How to Diagnose the Cloudy Eye

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1. Introduction
Diagnosing the cloudy equine eye is often met with trepidation in the field setting because of the variety of differentials for this condition, many of which are clinically difficult to distinguish. Most equine veterinarians feel comfortable with diagnosis and treatment of uncomplicated corneal ulceration because of its high prevalence in equine practice. However, the cloudy eye with intact epithelium is a less common complaint and can prove to be a diagnostic challenge. Furthermore, accurate diagnosis is vital. Treatment for one condition is often contraindicated for another, particularly with regard to the use of corticosteroids. The importance of accurate diagnosis and treatment is accentuated by the fact that maintenance of a clear visual axis is often a necessity for the career of the equine patient. Equine eyes have the propensity to degenerate rapidly, leaving very little room for error. The objective of this report is to present a stepwise approach to diagnosis of the cloudy equine eye. Correct diagnosis will allow accurate treatment.

The disease processes that will be discussed include the following:

- Stromal abscess
- Calcific band keratopathy
- Eosinophilic keratitis
- Nonulcerative keratouveitis
- Onchocerciasis
- Squamous cell carcinoma
- Subepithelial keratomycosis
- Immune-mediated keratitis
- Equine recurrent uveitis
- Glaucoma

2. Materials and Methods
For the initial ophthalmic examination, the same basic tools are needed as for any ophthalmic ambulatory procedure.

- Fluorescein stain
- Mepivacaine or lidocaine for local nerve blocks
- Chemical restraint: $\alpha_2$-agonist sedation (xylozine, detomidine)
- Focal light source with cobalt-blue filter
- Dimly lit area

Step 1: Is the Eye Painful?
Examination should start with a patient who has not yet been sedated and whose eyelids have not
been blocked, to allow accurate assessment of ocular pain. Hallmark clinical signs of ocular pain include epiphora and blepharospasm. Determining the degree of ocular pain is important for formulation of differential diagnoses of corneal opacity (Fig. 1). After gross assessment for pain through a visual examination, the function of cranial nerves II, III, V, and VII is assessed by the menace response, dazzle reflex, pupillary light reflexes (direct and indirect), and palpebral reflex. Pupil size, shape, and symmetry between right and left pupils should be evaluated. Miosis, mydriasis, and anisocoria may occur coincident with corneal disease, the most common examples being when the corneal opacity is associated with anterior uveitis, synchiae, or glaucoma.

Step 2: Is There an Ulcer?
After assessment of vision and reflexes, the horse can be sedated and perineural anesthesia can be performed if needed. If corneal culture is warranted, that should occur before instilling any topical solutions into the eye. The eye must be stained with fluorescein, even if it does not appear that a corneal ulcer is present. The only way to determine fluorescein stain uptake accurately is with use of a cobalt-blue filter light. Use of a focal light source is key to careful examination of corneal opacities. A systematic approach should be used every time, so that no area is missed, even if the lesion is immediately apparent. Start at the limbus and examine circumferentially, moving axially toward a more central part of the cornea as you proceed. Often dimming the focal light source and taking breaks will improve the tractability of the patient. Be sure to examine both eyes.

Step 3: What Color Is the Opacity?
The cornea readily displays pathologies as the result of its biologically clear appearance. Furthermore, it has a limited number of characteristic reactions to disease. The ability to visually recognize these reactions allows for accurate differentiation of keratopathies. The following is a list of the equine cornea reaction to disease accompanied by its clinical appearance:

- Edema: hazy gray-blue, can be focal or diffuse (Fig. 2)
- Vessels: originate from the limbus
- Perfused or ghost
- Depth indicates location of inciting lesion
- Superficial–branching
- Deep–hedge
- Fibrosis: gray, may note associated ghost vessels
- Inflammatory cell infiltrate: yellow to green discoloration
- Lipid or mineral infiltrate: shiny white, crystalline (cholesterol or calcium)

It is vital to be able to recognize these processes when examining an eye with corneal disease.

Step 4: Making the Diagnosis

(1) Diseases Generally Characterized by a Nonpainful Eye
If initial assessment shows the patient to have normal ocular comfort, the differential diagnosis list is significantly shortened. Any disease that has a component uveitis is excluded from this category, because the condition is typically painful (Fig. 3).

