Corneal colors in cats and dogs: what do they mean?

Kleuren van het hoornvlies bij kat en hond: wat betekenen ze?

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ABSTRACT

The cornea forms the anterior portion of the outer tunic of the eye and its transparency plays a vital role in the eye's refractive system. This transparency is achieved by a combination of physiological and anatomical adaptations, including a non-keratinized surface epithelium, its relative acellularity, lack of pigment, lymphatic vessels and blood vessels and the presence of non-myelinated corneal nerves. Any process that alters the cornea's epithelial or stromal architecture, increases corneal pigmentation, contributes to blood vessel migration, or predisposes to corneal edema, impairs transparency and is indicative of corneal disease. Infection and inflammation as well as traumatic or surgery-induced lesions of the cornea are common causes of such a loss of transparency. There are numerous ways to classify corneal diseases, and the color of their presenting lesions may be helpful for the clinician in determining the underlying cause and therefore give direction regarding the appropriate treatment selection.

SAMENVATTING

Het hoornvlies vormt het voorste gedeelte van de buitenste laag van het oog en de doorzichtigheid ervan speelt een vitale rol in het oculaire refractieve systeem. Deze transparantie wordt bereikt door een combinatie van fysiologische en anatomische aanpassingen, waaronder een niet-verhoornd oppervlakte-epitheel, de relatieve acellulariteit, een gebrek aan pigment, lymfevaten en bloedvaten en niet-gemyeliniseerde corneazenuwen. Elk proces dat de epitheliale of stromale architectuur van het hoornvlies wijzigt, leidt tot meer corneapigment en bijdraagt tot de migratie van bloedvaten of predisponeert voor cornea-oedeem, tast deze doorzichtigheid aan en duidt op ziekten van het hoornvlies. Infecties en ontstekingen, evenals traumatische of operatie-geïnduceerde letsels van het hoornvlies zijn veelvoorkomende oorzaken van een dergelijk verlies van transparantie. Er zijn meerdere manieren om hoornvliesaandoeningen te classificeren, en de kleur van de aanwezige letsels zou de dierenarts kunnen helpen bij het bepalen van de onderliggende oorzaak en als leidraad kunnen dienen bij de keuze van de juiste therapie.

INTRODUCTION

The cornea is the clear portion of the outer, fibrous tunic of the eye. Transmitting incident light, refracting it, and protecting intraocular structures from trauma and pathogens constitute its primary physiological functions (Meekins et al., 2021). In cats and dogs, the cornea provides two-thirds of the eye's refractive power, and each of its characteristics is critical to maintaining the tissue's transparency and viability (Maggs, 2016). A non-keratinized surface epithelium, the size and organization of the stromal collagen fibrils, non-myelinated corneal nerves, its relative acellularity, the lack of blood vessels, lymphatic vessels and melanin and the state of dehydration achieved by the endothelium and to a lesser degree by the epithe-

lium, are all factors that preserve this unique anatomic property of corneal transparency (Qazi et al., 2010). Limbal stem cells also appear to play an important role in the maintenance of corneal epithelial health and corneal clarity (Sanchez and Daniels., 2016). Changes in these anatomic and physiologic states are evident to the clinician as decreased corneal clarity, corneal opacification, corneal neovascularization, corneal pigmentation, or corneal edema (Maggs, 2016). Any of these corneal changes may act as a presenting sign but they are not, in themselves, specific diseases (Qazi et al., 2010).

The intact and healthy canine cornea is highly resistant to bacterial infection (Whitley and Hamor, 2021). Using its non-keratinized stratified epithelial cells, the ocular surface acts as a barrier against microorganisms. Due to its tight junctions between the epithelial cells and its rapid cell turnover, the cornea's deeper layers are protected from potentially infected epithelium (Hodges and Dartt, 2013). As a result of external injury or diseases like keratoconjunctivitis sicca (KCS), the corneal anatomical and physiological defences may be compromised and in turn may predispose to bacterial keratitis. Normal healthy corneal stroma consists primarily of collagen fibrils, keratocytes, nerves, and glycosaminoglycans and is free of infectious agents and inflammatory cells (Whitley and Hamor, 2021). As a result of a breach in the corneal epithelium's barrier functions, stromal leukocyte infiltrates with concurrent anterior uveitis are common clinical findings (Maggs, 2016).

There are very few objective corneal clarity grading scales in human and veterinary medicine (Whitley and Hamor, 2021), but in 2015, Sanchez et al. introduced a novel corneal clarity score in dogs. Together with photography, these clarity scores can help clinicians describe the transparency of corneal lesions and their progression over time (Sanchez et al., 2016).

