Review Article

Equine corneal stromal abscesses: An evolution in the understanding of pathogenesis and treatment during the past 30 years

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Summary

The last 30 years have seen many changes in the understanding of the pathogenesis and treatment of equine corneal stromal abscesses (SAs). Stromal abscesses were previously considered an eye problem related to corneal bacterial infection, equine recurrent uveitis, corneal microtrauma and corneal foreign bodies in horses. They were more commonly diagnosed in horses living in subtropical climatic areas of the world. Therapeutic recommendations to treat equine SAs were historically nearly always a medical approach directed at bacteria and the often associated severe iridocyclitis. Today the pathogenesis of most equine SAs appears to be more often related to fungal inoculation of the anterior corneal stroma followed by posterior migration of the fungi deeper into the corneal stroma. There is also now an increased incidence of diagnosis of corneal SAs in horses living in more temperate climates. Medical and surgical treatments are now directed towards elimination of fungal and bacterial infections, reduction and replacement of diseased corneal stroma, and suppression of iridocyclitis. If the abscess and anterior uveitis do not respond satisfactorily to medical therapy, full thickness or split thickness lamellar keratectomy to remove the fungal hyphae and diseased stroma, followed by transplantation of healthy corneal allografts has a high rate of success in speeding healing and preserving sight. This paradigm shift in the ability to diagnose and institute therapy for corneal SAs in horses has evolved over the last 30 years, and is the focus of this paper.

Introduction

An abscess is a focal mixture of cellular debris, necrotic tissue, leucocytes and possibly an infectious agent that initially created the lesion surrounded by a zone of reactive inflammation (Rebhun 1992; Rigler 1997). Rebhun (1982) was the first to describe clinically the corneal stromal abscess (SA) of the horse in the USA, and since then stromal abscessation has been increasingly recognised as a painful eye condition with a high potential for blindness in horses. The diagnosis of a SA can be relatively difficult in some eyes with severe iridocyclitis and extensive corneal oedema, and is best made by the clinical appearance, history and slit lamp biomicroscopy. Medical and surgical treatments have been developed and have evolved over many years for treatment of corneal SA. This paper aims to review the pathogenesis of SA, and the past, present and future treatment options.

The equine cornea

The equine ocular surface is a functionally integrated optical unit consisting of the precorneal tear film, cornea, limbus, conjunctiva and eyelid. The function of the transparent cornea is to refract and transmit light for the visual process (Mishima 1965; Rauz and Saw 2010). The precorneal tear film provides an optically smooth surface to the cornea and aids corneal nutrition. The precorneal tear film is on an average 234 µl in volume, 93 µm in thickness, and is replaced approximately every 7 min in the horse (Chen and Ward 2010). The horse cornea is 0.77–1.50 mm thick, and is thickest in the central part and thinnest at the limbus (Andrew *et al*. 2000; Samuelson 2007). The cornea is divided into 3 functional and anatomic parts with the epithelium as the most superficial anterior layer. The epithelial cells are further subdivided into the most superficial squamous cells (normally with a 3 cell layer thickness), the cuboidal cells of the middle part of the epithelium (normally 3–4 cells layer thick), and the posterior deeper basal cell layer (normally 1–2 cells in thickness; Andrew *et al*. 2000; Brooks and Matthews 2007). The cell membranes of the basal epithelial cells are attached with hemi-desmosomes and transmembrane cell adhesion proteins such as integrin $\alpha 6\beta 4$ to an epithelial basement membrane present between the corneal epithelium and stroma (Samuelson 2007; Carter 2009). The stroma is the dominant component of the cornea as it comprises about 90% of the corneal thickness. It is mainly composed of precisely arranged fibres of collagen *type I* (Samuelson 2007). Descemet's membrane is the basement membrane of the corneal endothelium located in the most posterior aspect of the stroma. There does not appear to be a rigid, strong attachment between the posterior stroma and Descemet's membrane in the horse. Descemet's membrane consists mainly of collagen *type IV* (Waltman and Hart 1987; Andrew *et al*. 2000; Samuelson 2007; Plummer *et al*. 2008). The endothelium is a single layer of cells attached to the posterior deep side of Descemet's membrane. It is a metabolically active cell layer with intracellular ATPase pumps used to maintain corneal deturgescence by moving water out of the cornea (Andrew *et al*. 2000). Severe corneal oedema will develop if the endothelial cells are dysfunctional (Watsky *et al*. 1995; Samuelson 2007). Neural innervation to the cornea is derived from ciliary nerves, which are end-branches of the ophthalmic division of the fifth cranial nerve (trigeminal nerve). These nerve fibres enter the cornea at the limbus in

the anteriorand midstromal layers such that the cornea is one of the most sensitive organs in the body (Waltman and Hart 1987).

Presumed pathogenesis of equine corneal stromal abscesses

A number of different hypotheses for the pathogenesis of SAs in horses have been proposed. One likely theory for some eyes with SAs is that they occur by traumatic micropuncture of the intact corneal epithelium and injection of a pathogen or foreign body into the stroma such that the microbe or foreign material is trapped in the stroma during the healing process of the inoculation site ulcer (Rebhun 1982). Such micropunctures could result in a superficial SA localised to the anterior stroma, a full thickness SA involving all layers of the stroma, or deep stromal abscesses (DSAs) present near Descemet's membrane. Other authors have hypothesised that a SA could develop in the deeper layer of the corneal stroma via vertical or posterior migration of fungi from the superficial cornea to the deeper stroma, and possibly by haematogenous spread of embolic abscess material leaving the iris capillaries to reach the anterior chamber and attach to the corneal endothelium (Brooks *et al*. 2009). In this latter proposal, systemic infection could be the cause of some SAs and DSAs. Some limbal SAs may also arise from embolic microbial spread from the limbal vasculature. That type of SA might also be a manifestation of a systemic infection with a haematogenous pathogenesis, and might explain why bilateral cases of SA occur, and also why some farms suffer simultaneous multiple cases of SA (Brooks *et al*. 2009).

