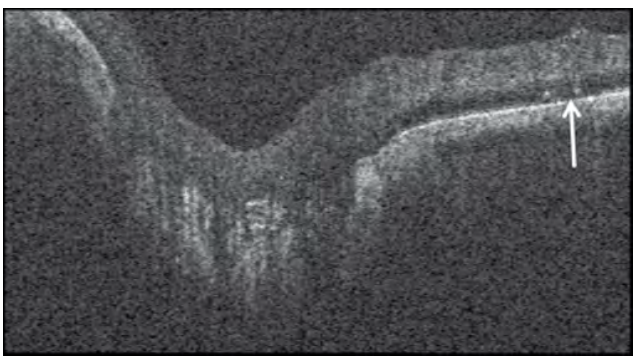
A VEP can be recorded from birth onward, with similar waveforms noted between foals and adults, except for higher amplitudes in the VEPs recorded from foals [41]. Sedation with both detomidine and xylazine have been used when recording VEPs [41]. Generally, detomidine was preferred as adequate sedation depth was easier to achieve [41]. The impact of sedation on the latencies and amplitudes is not yet known [41]. See Chapter 1 for more information.

Fluorescein angiography

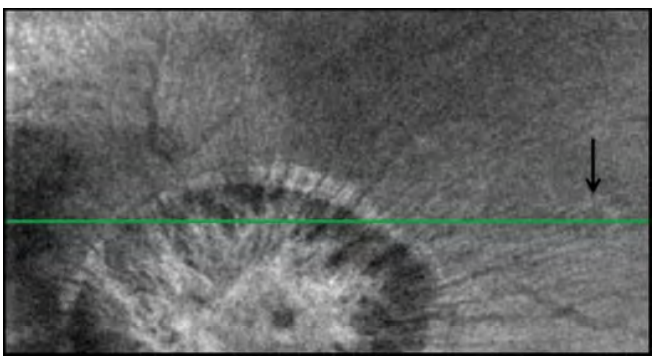
The technique and results of fluorescein angiography have been described in the normal horse [38]. Two successive angiographic phases were described: the choriopapillary phase, starting at 46.95 ± 9.48 seconds, and the retinal vascular phase, starting at 47.79 ± 10.38 seconds. The retinal vascular phase was divided into three parts: filling phase, maximum fluorescence point, and fading phase. During the filling phase, the dye progressed into the retinal vessels, obtaining maximum fluorescence at 59.79 ± 10.39 seconds, termed the maximum fluorescence point. The fading phase started immediately following the maximum fluorescence point. During this phase, vascular fluorescence decreased to complete reduction at 74.76 ± 9.81 seconds. Areas of delayed choroidal filling, the presence of short retinal vessels in the ventral region of the optic disc, and a trapezoidal ventral area of the optic disc that did not fluoresce were also observed [38]. Fluorescein angiography may have value in evaluating diseases of the retina, choroid, RPE, and optic nerve versus incidental findings (Figure 11.35). See Chapter 1 for more information.

Computed tomography and magnetic resonance imaging

Both CT and MRI can be used to image the equine eye, with MRI reportedly most useful [42]. Using MRI, the cornea, anterior and posterior chambers, ciliary body, lens, vitreous, optic nerve, and sclera can be identified [42]. However, the retina, choroid, and sclera cannot be differentiated in normal eyes [42]. See Chapter 2 for more information.



(A)



(B)

Figure 11.34 B-scan (A) and en-face view (B) OCT image of the lesion seen in Figure 11.36. **Arrows** correspond to the same areas in the retina. There is increased opacity in the B-scan area at the site of the bullet-hole lesion, indicating glial-cell proliferation. This is likely a result of inflammation or trauma. The retina is not thinned in this area nor is there overt disorganization of retinal layers.

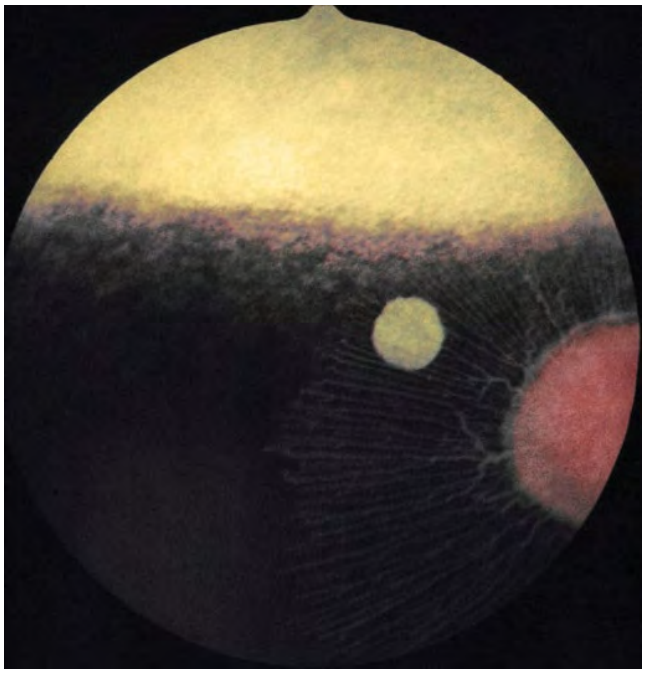


Figure 11.35 Late-phase fluorescein angiogram of a horse with an incidental RPE coloboma. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

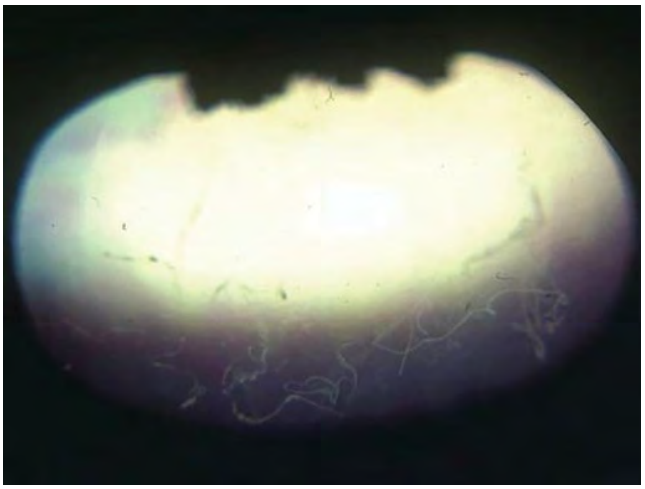


Figure 11.36 Embryonic vascular remnants are visible as fine, tortuous, pale, tubular structures floating free within the anterior vitreous. (*Source*: Reproduced with permission from Andy Matthews, Angus, Scotland.)

Diseases of the posterior segment

Vitreous

Persistent hyaloid artery

The hyaloid artery travels from the optic nerve anteriorly to the posterior lens capsule, where it connects with the posterior portion of the tunica vasculosa lentis. This vascular network generally disappears before or at the time of birth [4, 32]. In one study of the hyaloid apparatus in neonatal Thoroughbred foals, some portion of the hyaloid was present in over 80% of 169 foals examined [43]. The entire hyaloid artery was observed in approximately 60% of foals examined [43]. In general, the presence of the hyaloid appartus was bilateral, symmetrical, correlated with the presence of the posterior pupillary membrane, and not associated with any significant ocular problems [43]. In a survey of 204 Thoroughbred racehorses in Australia, a persistent hyaloid remnant was described in one horse [2].

Clinical appearance and diagnosis

Persistence of the hyaloid vasculature is uncommon in the horse compared with other domestic animals. Typically, a persistent hyaloid artery in adult horses appears as a fine, white, vermiform structure extending from the axial posterior lens capsule into the vitreous or from the optic nerve into the vitreous [44]. Alternatively, smaller embryonic vascular remnants may be visible as fine, tortuous, pale, tubular structures floating free within the anterior vitreous (Figure 11.36). A persistent hyaloid can be seen as an isolated finding or in association with other congenital anomalies such as posterior lenticonus, cataract, retinal dysplasia, coloboma, microphthalmia, or retinal detachment. If a posterior, axial cataract is noted, the cataract should be monitored for progression.

Treatment

No treatment is indicated.

Prognosis

Most instances of an isolated persistent hyaloid artery will spontaneously regress by 6–9 months of age [4]. There is no known genetic component to this disease.

Hyalitis

Hyalitis or inflammation of the vitreous can be seen with ERU or as an extension of chorioretinitis. In one retrospective study, horses with ERU and hyalitis had a poorer prognosis for vision than those without vitreal inflammation, and 80% of the horses with hyalitis were diagnosed with positive leptospirosis titers [45]. In Europe, hyalitis appears to be a common manifestation of equine uveitis. When 130 vitreous samples from 117 European horses affected with ERU which were collected during vitrectomy were evaluated, leptospires were isolated in 35 samples (26.9%) [46]. The most common serovar was Grippotyphosa [46]. In addition, 92 vitreous samples (70.7%) were positive for leptospiral antibodies [46]. Results of other similar studies have also confirmed the presence of leptospires in the vitreous of horses with ERU, with an additional finding of *Leptospira interrogans* in the vitreous of 52% of horses with ERU, but not in any control eyes [47–49]. Similar results have been reported in the southern USA with leptospiral DNA detected by quantitative polymerase chain reaction (qPCR) in 45% of horses, isolation of leptospires by culture in 21% of horses with ERU, and antileptospiral antibodies present in the ocular fluid of 70% of horses [50]. Antibodies to the serovar Bratislava were most commonly

identified on microscopic agglutination titers from both serum and ocular fluids [50]. However, the serovars Pomona and Grippotyphosa were isolated from cultures of ocular fluids [50]. In addition, horses with ERU have an increase in vitreous immunoglobulin A (IgA) as compared with serum IgA, suggesting a local immunologic reaction to antigens within the eye [51]. See Chapter 8 for more information on equine uveitis.

With hyalitis, the vitreous may take on a yellow-green appearance as a result of serum pigments (Figure 11.37). Thickened vitreal membranes, vitreal debris, fibrin, and inflammatory cells may be seen suspended within the vitreous or adhered to the posterior lens capsule (Figure 11.38). Strands of condensed vitreal collagen may float or swirl within vitreous that has undergone syneresis due to previous inflammation (see section **Vitreous syneresis**). Posterior cortical cataract and retinal detachment may occur as a result of hyalitis.



Figure 11.37 The vitreous has a yellow-green appearance in this horse with uveitis.

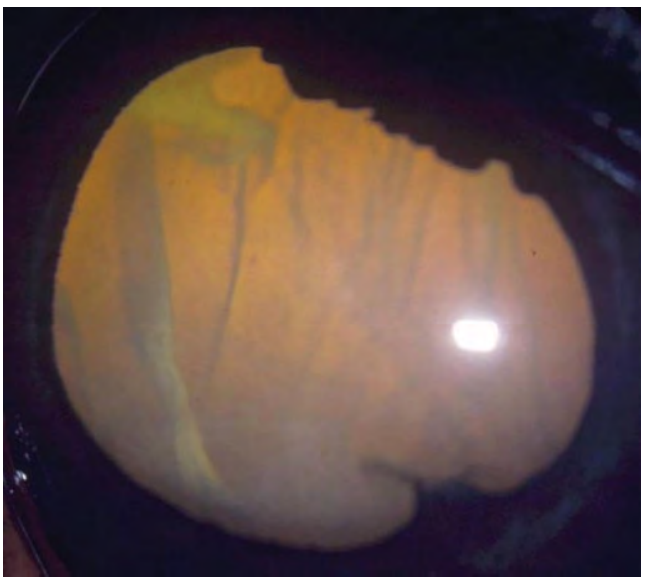


Figure 11.38 Thickened vitreal membranes are visible behind the lens following panuveitis. (*Source*: Reproduced with permission from Andy Matthews, Angus, Scotland.)

Vitreous syneresis

Vitreous degeneration or syneresis is more common in aged horses and in such cases is a benign condition. Vitreous syneresis can also be a pathologic change associated with inflammation [4]. In one study of 83 geriatric horses, vitreous degeneration was the most common abnormality, being present in 38 animals and 72 eyes [52]. In another study of 200 geriatric horses, vitreous degeneration was noted in 191 of 400 eyes [53]. The prevalence of vitreous degeneration increased with age [52, 53]. With syneresis may come vitreous floaters that can affect behavior, causing shying or head shaking (Figure 11.39). Although examination for vitreous floaters in horses with the complaint of head shaking is an essential part of the ophthalmic examination, seldom are these the cause. Evaluation for photic head shaking, refractive errors, ear or nasal disease, or various behavior concerns is more likely to result in a diagnosis.

Asteroid hyalosis (deposits of calcium-phosphate crystals in the vitreous) also occurs in horses (Figures 11.40 and 11.41). This is an incidental finding and is more common in aged horses.

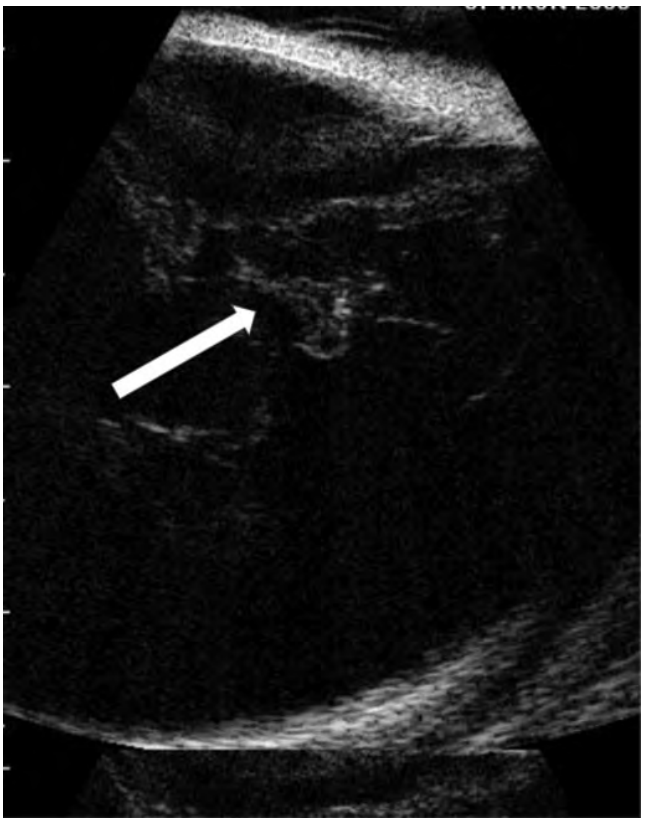


Figure 11.39 Ultrasound examination of an equine eye with a cataract and vitreous degeneration. Echogenic material is observed in the mid to anterior vitreous (**white arrow**) and is seen to move when evaluated in real time.

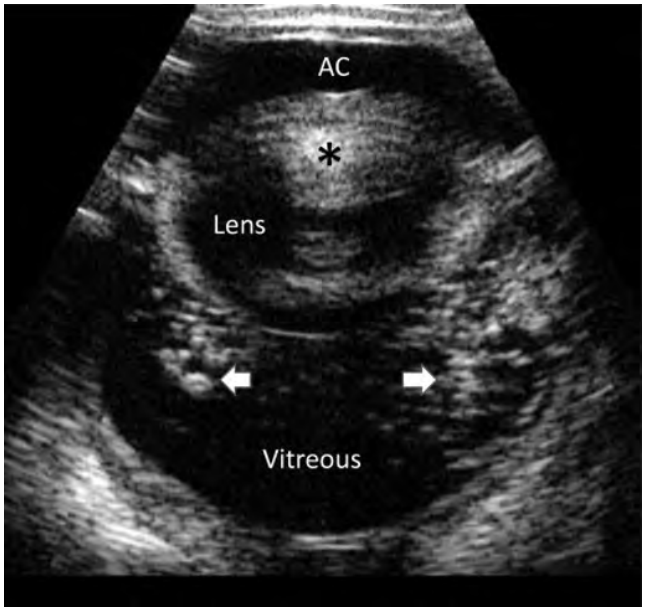


Figure 11.40 Ultrasound examination of an equine eye with a cataract (a portion of which is denoted by the **asterisk**) and asteroid hyalosis (**white arrow heads**). AC, Anterior chamber.

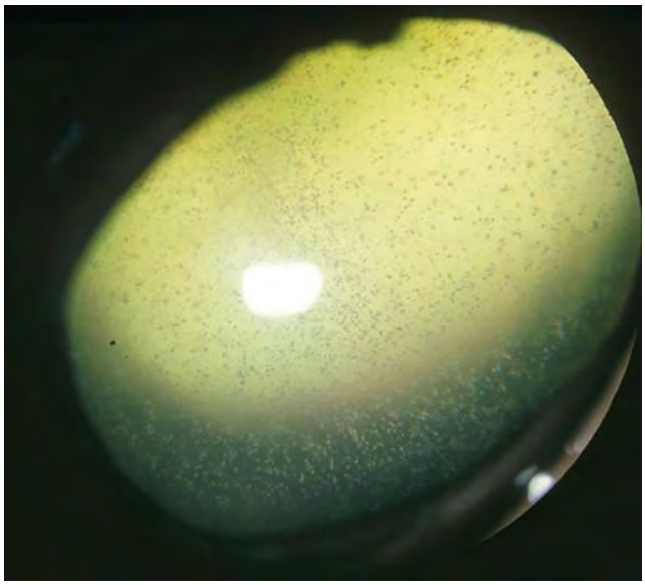


Figure 11.41 Asteroid hyalosis appears as multifocal, whitish refractile inclusions suspended in the vitreous, and only limited motion of opacities is noted with ocular movement. (*Source*: Reproduced with permission from Andy Matthews, Angus, Scotland.)

Retina

Retinal hemorrhages

Subretinal and intraretinal hemorrhages may be noted in neonatal foals (Figure 11.42) [54, 55]. In one study of 167 neonatal Thoroughbreds, 27 (16%) were found to have retinal hemorrhages [54]. Most hemorrhages were bilateral, and females were more commonly affected than males [54]. Hemorrhages were punctate

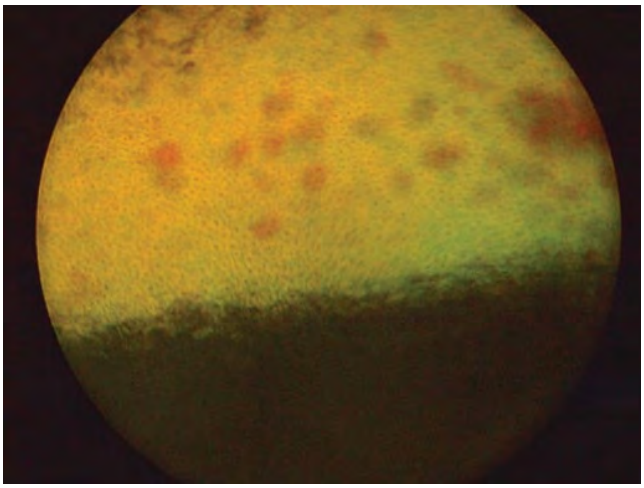


Figure 11.42 Multifocal retinal hemorrhages in a 2-day-old Standardbred foal. (*Source*: Photograph courtesy of Dr Ralph Hamor, University of Illinois.)

in 36% and "splash-like" in 56%; the number of hemorrhages per eye ranged from 1 to 20 [54]. In a study of 70 neonatal foals evaluated for nonophthalmic disease, retinal hemorrhages were seen in eight (11%), with no sex predilection noted [55]. Such hemorrhages may be the result of intraocular vascular hypertension with capillary rupture during parturition [18]. Hemorrhages will typically resolve over a few weeks with no visual or residual abnormalities [54].

Retinal dysplasia

Retinal dysplasia is a congenital malformation of the retina with the formation of folds or rosettes that appear clinically as retinal folds or larger areas of geographic dysplasia. Retinal dysplasia can be developmental or occur as a result of inflammation. It accounted for 3.5% of all congenital ocular anomalies in one study [56].

Clinical appearance and diagnosis

On ophthalmoscopic examination, dysplasia can appear as gray or hyperpigmented areas caused by retinal disorganization and RPE proliferation, respectively (Figure 11.43). Histologically, the NSR is folded and disorganized, often forming rosettes (Figure 11.44). The rosettes can be single or multiple and unilateral or bilateral. Retinal folds can be associated with *in utero* infections and have been attributed to various viral infections. In the horse, retinal dysplasia is most often associated with equine multiple congenital ocular anomalies (MCOA) syndrome [57]. Congenital megaloglobus has been associated with severe retinal dysplasia.

Treatment

Retinal folds are nonprogressive, and no treatment is required.

Prognosis

Although one author states that it is not heritable [37], not all veterinarians share this opinion. Others comment that the Thoroughbred may be predisposed to retinal dysplasia [18].

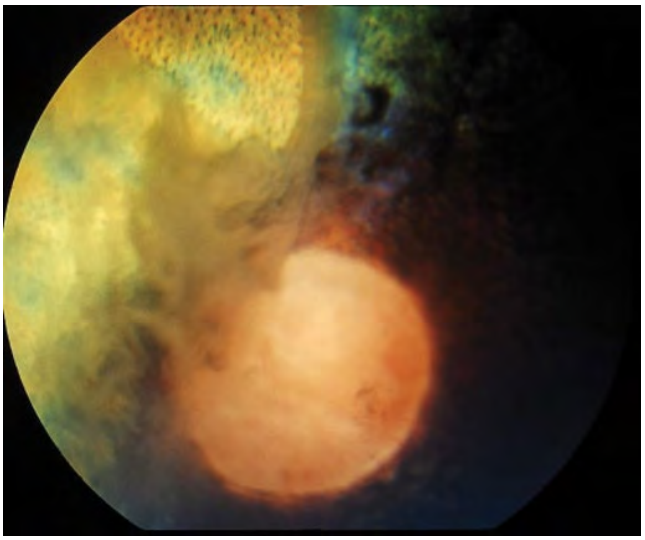


Figure 11.43 Congenital retinal dysplasia and retinal nonattachment in a foal. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

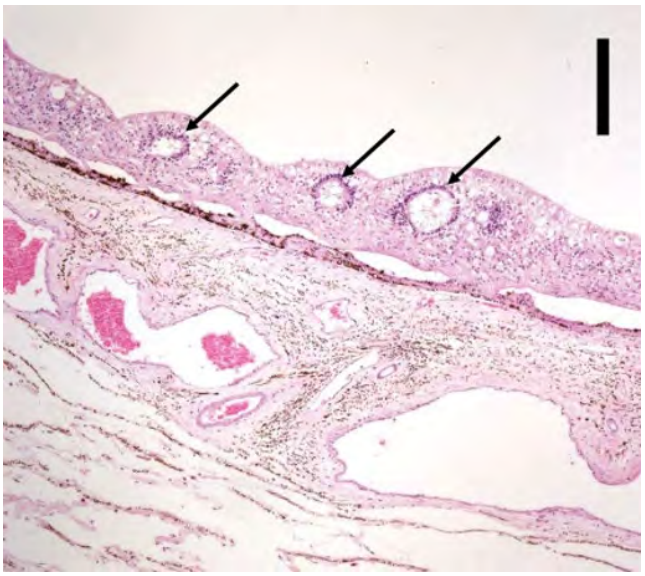


Figure 11.44 Histopathologic examination of the retina of the horse in Figure 11.43. The retina shows retinal atrophy, disorganization, and rosette formation (**black arrows**) (H&E; bar = 400 μm.) (*Source*: Photograph courtesy Drs Ingo Walde and Barbara Nell, University of Vienna.)

Breeding of horses with severe retinal dysplasia and/or MCOA should be discouraged.

Congenital retinal detachment

Congenital retinal detachment can be an isolated finding or can be associated with the anterior segment dysgenesis of MCOA; severe retinal dysplasia; or multiple congenital defects such as coloboma, microphakia, microphthalmos, and lens luxation [31]. Retinal detachment accounted for 6.2% of all congenital ocular anomalies in one study [56]. In a study of 40 horses with retinal detachment, congenital detachment was noted in only two horses (5%) [58]. One proposed cause is a failure of attachment of the NSR to the underlying RPE, which occurs as a result of incomplete invagination of the optic vesicle [18].

Clinical appearance and diagnosis

The affected eye is blind, with a dilated, nonresponsive pupil. Clinically, a veil of gray tissue radiating forward from the optic nerve is observed. If the retina is torn from the ora and falls ventral, tapetal hyper-reflectivity will be noted. Hyphema, cataract, and secondary glaucoma may occur as a result of chronic retinal detachment.

Treatment

There is no treatment, and affected animals should not be used for breeding.

Prognosis

A predilection for the Standardbred and Thoroughbred has been suggested [18, 31, 32]. Hyphema, cataract, and secondary glaucoma may occur as a result of chronic retinal detachment.

Multiple congenital ocular anomalies syndrome

Multiple, congenital anterior and posterior segment abnormalities have been described in many breeds including the Rocky Mountain, Kentucky Saddle, Mountain Pleasure, Morgan, Icelandic, American Miniature, Shetland, Deutsches Classic, Exmoor, and Comtois horse and pony breeds [57, 59–65]. The majority of affected horses have a silver (also termed chocolate) coat color with a white or flaxen mane and tail due to dilution of black pigment in the hair [60]. Coat color and ocular manifestations of the genetic mutation are visible in silver horses with a eumelanin base color; however, chestnut horses can possess the *Silver* mutation without expressing the coat color phenotype (it does not act on pheomelanin) while still demonstrating the ocular disease phenotype [66].

Clinical appearance and diagnosis

Abnormalities can affect the cornea, iris, ciliary body, lens, and retina. The anterior segment anomalies include temporal ciliary cysts, iridal hypoplasia, iridocorneal angle abnormalities, cornea globosa, and cataract. With respect to the posterior segment, temporal peripheral retinal cysts, retinal dysplasia, RPE proliferation, focal retinal degeneration, and retinal detachment have been described in affected horses [57]. Cysts can involve the posterior iris, ciliary body, or peripheral retina and are typically located temporally, although nasal cysts may be present as well [65]. Cysts can be unilateral or bilateral and affected 48% of Rocky Mountain horses examined [57]. Ultrasound was superior to direct ophthalmoscopy for detection of the uveal cysts [67]. Retinal dysplasia appeared as linear folds, most commonly in the temporal retina; it affected 24% of the horses examined and was only found in association with retinal or

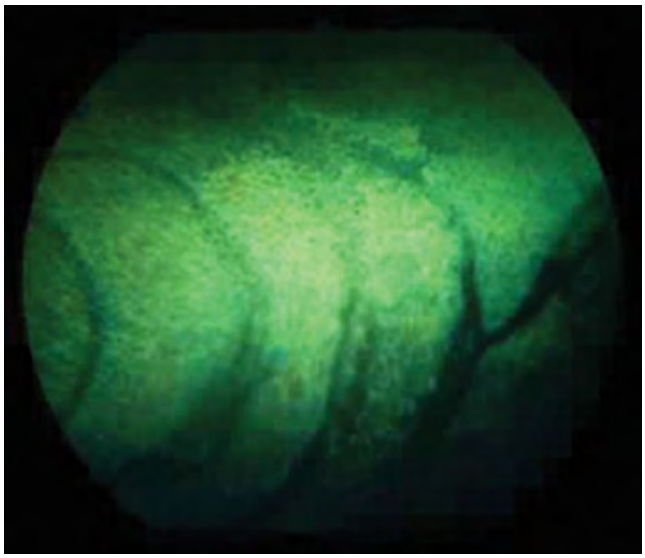


Figure 11.45 Pigment streaks of RPE extending outward from the ora. These are suggestive of previous retinal detachment. (*Source*: Photograph courtesy of Dr David Ramsey.)



Figure 11.46 Appaloosa horse affected with CSNB demonstrating dorsomedial strabismus. (*Source*: Photograph courtesy of Dr Lynne Sandmeyer, University of Saskatchewan.)

ciliary body cysts [57]. Lesions have been confirmed by histologic examination as retinal dysplasia, hypoplasia, rosette formation, and RPE proliferation. Proliferation of the RPE appearing as pigmented, curvilinear streaks that originate and terminate at the ora and extend toward the optic disc is believed to indicate previous retinal detachment (Figure 11.45) [57]. Retinal detachments appear to be associated with peripheral retinal cysts and most commonly occur temporally. Rhegmatogenous detachments were also observed in 16% of horses examined [57]. Persistent miosis or cataract may preclude fundic examination [65]. Ultrasound examinations of 67 Comtois and 18 Rocky Mountain horses detected five (7%) partial retinal detachments and one (1%) complete detachment, of which only the latter could be seen with direct ophthalmoscopy [67].

Treatment

Selective breeding for the desirable silver coat color has increased the frequency of MCOA; however, there is no treatment for the condition, and affected animals should not be used for breeding. If necessary, affected horses should only be bred to horses free of the silver mutation as confirmed by a genetic test to minimize ophthalmic abnormalities.

Heritability

The MCOA syndrome is inherited as an incompletely dominant trait [57, 59, 60, 66]. Affected horses that are heterozygous for the disease-causing allele have the less severe cyst phenotype with or without adjacent retinal changes, while those that are homozygous have multiple anterior and posterior segment anomalies that may result in blindness [66]. The MCOA syndrome is due to missense mutation in exon 11 of *premelanosome protein* (*PMEL*) on horse chromosome 6, with pleiotrophic effects causing both the silver coat color and MCOA [66]. The mutation causes an arginine to cysteine change in the second codon of the cytoplasmic region [66].

Congenital stationary night blindness

Congenital stationary night blindness (CSNB) has been reported in Appaloosas, Quarter horses, Miniature horses, Thoroughbreds, Paso Finos, Knabstruppers, and Standardbreds [32, 68–75]. This condition is similar to CSNB in humans [72]. It accounted for 3.5% of congenital ocular anomalies in one study [56]. In another study of Appaloosa horses, CSNB was present in one-third of the horses studied and a significant association was noted between CSNB and the leopard complex gene (*LP*) [74].

Clinical appearance and diagnosis

Affected horses have severely compromised vision in low-light conditions (nyctalopia) [70, 76]. Owners may notice a reluctance to enter darkened areas such as barns or difficulty riding in evening conditions. More severely affected horses may have abnormal day vision as well [69]. Findings on posterior segment examination are normal. Some affected horses also exhibit microphthalmia, dorsomedial strabismus, nystagmus, and an unusual gaze associated with head elevation, which has been termed **star gazing** (Figure 11.46). Myopia is common in humans with night blindness and may contribute to the visual impairment in horses with CSNB, although no significant difference in refractive error has been found between affected and unaffected Appaloosas [69, 74, 77, 78].

There are no histologic or ultrastructural differences between affected and normal equine retinas. Diagnosis can be confirmed by ERG in which a normal a wave but a decreased photopic and absent scotopic b wave are noted [70, 72]. This is refered to as a "**negative ERG**" (Figure 11.47). A differential diagnosis is a long-standing vitamin A deficiency, which leads to complete blindness, a dull brittle hair coat, and hyperkeratinization [73].

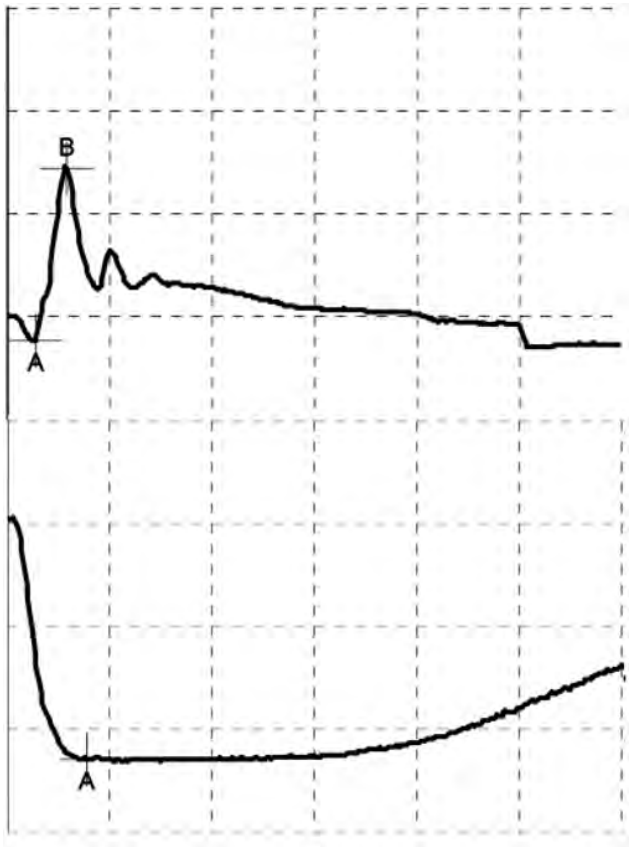


Figure 11.47 ERG tracings. The **top image** demonstrates a normal a and b wave in an unaffected horse. The **bottom image** is from a horse affected with CSNB and demonstrates the "negative ERG" due to absence of the b wave. (*Source*: Image courtesy of Dr Lynne Sandmeyer, University of Saskatchewan.)

Treatment

As indicated by the name, the condition is congenital and nonprogressive. There is no treatment, and affected animals should not be used for breeding. If an affected animal is used for breeding, it should only be bred to a homozygous normal to avoid producing CSNB.

Heritability

The leopard complex gene (*LP*) is responsible for the white spotting patterns of the Appaloosa, British Spotted Pony, Pony of the Americas, Knabstrupper, and Miniature horse [75]. This is an incompletely dominant gene. Both heterozygotes and homozygotes demonstrate the leopard spotting pattern, but only homozygotes for *LP* (*LP/LP*) develop CSNB [79]. The causative mutation for CSNB is a 1378 base-pair insertion from an endogenous retrovirus within intron 1 of the *transient receptor potential cation channel, subfamily M, member 1* (*TRPM1*) gene [80]. The insertion has been in the equine genetic pool for at least 17,000 years [80].

Night vision is typically controlled by depolarizing currents from the ON bipolar cells in which TRPM1 channels are present [80]. Normally, in the dark, glutamate is released by rod photoreceptors, binds to the G protein receptor on ON bipolar cells, and keeps the TRPM1 cation channels closed, causing hyperpolarization of the ON bipolar cells [80]. When a photon of light is absorbed, the cation channels of the rod photoreceptor close and the cell becomes hyperpolarized (the a wave of an ERG), interrupting the release of glutamate [80]. The loss of glutamate inhibition allows TRPM1 channels to open, causing depolarization of the ON bipolar cells (the b wave of an ERG) [80]. However, the mutation disrupts *TRPM1* transcription, which keeps TRPM1 from responding to a loss of glutamate inhibition [80]. Therefore the TRPM1 channels cannot open, the ON bipolar cells cannot depolarize to propagate the signals, so the horse cannot see at night, and no b wave is seen on the ERG [80]. In horses with CSNB that do not have the *LP* gene, mutations in *nyctalopin* (*NPX*) might be the cause, as mutations in *NPX* cause some forms of night blindness in humans [80].

Chorioretinitis

Chorioretinitis (inflammation of the choroid and retina) may be the result of ERU or may be a manifestation of systemic disease. Chorioretinitis is the most common abnormality identified on examination of the equine fundus. ERU is a CD4+ T-cell-mediated immune disease with both anterior and posterior segment manifestations. The retina has been demonstrated to be a specific target in ERU, and retinal Müller cells play a key role in this autoimmune inflammatory process [81–84]. It has been demonstrated that autoantigens such as S-antigen, interphotoreceptor retinoid-binding protein, cellular retinaldehyde-binding protein, and synaptotagmin-1 may also have a role in ERU [82, 85–88]. See Chapters 8 and 15 for complete discussions of uveitis, ERU, and ocular manifestations of systemic disease.

Clinical appearance and diagnosis

The appearance of chorioretinitis on fundic examination depends on whether the lesions are active or inactive and on whether the etiology results in focal or diffuse changes. Active lesions are characterized by edema, cellular infiltrate, and hemorrhage or retinal detachment; and they often appear gray, white, or hazy. The retina may be elevated by subretinal fluid and inflammatory cells (Figures 11.48, 11.49, and 11.50). Inactive lesions, or chorioretinal scars, appear as hyper-reflective or hyperpigmented in the tapetal fundus and may appear to be depigmented or to have pigment clumping in the nontapetal fundus (Figures 11.51 and 11.52).

If the retina was elevated during the active phase of the disease, it may reattach in a wrinkled or folded fashion, appearing as gray linear folds (Figure 11.53). These folds are most commonly seen radiating from the optic nerve (Figure 11.54). Chorioretinitis lesions can be focal or diffuse and unilateral or bilateral and are most commonly seen in the peripapillary region.

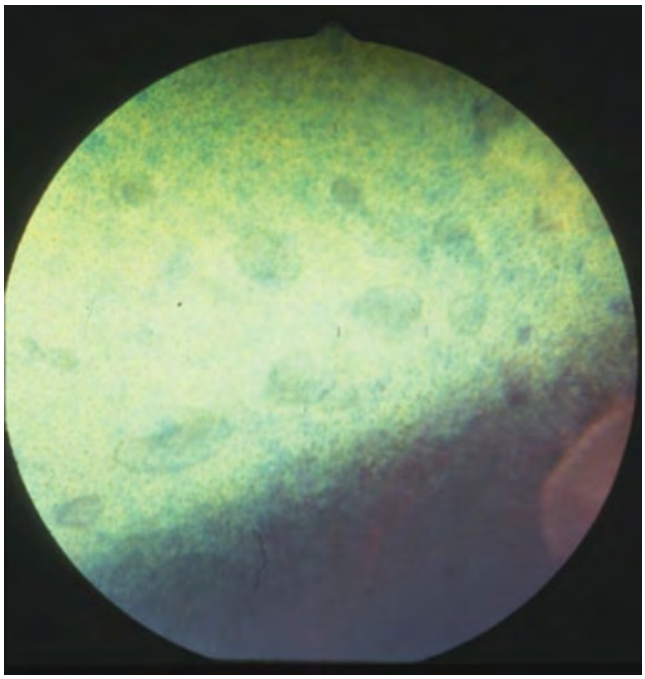


Figure 11.48 Multifocal chorioretinitis characterized by subretinal edema and tapetal hyporeflectivity.

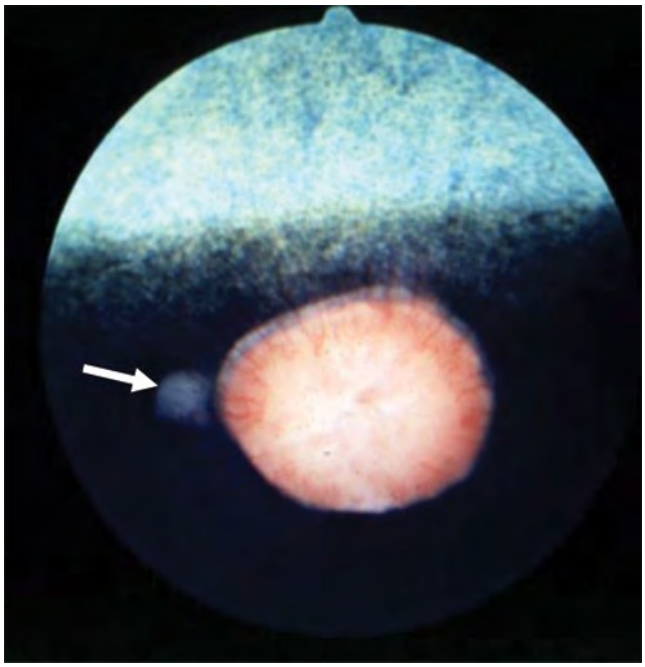


Figure 11.49 Focal area of retinitis with cellular infiltrate seen as a gray-white lesion (**white arrow**) adjacent to the optic nerve.

The "classic" inactive chorioretinal scar is circumpapillary and is termed a butterfly lesion (Figure 11.55). The butterfly lesion is an area of depigmentation and pigment clumping that typically radiates nasally and temporally from the optic nerve, although lesions can be confined to one side of the optic nerve.

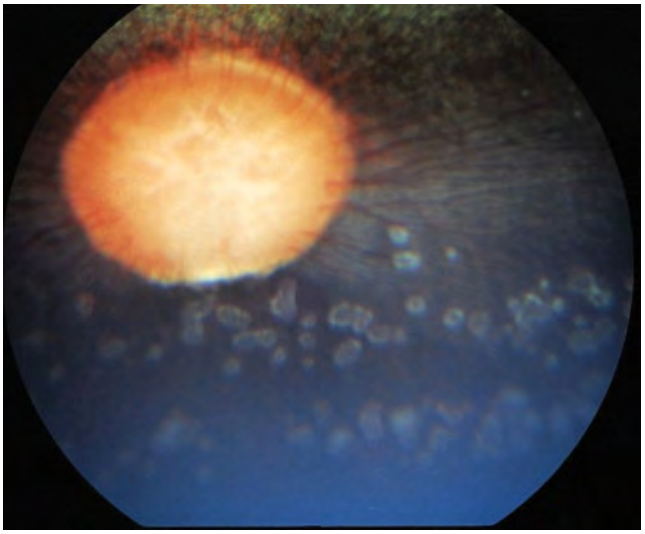


Figure 11.50 Multifocal chorioretinitis lesions. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

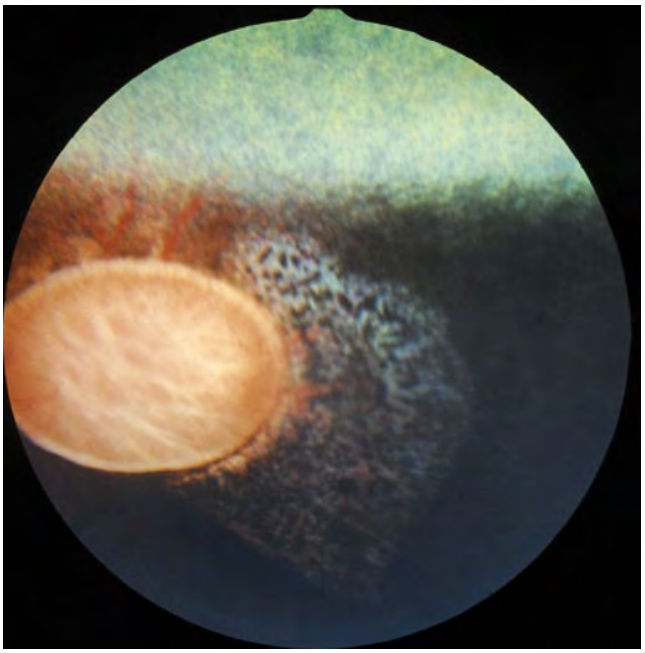


Figure 11.51 Peripapillary depigmentation and associated retinal vascular attenuation. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

During the active phase of the chorioretinitis, the peripapillary retina may be elevated; soft or hard exudates may be present; and retinal vasculitis, seen as indistinct margins and vascular cuffing, may be observed [32]. A butterfly lesion can be associated with ERU, but in many eyes the anterior segment often appears normal and no changes are noted in the retinal blood vessels or potentially retinal structure. The prevalence of peripapillary chorioretinal lesions in otherwise normal eyes has been reported to be 5–8% [28, 89]. In a survey of 204

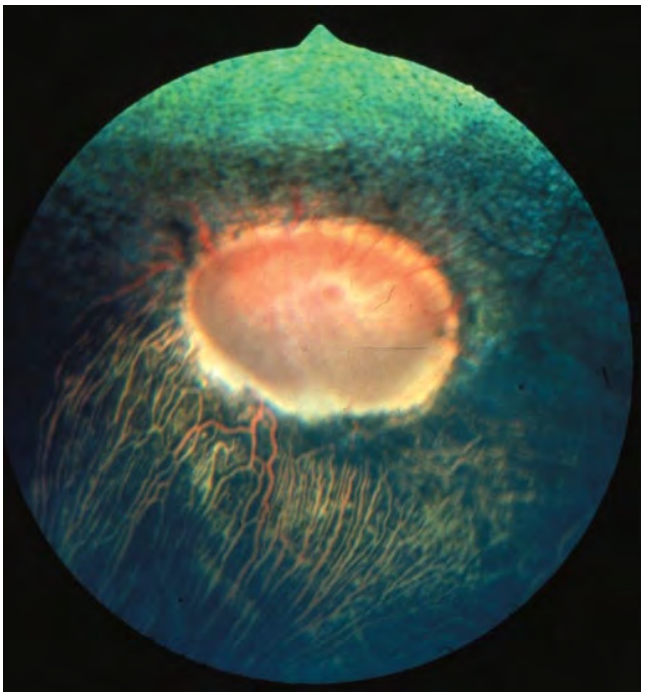


Figure 11.52 Choroidal depigmentation and degeneration of the ventral optic nerve after inflammation.

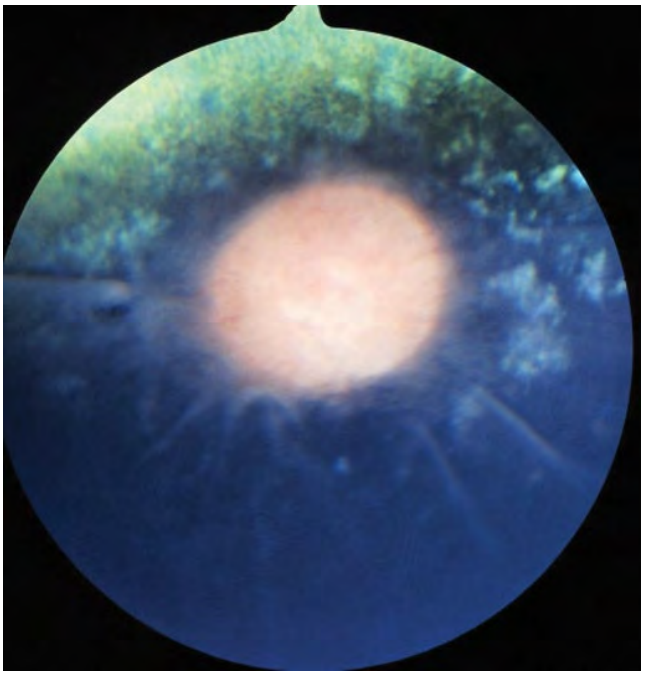


Figure 11.54 Peripapillary edema, retinal elevation, and retinal folds secondary to retinal detachment. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

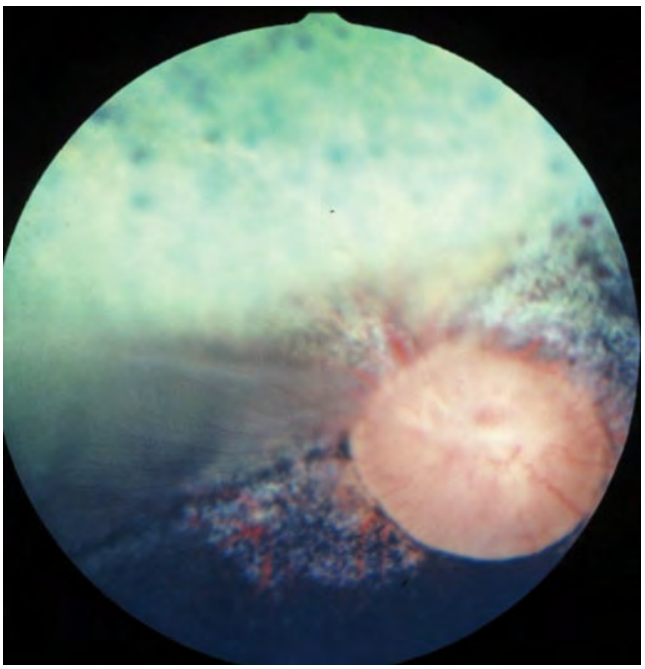


Figure 11.53 Peripapillary depigmentation and associated retinal detachment. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

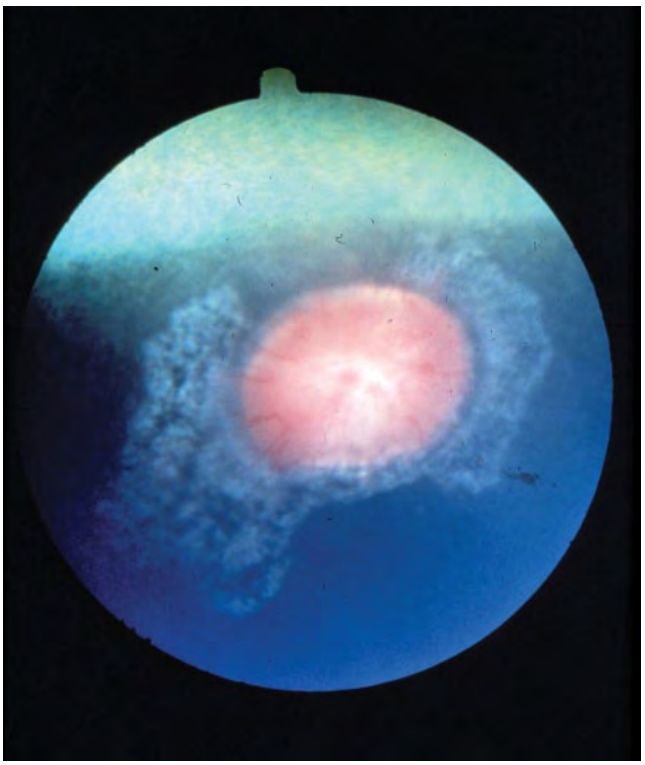


Figure 11.55 Peripapillary chorioretinal scar, also called a butterfly lesion.

Thoroughbred racehorses in Australia, peripapillary butterfly lesions were described in five horses (2.5%), with an additional 16 horses (7.9%) described with linear peripapillary hyperpigmented bands [2]. Posterior segment changes, in the absence of anterior segment disease, can and do occur with ERU; however, any optic neuritis or peripapillary chorioretinitis could result in similar changes. See Chapter 8 for more information on ERU effects on the equine retina.

Immunohistochemical examination of retinas from horses with naturally occurring ERU and from ponies with experimental *Leptospira*-induced uveitis demonstrated a range of findings [90]. Minimal to severe retinal changes were observed and were characterized by major histocompatibility complex class II antigen-expressing cells and T lymphocytes, suggesting an immunologic cause of retinal damage [90]. Ponies with *Leptospira*-induced uveitis demonstrated B lymphocytes that were seroreactive for *L. interrogans* serovar Pomona [90]. Additional studies have confirmed chorioretinal changes in horses with ERU that are characterized by T-lymphocyte infiltration and destruction of photoreceptor outer segments and inner retina [91]. T-cell-rich lymphoid follicle formation was noted in the iris and choroid [91]. Analysis of vitrectomy samples from horses with ERU demonstrates IgG antibodies and autoreactive T lymphocytes specific for retinal antigens, which provides support for the possibility of a local autoimmune-mediated disease involving the posterior segment [92]. In addition, analysis of vitrectomy samples from horses with ERU shows a frequent IgM response to a myriad of retinal proteins, demonstrating an ongoing immune response [93]. For a complete discussion see Chapter 8.

In experimental infection with EHV-1, chorioretinal lesions have been produced 6–8 weeks after intranasal infection [33, 94]. Clinically, this appears as multifocal white lesions in the peripapillary nontapetal fundus [33]. In recent studies, after experimental infection with a neuropathogenic strain of EHV-1, between 50% and 90% of the infected horses developed small, focal or multifocal, donut-shaped depigmented lesions with pigmented centers located in the nontapetal fundus, typically within the limits of the retinal vasculature [95]. The lesions appeared 20–111 days post-infection and were unilateral or bilateral [95]. No signs of uveitis or active chorioretinal disease were detected [95]. On the basis of findings from fluorescein angiography it is hypothesized that EHV-1 infection can result in infarction of the choroidal vasculature and subsequent focal loss of RPE [33, 95].

Focal chorioretinopathy, termed **bullet-hole chorioretinitis**, has been described [31, 32, 37]. Lesions are generally multifocal, appear ventral to the optic disc, and are white with a pigmented center (Figures 11.56 and 11.57). They are small and do not appear raised or depressed.

On histologic examination, a loss of normal retinal architecture with RPE hyperplasia and migration of RPE cells into the retina can be observed (Figure 11.58) [4]. It has been suggested that these lesions may be the result of previous chorioretinitis and may have a viral cause [31]. An association with respiratory disease in foals has been suggested [32]. Lesions are similar in appearance to those described in experimental EHV-1 infection [33].

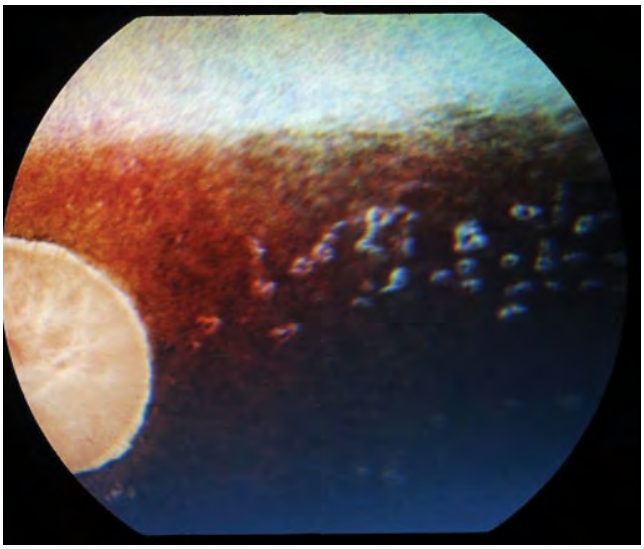


Figure 11.56 Bullet lesions at the tapetal–nontapetal junction adjacent to the optic nerve. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

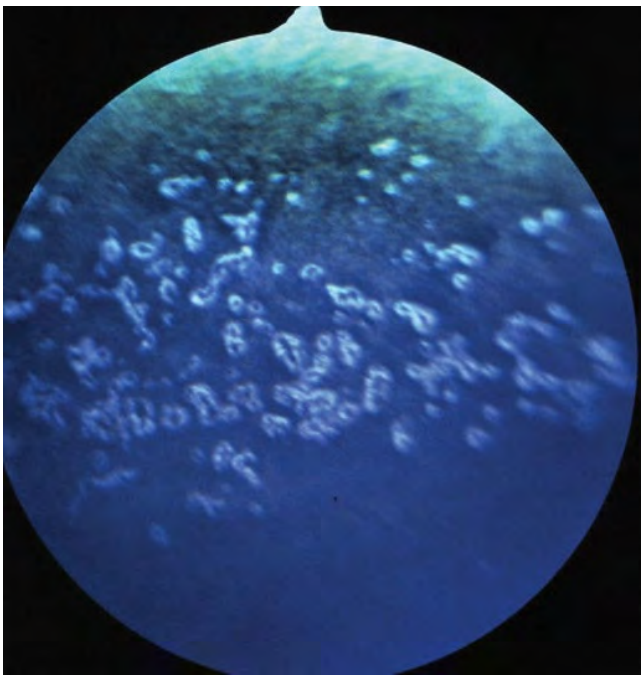


Figure 11.57 Numerous bullet lesions adjacent to the optic nerve near the tapetal–nontapetal junction. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

These lesions have been seen, as incidental findings, in many horses of all age groups. One report suggests that 10–20% of horses are affected with bullet-hole scars [32]. Another report found that horses with depigmented punctate chorioretinal foci

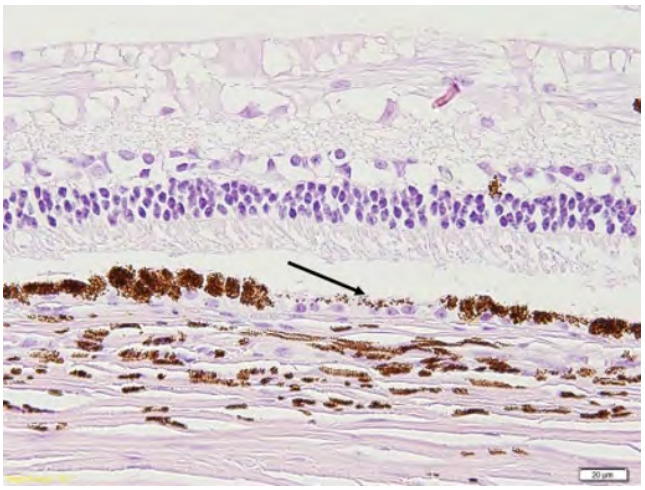


Figure 11.58 Histopathologic section of the retina from a horse with "bullet-hole" chorioretinopathy. Note focal loss of RPE (**arrow**). (*Source*: Photomicrograph courtesy of Dr Richard Dubielzig, Comparative Ocular Pathology Laboratory of Wisconsin.)

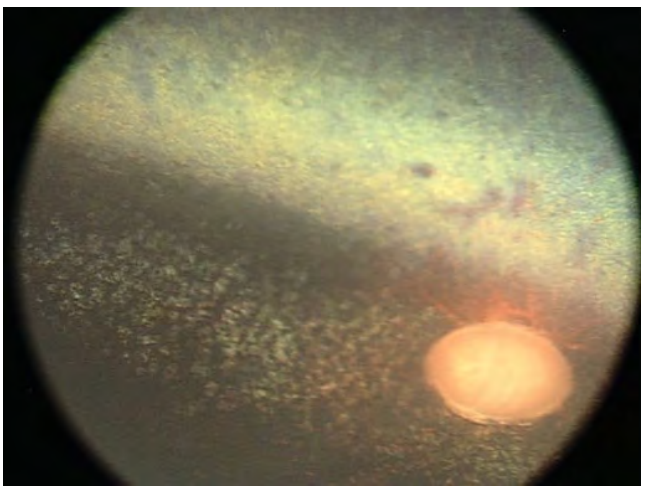


Figure 11.59 Hundreds of bullet-hole lesions in the nontapetal fundus of a clinically normal horse.

as the only fundic abnormality were no more likely to have intraocular disease than horses with clinically normal fundi [96]. In a survey of 204 Thoroughbred racehorses in Australia, peripapillary inactive "bullet-hole" chorioretinal lesions were described in 108 (52.9%) horses. In the majority of these horses (103/204) the lesions numbered less than 20, while in five horses (2.5%) the lesions numbered more than 20 and were considered potentially vision threatening, although no visual deficits were noted by trainers or detected on ophthalmic examination [2]. In a recent study, retinal function as determined by full-field ERG was within normal limits in two horses with extensive bullet-hole lesions (Figure 11.59) [97]. Since inactive focal or multifocal chorioretinopathy does not appear to affect vision and is non-progressive, despite the potential to be a post-inflammatory change, it is best considered an incidental finding.

A more diffuse chorioretinitis has been described in which lesions that are vermiform, circular, or band-shaped and are hyper-reflective in the tapetum and depigmented in the nontapetal region [32]. Similar lesions have occurred in association with severe blood loss (see section **Ischemic optic neuropathy**). Optic nerve degeneration may be present in some instances. Vision is generally decreased, especially if the optic nerve is affected. Trauma and vascular infarction are also possible causes [32].

Chorioretinitis or panuveitis may also be a manifestation of systemic disease and has been documented with equine infectious anemia [98], adenovirus [99, 100], West Nile virus [101, 102], neonatal septicemia [103], *Rhodococcus equi* [104], *Streptococcus equi* var *equi* [105, 106], Lyme disease [100, 104], brucellosis [107], *Leptospira interrogans* Pomona, equine granulocytic ehrlichiosis [108], toxoplasmosis [109], *Halicephalobus gingivalis* (*H. deletrix*) [110, 111], and onchocerciasis [112]. In general, any infectious or parasitic agent that is hematogenously disseminated is capable of causing vasculitis, or exhibiting aberrant migration, and could result in anterior or posterior uveitis. Neonatal foals with septicemia or bacteremia are often presented with anterior uveitis, which may occasionally extend to the posterior segment as a panuveitis. For a complete discussion of the effects of systemic disease on the equine eye see Chapter 15.

Treatment

Treatment is directed at the underlying cause, but there is no specific medical or surgical therapy for focal or diffuse chorioretinitis. Systemic nonsteroidal therapy may help minimize inflammation and subsequent damage, or systemic corticosteroids may be used at an anti-inflammatory dose provided there is no contraindication.

Prognosis

Focal lesions are usually of no significance. Although it is hypothesized that numerous or diffuse lesions could result in visual changes, clinically, these lesions appear to have no detectable effect on vision. However, vision should be assessed in affected animals, and attention should be paid to the purpose of each animal and the effect vision loss may have on function. In one report, when these lesions numbered more than 20 the authors considered this to be potentially vison-threatening [2]. Lesions in the peripapillary region have a greater impact on vision as they will affect a larger proportion of axons. In cases of peripapillary depigmentation, the veterinarian should perform a careful examination of the anterior segment, looking for subtle atrophy of the corpora nigra, diffuse iris hyperpigmentation, pigment rests on the anterior lens capsule, and yellowing of the lens or vitreous—all of which suggest previous inflammation and support a diagnosis of ERU. See Chapter 8 for more information.

Retinal detachment

A retinal detachment is the separation of the NSR from the outer RPE. The retina is normally supported in place by the vitreous and the RPE, which has metabolic pumps to maintain

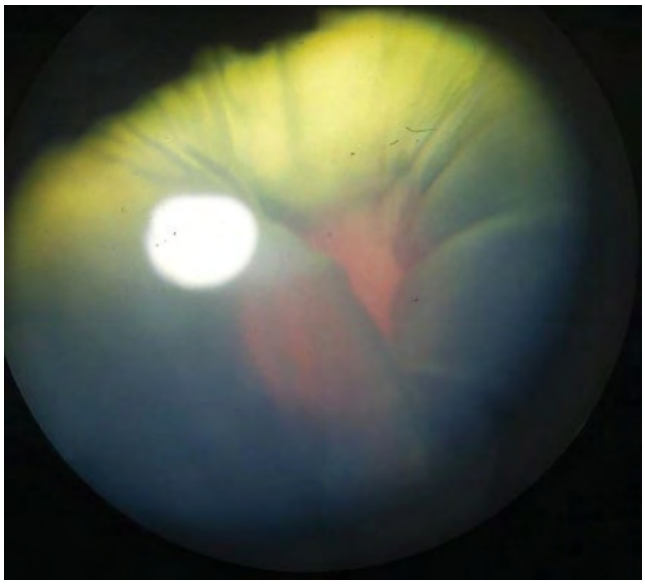


Figure 11.60 Complete bullous retinal detachment of unknown cause. The retina remains attached peripherally at the ora ciliaris retina. (*Source*: Reproduced with permission from Andy Matthews, Angus, Scotland.)

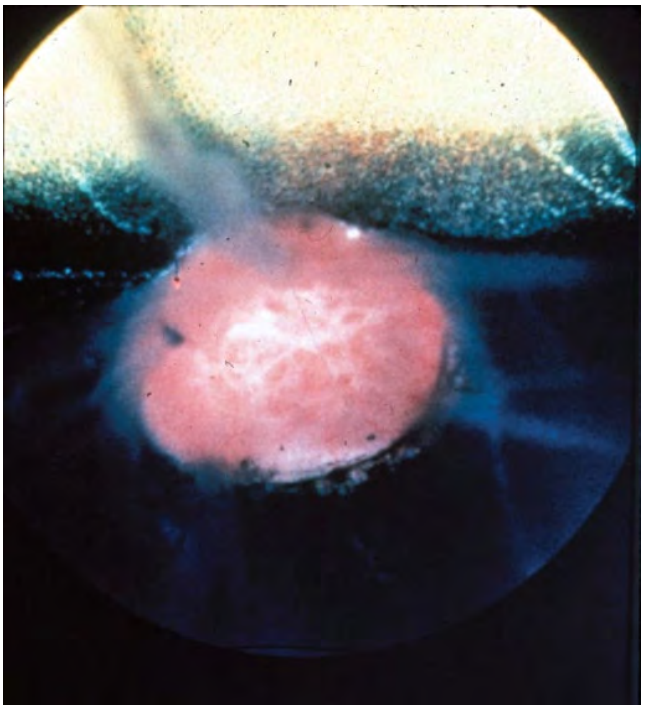


Figure 11.61 The peripapillary retina is detached, appearing as a gray veil of tissue over and around the optic nerve.

an osmotic gradient that keep the NSR in apposition with the RPE. The retina can detach as a result of fluid accumulation between the NSR and RPE, a retinal tear and migration of fluid from the vitreous into the subretinal space, blunt force trauma, or traction toward the vitreous secondary to resolution of vitreal hemorrhage or after hyalitis. Accumulation of fluid between the NSR and RPE results from inflammation, with ERU being the most common cause. This is termed a **bullous detachment** (Figure 11.60), and reattachment can occur if the inflammation is resolved and the RPE is able to pump the fluid out of the intraretinal space. The retina may reattach with folds or wrinkles, most commonly radiating outward from the optic nerve. Such folds indicate previous bullous detachment.

Retinal detachments associated with a retinal tear are termed **rhegmatogenous detachments**. In such cases, fluid migrates from the vitreous side of the retina, through the tear, forcing the NSR from the RPE. Dorsal tears are more likely to progress as gravity works to pull the retina down. Trauma, rupture of peripheral retinal cysts, MCOA, and complications from intraocular surgery such as phacoemulsification and vitrectomy are all associated with rhegmatogenous detachments.

In a retrospective study of 40 horses (46 eyes) with retinal detachment, the detachment was unilateral in 34 horses and bilateral in 6 horses [58]. The detachment was partial in 14 horses and complete in 32 horses. The diagnosis of retinal detachment was made clinically in 20 eyes and on ultrasound in 26 eyes. While there was no sex or breed predilection for retinal detachment, the mean age of affected horses (8.5 years) was significantly younger than the general hospital population. The etiology was diagnosed to be ERU in 27 horses (33 eyes) (67.5%) and trauma in 10 horses (10 eyes) (25%) [58]. The prognosis for vision in horses with retinal detachment is grave, with many eyes going on to enucleation or evisceration [58].

Clinical appearance and diagnosis

Clinically, a retinal detachment can be partial or complete (see Figures 11.53 and 11.61). Partial detachments are not associated with detectable vision loss by the owner in most instances. They are most often discovered on a pre-purchase examination or during examination of an eye for anterior segment disease. A focal bullous detachment appears as an elevated, hazy area of retina with subretinal fluid. Bullous detachments may occur as a result of systemic disease. (See section **Chorioretinitis**.)

With a complete detachment, the retina appears as a gray, floating veil of tissue extending into the vitreous toward the lens. If it is displaced far enough anteriorly, the retina may be visible by penlight examination (Figure 11.62). The retina is normally attached at the optic nerve and ora ciliaris retinae. As a consequence of a retinal detachment, the retina may tear at the ora and fall ventrally, obscuring the optic nerve (Figure 11.63). This is called a **giant tear** or **retinal disinsertion**.

Traction detachments occur after intravitreal hemorrhage or inflammation, termed hyalitis. Trauma, ERU, and extension of chorioretinitis can result in vitreal hemorrhage and hyalitis. Traction bands may form, appearing as tan to gray strands in the vitreous. These may attach to the inner retina and undergo contracture, elevating the retina and leading to a retinal detachment.

Retinal detachment may also be noted in horses presented for examination because of a congenital or juvenile cataract or a

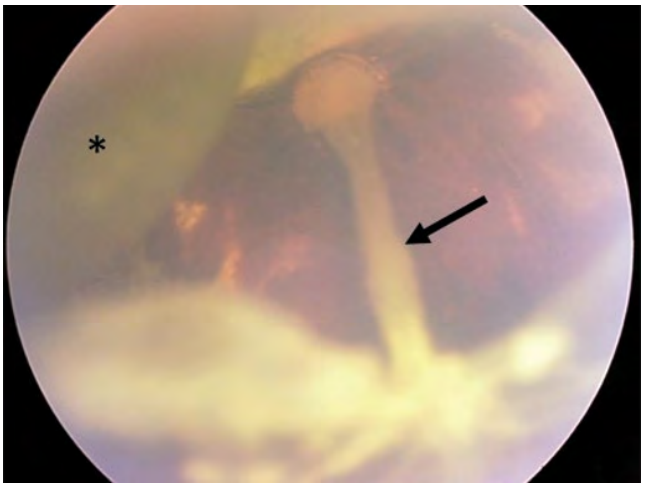


Figure 11.62 A fibrous traction band has caused a complete retinal detachment (**arrow**). The lens is posteriorly luxated (**asterisk**) as well. Althought the image shown here was taken with a fundic camera, the findings were clearly visible during examination with a transilluminator.

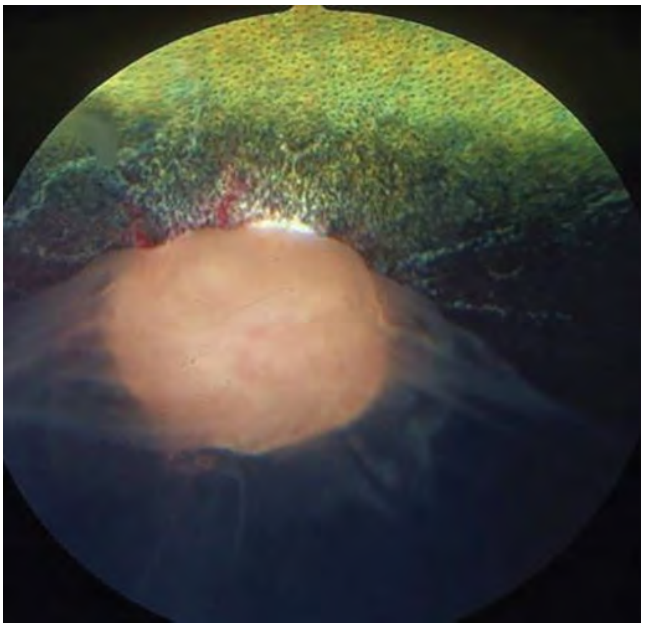


Figure 11.63 A complete retinal detachment with a giant tear and disinsertion as seen on fundic examination. The retina has fallen ventrally and is lying over and obscuring the optic nerve head. (*Source*: Reproduced with permission from Andy Matthews, Angus, Scotland.)

cataract caused by chronic uveitis. An ocular ultrasound examination is indicated to evaluate the posterior segment in horses with a mature or hypermature cataract (see Figures 11.28, 11.64, and 11.65).

Treatment

The underlying cause of inflammation needs to be managed, and if management is successful, a bullous detachment may reattach if the inflammation is resolved and the RPE is able to pump the fluid out of the intraretinal space. Once a retinal disinsertion or giant tear occurs, little treatment can be offered. Surgical retinal reattachment has been attempted in a few cases but is still a very new technique for equine globes.

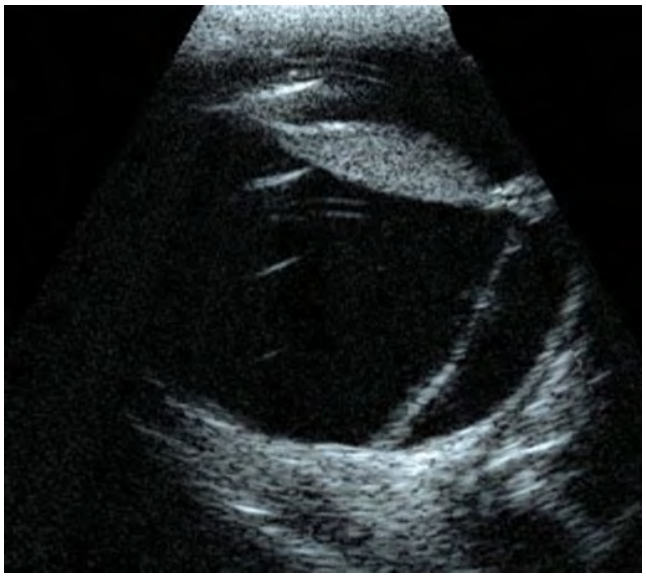


Figure 11.64 Ultrasound examination of a horse presented for cataract evaluation. The retina is partially detached, with a hyperechoic line present in the vitreous extending from the optic nerve posteriorly to the ora anteriorly. The lens is cataractous based on its echogenicity and is reduced in the anterior–posterior axial dimension, indicating a hypermature cataract with resorption.

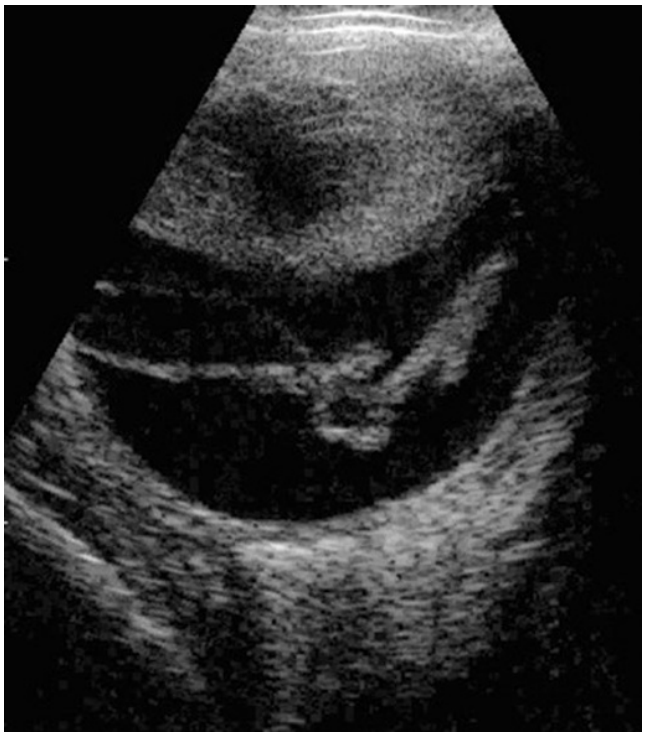


Figure 11.65 Complete retinal detachment with a mature cataract.

If detected early, retinal tears (rhegmatogenous detachments) can be isolated and prevented from progressing by laser retinopexy. The technique consists of delivering laser energy across the pupil through an indirect ophthalmoscope and a condensing lens. The diode laser is the instrument of choice, delivering a wavelength of 810 nm, which is preferentially absorbed by melanin. The energy is transformed into heat, resulting in thermal coagulation and a focal scar. Multiple scars are created to surround and isolate the tear, preventing progression of the detachment. Treatment of traction band retinal detachment requires severing of the traction bands, but concurrent intraocular disease generally precludes this as a viable option. (See section **Vitrectomy**.)

Prognosis

The prognosis for a retinal detachment depends on the severity, underlying cause, and chronicity of the lesions, but is generally poor.

Retinal degeneration

Retinal degeneration is far less common as a primary disease in horses than in dogs and cats. Primary retinal degeneration or progressive retinal atrophy will be bilateral and progressive, and Thoroughbreds may be predisposed [18, 32]. Affected horses show progressive vision loss with areas of nontapetal depigmentation and hyperpigmentation, and, in the later stages, optic nerve atrophy [32]. Similar changes can occur in association with aging and are referred to as senile retinal degeneration [18, 113]. Retinal degeneration has also recently been found to occur in horses infected with the Borna disease virus (BDV) [114]. It is thought that BDV spreads via the cerebrospinal fluid (CSF) and intra-axonal transport from the CNS along the optic nerve and to the retina [114].

Clinical appearance and diagnosis

Retinal degeneration appears as hyper-reflective changes in the tapetal retina and as multifocal depigmentation and hyperpigmentation in the nontapetal retina (Figure 11.66) [18]. The optic nerve becomes pale, and the peripapillary retinal vessels are attenuated. Vision loss may begin with nyctalopia (night blindness) and progress to day vision loss. Peripheral cystoid retinal degeneration has also been noted in some geriatric eyes [21, 52, 115]. Peripheral cystoid retinal degeneration occurs at the ora and is observed in many species. Although generally an incidental finding, it can predispose to rhegmatogenous retinal detachment if a cyst ruptures. Unilateral retinal degeneration can be associated with glaucoma, trauma, or vascular ischemia.

A lysosomal storage disease, neuronal ceroid lipofuscinosis, has also been described in three horses that demonstrated neurologic symptoms and vision loss in one instance [116]. Clinical symptoms were noted by 1 year of age, and euthanasia was performed by 1.5 years of age. Eosinophilic, autofluorescent material was found in the perikarya of neurons in the brain, spinal cord, retina, and mesenteric ganglia [116]. Immunohistochemistry confirmed the diagnosis as ceroid lipofuscinosis.

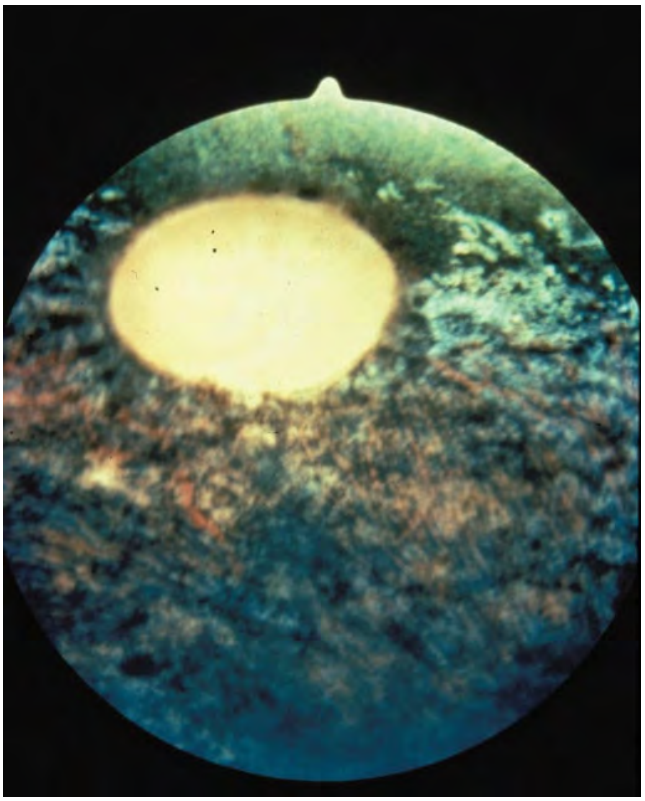


Figure 11.66 Retinal and optic nerve degeneration. Optic nerve pallor, pigment clumping, and depigmentation are all present.

Treatment

There is no treatment, and affected animals should not be used for breeding unless a definitive noninherited etiology can be documented.

Prognosis

The long-term prognosis for retinal degeneration in general is poor, but depends on the severity and the underlying cause. A mild, slowly progressive lesion may cause minimal visual disturbance. Neuronal ceroid lipofuscinosis is an inherited neurodegenerative disorder, and affected horses, their sires and dams, and siblings should not be used for breeding.

