35èmes Journées AVEF
18, 19 & 20 octobre 2007
Centre International de Deauville
Equine corneal ulceration is very common in horses and is a sight threatening disease requiring early clinical diagnosis, laboratory confirmation, and appropriate medical and surgical therapy. Ulcers can range from simple, superficial breaks or abrasions in the corneal epithelium, to full-thickness corneal perforations with iris prolapse. The prominent eye of the horse may predispose to traumatic corneal injury. 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. 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. Globe rupture, phthisis bulbi, and blindness are possible sequelae to corneal ulceration in horses.

**Corneal sensitivity in foals and adult horses**

Corneal sensation is important for corneal healing. The cornea of the adult horse is very sensitive compared to other animals. Corneal touch threshold analysis revealed the corneas of sick or hospitalized foals were significantly less sensitive than those of adult horses or normal foals. The incidence of corneal disease is also much higher in sick neonates than in healthy foals of similar age. Ulcerative keratitis in the equine neonate often differs from adult horses in clinical signs and disease course. Foals may not show characteristic epiphora, blepharospasm, or conjunctivitis, and the ulcers may be missed without daily fluorescein staining. This decreased sensitivity may partially explain the lack of clinical signs often seen in sick neonates with corneal ulcers.

**Corneal Healing in the Horse**

The thickness of the equine cornea is 1.0 to 1.5 mm in the center and 0.8 mm at the periphery. The normal equine corneal epithelium is 8 to 10 cell layers thick, but increases to 10 to 15 cell layers thick with hypertrophy of the basal epithelial cells following corneal injury. The epithelial basement membrane is not completely formed six weeks following corneal injury in the horse, in spite of the epithelium completely covering the ulcer site. Healing of large diameter, superficial, noninfected corneal ulcers is generally rapid and linear for 5-7 days, and then slows. Healing of ulcers in the second eye may be slower than in the first and is related to increased tear proteinase activity. Healing time of a 7-mm diameter, midstromal depth, noninfected corneal trephine wound was nearly 12 days in horses (0.6 mm/day).
The Equine Corneal Microenvironment

The environment of the horse is such that the conjunctiva and cornea are constantly exposed to bacteria and fungi. The corneal epithelium of the horse is a formidable barrier to the colonization and invasion of potentially pathogenic bacteria or fungi normally present on the surface of the horse cornea and conjunctiva. A defect in the corneal epithelium allows bacteria or fungi to adhere to the cornea and to initiate infection. *Staphylococcus*, *Streptococcus*, *Pseudomonas*, *Aspergillus*, and *Fusarium* spp. are common causes of corneal ulceration in the horse. Infection should be considered likely in every corneal ulcer in the horse. Fungal involvement should be suspected if there is a history of corneal injury with vegetative material, or if a corneal ulcer has received prolonged antibiotic and/or corticosteroid therapy with slight or no improvement. Tear film neutrophils and some bacteria and fungi are associated with highly destructive proteinase and collagenase enzymes that can result in rapid corneal stromal thinning, descemetocele formation, and perforation. Excessive proteinase activity is termed “melting”, and results in a liquefied, grayish-gelatinous appearance to the stroma near the margin of the ulcer. Total corneal ulceration ultimately requires the degradation of collagen that forms the framework of the corneal stroma. Horse corneas demonstrate a pronounced fibrovascular healing response. The unique corneal healing properties of the horse in regards to excessive corneal vascularization and fibrosis appear to be strongly species specific.

Many early 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. A vicious cycle may be initiated after the first injury to the cornea, with “second injury to the cornea” occurring because of the action of inflammatory cytokines. Ulcers, uveitis, blepharitis, conjunctivitis, glaucoma, and dacrocystitis must be considered in the differential for the horse with a painful eye. Corneal edema may surround the ulcer or involve the entire cornea. Signs of anterior uveitis are found with every corneal ulcer in the horse, and include miosis, fibrin, hyphema or hypopyon. Persistent superficial ulcers may become indolent due to hyaline membrane formation on the ulcer bed.

Fluorescein dye retention is diagnostic of a full thickness epithelial defect or corneal ulcer. Faint fluorescein retention may indicate a microerosion or partial epithelial cell layer defect due to infiltration of fluorescein dye between inflamed epithelial cell junctions. All corneal injuries should be fluorescein stained to detect corneal ulcers. Rose bengal retention indicates a defect in the mucin layer of the tear film. RB can be obtained at www.akorn.com

Horses with painful eyes need to have their corneas stained with both fluorescein dye and rose bengal dye as fungal ulcers in the earliest stage will be negative to the fluorescein but positive for the rose bengal. Fungi may induce changes in the tear film mucin layer prior to attachment to the cornea. Early fungal lesions that retain rose bengal are multifocal in appearance and may be mistaken for viral keratitis.

