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How to Use a Smartphone Camera for Ocular Photography in the Horse

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1. Introduction

Smartphones are becoming quite ubiquitous and all have digital photographic and video capability (Fig. 1). They are always with us. The imaging technologies of these smartphones are increasingly quite impressive. Utilizing these capabilities will allow rapid telemedicine consults and are accessible for owners for use in monitoring eye conditions. An unintended consequence of this photographic capability is it can allow veterinarians to view and image the adnexa, cornea, iris, lens, retina, and optic disc of the horse. The technique mimics the distant direct technique of the ophthalmoscope. Adaptors, macro lenses, and other accessories also allow slit lamp photography and imaging of cytologic specimens. Software apps are already available to aid photography of the horse globe to levels that are, with a little practice, astonishing! The views with some smartphones are often superior to that of the direct ophthalmoscope.

One major problem with ocular photography is how to properly illuminate the eye so that the camera autofocus can discriminate the tissue that is to be imaged (Figs. 2 and 3). Software apps are available to utilize the “flash” of the camera as an illumination beam to view the cornea, lens, and fundus.

Fig. 1. Smartphone cameras can be utilized to photograph the eyelids, cornea, iris, lens, and fundus of the horse.
These light-emitting diodes (LEDs) are unfortunately very bright such that adjunctive methods are needed in some cases to reduce the illumination intensity.

2. The “Camera Awesome” App

The “Camera Awesome” app is compatible with iPhone and iPad and recently released a version for Android phones. It is simple to use and allows the veterinarian to obtain both photographic images and videos of the horse eye. Some selective editing is possible. It does not allow dimming of the illumination beam such that a diffuser must be utilized (Figs. 4 and 5).

Camera Awesome is easy to use, and this starts with the main interface. Most of the screen is given to image space with the vitals hidden away, easily accessed with a single touch.

Unlike the default camera app that comes with the iPhone, Camera Awesome allows for separate focus and metering points (Figs. 6–8). This is similar to using the exposure or focus lock on a digital single lens reflex camera and recomposing, without the need to recompose. Tapping the screen will recombin the focus and metering points. If you want to return the focus and metering points to the middle of the screen, a double tap anywhere will do.

On the video side, the controls are fairly simplistic and the Awesomize feature is not available. But the camera does have the ability to prerecord for five seconds before you hit the record button. This is useful if you are trying to get a horse to stand still. The video also allows for splitting focus and light metering and will adjust these during recording.
enabling simplistic racking functions. The flash can also be turned on or off while shooting video.

3. Camera+ App

The Camera+ app allows for photographic images only. It does not have video capability. It does have a rheostat for adjusting light intensity! Several drop down menus are available in Camera+ (Figs. 9–12).

The exposure can be adjusted separately from focus to more easily control the darkness or lightness of the images. The specific area to be imaged can be delimited with the focus box. The stabilizer mode achieves the sharpest photos. Rapid streams of shots in Burst mode can help get a focused image in the moving target.
The iPhone’s flash can be used as a continuous fill light to improve photo quality for macro shots. Up to 6× zoom with advanced digital processing is also available in the Camera+ app. Multiple images can be “stitched” together with software such as Panorama’s AutoStitch (Figs. 13–15).

4. Other Uses for the Smartphone and Ocular Photography

The camera of the smartphone is also capable of photographing cornea, lens, and lid problems in horses and can be used to photograph microscope specimens (Figs. 16 and 17).

5. Tips for Smartphone Photography of the Horse Eye

1. Use your camera’s flash as a light. It is important to get as much light as you possibly can on the tissue to be imaged but NOT too much as bright light really hurts.

2. Clean your lens. It may seem silly, but give your lens a wipe down before you start snapping photos with your phone. While most people are pretty good about keeping their...
grubby fingers away from camera lenses, it's not as easily done with smartphones.
3. Check your resolution. Use the largest resolution and highest image quality possible.
4. Videography may be simpler than still photography in the moving horse eye. The shutter lag inherent in digital cameras is often too slow to get the image you wanted. Videos can be saved and images easily captured from the video using software such as Windows Live Movie Maker or any Apple computer.
5. Equine phoneoscopy was done initially with the iPhone 4 or 4s as the distance between the camera aperture and flash was close. The iPhone 5 and other cameras may have too much space between camera and flash.
6. It is easiest to image lens, vitreous, and retinal regions if the pupil is dilated.
7. The camera must be held close to the cornea to get good images.
8. The flash should be reduced with sticky tape to reduce photophobia and blepharospasm. The Camera+ app has a rheostat to reduce the light intensity.

9. Software is available for automatic stitching of multiple photographs of the same subject (Panorama’s AutoStitch app).

10. The iPhone light is great for “dazzle reflex” testing.

11. Practice photography on enucleated eyes or anesthetized animals.

Acknowledgments
Tim Knott from the UK is the true leader in equine phoneoscopy and deserves credit for seeing the potential of the smartphone for helping horses with eye problems. Brian Patterson and Rob Lowe from the UK also piqued my interest.

Conflict of Interest
The Author declares no conflicts of interest.

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How to Use Ophthalmoscopes

Dennis E. Brooks, DVM, PhD, DACVO

1. Introduction
The posterior segment or fundus (the internal structures of the globe behind the lens) consists of the vitreous, retina, and optic nerve and is examined using low magnification indirect ophthalmoscopy followed by high magnification direct ophthalmoscopy. The two methods are complementary rather than exclusive.1 The results of an examination of the horse fundus are always more easily achieved in a dark environment with a dilated pupil.

2. Methods
Examination in the Dark

Indirect and Direct Ophthalmoscopy
The normal appearance of the equine fundus requires considerable practice for correct interpretation, because there is much normal variation. Most pathologic lesions of the fundus are identified near and below the optic nerve head and typically involve hyperpigmentation or depigmentation.

Indirect Ophthalmoscopy
This is a useful technique for screening the ocular fundus and can be performed most simply using a bright pen light or transilluminator and a condensing lens. The system produces a low magnified reversed inverted virtual image, such that a large field of view is produced (Figs. 1–4). Mydriasis, a bright light source, and darkness are essential for a detailed fundic examination.

3. Results and Discussion
How to Do Indirect
A condensing lens is held some 2–8 cm from the horse’s eye and the light source is held level with the bridge of the observer’s nose (Figs. 1, 3, and 4). The aim is that the observer’s eye, the light source, the lens, and the patient’s pupil should all lie in the same axis. The plane of the lens must be parallel to

Fig. 1. Indirect ophthalmoscopy is best used for low magnification screening of the horse fundus for lesions.
that of the horse’s iris and pupil. The light is directed into the horse’s eye so that the tapetal reflection is obtained and the lens is moved to and fro until a sharp clear image is produced. The observer-patient distance is approximately 50–75 cm.

In horses a +20 diopter (D) condensing lens is the most versatile in use, although the image is miniﬁed. A 20 D lens miniﬁes the fundic view with 0.79× and 0.84× magniﬁcation laterally and axially, respectively. The 20 D lens provides a nice panoramic, screening view of the equine fundus, but it is not satisfactory for detailed highly magniﬁed observations. Indirect ophthalmoscopy with a 14 D lens provides a magniﬁed view of 1.18× lateral magniﬁcation and 1.86× axial magniﬁcation. Indirect ophthalmoscopy with a 5.5 D lens provides 3.88× lateral magniﬁcation and 20.10× axial magniﬁcation in the horse.

Direct Ophthalmoscopy

The use of a standard direct ophthalmoscope produces an upright image of greater magniﬁcation than is possible with the indirect ophthalmoscope when used close to the patient’s eye (Fig. 5). However, viewing the fundus directly along a beam of light necessarily restricts the ﬁeld of view. The direct ophthalmoscope provides the most magniﬁed view of the fundus in the horse, with a lateral magnification of 7.9× and an axial magnification of 8.4×. Both distant direct ophthalmoscopy and close direct ophthalmoscopy should form part of a direct ophthalmoscopic examination.
There are also controls on the head of the ophthalmoscope for spot size (use the largest diameter, Fig. 6) and brightness (use as bright as the animal will tolerate). There may be controls for a red-free filter (rarely used) and a cobalt blue filter (use to look for corneal ulcers).

Red is seen as black with a “red-free” or green filter. The “red-free” (don’t call it “green”) filter is useful for enhancing the appearance of blood vessels and hemorrhages by making blood show up black. The “red-free” filter in the ophthalmoscope is used to differentiate between small retinal melanomas, or nevi, and a choroidal nevi. The retinal blood supply and its retinal pigment epithelium act like a red filter. Therefore, a melanoma located in the choroid will not be seen when viewed with the “red-free” filter since red and green cancel each other out. On the contrary, a melanoma located on or in the retina will still be seen with the “red-free” filter in place.

