Eyelid and corneal neoplasia

Ocular squamous cell carcinoma (OSCC) is mostly seen in older, color dilute horses. OSCC is most commonly seen on lower lid margins, medial canthi, third eyelids, bulbar conjunctiva, and beginning at the corneoscleral limbus extending onto the cornea. On the lids, OSCC can appear as a “wart-like” mass, as an ulcerated area that becomes secondarily infected, or even as a smooth eyelid stromal mass. Diagnosis is based on cytology of scrapings (make sure and get a representative sample of the mass and not of the surface necrotic debris) and/or histopathologic evaluation of biopsy.

Therapy for OSCC may involve excision alone (low yield in my hands because of the extension of this type of neoplasia into the surrounding eyelid tissue. Surgical excision is more effective with third eyelid OSCC where clean margins can be more easily obtained), excision/debulkment followed by liquid nitrogen cryosurgery (one of my most commonly used treatments for lids and even cornea. Cool Renewal™ system ([www.cool-renewal.com](http://www.cool-renewal.com)) used in Man may be useful for small lid OSCC. Cool Renewal cryogen only -70°C centigrade versus -196°C for liquid nitrogen.), radiofrequency hyperthermia (not as high a yield for lid masses as liquid nitrogen therapy in my hands due to the poor penetration and ineffectiveness of the radiofrequency waves on tumor cells deep in tissue), CO₂ laser therapy following debulkment (due to the very limited penetration of the CO₂ laser energy into tissue, this modality usually only effective for corneal or limbal lesions), cisplatin powder in oil injections (JAVMA, 1993;202: 261-267), 5-fluorouracil injections (50mg/ml in 10 ml vial, Roche, used to be dirt cheap, is no longer. Either inject undiluted or mix 1/3 ml of 1:10,000 epinephrine with 1 ml 5-FU. Inject around edges and into tumor mass (saturate). Will require frequent re-injection and monitoring. I have not been altogether impressed with this technique used as the only treatment. In my hands, recurrence is common.), repeated intralesional injections with Bacillus-Calmette-Guerin (BCG, “Regressin”, this has been fairly useless in my hands for OSCC, however, I have had very good success with this drug for the treatment of sarcoids), radiation therapy (brachytherapy with gold-198 or iridium-192 “straws” with implant beads. This modality requires isolation and a radiotherapist. University of Tennessee, CVM and NC State, CVM has this modality available).

Implantation of cisplatin beads (Wedgewood pharmacy in N.J. is the only place you can obtain biodegradable cisplatin impregnated beads) is touted by some as being highly effective. Following debulkment procedure, beads are implanted ~1-3 cm apart and sutured into the surrounding tissue. Slow release of drug supposedly kills tumor cells and stimulates immune system to attack residual tumor cells. I have had some successes using this therapy.

The use of COX-2 inhibitors (piroxicam) for treatment of primary and locally metastasized OSCC is anecdotal. Early studies have shown levels of COX-2 expression in certain head and neck neoplasias in man (including SCC) as well as in SCC in horses. Some have recommended 80 mg/day for at least 90 days followed by 80 mg/48 hours indefinitely. Although we have used this modality in conjunction with other treatments in cases where complete excision was impossible or obvious local lymphatic metastasis had occurred, I personally cannot say one way or the other that this treatment is effective.
The newest and greatest technique from University of Missouri involves surgical debulkment followed by intralesional injection with photosensitizing substance (verteporfin – Visudyne™) followed by photodynamic therapy using a 665 nm wavelength diode laser light source. After injection, each 3 cm diameter area of the tumor mass is exposed to 15 minutes of the monochromatic light source until entire mass has been exposed (Vet Ophthal 2008 Sept; 11 (s1): 27-34). Long-term follow-up on cases treated this way show excellent results (lack of recurrence). Cost of the photosensitizing agent and lack of availability of the light source make this modality expensive and only available at Mizzou.

In summary, prognosis for eyelid OSCC is always guarded. The chance of recurrence is high with most treatment modalities used (with the exception of the new photodynamic therapy). In addition, the chance of local lymphatic metastasis is much higher for medial canthus, third eyelid, and eyelid masses than for masses on the eye alone.