DIFFERENTIALS AND KEY POINTS

- **SCAR TISSUE/FIBROSIS** (Figure 2)
- **LIPID**
  - Often shiny white and well demarcated lesion
    - **Corneal dystrophy** (Figure 5)
      - Hereditary in many breeds
      - Bilateral but not always symmetrical, usually central or paracentral
      - Often circular or oval shape
      - No signs of inflammation present
    - **Lipid keratopathy** (Figure 6)
      - Secondary to other diseases (e.g. diabetes mellitus or pancreatitis)
      - Unilateral or bilateral with or without blood vessels
    - **Arcus lipoides** (Figure 4)
      - Very rare
    - **Secondary to long-term topical steroids** (Maggs, 2016)
- **CALCIUM**
  - Often gritty white and less demarcated lesion
    - **Calcareous corneal degeneration**
      - Associated with blood vessels in chronic fase and usually whiter than lipid (Figure 8)
      - Often in very old dogs of small breeds (e.g. West Highland White Terrier)
      - Often associated with deep ulcers (Figure 9)
    - **Abnormal calcium metabolism**
    - **Sequel to parotid duct transposition** (Figure 7)
- **KERATIC PRECIPITATES** (Figures 10, 11)
  - Always situated on the corneal endothelium
  - Always in the ventral cornea and represents a specific sign of uveitis
  - Slit-lamp is often paramount for diagnosis
- **EOSINOPHILIC KERATITIS**
  - Usually white elevated plaques (Figure 12)
  - Clinical diagnosis of eosinophilic keratitis in cats

Figure 1. Differential diagnosis and key points of corneal lesions in dogs and cats with a white/grey appearance.

Keratitis and other corneal diseases are among the most common eye diseases in small animals, with a wide range of causes and appearances. Presenting signs vary on a case-to-case basis depending on the etiology, severity and chronicity (Sanchez, 2014; Maggs, 2016; Whitley and Hamor, 2021). The cornea in small animals can suffer from developmental and acquired problems and the latter may include a myriad of different disease processes, which all need to be considered when formulating a differential diagnosis (Whitley and Hamor, 2021). The general practitioner encounters a variety of corneal pathological conditions and some aspects of lesion recognition can be simplified by grouping certain problems according to their color (Sanchez, 2014). In this article, a brief overview of the canine and feline corneal pathologies is provided classified according to their color.

WHITE-GREY

Fibrosis

Etiology

In dogs and cats, corneal fibrosis or corneal scarring is a common sequel to various keratopathies that potentially could impair vision (Hu et al., 2009). Injuries or infections can lead to fibrosis as a result of uncontrolled stromal healing (Tandon et al., 2010). Due to the irregular pattern of the novel collagen fibrils, light transmission may be affected (Maggs, 2016). Injury-induced corneal haze is dynamic and may change over the course of years after the initial event (Qazi et al., 2010).

Diagnosis

Based on color alone, fibrosis could be confused with white blood cell infiltration or edema. By comparison, fibrosis has more distinct margins and is not associated with other inflammatory signs except perhaps some residual corneal blood vessels (Figure 2). Scars may become less visible over time, but rarely disappear completely. The tendency to clear is greater in young animals, especially in cats. In dogs, lipid and melanin deposition may also occur near the scar. The deeper the initial injury, the denser and more permanent the scar (Maggs, 2016).

Treatment

Currently, specific agents against corneal scarring are not routinely used in veterinary ophthalmology but new gene therapies, novel treatments against certain cytokines and antifibrotic agents may have the potential of modulating corneal scarring (Gupta et al., 2011; Bosiack et al., 2012; Gronkiewicz et al., 2016).

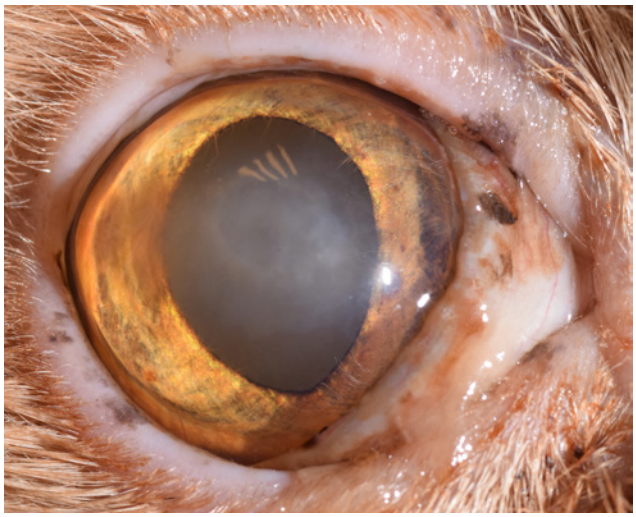

Figure 2. Corneal scarring in a cat after a healed superficial corneal ulcer presumably secondary to a herpes virus infection.