The slit on the ophthalmoscope is designed to look at the optic disc and is too wide at 2.2 mm for detecting trace aqueous flare (Fig. 7). This is especially true if there is corneal edema. In attempting to look for aqueous flare or evaluate the anterior chamber depth, the slit should be aimed from the front and the examiner look from the side to get the best view. If the scope has a cobalt blue filter (Fig. 8) this can be used to look for subtle corneal abrasions and corneal ulcers following the use of topical fluorescein dye.

How to Do Direct

Distant Direct Ophthalmoscopy

This technique uses the tapetal fundus as a means of retro-illuminating the structures anterior to it. The ophthalmoscope is set to 0 diopter (no magnification) and directed to find the tapetal reflex in the pupil at an observer-patient distance of 25–40 cm (Figs. 9 and 10). It is a useful way of assessing whether there are any opacities between the observer and the fundus and is usually used as a quick screening method prior to a more detailed assessment. Any opacities present in the ocular media (cornea, aqueous, lens, vitreous) will appear as black forms against the fundus reflex. An assessment of comparative pupil sizes may also be made using this technique.
Close Direct Ophthalmoscopy

Direct ophthalmoscopy can be performed with direct ophthalmoscopes. Direct ophthalmoscopy can be used to examine all aspects of the eye and adnexa but is most commonly done to examine the retina and optic nerve head. The aperture of the instrument must be held as close as possible to the observer’s eye and the subject’s eye (Figs. 11 and 12). As the examiner reduces the strength of the plus lenses, the focus of observation gradually extends posteriorly, so that magnified details of the lids, cornea, angle, aqueous, iris, lens, and vitreous are successively visualized until the features of the fundus are brought into focus. For a detailed examination, darkness is essential and mydriasis is helpful.

For examination of the external eye and adnexa a setting of +20 to +15 D (green numbers are plus) is required. The iris and angle may be examined with a setting of +15 to +12 D (Fig. 13). For the lens, the setting will be about +12 to +8 D, depending on whether the anterior or posterior parts are being examined. Intermediate settings will be required for the aqueous and vitreous (Fig. 14). Close examination of the fundus is usually performed with the ophthalmoscope placed some 2 cm from the eye and a setting between +2 D or −2D (red numbers are minus; usually 0) is required. The examination is often made easier and safer if the hand holding the ophthalmoscope is rested lightly against the horse’s head, so that sudden movements do not damage the eyes of the horse or the examiner.

Acknowledgments

Conflict of Interest

The Author declares no conflicts of interest.

Reference

How to Reach the Medical Standards of Care for Ulcerative and Non-Ulcerative Equine Keratopathies

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1. Introduction
Keratopathies may be ulcerative or nonulcerative in the horse. Ulcerative keratopathies may be infectious or sterile but are always associated with increased tear film protease activity. Ulcerative infectious keratopathies in horses may be caused by bacteria, fungi, and possibly viruses. Sterile ulcers may be caused by foreign bodies, tear film problems, corneal denervation, or basement membrane corneal dystrophies.

Nonulcerative keratopathies may also be infectious or sterile and range from cellular invasions of the stroma by inflammatory or neoplastic cells to persistent corneal edema. Infectious stromal abscesses, glaucoma-induced stria, uveitis-associated endothelial edema, eosinophilic keratitis, calcific band keratopathy, neoplasia, and immune mediated keratitis (IMMK) are major concerns.1,2

2. Medical Standards of Care
Ulcers
The current medical standard of care of treatment of ulcerative keratitis (Fig. 1) in the horse is a topical broad spectrum, nonirritating antibiotic, careful utilization of a mydriatic/cycloplegic, and an antiprotease compound such as serum. A systemically administered nonsteroidal drug is also critical to quick healing.

Ulcer Expectations
If the ulcer does not diminish in size at a rate of ~1 mm/day, the cornea does not vascularize at a rate of...
1 mm/day, and/or the signs of uveitis do not improve when therapy is initiated, then consider culture and/or cytology to document a change in the infection to decide if different antimicrobials are indicated. Additional antiproteases may also be beneficial. A suspicion of fungal involvement should always exist in ulcers that do not vascularize or heal. If the ulcer deepens, then amnion, conjunctival, or corneal grafting surgery is recommended. Contact lenses, chemical cautery with phenol or trichloroacetic acid, debridement of loose epithelium, gridding, and/or burring can be used for superficial noninfected ulcers.

**Stromal Abscesses (SA)**

The current medical standard of care of treatment of superficial and deep stromal abscesses (Fig. 2) is topical antimicrobials (including antifungals), atropine, and systemic antimicrobials and NSAIDs.

**SA Expectation**

Stromal abscesses must vascularize to heal. Therapy may take weeks. Vascularization and a reduction in the associated uveitis are signs of improvement. As the SA resolves, the blood supply leaves and the lesion will appear pale and then white. Superficial SAs tend to respond better to medical therapy than deep SAs. Intrastromal voriconazole may have some use in specific cases of SA. Surgery may be necessary to remove the abscess if medical therapy fails to resolve the inflammation in 2 to 4 weeks.

**Linear Keratopathy or Stria**

Broad white linear opacities can follow blunt globe trauma or immune mediated endotheliitis in the horse. These are single and nonprogressive (Fig. 3). Stria are breaks in Descemet’s membrane following elevated IOP in glaucoma. Stria in glaucoma are multiple and branching in nature (Fig. 4).

**Linear Keratopathy and Stria Expectations**

Intraocular pressure measurement is important. Careful monitoring over months to years is recommended. Therapy is generally not available or helpful, but if edema is present topical steroids are indicated.

**Corneal Neoplasia**

The current medical standard of care of treatment of epithelial dysplasia (Fig. 5) is topical 1% 5FU or 0.04 mitomycin C. Corneal squamous cell carcinoma (SCC) requires keratectomy and cryotherapy or ra-

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Fig. 2. A deep stromal abscess is present with corneal edema and vascularization.

Fig. 3. A single band opacity is present. Intraocular pressure was normal.

Fig. 4. Multiple band opacities from glaucoma are called stria.

Fig. 5. Epithelial dysplasia is a precursor to SCC and benefits from topical therapy.
diotherapy. Preferably, the keratectomy should be covered with an amnion graft, but conjunctiva can be used.

**Neoplasia Expectations**

Scarring of the cornea may be difficult to differentiate from tumor recurrence. Keratectomy and adjunctive therapies are needed for carcinoma *in situ* and SCC. Rapidly progressive and invasive SCC may necessitate enucleation.

**Eosinophilic Keratitis (EK)**

Eosinophilic keratitis is an immune-mediated corneal condition that is probably related to systemic parasites. It can be ulcerated or nonulcerated and infected with bacteria and fungi in some cases. The current medical standard of care of treatment of eosinophilic keratitis (Figs. 6 and 7) is topical steroids and antimicrobials. Ulcers can complicate the treatment.

**EK Expectations**

These lesions are typically slow to heal. Scarring of the cornea occurs. Cyclosporine A (2%), in combination with systemic nonsteroidal anti-inflammatory drugs (NSAIDS), are indicated. Topical cromolyn sodium (4.0% TID) or lodoxamide (0.1% TID) can also aid healing. Systemic corticosteroids may be necessary. Horses should be dewormed twice with ivermectin 10 days apart. Switching to moxidectin may also be beneficial. Superficial lamellar keratectomy to remove plaques speeds corneal healing.

**Subepithelial Keratomyocosis (SEK)**

Fungal infections in horses may begin as faint corneal opacities that are slightly painful. Fluorescein retention may be faint (Fig. 8) or absent. Rose bengal retention may be present. Slitlamp examination finds opacification beneath the epithelium. Cytology and culture following corneal scraping are diagnostic. Horses with the diagnosis of SEK are treated with topical antifungals.

**SEK Expectations**

Resolution of SEK will take several weeks. Immune-mediated keratitis should be considered in the differential diagnosis.

**Immune Mediated Keratitis (IMMK)**

Epithelial, subepithelial, stromal, and endothelial forms are possible. Immune mediated keratitis is a diagnosis made by appearance, biopsy and cytology, and response to therapy (Fig. 9). The current medical standard of care of treatment of IMMK is topical corticosteroids, nonsteroids, or cyclosporine A.
**IMMK Expectations**

Topical dexamethasone rapidly resolves many of these eyes, but co-infection is always a concern. Consider adding topical cyclosporine, and erythromycin or doxycycline, and systemic steroids and/or doxycycline to difficult cases. Corneal biopsy is recommended for recalcitrant eyes. Topical NSAIDS such as diclofenac or flurbiprofen are also indicated for IMMK eyes that recur.

**Calcific Band Keratopathy (CBK)**

Corneal degeneration from uveitis or chronic ulcers can result in calcium deposition into the diseased cornea. It can be a very irritating and painful problem. The current medical standard of care of treatment of calcific band keratopathy (Fig. 10) is topical 0.2% EDTA and debridement. Any accompanying ulcers are also treated with antimicrobials and antiproteases. Many of these horses also have equine recurrent uveitis (ERU) and the topical steroids may have induced the calcium deposition.