Corneal or bulbar conjunctival OSCC is usually seen as a slowly enlarging, initially white later becoming pink, proliferative mass that usually begins at the limbus and slowly moves across cornea. Signalment is usually (but not always) older, color dilute horses with high exposure to sunlight. Cytology of corneal/conjunctival scrapings is usually suggestive, but surgical biopsy and histopathology are usually definitive for a diagnosis of OSCC.

Surgical and adjunctive therapies are many, with varying results. Superficial keratectomy alone can be curative if all neoplastic tissue is removed, but there is a high incidence of recurrence due to the invasive nature of the tumor into the corneal tissue. In conjunction with superficial keratectomy, nitrous oxide or liquid nitrogen cryosurgery increases the chance of success for a cure of these tumors. One can “spray” liquid nitrogen onto the corneal surface or use a contact probe with liquid nitrogen or nitrous oxide refrigerant to kill residual cancer cells. A “double freeze-thaw” technique is used to freeze the tissue quickly, followed by a slow thaw, followed up by a second freezing of the tissue. Symptomatic treatment of the post-op ulcer with broad spectrum antibiotics and antifungals and the secondary anterior uveitis with topical atropine and systemic NSAID’s usually results in good wound healing and preservation of vision. Unlike with eyelid masses, radiofrequency hyperthermia following superficial keratectomy carries a good prognosis for minimizing tumor re-growth. The thin corneal tissue allows for adequate penetration of the radiofrequency waves unlike the situation with thicker eyelid skin. Following superficial keratectomy, irradiation with a Strontium-90 beta radiation emitting probe (5000-9000 rads per site over corneal tissue, 10000-20000 rads per site over scleral tissue) reduces the incidence of tumor re-growth due to residual tumor cells being left behind.

Carbon dioxide laser therapy following superficial keratectomy (JAVMA 1990;196:439-442) has been touted as being effective at preventing tumor re-growth. In my hands, CO₂ laser therapy alone has been ineffective at preventing recurrence. In 2010 Univ Penn paper, topical 5-fluorouracil (Wedgewood pharmacy, 1 or 5% ointment) application following keratectomy showed good promise at preventing tumor re-growth. In this paper, researchers performed superficial keratectomy, followed by liquid nitrogen cryo therapy. Once the keratectomy site had epithelialized, they followed surgery with topical 5-FU application, tid (5% 5-FU solution diluted to 1% with over the counter boric acid eye rinse solution through a lavage system. However, 5-FU is very basic, and the solution is quite unstable, so many use 1% 5-FU ointment.). Treatment was one week on medication, one week off medication, for a minimum of three medical treatment cycles. 84% of the treated cases followed for one year showed no recurrence of tumor. Adverse side effects included some cases of surface
and adnexal irritation due to the 5-FU and nasolacrimal duct punctum fibrosis with secondary epiphora.

In a retrospective study from North Carolina State University (Vet Ophthalmol 2012 Jul; 15(4):254-62), success rates were compared between groups of OSCC horses following excision and CO₂ laser therapy versus excision followed by treatment with 0.4% (4 mg/ml) mitomycin C solution (Wedgewood Pharmacy) through a lavage system (0.1-0.2 ml, q8h, for 7 days, followed by 7 days off, followed by repeat treatment either 2 or 3 treatment regimens). Success (lack of tumor recurrence) was equal (~82+%%) with both protocols. At Virginia Tech, we currently do excision, CO₂ laser, followed by mitomycin C (at least 2 treatment regimens), and have had good results concerning tumor regrowth. Side effects of the mitomycin include surface ocular irritation as well as periocular skin irritation.

In conclusion, OSCC in the horse is a vision/eye and potentially life threatening disorder. EARLY detection and treatment followed by periodic re-examinations and retreatment yields the highest potential for long-term success.