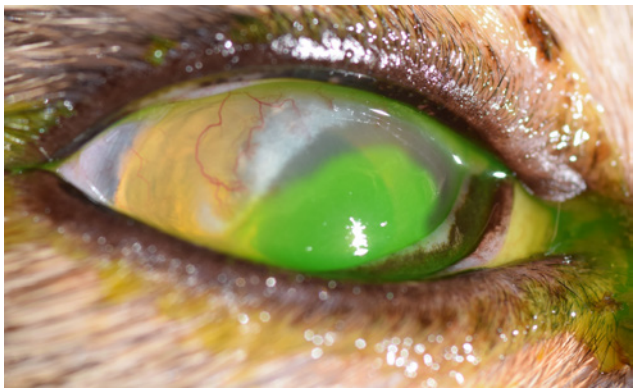

Figure 3. Mineral deposition in the right eye of a cat, presumably lipid deposition secondary to a corneal ulceration.

Lipid

Etiology

Corneal lipidosis refers to any disease in which lipid deposits are found on the cornea, including crystalline stromal dystrophy, lipid keratopathy, and in extremely rare situations corneal arcus (Crispin, 2005; Sanchez, 2014). A variety of dog breeds (including cavalier King Charlies spaniel, beagle, Shetland sheepdog, Siberian husky, rough collie, Airedale terrier) may be affected by familial corneal crystalline dystrophy. In this hereditary condition, lipid is deposited in the central or paracentral corneal stroma of both eyes, without any sign of inflammation (Crispin, 2005; Sanchez, 2014; Whitley and Hamor, 2021).

Lipid keratopathy is defined as a corneal lipid deposition secondary to other disease processes, such as hypothyroidism, pancreatitis or diabetes mellitus (Harrington and Kelly, 1980; Crispin, 2005; Sanchez,

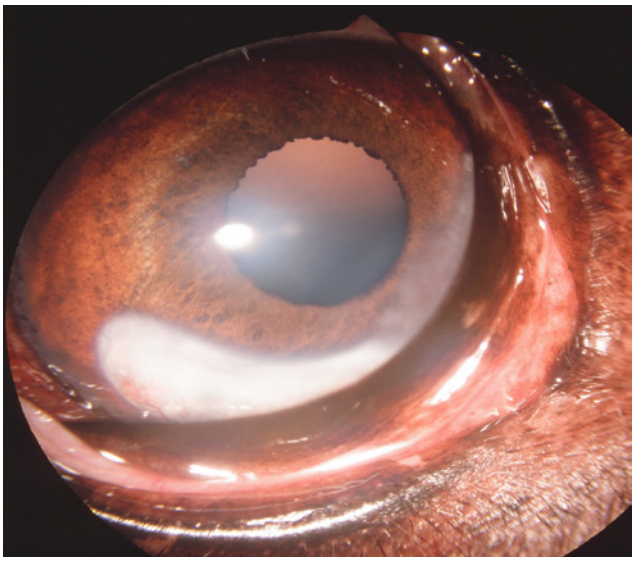

Figure 4. Corneal arcus in a dachshund (Photo courtesy of P. Hansen).

2014; Whitley and Hamor, 2021). Lipid is thought to accumulate in the cornea as a result of perilimbal blood vessels or by in situ lipid deposition (Whitley and Hamor, 2021). Lipid keratopathy is rarely encountered in cats and is almost always associated with prior corneal damage (Crispin, 2002) (Figure 3).

Arcus lipoides corneae or corneal arcus represents a very rare condition in dogs and refers to a bilateral infiltration of lipid into the peripheral cornea, following the curvature of the limbus (Crispin, 2002; Crispin, 2005) (Figure 4). It has been reported in German shepherds affected by hyperlipoproteinemia, most commonly secondary to primary acquired hypothyroidism (Crispin, 2005).

Diagnosis

The diagnosis is usually based on the history, signalment and the clinical appearance of the lesion (Sanchez, 2014; Maggs, 2016; Whitley and Hamor, 2021). Crystalline stromal dystrophy is most commonly seen in young adults of certain breeds and tends to be slowly progressive (Sanchez, 2014). The majority of canine corneal dystrophies appear clinically as gray-white or silver, crystalline or metallic opacities (Figures 5A and 5B). The condition is bilateral and in many cases lesions appear nearly symmetric (Whitley and Hamor, 2021). The opacity is typically oval or circular, with well-defined lesion margins. On slit-lamp biomicroscopy, small, fine shiny particles are usually seen in the anterior stroma with intact epithelium (Sanchez, 2014; Maggs, 2016; Whitley and Hamor, 2021). Typically, corneal dystrophy is not associated with corneal vascularization. However, chronic lipid accumulation causes subsequent inflammation and may trigger corneal vascularization in a process called corneal degeneration (Crispin, 2005; Whitley and Hamor, 2021).