**CBK Expectations**

The calcium is generally chelated in a manner of days, but superficial keratectomy may be necessary if the calcium deposition is deeper in the stroma. Debridement, keratectomy, and/or burring may be necessary for resolution.

**Herpes and Viral Keratitis**

Multiple, superficial, white, punctate, or linear opacities of the cornea, with or without fluorescein dye retention, are found associated with equine herpes virus 2 and perhaps other viruses. The focal punctate corneal opacities (Fig. 11) may be found at the end of superficial corneal vessels and may retain rose bengal stain. Varying amounts of ocular pain, conjunctivitis, and iridocyclitis are present. Multiple foals in a herd may be affected. The current medical standard of care of treatment of suspected herpes keratitis is topically administered 0.1% idoxuridine, 1.0% trifluorothymidine, or 3.0% acyclovir.

**Herpes Expectations**

Viral keratitis is overdiagnosed, in the author’s view, but still exists in nature. The response to therapy can be quite variable and the clinician may become frustrated. Further diagnostic workups and cultures of ulcerated lesions can be helpful. Topical NSAIDs for treatment of equine herpes ulcers may have as much benefit as antivirals.

**Keratoconjunctivitis Sicca (KCS)**

The horse more commonly develops a qualitative KCS rather than the quantitative KCS in dogs. Diagnosis is based on Schirmer tear tests, rose bengal retention, and increased tear film breakup time. Equine KCS can be found with fungi and equine herpes, but can also be found with corneal edema and corneal fibrosis.

**KCS Expectations**

Qualitative KCS may be temporary and associated with corneal abrasions. Topical antimicrobials, serum, and a fly mask are indicated. Careful monitoring is indicated.

**Traumatic Bullous Keratopathy**

Blunt trauma to the globe can result in generalized and dramatic corneal edema (Fig. 12). Uveitis may...
or may not be present. The edema can triple the corneal thickness. The hyperosmotic, Muro 128 (5% NaCl), is indicated TID for these eyes.

**Traumatic Bullous Keratopathy Expectations**

Traumatic bullous keratopathy should resolve, beginning in the periphery first, over 3 to 6 weeks. Thermal keratoplasty or a Gundersen flap may help recalcitrant eyes. The edema is permanent if Descemet's membrane detaches.

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**References**

How to Diagnose and Treat Immune-Mediated Keratitis of the Horse

Dennis E. Brooks, DVM, PhD, DACVO

1. Introduction

The pathogenesis of many nonulcerative keratopathies of horses is believed to be mediated by a dramatic corneal immune response to a foreign protein, microbial antigen, or a self-antigen. Such suspected immune-mediated keratitis (IMMK) of horses has been classified primarily according to the apparent depth of the inflammatory response. Geographic differences in primary corneal insult, antigen exposure, and in the duration of the IMMK prior to its recognition have led to some discrepancy in the clinical presentations and responses to therapy. It does seem that the more chronic the duration of IMMK, the poorer response to medical therapy. The diagnosis of IMMK is based on clinical signs and response to therapy.

2. Epithelial IMMK

This is a unilateral disease affecting horses of any age. Vascularization is not a prominent feature of the disease. There is a diffuse central superficial corneal opacity usually associated with very slight blepharospasm and discomfort. There may be some slight associated conjunctival hyperemia or chemosis. The superficial opacity represents irregular coalescing clumps or islands of thickened epithelium with no underlying stromal edema. The unaffected areas of cornea appear normal. Fluorescein is weakly and transiently retained in the interstices between the islands of abnormal epithelium. Topical dexamethasone results in rapid corneal clearing in most cases and the disease has not been observed to recur after successful treatment.

A Note of Caution

Subepithelial keratomycosis has recently been identified in Florida, Canada, Brazil, Mexico, Denmark, and Germany. It looks identical to some cases of the epithelial keratitis form of IMMK. Biopsy and response to topical antifungal therapy are factors in making the diagnosis of subepithelial keratomycosis. It does seem capable of self-resolution in a few cases which is quite confounding!!

3. Chronic Superficial Stromal IMMK

This disease is characterized by an insidious onset with affected eyes showing only slight to moderate discomfort. The lesions appear to be initially restricted to the area under the upper lid (Fig. 2) and, less frequently, the third eyelid and lower lid. The paracentral cornea is commonly involved in the U.S. There is prominent subepithelial arborizing vascularization from the limbus, perivascular epithelial edema, and a superficial yellow-white stromal cell
infiltrate. Tear production is normal and no fluorescein uptake occurs. The apposing palpebral conjunctiva is moderately hyperemic.

The disease is initially unilateral but the contralateral eye may become affected with time. Topical treatment with cyclosporine A twice daily usually results in clearing of the cornea in 7 to 10 days in cases of short duration. Long-standing cases may be refractory to CsA. Most cases of chronic superficial keratitis are not responsive to topical corticosteroids. Subconjunctival CsA implants are helpful for this condition. Successful resolution of refractory cases of chronic superficial keratitis in the U.S. required superficial keratectomy and conjunctival grafting.

4. Chronic Deep Stromal IMMK
This is an episodic keratitis recurring at irregular intervals of up to several years. There is frequently history of initiating ocular trauma and the disease may derive from a local adaptive response to autoantigen in an immunocompetent cornea.

In the acute or active phase of the disease there is an extensive and dense, deep, stromal edema, white cellular infiltrate, and fibrovascular response with isolated blood vessels encroaching on the affected stroma at various levels. The intensity of the stromal changes varies between cases and between episodes. Despite the dramatic appearance of affected eyes, the disease is associated with no ocular pain. Subepithelial bullae may form and rupture, however, to create fluorescein positive superficial erosions that are associated with transient ocular discomfort. In some eyes, a yellow-green tinged coloration may appear within the midstromal central and paracentral cornea (Fig. 3). The ventral paracentral cornea is most commonly affected. Subepithelial calcium deposition may occur in some eyes. In the quiescent or inactive phase of the disease there is a modest diffuse stromal fibrosis with some superficial vascularization.

The therapeutic benefit of topical corticosteroids is very limited in acute episodes of chronic deep keratitis although they may slowly accelerate clearing of the cornea. Topical cyclosporine A twice daily results in significant suppression of the acute corneal reaction and clearing of the cornea within 10 to 14 days in eyes with chronic deep keratitis. However, treatment may need to be maintained for long periods to prevent recrudescence of the disease. Spontaneous clearing of the cornea can also occur. Topical and/or systemic doxycycline aids healing of chronic deep keratitis with the yellow-green stroma. Topical NSAIDs are also often beneficial. Superficial keratectomy and conjunctival grafting are necessary for healing of cases of chronic deep keratitis in a few cases.

5. Endotheliitis
This type of IMMK is characterized by acute, uni- or bilateral, central edema, and deep vascularization. Endothelial immunoreactivity to a persistent, possibly viral, heteroantigen may be involved in the pathogenesis. Affected eyes are nonpainful with no evidence of anterior uveitis in the UK, but can be very painful in horses in North America. There is a deep diffuse fibrocellular infiltrate, opacification,
and stromal edema in the central cornea which may evolve rapidly into bullous keratopathy (Figs. 4 and 5). Isolated arborizing blood vessels encroach upon the affected area at the level of Descemet’s membrane and/or endothelium. In some cases, dense clumps of cells may be evident adherent to the endothelium in the region of the terminal blood vessels. In long-standing cases stromal mineralization can occur. Rapid clearing of the cornea and regression of the blood vessels using topical dexamethasone occurs in many cases of endotheliitis in the UK. It is a difficult disease in control in North America. Endotheliitis may be a precursor to glaucoma in the horse. Treatment should continue for a weeks following any corneal clearing. Recurrence of the disease is possible in a small number of long-standing cases. A successful outcome following penetrating keratoplasty has been reported in the U.S.

Acknowledgments

Conflict of Interest

The Author declares no conflicts of interest.

References


Fig. 4. There is a deep diffuse stromal edema in the central cornea of this eye with immune mediated endotheliitis.

Fig. 5. The other eye in the horse in Fig. 4 has more diffuse edema.
How to Use the Clinical Examination to Determine the Significance of Abnormalities of the Horse Cornea and Adnexa

Dennis E. Brooks, DVM, PhD, DACVO

1. Introduction

The normal tear film is continuous over the entire surface of the horse cornea and conjunctiva. The tear film “breaks up” from instability and discontinuity of the ocular surface if the cornea is scarred, infected or edematous, and if blinking does not occur often enough.1,2

Precorneal Tear Film

The precorneal tear film is a trilayered mucin-dominated gel produced by the meibomian glands (outer oily layer), the lacrimal and nictitans glands (aqueous layer), and the conjunctival goblet cells (inner mucin layer). The tear film serves as an extracellular matrix to the cornea, which provides an optically smooth surface and aids nutrition to the cornea. It contains vitamin A, proteinases, proteinase inhibitors, growth factors, and cytokines that affect corneal health. The tear film is replaced every 7 min in the horse.3

Third Eyelid

The nictitans or third eyelid (TE) of the horse is located at the medial canthus. It displays rapid, near horizontal movement as it protects the cornea and distributes the tear film. The TE conjunctiva may be completely pigmented or may contain no melanin. A large gland produces part of the tear film and is found at the base of a T-shaped piece of supportive TE cartilage.