Equine sarcoid is usually seen in younger horses than OSCC. It is not usually a life-threatening disorder like OSCC. Equine sarcoid can appear as “warty” flat or raised lesions, a pedunculated smooth lesion, or as a solid mass within eyelid stroma. Definitive diagnosis requires a biopsy and histopathologic evaluation. Etiology is believed to be due to exposure to the bovine papilloma virus, but there also appears to be a breed predisposition (AQH, Appaloosas, Arabs, and Saddlebreds). Therapy can take the form of topical application of irritants such as XXTERRA (bloodroot extract), repeated 5-FU injections like with OSCC, one time or repeated implantation of cisplatin beads (this seems to be one of our best treatment modalities at Virginia Tech), repeated intralesional injections with Bacillus-Calmette-Guerin (BCG, Nomagen- Fort Dodge or Regressin-V – Vetropharm)(Eq Vet Journal, 17(6): 445-448, 1985), excision with either radiofrequency hyperthermia or liquid nitrogen cryotherapy ancillary therapy, or brachytherapy using iridium-192. Prior to the availability of cisplatin beads, I had the best luck with BCG injections for treatment of equine sarcoid. Treatment to resolution usually required 3-6 injections before body’s immune system was stimulated to “attack” the tumor. Once the immunostimulant activated to body’s defense system, sloughing of the mass is seen, followed usually by good healing. Some have successfully treated equine sarcomas with aggressive debulkment and radiofrequency hyperthermia, but attempts at surgical excision or carbon dioxide lasering have been fraught with near disastrous re-growth of the mass.

Equine recurrent uveitis (ERU or “moon blindness”)

Recognized since ancient Greece, “moon blindness” refers to the periodic nature of ERU. The ancients felt the cyclic nature of this malady had something to do with stages of the moon.

ERU is pretty much now recognized as having an immunologic basis. Histopathological evaluations of ERU eyes show “lymph node-like” aggregations of lymphocytes in the ciliary body and other uveal tissues within afflicted eyes. These CD-4+ T-lymphocytes are primarily T-helper (TH-1) cells. They release high concentrations of interleukin-2, gamma interferon, and low levels of interleukin-4. So in cases of chronic recurrent (or actually persistent) uveitis, ocular inflammation is non-specific and immune mediated. Once initiated, inflammation does not necessarily develop in response to specific antigens (micro-organisms) (AJVR 2001 62(12): 1892-1896). In the past, ERU was felt to occur when animals had been exposed to an antigen, and had developed
immune competent cells in the uvea. With each re-exposure to the antigen, another “flare-up” of uveitis was felt to occur due to Ag-Ab response. In the past, much work was done to look at cross-reaction of antibodies to “self” antigens within the eye. Some classic “antigens” described for ERU initiation included: leptospirosis, strongyles, onchocerca, and streptococcus or rhodococcus. Other infectious diseases felt to initiate the immunologic cascade that led to ERU were brucellosis, toxoplasmosis, Lyme borreliosis, equine infectious anemia, and Potomac Horse fever.

For almost 100 years, there has been a known association between *Lepto interrogans* and ERU. In 1950’s and 1960’s, work done at UC-Davis showed that horses inoculated with serovar *pomona* would develop clinical signs of ERU MONTHS after inoculation. *Lepto interrogans* has many serovars (*pomona, griptophyosa, canicola, hardjo, bratislava, autumnalis*) that have all been serologically implicated as being an initiating event for ERU. In the upper Midwestern USA, many ERU horses are seropositive for *pomona* (cattle and swine reservoir?). In Virginia, Kentucky, and West Virginia, many ERU horses are seropositive for *bratislava* and *autumnalis* (which also cause equine abortions and have many wildlife vectors, e.g. whitetail deer). The current testing available (Micro Agglutination Test, MAT) for leptospirosis is poor. The MAT does not differentiate IgG and IgM, so evaluation for “acute” infection versus a long-term antibody titer is impossible.