Lipid keratopathy can present uni- or bilaterally, and the corneas may be vascularized or non-vascularized (Crispin, 2005; Sanchez, 2014; Whitley and Hamor, 2021) (Figure 6).

All dogs with presumed lipid keratopathy, as well as all cases that do not fit the criteria of typical hereditary dystrophy should undergo ancillary blood tests. These patients should be screened for thyroid function, pancreatitis and diabetes mellitus. Additionally, their total serum and plasma cholesterol, triglyceride levels, and lipoprotein profile should be analyzed (Crispin, 2005; Whitley and Hamor, 2021).

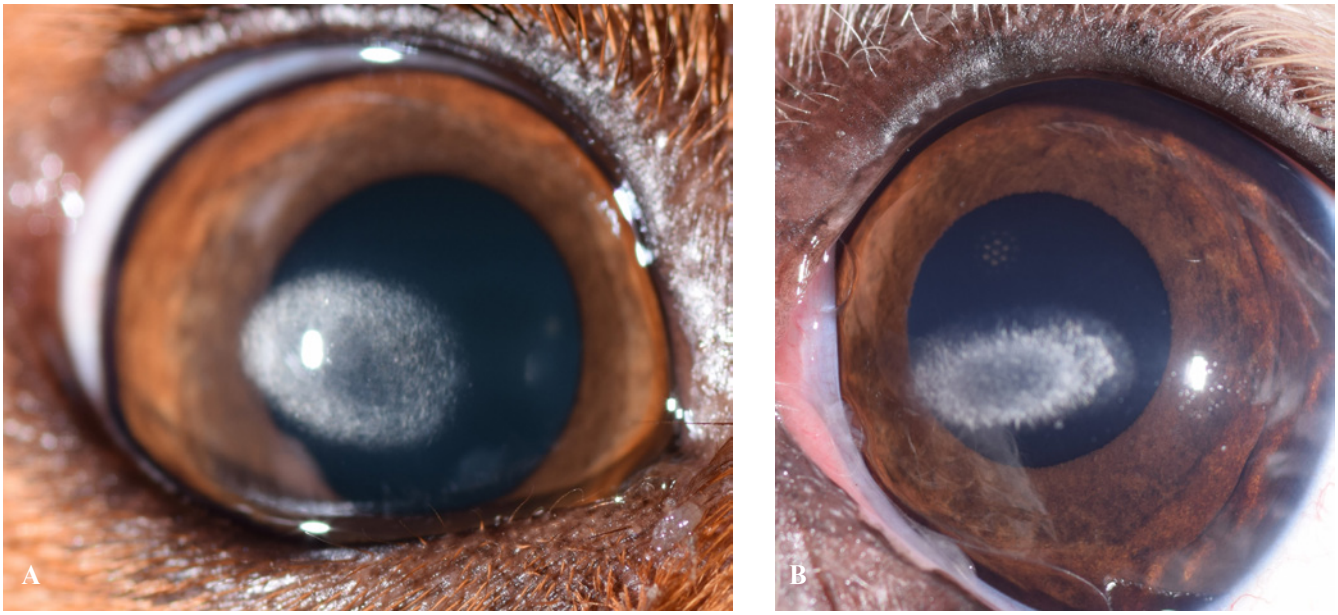

Figure 5. Corneal dystrophy in A. a Basenji and B. a Shih-tzu. The other eye was equally affected.

Treatment

In general, corneal dystrophies are not responsive to medical treatment and topical anti-inflammatory agents may exacerbate the lesion (Whitley and Hamor, 2021). As this condition is usually not associated with serum lipid elevations, the instigation of low-fat diets is unlikely to have an effect (Barsotti et al., 2008; Sanchez, 2014; Whitley and Hamor, 2021). Regardless of its cause, lipid infiltrates rarely interfere with vision, so their surgical removal is seldom indicated. In cases where surgical removal is required, recurrence is likely (Sanchez, 2014; Maggs, 2016). Most of the lipid lowering drugs currently used in human medicine are not applicable to the management of dyslipoproteinemia in small animals (Crispin, 2005).