Conjunctiva

Conjunctiva is a mucous membrane that is pigmented near the limbus in some horses. The conjunctival epithelium covering the globe (bulbar conjunctiva) begins at the corneoscleral junction or limbus, lies superficial to the sclera, and reflects forward at the fornix where it becomes palpebral conjunctival epithelium. The palpebral conjunctival epithelium lines the inner eyelid surface and continues to the mucocutaneous junction at the lid margin. The ventromedial portion of the palpebral conjunctiva covers the nictitating membrane. Components of the ocular immune system and tear-producing cells are present in the conjunctiva.

2. The Clinical Examination: Observations

The Cornea Looks “Dry”

Keratoconjunctivitis Sicca

“Dry eye” or keratoconjunctivitis sicca (KCS) is an abnormality of the tear film and may be commonly...
due to qualitative changes in the tear film or, rarely, due to reduced quantity of tears in the horse. Environmental, immunologic, traumatic, and infectious causes of KCS are reported. Mild to severe ulcerative keratitis and conjunctivitis can be present. The corneal surface is not shiny in KCS (Fig. 1). Treatment with a fly mask, topical serum, and cyclosporine A can be beneficial. This may not be a permanent condition.

The Conjunctiva is “Red”

Conjunctivitis

Because the eye has limited ways to react to injury, the conjunctiva gets red (Fig. 2) or becomes inflamed in nearly all types of eye disease. Conjunctivitis is a nonspecific finding that indicates ocular inflammation, but may also be seen in systemic diseases. Infectious and noninfectious diseases of the eyelids, cornea, sclera, anterior uvea, nasolacrimal system, and orbit can result in conjunctivitis in the horse.

Habronemiasis is a parasitic disease resulting in conjunctival and ocular granulomas. *Thelazia lacrymalis* is a commensal parasite of the conjunctival fornices and nasolacrimal ducts of horses, which can incite conjunctivitis, superficial keratitis, dacryocystitis, and mild eyelid swelling.

Foal conjunctivitis is associated with neonatal maladjustment syndrome, septicemia, immune-mediated hemolytic anemia, environmental allergens and irritants, dermoids, and subconjunctival or episcleral hemorrhages secondary to birth trauma.

Allergic conjunctivitis due to exposure to environmental antigens is treated with topical corticosteroids and is often difficult to eliminate completely due to the nature of the horse’s environment.

Conjunctival neoplasia may be focal or diffuse and includes squamous cell carcinoma, hemangiosarcoma, and lymphoma. Tumors of the conjunctiva may resemble conjunctivitis in the early stages. The eyelid, globe conjunctiva, and third eyelid conjunctiva are susceptible to neoplasia.

3. Cornea

The horse cornea should normally be clear, smooth and shiny.

The Cornea is “Red”

Vascularization of the cornea will result in the entire or focal regions of the cornea being red (Fig. 3). The position of the redness can indicate the location of inflammation. The higher the intensity of redness, the more the incitatory activity there is for the neovascularization at the corneal site.

The Cornea is Hazy or “Blue”

Edema causes a blue color of the cornea if severe and more subtle haziness if the edema is slight (Figs. 3 and 4). Severe edema can result in bullae or “bubbles” in the epithelium if very severe. Corneal edema may surround a focal ulcer, foreign body or abscess, or involve the entire cornea in uveitis and glaucoma.
The Cornea is “White or Yellow”
Neutrophil and macrophage invasion of the cornea causes a yellow/white opacity (Figs. 3 and 4).

The Cornea is “Shiny” or “Dark”
A very shiny area of the cornea indicates that the cornea is thin (Fig. 2). A dark area can also be from a thin area of cornea (Figs. 5–8), or can be from rupture of the cornea and iris prolapse. Fibrin covering an iris prolapse can be red to pink in color.

Fig. 6. A thin (shiny) corneal ulcer with edema and hypopyon are present.

Fig. 7. A cellular infiltrate, central melting, and a thin cornea are present. The tapetal reflection is very apparent through the thinned cornea in the ulcer.

The Cornea is “Soft and Gelatinous”
Excessive tear film proteinase activity is termed “melting” and results in a liquefied grayish-gelatinous appearance to the stroma of the ulcer (Fig. 9).

Fig. 8. Corneal cellular infiltrate with thinning of the center and hypopyon are present.

Fig. 4. A prominent white cellular infiltrate with a darker thin center is present.

Fig. 5. Deep corneal injuries may allow the observation of a darker corneal area if the tapetal reflection is not detectable as in this descemetocele. Fluorescein dye is retained ventral to the deep lesion.
The Cornea is “Dry”
The cornea will appear dry if there is a deficiency of the precorneal tear film.

Corneal Ulcers
Equine corneal ulceration is very common in horses and is a sight-threatening disease requiring early clinical diagnosis and appropriate medical and surgical therapy.

Ulcers can range from simple superficial breaks or abrasions in the corneal epithelium (Figs. 10–12) to full-thickness corneal perforations with iris prolapse. Both bacterial and fungal keratitis in horses may present with a mild early clinical course, but require prompt therapy if serious ocular complications are to be avoided.

Many severe cases of equine ulcerative keratitis present initially as minor corneal epithelial ulcers or infiltrates with slight pain, blepharospasm, epiphora, and photophobia. At first, anterior uveitis and corneal vascularization may not be clinically pronounced. Slight droopiness of the eyelashes of the upper eyelid may be an early, yet subtle, sign of corneal ulceration.

Fluorescein dye retention is diagnostic of a corneal ulcer. Faint fluorescein dye retention may indicate an abrasion or partial epithelial cell layer defect due to infiltration of fluorescein dye between inflamed epithelial cell junctions. Cobalt blue filters can enhance detection of abrasions (Fig. 13). Fluorescein dye retention is bright in color when the entire corneal epithelium is missing to expose the stroma.

Corneal destruction results from the excessive production and release of proteinases and other en-
zymes from microbes, tear film leukocytes, and keratocytes. These proteinases can lead to rapid degeneration of collagen and other components of the stroma, potentially inducing keratomalacia or corneal “melting.”

Corneal ulcers in horses should be aggressively treated no matter how small or superficial they may be. Corneal infection and iridocyclitis are always major concerns for even the slightest corneal ulcerations. Iridocyclitis or uveitis is present in all types of corneal ulcers and must be treated in order to preserve vision. Some fungi may produce anti-angiogenic compounds that inhibit vascularization.

The healing time of a superficial, noninfected corneal ulcer is about 1 mm/day, i.e., a 5 mm diameter ulcer should take around 5 days to re-epithelialize or heal.

4. Eyelids

Which Lid is Affected?
The eyelids are thin and highly vascular and have several important functions. They protect the eye, produce and distribute the precorneal tear film, prevent corneal drying, pump tears into the lacrimal puncta, and help control the amount of light entering the eye. Eyelid blinking maintains the continuity of the tear film. The tear film “breaks up” to cause discontinuity of the ocular surface if blinking does not occur often enough.

Upper eyelid disease is more significant than lower lid disease as most (75%) of the eyelid movement is in the upper eyelid.

Nasal canthal disease is more significant than lateral canthal disease due to the location of the tear drainage apparatus in the nasal region. The eyelashes of the upper lid are normally perpendicular to the cornea. If the conjunctiva, cornea, or iris become inflamed, the horse will pull the eyeball posteriorly such that the eyelashes begin to droop (Fig. 14).

The Eyelids are Swollen
Blepharitis or inflammation of the eyelids can be caused by infection, parasites, allergy, immune disease and trauma in the horse (Figs. 15–17). Traumatic blepharitis can develop into eyelid abscesses and may be associated with orbital fractures, penetrating and lacerating trauma, subpalpebral lavage system irritation, and bony sequestra. Demodex infestation may lead to lid alopecia, meibomianitis, and blepharitis. *Thelazia lacrimalis* is a spirurid nematode and a commensal parasite of the equine conjunctival fomices and nasolacrimal ducts. This parasite can cause diffuse blepharitis. Habronemiasis, a common cause of granulomatous blepharitis,
occurs mainly in the summer months when house and stable flies serve as vectors. Dying microfilaria in the eyelids, conjunctiva, lacrimal caruncle, medial canthus, and nictitans are thought to incite an immune-mediated hypersensitivity. Fly-bite blepharitis, dermatophilus, and staphylococcal folliculitis are other causes of blepharitis, especially in young foals.