Thirty years ago most equine SAs were believed to be caused by bacterial infections (Rebhun 1982). We now know that fungi are commonly involved as the cause of SA in horses (Hamilton *et al*. 1994; Hendrix *et al*. 1995; Andrew *et al*. 2000; Gilger *et al*. 2005). Bacterial SA and mixed bacterial and fungal SA are diagnosed, but fungi, due to their unexplained affinity for the deeper layers of the cornea, including Descemet's membrane, must be considered critically involved in the pathogenesis of equine DSA (Hamilton *et al*. 1994). It may be that fungi able to produce high amount of proteinases are capable of moving deep vertically and posteriorly in the cornea to cause the particularly inflammatory DSA (Gaarder *et al*. 1998; Brooks 2004; Dong *et al*. 2005; Plummer *et al*. 2008).

The most common fungi isolated from SA from horses are *Aspergillus*, *Fusarium*, *Candida* and *Alternaria* spp. Bacteria cultured from SA in horses include *Pseudomonas aeruginosa*, beta-haemolytic streptococci (in particular *Streptococcus zooepidemicus*), and *Staphylococcus* spp. (Hamilton *et al*. 1994; Hendrix *et al*. 1995; Brooks and Matthews 2007).

Immune response of the normal cornea and the cornea with a stromal abscess

The function of the cornea is to be a transparent, supportive optical structure. The transparency is maintained during corneal inflammatory disease by the ocular immune privilege that makes it possible for the cornea to avoid massive attraction and infiltration of leucocytes, and inhibits mechanisms of generalised vascularisation and fibrosis (Hamrah *et al*. 2003; Cursiefen 2007). Down regulation of innate ocular surface defences may allow a pathogen that has been introduced to the equine corneal stroma to initiate stromal inflammatory disease. The fact that leucocytes are attracted very aggressively in the formation of SAs and DSAs suggests, however, that the immune system of the horse cornea with a SA or DSA is acting quite effectively. Focal angiogenic and vasculogenic responses can also be initiated in equine SA and DSA (**Fig 1**) (Hamilton *et al*. 1994; Hendrix *et al*. 1995; Brooks and Matthews 2007). Chronic SA may be more associated with dysfunction of the immune system of the cornea due to the fact that histopathology from many chronic SA cases will show only an inflammatory reaction in the SA tissue, and no pathological agent (Brooks and Matthews 2007).

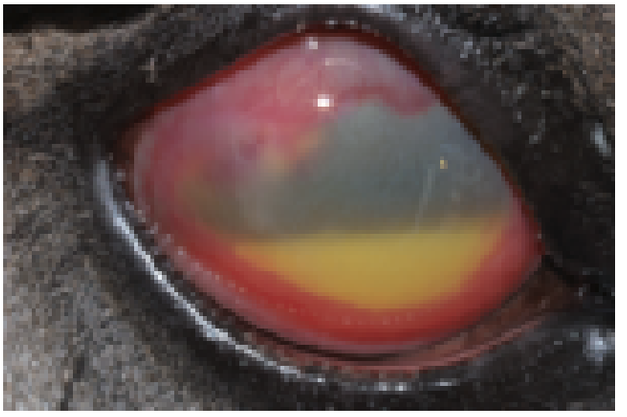


Fig 1: Leucocytes are attracted very aggressively in the formation of a stromal abscess suggesting that the immune privilege of the cornea has been disrupted. Vascularisation over the abscess and ventrally is very prominent. Severe uveitis with breakdown of the blood-aqueous barrier and hypopyon can be appreciated in this horse eye.

The formation of a SA may be divided into 3 different stages. During the first stage of a SA formation, the cornea will be infiltrated with different inflammatory cells, but particularly neutrophils and multinucleated giant cells. Chemoattraction of leucocytes is caused by infection, epithelial cell loss, and keratocyte damage. Vascularisation of the abscess region is slower to develop but will also eventually be seen arising from the limbus (**Fig 2**). This inflammatory response in the cornea will normally also create mild to severe anterior segment inflammation or uveitis that manifests as a breakdown of the blood-aqueous barrier and development of aqueous flare, hypopyon, occasionally hyphaema, and a miotic pupil (Rebhun 1992; Hamilton *et al*. 1994; Hendrix *et al*. 1995). During the second stage of SA formation (**Fig 3**), vascularisation is observed in areas of the stroma where cellular infiltration is present. The vascular response in the areas adjacent to the SA is prominent in the degree of intensity but, distant from the SA, the intensity of vascularisation will be less pronounced resulting in an asymmetrical vascular pattern. The initially rather diffuse cellular infiltration will slowly consolidate to a smaller, but more dense focal area, and in many cases the cellular infiltrate will migrate to the deeper stroma and Descemet's membrane (Brooks and Matthews 2007; Plummer *et al*. 2008). The concurrent uveitis will at this point be severe if medical treatment has not been initiated (Andrew *et al*. 1998; Brooks and Matthews 2007). Thethird stage in SA formation (**Fig 4**) is characterised by vascularisation of the superficial cornea anterior to the SA. For reasons as yet unknown, new blood vessels will not easily directly invade the abscess but can be