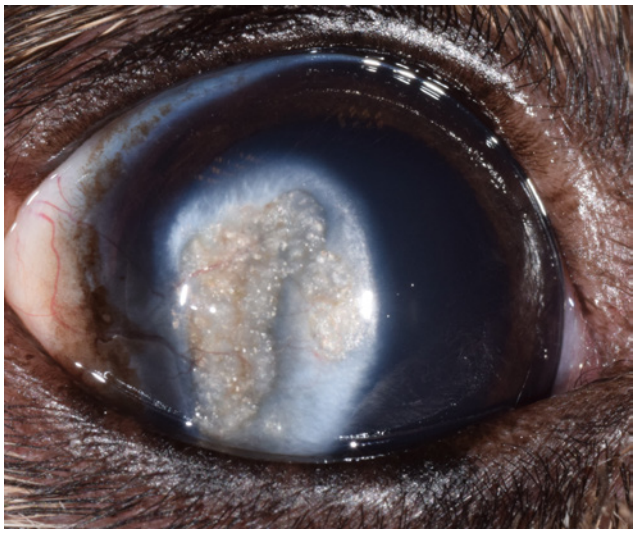

Figure 6. Lipid deposition in the right eye of a five-year-old Shetland sheepdog. No abnormalities were found on hematology. A superficial keratectomy was subsequently performed.

Calcium

Etiology

Corneal calcium deposits may occur with corneal ageing, termed calcareous corneal degeneration (Crispin and Barnett, 1983) or may be a consequence of an ocular or systemic disease (Whitley and Hamor, 2021). Many dogs with calcareous corneal degeneration have no history of underlying ocular or systemic disease, and therefore it is often considered a spontaneous corneal condition (Bellhorn et al., 1988; Nevile et al., 2016).

Secondary corneal calcification may be associated with any disease affecting calcium metabolism, such as hypercalcemia, hyperphosphatemia, hyperadrenocorticism, uremia and hypervitaminosis D (Whitley and Hamor, 2021).

Compared with tears, saliva contains a higher mineral concentration. Superficial calcium deposits on the cornea and eyelids are a normal sequelae to parotid duct transposition (PDT) surgery for the management of severe and intractable KCS (Rhodes et al., 2012) (Figure 7).

Figure 7. Left eye of an eight-year-old dachshund with corneal calcium deposition secondary to a parotid duct transposition.

Diagnosis

Generally, calcareous corneal degeneration is diagnosed in old animals. In the initial stages, calcium is scattered within the cornea without clear vascularization. As the lesion becomes more chronic and more calcium is deposited, vascularization is often present (direct communication with P. Hansen) (Figure 8). Any part of the cornea can be affected, but degenerations generally appear axial, paraxial or in the inferior cornea. The corneal surface becomes rough and signs of corneal irritation such as lacrimation and blepharospasm are often noticed (Whitley and Hamor, 2021). The presence of calcium may cause deep ulcers or delay corneal healing (Sanchez, 2014) (Figure 9). Corneal scraping for cytology or manipulation of the cornea during surgery may reveal a gritty or sandpa-

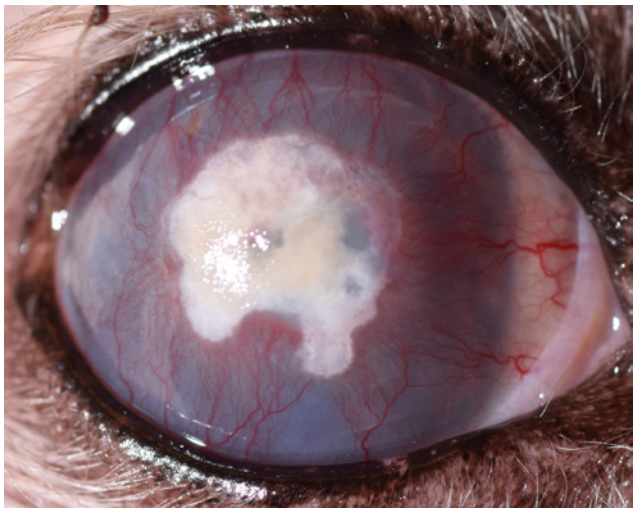

Figure 8. Calcareous corneal degeneration in a dog.

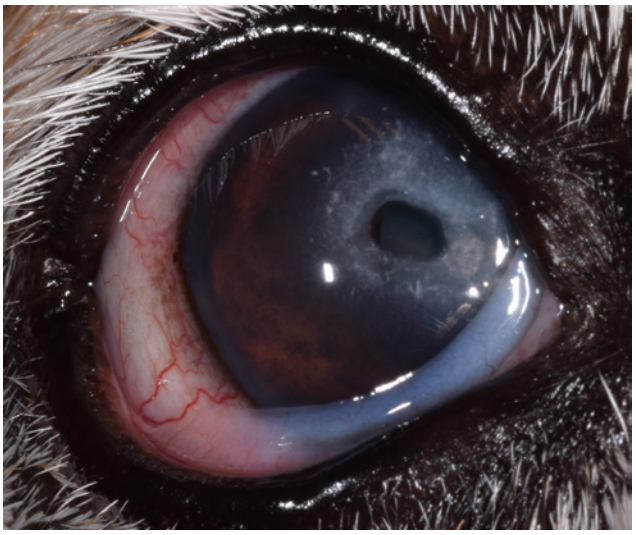

Figure 9. Descemetocele in the right eye of a twelve-year-old crossbreed secondary to corneal degeneration.