(a) Immune-mediated keratitis (IMK) should be considered as a differential for a nonpainful eye with corneal vascularization. In IMK, vascularization depth generally corresponds to the depth of the lesion. There are often striking corneal changes while the eye is quiet and comfortable (Fig. 4). The specific pathogenesis of this disease is not known, and the clinical presentation can be highly variable. The unifying characteristics of the disease are the ocular comfort of the patient and the lesion response to immunosuppressive therapy.
Ruling out an infectious cause through culture or empirical antimicrobial therapy is important when making this diagnosis because the cornerstone of therapy for IMK is immunosuppression with corticosteroids.

(b) Similar in appearance to IMK but of infectious origin is subepithelial keratomycosis. Horses with this disease only exhibit mild to no blepharospasm. Hallmark corneal changes are multifocal punctate to geographic cellular infiltrate opacities that resolve with anti-fungal therapy. Culture results of these lesions are variable. Therefore, it is important to rule out an infectious disease such as this, for example, with initial treatment of empirical antimicrobial therapy before treating for immune-mediated disease.

(c) Another differential for a nonpainful corneal opacity is the most common tumor of the equine cornea—corneal squamous cell carcinoma. This can originate from the cornea, conjunctiva, or limbus. Although lesions commonly appear nodular and elevated, some may appear simply as stromal infiltrate (Fig. 5). Notably, all of the forms should cause little to no discomfort. When squamous cell carcinoma is high on the differential diagnosis list, biopsy is needed for diagnosis. This may be in the form of keratectomy under general anesthesia if the lesion is smooth and cannot be grasped for easy removal.

(d) End-stage glaucoma can manifest as a comfortable, cloudy eye. The corneal opacity in this case is usually edema. This corneal change is often accompanied by other gross changes such as buphthalmos and striae, and the eye is usually blind.

(e) Despite its chronicity, fibrosis may be newly noted by a client or seen on initial examination such as during a pre-purchase exam. Corneal scars vary
significantly in size and density. The deeper the injury, the denser the scar; they should appear white, consolidated, and smooth, with no ocular discomfort (see Fig. 6).

(2) Diseases Generally Characterized by a Painful Eye

If the eye is painful, a wide variety of conditions are possible (Fig. 7).

(a) Both eosinophilic keratitis and calcific band keratopathy appear as raised corneal lesions. However, they can be differentiated on the basis of cytology and location. Eosinophilic keratitis is characterized by numerous eosinophils on cytology and is typically limbal (Fig. 8). Conversely, calcific band keratopathy should be both negative for eosinophils and infectious causes and is typically distributed in the interpalpebral fissure.

(b) For a smooth, intact epithelium, differentiating between a focal lesion and segmental disease can sometimes be difficult. Anterior uveitis is often secondary to discrete opacities created by nonulcerative keratouveitis (NUKU) and stromal abscessation (Fig. 9). Severe, diffuse corneal edema may mask the whitish to yellow cellular infiltrate that is characteristic of these diseases. This infiltrate may be located in any area of the cornea and at any depth. Nonspecific signs of ocular pain and severe inflammation are concurrent. The gold standard for diagnosis and differentiation of both diseases is histopathology; however, this requires general anesthesia. Therefore, often the diagnosis may be made by response to therapy because the intact epithelium usually prevents adequate cytology and culture.

(c) A differential for the cloudy, painful eye with diffuse or focal corneal edema is uveitis. Anterior uveitis alone without primary corneal disease may manifest as the result of equine recurrent uveitis or ocular trauma. In these cases, the predominant corneal change is diffuse corneal edema. Extensive neovascularization or cellular infiltrate should not be present. Clinical signs of note are miosis, often severe, and circumlimbal vascularization. Careful inspection of the quality, opacity, and coloration of the cornea should allow for differentiation.

(d) Early glaucoma is another differential for painful, diffuse corneal edema, especially that which does not respond to anti-inflammatory medication. In the early, acute stage, the eye may be painful. Measurement of intraocular pressure is the gold standard for diagnosis of this disease and will be discussed later. However, a sign to differentiate this edema from that of uveitis without the ability to measure pressure is through pupil size. A uveitic pupil is most often miotic, whereas an early glaucoma pupil without synechia should be at least slightly mydriatic. Often, vertical corneal edema with linear band opacities is noted.