Senile retinopathy

Senile retinopathy, or senile retinal degeneration, is a common incidental finding in geriatric horses. Its prevalence has been noted to increase with age [52, 53]. In one study of 83 geriatric horses, 35 animals (42%) and 64 eyes were noted to have senile retinopathy or retinal degeneration [52]. In most cases, the lesions were bilateral and in the peripapillary region [52]. In another study of 200 geriatric horses, 190 of 400 eyes (48%) were noted to have senile retinopathy [53]. In horses over 30 years of age, 73% had senile retinopathy [117].

Clinical appearance and diagnosis

Ophthalmoscopically the lesions appear as irregular linear hyperpigmentation in the nontapetal fundus, sometimes accompanied by adjacent depigmentation (Figures 11.67 and 11.68) [52]. Horses may also have areas of tapetal hyper-reflectivity and retinal vessel attenuation [52]. Histologically the lesions are characterized by variable loss of inner and outer retinal layers and retinal gliosis [52]. In all affected eyes the RPE is disrupted, with proliferation and focal loss of the epithelial cells [52]. The loss of the RPE is similar to that seen in retinal paving-stone (or cobblestone) degeneration in elderly people [118]. In other older horses, a focal peripheral retinal degeneration consisting of small areas of fibrosis has been described [21].

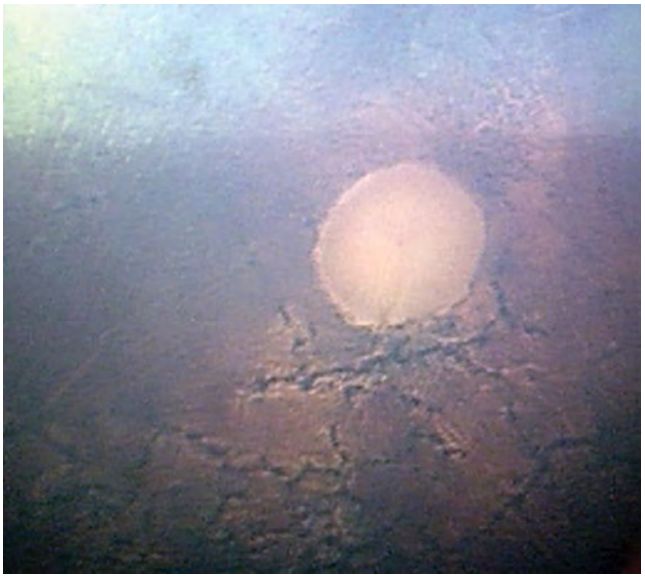


Figure 11.67 The irregular, linear hyperpigmentation ventral to the optic disc is characteristic of senile retinopathy. This horse had no demonstrated visual deficits. The optic nerve head appears pale, as this image was taken after the horse had been euthanized for reasons unrelated to the ocular condition.

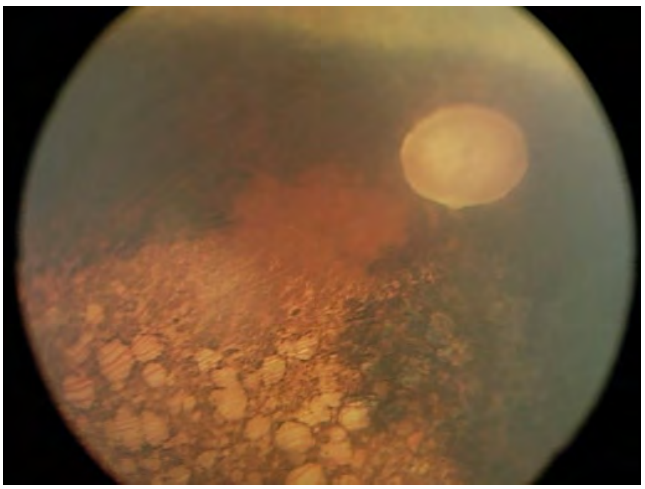


Figure 11.68 Extensive senile retinopathy. Despite the extent of the lesions the horse did not appear to have visual deficits. Histologically these lesions were similar to retinal paving-stone degeneration as seen in elderly humans.

Treatment

There is no treatment, and, despite the changes present, most horses maintain functional vision with no observable deficits.

Equine motor neuron disease

Equine motor neuron disease (EMND) is a neurodegenerative disease that occurs as a result of a chronic dietary deficiency of the antioxidant vitamin E [119–121]. Ceroid-lipofuscin subsequently accumulates in the RPE in the tapetal and nontapetal fundus (Figure 11.69) [119].

Clinical appearance and diagnosis

On examination with an ophthalmoscope, EMND appears as an irregular, reticulated, or honeycomb pattern of accumulations of yellow-brown to black pigment in the tapetal and nontapetal retina (Figures 11.70). In one study of 42 EMND affected horses, 40 had ophthalmoscopic lesions [119]. Although vision impairment is inconsistent, a 50% reduction in the ERG b-wave amplitude has been documented [119]. The ophthalmoscopic findings are used in conjunction with musculoskeletal signs to make a diagnosis of EMND. The plasma vitamin E levels in unsupplemented EMND-affected horses have been found to be

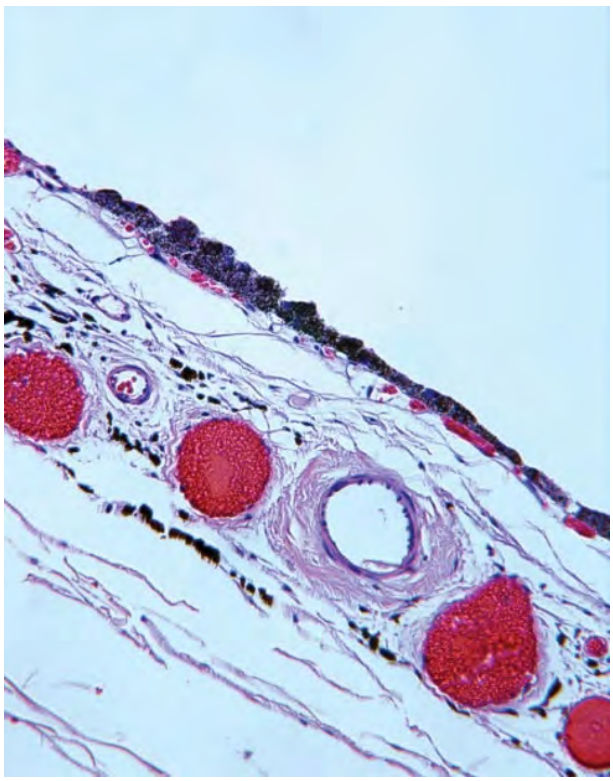


Figure 11.69 Histopathologic examination of the choroid and RPE of a horse with equine motor neuron disease. Note the accumulation of ceroid-lipofuscin in RPE.

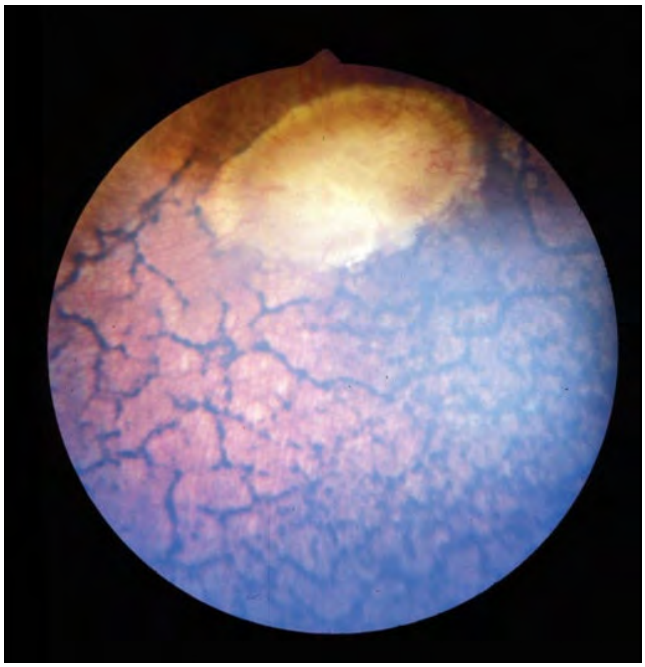


Figure 11.70 Optic nerve and nontapetal fundus of a horse with equine motor neuron disease. Note the honeycomb pattern of pigment deposits in RPE.

less than 1.0 μg/mL [119]. When testing serum or plasma for vitamin E levels the sample should be refrigerated or frozen and protected from prolonged exposure to light. Serum samples should be centrifuged to separate serum from the clot and the serum removed (according to the Michigan State Diagnostic Center for Population and Animal Health). Clinically, horses affected with EMND may exhibit weight loss, weakness, muscle atrophy, trembling, low head carriage, and an abnormal stance. In North America the risk factors for a horse having EMND were absence of grazing for more than a year and provision of poor quality hay; however, EMND has been described in Europe in horses with access to adequate pasture [122, 123].

Treatment

Supplementation with vitamin E and provision of fresh forage may stabilize the neurologic signs but do not appear to reverse the RPE changes. See Chapter 15 for further information.

Prognosis

The prognosis depends on severity of disease and response to therapy.

Photic head shaking

A condition of head shaking or head tossing induced by exposure to light and eliminated by blindfolding, a darkened environment, and contact lenses has been reported in the horse [124, 125]. The problem is usually seen in the spring and summer, is exacerbated by exercise, and may be accompanied by sneezing, snorting, and nasal rubbing [124]. See Chapter 14 for further information.

Optic nerve

Colobomas

Colobomas are absences of or defects in normal ocular tissue and typically occur in the area of the embryonic optic fissure, which is ventral to slightly ventronasal; if colobomas are noted elsewhere, they are considered atypical. Colobomas can be unilateral or bilateral and may affect the iris, ciliary body, lens, retina, choroid, optic disc, and sclera [29, 31, 32, 126–129]. They can occur alone or in association with MCOA. One report of a Thoroughbred with bilateral optic disc colobomas also included mention of microphthalmos, microcornea, and iris and lens abnormalities [130]. In a survey of 204 Thoroughbred racehorses in Australia, optic nerve coloboma and "unusual optic nerve head anatomy" was described in two horses [2]. In a survey of 30 Exmoor ponies, typical optic nerve colobomas were seen in four closely related ponies [64]. Bilateral colobomas involving the iris, ciliary body, lens, choroid, retina, and optic nerve have been described clinically and using fluorangiography in a donkey [129]. Posterior segment colobomas have been found to affect the optic disc in horses, most commonly the Quarter horse [126–128]. Others report a predisposition in the Appaloosa [18]. Optic nerve colobomas accounted for 1.8% of all congenital ocular anomalies in one study [56]. Small colobomas must be distinguished from the small 6 o'clock notch and peripapillary ring that can be normal in some horse optic nerves (see Figure 11.3) [18]. Severe colobomas involving the optic disc have been associated with vision deficits, specifically in the Quarter horse (Figure 11.71) [126–128].

Clinical appearance and diagnosis

Colobomas can involve other areas of the fundus and appear white (complete absence of choroid) or orange and white (some choroidal vasculature present). Involvement of the area centralis will have a more significant impact on vision, although most horses with colobomas are asymptomatic. On ophthalmoscopic examination, the edges of the coloboma may appear recessed below the surrounding tissue (Figure 11.72).

Additionally, a "window defect" involving the RPE has been described as an RPE coloboma (Figures 11.73 and 11.74) [18, 29]. This abnormality occurs most commonly in the nontapetal fundus adjacent to the optic disc and appears as a sharply demarcated focal area of decreased pigmentation. Such an abnormality has no known visual or genetic significance.

Treatment

There is no treatment.

Prognosis

Given the predisposition of optic disc colobomas in Quarter horses, breeding of affected animals and their sires and dams should be avoided.

Optic nerve hypoplasia

Optic nerve hypoplasia can be unilateral or bilateral and is a rare congenital abnormality [115]. Optic nerve hypoplasia

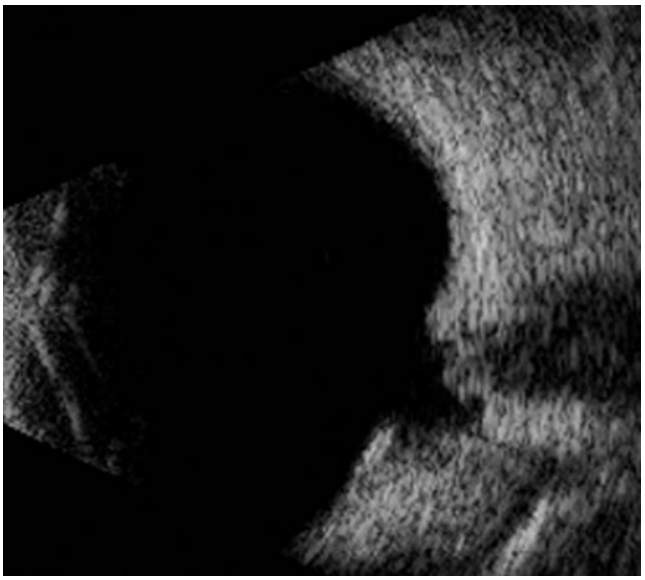


Figure 11.71 Ultrasound examination of a posterior segment coloboma. The posterior eye wall extends posteriorly toward the orbit in the area of the optic nerve.

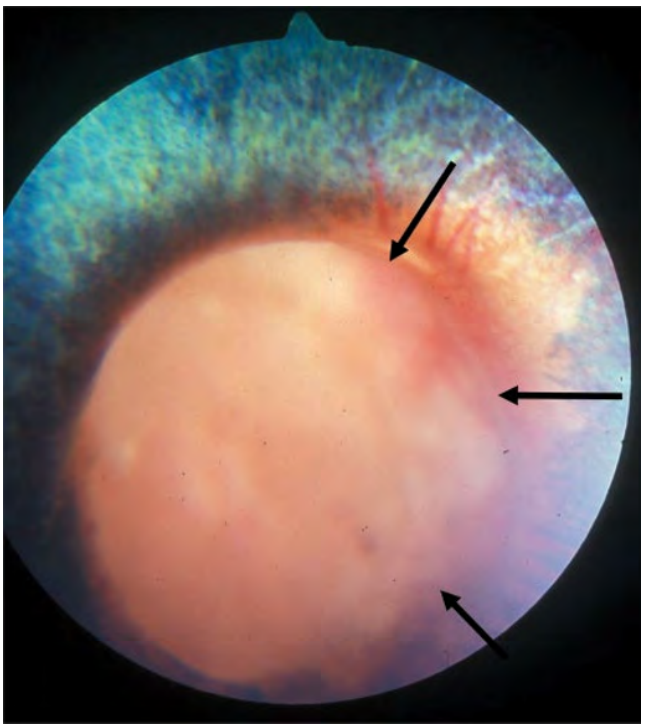


Figure 11.72 Extensive nasal optic nerve coloboma (**arrows**). The coloboma is not as well focused because it is posterior to the plane of focus.

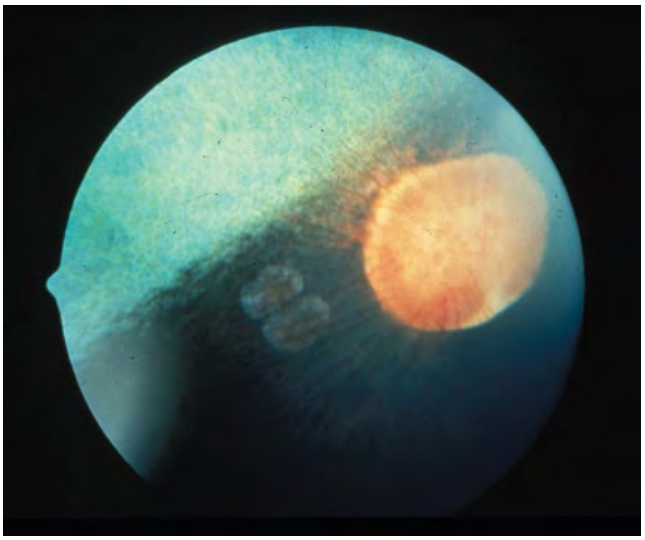


Figure 11.73 Two "window defects" or RPE colobomas are noted adjacent to the optic nerve.



Figure 11.74 Circular depigmented lesion in the nontapetal fundus located ventral to the optic nerve consistent with a typical RPE coloboma. (*Source*: Photograph courtesy of Dr Tim Knott, United Kingdom.)

accounted for 0.9% of all congenital ocular anomalies in one study [56].

Clinical appearance and diagnosis

In optic nerve hypoplasia, the optic nerve appears pale, is smaller than normal, and may be depressed or recessed; retinal vessels are difficult to visualize [18, 131]. Numbers of retinal ganglion cells are reduced, the pupil is dilated, and the pupillary light response is reduced or absent [18]. Nystagmus and decreased to absent vision are also observed.

Treatment

There is no treatment.

Prognosis

The cause is not known, visual loss depends on severity, and affected horses should not be used for breeding.

Optic nerve atrophy

Atrophy of the optic nerve is not a primary disease but occurs as a result of ocular and cranial trauma, inflammation, glaucoma, retinal degeneration, ischemia, pituitary neoplasia, orbital neoplasia, sinusitis, and compression.Sinusitis involving the spheno-palatine sinuses has been reported to result in optic nerve degeneration and blindness in three horses [132]. Distension of the spheno-palatine sinuses secondary to infection resulted in pressure on the optic nerves with subsequent atrophy. Acute blood loss has also been implicated in optic nerve degeneration with or without retinal degeneration [115, 133]. Optic nerve atrophy may also be seen in older horses without a definitive cause. In one study of 83 geriatric horses, optic nerve atrophy was observed in seven eyes of four horses [52].

Clinical appearance and diagnosis

Immediately following traumatic optic nerve injury, the pupil will be fixed and dilated and the optic nerve will appear normal on ophthalmoscopic examination. If the lesion is unilateral there will be an absent consensual PLR from the affected eye and an absent dazzle reflex in the affected eye. In many instances, on examination several days after the onset of sudden blindness, peripapillary edema/exudates are observed and the optic nerve may appear hyperemic. Regardless of the cause, optic nerve pallor, visualization of the lamina cribrosa, and peripapillary vascular attenuation are common end points (Figure 11.75).

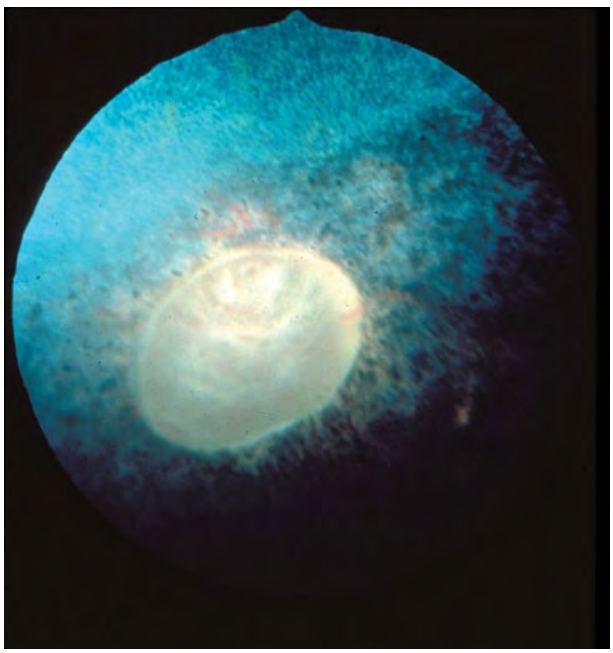


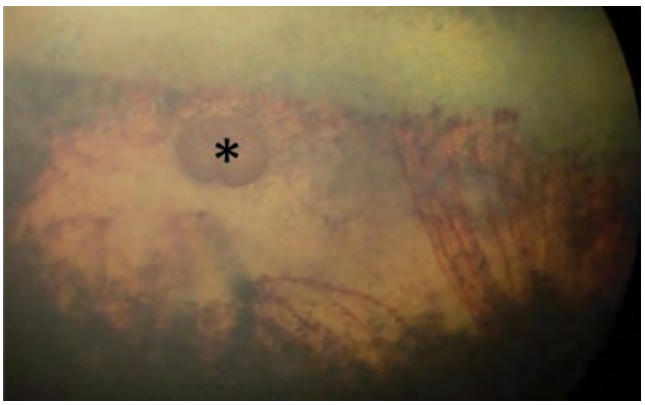
Figure 11.75 Post-traumatic optic nerve atrophy with retinal vascular attenuation and peripapillary depigmentation.

If inflammation has been present, peripapillary depigmentation and pigment clumping may be present (see Figure 11.52).

Orbital mass lesions can result in compression of the optic nerve and are often also associated with exophthalmos (Figure 11.76). Orbital masses can be inflammatory or neoplastic. Lymphosarcoma and extra-adrenal paraganglioma are the most common equine orbital neoplasms [134]. MRI or CT scan may be of value in cases where trauma or sinusitis is suspected as the cause of the optic nerve degeneration [132]. Chronic glaucoma can also result in retinal and optic nerve degeneration (Figure 11.77) [135]. Histologically, hypercellularity of the optic nerve has been noted in 93% of eyes with chronic glaucoma. See Chapter 10 for more information on equine glaucoma [136].



(A)



(B)

Figure 11.76 (A) Marked exophthalmos and dorsomedial strabismus of the right eye due to an orbital mass. (B) Fundus of the same horse demonstrating marked retinal and optic nerve (**asterisk**) degeneration, particularly of the nontapetal fundus.

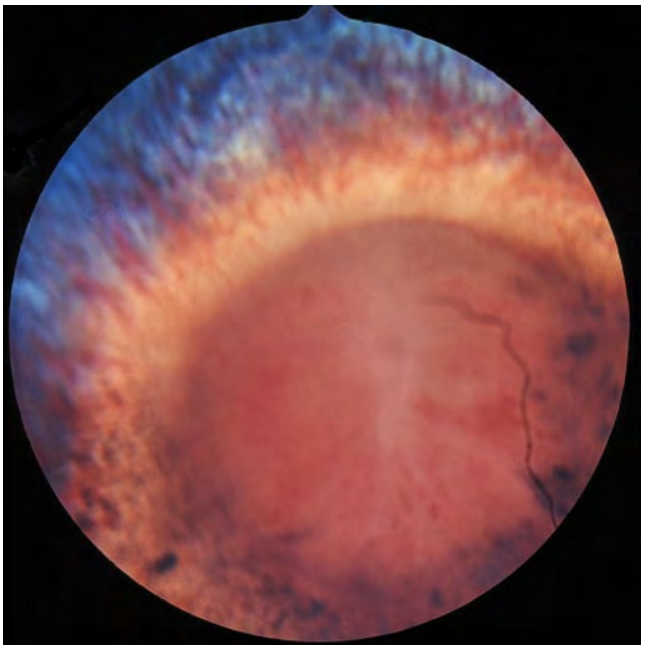


Figure 11.77 Optic nerve atrophy with retinal vascular attenuation, peripapillary depigmentation, and cupping secondary to chronic glaucoma. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

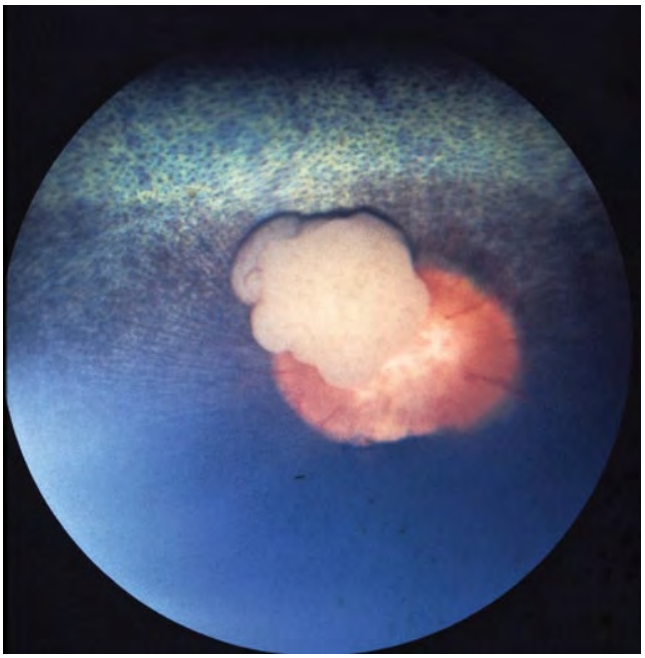


Figure 11.78 Proliferative optic neuropathy. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

Treatment

There is no treatment. Systemic anti-inflammatory therapy implemented immediately following cranial trauma does not appear to affect long-term outcome. Treatment of spheno-palatine sinusitis has been associated with a transient improvement in vision, but vision loss progressed following cessation of treatment [132]. Control of IOP may help prevent further optic nerve degeneration associated with glaucoma.

Prognosis

The prognosis for vision is poor.

Proliferative optic neuropathy

Proliferative optic neuropathy (PON) typically occurs in aged horses (more than 15 years) and is generally an incidental finding [32]. It is usually unilateral and vision remains within normal limits. In one study of 83 geriatric horses, PON was noted in two animals and was unilateral in both [52]. Rarely, proliferative lesions may enlarge and can result in vision or behavior changes if they become large enough to obscure portions of the retina [32].

Clinical appearance and diagnosis

PON appears as a white or gray, well-defined, pedunculated mass that protrudes from the optic nerve into the vitreous cavity with an otherwise normal-appearing optic nerve and retinal blood vessels (Figure 11.78) [18, 31, 32, 115, 137, 138]. Astrocytomas or schwannomas of the optic nerve can clinically look very similar to PON and can only be differentiated histologically by the presence of large, thin-walled cells with foamy cytoplasm that are thought to contain lipid [137, 139]. PON must be distinguised from exudative optic neuritis and ischemic optic neuropathy. However, those two conditions cause acute blindness in the affected eye, may be bilateral (especially exudative optic neuropathy), and affect the majority of the optic nerve head.

Treatment

No treatment is required.

Prognosis

The prognosis for vision is excellent, because these lesions are usually incidental findings.

Ischemic optic neuropathy

Ischemic optic neuropathy is caused by sudden hypoxemia of the optic nerve as a result of acute hypovolemia, thromboembolic disease, or surgical occlusion of the internal or external carotid artery [18, 140]. Ligation of the internal or external carotid artery is used as treatment for guttural pouch mycosis to prevent epistaxis associated with vascular invasion by fungal plaques [140]. With arterial occlusion, the affected eye will be ipsilateral to the surgical site.

Clinical appearance and diagnosis

Initially, the affected optic nerve appears normal, but the affected eye is blind. The nerve becomes edematous and hyperemic within 24 hours. Focal peripapillary hemorrhages and accumulation of axoplasmic material may be observed in 24–48 hours. This appears as white material extending vitreally from

the optic nerve (Figure 11.79). Optic nerve degeneration, characterized by pallor and vascular attenuation, becomes apparent in 2–4 weeks (Figure 11.80).

Treatment

There is no treatment.

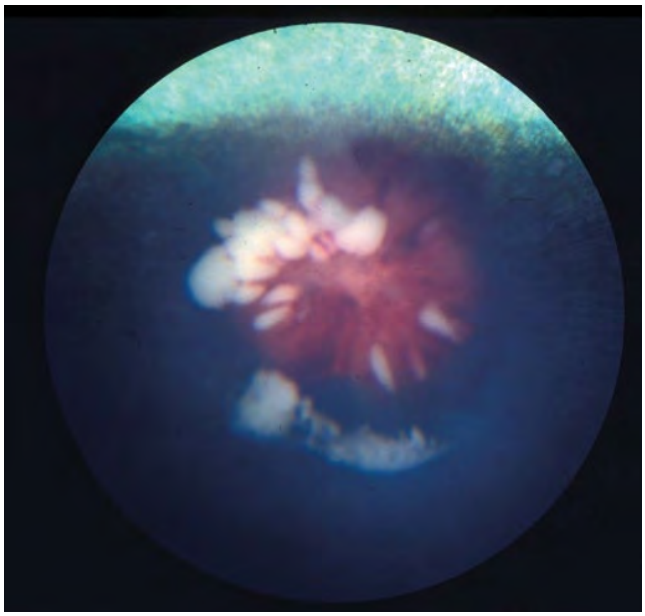


Figure 11.79 Several days after vascular occlusion, peripapillary hemorrhages, optic nerve hyperemia, and accumulation of axoplasmic materials are observed.

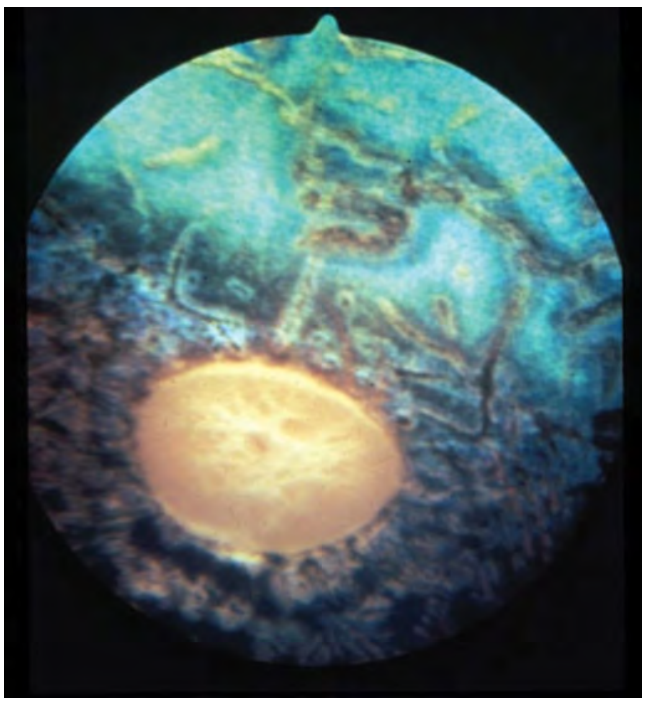


Figure 11.80 Retinal and optic nerve degeneration caused by severe blood loss.

Prognosis

Prognosis for vision is grave.

Traumatic optic neuropathy

Blunt trauma to the head can result in sudden unilateral or bilateral blindness without associated compromise of the globe [141–144]. Trauma may include rearing or falling backward; striking the poll; or blunt injury to the side of the face caused by a kick, twitch handle, or other blunt device. The trauma may result in fracture of the basi-sphenoid bone and compression or hemorrhage in the intracanalicular area of the optic nerve. Additionally, motion of the brain away from the fixed intracanalicular portion of the optic nerve causes stretching of the optic nerve, with resultant neuropraxia of the retinal ganglion cell axons. Cranial trauma may result in unilateral or bilateral optic nerve degeneration.

Clinical appearance and diagnosis

The pupil is fixed and dilated, with absent menace response in the affected eye and an absent consensual PLR to the contralateral eye in the case of a unilateral lesion. Initially, the optic nerve appears normal on fundic examination. Papilledema, focal hemorrhages, hyperemia, and accumulations of axoplasmic materials may occur in the first 24–48 hours but are not seen in all cases (Figures 11.81). Within 2–4 weeks, the optic nerve becomes pale, and the fibers of the lamina cribrosa become apparent as the axons of the retinal ganglion cells disappear (see Figure 11.75). Over time, atrophy of the NSR and hypertrophy of the RPE, which appears clinically as vascular attenuation, tapetal hyper-reflectivity, and areas of hyperpigmentation, will be observed on histologic examination [142]. Necropsy of

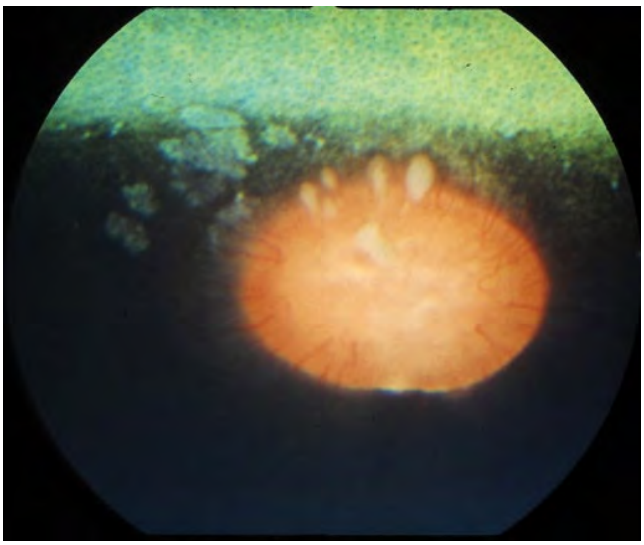


Figure 11.81 Peripapillary white exudates, likely axoplasmic material, are observed 10 hours following an observed head trauma and associated optic nerve blindness. This eye was blind with a dilated, nonresponsive pupil. (*Source*: Photograph courtesy of Drs Ingo Walde and Barbara Nell, University of Vienna.)

affected horses demonstrated focal constriction of the optic nerves at the point of exit from the optic foramina and entry into the cranial cavity [143, 144]. Histologically these regions demonstrated severe loss of nerve fibers, with replacement by astrocytes and gitter cells [143].

Treatment

Horses often receive immediate treatment with anti-inflammatory agents such as systemic corticosteroids or nonsteroidal anti-inflammatory drugs [144]. However, the treatment appears to be of little benefit [144].

Prognosis

The prognosis for vision after traumatic optic neuropathy is poor. If vision has not returned within 2 weeks, the prognosis is grave.

Exudative optic neuritis

Exudative optic neuritis is characterized by an acute onset of sudden bilateral blindness and severe optic nerve inflammation [18, 31, 115]. The pupils are dilated and PLRs are depressed or absent.

Clinical appearance and diagnosis

Exudative optic neuritis is bilateral and appears as a white to gray material obscuring the optic nerve, which, if visible, is edematous with or without hemorrhages (Figure 11.82) [145]. The cause is not known, but it is hypothesized to be an ocular response to a variety of systemic diseases such as infection with *Streptococcus equi* or *Actinobacillus equuli*, septicemia, EHV-1, and possibly ERU [18].

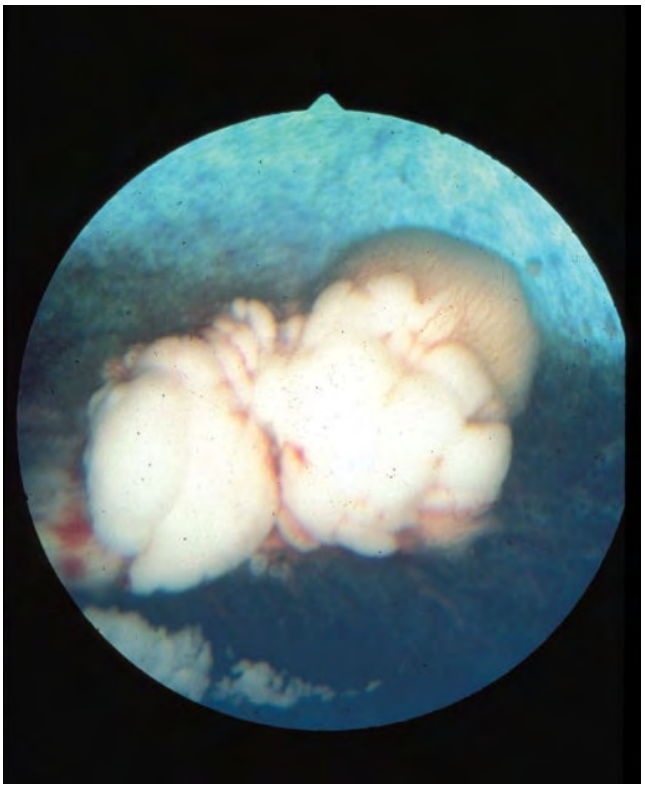


Figure 11.82 Exudative optic neuropathy.

Treatment

There is no treatment unless an underlying condition can be identified and treated.

Prognosis

The prognosis for vision is grave. In the few reports in the literature, vision has not returned. Over time, the optic disc may become atrophied [146].

Optic neuritis

The optic nerve is an anterior extension of the CNS, and, as such, is subject to diseases that result from inflammation, edema, infection, parasitism, and neoplasia of the CNS. Diseases of the CNS must be considered when optic neuritis is diagnosed, but the converse is just as important. A complete ophthalmic examination, with special attention to the optic nerve, should be performed in all horses with diseases of the CNS. This would include in cases of viral encephalitis (arbovirus, herpesvirus, BDV), CNS parasitism (*Trypanosoma evansi*, *Halicephalobus gingivalis*), and mycotic (*Cryptococcus neoformans*) or bacterial meningitis (*Rhodococcus equi*, *Streptococcus equi*). Parasites, such as *Halicephalobus gingivalis* (*H. deletrix*), have been demonstrated to result in chorioretinitis and optic neuritis [110, 111]. These are typically disseminated, with lesions in multiple organ systems. Optic neuritis can occur with ERU. Borna disease, a viral encephalomyelitis exotic to North America, has also been reported to cause optic neuritis and retinal degeneration [32, 114, 115]. See Chapter 15 for more information regarding systemic diseases and the equine eye.

Clinical appearance and diagnosis

Clinically, the optic nerve may appear hyperemic, hazy, and edematous, often with white exudates and hemorrhage (Figure 11.83). The peripapillary retina may be elevated. Vision is generally decreased to absent, and the PLR will be slow to absent, with a mydriatic pupil. In cases of retrobulbar optic neuritis without intraocular involvement, the fundic examination may be normal. In these cases there will be a visual deficit and mydriasis with a PLR deficit. An ERG will confirm a functional retina and should be followed by a complete physical and neurological examination. Additional diagnostic options include VEPs, CSF analysis, and CNS imaging by CT scan or MRI.

Treatment

Treatment is directed at the underlying cause. A case of cryptococcus meningitis and optic neuritis has been reported in a horse and was successfully treated with systemic fluconazole, with return of vision and PLRs [147].

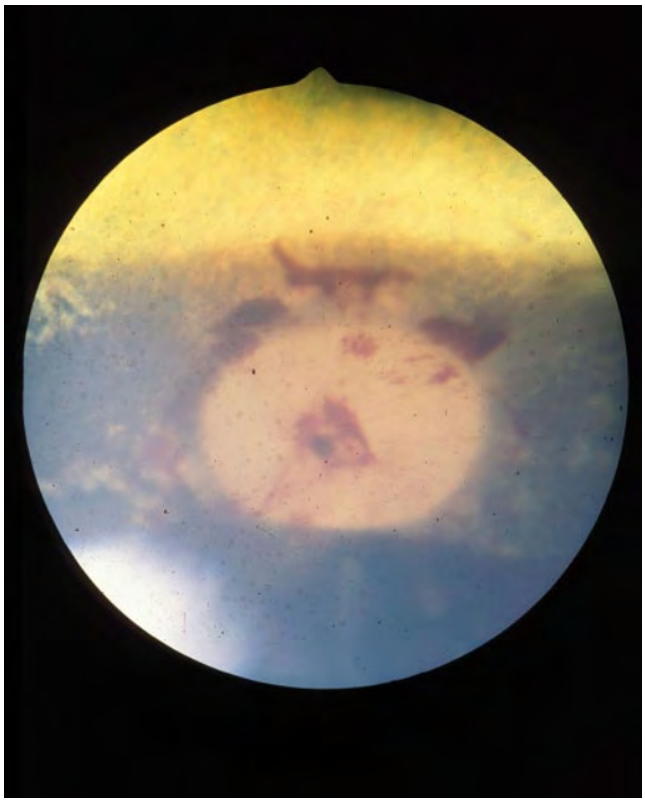


Figure 11.83 Optic neuritis is observed, along with hemorrhage, peripapillary edema, and cellular exudates.

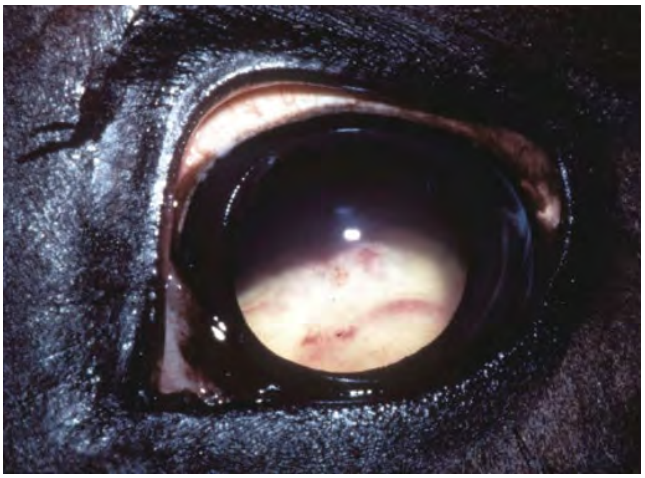


Figure 11.84 Foal with leucocoria caused by a teratoid medulloepithelioma of the posterior globe.

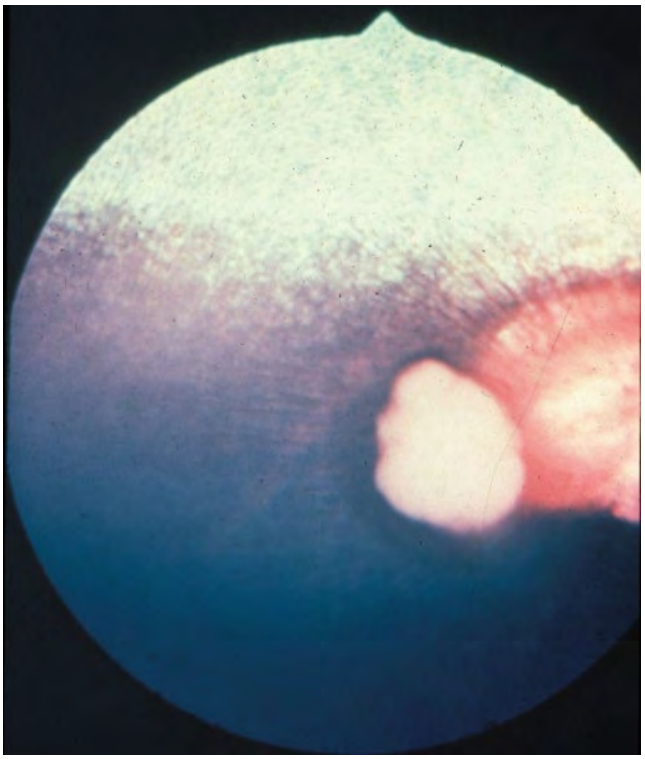


Figure 11.85 Astrocytoma of the optic nerve.

Prognosis

Prognosis for vision is dependent on the severity of disease and response to treatment.

Neoplasia

Primary neoplasia of the equine posterior segment is rare. Retinal detachment, hyphema, glaucoma, blindness, and pain may be observed with primary or metastatic neoplasia. Medulloepitheliomas (teratoid and nonteratoid) appear as white masses in the vitreous (leucocoria) and are seen most commonly in young horses (Figure 11.84) [148–151]. However, in one case report an 11-year-old horse presented with glaucoma caused by a teratoid medulloepithelioma [148]. The medulloepitheliomas can be rapidly growing. Enucleation is indicated and usually curative. A primary primitive neuroectodermal tumor (retinoblastoma) was diagnosed in a 14-year-old gelding and resulted in unilateral blindness [152]. Choroidal melanoma is also a possible primary tumor of the posterior globe, and enucleation is advised.

Astrocytomas, gliomas, and schwannomas may occur and are typically benign (Figure 11.85) [153]. These are difficult to differentiate from PON without histologic examination, but as the lesions are typically benign, treatment consists of monitoring and only considering enucleation if the lesion is rapidly enlarging or the eye loses vision.

Metastatic tumors can also occur, with lymphosarcoma being most common. In general, metastatic tumors are associated with more significant inflammation and hemorrhage than are primary tumors. A metastatic adenocarcinoma has been reported in a horse [154]. The horse presented with a unilateral fleshy, pink, raised iridal mass and bilateral, multifocal, brown to black raised lesions throughout the tapetal fundus (Figure 11.86) [154]. A diagnosis of pulmonary adenocarcinoma with extensive metastases was made at necropsy [154].

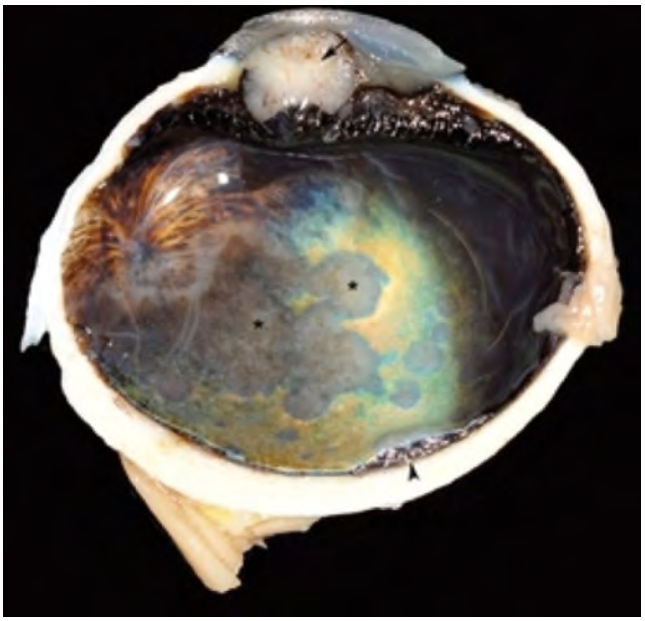


Figure 11.86 Hemisection of the eye after formalin fixation, showing the anterior segment iris mass (**arrow**) and neoplastic chorioretinal infiltrates (**asterisks**). Neoplastic thickening of the choroid is obvious at the sectioned edge (**arrowhead**). (*Source*: Matheis et al., 2013 [154]. Reproduced with permission from John Wiley & Sons.)

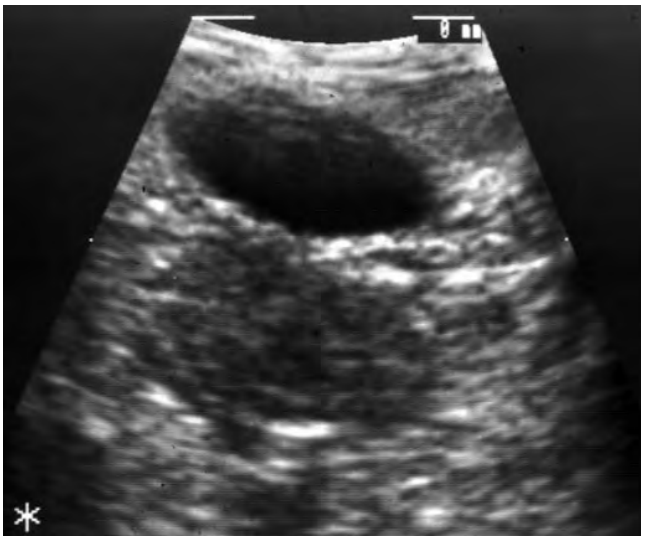


Figure 11.87 Ultrasound examination of a globe with acute blunt trauma. The lens appears anechoic, vitreous contains echoic blood, and posterior eye wall has been ruptured.

Ocular trauma

The equine eye is often subject to severe traumatic injury, perhaps as a result of its prominent position in the head. Traumatic injuries are divided according to the tissues involved and the severity of the injury: contusions (overlying tissue is intact), penetrating injuries (tissue is abraded or partially cut), and perforating injuries (tissue is cut completely). Blunt trauma—whether contusive, penetrating, or perforating—generally results in more severe ocular damage than injury caused by a sharp object. Unfortunately, most ocular trauma in the horse is blunt in nature. In contrast to sharp perforating injuries, blunt trauma results in a rapid increase in IOP, an explosive rupture from the inside outward, and the expulsion of the intraocular contents. The resulting rent in the fibrous tunic is often large and irregular, and portions of the cornea or sclera may be lost. The typical wound is one that originates at the limbus and extends forward into the cornea and posterior into the sclera. However, the posterior portion of the eye may rupture, and the horse may be presented with hyphema and decreased IOP.

Clinical appearance and diagnosis

Vitreous hemorrhage, lens luxation, retinal tears, retinal hemorrhage, retinal and choroidal detachment, and optic nerve damage are all associated with blunt trauma to the eye and orbit [32, 141]. If the hyphema is complete and precludes the evaluation of intraocular structures, ocular ultrasound examination is indicated to assess the lens position, vitreous, retina, and posterior eye wall. If the cornea is intact, the probe can be placed directly on it; if the cornea is compromised, imaging can be performed through the eyelid or an offset device. Evaluation for lens rupture or luxation, vitreous hemorrhage, retinal and choroidal detachment, and posterior eye wall rupture should be performed (Figure 11.87). However, extensive intravitreal hemorrhage can make identification of retinal detachments more challenging [34].

Treatment

Repair of these explosive ruptures is difficult, and the treatment of choice is often enucleation. If cosmetic repair is important, an intraocular silicone prosthesis can be used in some patients, provided there is sufficient tissue left to close the fibrous tunic. This procedure should be performed as soon as possible after injury. If the injury is chronic and atrophy of the globe has occurred, placement of an intraocular prosthesis is not possible. The only cosmetic alternative in these horses is an orbital implant with a cosmetic corneoscleral prosthesis [155]. This requires multiple procedures and referral to an ophthalmologist and ocularist to achieve an acceptable cosmetic outcome.

Prognosis

In general, damage to the posterior segment, especially in association with hemorrhage, carries a grave prognosis.

Surgery of the posterior segment

Vitrectomy

Surgical management of ERU with vitrectomy has been described [46, 47, 156]. Complications include cataract formation, phthisis bulbi, and retinal detachment [157]. Vitrectomy has been more accepted among European veterinary ophthalmologists, and a large number of horses have been treated with this technique. ERU in European horses may differ in its manifestation as a posterior segment disease with marked hyalitis, and therefore this technique has received more widespread recognition in

Europe. However, this posterior manifestation of ERU does appear to be increasing in prevalence in North America. This is evidence that the vitreous may have a role as an effector in some instances of ERU and pars plana vitrectomy has been advocated to control recurrent inflammation in ERU [6, 92, 93]. The success rate for controlling ERU with vitrectomy is much higher for horses with vitreal antibodies against leptospirosis (83%) than for those without detectable vitreal antibodies (14%) [158]. Therefore screening for the presence of vitreal leptospiral antibodies may be an important factor for case selection [158]. The anatomy for surgical entry into the vitreous through the pars plana has been described [3]. For a more detailed discussion see Chapter 8.

Retinal reattachment surgery

To the authors' knowledge, retinal reattachment has been attempted in only a limited number of horses. A pars plana vitrectomy was performed, perfluorocarbons were used to reposition the retina, endolaser retinopexy was performed, and a silicone oil/perfluorocarbon exchange was performed using a technique similar to that described in dogs [159]. However, the success rate has been poor, with either failure to reattach the retina or lack of vision despite retinal reattachment.

Future Research

Future areas of investigation regarding the equine posterior segment should expand our knowledge of infectious diseases and ocular immunology with respect to inflammation of the posterior segment. Examination of the equine posterior segment using advanced diagnostic procedures and *in vivo* imaging systems such as multifocal ERG and OCT should greatly improve our ability to distinguish variations of normal from pathologic concerns. In addition, the potential significance lesions have on vision should become easier to discern as the layers affected and the extent of the damage can be directly visualized and measured. Furthermore, the pathogenesis of various retinal and optic nerve conditions will be able to be more fully ascertained. Surgery of the posterior segment is also an area in need of improved techniques and further research. Studies should be done to help determine prognostic indicators so that the best candidates are selected for vitrectomy. In addition, further attempts to reattach equine retinas will allow refinement of the surgical technique, leading to improved visual outcomes.

Additional content

The book companion website at

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CHAPTER 12

Equine vision

Paul E. Miller and Christopher J. Murphy

Introduction

An understanding of equine vision is important for a number of reasons. Equine practitioners are frequently asked to judge the suitability of a particular horse for specific uses, ranging from the visually demanding (e.g., identification and isolation of a calf) to those that can be performed by nearly blind animals, such as a broodmare walking in an enclosed pasture without injuring herself. Additionally, effective therapy of equine ocular disease requires that the clinician possess a good working understanding of not only the normal visual capabilities and visually guided behaviors of the horse, but also how various ocular diseases alter the animal's vision and hence its utility. An understanding of equine vision also allows the clinician to provide a more accurate prognosis prior to initiating therapy and to more intelligently select from a range of potential therapeutic options for a particular disorder to maximize the probability of optimally preserving the eye's visual capabilities. After preservation of the globe and achieving a comfortable result for the patient, the clinician's therapeutic strategy must be one that best preserves vision.

Ophthalmic disorders add another layer of complexity to estimating a horse's visual capabilities. Some ocular diseases do not alter vision at all, whereas others have such a profound impact that even the ability to perceive light is lost. The externally apparent severity of the disease or size of an opacity does not always correlate with the impact the disorder has on the animal's vision. For example, eyes with copious ocular discharge or a large cataract in the lens periphery may retain essentially normal visual performance, but the presence of a small axial opacity in the posterior nucleus of the lens may significantly degrade visual acuity. In other instances, the clinician may be asked to examine a horse to determine whether an ocular disorder is the root cause of undesirable behaviors such as shying from objects or head shaking. The purpose of this chapter is to provide the clinician with a review of the normal visual abilities of the horse and describe how select ocular abnormalities may alter the animal's vision and behavior.

"Seeing"

Although a seemingly esoteric concept, it is critical to recognize that "seeing" is a perception and not a faithful rendition of the external world in all its factual detail. Indeed, the visual system of all species that have been studied to date takes great liberties with the data it receives from the external environment and uses a number of shortcuts to more rapidly process the image into information that can be used to guide behaviors. One such shortcut is to "see" things in context rather than as they truly are. Both horses and humans have been shown to be subject to the Ponzo illusion in which two horizontal lines of the same size are perceived by the brain to be two different sizes if they are presented in the context of a background set of lines similar to a converging pair of railroad tracks (Figure 12.1) [1]. Similarly, it is quite probable that horses also perceive light and dark in relative rather than absolute terms, potentially explaining certain behaviors such as resistance to crossing certain visual barriers or entering trailers or stalls (Figure 12.2). In general, illusions such as these offer insight into how the brain processes images; objects in the environment may not be seen as they really are but in context with their surroundings.

The eye is often compared to a camera, possessing optical elements (cornea and lens) capable of changing focus (lens) and an adjustable diaphragm (iris) that assists in controlling the amount of light that passes to the photosensitive layer (retina) that captures the image. This represents only the initial process of vision, however, as there is active manipulation of the image captured by the photoreceptors, both within the neural retina and subsequently by the central nervous system. Seeing is a complex process that depends on (1) light from the outside world entering the eye and being properly focused onto the retina, (2) the retina changing light energy into chemical energy and subsequently into electrical energy, (3) segregation of these responses into various categories (brightness, motion, location, etc.) and transmission of this information to the brain, (4) the brain processing this information to make it useful,

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and (5) selection of the relevant portions of the image for attention and further action (Figure 12.3) [2].

The first two steps are comparable to a camera, but the act of seeing is not simply faithfully recording every feature of a scene as a camera would do, because that would quickly overwhelm the brain with huge amounts of information that would be irrelevant to the horse's lifestyle or survival. Instead the brain must decipher the relevant aspects of an image from the billions of photons that interact with more than 100 million photoreceptors in each eye every second. In reality, the optic nerves are flooding the brain with massive amounts of information, much like a large telephone cable serving a major metropolitan area simultaneously carries millions of phone conversations. The brain has coped with this information overload by evolving to not consciously "listen" to all these "conversations" at the same time, but instead to categorize them into specific "topics," which are channeled to specific areas of the brain for further processing [3–6]. Unlike a camera, the brain compares this input with previous images (emphasizing changing aspects of the image), images from the other eye, and input from other senses such as hearing, smell, and touch. Once this is completed, only the information relevant to the task at hand or the horse's survival rises to the level of conscious attention (Figure 12.4). Interference with the process by which an object is determined to merit visual attention, even though it is clearly visible, is a common cause of accidents such as running into fences, the horse hitting its head on stall doors, or throwing its rider. The act of seeing depends not only on the function and health of the eye but also on the cognitive processes in the brain that decide what information merits conscious attention and what is to remain subconscious or be discarded.

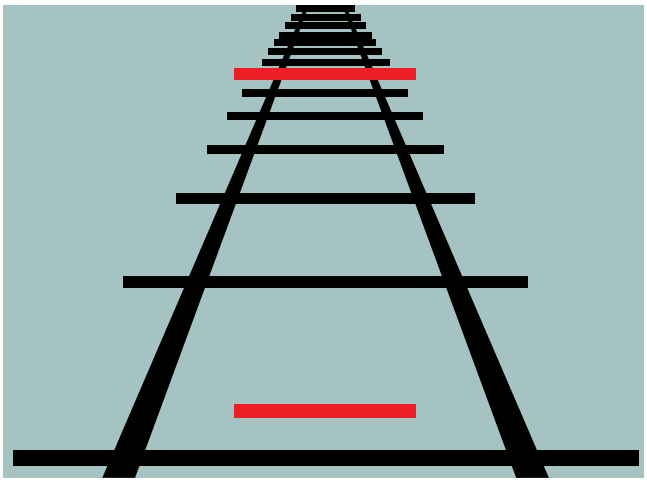


Figure 12.1 The Ponzo illusion. Both horses and humans are subject to this illusion in which the brain estimates the size of an object (**red line**) based on its surroundings and not its true size. The two red lines are the same length, yet the upper line looks longer, since the brain interprets the converging **black lines** as receding into the distance. This perspective clue suggests to the brain that because the size of the image of the two red lines is the same on the retina, the upper red line must be larger—when in fact it is not.

Extensive research into the visual pathways of numerous species, including the horse, has revealed that the information carried from the eye is packaged into many discrete topics, such as an object's brightness and size, location of its edges, its "internal" features such as texture and contrast, direction of movement, velocity, overall orientation as represented on the retinal surface, shape, color, and many other parameters. The most critical aspect of vision, however, is the ability to identify an object (a wolf, for example) as separate from its surroundings (dense vegetation). Because this distinction is so important for survival, animals (including humans) with normal vision can "see" an object if it differs sufficiently from its surroundings in any one of six different aspects: luminance (brightness), motion, depth, texture (which is related to visual acuity), orientation, or color (Figure 12.5) [6]. On the basis of their luminance, motion, depth, and texture, objects are roughly differentiated equally well, but separations based on color are less easily made [3–6]. In this chapter, we describe these fundamental ways of seeing objects as different from their surroundings, but in reality, a complete description of how well a horse sees requires an

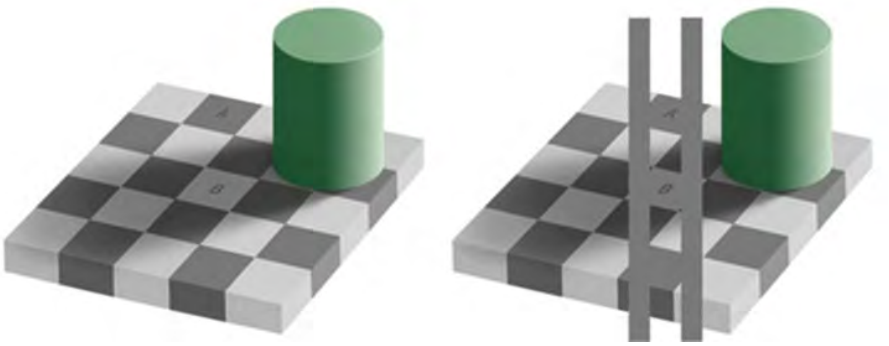


Figure 12.2 The checkerboard illusion. Although they appear different, blocks **A** and **B** are the same shade of gray. They appear different because the brain sees these blocks in the context of their surroundings and not as a light meter would. **B** appears lighter than it really is because it is surrounded by darker checks; it is in the shade. When bands of gray bridge the gap between **A** and **B**, the brain now recognizes that the two are actually the same shade of gray. This illustrates that the brain sees images in context and not as they really are. (*Source*: Courtesy of Edward H. Adelson.)

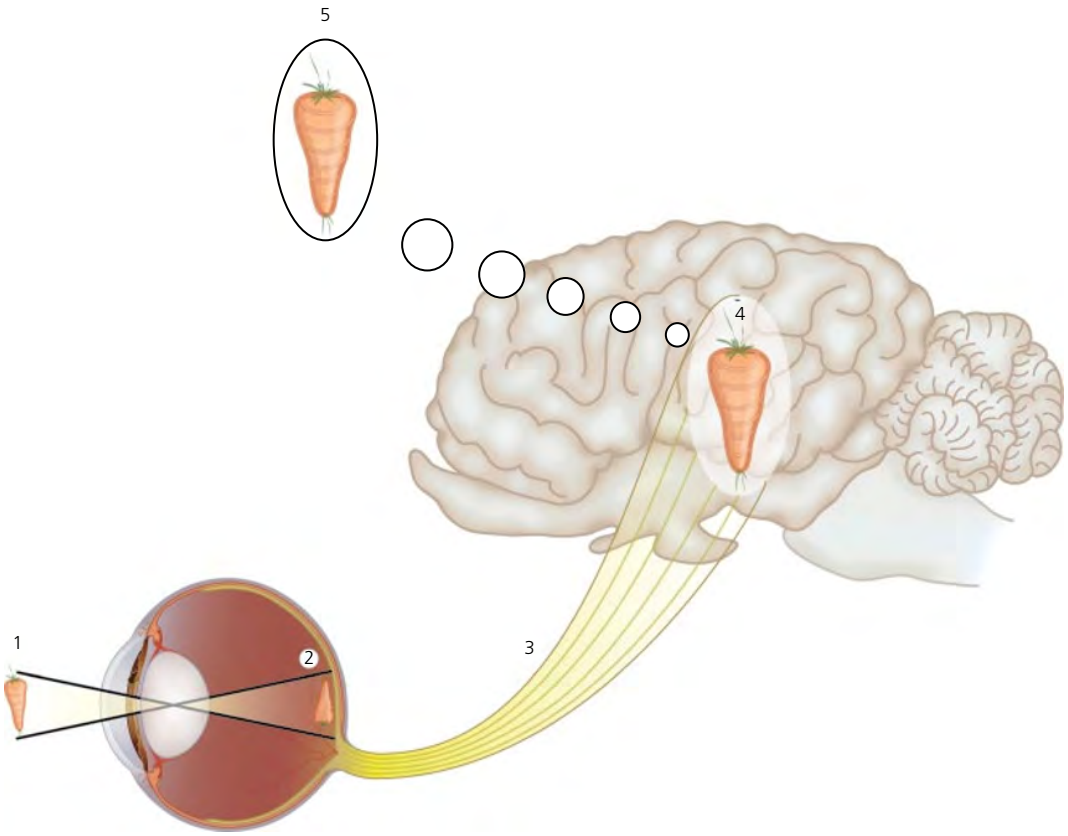


Figure 12.3 The steps in "seeing." **1,** Light enters the eye and is properly focused onto the retina. **2,** The retina interacts with these photons and biochemically triggers an electrical signal. **3,** These responses are segregated into various categories (brightness, motion, location, etc.) and transmitted to the brain. **4,** The brain further processes the information to make it useful. **5,** Relevant portions of the image are selected for attention and further action. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

understanding of not only each of these facets of vision but also how the brain integrates the constituent parts into a unified perception of the world. Unfortunately, the horse's higher visual pathways remain poorly understood, so our understanding of equine visual perception has significant gaps.

Luminance and the perception of light

The ability to perceive light is the most basic aspect of vision. Although some birds are able to see into the ultraviolet spectrum and some snakes use infrared wavelengths to hunt (using specific nonocular receptors located in pits), the eyes of most mammals, including horses and humans, are capable of detecting photons located in only a tiny portion of the electromagnetic spectrum—typically between 380 and 760 nm (Figure 12.6) [7–10]. Even in this visible spectrum, not all photons are detected equally well, and the specific photoreceptors which are optimally tuned to specific wavelengths are not uniformly distributed across the retina. For these reasons, light perception depends not only on the number of photons "raining" onto the retina but also on the spectral composition of the light entering the eye and the sensitivity of the eye's photoreceptors to particular wavelengths [3, 4]. In other words, the ability to detect light in the visible spectrum depends on the type, density, and spatial distribution of photoreceptors that are present, and this will vary from species to species and even individual to individual.

The term **luminance** (sometimes called **value** by artists) is the perceived lightness of an object [6, 11]. Luminance is not purely a physical phenomenon, because the perception of dim-appearing "blue" light and bright-appearing "yellow" light may result from exactly the same number of photons of these different wavelengths striking the retina. Luminance also depends on how sensitive the rod and cone retinal photoreceptors are to the wavelength of light striking the retina [3, 11].

In bright light, where the cone photoreceptors are most active, the equine eye is generally more sensitive to wavelengths in the yellow end of the visible spectrum. Light in the green range of the visible spectrum is detected somewhat less effectively, followed by lesser sensitivity to red, and even less sensitivity to wavelengths in the blue portion of the visible spectrum. In dim light, where the rod photoreceptors are most active, light in the green-blue end of the spectrum is better perceived (peak sensitivity of rhodopsin is approximately 500 nm). Therefore a yellow leaf may appear brighter than a green leaf under bright-light



Figure 12.4 Visual attention: find the cat. Although all the information is available all at once in this image, the brain must select which portions of the image to pay attention to in order for the information to be useful. It locates the cat amongst the plants by first identifying the main outlines or features of the object (eye, ear, white nose, back, and overall "cat-like" shape). It then begins to find where the rest of the "cat-like object" is in the field of view and begins to look for further confirmation by trying to identify more specific confirmatory details such as legs and tail. This process can take some time, and interference with the process of visual attention is a major cause of accidents, even though the object was clearly visible.

viewing conditions, which favor the use of cone photoreceptors that are most sensitive to yellow (peak sensitivity is approximately 545 nm). Under dim-lighting conditions, when the rod photoreceptors are most active, the green leaf may now appear brighter or more luminous than the yellow one. This phenomenon, called the **Purkinje shift**, also explains why blue objects appear lighter and red ones appear darker in twilight versus daylight (Figure 12.7) [12].

Another way of appreciating the difference between luminance and color is to remove all the color information with a computer program and look at a scene in shades of gray [11]. When this is done, it becomes obvious that many objects can be differentiated on the basis of their luminance alone; color is a less important clue (Figure 12.8). Luminance is important because the perception of depth, three-dimensionality, movement (or lack thereof), and spatial organization are all carried by a part of the visual system that responds only to luminance differences and is insensitive to color [4, 5, 11, 13].

A major challenge confronting horses is to adapt to light intensities that vary from the dimmest star to bright sunlight on snow, a factor of as much as 1 to 40 billion [14, 15]. As noted previously, humans, and undoubtedly horses, are largely unaware of this enormous variation in light intensity, principally because objects are perceived in the context of their surroundings and not in absolute terms. Several mechanisms are used to adjust to this wide range of illumination, one of which is the previously mentioned Purkinje shift wherein a duplex retina (possessing both rods and cones) uses rod photoreceptors for dim light and cones for bright light [3, 14, 16–18]. Rod photoreceptors can reliably respond to a single photon of light and are the primary receptors used when the light levels range from virtually complete darkness on an overcast moonless night to those found at dawn and twilight [14, 19]. By mid-morning on a sunny day, the rods have become saturated by light, and in order for useful vision to be maintained, the eye must shift over to using primarily cones. This is analogous to a photographer switching from a fast-speed, "coarse-grain" black-and-white film designed for obtaining less detailed grayscale images in low light to a slow-speed, "fine-grain" film designed to produce highly detailed color images in bright light. However, as the eye shifts from rod to cone photoreceptors, what is lost in terms of sensitivity to light is replaced by improved color vision and visual acuity.

In addition to switching between rod and cone photoreceptors, there are several other mechanisms for adjusting to the wide range of lighting intensities that occur in the real world. Changing pupil size can rapidly alter the amount of light that reaches the retina, but this mechanism limits the range of light intensities only by about ten-fold in humans [14] and probably only by a few fold more in horses. The horse eye is superior to the human in this regard because its pupil diameter has a greater dynamic range [20, 21]. Another relatively rapid but more robust mechanism involves changing neural processing by the retinal bipolar and ganglion cells. These cells can sum the light signals from a group of photoreceptors (spatial summation) or over time (temporal summation), and the retina can facilitate adaptation over a range of about 1000-fold [14]. The large size of the horse's eye serves to facilitate this process because it allows the light signal from neighboring photoreceptors to be summated, thereby brightening the retinal image. The summation process would potentially result in loss of the ability of the eye to resolve detail, but the large eye of the horse compensates for this by providing for a greater number of photoreceptors [21].

The major but slower mechanism for adjusting to varying light intensity is to chemically alter the sensitivity of the photoreceptors to light [3, 22]. Light chemically dissociates the retinal photopigments into their constituent parts, and this depletion (photoreceptor bleaching) leads to a proportional increase in the amount of light required to trigger a response by the photoreceptor [3, 14, 22]. Conversely, when an animal is placed in



Figure 12.5 The ability to see an object as separate from its surroundings is critical for a horse's visual performance. Objects can be seen as separate if they differ in luminance ("brightness"), motion (or relative movement), texture (how "grainy" an object is), depth (binocular disparity), or color. The inside rail and the outer perimeter fence of this race track can be differentiated from the dirt track by any one of these features.

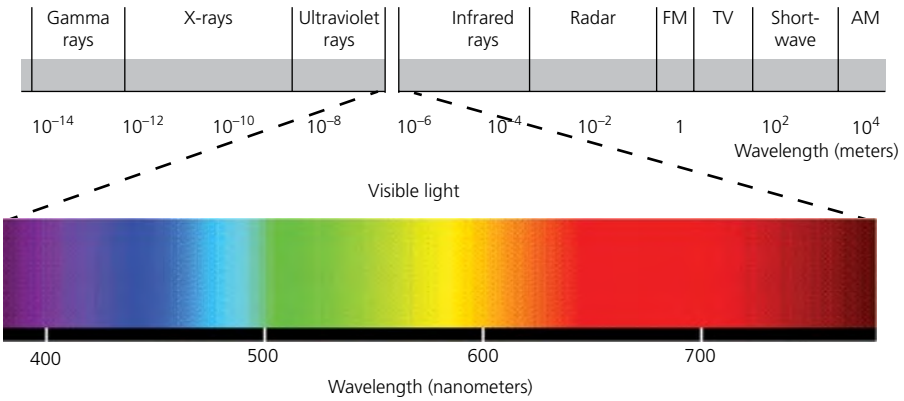


Figure 12.6 The electromagnetic spectrum and visible light. Although some birds can see into the ultraviolet (UV) range and some snakes use infrared imaging to locate prey, most mammals including horses see only a tiny fraction of the electromagnetic spectrum. (*Source*: Gilger, 2011 [174]. Reproduced with permission from Elsevier.)



(A) (B)

Figure 12.7 Purkinje shift. (A) A coffee plant under conditions favoring cone vision. The yellow colors in the leaves are brighter because this color more closely approximates the peak sensitivity of the cones. (B) The same scene under conditions favoring rod vision. The green leaves are brighter than the yellow and red because these colors are closer to the peak sensitivity of the rods.



(A)



(B)

Figure 12.8 Luminance. (A) A racetrack. (B) The same scene with all color cues removed. It is still readily possible to distinguish objects based on their differences in luminance; for example, the poles and rails appear much brighter than the track and the outer wall and trees.

darkness, the photopigment is reconstituted into its active form, and the eye becomes more sensitive to light. This light and dark adaptation occurs over a period of minutes (5 minutes for cones and 20–30 minutes for rods) and can easily be appreciated by simply walking into and out of a dark barn on a bright, sunny day [3, 14]. In humans these photochemical changes can provide a range of adaptation to light intensity that varies in the order of 100 million-fold [14]. Hence, vision is maintained over an enormous range of light intensities by making relatively slow but massive changes in photoreceptor sensitivity and then fine-tuning the intensity by faster alterations in pupil size and retinal processing.

Other ocular adaptations

In addition to these mechanisms, horses have a number of other adaptations that improve vision in dim light that humans do not (Figure 12.9). The horse has one of the largest eyes among the terrestrial vertebrates, and this allows more light to enter the eye through a large cornea and the pupil [23, 24]. Admission of light to the eye is further enhanced by horizontal elongation of the cornea and pupil [25, 26] and by the equine pupil's ability to dilate to an area six times larger than that of a human pupil (3–3.5 times greater than that of a cat or dog) [20, 27, 28]. An elongated slit-like pupil is common in species that are active at night and daytime, because in bright light this shape closes more completely than a round pupil, thereby better protecting a highly light-sensitive retina from very bright light [29, 30]. Because the pupil is located in front of the nodal point of the optical system of the eye, the horizontally elongated, roughly rectangular shape of the horse's pupil in daylight also provides it with a wider view of the horizon than it would obtain with a circular pupil with identical surface area [29]. This allows the horse to scan the visual horizon while at the same time reducing the variations in luminosity the retina must cope with between the usually brighter sky and the usually darker ground. The equine version of the rod photopigment, rhodopsin, also differs somewhat from that of humans [31], and like that of dogs and other species adapted for vision in dim light, it may continue to increase in sensitivity to light for a longer period when the animal is placed in the dark [32–34]. Indeed, it may take more than 30 minutes or more for a horse to fully adapt to dim light conditions [18].

The horse's vision in dim light is also improved by a large, superiorly located, roughly triangular reflective tapetum lucidum that provides the photoreceptors a second chance to capture each photon (Figure 12.10) [35–43]. However, this improved ability to capture light may come at the price of reducing the potential visual acuity of the eye, because the retina is unable to determine whether the photon hit the photoreceptor on the first

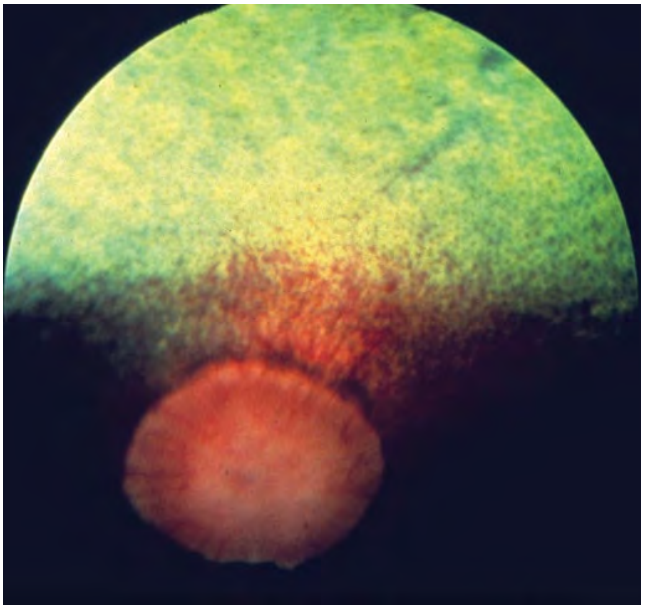
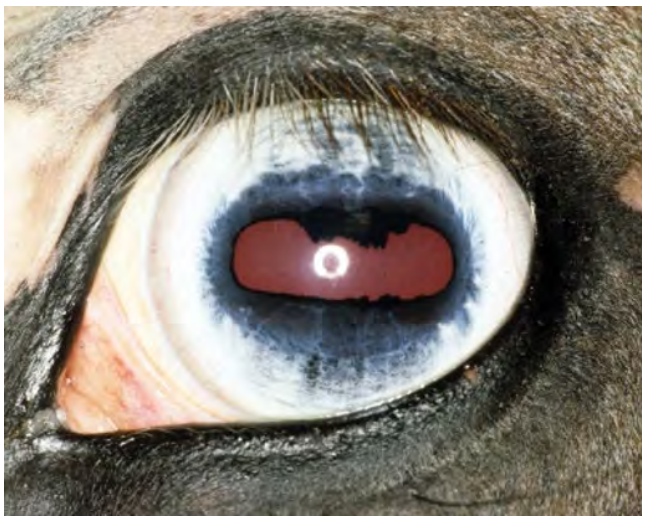


Figure 12.10 The fibrous tapetum of horses reflects light to enhance vision in dim light. However, this reflection may also scatter light and reduce visual acuity.



(A)



(B)

Figure 12.9 (A) Normal equine eye, demonstrating several adaptations to vision in dim and bright light: a large elongated cornea, a horizontal rectangular pupil, and corpora nigra. (B) Note how the superior corpora nigra functions as an "awning" and shields the retina from bright light originating from above. Similarly, the inferior corpora nigra may partially shield the retina from rays reflected off the ground.

pass or was reflected there from a slightly different point in space. However, recently it has been suggested that light scattering by the tapetum may have minimal effect on equine visual resolution because the wavelengths that it reflects are closer to the peak sensitivity of the rods (which are used in low and mid-level lighting conditions) rather than the cones (which are used in bright lighting conditions), thereby increasing its impact in dim light and decreasing its impact in bright light [43]. Additionally, the greatest density of cones is just ventral to the brightest region of the tapetum and partially covered by slightly pigmented retinal pigmented epithelium—both of which may partially shield these cells from scattered light [43]. Finally, estimates of equine visual acuity based on behavioral testing in bright light correlate closely with those based on the anatomy of the retina (without the input of the tapetum), suggesting the tapetum may not substantially degrade vision in bright light in horses.43

In horses, the tapetal reflection is accomplished by the regular spacing of uniform-diameter collagen fibrils in the choroid [36, 39, 41, 43]. The color of the tapetum as seen with an ophthalmoscope is the result of the physical interaction of light with the fibrous tapetum, not the result of colored pigments in the tapetum [36, 39, 41, 43] Yellow or green tapetal reflections represent regions where these fibrils are more numerous, whereas deep blue to purple reflections represent thinner regions of the tapetum [43]. In contrast to the fibrous tapetum characteristic of most mammalian herbivores, the tapetum of carnivores is typically composed of cellular elements [35, 36, 39, 41, 43]. Although the equine tapetum is not as efficient a reflector as the cellular tapetum of some nocturnal carnivores such as the cat (which can reflect up to 130 times more light than the human fundus) [42, 43], it is undoubtedly superior to the human eye, which lacks a tapetum altogether. The modification of different constituents (collagen, cells, or even crystals in some species) to create a reflective layer in the fundus and thereby improve vision in dim light suggests that the tapetum has evolved separately on a number of occasions and represents an evolutionary "arms race" between various predator and prey combinations in which each is seeking a distinct survival advantage over the other [24, 26, 35, 37–41, 43].