Eyelid Lacerations Need Repair
Eyelid lacerations should be carefully repaired with a two layer closure (Figs. 18 and 19). Extra care should be directed at repositioning the eyelid margin. Removal of a torn eyelid may have serious consequences for the eye and life of the animal.

Eyelid Masses are Most Commonly Tumors
Eyelid melanomas are found in grey horses, with Arabians and Percherons also at increased risk. Melanomas may be single or multiple. Treatment is surgical excision and cryotherapy.

Squamous cell carcinoma (SCC) is the most common tumor of the eye and adnexa in horses (Fig. 20). The etiopathogenesis may be related to the ultraviolet (UV) component of solar radiation, periorcular pigmentation, and an increased susceptibility to carcinogenesis. The UV component is the most plausible carcinogenic agent associated with SCC, as it targets the tumor suppressor gene p53, which is altered in equine SCC.

The prevalence in horses increases with age with the mean age at diagnosis 11.1 ± 0.4 years in one report. Belgians, Clydesdales, and other draft horses have a high prevalence of ocular SCC, followed by Haflingers, Appaloosas, and Paints. Squamous cell carcinoma is least prevalent in Arabians, Thoroughbreds, and Quarter Horses. Cryotherapy, immunotherapy, irradiation, radiofrequency hyperthermia, CO₂ laser ablation, or intralesional chemotherapy should follow surgical excision of equine ocular SCC.

Sarcoids are solitary or multiple tumors of the eyelids and periorcular region of the horse (Fig. 21). Retroviruses and papilloma viruses may be involved in the etiology. It is suspected that flies may be able to transfer sarcoid cells from one horse to trau-
matic skin lesions in other horses. There are geographic differences in the aggressiveness of the sarcoid in horses. Mules appear to suffer from an aggressive form of sarcoid. Immunotherapy for sarcoids includes autogenous vaccines and immunomodulators of mycobacterial products.

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Conflict of Interest

The Author declares no conflicts of interest.

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How to Diagnose and Treat Common Ophthalmic Diseases in the Neonatal Foal

Sarah L. Czerwinski, DVM, BSc*; and Dennis E. Brooks, DVM, PhD, DACVO

1. Introduction
Examination of the neonate typically occurs at 12–24 hours for healthy foals with a normal foaling. The ocular portion of the exam includes a thorough evaluation of the ocular and periocular structures. The globe and adnexa of the normal foal are fully developed at birth, but there are several normal anatomic and physiologic differences between the neonate and adult eye. Ocular diseases in foals can be classified as congenital, inherited, or acquired. It is important for the veterinarian to be able to recognize these conditions so that any therapy can be instituted and so the owner can be informed about conditions which may impact the foal's future life.

2. Materials and Methods
A quiet dark stall is the ideal place in which to perform the ophthalmic examination. The mare should be restrained by a handler using a halter and lead rope. The exam is typically well-tolerated by the foal; a hand stabilizing the ventral mandible while an assistant supports the chest and tail is often sufficient.

The veterinarian attending to neonatal foals should carry the equipment required to perform an ophthalmic examination in order to identify and treat common ocular conditions.

Equipment for Performing the Examination
- direct ophthalmoscope or smartphone camera
- transilluminator
- 14 or 20 D lens
- sterile fluorescein strips
- balanced saline solution
- tropicamide 1% ophthalmic solution for mydriasis
- lidocaine 2% for auriculopalpebral nerve block
- 3 cc syringe and 25 g needle to administer topical medications
- topical anesthetic (tetracaine or proparacaine)
- culturettes
- sterile cotton swabs
- scalp for cytology
- microscope slides

Equipment for Placing Tacking Sutures for Entropion
- sedation—diazepam/butorphanol
- lidocaine cream or 2% injectable for local anesthesia
- needle drivers, small forceps, scissors
- 4–0 nonabsorbable suture (nylon or silk on a P-3 or similar needle)
Normal Ocular Characteristics of the Equine Neonate

The cornea of a normal foal should be bright and glossy. Foals with systemic illness have decreased corneal sensitivity compared to adults, which may predispose them to injury.\textsuperscript{1} Downward orientation of the eyelashes is a subtle indicator of ocular pain in horses.

The iris is slightly gray in color and the pupil slightly circular compared to an adult, becoming horizontal over the first month of life.\textsuperscript{2,3}

The lens should also be clear, although the anterior and posterior lens sutures may be visible.\textsuperscript{4} These should be differentiated from larger cataracts.

Examination of the fundus reveals tapetal color that relates to the coat color. The optic disc is round and pale to deep pink in color. Pale grey streaks may be visualized radiating from the optic nerve and are bundles of axons traveling from the retina to the nerve.\textsuperscript{5–7}

Assessment of Vision and Reflexes

The menace response is learned; thus, it is absent until about 2 to 3 weeks of age.\textsuperscript{5} The dazzle reflex and observing ambulation are beneficial in determining the visual status of the foal. It is important to use a very bright light source to assess the dazzle reflex. The pupillary light reflexes are often sluggish for the first several days of life.\textsuperscript{4} The palpebral reflex may yield lagophthalmos in the young foal.\textsuperscript{8} Physiologic rotational strabismus results in a mild ventronasal rotation of the globe, giving the appearance that the foal is gazing downwards.\textsuperscript{9} This typically resolves after 2 to 4 weeks.

Fig. 1. Immature cataract in a foal. Note the clear area of lens nasally. Nonetheless, this cataract causes significant visual impairment.

Fig. 2. Microphthalmos in a foal. Note the flattened orbit and prolapsed nictitans.

Fig. 3. Microphthalmos in a foal. Note small cornea and globe and conjunctival exposure.

3. Results

Congenital or Inherited Diseases

Cataracts

Cataracts are opacities in the lens and are a common ocular congenital abnormality in foals. Cataracts are inherited in Thoroughbreds and Quarter Horses. Rocky Mountain Horses also have inherited cataracts, but often in conjunction with other signs of anterior segment dysgenesis, such as microphthalmia, persistent pupillary membranes, and aniridia.\textsuperscript{10}
It is important to assess all foals with cataracts for these other abnormalities.

The location and extent of the cataract within the lens is important for prognosis (Fig. 1). A mature cataract occupies the entire lens, thus is blinding. Cataracts within the nucleus of the lens typically don’t progress and become smaller relative to the rest of the lens with growth. Perinuclear cataracts occur soon after birth and may progress. The Morgan horse is predisposed to inherited nuclear or perinuclear cataracts. Cataracts may also occur as an acquired condition secondary to uveitis.

Phacoemulsification cataract surgery is a treatment option for foals with cataracts. It has a high initial success rate in foals; however, the prognosis for long term vision in horses, regardless of age and etiology, following cataract surgery is guarded; in a recent study approximately 30% horses were visual two years after phacoemulsification. An electroretinogram and ocular ultrasound are performed pre-operatively to ensure normal retinal structure and function.

**Microphthalmia**

Microphthalmia is characterized by an abnormally small globe. The globe may be normally proportioned and visual, or present in conjunction with other abnormalities causing blindness. The palpebral fissure is usually small and the third eyelid prominent (Figs. 2 and 3). Entropion is a possible sequela, leading to chronic irritation. The affected orbit is also abnormally flat and small; this becomes more prominent as the animal ages.

**Dermoids**

Dermoids are plaques of epidermal tissue in an abnormal location, such as on the cornea, conjunctiva, or eyelid. They most often occur in the dorsotemporal limbus. They are pigmented and may contain hair follicles, which can cause irritation and ulceration. Surgical removal via keratectomy or blepharoplasty is the recommended treatment for corneal and eyelid dermoids, respectively.

**Persistent Pupillary Membranes (PPMs)**

Persistent pupillary membranes are strands of iris connecting to the iris, cornea, or lens. Focal opacities may be present in the lens or cornea, usually without affecting vision. Surgical transection of the membranes is not necessary.

**Persistent Hyaloid Artery**

The hyaloid artery is responsible for vascular supply of the lens in utero. It typically regresses with age, sometimes leaving a translucent band running from the posterior lens capsule to the optic nerve. A persistent hyaloid artery remnant was noted in about 85% of foals, often bilaterally.

**Aniridia**

Aniridia is a partial or total absence of the iris. It is a rare condition and has been reported in Belgians and Quarter Horses. Aniridia in conjunction with congenital cataracts has been reported in Thoroughbreds. The ciliary processes and lens equator are visible in these horses (Fig. 4). These foals will not tolerate bright light and exhibit photophobia and blepharospasm.

**Dorsal strabismus**

Dorsal strabismus is observed in Appaloosa foals with congenital stationary night blindness, although the relationship is unclear. These foals have a “stargazing” appearance (Fig. 5). This should be differentiated from physiologic rotational strabismus that resolves 2 to 4 weeks postnatally.