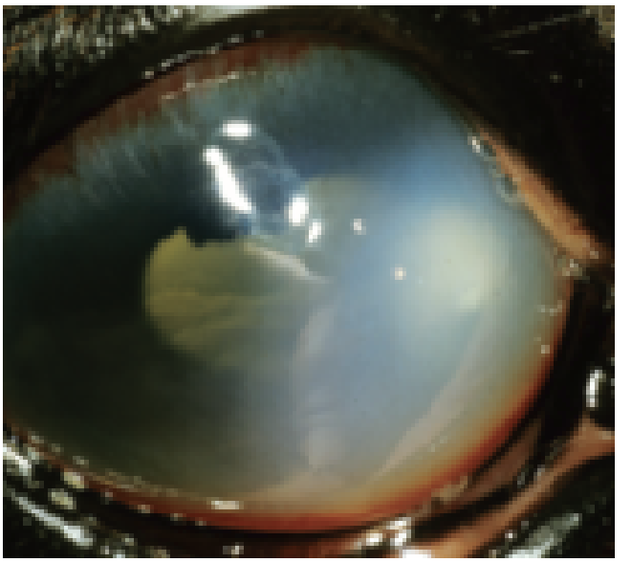


Fig 2: The first stage in the development of a stromal abscess is the presence of a diffuse circular cellular infiltrated area found in this case at the 3 o'clock position in the cornea. Perilimbal neovascularisation has begun but has not moved more than a couple of millimetres into the cornea. The abscess area is surrounded by moderate corneal oedema and the pupil is starting to dilate due to medical treatment.

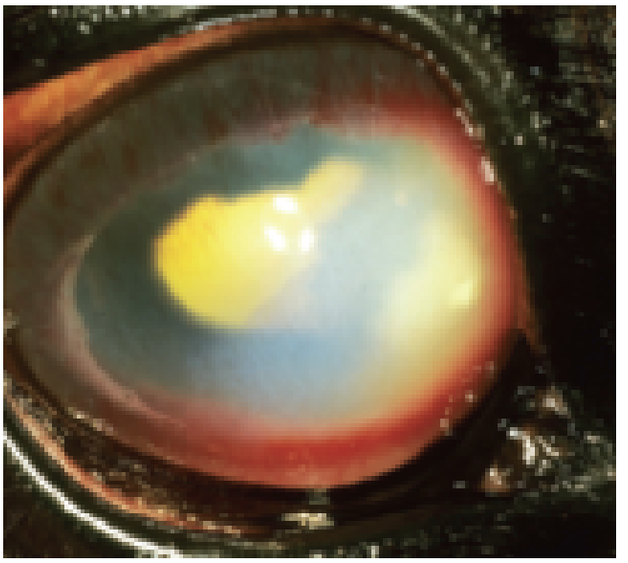


Fig 3: This image shows the same horse as in Figure 2 one week after medical treatment for the nonulcerative stromal abscess (SA). In this second stage of SA formation, the cellular infiltrated area in the cornea is more consolidated and dense (compared with the first stage of Figure 2). The perilimbal neovascularisation has almost reached the deep SA (DSA) at 3 o'clock, the corneal oedema has increased severely in the area of the DSA, but the pupil has not dilated much more than at the earlier stage despite medical treatment indicating uncontrolled uveitis.

adjacent to or deep to the abscess in the posterior cornea. It is possible that cytokines or other chemical agents derived from fungi, bacteria or leucocytes secrete anti-angiogenic factors that inhibit vascularisation of the SA (Welch *et al*. 2000; Brooks and Matthews 2007).

The healing process of a stromal abscess

Stromal abscess in the anterior stroma are more likely to be bacterial and respond to medical therapy, while abscesses of the posterior stroma and those involving the entire corneal thickness heal quicker with surgical removal of the abscess (Brooks and Matthews 2007). The absence of vascularisation to the area of a SA or DSA inhibits beneficial components of the inflammatory reaction reaching the lesion to aid rapid resolution of the condition (Brooks and Matthews 2007). The purulent material, which in other equine tissues is liquefied (Barber 2008), remains firm in most equine corneal SA (Hamilton *et al*. 1994; Brooks and Matthews 2007) and therefore this material is difficult or impossible to drain or evacuate. Vascularisation of the SA is necessary for resolution of the leucocyte response and for abscess healing. The vascular response is initially rather weak and may be confined to stromal lamellae adjacent or anterior to the abscess. It seems that blood vessels have difficulty invading SA tissue during the early clinical stages of this disease due to some unknown mechanism. Blood vessel invasion of the SA can become quite robust with time during the healing phase of an abscess, and then attenuates over several weeks to result in stromal fibrosis of the stromal abscess. The fibrosis from extreme vascularisation in large SA may be severe (Brooks and Matthews 2007).

The pro- and anti-inflammatory mediators, including cytokines, involved in formation and maintenance of equine

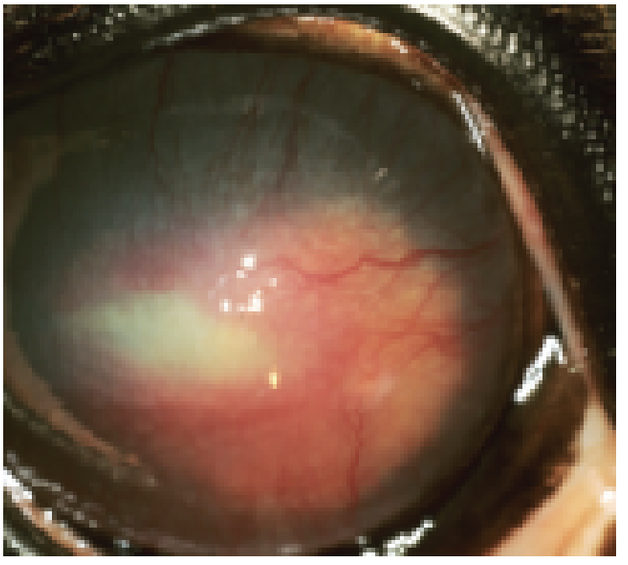


Fig 4: The third stage of development of a stromal abscess has the vascularisation completely infiltrating the stroma anterior to the deep stromal abscess. The corneal oedema has started to clear in the periphery.