In two classic papers (Proceedings ACVO 1998, p. 49 and *JAVMA* 2001 219(6): 795-800), the authors showed (via culture and PCR testing for bacterial DNA) that leptospiral organisms were actually within ERU afflicted eyes at some stage in the early development of ERU. Historically, in the 50’s, 60’s, and even into the 70’s and beyond, equine practitioners would treat ERU cases with “Combiotic” (pen-strep) as well as supportive care, and some of these cases would “clear” and not be plagued with recurrent episodes of uveitis with ultimate blindness. Approximately 20 years ago, Dr. Bill Rebhun (Cornell) proposed treating “early” ERU cases with penicillin-streptomycin (later penicillin-gentamicin) in an attempt to “clear” horses of leptospirosis. In his hands, many cases were “cured” of ERU, with no long-term sequela. Interestingly, epidemiologic studies done in New York’s Genesee River valley by Dr. Anne Dwyer (*JAVMA* 1995, 207(10): 1327-1331) showed a high association between ERU cases and positive Lepto titers. Her findings showed that horses with positive *pomona* titers (1:100+, MAT) were 13.2X more likely to have ERU than a horse with a negative titer and that horses with ERU and positive Lepto titers were 4.4X more likely to go blind than were ERU horses with negative Lepto titers. In addition, she found that seropositive Appaloosas were 8.3X more likely than other breeds to develop ERU and that seropositive Appaloosas were 3.8X more likely to go blind than other seropositive breeds. In the early 1990’s in Bangladesh, leptospiral induced uveitis in man was treated with penicillin, and those without therapy would have chronic uveitis, cataract formation, etc. and eventual blindness, much like our equine cases. I personally have treated a few “early” cases that were leptospira positive with either gentamicin or pen-gent that “resolved” and were able to be gotten off all anti-inflammatory medications eventually without the chronic uveitis of ERU. Some ophthalmologists recommend systemic therapy with doxycycline in an attempt to rid the body of leptospires before the immune system sets up shop in the eye. Recent work from Cornell has shown that systemic administration of enrofloxacin will penetrate into ocular tissues with a drug level adequate to kill leptospiral organisms.
With the more chronic disease we know that immune competent cells (CD-4 T-lymphocytes) are deposited into uvea (ciliary body, iris, and choroid). In the 80’s, one study showed that in ERU horses, higher MAT titers were seen in the aqueous humor than in the serum. At that time, it was recommended to “limit exposure” to Ag (don’t drink nasty pond water, etc.) in an attempt to reduce the recurrent episodes and long-term effects of ERU. In the late 1990’s, Dr. Brian Gilger at NC State developed subscleral/suprachoroidal implants of cyclosporine A to try to counteract the immunologic cascade of ERU (AJVR 2001 62(12) 1892-1896.). Long-term follow up has shown that in many horses, these implants calm the inflammation of ERU for 3+ years. These cyclosporine implants are not available commercially (probably never will be due to stringent FDA regulations). Other drugs (e.g., rapamicin) have been evaluated, but the suprachoroidal CsA implants are still considered the therapy of choice.

As far as a clinical course/diagnosis is concerned, there should be an increased index of suspicion in a horse with recurrent/persistent bouts of uveitis and no history of systemic disease or other ocular disease (esp. corneal disease such as previous corneal ulcers, stromal abscesses, etc.). A diagnostic workup should be done for other disease (lepto, brucella, EIA, toxoplasmosis, Lyme borreliosis, fecal for strongyles, history of Strep?, CBC, good physical and ophthalmic examination). Unfortunately, many horses have absolutely nothing wrong with them other than ocular disease. For years, Dr. Gilger at NC State stated that they rarely saw ERU horses with positive leptospiral titers or any other predisposing disease (unlike my experience with leptospirosis in Virginia and when I worked at the University of Wisconsin). In a recent retrospective study from NC State, however, it was found that 45% of horses TESTED (only 40% were tested) had a positive titer for one or more serovars of leptospirosis. Unfortunately, a diagnosis of ERU many times is made based on clinical signs, elimination of other causes, and history.

In the past, therapy has been mostly supportive until the horse went blind. Topical steroids (dexamethasone and prednisolone are the most effective) reduce inflammation, subconjunctival corticosteroids would help reduce the frequency needed to control the clinical signs but were not without ill effects if the horse had an infectious corneal disease or developed a corneal ulcer. Topical atropine reduced painful ciliary spasm and dilated the pupil to hopefully prevent posterior synechia and the occurrence of a blinding secluded pupil. Systemic NSAID’s reduce pain and help restore the blood-aqueous barrier integrity. Most eyes were treated aggressively until inflammation calmed down, and then we SLOWLY weaned off drugs (maybe chronic drug therapy such as daily aspirin) and hoped that the eye would remain stable without recurrent episodes of inflammation with ultimate blindness.