**Congenital Glaucoma**

Congenital glaucoma is uncommon, resulting in rapid enlargement of the globe (buphthalmos). Management is challenging and blindness is inevitable.
Congenital Retinal Detachments
Congenital retinal detachments are another uncommon disease with a poor prognosis for vision and no therapeutic options (Fig. 6).8

Multiple Congenital Ocular Anomalies
Signs of multiple congenital ocular anomalies include congenital miosis, iris hypoplasia, cataracts, increased corneal curvature (cornea globosa), uveal cysts, and retinal dysplasia.16

This disease is linked to an autosomal dominant gene.17 These abnormalities are associated with the silver coat color, common in the Rocky Mountain Horse, the breed in which these abnormalities were first described.

Acquired Diseases
Entropion
Entropion is a common ocular abnormality in foals and requires immediate therapy. It most commonly involves the lower eyelid (Fig. 7); however, both the upper and lower lids may be affected. Enophthalmos results from dehydration secondary to systemic illness or maladjustment. Other causes include loss of orbital fat from cachexia, trauma, scarring, or congenital microphthalmos.10

When the globe is displaced caudally in the orbit, the eyelids are no longer supported by the globe and roll inwards. The inversion of the eyelids means that the hairs from the lids are contacting the cornea, often causing ulceration. This painful irritation causes the globe to retract further (spastic entropion), worsening the degree of entropion.

Treatment for entropion involves correcting the eyelid position with tacking sutures or a tarsorrhaphy while the foal is treated for systemic disease and any secondary corneal ulcerations heal. This can be performed with mild sedation and topical anesthesia using lidocaine. A nonabsorbable suture such as 4–0 silk or nylon is preferred in a vertical mattress pattern (Fig. 8). The space between the bites of skin correlates to the amount of eyelid rolling in. The suture end closest to the cornea should be cut short to avoid subsequent ulceration from contacting the cornea. These sutures may be left in place for 2 to 4 weeks, but should be monitored daily to make sure that they have not become loose.

If the entropion is suspected to be a primary anatomic problem, permanent surgical correction of
the eyelid inversion is advised. Because the foal will continue to grow, it is important to delay this procedure as long as possible to avoid overcorrection and potential ectropion and poor cosmesis.\textsuperscript{18}

**Ocular Hemorrhage**

Subconjunctival and episcleral hemorrhage are frequently observed following dystocia. It is self-limiting and resolves within several days.\textsuperscript{5} Episcleral hemorrhage may be seen secondary to systemic illness, such as neonatal maladjustment syndrome.\textsuperscript{14} Retinal hemorrhages are typically visualized in the tapetal fundus (Fig. 9), ranging from 16 to 29% in two studies.\textsuperscript{4,19} These were self-limiting and not related to ophthalmic or neurologic disease.\textsuperscript{19}

**Corneal Ulceration**

Foals, especially systemically ill foals, have decreased corneal sensitivity.\textsuperscript{1} This, combined with an absent menace response for the first couple of weeks of life, may predispose the neonatal foal to corneal trauma. It also means that the clinical signs of corneal ulceration may be more difficult to detect than in an adult; the level of discomfort may be mild despite serious corneal disease.

Uncomplicated corneal ulcers are superficial, non-infected, and associated with minimal uveitis (Fig. 10). Close monitoring is essential as these ulcers do have the potential to melt. Therapy includes topical serum, prophylactic antimicrobials (usually triple antibiotic ointment), and atropine for underlying uveitis. Systemic nonsteroidal anti-inflammatory drugs (NSAIDs) provide analgesia and minimize uveitis.

Complicated ulcers may be melting, deep, or infected. Targeted therapy based on results from cytology and bacterial culture and sensitivity results is prudent. Topical atropine and systemic NSAIDs are required. Aggressive therapeutic regimes may be necessary with administration of serum and selected antimicrobials every 1 to 4 hours. Surgery is recommended for corneal ulcers \( >50\% \) of stromal depth.

**Uveitis**

Iridocyclitis is inflammation of the anterior uvea. It may be unilateral or bilateral. In foals this occurs most often secondary to sepsis associated with *Salmonella*, *E. coli*, and *Streptococcus*. One study found that uveitis was a negative prognostic indicator in septic foals.\textsuperscript{20} Other organisms associated with uveitis in horses include *Actinobacillus equuli*, adenovirus, and equine viral arteritis.\textsuperscript{8} Clinical signs include blepharospasm, epiphora, conjunctival and scleral hyperemia, miosis, variable corneal edema, aqueous flare, fibrin in the anterior chamber, hypopyon, and hyphema (Fig. 11).

Aggressive treatment is essential as uveitis has the potential to cause blindness. Therapy for uveitis involves systemic antibiotics and NSAIDs and topical corticosteroids (such as prednisolone acetate 1% or dexamethasone 0.1%). Topical steroids should be administered as frequently as q 4 h, depending on the severity of the uveitis. Topical atropine reduces painful ciliary muscle spasm and treats uveitis by stabilizing the blood-aqueous barrier and is administered q 24 to q 12 h. Gastrointestinal motility must be closely monitored as atropine is a parasympatholytic and can be absorbed into the systemic circulation through the eye. In some cases, tissue plasminogen activator can be injected into the anterior chamber to dissolve fibrin.\textsuperscript{10}

4. Discussion

The ophthalmic examination is an essential part of the neonatal examination. It is important for the equine practitioner to be able to recognize normal
features of the foal's globe, in addition to common
diseases. Ophthalmic disease is common in foals
admitted to the University of Florida's ICU; 21%
have corneal ulcers and 19% have entropion. The
practitioner should be proficient at managing com-
mon ocular disease in the neonate including entro-
pion, corneal ulceration, and uveitis.

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Conflict of Interest

The Authors declare no conflicts of interest.

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How to Navigate Topical Antifungal Ophthalmic Products

Caroline Monk, DVM*; Caryn Plummer, DVM, DACVO; and Dennis E. Brooks, DVM, PhD, DACVO

1. Introduction

Keratomycosis is a common and dangerous disease of the equine eye. Case presentation and disease course is variable. Cytology gives the best side identification of etiologic organism. A sample with good yield enables the practitioner to determine bacteria from fungi and additionally should provide fungal differentiation of multicellular hyphae from unicellular yeast. However, occasionally cytology cannot be performed due to the nature of the lesion (intact epithelium, deep lesion). Furthermore, culture or polymerase chain reaction (PCR) is required to obtain actual species identification. Since fungi are typically slower growing than other organisms, it may be weeks into treatment before a culture result is produced. Once a positive culture has been obtained, additional testing must be requested if sensitivities are desired. Therefore, instead of therapeutic treatment to target an organism, antifungal treatment is often empirical.

Empiric antifungal therapy can vary based on region. Retrospective studies collecting data on fungal species involved in keratomycosis have been performed in multiple regions within the United States.1-4 Regional isolates associated with fungal keratitis vary. Fungi appear in three main forms—yeast (single cell, budding), mold (hyphae, branching), and dimorphic populations. Regardless of the region, Aspergillus, the filamentous multicellular hyphae, appears to be the most common organism implicated in the disease. In the southeastern U.S., most studies point to primarily Aspergillus and another filamentous organism Fusarium.1,5 Conversely, in the northeast, the yeast Candida is more frequently isolated.2 Finally, a recent study originating from the west, specifically California, confirmed Aspergillus in almost all of the keratomycosis cases that cultured positive.3

Because of their structural commonalities with mammalian cells, specific pharmacologic targeting is more difficult. Most antifungals act on the fungal cell wall. Topical antifungal therapy offers increased concentrations at the site of disease, decreased systemic side effects, improved economics, and improved ease of administration. However, topical antifungal medications are fairly new, with only one product gaining FDA approval. They vary substantially in cost, formulation, and availability. The purpose of this paper is to illustrate the antifungal options currently available and provide a basis behind choosing them to treat keratomycosis in the horse.
2. Materials and Methods

Formulation for Topical Medications

Topical medications are formulated as a solution, a suspension, or an ointment. These medications are deposited into the precorneal tear film where they follow one of three routes. The two nontherapeutic routes are nasolacrimal drainage and into the systemic circulation via the conjunctiva and nasopharynx. Ocular absorption is the third desired route for therapy. This is through both the cornea and conjunctiva/sclera. Corneal absorption is limited by the hydrophilic or phobic affinity of the drug and the integrity of the cornea. The epithelium is the rate-limiting barrier for absorption of hydrophilic drugs, while the stroma is the rate-limiting barrier for lipophilic drugs. Therefore, drug penetration can improve in the presence of a corneal ulcer. For example, it has been demonstrated that when 25% to 50% of the corneal epithelium is removed drug penetration into the cornea and anterior chamber can be increased over ninefold.6 Other considerations that can significantly impact concentration of drug in the ocular tissues include lacrimation, blink rate, and protein content of tears—all of which can be substantially altered in horses with keratomycosis.