The presence of a tapetum suggests that the horse's lower limit for vision in dim light is much less than that for humans. It is not as low as that for cats, however, (5.5–7 times less than that for humans [44]) and perhaps that of certain other predators with a bright, reflective tapetum. A recent behavioral study that required horses to discriminate between circles and triangles in a variety of dim-light circumstances in order to receive a food reward found that horses could readily make these kind of visual discriminations and navigate a room with obstacles at light levels that were so low a dark-adapted human could not see at all [45]. They were fully capable of discriminating between shapes at light levels approximating those of moonlight, starlight on a moonless night, or under cloud cover at night. In fact, only when light levels approximated those of a dense forest with minimal visible sky at night-time, or a dark enclosure devoid of almost all light, did they lose their ability to make visual discriminations. Even in this very dim-lighting circumstance, however, the horses were still able walk around the testing area, locate a feed bowl, and walk through a small testing station set of stocks without bumping into objects [45]. These experimental observations are consistent with anecdotal observations that wild mustangs are able to run at full gallop over rough terrain while negotiating sagebrush, rocks, hills, and gullies with only starlight as the light source [45].

Although the equine visual system appears to have evolved to function well in dim-lighting circumstances, it also has several features that improve vision in bright light, suggesting that the horse is adapted for an arrhythmic photic lifestyle. For example, the nuclear region of the equine lens contains yellow pigments (Figure 12.11) [46], as do human lenses and those of other highly diurnal species such as squirrels [46, 47]. These pigments filter out shorter (blue) wavelengths of light, much as yellow-tinted sunglasses do for humans, thereby reducing glare in bright light and improving the contrast of some objects against their background, since blue wavelengths of light are scattered 16 times more easily than red wavelengths [47, 48]. This pigment also filters out higher-energy rays that are more likely to damage the retina, thereby protecting the delicate photoreceptors of the ventral retina in bright daylight [47, 48]. The large corpora nigra on the central superior border of the iris also improves vision in bright light by augmenting pupillary constriction and acting as an internal visor that decreases the amount of light entering the eye from the superior visual field (where the sun is located), further reducing glare and improving vision in bright light. The much smaller corpora nigra on the inferior pupillary border

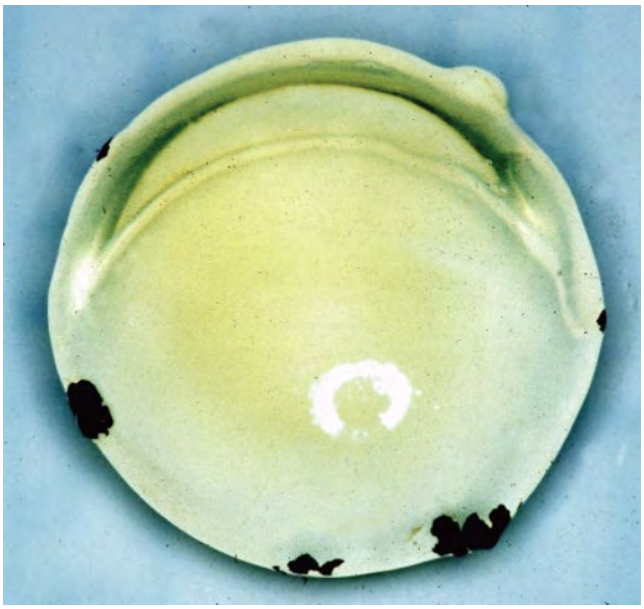


Figure 12.11 Yellow pigments present in the equine lens may filter out blue light, thereby reducing glare and improving contrast in bright light.

may behave in a similar way to reduce the impact of light reflected off the ground. In fact, in very bright light, the horse's pupil may constrict to such a degree that the superior corpora nigra apposes the border of the inferior iris, effectively dividing the pupil into two segments. The impact of this on the animal's vision is unclear, but two pupils oriented in the same plane as the visual streak on the retina may improve the animal's vision in bright light [29] (see section **Optical consequences of pupil shape**). In a sense, the horse has evolved to be a visual generalist, with some degree of vision under all lighting circumstances, unlike humans who tend to function best in bright light and cats who function well in dim light.

Detecting motion

Detecting motion is another fundamental component of vision with great biological importance. Moving objects are more likely to demand some type of response on the part of the horse than stationary ones, and horses, like humans, detect moving objects more easily than stationary ones. This is especially true for objects in the horse's peripheral visual field, which has a visual acuity so low that it may permit only movement and brightness, rather than discrete objects, to be seen [49, 50]. This poor peripheral visual acuity coupled with a prey mentality may explain why horses often shy from even innocuous objects that move in their peripheral visual field. Although the peripheral retina has often been described as being best at detecting motion, it is inaccurate to infer that animals with large peripheral visual fields are better at motion detection than those with better-developed central visual areas such as a fovea. The peripheral retina does have a greater number of the ganglion cell subtypes devoted to motion detection [49, 50], but the central retina has more densely packed photoreceptors. Because of this higher resolution, it actually has a much greater ability to detect motion than does the peripheral retina. In one study, the more densely packed human fovea had a 10- to 12-fold lower threshold for detecting motion than that of a cat [51, 52]. Horses have significantly better visual acuity than cats, so it is likely they are better at detecting motion than cats, but not quite as good at it as humans. It remains to be determined, however, whether there are differences between the peripheral retina and central retina of horses that would render their peripheral vision more sensitive to objects that are moving at specific speeds, in certain directions, or possess features that make them more "attention grabbing" for some reason.

In real life, detecting motion can be quite complex because movement may occur on the part of the object, the horse, or both. Motion detection is most easily accomplished if the horse itself is stationary and the object is moving. In that circumstance, any change in the position of the object on the retina generally signals that it is moving. If both the horse and the object are moving, however, motion detection becomes quite complicated because the animal must now closely coordinate the movements of its eyes, head, neck, and entire body to prevent the retinal image from "bouncing" in such a jerky manner (like the image captured on a video camera when the operator is running) that the animal would be functionally blind [14]. When a horse is trotting, some compensatory mechanisms can be seen at work: the head and therefore the eyes bob only slightly because of a series of reflexive counterbalancing motions by the body and neck (Figure 12.12).

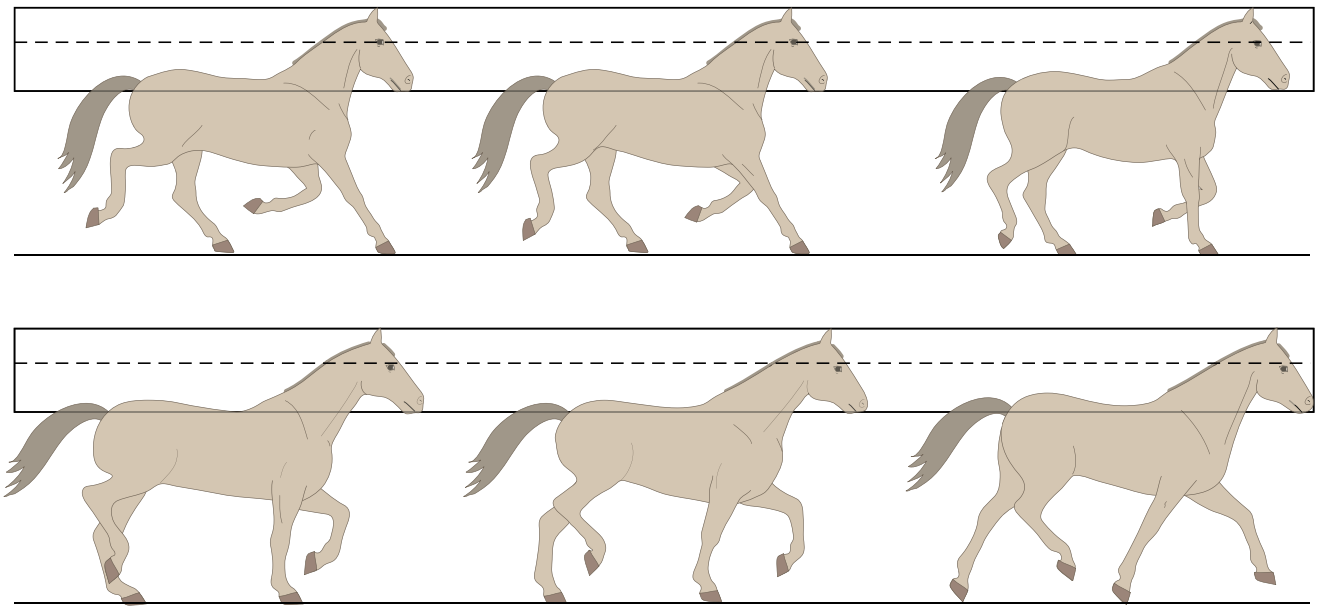


Figure 12.12 When trotting, the image on the retina remains relatively stationary during movement through a series of carefully coordinated movements of the head and neck. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

Because maintaining vision while the horse or an object is moving is so critical to the animal's survival, several different systems have evolved to stabilize images on the retina. Virtually all mammals, including horses, use a stabilization (fixation) system, a vestibulo-ocular reflex system, and an optokinetic system to stabilize images on the retina [53–55]. An additional set of more complicated eye movements—saccades, smooth pursuit movements, and vergence eye movements—are found in species that have forward-looking eyes, comparatively smaller fields of view, relatively well-developed extraocular muscles, a fovea (or at least a localized central region with heightened photoreceptor density, such as the area centralis in cats), and improved binocular vision [53–55]. These movements allow the region of the retina with the greatest visual acuity to be aimed at and track an object, especially while both the animal and the object of interest in the environment are moving.

Most of a human's perception of vision (and presumably that of a horse) occurs when we fixate our gaze. The fixation system (1) attempts to keep objects of interest in a relatively stable position on the area of the retina with the greatest visual acuity, and (2) helps prevent the image from being so stable on the retina that the retina undergoes sensory adaptation and the image no longer becomes visible. Although these two aims appear to be at odds with each other, it is important to remember that because the brain takes shortcuts and emphasizes changes in an object rather than its true physical nature, perfect stabilization of an object on the retina would soon result in it being no longer apparent (Figure 12.13). Hence, the fixation system consists of both eye movements that keep the area of greatest visual acuity directed at an object and a set of very small, involuntary eye movements that prevent the image from being perfectly stable on the retina. The precision of these movements means that the fixation system works well only if the object is completely still or moving very slowly. It tends to quickly become inoperable if the object, the horse, or both are rapidly moving.

Two even faster reflexive eye movement systems also participate in retinal image stabilization. These pathways work to cancel out motion of an object across the retina when the horse itself is moving (the vestibulo-ocular reflex or "doll's eye" reflex) or when an object is moving across the horse's visual field and the horse is stationary (optokinetic nystagmus). The differences between these two methods of stabilizing an image can be appreciated by holding up one finger at arm's length. The vestibulo-ocular reflex can be simulated by rotating your head side to side while at the same time having both eyes remain focused on your finger. You will notice that although your head is moving, the image of your finger remains relatively stable. This is because the semicircular canals of the vestibular system detect movement of the head, and this information can be used to rapidly direct the eyes to move to counteract the anticipated effects of that motion and keep the object in focus. In contrast, the optokinetic system can be simulated in this example by keeping your head stationary and moving your finger rapidly from side to side. In this situation, the image of your finger is much less stable and appears blurred. Here the stimulus for perceiving motion is not movement in the semicircular canals, but the retina detecting an image "slipping" very quickly across the visual field. Because the image must move before it can be detected, and only then can this information be used to redirect the eyes, the brain is always one step behind where the finger was in space, so the image appears blurred. Although the vestibulo-ocular reflex is better at stabilizing an image on the retina as the head is accelerating or decelerating, if the head begins to move at the same speed, the fluid in the vestibular canals soon begins moving at or near the same rate as the head and can no longer be used to direct the compensatory eye movements. The image, however, is still slipping across large regions of the retina, and now the phylogenetically old optokinetic nystagmus system takes over, and the brain switches over to using this visual stimulus to continue to direct the eye movements in an attempt to keep the image stationary on the retina [53–55].

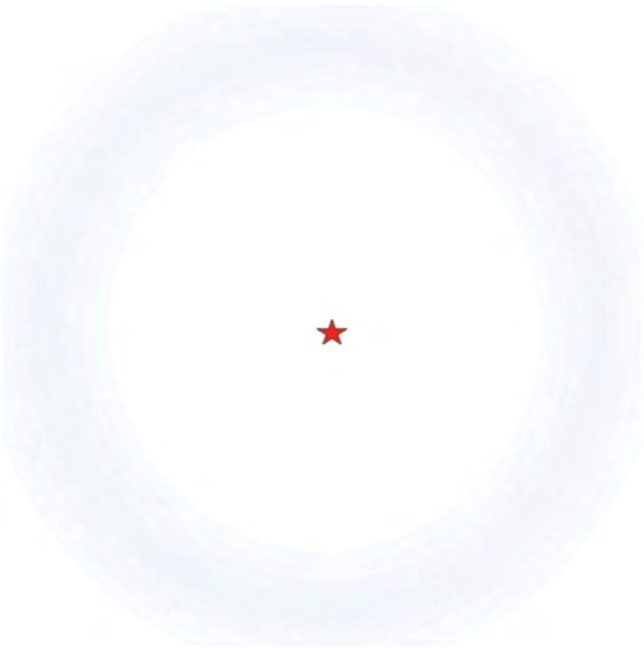


Figure 12.13 Visual "shortcuts." Fixate on the **red star** while paying attention to the **light-blue annulus**. After a few seconds, the blue annulus will disappear, and the red star will appear to be completely surrounded by a white field. Any movement of the eyes brings the blue annulus back into view. This exemplifies how the brain takes shortcuts in processing images by emphasizing changes; perfect stabilization of an image object on the retina would soon result in it being no longer apparent. This occurs because the receptive fields of the peripheral retina are much larger than those of the central retina, so the image appears stable in the peripheral visual field. Receptive fields of the central retina are much smaller than the red star, and micromovements of the eyes prevent that image from fading.

It is also possible to trick the brain into activating the optokinetic nystagmus system by keeping the animal stationary and making the surrounding environment appear to rotate around it. The latter trick, consisting of a rotating drum or projected series of bars (Figure 12.14), has been used to estimate an animal's visual acuity, because this type of nystagmus only occurs if the

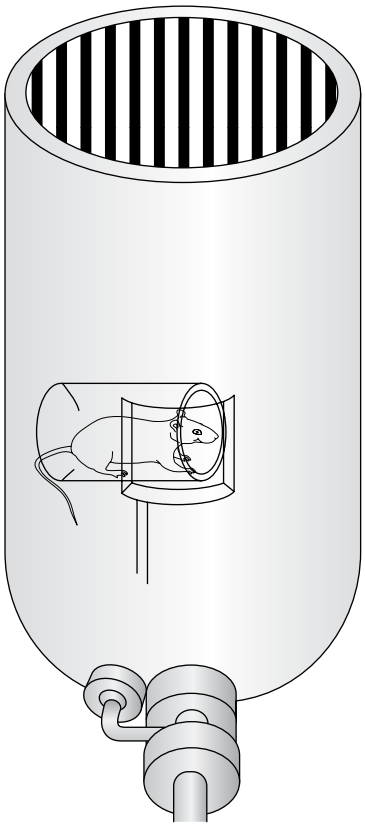


Figure 12.14 Optokinetic nystagmus testing for visual acuity. The animal is held stationary, and a grating pattern consisting of black and white bars is rotated around the animal's head. If the grating pattern is discernable, nystagmus will be detectable. If the pattern is not discernable, it will appear gray, and there will be no nystagmus. Alternatively, the animal can be placed in front of a computer screen and its ocular movements noted as the grating pattern is varied in frequency and made to move across the screen. (*Source*: Adapted from Cahill and Nathans 2008 [175].)

animal is actually able to distinguish the object in question (usually a series of light and dark bands) as separate from the background [56]. The limit of visual resolution in this case is determined by varying the width of the lines on the drum (or the speed with which the drum rotates) and establishing the maximum line width (or speed) at which the optokinetic response is no longer initiated. In effect, when the nystagmus disappears, the animal no longer sees individual light and dark bars, and the image appears uniformly gray. The spacing between the bars at which this occurs can be used to calculate the animal's visual acuity or ability to resolve fine details. This is a less than ideal method. The stimulus for the optokinetic reflex is the image "slipping" on large regions of the retina, rather than the fine details of the object as viewed by the visual streak or fovea [53–55]. Because estimates of visual acuity obtained in this manner are not limited to the regions of the retina responsible for the greatest visual acuity (visual streak) but include larger parts of the retina that have lesser acuity, this method may result in underestimating visual acuity. Nevertheless, the vestibulo-ocular reflex and the optokinetic system can be thought of as a single system that uses two different sensory signals, vestibular and visual, to help solve the same problem: maintaining retinal image stability during self-rotation and movement.

In addition to these three involuntary stabilizing reflexes, many species that have been investigated (and probably the horse) have voluntary eye movements such as saccades and smooth pursuit movements that allow the animal to voluntarily shift its gaze to keep images on important regions of the retina [53–55]. **Saccades** are rapid (0.02- to 0.1-second) voluntary movements that quickly shift the eyes to keep a moving or new image on the area of the retina with the greatest visual acuity. These "jumping-ahead" movements may be quite large, covering up to 100 degrees in humans [54]. When the head is stationary, some species such as the rabbit and goldfish do not make saccades for all practical purposes [54]. These species have little need to do so because their laterally placed eyes already provide them with a large field of view, and their horizontally oriented visual streak allows them to scan the horizon without moving the globe. When a rabbit (and under certain conditions, a horse) makes a voluntary head movement, a saccade is initiated simultaneously with, or just before, the head movement in the direction the head is turning [54]. This causes the gaze to jump ahead, and while the head is moving, the eye holds its new position by means of the vestibulo-ocular reflex until the head catches up and the gaze is again properly aligned [54]. Humans and animals with a central area of particularly acute vision (area centralis), such as dogs and cats, can make voluntary saccadic eye movements without moving the head. Although the horse also has laterally placed eyes and a large field of view, it appears to be capable of making saccades without moving its head, especially when it is apprehensive, but it does not seem to make these movements as often as animals with more frontally located eyes.

Because the eye rapidly "skips ahead" during a saccade, there is no time for the retina to process the intervening visual information or for the brain to correct or refine the movement during the shift. In effect, the eye is functionally blind during a saccade, and the target may be slightly undershot or overshot [53–55]. If the eye is shifting a large distance, the initial saccade moves the eye about 90% of the distance, and one or more smaller corrective saccades make up the remainder. The "smearing" of the image on the retina during a saccade is generally not consciously appreciated, and even though the eye has moved a large distance, the external world is perceived to be stable [53–55]. This is another way the eye differs from a camera; when a camera moves, the external world would also appear to move. Once the image stabilizes on the retina at the end of a saccade, the new information overpowers that which may have started during the saccade, and higher visual pathways "backward mask" the old information, thereby smoothing the image and rendering the animal unaware of the rapid, large shift that occurred [54]. It is tempting to speculate that because the horse has a large field of view, it needs to make fewer saccades, and this improves its vision (at least to a minor degree) by virtue of a reduction in the image smearing that occurs during these movements.

In many species, once the image has been captured on the visual streak by a saccade and any small catch-up saccades have been made, relatively voluntary, smooth-pursuit eye movements track a moving object so that its image remains on the retinal area with the greatest visual acuity (fovea or area centralis) [53–55]. Like the saccadic system, smooth pursuit evolved with the development of retinal areas of greater resolution and is most well developed in species equipped with this type of retinal architecture. Under normal conditions, the stimulus for smooth pursuit is similar to that for the optokinetic system—for example, movement of the image across the retina (retinal slip) [54, 55]. Smooth pursuit differs in that the movement of the object is the point of interest. With the optokinetic system, the stimulus is much larger, and the goal is to follow the background, which is moving in the opposite direction, as the point of interest. Smooth-pursuit movements are driven by images that stimulate the fovea or area centralis and are usually small and relatively slow, whereas the slow phases of the optokinetic system are induced by large patterns that stimulate large areas of the retina [53]. To be effective, smooth-pursuit eye movements must override not only the fixation maintenance system, which tries to keep the eyes fixated on the same point in space, but also the optokinetic system, which tries to follow the massively slipping background images instead of the target [54]. If the horse's head is also moving, the vestibulo-ocular reflex needs to be cancelled out if smooth-pursuit movements are to allow the image to be examined more closely [54]. In all these circumstances, the central visual processing system of the horse must decide whether to consciously pay attention to the background or the more focal point of interest, and which system to override to achieve this goal.

Stationary objects are also viewed with smooth-pursuit eye movements, because there is always slight motion of the image on the retina as the muscles of the head, neck, and body attempt to maintain a steady posture [14, 53–55]. Because smooth-pursuit eye movements track an image by using "retinal slip," the image on the retina is always moving to some degree. This is another way in which the visual system differs from a camera: in effect, it requires some degree of movement to function properly. Although the image of the object being observed may seem to be stationary, this is purely a perceptual phenomenon and is the result of central visual pathway processing of the image. Animals with visual streaks (such as horses) typically do not show smooth-pursuit movements when an object moves horizontally along the direction of the streak, but they appear to do so when an object moves vertically across the streak [14].

Saccadic and smooth-pursuit movements result in the two eyes moving equally in a synchronous (conjugate) fashion, and the viewing angle between the two eyes remains the same. Typically, these movements are elicited when the object of interest is moving from side to side or up and down. If the object of interest is moving toward or away from the viewer, convergent or divergent "vergence" eye movements, respectively, are used to change the viewing angle between the two eyes to keep the object in proper focus. Convergence is also usually accompanied by accommodation (adjusting the focal power of the lens so that near objects are seen more clearly) and miosis that optically increases the animal's depth of field, thereby enhancing depth perception and visualization of near objects [57]. These three responses—convergence, accommodation, and miosis—are neurologically distinct, but because they generally occur simultaneously, they are referred to as the **near response** [57]. Vergence eye movements are typically fairly slow (taking up to 1 second in humans) [53], and as during a saccade, visual sensitivity is markedly reduced during the movement itself. The extent to which horses perform vergence eye movements has not been carefully investigated, but the relatively large area of binocular overlap and certain behaviors (see section **Perception of depth**) suggest that they are readily capable of performing these types of movements. However, the comparably slower rate of pupillary constriction of horses versus that of humans suggests that horses may perform vergence movements more slowly than humans do.

Perception of depth

Visual perspective and field of view

The ability to differentiate objects on the basis of depth depends on a number of factors: the animal's visual perspective, field of view, the difference between the images acquired when both eyes view the same object (binocular disparity), and higher processing by the brain to fuse these images into a novel image that allows for depth to be perceived. The horse's visual perspective can vary greatly and depends to a large extent on whether the head is down and the animal is grazing, or the head is up and the animal is scanning the horizon. Furthermore, breed differences can result in the same environment being perceived quite differently. A field of tall grass may appear to be a dense, impenetrable brush to a Miniature horse but a wide-open savanna to a Clydesdale (Figure 12.15).

The lateral position of the eyes in the skull affords the horse a wide panoramic view (Figures 12.16 and 12.17) [16, 24, 30], and the nasal extension of the retina further enhances the horse's temporal peripheral visual field. On the basis of anatomic relationships, the horse is believed to have a total monocular visual field in the horizontal meridian (i.e., the portion of the horizon that can be seen by an eye when fixed on one point) of approximately 190–195 degrees, and up to 178 degrees in the vertical (superior to inferior) meridian. When the visual fields of the two eyes are combined, the total horizontal visual field is up to 350 degrees, and the horse has virtually a complete sphere of vision around its body, with only a few minor "blind spots" [16, 24, 30]. Recent behavioral studies have confirmed that horses can detect objects within an almost fully encompassing circle and that they are able to identify the type of object within most, but not all, of their panoramic field of view [58]. The blind spots in the equine



Figure 12.15 The visual perspective of horses varies greatly by breed, even when standing in the same location. (A) A Miniature horse only sees a stone wall. (B) An Arabian sees to the top of the wall. (C) A Belgian draft horse sees what is on the other side of the wall.

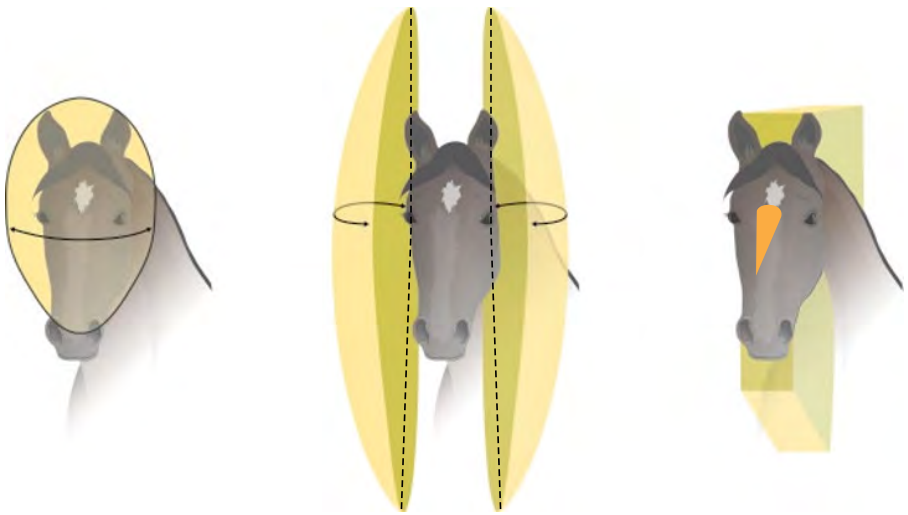


Figure 12.16 Visual field of view of the horse. (*Source*: Illustrations by Samantha J Elmhurst BA Hons/LivingArt.)

visual field are small and located superior and perpendicular to the forehead, directly below the nose, in a small oval region in the superior visual field where light strikes the optic nerve itself, and the width of the animal's head directly behind it. Clearly, this extensive visual field makes it very difficult for a predator or human handler to sneak up on a horse.

The visual fields of the two eyes overlap anteriorly and below the nose for 55–65 degrees, although some authors suggest the



(A)

(B)

Figure 12.17 Simulation of the view seen by the left eye of a human and a horse looking over the city of Perth, Australia. (A) Simulated view of a human, with a small, high-acuity central region surrounded by a peripheral region of lower visual acuity. (B) Simulated view of a horse. Note the much wider field of view with a linear area of higher acuity and a horizontal strip of lower acuity above and below. (*Source*: Harman et al. 1999 [16]. Reproduced with permission from John Wiley & Sons.)

overlap may be as great as 70–80 degrees [16]. This degree of binocular overlap rivals or exceeds that of domestic dogs, which ranges from 30 to 60 degrees, depending on breed [24, 59–61]. This would seem to challenge the generally accepted view that predators have binocular vision superior to that of prey species. In reality, however, depth perception plays a significant role in breaking the camouflage of an object (e.g., a wolf) against its background, and this would be of distinct advantage to prey species [62]. As has been described for certain bird species, it is also possible the animal's lifestyle and the extent of the binocular field do not necessarily predict the quality of its stereoscopic vision [63, 64].

Stereopsis (binocular depth perception) results when the two eyes view the world from slightly different vantage points, and the images from the overlapping visual fields are fused into one [62]. If the relatively disparate images on the two retinas were not blended, viewing a scene with both eyes would simply result in double vision (diplopia), and depth perception would actually be impaired. The new information that stereopsis provides is as qualitatively important to the overall sense of vision as is the perception of motion, color, or contrast. The ability to perceive depth varies greatly between individual humans [65, 66] and cats [67], and although similar work has not been done with horses, some horses undoubtedly are better than others at detecting depth. How these differences may affect their usefulness for certain types of work is uncertain, because most horses with one eye have been observed to still function well as jumpers or barrel racers, even though these tasks would seem to demand excellent depth perception [68]. Also, several horses with only one functional eye have performed well in top-tier races such as the Kentucky Derby [69].



Figure 12.18 Depth perception with one eye. Several cues allow depth to be perceived with one eye or in a two-dimensional photograph. These cues include apparent size (the left tower appears closer because it is larger than the right), looming (cars moving toward the viewer appear to become progressively larger), interposition (near objects, such as the bridge, overlie the more distant hills), aerial perspective (water vapor and dust in the air make the more distant hills less distinct and relatively color desaturated), shading (shadows on the tower suggest depth), perspective (the parallel roadways appear to converge toward the horizon), relative velocity (the nearer cars appear to move faster than the more distant ones), and motion parallax (if the eye is fixed on the center of the bridge, the images of near objects appear to move opposite the direction in which the observer moves his or her head, whereas distant objects move in the same direction as the head).

Integration of binocular visual inputs is not the only means available to an animal to accomplish depth perception, however. As any artist can attest, animals and humans can appreciate depth with only one eye by using specific visual clues. These include relative brightness (brighter objects tend to be closer), size (larger objects are closer or objects progressively increasing in size are getting closer), contour and areas of light and shadows (the gradation in the intensity of a shadow on a curved object makes it appear to be projecting away from or toward the observer), object overlay (closer objects block distant ones), linear perspective (parallel lines like those of a railroad track converge onto a vanishing point at distance), aerial perspective (water vapor, dust, and smoke in the atmosphere make distant objects indistinct and relatively color-desaturated), density of optical texture (the fine details of the surface of an object become less apparent the farther away it is), relative velocity (near objects appear to move faster than distant ones), and motion parallax (objects at different distances appear to move at different speeds or in different directions, depending on the observer's point of fixation) (Figure 12.18) [62]. There is good evidence that horses are able to use at least some of these static monocular clues to recognize depth in two-dimensional photographs, and it appears they are even susceptible to some of the pictorial visual illusions to which humans are susceptible [1, 70]. Because of their huge monocular visual fields, it is clearly advantageous for horses to be able to use monocular clues to estimate depth.

Nevertheless, two eyes are better than one, because the binocular threshold for depth perception in horses is five times better than the monocular threshold [71]. Although the two eyes of horses are farther apart than those of humans (resulting in a greater relative disparity between the two retinal images and theoretically better depth perception), humans still have better depth perception than horses. From 2 m away, humans can detect a few millimeters' difference in depth, whereas from the same distance, horses can detect only a 9-cm difference

(a 10- to 20-fold poorer performance) [71]. The latter value approximates that of cats [72, 73] and may have some biological relevance because it is also approximately the same difference in depth between grass in a pasture and the ground under it. The familiar behavior of a horse rotating its nose upward to better observe distant objects has been suggested to be a response to exploit improved depth perception, since binocular overlap is said to be oriented down the nose in horses (rather than straight ahead as it is in humans) [16, 24, 74]. Evaluation of the eye position and forward visual field of the horse, however, would suggest that they are still capable of binocular overlap when viewing objects with their noses down and their eyes directed forwards, as when riding "on the bit" [75].

When stereopsis is combined with the perception of motion, horses and humans are able to make accurate judgments regarding the trajectories and distances of moving objects so as to allow them to be intercepted or avoided. A similar phenomenon occurs if the object is stationary and the horse is moving. If a fixed point of reference is present, it is easier to detect motion-in-depth than if the object is effectively by itself [76]. For example, it is easier to detect the motion-in-depth of a baseball bouncing along the ground than it is to detect its motion-in-depth against a clear blue sky. Predators use stereopsis and stereomovement (the ability to detect motion-in-depth) to improve the accuracy of their attacks, but these visual components are equally important to prey species such as horses because they enhance their ability to detect the predator's camouflage and avoid objects during their escape [62].

The ability of humans with normal vision to detect motion-in-depth is 5–28 times poorer than their ability to detect a difference in depth if the object remains static (stereoacuity) [76, 77]. At first, this is somewhat surprising because (1) objects that are moving from side to side (e.g., in the frontoparallel plane) are much easier to detect than stationary objects, and (2) each eye working alone is readily able to detect objects that are moving across the visual field from nasal to temporal and also moving away from or toward the eye [78]. This phenomenon appears to be due at least in part to the fact that stereomotion detectors average the motion individually detected by the left and right eyes [78]. Additionally, objects moving across the visual field stimulate a series of photoreceptors over more widely separated regions of the retina, whereas objects moving in depth stimulate regions of the retina that are much closer to each other. Finally, this difference is not so much because detection of motion-in-depth is so poor, but more because stereoacuity is so good. Brain processing of the images from both eyes allows details of an object that are not visible to either eye alone to be detected (see discussion of hyperacuity in section **Retinal factors affecting visual acuity**).

The ability to perceive depth develops after birth and depends on images being presented to both eyes for comparison purposes. This ability goes through a critical developmental period, and kittens that have had the eyelids of just one eye sutured closed for a brief period (5 days) will experience substantial permanent deficits in binocular depth perception. This is especially true if the deprivation occurs between 35 and 45 days after birth [79]. This developmental age may correlate with that of a newborn foal and suggests that if the vision in one eye is impaired by a corneal ulcer or the placement of a third eyelid flap during critical periods of maturation of the visual system, depth perception may fail to develop normally in that animal, despite subsequent resolution of the problem.

Visual texture

All surfaces of an object have a tactile texture—how they feel when touched. They also have a visual correlate of this called visual texture, which for our purposes refers to the appearance of the surface's texture. In other words, does the surface appear rough or smooth, homogenous or fragmented, full of fine details or uniform, composed of randomly arranged elements or elements that occur in a regular pattern, and so on. Visual texture can be a powerful mechanism for seeing an object as separate from other objects in the visual field (Figure 12.19). Visual acuity and form perception are other critical elements in the horse's ability to see objects as separate from their surroundings.

Visual acuity

In general, visual acuity refers to the ability to see the details of an object separately and without blurring. It depends on (1) the optical properties of the eye, (2) the retina's ability to detect and process images, and (3) the ability of higher visual pathways to process and interpret these images. Visual acuity can be evaluated in many ways, and, at times, the methods and terminology can be quite confusing. Measurements of visual acuity may be based on the size of a letter on an eye chart, the angle the object's image subtends on the retina (in seconds, minutes, or degrees of arc), or how close together an alternating pattern of black and white lines can be before they appear to be uniformly gray (the so-called grating acuity, which is measured in cycles per degree). All of these measurements are interrelated, and tables that allow one set of units to be compared with another have been created (Table 12.1) [80].

In humans, one of the most familiar methods of measuring visual acuity is to ask an observer to read a Snellen eye chart, which consists of rows of progressively smaller black letters on a white background (Figure 12.20) [81]. The size of the letters between rows varies in a geometric fashion (0.1 log unit), and the smallest line that can be reliably discerned in this high-contrast setting is called the **minimum resolvable** or **resolution acuity** [81]. There are a number of variations on the classical Snellen eye chart, and because not all letters are equally easy to read, other commonly used charts use only one letter (typically a "tumbling E" or "Landolt's C") and ask the observer to indicate the direction in which the letter is pointing (up, down, right, or left). The size of each letter in a row is based on the assumption



Figure 12.19 Visual texture. Objects may be differentiated from their background on the basis of differences in texture of their constituent elements. In this image, the deer can be identified in part because its coat has a more homogenous texture than either the forest floor or the oak trees.

Table 12.1 Comparison of terms used to describe visual acuity.

Snellen value	Numerical value	Minutes of arc	Minutes/seconds of arc	Cycles per degree
20/20	1.0	1	1′ 0″	30
20/25	0.80	1.25	1′ 15″	24
20/30	0.667	1.5	1′ 30″	20
20/35	0.571	1.75	1′ 45″	17.2
20/40	0.50	2.0	2′ 0″	15
20/45	0.444	2.25	2′ 15″	13.4
20/50	0.40	2.5	2′ 30″	12
20/55	0.364	2.75	2′ 45″	10.9
20/60	0.333	3.0	3′ 0″	10
20/65	0.308	3.25	3′ 15″	9.2
20/70	0.286	3.5	3′ 30″	8.6
20/75	0.267	3.75	3′ 45″	8
20/80	0.25	4.0	4′ 0″	7.5
20/85	0.235	4.25	4′ 15″	7.1
20/90	0.222	4.5	4′ 30″	6.7
20/95	0.21	4.75	4′ 45″	6.3
20/100	0.20	5	5′ 0″	6
20/150	0.133	7.5	7′ 30″	4
20/200	0.10	10	10′ 0″	3

(*Source*: Data from Borish, 1975 [80].)

that under these optimal but artificial conditions, normal human visual acuity is 1 minute of arc, so the width of the strokes forming the E or the gap in the C will subtend 1 minute of arc on the retina at a specified distance (e.g., 20 ft, 60 ft, 200 ft) [81]. The results of these tests are then typically recorded as 20/20, 20/40, 20/60, and so on—the numerator representing the distance the subject is from the target (chart), and the denominator representing the maximal distance from which a person with statistically normal vision could identify a letter this size. In other words, 20/200 vision means that the test subject can only make

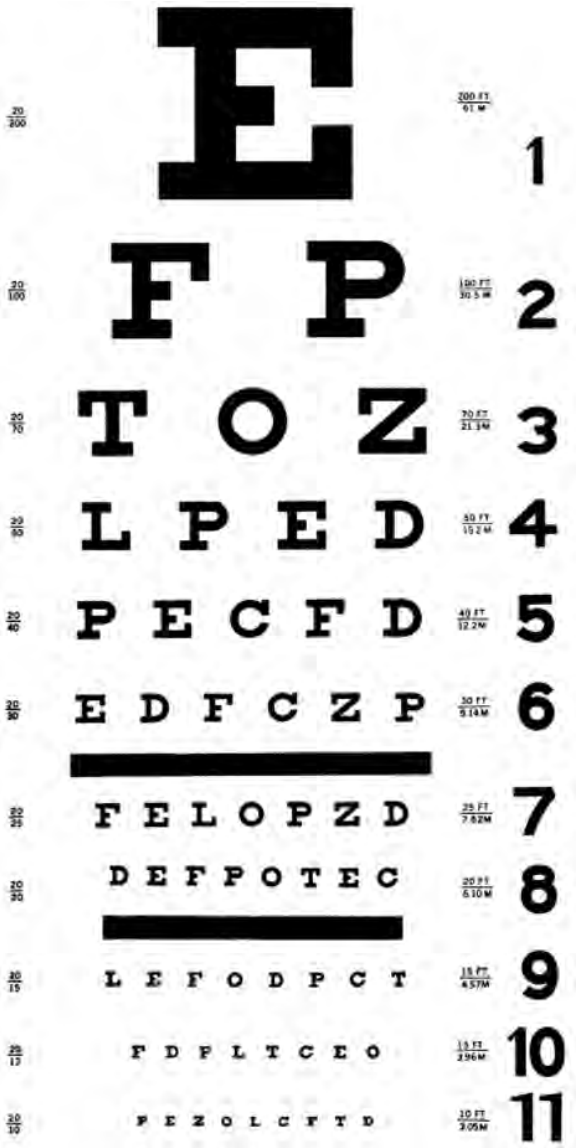


Figure 12.20 A Snellen-type visual acuity chart.

out the details of a letter from 20 ft away that a person with normal visual acuity could make out from 200 ft away.

In using Snellen acuity values to express visual acuity for animals, it must be recognized that the denominator is still using a statistically normal person for comparison. With this type of notation, equine visual acuity varies from about 20/30 on behavioral testing [82], 20/35 to 20/40 according to ganglion cell density calculations [16], and approximately 20/60 when estimated electrophysiologically with the horse under general anesthesia [10, 83]. By comparison, normal canine visual acuity is approximately 20/75 and normal feline visual acuity is 20/100 to 20/200 [84–86]. In one study it was shown that the horse could better visually discriminate between objects if they were located on the ground versus being placed 70 cm above the ground, although other behavioral studies found no effect of stimulus height at ground level versus 80 cm above the ground [58, 87]. Nevertheless, horses may learn tasks better when they are allowed to use natural head and body postures to visualize objects [58].

The largest row of letters on most eye charts usually corresponds to 20/400 visual acuity. Vision poorer than this is commonly described as "counting fingers" (at a certain distance), "hand motion" (at a certain distance), "light perception," and "no light perception" [88]. The latter two descriptions do not actually measure visual acuity but simply indicate whether any stimulus can be detected at all. If a person's best corrected (e.g., with glasses or contact lenses) visual acuity is 20/200, he or she is considered to be legally blind. In comparison, counting fingers vision at 2 ft corresponds to a visual acuity of approximately 20/2000, and hand motion vision at 2 ft corresponds to a visual acuity ten times worse than this, or 20/20,000 [88]. Because the stimulus for a menace response is essentially identical to that of hand motion vision, the veterinarian should be cautious about interpreting a horse's positive menace response to mean that it has useful vision. In reality, a positive menace response from 2 ft away only indicates that the animal's vision is at least 20/20,000, but such a response could also be present in a person with a visual acuity 100 times worse than someone who is legally blind. Unfortunately, in veterinary medicine there is no simple method such as an eye chart that allows the clinician to more precisely determine a horse's visual acuity, and the clinician is often forced to extrapolate the impact of a given disorder from humans to horses.

Lay people often regard Snellen visual acuity to be synonymous with how well an animal or person sees, but, in fact, this is not the case. In the real world, the ability to see all the features present in a complex visual environment cannot be reduced to one number such as 20/20, and a horse or human may have "normal" Snellen visual acuity and still have marked visual impairment. This is because, in part, Snellen acuity is so highly tied to the performance of a very small region of the retina with the greatest photoreceptor density [3]. For example, if the entire retina except for the fovea is lost, a person's visual acuity would still be 20/20, but the field of view would be only a few degrees in diameter and, for all practical purposes, not very useful. Such a situation occurs in people with advanced retinitis pigmentosa in which the photoreceptors of the peripheral retina degenerate and only foveal vision is preserved. Similarly, if only the fovea is lost, visual acuity drops to that of the peripheral retina (20/200 or worse in humans) even though most of the retina is still performing normally [3]. Although the horse lacks a fovea, and the reliance on such a very small region of the retina is lessened, lesions that affect the horse's visual streak, especially the temporal arm, will undoubtedly have an appreciable impact on an animal's ability to resolve fine details in its environment [10, 16].

For this and other reasons, a variety of other stimuli have been employed in assessing vision, including presenting targets with varying shades of gray, alternating bars or checkerboards, objects arranged according to depth, various sets of colors, and a series of dots or short lines arranged in a row. Each type of

target tends to activate different portions of the visual system, and the results are expressed in relatively unique ways. When the stimulus and viewing conditions are varied, it becomes apparent that a number of factors influence visual acuity:

- Contrast: reduced contrast reduces resolution.
- Luminance: visual acuity decreases in dim light.
- Refractive error: errors reduce visual acuity.
- Pupil size: small pupils lead to greater depth of field and, to a certain degree, improve visual acuity for targets located outside the plane of focus of the eye.
- Retinal eccentricity: the farther from the fovea or visual streak, the greater the reduction in visual acuity.
- Exposure duration: visual acuity is decreased for target exposures in the 100- to 500-millisecond range compared with longer exposures.
- Target and eye movements: saccades and rapid target movements reduce acuity, but moderate movements do not [81].

The degree of contrast between the brightest and dimmest components of an object can greatly affect the object's visibility (Figure 12.21) [6]. Although it is important to use a highly contrasting standard such as black letters on a white background (e.g., the standard Snellen target), if the maximal visual acuity a visual system is capable of is to be determined, this situation is seldom encountered in the real world. It may be far more important for the horse to be able to differentiate between varying shades of gray, because its rod-rich retina has evolved primarily to perform well in dim light where contrast is not as great.

In a laboratory setting, contrast sensitivity is tested by using repetitive stimuli such as alternating lighter and darker bars (grating patterns), checkerboards, or varying shades of gray letters on a white background [6]. When this type of stimulus is used, visual acuity varies not only with the spatial grain of an image (how thin the black bars are and how far apart the alternating bars are from each other) but also with the contrast between various elements of the image. Very coarse patterns (very wide bars) can be seen at very low contrast (relatively little difference between the bars in terms of their shades of gray), but as the spatial grain is made finer (the bars become thinner), a higher degree of contrast is needed to see the pattern [6]. In general, objects with low degrees of contrast are more difficult to distinguish as separate from the background than highly contrasting objects, even if the objects are the same size and are viewed from the same distance. Therefore, although resolution acuity of black objects on a white background is important for establishing a minimum threshold for detection of an object, it is in reality only one small point on the contrast sensitivity continuum, and it does not fully describe an animal's visual capabilities [6].

The degree of illumination of an object also affects visual acuity. In very dim light, visual acuity is reduced in humans and horses, with the human rod system being able to support a peak visual acuity of approximately 20/150 [81]. As the light intensity increases to the point that cones can be used effectively, human visual acuity rises to 20/20 because the cones are more densely packed in the fovea than the rods. In very bright light (e.g., that exceeding a bright sky on a sunny day), human visual acuity tends to level off or be reduced from expected values [81]. Although these findings are likely to be applicable to horses in general terms, similar studies have not been performed in horses, and the presence of a large number of rod photoreceptors in the central retina of the horse may alter these values to some degree. For example, one study demonstrated that a 1-inch-wide stimulus on an overcast day was more visible to a horse than a 2-inch stripe on a sunny day [74]. This suggests that the rod-dominated central area of the equine visual streak has impaired visual discrimination under bright light conditions compared with that of a human with a cone-rich fovea. In another experiment, it appeared that contrast stimuli underfoot were less visible to younger animals than older ones, but a subsequent examination of head/neck carriage showed that younger horses did not lower their heads to the same degree as older, more trained horses [74]. These types of findings indicate the difficulties associated with performing visual evaluations in horses and also highlight the role learning plays in a horse's visual performance.



Figure 12.21 Reduced contrast sensitivity, glare, and reduced visual acuity. The entire image is "washed" with light, and the contrast between objects is diminished in addition to a reduction in the visibility of fine detail (reduced visual acuity). Extreme glare is also present, which can occur naturally as in this case or as a frequent sequela of corneal scarring, cataracts, and other ocular opacities that scatter light towards the retina (versus bouncing it back out of the eye). All three can be quite debilitating and are frequent causes of accidents.

Optical factors in visual acuity

In the ideal situation, the transparent optical elements of the eye (cornea, lens, aqueous and vitreous humors) would capture light emanating from every infinitesimal point in a scene and precisely focus these onto a correspondingly infinitesimal point on the retina [89–91]. However, in actuality, the optics of the eye invariably distort a precise point of light from a scene into a circular blur on the retina. When severe, this distortion can substantially limit the visual acuity of the eye, but humans and animals are relatively insensitive to small amounts of blurring, so objects located at a range of distances from the eye appear to be in sharp focus (depth of field) [3].

Refractive state

The refractive state of the eye has a direct impact on visual performance. For all the elegance of the retina and the higher visual pathways, their function is for naught unless an accurately focused image of the environment is formed on the retina. In ophthalmology, the term **resting refractive state** is generally used to refer to the plane in space where the eye is focused when at rest (not accommodating). When an object is placed approximately 20 ft away from the eye, all light rays emanating from the object that enter the pupil are essentially parallel (hence this distance is regarded as essentially the same as optical infinity and is used for Snellen visual acuity testing). Proper focusing of parallel rays emanating from an object on the retina is called **emmetropia**, whereas focusing of the image in front of or behind the retina are called **myopia** (near-sightedness) and **hyperopia** (far-sightedness), respectively (Figure 12.22). In astigmatism, the cornea, lens, or both have an uneven curvature (e.g., a football versus a sphere), causing the eye to have two (or more) focal points.

The extent of a refractive error is expressed in terms of the dioptric power of a lens that is needed to allow the eye to correctly focus on an object that is infinitely far away (e.g., ≥20 ft

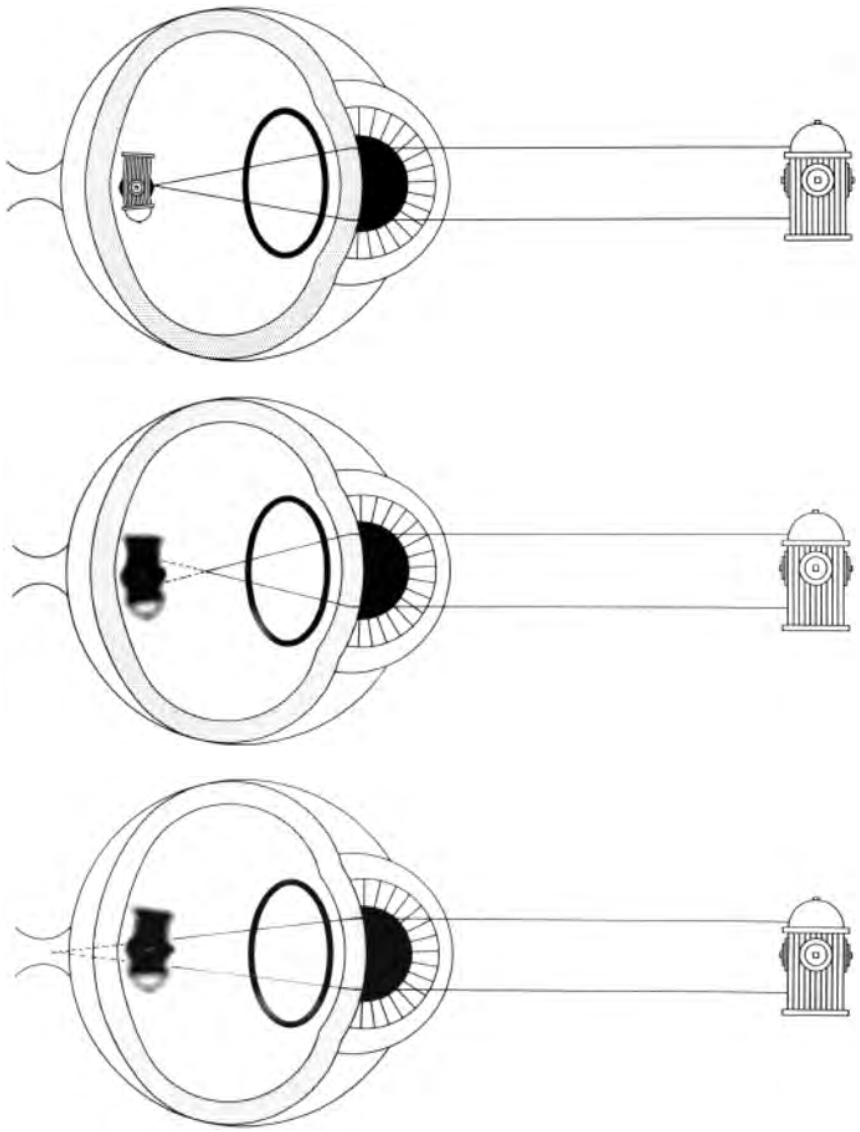


Figure 12.22 Ray diagrams showing emmetropia (proper focusing of images on the retina, **top**), myopia (near-sightedness, or focusing of images in front of the retina, **middle**), and hyperopia (far-sightedness, or focusing of images behind the retina, **bottom**). (*Source*: Miller and Murphy, 1995 [85]. Reproduced with permission from American Veterinary Medical Association.)

for practical purposes). The unit of optical power of a lens system is the diopter (D = 1/focal length in meters). This means that an eye that is in focus at rest 1/3 m away from the eye is 3 D myopic. In humans, simple myopic or hyperopic refractive errors can be corrected by placing appropriately powered spherical lenses in the form of glasses or contact lenses in front of the eyes. In the previous example, placement of a 3-D, concave (negative) lens in front of the eye would now allow images greater than or equal to 20 ft away to be properly focused on the retina. Astigmatism is more complicated, but it can be corrected by adding cylindrical-shaped lenses that refract (bend) light in one plane but not the other. Alternatively, refractive errors can be corrected by surgically recontouring the cornea with any one of several different procedures (e.g., LASIK). In theory, these procedures are also applicable to horses, but only rarely are contact lenses used to attempt to correct refractive errors in horses.

The resting refractive state of the living equine eye can be objectively determined by streak retinoscopy, and numerous studies involving more than 16,000 equine eyes have been performed in which this technique was predominately used [16, 24, 92–105]. As is often the case, in most recent reports, the large number of studies performed in the 1800s and early to mid-1900s have been ignored. Each of these reports varies as to the mean refractive state and the relative frequency and magnitude of reported myopia and hyperopia [16, 24, 92–104]. This may reflect regional and perhaps temporal variations in the equine populations screened, rather than inconsistencies in technique. It has been well documented in dogs that the refractive state can vary with breed and with selective pressures imposed by performance requirements [106–108].

In general, the average resting refraction of the horse in most modern studies is near emmetropia (normal), but some individuals are significantly (≥3 D) myopic or hyperopic. In a study of 333 horses and ponies in the UK, 69% were emmetropic in both eyes, but refractive errors greater than 1.5 D (in either direction) occurred in only 2.7% of eyes tested [104]. In another study of 215 equine eyes in Europe [103], 3% were hyperopic, 15% were emmetropic, and 82% were myopic, although most of these were within a diopter of emmetropia. Significant astigmatism was not found in this study [103]. Finally, a survey of 83 horses of varying breeds, ages, and performance demands living in the midwestern USA [101] revealed a mean resting refractive state after cycloplegia of +0.25 D and low frequencies of astigmatism (≥0.5 D in six horses) and anisometropia (a difference in refractive status between the two eyes of 0.5 D in ten horses). In this study, 55% of horses were within 0.5 D of emmetropia, whereas 24% were greater than or equal to 0.5 D hyperopic and 21% were greater than or equal to 0.5 D myopic [101]. Horses with moderate to severe vitreal degeneration tended toward myopia, although this was not statistically significant [101]. In a study by Wouters and De Moor [103] that demonstrated a high frequency of myopia, a high incidence of vitreal degeneration was recorded in the study population.

The resting refractive state of a species can also be estimated from analysis of ray tracings with schematic eyes. A schematic eye is an internally consistent mathematical model that is constructed for a particular species with three sets of data: (1) the refractive index of the optical media, (2) the position along the optical axis of each optical interface (front and back of the cornea, the front and back surfaces of the lens, and the retina), and (3) the radius of curvature of each optical interface. Three schematic eyes for horses have been reported [96, 99, 105]. As pointed out by Farrall and Handscombe [95], an unresolved issue in the schematic eyes presented by Sivak and Allen [99] and Knill et al. [96] is the prediction of marked hyperopia, a finding incongruous with the data obtained by refraction of the living horse eye. In contrast, the schematic equine eye constructed by Coile and O'Keefe [105] predicts a refractive state of +1 D, which is closer to that obtained by streak retinoscopy.

Diffraction

Even in the absence of any optical abnormalities, an infinitesimal point of light cannot be brought into focus on the retina because light waves are bent (diffracted) as they pass through a hole in an obstruction, in this case the pupil [3, 90]. This results in a precise point of light being converted to a fuzzy disc surrounded by dimmer rings (airy disc) by the time it reaches the retina. The smaller the pupil, the greater the impact diffraction has on vision [3, 90]. Although diffraction is a fundamental physical phenomenon and may significantly affect human visual acuity, the role it plays in equine vision is unclear [81]. This is due in part to differences between humans and horses in the shape and size of the pupil and to the fact that in very bright light, the equine pupil may have two distinct pupillary apertures, as described in the following section.

Optical aberrations

Optical aberrations occur when the light rays originating from a point light source are not brought to a point of focus on the retina, typically as a result of inaccuracies and irregularities in the shapes of the curved refracting surfaces of the cornea and lens [3]. Along with diffraction, optical aberrations are potentially more serious than simple refractive errors because they are not easily correctable with the usual spherical or cylindrical lenses [3]. Aberrations can be classified as monochromatic, which may be seen with only one wavelength of light, or chromatic, which involves the differential focusing of various wavelengths (e.g., colors) of light on the retina [90]. Monochromatic aberrations can be further classified as spherical or cylindrical refractive errors and spherical aberrations, comas (in which a point source of light is distorted into a comet-shaped blur), and "higher-order" aberrations that are an amalgam of deviations that can take on complex patterns [90].

Spherical aberration is a major distortion in many optical systems, inducing up to 2 D of blur in humans (Figure 12.23) [89]. Positive spherical aberration occurs when light rays passing through the periphery of the cornea and, to a lesser extent, the

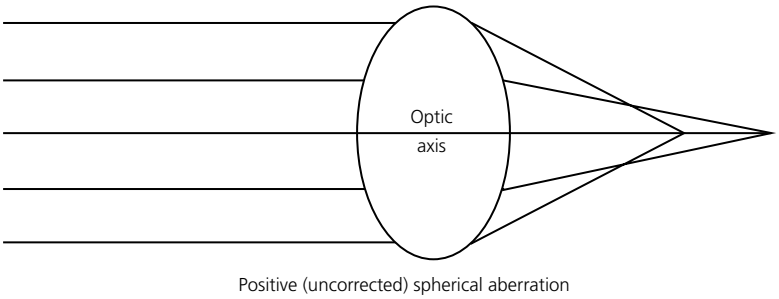


Figure 12.23 Spherical aberration. With positive spherical aberration, the more highly curved peripheral portion of the lens focuses light in front of light rays that pass centrally. (*Source*: Miller and Murphy, 1995 [85]. Reproduced with permission from American Veterinary Medical Association.)

lens are brought into focus in front of those passing through the central portion of the cornea and lens. Negative spherical aberration occurs when the more peripheral rays are brought into focus behind the paraxial rays. At the level of the retina, the result is a focal light source appearing as a relatively intense circle of light surrounded by a less intense halo, provided that the eye is emmetropic [90].

Because the iris controls the amount of peripheral light that reaches the retina, spherical aberration is greatest when the pupil is large. In bright light, it is essentially negligible in humans. The proportionally larger, horizontally elongated cornea [25, 26] and the large rectangular pupil in horses suggest that either spherical aberration plays a more significant role in horses than in humans, or horses have other mechanisms for controlling this aberration. Spherical aberration can be reduced by flattening the peripheral cornea, thereby reducing its optical power, or by reducing the refractive index of the peripheral lens versus the axial lens. The equine cornea does appear to have a flatter peripheral corneal curvature, although precise measurements have not been made [25, 26]. In the equine pupil that is fully constricted, thereby creating two pupillary apertures as a result of occlusion of the mid-portion of the pupil by the corpora nigra, spherical aberration would be minimized. This is because rays would pass through portions of the lens that are roughly equidistant from the center of the lens. Spherical aberration may also be less of a problem for horses because they also rely more heavily on rod photoreceptors with larger receptive fields and because identification of large shapes or movement is more important than discrimination of fine details.

Chromatic aberrations occur when light of different wavelengths is focused at different distances from the posterior nodal point of an optical system (e.g., at different planes relative to the retina) (Figure 12.24). In humans, the total chromatic aberration is about 1.5–3 D under daytime conditions [89, 109]. Green light (medium wavelength) tends to be focused on the retina, red light (long wavelength) is bent less and is focused behind the retina, and blue light (short wavelength) is bent more and focused in front of the retina [89, 109]. All things being equal, this would produce colored fringes around a focused point of light, much like a rainbow is created by the chromatic aberration of water droplets in the atmosphere. Despite this physical phenomenon, humans do not see colored fringes around objects, in part because red and blue are less likely to be detected

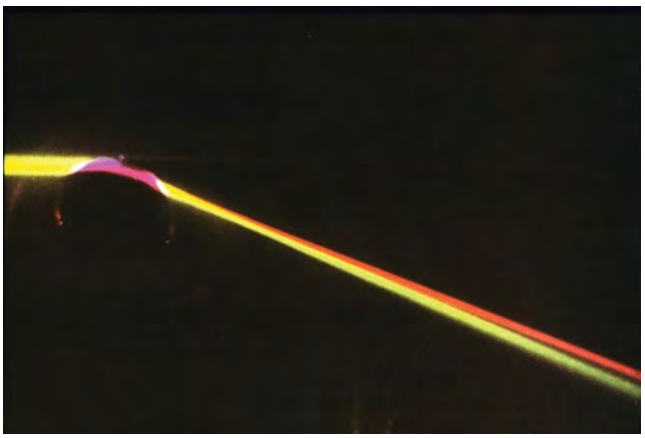


Figure 12.24 Chromatic aberration. Red and green lasers have been superimposed and subsequently passed through the isolated lens of a fish. The shorter-wavelength light (**green**) is focused in front of the longer-wavelength light (**red**). (*Source*: Photograph courtesy of Dr Jake Sivak.)

because of the cones' relative insensitivity to wavelengths at the ends of the visible spectrum [89, 109]. Additionally, visual processing in the human retina and brain appears to be able to sharpen the edges of images and "erase" the colored blur [89]. The relatively minor effect of chromatic aberration is verified by studies that show that human visual acuity is not materially improved by wearing achromatic lenses that neutralize this phenomenon [109].

Chromatic aberration has been suggested to be an important factor in guiding accommodation, because the differential bending of various wavelengths of light can provide feedback to ensure that the image of interest is in as sharp focus as possible [110]. Chromatic aberration, however, may be relatively unimportant to horses because their cone photoreceptors are less numerous than those in humans, they accommodate little, they have yellow pigment in their lens (which reduces blue light reaching the retina), and they too are less sensitive to wavelengths at the ends of the visible spectrum.

The posterior nodal point

The optics of the eye are such that the majority of light rays emanating from objects in the environment pass through certain key points along the optic axis before continuing on to strike the retina (Figure 12.25). One of these critical points is the posterior

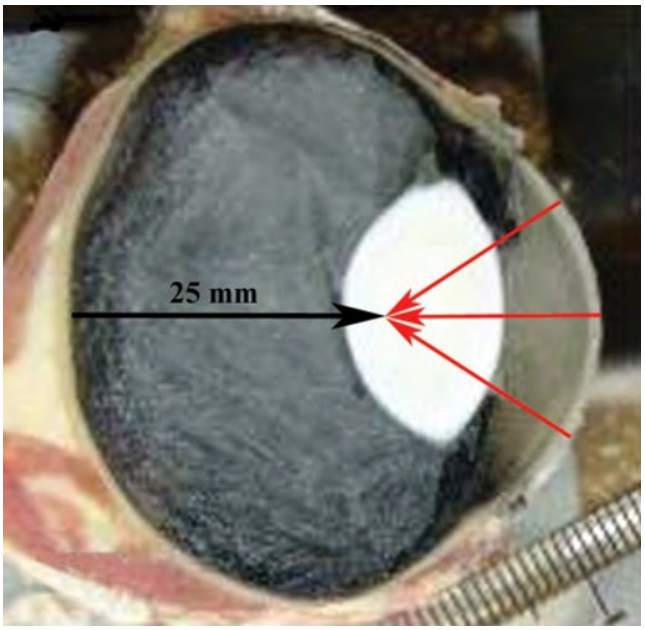


Figure 12.25 Location of the posterior nodal point of the equine eye (**tip of black arrow**). The majority of light rays (**red lines**) passing through the pupil are focused through this point. Opacities in this location will create substantially more visual impairment than anywhere else in the lens. (*Source*: Adapted from Roth et al. 2008. The absolute threshold of colour vision in the horse, *PLoS ONE* 3:e3711, Epub 2008.)

nodal point, which is located approximately at the level of the posterior lens capsule in humans. In the horse, it is estimated that this point is somewhat more anterior than in humans and located approximately 2.4–2.9 mm posterior to the center of the lens, or roughly in the posterior lens nucleus. Coile and O'Keefe's [105] schematic eye for the horse calculates the posterior nodal point to be located 2.94 mm posterior to the center of the lens. The value of 2.4 mm posterior to the lens center is obtained by using a calculation that estimates the anterior focal length of the eye to be approximately 0.665 times the axial length [111] and then using the following values from the literature: the average axial length of the eye is 43.68 mm [112], the anterior focal length (equal to the posterior nodal distance in emmetropic animals) of the equine eye is 31.6 mm [111], the equine lens is 12.7 mm thick axially [112], and the posterior lens capsule is 19 mm posterior to the cornea [112]. Others have used frozen sections of the eye to calculate that the posterior nodal point of the equine eye is approximately 25 mm from the retina, which again puts it roughly at the level of the posterior lens nucleus [21].

Because of the critical importance of the posterior nodal point to the performance of any optical system, even small opacities in this region of the lens have a substantial impact on visual acuity. In humans, small cataracts present at this location can reduce visual acuity to the legally blind range. Because this phenomenon is a function of the physics of every lens system, animate or inanimate, there is no doubt that small opacities in this region can significantly impair a horse's vision as well. The fact that these visual deficits may not be discernable on routine examination is more of a testament to the crudeness of one's ability to fully evaluate the visual performance of the horse than to the real impact of these opacities.

Glare

Scattering of light within the eye (glare) reduces the contrast of an object against its background and renders low to moderately contrasting objects difficult to see in a high-glare environment (see Figure 12.21) [6]. Anyone who has driven a car in the direction of the sun, faced a car with "bright" headlights on at night, or gazed at the water from a beach on a sunny day has experienced the visually disabling effects of glare [6]. Given these situations, it is easy to understand why glare is a notorious cause of motor vehicle accidents. Undoubtedly, glare also plays a substantial role in some accidents in which a horse inadvertently runs through a low-contrast object such as a barbed wire fence.

Disease states may increase glare by further increasing forward light scattering in the eye. Some of the causes of pathologic glare include early cataract (especially posterior subcapsular cataracts), light entering through the iris (especially in blue eyes or those with iris atrophy and polycoria), and corneal edema or scarring [6]. In humans, a 30% increase in corneal thickness caused by stromal edema may not alter Snellen visual acuity, but it can produce significant alterations in contrast sensitivity and susceptibility to glare [113]. It is likely that a similar phenomenon occurs in horses. Slit-lamp biomicroscopic examinations highlight cataracts by scattering light back toward the examiner, whereas the disabling effect of glare is caused by light that is scattered forward onto the retina [6]. Consequently, slit-lamp examinations do not necessarily indicate the degree of glare disability experienced by individual patients [6]. The equine eye's defense against glare includes yellow pigments in the lens that preferentially absorb the more highly scattered blue light, the dark brown pigment of the uveal tract and retinal pigment epithelium, an eyebrow, eyelid, and granula iridica (superior ones may block the sun, smaller inferior ones may block reflected light), and an orientation of the rods and cones such that they behave as light guides in which light must enter at a specific (nonscattered) angle to be sensed.

Accommodation

A method of adjusting the focus of the eye (accommodation) is needed if objects at different distances are to be seen with equal clarity. As an object is moved closer than 20 ft to the eye, more divergent rays emanating from the object can pass through the pupil. Because these rays are no longer roughly parallel to each other, the refractive status of the eye must be altered to maintain the image in sharp focus on the retina. In older texts, the horse is said to have a "ramp retina" that obviates the need for an active accommodative mechanism. In a true ramp retina, such as that possessed by the sting-ray, the retinal plane is "ramped"

relative to the optic axis such that the superior retina is farther from the nodal point than the inferior retina [114]. In such a situation, near objects would be imaged on the superior retina, whereas distant objects would be imaged on the inferior retina. More recent research has indicated that although there are small variations in the distance from the nodal point to the retina, the horse does not possess a true ramp retina [16, 99].

Humans are generally believed to accommodate by contracting the sphincter-like ciliary muscle, thereby reducing the resting tension on the lens zonules [110]. This frees the elastic lens capsule to bring the remainder of the lens into a more spherical shape and increase its focal power, improving near vision [110]. This method of accommodation, however, is not used by all animals. A few of the many ways in which different species affect accommodation include moving the lens anteriorly or posteriorly, changing the curvature of the cornea, and squeezing the lens with the ciliary musculature or iris [110, 115]. Mammals typically accommodate by either increasing the curvature of the lens [24, 80, 110] or forward translocation of the lens within the eye [115]. When streak retinoscopy and dynamic photorefraction (which allows real-time imaging of the refractive state of the eye [116, 117]) are used, horses rarely evidence accommodative shifts greater than 1–2 D. This is in accordance with estimates of less than 2 D of accommodative range for the horse, on the basis of an evaluation of the optics of the equine eye [100]. In an emmetropic eye, an accommodative shift of 2 D would allow the horse to bring into sharp focus objects located from visual infinity to 0.5 m from the eye. This accommodative range is well suited to the lifestyle of the horse.

The exact mechanism by which the horse accommodates is not fully understood. Over 100 years ago, Tscherning suggested that accommodation in horses and cattle may be the result of flattening of the peripheral lens surface and increasing the curvature of the central lens surface [118]. He noted, in contrast to the previously described mechanism of accommodation in humans, that if he pulled on the lens zonules, the lens curvature actually increased in these species [118]. Similarly, in a more recent study of bovine lenses, Schachar et al. [119] found that when the sclera and ciliary body were stretched radially, the equatorial diameter of the lens increased, and the effective optical power of the lens also increased. The mechanism underlying this phenomenon is unclear, but it has been proposed that constriction of the ciliary muscle increases the tension on the lens zonules that insert on the equatorial lens capsule (thereby increasing lens diameter and flattening the peripheral region of the lens) and relaxes the tension on the zonules that insert on the anterior and posterior portions of the lens capsules (thereby allowing the central lens surface curvature to increase) [120]. Definitive evidence to support this theory remains to be presented, and this mechanism of accommodation is controversial. If the functional structure of the equine eye is carefully considered—ciliary muscles are strictly longitudinal in orientation and relatively poorly developed—it is more likely that accommodation occurs in the horse by anterior translocation of the lens during accommodative excursions. This hypothesis could be tested by using ultrasonography in combination with pharmacologic agents.

Regardless of the mechanism by which it occurs, the stimulus for accommodation is blurring of the retinal image and/or divergence of the two eyes. As noted previously (in section **Optic aberrations**), the eye may detect that the image is defocused on the retina by using chromatic aberration to fine-tune accommodation [110, 121–123]. This then drives the parasympathetic nervous system to cause the ciliary musculature to constrict and also evokes pupil constriction and convergence of the two eyes (the near response) [110]. The two eyes are linked so that if one eye is made to accommodate, the other will as well [110]. Although the impact on the optics of the eye is often overlooked by veterinarians, drugs such as pilocarpine also elicit accommodation, and atropine inhibits it. Whether topical atropine interferes with ciliary muscle motility and accommodation for the same prolonged period during which it can affect pupil size is unknown [20]. If the musculature of the equine ciliary body contracts at the same relatively slow rate as the iris sphincter muscle, it is likely that the horse is slower to accommodate than humans and domestic carnivores. For the same reasons, it is also likely that the "near response" in horses is quite slow to develop.

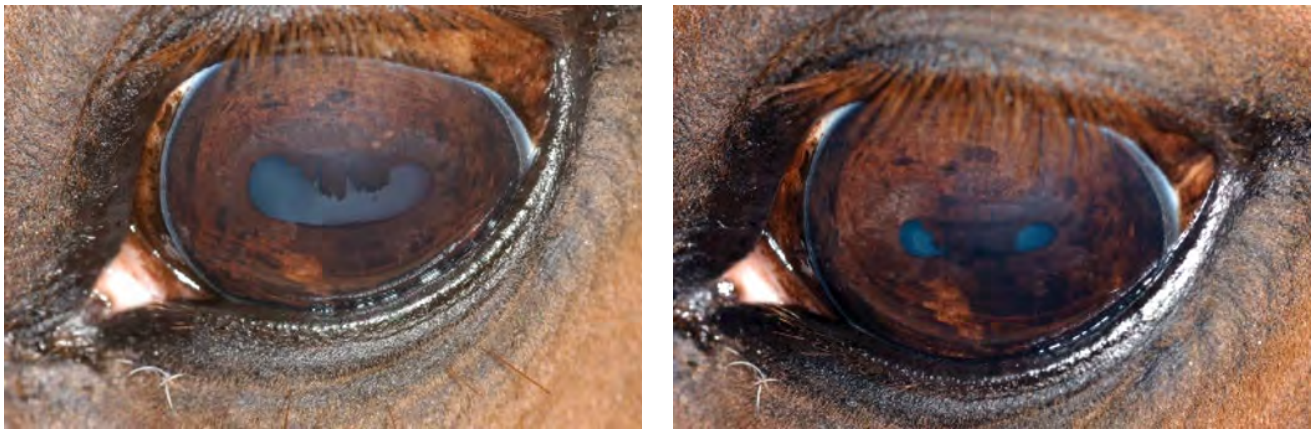
Effect of pupil size

The exact magnitude of the loss of image quality resulting from focus errors, aberrations, and diffraction depends on the size of the pupil. A small pupil not only reduces spherical aberration but also increases the depth of field. However, when the pupil diameter becomes exceedingly small, the impact of diffraction increases, and the image projected onto the retina is degraded. These competing factors balance out for humans when the pupil is about 3 mm in diameter, or about the size it tends to achieve under normal bright-light conditions [3]. When the pupil is this size, the quality of the retinal image is quite high and deviates only slightly from an ideal system limited by diffraction [3].

Optical consequences of pupil shape

At mid-dilation, the equine pupil is horizontally elliptical. Because the pupil is located in front of the nodal point of the optical system, the field of view will be greatest in the horizontal plane, a situation that is best suited for scanning the horizon [124]. The vertical field of view will be further limited by the presence of the granula iridica, located superiorly and inferiorly. In bright daylight, the superior granula can contact the inferior pupil edge, occluding the central region and creating two roughly spherical pupillary apertures at the lateral and medial extent (Figure 12.26).

Walls [24] reports that many felids will form two apertures at the superior and inferior limits of the pupil under bright-light conditions. The provision of two pupils located in front of the posterior nodal point of the eye has several optical consequences, including provision of a relatively larger visual field



(A) (B)

Figure 12.26 (A, B) In bright light, the equine pupil can constrict to the point at which two pupils are effectively created. This phenomenon may reduce spherical aberration and also serve as a range-finding device.

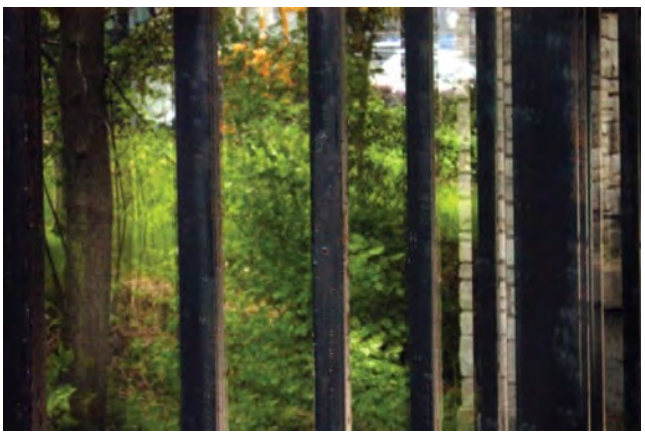


Figure 12.27 Simulated view through the multiple pupillary apertures. Only objects that reside in the plane of focus of the eye form a single image on the retina. Objects located in front and behind the plane of focus form two images on the retina. Some species have been reported to be able to use this Scheiner's disc-like phenomenon as a focusing indicator.

than would be achieved with a circular pupil of equivalent surface area [24]. By limiting the passage of rays to regions that are roughly equidistant from the axis of the lens, the presence of two pupillary apertures would also serve to diminish any spherical aberration that may be present in the optical system.

Additionally, the possession of multiple pupillary apertures creates a Scheiner's disc phenomenon [29, 125]. Scheiner's disc is an optometric device that has two pinpoint apertures separated by several millimeters; it is used to determine the near-point focus of the human eye. When both apertures are situated over the pupil of the human patient, only objects that reside in the plane of focus of the eye form a single image on the retina. Objects in front of or behind the plane of focus form two images on the retina (Figure 12.27). In the horse, the presence of two pupils in very bright light may decrease the light flux to the retina while preserving a shallow plane of focus (a single, small pupillary aperture would greatly increase the depth of field). In the chameleon, which has a well-developed fovea that can be used as a focusing indicator, it has been shown that the degree of accommodative effort is able to be integrated by the brain to provide a type of automatic range finder [126, 127]. Although the horse lacks a fovea and has limited accommodative ability, it is possible that the presence of two pupils in very bright light would allow the horse to better discriminate relative distances, a distinct advantage in determining how far away a predator may be.

Retinal factors affecting visual acuity

The size of each photoreceptor and the spacing between adjacent photoreceptors are two of the rate-limiting factors in determining how small of an object can be resolved. In a sense, this packing is analogous to the number of pixels on a computer screen or the number of brush strokes in a painting. Humans have the greatest density of photoreceptors in a roughly circular, densely packed fovea temporal to the optic disc. Horses have a relatively thin (1-mm-wide) visual streak located about 3 mm dorsal to the disc in or near the ventral aspect of the tapetal zone and extending approximately 22 mm in the nasal and temporal directions [16, 17, 50]. In the temporal arm of this visual streak, ganglion cell density increases slightly (area centralis rotunda), but an indistinct field of relatively high density also continues along the nasal arm to near the ora serrata (Figures 12.28 and 12.29). As in all species, there are many fewer ganglion cells in the periphery of the retina than in the center, greatly reducing the visual acuity of the peripheral visual field [50, 128, 129]. The temporal portion of the streak provides the greatest visual acuity and perhaps some color vision, because this region appears to have a three- to four-fold increased density of cones [130]. Mammals that live on the open plains (or steppes in the case of horses) generally have a visual streak pattern that conforms to the projection of the horizon at the intersection of the earth and sky, and this provides a particularly acute image of this part of the environment. Indeed, horses tend to keep the pupillary aperture parallel to the horizon whether the head is down or

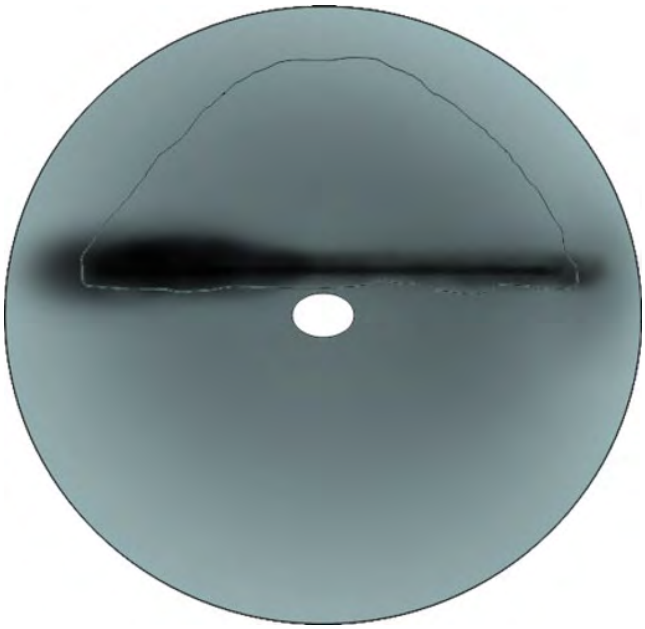


Figure 12.28 Schematic representation of the visual streak of the right eye of a horse. The greater the density of ganglion cells and photoreceptors, the darker the shading is in this image. The density of these cells is greatest immediately superior to the optic disc (**oval**), which facilitates scanning the horizon. There also is a somewhat greater density of these cells temporal to the disc, which facilitates greater visual acuity, binocular vision, and some color vision, because there are three to four times more cones in this area. (*Source*: Modified from Hebel, 1976 [17]. Reproduced with permission from Springer.)