SA are currently being investigated (Hamilton *et al*. 1994; Brooks and Matthews 2007). Vascular endothelial growth factor (VEGF) has been shown to have an important role in the cornea vascularisation response in other animal species, and could therefore also have an important role in the

vascularisation process in the horse cornea (Coman *et al*. 2010; Perez-Santonja *et al*. 2010). Pigment epithelium-derived factor (PEDF) acts in balance with VEGF and is an anti-angiogenic cytokine that is normally present in the equine retina and in the cornea of other animals. The presence of PEDF will inhibit vascularisation. It is thought that PEDF also has a very important role in maintaining the immune privilege of the eye (Stuart *et al*. 2003; Zipplies *et al*. 2009). Pigment epithelium-derived factor may be involved in the absence of vascularisation of the surrounding tissue of a SA in the horse but further studies are required to determine which cells or agents produce this cytokine in the cornea.

Corneal inflammatory cytokines identified in animals include interleukin-1 (IL-1) alpha and beta. Interleukin-1 is well studied in the inflammatory reaction of septic and degenerate arthritis in horses, and has also been investigated in the cornea of different animals (Moore *et al*. 2002). The receptor antagonist for the IL-1 is currently being investigated for possible anti-inflammatory effects and a role in neovascularisation of the cornea, but studies of IL-1 in the equine cornea have been inconclusive to date (Dana *et al*. 1998; Lu *et al*. 2009). Another substance possibly involved in equine SA is FAS-ligand (FasL), which is an apoptotic transmembrane protein known to protect immune privileged sites, and to regulate and terminate immune responses by T cell apoptosis (Murphy *et al*. 2008). FasL has been shown to be present in the cornea, where it acts as a barrier to inflammatory cells and neovascularisation. There may be a connection between PEDF and FasL in inhibiting neovascularisation caused by inflammation or infection in the cornea (Stuart *et al*. 2003). It is possible that a loss of homeostatic balance between VEGF and PEDF may play a role in the absence of vascularisation to a SA (Gao *et al*. 2001).

Diagnosis and medical treatment of stromal abscesses

The diagnosis of a SA is based on the slit lamp visualisation of a focal, yellow-white, stromal infiltrate with associated corneal oedema. Single or multiple abscesses may be present. Fluorescein dye retention is either negative or faintly positive over the SA. A mild to fulminating iridocyclitis can occur to cause ocular pain and possible blindness. Corneal vascularisation varies according to the stage of SA progression. Some SAs are adjacent to Descemet's membrane and/or projecting into the anterior chamber.

During the 1980s, surgical treatment of equine SAs was more or less condemned because of poor outcome and medical treatment alone was recommended (Rebhun 1982) (**Table 1**). These recommendations have since changed, although medical treatment of superficial SA is still most economical and can result in good visual outcomes with mild scarring. Deep stromal abscesses are, however, often unresponsive to medical therapy. Medical treatment of DSAs is always necessary as the first step to address the infection and uveitis but surgical therapy may be necessary for DSAs to most often quickly resolve the condition (Brooks 2004) (**Table 2**).

Signs of healing of a SA would be vascularisation of the entire abscess although what occurs in most DSAs is vascularisation of the stroma anterior to the DSA but not the DSA itself. The whitish yellow cellular infiltrate of the SA or DSA will be replaced with beige to grey fibrotic tissue during healing if the lesion is responding to medication (**Fig 5**), and the uveitis will diminish and be more easily controlled despite utilising relatively low dosages of systemically administered anti-inflammatory medications (Andrew *et al*. 2000; Brooks *et al*. 2008; Plummer *et al*. 2008). Most SA cases do not require high doses of systemic nonsteroidal anti-inflammatory drugs (NSAIDs) to control the uveitis if the disease is medically responsive. However, uveitis 'flare-ups' when using low dose systemically NSAID therapy indicate continued activity of the SA or DSA and may require use of a higher dose of NSAID, a change in antimicrobial therapy, and/or surgical management (Brooks and Matthews 2007; Clode 2011). During medical therapy, if no signs of recovery can be appreciated, or if the anterior segment inflammation persists despite the aggressive medical treatment, surgical options should be considered (Andrew *et al*. 1998; Brooks and Matthews 2007; Plummer *et al*. 2008).

Medical treatment consists of a combination of topically administered antimicrobial medications, mydriatic/cycloplegic drugs and anti-inflammatory medications. Subpalpebral lavage systems may aid aggressive medical therapy. The antimicrobial medication will normally be a combination of antibacterial and antifungal drugs. The most common topical antibiotics used at the Veterinary Ophthalmology Service at the University of Florida (UF) for equine SA are neomycin, polymyxin B, gramicidin ophthalmic solution[1], or a combination of compounded cefazolin (55 mg/ml) ophthalmic solution and tobramycin (0.3%) ophthalmic solution[2]. The most common topical antifungal medication used at UF is compounded voriconazole 1% ophthalmic solution. Compounded miconazole (1%) ophthalmic solution and natamycin (5%) ophthalmic solution[2] are also used at UF in selected cases. These topical medications may need to be administrated to the cornea 4–6 times daily for 4–6 weeks (Andrew *et al*. 1998; Brooks and Matthews 2007; Clode 2011). Intrastromal injection of antifungal agent such as amphotericin B and voriconazole has been effective in some SA cases. This procedure has been performed in standing sedated horses and in horses under general anaesthesia. The advantage of this procedure is the low cost. The risk is the possibility of introducing infectious agents into the anterior chamber, and cataract formation (Cutler 2010).