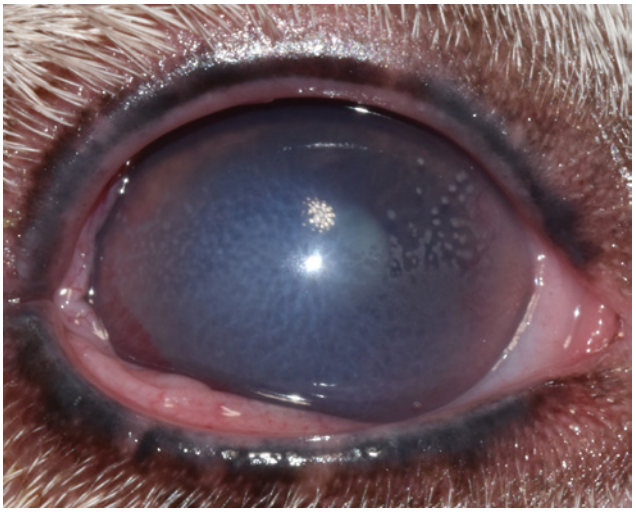

Figure 10. Keratic precipitates in a Staffordshire terrier with anterior exsudative uveitis.

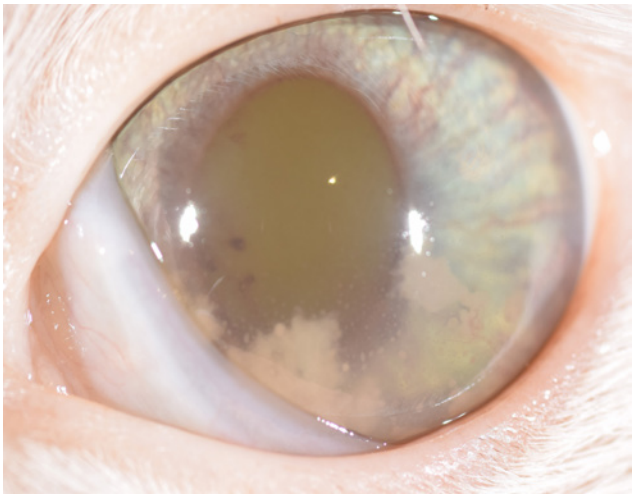

Figure 11. Mutton fat keratic precipitates in the left eye of a one-year-old cat with a presumed FIP virus infection. The right eye had a chorioretinitis. The cat was lethargic and had a distended, fluid-filled abdomen.

per-like feel (Whitley and Hamor, 2021). A thorough history can reveal a previous parotid duct transposition surgery (Leiva and Giménez, 2016). It may be difficult to distinguish calcium deposition from lipid on ophthalmic examination, and to make a definitive diagnosis, histopathology is required (Laus et al., 2002).

Treatment

Patients with corneal degeneration should be treated when they experience discomfort, refractory corneal ulcers, or have decreased functional vision (Whitley and Hamor, 2021). Most animals with calcareous corneal degeneration will develop a deep ulcer at some point and will require a surgical grafting procedure (Sansom and Blunden, 2010). In addition to superficial keratectomy with or without additional grafting procedures, chelating agents such as topical EDTA are sometimes used to treat corneal calcium deposits (Sanchez, 2014). Diamond burr debridement with or without topical EDTA has also been shown to be effective in resolving superficial corneal ulcerations and ocular pain caused by presumed calcareous degeneration in dogs (Nevile et al., 2016; Anastassiadis et al., 2022). Corticosteroid therapy should be avoided as this will decrease vascularization and macrophage function and therefore healing. Furthermore, the use of steroids will promote the attraction and binding of additional calcium by inducing rearrangement of the corneal molecular structure (Laus et al., 2002; Whitley and Hamor, 2021).

Keratic precipitates

Etiology

Keratic precipitates (KPs) are accumulations of inflammatory cells, fibrin, and iris pigment that settle on the corneal endothelium (Hendrix, 2021). KPs are usually located ventromedially on the cornea in a triangular shape, with the apex located dorsally. It is thought that the thermal currents within the anterior chamber that influence aqueous humor circulation, are responsible for this characteristic formation (Crispin, 2005). KPs consist most frequently of neutrophils, lymphocytes or macrophages and are a specific sign of anterior uveitis (Miller, 2016).