(e) Finally, onchocerciasis may also appear as a painful opacity usually located limbally with accompanying signs of corneal inflammation (edema, vascularization). The most common concurrent clinical sign, conjunctivitis, distinguishes it from other corneal infiltrates. Definitive diagnosis is made through a conjunctival snip biopsy.

Step 5: Further Diagnostics

Once the initial examination has been performed, further diagnostics are often warranted for definitive diagnosis.

(a) Applanation or rebound tonometry. This is needed to accurately diagnose glaucoma and uveitis by providing an objective measurement of intraocular pressure. Tonometry facilitates early diagnosis of glaucoma, which is often subtle. Comparison between globes within a horse as well as comparison of published reference ranges is helpful. This diagnostic is vital to monitoring response to treatment for glaucoma.

(b) Culture and cytology. Culture and cytology are a frustrating aspect to nonulcerative corneal disease. Because of the intact epithelium, a diagnostic sample is difficult to obtain. Cytology is a requirement for diagnosis of certain conditions (eosinophilic keratitis). It also can guide therapeu-
tic choices even if definitive diagnosis cannot be obtained. Therefore, an attempt at culture and cytology can be made with the knowledge that an inconclusive sample or sterile culture is not definitive. Culture can be obtained with the use of a sterile cotton-tipped applicator culturette on the corneal surface. After this, cytology can be obtained after the application of topical anesthetic agent (proparacaine, tetracaine) with the use of the blunt end of a sterile scalpel blade. Gently scrape the margins of the opacity, and smooth the sample onto glass slides. The slides should then be stained before analysis. If scraping of the lesion for cytology has created ulceration caused by poorly adherent epithelium, a second culture should be obtained of the exposed stroma.

(c) Biopsy. Biopsy of corneal tissue should only be performed with extreme caution. Rupture of the globe as the result of structural instability is more common in equids than other veterinary species. Globe rupture is a surgical emergency, and eyes can only be saved if prompt surgical intervention is performed. A proliferative, nonpainful lesion is the best candidate for corneal field biopsy.

(d) Referral for keratectomy. This procedure requires heavy sedation or general anesthesia. It is indicated both for diagnosis of a deep stromal opacity through histopathology but also is a treatment to remove neoplastic or infected corneal tissue. The importance of an accurate diagnosis is highlighted by the decision to treat the eye with topical corticosteroids. Corticosteroids have been shown to decrease vascularization and limit potentially blinding anterior uveitis.\(^{10}\) Conversely, they also inhibit epithelial regeneration and can predispose the ocular surface to infectious colonization.\(^{11–13}\) It is veterinary dogma never to use a topical steroid when a corneal ulceration is present. However, other contraindications also exist. An infection may still be present because of the difficulty to obtain a positive culture through the intact epithelium. Furthermore, horse eyes appear to be more susceptible to the adverse effects of topical corticosteroids and infectious colonization. If a culture cannot be obtained and diagnosis is open, initially, presumptive treatment with topical antimicrobials...
is indicated. If the eye fails to respond, corticosteroids then may be justified with caution. Finally, frequent reassessments are vital because eyes are highly dynamic, and clients may not perceive subtle changes in disease processes.

3. Results

When a systematic and consistent approach is used to examine and diagnose ocular lesions, you are less likely to miss subtle clinical signs and prescribe inappropriate therapy. Once the correct diagnosis is made, searching for current therapies is simplified. Inappropriate use of corticosteroids can be disastrous in the equine eye, and therefore careful examination and thought should be given before their administration.

4. Discussion

Characterizing a lesion on the basis of the hallmark corneal changes as well as the use of a stepwise, logical approach allows for the more accurate diagnosis of corneal disease. Ideally, all corneal lesions would be examined through the use of slit-lamp biomicroscopy. This allows for a more precise assessment of depth and composition by means of microscopic inspection. However, the cost and learning curve associated with these devices typically precludes their use for the general practitioner. Instead, the general practitioner is often put in a position of doing an in-depth corneal examination with limited tools and must therefore be careful not to miss any subtle clinical signs. Referral should always be offered, especially in cases in which the diagnosis is not straightforward or the eye fails to respond to therapy.

References


Fig. 9. Severe inflammation and pain accompany stromal abscessation.