TABLE 1: Medical therapy for stromal abscesses, 30 years ago (Rebhun 1982) – superficial stromal abscess therapy

Drug/procedure	Dose and frequency
Topical and subconjunctival chloramphenicol or gentamicin	q. 1–4 h
Topical atropine (1%)	Until pupil is dilated
Systemic flunixin meglumine	0.5–1 mg/kg bwt i.v., i.m., b.i.d.
Systemic antimicrobials: chloramphenicol or gentamicin and itraconazole or fluconazole	Itraconazole: 3 mg/kg bwt *per os* b.i.d. Fluconazole: 4 mg/kg bwt *per os* s.i.d.

TABLE 2: Deep stromal abscess therapy circa 2012 – used most commonly at the Veterinary Ophthalmology Service at the University of Florida, Large Animal Hospital. Penetrating keratoplasty (PK), posterior lamellar keratoplasty (PLK), deep lamellar endothelial keratoplasty (DLEK) (Brooks 2004; Brooks *et al*. 2008)

Drug/procedure	Dose and frequency
Topical antifungal: voriconazole (1%), or a combination of natamycin (3.33%) and miconazole (1%)	q. 4–6 h
Topical antibiotic: Neomycin, polymyxin B, bacitracin, or a combination of tobramycin (0.3%) and cefazolin (55 mg/ml) ophthalmic solution	q. 4–6 h
Topical atropine (1%)	q. 6 h (until pupil is dilated/inflammation controlled and then decrease to q. 8–12 h)
Systemic flunixin meglumine	1.1 mg/kg bwt i.v. *per os* b.i.d.
Systemic antibiotics: Doxycycline; trimethoprim sulphur	Doxy: 10 mg/kg bwt *per os* b.i.d. TMS: 25 mg/kg bwt *per os* b.i.d.
Systemic antifungals: Itraconazole or fluconazole	Itra: 3 mg/kg bwt *per os* b.i.d. Fluc: Loading dose: 14 mg/kg bwt *per os* once, then 5 mg/kg bwt *per os* s.i.d.
Surgical PK, PLK, DLEK	Healing time post surgery: PK: 46.7 ± 23.1 days PLK: 30.8 ± 9.5 days DLEK: 35.8 ± 14.7 days

A mydriatic/cycloplegic drug such as atropine 1% ophthalmic solution will need to be administered topically 1–4 times daily to achieve pupil dilation and cycloplegia. Atropine should be used with caution since horses treated with atropine have decreased motility of the intestine (Williams *et al*. 2000; Brooks and Matthews 2007). This risk should, however, not prohibit the use of atropine for horses since it is essential to treat the often severe secondary inflammation in the anterior segment (Brooks and Matthews 2007; Herring 2007).

Systemically administered NSAIDs are also critical in the medical treatment of SA. Flunixin meglumine is presently the systemically administered NSAID of choice for inflammatory eye diseases in horses but phenylbutazone may also be used. The specific mechanism of the inflammatory response in the anterior segment of the horse is not well described, and to date it is not known whether uveitis in the horse is either initiated by a Cox-1 or Cox-2 pathway. A study in dogs indicated that uveitis in this species could be caused by a Cox-1 induced inflammatory reaction. If that is also the case in horses, this could explain why NSAIDs with a primary Cox-1 inhibitor pathway such as flunixin meglumine seem to be most effective against controlling uveitis in horses (Gilmour and Lehenbauer 2009). A recent study has shown that systemically administered nonsteroidal Cox-2 inhibitor firocoxib reaches a higher concentration in the aqueous humour of the horse than systemically administered flunixin meglumine and might be a useful treatment of uveitis in horses (Hilton *et al*. 2011). More research is required before recommending firocoxib over flunixin as the 'drug of choice' for inflammatory equine eye diseases. It is therefore recommended to treat SA horses with an initial dose of 1.1 mg/kg bwt flunixin meglumine every 12 h i.v. or *per os* until the inflammation in the anterior segment decreases. When the horse is comfortable and signs of inflammation are decreased in the anterior segment, the NSAID dose may be decreased. It is not recommended to continue high dose anti-inflammatory medication for extended periods of time because the anti-inflammatory effects of flunixin meglumine also reduce corneal vascularisation due to an anti-angiogenic effect on the cornea. Also, the well known side effects of flunixin to the horse kidney, liver and alimentary systems should be considered (MacAllister *et al*. 1993). It is usually necessary to continue NSAID therapy through the length of the treatment period for the SA. In many cases, this drug will be the last medication to be discontinued (Giuliano 2004; Brooks and Matthews 2007). Omeprazole may be administrated to decrease the possibility of gastric ulceration caused by the long time use of a systemic NSAID medication (MacAllister *et al*. 1993; Plummer *et al*. 2008).

Other drugs, which may be utilised for SA cases include topical antiproteinases and hypertonic saline. Antiproteases such as serum are only recommended if there is an epithelial or stromal defect with positive fluorescein retention (Ollivier *et al*. 2007). Corneal oedema may interfere with healing of the SA by causing corneal bullae that will increase the possibility for complications as secondary corneal ulcerations if the bullae rupture (Plummer *et al*. 2008). Hypertonic saline (5% NaCl, ointment or solution) is recommended if severe corneal oedema is present in a SA case.

Surgical treatment for stromal abscesses

Medical treatment may need to be continued for months in eyes with SAs and DSAs. If there is not a dramatic resolution to the size and colour of the SA or DSA, and a reduction in the uveitis after a week of medical therapy we strongly recommend that surgical alternatives be considered. Various surgical options for surgical removal of SAs and DSAs depend on the depth and location of the abscess in the stroma and cornea (Andrew *et al*. 2000; Brooks and Matthews 2007; Brooks *et al*. 2008; Plummer *et al*. 2008; Clode 2011).