Diagnosis

KPs appear as fine, white to yellow spots on the corneal endothelium (Figure 10) and on retro-illumination, they can take on a darker, grey to brown color (Watté and pot, 2014). KPs can form large, white to yellow, waxy deposits on the ventral cornea in some granulomatous conditions, like FIP in cats. These deposits are then referred to as ‘mutton fat’ precipitates (Crispin, 2005; Hendrix, 2021) (Figure 11). Varying amounts of pigment can be present in KPs, with more

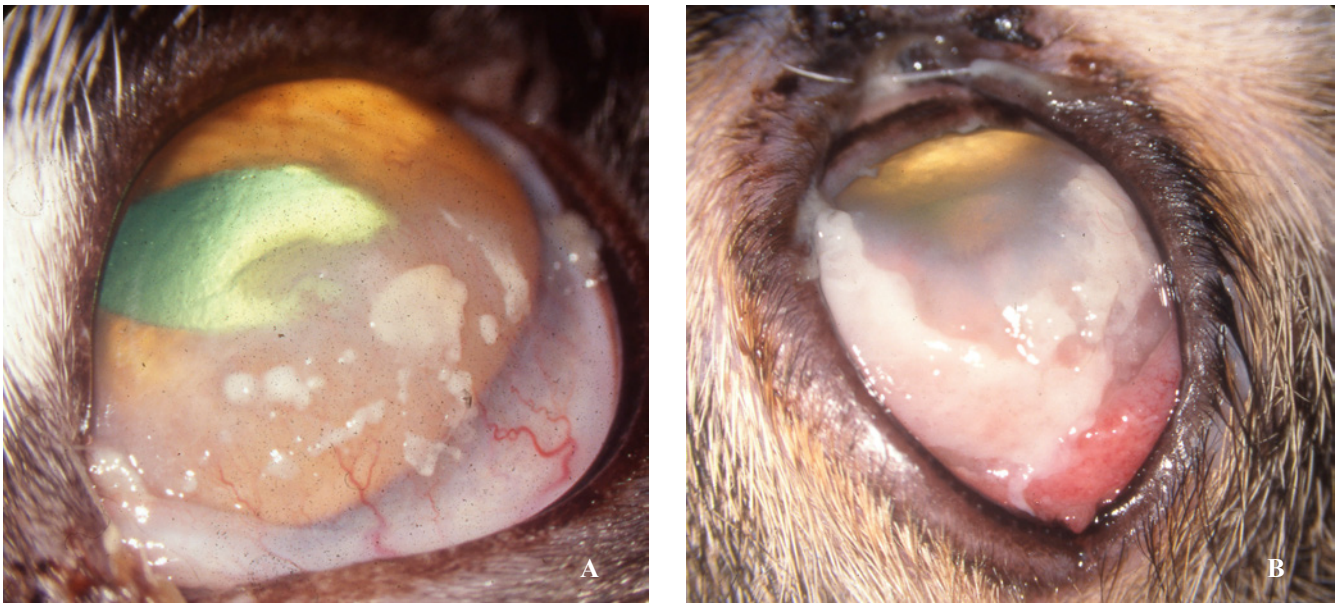

Figure 12. A. Eosinophilic keratitis in a cat. Note the white-yellow spots at the limbus and within the cornea. B. More extensive eosinophilic keratoconjunctivitis in a cat with plaque formation and infiltration of the lateral conjunctiva. (Photo courtesy of P. Hansen)

pigment appearing with chronicity (Hendrix, 2021).

KPs can easily be overlooked, especially if the examiner is not specifically searching for them. Slit-lamp examination is paramount to confirm their endothelial localization and gently tilting the animal's head downward can facilitate visualization of the ventral corneal (Watté and Pot, 2014; Hendrix, 2021). KPs are especially difficult to see in painful eyes where the nictitating membrane is covering the eye (Hendrix, 2021). Once anterior uveitis is diagnosed, all efforts should be made to determine its exact etiology in order to start the most effective treatment (Miller, 2016; Hendrix, 2021). A long list of differential diagnoses can be narrowed down by obtaining a detailed history, performing a thorough ophthalmic and physical examination, and often carry out additional diagnostic tests (e.g. blood tests, urinalysis and imaging) (Watté and Pot, 2014; Miller, 2016).