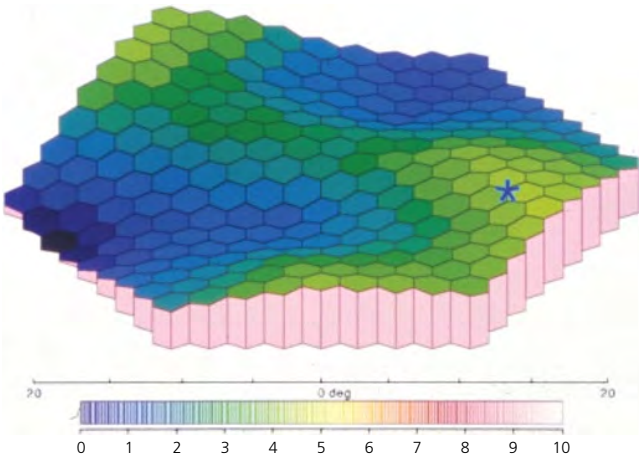


Figure 12.29 The visual streak of a horse as determined electrophysiologically with multifocal electroretinography. Green indicates relatively higher sensitivity, whereas blue indicates lower sensitivity. The optic disc is just to the left of the dark black region. A band of heightened retinal sensitivity corresponds to the location of the horizontally arranged visual streak. (*Source*: Gilger, 2011 [174]. Reproduced with permission from Elsevier.)

upright [75]. The tapetal location of the streak further enhances vision in dim light.

Unlike a computer screen or a painting, the images collected by the photoreceptors are then passed up to the brain via a series of neurons, and visual acuity becomes limited by the least densely packed element in this chain, which is typically the ganglion cells of the optic nerve. To make matters more complex, there are a number of ganglion cell types, each most responsive to a specific component of a visual stimulus, and each point on the retina is covered by at least one ganglion cell of each functional class [131]. This arrangement means that a single visual stimulus is reported in several ways to the higher visual centers [131]. The optic nerve of the horse is somewhat unique in that it also contains a substantial number of large-diameter axons that are involved in motion detection, depth perception, and sensitivity to dim light [49, 50]. Although the horse has the lowest ganglion [16, 17, 51, 129] and Müller [132] cell density of the domestic mammals (peak ganglion cell density ranging from 4000 to 6500/mm2), its very large eye means that its total number of ganglion cells (hence information-carrying capacity) is comparable to that found in humans. In this packing of ganglion cells, the tradeoff between high visual acuity and improved vision in dim light is made because optimizing visual acuity requires a 1:1 ratio between the numbers of photoreceptors and the numbers of ganglion cells, whereas optimizing light detection requires a greater number of photoreceptors to synaptically converge on a single ganglion cell. Although this convergence improves vision in dim light, it also reduces visual acuity, just as high-speed film produces a "grainy" image in daylight.

In the human fovea, the ratio of cones to ganglion cells is approximately 2:1, but because the ganglion cell output is divided into parallel on and off channels, the functional relationship is approximately 1:1 [131]. This close association, even in just a small area, results in an eye with quite high visual acuity. The exact peak ratios for horses have not been determined, but because of what is known about their relatively high visual acuity, it seems likely that there is at least a small region of retina in which the ratio is only a little greater than 1:1. In the human peripheral retina, the ratio of cones to ganglion cells increases to roughly 10 cones per ganglion cell; allowing for the same on/off channels, the functional ratio is 5 cones per ganglion cell [131]. Because horses have a lower peak cone density and perhaps fewer cones than humans, it is likely this ratio is substantially greater for horses and that rod photoreceptors rather than cones may be the operative elements. In cats, it has been estimated that in the peripheral retina, approximately 75,000 rod photoreceptors drive 5000 rod bipolar cells, which in turn drive 250 amacrine cells, which then converge on one ganglion cell [133]. A similar phenomenon occurs in humans, and although the density of the rods in the mid-peripheral retina is nearly as high as the density of cones in the fovea, the visual acuity of the peripheral retina is poor because of the convergence of so many rods onto a single ganglion cell [131]. The tradeoff is that in dim light, the peripheral retina is much better at detecting light than the foveal region.

In certain circumstances, it appears that the eye is able to get around the limits to ordinary resolution acuity (also called the **minimum resolvable acuity**) imposed by the diameter of the smallest photoreceptor [81]. In humans, the shortest distance

between the foveal cone photoreceptors is approximately 25 seconds of arc, and this forms the basis for the ordinary visual acuity limit of about 30 seconds of arc [81]. If the task is switched from determining in which direction a letter (e.g., an E) is pointing to determining whether an object is present or absent (minimum visible) or identifying the relative relationship of two objects to each other (minimum discriminable), the eye can resolve differences as little as 1 second of arc and 3 seconds of arc, respectively [81]. A classic method of determining the minimum visible is to measure the width of a telephone wire that can be seen against a uniformly blue sky. This task is actually a difference-in-brightness discrimination and not a true spatial discrimination [81], because under these conditions an individual photoreceptor is being struck by many photons, and all that is being determined is how many photons the wire needs to block before a detectable change in brightness occurs in an individual photoreceptor. Hence the sensitivity of this discrimination is much less than the diameter of one photoreceptor.

Minimum discriminable acuity does require making a spatial discrimination. Because it is approximately ten times better than ordinary acuity, it is sometimes called **hyperacuity**, and it appears to have a fundamentally different physiologic basis rooted in the neural processing of images at the level of the brain or retinal ganglion cells [81, 134–137]. There are several types of hyperacuity, and they are usually evaluated by tasks that require determining the relative relationship of two or more objects to each other. For example, the most common task is the so-called alignment or vernier acuity in which the subject is asked to determine whether the two line segments in "--" are offset from each other. In other circumstances, the subject may be asked to determine the relationship of a line segment to the point of a chevron (>-) or whether a line is perfectly vertical. Stereoacuity is also a form of hyperacuity, as is the ability to make color discriminations, because in the latter the just-noticeable difference in wavelength (color) is far less than the range of wavelengths to which any of the three cone types responds [81]. Hyperacuity-like phenomena are not unique to the eye but appear to be used by many senses, including echolocation in bats, the jamming avoidance response of electric fish, and differential pitch sensitivity experiments in humans to enhance detection of various forms of energy in the environment [138]. Although the magnitude of the minimum detectable difference in cats varies from that seen in humans, cats have vernier acuity that is approximately six times better than their ordinary grating visual acuity, so hyperacuity is not limited to humans [139].

Perception of form

Several studies evaluating equine form perception have been conducted [46, 140–144]. In general, these are behavioral studies in which a food reinforcer is used to "chain" a series of behaviors together (e.g., walk into the testing area, look at a visual target, walk up to the target, touch the target, walk back to the stocks for the next trial) that teaches the horse to work independently of the evaluator (Figure 12.30) [41, 140–144]. This minimizes the potential for inadvertent cueing by the examiner or other observers, as in the case of "Clever Hans" who was carefully reading the body language of human observers instead of actually doing arithmetic and other calculations [145]. Although time consuming to perform, these types of studies evaluate not only the eye but also the shortcuts the brain takes to use this information in the real world, and they provide hints as to what features a horse considers important.

Behavioral studies have demonstrated that horses can understand the general concept of size and learn to select the largest object regardless of its shape [142]. It was also found that horses can visually learn to prefer one object over another even though they differ only in color (e.g., a blue toolbox over a red one) or shape (an orange ball over an orange tube). Furthermore, these learned visual discriminations can be remembered for many years even though they are not reinforced in the intervening time period [144]. Horses have been demonstrated to be capable of visually transferring information between three-dimensional (3D) objects and two-dimensional (2D) photos [143]. For example, once the horse is trained to select a specific 3D toy over another 3D toy, this behavior can be readily transferred to 2D photographs of the toys. Horses have also been shown to categorize visual stimuli into specific classes, such as open center versus solid center, by being trained to select a triangle or square with an open center over a triangle, circle, square, or keyhole with a solid center [141]. Behavioral studies have dispelled the common myth that what horses see with one eye is "novel" and possibly frightening if seen with the other eye [140]. In these studies, it was shown that horses can recognize with one eye an object that was previously learned about only with the other eye [140].

Orientation

The orientation of the "broad strokes" of an object provides considerable information very rapidly at even very low levels of visual acuity (Figure 12.31) [146]. In fact, much of the information we act on is at this low level of acuity. Work ultimately leading to a Noble Prize by David Hubel and Torsten Wiesel in 1981 demonstrated that at a fundamental level, the brain is geared towards identifying the orientation of lines and edges of an object that define it [147]. The neurologic wiring associated with this phenomenon is complex, but at its basis are single neurons that only respond to lines with specific orientations and surrounding cells that respond in an on/off fashion so as to further highlight this orientation or the edges of an object [147, 148].

Color vision

The perception of color is another fundamental component of vision that allows for objects to be seen as separate and distinct from their surroundings. The basis for this distinction comes not from the intensity of the light but instead from the differential retinal response to differing wavelengths of light



(A)



(B)



(C)



(D)



(E)

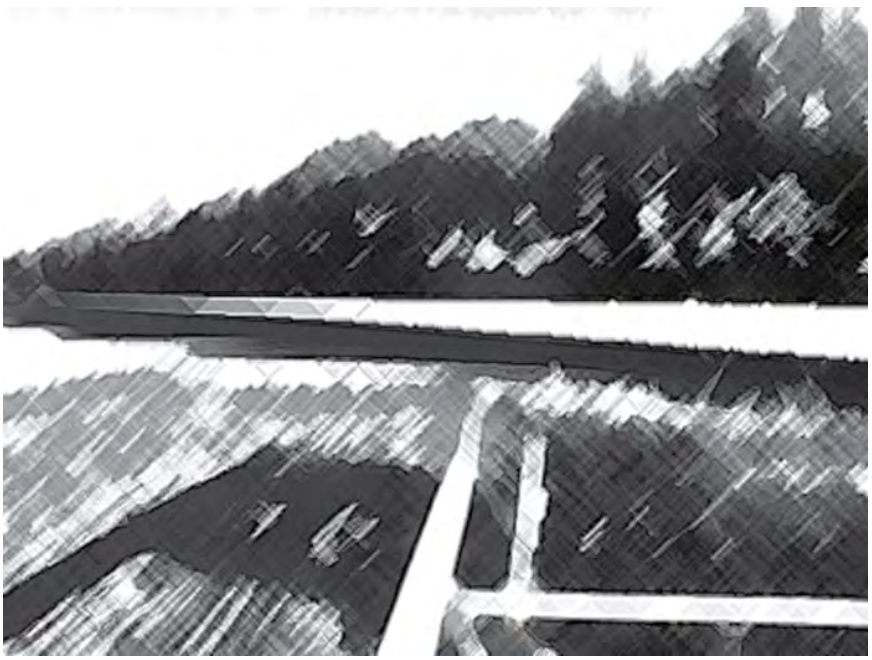


(F)

Figure 12.30 Chaining behaviors for visual performance testing to avoid inadvertent cueing. **(A)** and **(B)** The horse in the station awaiting a trial. **(C)** If the horse selects the correct stimulus, it receives a food reinforcer. **(D)** It then walks away from the apparatus, **(E)** enters the station, and **(F)** stands quietly while waiting for the next trial. Typically the correct stimulus must be chosen at least 80% of the time to be considered a visible stimulus. (*Source*: Hanggi et al., 2007 [166]. Reproduced with permission from American Psychological Association.)



(A)



(B)

Figure 12.31 Discrimination on the basis of orientation. (A) A racetrack. (B) Simulation of the principal orientation of the visual elements in the image. Even though orientation provides only black-and-white clues with very low visual acuity, it is a very rapid method of identifying critical features in an image and using that information to direct gross behaviors.

striking the retina. The ability to detect color has gone through numerous permutations during evolution, and this informs our understanding of the differences between human and equine color perception. Approximately 350–400 million years ago, vertebrates developed five major families of visual pigments (one rod and four distinct cone classes), enabling color vision that was based on four cone pigments (tetrachromatic color vision) [149–151]. One of these cones was also sensitive to ultraviolet light, which is retained by many modern-day birds and used for foraging, mate selection, and perceiving color in a region of the electromagnetic spectrum humans cannot discern [8, 149–151]. Over time, as mammals evolved to exploit a more

nocturnal niche, two of these four cones (including the UV cone) were lost, resulting in color vision that was based on only two cone types (dichromatic color vision) [149–151]. Modern horses and the substantial majority of other mammals alive today have only these two cone pigments. As primates evolved approximately 35 million years ago, the long wavelength-sensitive cone pigment underwent a favorable mutation that allowed the animal to distinguish yellow-orange fruits from green foliage, resulting in trichromatic color vision in a few primates and humans [10, 100, 151–155]. Even within a species, numerous mutations have continued to occur in the genes coding for these pigments such that there are subtle differences in the peak sensitivity of the two cone pigments from individual to individual. The relative ratios of the three cone types may vary by as much as 30-fold among humans with normal color vision [152, 156–159]. This considerable diversity suggests that even within the same species, there may be substantial differences in color perception among individuals with normal vision [152, 156–159].

The basis for equine or human color vision is how different wavelengths of light interact with each of the distinct cone pigments [3]. Each cone pigment has a unique sensitivity to different wavelengths of light, with a peak sensitivity to one wavelength and diminished sensitivity to adjacent wavelengths (Figure 12.32). Once receiving input from two or more types of cones, the brain compares the relative stimulation of the different cone types and uses this to ascribe a certain color to an object even though the wavelengths themselves have no inherent color. Therefore color vision does not occur at the level of the eye, but instead at the level of the brain. Although there is considerable overlap in sensitivity to different wavelengths of light, each cone has a peak sensitivity which is used to categorize the cone as to type. In humans, the three cones have peak sensitivities near 430 nm (called the **blue wavelength-sensitive**, **short**, or **S cone**), 530 nm (called the **green wavelength-sensitive**, **middle**, or **M cone**), and 560 nm (**red wavelength-sensitive**, **long**, or **L cone**) [149, 160]. In horses, the peak cone sensitivities are at approximately 428–429 nm (blue or short cone) and 539–545 nm (middle to long wavelength-sensitive cone) which is intermediate between the human red and green cones [152, 154, 159].

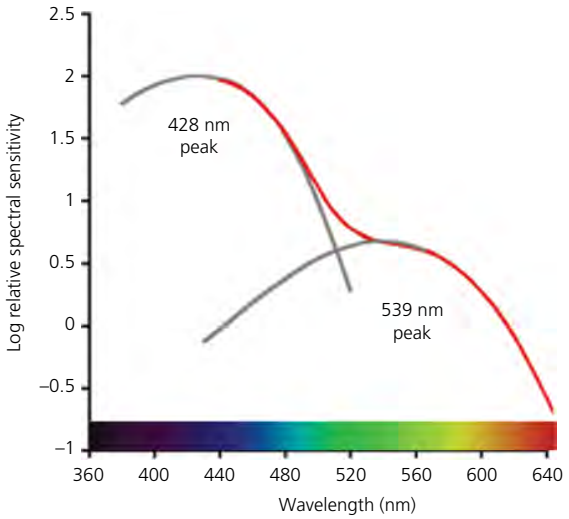


Figure 12.32 Sensitivity curves of the two principal cones of the horse. Each cone pigment has a uniquely varying sensitivity to different wavelengths of light. The relative stimulation of each of the cones is used by the brain to ascribe a certain color to an object. (*Source*: Modified from Carroll et al. 2001 [7]. Reproduced with permission from Association for Research in Vision and Ophthalmology.)

The number and location of cones within the retina is also important. In both humans and horses, the overall ratio of rod to cone photoreceptors is approximately 20 to 118 [161], but the distribution of these cells is quite different between the two species. In humans, the blue wavelength-sensitive cones comprise about 7% of all cones and are roughly uniformly distributed over the retina [149, 151], whereas the green wavelength-sensitive and red wavelength-sensitive cones (at least in monkeys) are concentrated primarily in the fovea and the immediately adjacent central retina [162]. In humans, the cones are densely packed in the central retina (fovea) and rapidly fall off to low numbers just 1–2 mm away from the fovea [161]. The distribution of cones is believed to be more uniform across the retina in horses, with perhaps an increase in the temporal region of the visual streak [17, 129]. Horses have a significant population of patchily distributed blue cones, which comprise approximately 10% of all cones in the visual streak and 20–25% in the mid-peripheral and peripheral retina, and a larger population of a more regularly arranged second type of cone, with its peak concentration in the region of the visual streak and declining toward the peripheral retina [130, 163]. Cone densities in the horse range from around 5000/mm2 in the peripheral retina to 15,000–20,000/mm2 in the visual streak, whereas in humans, peak cone density averages almost 200,000 cones/mm2 [161]. This density suggests that in order to differentiate an object on the basis of color, the stimulus may need to be larger for horses than for humans, especially if it is in the animal's peripheral visual field.

Humans with normal vision see four basic unique hues—blue, green, yellow, and red—and about 100 intermediate colors, which can be thought of as varying blends of pairs of the four unique colors—for example, yellow-green, reddish-yellow (orange), reddish-blue (violet), and so forth (Figures 12.6, 12.32, and 12.33) [152, 164]. Similarly, if different combinations of wavelengths of light produce the same pattern of activity among the cone subtypes, the two different wavelengths will be perceived to be the same (so-called color-blindness) even though the composition of the light is quite different. However, color-blindness does not mean that an individual person or animal is blind and unable to detect photons with these wavelengths. Instead, it only means that the individual has difficulty using this information to differentiate between two colors solely on the basis of their hue. Various degrees of congenital color-blindness such as red-green color deficiency (daltonism) can affect up to 8% of white men [3, 149].

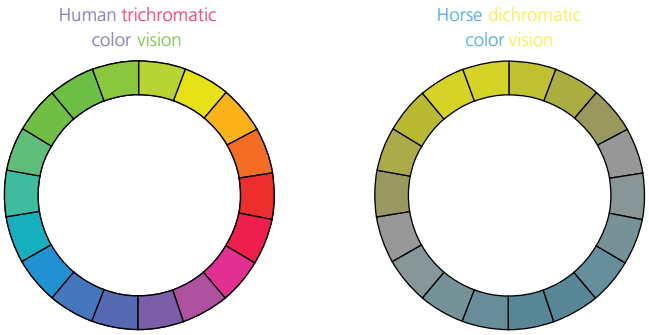


Figure 12.33 Difference between dichromatic color vision of the horse and normal human color vision. Color wheel (**left**) representing the spectrum of colors perceived by the trichromatic human visual system. Reducing the number of types of cone from three to two results in dichromatic color vision (**right**) and an enormous reduction in the number of different colors seen. (*Source*: Carroll et al. 2001 [7]. Reproduced with permission from Association for Research in Vision and Ophthalmology.)

All studies of equine color vision to date suggest that it is very likely horses perceive colors differently than humans, because they have only two types of cones, their cone types have different peak sensitivities than those in humans, and they have many fewer cones in the central retina than do humans [10, 21, 100, 152–155, 165, 166]. The most dramatic impact of having two cone types instead of three is that dichromatic horses (and humans with red-green color deficiencies) have only two unique hues, believed to be something similar to blue and yellow. When both cones are approximately equally stimulated (as white light would do for us) the result is a so-called neutral point at about 480 nm (blue-green for humans with normal color vision). In theory, light of this wavelength should be perceived as colorless and a variation of white/gray/black depending on the intensity of the illumination [152, 167]. As the illuminating wavelength is shifted to either side of the neutral point, the two cones again become differentially stimulated, and color may again form a basis for making distinctions between objects. It is quite possible that because horses have many fewer cones in the central retina than do humans, their perception of color may not be as vivid as a human's and colors may appear as washed-out pastels or sepia [10, 152]. Additionally, because cones in horses, and even humans, are primarily located in the central retina, color vision is largely restricted to the central retina in horses (the fovea in humans), and the ability of the peripheral retina to detect color is substantially reduced [3, 10, 21, 100, 152–155, 165, 166].

Behavioral tests of equine color vision have been conducted to verify that the cone pigments identified histologically and electrophysiologically are actually useful to the horse [21, 100, 144, 153–155, 165–167]. Such studies are confounded by the need to ensure that the brightness of the test objects is not also a cue, and the various filters used to create different colors (e.g., different shades of green) do not actually allow other color cues to pass through as well (e.g., yellow) [73, 165, 166]. Although these behavioral studies have somewhat different conclusions, most of them show that horses can differentiate blue (470–482 nm) and yellow (579–583 nm) from gray (Figures 12.33 and 12.34). Green (532–545 nm) and red (609–615 nm) are less accurately differentiated from gray in many but not all studies, suggesting that in the aggregate, horses behaviorally have a form of red-green color-blindness [101, 153–155, 165, 166, 168, 169]. Electrophysiologic studies would suggest that for horses, orange and light blue appear similar (i.e., neither may have much if any color and appear to be similar to gray). This process is similar to color vision in human dichromats who are red-green color-blind and cannot differentiate between red and green, but it is shifted for horses such that they are orange-blue color-blind (see Figures 12.33 and 12.34). Despite these "deficiencies," the absolute threshold for discriminating between objects on the basis of color is comparable between horses and humans [21]. In this study, one horse and most humans were able to discriminate between colors at a light intensity level that approximated that of moonlight (0.02 cd/m2) [21].

The real question, however, is how horses perceive colors, especially those near the neutral point. This is important because much of the food a horse consumes is in the green spectrum, and yet this is also near the neutral point and would seem to be evolutionarily nonadaptive. Although we cannot know for sure, Figure 12.34 offers a suggestion as to how specific colors may appear to a horse. Recent behavioral studies into how horses perceive the color spectrum suggest that horses "think" of colors in relation to each other (e.g., this one is more green or less blue than that one) and not on the basis of an absolute scale [167]. Work with human dichromats, who have a similar neutral point, recently found that they use the term **green** to describe all colors at the neutral point, rather than describing the neutral point as being shades of gray, as would be predicted solely on the basis of photopigment sensitivity profiles [170]. This is interesting because humans readily see gray/white as qualitatively different from colors such as red and green, and presumably so would a horse [170]. Although requiring confirmation via other methods, behavioral tests also suggest that the neutral point does not divide the colors horses perceive into two separate categories (a short-wavelength blue and a longer-wavelength green-yellow), but instead, like human dichromats, they perceive the neutral point as a "color" (e.g., a type of green) just like any other they can distinguish (Figure 12.35) [167]. It has been suggested that this phenomenon is the result of color information being carried to the brain in two channels: one that is the more traditionally understood and based on the relative ratios of the stimulation of each cone a specific wavelength affords, and a second channel that codes color in a nonlinear way with high gain and rapid saturation [167]. This second channel may provide some color-based information at the neutral point that allows the brain to put the wavelengths near the neutral point into a general category such as "green."

Although the added information obtained by differentiating between photons on the basis of their wavelengths can be very useful in certain circumstances, black and white images alone

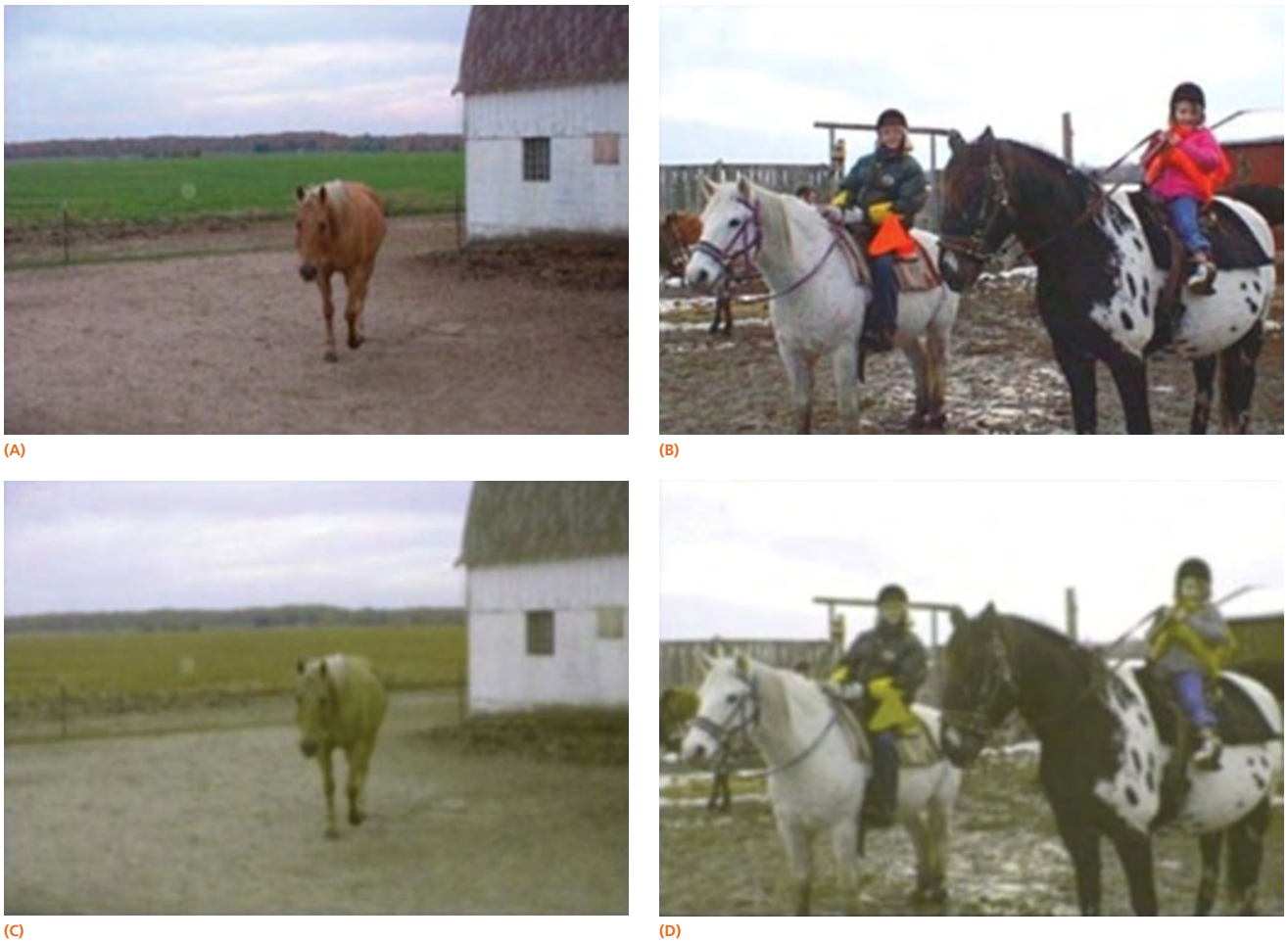


Figure 12.34 Real-life implications of dichromatic color vision for the horse. (A) and (B) Two unaltered digital images. (C) and (D) Digitally altered forms of the same pictures simulate the dichromatic color vision of the horse. The images were also adjusted to take into account the reduced visual acuity of the horse to more closely approximate the horse's visual experience. (*Source*: Carroll et al., 2001 [7]. Reproduced with permission from Association for Research in Vision and Ophthalmology.)



Figure 12.35 Two theories as to how the neutral point may be perceived by a horse. (A) As a divided chromatic space, with the white/gray-appearing neutral point separating the two ends of the spectrum. (B) As a continuous chromatic space. Electrophysiologic and biochemical studies of the human and equine cones suggest that the neutral point would suggest **(A)** is how the neutral point should be perceived. Behavioral studies of both horses and humans with comparable color vision abnormalities, however, suggest that the brain alters this input, and the neutral point is perceived as if it were a shade of green, as proposed in theory **(B)**. (*Source*: Adapted from Roth et al., 2007 [176].)

can capture most of the visual content in the environment. Even in species with highly developed color vision, distinguishing form, shape, depth, and movement is far more important than distinguishing color [3–5, 11]. Additionally, as vibrant and real as color vision may appear, it is not only the result of the physical interaction of photons with a set of cone photopigments, but also a cognitive and psychological sensory experience in the central nervous system that does not even begin to accurately represent physical reality. For example, very different stimuli such as a combination of green (544 nm) and red (679 nm) lights can appear exactly the same as a pure yellow light (589 nm), even though the actual wavelengths of the photons composing these lights are completely different [3, 11]. Similarly, changes in wavelength of only a few nanometers in the green portion of the spectrum result in humans perceiving quite different colors, but similar changes in the red region (680 nm onward) do not (see Figure 12.6). Again, photons in the yellow portion of the spectrum are more easily detected than photons in the blue portion, making yellow lights appear brighter than blue ones, even though the same number of photons are striking the retina. Finally, the exact color a person experiences depends not only on the object itself but also on the illuminating light, the spectral properties of the objects immediately surrounding it, and the fact that the brain attempts to maintain the perception of the constancy of colors even though dramatic changes may be

occurring [3, 11]. In aggregate, these studies suggest that in humans there is no simple correspondence between the spectral properties and physical stimulus of an object and the color humans perceive, and it is highly probable that a similar phenomenon occurs in horses.

When color vision is considered, it is tempting, especially from an anthropocentric point of view, to conclude that compared to humans, most mammals have inferior visual abilities, and only humans and some primates have achieved the pinnacle of vision by possessing the ability to detect a greater range of colors. However, this does not take into account the fact that mammals with only dichromatic color vision have been extremely successful on an evolutionary basis or that up to 8% of Caucasian men have congenital red-green color vision abnormalities [3, 149] An alternative perspective is that humans have acquired the ability to see more colors at the expense of the light sensitivity of their retinae—a "choice" the majority of other mammals would not make [166]. Therefore, instead of developing color vision so as to better identify a ripe, yellow fruit hanging in a green tree, the equine visual system, like that of most mammals, has evolved to function under a greater range of lighting conditions and to afford a more panoramic view so as to avoid predators. Because the horse's food is essentially immobile and not particularly challenging to identify or capture, being able to perceive a broader palette of hues does not offer as much advantage to a horse, especially if it comes with the tradeoff of degrading its visual capabilities for detecting predators. Dichromatic color vision may also present an adaptive advantage for horses. Humans with dichromatic color vision can "break the camouflage" of certain colored objects that humans with normal color vision cannot [172], and it is debatable whether humans with color vision abnormalities actually have a lower light perception threshold than those with normal color vision [171, 173]. Therefore, because many predators have also evolved coat colors that closely match the background in terms of color and in some cases visual texture, color may be a relatively poor way of breaking the camouflage of a predator; and dichromatic color vision, instead of being detrimental, may actually confer a survival advantage to the horse.

Summary

The act of seeing is a complex process that involves not only the eye focusing and detecting light, which may vary in intensity by as much as 40 billion-fold, but also the brain perceiving the resulting image. Because the horse's food is essentially immobile and not particularly challenging to identify or capture, much of the horse's visual capabilities appear to be defensive and devoted to ensuring the animal's survival by more easily identifying potential threats (as in the case of a predator) rather than capturing prey.

Horses have several adaptations to both dim light (a large cornea and pupil, and a reflective fibrous tapetum lucidum) and bright light (yellow-filtering pigments in the lens and the corpora nigra, which act as "internal visors," and a significant population of cones). They maintain the image on the retina during motion in much the same way as humans do, and, like humans, they detect moving objects more easily than stationary ones. Their visual field is enormous (up to 350 degrees) and provides nearly a complete sphere of vision, with only a few small blind spots. The degree of binocular overlap (55–65 degrees) rivals or exceeds that of dogs, and horses use both monocular and binocular clues to estimate depth, although the binocular depth threshold is five times better than for one eye. From 2 m away, horses can detect a 9-cm difference in depth, which approximates the ability of a cat. Accommodation is limited (less than 2 D), but only small changes by the lens are needed to maintain a focused image on the retina. Although some individuals are greater than or equal to 3 D myopic or hyperopic, the average resting refraction is near emmetropia (normal). Horses possess a visual streak located in the tapetal zone, oriented so it conforms to the projection of the horizon on the retina, and an optic nerve that contains approximately the same number of fibers as a human's. At 20/30 to 20/60, the horse's visual acuity is among the best of the domestic mammals, including predators, and is better than that of many humans. Horses have dichromatic color vision with two cone types: a short wavelength-sensitive (blue) cone with a peak sensitivity of approximately 428 nm, and a second cone with a peak sensitivity around 540 nm, which is between the human red and green cones. It is probable that this results in colors appearing as washed-out pastels or sepia, and horses have difficulty in differentiating orange and blue, much like some color-blind men have difficulty differentiating between red and green. Because many predators have also evolved coats that closely match the background in terms of color, and, in some cases, visual texture, color may be a relatively poor way for the horse to "break the camouflage" of a predator. Instead, objects can be differentiated from their surroundings if they are suitably different in any one of five different aspects: luminance ("brightness"), motion, texture, binocular disparity (depth), or color.

The current inability to clinically recognize anything but the most massive visual impediments in horses is not because the horse is unusually resistant to disorders that impair vision in other species, but because of the crudeness of the tools the clinician currently has available to determine how well a particular horse can see.

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CHAPTER 13

Inherited ocular disorders

Lynne Sheila Sandmeyer and Rebecca Bellone

Introduction

Hereditary ocular diseases and those with ocular manifestations have been described in several breeds of horses (Table 13.1); however, not many have been studied in as much detail as similar disorders in other species. The genomes of many species, including the horse, have now been sequenced (see http://www.ncbi.nlm.nih.gov/Genomes/index.html for updated information). In 2009, the equine genome sequence was reported [1], and this has facilitated the investigation of equine genetic traits with both simple modes of inheritance and polygenetic traits (those caused by more than one gene), but we still have much to learn. The purpose of this chapter is to review some basic concepts of genetics and describe those ocular conditions for which a genetic basis is known or suspected in the horse.

Basic concepts and terminology

DNA and genes

Deoxyribonucleic acid (DNA) is the biological material that is inherited from generation to generation. DNA is associated with proteins and tightly packaged to form chromosomes, which reside in the nucleus of the cell. Structurally, DNA is a double helix that consists of two complementary parallel chains joined by hydrogen bonds. The building blocks of each of these chains are nucleotides comprised of a sugar molecule (deoxyribose), a phosphate group, and one of four nitrogenous bases: adenine (A), thymine (T), guanine (G), and cytosine (C). Each nucleotide is linked to the next through a bond between the sugar of the first nucleotide and the phosphate of the next. The double helix is formed by pairing of the nucleotides on one strand to the other strand through hydrogen bonds, this is known as a base pair (bp). Adenines always base pair with thymines and guanine always pairs with cytosine (thus termed complementary base pairs, as A complements T, C complements G, and vice versa). The genetic code of an animal lies in the order of the bases in the DNA strand.

The genome of the horse is made up of approximately 2.4–2.7 billion base pairs. It is estimated that the horse genome contains about 20,000 genes [1]. A gene is described as a region of DNA that codes for a functional unit in the cell (most often a protein). The gene itself is made up of both exons and introns. **Exons** are regions of DNA with information to code for protein. Exons are separated by sequences of bases that do not code for protein and thus are considered to be intervening sequences and have been called **introns**. Roughly 2% of the horse genome codes for proteins (exons). The function of the rest is not fully elucidated but thought to be regulatory, controlling for gene expression. When genes are expressed, the DNA is first transcribed in the nucleus into **ribonucleic acid** (RNA). This process essentially uses one strand of the DNA as a template and makes a complementary RNA copy of that template. RNA is made of the same building blocks as DNA; however, the nitrogenous base uracil replaces thymine and the sugar molecule is ribose and not deoxyribose. In addition, RNA is single stranded (except for secondary structure formation). The resulting RNA that is produced from transcription of the DNA template of a gene will have the introns removed and exons brought together by a process called splicing; this results in the mRNA that is an uninterrupted code for protein production. mRNA is exported out of the nucleus into the cytoplasm, where it is then translated by ribosomes (protein-manufacturing machinery) into proteins whose building blocks are amino acids. Which genes are expressed, when they are expressed, and how much they are expressed are controlled by highly regulated processes that involve many proteins and signaling molecules, and their association with DNA. For example, the beginning of a gene typically has a stretch of sequence that does not code for proteins but does control the expression of the gene. These regions have been defined as **promoters**, as they promote gene expression; in other words, they promote transcription.

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Table 13.1 Inherited ocular disorders and manifestations. Presented are the breeds affected, mode of inheritance, genes and mutations associated, and available genetic tests.

Disorder	Breed	Mode of inheritance for disorder	Clinical associations	Gene mutation	Genetic markers	Genetic test available
CSNB	Appaloosa, Knabstrupper, American Miniature	Autosomal recessive	Leopard complex spotting (*LP*) coat pattern	*TRPM1* LTR insertion in intron 1 (ECA1g.108, 297, 929_108, 297, 930 ins1378)		Yes—same test as *LP*
MCOA	Rocky Mountain, Kentucky Mountain, Mountain Pleasure, Icelandic, Shetland Pony, American Miniature, Belgian, Morgan, Comtois	Incomplete dominant	Silver coat dilution	*PMEL* missense mutation in exon 11 (p.Arg625Cys)		Yes—same test as Silver
ERU	Appaloosa	Complex	Leopard complex spotting (*LP*) coat pattern	Not identified	(1) SNP in intron 11 of *TRPM1* (ECA1g. 108249293 C>T) (2) MHC I microsatellite (*427–260*) (3) MHC II microsatellite (*eqMHC1*)	(1) Yes—*LP* test (2) Not available (3) Not available
ERU	German Warmblood	Complex	Not identified	Not identified	(1) MHC I haplotype ELA-A9 (2) SNP (ECA20g. 49,349,056G>A) close to IL-17A and IL-17F)	Not available
Limbal SCC	Haflinger	Suspect autosomal recessive	Not identified	Not identified	Not identified	Not available
Corneal dystrophy	Friesian	Not determined	Not identified	Not identified	Not identified	Not available
Aniridia	Belgian, Quarter horse	Autosomal dominant	Not identified	Not identified	Not identified	Not available
Aniridia	Welsh Thoroughbred, Swedish Warmblood, Tennessee Walking horse	Not determined	Not identified	Not identified	Not identified	Not available
Cataract	Morgan	Autosomal dominant	Not identified	Not identified	Not identified	Not available
Cataract	Quarter horse, Arabian, Thoroughbred, Exmoor pony	Not determined	Not identified	Not identified	Not identified	Not available
HERDA	Quarter horse	Autosomal recessive	Not identified	*PPIB* missense mutation (p.Gly39Arg)		Yes
HYPP	Quarter horse	Autosomal semidominant	Heavy Musculature	*SCN4A* missense mutation (Phe > Leu)		Yes
JEB	Belgian draft, Italian draft, Trait Breton, Trait Comtois	Autosomal recessive	Not identified	*LAMC2* frameshift mutation (c.1368_1369insC)		Yes
JEB	American Saddlebred	Autosomal recessive		*LAMA3* deletion of exons 24–27 (ECA8g.3724_10312del6589)		Yes
LWFS	American Paint	Autosomal recessive		*EDNBR* dinucleotide missense mutation (p.Ile118Lys)		Yes
SCID	Arabian	Autosomal recessive		*PRKDC* frameshift mutation (p.Ser3155Asn*4)		Yes

Promoters contain sequence information that allows for the binding of proteins that respond to changes in stimuli to increase or decrease expression.

The 2.4 billion base pairs of the horse genome are divided up among 32 chromosomes. A horse has two copies of every chromosome, inheriting one copy from each of its parents. Chromosomes that do not determine the sex of the horse are called autosomes and each autosomal pair (maternal and paternal) is the same length and carries the same genes (at the same position) and is thus said to be homologous. Autosomes are numbered according to size, with the longest chromosome being horse chromosome 1. Genes have defined locations on the chromosome termed loci (loci plural or locus singular). Every animal of the same species has the same gene at the same locus

on the same chromosome (unless of course there is a mutational event causing an insertion or deletion of a section of DNA). However, these genes can differ in the exact order of bases, and therefore genes can come in alternative forms, or alleles. These alternative forms are the variations that exist in populations.

One pair of chromosomes is known as the sex chromosomes as they determine the sex of the organism (XX for females and XY for male mammals), and these do not carry all of the same genes or have the same morphology. In females, one X chromosome is inactivated in each cell and is seen as the barr body. The process by which this occurs is called **random X chromosome inactivation** and happens during embryonic development. Once one X chromosome is inactivated in a cell, all daughter cells resulting from that cell will have the same X chromosome inactivated. Because this process occurs during embryonic development, the result is that patches of tissues (derived from the same parental cell) will have the same X chromosome inactivated.

Meiosis and linkage disequilibrium

Meiosis is the type of cell division that occurs in the ovaries and testes to produce gametes. During meiosis the single cell replicates its DNA, then divides twice to produce four cells, each with half the amount of DNA as the original cell (haploid or half the number of chromosomes). The new cells have one copy of all the chromosomes from the original cell. During the formation of gametes, crossing over (or the exchange) of genetic material from homologous chromosomes occurs such that the original paternal chromosome may get a section of homologous chromosome that originally was inherited maternally, and vice versa. This is one level that allows for genetic diversity, as alleles (or alternative forms of genes) can get shuffled, allowing for new combinations along the chromosome (Figure 13.1).

When genes are on separate chromosomes, there is random segregation of these chromosome pairs into gametes. While each gamete will receive only one copy of each chromosome, some of these will be paternal and some maternal, and this process is random in that one chromosome segregation is independent of the next. However, when two genes are close together on the same chromosome, they are more likely to be inherited together during meiosis, and the closer they are, the less likely there will be a crossing over event occurring between them. Two such genes are described as being linked. When two alleles at different loci are inherited together more frequently than they would be by chance (random assortment), those two alleles are considered to be in linkage disequilibrium (LD) [2]. Genes on the sex chromosomes are said to be sex-linked. The X chromosome is always much larger than the Y chromosome, so most of the sex-linked genes are located on the X chromosome.

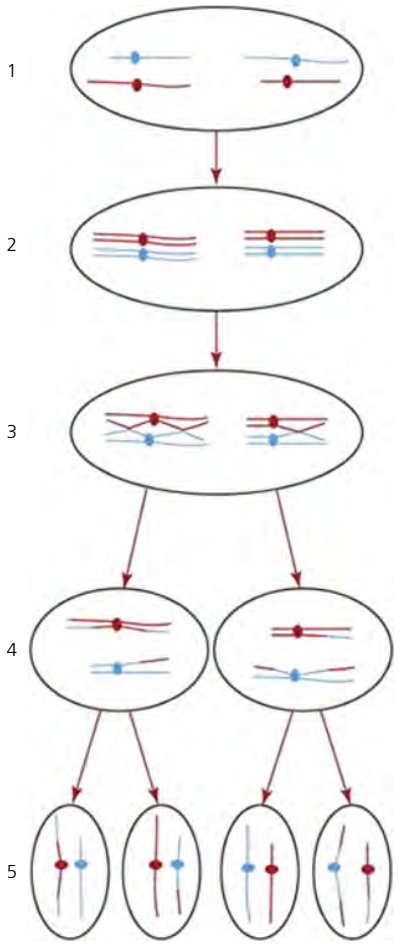


Figure 13.1 In this diagram of meiosis, the cell has two pairs of chromosomes (for simplicity). Maternally derived chromosomes are red and paternally derived ones are blue. 1, Cell with a diploid (2n) number of chromosomes (n); here the diploid number would be 4. Each chromosome has one chromatid. 2, During S phase of the cell cycle, DNA from each chromatid is replicated (so that now each of the pair of chromosomes has a sister chromatid). During meiosis, maternally and paternally derived versions of each chromosome will pair together. 3, Crossover between one chromatid of each pair of chromosomes is occurring and this allows for exchange of genetic information between maternally and paternally derived chromatids. In this figure one chromosome pair represents recombination events and the other represents only one. 4, The cell divides (meiosis I—reductional division) to produce two cells, each containing one copy of each chromosome, with each copy having two sister chromatids (1n). Note exchanged chromosomal material between maternally and paternally derived chromosomes. 5, Meiosis II, the final division to produce gametes. Each gamete has one copy of each chromosome, and each chromosome has one chromatid. Note recombination of material within chromosomes in comparison with paternally and maternally derived chromosomes in *1*. (*Source*: Gilger, 2011 [203]. Reproduced with permission from Elsevier.)

Genetic variation

Sometimes when a cell replicates the DNA, a mistake in copying the order of nucleotides is made. When the mistake does not get repaired, the new strand of DNA will have a change in the sequence of bases in the DNA molecule and this mistake is termed a **mutation** (also called a **polymorphism** or change in form). If a single base is changed, it is termed a single nucleotide polymorphism (SNP). Mutation is the main source of variation. If a mutation occurs in the sequence of bases that code for

protein, the resulting protein may also have a mistake that will get passed on in each new daughter cell. The mistake in the protein can allow for the protein to be more active (gain of function) or diminish or abolish function (loss of function). If a loss-of-function mutation occurs in a vital gene for survival, then this is said to be a lethal mutation. Mutations can also occur in introns or other regulatory regions that may affect gene expression and not coding sequence. If the mutation has occurred in a gamete, then the gene can be passed on to the next generation and this process results in new alleles. Within a population, there can be a number of alleles for a single gene; however, because there are only two copies of each autosomal chromosome, an individual animal can only have two alleles for a single gene. When there are two different alleles present, the individual is said to be **heterozygous** for that allele. If the alleles are the same, then the individual is said to be **homozygous** for the allele. The genetic makeup or which alleles are inherited for a given locus is termed the **genotype**.

Phenotype and expression

Phenotype is defined as the observable characteristic of a trait, such as morphology (tall versus short), pigmentation (black versus chestnut), and status of an eye disease (affected versus unaffected). However, it is not just defined by what can be seen; it also includes biochemical and physiologic properties. Phenotype is the product of the genotype and environmental influences. **Expressivity** is the extent to which a genotype exhibits its phenotypic expression. Variable expressivity occurs when all animals carrying a gene express the trait but to variable degrees. Variable expressivity can occur if the characteristic is governed by a number of genes (polygenic), or a genotype/environment interaction; for example, equine recurrent uveitis (ERU) in Appaloosas (which is explained in greater detail in the section **Equine recurrent uveitis**) exhibits variable expression, with some horses more severely affected than others, and this is thought to be governed by several loci along with other non-inherited causes [3]. **Penetrance** is a measurement of the proportion of individuals in a population who carry the allele for a trait and express the phenotype. Incomplete penetrance occurs when all animals in a group are known to carry a particular gene but only some exhibit the trait; thus the gene appears to penetrate and be expressed by some animals but not others (MCOA syndrome is an example and is discussed in the section **Multiple congenital ocular anomalies syndrome**).

Modes of inheritance

Pedigree analysis is useful in the investigation of the possible genetic basis for a trait. If the phenotype is caused by a genetic mechanism, then the inheritance of the characteristic will be higher in related compared to unrelated individuals. Pedigrees can be used to determine how often the condition occurs and to determine the pattern of inheritance, and this is helpful to genetic studies with the aim of identifying associated or causative polymorphisms.

Autosomal recessive

In autosomal recessive inheritance, the causal gene mutation lies on an autosome. Any autosomal gene is just as likely to be inherited by males as females, so the incidence of the characteristic should be relatively the same in males and females. Recessive traits are only expressed in individuals that are homozygous for the causative allele. Animals with one mutant and one normal allele (heterozygous for the mutation) do not express the disease phenotype and are described as **carriers**. The offspring from a mating between two heterozygous animals have a one in four chance of being homozygous for the mutation and thus expressing the disease phenotype. All offspring from a mating between two homozygous individuals will be affected. Because carriers of autosomal recessive traits are phenotypically normal, the disease tends to skip generations (unless the mutant allele becomes very common in the population).

Autosomal dominant

In autosomal dominant inheritance, as with autosomal recessive, the causal genetic mutation lies on an autosome and is just as likely to be inherited by males as females, so the incidence is approximately the same in males and females. Phenotypes caused by dominant alleles will be expressed in every individual carrying the allele regardless of whether there is one copy or two. The defect is transmitted from one generation to the next without skipping a generation. Every affected offspring must have at least one affected parent. Normal offspring from affected parents will not carry the gene and so will produce normal individuals. Mating between an affected individual (who is heterozygous for the affected allele) and an unaffected individual will result in a 50% chance of producing an affected offspring.

X-linked recessive

In X-linked recessive inheritance, the causal gene mutation lies on the X chromosome. In examining pedigrees, an X-linked recessive mode of inheritance is implicated when there are predominantly more males with the phenotype. This is because males only have one X chromosome, and thus one mutated allele will result in the phenotype. The incidence of disease is therefore higher in male animals that inherit an X chromosome with the mutant gene from their dams. In the event that both X chromosomes of a female animal have the mutant allele, that female will have the disease. All female offspring from an affected male will at least be carriers of the mutant allele. Male offspring from a carrier female will have a 50% chance of being affected, whereas female offspring from a carrier female bred to a healthy male will have a 50% chance of being carriers.

X-linked dominant

In X-linked dominant inheritance, the causal gene mutation lies on the X chromosome. All animals carrying the gene will be affected. Every affected offspring must have at least one affected parent. Affected males mated to normal females will not pass the gene on to any of their sons because the sons receive the

Y chromosome. Affected males mated to normal females will pass the gene to all the daughters because the daughters receive the father's X chromosome. Both male and female offspring of a heterozygous female will have a 50% chance of being affected. Heterozygous females may have a less severe phenotype than hemizygous males or homozygous affected females. This is because in each cell, only one of the X chromosomes is active; the other is inactivated, so heterozygous females may have more cells with the normal allele on the active X chromosome.

Mitochondrial inheritance

Mitochondria within eukaryotic cells contain their own genomes. Mitochondria are only transmitted in the ova, not in the sperm, so each animal inherits mitochondria from the dam only. Diseases resulting from defects in mitochondrial DNA are therefore maternally inherited, but to date, no ocular diseases in the horse are known to be caused by genes in the mitochondrial genome.

Ocular disorders of the horse with known or suspected genetic basis

Congenital stationary night blindness

Congenital stationary night blindness (CSNB) was first reported in the Appaloosa in 1977 by Witzel et al. [4, 5]. Horses with this condition are born with the inability to see in the dark. The condition is nonprogressive and the retina is morphologically normal [4–6]. Under scotopic conditions, the electroretinogram (ERG) has a characteristic "negative" response; the dark-adapted ERG recording consists of an absent b wave and a depolarizing a wave (Figure 13.2) [4–6]. The pathogenesis of CSNB is defective neural transmission within the rod pathway, specifically an inability of the ON bipolar cells to respond following hyperpolarization of the rod photoreceptors [4, 7, 8].

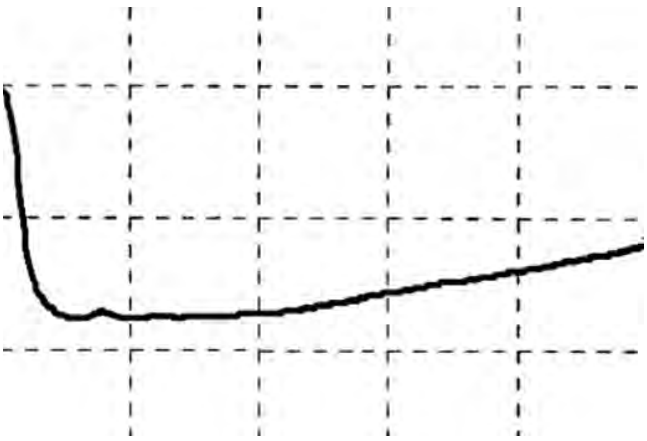


Figure 13.2 Characteristic "negative ERG" of a dark-adapted Appaloosa with CSNB (50 milliseconds/box × 100 μV/box). There is a large a wave of 172 μV and no b wave.

CSNB has been associated with specific coat patterns in the Appaloosa [7]. These coat-spotting patterns are collectively referred to as the leopard complex spotting and are caused by a single incompletely dominant autosomal allele (*LP*). In addition to the Appaloosa, leopard complex spotting occurs in the Knabstrupper, Noriker, pony of the Americas, American Miniature horse, and British spotted pony, among others. CSNB is likely to exist in all breeds with *LP* spotting characteristics, and has been confirmed by ERG in the Appaloosa, American Miniature Horse, and Knabstrupper [9].

Leopard complex spotting is characterized by patches of white in the coat that vary in size but tend to be symmetrical and centered over the hips. Additional pigmentation traits include striped hooves, readily visible nonpigmented sclera around the eye, and mottled pigmentation around the anus, genitalia, and muzzle (Figure 13.3) [10]. Horses also experience varnish roaning, which is the progressive loss of pigment in the coat as the horse ages, while maintaining full pigment on the bony surfaces of the face, hips, and lower legs.

Horses homozygous for *LP* (*LP/LP*) have white-patterned areas with few to no spots of pigment. Horses heterozygous for *LP* (*LP/lp*) have characteristic pigmented oval spots known as "leopard spots" observed in the white-patterned areas (Figure 13.4). The patterns differ by the extent of white on the individual, and range from horses that display only a few white flecks on the rump to those that are nearly all white (Figure 13.5). Modifier genes are thought to be responsible for determining the amount of white patterning that is inherited [11–13].

Horses that are homozygous *LP/LP* are affected by CSNB [7, 9]. The cause of both CSNB and *LP* is a defect in expression of the *TRPM1* gene [14]. TRPM1 is a member of the transient receptor potential (TRP) channel family. TRPM1 has been determined to be a cation channel of the ON bipolar cell [15–18].

Identifying the causative mutation for both *LP* and CSNB involved first mapping the locus to equine chromosome 1 (ECA1) [19]. Investigating the positional candidate gene *TRPM1* determined that the expression of this gene was downregulating in both skin and retina, but sequencing the exons did not identify a causative mutation [14, 20–23]. However, RNA sequencing identified a structural variation, specifically a 1378-bp-long terminal repeat (LTR) insertion in intron 1 of *TRPM1* that was associated with CSNB and *LP* [12]. This LTR of an endogenous retrovirus is believed to disrupt normal transcription of TRPM1 by premature polyadenylation, and thus it has been suggested that no functional TRPM1 protein is present in horses homozygous for *LP*. Several polymorphisms in TRPM1 have been identified as causal mutations for autosomal recessive complete CSNB in humans. These represent a variety of mutations; however, none involves insertions or transposable elements [24–28].

Lack of expression of TRPM1 in CSNB-affected horses explains the "negative ERG" in these animals. Under scotopic conditions, the rods normally exist in a depolarized state.



Figure 13.3 Physical traits associated with *LP* (mottled skin, striped hooves, nonpigmented exposed sclera, and *LP*-caused progressive roaning). (*Source*: Reproduced with permission from Sheila Archer, Moose Jaw, SK.)

The photoreceptors hyperpolarize in response to light and signaling occurs through reduction in glutamate release [29]. This hyperpolarization is responsible for the a-wave of the ERG. Normally, this results in stimulation of the ON bipolar cells. The glutamate receptor of the ON bipolar cell is a metabotropic glutamate receptor (MGluR6) which senses the reduction in synaptic glutamate and produces a response that depolarizes the ON bipolar cell. This results in the b wave of the ERG. In contrast, a horse with CSNB has a lack of expression of TRPM1, and thus rod cells will hyperpolarize in response to light, causing the-a wave, but the ON bipolar cells cannot depolarize and no b wave appears [17, 18]. TRPM1 has also been localized to the synaptic ribbons of rods and melanopsin-expressing photosensitive retinal ganglion cells, suggesting yet undiscovered roles for this gene in vision [30, 31].

The role if TRPM1 in pigmentation and production of the spotted coat patterns is less clear. *LP*-associated characteristics appear to result from a reduction of pigmentation, and it is hypothesized that this is caused by a reduction in melanocytes [12]. TRPM1 knockout mice are night blind, but they do not exhibit a pigmentation phenotype, and, in addition, humans with cCSNB caused by one of 39 mutations in TRPM1 also do not exhibit any pigmentation differences [32].

TRPM1 is also known as melastatin 1 (MLSN1) and is a tumor suppressor gene in melanomas, as its expression declines with increased metastatic potential [33–35]. TRPM1 has been shown to be involved in pigment storage and UV-regulated calcium homeostasis in human melanocytes [36, 37], suggesting that this gene may be involved in Ca^{2+}-dependent signaling related to melanocyte proliferation and/or survival. Cell cultures from *LP/LP* horses reveal an absence of melanocytes in the white-patterned areas, and that melanocytes from pigmented spots within the white-patterned areas have irregularly shaped melanosomes. This suggests that pigmentation in *LP* horses could be disrupted by improper melanosome maturation [12]. It is possible that this may stimulate melanocytosis, resulting in white-patterned areas during development and progressive roaning during the life of the animal.

A genetic test is now available for CSNB and *LP*. Electroretinography and genetic testing are the most accurate ways



Figure 13.4 Homozygous *LP/LP* **(A, B)** and heterozygous *LP/lp* **(C, D)** Appaloosa foals. Heterozygotes have pigmented spots within the white-patterned areas, while homozygotes do not. (*Source*: (A, C) Reproduced with permission from Cheryl Woods, South Wood, SD. (B) Reproduced with permission from Vicki Johnson, Asquith, SK. (D) Reproduced with permission from Sheila Archer, Moose Jaw, SK.)

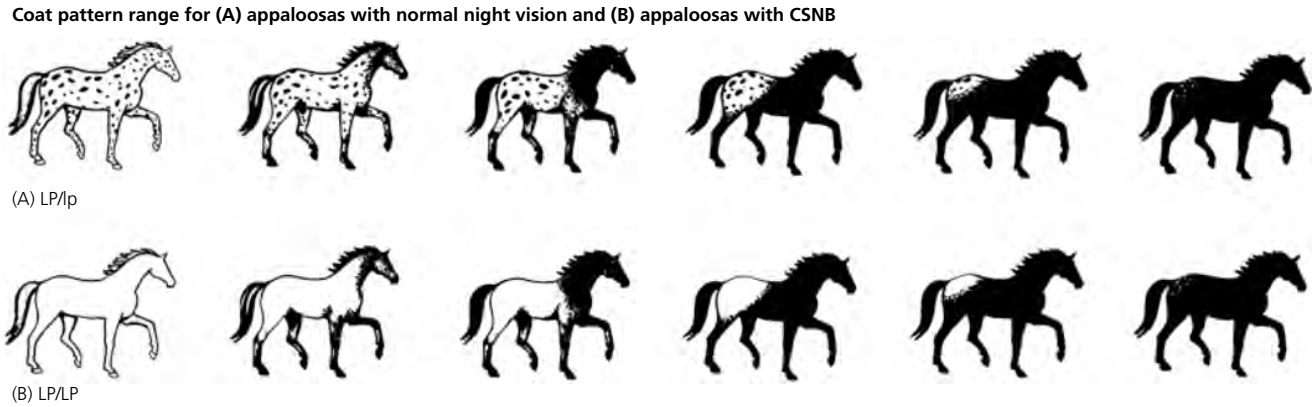


Figure 13.5 Leopard complex coat pattern continuum. Patterns differ by the extent of white on the individual. The **top panel** represents the range of pattering occurring in heterozygotes (*LP/lp*), while the **bottom panel** depicts homozygotes (*LP/LP*). (*Source*: Reproduced with permission from Sheila Archer, Moose Jaw, SK.)

of confirming a diagnosis of CSNB and the *LP* genotype, respectively. Genotype cannot be assumed based on assessment of the spotting pattern phenotype for several reasons. Incorrect classification of homozygous *LP/LP* can occur in horses with additional white spotting mutations (sabino, tobiano, splash, overo, and classic roan) and in those with gray in the genetic background, as these additional pigmentation phenotypes may mask or make it difficult to distinguish the leopard complex patterns. Additionally, horses with little or no white patterning at birth cannot be easily classified by phenotype alone.

LP genotype is important from a breeding and management perspective. Horses homozygous for *LP* (*LP/LP*) are important breeding animals to produce the desired coat patterns; however, since *LP* and CSNB are likely caused by the same mutation, it is impossible to eliminate CSNB from the population without also eliminating the desired coat patterns. Fortunately, most horses with CSNB function very well and visual deficits are often not obvious. Confirming a diagnosis of CSNB is important, however, because this knowledge allows adjusted management conditions, and training and handling strategies that optimize safety for these horses and their human contacts.

Multiple congenital ocular anomalies syndrome

Another ocular disease coupled with coat pigmentation is MCOA syndrome, which has been identified as a pleotropic effect of the silver coat color dilution in the horse [38]. The original description of this condition (previously called **anterior segment dysgenesis**) was in relation to Rocky Mountain horses by Ramsey and colleagues in 1999 [39, 40]. MCOA syndrome has since been confirmed in the Icelandic horse, Shetland pony, American Miniature, Belgian draft, Morgan, and Comtois horse, as well as the Kentucky Mountain Saddle horse and the Mountain Pleasure horse [41–46].

The silver coat color is a dilution of eumelanin (black) pigment controlled by a dominant gene which phenotypically greatly influences the color of the mane and tail, producing a silver or flaxen color. On black base color it also reduces the pigment in the coat, lightening the deep black-colored coat to a dark-chocolate-colored coat with dappling in the coat (a network of dark and light hairs, with the center usually lighter than the periphery) (Figure 13.6) [47]. The body color of a bay silver horse stays relatively unchanged apart from the legs, which are dark-grayish, but the mane and tail are diluted to a mixture of white and gray hairs. Horses with a chestnut background will not show phenotypic changes in coat color as this dilution does not affect pheomelanin (red pigment).

The *silver* gene encodes for premelanosome protein (PMEL). PMEL is a pigment cell-specific integral membrane protein found in the melanosomes, synthesizing primarily the black and brown pigment eumelanin [48, 49]. This protein forms amyloid fibrils in melanosomes on which precursors of melanin synthesis are deposited and concentrated [50]. The exact function of the sheets is not known, but they are thought to have a role in processing of melanin intermediates, facilitating in the polymerization, intracellular transfer, and/or detoxification [49, 51, 52]. Mutations in PMEL regulate hypopigmentation phenotypes in many species, including horses, mice, chickens, zebrafish, dogs, and cattle [53–58]. The zebrafish and dog also have been



Figure 13.6 Silver coat color in the Rocky Mountain horse. The silver mutation causes a black base coat to lighten to a dark-chocolate color with a flaxen mane and tail. (*Source*: Photograph courtesy of Lucinda Nold.)

reported to have concurrent ocular anomalies, although these are different clinically from those noted in the horse [59]. In dogs, PMEL mutations cause the merle coat pattern, which is characterized by patches of diluted pigment intermingled with normal melanin. Ocular lesions associated with this mutation include microphthalmia, cataract, colobomas, and retinal dysplasia [59]. In the **fading vision** zebrafish pigmentation mutant, the retinal pigment epithelium (RPE) is also hypopigmented and this causes the outer segment of the photoreceptors to be reduced in length [57].

Ocular manifestations of MCOA syndrome in the horse exist as two distinct phenotypes: (1) temporal cysts originating from the ciliary body or peripheral retina (cyst phenotype), and (2) multiple congenital ocular anomalies (MCOA phenotype) including ciliary or peripheral retina cysts coincident with iris hypoplasia (Figure 13.7). Clinical manifestations of iris hypoplasia include miosis, dyscoria, absence of a discernible collarette, a visible pupillary sphincter muscle, flattened granula iridica, and incomplete pupillary dilation following mydriatic drugs [39]. Additionally, some horses with the MCOA phenotype manifest with an abnormal corneal contour (corneal globosa, previously called megalocornea), megaloblepharon, retinal dysplasia, immature nuclear cataracts, and iridocorneal angle adhesions or hypoplasia [39, 41, 60].

Animals presumed to be heterozygous for the mutant allele express the cyst phenotype, while those predicted to be homozygous for the allele express the MCOA phenotype [38]. Thus the mutation is incompletely dominant where homozygotes have more serious ocular defects than heterozygous horses. Examining the pedigree records of 516 Rocky Mountain horses in the USA and 97 Rocky Mountain and Rocky Mountain crosses also suggested incomplete penetrance of this dominant allele [40, 41].

A linkage analysis followed by targeted sequencing identified a missense mutation in exon 11 of the *PMEL* gene on ECA6 as the cause of silver coat coloration [61]. To investigate if this mutation was also the cause of MCOA, a separate genetic study mapped MCOA to a 208-kb interval on ECA6 that contains *PMEL* and 14 additional genes [62]. By next-generation DNA sequencing, Andersson et al. [62] refined this location to a 193.3-kb region and identified 609 SNPs for further investigation. They systematically excluded polymorphisms in all genes, except for two in *PMEL*. These authors thus concluded that the ECA6 g.73665304C>T (Arg625Cys) polymorphism is causative for both the MCOA syndrome and silver coat color in horses [38]. However, there are instances where horses who have the ECA6 g.73665304C>T (Arg625Cys) mutation do not exhibit a disease phenotype (nonpenetrant horses); therefore it is still possible that another mutation is causative for this disease or that these horses harbor another genetic mutation that could rescue the phenotype. This will likely be addressed further in future studies.

Molecular consequences of the missense mutation in PMEL have been investigated. Analyzing human protein modified to include the horse mutation demonstrated that this missense mutation (replacing cysteine for arginine) results in a gain of function allowing the protein to self-oligermize, which does not happen with the wild-type protein. Furthermore, cell cultures expressing an analogous PMEL mutation to that in the horse support the role PMEL in the silver phenotype, as anomalies in the formation of the fibrillary sheet structure were detected and these melanosomes lacked pigment [51]. However, the basis for

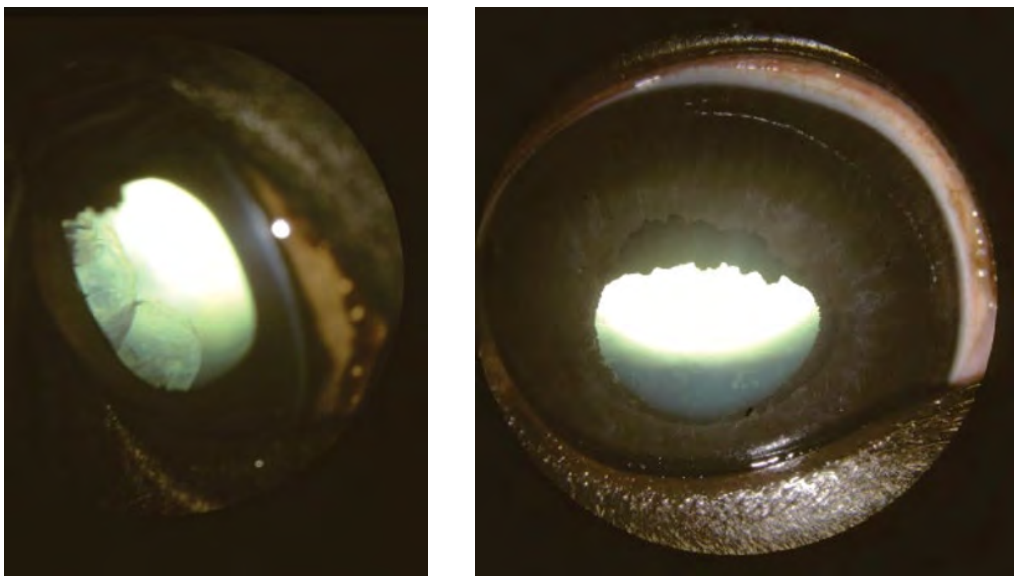


Figure 13.7 Rocky Mountain horse eyes. (A) With cyst phenotype, in which large translucent cysts originate from the ciliary body or peripheral retina. (B) MCOA phenotype, in which ciliary/peripheral retinal cysts are accompanied by multiple other anomalies, which in this horse includes miosis, absence of a collarette, and incomplete pupillary dilation. (*Source*: Reproduced with permission from Bruce Grahn, Saskatoon, SK.)

how this gain of function self-oligomerization causes the ocular anomalies associated with PMEL mutations is not yet known.

In order to eliminate the risk of breeding foals affected by the MCOA phenotype, it is advisable to avoid breeding silver horses to each other. In addition, since only bay- and black-based coat patterns will display the phenotype, it is advisable to have chestnut-based horses that come from silver breeding programs tested for the *PMEL* mutation, and again avoid breeding those horses with the silver mutation to each other.

Equine recurrent uveitis

ERU is a common condition with worldwide distribution and high prevalence [63]. It is characterized by chronic recurring bouts of inflammation of the uveal tissue. This inflammation leads to secondary changes which ultimately result in blindness, and ERU is considered to be the most common cause of blindness in horses [63]. The condition is usually bilateral, although the severity may differ between eyes. Three clinical forms of ERU, classic, insidious, and posterior, have been described [63]. **Classic** ERU is the most common form and is characterized by active inflammatory episodes in the eye followed by periods of minimal observable ocular inflammation. **Insidious** ERU is characterized by persistent low-grade intraocular inflammation, with a gradual and cumulative destructive effect rather than the typical manifestation of outwardly painful episodes. The insidious form is most commonly seen in the Appaloosa and draft breeds. In **posterior** uveitis, the inflammation predominates in the posterior segment, mainly involving the vitreous, retina, and choroid. The posterior syndrome is most common in Warmbloods, draft breeds, and horses imported from Europe to the USA [63].

The pathophysiology of ERU is complex and not completely resolved. It is thought to be an autoimmune disease; however, the mechanisms of the inciting cause and reasons for recurrence of inflammatory episodes are not fully known. Although the association of *Leptospira* spp. with ERU is well established, it is also incompletely understood. *Leptospira interrogans* serovar Pomona is the most common and well-documented infectious agent associated with ERU. High serum antibody titers have been found in some horses with ERU [64–67]. *Leptospira* spp. antibodies have also been found within the ocular fluid of horses with ERU [66, 67]. Additionally, *Leptospira* spp. organisms, as well as their DNA, have been isolated from ocular tissues and fluids of horses with ERU [65, 68–73]. It is theorized that for at least some horses, infection with *Leptospira* spp. is the inciting cause of uveitis [64, 66, 73, 74]. Its role in chronic recurrences of the disease is debated, but likely involves interaction with the immune system. There is ample evidence of cross-reactivity of *Leptospira* spp. antibodies with equine ocular tissues—including the cornea, lens, and retina [75–81]. See Chapter 8 for more information regarding ERU and leptospirosis.

The cells infiltrating the uvea of horses with ERU are predominantly CD4+ T cells. Increased transcription of interleukin 2 (IL-2) and interferon-γ (IFNγ) and low IL-4 mRNA expression in ERU-affected eyes support a T-helper type 1 (Th1)-mediated disease process [79, 80, 82, 83]. Cytokines including IL-17, IL-23, and IL-6 have also been identified in ERU-affected eyes, suggesting that IL-17 secreting CD4+ T Cells (Th17 cells) are another important cell population in the uvea of ERU-affected horses [83, 84]. Th1 and Th17 cells are thought to play overlapping roles in autoimmune inflammation and are both important directors of the immune response in ERU [85]. However, since ERU presents differently in each subclinical classification and there are different breed dispositions, breed-specific characterization of the immune response involved is lacking.

As ERU has an autoimmune-mediated pathogenesis, it is likely that the genetic make-up of the individual plays an important role in determining the susceptibility to inciting infections, as well as the development and severity of subsequent uveitis episodes. Genetic associations for ERU have been identified in the Appaloosa and the German Warmblood horse breeds (see sections **ERU in the Appaloosa** and **ERU in the German Warmblood**) [3, 86]. In both breeds, associations with genes involved in immune function, specifically the major histocompatibility complex (MHC), have been identified.

The most important known function of the gene products of MHC is the processing and presenting of antigens to T cells, although some have other roles in the immune system [87]. MHC class I molecules function to display fragments of proteins from within the cell (i.e., cytosolic or endogenous peptides), while MHC class II molecules function to display peptides derived from extracellular proteins (endocytic or exogenous peptides) [87]. The MHC is polygenic; it contains several different MHC class I and MHC class II genes, so that every individual possesses a set of MHC molecules with different ranges of peptide-binding specificities [87]. MHC is also among the most polymorphic genes in the vertebrate genome in that there are multiple variants of each gene within populations. Loss of genetic diversity in MHC genes has been associated with reduced ability to cope with new and changed diseases [88].

In humans the MHC is called human leucocyte antigen (HLA), and in horses it may be referred to as equine leucocyte antigen (ELA). Several types of uveitis have been associated with different HLA phenotypes [89–93]. Clinical evaluation of HLA phenotypes has become an important tool in assessing the differential diagnoses in human patients with uveitis. HLA typing not only helps diagnose their ocular condition, but also provides information regarding familial risk of inflammatory syndromes [94, 95]. In addition, while there have been studies showing the link between MHC and ERU in both Appaloosas and Warmblood horses (see sections **ERU in the Appaloosa** and **ERU in the German Warmblood**), to date, ELA typing has not been used to routinely diagnose or ascertain genetic risk in horses.

ERU in the Appaloosa

The frequency of ERU in the Appaloosa horse is much higher than in the general population, and ERU is often more severe and more likely to cause blindness in this breed [64, 96].

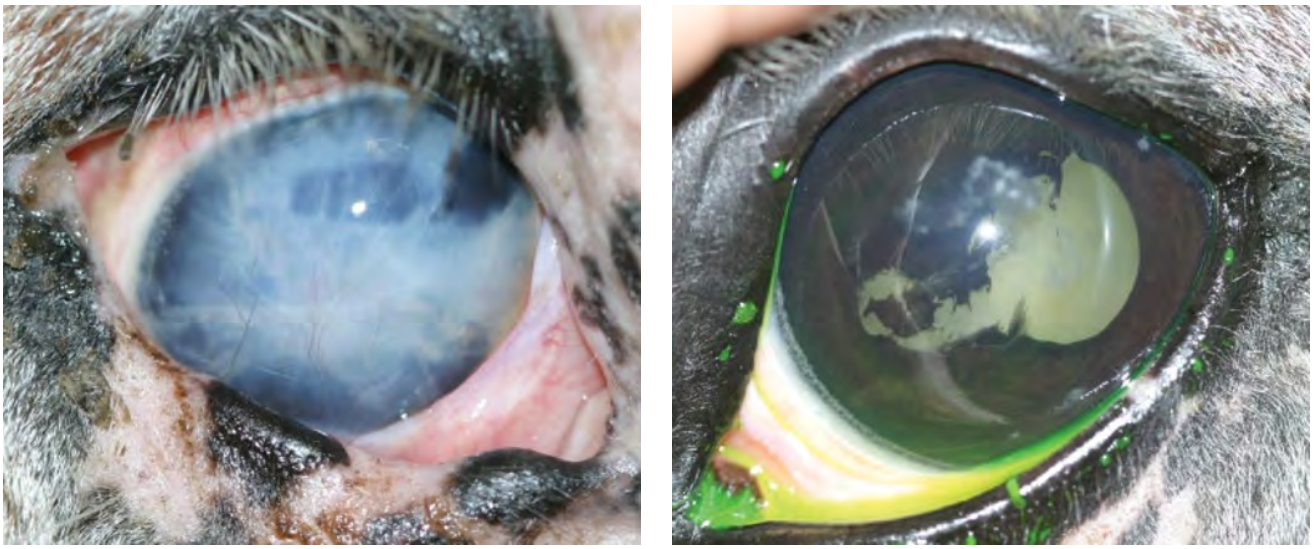


Figure 13.8 Right and left eyes of an Appaloosa horse with insidious ERU. The right eye has developed phthisis bulbi. The left has extensive posterior synechia, immature cataract, and corneal degeneration.

The insidious form of ERU is more common in the Appaloosa, resulting in a gradual cumulative destruction of ocular tissues, and bilateral blindness often occurs by middle age (Figure 13.8). See Chapter 8 for more information regarding ERU and Appaloosa horses.

Recent investigations using a candidate gene approach identified three genetic markers significantly associated with insidious ERU in Appaloosa horses [3]. These included an SNP within intron 11 of the *TRPM1* gene (the gene causing the white coat spotting pattern for which this breed is known; see section **Congenital stationary night blindness**) on ECA1, an MHC class I microsatellite (472-260), and an MHC class II microsatellite (*eqMHC1*) in intron 1 of the *DRA* gene; both of the microsatellites are located on ECA20. The A allele at the *TRPM1* locus, 224 and 227 alleles at the MHC class I microsatellite locus, and 205 and 207 alleles at the eqMHC1 locus were found more frequently in ERU cases compared to unaffected horses. There was a strong correlation between the MHC I and II microsatellites, suggesting that certain combinations of alleles of MHC class I and II genes may be under selective pressure to segregate together [3]. Thus both MHC class I and II are likely to play a role in the susceptibility for ERU in Appaloosas.

For this population of Appaloosa horses, the relative risk of ERU was two to three times higher with each A allele for the *TRPM1* intron 11 SNP G>A [3]. *TRPM1* is the gene responsible for the leopard complex spotting (*LP*) patterns for which the Appaloosa has been selected [12]. *TRPM1* expression is reduced in the retina and skin of Appaloosa horses [14]. Reduced expression in the retina of *LP/LP* horses is the cause of CSNB; however, as described in the section **Congenital stationary night blindness**, its role in pigmentation in the Appaloosa is not understood. Some forms of uveitis in humans and dogs are linked to autoimmune reactions against melanocyte-expressed proteins within the uveal tract [97, 98]. It is possible that the link between the coat patterns of the Appaloosa and an increased risk of insidious ERU may be an autoimmune reaction to altered *TRPM1* in uveal melanocytes; however, this has yet to be investigated. Alternatively, *TRPM1* may have a primary role in immune function as it is also known to be expressed in human B and T lymphocytes, monocytes, and hematopoietic cell lines [99, 100]. However, the biological functions of TRPM1 cation channels in immune cells are also currently unknown. Additionally, the risk of ERU in other *LP* breeds has not been investigated.

ERU in the German Warmblood

German Warmblood horses are also known to have a high frequency of ERU and heredity has also been shown to play a role in ERU in this breed [101]. A serological study in this breed demonstrated an association between ERU and equine MHC class I haplotypes: at least one copy of the ELA-A9 haplotype appeared in 41% of ERU cases and none of the normal controls [102]. In addition, a genome-wide association study (GWAS) in German Warmbloods identified a significantly associated SNP on ECA20 located close to the candidate genes IL-17A and IL-17F. The haplotype containing the SNP closest to IL-17A resulted in the highest haplotype association for this ECA20 region [101]. IL-17 is a pro-inflammatory cytokine associated with cell damage during autoimmune disease, including uveitis (see section **Equine recurrent uveitis**) [83, 103]. Thus this association and link to IL-17 warrants further investigation in German Warmbloods. In the same study, the GWAS data were also analyzed for severity and an SNP near the crystalline gene cluster on ECA18 was strongly associated with the most severe cases. It was hypothesized by these investigators that genetic variants in mutations in crystalline genes may contribute to cataract formation in the course of ERU [101].