Recent therapies have included vitrectomies (Vet Ophth 1998 1(2-3): 137-151), which have a high incidence of cataract formation and blindness post-op, and subscleral/ suprachoroidal CsA implants (see reference above). Cyclosporine A implants have by far shown the most benefit thus far. Early systemic antimicrobial therapy (gentamicin, penicillin, tetracycline, or enrofloxacin) may be of some help. Other therapies have included intravitreal gentamicin therapy in those cases believed to be early leptospiral induced and intravitreal triamcinolone (associated with very high incidence of fungal keratitis, Gilger and others, personal communication).

To summarize, ERU continues to be the leading cause of blindness in horses. We know that a “hyperactive” immune system within the afflicted eye results in an inflammatory cascade that ultimately can lead to cataract formation, phthisis bulbi, retinal
detachments, and other blinding sequelae if left unchecked. Although exposure to leptospirosis may be a triggering mechanism for many cases, it is not the only cause of this devastating disorder.

**Corneal ulcers**

Despite the large numbers of bacteria and fungi that are “normal flora” on the surface of the equine eye, there really is no infectious agent that by itself CAUSES ulcerative keratitis (+/- EHV-2 or -5). The most common cause of ulcerative keratitis is trauma/frictional irritation from herbaceous environmental material (hay, straw, bedding, weeds, etc.). Very seldom will we see exposure or tear deficiency problems in horses like in dogs. Weed seeds, burdock pappi seen in fall of the year and other environmental hazards may strip the corneal epithelium from the underlying stroma. Caustic substances can damage the epithelium and stroma, the worst of which are alkali-type substances (lime, strong detergents).

Because of the typical severe blepharospasm in horses, sedation, palpebral nerve block, +/-topical anesthesia is essential to look for a foreign body or other cause of an ulcer. If an ulcer bed is necrotic or “melting”, “deep”, or more than 24 hours old, scrapings for cytology and Gram’s stain and culture and sensitivity are recommended.

Initial therapy for uncomplicated cases includes debridement of any necrotic debris from ulcer bed with Betadine soaked Q-tip, topical antibiotic (broad spectrum or based on cytology/Gram’s stain), topical antifungal if herbaceous material caused ulcer (silver sulfadiazine, miconazole, or itraconazole/DMSO ointments), and symptomatic treatment of secondary anterior uveitis (topical atropine and NSAIDs such as phenylbutazone or flunixin). I suggest re-examine the eye in 24-48 hours to make sure it is healing, don’t take the owner’s word for how the horse is doing.

If you are faced with a more complicated case, or if the eye is not healing as you would expect, you could have a bacterial infection or a fungal infection of the exposed corneal stroma. In the case of bacteria, either “normal” flora inoculates exposed corneal stroma after damage to epithelium, or whatever traumatized the cornea was contaminated with bacteria. Proteolytic enzymes (MMP-2 and -9 and other elastases) from bacteria, neutrophils, or traumatized epithelium and/or stroma cause “meltdown” of corneal stromal protein fibrils and interfibril proteins. This proteolytic “meltdown” can lead to extensive stromal destruction that can lead to corneal perforation in as little as 24 hours if untreated. Gram-negative organisms (especially *Pseudomonas*) are usually the worst, but some Gram-positive *Strep* and *Staph* can also cause extensive proteolytic enzyme destruction. Medical management of these types of ulcers should be swift and intensive. Diagnostics should be performed first (scrapings for cytology and Gram’s stain followed by cultures for bacteria and fungi). Necrotic debris should be debrided from the ulcer using a Betadine soaked Q-tip. Anti-proteolytic agents such as 2-4% acetylcysteine, NaEDTA, serum, and oral doxycycline will reduce proteolytic enzyme degradation of the corneal stroma. Choices of antibiotics include: gentamicin, tobramycin, ciprofloxacin for Gram-negative organisms and chloramphenicol, cefazolin or ciprofloxacin for Gram-positive organisms while awaiting culture and sensitivity results. “Ulcer mix” cocktails that I use are made up of 15 ml saline based artificial tears, 2 ml 100 mg/ml injectable gentamicin or chloramphenicol (based on Gram stain or culture results), and 2-4 ml of 20% acetylcysteine. Supportive care such as topical atropine and NSAID’s for the secondary anterior uveitis is essential. Since sore-eyed horses are quickly difficult (and potentially dangerous) to treat, implantation of a
subpalpebral lavage system (Mila™) is almost essential. Aggressive hourly treatment for the first 24 hours may make the difference between a mess that turns around and heals versus a case that requires surgery or perforates resulting in loss of the globe. For cases of fungal keratitis, immediate antifungal therapy is essential. Unfortunately, dying fungi can contribute to proteolytic enzyme destruction of the corneal stroma, so supportive anti-proteolytic agents are needed to prevent further “melting” and perforation in cases where the deep corneal stroma appears to be infiltrated with infection. Topical antifungals that can be used include natamicin (expensive) suspension, miconazole (as a compounded solution to run through a lavage system or as a compounded ointment or as Conofite™ dermatological cream, NOT the 50% ethyl alcohol containing lotion), silversulfadiazene cream (Silvadene™), a compounded itraconazole-DMSO ointment (Wedgewood and others), or compounded voriconazole solution (expensive as well).