Microbiologic culture and sensitivity for bacteria and fungi are recommended for horses with rapidly progressive, and deep corneal ulcers. Corneal cultures should be obtained first and then followed by corneal scrapings for cytology. Mixed bacterial and fungal
infections can be present. Vigorous corneal scraping at the edge and base of a corneal ulcer is used to detect bacteria and fungal hyphae. Samples can be obtained with the handle end of a sterile scalpel blade and topical anesthesia. Superficial scraping with a cotton swab cannot be expected to yield organisms in a high percentage of cases.

A “crater-like” defect that retains fluorescein dye at its periphery and is clear in the center is a descemetocele, and indicates the globe is at high risk of rupture. Descemet’s membrane does not retain fluorescein dye, whereas deep ulcers that continue to have stroma anterior to Descemet’s membrane will retain fluorescein. Deep penetration of the stroma to Descemet’s membrane with perforation of the cornea is a possible sequelae to all corneal ulcers in horses.

Medical therapy
Once a corneal ulcer is diagnosed, the therapy must be carefully considered to ensure comprehensive treatment. Medical therapy almost always comprises the initial major thrust in ulcer control, albeit tempered by judicious use of adjunctive surgical procedures. This intensive pharmacological attack should be modified according to its efficacy. Subpalpebral or nasolacrimal lavage treatment systems are employed to treat a fractious horse or one with a painful eye that needs frequent therapy. The clarity of the cornea, the depth and size of the ulcer, the degree of corneal vascularization, the amount of tearing, the pupil size, and intensity of the anterior uveitis should be monitored. Serial fluorescein staining of the ulcer is indicated to assess healing. As the cornea heals the stimulus for the uveitis will diminish, and the pupil will dilate with minimal atropine therapy. Self-trauma should be reduced with hard or soft cup hoods.

Antibiotics
Bacterial and fungal growth must be halted and the microbes rendered non-viable. Broad-spectrum topical antibiotics are usually administered with culture and sensitivity tests aiding selection. Topical antibiotic solutions interfere with corneal epithelial healing less than ointments. Gentamicin should be used in ulcers with evidence of stromal melting only. Topically applied antibiotics, such as bacitracin-neomycin-polymyxin B, gentamicin, ciprofloxacin, or tobramycin ophthalmic solutions may be utilized to treat bacterial ulcers. Frequency of medication varies from q2h to q8h. Cephalothin (55mg/ml), bacitracin, and carbenicillin are effective against beta hemolytic Streptococcus. Ciloxan (ciprofloxacin), amikacin (10 mg/ml), and polymyxin B (0.25% IV solution) may be used topically for gentamicin resistant Pseudomonas.

The fungi are overall more susceptible to antifungal drugs in this order: natamycin = miconazole > itraconazole > ketoconazole > fluconazole. Natamycin, miconazole, itraconazole/ DMSO, fluconazole, amphotericin B, betadine solution, chlorhexidine gluconate, posaconazole, voriconazole, and silver sulfadiazine can be utilized topically. The antifungals can be given q2h to q8h.
Proteinases in the tear film

Tear film proteinases normally provide a surveillance and repair function to detect and remove damaged cells or collagen caused by regular wear and tear of the cornea. These enzymes exist in a balance with inhibitory factors to prevent excessive degradation of normal tissue. Two major families of proteinases that may affect the cornea include the matrix metalloproteinases (MMP) and the serine proteinases. MMPs predominate in the horse.

Bacterial and fungal pathogens induce corneal epithelial cells, corneal stromal fibroblasts, and leukocytes (PMN) in the tear film to upregulate cytokines (IL-1, IL-6 and IL-8) that induce MMP production and elicit inflammatory and degradative processes. Proteinases that may contribute to corneal ulceration in the early stages of infection could be of bacterial or corneal cell origin. In the later stages as PMNs accumulate, PMN-derived proteinases predominate as the main factor in corneal tissue destruction. In pathologic processes such as ulcerative keratitis, excessive levels of these proteinases can lead to rapid degeneration of collagen and other components of the stroma, potentially inducing keratomalacia or corneal “melting”.

Collagenolysis prevention

Severe corneal inflammation secondary to bacterial (especially, Pseudomonas and beta hemolytic Streptococcus) or, much less commonly, fungal infection may result in sudden, rapid corneal liquefaction and perforation. Activation and/or production of proteolytic enzymes by corneal epithelial cells, leucocytes and microbial organisms are responsible for stromal collagenolysis or “melting”. Serum is biologically nontoxic and contains an alpha-2 macroglobulin with antiproteinase activity. Autogenous serum administered topically can reduce tear film and corneal protease activity in corneal ulcers in horses. The serum can be administered topically as often as possible, and should be replaced by new serum every 8 days. Five to 10 per cent acetylcysteine, and/or 0.05% sodium EDTA can be instilled hourly, in addition to the other indicated drugs, for antimelting effect until stromal liquefaction ceases. It may be necessary to use serum, EDTA, and acetylcysteine simultaneously in severe cases. Subconjunctival tetanus antitoxin contains macroglobulins with anticollagenase effects and can also slow corneal melting.