There are major limitations in our understanding of the genetics of autoimmune diseases in horses and other species. In the Appaloosa and German Warmblood horses, association studies identified five genes; however, the precise role these genes and/or variants of these genes play in disease pathogenesis is not yet known. Future genetic studies will likely unravel novel genes that will help to explain the variability and severity of disease both within and between sub-clinical classifications and should enable a more complete understanding of the pathogenesis of this disease. Further, having DNA testing available to predict risk of ERU in the susceptible breeds could aid clinicians in early diagnosis and a better prognosis for the horse.

Squamous cell carcinoma

Squamous cell carcinoma (SCC) is the most common tumor of the eye and adnexa in horses [104]. The nictitating membrane and the limbus are the most common ocular sites, followed by the eyelids [104, 105]. Among all breeds examined, prevalence seems to increase with age and the disease may be more common in geldings than in mares [104]. Gray, white-pattered, and dilute chestnut (cremello and palomino) horses are more likely to develop SCC than bay, brown, and black horses [104, 105]. Horse breeds at increased risk include those with minimally pigmented ocular and periocular tissue, such as the Appaloosa and American Paint horse [104–108]. Thoroughbreds, Draft horses, and Haflingers are also reported to be at increased risk [104, 105, 108–112]. The Haflinger horse is particularly over-represented for the development of limbal SCC; in two retrospective studies, 69% and 26% of the affected horses were Haflingers, respectively [108, 111, 113]. Haflingers are also known as Avelignese and are always some shade of chestnut in coloration with a flaxen mane and tail (Figures 13.9 and 13.10). To date, no association with shade of chestnut coloration and disease states has been observed in Haflingers. The disease appears to have a lower age of onset in the breed, with an average of 8.7 years compared to 12.9 years for horses of other breeds [113]. Four-generation pedigree analysis revealed that all affected Haflinger horses share a single common ancestor who is a prominent sire, suggesting that genetics plays a role in the pathogenesis of limbal SCC in the breed. A recessive mode of inheritance is suspected [113]. Research to identify genetic risk factors is on-going.

The prevalence of periocular SCC in horses increases with an increase in longitude, altitude, and mean annual solar radiation [104]. Ultraviolet (UV) radiation is believed to be the primary carcinogen associated with SCC. This belief is supported by evidence that UV light radiation damage has been shown to cause mutations in the tumor-suppressor gene p53, and gene expression of p53 is altered in equine, bovine, canine, and feline ocular SCC [114]. This gene encodes for a 53-kDa nuclear phosphoprotein which functions as a regulator of cellular growth and proliferation. Higher concentrations of p53 protein switch off DNA replication by arresting the cell cycle in the G1 phase to allow extra time for DNA repair. Cells containing mutant p53 protein or lacking p53 are unable to arrest the cell cycle and continue unchecked into the S phase before repair of DNA is completed. This allows for the accumulation of mutations at an increased rate, leading to selection of neoplastic clones and tumor development [115, 116]. Overexpression of mutant p53 antigen can be detected immunohistochemically in tissues of SCC, and this is particularly true for equine ocular SCC [114, 117].

Immunoreactivity for cyclo-oxygenase (COX)-1 and -2 is also high in equine corneal SCC, possibly indicating that COX plays a role in oncogenesis or progression of this tumor type at



Figure 13.9 Typical chestnut coloration with flaxen mane and tail of the Haflinger horse. (*Source*: Photograph courtesy of Van Horn/Der Haflingerhof.)



Figure 13.10 Limbal SCC in a 6-year-old Haflinger horse. (*Source*: Photograph courtesy of Mary Lassaline.)

this site [112, 118]. COX are a family of enzymes responsible for conversion of arachidonic acid to prostaglandins. The COX-1 isoform is described as being constitutively expressed in healthy tissues and active in numerous homeostatic functions. The COX-2 isoform is described as an inducible enzyme which is overexpressed in inflammatory and neoplastic conditions through cytokine, hormone, and tumour promotor signals. Overexpression of COX-2 in some neoplasms has been associated with a higher degree of tumour aggression and poor prognostic indicators [119–124]. The reason for this is not known; however, it is possible that COX-2 expression may enhance oncogenesis via stimulated angiogenesis and mitosis and inhibition of apoptosis [125–127]. Thus both p53 and COX-2 are potential candidate genes worthy of investigation in the Haflinger horse and other breeds where a genetic component is expected. Currently, a GWAS is being conducted in Haflingers to elucidate the genetics and pathophysiology of limbal SCC in the breed.

Corneal dystrophy in Friesian horses

A spontaneous and progressive thinning condition of the cornea is reported in Friesian horses in the USA and Europe for which an inherited disease process is likely. The condition has been classified as a dystrophy due to its bilateral nature, symmetric location, and absence of accompanying uveitis [128–130].

The corneal lesions vary in severity from shallow facets to deep corneal ulcers that may progress to perforation. Lesions are on average 5 mm in diameter (range 2–8 mm) and are most commonly located in the inferotemporal quadrant of the cornea, although inferonasal and inferior and superior temporal locations have also been reported (Figure 13.11) [131]. Blepharospasm, epiphora, conjunctival hyperemia, corneal edema, corneal vascularization, aqueous flare, and miosis are not present until the condition progresses to corneal perforation [131]. The disease may present unilaterally, with spontaneous development and progression of similar lesions in the second eye. Dehiscence of conjunctival grafts placed to surgically repair corneal ulcers was not uncommon, occurring in 5/9 eyes treated, indicating that there may be a progressive degenerative process even after surgical repair [131]. The average age of diagnosis of the first eye was reported as 10.7 years and this disease was more common in male horses, with only one of the nine affected horses being female [131].



Figure 13.11 Deep corneal ulceration in the inferotemporal quadrant of the left eye as a manifestation of corneal dystrophy in the Friesian horse. (*Source*: Photograph courtesy of Mary Lassaline.)

The condition has some similarities to pellucid marginal degeneration (PMD), which is a progressive, noninflammatory, thinning disease of the cornea in people. The clinical appearance of PMD is that of peripheral, crescent-shaped regions of thinning, typically involving the inferior cornea where the cornea remains clear, without vascularization or infiltrate [132]. PMD is more common in males in the second to fifth decade. While most of these symptoms are the same in horses (with the exception being the lesions that have been reported to be round in Friesian horses and not crescent shaped), there is little evidence to support the idea that PMD is genetically inherited in humans [133]. Ultrastructurally, however, there is disorganization and degeneration of collagen fibrils within the PMD lesions [134], thus suggesting that collagen fibril disorganization might contribute to disease in Friesian horses, but ultrastructural analysis has not been performed.

Other nonocular conditions appear to be more common in the Friesian breed. These include retained placenta, megaoesophagus, dwarfism, hydrocephalus, and aortic rupture [135–139]. It has been suggested that these may be multisystem manifestations of a collagen disorder, possibly associated with selection of their baroque phenotype of an upright neck and hyperreflective locomotor pattern [140].

The bilateral nature and breed predisposition to corneal dystrophy suggests a genetic component to the disease. Pedigree analysis of nine Friesian horses affected bilaterally and four with unilateral disease revealed a common ancestor within six generations. The presence of a close common ancestor is thus consistent with the hypothesis that the disease has a genetic basis. Molecular work to better characterize the genetics of this disease is ongoing. In addition to genetics, more work is needed to investigate the pathophysiology and etiology of the condition, including histologic and ultrastructural studies.

Cataract

Congenital and developmental cataracts have been reported in several horse breeds; however, investigation of the heritability of cataracts in horses is limited. In young horses, the occurrence of cataract, particularly those that manifest bilaterally, is suggestive of the defect having a hereditary basis. Sporadic familial occurrences of cataracts are reported in the Quarter horse, Arabian, and Thoroughbred breeds [141–144]. Reports often represent observations of veterinary ophthalmologists and the true hereditary nature in these cases is unconfirmed. Lavach reported cataracts in three successive foals of a Quarter horse mare that were sired by three different stallions, implying a dominant mode of inheritance [141]. Whitley shows similar results, mentioning

unpublished data of cataracts in two foals from an affected Quarter horse mare [142]. Millichamp and Dziezyc noted two independent families of Arabians in which cataracts occurred in related animals, suggestive of an inherited etiology, but no mode of inheritance was investigated or reported [143]. Severin lists congenital nuclear cataract as a dominant mode of inheritance in the Thoroughbred as supported by test breeding, but does not include specific details [144].

The Morgan is a breed thought to have an inherited form of congenital nuclear cataracts [145, 146]. These are bilateral, nonprogressive, and described as finely reticulated, spherical translucencies of the embryonal and fetal nucleus that sometimes extend to the region of the posterior "Y" suture. Morgan cataracts are not associated with any other ocular defect and do not impair vision. Pedigree analysis has shown that these are inherited as an autosomal dominant trait, as 10 out of 12 affected animals were all sired by the same stallion [146]. The authors also noted that more females were affected than males. However, to date, no molecular studies have been conducted to examine what genes may be involved.

High prevalence of cataract was also reported in a herd of Exmoor ponies in Canada [147]. The cataracts varied in severity, with the majority being punctate or intermediate and most were located in the anterior cortex or capsule. Progression was not documented. Although it is likely that there is an inherited etiology for these cataracts, the mode of inheritance has not been definitively determined. Based on this study, inheritance did not appear to follow a simple autosomal dominant or recessive pattern. However, females were more often affected, similar to the study in the Morgan, but also showed greater severity. Taken together, this suggests a sex-linked or sex-influenced inheritance pattern [145–147].

Cataracts are reported in association with other known inherited ocular anomalies, including iridial hypoplasia in the Belgian and Quarter horse breeds and MCOA syndrome in horses with the Silver mutation [39, 41–46, 148–150]. Finally, ERU is considered to be the most common cause of cataract in horses. Cataracts are thought to form as a consequence of degenerative changes to the lens secondary to the intraocular inflammation. Heredity has been shown to play a role in development of ERU in the Appaloosa and German Warmblood breeds [3, 86, 101]. Interestingly, as described above (see section **ERU in the German Warmblood**), a GWAS in German Warmbloods identified a significant SNP near the crystalline gene cluster on ECA18. Although the role of this mutation is not known, it is suggested that it may be associated with cataract formation in the course of ERU in this breed [86].

Aniridia

The term aniridia is often used in the literature to describe partial or complete absence of the iris. Although iridal hypoplasia is a more appropriate term when some rudimentary iris tissue is present, this can be difficult to differentiate without light microscopic examination. Inherited aniridia/iridal hypoplasia has been reported in the Belgian and Quarter horse breeds.

Inherited aniridia was first reported by Eriksson in 1955 [148]. Bilateral aniridia with cataracts was seen in a Belgian stallion and 65 of his offspring. Affected animals were photophobic with large circular pupils that were nonresponsive to light. Dermoids and a nonulcerative keratitis were concurrently present in several of the affected horses and cataracts developed in affected offspring after 2 months of age. Pedigree analysis was consistent with an autosomal dominant mode of inheritance. After affected animals were eliminated from the breeding pool there have been no further reports of the condition in the Belgian breed.

Bilateral congenital aniridia was also reported in a Quarter horse stallion and in several of his offspring [149, 150]. Mild nonulcerative, pigmented, and vascularized keratitis and nodular tissue masses were present at the dorsal limbus of affected horses. Some of these were smooth and appeared similar to follicular hyperplasia, and some had short, sparse, fine hairs protruding from them. Cataracts were present on clinical examination in most eyes of the affected offspring. Cataracts were not observed clinically in the stallion at 18 months of age; however, they were present and extensive on light microscopic examination after he was euthanized at 38 months of age, indicating a progressive course. Light microscopic examination of affected eyes showed rudimentary iris tissue to be present, indicating iridal hypoplasia rather than true aniridia, and the limbal nodules were consistent with dermoids. The authors hypothesize an autosomal dominant mode of inheritance, as seven of eight of the Quarter horse stallions foals out of unaffected and unrelated mares were affected [149].

Similar associations of iris hypoplasia, dorsal nonulcerative keratitis, and cataract have been reported in single case reports of a Welsh Thoroughbred-cross filly and a Thoroughbred colt, a case series of Swedish Warmblood horses, and two related Tennessee Walking horses—a mare and her foal (Figure 13.12). The mode of inheritance of the condition was not determined in

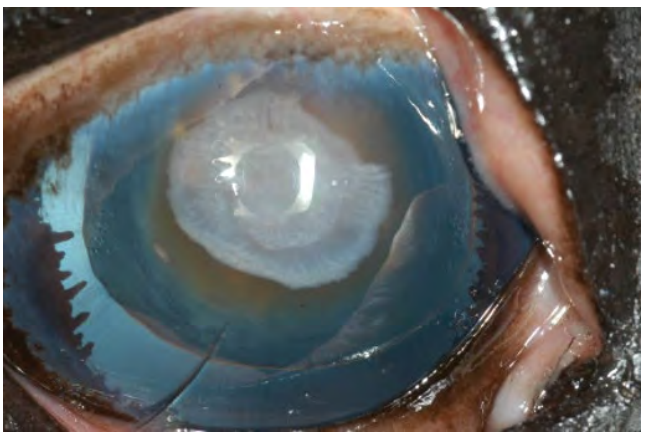


Figure 13.12 Aniridia in a Tennessee Walking horse. The tips of the ciliary processes are visible and the iris cannot be identified. The dorsal limbus has fine cilia-like hairs protruding from dermoid tissue. Immature nuclear cataract was present. These abnormalities were present bilaterally. (*Source*: Reproduced with permission from Dan Ward, Knoxville, TN.)

these reports, although dominant inheritance was ruled out in one Swedish Warmblood, suggesting different genetic mechanisms in different breeds [151–154].

The underlying pathophysiology of aniridia is not known. Aniridia in humans is a panocular disorder associated with other ocular defects including keratopathy, cataracts, ectopia lentis, glaucoma, and macular and optic nerve hypoplasia [155, 156]. Most cases in humans are inherited in an autosomal dominant fashion and involve defects in the paired box protein (*PAX*)-6 gene [157]. *PAX-6* is one of a family of transcriptional regulators that has a key role in directing development of the eye and brain [155, 156]. It is known to be important in the many aspects of ocular development, including the iris, cornea, lens, optic nerve, retina, and iridocorneal angle [158–161]. Therefore mutations in the gene can explain the simultaneous clinical features of the aniridia syndrome. To date, no molecular work on this condition has been reported; however, given the similarity to the human disorder, *PAX-6* is a viable candidate worthy of investigation in the horses and breeds affected.

Ocular manifestations of equine diseases caused by known genetic mutations

Hereditary equine regional dermal asthenia

Hereditary equine regional dermal asthenia (HERDA), also known as hyperelastosis cutis, is an autosomal recessive disorder seen in American Quarter horses and their lineages [162, 163]. HERDA is characterized clinically by loose, hyperextensible, and abnormally fragile skin that tears easily and has impaired healing [162, 164, 165]. Subtle signs of the condition, such as increased joint flexibility or a loose mane, may be present at birth; however, HERDA is most commonly noticed around 18–24 months when skin lesions begin to develop [166]. Lesions have regional distribution most commonly occurring along the dorsum, gluteal region, neck, lateral thorax, and abdomen [162]. Temperature and UV light exposure are believed to play a role in disease progression and the most common lesions occur over the dorsal midline, where both are more intense [166]. Tendonoligamentous structures have been shown to be weaker in horses with HERDA and there may be an increased susceptibility to infection and certain types of cancer, such as disseminated SCC, related to reduced immune surveillance due to T-cell malfunction [166]. Particular to ophthalmic pathology, horses with HERDA have significantly thinner corneas and an increased incidence of corneal ulcers than normal horses [167]. Additionally, the corneal curvature and diameter are significantly larger than normal horses [168].

The pathogenesis of lesions seen in HERDA relate to defects in collagen biosynthesis and organization of collagen microarchitecture [166, 168–171]. Increased content of soluble collagen and reduced tensile strength of the skin have been described [169, 172]. Light microscopic examination shows reduced density and loose arrangements of collagen fibers within the deep dermis in the skin of HERDA horses [162, 173]. Similarly, light and scanning electron microscopy reveals areas of collagen disarray and disruption of the typical collagen lamellar pattern in corneas from horses with HERDA [167].

A missense mutation in the *cyclophilin B* gene (*PPIB*) has been identified as the likely cause of the disorder, as this mutation causes a nonconservative amino acid change in the protein (p.Gly39Arg) [163]. Thus, while light microscopic examination of skin biopsy samples may be suggestive of this condition, genetic testing is the most definitive choice for diagnosis [166]. Cyclophilin B is a member of the peptidyl-prolyl *cis*-trans isomerase family of proteins, which catalyze prolyl-containing bonds in procollagen to the trans configuration, and is critical in procollagen trafficking, processing, and chain association [166]. The HERDA mutation does not alter prolyl isomerization activity but delays collagen folding and secretion and decreases post-translational modifications of lysine residues. Such modifications are fundamental to the formation and stability of collagen intermolecular cross-links, which play a role in maturation of insoluble collagen and development of tensile strength of collagen fibrils [170, 171, 174, 175].

Hyperkalemic periodic paralysis

Hyperkalemic periodic paralysis (HYPP) is an autosomal dominant trait affecting Quarter horses and horses with Quarter horse lineage. The clinical signs of the condition are variable, and range from asymptomatic to daily muscle fasciculations and weakness which may result in recumbency. Ocular manifestations relate to muscle weakness and include third eyelid prolapse secondary to globe retraction [176]. The genetic defect has been traced back to a single Quarter horse stallion. He and his descendants were likely selected as breeding stock because of the well-developed musculature resulting from the genetic mutation [177–179].

The molecular basis for HYPP is a missense mutation in the alpha-subunit of the voltage-dependent skeletal muscle sodium channel alpha-subunit (*SCN4A*) [180]. The mutation causes a failure of sodium channel inactivation when serum potassium concentrations are increased, for example following intense exercise or in renal disease. This failure leads to excessive inward flux of sodium and outward flux of potassium causing persistent depolarization of the skeletal muscle cells and thus temporary weakness [179, 181]. A genetic test for the disease is available.

Junctional epidermolysis bullosa

Junctional epidermolysis bullosa (JEB) is an autosomal recessive trait affecting Belgians, other draft breeds, and American Saddlebred horses [182–185]. Clinically, the disease is characterized by mechanical stress-induced blistering of the skin and mucous membranes. Blisters rapidly progress to erosions and ulcerations and are typically seen at sites of minor frictional

trauma such as the lips, oral mucosa, distal extremities, and coronary band [185, 186]. Lesions may be present at or shortly after birth and affected foals often fail to thrive due to inability to suck [185]. Other symptoms described in affected foals include dystrophic teeth and the ocular manifestation of corneal ulcers [182, 186–188].

JEB is characterized histologically by separation of the epidermis and dermis within the lamina lucida leaving the epidermis and dermis intact. The lesion is caused by a defective basement membrane zone [183, 184]. Mutations involving two different genes coding for the laminin 332 protein complex have been associated with the disease in horses [189, 190]. Laminin is a basement membrane protein integral to the structure and function of the dermal–epidermal junction and consists of three glycoprotein subunits: the alpha3, beta3, and gamma2 chains encoded by the *LAMA3*, *LAMB3*, and *LAMC2*, respectively [181]. In Draft breeds (Belgian, Italian, Trait Breton, Trait Comtois) the genetic defect is a cytosine insertion creating a premature stop codon in the *LAMC2* gene [184, 185, 190]. The mutation in American Saddlebreds has been identified as a 6589-bp deletion in the *LAMA3* gene [189]. A genetic test for both of the identified mutations exists. The mutations may underlie the development of corneal ulceration noted in some affected animals.

Lethal white foal syndrome (lethal white overo syndrome)

Lethal white foal syndrome (LWFS) is an autosomal recessively inherited trait seen in American Paint foals (and related breeds) that are homozygous for the pigmentation mutation known to cause the frame overo pattern. The term "frame" comes from the phenotypic appearance in which pigment frames the horse and the white spotting occurs in the middle of the flanks and neck as well as on the ventral surface. However, the amount of white is variable and sometimes this pattern is confused with other white spotting patterns [191]. Affected foals are all- or nearly all-white with blue eyes, and die from complications of intestinal aganglionosis [192].

This disorder is caused by a missense mutation (p.Ile118Lys) in the *endothelin-B receptor* gene (*EDNBR*) [193]. *EDNBR* is involved in developmental regulation of neural crest cells that are precursors to neurons in the peripheral nervous systems including the enteric nervous system, as well as melanocytes that populate the skin and eyes. In addition, neural crest cells migrate to the inner ear where they are important for maintenance of normal hearing. One study showed that 91% of horses confirmed or suspected to be deaf had this frame overo mutation [194]. Consequently, foals with LWFS are white with blue eyes, have an aganglionic colon resulting in gastrointestinal motility dysfunction, and may also be deaf [194]. Not all white foals with blue eyes will be homozygous for the mutation; however, there is a genetic test available to screen for carriers and test white, blue-eyed foals [191]. It is important to note that this is not the only mutation known to cause blue eyes in horses and it is also not known if vision is altered by the reduction in pigment.

Severe combined immunodeficiency

Severe combined immunodeficiency (SCID) is an autosomal recessive trait in Arabian horses characterized by a lack of functional B and T lymphocytes [195]. Affected foals are clinically normal at birth, as passive transfer initially provides protective immunity. However, they become susceptible to infection as colostral immunity wanes [196]. Onset of infection is usually around 6–10 weeks depending on the adequacy of passive transfer and exposure to pathogens. Foals most often die of respiratory tract diseases such as adenovirus pneumonia, *Pneumocystis carinii*, or bacterial infection [197]. Because of insufficient immunity, affected foals may develop uveitis related to sepsis or disseminated opportunistic pathogens [176].

SCID in Arabian horses results from a frameshift mutation in the gene encoding deoxyribonucleic acid-protein kinase catalytic subunit (DNA-PKcs), a subunit of deoxyribonucleic acid-protein kinase (DNA-PK) which is an enzyme important to DNA repair [198]. This mutation leads to nonfunctional DNA-PK, which is required in the gene rearrangement that leads to T-lymphocyte antigen-specific and B-lymphocyte surface Ig receptors [190, 200]. Thus B- and T-lymphocyte precursors fail to differentiate into mature lymphocytes, leading to lack of antibody- and cell-mediated immunity, respectively.

Definitive diagnosis of SCID in the Arabian is based on the results of the genetic test [199]. The clinical syndrome of SCID has also been described in a single Appaloosa and a Caspian foal. Genetic testing was not available at the time of the Appaloosa case report, and the defective allele was not detected in the Caspian horse [201, 202]. Thus it is possible that other mutations exist, at least in the Caspian breed.

Conclusions and genetic testing in the horse

Causative mutations have been discovered for a limited number of ocular conditions (CSNB and MCOA syndrome) and several systemic conditions with ocular manifestations (HERDA, HYPP, JEB, LWFS, and SCID). Genetic tests now exist for those with known mutations (see Table 13.1). For many conditions, a simple genetic basis is supported (limbal SCC in the Haflinger; corneal dystrophy in the Friesian; cataract in the Quarter horse, Arabian, Thoroughbred, and Exmoor pony; aniridia in the Welsh Thoroughbred, Swedish Warmblood, and Tennessee Walking horse). Other ocular disorders appear to be more complex involving several genes, and genetic associations have been detected (ERU in the Appaloosa and German Warmblood). Inheritance patterns and causative mutations for these have yet to be identified and confirmed. For other ocular disorders, single gene inheritance patterns are highly suspected but little else is known (cataract in the Morgan; aniridia in the Belgian and Quarter horse). Until recently, the study of equine genetic

diseases has been limited, but advances in genetic and genomic technologies and the availability of the horse genome sequence have helped to overcome some of the limitations in doing horse genetic research. With the rapidly advancing molecular tools, it is likely that the genetics of several of these aforementioned ocular disorders will be unraveled in the near future.

Once a mutation that causes a disease (or is associated with a disease) has been identified and a DNA test is commercially available, informed breeding decisions can be made with the hope of lowering the incidence of the disease in affected breeds. Furthermore, when "risk" alleles are identified for inherited ocular disorders, such as ocular cancers and ERU, clinicians can utilize DNA testing to identify animals that should be examined more frequently, thus enabling earlier detection, treatment, and a better prognosis. There are several laboratories in the USA, Canada, and around the globe that offer equine coat color and disease genetic testing. For example, the University of California Davis Veterinary Genetics Laboratory offers DNA testing for most of the available DNA tests listed in Table 13.1 (for more information see https://www.vgl.ucdavis.edu/services/horse.php). Furthermore, some tests are patent protected and licensed to specific laboratories, and some breed organizations have contracts with specific laboratories to perform testing for their breed. Considerations for responsible testing should include both the laboratory used and application of the results. Breeding decisions should be made to avoid producing animals that express serious or lethal diseases. Such decisions are not always straightforward, however. Elimination of affected and carrier animals may have greater effects on genetic diversity of some small horse breeds, and, in some breeds, eliminating the disease would greatly impact breed characteristics. For example, in the Appaloosa and related breeds, elimination of CSNB would result in elimination of the *LP* spotting pattern and characteristics typical of these breeds.

In recent years, the genetics of several ocular disorders have been extensively studied, while several additional studies are now currently underway and with the aid of new tools and technology new molecular mechanisms should be elucidated. Combining these discoveries with DNA testing and the development of new therapeutic targets, genetics will positively impact the ocular health of the horse.

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CHAPTER 14

Equine neuro-ophthalmology

Elsa Beltran, Kaspar Matiasek, and Claudia Hartley

Introduction

Diseases causing neuro-ophthalmic signs are emerging in equine veterinary medicine. The visual pathways and their related structures involve motor, sensory, and autonomic functions from the central and peripheral nervous system. Dysfunction of any of these systems can cause a variety of clinical signs (decreased vision, blindness, abnormal pupillary light reflex (PLR), anisocoria, abnormal eye movements, neurogenic keratoconjunctivitis sicca (NKCS), neurotrophic keratopathy, facial paresis-paralysis, and fixed strabismus alone or in association with multifocal neurologic/systemic signs). It is important to understand the functional neuro-ophthalmic anatomy prior to interpreting its dysfunction.

This chapter focuses on the basic understanding of neuroanatomic pathways and their clinical assessments, which permit localizing the lesion in the nervous system and therefore having a neuroanatomic diagnosis. In order to list the differential diagnoses, we have to take into account signalment, history, systemic assessment, and neuroanatomic diagnosis of the affected horse. The list of differential diagnoses will allow us to formulate an appropriate diagnostic plan. This chapter reviews neuro-ophthalmic anatomy and function, the clinical examination, and the most common diseases resulting in neuro-ophthalmic dysfunction. General neuroanatomy and full neurological examination that are not involved in the neuro-ophthalmology system are beyond the scope of this chapter.

Neuro-ophthalmic anatomy and function

Neurosensory retina and optic nerve

The retina is histologically divided into ten layers [1]. Nine layers form the neurosensory retina (embryonic derivative of the prosencephalon, neuroectoderm), and the tenth and most external layer (on the scleral surface and closest to the choroid) is the supportive retinal pigmented epithelium [1]. The nine identifiable layers of the neurosensory retina (from the outer (scleral) surface to the inner (vitreal) surface) are the photoreceptor layer, external limiting membrane, external nuclear layer, external plexiform layer, internal nuclear layer, internal plexiform layer, ganglion cell layer, nerve fiber layer (NFL), and internal limiting membrane [1] (Figure 14.1). The neurosensory retina layers contain seven types of major cells (six neuronal and one glial): outer retina photoreceptors (rods and cones), bipolar neurons, horizontal neurons, amacrine cells, Müller cells (retinal astrocytes, radiating glia), and retinal ganglion cells (RGCs) [1, 2] (Figure 14.1). These cells convert light into electrical impulses, which are sent, via the optic nerve, to the visual cortex (to be transformed into images) and reflex pathways (to coordinate pupil size, head, neck, and eyeball movements in response to visual stimuli) [3].

The outer photoreceptors (rods and cones) are the first neurons in the visual/reflex pathway and are located in the photoreceptor layer. The horse has a predominance of the rod system, with approximately 95% rods and 5% cones [4]. The rods function in dim light and detect shapes and motion, while the cones function in bright light and provide sharp visual activity and color sensitivity [5, 6]. The second neurons of the visual/reflex pathway are the horizontal and bipolar neurons, which are located in the internal nuclear layer. The horizontal cells are interneurons that modulate the synaptic transmission between the outer photoreceptors and bipolar neurons. The nuclei of the horizontal cells are entirely located close to the center of the globe and next to the inner plexiform layer [1, 2]. The bipolar neurons connect (directly or indirectly) the outer photoreceptor neurons (rods and cones) with the RGCs (third neuron in the visual/reflex pathway), which are the last neurons within the retina [1, 5, 6].

The amacrine cells are other interneurons located in the internal nuclear layer with their axons extending to the external and internal plexiform layers [2, 7]. The amacrine cells are mainly inhibitory interneurons that form a complex network between bipolar neurons, RGCs, and other amacrine cells, contributing to increase the sensitivity of RGCs to changes in illumination [8, 9].

Müller glial cells are the only glial cells located in the retina and are essential to maintain retinal physiology. They span the

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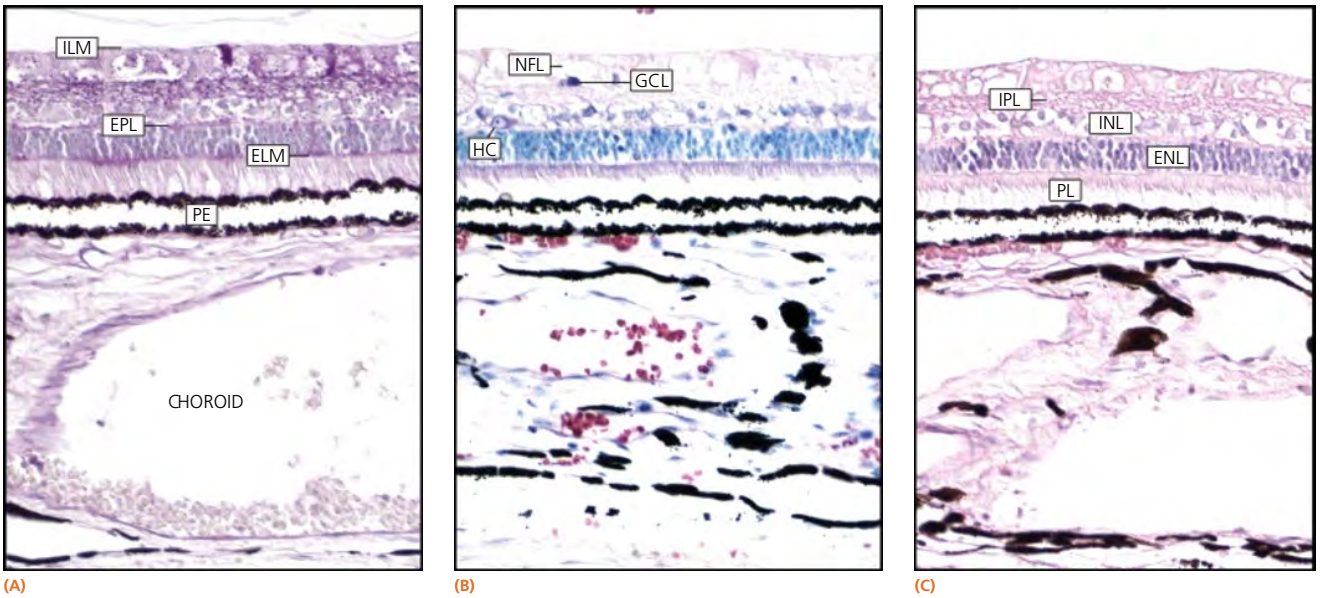


Figure 14.1 Microscopic cross section of the retina of a horse's eye stained with periodic acid-Schiff (A), Giemsa (B), and hematoxylin and eosin (C). PE, Pigmented epithelium; PL, photoreceptor layer; ELM, external limiting membrane; ENL, external nuclear layer; EPL, external plexiform layer; HC, horizontal cell; INL, internal nuclear layer; IPL, internal plexiform layer; GCL, ganglion cell layer; NFL, nerve fiber layer (8); ILM, internal limiting membrane.

entire thickness of the retina, with the cell body located in the inner nuclear layer and the axons extending from the internal limiting membrane (vitreal surface) to the external limiting membrane (scleral surface) [1, 2, 10, 11].

The ganglion cell layer contains the cell bodies and nuclei of the RGCs. The term of this layer is a misnomer, as "ganglion" implies that these neurons are outside of the central nervous system (CNS), which is not correct, as the retina is an extension of the CNS [3]. A new subgroup of RGCs has been identified called melanopsin-containing RGCs (intrinsically photosensitive RGC (ipRGCs)) that are also photosensitive, with melanopsin as the photosensitive pigment. This subgroup can respond to changes in light without the input of the outer photoreceptors (cones and rods) and contribute to regulation of circadian behavior, seasonal reproductive rhythm, and PLR [12–15].

There is an area in the retina with the highest number of photoreceptors and RGCs, called the area centralis, which is specialized for high resolution with maximal visual acuity [1, 2, 7]. The equine area centralis contains two areas: the area centralis rotunda (small, circular area dorsolateral to the optic disc (in the temporal region of the retina)) with slightly higher RGC density; and the area centralis striaeformis (visual streak, horizontal band above the optic disc spanning the entire width of the retina) [7]. A strong positive correlation has been found between the density of the RGCs in the area centralis striaeformis and nasal length in horses; however, the functional significance of this relationship remains to be defined [7].

The NFL is mainly formed by axons of the RGCs, which course on the vitreal surface of the retina to the optic disc (optic nerve head or optic papilla), and this point is the origin of the optic nerve (cranial nerve (CN) II). The thickness of the NFL depends on the density of the RGCs, which changes throughout the retina, and increases towards the optic disc [1]. The thinnest NFL is located in the ventral retinal quadrant, which correlates with lower populations of RGCs [16]. In the NFL the axons lack myelin to maintain the transparency of the retina. Myelination starts at the level of the scleral canal in horses, which explains the shape and color of the optic disc (Figure 14.2), although

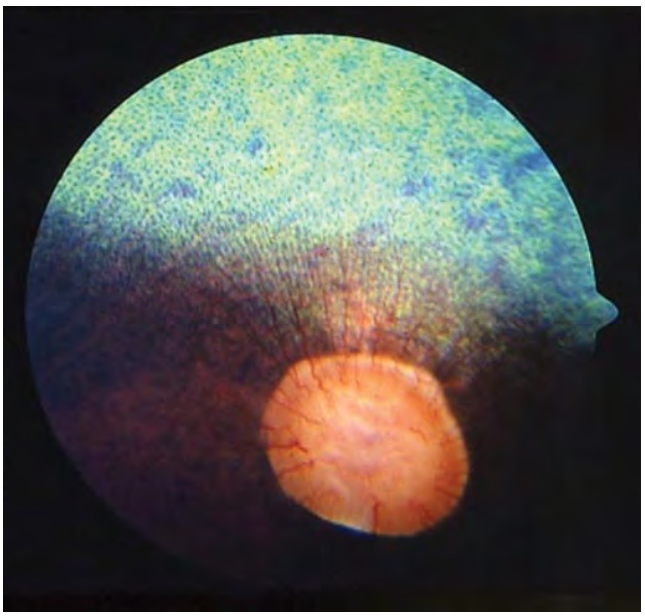
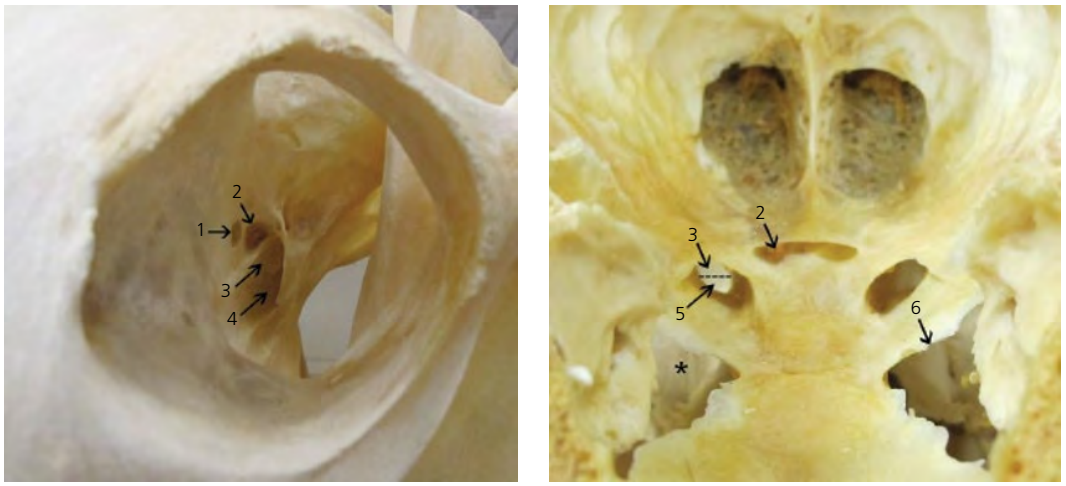


Figure 14.2 Ocular fundus of a normal horse. Notice that the optic disc is mildly concave, ellipsoidal, and located in the nontapetal zone. The vascular pattern consists of cilioretinal blood vessels that emerge from the edge of the optic disc.



(A) (B)

Figure 14.3 Equine skull. (A) Lateral view through the left orbit. (B) Dorsocaudal view of the rostral and middle cranial fossae of a normal horse after the calvaria has been removed. **1**, Ethmoidal foramen; **2**, optic canal; **3**, orbital fissure; **4**, rostral alar foramen; **5**, round foramen; **6**, oval notch of the oval foramen; the foramen lacerum (**asterisk**). The **dotted line** represents a thin bony lamina that was not preserved on this skull.

some horses may have myelinated axons of the NFL in the horizontal quadrants of the retina (seen as "medullary rays").

The optic nerve is a white matter tract of the diencephalon, formed by RGC axons and glial cells (mainly astrocytes and oligodendrocytes). Optic nerve is actually also a misnomer, as the term "nerve" involves a bundle of axons in the peripheral nervous system (PNS) myelinated by Schwann cells; however, the optic nerve is a tract of the CNS and is myelinated by oligodendrocytes [3]. The optic nerve after the lamina cribosa is surrounded by meninges (dura mater, arachnoid membrane, and pia mater) with a subarachnoid space and cerebrospinal fluid [3]. The RGC axons in the optic nerve are arranged in a retinotopic manner to maintain the spatial arrangement of the retina [6, 17, 18]. The optic nerve is divided into four regions: intraocular (ganglion layer, NFL, optic disc, and intralaminar region within the sclera), intraorbital (retrobulbar, posterior to the lamina cribosa), intracanalicular (within the optic canal), and intracranial (just before merging into optic chiasm). RGC axons course caudally and enter the skull through the optic canals, located in the presphenoid bone, to merge into the optic chiasm (Figure 14.3). The optic canals are of a considerable length in the horse compared to other species [3].

Chiasm and retrochiasm pathways to the visual cortex

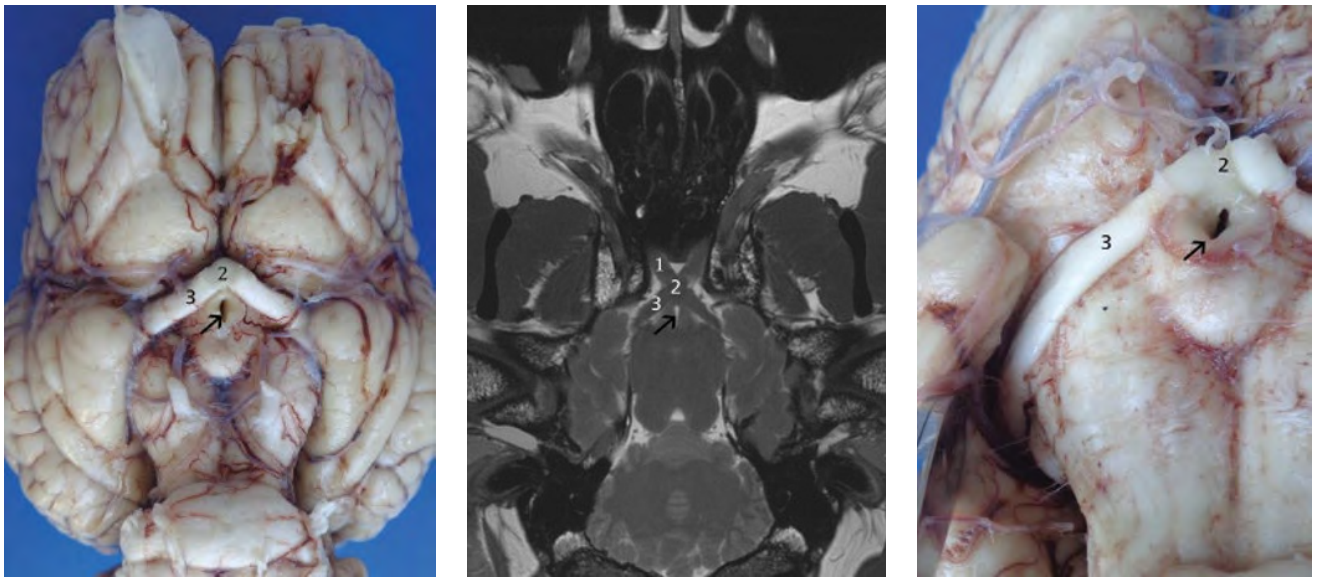
About 80% of the RGC axons decussate at the optic chiasm and about 20% remain ipsilateral [17, 18]. The axons that decussate come from the RGCs in the medial aspect of the retina, while the ipsilateral axons come from the RGCs in the lateral aspect of the retina [3]. The optic chiasm is located on the floor of the rostral cranial fossa (presphenoid bone) and rostral to the pituitary gland (Figure 14.4); after the optic chiasm, the RGC axons continue as the optic tract and course caudodorsolaterally over the side of the diencephalon.

The majority of the optic tract axons synapse in the lateral geniculate nucleus (LGN), located caudodorsolaterally in the thalamus (Figure 14.5) [3]. Some (including melanopsin-containing RGC axons) leave the optic tract before reaching the LGN to relay information to extracortical nuclei (pretectal nucleus, rostral colliculus, and suprachiasmatic nucleus) [3, 18, 19]. The axons from the neuronal cell bodies in the LGN project into the internal capsule and course caudally as the optic radiation, to terminate in the visual cortex (lateral, caudal, and medial aspect of the occipital lobe) and produce conscious visual perception (Figure 14.6) [3].

Eye globe position and eye movements

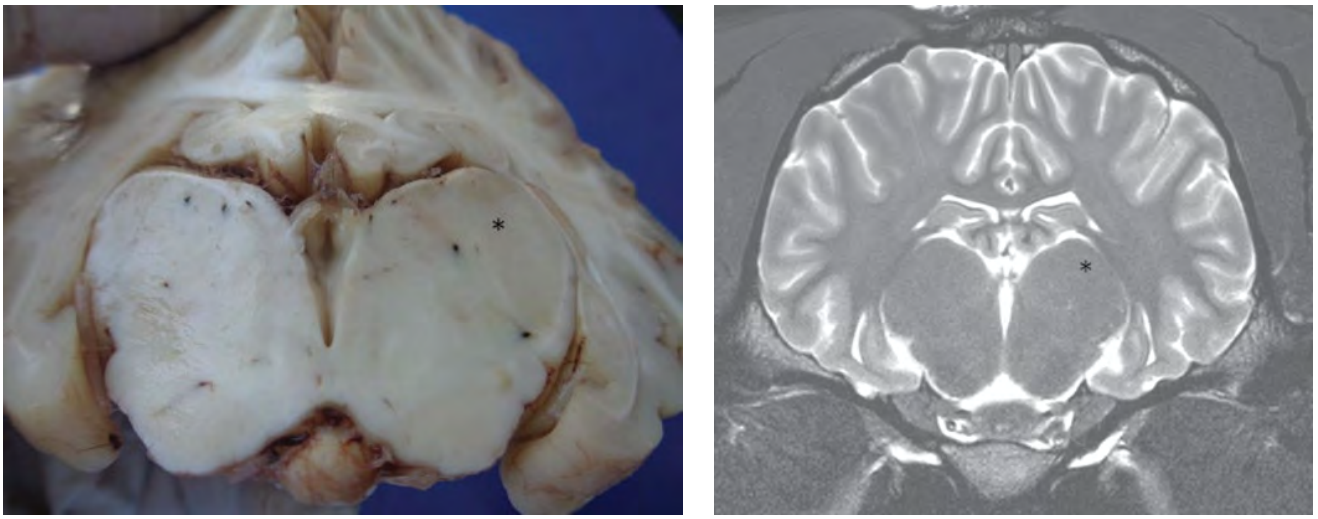
The centered eye position in each orbit and the eye's movements depend on the coordination of three cranial nerves—the oculomotor nerve (CN III), trochlear nerve (CN IV), and abducent nerve (CN VI)—their associated extraocular muscles (dorsal, ventral, lateral, and medial rectus muscles, dorsal and ventral oblique muscles, retractor bulbi muscle), the visual system, and the vestibular system (VS) [20].

The VS is the primary component of the nervous system responsible for maintaining equilibrium. The components of the VS can be functionally divided into peripheral and central systems. The peripheral system mainly includes the sensory receptor and the vestibular division of the vestibulocochlear nerve (CN VIII). The sensory receptor is located in the inner ear (within the petrous temporal bone) and consists of three semicircular canals with ampullae, the utricle, and the saccule [21]. Movement of the head (acceleration–deceleration) induces movement of the endolymph within the semicircular canals, which stimulates the sensory receptors and sends tonic excitatory input towards the CNS [20]. The vestibular division of CN VIII has dendritic connections with these receptors, and its axons course (with the cell bodies located in the vestibular ganglion within the petrous



(A) (B) (C)

Figure 14.4 (A) and (C) Ventral surface of the brain. (B) Three-dimensional, water-selective sequence, dorsal plane reconstruction at the level of the optic chiasm. **1**, Optic nerve; **2**, optic chiasm; **3**, optic tract. The **arrow** points to the infundibulum (pituitary stalk).



(A) (B)

Figure 14.5 (A) Transverse section at the level of the caudal part of the thalamus. (B) Transverse T2-weighted image at the same level as **(A)**. The lateral geniculate nucleus is marked with an **asterisk**.

temporal bone) through the internal acoustic meatus to reach the components of the central vestibular system at the level of the cerebellomedullary angle (rostral medulla oblongata) [20].

In the central vestibular system, the vestibular axons project to the vestibular nuclei in the brainstem, and from these nuclei, axons project to the spinal cord, other parts of the brainstem, thalamus, and cerebellum. The axons projecting from the vestibular nuclei to the motor nuclei of the CNs III, IV, and VI, via the medial longitudinal fascicle within the brainstem provide coordinated conjugate ocular movements (both eyes involved) as the head changes position. This pathway is responsible for the physiologic nystagmus, which preserves image stability on the retina while the head moves to optimize performance of the visual system. This pathway can be assessed clinically by evaluating the vestibulo-ocular reflex (physiologic nystagmus) (Figure 14.7) [20].

The somatomotor nucleus of the oculomotor nerve, CN III, is located in the rostral mesencephalon (midbrain), caudal to the parasympathetic (visceromotor) nucleus of the same cranial nerve, lateral and dorsal to the medial longitudinal fasciculus, and at the level of the rostral colliculi. Axons of the oculomotor nerve emerge on the ventrolateral side of the mesencephalon and course rostrally on the floor of the middle cranial fossa and

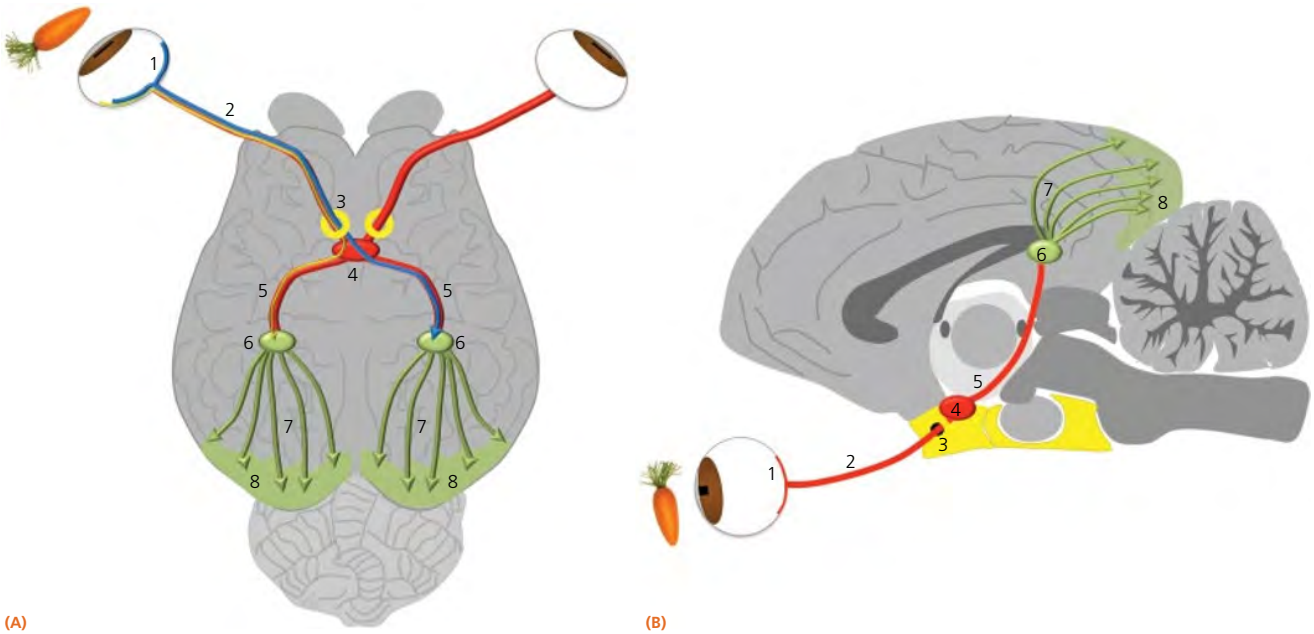


Figure 14.6 Neuroanatomic pathway for conscious vision. (A) Dorsal and (B) lateral views. **1**, Retina; **2**, optic nerve; **3**, optic canal; **4**, optic chiasm; **5**, optic tract; **6**, lateral geniculate nucleus; **7**, optic radiation; **8**, occipital cortex.

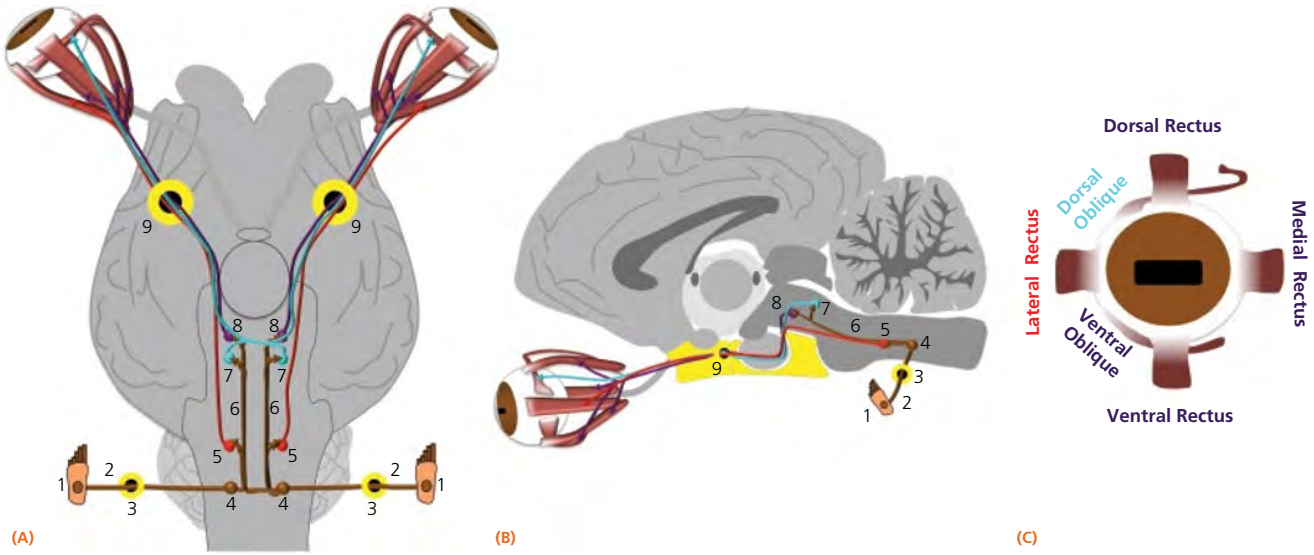


Figure 14.7 Neuroanatomic pathway for VOR. (A) Dorsal and (B) lateral views. (C) Extra-ocular muscles of the right eye. **1**, Sensory receptors in the inner ear; **2**, vestibulo-cochlear nerve; **3**, internal acoustic meatus; **4**, vestibular nucleus; **5**, abducent nucleus and nerve; **6**, medial longitudinal fasciculus; **7**, trochlear nucleus and nerve; **8**, oculomotor nucleus and nerve; **9**, orbital fissure.

lateral to the pituitary gland to leave the cranial cavity through the orbital fissure. The orbital fissure is a cleft between the presphenoid and basisphenoid bones (see Figure 14.3). After emerging from the orbital fissure, the oculomotor nerve divides into two branches (dorsal and ventral). The dorsal branch supplies the dorsal rectus muscle and the levator palpebrae superioris. The ventral branch supplies the medial and ventral rectus muscles and ventral oblique muscle of the eyeball (see Figure 14.7) [22–24].

The motor nucleus of the trochlear nerve, CN IV, is the smallest of the cranial nerves and is the only cranial nerve that emerges from the brainstem dorsally and crosses entirely to innervate a contralateral extraocular muscle (see Figure 14.7). The nucleus of CN IV is located in the caudal mesencephalon, caudal to the motor nucleus of the oculomotor nerve, lateral and dorsal to the medial longitudinal fasciculus, and at the level of the caudal colliculi. The axons of CN IV course dorsally around the mesencephalic aqueduct to enter the rostral medullary

velum and as trochlear decussation cross to the opposite site. The axons then course rostroventrally lateral to the mesencephalon within the membranous tentorium cerebelli, continue on the floor of the middle cranial fossa, lateral to the pituitary gland, to leave the cranial cavity through the contralateral orbital fissure and innervate the contralateral dorsal oblique muscle of the eyeball (see Figure 14.7) [22–24].

The motor nucleus of the abducent nerve, CN VI, is in the rostral medulla oblongata, ventral to the floor of the fourth ventricle. The axons of the abducent nerve course ventrolaterally through the medulla and emerge from the brainstem just lateral to the pyramid of the medulla oblongata, and course rostrally on the floor of the middle cranial fossa and lateral to the pituitary gland to leave the cranial cavity through the orbital fissure. The abducent nerve branches in the orbit to innervate the lateral rectus and the retractor bulbi muscles of the eyeball [22, 23].

Motor and autonomic nerve supply to the eyelids

The principal muscle elevating the eyelid under voluntary contraction is the levator palpebral superioris muscle, which is innervated by the oculomotor nerve (CN III) [24, 25]. There is a very thin muscle, levator anguli oculi medialis muscle, which assists in raising the superior eyelid and it is innervated by the auriculopalpebral branch of the facial nerve (CN VII) [25]. The resting tone of the eyelid and eyelashes is supplied by Müller's superior tarsal and the arrectores ciliorum muscles, which are innervated by the sympathetic system [25].

The orbicularis oculi muscle is the principal muscle to close the eyelid, which is innervated by the auriculopalpebral branch of the facial nerve (CN VII) [24, 25]. The somatic motor nucleus of the facial nerve is in the rostral medulla oblongata, ventral to the floor of the fourth ventricle. The axons of the facial nerve emerge from the brainstem at the lateral part of the trapezoid body, the rostral medulla oblongata, and course rostral to the vestibulocochlear nerve (CN VIII). These two cranial nerves (CN VII and VIII) leave the cranial cavity within a common sheath of dura mater through the internal acoustic meatus. At the base of the internal acoustic meatus, the facial nerve continues laterally through the facial canal of the petrous temporal bone and then curves caudoventrally in the caudal wall of the tympanum to exit the skull through the stylomastoid foramen. This caudoventral bend formed by the facial nerve is known as the "knee" of the facial nerve (geniculum) within the facial canal. After emerging from the stylomastoid foramen, the facial nerve runs ventral, lateral, and rostral to the guttural pouch, crosses the caudal border of the ramus of the mandible, and branches as the auriculopalpebral nerve. The auriculopalpebral nerve ascends towards the parotid gland to terminate in zygomatic and rostral auricular branches. The zygomatic branch runs to the medial angle of the eye to innervate the orbicularis oculi, levator anguli oculi medialis, and levator nasolabialis as palpebral branches [24, 25]. There are other branches from the facial nerve that are beyond the scope of this chapter.

Sensory nerve supply to the eye and surrounding areas

Sensory innervation of the eye and surrounding areas of the face involves components of the trigeminal nerve (CN V) through its ophthalmic, maxillary, and mandibular branches (Figure 14.8). The ophthalmic branch is purely sensory, leaves the cranial

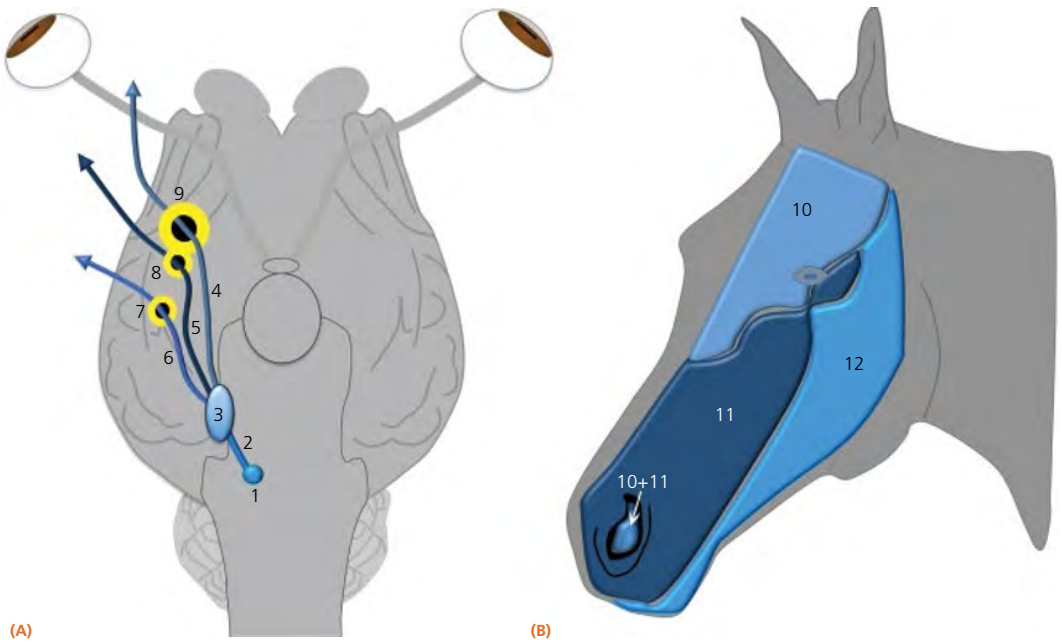


Figure 14.8 (A) The origin, course, and distribution of three branches of the trigeminal nerve. **1**, Trigeminal nucleus; **2**, trigeminal nerve; **3**, trigeminal ganglion; **4**, ophthalmic branch; **5**, maxillary branch; **6**, mandibular branch; **7**, oval foramen; **8**, round foramen; **9**, orbital fissure. (B) Dermatome distribution of the ophthalmic (**10**), maxillary (**11**), and mandibular (**12**) branches of the trigeminal nerve.

cavity through the orbital fissure, and subdivides into three further branches: the lacrimal nerve (which innervates the lacrimal gland), the frontal nerve (which innervates the skin of the forehead and upper eyelid), and the nasociliary nerve (which innervates the corneal epithelium, skin of the medial canthus of the eye, septum, and parts of the wall of the nasal cavity) [24, 25]. The maxillary branch is also purely sensory, leaves the cranial cavity through the round foramen (located in the basisphenoid bone, on the external surface known as rostral alar foramen) (see Figure 14.3), and divides into three further branches: the zygomatic nerve (which innervates the inferior eyelid and the lateral canthus of the eye; and anastomoses are formed with branches of the lacrimal nerve to also innervate the lacrimal gland); the pterygopalatine nerve (which innervates part of the nasal mucosa, mainly in the ventral meatus of the nasal cavity and the hard and soft palate); and the infraorbital nerve that continues in the infraorbital canal (which innervates the cheek, superior teeth, alveolar periosteum, and gums) [22, 24].

The zygomatic nerve is not to be confused with the zygomatic branch of the facial nerve. The mandibular branch is sensory and motor (motor component to the muscles of mastication). The sensory part of the mandibular branch innervates the skin of the temporal area, lower mandible, and oral mucous membrane. The axons form the ophthalmic, maxillary, and mandibular branches of the trigeminal nerve, and course from the mentioned receptor organs towards the cranial cavity through the orbital fissure, rostral alar foramen (round foramen internal surface), and oval foramen, respectively, to reach the trigeminal ganglion, where the cell bodies from these sensory nerves are located (see Figure 14.8). The trigeminal ganglion is located inside the cranial cavity, rostrolateral to the foramen lacerum, and in the canal of the trigeminal nerve (the rostral part of the petrous portion of the temporal bone). These axons then enter the brainstem at the level of the pons to terminate in the sensory nucleus of the spinal tract of the trigeminal nerve, which extends from the pons to the sixth cervical segment of the spinal cord [22, 26]. From this nucleus, reflex pathways (such as corneal reflex) and conscious perception of nociception from the innervated areas are processed [26].

Autonomic innervation to the eye

Autonomic innervation to the eye has central and peripheral components, including higher centers in the hypothalamus and midbrain and also tracts and nuclei in the pons, medulla oblongata, and spinal cord. The autonomic system has mainly two components: the general visceral afferent system and the general visceral efferent system with its parasympathetic and sympathetic divisions [19]. Parasympathetic innervation to the eye regulates pupil response (more precisely iris size) to the amount of environmental light, while sympathetic innervation to the eye regulates pupil response (iris size) to central factors such as emotion, pain, and distress. In other words, the iris sphincter muscle is primarily under the control of the parasympathetic nervous system, while the iris dilator muscle is primarily under the control of the sympathetic system. Pupil constriction (miosis) is produced by contraction of the iris sphincter muscle and relaxation of its antagonist muscle (iris dilator muscle). On the other hand, pupil dilation (mydriasis) is produced by contraction of the iris dilator muscle and relaxation of its antagonist muscle (iris sphincter muscle). This is referred to as reciprocal innervation [5, 27, 28].

The afferent pathways that contribute to parasympathetic innervation to the eye arise from the retina, where the impulses originate after light stimulation to the photoreceptors (rods, cones, and ipRGCs). These impulses travel within the RGC axons (optic nerve) and reach the optic chiasm. The majority of the RGC axons decussate at the level of the optic chiasm (around 80%) and continue as part of the optic tract. Some optic tract RGC axons bypass the LGN and course caudally to synapse in the pretectal nucleus, particularly the pretectal olivary nucleus (PON). The PON is located rostral in the midbrain tectum and contributes to the PLR pathway. From the PON, the majority of the axons (around 80%) cross over to the contralateral side through the caudal commissure and reach the parasympathetic nucleus of the oculomotor nerve (known as the Edinger–Westphal nucleus in human neuroanatomy), which is located in the rostral part of the midbrain and very close to the midline. The remaining axons from the PON (around 20%) reach the ipsilateral parasympathetic nucleus of the oculomotor nerve [17, 19].

The efferent parasympathetic fibers (preganglionic fibers) from the oculomotor nucleus travel with the motor fibers of the oculomotor nerve, coursing ventrally and emerging on the medial side of the crus cerebri. The parasympathetic fibers are located medially to the motor fibers of the oculomotor nerve on the floor of the middle cranial fossa and therefore they are the first to be affected when a structural lesion (such as a pituitary gland mass) arises and extends laterally from the midline [19].

The parasympathetic fibers leave the cranial cavity through the orbital fissure and synapse in the ciliary ganglion caudal and lateral to the eyeball. These postganglionic parasympathetic fibers (five to eight short ciliary nerves) innervate the iridal sphincter muscle and give reciprocal cholinergic inhibition to the iridal dilator muscle, causing iridal sphincter contraction and dilator muscle relaxation (pupillary constriction) (Figure 14.9) [5, 19, 22, 24]. There is an accessory ciliary ganglion (5 mm distal to the main ciliary ganglion) that has been found in horses and other mammals, which is connected mostly with short ciliary nerves [29].

Sympathetic innervation to the eye is described as a three-order neuron pathway (Figure 14.10). Cell bodies of the first-order neurons are located in the caudal nuclei of the hypothalamus, which are activated by emotional factors or noxious stimuli. These first-order neurons project caudally and ipsilaterally via the lateral tectotegmental spinal tract (located in the lateral funiculus of the spinal cord) to the preganglionic cell bodies (second-order neurons), which are located in the lateral

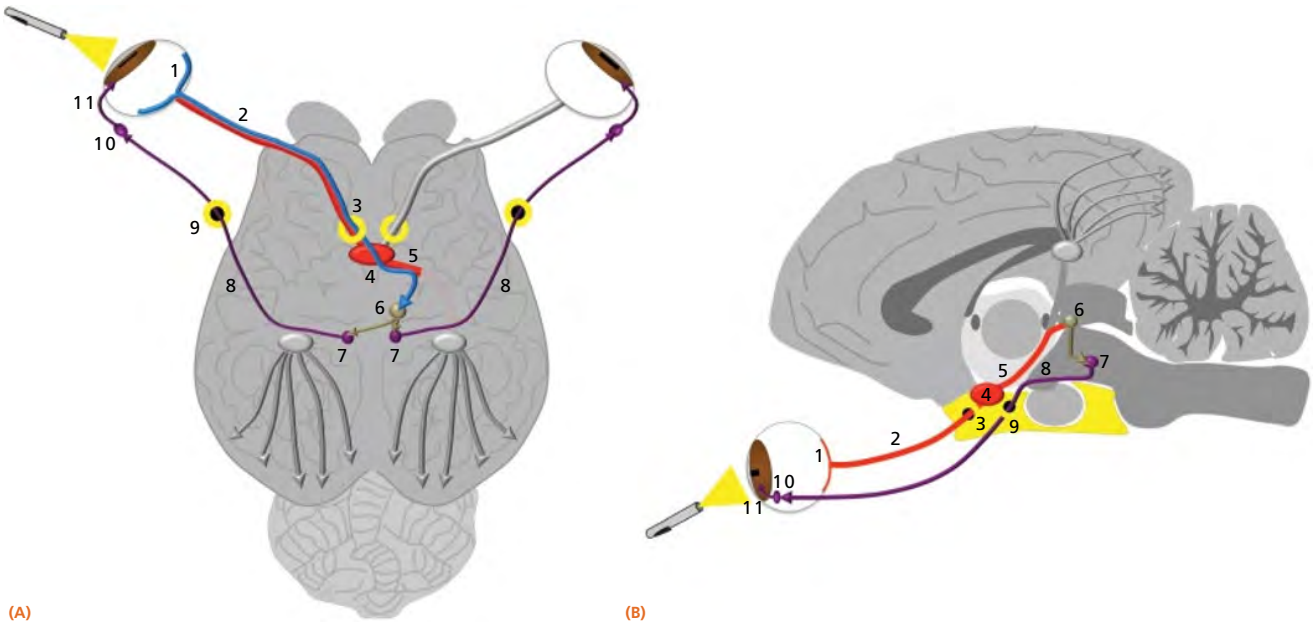


Figure 14.9 Neuroanatomic pathway for PLR. (A) Dorsal and (B) lateral views. **1**, Retina; **2**, optic nerve; **3**, optic canal; **4**, optic chiasm; **5**, optic tract; **6**, pretectal nucleus; **7**, parasympathetic component of the oculomotor nucleus (Edinger–Westphal nucleus); **8**, oculomotor nerve; **9**, orbital fissure; **10**, ciliary ganglion; **11**, short ciliary nerve.

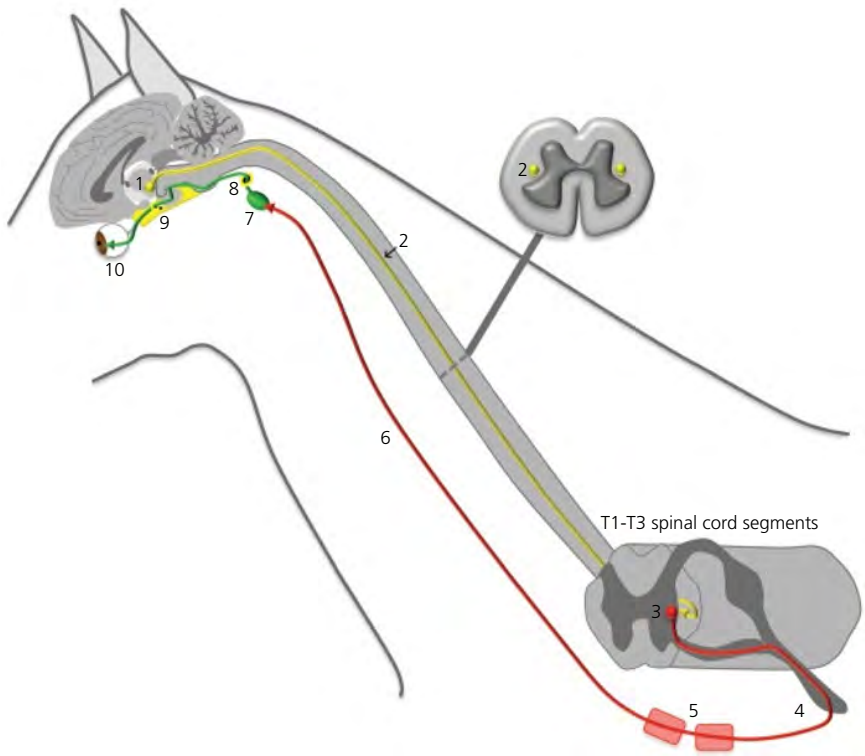


Figure 14.10 Neuroanatomic pathway for sympathetic innervation to the eye. **1**, Cell bodies of the first-order neuron located in the caudal nuclei of the hypothalamus; **2**, tectotegmental spinal tract; **3**, cell body of the second-order neuron located in the lateral gray column of the first thoracic spinal cord segments; **4**, ramus communicans; **5**, sympathetic chain ganglia; **6**, vagosympathetic trunk; **7**, cranial cervical ganglion and cell body of the third-order neuron; **8**, tympano-occipital fissure; **9**, orbital fissure; **10**, muscles of the iris.

gray column (nucleus intermediolateralis) at the level of T1–T3 or T4 spinal cord segments (Figure 14.10). Axons from the preganglionic neurons join the ventral roots of the segmental spinal nerves at the same level, emerge through the intervertebral foramen, and leave the spinal nerves in the segmental ramus communicans to join the thoracic sympathetic trunk. The preganglionic fibers continue cranially as part of the cervical vagosympathetic trunk. This sympathetic trunk is associated with the vagus nerve (CN X) and located in the carotid sheath. At the level of the caudal wall of the medial guttural pouch

compartment, ventral to the atlanto-occipital articulation, the preganglionic fibers terminate in the cranial cervical ganglion (CCG), where they synapse with postganglionic neurons (third-order neurons) [30].

The exact route of these postganglionic fibers to reach the smooth muscles of the iris remains undefined. One of the recent reported possible routes describes that the postganglionic axons leave the CCG as the internal carotid nerve and direct cranially through the tympano-occipital fissure to enter the carotid canal of the temporal bone (see Figure 14.10). At the rostral end of the carotid canal, postganglionic sympathetic axons access the cranial cavity through the foramen lacerum, joining the ophthalmic branch of CN V, course on the floor of the middle cranial fossa, and emerge through the orbital fissure [19, 31]. Postganglionic sympathetic fibers innervate the smooth muscles of the periorbita, superior and inferior (Müller's) tarsal muscles of the eyelid, and dilator muscles of the iris. The sympathetic input to the dilator muscle causes contraction of this muscle and therefore mydriasis.

As previously described regarding parasympathetic innervation (see section **Autonomic innervation to the eye**), sympathetic innervation causes a reciprocal inhibition of the other antagonist muscle (iris dilator muscle) and therefore further relaxation of the iris sphincter muscle [5]. The sympathetic system also seems to innervate the sweat glands of the skin and their cutaneous vascular supply from the face and neck; however, the exact sudomotor pathways in horses are still not fully elucidated [32]. Cell bodies of the postganglionic axons that supply innervation to the sweat glands (and their cutaneous vascular supply) of the skin of the neck from C3 to C8 spinal cord segments are located in the cervicothoracic ganglion at the level of the cranial dorsal thorax. These postganglionic axons continue cranially with vertebral vessels running in the lateral vertebral foramina to segmentally join the vertebral nerves supplying each cervical dermatome. Postganglionic axons (third-order neuron) supply sympathetic innervation to the sweat glands of the skin (and their cutaneous vascular supply) of the head and the cranial cervical spine to the level of C2 vertebra, likely following branches of the trigeminal nerve [33].

Autonomic nerve supply of the lacrimal glands originates from the parasympathetic nucleus of the facial nerve (rostral salivary nucleus (RSN)) within the rostral medulla oblongata. The preganglionic parasympathetic fibers that arise from the RSN emerge from the medulla oblongata as the intermediate nerve and join the somatic motor axons of the facial nerve, before leaving the cranial cavity accompanied by the vestibulocochlear nerve (CN VIII) within a common sheath of dura mater through the internal acoustic meatus. The preganglionic parasympathetic axons of the intermediate nerve leave the main trunk of the facial nerve at the level of the geniculate ganglion (located at the "knee" of the facial nerve) in the facial canal of the petrous temporal bone and continue as the greater (major) petrosal nerve (GPN) in the small petrosal canal. The GPN (preganglionic parasympathetic fibers) emerges from the petrosal canal adjacent to foramen lacerum and continues through the pterygoid canal into the pterygoid fossa, where it synapses in the pterygopalatine ganglion (located on the floor of the orbit). Postganglionic parasympathetic fibers join sensory branches of the ophthalmic nerve (lacrimal nerve) and maxillary nerve (zygomatic nerve) to project to the lacrimal gland [24]. Other postganglionic parasympathetic fibers project to glands of the nasal cavity [24].

Neuro-ophthalmic examination

The aim of the neuro-ophthalmic examination is to detect if there are any ophthalmologic dysfunctions related to a disorder affecting the nervous system. Neuro-ophthalmic examination begins by taking an accurate history and reviewing any systemic problems that could be relevant. A complete physical, neurological, and ophthalmological examination must be performed in any horse with a suspected neuro-ophthalmologic disorder. In this chapter we describe only the clinical assessment of the neuro-ophthalmologic pathways.

Vision

The pathways of conscious visual perception have been previously described (see Figure 14.6), and a lesion at any level can cause visual deficits. Clinical assessment of conscious vision (in dim- and bright-light conditions) is mainly performed by observing the horse moving in an unfamiliar environment, negotiating an obstacle course (maze test), and by assessing menace response [3, 5]. Unilateral visual deficits may be difficult to detect and this requires blindfolding each eye in turn.

The menace response is elicited by making a threatening gesture to the eye, involving the visual fields, and observing closure of the eyelids. It is important to avoid touching the eye/eyelashes or creating excessive air currents as this can trigger the palpebral and/or corneal reflex and therefore a false-positive menace response. The menace response should be undertaken in both medial and lateral visual fields. It requires an intact sensory pathway (i.e., optic nerve, optic chiasm, contralateral optic tract, contralateral LGN, contralateral optic radiation, and contralateral occipital cortex) and an intact motor pathway to elicit the expected response (closure of the eyelids) [3, 5].

From the visual cortex (occipital cortex), impulses are transmitted by association fibers to the primary motor cortex (frontal cortex) where the motor pathway of the menace response begins. This pathway has not yet been fully described. Axons from the motor cortex reach the pontine nucleus via projection fibers. Axons from the pontine nucleus decussate and enter the cerebellum via the middle cerebellar peduncle, reaching the cerebellar cortex, which is ipsilateral to the eye where the menace response is elicited. The cerebellum then coordinates this response by efferent cerebellar pathways that activate the facial nuclei in the ventrolateral part of the rostral medulla oblongata [3]. A recent study [34] has demonstrated by trans-synaptic

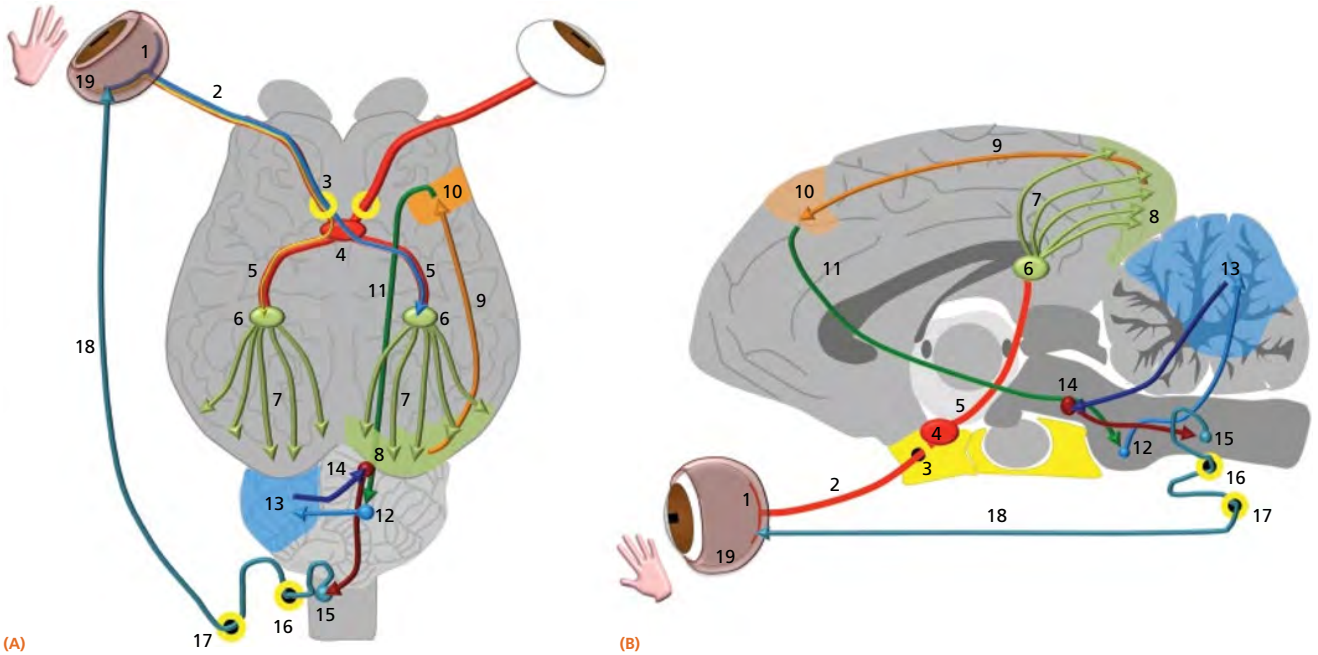


Figure 14.11 Neuroanatomic pathway for the menace response. (A) Dorsal and (B) lateral views. **1**, Retina; **2**, optic nerve; **3**, optic canal; **4**, optic chiasm; **5**, optic tract; **6**, lateral geniculate nucleus; **7**, optic radiation; **8**, occipital (visual) cortex; **9**, association fibers; **10**, frontal cortex; **11**, projection fibers; **12**, pontine nucleus; **13**, cerebellar cortex; **14**, red nucleus; **15**, facial nucleus; **16**, internal acoustic meatus; **17**, stylomastoid foramen; **18**, facial nerve; **19**, orbicularis oculi muscle.

tracing in mice that Purkinje cells in the cerebellar cortex project to the cerebellar interposital nucleus (CIN), the CIN sends projection fibers to the red nuclei in the midbrain (mainly to the red nucleus contralateral to the eye tested), and the red nuclei send projections to the facial nuclei (mainly ipsilateral to the eye tested) in the medulla oblongata [34, 35]. The axons emerge from the medulla oblongata and leave the cranial cavity via the internal acoustic meatus. At the base of the internal acoustic meatus, the facial nerve continues laterally through the facial canal of the petrous temporal bone and then curves caudoventrally in the caudal wall of the tympanum to exit the skull through the stylomastoid foramen [24].