If medical therapy does not result in healing of the ulcer or if the ulcer progresses to more than 2/3 corneal depth or a descemetocele, surgery in the form of a keratectomy to remove as much necrotic debris as possible followed by a conjunctival flap is indicated. Reducing the amount of necrotic tissue and proteolytic enzymes present and application of healthy vascularized tissue to the corneal stroma may result in a corneal scar, but some vision is better than a ruptured, blind/enucleated eye.

**Stromal abscesses/cellulitis**

Stromal abscess/cellulitis is an uncommon entity in other species, but occurs with some regularity in the horse. There is usually a nebulous history of trauma to the cornea, +/- a corneal ulcer early on. The stroma of the cornea may be “seeded” with bacteria or fungi from a superficial puncture, or there can be a “sterile” abscess of degenerate inflammatory cells from stromal necrosis. A 2007 ACVO report from Ohio State showed with culture, cytology, PCR, and histopathology, 90+% of these stromal abscesses were infected with fungi. Following a puncture wound, the epithelium quickly grows over the necrotic stroma, and these lesions are usually fluorescein dye negative. Subsequently, inappropriate therapy with topical steroids may be used for the painful eye. This initially decreases the anterior uveitis and pain, but the stromal degradation “spreads”, and eventually the horse becomes even more painful and the white foci of necrotic debris gets wider and/or deeper. Usually these horses are very painful, with anterior uveitis, and hypopyon is not uncommon. These horses usually have an intact corneal epithelium with subepithelial necrosis. The affected area may be yellow to green discolored. If steroids have not been used, there will be deep corneal neovascularization beginning at limbus. If one debrides the epithelium and gets into the stromal debris, you may well culture bacteria or fungi, and will see inflammatory cells on cytology.

Therapy can be conservative medical or aggressive surgical. If a horse has a painful eye with corneal neovascularization, do not attempt to temper that neovascularization with corticosteroid therapy. I learned years ago by painful experience that vessels do not usually grow across a horse’s cornea for no reason. If the area is not too deep, debridement of the epithelium and getting cytology and culture of the debris can give you a quick diagnosis. If the area is deep in the corneal stroma, a “shotgun” approach to medical management may be taken to see if the cornea will heal on its own. Broad-spectrum antibiotics that penetrate the intact corneal epithelium and stroma both (e.g. chloramphenicol or ciprofloxacin) and antifungals that penetrate the cornea well (miconazole, voriconazole, or one of the compounded itraconazole-DMSO cocktail ointments) as well as supportive therapy (atropine and NSAID’s for uveitis control) may
be tried. Removal of the surface epithelium daily may enhance penetration of the antimicrobial drugs (especially if using drugs that do not penetrate an intact corneal epithelium such as the aminoglycosides, silver sulfadiazine, or natamicin). If medical therapy is successful, the cornea will vascularize to the foci and with time the corneal vessels will regress, the cornea will remodel, and there will be a focal scar at the site of the original lesion. This process may take weeks/months to run its course. A good sign after beginning medical therapy is that the horse is more comfortable and the vascularization process is progressing well.