Treat Uveitis

Atropine sulfate is a common therapeutic agent for equine eye problems. Topically applied atropine (1%) is effective in stabilizing the blood-aqueous barrier, reducing vascular protein leakage, minimizing pain from ciliary muscle spasm, and reducing the chance of synechia formation by causing pupillary dilatation. Atropine may be utilized topically q4h to q6h with the frequency of administration reduced as soon as the pupil dilates.

Topical atropine has been shown to prolong intestinal transit time, reduce and abolish intestinal sounds, and diminish the normal myoelectric patterns in the small intestine and large colon of horses. Some horses appear more sensitive than others to these atropine effects, and may «respond» by displaying signs of colic and/or prolonged intestinal transit time. Horses receiving topically administered atropine should be monitored for signs of colic.

Systemically administered NSAIDs such as phenylbutazone (1 gm BID PO) or flunixin meglumine (1 mg/kg BID, IV, IM or PO) can be used orally or parenterally, and are effective in reducing uveal exudation and relieving ocular discomfort from the anterior uveitis in horses with ulcers. Topical nonsteroidal antiinflammatory drugs (NSAIDs) such
as profenol, flurbiprofen and diclofenamic acid (BID to TID) can also reduce the degree of uveitis. Horses with corneal ulcers and secondary uveitis should be stall-rested till the condition is healed. Intraocular hemorrhage and increased severity of uveitis are sequelae to overexertion.

Adjunctive surgical therapy
Bandage soft contact lens (SCL). Bandage SCLs help to maintain apposition of the healing epithelium to the stroma, reduce pain, and protect the new epithelium. Disadvantages include an occasional poor fit in horses thereby resulting in limited retention times. Contact lens retention time may be improved by partial temporary lateral tarsorrhaphy.

Debridement, Keratectomy and Keratotomy
Removing necrotic tissue and microbial debris by keratectomy speeds healing, minimizes scarring, and decreases the stimulus for iridocyclitis. Persistent superficial ulcers may need surgical debridement and keratotomy to remove the hyaline membrane slowing epithelial healing. Debridement to remove abnormal epithelium of refractory superficial erosions can be accomplished with topical anesthesia and a cotton-tipped applicator.

Conjunctival Flaps
Conjunctival grafts or flaps are used frequently in equine ophthalmology for the clinical management of deep, melting, and large corneal ulcers, descemetocceles, and for perforated corneal ulcers with and without iris prolapse. To augment lost corneal thickness and strength, deep corneal ulcers threatening perforation may require conjunctival flap placement. Conjunctival flaps are associated with some scarring of the ulcer site. Coverage with a 360 degree, hood, island, pedicle, or bridge flap should be maintained for 4 to 12 weeks. Reoccurrence of the inflammation may occur following flap removal.

Penetrating Keratoplasty
Corneal transplantation is recommended for corneal ulcers with iris prolapse. It is a very viable surgery for the horse eye. It may be combined with a conjunctival graft.

Amniotic Membrane Flaps
Amniotic membrane transplantation may provide decreased fibrosis, reduced vascularization of corneal ulcers, and faster reepithelialization in horses with superficial and/or deep corneal ulcers. They may be used alone or with conjunctival flaps.

Third-Eyelid (TE) Flaps
Nictitating membrane flaps are used for superficial corneal diseases including corneal erosions, neuroparalytic and neurotropic keratitis, temporary exposure keratitis, superficial corneal ulcers, superficial stromal abscesses, and to reinforce a bulbar conjunctival graft.

Temporary tarsorrhaphy
Horizontal mattress sutures enter the eyelid two to three millimeters from the eyelid margin with the cutting needle emerging from at the central aspect (Meibomian gland line) of the eyelid margin, and then reentering the apposing lid margin to exit in the skin. 4-0 silk or nylon is commonly used for this procedure.
Enucleation

Panophthalmitis following perforation of an infected corneal stromal ulcer has a poor prognosis. Phthisis bulbi is likely to result after a chronically painful course. Affected horses can be febrile and manifest signs of septicemia. To spare the unfortunate animal this discomfort, enucleation is the humane alternative.

Inappropriate therapy and ulcers

Topical corticosteroids may encourage growth of bacterial and fungal opportunists by interfering with non-specific inflammatory reactions and cellular immunity. Corticosteroid therapy by all routes is contraindicated in the management of corneal infections. Even topical corticosteroid instillation, to reduce the size of a corneal scar, may be disastrous if organisms remain indolent in the corneal stroma.

References/Suggested Reading