Superficial keratectomy may aid penetration of drugs to a superficial stromal abscess (Rebhun 1982). Superficial keratectomy with conjunctival graft (Hendrix *et al*. 1995), penetrating keratoplasty (PK) (Denis 2004; Brooks *et al*. 2008), posterior lamellar keratoplasty (PLK; Andrew *et al*. 2000), deep lamellar endothelial keratoplasty (DLEK; Plummer *et al*. 2008), carbon dioxide laser keratectomy (CDLK) with conjunctival graft (van Zyl and Rayner 2010), and enucleation have been utilised for eyes with SAs and DSAs. Surgical drainage of the SA has been successful in few cases but most often the SA is not sufficiently liquefied for drainage (Brooks and Matthews 2007).

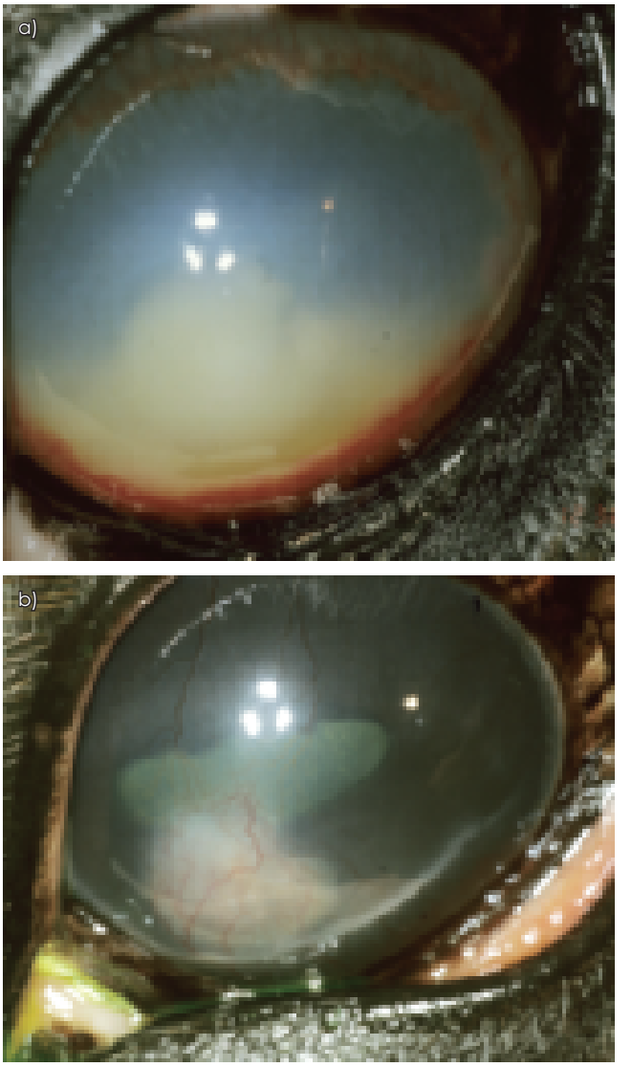


Fig 5: a) In this image a stromal abscess (SA) with a diffuse cellular infiltrated area in the cornea near 6 o'clock has neovascularisation and corneal oedema surrounding the SA. The pupil can barely be appreciated due to corneal oedema but it seems that the pupil is miotic, indicating secondary uveitis. b) The same horse as in Figure 5a after medical treatment for 2 months. The SA has become fibrotic and only mild vascularisation can still be appreciated. The secondary uveitis is no longer present, although the pupil is dyscoric and slightly miotic due to posterior synechia.

Penetrating keratoplasty is full thickness microsurgical transplantation of the corneal epithelium, stroma, and Descemet's membrane/endothelium. Full thickness penetrating keratoplasty may be performed in horses for therapeutic and tectonic reasons for melting ulcers with extensive stromal loss, iris prolapse/descemetoceles, and full thickness stromal abscesses. Penetrating keratoplasty has become a viable, routine and successful surgical technique in horses with severe keratitis, and is associated with a very good visual outcome in most cases (approximately 80%). This is despite the fact that nearly all the corneal transplant donor allografts in horses vascularised post operatively and exhibited troubling degrees of full thickness corneal opacification at the surgical site (Brooks 2005, 2010; Brooks *et al*. 2008).

The concept of lamellar keratoplasty (LK) is to target and replace only diseased corneal tissue while retaining the normal healthy corneal tissue (Kawakita *et al*. 2007; Brooks 2010). Lamellar keratoplasty is utilised for tectonic reasons to replace damaged stroma in melting corneal ulcers of human patients as it provides enhanced donor graft survival and improved visual outcomes compared to PK (Tan and Mehta 2007). Deep lamellar endothelial keratoplasty and PLK are split thickness LKs utilised to replace diseased endothelium from endothelial dystrophy and bullous keratopathy in man. The remaining healthy corneal layers are preserved in DLEK and PLK (Tan and Mehta 2007). This targeted replacement of individual diseased components of the cornea is also suitable for treatment of equine keratopathies (Brooks *et al*. 2008).

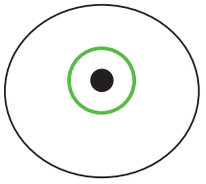
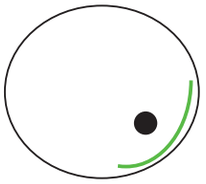
Posterior lamellar keratoplasty in horses is recommended for SAs and DSAs in the axial cornea that are 12 mm or less in diameter. The overlying epithelium may be oedematous but is intact, and the anterior stroma may be vascularised, but should not have a cellular infiltrate. This procedure replaces the diseased posterior stroma, Descemet's membrane and endothelium, and has proven successful for surgical therapy of DSA in the horse (Brooks 2005; Brooks *et al*. 2008).