Indications for Topical Antifungal

Indications for use of a topical antifungal can be either empiric or therapeutic. A positive cytology or culture necessitates the use of a topical antifungal as a therapeutic. However, indications for empiric therapy are less well defined. Specific factors such as appearance of the lesion, geographic location, season, and clinician preference can all guide empiric use.

Appearance

Fungal keratitis can vary widely in presentation. Superficial keratomycosis can manifest as a gritty or dull lesion with minimal vascular response. Midstromal lesions may form central plaques or areas of malacia surrounded by a deeper furrow. Deep lesions may be epithelialized in the form of a deep stromal abscess.

Geographic Location

Horses everywhere are at risk. However, while fungal keratitis has been reported to occur all across the United States, the most frequent reports emerge from the southeastern U.S. The clinical manifestations may vary by region.

Season

Similarly to the increased prevalence in the southeast, hot and humid summer months are thought to yield a higher prevalence of keratomycosis in horses.

Categories of Antifungals

The following is not an exhaustive list of antifungal therapies available. Instead they are the most common antifungals for ophthalmic topical use. Please refer to Table 1 for a quick comparison of their benefits and drawbacks.

Polyenes

Polyenes target ergosterol in the cell membrane of fungi. Amphotericin B has been validated for use topically.7 However, its penetration is limited when the corneal epithelium is intact (e.g., deep stromal abscess). Natamycin is another polyene. This is the only FDA-approved topical antifungal agent and is formulated as a 5% suspension. However, this formulation is irritating to healthy corneal cells, and therefore it is often compounded to a 3.33% suspension. It has better coverage of filamentous organisms than amphotericin, often making it a better choice in equine keratomycosis.

Azoles

Azoles also target ergosterol, but instead they inhibit its synthesis through the cytochrome P450 system. A concurrent action is inhibition of mitochondrial oxidative and peroxidative enzymes. The first sub-group within the azoles is the imidazoles (named based on parent ring structure).

### Table 1. Quick Reference of Topical Ophthalmic Antifungal Options

<table>
<thead>
<tr>
<th>Name</th>
<th>Formulation</th>
<th>Cost</th>
<th>Availability</th>
<th>Penetration</th>
<th>Spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>0.15% to 3%</td>
<td>$$$</td>
<td>Less common compound</td>
<td>Limited</td>
<td>Both</td>
</tr>
<tr>
<td>Natamycin*</td>
<td>5% suspension; 3.33%</td>
<td>$$</td>
<td>Common</td>
<td>Some Corneal</td>
<td>Filamentous, Most yeast</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>1% to 5%</td>
<td>$$</td>
<td>Less common compound</td>
<td>Corneal</td>
<td>Poor filamentous</td>
</tr>
<tr>
<td>Miconazole</td>
<td>1% ophthalmic</td>
<td>$$</td>
<td>Commonly compounded</td>
<td>Corneal</td>
<td>Filamentous</td>
</tr>
<tr>
<td>2% derm, 2% vaginal</td>
<td>$</td>
<td></td>
<td>Over the counter</td>
<td>Limited</td>
<td>Filamentous</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>2 mg/ml</td>
<td>$$</td>
<td>Less common compounded</td>
<td>Intraocular</td>
<td>Yeast</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>1% (± in 30% DMSO)</td>
<td>$$</td>
<td>Commonly compounded</td>
<td>Corneal</td>
<td>Filamentous (not Fusarium)</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>0.5%, 1%, 3%</td>
<td>$$$</td>
<td>Less commonly compounded</td>
<td>Intraocular</td>
<td>Both</td>
</tr>
<tr>
<td>SSD</td>
<td>1% cream</td>
<td>$</td>
<td>Widely</td>
<td>Limited</td>
<td>Both</td>
</tr>
<tr>
<td>Povidone-Iodine</td>
<td>0.2% (1:50) solution to 5%</td>
<td>$</td>
<td>Widely</td>
<td>Limited</td>
<td>Both</td>
</tr>
</tbody>
</table>

Note: * denotes FDA approval.
**Ketoconazole** is an imidazole with fairly limited spectrum but good corneal and intraocular penetration.\(^4,5\)

**Miconazole** has variable reported activity against the filamentous fungi.\(^2,4\) It comes as a 1% compounded suspension; however, the over-the-counter 2% dermatologic and 2% vaginal cream preparations have also been used as an ophthalmic treatment. Please see the below discussion for additional details on these formulations.

The second group of azoles is the triazoles, again named for their parent ring structure.

Despite being well absorbed, **fluconazole** primarily targets yeast, which limits its usefulness in equine keratomycosis.

**Itraconazole** is a triazole with a broader spectrum but has a reduced penetration relative to fluconazole. This penetration is believed to be improved by the addition of 30% dimethyl sulfoxide (DMSO) and is commonly available. This formulation has been seen to penetrate into the corneal stroma but has not been found in measurable levels within the aqueous humor.\(^8\) In a study by Mathes et al, itraconazole and DMSO were found to have the least keratocyte damage relative to miconazole and natamycin.\(^9\)

With excellent penetration and good efficacy against yeast and hyphae, voriconazole has emerged as a good option for antifungal therapy. Clode et al tested three concentrations (0.5%, 1%, and 3%) and found 1% delivered the best combination of penetration and mitigation of side effects.\(^10\) Voriconazole was found to outperform natamycin, fluconazole, itraconazole, ketoconazole, and miconazole against in vitro isolates in a study by Pearce et al.\(^4\)

**Betadine (Povidone-Iodine) Solution**

**Betadine solution** is an antiseptic with both antibacterial and antifungal properties. Widely used as a surgical preparation, there is also some who advocate its use as a therapy. Concentrations from 0.5% to 1.0% betadine have been validated to disinfect the surgical site or donor cornea as a protocol for preoperative antisepsis.\(^11\) The use of a 2% dilute betadine solution every 24 hours has been suggested in the treatment of fungal keratitis.\(^12\) However, this should be limited to adjunctive therapy only. A large metastudy concluded that 5% betadine solution did not reduce the bacterial load of human corneal ulcers significantly. This was theorized to be due to the lack of penetration into the corneal stroma.\(^13\)

**Silver Sulfadiazine**

**Silver sulfadiazine (SSD)** is a 1% dermatologic cream with broad antibacterial and antifungal activity historically used to treat burns. Use as a corneal antifungal with topical application every 12 to 24 hours has been suggested.\(^14\) There has been limited in vitro data in horses\(^14\) that it is fungicidal when used as an ophthalmic topical. A large meta study\(^15\) investigated topical drug trials for fungal keratitis in people. This study showed that based on the trials included, there was no evidence that any particular drug was more effective in the management of fungal keratitis. One specific comparison was topical SSD vs miconazole. However, the study noted that the trials included in this review were of variable quality and were generally underpowered. Therefore, the evidence behind use of SSD as an antifungal ophthalmic remains inconclusive.

**Dosage: Frequency and Duration**

Dosage of ophthalmic drugs is significantly different from other pharmacokinetics. Most topical drugs follow first-order kinetics (maximum concentration then exponential decline). Unlike systemic drugs where usually >75% is bioavailable, after topical application of an ophthalmic solution less than 1% and no more than 10% of the dose enters the eye. Furthermore, the lacrimal lake limits the volume that can be administered, and the concentration is limited by what is tolerable to the corneal surface. Therefore, frequent application of low-volume, dilute solution is a mainstay to equine topical treatment. For example, a dosing regime may use topical antifungals every 2 to 4 hours initially and only reducing to six-times a day once clinical improvement is seen.

Ointments are a good option for decreasing the frequency of application. Rate of dissipation from the precorneal tear film of drugs administered in an ointment is significantly slower than a liquid. This is because less of the drug is immediately lost to nasolacrimal drainage, increasing bioavailability. Eye ointments can be dosed anywhere from every 4 to 12 hours. Disadvantages include danger if corneal perforation is imminent, imprecise dosing, and a creation of a film on the cornea significantly distorting vision.

Regardless of topical of choice, a positive cytology or culture of fungus should necessitate a continued course of topical antifungal therapy. Recrudescence is common. Durations from 3 to 8 weeks depending on response have been reported. Preparing clients for a minimum of 6 weeks of topical therapy is usually realistic.

**Specific Questions**

Is vaginal and athlete’s foot preparation of miconazole acceptable to apply topically to the horse eye?

Two percent miconazole is available as a dermatologic and vaginal cream over-the-counter (OTC) preparation. These have been used as topical medications in horses. While this is an economic option, these formulations are not designed for the ocular surface. There are anecdotal reports of ophthalmic problems resulting from its use in horses and, therefore, use is with risk. The primary inactive ingredient in vaginal miconazole is benzoic acid.
Benoic acid causes moderate eye irritation in the form of chemosis, hyperemia, and keratitis. This medication is the fourth most common ingredient in the dermatologic preparation. Furthermore, the pH and osmolality have not been investigated with regards to ophthalmic tolerance. At this time neither formulation is recommended. However, it should be noted that miconazole ophthalmic ointment is readily available from compounding pharmacies that ship and is reasonably priced (approximately $25 for a tube vs $10 for nonophthalmic OTC formulations).