The facial nerve (CN VII) innervates the orbicularis oculi muscle, eliciting a blink (menace response) (Figure 14.11). If the menace response is decreased or absent, the facial nerve needs to be evaluated by the palpebral reflex (see section **Palpebral reflex**) because facial nerve paresis/paralysis may result in reduced/lack of menace response without involving deficits of visual perception. Cerebellar lesions can also result in a lack of menace response from/to the ipsilateral side without involving deficit of visual perception, but signs of cerebellar dysfunction will also be present [33, 35, 36].

The menace response is a learned response and therefore is usually absent during the first 1–2 weeks of age [3]. It is important to remember that menace response is a cortically mediated response and therefore horses that are stressed, lethargic, or disorientated may not respond appropriately, without necessarily being affected by a lesion in the menace response pathway.

Palpebral reflex

Palpebral reflex is elicited by touching separately the lateral and medial canthus of the eye, which induces contraction of the orbicularis oculi muscle and therefore a blink (Figure 14.12). The sensory (afferent) arm of this reflex is mediated by small myelinated afferents of the trigeminal nerve, CN V (ophthalmic branch (medial canthus) and maxillary branch (lateral canthus)), while the motor (efferent) arm is mediated by the zygomatic branch (palpebral branches) of the auriculopalpebral nerve, which is a major branch of the facial nerve, CN VII. The palpebral reflex is present immediately after birth in foals [37]. The blink is the endpoint of some neuro-ophthalmologic tests (such as menace response, corneal reflex, and dazzle reflex); therefore the palpebral reflex should be performed before those mentioned tests in order to avoid false-negative results.

Pupillary light reflex

PLR is a subcortical reflex that regulates pupil size in response to the intensity of light that falls on the retina. This reflex assists in adaptation to various levels of darkness/brightness and is driven by activation of the photoreceptors (rods, cones, and ipRCGs) in different degrees of contribution. PLR is present immediately after birth; however, this reflex may be sluggish until the normal retina is fully developed [37]. Qualitative PLR is evaluated by shining a focal, bright light into the eye and assessing the ipsilateral (direct PLR) and the contralateral (indirect or consensual PLR) pupillary constriction.

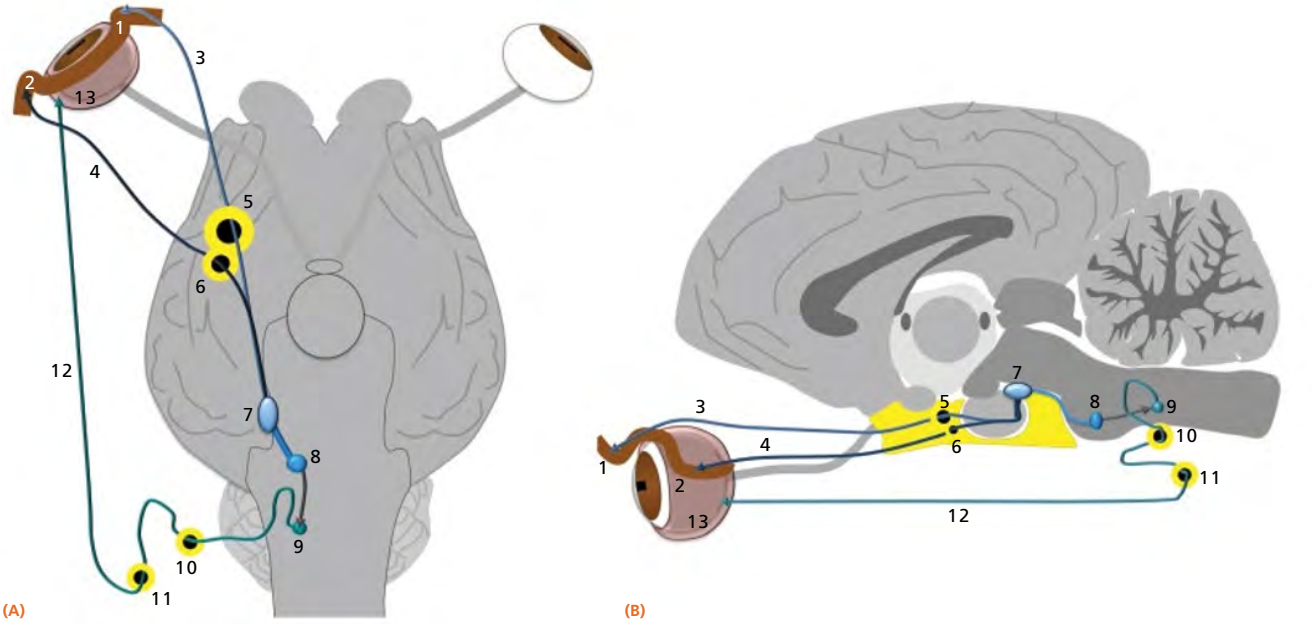


Figure 14.12 Neuroanatomic pathway of palpebral reflex. (A) Dorsal and (B) lateral views. **1**, Medial canthus of the eye; **2**, lateral canthus of the eye; **3**, ophthalmic branch; **4**, maxillary branch; **5**, orbital fissure; **6**, round foramen; **7**, trigeminal ganglion; **8**, trigeminal nucleus; **9**, facial nucleus; **10**, internal acoustic meatus; **11**, stylomastoid foramen; **12**, facial nerve; **13**, orbicularis oculi muscle.

Adult horses and foals have a diphasic PLR [37, 38]. The initial response to bright light is a rapid but small reduction in pupil diameter, followed by a second response, which is slower and causes further pupillary constriction. The anatomic pathway has been previously described (see Figure 14.9). PLR is stronger if the bright light is directed towards the area centralis (slightly dorsal to the optic nerve in the lateral retina). Consensual PLR is difficult to evaluate in the horse, as it is less prominent due to the amount of decussating fibers (around 20%) that contribute to indirect PLR. Moreover, evaluation of consensual PLR is awkward if the practitioner is alone, but, in these circumstances, the swinging light test could be a convenient substitute [33].

Assessment of consensual PLR is not necessary if menace response and direct PLRs are present in both eyes. However, consensual PLR can be of great value when assessing the afferent pathways (optic nerve and optic chiasm) in an eye where the posterior segment cannot be visualized, which means that direct PLR cannot be then assessed (such as in severe corneal edema). Retinal pathology detection benefits from chromatic PLR in dogs, which can distinguish between disorders affecting the outer photoreceptors (rods and cones) and the ipRCG, but this still needs to be validated in equine ophthalmology [39–41]. Stressful environments and noxious stimulation can result in pupil dilation (without any to little change in PLR response), due to the influence of the locus coeruleus on pupillary control via sympathetic activation and parasympathetic inhibition [42]. The locus coeruleus is a nucleus located at the level of the pons and is involved with physiological and psychological responses to stress and pain [42].

Other factors that may cause PLR to be reduced or absent include a low-intensity light source, iris atrophy, posterior synechiae, developmental anomalies of the iris, iris or ciliary body masses, and prior topical administration of a mydriatic agent [3, 43].

Swinging light (flashing) test

The anatomical pathway of the swinging light (flashing) test follows the same course as PLR. This test is performed using a bright light into one eye and, after direct PLR is achieved (pupillary constriction), the light source is quickly pointed to the other eye, in which further pupillary constriction is expected. The test is then performed in a reverse and repeated manner (swinging movements). If the pupil dilates when the light reaches the second eye, then an afferent optic pathway lesion (optic nerve, optic chiasm, or contralateral optic tract) is present in that second tested eye [33].

Dazzle reflex (photic blink reflex)

Dazzle reflex is another subcortical reflex induced by flashing the eye with a very strong light, which causes an eyelid blink. The blink is usually bilateral, but may be more complete in the tested eye. This reflex is present from birth in horses [37]. The afferent arm is similar to PLR; however, the efferent arm is mediated via the facial nerve, CN VII. Optic tract axons synapse in the rostral colliculus, and then tectonuclear axons course caudally to synapse in the facial nucleus at the level of the rostral medulla oblongata to elicit an eyelid blink (from here, the same efferent pathways as the palpebral reflex are followed). This reflex can be useful when the pupils cannot be visualized to

evaluate PLR, such as in patients with hyphema or severe corneal edema. However, the exact anatomical pathways have not been fully elucidated yet and therefore this reflex cannot be used on its own to localize subcortical lesions.

Corneal reflex

Corneal reflex is elicited by gently touching the cornea (avoiding the visual field) with a moistened and sterile stick swab, which results in the retraction of the eye globe (triggered by contraction of the retractor bulbi muscle, innervated by the abducent nerve, CN VI) and an eyelid blink (triggered by contraction of the orbicularis oculi muscle, innervated by the zygomatic branch of the auriculopalpebral nerve, which is a major branch of the facial nerve, CN VII) (Figure 14.13). Therefore this reflex requires an intact sensory (afferent) arm (ophthalmic branch (long ciliary nerves) of the trigeminal nerve, CN V) and an intact motor (efferent) arm (abducent nerve, CN VI, and facial nerve, CN VII) (Figure 14.13). The sensitivity of the cornea can be quantified by a corneal esthesiometer, which measures the corneal touch threshold (CTT) (minimum pressure against the cornea to elicit corneal reflex). A recent study has shown major differences in CTT between species, with the horse and the sheep having the most sensitive cornea [44]. Regions of the cornea that are less exposed to potential injury (near the eyelid margins) are less sensitive than the central cornea, and these regions may elicit a weaker reflex [5].

Vestibulo-ocular reflex: physiological nystagmus

Vestibulo-ocular reflex (VOR) is a type of involuntary ocular movement evoked in response to vestibular stimuli. The aim of this physiological reflex is to stabilize the gaze in space, proving a clear vision while the head is moving or during locomotion. VOR is elicited by moving the head from side to side in a horizontal plane (physiological nystagmus), which induces slow compensatory intervals (slow-phase: eyes move in the opposite direction to head movement) and high-velocity reorientating movements (fast-phase: eyes move in the direction of head movement). The visual afferent system is not involved in this reflex; if you close your eyes and move your head from side to side, you can feel your eyeballs moving with your finger tips—this is your VOR. However, active visual experience is required during early and adult life to develop and maintain a normal VOR [45–47]. The anatomical pathway of this reflex has been previously described (see Figure 14.7) [20].

Clinical presentation and aetiologies of neuro-ophthalmic disorders

This section describes disorders related to post-retinal visual deficits, post-retinal pupillary dysfunction, abnormal eye movements, abnormal eyeball position, NKCS, neurotrophic keratitis, facial nerve dysfunction, middle cranial fossa syndrome, and photic head shaking.

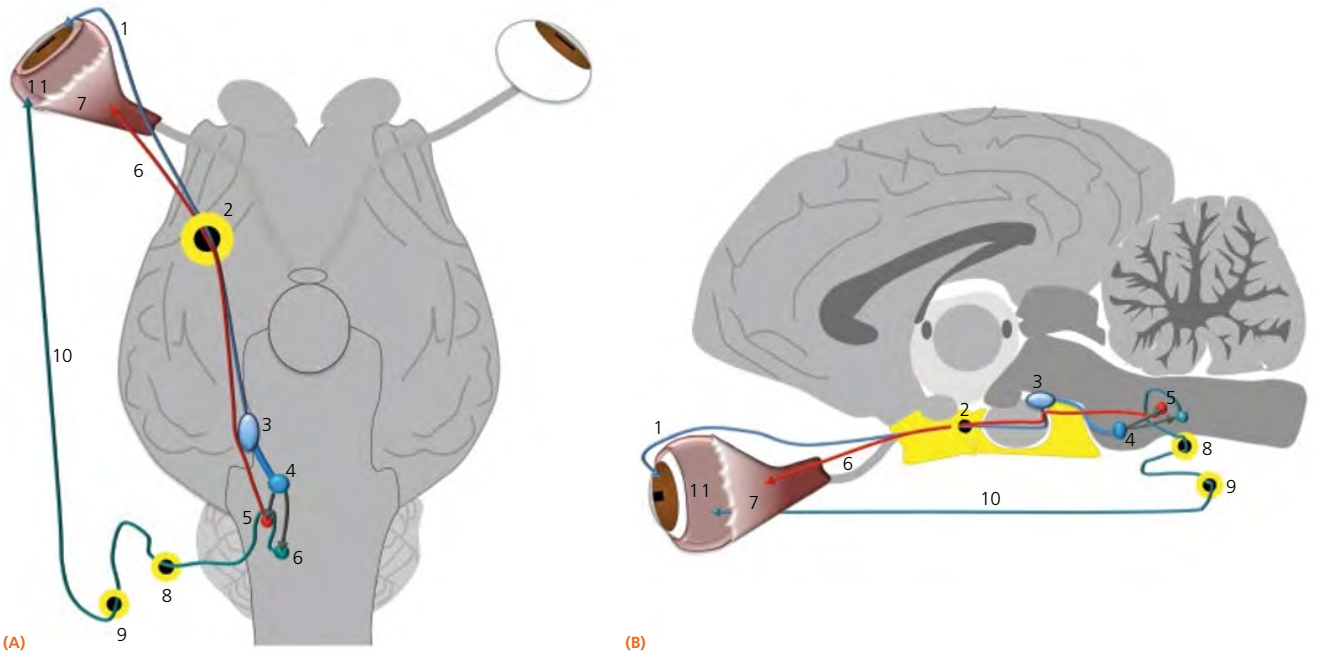


Figure 14.13 Neuroanatomic pathway of corneal reflex. (A) Dorsal and (B) lateral views. **1**, Ophthalmic branch; **2**, orbital fissure; **3**, trigeminal ganglion; **4**, trigeminal nucleus; **5**, abducent nucleus and abducent nerve; **6**, facial nucleus; **7**, retractor bulbi muscle; **8**, internal acoustic meatus; **9**, stylomastoid foramen; **10**, facial nerve; **11**, orbicularis oculi muscle.

Neurologic causes of post-retinal visual deficits

Signalment, clinical history, ophthalmic examination (particularly of the fundus), and electroretinography (ERG) are essential in cases with visual deficits to differentiate lesions affecting the retina from post-retinal lesions. Retinal lesions that may result in visual deficits such as congenital stationary night blindness, retinal dysplasia (as part of multiple congenital ocular abnormalities (MCOA) in the Rocky Mountain horse, or in isolation), retinal degeneration (including equine motor neuron disease (EMND)), chorioretinitis, retinal detachment, and other retinopathies are discussed in Chapter 11.

The use of handheld spectral-domain optical coherence tomography (SD-OCT) has been recently proven feasible to characterize normal corneal, retinal, and optic nerve head anatomy *in vivo* in sedated standing horses [16]. However, further studies are needed to evaluate the diagnostic potential of SD-OCT for the equine eye with vision loss. Lesions affecting any of the structures involving visual perception can cause post-retinal visual deficits in the following structures: optic nerve (optic neuropathy), optic chiasm, optic tract, LGN, optic radiation, and/or visual cortex, either unilaterally or bilaterally (see Figure 14.6).

If visual deficits are present, PLR is sometimes useful to differentiate between cortical and subcortical lesions. PLR will be present in both eyes if the lesion is only affecting the LGN, the optic radiation, or the visual cortex. If there is absent/decreased direct and indirect PLR with post-retinal visual deficits, the lesion is located in either the optic nerve (ipsilateral to absent direct PLR and visual deficits), optic chiasm (bilaterally absent direct and indirect PLR and visual deficits), or optic tract (contralateral to the absent direct PLR and visual deficits).

Optic neuropathy

Lesions affecting the optic nerve are divided into congenital and acquired lesions. Congenital optic neuropathies are discussed in Chapter 4. Acquired optic neuropathies mainly involve inflammatory/infectious, neoplastic, vascular, compressive, degenerative, traumatic, and toxic disorders. A rapid onset of visual deficits is usually seen in inflammatory, vascular (mainly ischemic), and traumatic causes. A chronic course of visual impairment is usually caused by compressive, neoplastic, and degenerative disorders.

The main neurologic signs of optic neuropathy include visual deficits and decreased to absent direct and consensual PLR. Fundus examination may identify a normal, swollen, or pale optic disc, peripapillary vascular attenuation, prominence of the lamina cribosa, and/or proliferation of neural tissue within/from the optic nerve head [48]. Magnetic resonance imaging (MRI) is currently the optimal imaging modality to diagnose optic neuropathy and delineate the extent of the lesion in horses with a normal fundus examination. Computed tomography (CT) is of advantage for evaluating bony structures and osteolytic/osteoproliferative lesions; however, CT is limited in defining soft-tissue structures.

Optic neuritis

Inflammatory disorders affecting the optic nerve in horses are usually seen in association with uveitis and chorioretinitis, and they may also occur in septicemia and multifocal CNS diseases. Underlying etiologies can be divided into infectious and noninfectious causes. Infectious etiologies of optic neuritis include viral (Borna disease, equine herpesvirus type 1, Suid herpesvirus type 1, *Flaviviridae* (West Nile virus, Japanese encephalitis virus), *Alphaviridae* (Eastern equine encephalitis, Western equine encephalitis, Venezuelan equine encephalitis), bacterial (*Actinobacillus equi*), fungal (*Cryptococcus neoformans*, *Aspergillus* spp.), and parasitic (*Halicephalobus gingivalis*) [49–57]. Infectious diseases usually involve multiple organ systems and therefore systemic signs are often present. Noninfectious optic neuritis can be caused by exudative optic neuritis (often with a history of trauma, haemorrhage, or colic) or has an immune-mediated cause.

Clinical signs associated with optic neuritis usually have an acute onset and include unilateral or bilateral visual deficits with dilated pupils, and decreased to absent PLRs. Diagnosis is based on the history, signalment, physical and neuro-ophthalmic examination, and advanced imaging [58].

Treatment of optic neuritis is based on the underlying cause, but if the etiology remains unknown, and infectious causes have been excluded, a trial with immunosuppressive medications may be indicated. Prognosis is variable and depends on the underlying cause [58]. However, studies that analyze prognostic factors of vision recovery in cases of equine optic neuritis are lacking.

Optic nerve neoplasia

Neoplasia of the optic nerve is rare in horses. There are only single case reports describing meningioma, astrocytoma, and malignant medulloepithelioma affecting the optic nerve [59–62]. The clinical signs include unilateral vision loss and absent to decreased PLR. Fundus examination may be normal and exophthalmia has been reported in a horse with retrobulbar meningioma [59]. Presumptive diagnosis of optic neoplasia is based on history, signalment, neuro-ophthalmic examination, and advanced imaging [59]. Prognosis of optic nerve meningioma with unilateral vision is considered good after surgical treatment (enucleation) followed by radiotherapy [59].

Ischemic optic neuropathy

Ischemic optic neuropathy can occur due to sudden onset of hypoxia or hypotension to the optic nerve. The underlying causes include systemic illness and severe blood loss (such as might occur in mycosis of the guttural pouch). Surgical occlusion of the external and internal carotid and greater palatine arteries, performed as part of the management of guttural pouch mycosis, has also been reported as a cause of ischemic optic neuropathy [63, 64]. The clinical signs are associated with acute onset of blindness (unilateral or bilateral absent vision and

absent/decreased PLR) within 24–48 hours of the severe hypoxemia or hypotension. Diagnosis is made according to the clinical history and physical and neuro-ophthalmic examinations. Fundus examination may be normal or show optic disc pallor, retinal edema, and/or hemorrhages, depending on time of presentation after injury. With time, the lesion resembles optic nerve atrophy and peripapillary retinal degeneration. Treatment is based on addressing the underlying systemic cause, but prognosis for return of vision is very poor [56, 58, 63].

Compressive optic neuropathy

Compressive optic neuropathy can result from infectious, inflammatory, and neoplastic processes affecting the surrounding tissues, including the sphenoid and palatine sinuses. Clinical signs include vision loss and decreased/absent direct PLR. Other cranial nerve deficits can be present if the lesion extends caudally (including CN III, IV, and VI, and the ophthalmic branch of CN V). Advanced imaging (CT or MRI) is optimal to diagnose disorders involving the optic nerve(s) and delineate the extent of the lesion [65]. Treatment and prognosis vary with the cause of the compressive disease.

Proliferative optic neuropathy

Proliferative optic neuropathy is a disorder primary found in old horses (more than 15 years of age). The underlying cause is unknown, but it has been postulated that it may represent reaction of the glial cells to a non-specific insult [66]. Some authors have hypothesized that these lesions represent an astrocytoma or a granular cell tumor [60]. Clinical signs may include mild vision loss (usually unilateral) and occasionally head shaking, but it may also be asymptomatic. Fundus examination reveals a protruding mass from the optic disc into the vitreous (Figure 14.14). There is no treatment and prognosis is fair as there is little effect on visual perception [66, 67].

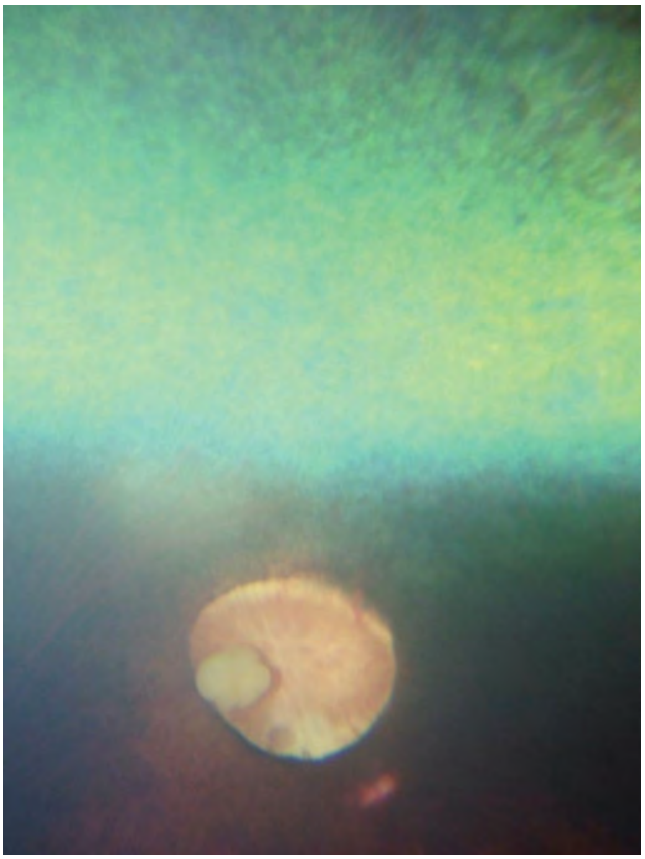


Figure 14.14 Proliferative optic neuropathy in a 14-year-old Fell pony gelding as an incidental finding. Note the cream protruding mass at approximately 8 o'clock position on the optic nerve head, and a small coloboma of the optic nerve head (small circular gray-colored cup-like lesion) at 6 o'clock as an additional incidental finding.

Traumatic optic neuropathy

Traumatic optic neuropathy results as a focal damage from rapid deceleration and stretching of the optic nerve(s) following traumatic brain injury [68]. This type of neuropathy is mainly characterized by hemorrhage, edema, pronounced ischemia, and irreversible neuronal damage. Avulsion of both optic nerves has also been reported after head trauma in horses [69]. Clinical signs include vision loss with absent PLR (usually bilaterally). Fundus examination may reveal peripapillary hemorrhage or edema in some cases, but many cases appear normal if the optic nerve damage is retrobulbar in nature. The presumptive diagnosis is made based on the history of head trauma, vision loss, absent PLR, and fundus examination. Advanced imaging of the head can document further the consequences of traumatic brain injury with optic neuropathy [68, 70]. Treatment is limited and high doses of corticosteroids should be avoided due to lack of demonstrated clinical efficacy on traumatic optic neuropathy [71]. Current suggested therapies in horses include systemic iron, calcium chelation therapy, and nonsteroidal anti-inflammatory therapy [68]. Prognosis is guarded and there are no reports of horses recovering vision with traumatic optic neuropathy following traumatic brain injury to date [68].

Toxic optic neuropathy

Ivermectin and pyrantel toxicosis have been reported as potential causes of bilateral blindness with absent PLR in combination with other neurological signs (depression, all four limb ataxia, drooping of the superior and inferior lips, muscle fasciculation, absent palpebral reflexes) [72, 73]. Diagnosis of ivermectin toxicosis was based on history of exposure, clinical signs, and brain tissue concentration; however, histopathologic changes on optic nerves have not yet been reported in horses [72]. On the other hand, the horse with suspected pyrantel toxicosis underwent post-mortem examination, which revealed myelin loss axonal degeneration, gitter cells, and patchy lymphocyte accumulation affecting both optic nerves and optic tracts [73]. Treatment is mainly based on supportive care and time. Visual recovery is possible if the horse survives the initial toxicity.

Optic chiasm lesions

An optic chiasm lesion can result in bilateral vision loss and bilateral decreased to absent PLRs. Disorders affecting the optic chiasm include intracranial extension of orbital lesions (neoplasia or inflammation), disease of the sphenopalatine sinus, traumatic brain injury, CNS diseases (neoplasia, inflammatory or congenital), and tumors of the pituitary area that extend rostrodorsally through the incomplete pituitary diaphragm [3, 65, 68]. CT or MRI are the optimal imaging modalities to diagnose disorders involving the optic chiasm and delineate the extent of the lesion. Cerebrospinal fluid analysis may also contribute to the diagnosis. Treatment and prognosis depend on the underlying cause.

Optic tract, LGN lesions, optic radiation, and visual cortex

Lesions (inflammatory, infectious, metabolic, neoplastic, traumatic, and vascular) in the optic tract, LGN, optic radiation, and visual cortex will cause contralateral vision deficits. Lesions in the thalamic area can also affect the optic tract and LGN. It is important to remember that if the lesion affects the rostral part of the optic tract, PLRs could also be affected. Horses with cerebral cortex involvement may also present with seizures, decreased consciousness, contralateral postural reaction deficits, and ipsilateral head turn.

Metabolic causes, such as hepatic encephalopathy, usually cause bilateral involvement of the cerebral cortex and therefore reduced vision or blindness in both eyes with normal PLRs. Ischemia and/or hypoxia during anesthesia are potential factors in the development of post-anesthetic cortical blindness due to cerebrocortical necrosis, and this type of blindness can be transient or irreversible, depending on the severity of cerebral damage [74, 75]. Blindness after iatrogenic intracarotid injection may result in ipsilateral forebrain cerebrovascular ischemia/toxicity, which has been reported to cause contralateral vision loss with normal PLR [76].

Transient vision loss (cortical blindness) of variable duration after an epileptic event can be present in horses, and the exact pathophysiology remains unknown. There is no correlation between the severity and length of seizures and the transient cortical blindness [3]. Transient blindness has also been reported in a horse with cholesterinic granuloma in the lateral ventricles, which was likely associated with intermittent release of noxious substances from the cholesterinic granulomas or unrecognized ictal or postictal activity [77].

CT and MRI are the optimal imaging modalities to diagnose disorders involving the thalamic area and visual cortex and also to delineate the extent of the lesion. Cerebrospinal fluid analysis may contribute to the diagnosis. Treatment and prognosis depend on the underlying cause.

Neurological causes of strabismus and pathological nystagmus

Strabismus is an abnormal position of the eyeball relative to the orbit. There are two main types of strabismus: positional or vestibular strabismus and fixed or neuromuscular strabismus [20, 23, 78]. Vestibular strabismus is a clinical sign of vestibular dysfunction and it is seen when the head and neck move dorsal or ventral due to loss of antigravity tone (ventrolateral deviation of one eye in certain positions of the head (ventrolateral strabismus)) [20, 78]. With neuromuscular strabismus the eyeball is fixed in a deviated position regardless of head position. Neuromuscular strabismus can be due to loss of innervation of the extraocular muscles or myopathy of the extraocular muscles. The direction of the neuromuscular strabismus depends on the affected cranial nerve or extraocular muscle(s) (see Figure 14.7). Dysfunction of the oculomotor nerve, CN III, results in ventrolateral strabismus; dysfunction of the trochlear nerve, CN IV, results in rotation of the globe (the ventral aspect of the pupil moves dorsomedially); and dysfunction of the abducent nerve, CN VI, results in medial strabismus and enophthalmos [69]. Neuromuscular strabismus can be caused by orbital or intracranial disorders, including congenital, inflammatory, infectious, neoplastic and traumatic processes. With intracranial disorders, neuromuscular strabismus is usually seen as part of the middle cranial fossa syndrome (see section **Middle cranial fossa syndrome**).

Physiological jerk **nystagmus** is a rhythmical and reflexive eyeball movement, which can be assessed clinically by performing the VOR (see section **Vestibulo-ocular reflex: physiological nystagmus**). Pathological jerk nystagmus occurs with unilateral dysfunction of the vestibular system. Physiological jerk nystagmus and pathological jerk nystagmus are absent with bilateral vestibular dysfunction. The abnormal nystagmus may be continuous (resting or spontaneous nystagmus) or may be observed when the head changes position (positional nystagmus). The direction of nystagmus is defined as the direction of the fast phase of the nystagmus (right or left), and also as the plane of rotation (horizontal, vertical, or rotatory). The fast phase direction is usually away from the side of the lesion, except in cases of central vestibular disease with a paradoxical vestibular dysfunction. Pathological vertical nystagmus has been associated with dysfunction of the central vestibular system; however, this clinical sign should not be the only sign used to differentiate between a central and peripheral vestibular dysfunction [20].

Anisocoria and Horner's syndrome

Anisocoria is a condition characterized by unequal pupil size. Resting pupil size and possible asymmetry should be assessed (by distant direct ophthalmoscopy) in normal light and then in a darkened room. Neurological causes of anisocoria with normal vision involve lack of parasympathetic tone to the iris constrictor muscles (mydriatic pupil) or lack of sympathetic tone to the iris dilator muscles (miotic pupil, Horner's syndrome) [19].

The parasympathetic component of the oculomotor nerve can be affected by a lesion located between the rostral midbrain and the periorbita and cause a dilated and unresponsive pupil with normal vision (normal menace response, absent direct PLR when the affected pupil is tested, and absent indirect PLR



Figure 14.15 Equine dysautonomia in a 16-year-old horse. The horse showed bilateral ptosis with ventral deviation of the eyelashes secondary to loss of sympathetic eyelid tone.

when the contralateral eye is tested). In some cases, a mydriatic pupil with normal vision (internal ophthalmoplegia) could be the first indication of middle cranial fossa syndrome (see section **Middle cranial fossa syndrome**) and it is also presented in conjunction with a ventrolateral neuromuscular strabismus due to involvement of the motor component of the oculomotor nerve [23].

Horner's syndrome is a clinical disorder caused by a lack of sympathetic innervation to the head. The most common clinical signs include ptosis of the upper eyelid, lowering the upper eyelashes (Figure 14.15), decreased tone of the lower eyelid, hyperthermia, and sweating of the face and/or neck (marked sweating persists for 24–48 hours). Enophthalmos, protrusion of the nictitating membrane, and a mildly miotic pupil (the degree of miosis seen in horses is not as dramatic as the miosis seen in small animals with Horner's syndrome) are less commonly reported signs. The miotic pupil in patients with Horner's syndrome is most noticeable in the dark because the normal pupil dilates and the affected pupil remains miotic.

Horner's syndrome results from lesions affecting the first-, second- (preganglionic), or third-order (postganglionic) neurons (see Figure 14.10). Because of the proximity of other structures within the hypothalamus, brainstem, or spinal cord (tectotegmental spinal tract), first-order Horner's syndrome in isolation is unlikely (Table 14.1). Preganglionic Horner's syndrome (second-order Horner's syndrome) is frequently caused by a tumor or trauma (including iatrogenic trauma after perivascular jugular vein injections). Nerve root avulsion disrupting the preganglionic axons may produce symptoms referable to the brachial plexus distribution. Postganglionic Horner's syndrome (third-order Horner's syndrome) can be caused by conditions ranging from the relatively insignificant or even idiopathic to life threatening (Table 14.1). The anatomical distribution extends from the internal carotid artery to the middle cranial fossa, orbital fissure, and eyeball.

Presence of other clinical signs in association with Horner's syndrome can help to localize the lesion and formulate the differential diagnosis list (Table 14.1). Treatment is directed at treating the underlying cause; however, even if the underlying cause is resolved, permanent deficits are still possible.

Equine dysautonomia (syn. equine grass sickness) is a disorder characterized by neuronal degeneration in the autonomic and in the enteric nervous systems. The disease has been reported mainly in the UK, but also in other areas of Europe, and in a mule in the USA [79–81]. It has been strongly associated with grazing (as the name suggests) and only a few cases had no exposure to pasture. Young adult horses are usually affected with an acute, subacute, or chronic presentation. The underlying cause still remains unknown; however, the current theory states that equine dysautonomia represents a toxin-mediated infection with *Clostridium botulinum* type C, where the neurotoxin is ingested, causing chromatolytic degeneration and neuronal loss in the autonomic, somatic, and myenteric nervous systems. The main neuro-ophthalmologic signs include bilateral ptosis, which results from sympathetic denervation of the Müller's superior tarsal muscle (Figure 14.15). Other systemic and neurologic signs are present, including anorexia, dullness, abdominal pain, nasogastric reflux, dysphagia, tachycardia, patchy sweating, gastrointestinal distension, and weight loss. Definitive diagnosis is made by histopathologic demonstration of the pathognomonic lesions in autonomic/enteric ganglia [82, 83]. Additional diagnostic information to achieve the presumptive diagnosis of equine dysautonomia is the use of phenylephrine (diluted to 0.5% with normal saline) eyedrops in horses with bilateral ptosis, which results in temporary reversal of this clinical sign [84]. These results have to be assessed in the context of the signalment, clinical presentation, and the results of other ancillary diagnostic tests [79].

Pharmacological testing procedures can be used to determine if the dysfunction is preganglionic or postganglionic in both parasympathetic and sympathetic denervation. These tests rely on denervation hypersensitivity, and postganglionic lesions will respond quicker. Denervation hypersensitivity takes about 7 days to occur after the onset of clinical signs, which limits their use. Moreover, these tests should not be used as the only method to localize the lesion, as, by some authors, they are considered not reliable [19].

Neurogenic keratoconjunctivitis sicca

KCS in the horse is a progressive inflammatory condition of the cornea and conjunctiva caused by a lack of aqueous tears. It is considered neurogenic (NKCS) when the lesion affects any part of the parasympathetic innervation to the lacrimal gland by the facial nerve, CN VII. Depending on the location of the lesion along this parasympathetic pathway, other neurological deficits may be present (Table 14.2).

NKCS may be present with ipsilateral dry nares if the lesion affects the preganglionic parasympathetic fibers or if the lesion is located at the level of the pterygopalatine

Table 14.1 Lesion location, associated clinical signs, and differential diagnoses for Horner's syndrome.

Order of Horner's syndrome	Localization	Possible signs of dysfunction that *could* be present ipsilateral to Horner's syndrome	Possible underlying causes
First-order neuron	Brainstem	Altered level of consciousness CN deficits from CN III to XII General proprioceptive ataxia Central vestibular dysfunction Paresis or plegia on ipsilateral side of the body Sweating and hyperthermia of the entire ipsilateral side of the body	Equine protozoal myeloencephalitis Traumatic brain injury Vascular CNS neoplasias
First-order neuron	Lateral tectotegmental spinal tract (C1–C5 spinal cord segments)	General proprioceptive ataxia Paresis or plegia on all four limbs or ipsilateral Cervical spinal hyperalgesia Cervical muscle spasm/rigidity Sweating and hyperthermia of the entire ipsilateral side of the body	Equine protozoal myelitis Aberrant helminth migration Vertebral fractures Vascular CNS neoplasias
First-/second = order neuron	C6–T2 spinal cord segments	General proprioceptive ataxia Paresis or plegia on all four limbs or ipsilateral Decreased spinal reflexes in thoracic limb(s) Increased spinal reflexes in pelvic limb(s) Lameness (nerve root signature) Cervicothoracic spinal hyperalgesia	Same as C1–C5 spinal cord segments
Second-order neuron	T3–L3 spinal cord segments	General proprioceptive ataxia Paresis or plegia on pelvic limb(s) Increased spinal reflexes in the pelvic limb(s) Cranial thoracic spinal hyperalgesia Cutaneous trunci muscle decreased or absent Dysfunction of micturition (upper motor neuron bladder) and defecation	Same as C1–C5 spinal cord segments
Second-order neuron	T1–T3 ventral nerve roots	Lameness (nerve root signature) Cutaneous trunci muscle reflex decreased or absent	Cranial thoracic neoplasia Infection Trauma
Second-order neuron	Vagosympathetic trunk	Laryngeal paralysis Dysphagia Cough Regurgitation	Thymoma Lymphoma Thyroid tumor Trauma Iatrogenic trauma after perivascular jugular vein injections
Third-order neuron	Guttural pouch	Facial paresis/paralysis Masticatory muscle atrophy Decreased sensation in the inferior lip Dysphagia Dorsal nasopharyngeal collapse Inspiratory dyspnea (laryngeal paralysis/paresis) Neck muscle atrophy Tongue dysfunction	Guttural pouch empyema Mycosis Guttural pouch hemorrhage (mycosis or longus capitis avulsion) Tympani
Third-order neuron	Middle cranial fossa Retrobulbar area	Exophthalmos Hyperesthesia on palpation CN deficits II, III, IV, V (ophthalmic), VI	Orbital tumors Inflammation Trauma Invasive pituitary tumor
Second-/third-order neuron	Bilateral Horner's syndrome	Colic Dysphagia Tachycardia	Equine dysautonomia

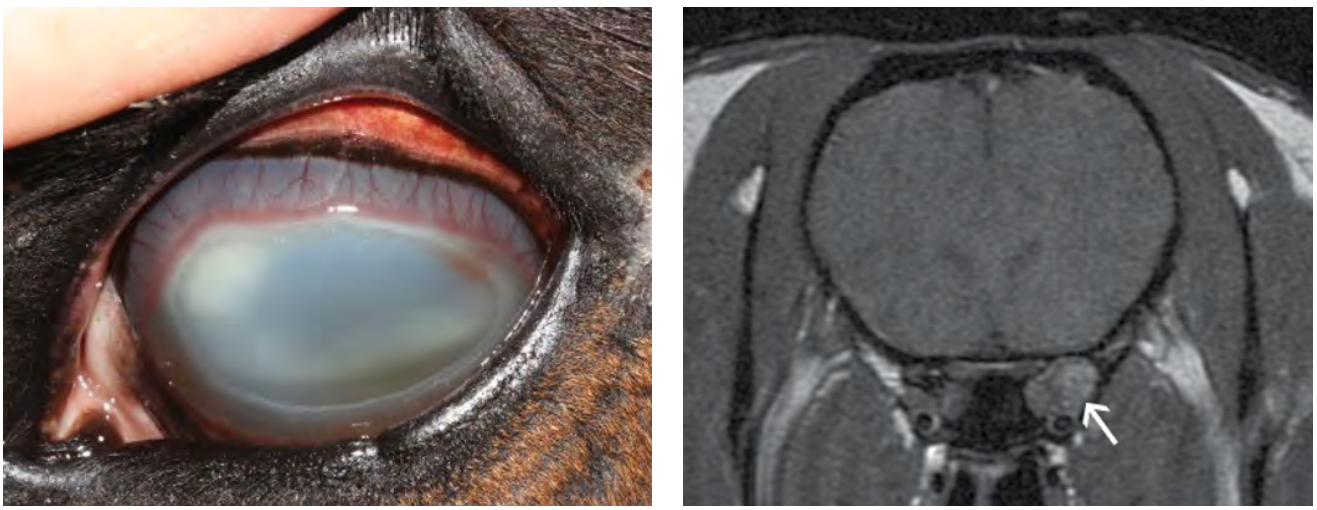
ganglion. Ipsilateral facial paralysis and ipsilateral dry nares may be present in conjunction with NKCS if the lesion occurs proximal or at the level of the geniculate ganglion. If the lesion occurs at the level of the internal acoustic meatus, then peripheral vestibular signs may also be present in conjunction with facial paralysis and dry nares. If the lesion is at the level of the medulla oblongata, other brainstem signs in conjunction with the facial paralysis and NKCS will be present (altered mental status, ipsilateral postural reactions deficits, facial paralysis, and the possibility of other cranial nerves affected) [23, 24].

Facial neuropathy due to trauma (e.g., fracture of the mandible) is considered one of the most common underlying causes for NKCS; however, other possible causes should be taken into account. Possible associated clinical signs and underlying causes of NKCS are summarized in Table 14.2.

Table 14.2 Lesion location, associated clinical signs, and differential diagnoses for NKCS.

Location of the lesion	Possible signs of dysfunction that *could* be present ipsilateral to NKCS	Diseases
Brainstem (rostral medulla oblongata)	Altered level of consciousness Facial paralysis Dry nares Ipsilateral postural reaction deficits Central vestibular syndrome (if CN VIII is also affected)	Traumatic brain injury EPM Other infectious CNS diseases Vascular
Facial nerve in IAM, facial canal, or at the level of the GG (preganglionic PF)	Facial paralysis Dry nares Peripheral vestibular syndrome (if CN VIII is also affected)	Otitis media/interna Guttural pouches disease Head trauma (skull fractures) Temporohyoid osteoarthropathy Polyneuritis equi
Small petrosal canal, pterygopalatine canal, pterygopalatine fossa (preganglionic PF distal to the GG and pterygopalatine ganglion)	Dry nares Decreased to absent facial/corneal sensation (if ophthalmic and maxial branches of CN V are also affected)	Temporohyoid osteoarthropathy Hypothyroidism Parotid gland disease Periorbital cellulitis Dental abscess
Postganglionic parasympathetic fibers	Decrease to absent periocular sensation (maxillar branch of the CN V)	Hypothyroidism

CN, Cranial nerve; EPM, equine protozoal myeloencephalitis; CNS, central nervous system; IAM, internal acoustic meatus; GG, geniculate ganglion; PF, parasympathetic fibers.



(A) (B)

Figure 14.16 (A) A 16-year-old Warmblood gelding presented with a 2-week history of a nonhealing corneal ulcer in the left eye. There was loss of corneal sensation with mild depth stromal ulcer (consistent with neurotrophic keratitis). (B) Transverse T1-weighted image at the level of the orbital fissure and round foramen. There is an enlargement of the ophthalmic and maxillary branches of the left trigeminal nerve (**arrow**). Histopathology was consistent with severe granulomatous neuritis.

Neurotrophic keratitis

Neurotrophic keratitis is a type of neurogenic keratitis, and poor corneal healing is due to loss of corneal sensation (general somatic afferent system), which is provided by the ophthalmic branch of the trigeminal nerve (Figure 14.16). In horses with neutrophic keratitis, the corneal reflex (see Figure 14.13) is severely decreased to absent [26, 85]. If clinical signs are consistent with a dysfunction of the ophthalmic branch, further neurological evaluation should be done to assess all the areas innervated by the trigeminal nerve (see Figure 14.8).

Neurogenic keratitis may be the first clinical sign that a horse with trigeminal neuropathy exhibits [85]. Facial hypalgesia or analgesia is caused by a lesion affecting the ipsilateral trigeminal nerve, ipsilateral trigeminal ganglion, or ipsilateral trigeminal nucleus in the brainstem and/or the contralateral forebrain. If facial hypalgesia/analgesia is presented together with a decreased to absent palpebral reflex and corneal reflex, then the lesion is limited to the ipsilateral trigeminal nerve, ipsilateral trigeminal ganglion, and/or ipsilateral trigeminal nucleus. The most likely underlying causes for a trigeminal neuropathy

involve inflammatory and neoplastic disorders arising either from the trigeminal nerve or from surrounding structures (see Figure 14.16) [26, 85, 86]. However, if facial hypalgesia is presented in all the areas innervated by the trigeminal nerve but their associated reflexes are normal, then a lesion in the ipsilateral midbrain or the contralateral forebrain should be suspected and other intracranial signs are also likely to be present (such as seen in equine protozoal myeloencephalitis, cerebral abscesses, and filarid nematode infection) [86]. Diagnosis of neurotrophic keratitis is based on neuro-ophthalmic examination, but to investigate the possible underlying causes, advanced imaging of the head may be required (see Figure 14.16). Treatment and prognosis depend on the underlying cause.

Facial nerve paresis/paralysis

Lesions affecting the facial motor nucleus (rostral medulla oblongata) or anywhere in the course of the facial nerve can result in facial paresis (some motor function still present) or facial paralysis (complete loss of motor function) [23]. If the lesion occurs anywhere from the facial motor nucleus to the exit of the facial nerve through the stylomastoid foramen, complete facial paralysis/paresis of the muscles of facial expression will be evident. However, if the lesion affects individual branches of the facial nerve along their course to the muscles they innervate, then the clinical signs will be associated with paresis/paralysis of the specific muscle or group of muscles [23] (Figure 14.17).

Clinical features of acute complete paralysis of the muscles of facial expression include a dropped ear, lagophthalmos, a decreased palpebral fissure, a dropped lip, ptosis (due to paresis/paralysis of the levator anguli oculi medialis), and deviation of the nose and superior lip towards the unaffected side (this is due to contraction of the muscles of the lip and nose of the unaffected side (see Figure 14.17)) [19]. In chronic facial paralysis, the facial muscles undergo atrophy with fibrous contracture due to the lack of nerve stimuli. Therefore horses with chronic facial paralysis may have deviated lips and the nares towards the paralysed side, which deforms the facial expression permanently. Collapse of the external nares can also be observed in horses with facial paralysis during exercise. The palpebral reflex is also absent on the affected side. It is important to remember that blink is the endpoint of some neuro-ophthalmologic tests (such as menace response, corneal reflex, and dazzle reflex); therefore the palpebral reflex should be performed before those mentioned tests in order to avoid false-negative results.

A Schirmer tear test (STT) is indicated in every facial paralysis case (normal STT is 11–30 mm wetting/min, and may be reduced in systemically sick foals) to assess the parasympathetic innervation to the lacrimal gland, also provided by the facial nerve. The cornea should also be assessed carefully for any signs of keratitis, with or without ulceration.

If the horse has facial paralysis/paresis with NKCS due to lack of parasympathetic innervation to the lacrimal gland, the lesion has to be located before branching of the nerve at the level of the geniculate ganglion in the petrous temporal bone. The facial nerve and the vestibulocochlear nerve are closely associated from the medulla to the petrous temporal bone, where the internal acoustic meatus is located. If the lesion is located at this level, then facial paralysis and vestibular dysfunction are often present together (such as in the case of otitis media/interna, temporohyoid osteoarthropathy, meningitis, and multicentre



(A) (B) (C)

Figure 14.17 A 7-year-old Thoroughbred gelding with left facial paralysis limited to the nose and the lip muscles. Note that (A) the ear and eyelid position are normal, (B) the horse is able to blink spontaneously, and (C) palpebral reflex is present. The cause was due to compression of the buccal branches of the facial nerve (on their external course over the ramus of the mandible) after prolonged lateral recumbency for cataract surgery on the right eye. Neuropraxia (loss of function without loss of axonal continuity) of those branches was suspected as the horse recovered after 3 weeks.

lymphoma) [87–90]. Disorders affecting the rostral medulla oblongata could cause facial paralysis, NKCS, and clinical signs associated with dysfunction of other systems located at the same level (hemiparesis, tetraparesis, proprioceptive/vestibular ataxia, lethargy, and other cranial nerves), such as is seen in equine protozoal myeloencephalitis, hematomas, intracarotid drug injection, and bacterial meningoencephalitis [89, 91, 92].

Facial trauma (due to prolonged lateral recumbency after surgical procedures, fractures of the stylohyoid bone, fractures of the petrous temporal bone, or fractures of the vertical ramus of the mandible) is a common cause of facial paralysis [23]. Idiopathic facial paralysis is also possible in horses and its diagnosis is made by exclusion [23].

Treatment is based on addressing the underlying cause of the facial paralysis if possible. Frequent lubrication of the cornea with artificial tears is necessary in horses that have lost the ability to blink, to provide protection to the cornea and avoid exposure keratitis. Temporary partial tarsorrhaphy may also be necessary in these cases if the facial nerve function has not returned within 7–10 days [58]. Electroacupuncture may promote recovery and hasten time to recovery in horses with traumatic facial paralysis [93]. In racing horses with highly demanding athletic activity, surgery may be required to prevent collapse of the alar cartilage and therefore increase airflow through the nares [94–96]. The prognosis for full recovery depends on the underlying cause; recovery can take weeks, months, or even years [58].

Middle cranial fossa syndrome

Middle cranial fossa syndrome (also known as cavernous sinus syndrome) is a clinical disorder characterized by dysfunction of several cranial nerves that course at the level of the middle cranial fossa and pass through the orbital fissure, which include: CN III (motor and parasympathetic component), CN IV, CN VI, the ophthalmic branch of the CN V, and postganglionic sympathetic nerve fibers. The maxillary branch of the CN V, which passes through the round foramen, can also be affected [23].

The most common clinical signs involve internal and external ophthalmoparesis/plegia. Internal ophthalmoplegia refers to paralysis of the iris and ciliary muscles (mydriasis), whereas external ophthalmoplegia refers to paralysis of the extraocular muscles (ipsilateral absent vestibulo-ocular reflex). The term pan-ophthalmoplegia can also be used if there is external and internal ophthalmoplegia. When the iris or ciliary or extraocular muscles are incompletely paralysed (some movements are still present), the term ophthalmoparesis is applied. Fixed mid-range pupil can also be present if there is involvement of both the parasympathetic and the sympathetic innervation of the iris. Ipsilateral sensory deficits of the ophthalmic (reduced to absent corneal sensation; reduced to absent corneal reflex; and nasofacial hypalgesia) and maxillary (periorbital hypalgesia) branches of the CN V can also be present.

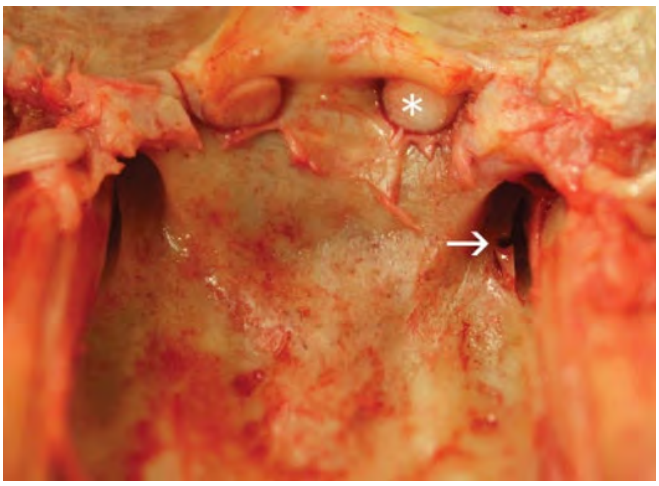
Middle cranial fossa syndrome is an anatomical diagnosis, and the most common reported etiologies in cats and dogs are neoplasia or infectious disorders. The authors of this chapter have seen a yearling Thoroughbred with middle cranial fossa syndrome following head trauma (unpublished data) (Figure 14.18) and the syndrome has been recently reported in cattle due to an infectious cause [97]. Therefore it should be considered in horses if clinical signs are compatible.

Advanced imaging (MRI or CT) should be performed if retrobulbar ultrasound fails to identify a lesion, in order to further determine the possible underlying cause.

Treatment is based on the underlying cause. Mean survival time for dogs has been reported as 135 days; however, all the dogs in that study presented with extensive tumors [98]. Overall prognosis in dogs and cats is considered guarded to poor, although published cases are limited to severe infectious disease



(A)



(B)

Figure 14.18 (A) Unilateral internal ophthalmoplegia and neuromuscular medial strabismus (due to abducent neuropathy) in the right eye of a yearling Thoroughbred after head trauma. (B) Post-mortem image of the rostral and middle cranial fossae. The optic nerve (**asterisk**) is visible. There is a small fracture (**arrow**) at the level of the rostral end of the right pterygoid process of the basisphenoid, which involves the medial part of the right orbital fissure.

or extensive neoplasia [98, 99]. Unfortunately this information is currently lacking in equine veterinary medicine.

Photic head shaking

Equine head shaking is a spontaneous clinical syndrome mainly characterized by violent head flicks (usually vertical), jerks of the head, muzzle rubbing, "distressed" facial expression, and snorting [100–102]. Any breed, sex, and age can be affected, but Thoroughbreds, geldings, and adult horses appear to be over-represented [102, 103]. Clinical signs can be intermittent or continuous and up to 82% of affected horses have been reported to have seasonality of clinical signs (head shaking begins in spring and ceases in late summer or fall) [102].

Trigeminal neuropathy is involved in the pathophysiology of this syndrome, but, in the majority of the horses (up to 90%), the underlying cause remains unknown, and therefore the term idiopathic head shaking is still currently used [104–106]. However, due to proven involvement of the trigeminal nerve in the pathophysiology of this syndrome, "trigeminal-mediated head shaking" has been recently proposed as a more accurate term [105]. Involvement of the trigeminal nerve has been demonstrated by differences in the threshold of activation of the infraorbital nerve (branch of the maxillary division of the trigeminal nerve) between horses affected by head shaking and a control group [104]. This reduced threshold and neural sensitization appears to result in neuropathic pain. The underlying cause for this sensitization in affected horses remains unknown. Horses affected by photic head shaking exhibit severe clinical signs during bright light and show a reduction of the signs at night. The etiopathogenesis of this photic trigger has been postulated to be similar to the human photic sneeze reflex [103]. One of the theories for this light-induced sneezing is that stimulation of the optic nerve active central pathways, which involves the trigeminal nucleus, causes a subsequent tickling and sneeze as a referred sensation [107]. Another theory implicates stimulation of the parasympathetic pterygopalatine ganglion [108]. This ganglion is activated by light and causes congestion and secretion inside the nares, which irritates the trigeminal nerve branches and triggers the subsequent behavior seen in horses [103, 108]. Horses affected with photic idiopathic head shaking exhibit the same clinical signs as those with non-photic head shaking, with the unique phenomenon that the trigeminal response appears to be triggered by daylight [109].

Diagnosis is based on evaluation of the signalment, history, and clinical signs. Other possible underlying causes that could exhibit similar clinical signs should be ruled out (middle ear disorders, uveal/corpora nigra cysts, guttural pouch diseases, dental and nasal disease, vitreous floaters, temporomandibular osteopathy, upper respiratory tract disease) [103]. Electrodiagnostic tests demonstrating a reduced threshold for infraorbital nerve activation are accurate tests for trigeminal-mediated head shaking in horses; however, these studies require a level of expertise, are invasive, and need to be done under general anesthesia [106]. Bilateral local analgesia of the rostral portion of the infraorbital nerve at the level of the infraorbital foramen has not proven useful for diagnosis [110]. Bilateral local anesthesia of the posterior ethmoidal nerve (PET block) proved more useful for diagnosis, with 76–85% of affected horses showing a positive response; however, an experienced operator is required to decrease the probability of false-negative results with this procedure [110–112].

There are no current effective treatments, since the etiology is still unknown. Environmental management (such as keeping the horse indoors) can improve clinical signs, but this is an unrealistic permanent treatment in the majority of cases. Face masks and nose nets are currently the most successful therapies, with improvement reported in 50–75% of affected horses, but horses can be irritated by the mask and also have reduced vision [105, 113]. There are different options for medical therapy, including cyproheptadine, carbamazepine, hydroxyzine, fluphenazine, phenobarbitone, gabapentin, and corticosteroids [101, 102, 105, 106, 110, 113]. These medications have shown variable success rates, all have been reported to have potential adverse side-effects, and the use of multiple medications should be avoided [105]. The only current recommended surgical therapy involves the use of platinum coils to provide permanent compression of the caudal infraorbital nerve, but due to the adverse effects, this procedure should only be considered for horses in which the only other option is euthanasia [111]. Oral supplementation with magnesium has been shown to improve clinical signs in up to 40% of affected horses [105]. Neuromodulation using percutaneous electrical nerve stimulation has been recently proven to be a safe and potential effective method to treat affected horses; however, further studies with larger study populations are needed to standardize treatment protocols [114].

Prognosis is variable and current treatments have low efficacy for many affected horses, which warrants the need for further investigations in this field. Some affected horses might go into spontaneous remission regardless of the treatment, and this postulates that the aberrant activity of the trigeminal nerve might not represent a permanent damage.

Future research

Future areas of investigation include use advanced imaging modalities, in particular MRI, to better characterize the different intracranial causes and associated prognostic factors in horses presenting with neuro-ophthalmic dysfunction.

Use of handheld spectral-domain optical coherence tomography (SD-OCT) is feasible to characterize normal corneal, retinal, and optic nerve head anatomy *in vivo* in standing sedated horses. However, further studies are needed to evaluate the diagnostic potential of SD-OCT for the equine eye with vision loss. For instance, assessment of the optic nerve head by SD-OCT in cases with optic neuritis may contribute towards analyzing the prognostic factors of vision recovery. In addition,

retinal pathology detection benefits from chromatic PLR in dogs, but this still needs to be investigated and validated in equine ophthalmology.

There are no current safe and effective methods to treat trigeminal-mediated head shaking in horses. Neuromodulation using percutaneous electrical nerve stimulation has been proven to be a safe and potentially effective method, but further studies with a large study population are needed to standardized treatment protocols.

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CHAPTER 15

Ocular manifestations of systemic disease

Jennifer L. Davis

Introduction

The ocular examination is greatly underused in the diagnosis of systemic diseases in horses. Ocular clinical signs may provide the practitioner with a shorter list of differential diagnoses and a prognosis. Numerous systemic diseases cause ocular changes in horses. This chapter has two purposes: (1) to allow the equine practitioner to become more aware of the changes that can occur in the eye and be able to use them as diagnostic aids; and (2) to enable the veterinary ophthalmologist to recognize the systemic diseases associated with some ocular diseases in the horse.

Neuro-ophthalmic diseases

Equine protozoal myeloencephalitis

Equine protozoal myeloencephalitis (EPM) is an important neurologic disease in North and South America, caused by *Sarcocystis neurona* or *Neospora hughesi*. To date, there are no reported visual deficits associated with EPM, although cerebral lesions could result in blindness.1 No fundic lesions were seen in an extensive unpublished evaluation of EPM cases. However, cranial nerve involvement leading to potential ocular manifestations occurs in approximately 12% of cases. Any cranial nerve nucleus may be involved, and if EPM affects the brainstem, cranial nerves (CNs) VII and VIII are usually affected, resulting in facial nerve paralysis (Box 15.1) and vestibular disease [1].

Ocular clinical signs associated with facial nerve paralysis include ptosis, absence of the menace response, and absence of the palpebral reflex (Figure 15.1). If the parasympathetic nucleus of CN VII is affected, neurogenic keratoconjunctivitis sicca will occur, predisposing the cornea to ulceration and secondary infectious keratitis. Involvement of CN III, IV, and VI may result in unilateral strabismus. The presence of ventrolateral strabismus plus the absence of a pupillary light reflex (PLR) in the stimulated eye, with a normal consensual PLR, indicate an ipsilateral lesion in the oculomotor nerve. Involvement of CN VIII may also result in a positional strabismus, noted only when the head is raised (Figure 15.2).

If ocular manifestations are present, they are usually accompanied by other cranial nerve deficits. EPM affecting the cervical spinal cord can cause Horner's syndrome (Box 15.2) [2], and clinical signs are listed in the discussion of Horner's syndrome (please see online material for discussion on this topic).

Classic clinical signs associated with EPM include ataxia, weakness, and muscle atrophy [1]. Ataxia occurs in almost 95% of cases, and signs are typically asymmetrical (69%). Muscle atrophy occurs in approximately 40% of cases and is also typically asymmetrical, with the gluteal muscle groups being the most commonly affected. Forebrain signs with seizures are rare and reported to only occur in 6% of cases. Some horses may have acute paraplegia or tetraplegia associated with periods of stress such as shipping, pregnancy, or concurrent illness [3].

Diagnosis of EPM is based on typical clinical signs, exclusion of other disease processes, plus the results of immunodiagnostic testing. The best validated immunodiagnostic tests include the indirect fluorescent antibody test (IFAT) and the surface antigen (SAG) 2, 4/3 enzyme-linked immunosorbent assay (ELISA) on serum or cerebrospinal fluid (CSF) [4]. One advantage of the IFAT is that it provides an actual quantitative titer, with serum titers greater than 1:640 and CSF titers greater than 1:5 being associated with a more than 92% probability of active disease. When using the SAG2, 4/3 ELISA, the most accurate results are obtained using a CSF:serum titer ratio of less than 100 [4]. Positive results on serum titers with any test are only indicative of exposure and should not be used alone to diagnose central nervous system (CNS) disease; however, a negative result remains a good means of ruling out EPM [5]. Intrathecal production of antibodies without actual invasion of the CNS, or serum-derived antibodies crossing the blood–brain barrier (as occurs with vaccinated horses) are also potential causes of false-positive results. There is no one single ideal test for EPM; the best means of ruling out the disease is a negative result for serum or CSF.

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Box 15.1 Systemic illness causing facial nerve dysfunction.

- Equine protozoal myeloencephalitis
- Polyneuritis equi
- Eastern equine encephalomyelitis, Western equine encephalomyelitis, Venezuelan equine encephalomyelitis
- Vestibular disease
- Aspergillosis
- Trauma
- Lyme disease
- Hypothyroidism



Figure 15.1 Left-sided facial nerve paralysis in a horse.



Figure 15.2 Unilateral right-sided positional strabismus due to central vestibular disease caused by equine protozoal myeloencephalitis in a horse.

Box 15.2 Systemic illness causing Horner's syndrome.

- Equine protozoal meningitis
- Guttural pouch disease (aspergillosis)
- Polyneuritis equi
- Trauma to the basisphenoid bone
- Esophageal rupture
- Extravasation of an irritating drug (phenylbutazone)
- Trauma

Numerous treatments are licensed in the USA for the treatment of EPM [6]. A combination product of sulfadiazine and pyrimethamine (ReBalance Antiprotozoal Oral Suspension (IVX Animal Health Inc., St. Joseph, MO)) has been used successfully, although treatment is often prolonged, and bone marrow suppression may occur. Ponazuril (Marquis Antiprotozoal Oral Paste (Merial Inc., Duluth, GA)) is available in the USA and comes in a paste formulation for easy administration. A loading dose of 15 mg/kg orally followed by 5 mg/kg once daily for 28 days is recommended. Diclazuril (Protazil Antiprotozoal Pellets (Merck Animal Health, Madison, NJ)) is the newest product licensed for EPM treatment in the USA and is administered as a daily top-dress at 1.0 mg/kg for 28 days. Although label treatment duration is only 4 weeks for both ponazuril and diclazuril, extended treatment with either drug is safe and it is recommended to treat until there is no further improvement in neurologic status. It is not recommend

Box 15.3 Systemic illness causing blindness.

- Equine leukoencephalomyelitis
- Eastern equine encephalomyelitis, Western equine encephalomyelitis, Venezuelan equine encephalomyelitis
- Thiamine deficiency and plants containing thiaminase
- Equine protozoal myeloencephalitis
- Bacterial meningoencephalitis
- Cryptococcal meningitis
- Ischemic optic neuropathy
- Intracranial neoplasia
- Rabies
- Strangles (brain abscess)
- Aspergillosis
- *Halicephalobus deletrix*
- Vitamin A deficiency
- Trauma
- Optic neuritis
- Plants containing pyrrolizidine alkaloids
- Trypanosomiasis
- Ivermectin toxicosis
- Air embolism

to retest serum or CSF. Regardless of which treatment is used, approximately 65% of horses show an improvement in neurologic scores of one to two grades [1].

Equine leukoencephalomalacia

Blindness (Box 15.3) caused by equine leukoencephalomalacia, also called **blind staggers** and **moldy corn disease**, occurs when the midbrain (cortex-cerebrum) is affected, resulting in central blindness that may be unilateral or bilateral [7, 8]. Other clinical signs relate to the cerebrum and brainstem and include anorexia, dullness, drowsiness, hyperexcitability, muscle tremors, compulsive walking, head pressing, circling, difficulty chewing, ataxia, decreased eyelid reflex, decreased tone of the tongue and lips, loss of sensitivity of the face, paralysis of the jaw, and recumbency [8].

The disease is caused by chronic ingestion of moldy corn infested with *Fusarium verticilliodes* (formerly *F. moniliforme*) and its associated toxin, fumonisin B1 [9, 10]. Even though the ingestion of the toxin is chronic, clinical signs occur abruptly and may not be present until after infected feed is withdrawn. If one horse on the farm is affected, the other horses have most likely been exposed, and the feed should be checked for presence of the mold. Hepatic enzyme activities—in particular, activity of gamma-glutamyl transferase—are often high in horses exposed to the toxin, and this can be used as a screening test for other horses on the farm [11]. If treatment is attempted, it should consist of supportive care, provision of fluids, and administration of activated charcoal to decrease absorption of the toxin. Morbidity rates are 4–100%, and case fatality rates are nearly 100%. Partial recovery has been reported in some cases, although this is rare and most affected animals die within 6–24 hours [8]. Gross and histopathologic changes include liquefactive necrosis of the white matter in the brain (Figure 15.3).

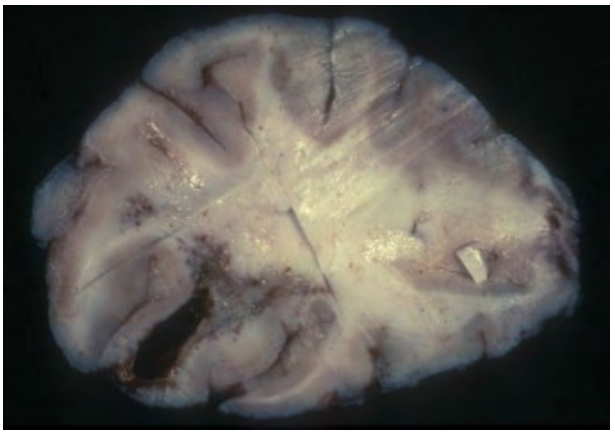


Figure 15.3 Liquefactive necrosis of the white matter in a horse with equine leukoencephalomalacia. (*Source*: Photograph courtesy of Dr Geoffrey Smith.)

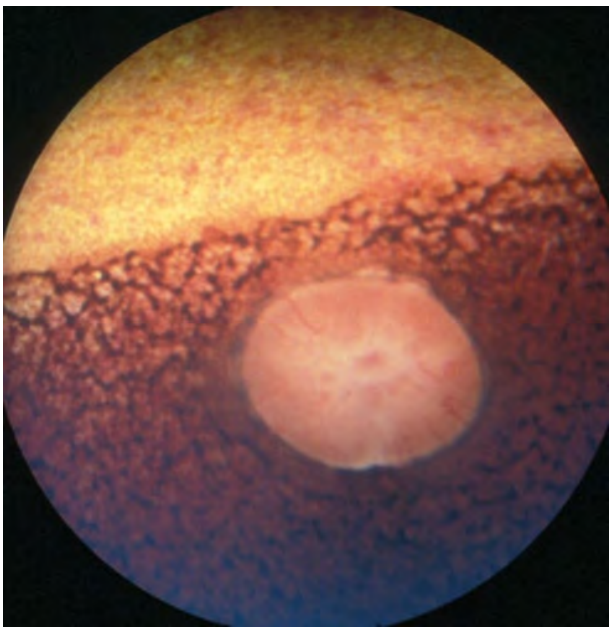


Figure 15.4 Ceroid/lipofuscin accumulation in the retinal pigment epithelium caused by equine lower motor neuron disease. This dark-brown to yellow pigment is deposited in a honeycomb mosaic pattern in the area of the tapetal fundus, with a distinct band of pigment at the tapetal/nontapetal junction.

Equine motor neuron disease

Equine motor neuron disease (EMND) is an acquired neurodegenerative disease of middle-aged to older horses that affects the motor neurons in the spinal cord ventral horn cells and brainstem. Visual deficits are not usually reported, but approximately 50% of affected horses will have characteristic fundic changes caused by ceroid/lipofuscin accumulation in the retinal pigment epithelium, considered pathognomonic for the disease. This dark-brown to yellow pigment is deposited in a honeycomb mosaic pattern in the area of the tapetal fundus, with a distinct band of pigment at the tapetal/nontapetal junction (Figure 15.4). PLRs may be abnormal [12].

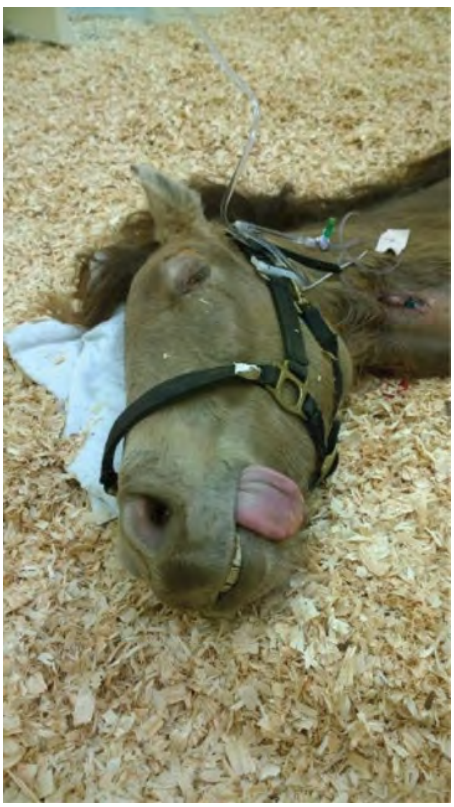
Clinical signs include muscle fasciculations, a base narrow stance, weight shifting, patchy sweating, elevations of the tailhead, low head carriage, excessive recumbency, muscle atrophy, and weight loss despite a ravenous appetite. The severe weakness and muscle atrophy are associated with denervation atrophy of type I muscle fibers [13]. Affected horses are not ataxic, and clinical signs actually improve when horses are in motion [13]. Chronic vitamin E deficiency has been associated with an increased risk of developing the disease and may be related to the pathophysiology, as evidenced by oxidative injury to the spinal cord, particularly in the somatic ventral motor neuron cells [14, 15]. Diagnosis is often made on the basis of clinical signs, and decreased serum vitamin E levels with concurrent and consistent elevations in muscle enzymes (creatine kinase (CK) and aspartate aminotransferase (AST)). Confirmation of the diagnosis can also be achieved through biopsy of the spinal accessory nerve or sacrodorsalis caudalis muscle, which reveals neurogenic atrophy [14, 15]. The disease is slowly progressive, and while progression is often slowed with vitamin E supplementation, full recovery is unlikely.

Some horses with clinical signs of EMND and a deficiency in vitamin E lack evidence of neurogenic atrophy in the sacrocaudalis dorsalis muscle. These horses represent a specific myogenic presentation of vitamin E deficiency and greatly improve with vitamin E supplementation [16]. Vitamin E-deficient myopathy could be an entity unto itself or a predecessor to development of EMND. The retinal pigment changes associated with EMND have not been reported for vitamin E-deficient myopathy, nor for equine degenerative myelopathy, another vitamin E-deficient neurologic disease [16, 17].

Viral encephalitides

Eastern/Western/Venezualan equine encephalitis

The Togaviral encephalitides, including Eastern/Western/Venezualan equine encephalitis viruses (genus *Alphavirus*), are transmitted by mosquitoes and tend to have a typical geographic distribution according to antigenic variation [18]. North American strains are considered more virulent than South American strains, and Eastern equine encephalomyelitis is considered the most pathogenic of the three. Typical early clinical signs include fever, conscious proprioceptive deficits, and behavioral changes. Viremia occurs during this period. Rapid progression of cerebral or cerebrocortical and cranial nerve dysfunction occurs over the next 2–14 days, with progression being most rapid in unvaccinated horses. Neurologic signs include blindness; facial, lingual (Figure 15.5A), and pharyngeal paralysis; ataxia; hypermetria; circling; head pressing; and proprioceptive deficits or paresis of the trunk and limbs (see Boxes 15.1 and 15.3), progressing to nonresponsiveness and recumbency [19]. When the brainstem becomes involved, strabismus (Figure 15.5B), nystagmus, pupil dilatation, and head tilt ensue [20].



(A)



(B)

Figure 15.5 (A) and (B) Severe obtundation and cranial nerve deficits in a 1-year-old Warmblood horse with Eastern equine encephalitis.

Diagnosis is based on clinical signs, viral titers, and, often, post-mortem findings. CSF cytology may reveal a neutrophilic inflammation, and histopathologic examination reveals a nonseptic suppurative inflammatory infiltrate. An immunoglobulin (Ig) M capture ELISA may be used to differentiate actual infection from vaccine responses [21].

Treatment involves supportive therapy with fluids, antiinflammatory drugs, and management of the recumbent horse. There are no currently available antiviral drugs that have demonstrated efficacy against alphaviruses. The mortality rate for Eastern equine encephalitis is the highest and is reported to be 75–100%, compared with mortality rates for Venezuelan equine encephalitis at 40–80% and Western equine encephalitis at 20–50% [18]. If the horse does recover from the acute phase of the disease, residual neurologic deficits are common, especially with Eastern equine encephalitis. A vaccine that provides adequate protection for 6–8 months is available and is considered a core vaccine for horses [22]. These viruses are zoonotic and are therefore reportable diseases in the USA.

West Nile virus

West Nile virus encephalitis is caused by a flavivirus with a worldwide distribution. It is considered endemic in Europe, Africa, Asia, and the Middle East. It was not introduced into the western hemisphere until 1999; however, it has spread rapidly across North America, and outbreaks have now been reported in almost every state in the USA, as well as in most provinces in Canada. The disease affects horses, humans, and susceptible bird populations. Cases in dogs, cats, camelids, and squirrels have also been reported [23]. The virus is spread by arthropod vectors, notably *Culex* spp. and *Aedes* spp. mosquitoes [24]. The normal life cycle includes birds and mosquitoes, with horses and humans considered to be dead-end hosts [25].

Clinical signs vary widely, depending on the portion of the CNS affected, and some horses may be asymptomatic even after experimental infection [26]. The most common neurologic sign in horses is hindlimb ataxia or paresis [27]. In one retrospective study, fever was noted in 65% of the cases [27]. Muscle fasciculations are also commonly noted and are thought to be due to either muscular weakness or lesions of the basal ganglia, as documented in humans [28]. Other clinical signs include behavioral abnormalities, depressed mentation, cranial nerve abnormalities, anorexia, bruxism, ptyalism, seizures, and recumbency [27, 29]. The most common ophthalmic clinical sign is unilateral or bilateral facial nerve paralysis (see Figure 15.1 and Box 15.1). Loss of menace response is also reported, although its pathogenesis was not mentioned, and it was only found in 3 out of 46 horses [27]. Corneal ulceration and mild keratitis, possibly caused by recumbency, and protrusion of the third eyelid were noted in horses that recovered from the disease [27, 29]. Blindness, presumably caused by encephalitis, was diagnosed in 5% of cases in one report [30]. In humans, the virus has been reported to cause optic neuritis, uveitis, and chorioretinitis [28, 31, 32].

Diagnosis is typically made by IgM capture ELISA of serum or CSF. This test has the advantage of differentiating between an acute infection and a vaccine response; however, hemagglutination inhibition is considered a more sensitive test [30]. CSF analysis may show xanthochromia with or without hyperproteinemia, and a monocytic pleocytosis [27]. Treatment is supportive as no currently available antiviral drugs have demonstrated efficacy against flaviviruses. Nonsteroidal antiinflammatory drugs (NSAIDs) are helpful in ameliorating the muscle fasciculations. Corticosteroids are often administered to severely affected cases; however. this is controversial, as they may increase serum and CSF viral load. Diuretics, such as mannitol, are used to decrease cerebral edema. A hyperimmune plasma labeled for use in horses with West Nile virus encephalitis has also been recommended, and may decrease the risk of recumbency.

Preventative measures against infection are highly recommended and West Nile virus vaccines are included in core vaccination protocols for horses. There are currently three vaccines available for use in horses: an inactivated whole virus vaccine, a recombinant canarypox vector vaccine, and a modified live chimera vaccine [33, 34]. The incidence of the disease in horses is decreasing, which may be due to naturally acquired immunity or the prudent use of vaccinations. The mortality rate is around 30–38% in horses that do not become recumbent and may be as high as 71% in horses that are unable to rise [27, 30]. West Nile virus is a zoonotic and reportable disease.