Deep lamellar endothelial keratoplasty is a similar technique that is recommended for medically nonresponsive SAs and DSAs in the peripheral cornea, DSAs that are 12 mm or less in diameter, and have moderate vascularisation and oedema of the overlying epithelium and anterior stroma with no anterior stromal cellular infiltrate are ideal candidates for DLEK. The DLEK transfers healthy Descemet's membrane and endothelium while preserving the horse's corneal surface and topography. The difference between PLK and DLEK is the placement of sutures in the cornea in PLK surgery compared with only sutures in the limbus when DLEK surgery is performed (Brooks 2005). The overall success rate for rapid return to visual function for surgical therapy of DSA by DLEK and PLK approaches 90% in horses, and is higher than for PK (Brooks 2005; Brooks *et al*. 2008) (**Table 3**).

Visual outcome for both medical and surgical treatment of stromal abscesses

The visual outcome for SA depends on whether the healing process has been completed with medical treatment or with one of the surgical approaches. Less scarring of the cornea can be seen with small SA or DSA treated medically if they respond to medical treatment alone (**Fig 6**). If this is not possible PK, PLK or DLEK is recommended depending on the localisation and depth of the SA or DSA (Brooks and Matthews 2007; Brooks *et al*. 2008). These surgical techniques will all leave some type of corneal scar, since a full or partial thickness corneal allograft is respectively used to close the corneal defect. It has not been possible to date to inhibit the rejection of the corneal transplant and thus all grafts eventually become opaque as part of the rejection process. The rejection to the equine corneal graft will be seen as a fibrotic grey area with some degree of vascularisation (**Fig 7**), and thus has a tectonic rather than optical function. The horse will retain vision in the areas outside the graft opacity as long as there has not been extensive damage to the interior of the eye from the uveitis. It is not generally recommended to perform a corneal graft surgery larger than 15 mm due to graft scarring if good

TABLE 3: Three different corneal graft surgeries have been described as the surgical treatment for stromal abscess (SA) and deep stromal abscess (DSA). The penetrating keratoplasty (PK) will be used for a full thickness stromal abscess. The 2 split thickness lamellar keratoplasty surgeries are being used for the DSA depending of the location of the abscess. The DSA located in the central aspect of the cornea will be treated with the posterior lamellar keratoplasty (PLK) and the DSA located by the limbus will be treated with the deep lamellar endothelial keratoplasty (DLEK). The success rate for positive visual outcome for the 3 different surgeries is for PK: 77.9%, PLK: 98.1%, DLEK: 89.4% (Brooks *et al*. 2008)

Surgical procedure	Location of the stromal abscess in the cornea	Location of the stromal abscess (black) and surgical incision (green) on the cornea surface	Description of the surgical procedure	Success rate by Brooks *et al*. 2008
PK Used for full thickness stromal abscesses			With a full thickness SA, the SA will be removed full thickness and replaced by a corneal graft	77.9% (86 horses)
PLK Used for a deep stromal abscesses located in the central cornea			In the PLK type of lamellar keratoplasty the diseased deep corneal tissue including the DSA is removed and the anterior healthy tissue preserved. The incision in the cornea will be made around the stromal abscess	98.1% (54 horses)
DLEK Used for a deep stromal abscess located by the limbus			In the DLEK type of lamellar keratoplasty the DSA is located in the periphery of the cornea and is removed by an incision at the limbus.	89.4% (66 horses)

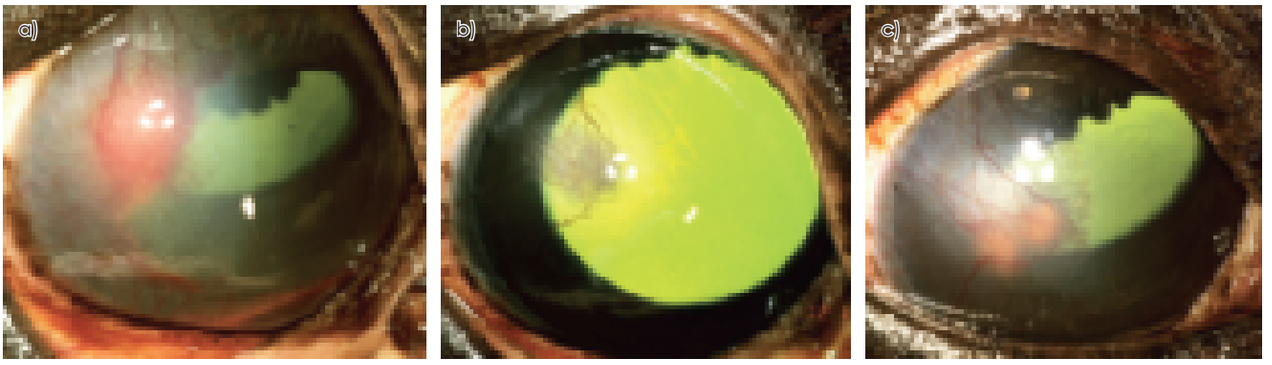


Fig 6: a) Aggressive medical treatment for a deep stromal abscess (DSA) should be tried for 1–2 weeks before surgical intervention is performed to see if the DSA is responsive to the medical therapy and to calm the uveitis. This horse was presented with a deep corneal cellular infiltrate which had vascularised completely in the anterior portion of the cornea. The horse had uveitis indicated by aqueous flare and a miotic pupil, and the horse was started on medical treatment. b) This is a picture of the same horse as in Fig 6a after a month of aggressive medical treatment. The deep stromal abscess had healed with fibrosis of the cornea (scar) which can be seen at 9 to 10 o'clock. The vascularisation had decreased in intensity and there were no signs of inflammation in the anterior chamber. The medical treatment of the horse was then discontinued. c) Two weeks later after the medical treatment had been discontinued for the horse in Fig 6a and 6b, 2 new DSAs could be appreciated in the cornea at 6 to 7 o'clock, just ventral to the area with the 'healed' DSA. This horse had deep lamellar endothelial keratoplasty surgery and healed completely post surgery.