Should I use an empiric antifungal on every case of corneal ulceration?

When evaluating a painful eye, efforts should be made to obtain a diagnosis—specifically through at minimum, cytology. More severe cases additionally warrant a culture. However, in the face of an open diagnosis, empiric therapy may sometimes still be warranted. A simple case of corneal ulceration is unlikely to necessitate empiric or prophylactic treatment with an antifungal. Simple corneal ulcers are superficial, uninfected, and heal within 3 to 5 days. A wound or lesion deeper than superficial epithelium, the presence of cellular infiltrate or corneal melting or malacia, secondary uveitis, or an appearance typical of fungal keratitis all indicate that fungal infection may be present.

While we have discussed the use of empiric and treatment antifungals, no studies have been performed on the use of prophylactic topical antifungal therapy. Prophylactic systemic antifungals are used in human patients at risk of infection. Therefore, in areas where fungal keratitis is endemic or during high-risk seasons (summer), prophylactic therapy may be warranted. However, the overall rate of keratomycosis seen at the field level is low. Based on retrospective studies comprised of referral institutions, the rate of equine keratomycosis was anywhere from 5.7% of all horses presenting to the ophthalmology service1 to 25% cases of severe ulcerate keratitis.16 These numbers may even be overrepresented, as pretreatment with antibiotics and topical steroids has been shown to be predisposing factors in fungal keratitis.

3. Results

Resolution of fungal keratitis is characterized by an increase in comfort, decrease in uveitis, decrease in the severity of corneal infiltrate and edema, and epithelization (if applicable). In a recent retrospective study on keratomycosis at a referral institution, 73% of horses were treated with medical therapy alone.8 Of the investigated cases, 77% retained their globes and 53% retained vision. However, this prognosis is likely significantly worse than what would be encountered on a primary field case due to the severity of the cases.

Lack of resolution may be due to inadequate duration of therapy, lack of susceptibility of the organism, lack of penetration of the medication to the site of infection, infrequent medication administration, continued stimulus (thick plaque, foreign body), or other factors. Steps in reevaluation of a nonhealing ulcer include repeat detailed examination, repeat cytology, obtain or repeat culture, and potentially referral.

Conflict of Interest

The Authors declare no conflicts of interest.

References and Footnote


*Natacyn (natamycin) 5% Ophthalmic Suspension, Alcon Laboratories, Irvine, CA 92618.*
Stability of Voriconazole by Constant-Rate Infusion for Ocular Delivery in Horses

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Voriconazole 1% solution is not compatible with constant-rate infusion delivery and the use of other aqueous-based medications may have similar results. Voriconazole 1% solution is stable when stored in the commercial glass vial at controlled temperatures between 23 and 40°C up to 30 days. Authors’ addresses: Department of Veterinary Clinical Sciences, Center for Veterinary Health Sciences (Smith, Gilmour); Department of Physiological Sciences, Center for Veterinary Health Sciences (Maxwell); Department of Veterinary Pathobiology, Center for Veterinary Health Sciences (Gull); and Department of Statistics (Payton), Oklahoma State University, Stillwater, OK 74078; e-mail: kathryn.m.smith@okstate.edu. *Corresponding and presenting author. © 2014 AAEP.

1. Introduction
The study objective was to establish the effect of storage in a constant-rate infusion (CRI) pump on the sterility and stability of voriconazole 1% solution.

2. Materials and Methods
Nine vials of voriconazole 1% solution were prepared. Each vial was used to prime a commercially-available CRI pump and attached subpalpebral lavage system (CRI/SPL unit), with the remaining solution stored in the commercial glass vial. Three CRI/SPL units and their 3 corresponding vials were stored at 23°C, 33°C, and 40°C. Fungal and aerobic bacterial cultures were performed on all solutions on the first and last storage day. Samples obtained at regular intervals were analyzed for voriconazole concentration using high-performance liquid chromatography.

3. Results
No bacterial or fungal contamination was identified in any solution. All solutions stored in the glass vial remained stable throughout the study. Voriconazole concentration significantly increased (by 35–134%) after passage through the SPL and several units became blocked with precipitate ($p < 0.05$).

4. Discussion
Voriconazole 1% solution was not compatible with CRI/SPL delivery but remained stable when stored in the commercial glass vial.

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Conflict of Interest
The Authors declare no conflicts of interest.

Footnote
* Vfend I.V., Pfizer Pharmaceuticals, New York, NY 10017.
Safety of Subconjunctival Injection of Allogeneic Mesenchymal Stem Cells in Horses

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Clinical trials should be performed to assess subconjunctival injection of allogeneic mesenchymal stem cells (MSCs) in the treatment of equine eye disorders. Authors’ addresses: Large Animal Clinical Sciences, (Joswig, Hardy, Easterwood, and Watts); and Veterinary Integrative Biosciences (Cummings), Texas A&M University, College Station TX 77843; e-mail: AWatts@cvm.tamu.edu. *Corresponding and presenting author. © 2014 AAEP.

1. Introduction
Subconjunctival injection of allogeneic mesenchymal stem cells (MSCs) has the potential to become a new therapeutic in equine ophthalmology. Our objective was to evaluate the safety of allogeneic MSC subconjunctival injection. We hypothesized there would be no difference in adverse events after subconjunctival MSC injection versus control.

2. Methods
Upper-lid subconjunctival injection of 3 million MSCs in 0.5 mL was performed in a randomly assigned eye (n = 14 horses). The opposite eye was injected with cell-free medium (0.5 mL). Serial evaluations of both eyes were performed by investigators blinded to treatment assignment. The injections were repeated to the same eye 3 weeks later. Flow cytometry was used to determine major histocompatibility complex (MHC) II expression of MSCs.

3. Results
There were no adverse events or complications in either the MSC or control injected eyes. Redness and chemosis were significantly different (higher scores in the MSC treated eyes) on days 1, 22, and 28, but not at other time points. Blepharospasm, blepharoadema, and miosis were absent throughout the study. Eyes that had epiphora on day 0 continued to have epiphora throughout the trial and there were no significant differences in epiphora between groups. The MSCs were negative for MHC II.

4. Discussion
In preclinical models, subconjunctival injection of MSCs speeds healing after chemical keratitis. This may be due to the regulation of inflammation and healing. In the horse, subconjunctival administration of two injections of 3 million allogeneic MSCs appears to be safe.
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Conflict of Interest
The Authors declare no conflicts of interest.
Incidence of Colic in Ophthalmic Versus Orthopedic Patients in a Hospital Environment

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The incidence of colic in patients hospitalized with an ocular complaint was not significantly different from the incidence in those hospitalized with a nonocular complaint. Authors’ address: New Bolton Center, University of Pennsylvania School of Veterinary Medicine, Kennett Square, PA 19348; e-mail: scherrer@vet.upenn.edu. *Corresponding and presenting author. © 2014 AAEP.

1. Introduction
Ophthalmic patients have been suggested as an “at risk” group due to chronic pain, long-term hospitalization, use of atropine, and frequent sedation.

2. Materials and Methods
Records of ophthalmic (n = 105) and orthopedic (n = 197) horses admitted from July 1, 2011–June 30, 2012 were used to determine patient breed, age, and sex, presenting complaint, medical therapy, and surgical intervention for all included horses. An episode of abdominal discomfort was identified if the animal showed behavior that warranted abdominal palpation per rectum or fluid therapy administration (enteral or intravenous).

3. Results
Horses with ocular disease significantly differed from orthopedic cases in median age (10.7 vs 3.8 years), sex (3% vs 30% intact males), breed (28% vs 62% Thoroughbreds), likelihood of having general anesthesia (65% vs 80%), and median length of hospital stay (3 vs 2 days), but not in incidence of colic (8% vs 5%), respectively. A logistic regression model using disease category (ocular or orthopedic), general anesthesia (yes or no), age in years, and length of hospitalization in days as predictors of colic showed marginally good fit (log likelihood ratio = 7.69, P = 0.1). Only the length of hospitalization had significant predictive power (log odds = 1.09, P < 0.01). Amongst horses that experienced episodes of colic, 16/17 resolved without surgery, with no difference between ocular and orthopedic cases in median colic duration (1 day for both groups), median hospitalization time (7 vs 3 days), or duration of systemic nonsteroidal anti-inflammatory drug use (7 vs 5 days).

4. Discussion
Horses hospitalized with ocular disease were not at an increased risk of colic relative to orthopedic cases and episodes of colic in both groups were resolved with medical management in all but one case.

Acknowledgments
Conflict of Interest
The Authors declare no conflicts of interest.