Rabies

Rabies is caused by a neurotropic rhabdovirus that affects most warm-blooded mammals. The disease has a variable incubation period; however, once clinical signs occur, it is rapidly progressive and invariably fatal within 10 days of onset. Early clinical signs are nonspecific and often include muzzle fasciculations, behavioral changes, hindlimb lameness or paresis, colic, and pharyngeal paralysis [38, 39]. Self-mutilation, head pressing, circling, recumbency, and convulsions may occur as terminal events [35]. Ocular signs are rare and include blindness, prolapse of the third eyelid, nystagmus, and strabismus, most likely caused by diffuse cerebrocortical edema and hemorrhage [38–40]. The retinal ganglion cells, the inner plexiform layer, and the outer nuclear layer may be susceptible to infection with histopathologic demonstration of granular intracytoplasmic rabies virus [36, 37].

There is no treatment available for rabid animals, and euthanasia is recommended. Appropriate caution should be taken with all animals with acute neurologic signs, especially those horses that have not been vaccinated for rabies. Rabies vaccines are available and effective in prevention of disease. Vaccination against rabies is considered a core vaccination recommendation and should be repeated annually. There is also no reliable antemortem diagnostic test and confirmation of infection is by direct immunofluorescence with monoclonal antibodies performed

on brain tissue at an approved regional laboratory [39]. Rabies is a zoonotic and reportable disease.

Septic meningoencephalitis

Septic meningoencephalitis is rare in adult horses but more common in young foals. In the neonate, hematogenous spread is the most common cause of the disease, but in the adult, it is often a direct extension of infectious agents into the CNS as a result of skull fractures, sinusitis, otitis, or surgical procedures [35, 41]. Hematogenous spread may also occur in adult horses as a result of bacterial endocarditis or respiratory disease [35, 42].

Clinical signs in foals often begin with stiffness in the neck (Figure 15.6), photophobia, and hyperesthesia. These signs can then rapidly progress to behavioral changes, cranial nerve deficits, ataxia, coma, seizures, and death. Signs are similar in adult horses but tend to progress slowly over a period of several days [43]. Specific ocular signs that have been reported in horses with bacterial meningoencephalitis include blindness (see Box 15.3), lack of a menace response, lack of PLR, nystagmus, strabismus, decreased palpebral reflex, retraction of the globe, and elevation of the third eyelid [41–43]. A recent report of ten foals with bacterial meningoencephalitis documented ocular signs including spontaneous nystagmus (4/10), ventrolateral positional strabismus (1/10), decreased PLR (4/10), and absent PLR with or without mydriasis and ansiocoria (2/10) [44]. Concurrent uveitis secondary to sepsis was also noted in two out of ten foals in that report and one had uveitis and optic neuritis. Lesions have been reported to be unilateral or bilateral and result from inflammation of the cerebral cortex or individual cranial nerves [42, 43].

Diagnosis is made on the basis of findings from CSF cytology, Gram staining, and culture. Treatment can be difficult because of the well-developed blood–brain barrier. Antibiotic choices should be based on findings from culture and sensitivity testing, as well as the physicochemical properties of the drug. In general, lipophilic, nonpolar basic drugs with a broad spectrum of activity and bactericidal action should be considered. The most common bacterium isolated from foals with meningoencephalitis was *E. coli* [44]; therefore treatment with a third- or fourth-generation cephalosporin such as cefotaxime (40 mg/kg intravenous (IV) every six hours) or cefepime (11 mg/kg IV every 8 hours) are acceptable empiric choices. In horses that do not respond to typical antibiotic therapies, nonbacterial causes of meningitis should be considered. Fungal infections with *Cryptococcus neoformans* [45] and parasitic infections with *Halicephalobus gingivalis* [46] have also been reported to cause meningitis with concurrent blindness in the horse. Anti-inflammatory medications and anticonvulsants are also necessary. The prognosis should be considered guarded in all cases.



Figure 15.6 Abnormal posture and stiff neck in a foal with septic meningitis.

Thiamine deficiency

Thiamine deficiency in the horse can be induced by feeding a diet deficient in thiamine or by the ingestion of thiaminase-containing plants, such as bracken fern (*Pteridium aquilinum*) and horsetail (*Equisetum arvense*) [7, 35]. Amprolium has been used experimentally to induce thiamine deficiency [47]. Ataxia, conscious proprioceptive deficits, heart block, bradycardia, cortical blindness, and muscle fasciculations or rhabdomyolysis have all been reported. Electrolyte changes, hyperglycemia, decreased glucose tolerance, and high CK activities have also been described [35, 48]. Supplementation with injectable thiamine is successful at reversing clinical signs, including blindness, when administered in the early stages of the disease [7, 35].

Vestibular disease

Vestibular disease can be classified as peripheral or central. Peripheral vestibular disease causes head tilt toward the side of the lesion; horizontal or rotary nystagmus, with the fast phase occurring away from the side of the lesion [35]; falling; circling; and asymmetric ataxia without conscious proprioceptive deficits or weakness. Facial nerve paralysis can occur concurrently with peripheral disease due to the facial nerve's proximity to the petrous temporal bone. Ipsilateral Horner's syndrome occurs when the postganglionic sympathetic nerves are affected as they course through the petrous temporal bone. Positional ventrolateral strabismus may be noted with the head elevated. Common causes of peripheral vestibular dysfunction include trauma, otitis media, temporohyoid osteoarthropathy (Figure 15.7), and guttural pouch disease [49, 50].

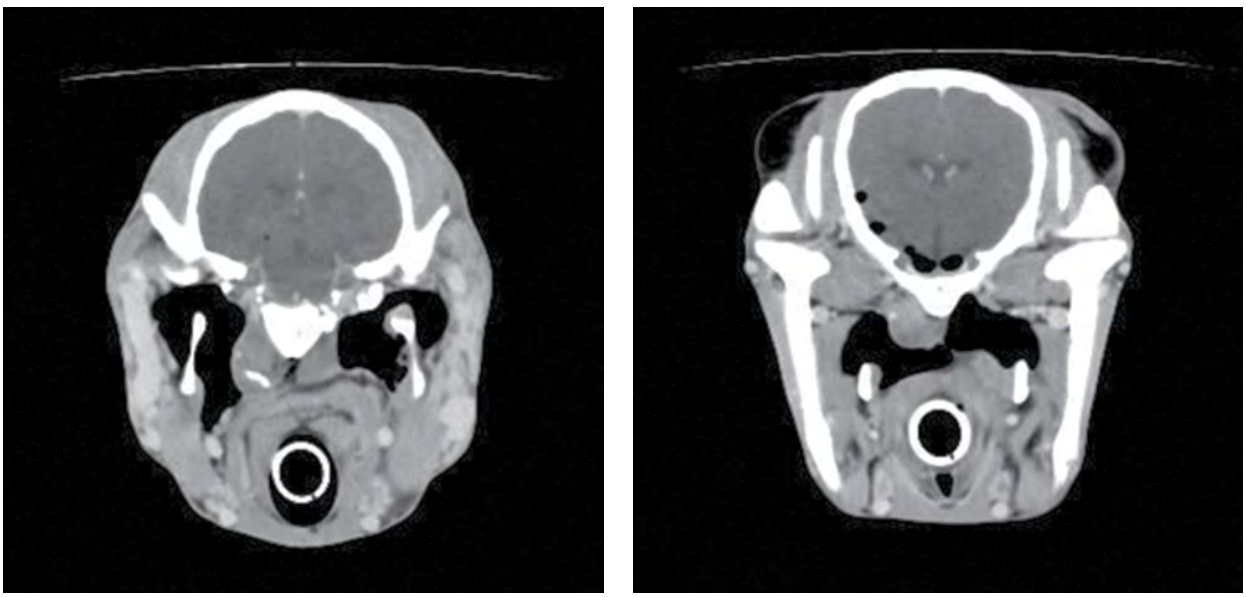
Central vestibular disease presents in a similar manner; however, conscious proprioceptive deficits, generalized weakness, involvement of multiple cranial nerves, and nystagmus may also be present. Nystagmus may be indistinguishable from peripheral disease but may also be vertical, diagonal, or disconjugate (different in each eye). The direction of the nystagmus may change with head position in horses with central vestibular disease [51].



Figure 15.7 Right-sided facial nerve paralysis and slight right-sided head tilt in a horse with temporohyioid osteoarthropathy.

Strabismus can be seen with central disease as well. Paradoxical central vestibular disease may occur with destructive lesions of the cerebellopontine angle or the flocculonodular lobe, resulting in clinical signs contralateral to the lesion [52]. The nuclei of CNs V–XII can be involved; therefore cranial nerve dysfunction, besides dysfunction of CN VII, indicates central disease. In addition, Horner's syndrome is not seen with central vestibular disease. Bilateral vestibular disease is difficult to differentiate from generalized cerebellar disease, and horses with bilateral vestibular disease do not exhibit typical clinical signs. Central vestibular dysfunction is commonly associated with space-occupying lesions such as tumors or abscesses but may also be caused by protozoal, viral, bacterial, or parasitic encephalitides [49].

Diagnostic techniques for determining the underlying cause should include radiographs of the skull, endoscopy of the pharyngeal region and guttural pouches, and possibly magnetic resonance imaging (MRI) or a computed tomography (CT) scan of the head (Figure 15.8A,B). CSF cytology and ancillary testing for viral or protozoal antibodies are indicated if central disease is suspected. Caloric testing by irrigating the ear canal with cold water and checking for induction of normal horizontal nystagmus can be done, although the test is not always reliable, and most horses will resist the procedure [53]. A decreased or absent reaction indicates the side of the lesion. Brainstem auditory evoked responses are also useful in demonstrating damage to the cochlea and CN VIII and can be used to differentiate between central and peripheral disease [54, 55]. The procedure is reliable and repeatable in the sedated horse. Treatment and prognosis should be related to the primary disease process.



(A) (B)

Figure 15.8 (A) CT image of a basisphenoid fracture in a 3-month-old Quarter horse colt that presented with unilateral vestibular disease secondary to trauma. (B) Distal CT image from the same foal, showing air within the calvarium.

Tetanus

Tetanus occurs after infection of a wound with *Clostridium tetani*, an anaerobic, motile, Gram-positive, nonencapsulated spore-forming bacteria ubiquitous in soils worldwide [56, 57]. The bacteria produce at least three toxins responsible for the clinical signs of the disease: tetanospasmin, tetanolysin, and a nonspasmogenic toxin. Tetanospasmin is responsible for the clinical signs typically associated with tetanus and is thought to work by inhibiting release of glycine and gamma-aminobutyric acid, the main inhibitory neurotransmitters in the CNS [35]. Tetanolysin causes local tissue necrosis, which helps promote bacterial proliferation, and the nonspasmogenic toxin produces overstimulation of the sympathetic nervous system.

The characteristic ocular sign in horses is "flashing" third eyelids (Box 15.4). **Flashing** refers to the rapid protrusion and retraction of the third eyelids coupled with eyeball retraction, usually in response to a menacing gesture [56]. Concurrent clinical signs often include lameness and a stiff gait that progresses to generalized spasticity and severe muscular rigidity. Sensory stimulation can produce muscle spasms, leading to recumbency and the sawhorse stance typical of tetanus. Ocular signs of advanced tetanus include ventrolateral strabismus and fixed, dilated pupils with normal vision [56]. Death usually occurs as a result of involvement of the respiratory tract muscles, leading to hypoxemia, and cardiac failure caused by systemic hypertension [58].

The principles of therapy center around providing muscle relaxation through the use of phenothiazine tranquilizers, barbiturates, benzodiazepines, or high doses of magnesium sulfate; preventing self-trauma by providing adequate bedding and good footing; decreasing external stimulation; and preventing further toxin absorption or binding by cleaning and debriding the wound, administration of appropriate antibiotics including high doses of penicillin, and administration of commercially available tetanus antitoxin locally in the wound, intramuscularly, or intrathecally.

The prognosis is poor, with a mortality rate of 80%. Prevention with annual administration of a tetanus toxoid vaccine is safe and effective and should be recommended for all horses on a routine basis and especially before surgical procedures. Administration of tetanus antitoxin has been associated with the development of acute necrotic hepatitis (Theiler's disease), and its use should be limited to horses at high risk for developing tetanus and those showing clinical signs [59].

Box 15.4 Systemic illness causing elevated nictitating membrane.

- Septic meningoencephalitis
- Hyperkalemic periodic paralysis
- Rabies
- Tetanus (flashing nictitating membrane)

Botulism

The clinical signs of botulism are caused by a neurotoxin elicited from the anerobic bacteria *Clostridium botulinum*. The toxin blocks the release of acetylcholine from the presynaptic peripheral cholinergic neurons, resulting in a neuromuscular blockade and generalized muscular weakness [60]. Botulinum toxin is considered to be one of the most potent known toxins, and horses are more sensitive to the toxin than most other species. Three causes of botulism occur in horses: ingestion of preformed toxin, ingestion of spores (toxicoinfectious botulism or shaker foal syndrome), and contamination of a wound.

Ocular signs include enophthalmos caused by retractor bulbi spasm, weak eyelids and upper eyelid ptosis [36], and mydriasis with slow PLRs [61]. Aside from the ocular signs, horses may be presented with limb weakness and ataxia that begins caudally and progresses cranially, decreased tail and anal tone, bladder paralysis, weakness of the tongue, and dysphagia. The presence of dysphagia at the time of admission to hospital has actually been associated with a higher survival in horses, as it is associated with early disease, and earlier diagnosis [62]. Colic may be present as a result of progressive ileus. Foals are most often presented in recumbency and, when forced to stand, will show generalized muscle tremors because of severe weakness. Death occurs as a result of paralysis of the intercostal muscles and the diaphragm.

Diagnosis of botulism is typically made by demonstration of the preformed toxin or *C. botulinum* spores in feed, serum, wounds, or gastrointestinal contents of affected horses [63]. Polymerase chain reaction (PCR) testing has recently become available and may be positive in approximately 60% of cases [62]. The mouse inoculation test commonly used in other species is positive in only 22–30% of cases, potentially because the amount of toxin necessary to kill a horse may not be enough to kill a mouse [62]. Diagnosis is frequently made by the exclusion of other neurologic diseases. Results of hematologic analysis are often normal in these horses, with the exception of an elevated pCO2.

Treatment consists of supportive care, ventilatory support, and administration of botulinum antitoxin. Aminoglycoside and tetracycline antibiotics should not be used as they can potentiate neuromuscular blockade, and cause a rapid progression of clinical signs. Antitoxins are available for treatment and the antitoxin used should be specific for the type of botulism involved, although the type is frequently not known. The most common type of botulism in North America is type B, although types C and A have been reported. A polyvalent antiserum is available, but the cost is prohibitive for most horse owners. Antitoxins are only effective against unbound toxin and must be given early in the course of the disease to be beneficial.

The prognosis in all cases of botulism should be guarded. Overall, survival in hospitalized cases is approximately 48%, with the most important predictor of survival being maintaining the ability to stand [69]. Vaccines against type B botulism are commercially available and are recommended on farms where the disease is endemic. This vaccine is considered effective; however, in a retrospective study of 92 cases, two affected horses

were fully vaccinated. Both these horses displayed mild clinical signs and fully recovered [62]. The vaccine does not produce cross protection among serotypes.

Trypanosomiasis

Trypanosoma evansi is a protozoal parasite that causes a chronic wasting syndrome in horses and numerous other species, including cattle and dogs. Less frequently, it can cause a severe encephalitis or myeloencephalitis with asymmetric leukoencephalomalacia, edema, demyelination, and lymphoplasmacytic perivascular cuffing [64]. Neurologic signs reported include ataxia, blindness, nystagmus, head tilt, circling, head pressing, proprioceptive deficits, and hyperexcitability leading to obtundity and death [64, 65]. The use of subtherapeutic doses of antitrypanosomal drugs, such as diminazene aceturate or quinapyramine sulfate, may clear the organism from peripheral tissues but appears to predispose the animal to developing CNS infection [66]. Introduction of naïve animals into endemic areas may also account for the severity of signs seen with the neurologic disease. Serology or PCR can be used for diagnosis. Once horses develop neurologic signs, the prognosis is grave.

Photic head shaking

No visual abnormalities are associated with photic head shaking [56, 67]. The underlying cause of head shaking in most horses is unknown. Proposed causes include iris cysts [56], guttural pouch disease, nasal and dental disease, middle ear disorders, and ear mite infestation (*Trombicula autumnalis*). A thorough examination should include endoscopy and radiography of the guttural pouches and upper airways and complete ophthalmic, otoscopic, and dental examinations [68]. A more detailed examination should include observation of the horse during exercise and at rest with a fitted nasal mask and tinted contact lenses, as well as during anesthesia of the infraorbital and posterior ethmoidal branches of the trigeminal nerve [69].

Medical management may include administration of cyproheptadine, an antiserotonergic drug thought to decrease neuropathic pain, with or without concurrent administration of carbamazepine, a drug related structurally to the tricyclic antidepressants, which is thought to reduce nerve impulses in the trigeminal nerve and has been used frequently for the treatment of trigeminal neuropathy in humans [69, 70]. Gabapentin, another potential therapeutic for neuropathic pain, has also been used with some success in these cases. Additional procedures that have been recommended include posterior ethmoid nerve sclerosis and infraorbital neurectomies, although significant adverse effects may be associated with these procedures [68, 69]. See more information on photic head shaking in Chapter 14.

Ischemic optic neuropathy

Epistaxis caused by guttural pouch mycosis can be treated with arterial occlusion of the internal carotid, external carotid, and greater palatine arteries. This treatment can result in sudden irreversible blindness of the eye on the affected side. Clinical lesions include congestion of the optic nerve head and involvement of the nerve fiber layer (see Chapters 9 and 14) [71]. Severe blood loss can result in bilateral blindness caused by an unknown mechanism [72].

Intracranial neoplasia

Intracranial neoplasia is rare in the horse. Clinical signs usually relate to the size and location of the tumor and whether metastasis has occurred. Exophthalmos, ocular discharge, and facial deformity may be observed with masses involving the sinuses or nasal passages [73–76]. Unilateral blindness, ventrolateral strabismus, and a lack of physiologic nystagmus have been described in a horse with intracranial neoplasia that involved the retrobulbar space [77]. These lesions were thought to be due to involvement of CNs II, III, and IV and possibly CN VI through compression by a space-occupying mass or metastasis of the tumor to involve the peripheral nerves. An immune-mediated paraneoplastic peripheral neuropathy may also have contributed to the dysfunction of these peripheral nerves [77]. CSF cytology, radiography, endoscopy of the nasal passages, and CT or MRI can all be used to assist in making the diagnosis [77, 78]. A prognosis should be determined according to the extent and nature of the lesion and the possibility for surgical removal or adjunctive therapy.

Polyneuritis equi

Polyneuritis equi is a chronic disease characterized initially by hyperesthesia, followed by progressive hypoesthesia and subsequent paralysis of regions innervated by the corresponding nerve roots. Common areas affected include the tail, anus and perineal area, bladder, and CNs V, VII, and VIII, although other cranial nerves may be affected [79]. CNs VII and VIII are more commonly affected than CN V [80]. Facial nerve paralysis and decreased tear production can occur leading to secondary corneal disease [81]. Colic, as a result of fecal retention and bladder distention, is a common clinical sign.

The cause is unknown, but a viral or immune-mediated etiology has been proposed. This is supported by the presence of antibodies to P2 myelin protein that are found in some horses with the disease [82]. This antibody has also been found in horses with equine herpesvirus 1 (EHV-1) and adenovirus infections, however, and should only be considered as a supportive test. Other diagnostic tests should include a complete blood count, which often shows signs of chronic inflammation (mature neutrophilia with hyperfibrinogenemia), and CSF cytology, which may be normal or may show high white blood cell counts or protein levels [82, 83]. Additional supportive evidence can be gained through transrectal ultrasound examination showing enlargement and diffusely mottled, hypoechoic appearance of extradural sacral nerve roots as they exit the ventral sacral foramina [84]. Biopsy of the sacrocaudalis dorsalis muscle may show extensive mononuclear cellular infiltrations in intramuscular nerve branches along with neurogenic atrophy [84].

The definitive diagnosis is often made at necropsy where histopathologic examination may reveal inflammation and infiltration of the extradural or intradural nerve roots [85]. Treatment with steroids may improve clinical signs in the early stages of the disease, but the lesions are progressive, and euthanasia is often required.

Viral diseases

Equine viral arteritis

Equine viral arteritis is caused by a togavirus and is spread by aerosolization and inhalation or through sexual contact. Carrier stallions are considered responsible for maintaining the disease in the population and may shed the virus in their semen for months to years [86]. Outbreaks have occurred in New Mexico (2006), France (2007), and Argentina (2010) that highlight the potential for the quick dissemination of the disease among breeding farms [87, 88]. The incubation period is 2–14 days.

There are two major syndromes associated with equine viral arteritis in the horse: a respiratory syndrome and an abortion syndrome. Many cases are asymptomatic, particularly in mares that are exposed to persistently infected stallions. Young, old, debilitated, or immunocompromised horses or those exposed to more virulent strains of disease (i.e., equine arteritis virus (EAV) KY84, EAV AZ87, EAV IL93, and EAV PA96) show moderate to severe clinical signs, including pyrexia up to 41 °C (105.8 °F), upper respiratory tract disease, severe dependent edema, and abortion 3–8 weeks after infection with the virus [88, 89]. Ocular signs include serous to mucoid ocular discharge, supraorbital and periorbital edema, conjunctivitis, corneal opacity, and photophobia (Box 15.5). Genetic factors may also play a role, as a genome-wide association study identified a common, genetically dominant haplotype associated with the *in vitro* susceptible phenotype in the region of equine chromosome 11, and stallions with EAV-susceptible CD31 T lymphocytes are at a higher risk of becoming persistently infected [88]. The disease is often fatal in neonatal foals, causing a fulminating interstitial pneumonia. Older foals may develop a progressive pneumoenteric syndrome where EAVAg may localize within enterocytes and vascular endothelial cells [88, 89].

The pathophysiology involves a necrotizing vasculitis, mainly of the small arteries in the muscle tissue of affected animals [68]. Diagnostic samples to collect in clinical cases include nasopharyngeal swab or nasal washing or swab, conjunctival swab, whole blood (in ethylenediaminetetra-acetic acid (EDTA) or citrate), and paired serum samples (21–28 days apart). Virus isolation is considered the gold standard diagnostic test, although viral nucleic acid or antigen detection, and serology can be used [88, 91]. Leukopenia with a lymphopenia is a consistent finding on hematologic analysis.

There is no specific treatment; however, severely affected horses should be treated symptomatically with NSAIDs, antipyretics to control fever, and diuretics and support wraps to reduce edema. It is rarely fatal in adult horses and the prognosis for recovery is good. Prevention involves vaccination of mares and pre-pubertal stallions and routine testing of breeding stallions, as well as implementing proper biosecurity or infection control programs [88]. Freezing of the semen will not deactivate the virus, and both freshly collected and frozen semen are considered infective [92].

Box 15.5 Systemic illness causing conjunctival disease.

- Equine viral arteritis
- Equine herpesvirus 2 (EHV-2)
- African horse sickness (chemosis)
- Equine influenza
- Equine granulocytic ehrlichiosis
- Babesiosis
- Epizootic lymphangitis
- Onchocerciasis
- Habronema
- Pemphigus
- Neonatal isoerythrolysis (icterus)
- Cushing's disease

Equine infectious anemia

Equine infectious anemia (EIA) is caused by a nononcogenic retrovirus that produces an immune-mediated hemolytic anemia in affected horses [93]. Control programs in the USA have resulted in near eradication of the disease, but EIA is still endemic in many countries. The disease originally presents as an acute syndrome characterized by fever, anorexia, depression, and petechial hemorrhages caused by thrombocytopenia. Thrombocytopenia can have associated ocular lesions, including conjunctival and intraocular hemorrhages. Choroiditis has also been documented with EIA [40]. Anemia develops in the subacute to chronic stage, and horses with EIA may have a recrudescence of the disease. Chronic carriers have also been described, and these horses are clinically healthy and hematologically normal.

Diagnosis in the USA is most frequently made by agar gel immunodiffusion (Coggins test), which is highly specific and can show a positive result as early as 10 days after infection and remain positive as a result of chronic antigenic stimulation from the virus [100]. Newer tests such as the ELISA and Western blot may have higher sensitivity; however, and for positive cases, a multitiered approach to testing is recommended. Samples screened by ELISA tests and found to be positive for EIA are confirmed by agarose gel immunodiffusion assay (AGID), or vice versa. In the few cases where these results do not agree, additional immunoblot tests are performed [94].

No treatment or vaccine is available for EIA, and infected horses are considered contagious. The disease must be reported, and euthanasia is recommended. If a positive horse is found on the premises, the remaining horses should be quarantined and retested at 30- to 60-day intervals until no new cases are reported.



(A) (B)

Figure 15.9 (A) Bulging of the supraorbital fossae in a horse with African horse sickness (AHS). (B) Marked chemosis in a horse with AHS. (*Source*: Photographs courtesy of Prof. Montague N. Saulez.)

African horse sickness

African horse sickness is not present in North America but is endemic in sub-Saharan Africa. The virus is a noncontagious, arthropod-borne (*Culicoides imicola* and *bolitinos)* orbivirus that affects all equidae; however, mules, donkeys, and zebras are less susceptible than horses [95]. Four forms of the disease are recognized: the pulmonary or peracute form, the cardiac or subacute form, the mixed form, and a milder horse sickness fever [103]. The mixed form is the one most commonly diagnosed and has clinical signs from both the pulmonary and cardiac forms of the disease, which may include pyrexia; tachypnea; sweating; cough; mucosal congestion; pleural effusion; and pulmonary, interfascial, and subcutaneous edema [102, 104]. Bulging of the supraorbital fossae (Figure 15.9A,B) occurs in 10–20% of cases, but it is a hallmark sign considered diagnostic for the disease (Box 15.6). This is likely due to retrobulbar edema and increased vascular pressure. Another possible ocular sign is marked chemosis (conjunctival edema) [97].

The mortality rate is between 50% and 95%. Diagnosis is based on virus isolation or neutralization and serology. Prevention involves quarantine of affected animals and vaccination of animals in endemic areas [98].

Box 15.6 Systemic illness causing exophthalmos.

- Neoplasia
- African horse sickness (bulging of supraorbital fossa)
- Echinococcosis
- Cryptococcosis

Equine herpesvirus

Equine herpesvirus 1 (EHV-1) is a common cause of upper respiratory tract infection, abortion, and neurologic disease in horses. Respiratory signs are more common in young horses and show/race horses and include fever, cough, and a mucoid nasal discharge that may progress to mucopurulent discharge with secondary bacterial infections. Abortions tend to occur after the seventh month of gestation and are sudden, without premonitory signs [99]. Stillbirths may also occur, and foals born alive are often weak, have severe interstitial pneumonia, and typically die within the first few days of life. The neurologic form of EHV-1 frequently presents with hindlimb ataxia, decreased tail and anal tone, and fecal and urinary retention. Signs may progress to the forelimbs, and horses may eventually become recumbent, which indicates a poor prognosis.

Ocular signs associated with EHV-1 and EHV-4 include hyperemia of the conjunctiva or sclera. Experimental infection of a foal with EHV-1 led to signs of severe visual dysfunction and chorioretinitis 28 days after exposure [100]. Ophthalmic examination revealed severe degeneration of the neurosensory retina, retinal pigmented epithelium, and choroidal layers, with EHV-1 DNA present in the ocular tissues. In a recent study designed specifically to monitor the development of ocular lesions following experimental infection with EHV-1, multifocal choroidal lesions developed in 50–90% of horses; however, lesions did not appear until 3 weeks to 3 months post-infection [101]. Infection with the neuropathic strain of EHV-1 may result in diffuse cerebral dysfunction and cranial nerve involvement.

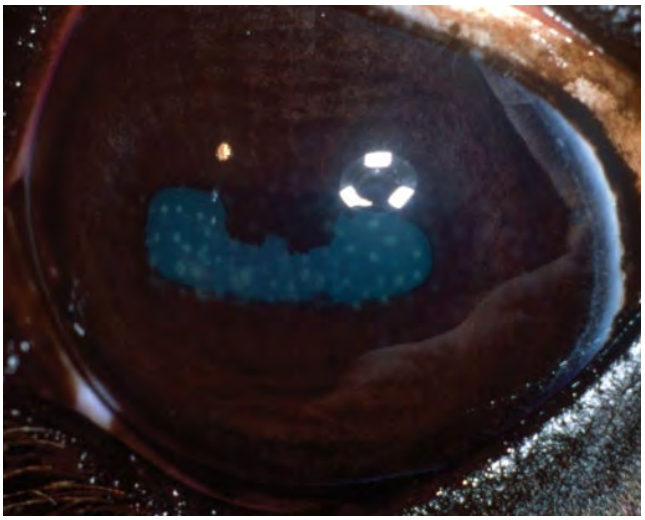


Figure 15.10 Left eye of a 4-year-old Warmblood stallion with equine herpesvirus 2 (EHV-2) keratitis. There are multiple focal, punctate, white lesions in the superficial cornea that are rose bengal positive and fluorescein positive. (*Source*: Photograph courtesy of Dr Stacy Andrew.)

Specific antiviral treatments studied for EHVs include acyclovir, valacyclovir, and ganciclovir. Due to the cost of treatment, as well as relatively mild signs of disease in most animals, these treatments are typically reserved for horses with severe herpes myeloencephalitis [102]. Supportive care including anti-inflammatory treatments, stall rest, and adequate nursing for horses with the neurologic form of the disease is recommended. Commercial vaccines against EHV-1 and EHV-4 are available, although protection is only short lived, and the vaccines may not protect against the neurologic form of the disease.

EHV-2 is a cytomegalovirus not known to cause disease by itself but considered important in the pathogenesis of other diseases through immunosuppression or possible transactivation of EHV-1 [103, 104]. The virus has been detected in pulmonary macrophages of up to 90% of horses with chronic pulmonary disease [105]. There are numerous reports of ocular signs associated with EHV-2, including serous to mucopurulent ocular discharge, conjunctival hyperemia and chemosis, superficial dendritic-type corneal lesions, which may be linear or punctate, and corneal edema and vascularization (Figure 15.10) [7, 106]. Response to topical antiviral medications is often favorable [107, 108]. See Chapter 7 for more information.

Adenovirus

The most frequent manifestation of adenovirus in the horse is as a lower respiratory tract pathogen in foals with severe combined immunodeficiency [109, 110]. The virus has also been co-isolated from foals with diarrhea caused by rotavirus [111]. It is not considered a pathogen in nonimmunocompromised animals. Bronchopneumonia is accompanied by mucopurulent nasal and ocular discharge. Conjunctival epithelial cells are histologically necrotic with intranuclear inclusions, and a neutrophilic infiltrate is present in the uveal vasculature, which is consistent with panuveitis [7, 112].

Equine influenza

Clinical signs of equine influenza virus are virtually indistinguishable from those of upper respiratory tract disease caused by EHV-1 and EHV-4. Fever, cough, and a serous or mucoid nasal and ocular discharge are often present, along with conjunctival hyperemia (see Box 15.5) [7]. The disease most often affects young horses, and there is usually a history of travel or introduction of a new horse into the herd. The virus spreads extremely rapidly, with an onset of fever within 2–3 days, which may last for up to 10 days, and a harsh, dry cough, which may persist for 2–3 weeks [113].

Treatment consists of supportive therapy, administration of NSAIDs, and stall rest for several weeks after resolution of clinical signs. Immunity after natural infection may last for more than 1 year; however, immunity after vaccination usually only lasts for 2–3 months because of antigenic drift in the virus [113, 114]. The modified live intranasal vaccine may provide extended immunity (for more than 6 months) and has proven effective in challenge studies [115]. Studies have shown that early vaccination may actually decrease the immune response, and therefore it is recommended that the initial vaccination not take place until the foal is 8 months old. The mortality rate is very low unless the patient is debilitated or complications such as myositis or secondary bacterial pneumonia develop.

Bacterial and rickettsial diseases

Neonatal septicemia

Neonatal septicemia is frequently associated with prematurity or dysmaturity, placental insufficiency, or failure of passive transfer. The foal is often healthy at birth, but signs of septicemia develop within the first 24–48 hours. Clinical signs vary widely but often include transient fever or hypothermia, loss of suckle, mild to severe depression, constipation or diarrhea, and bacterial seeding of other organs, including the joints, the lungs, and the umbilicus, as well as the eye. The earliest sign of septic uveitis is a green hue to the iris caused by fibrin seeping from the uveal vessels (Figure 15.11A). With progression, classic signs of uveitis are present: miosis, hypotony, aqueous flare, hypopyon, hyphema (Figure 15.11B), hyperemia of the conjunctival and ciliary vessels, and deep peripheral corneal vascularization. Most cases will present bilaterally.

If the foal survives, the prognosis for vision is good [116]. Diagnosis is based on clinical signs, hematologic analysis, and a positive blood culture. Treatment includes appropriate antibiotic therapy, administration of colostrum or hyperimmune plasma, gastroprotectants, treatment of endotoxemia, pressor therapy, fluid and nutritional support, flushing of septic joints, or removal of an infected umbilicus if necessary, and general supportive care for recumbent foals, including appropriate



(A) (B)

Figure 15.11 (A) Acute uveitis associated with neonatal septicemia. The earliest sign of septic uveitis is a green hue to the iris caused by fibrin seeping from the uveal vessels. (B) Intraocular hemorrhage and uveitis secondary to disseminated intravascular coagulopathy in an adult horse with salmonellosis.

ventilatory support. Gram-negative bacteria are frequently isolated from foals with sepsis, and initial antibiotic therapy should include broad-spectrum antibiotics with good Gram-negative coverage while results of culture and sensitivity are pending. Prognosis often depends on the initial response to treatment and the development of secondary complications.

Strangles

Strangles is a common disease caused by *Streptococcus equi* var. *equi*, a Gram-positive bacteria with a predilection for lymph tissue. The classic presentation involves acute onset of fever and nasal discharge, with swelling and abscessation of the retropharyngeal and submandibular lymph nodes (Figure 15.12A). Initial ocular signs include serous discharge followed by mucopurulent discharge; panophthalmitis [117] and chorioretinitis [118] have also been reported. In a separate case, blindness was caused by a brain abscess [119].

Diagnosis is based on culture of the abscess fluid or PCR of nasopharyngeal or guttural pouch washes. The disease is highly contagious and spreads through direct contact or aerosolization or by fomites. In rare instances, horses with long-term carrier status have been described and may serve as reservoirs that can introduce the disease into naïve herds, possibly by harboring the bacteria in the guttural pouch or, rarely, in the sinuses [120]. Culture of purulent discharge from abscesses is often positive, unless extended antimicrobial administration has occurred. Nasopharyngeal lavage analyzed by a combination of real-time PCR directly and after culture or, alternatively, real-time PCR directly on a nasopharyngeal lavage and a nasal/nasopharyngeal swab can identify *S. equi* in over 90% of acute strangles cases [121]. Treatment remains controversial. Recommendations on the use of antibiotics depend on the stage of the disease [122]. Horses that are at risk for exposure to strangles but do not yet have a fever or any other clinical signs will often benefit from vaccination with or without a short course of antibiotics. Horses that have been exposed and are already exhibiting fever and anorexia should not be vaccinated, and antibiotic administration at this time must be prolonged because horses may be more susceptible to the disease once the therapy is stopped. Many veterinarians recommend letting the disease run its course, rather than administering antibiotics at this stage. Once a horse has abscesses in the lymph nodes, antibiotics are thought to only prolong the course of the disease. Rupture and drainage of the lymph nodes should be encouraged by hot packing the area or establishing open drainage. NSAIDs may be given at this time if the horse has a high fever or is not eating or drinking well. Horses that have complications from strangles should be treated with appropriate antibiotics. Penicillin or ceftiofur are the antibiotics of choice for treating infections with *S. equi*. The organism may also be sensitive to tetracyclines, chloramphenicol, and macrolides, although culture and sensitivity testing are recommended if one of these drugs is to be used. Although *in vitro* sensitivity to trimethoprim-sulfa combinations is frequently documented, these formulations are rarely effective *in vivo*, potentially due to inactivation by bacterial para-aminobenzoic acid (PABA) at the infection site.

Vaccination against strangles is possible, but currently available vaccines are not considered fully protective against the disease. Vaccination should be avoided in horses with clinical signs of strangles or those that have recently recovered from the disease, as high levels of immunity can predispose horses to immunologic complications. Serum titers should be measured before vaccinating recovered horses, and the vaccine should not be administered unless the titer is less than 1:1600 [122, 123]. Two vaccines are currently available in the USA: an intramuscular (IM) M protein extract vaccine, and a modified live intranasal (IN) vaccine. The IM vaccine is less effective but can reduce the amount and severity of clinical cases. The IN vaccine may be more effective but has a higher risk of complications, particularly in young and debilitated animals [123].



(A)



(B)

Figure 15.12 (A) A 17-year-old Tennessee Walking horse gelding with retropharyngeal swelling characteristic of strangles. The classic presentation of strangles involves acute onset of fever and nasal discharge, with swelling and abscessation of the retropharyngeal and submandibular lymph nodes. (B) A 12-year-old Quarter horse gelding with severe vasculitis attributed to purpura hemorrhagica that developed 2 months after he recovered from an episode of strangles. Purpura hemorrhagica is an immune-mediated leukocytoclastic vasculitis that causes mucosal petechiation and severe edema of the head, limbs, and ventral abdomen.

Complications include acute upper airway obstruction, bastard strangles, guttural pouch empyema, and immunological complications, including purpura hemorrhagica and myositis. The enlarged lymph nodes and associated pharyngeal swelling may occlude the upper airway, necessitating an emergency tracheostomy. Once a patent airway has been established, the lymph nodes should be drained to further improve airflow. The term **bastard strangles** refers to spread of the infection to distal sites, including the cranial, mediastinal, mesenteric, and inguinal lymph nodes, or other organs such as the lungs, liver, kidneys, and brain [124]. This form of the disease is often difficult to treat and requires long-term antibiotic therapy unless a discrete abscess is found and can be successfully removed or drained. Guttural pouch empyema may result from rupture of the retropharyngeal lymph node directly into the pouch, or it may be a consequence of hematogenous spread. Daily lavage of the guttural pouches and establishment of ventral drainage for the abscess are often successful in clearing the organism, although surgical drainage of the affected pouch or pouches may be necessary. Instillation of a gel containing sodium penicillin into the affected pouches may shorten the course of the disease [125]. Purpura hemorrhagica is an immune-mediated leukocytoclastic vasculitis that causes mucosal petechiation and severe edema of the head, limbs, and ventral abdomen (Figure 15.12B). Clinical signs usually develop 2–4 weeks after acute infection, although they have also been documented to occur after vaccination with products containing the M protein of *S. equi* in horses exposed to the disease that did not have clinical infection or horses that have recovered from the disease and are re-exposed [126]. Anemia, neutrophilia, hyperproteinemia caused by a hyperglobulinemia, hyperfibrinogenemia, high muscle enzyme levels, and azotemia are frequently noted [122, 123, 126]. The azotemia may be prerenal, or it may be a result of glomerulonephritis caused by immune complex deposition in the kidneys [127]. Treatment consists of corticosteroids, antibiotics (preferably intravenous potassium penicillin), bandaging of the lower limbs to help decrease the edema, and supportive care with treatment of any secondary infections. The prognosis is good if horses are treated early and aggressively [126]. Cellulitis, myositis, sloughing of the skin, laminitis, diarrhea, and pneumonia may all occur as a result of purpura and should carry a poor prognosis. Other less common complications associated with strangles include rhabdomyolysis and myositis, endocarditis, myocarditis, laryngeal hemiplegia, bronchopneumonia, and septicemia.

Rhodococcus equi

Ocular manifestations of *Rhodococcus equi* infection typically include uveitis and hyphema and may relate to septicemia or

Box 15.7 Systemic illness causing anterior and/or posterior uveitis.

- Adenovirus
- Equine infectious anemia
- Neonatal septicemia
- Strangles
- *Rhodococcus equi*
- Lyme disease
- Brucellosis
- Leptospirosis
- Equine granulocytic ehrlichiosis
- Onchocerciasis
- *Setaria* spp.
- *Dirofilaria immitis*
- Mare reproductive loss syndrome



Figure 15.13 Uveitis secondary to *Rhodococcus equi* infection in a 4-month-old Saddlebred colt.

immune-mediated causes (Box 15.7) [7]. Clinical signs of uveitis include epiphora, blepharospasm, photophobia, corneal edema, conjunctival hyperemia, aqueous flare, hyphema, hypopyon, fibrin in the anterior chamber and/or vitreous, and miosis (Figure 15.13) [67]. The posterior segment may be difficult to examine because of anterior segment changes. Severe infections can present with panuveitis and vitreal abscess formation [81]. In a retrospective study of extrapulmonary disorders (EPD) associated with *R. equi* infection in foals, uveitis was the sixth most common EPD reported, with 11% of foals showing ocular signs [128].

Rhodococcus equi is a Gram-positive pleomorphic bacillus that survives for long periods in the soil. Adult horses are resistant to infection unless an underlying immunodeficiency is present. Young foals exposed to the organism within the first few weeks of life are most susceptible to the disease; however, they do not often show clinical symptoms until they are between 1 and 6 months of age, with signs of fever, cough, nasal discharge, and varying degrees of respiratory distress [129]. Radiographically, the disease is characterized by the presence of nodules (pyogranulomas) throughout the lungs and areas of consolidation,

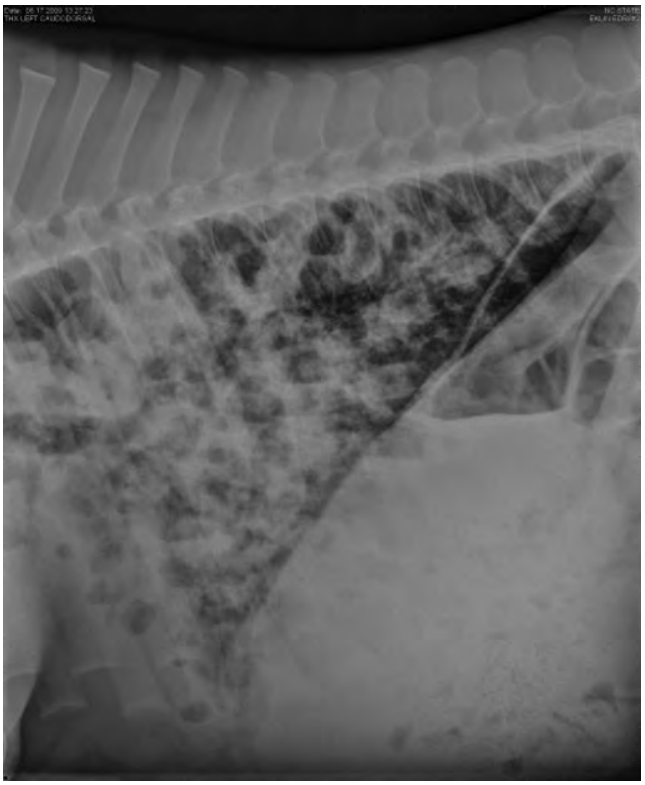


Figure 15.14 Radiograph of multiple pyogranulomas in a severe case of *Rhodococcus equi* infection in a 3-month-old Quarter horse filly.

typically found in the ventral lung fields (Figure 15.14). Abscesses associated with the pleural space can be easily discerned with ultrasound. Diarrhea, peritonitis, subcutaneous abscessation, joint effusion, osteomyelitis, or septic physitis may also be present [128, 129]. Diagnosis can be made on the basis of clinical presentation in an appropriately aged foal, radiographic and ultrasonographic signs, and positive culture or PCR for the organism from transtracheal wash or bronchoalveolar lavage fluid. Blood work and serology can be used as screening tests for other foals on the farm. Neutrophilia and hyperfibrinogenemia will often be present before any clinical signs of the disease.

Rhodococcus equi tends to form pyogranulomatous lesions that make the disease difficult to treat. The organism can also survive and replicate intracellularly within alveolar macrophages and neutrophils [130]. Historically, treatment has consisted of combination therapy with erythromycin estolate (25 mg/kg orally (PO) every 6–8 hours) or erythromycin phosphate (37.5 mg/kg PO every 12 hours) and rifampin (5–10 mg/kg PO every 12 hours) for several months. Newer macrolide and azalide antibiotics such as clarithromycin (7.5 mg/kg PO every 12 hours) and azithromycin (10 mg/kg PO every 24–48 hours) offer a better choice for therapy, as treatment courses are shortened, less frequent dosing is required, higher intracellular drug concentrations are achieved, and there is a lower incidence of adverse effects [131]. Rifampin is often added to treatments, with either clarithromycin or azithromycin as well.

Recent studies of *R. equi* on endemic farms have shown that not all foals need treatment. It is currently not recommended to treat subclinical foals, or foals with small pulmonary lesions (total abscess scores between 1 and 10 cm on ultrasound), as they may be able to resolve the disease without antibiotic therapy [132]. Establishing guidelines for when to treat or not is essential, as macrolide-resistant strains of *R. equi* have been increasing over the years. Additional supportive therapy such as provision of fluids, nasal insufflation of oxygen, administration of NSAIDs for high fevers, and ulcer prophylaxis may be necessary. Hyperimmune plasma is available for administration on farms with confirmed cases of *R. equi* infection. The plasma should be administered within the first week of life and has been shown to reduce the incidence of disease [133]. No effective vaccine is currently commercially available. The prognosis for foals with *R. equi* pneumonia is good so long as treatment is early and aggressive. Antibiotic therapy should be continued until all radiographic evidence of pneumonia has resolved. No significant adverse effects were seen in adult horses that had survived the disease as foals [134].

Lyme disease

Ocular manifestations of Lyme disease are nonspecific and include severe panuveitis and hyphema [7, 81]. Spirochetes have been found within eyes with panuveitis, but antibodies to the organisms may not be found [135]. A more recent report definitively diagnosed the organism in cases of uveitis using PCR techniques on ocular fluids [136]. The cases presented in that paper had concurrent clinical signs, including weight loss and pruritis, with unilateral or bilateral blindness. Neurologic disease affecting the eye can include facial nerve paralysis and resulting corneal disease (see Figure 15.1 and Box 15.1) [137].

Lyme disease is caused by *Borrelia burgdorferi*, a tick-borne bacteria found throughout North America, Europe, and Asia. Diagnostic Lyme antibody testing in horse serum has traditionally been performed by ELISA followed by a confirmatory Western blot; however, the test currently recommended for diagnosis is the fluorescent bead-based multiplex assay for the detection of antibodies to *B. burgdorferi* outer surface proteins (Osp) OspA, OspC, and OspF [138]. The advantage of this test is that it can differentiate between acute (OspC) and chronic (OspF) infection. In the USA, seroprevalence of the disease varies greatly depending on the region of the country, ranging from 0.2% in Texas to 45% in the northeast [139, 140]. Clinical disease is considered rare. Polysynovitis, arthritis, and reluctance to move in seropositive horses from endemic areas are signs frequently attributed to *B. burgdorferi* infection [140]. Reproductive dysfunction and neurologic disease have also been associated with Lyme disease [135, 141].

Definitive diagnosis of the disease can be difficult because of the high seroprevalence in some areas. A positive response to treatment is considered a useful diagnostic aid in many cases. The organism is typically sensitive to tetracyclines, penicillins, and cephalosporins; however, treatment is more successful if begun early in the disease. Doxycycline (10 mg/kg PO every 12 hours) is considered the antibiotic of choice.

Brucellosis

Brucella abortus was a significant cause of uveitis (see Box 15.7) in horses until its near-eradication in the 1940s [142]. The organism has not been isolated from ocular tissues in horses with positive serum agglutination titers, so its role in recurrent uveitis is unclear [143]. *Brucella abortus* is now most frequently implicated as a cause of inflammation of the supraspinous bursa, known as **fistulous withers** in the horse. Initial clinical signs include heat, pain, and swelling over the withers. Eventually, a draining tract forms, and secondary contamination with other bacteria may occur. In one retrospective study of horses with fistulous withers, 37.5% were seropositive for *B. abortus*, and those horses usually had a history of being pastured with cattle and were significantly more likely to have osteomyelitis of the underlying vertebrae than were seronegative horses [144]. Definitive diagnosis is made by culture of the organism, which requires special media and culture conditions [144]. Treatment options include radical surgical excision of the affected area and subcutaneous injections of available cattle vaccines [144, 145]. Recurrence after surgery is common, and reactions have been noted with vaccine administration. Brucellosis is a reportable disease, and personnel handling affected animals should wear gloves and masks to avoid exposure. Abortions are not associated with brucellosis in horses.

Leptospirosis

Leptospirosis is one of the most commonly associated systemic diseases linked to equine recurrent uveitis (ERU). Experimental infection with leptospiral organisms results in clinical uveitis approximately 1 year after initial inoculation [146]. Blindness often results from chronic ERU that is poorly managed. For a more complete description of ERU and the role of leptospirosis in ERU, see Chapter 8.

Leptospires are spirochete bacteria that are associated with disease in many species. Chronically or subclinically infected animals are the main source for spread of the disease. The *Leptospira interrogans* complex is associated with disease in humans and domestic animals. The serovars most frequently isolated in horses include *L. pomona*, *L. icterohaemorrhagiae*, *L. bratislava*, and *L. autumnalis* [147]. In horses, clinical manifestations aside from uveitis include acute renal failure in foals and stallions, hepatic failure in foals, neonatal deaths, and late-term abortions in mares [148–151]. Diagnosis is based on culture of the organism from blood, tissues, aborted fetuses, or urine. The presence of leptospiral DNA has been found in the vaginal fluid of mares, particularly *L. bratislava*, suggesting possible sexual transmission of disease [152]. Administration of furosemide may help dislodge the organism from the bladder wall and increase the chance of a positive culture [153]. Dark-field microscopy and serology (ELISA or microscopic agglutination test) may also be useful, because culture is often difficult and may take as long as 6 months [154]. Treatment usually consists of antibiotic therapy with penicillins, tetracyclines, or dihydrostreptomycin, although these antibiotics have not been shown to prevent shedding of leptospires in the urine [147].

Equine granulocytic ehrlichiosis

Equine granulocytic ehrlichiosis is caused by a rickettsial organism, *Anaplasma phagocytophilum* (formerly *Ehrlichia equi*), and has recently been discovered to be identical to the causative agent of human granulocytic ehrlichiosis and tick-borne fever of cattle and sheep in Europe [155]. Transmission occurs through *Ixodes* spp. ticks, and experimental transmission with infected tick vectors has been demonstrated [156]. The organism can be found in the cytoplasm of neutrophils and eosinophils of infected horses during the febrile period and can be detected with Giemsa stain or new methylene blue stain. Ocular signs include icteric sclera and petechiation of the bulbar and third eyelid conjunctival mucosa; uveitis may also be present [157]. Systemic clinical signs and blood work abnormalities can include fever, thrombocytopenia, leukopenia, edema of the limbs, mucosal petechiation, icterus, and ataxia. The underlying pathology involves a vasculitis with decreased maturation or release of platelets from the bone marrow [158]. Cardiac arrhythmias may also be seen, possibly as a result of myocardial vasculitis [159]. Clinical signs are less severe in younger horses (less than 3 years old) [159]. Diagnosis is based on clinical presentation, characteristic changes in laboratory blood tests, serology, and demonstration of the organism in buffy coat smears. Treatment with tetracyclines often results in resolution of fever within 12–24 hours and resolution of other clinical signs within 7–10 days [159]. The prognosis is good in most cases unless complications such as laminitis or secondary bacterial infections occur. No vaccine is currently available, but natural immunity persists for up to 300 days after infection, and no latency or carrier state has been detected [160].

Protozoal diseases

Piroplasmosis

Ophthalmic signs of piroplasmosis include icteric conjunctiva and sclera, blepharoedema, and petechiae and ecchymoses of the conjunctiva, including the third eyelid conjunctiva [161]. Other signs include red-tinged and serous ocular discharge and distension of the supraorbital fossa [7].

Piroplasmosis is a tick-borne hemolytic disease of horses caused by the obligate intraerythrocytic parasites *Theileria equi* (formerly *Babesia equi*) and *Babesia caballi*. Neither of these are considered endemic in the USA or Canada; however, outbreaks may sometimes occur, particularly in the southern USA. After infection, clinical signs typically appear within 12–19 days for *T. equi* and 10–30 days for *B. caballi* [162]. Horses that survive acute infection become inapparent carriers of disease and a potential source for outbreaks. Diagnosis can easily be made from blood smears during the early febrile stages of the disease. *Babesia caballi* is large and appears as pairs visualized within the red blood cells. *Theileria equi* is smaller and is found in groups of four [162, 163]. A negative complement fixation test result is required before a horse can be imported into the USA. An indirect immunofluorescent antibody test, Western blot, and ELISA are also available, and these tests are more sensitive in detecting chronic disease and inapparent carriers. Laboratory findings often seen include hemolytic anemia, jaundice, and hemoglobinuria.

The severity of clinical signs (fever, anorexia, depression, ataxia, paresis, icterus, and ocular signs) depends on the organism, and *T. equi* is considered the more pathogenic of the two [162]. Chronic disease may occur, with nonspecific signs including lethargy, partial anorexia, weight loss, poor hair coat, and poor performance; mild anemia and an enlarged spleen may be present on rectal palpation.

Treatment goals vary according to location. For horses in endemic areas, the main goal is survival of acute infection, with maintenance of a carrier state and, presumably, maintenance of long-term immunity. For horses in nonendemic areas, complete clearance of the parasite is necessary to avoid the animal becoming a possible source of transmission. Treatment involves administration of imidocarb dipropionate (2.2–4.4 mg/kg given IM once, followed by 2.2 mg/kg IM every 24–72 hours for two to three treatments) and this will eliminate or reduce clinical signs in acutely infected horses. To eliminate carriers, dosing of 4 mg/kg IM every 72 hours for four doses is needed [162, 164]. Adverse effects of imidocarb are related to its anticholinesterase activity and include colic, agitation, hypersalivation, sweating, and diarrhea. Injection site inflammation and transiently elevated hepatic enzyme activity may also be noted. Donkeys and mules are extremely sensitive to the adverse effects of imidocarb and administration may prove fatal in these animals. Addition of parvaquone or buparvaquone may help with therapy, but, when given alone, may cause treated horses to become carriers [164, 165]. Fluids, NSAIDs, and blood transfusions may be necessary as supportive therapy.

In the USA, if a horse is to undergo treatment, the owner and veterinarian must enroll the horse in the US Department of Agriculture (USDA) treatment program, and clearance with subsequent release from quarantine is not allowed unless serial negative PCR or serologic testing results are available, and the parasite is not transmitted to a naïve splenectomized horse via blood transfusion.

Toxoplasmosis

Seroprevalence of antibodies to *Toxoplasma gondii* in horses in the USA ranges from 7% to 10%, but cases of actual clinical disease are rare [166]. Horses fed viable oocysts will have cysts; however, they do not shed the organism [167]. *Toxoplasma gondii* was originally thought to be the causative agent of EPM, but this has since been disproved. It is a rare cause of abortion in the horse. Horses seem to be resistant to ocular manifestations of toxoplasmosis. One case of peripapillary and partial optic nerve atrophy in a horse with toxoplasmosis has been reported [168], but there are no other cases in the literature in which *T. gondii* is cited as the cause of ocular disease in horses. In one study, investigators examined three separate horse populations in India and

found that in the few horses with ocular lesions, there was no correlation with positive titers for *T. gondii* [169]. Another study of 71 horses showed that toxoplasmosis was not associated with ERU [170].

Fungal diseases

Cryptococcosis

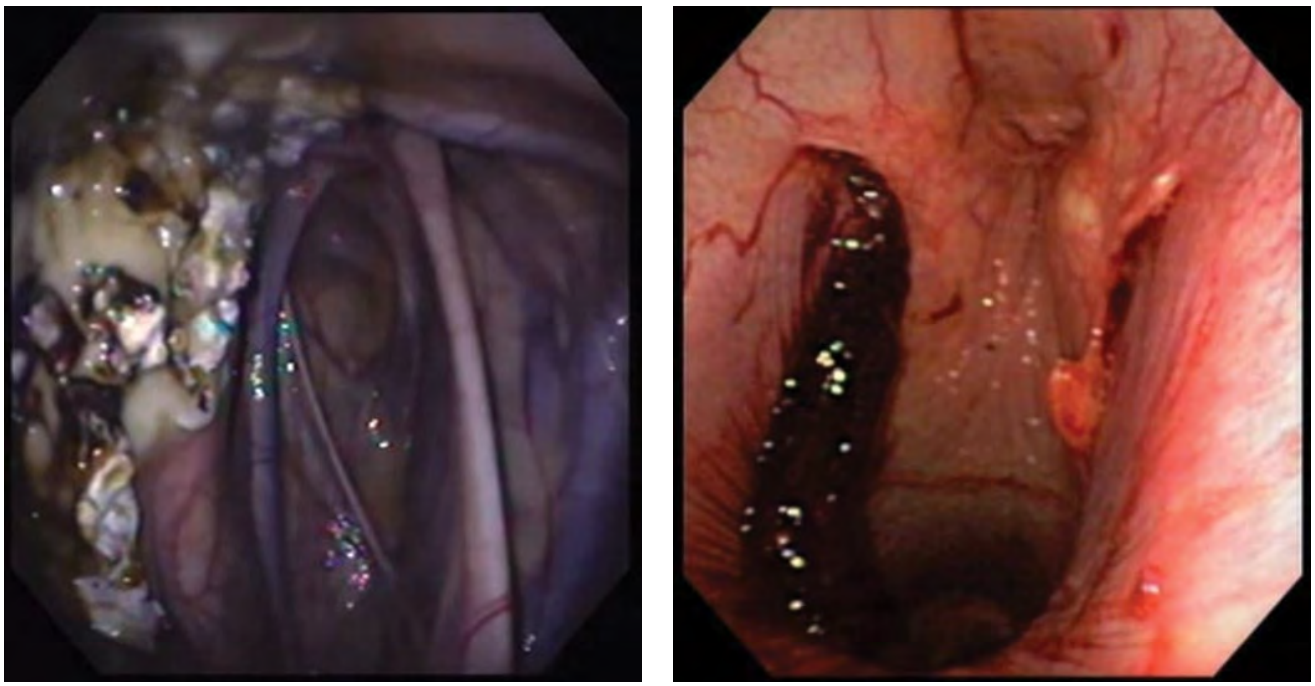
Cryptococcus neoformans is a pathogenic fungus that has been known to infect both healthy horses and those with a history of severe illness. Clinical manifestations include abortion, pneumonia, and, less commonly, abdominal abscesses, meningitis, and subcutaneous, nasal, or sinus granulomas [171–175]. Direct ocular infection of equine cryptococcosis has not been noted, although blindness and optic neuritis secondary to meningitis [45] and a retrobulbar mass causing exophthalmos and periorbital distension [176] (see Box 15.6) have been reported. Diagnosis is based on histopathologic evidence of the organism in tissue samples or on cytology, as well as a positive culture. Lung biopsy should be performed to confirm the presence of fungal infection in cases of pneumonia, because fungal organisms have been identified in transtracheal aspirates from healthy horses [177]. Systemic cryptococcosis has a very poor prognosis, and treatment is often not attempted [173]. Cryptococcal organisms are typically sensitive to fluconazole, and this may provide an effective and affordable option if treatment is attempted. Prolonged treatment is recommended and may be as long as 6 months [45]. Abortions caused by *Cryptococcus* spp. usually occur in late gestation and may be associated with infertility [178].

Epizootic lymphangitis

Epizootic lymphangitis is caused by *Histoplasma farciminosum*, a fungal agent found mainly in Africa. It causes cordlike lesions of the subcutaneous lymphatic system or cutaneous pyogranulomas [179]. A conjunctival form of this disease occurs as a result of deposition of the organism on the ocular mucous membranes by biting flies (*Musca* and *Stomoxys* spp.). The initial lesion is a medial canthal swelling that causes purulent discharge and tear eczema [180]. Progression of the disease can result in obstruction and erosion of the lacrimal duct, which can eventually create a fistula between the orbit and the maxillary sinus [181]. Diagnosis is mainly made by cytology and culture, although serologic assays are also available [181]. Amphotericin B is the treatment of choice, and a vaccine is available for horses in endemic areas.

Aspergillosis

Aspergillus spp. are considered opportunistic fungi that rarely cause disease in nonimmunocompromised horses. Ocular signs of aspergillosis are often manifested as corneal ulceration or abscessation caused by direct trauma. This manifestation is described in Chapter 7. Aspergillosis is a cause of guttural pouch mycosis (Figure 15.15A,B), and ocular manifestations can include Horner's syndrome, facial nerve palsy, and blindness



(A) (B)

Figure 15.15 (A) Fungal plaque in the left guttural pouch of an 11-year-old Percheron mare caused by *Aspergillus* spp. Lesions were actually bilateral. (B) Later endoscopic view of the same horse showing severe hemorrhage from the right guttural pouch.

caused by ischemic optic neuritis resulting from compression of the optic nerve or chiasm by a granuloma or infarction [182–186]. Other systemic clinical syndromes seen are similar to those described for cryptococcosis.

The development of pulmonary aspergillosis has been significantly associated with severe enteritis in the horse, indicating hematogenous spread through a breakdown in the mucosal barrier of the gut wall [187]. The organisms are ubiquitous in the environment, and horses are frequently exposed. Inhalation of the antigen can produce a severe inflammatory reaction in the lungs of horses with recurrent airway obstruction [188]. Pulmonary infections can spread, resulting in disseminated disease, including encephalitis and possible blindness [189]. Late-term abortions can also be seen as a result of aspergillosis. Treatment with systemic antifungal agents may be attempted, but the prognosis is always guarded because of the underlying disease process present and the severity of the lesions [190]. The organism is susceptible to many of the azole antimicrobial drugs, such as ketoconazole, itraconazole, and voriconazole; however, it is often resistant to fluconazole [191].

Parasitic diseases

Onchocerciasis

Onchocerca cervicalis is spread by *Culicoides* spp. and is a common cause of dermatitis in horses. Adult parasites live in the nuchal ligament and can produce microfilaria for up to 5 years. The microfilaria then migrate through the subcutaneous tissues, particularly to the ventral midline, base of the mane, proximal forelimbs, and pectoral region. Actual disease is due to an immune reaction to the death of circulating microfilaria that causes a perivascular mononuclear dermatitis [192]. Ocular microfilariae have been reported in horses, and the prevalence varies by geographic location. The eastern USA has the highest prevalence, with 49% of 121 horses affected [193], and the Midwest has the lowest prevalence, with 11% of 368 horses affected [194].

The most common ocular lesion evident is depigmentation of the conjunctiva at the temporal limbal region (Figure 15.16) [195]. Similar to systemic onchocerciasis, ocular disease is usually due to dead parasites releasing antigens that result in marked inflammation [194]. Other ocular manifestations include conjunctivitis, peripheral keratitis, and anterior and posterior uveitis. Conjunctivitis and keratitis are characterized by chemosis, corneal edema, corneal vascularization, and subepithelial yellow to white corneal opacities [195]. Keratitis is typically seen at the temporal limbus but can extend axially; this results from aberrant migration of the microfilariae that die in the corneal stroma, and keratitis can be accompanied by temporal conjunctivitis and anterior uveitis. Clinical signs of uveitis include epiphora, blepharospasm, miosis, and aqueous flare [195]. Signs of posterior uveitis, including peripapillary chorioretinitis and chorioretinal scarring (i.e., butterfly lesions), are often evident.

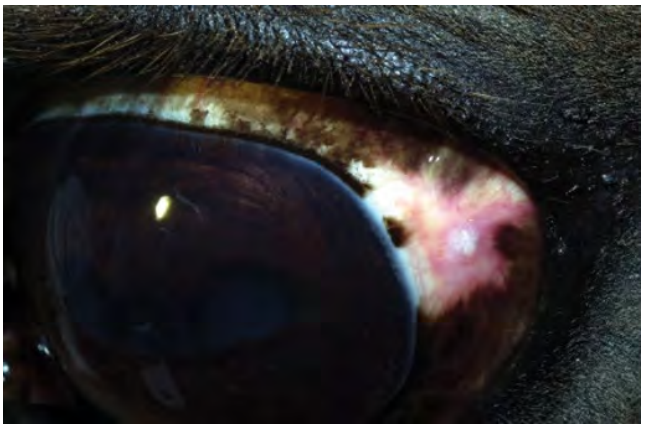


Figure 15.16 Onchocerciasis infection in a horse. The most common ocular lesion evident is depigmentation of the conjunctiva at the temporal limbal region.

Although onchocerciasis is often implicated in the pathogenesis of ERU, it is difficult to ascertain the true relevance of this disease because of the prevalence of the parasite in healthy horse populations. Ivermectin is effective in killing the microfilaria, but it will not kill the adult parasites [196]. Treatment may initially worsen clinical signs, and the disease may recur. Lesions are nonseasonal, and older horses are more likely to be infected than younger horses [192].

Cutaneous habronemiasis

Also known as **summer sores**, cutaneous habronemiasis is caused by aberrant intradermal migration of the larvae of *Habronema* or *Draschia* spp., which are normally found in the stomach. Lesions develop in areas of traumatized skin and are caused by a hypersensitivity reaction to death of the larvae. Granulomas with necrotic centers are typically seen on the lower limbs and the urethral process, as well as the eye; mineralized larvae can often be found in the center of the lesion. Specific common ocular locations for habronemiasis include the eyelids, conjunctiva, lacrimal caruncle, and the third eyelids (Figure 15.17; also see Chapter 6) [197]. Conjunctival lesions are typically located near the medial canthus. Periocular or eyelid lesions have a raised, irregular, yellow appearance, often referred to as **sulfur granules** [7].

Biopsy of the affected area should be performed to aid in diagnosis and rule out other causes of ulcerative skin lesions, such as neoplasia, proud flesh, and bacterial or fungal granulomas [198]. On histopathologic examination, an eosinophilic infiltrate is seen in a fibrous stroma [199]. Treatment consists of an adequate deworming program that includes ivermectin, debridement of the lesions, topical and systemic anti-inflammatory therapy, and adequate fly control [200, 201]. Clinical experience indicates that resistance to ivermectin may be increasing, necessitating the use of multiple doses, higher doses, or switching to the use of moxidectin.

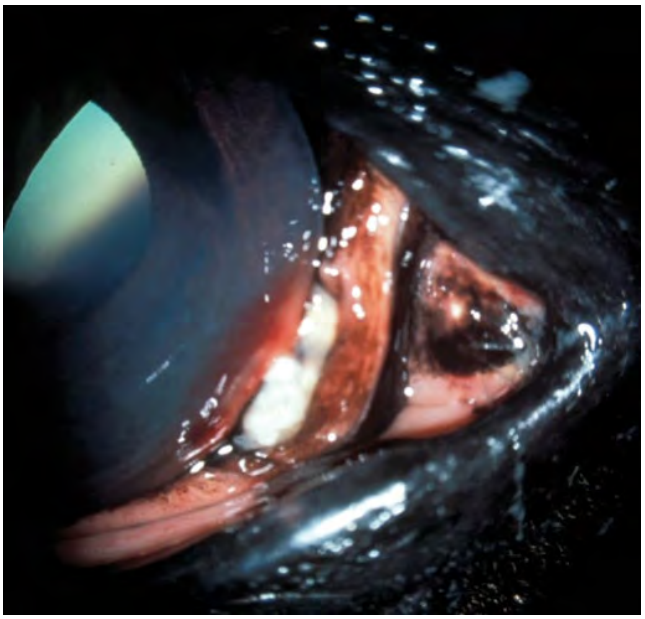


Figure 15.17 Habronemiasis of the medial canthus and third eyelid. (*Source*: Photograph courtesy of Dr Mike Davidson.)

Setaria

Setaria spp. have been documented as a cause of microfilaremia in horses. Systemic clinical signs include poor body condition, depression, stiff gait, and fever. Other clinical signs may be present based on aberrant migration of the parasite to distant sites such as the CNS and eye. *Setaria* spp. have been implicated as a cause of cerebrospinal nematodiasis in horses, sheep, and goats. Cattle are the natural hosts, and the parasites are transmitted to horses through mosquitoes and other blood-sucking insects [202]. Aberrant parasite migration can occur anywhere in the CNS. Spinal cord lesions are more common, and signs include an atonic tail and bladder, ataxia, and conscious proprioceptive deficits [203]. In horses, aberrant migration of *Setaria* into the eye also occurs, resulting in severe intraocular inflammation, photophobia, corneal opacity, blepharospasm, and lacrimation [204–206]. Cutaneous lesions on the face, ears, and limbs have also been described [207].

Diagnosis can be made based on visualization of the parasite in the aqueous humor and detection of the microfilaria in the blood. Knott's test is an easy and sensitive technique for detection of microfilaremia and can be used to monitor for *Setaria* spp. [207]. Successful removal of the nematode from the anterior chamber has been reported [208], although complications from the surgery can include phthisis bulbi, corneal edema, and scarring and prolapse of the iris. Treatment with diethylcarbamazine (20 mg/kg IM) has been shown to resolve microfilaremia, but requires multiple treatments and has not been documented to kill adult parasites in the eye [206]. A more recent report [205] documented successful treatment of equine ocular microfilariasis caused by *Setaria digitata* in three horses with a single subcutaneous dose of ivermectin (300 mcg/kg). Microfilaremia was resolved by day 7 after treatment, and adult ocular parasites died between 15 and 17 days after treatment. Removal of the dead parasites was not necessary, and all ocular signs had resolved by 90 days after treatment. Anti-inflammatory therapy should be instituted along with administration of antiparasitic agents.

Dirofilaria immitis

Arteriosclerosis secondary to adult *Dirofilaria immitis* parasites in the pulmonary vasculature has been diagnosed in a 20-month-old Quarter horse stallion [209]. Intraocular migration of *D. immitis* is less common in horses than in carnivores, although successful removal of the nematode from the anterior chamber of a horse has been reported [210].

Echinococcus

Echinococcus granulosus is a small tapeworm. Dogs are the definitive hosts, and horses are considered intermediate hosts. Hydatid cysts with viable protoscolices have been found in the livers of some horses [211]. Exophthalmos is the only reported ocular manifestation of hydatid cyst disease in horses, and it is due to cysts in the orbital tissues. The only definitive treatment is surgical excision, and diagnosis is based on positive histopathologic identification [212]. Cysts are usually an incidental finding at necropsy, but they are of particular concern because they can cause severe disease in humans, who are also intermediate hosts [213].

Halicephalobus deletrix

Halicephalobus gingivalis (formerly *Micronema deletrix* or *Halicephalobus deletrix*) is a small roundworm that is considered to be saprophytic, but it occasionally acts as a facultative parasite in horses and humans. Common organs affected include the brain, spinal cord, nasal and oral cavities, kidneys, and pituitary gland. Less affected organs include the lymph nodes, heart, lungs, liver, bones, and stomach. As with *Setaria* spp., the neurologic signs depend on the part of the CNS affected. Ocular related signs including inconsistent menace response and facial nerve dysfunction have been reported with CNS involvement [214]. *Halicephalobus gingivalis* is known to have a predilection for the basilar pituitary region of the brain, which may explain the high incidence of blindness reported with this disease [215]. Renal dysfunction caused by larval migration in the renal parenchyma and granulomatous nephritis may be found, often in combination with neurologic signs [216]. Clinical ocular signs include uveitis, granulomatous chorioretinitis, optic neuritis, and blindness [217, 218]. Transmission of the parasite through the colostrum from dam to foal has been reported [219]. Antemortem diagnosis is difficult, and necropsy reveals granulomatous lesions in affected organs. Treatment is often unsuccessful once neurologic signs have been noted. For single peripheral granulomatous lesions, ivermectin and diethylcarbamazine combined with surgical excision and anti-inflammatory medications may be useful [220].

Miscellaneous disorders

Neoplasia

Ocular and clinical signs of metastatic neoplasia depend on the site and extent of metastasis. Metastasis to the eye may present as a discrete mass, or as uveitis that is not responsive to traditional therapy [221, 222]. Endoscopy, radiography, CT, ultrasonography, cytology, or biopsy of accessible lesions all aid in the diagnosis of neoplasia in the horse. Aspiration and cytology of ocular fluids may also aid in diagnosis of the actual tumor type [222]. Chemotherapy and radiation treatment are available, but these treatments are often cost prohibitive and not attempted because of the grave prognosis associated with most metastatic tumors [223, 224].

Hyperkalemic periodic paralysis

Hyperkalemic periodic paralysis (HYPP) occurs as an autosomal dominant trait in Quarter horses, American Paint horses, Appaloosas, and Quarter horse crosses that can trace their lineage back to the Quarter horse stallion Impressive [225]. Horses with HYPP tend to be well muscled and, as such, have been preferentially selected, and it is estimated to occur in 56.4% of halter horses [226]. The frequency of the allele is much less in other performance horses of the same breeds [227]. The defect involves a point mutation in the sodium channel of the muscle cells that results in a phenylalanine–leucine substitution [228]. When serum potassium levels are increased as a result of exercise, diet, or disease, the sodium channels fail to deactivate, leading to an influx of sodium into muscle cells and an outflow of potassium from the cells. This leads to persistent depolarization and muscular weakness.

Horses often appear healthy between attacks. In the early stages of an attack, horses may appear hyperexcitable, sweat profusely, and have focal muscle fasciculations. As the episode progresses, the fasciculations may spread to other muscle groups and produce a generalized weakness, which may result in ataxia, dog sitting, or total recumbency in severe cases [229, 230]. The only ocular sign associated with HYPP is retraction of the globe by spasm of the retractor bulbi muscle, resulting in third eyelid elevation (Figure 15.18) [7].

Electromyography may reveal complex repetitive discharges, myotonic potentials, and abnormal fibrillation potentials, even between attacks [230]. Homozygotes experience more frequent and severe episodes and may develop pharyngeal edema or laryngeal paralysis, which may become life threatening, especially in foals [231]. Serum potassium concentrations may or may not be elevated during an attack, but serum creatinine kinase activity is not high unless the horse becomes recumbent. A diagnosis of HYPP can be presumed on the basis of characteristic clinical signs and bloodlines. A DNA test has been developed for definitive diagnosis of the disease.

Treatment is aimed at correcting hyperkalemia. Some mild cases may respond to light exercise. Slow intravenous infusion of calcium gluconate, glucose, or sodium bicarbonate can be used to treat a more severe attack. These treatments should be given as a solution in 0.9% sodium chloride and administered to effect. Lactated Ringer's solutions should not be given to horses with HYPP, because they contain potassium. Acetazolamide, a carbonic anhydrase inhibitor that acts as a potassium-wasting diuretic, can be given orally in doses of 2–4 mg/kg twice a day as a preventative therapy in horses that experience frequent attacks. A proper diet is also important in preventing attacks. Legume hays such as alfalfa should be avoided, as well as foods containing molasses or oils. Grass hays, oats, corn, wheat, barley, and beet pulp are good alternatives. Medications should be given in corn syrup rather than molasses, as molasses has a high potassium content. Small, frequent feedings and regular exercise may also help decrease the incidence of attacks.



Figure 15.18 Retraction of the globe and protrusion of the third eyelid in a horse experiencing an episode of HYPP.

Vitamin A deficiency

Vitamin A has important functions in an animal's growth and development, maintenance of the immune system, and vision. For vision, specifically, vitamin A is necessary for the retina in the form of retinal, which combines with the protein opsin to form rhodopsin, a light-absorbing molecule necessary for

low-light and color vision. Vitamin A deficiency is rare in horses grazing pastures or fed good-quality commercially available diets. Those animals that are deficient may show stunted growth, decreased hematopoiesis, or reproductive problems [232, 233]. Ocular signs associated with hypovitaminosis A include epiphora and night blindness [234]. In addition, the cornea may become hyperkeratinized, and the conjunctival goblet cells may become atrophied. Chronic vitamin A deficiency can result in complete blindness with dilated unresponsive pupils [235]. Decreased serum concentrations of iron, albumin, and cholesterol may also be observed [232]. Serum retinol concentrations or the retinol dose-response test may be used for diagnosis [233]. Vitamin A supplements are available for horses fed deficient diets.

Systemic lupus erythematosus

A 2-year-old Standardbred filly with weight loss, alopecia, seborrhea, oral ulceration, lymphadenopathy, and hemolytic anemia with positive Coombs and antinuclear antibody test results was given a diagnosis of systemic lupus erythematosus [236]. A skin biopsy specimen revealed characteristic interface dermatitis with immunoglobulin deposition in the basement membrane. Immunosuppressive therapy was attempted but was not successful. Ocular lesions, though not noted in this report, may include alopecia of the periorbital skin and lesions of the mucocutaneous eyelid margins [81, 237].

Pemphigus

Pemphigus foliaceus is an autoimmune vesiculobullous disorder characterized by intraepidermal acantholysis (loss of cell–cell adhesions), intercellular deposition of IgG and complement on mucocutaneous junctions, and circulating autoantibodies [238]. Appaloosas are predisposed to the disease, although it can occur in other breeds [239]. Clinical signs may wax and wane but initially consist of vesicles or pustules that rapidly progress to crusts and erosions with alopecia, scaling, and epidermal collarettes (Figure 15.19) [239]. Lesions are most commonly seen on the head, ventrum, and limbs, especially around the coronary band. Anorexia, weight loss, edema, fever, and, rarely, pruritus may be evident. Pemphigus may affect the eyelids and conjunctiva [240].



Figure 15.19 Pemphigus foliaceus with scaling and crusting of the head in a 2-year-old Standardbred gelding.

Diagnosis is based on the characteristic histologic changes seen on cytologic examination of skin biopsy specimens or vesicular fluid. Treatment consists of immunosuppressive therapy such as corticosteroids (prednisolone, 2 mg/kg given PO every 24 hours, or dexamethasone, 0.2–0.5 mg/kg given IV every 24 hours initially, then tapered to the lowest dose that controls clinical signs) or injectable gold salts (aurothioglucose 1 mg/kg given IM once a week until a response is seen, then once monthly) [239, 241]. The prognosis is guarded in adult horses, although in foals and younger horses, the disease may spontaneously regress by 1 year of age [239].

Neonatal isoerythrolysis

Neonatal isoerythrolysis (NI) is a primary immune-mediated hemolytic anemia of foals that occurs when the mare produces antibodies (alloantibodies) against a red blood cell antigen inherited from the stallion (alloantigen) that is not present in the mare [242]. In most cases, the antibodies are directed against the Aa or Qa factor. These antibodies are then passed to the foal in the mare's colostrum, resulting in lysis of the red blood cells and hemagglutination. Before development of these alloantibodies by the mare, the dam must become sensitized to the red blood cell factor, by either exposure during a prior pregnancy or blood transfusion, or, rarely, by transplacental exposure during the current pregnancy. The foal must have inherited the factor from the sire.