vision is necessary and expected (Denis 2004; Brooks and Matthews 2007; Brooks *et al*. 2008). A study by Brooks *et al*. (2008) indicated that a positive visual outcome from PK surgeries from 86 horses was achieved in 77.9% of the cases, from PLK surgeries of 54 horses was 98.1%, and from DLEK surgeries of 66 horses was 89.4% (Brooks *et al*. 2008). A series of case reports describing laser treatment for SA via CDLK surgery that compared DLEK/PLK and PK surgeries with the CDLK

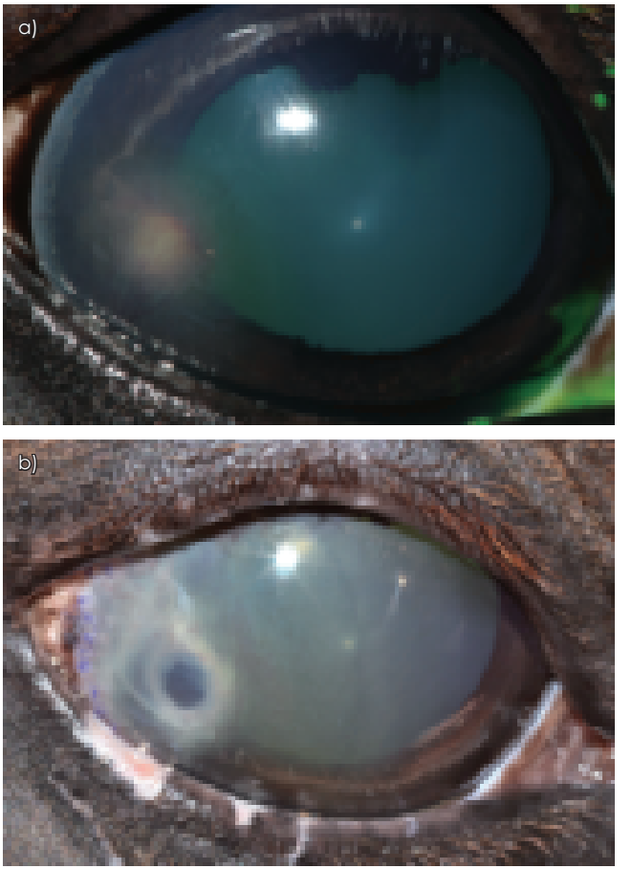


Fig 7: a) We generally recommend surgical therapy for most deep stromal abscesses (DSA). In this eye, the DSA can be appreciated at 7 o'clock in the cornea as a focal circular cellular infiltrated area with surrounding vascularisation. No signs of uveitis can be appreciated due to topical therapy and systemic NSAID therapy. b) Three weeks post deep lamellar endothelial keratoplasty surgery of the eye in Figure 7a, the sutures in the limbus can be appreciated together with corneal fibrosis and corneal oedema in the area of the surgery site. The horse has a completely dilated pupil due to topical atropine treatment.

method found few complications but did not report the visual outcome (van Zyl and Rayner 2010).

Future perspectives

There have been many advances in the diagnosis and treatment of SAs and DSAs in the last 30 years, but a lot of questions regarding SAs and DSAs in horses remain unanswered. Why are SAs and DSAs so common in the horse and not other species? Does the relatively low temperature of the horse cornea act as a possible predisposing factor for fungal infection since fungal growth is inhibited at high temperatures (Galle and Moore 2007)? Why is the purulent material in an equine SA firm? The answers to these questions are not yet known but it has been speculated that fungi alter the corneal immune response and that the inflammatory response that occurs in the cornea is blunted compared to other equine tissues (Brooks *et al*. 2008).

Another question regarding equine SAs is why the vascularisation does not infiltrate the deeper layers of the cornea where the DSA is located. Perhaps therapeutic approaches to stimulate vascularisation and vascular infiltration of the SA will be important in improving clinical healing and outcomes. Vascularisation is necessary to heal many DSAs but this vascularisation is often slow, aberrant or is inhibited for unknown reasons. Studies to investigate this phenomenon with the goal of creating drugs or biologically active substances that support vascularisation and healing, without disturbing the immune privilege of the cornea, will be important for SA and DSA therapy.

Many equine SA that have a large diameter will heal with profound corneal fibrosis. The challenge remains for the cornea to heal without a subsequent blinding scar. Further research in this area may also lead to better therapeutic results in affected horses. Varied surgical approaches are being investigated in hopes of decreasing the fibrosis of the healing cornea. The CDLK techniques are examples of these approaches.

Stromal abscesses and DSAs, which until now have been quite a geographically localised equine eye disease, are now being diagnosed in more temperate climates where they were once considered sporadic or rare. More basic and clinical research is therefore needed in order to elucidate the pathogenesis of SA in horses in order to develop a better treatment regimen for this painful and blinding disease in horses.

Authors' declaration of interests

No conflicts of interest have been declared.

Manufacturers' addresses

[1]Bausch and Lomb, Rochester, New York, USA.
[2]Alcon Laboratories Inc., Fort Worth, Texas, USA.

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