If the medical therapy does not show improvement of pain and intraocular inflammation in a few days, aggressive surgical therapy may be in order. Full thickness keratectomy, lamellar keratectomy, and other surgical manipulations to remove the infected/necrotic tissue with or without placement of a conjunctival flap are best left to those with experience and equipment necessary to do these microsurgical procedures. As was the case with keratectomies and conjunctival flaps for deep ulcers, a scarred, partially visual eye is better than a blind/enucleated eye in these cases.

**Eosinophilic keratoconjunctivitis**

An emerging ocular disease in horses in the Mid-Atlantic and Midwestern states, eosinophilic keratoconjunctivitis is a seasonal disorder (late spring through summer months) seen mostly in adult horses. Clinical signs include pain (blepharospasm, tearing, +/- photophobia), corneal/conjunctival “plaques”, and superficial corneal ulcerations. Over the past 10 years, we have seen 1-6 cases per summer at the VMRCVM, plus we have consulted on many cases with RDVMs. Dr. Utter, et al, published an excellent retrospective study from University of Pennsylvania cases (Vet Ophthalmol (on line) 14: Jun 2013, Eosinophilic keratitis in 46 eyes of 27 horses in the Mid-Atlantic United States (2008-2012).

Most horses present early in the summer with pain and characteristic white-grey/yellow plaque-like grainy debris of the lateral or medial limbus, extending onto the bulbar conjunctiva and corneal surfaces. Cytology of this debris reveals eosinophils and eosinophilic granules with occasional neutrophils and mast cells. Few will culture positive for bacteria or fungi, and if they do, organisms are usually in low numbers and are typical surface ocular flora for the horse. When the plaque is removed from the ocular surface, a superficial discontinuity of the corneal epithelium may be seen. Underlying etiology for this disorder is uncertain, but a history of fly infestation is common for the cases reported. In addition, aggressive fly control about the face and in general has lead to resolution of clinical signs as well prevented recurrence in subsequent years for at risk patients. Some cases have cleared in the late summer/early fall only to recur the following spring. Some horses have other clinical signs of hypersensitivity phenomena (hives, wheals, food and pollen allergies), but most do not. Severe cases seen in Virginia and in Kentucky may also have severe decrease in tear production due to apparent dacrtyoadenitis of the lacrimal glands.

Therapy is in the form of topical and systemic corticosteroids. Some cases will respond with regression of the plaques with topical dexamethasone or prednisolone, but those cases with superficial ulceration may take weeks/months for the area to re-epithelialize. Systemic dexamethasone (up to 30 mg/day orally), will greatly reduce the time to resolution for many cases, and may help resolve those cases with superficial ulcerations. At Virginia Tech, we found (as have others) that the cases with superficial ulceration will resolve quicker if the corneal ulcer area undergoes a superficial
keratectomy to remove the abnormal tissue. Histopath and ultrastructural studies of this abnormal tissue reveals a layer of hyalinized necrosis of the anterior corneal stroma with no viable keratocytes that inhibits proper corneal healing and repair. Broad-spectrum antibiotics and anti-fungals should also be administered to prevent secondary bacterial or fungal infection, as cases that have become infected with secondary invaders have taken longer to resolve (cases with active bacterial/fungal infection should not be treated with topical steroids, rather should be managed with systemic steroids alone). Our experience with using a diamond burr to perform a superficial keratotomy has been unrewarding, but some anecdotal reports indicate that this therapy is useful at shortening the period to final resolution. Additionally, systemic anti-histamine therapy (cetirizine, Zyrtec\textsuperscript{TM}, 0.4 mg/kg bid) has been shown to reduce the incidence of recurrence, and may help reduce the time to clinical resolution.

Mean time to resolution of signs for all horses in the Penn study was 3.7 months (S.D. 2.3 months) with horses receiving systemic dexamethasone resolving in 2.23 months (S.D. 1.13 months) and horses not receiving systemic steroids resolving in 4.2 +/- 1.47 months. Prophylactically cetirizine treated horses were less likely to have recurrence the following year (8\%) versus horses not prophylactically treated with cetirizine (57\%).