Incidence varies among breeds, with Thoroughbreds and Standardbreds being more likely to have the disease. The incidence may be as high as 10% in mule foals, with antibodies directed against donkey factor, a red blood cell factor unique to mules [243]. Foals are usually healthy at birth, with clinical signs developing 12–36 hours after ingestion of colostrum. Weakness, lethargy, loss of suckle, and varying degrees of tachypnea, tachycardia, and dyspnea occur. The mucous membranes, including those of the conjunctivae, are initially pale, then become icteric as the disease progresses. Anemia, hyperbilirubinemia, thrombocytopenia, hemoglobinemia, and hemoglobinuria may be noted on blood tests and urinalysis. Other ocular signs can include conjunctival, episcleral, and intraocular hemorrhages [81]. In severe cases, seizures and death occur as a result of hypoxia.

Diagnosis is made on the basis of a hemolytic crossmatch between the mare's serum or colostrum and the foal's red blood cells, the result of a direct Coombs test, or a saline agglutination crossmatch [244]. Treatment should be aimed at preventing further colostrum absorption, ensuring adequate nutrition, supportive care, and stall rest; nasal oxygen or blood transfusions may be given as necessary [245]. Blood transfusions should be washed red blood cells from the mare or blood from an unrelated gelding. In the case of mules, any unrelated horse is

a suitable donor, because horses do not produce the donkey factor; however, blood from a mare previously bred to a donkey should not be used.

With prompt recognition of the disease, the prognosis for NI foals is good. Development of liver failure, kernicterus, and complications related to bacterial sepsis are the most common causes of death in foals with NI [246]. Liver failure is related to the amount of whole-blood products administered, as multiple transfusions can lead to iron intoxication and hepatopathy. Deferoxamine mesylate can be administered to foals requiring multiple transfusions to enhance urinary iron elimination and decrease hepatic iron accumulation [247]. Kernicterus is neurologic disease caused by extremely high levels of bilirubin, which readily crosses the blood–brain barrier. Plasmapheresis can be used to rapidly drop bilirubin concentrations in NI foals, and prevent the development of kernicterus [248].

Prevention is key. Owners should be educated that the mare should not be bred with the same stallion or other stallions with the same blood factor. If the mare is bred with a stallion that has the same blood factor, the next foal should not be allowed to suckle the mare's colostrum and will need an alternative source of antibodies, such as colostrum from another mare that does not have the alloantibodies or a commercially available hyperimmune plasma solution.

Equine Cushing's disease

Equine Cushing's disease (ECD) is caused by a dysfunction of the intermediate lobe of the pituitary gland, leading to hyperplasia resulting from a loss of dopaminergic inhibition. This produces an increase in the pro-opiomelanocortin-derived peptides produced in the pituitary, including corticotropin, α-melanocyte-stimulating hormone, endorphin, and corticotropin-like intermediate lobe peptide. Corticotropin, α-melanocyte-stimulating hormone, and endorphin all provide positive feedback to the adrenal glands, resulting in an increased production of glucocorticoids from the adrenal cortex [249]. The hyperplastic pars intermedia may also lead to compression of the adjacent pars distalis and pars nervosa.

Clinical signs include polyuria/polydipsia, hypertrichosis (Figure 15.20A), failure to shed, hyperhidrosis, muscle wasting, recurrent or chronic infections, delayed wound healing, laminitis, parasitism, pseudolactation, seizures, and, occasionally, secondary diabetes mellitus or diabetes insipidus [249, 250]. Ocular manifestations include bulging of the supraorbital fat pad caused by fat redistribution (Figure 15.20B) [251], conjunctival edema, and abnormal vision. Abnormal vision is due to compression of the optic chiasm (Figure 15.20C) or cataracts caused by chronic elevated cortisol levels. Additionally, corneal sensitivity has been noted to be decreased in older horses and in those with ECD [252]. Decreased corneal sensitivity is associated with impaired wound healing; therefore ECD may increase the risk for nonhealing or recurrent corneal ulcers in horses.

Diagnosis is often based on the typical history and clinical signs seen in an older horse. Changes may be noted on hematologic analyses, including a mature neutrophilia, lymphopenia, hyperglycemia, and high alkaline phosphatase activity, although these findings are inconsistent, and the results of blood tests may actually reflect an underlying disease process. Numerous laboratory tests for the diagnosis of ECD are available [253]. Endogenous corticotropin (adrenocorticotrophic hormone (ACTH)) and the low-dose dexamethasone suppression test (DST) are considered first-tier tests and are adequate for diagnosing most cases of ECD. ACTH is often preferred as it only involves a single blood draw; however, special handling procedures must be followed, including collecting into plastic tubes and immediately refrigerating the sample and then freezing the plasma within 8 hours of collection. Elevated concentrations are diagnostic for ECD. The DST is administered by collecting EDTA blood for the measurement of plasma cortisol levels immediately before and 19 hours after intramuscular administration of 40 mcg/kg dexamethasone. Horses with ECD will not show any significant decrease in cortisol production. This test should not be used in cases with an acute episode or history of laminitis. Horses may show a seasonal variation in ACTH secretion, as well as in response to DST; therefore reference ranges should be used that are specific for the time of year. Horses with equivocal results of either of these tests can undergo a thyrotropin-releasing hormone (TRH) stimulation test, with measurement of ACTH as a second-tier diagnostic. Horses with ECD will show an increase in ACTH at 15 and 30 minutes.

Treatment should always include excellent husbandry and preventive medicine. Horses should have proper and consistent farriery, dentistry, vaccination schedules, and parasite control. Proper diet and coat clipping of horses in hot climates are also essential. Many horses can be treated this way without additional therapy. In cases with severe clinical signs, including laminitis and secondary infections, pharmacologic intervention may be necessary [253]. Pergolide, a dopamine agonist, is the treatment of choice (0.25–2 mg PO every 24 hours). A Federal Drug Agency (FDA)-approved product is available for horses in the USA and should be used over compounded products, as pergolide has been demonstrated to be unstable in a variety of compounded formulations [254]. Once the horse is receiving the lowest dose that is effective according to the results of the endocrine tests and clinical signs, it will need to receive that maintenance dose for the rest of its life. Cyproheptadine (0.25–0.5 mg PO every 24 hours) or trilostane (0.4–1.0 mg/kg PO every 24 hours) can be used alone or in combination with pergolide for horses that do not respond to pergolide monotherapy. With proper management and therapies, the prognosis for horses that do not develop laminitis is good.

Hypothyroidism

Thyroid gland dysfunction in the adult horse is rare and often misdiagnosed [255]. Treatment of hypothyroidism is often initiated in overweight horses with cresty necks, based on single-point, low thyroid hormone levels. However, experimental induction of hypothyroidism in adult horses produces little to



(A)



(B)



(C)

Figure 15.20 (A) Classic haircoat (hirsutism) of equine Cushing's disease on a 19-year-old Quarter horse mare. (B) Bulging of the supraorbital fat pads and nasal discharge due to chronic sinusitis. (C) Gross necropsy photo of the pituitary gland in this same horse.

no clinical signs, and complete surgical removal of the thyroid gland typically results in mild, nonspecific signs such as cold intolerance, changes in the haircoat, lethargy, exercise intolerance, and decreased feed intake [256, 257]. True hypothyroidism can only be documented by use of TRH and thyroid-stimulating hormone (TSH) stimulation testing.

Ocular signs were not noted in any of the horses with experimentally induced hypothyroidism, but there is a report of hypothyroidism and polyneuropathy causing keratoconjunctivitis sicca (KCS) in a horse [258]. The horse presented with bilateral blepharospasm, hyperemic and edematous conjunctiva, and dull corneas, and had an abnormal Schirmer tear test. Signs of trigeminal and facial nerve dysfunction were also present, leading to a diagnosis of KCS secondary to damage to the parasympathetic pathways of the facial nerve. The KCS resolved after treatment with levothyroxine.

Trauma

Trauma to the head caused by falling over backward and striking the poll or blunt trauma from direct kicks or running forward into a fixed object are frequently associated with neurologic disease. Striking the poll can result in basilar skull fractures involving the nuchal crest, basisphenoid/basioccipital bone, occipital bone, or petrous temporal bone. Trauma to the poll can also result in acute unilateral or bilateral blindness caused by neuropraxia of the intracranial optic nerve [259]. The dural sheath that encases the optic nerve is fused with the periosteum of the optic canal, and traumatic concussive shock waves can cause stretching, shearing, or avulsion of the optic nerve and/or chiasm.

Initially, findings on fundic examination may be normal, or intraocular hemorrhage may be seen; but, with time, the optic nerve atrophies and the peripapillary retina degenerates [67, 259, 260]. Damage to the brain and spinal cord may also result, with or without the presence of a fracture. Basilar skull fractures often result in unilateral vestibular signs toward the side of the lesion, and bilateral nystagmus present in the early stages has a fast component away from the side of the lesion, similar to those previously described [261]. In addition, hemorrhage from the nose and ears may be noted. Damage to the region of the petrous temporal bone may result in facial nerve paralysis and/or Horner's syndrome [7, 259]. KCS secondary to a presumed basilar skull fracture and damage to the lacrimal gland innervation has also been reported in one horse [262]. Clinical signs that follow blunt trauma to the head may occur immediately after the incident or several days later if intracranial hemorrhage or inflammation is present. Depression, cranial nerve deficits, ataxia, and proprioceptive deficits in all four limbs are commonly seen [263, 264].

Diagnosis is based on the history of trauma combined with clinical signs and diagnostic imaging. A radiographic diagnosis may be difficult to establish because of the overlying soft tissue and bony structures, particularly for basilar skull fractures. CT or MRI is more sensitive, but anesthesia is risky in horses with intracranial hemorrhage and increased intracranial pressure. Treatment is aimed at reducing inflammation in the CNS with corticosteroids, NSAIDs, and dimethyl sulfoxide. Mannitol has also been used for its osmotic effects to help decrease brain and spinal cord edema; however, it may worsen active hemorrhage and should be used with caution, or substituted with hypertonic saline. Secondary infectious meningitis may result from skull base fractures; therefore broad-spectrum antibiotic coverage with drugs known to have good CNS penetration is recommended. If fractures are present and accessible, they should be stabilized as soon as possible to prevent further damage. The horse should be kept in a well-padded stall to prevent additional injury. Prognosis for horses with fractures is poor in most cases, and horses that do recover will often have residual deficits.

Air embolism

Venous air embolism via a jugular catheter is a rare cause of disease in adult horses [265, 266]. Large volumes of air (more than 0.25 mL/kg) are necessary to cause clinical signs, although the rate of air embolism may also influence the development of signs. Reports in the literature of two horses with suspected air embolism document severe agitation, pruritus, pulmonary edema, vestibular disease, and blindness. Clinical signs, including blindness, resolved without specific treatment.

Optic neuritis

Optic neuritis has been reported in association with septicemia, parasite migration, trauma, hemorrhage, anemia, orbital cellulitis, guttural pouch disease, and intra-arterial injections of phenylbutazone [7].

Mare reproductive loss syndrome

In the spring of 2001, and to a lesser degree 2002, a syndrome of early fetal loss, late-term abortions, stillbirths, and neonatal foal deaths occurred in Kentucky, Ohio, West Virginia, and Tennessee [267]. The syndrome was subsequently called mare reproductive loss syndrome (MRLS). Aside from the reproductive losses, epidemics of fibrinous pericarditis and uveitis were also reported in horses of any age, sex, or breed during the same time period. The uveitis is described as peracute, severe exudative endophthalmitis and has been unilateral in all cases. Corneal edema, hemorrhage from the iris, and thick, proteinaceous, tan-yellow exudates are present in the anterior and posterior chambers. Culture and cytology of the affected eyes were negative. Treatment is based on systemic and topical anti-inflammatory therapy but may not always be successful. Permanent visual deficits or blindness may result.

There is strong evidence that links MRLS to the presence of the eastern tent caterpillar (ETC). Ingestion of the caterpillars, either in feed or via nasogastric tube, has reproduced abortion in pregnant mares and swine. The setae (hairs) of the ETC embed into the submucosa of the alimentary tract, creating microgranulomatous lesions. These lesions may allow bacteria from the alimentary tract of the mare to invade the circulatory

system and then establish infections in tissues where the immune surveillance of the mare is reduced, such as the fetus and placenta. These infections then lead to fetal death and the abortion characteristic of MRLS [268, 269]. However, administration of ETCs to horses has not reproduced either the fibrinous pericarditis or the unilateral uveitis. The epidemic of MRLS in Kentucky and the surrounding states appears to be over, but similar abortion storms have been reported in Australia, Florida, and New Jersey between 2004 and 2006. ETCs were present at each site of the abortion outbreaks.

Ivermectin toxicosis

An overdose of the avermectin parasiticide ivermectin has been reported to cause mydriasis and cortical blindness in adult horses, foals, and other equidae such as mules and zebras [270–272]. Other clinical signs include ataxia, lethargy, depression, muscle fasciculations, drooping upper and lower lips, recumbency, coma, and potentially death. The mechanism of toxicity is thought to be related to the drug's effects on gamma-aminobutyric acid (GABA). Young animals may be more sensitive because of an incomplete blood–brain barrier and greater penetration of the drug into the CNS. Concurrent exposure to toxic plants in the *Solanum* family has also been implicated as predisposing horses to ivermectin toxicity, possibly through downregulation of P-glycoprotein efflux pumps, which results in higher than normal drug concentrations in the brain and CNS [280]. Moxidectin, another avermectin, is also associated with toxicity, particularly in foals. Although blindness has not been specifically associated with toxicity, foals often present comatose, so assessment of vision is difficult [274]. Treatment is mainly supportive; sarmazenil, a benzodiazepine, may speed recovery [275]. Horses that survive the initial toxicity do not appear to have residual visual defects.

Toxic plants

Numerous toxic plants have been associated with ocular changes in the horse. Many of these cause neurologic signs leading to central blindness. Black locust trees (*Robinia pseudoacacia*) are common in the eastern states, and ingestion of the plant may cause gastrointestinal ileus, weakness, ataxia, and blindness. The clinical signs, including blindness, resolve with treatment. Plants containing thiaminases—such as horsetail (*Equisetum arvense*), kochia weed (*Kochia scoparia*), and bracken fern (*Pteridium aquilinum*)—can produce cortical blindness as seen with thiamine deficiency. Bracken fern is also associated with retinal degeneration caused by stenosis of the optic vessels and progressive retinal atrophy in sheep, although this has not been reported in horses. The toxic principle involved in the retinal degeneration is ptaquiloside, which also causes myeloid aplasia and bladder tumors in cattle, as well as gastrointestinal tumors in humans [276, 277]. Locoweed (*Astragalus* spp.) can produce severe CNS signs in horses and is associated with poor vision.

Numerous other plants can cause cortical blindness by inducing severe hepatic failure. The most common plants associated with this are those containing pyrrolizidine alkaloids, including *Crotalaria* spp., *Amsinckia* spp., and *Senecio* spp. Pyrrolizidine alkaloids cause characteristic changes in the liver, such as megalocytosis, periportal fibrosis, and biliary hyperplasia, which are easily detected on biopsy specimens. The poisoning is usually chronic in nature, although signs of hepatic failure may develop immediately. Icterus of the sclera and mucous membranes often develops as a result of hyperbilirubinemia. Horses with hepatoencephalopathy show signs of depression, ataxia, aimless wandering, circling, head pressing, and blindness. Photophobia may also be present in horses that have secondary photosensitization if they lack pigment in the skin around the eyes or in the third eyelid. Once horses show signs of hepatic failure and encephalopathy, and the prognosis is poor. Serum gamma-glutamyl transferase activity can be used as an early screening test for subclinical hepatic disease in horses grazing pastures with pyrrolizidine alkaloid-containing plants [278]. Other toxic plants associated with hepatic failure and cortical blindness in horses include alsike clover (*Trifolium hybridum*), buckwheat (*Fagopyrum esculentum*), and cow cockle (*Vaccaria pyramidata*). St John's wort (*Hypericum perforatum*) causes a primary photosensitization and potential photophobia without elevations in liver enzyme levels. Icteric sclera may also be noted in horses with hemolytic anemias and oxidative injury to the red blood cells caused by ingestion of red maple (*Acer rubrum*) leaves or wild onions (*Allium* spp.).

One of the most common ocular signs of plant toxicity is mydriasis associated with the ingestion of plants containing tropane and other alkaloids. These compounds include atropine, hyoscine (scopolamine), hyoscyamine, and solanine and are found in jimson weed (*Datura stramonium*), horse nettle (*Solanum carolinense*), sacred datura (*Datura meteloides*), blindweed (*Convolvulus arvensis*), nightshade (*Solanum nigrum*), black henbane (*Hyoscyamus niger*), buffalo bur (*Solanum rostratum*), and ground cherry (*Physalis* spp.). The toxins work on the autonomic nervous system and have clinical signs similar to those seen with administration of atropine, including mydriasis, tachycardia, gastrointestinal ileus, and colic. Other toxic compounds have been associated with mydriasis. Oleander (*Nerium oleander*) causes mainly cardiovascular and gastrointestinal effects as a result of cardiac glycoside production, but mydriasis and impaired vision may also be seen. Water hemlock (*Cicuta* spp.) produces cicutoxin, a potent neurotoxin that causes violent convulsions, muscle tremors, and cardiac degeneration, as well as mydriasis. Organophosphate poisoning in horses is rare, but it can cause miotic pupils as it does in other species.

Some plants are not toxic in and of themselves but can produce toxic effects from the molds and fungi associated with them [279]. Yellow sweet clover infected with *Penicillium* or *Aspergillus* spp. can produce dicumarol, which, when ingested, interferes with the vitamin K-dependent coagulation factors (II, VII, IX, X). This can lead to a bleeding diathesis in the animal, with hemorrhage into the anterior chamber. Corn infested with *Fusarium* spp. that produce the toxin fumonisin

B1 can cause blindness (see section **Equine leukoencephalomalacia**). Although the major toxic effect seen in horses exposed to black walnut trees (*Juglans nigra*) is a severe acute laminitis, the walnuts, when infected with *Penicillium* spp., may produce penitrem-A, a toxin that causes convulsions, hyperthermia, tachypnea, frequent urination, and mydriasis in many species.

Finally, some plants that produce burs or sharp projections can induce corneal trauma and ulceration. These include burdock (*Arctium* spp.), buffalo bur, and cocklebur (*Xanthium* spp.).

Future research

It is likely that diseases other than those described in this chapter can cause changes in the eyes and surrounding structures of the horse. In the future, careful examination of the ocular structures in all horses with systemic diseases may lead to the discovery of more ocular manifestations of disease and potentially useful diagnostic tools for general practitioners as well as ophthalmologists.

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CHAPTER 16

National and international regulations on ophthalmic disease and medications

Mary Lassaline

Introduction

Veterinarians involved in the care of performance horses may be in a position to diagnose and treat ophthalmic disease in patients for whom the disease or its treatment may affect their performance. Implications of performance-altering disease may be professional, legal, medical, or even life threatening. The goals of this chapter are (1) to provide a guide to agencies regulating equine sport; (2) to review ophthalmic diseases that may affect performance; (3) to give examples of regulations regarding ophthalmic disease; (4) to review medications used to treat ophthalmic disease that may affect performance or may be regulated; and (5) to give examples of regulations regarding medications used to treat ophthalmic disease.

Because regulations at any level of administration, including international, national, state, and local organizations, have the potential to change at any time, this chapter carries with it the disclaimer that any information provided here is intended solely as a guide, rather than as a definitive resource. The veterinarian's role is to inform and advise, but responsibility for compliance with regulations lies collectively with the owner, trainer, and veterinarian.

Regulatory agencies

The Food and Drug Administration (FDA) is an agency within the United States Department of Health and Human Services which is responsible for assuring the safety, effectiveness, quality, and security of human and veterinary drugs, vaccines and other biological products, and medical devices. The US Congress passed a set of laws in 1938 collectively known as the Federal Food, Drug, and Cosmetic Act (FFDCA). The FFDCA gave authority to the FDA to oversee the safety of food, drugs, and cosmetics.

National and international agencies that more specifically regulate equestrian sports include the Fédération Equestre Internationale (FEI), the United States Equestrian Federation (USEF), the National Thoroughbred Racing Association (NTRA), and the Canadian Pari-Mutuel Agency (CPMA). Websites for these agencies are listed in Table 16.1.

The FEI, founded in 1921, is the sole controlling authority for all international events in Dressage and Para-Equestrian Dressage, Jumping, Eventing, Driving and Para-Equestrian Driving, Endurance, Vaulting, and Reining. It establishes the regulations and approves equestrian programs at Championships and Continental and Regional Games, as well as the Olympic and Paralympic Games.

The USEF is the national governing body for equestrian sport including 29 breeds and disciplines. The USEF, which was founded in 1917, trains, selects, and funds USEF teams, which compete at the highest level of international competition, including the Olympic Games. It also licenses equestrian competitions of all levels across the US each year.

The NTRA is a coalition of Thoroughbred racetracks, owners, breeders, trainers, and affiliated horse racing associations in the USA whose mission is to increase the popularity of horse racing and improve economic conditions for industry participants. In 2001, the NTRA Task Force on Racing Integrity and Drug Testing released a report on a 2-year investigation of drug testing in Thoroughbred racehorses, which led to formation of the RMTC. The RMTC is a consortium of stake holders in the horse racing industry whose mission is to provide an independent voice for uniform rules, policies, and testing standards through research-based recommendations. The goal of these recommendations was to ensure the integrity of horse racing and protection of the welfare of horses and other participants. Its 23 member organizations represent horsemen's groups, breed registries, race tracks, racing regulators, industry associations, and veterinarians, and it includes the American Association of Equine Practitioners, the American Quarter Horse Association, the National Thoroughbred Racing Association, and the Jockey Club.

The CPMA is an agency within Agriculture and Agri-Food Canada that, among other tasks, including regulation of pari-mutuel betting at horse racetracks across Canada, regulates

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Companion website: www.wiley.com/go/gilger/ophthalmology

Table 16.1 Agencies regulating equine sport.

Name	Abbreviation	Website
US Food and Drug Administration	FDA	http://www.fda.gov/AnimalVeterinary/default.htm
Fédération Equestre Internationale	FEI	http://www.fei.org/fei/about-fei/structure
United States Equestrian Federation	USEF	https://www.usef.org/_IFrames/AboutUs/WhoWeAre.aspx
National Thoroughbred Racing Association	NTRA	http://www.ntra.com/
Canadian Pari-Mutuel Agency	CPMA	http://www.agr.gc.ca/eng/about-us/partners-and-agencies/canadian-pari-mutuel-agency/?id=1204043533186
Racing Medication and Testing Consortium	RMTC	http://www.rmtcnet.com/content_organization.asp

drug testing in horses to deter the use of prohibited substances through the Equine Drug Control Program. In addition, the CPMA performs research on drug testing, and provides information on elimination guidelines for veterinary drugs.

Ophthalmic disease in performance animals

The rationale for regulating ophthalmic disease in performance animals is to protect the equine and human athlete from injury. Performing in equestrian sports carries risk for both horse and rider. Eventing, for example, which combines the disciplines of dressage, show jumping, and cross country, is a risk sport. There were 18 rider deaths in 2006–2008 associated with injuries sustained during the cross-country phase of eventing, often resulting from a rotational or somersaulting fall of the horse [1]. Statistics reporting equine injuries and fatalities are not easily available, but one source reported 19 equine deaths in 2007–2008 [1]. Steeplechase races have a 0.4% fatality rate for horses, according to the British Horseracing Authority, and a 1.6% equine fatality rate in one of the discipline's most popular races during the period 2000–2010 [2]. Equine deaths may be the direct result of injuries sustained while competing, or indirectly by euthanasia associated with injury or loss of use. While it is unknown whether vision played any role in falls, injuries, and fatalities, any impairment that could affect performance can certainly contribute to these statistics.

Diseases that may affect performance can be classified into two types: those that result in visual impairment or blindness, such as corneal opacity, cataract, and retinal disease, and those that cause ocular pain, such as corneal ulcer, uveitis, and glaucoma. The impact of visual impairment and of ocular pain on performance is quite simply unknown.

Animals with laterally placed eyes and large monocular visual fields, like horses, may not have good binocular vision or stereopsis [3] relative to species like humans that have frontally placed eyes, although research suggests that horses can use stereoscopic information when it is available [4]. It is unknown, however, whether horses with only monocular vision exhibit differences in spatial vision and motion processing relative to bilaterally visual horses that are analogous to differences seen in humans [5]. See Chapter 12 for more information on equine vision. However, the functional impact of loss of vision in one eye is unknown.

One study evaluating the performance of horses following unilateral enucleation found no significant effect on likelihood of return to performance in horses, for both right and left eyes, across ages and across disciplines [6]. In that study, the associations between age at enucleation, equine discipline, reason for enucleation, time to vision loss (acute versus gradual), and eye enucleated (right or left) were investigated. Pre-operative occupation and post-operative performance were determined by telephone communication with an owner or trainer, or by referring to the veterinarian familiar with the horse. Of 34 horses for whom this information was available, 29/34 (85%) returned to work in pleasure or trail riding (11/13), flat racing (7/10), hunter/jumpers (4/4), dressage (3/3), group lessons (1/1), eventing (1/1), steeplechase (1/1), and as a broodmare (1/1). One of the five horses that did not return to work was retired from racing for lameness issues unrelated to enucleation. The remaining four horses who were not returned to work, two pleasure horses and two racehorses, were retired due to anticipated or perceived decrease in performance or behavior change following unilateral enucleation. Twenty-two of 25 horses (88%) with acute vision loss returned to their pre-operative occupation. No performance measure was evaluated in that study. Again, the impact of visual impairment on performance in horses is unknown.

Regulations regarding ophthalmic disease

Regulations on performance associated with ophthalmic disease vary by discipline and agency, although the majority of disciplines allow performance with only one visual eye. Regulations are generally limited to statements about loss of vision in one eye or complete blindness, but more specific or detailed findings and rulings are typically left to an official's discretion.

According to the Rules and Governance Rule Book for the USEF, unless a specific division rule states otherwise, all animals except stallions and mares in Breeding classes "… must be serviceable sound for competition purposes" and "… Animals with complete loss of sight in either eye may be found serviceably sound at the Judge's discretion, except in a class over fences where a Judge may ask a rider to change horses" [7]. A summary of the 2014 USEF regulations on performance associated with vision loss by discipline is shown in Table 16.2.

Table 16.2 2014 United States Equestrian Federation rules governing competition by discipline, as listed in the USEF Rule Book.

USEF division	Rule #	Rule	Ability to compete unilaterally blind
General	GR841	Animals with complete loss of sight in either eye may be found serviceably sound at the judge's discretion, except in a class over fences where a judge may ask a rider to change horses	Yes, with exceptions
General	GR1204.4	The official veterinarian's decision, if requested by the judge as to the serviceable soundness of a horse (i.e., whether the horse shows evidence of lameness, broken wind, or complete loss of sight in either eye), will be final for the purpose of awarding ribbons in the class for which he has been called	N/A
Andalusian/Lusitano	AL101.2	Horses with loss of sight in one eye may compete in performance classes only	Yes, in performance classes only
Arabian, Half-Arabian, and Anglo-Arabian	AR105.1	Horses with loss of sight in one eye may compete in any class except Breeding/Gelding In-Hand classes and Sport Horse In-Hand Classes	Yes, in performance classes only
Arabian, Half-Arabian, and Anglo-Arabian	AR117.1	Horses must be serviceably sound (i.e., horse must not show evidence of lameness, broken wind, or complete loss of sight in either eye)	No
Arabian, Half-Arabian, and Anglo-Arabian	AR121.4	Glass eyes shall be penalized	
Carriage Pleasure Driving	CP107.2	Horses must be serviceably sound and must not show evidence of lameness, broken wind, or impairment of vision in **both** eyes	Yes
Dressage	DR119.1	Horses showing evidence of broken wind or complete loss of sight in either or both eyes are permitted to compete. Horses with complete loss of sight in both eyes may only participate in classes in which they are shown individually	Yes
English Pleasure Division	EP101	Animals with complete loss of sight in one eye may be found serviceably sound at the judge's discretion	Yes
Eventing	EV104.4	As an exception to the general requirements of GR841, a horse is eligible for venting competitions even though it has complete loss of sight in one eye, provided sight in the other eye is normal and provided it meets the other requirements	Yes
Friesian	FR101.10	Horse must possess one eye that is not visually impaired. One eye prosthetic or an eye that is damaged/impaired either by illness, injury, or due to birth defect is permissible in all performance classes. Exceptions: In Hand, Western Trail, Hunter Hack, and Combination Drive, Ride, and Jump classes	Yes, with exceptions
Hackney	HK104.5	In the event an animal has lost sight in one eye, it may still be shown	Yes
Morgan	MO102.3	Animals with complete loss of sight in one eye may be found serviceably sound at the judge's discretion, except in a class over fences, where a judge may ask a rider to change horses.	Yes, with exceptions
Paso Fino	PF102.13	Animals with complete loss of sight in either eye may be found serviceably sound at the judge's discretion	Yes
Saddlebred	SB103.2	Horses must not show evidence of lameness, broken wind, or complete loss of sight in both eyes	Yes
Saddlebred	SB104.3	In the event that a horse has lost the sight in one eye, it must appear to have vision and may be shown with an artificial eye or contact lens	Yes
Shetland Pony	SP101	Complete or partial loss of sight in either eye will not be a disqualification if the loss of sight results from traumatic injury. A licensed veterinarian must verify the etiology of the sight loss as traumatic. Any pony showing evidence of lameness, deformity in feet, broken wind, or complete loss of sight in either eye shall be refused an award	Yes, with limitations

In polo, the Federation of International Polo Rules specifically state, "A pony blind in an eye may not be played" [8]. In contrast, performing with only one visual eye is allowed for American Quarter horses and for Standardbred pacers and trotters. According to the Official Handbook Show Rules of the American Quarter Horse Association, "… the use of a pacemaker or prosthetic eye may be permitted if the owner files written request for permission … after which, if the request is approved, such authorization will be noted on the horse's registration certificate." [9] Similarly, the United States Trotting Association Rules and Regulations state that "No horse may race unless he had unimpaired vision in one eye" [10]. For Quarter horse racing, however, no statement regarding eligibility for horses with a blind eye was found. For Thoroughbred racing in the USA, rules regarding racing with one blind eye vary by state and are regulated by state racing commissions.

Medications used to treat ophthalmic disease in performance animals

Medications used to treat ophthalmic disease that may affect performance include nonsteroidal anti-inflammatories, corticosteroids, cyclosporine, sedatives, and atropine. These drugs can affect performance by masking pain, which can predispose the equine athlete to injury, and by impairing vision—either by a direct effect on the visual system, such as the use of atropine as a cycloplegic which results in mydriasis and potentially altered depth perception, or by a systemic effect on mentation and behavior, such as the use of sedatives to reduce anxiety but also that potentially affect visual attention.

The use of medication to treat ophthalmic disease can be categorized into legend, over-the-counter, and extralabel. Legend drugs, more commonly known as prescription drugs, are approved in the USA by the FDA and are required by federal or state law to be dispensed to the public for veterinary use only on prescription of a licensed veterinarian. Over-the-counter drugs are sold directly to the consumer without a prescription. Extralabel, or off-label, prescribing occurs when an animal or human drug is used in a manner not specified in the FDA's approved packaging label, including the dose, route, frequency, indication, and species given on the label. Before extralabel prescribing occurs, it is the veterinarian's responsibility to make certain there is no approved animal drug that is labeled for such use in that species, or that contains the same active ingredient in the required dosage form and concentration. Additionally, if an approved animal drug exists, but the approved drug is clinically ineffective for its intended use, extralabel use of an alternative medication is permissible.

Regulations regarding medications used to treat ophthalmic disease

Rules and regulations governing equine sport exist to protect the health of both human and equine athletes, as well as to preserve the integrity of the sport by allowing athletes to compete on an even playing field. Agencies governing sport in individual disciplines should be consulted for specific regulations regarding allowable drugs and withdrawal times. Regulations on medication by discipline/agency are summarized in Table 16.3.

The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) permits veterinarians to prescribe extralabel uses of certain approved new animal drugs and approved human drugs for animals under certain conditions. Extralabel use refers to the use of an approved drug in a manner that is not in accordance with the approved label directions. Extralabel use is defined by the FDA as:

> "Actual use or intended use of a drug in an animal in a manner that is not in accordance with the approved labeling. This includes, but is not limited to, use in species not listed in the labeling, use for indications (disease and other conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from labeled withdrawal time based on these different uses."
>
> (21 CFR 530.3(a)) [11]

Extralabel use of drugs may only take place within the scope of a valid veterinarian–client–patient relationship. Extralabel use is limited to circumstances when the health of an animal is

Table 16.3 Regulations on medication.

Regulation	Regulating agency	Website
Animal Medicinal Drug Use Clarification Act	FDA	http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/ActsRulesRegulations/ucm085377.htm
Clean Sport	FEI	http://www.fei.org/fei/cleansport
Equine Drugs and Medications Program	USEF	https://www.usef.org/_iframes/drugs/default.aspx
Controlled Therapeutic Substances	Racing Medication and Testing Consortium	http://rmtcnet.com/national-uniform-medication-program/controlled-therapeutic-substances/
National Uniform Medication Program	Racing Medication and Testing Consortium	http://rmtcnet.com/national-uniform-medication-program/
Equine Drug Control Program	CPMA	http://www.agr.gc.ca/eng/about-us/partners-and-agencies/canadian-pari-mutuel-agency/equine-drug-control-program/?id=1204670391600

threatened, or when it is suffering or death may result from failure to treat. Compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine is permitted, as long as there is no approved new animal or approved new human drug that, when used as labeled or in conformity with criteria established in this part, will, in the available dosage form and concentration, appropriately treat the condition diagnosed.

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CHAPTER 17

Management of blind horses

Ann E. Dwyer

Introduction

A variety of ophthalmic diseases may cause horses to lose their sight [1]. Recurrent uveitis is the most common cause of bilateral blindness; but glaucoma, corneal disease, cranial trauma, blunt or penetrating globe trauma, neoplasia, and infection also can cause vision loss. (See online material for further discussion.) In many cases, attending veterinarians have provided proper treatment and caretakers have followed medication schedules, but blinding sequelae still occur. Data on the incidence of blindness in horses are scant, but field experience suggests that at least 1% of horses lose sight in one or both eyes during their lifetime [2]. Several facts are of concern if vision loss is imminent:

- Horses have a natural history as grazing animals hunted by predators. This gives them a wary temperament. They are prone to display sudden fight or -flight responses. When cornered, frightened, or threatened, horses may kick, strike, or run.
- Horses are herd animals that follow a strict social hierarchy. Visual cues are paramount in establishing the dominance order of the group. Individual animals that ignore the visual cues of their herd mates are often bitten, shoved, or kicked by dominant individuals. Dominant herd members may limit the food and shelter access of nondominant members.
- Horses are large, strong creatures, usually weighing more than 500 kg. Yet their lower legs have a diameter not much larger than a baseball bat. Horses trapped in fences or other hazards often panic. The result can be fractured extremity bones and other severe injuries.

Given these truths of equine social life, behavior, and anatomy, how do horses cope with the loss of their primary orienting sense? Some horses adapt poorly and must be euthanized to protect the safety of their handlers and themselves. However, others show a remarkable ability to adjust to blindness. Adaptation to blindness depends on the inherent temperament of the horse, the dedication of the owner, and the presence of a safe and predictable environment.

While a large number of horses are euthanized if they become blind, many horse owners have an interest in blind horses and opt to provide for them throughout their natural lifespan. Some are kept at pasture as pets; others are used in a variety of ways. Ultimately, management choices for blind horses are made considering many factors, including how well the horse adapts to loss of sight, the horse's obedience and aptitude for training, and the economics of the situation at hand.

Adaptation to blindness: give them time

Although blindness can occur suddenly, onset in most horses is gradual. Caretakers of horses with failing vision usually notice progressive uncertainty, especially in low-light situations. As sight dims, horses may bump into walls or fences and show reluctance to walk over terrain that is unfamiliar. Herd behavior changes, even among horses that have been pastured together for years. Horses that are ridden may shy frequently, refuse to obey simple commands, and show reluctance to move forward. Balance may be altered, and horses with minimal acuity may show a head tilt or postural change.

When vision finally fails, caretakers report that blind horses go through a "transition period" where their behavior is unpredictable, reflecting fear and anxiety [3]. Rapid circling, "freezing" in place, prolonged neighing, spooking, and aggressive body motions (e.g., crashing into walls, running over a handler) may be observed. This initial adjustment period can be dangerous to both the horse and handler, but it is usually transient, lasting anywhere from a few days to several weeks. Cautious handling, patience, and common sense are needed to help the horse adjust to vision loss during this critical period (Figure 17.1).

In most situations, newly blind horses should not be turned out with a large group of horses. They will do best if they are initially kept by themselves in a stall or turned out in a small corral or paddock with a single carefully chosen companion,

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(A)



(B)



(C)

Figure 17.1 (A) Contact with familiar handlers and stablemates facilitates adaptation to blindness. Mindy, a 38-year-old mare, has just gone blind from glaucoma. She is anxious but is calmed by the presence of her long-time companion Suntan. (B) Mindy shows a head tilt and wary posture the first time out of the barn, but she is settled by the voice and touch of her owner and by Suntan. (C) Soon Mindy accepts her vision loss, and grazes with contentment. (*Source*: Photographs courtesy of Deborah and Rocco Distaffen, Spencerport, NY.)



Figure 17.2 Hanging a bell on the halter or neck strap of a sighted pasture-mate helps blind horses locate their companion. (*Source*: Photograph courtesy of Jeannie Henderson, Honeoye Falls, NY.)

such as a quiet horse, goat, or donkey. It may be helpful to hang a bell on the halter or neck strap of the companion (Figure 17.2).

Newly blind horses show anxious behavior but appear to be settled by the voice, smell, and touch of people they knew and trusted when they had sight. While the transition/adaptation period is **not** a time to try to train a blind horse to do new things, frequent handling and attention are appropriate. All owners report that **talking** is a key part of blind horse management. The constant murmur of a handler's voice provides reassurance, lets the horse know where the handler is, and avoids surprise. Handlers also report that frequent **touch** in the form of grooming and petting is calming and comforting to blind horses. The blind horse soon learns that auditory and tactile signals from a trusted handler indicate a safe place.

Adjustment to vision loss is helped if the horse is given a predictable daily routine. Feeding should be done at the same time and in the same place every day. Fresh water should always be available. If the horse is turned out, it should be led out along the same path each time and released at the same spot. Free-choice access to hay is a good settling aid. If the horse is being managed with a companion, the pair should not be separated during the adjustment period. Personnel visiting the farm must be aware of the status of the newly blind animal and should be cautioned to act with common sense and respect. Startling stimuli (farm vehicle traffic, aggressive dogs, flapping tarps, etc.) should be kept to a minimum.

Acceptance of vision loss and adjustment to blindness occurs in most innately calm horses over a period of days to weeks. A few horses take several months to display full adaptation but still exhibit progressive acceptance and increasingly confident behavior. Well-adapted blind horses tend to be cautious and careful and do not have a high rate of injury. Some horses, particularly those that have innately high-strung temperaments, never adapt. Horses that do not adapt well continue to exhibit anxious behavior and are prone to injuring themselves and their handlers.

Decision-making for owners

Owning a horse is a big responsibility; owning a blind horse is an even greater one. Horses have a lifespan of approximately 30 years; owners who are faced with the decision of what to do with a horse that is blind should consider the ramifications of supporting that animal for many years to come. Decisions on whether to keep the horse as a pet, use the horse in some capacity, or choose humane euthanasia are dependent on many factors, including the horse's temperament, applicable herd dynamics, facility limitations, economics and welfare considerations. Decision-making must prioritize the security and welfare of the horse and the safety of the handlers.

Adaptation to blindness in the horse is highly dependent on the individual's temperament. Horses that are high strung, nervous, and reactive are usually the most challenged. When sight is lost these horses appear to experience more fear and anxiety than horses of calmer disposition. Frantic behavior such as constant stall circling, compulsive calling to former herd mates, and intolerance of lead rope or cross tie restraint may be displayed. Anxious blind horses may crash into walls or fences

or run over people who try to help them. Such behavior poses obvious risk to both the horse and its handlers. Blind horses that persist in exhibiting dangerous behavior after being allowed a generous trial period for adjustment may need to be euthanized for safety reasons (Figure 17.3).

Horses that exhibited calm behavior and quiet temperaments when they had sight are usually the best candidates for adapting to blindness. Once the adaptation period is complete, these horses usually transition to patterns of behavior that are predictable and easy to manage. However, the owner must commit to extra safety precautions that are implicit when an animal as large as a horse is kept on a property, especially if there are other horses on site and/or frequent visitors. These precautions include special care to "blind-proof the environment," vigilant handling of the blind horse, and prudent choices in confinement. The owner may need to provide turnout for the blind horse that is separate from the rest of the herd, and identify a quiet companion for that enclosure. People that handle a blind horse must be aware of its nonvisual status and be coached in safe handling protocols.

Some owners do not have the resources to provide a suitable environment for a sightless horse, even if it has adapted well to vision loss. Some of these animals are donated to sanctuaries or placed in foster homes, and some are euthanized. Ultimately, individual circumstances will dictate the choices that are made in managing every horse that loses sight.

Mapping their world—how do they do it?

"Experience is the cane of the blind" (popular Haitian saying).

Horses that have lost vision appear to have the ability to construct a "**mental map**" of their environment (Figure 17.4). Owners of blind horses cite remarkable stories of the navigational skills of their horses. Blind horses traverse the perimeter of their paddock or pasture boldly, following paths and laneways without hesitation. Blind horses often run and play in their fenced enclosures, halting just short of the boundary. "Dark-adapted" horses travel their home terrain with such confidence that outside observers may mistake them for sighted animals. No one knows just how blind horses are able to orient themselves so well, but current research on the neuroscience of vision and navigation in other species suggests a few mechanisms that may facilitate spatial awareness in blind horses:

Neuroplasticity of the visual cortex

Neuroplasticity is a term that describes the brain's ability to reorganize itself by forming new neural connections throughout life. In humans, the visual cortex region of the brain is massive, occupying over a third of the anatomy of the cerebral cortex. The visual cortex processes light signals in sighted individuals, and is an area of high activity. Abundant



Figure 17.3 Individual circumstances dictate the choices made in managing blind horses. The three horses in this photograph all had different fates. Nikki, the bay mare on the far right, is regularly used for riding. Lena, the chestnut mare in the center, is never ridden but is a calm and well-behaved companion. Destiny, the chestnut filly on the left, was blind at birth. She never adapted well to blindness and had to be euthanized at 3 years of age for dangerous behavior. (*Source*: Photograph courtesy of Steve Smith, Rolling Dog Farm, Lancaster, NH.)



Figure 17.4 Blind horses construct a mental map of their environment. Gideon, a blind Appaloosa, calmly roams his pasture and has no trouble locating food or water. (*Source*: Photograph courtesy of Jeannie Henderson, Honeoye Falls, NY.)

research has shown that the neuronal circuitry of the visual cortex in blind individuals of many species is not abandoned but is instead "rewired" and reallocated to the processing of other sensory input, particularly that associated with auditory and tactile stimuli [4, 5].

Spatial navigation and neural representation, or the brain's positioning system

A cellular basis for the higher cognitive function of spatial navigation and route recognition has been postulated in recent decades. Dr John O'Keefe, Dr May-Britt Moser, and Dr Edvard I. Moser shared the Nobel Prize in Physiology or Medicine in 2014 for related research investigating the cellular nature of a "positioning system" in the mammalian brain that governs spatial orientation and navigation [6]. This "internal GPS" is activated when certain cells in the brain are triggered because the host has moved into a new place. The activation occurs at the specific point in time that the change in position occurs. A unique "map" of activated neural cells is created, and the "map" changes as the animal moves through space. This "internal GPS" is thought to function to direct individual route navigation in a process termed "**path integration**".

Four groups of cells that are part of the path integration system have been studied in rats and mice [7–10], and functional MRI studies have demonstrated similar cells in human subjects [11]. "**Place cells**" are a group of cells in the hippocampus that become activated when the individual is in a very particular place, such as a corner of a room. "**Grid cells**" are another group of cells located in the entorhinal cortex (parahippocampus) that fire in a grid-like pattern when an individual moves and crosses a space. Firing activity of these cells creates a pattern of neuronal activity that forms a grid made up of 3-D equilateral triangles. The grid pattern is unique to the particular space traversed. Evidence is mounting that electrical activity of grid cells and place cells, working through networks with additional "**border cells**" (cells that are active in a closed environment) and "**head direction cells**" (cells that act like a compass), generates an internal navigation system—a kind of "cellular mental map" that can be imagined as a virtual model of the outside environment [6]. The network is activated through the visual cortex in sighted subjects, but subsequent research on blind subjects has shown that path integration can also develop in the visual cortex **in the absence of visual stimuli**. In these blind subjects the "plastic" visual cortex was retooled to process spatial information received by nonvisual senses such as touch. Moreover, "place cells" fire in response to certain exact "places" independent of visual stimuli in both sighted and blind individuals [12, 13].

Echolocation

Echolocation is a term that describes the acquisition of spatial information about the environment that is perceived when a subject senses sound waves that travel through the environment, bounce off nearby surfaces, and are reflected back to the ears of the recipient. Long studied in species like bats and marine mammals, the principle of echolocation is the same as that of sonar.

Some blind people have become highly skilled in echolocation [14]. Using distinct "tongue clicks" that propel sound waves into their surroundings, these individuals have trained their brains to process the reflected sound to generate a detailed "mental map" of the objects in the immediate environment. Information gathered on the location, dimension, and density of nearby objects allows these individuals to move easily in a complicated environment, often fooling observers into thinking they possess sight. As with the reallocated pathways of the cellular GPS system, and evidence showing reallocation of the visual circuitry to process tactile stimuli, research has shown that the visual cortex of the brain in blind individuals is very active in processing audible echo signals because it has undergone a "rewiring" process where resident neurons now respond to nonvisual stimuli [15].

Research on neuroplasticity, path integration, and echolocation has not been performed in horses, but these concepts have been studied extensively in multiple other mammalian species, including humans. It is interesting to speculate that similar neural processes may contribute to the remarkable ability that blind horses demonstrate in navigating a wide range of environments.

Coping in the dark

Whatever the underlying neurophysiologic mechanisms of their perception, simple observation confirms that blind horses rely heavily on increased use of their remaining special senses, just as blind people do. Blind horses consistently demonstrate increased use of their **sense of hearing**. Their ears move often, collecting sound waves like satellite dishes. They act as if their hearing is more acute than the average horse and orient themselves in their environment on the basis of the loudness and direction of the sounds they hear. They recognize the voices of their handlers and are calmed by learned verbal cues. Sounds from their regular pasture companions attract special attention.

The **sense of smell** of blind horses also appears enhanced. They often scent the ground or air, moving their noses toward perceivable smells as they search for other horses or food sources. They do not have difficulty locating hay, succulent pasture, grain, or water.

Blind horses use their **sense of touch**, specifically their muzzles, to investigate their environment. The muzzle is one of the most richly innervated regions of the horse's body. The density of sensory nerves in the equine lip and nose region is similar to the concentration of sensory nerves in the human hand. A blind horse running its nose over a pasture fence or stall gathers information in much the same way that a blind person reads Braille with his or her fingertips. Blind horses should be encouraged to explore their surroundings and touch new people and things with their muzzles. The long whiskers of the periocular region and muzzle should not be clipped because these structures help the horse "map" and understand the environment (Figure 17.5).

Blind horses with even temperaments often modify the fight-or-flight behavior that can be so hazardous to the health of a



Figure 17.5 Blind horses appear to use their nonvisual senses, especially touch, to navigate. Just a few days after his left eye was enucleated, Gideon methodically explores his turnout area. (*Source*: Photograph courtesy of Jeannie Henderson, Honeoye Falls, NY.)

sighted horse. Many anecdotes demonstrate that these animals override their natural tendency to panic when faced with a situation in which they are stuck or trapped. Many blind horses that get tangled in fences or farm machinery escape injury because they calmly wait for assistance. A sighted horse in a similar situation would be expected to panic and sustain severe trauma.

Common-sense safety concerns

A safe environment is important as blind horses can easily be traumatized. Walls and fences should be smooth and free of nails, sharp pieces of wood, or projecting pieces of wire. Stall entry and exit will be easiest if the stall has a sliding door or a door that swings out into the aisle. All hardware should be free of any sharp or hook-like projections. The J-shaped handles of water buckets should be taped over, as these often become gapped with use, presenting a hazard that can trap and tear an eyelid (Figure 17.6).

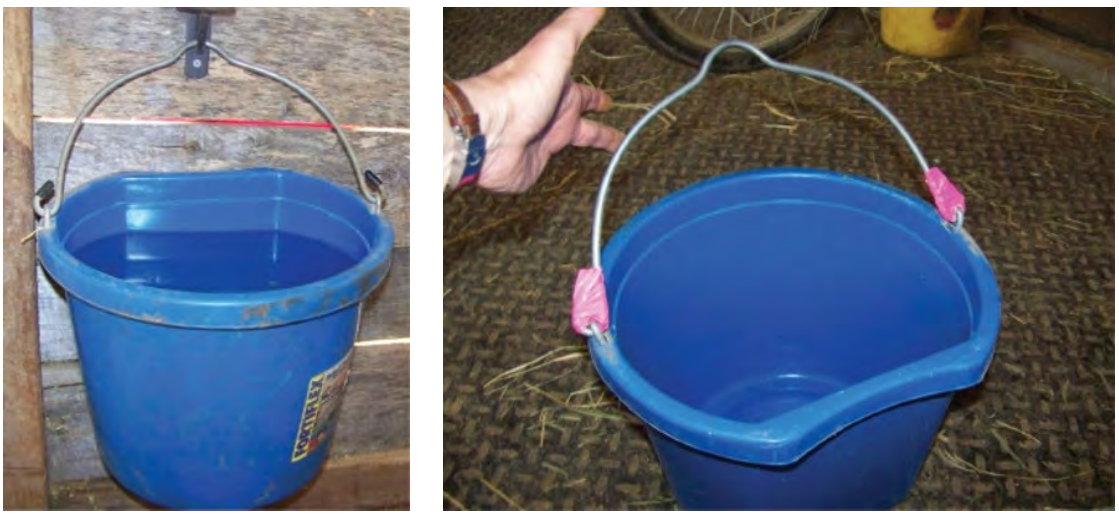
A blind horse may spook and jump sideways if something like snow sliding off a roof or a loose dog scares it. Another great stressor for blind horses is wind. The exact reason that wind causes alarm is not known, but it may be that wind interferes with the usual audible cues that blind horses use for orientation. People working with blind animals should be especially careful if high winds, unusual loud noises, or loose animals are present, and should always be prepared to take evasive action if the horse gets startled and makes a sudden move. Like all horses, blind horses can be dangerous to be around if they are frightened.

Signage can be posted on stalls or paddocks of blind horses to alert visitors to the animal's disability. Regular handlers should stand near a blind horse's shoulder when working with it, because this is the safest position from which to react if the horse makes any quick moves. Veterinarians and farriers must be aware that the horse is blind and should take a little extra time to reassure the horse using "talk" and "touch" before initiating any actions that might be painful or surprising to the horse.

The decision to turn a blind horse out into a pasture once it has adapted to vision loss is dependent on the horse and the safety of the pasture. It is a good idea to walk a horse around the perimeter to introduce it to the new pasture space. The process of "mental mapping" may be aided if the handler taps on the fence as it is circumnavigated. Extra time should be spent at the water trough and gate (Figure 17.7). Audible signals like "swishing" the water and rapping on the gate will help the horse locate the key features of the pasture [16].

The footing of all enclosure(s) should be level and free of holes. Obstacles like mounting blocks, jumps, or farm equipment should be removed. Corral or paddock fencing must be horse-safe. Post and pole, split rail, plastic or wooden boards, woven wire-mesh fencing, or metal pipe panels are good choices for fence boundaries. Barbed wire and stand-alone electric wire fences are inappropriate, as wire barbs pose obvious safety hazards and the electric shock transmitted from electrified wire can panic a blind horse, causing it to run through the fence. Smooth wire-strand fencing is not optimal for safety reasons, but if this type of fencing is the only option, strips of fabric can be tied to the wire at 1.5- to 2.5-m intervals. The strips will flutter in the wind and the associated noise will aid the horse in respecting the fence boundary.

Tree branches, holes, ponds, ditches, insecure fencing, and farm equipment are obvious hazards that should be eliminated



(A) (B)

Figure 17.6 (A) The handles of water buckets pose a risk for eyelid laceration as the J-shaped hooks can develop a gap wide enough to trap the lid margin if a horse rubs its face on the handle. (B) This hazard can be eliminated by taping up the bent hooks.



Figure 17.7 Handlers can help introduce blind horses to elements in the pasture. Here, TJ, a blind Standardbred gelding, is shown the water trough. (*Source*: Photograph courtesy of Susan Straumann, Woodstown, NJ.)



(A)



(B)

Figure 17.8 Immovable objects like trees can pose a major hazard to blind horses. (A) This blind mare sustained a facial laceration in her pasture. (B) Hoof-prints and bloodstains in the snow proved the injury was caused by contact with tree branches.

if possible (Figure 17.8). Immovable vertical obstacles like trees or poles can be made safe if they are rimmed with tires filled with sand, or marked by spreading an apron of gravel or rock around their base. The water trough should be located along the fence line and should not contain any sharp corners or rough edges. Seasonal hazards must be taken into consideration, as very wet weather can create dangerous bogs or high water in pasture creeks, and very cold weather paired with freezing rain can create ice patches that are treacherous for blind horses (Figure 17.9).



Figure 17.9 Seasonal hazards must be considered when choosing turnout space for blind horses. This photograph shows a blind horse that has slipped on a large ice patch. He became exhausted trying to rise and had to be lifted with a sling held up by a tractor bucket. Hay was spread around the horse's body to improve footing.

Bullies and buddies: social interactions with other horses

Horses in herd situations establish a social hierarchy, with dominant individuals ranking higher in the pecking order than submissive ones. In a herd situation, a blind horse usually falls to the bottom of the social order. Dominant sighted horses will take advantage of the blind one, chasing it away from feed sources. They will bully, bite, and push the handicapped horse, keeping it away from others. Blind horses are threatened and frightened by dominant individuals and will become skittish and nervous. Blind horses in herds tend to lose weight because of poor access to food and they may not come up to the pasture gate when other horses are being brought in. For all these reasons, it is generally not advisable to turn blind horses out in herds.

However, horses are social individuals and are usually happiest if they have a companion. Many calm horses are well suited to a "**buddy**" role for a blind horse. By all reports, bonding between two well-matched horses usually develops quickly. Once a compatible pair has been identified, the two equine friends can be turned out together in their own enclosure and will be content to live together as a pair (Figure 17.10). Often "buddies" are housed in adjacent stalls. In some cases they have the ability to touch noses and smell each other when stabled if the stall wall that separates them has a grating or does not go to the ceiling.

Companion horses that are visual act as "seeing eyes" and often appear to lead their unsighted companions over unfamiliar terrain. Sometimes the guidance is in the form of a nose-to-tail physical presence. Other times, the blind horse listens and scents for clues that define the location of the buddy. Vocal contact is frequent, with both individuals calling back and forth to each other. In some cases the sighted horse may wear a bell on its halter that provides guidance. Observers have seen buddy horses appear to lead the blind partner through lanes and gates.

Several sanctuaries have been developed that house multiple blind horses. Managers of these facilities often pair two compatible blind horses together as pasture companions or "buddies" (Figure 17.11). They report that the bond between the pair of blind horses is just as strong as the bond between a sighted and blind horse. The horses stick close together and figure out the boundaries of their world, navigating their environment together. They will groom each other's coats with their muzzles, use each other's tail as a fly switch, and graze nose to nose [17].

Whatever the visual status of the buddies, the attachment between the pair is usually strong (Figure 17.12). As such, one horse will become quite anxious if separated from the other, and this fact must be taken into consideration if the two are pulled apart. If circumstances arise where a pair must be separated permanently (e.g., if one becomes ill and dies), the remaining horse will go through a period of anxiety and distress. However, the horse will generally accept and bond quickly with a replacement "buddy" if their temperaments are compatible.

Blind broodmares with foals

Mares that become blind for nonheritable reasons are often bred, and may produce several foals during their lifespan [18]. Blind broodmares are as maternal as sighted mares and show strong protective behavior toward their offspring, especially in



Figure 17.10 A calm, sighted horse is a good "buddy" for a blind horse. Blind Mindy never strays far from buddy Suntan. (*Source*: Photograph courtesy of Deborah and Rocco Distaffen, Spencerport, NY.)



Figure 17.11 Two compatible blind horses can also make very good pasture companions. (*Source*: Photograph courtesy of Steve Smith, Rolling Dog Farm, Lancaster, NH.)



Figure 17.12 Whatever the visual status of the "buddies," the bond between them is usually very strong. (*Source*: Photograph courtesy of Steve Smith, Rolling Dog Farm, Lancaster, NH.)

the first few weeks of the foal's life. They need to know that their foal is nearby and are often more relaxed if the foal wears a halter with a bell. Like sighted mares, they show signs of panic if separated from their offspring. A blind mare that is stressed by separation and trying to reach her foal will be heedless of people or obstacles in her path and thus dangerous. Farm employees and veterinarians working on blind broodmares or their foals should always take care to restrain the pair in such a way that the mare is aware that the foal is near. This usually means holding the foal close to the mare's front end where she can swing her head and touch, hear, or smell the foal.

Training blind horses: talk and touch

Management of a blind horse is simplified if the horse is taught a "vocabulary" of a few simple commands that the horse will obey when being led or worked on. At the same time, the handler should establish rules and boundaries for acceptable behavior in any circumstance that can be anticipated. Training should include clear modeling and positive reinforcement of behavior that will maximize safety and ease of handling when the horse is being groomed, led, fed, and transferred from one place to another. As time goes on, additional training will teach the horse proper behavior for interventions like farrier and veterinary visits.

Blind horses must be well adjusted to vision loss before serious training begins. Handlers who practice constant **talking** and **touching** will help their horse adapt to blindness and set the stage for future lessons. Caretakers should speak in constant low soothing tones to calm the horse and help it become oriented. They should offer frequent hand contact and close physical presence. Blind horses will be steadied if they are led with a guiding hand on the neck or shoulder (Figure 17.13). With time and patience the horse will relax. Adaptation is complete when the horse navigates its environment with confidence and carries out all parts of the daily routine (eating, turnout, grazing, grooming, etc.) without undue anxiety. Basic training seeks to reinforce good behavior any time the horse is handled or moved, with the end goal of instilling habitual behavior that is safe for both horse and handler.

After the horse has adjusted to blindness, structured training sessions can begin. The habit of constantly touching and talking to the horse should be continued, respecting the fact that tactile and auditory senses are heightened in all blind animals. Trust will grow and basic commands will be learned quickly if the trainer gives consistent cues and stays relaxed and nonthreatening. Initially, commands such as "whoa," "step up," "step down," "stand," and "back" are taught. Verbal signals for the desired behavior are augmented by tactile cues that help "explain" the desired result.

"Whoa" can be taught by saying the command while restricting forward movement using pressure on the lead shank or rein and a hand on the chest (Figure 17.14). "Step up" can be learned by guiding the horse over a known elevation like a ledge entrance into a barn or the ramp of a trailer while voicing the chosen cue (Figure 17.15). "Stand" can be taught by speaking the command while emphasizing the halt stance with a hand on the body. The most important commands to master are the order to stop ("Whoa") and a cue to let the horse know there is an obstacle



Figure 17.13 Blind horses are steadied by the touch of a familiar handler. Daisy, a 38-year-old Shetland pony, who has had both eyes removed, follows her owner just by feeling his hand on her neck.

coming ahead [16]. Good trainers use consistent pronunciation of commands and inflections that do not vary in pitch to teach blind horses the exact meaning of the chosen set of cues. They keep their tactile cues consistent and clear.

As training goes on, the horse will learn to pick up additional nonverbal cues and will start to respond to the trainer's touch, footfalls, and body position. Blind horses benefit from natural horsemanship exercises that involve positive reinforcement of desired behaviors. Most of these natural horsemanship methods involve frequent auditory and tactile cues, so they are easily adapted to blind horses.

Safety concerns preclude veterinarians from advising their clients to ride their blind horses. Still, many owners choose to use their blind horses for riding. Trainers of blind riding horses report that these horses benefit from long sessions of ground work before any attempt is made to put weight on their back. Equipment like the saddle pad, saddle, bridle, and girth is put on and taken off over and over until the horse is thoroughly familiar with the sensation of being "tacked up" and accepts the pressure of any straps that hold equipment in place. Considerable time is spent teaching the horse the typical mounted aids by giving the same signals from the ground. The rein aids are taught by using rein pressure applied to the bit by a person walking beside the bridled horse, coupled with already learned verbal commands [16].

Advanced riding aids can also be taught from the ground using "long lining" sessions where two long straps or reins are affixed to the bit, one on each side. The straps can be used to "drive" the horse from behind, or do lunge work in a circle. The straps transmit signals that are similar to those that a rider on



Figure 17.14 Blind TJ is being taught to halt by his owner. While walking beside him, she gives the appropriate rein aids as she says the command "Whoa." (*Source*: Photograph courtesy of Susan Straumann, Woodstown, NJ.)



Figure 17.15 Commands are taught by a combination of talk and touch in the presence of a trusted handler. "Step up" and "Step down" commands can be learned by guiding the horse up and down a trailer ramp. (*Source*: Photograph courtesy of Steve Smith, Rolling Dog Farm, Lancaster, NH.)

the back would give, but the signals all originate from a handler who is actually on the ground [16].

Trainers advise that no one should attempt to ride a blind horse alone. Initial weight-bearing sessions should be done with a competent "spotter" on the ground who can help reinforce the cues that the rider gives and also provide an added measure of safety. As basic training is completed, trainers can then add aspects of work that match the intended use of the horse. It is important to introduce new stimuli slowly, and stop the lesson or "switch gears" to a familiar task if something is frightening to the horse.

Owners who work with tractable, well-adapted blind horses report that these horses learn their lessons quickly. The horses seem to enjoy regular training sessions and put absolute trust in their handlers. Working with a familiar sighted person seems to give blind horses a sense of "freedom in the dark." A trained blind horse trusts that the cues the trainer gives are safe and learns to obey directions with confidence.

Communication between a blind horse and its trainer is quite refined, especially in horses that are used for dressage or other riding purposes. Trainers, riders, and owners cite the rewards of working with blind horses, describing heightened awareness of their own special senses and a deep and satisfying sense of partnership with these animals.

Lives blind horses lead

There are thousands of bilateral blind horses alive in the world. Their owners choose to manage them in a variety of ways.

Most blind horses are kept as simple "**pasture pets**." They are not ridden but are treasured family members (Figure 17.16). Their owners enjoy caring for them and are happy to provide them with basic shelter, feed, and handling in return for their affection and companionship. If the horse has a calm and gentle temperament and has successfully adapted to blindness, it may provide a steadying influence in the form of company for flighty youngstock or older sighted horses who do not tolerate solitude.

Horses that are kept as blind **broodmares** (Figure 17.17) demonstrate breeding behavior that is similar to that of sighted mares. However, lacking photoreceptors, they do not respond to artificial light treatment for inducing estrus early in the year when the natural photoperiod is short. Most blind mares show normal heat cycles by April and thus can be bred relatively early in the year. Their gestational issues are exactly the same as those of sighted horses, and they should be placed on the same schedule for nutrition, deworming, and vaccination as other mares on the farm. If a mare became blind as a result of leptospirosis-associated uveitis, serologic testing is recommended for other broodmares on the farm, because leptospiral infection is well documented as a cause of abortion. Most sighted mares foal in the middle of the night, but blind broodmares tend to foal at any time of day or night, so extra vigilance is warranted when these mares near their due dates.

A veterinary consultation is advised if a blind or visually compromised mare or stallion is under consideration for breeding. Most Appaloosas with insidious uveitis or congenital stationary night blindness have genetic predisposition to visual



Figure 17.16 Many blind horses are kept as "pasture pets." Cloud, an Appaloosa mare that has been blind most of her life, is regarded as a member of the family. (*Source*: Photograph courtesy of James and Judith Griffin, Mendon, NY.)

problems [19], and horses that display silver dapple coloring often have a genetic predisposition to multiple congenital ocular anomalies (MCOA) syndrome [20–25]. European Warmbloods that are blind from uveitis commonly demonstrate a genetic predisposition to blindness secondary to an inherited equine leukocyte antigen (ELA) haplotype [26]. Animals that present with phenotypes associated with blindness or visual compromise should not be used for breeding.

The majority of blind horses are not ridden or driven: they are maintained as pets or are used as breeding animals. However, some blind horse owners do opt to train their animals to perform some kind of working role, as detailed below. Successful transition to a competitive or working role after sight loss is not guaranteed, but a small number of horses have achieved remarkable training and competitive success in disciplines that do not require navigation of fixed obstacles or work at high speed.

Some blind horses are used as **trail horses** (Figure 17.18). These animals have a strong bond with their riders and are highly cued to riding aids and voice commands. Mileage on unfamiliar trails cements the trust between horse and rider because the horse depends on the rider for guidance and avoidance of hazards. Blind trail horses are taught to step over logs and small obstacles in their path in response to voice or tactile cues from the rider. Anecdotal reports indicate that many blind horses adopt a very confident attitude on the trail. Some blind horses like to take the dominant "lead" position if riding is done in a group; others prefer to follow sighted horses. Most owners who maintain blind trail horses report that these animals are very agreeable mounts. They are eager to go out on rides and willing to enter and exit trailers. Like blind people who travel with service guide dogs, these horses seem to enjoy an outing using the rider as a pair of "seeing eyes."

Blindness is a common endpoint for horses, mules, and donkeys that work pulling carts, being ridden, or serving as pack animals to transport people or products in the developing world. Many blind equids continue to work as **driving**, **pack**, or **riding working equids**. They play a crucial role in the economic viability of the families that own them.

Some blind horses have been used in **therapeutic riding programs** where children and adults with disabilities learn to ride and practice horsemanship. Blind horses who succeed as therapeutic lesson horses must be well trained and quiet and have gentle dispositions. The riding therapy sessions usually involve at least two assistants on the ground. One assistant leads the horse and the other(s) provides guiding hands for rider stability and safety.

Caring for, riding, and observing a horse that has lost the sense of vision may help people who have disabilities. The horse's ability to cope with blindness may inspire the rider to overcome his or her own special challenges. Also, enucleated or phthisical blind animals have a "different" appearance that is at first a bit startling. These horses teach children and adult family members acceptance of altered appearance relating to physical challenges.

A few blind horses have gone on to celebrated careers as high-level athletes. **Dressage** is an English equestrian discipline



(A)



(B)

Figure 17.17 Blind broodmares can make excellent mothers. (A) Begam, one of the first daughters of the famed sire Alydar, was born blind with bilateral microphthalmia. Begam's breeder, Alice Headley Chandler, of Mill Ridge Farm in Lexington, Kentucky, raised her and bred her several times to the farm's resident stallions. (B) Begam produced six valuable Thoroughbred foals, three of which were stakes winners. All the foals had normal eyes. (*Source*: Photographs courtesy of Mill Ridge Farm, Lexington, KY.)



Figure 17.18 Some blind horses are used as trail horses. This photograph shows Domino, a blind Appaloosa, and Nikki, a blind Quarter horse, going out for a ride in Montana. (*Source*: Photographs courtesy of Steve Smith, Rolling Dog Farm, Lancaster, NH.)



Figure 17.19 Valiant, a Dutch Warmblood gelding, performing a dressage test in Florida. Bilaterally blind since the age of 6, this horse was trained to upper-level dressage. His rider provides performance cues or "aids" by subtle shifts in the position, pressure, and balance of her hands, legs, and body. (*Source*: Photograph courtesy of Dr Dennis Brooks and Jeanette Sassoon.)

practiced by some well-adapted blind horses (Figure 17.19). The sport involves a high level of precise communication between horse and rider. The signals that are used are primarily tactile because the rider uses subtle changes in the position and pressure of the hands, legs, seat, and body balance to tell the horse to change gait, speed, rhythm, and direction. Unlike other equestrian sports that involve obstacles (jumping), high speed (racing and polo), carriages (driving), or interaction with cows, poles, or barrels (many Western events), dressage takes place in a level arena at fairly low speeds and thus poses fewer hazards

for a blind animal. The rider tells the horse where the boundaries of the ring are by changes in his or her weight and body position and turns corners as part of the test pattern. A small number of blind horses have been trained to advanced dressage standards by skilled and empathetic trainers and have competed against sighted animals at a variety of levels [27].

Other blind horses have been shown with success in Western show ring events by both adult and youth riders (Figure 17.20). **Reining** is a discipline that has attracted a few blind competitors in Western shows. Like dressage, reining is a sport that does not involve obstacles but is highly dependent on training and precise communication between horse and rider.

Each horse's circumstances are unique, and safety considerations must take priority in any choice of equestrian activity. Veterinarians should not make recommendations about riding a blind horse, as their job is to tend to the medical and welfare concerns of the animal and only give advice on general management. Veterinarians must always stress safety for both horses and humans and educate their clients in handling methods that are conservative and safe.

Owners who are pondering decisions about working with their blind horse can be directed to several books [28, 29], articles [30], and websites [16, 31–35] where they can read about choices that other owners have made. They may also find useful information in books that discuss managing blindness in small animals [36].



Figure 17.20 Skips Golden Silk, a Palomino Quarter horse gelding, was performing and winning in Western show classes with 12-year-old owner Victoria Czech in the saddle just 2 months after losing sight in both eyes. (*Source*: Photograph courtesy of Mary and Victoria Czech of Chippewa Falls, WI.)

Horses with unilateral loss of sight

Many horses lose vision in a single eye for a variety of reasons, retaining normal vision in the fellow eye. Horses that lose vision in just one eye usually adapt well. If the blind eye has been enucleated they may show a head tilt for a short time after surgery, but generally revert quickly to a normal head carriage. Because they cannot see people or objects that approach on the blind side, they may be skittish when approached on that side. As a result, horses with unilateral vision loss are often led and approached on the visual side. Painful or unpleasant stimuli like injections are best administered on the sighted side. When the horse is handled on the blind half of the body, the handler should talk to the horse in a reassuring tone and keep a hand on the horse's body so that the animal is aware of the handler's position.

Veterinary ophthalmologists are not able to calibrate acuity or depth perception in either one- or two-eyed horses with certainty. Horses that have unilateral blindness have only half the visual field of a fully sighted horse, so safety questions arise when athletic use of these animals is debated. For this reason, owners are usually advised to use one-eyed horses as sport horses with caution. However, a review of 34 horses enucleated at a referral center showed that 85% (29/34) returned to work in their previous discipline soon after eye removal. Disciplines that the horses were used for prior to surgery included flat and steeplechase racing, dressage, eventing, hunter/jumper shows, trail riding, lesson work, and breeding. Most of the horses in the study had become acutely blind just prior to enucleation, and reasons for eye removal included ulcerative keratitis, perforation, uveitis, glaucoma, and neoplasia [37].

A survey of the world of equestrian competition shows that unilaterally blind horses can be found leading just about every type of sporting life that fully sighted horses lead. Half-blind horses have run in the Kentucky Derby and other premier stakes races, have competed in international combined training events, have won championships in Western events, and have had storied careers as driving, harness, dressage, and show horses. Riders often comment that these horses approach jumps with confidence and appear to gauge distance well.

The show hunter sport sector has a rule that may restrict unilateral blind horses from their sanctioned competitions. The rules of the governing body that oversees rated hunter competition, the United States Equestrian Federation, state: "Animals with complete loss of sight in either eye may be found serviceably sound at the Judge's discretion, except in a class over fences where a Judge may ask a rider to change horses" [38]. The language of this ruling is open to interpretation, but it implies that a unilaterally blind or enucleated horse may be dismissed from the hunter ring.

Polo matches governed by the rules of the United States Polo Association forbid match play by ponies that have lost the sight in one eye. However, collegiate rules allow unilateral blind ponies in their tournaments. Professional polo ponies that sustain a blinding eye injury may be "handed down" to collegiate teams and are often very successful athletes in that venue. See Chapter 16 for more information on national and international regulations regarding eye disease and medications.

Enucleation of blind eyes

Many conditions that cause an eye to lose sight are acutely painful or rapidly progressive. Such cases must undergo prompt enucleation for humane and medical reasons. Decision-making is usually clear in severe disease, like intraocular neoplasia, large globe perforations, or corneal infections that progress to endophthalmitis.

Some conditions that cause blindness are not associated with any apparent pain and are static. Examples include horses that have cortical blindness from old head trauma, and nonphthisical horses that have mature cataracts. These horses do not benefit from ocular surgery and should retain their globes.

However, other conditions that cause blindness may be associated with subtle, low-grade, or chronic discomfort that is debilitating for the horse. Decision-making in these cases is murky as it is difficult to quantify ocular pain in a horse with a misshapen or diseased eye. Horses with phthisis bulbi, insidious uveitis, persistent corneal infections, and certain types of glaucoma may show chronic tearing, conjunctivitis, keratitis, and blepharospasm (Figure 17.21). These horses may be somewhat ill-tempered and show aversive behavior if the periocular region is handled. When such horses have the abnormal eye(s) removed, they often show a great improvement in temperament. This fact suggests that some blind horses endure constant pain in their nonfunctional globes that compromises their quality of life. Veterinarians have a duty to look out for these patients, and thus have a responsibility to try to identify the subset of blind eyes that are accompanied by chronic pain or discomfort.

Veterinarians should explain to owners that disease does not "stop" in a blind horse when vision is lost. Many structures in a nonfunctional globe can still transmit pain or be subject to ongoing complications. Blind eyes that suffer frequent corneal ulceration or show continuous blepharospasm are candidates for removal. Many horses that develop glaucoma secondary to uveitis become painful and difficult to manage as they suffer episodes of corneal disruption, edema, bullous keratopathy, and secondary infection. A point of diminishing returns is often reached where it is not rational to continue treating corneal disease in a nonfunctioning globe. If signs of chronic pain are identified, the owner should be counseled as to the positive welfare benefits of enucleation, and urged to schedule surgery.

Enucleation techniques are discussed in Chapter 5.



(A)



(B)

Figure 17.21 Blind horses may still experience debilitating ocular pain. Enucleation is a humane option for these globes. (A) This Appaloosa gelding suffers from equine recurrent uveitis and both globes are phthisical. Bilateral blepharospasm is a sign of persistent pain and inflammation. (B) Jake, an aged Appaloosa who went blind at 16 years of age, suffered from painful calcific keratopathy. He showed a notable improvement in temperament after bilateral enucleation was performed. (*Source*: Photograph courtesy of Lisa and Greg Weren, Hilton, NY.)

Special partnerships: life lessons with blind horses

Working with horses that have lost a special sense such as vision is a humbling and powerful learning experience. Observing how blind horses navigate teaches lessons of perception, adaptability, and persistence. Watching the athleticism of well-trained blind riding horses emphasizes the remarkable communication that occurs between educated horses and their riders. Anyone who helps free a blind horse trapped in a fence will be humbled by the "horse sense" that prevails when the animal needs help.

Blind horses can be an inspiration to children and adults who live with mental or physical disabilities. They can also be beloved pets that teach lessons of tolerance and acceptance of diversity. They are living proof that communication and connection between species occurs on many levels and in many ways. Few sights are more heartwarming than watching blind horses enjoy a good roll and a playful buck in a pasture on a sunny summer afternoon. These horses are telling us that life is sweet and full of value even when it is not perfect (Figure 17.22).

The biggest factor that determines the success of adapting a formerly sighted horse to a life of blindness is the horse's temperament, but the owner's resources and dedication to the process also play a key role. Owners must have the patience and risk tolerance to commit to everything that is part of providing a good environment for the horse and to assume the role of visual guide when the horse is in human company (Boxes 17.1 and 17.2). The best human partners create a new perceptive vocabulary for the horse that is centered on verbal and tactile signals. They may also provide a "buddy horse" that acts as a set of "seeing eyes" and provides equine companionship.

Box 17.1 Making the environment safe for a blind horse.

- Fence paddocks and pastures with horse-safe boundaries
- Consider tying fabric strips to fences to increase boundary auditory signals
- Remove objects from the pasture that horse could run into
- Create a ground border (apron of stones, sand-filled tires) around immovable vertical objects in pasture
- Position water and feed receptacles against a fence or stall wall
- Ensure that water and feed tubs have smooth edges
- Police stall walls and doors and paddocks for hazards and sharp projections; remove or cover up
- Tape over all J-shaped bucket handle hooks
- Demonstrate the boundaries of any new enclosure
- Post signage to alert visitors that a blind horse is present

Box 17.2 Common-sense tips for managing blind horses.

Veterinarians can provide the following list of tips to owners of blind horses:

- **Talk** to the blind horse often, using a calm tone
- **Touch** the blind horse often, especially when a new stimuli is pending
- **Teach** the horse basic verbal commands: "Whoa," "Step up," "Back," etc.
- Choose a quiet companion for the blind horse and keep them as a pair
- Keep a consistent daily routine
- Keep food and water in a consistent location
- Do not clip the muzzle whiskers or vibrissae around the orbit
- Practice loading off and on a trailer
- Be aware that sudden noises or high winds may scare blind horses
- Set limits for behavior and reinforce them. Spoiling a blind horse is **not** a good idea!



Figure 17.22 Blind horses may enjoy life the same way a sighted horse does. This photograph shows Scout, a blind Appaloosa, enjoying a good roll in his field. (*Source*: Photograph courtesy of Steve Smith, Rolling Dog Farm, Lancaster, NH.)

The partnership that develops between a well-adapted blind horse and its human caretaker is a very special one, based on mutual trust and respect. It is sustained by the emotional satisfaction that comes from helping a creature with special needs. Many people that care for blind horses would not trade their sightless companions for sighted horses. They report great personal rewards and satisfaction from living and working with these horses and take pride in letting them live out their natural lifespan.

Additional content

The book companion website at

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includes additional text and figures that are not in the printed book or E-book.

Please see the "**About the companion website**" page at the start of the book for details on how to access the website.

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