Treatment

Inflammation suppression, analgesia and preventing adverse sequelae, such as posterior synechiae or secondary glaucoma, are the mainstays of uveitis therapy (Miller, 2016; Hendrix, 2021). Treatment should be tapered slowly once begun and systemic corticosteroids should only be instituted once the inciting cause of the uveitis has been ruled out (Hendrix, 2021). Should immediate systemic treatment deemed necessary for the preservation or return of vision, blood and serum should be collected for later testing, and careful monitoring for disease progression is warranted (Watté and Pot, 2014). Mydriatics or cycloplegics can be added to the treatment regimen to reduce the risk of posterior synechiae, relieve ciliary body spasm and stabilize the blood–aqueous barrier (Watté and Pot, 2014; Miller, 2016). Institution of appropriate glaucoma therapy is indicated if a normal or increased intraocular pressure (IOP) is observed on initial presentation (Watté and Pot, 2014).

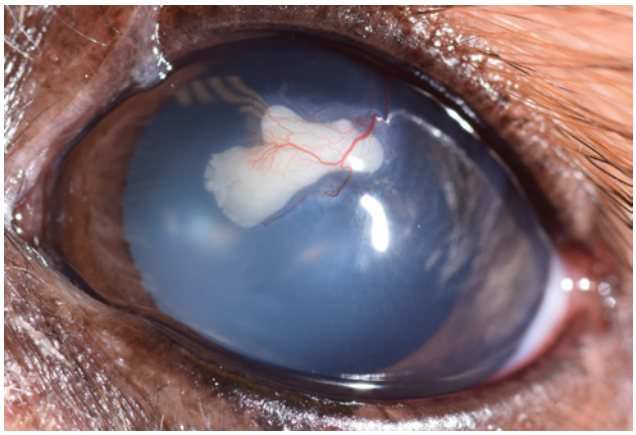

Figure 13. Typical appearance of an epithelial inclusion cyst in a dog.

Eosinophilic keratitis

Etiology

Eosinophilic keratitis is a slowly progressing, infiltrative condition whose name is derived from eosinophils found in samples of affected corneas (Glaze et al., 2021). Despite its unknown etiology, this disease may be related to FHV-1 infection (Morgan et al., 1996; Nasisse et al., 1998; Déan and Meunier, 2013). An aberrant immune response involving type

I or type IV hypersensitivity has also been proposed (Prasse and Winston, 1996).

Diagnosis

It is generally possible to make a presumptive diagnosis based on the clinical appearance alone, however, corneal scrapings should ideally be cytologically evaluated to confirm this (Whitley and Hamor, 2021). This condition often manifests clinically as white or yellow, slightly elevated spots (Figure 12A) or plaques (Figure 12B). The lesions may appear pink due to corneal vascularization (Sanchez, 2014).

Samples for cytology often contain a mixed cell population including epithelial cells, eosinophils, mast cells, neutrophils and lymphocytes, along with nuclear debris and eosinophilic granules from disrupted cells (Prasse and Winston, 1996). Eosinophils may not be the predominant cell type, but finding a single eosinophil on cytology is considered diagnostic (Spiess et al., 2009). A recent study reported on a large variability in the cytological characteristics and clinical features of affected cats, and was the first in which the globule leukocyte was identified (Lucyshyn et al., 2021).

Differential diagnoses for eosinophilic keratoconjunctivitis include fungal keratitis, neoplasia, foreign body granuloma, corneal trauma with second intention healing (Paulsen et al., 1987; O'Connell et al., 2017), or a lepromatous granuloma. Feline leprosy refers to a *Mycobacterium sp.* infection in which single or multiple granulomas form in the skin or subcutis with acid-fast bacilli that can be difficult to culture using routine bacteriologic methods. A conjunctivo-corneal leproma (mass) can occur as an unusual symptom of leprosy (Lamagna et al., 2009).

Treatment

Eosinophilic keratitis is more likely to be controlled than cured. The mainstay of treatment remains local immunosuppression with topical corticosteroids (Glaze et al., 2021). However, it is important to note that the use of immunomodulatory drugs in association with FHV-1 can reactivate the virus from latency and exacerbate clinical disease (Maggs, 2016).

After initial disease control has been achieved with steroids, cyclosporine may be more suitable for long-term maintenance (Sanchez, 2014). In a minority of cases, antivirals alone are enough to control the disease but more commonly, a form of immunomodulatory therapy must be added (Maggs, 2016; Whitley and Hamor, 2021).

In more recent publications, a topical regimen has been described of megestrol acetate and feline stem cell therapy to treat eosinophilic keratitis in cats (Carrade and Borjesson, 2013; Stiles and Coster, 2016; Villatoro et al., 2018).

Epithelial inclusion cyst

Etiology

Corneal epithelial inclusion cyst (CEIC) is an uncommon corneal disease in dogs (Bedford, 1997; Campos et al., 2002; Choi et al., 2010; Whitley and Hamor, 2021) and cats (Glaze et al., 2021). In small animals, the etiology is usually traumatic or iatrogenic. It is postulated that upon traumatic deposit of epithelium into the deeper cornea, epithelial cells grow and form a cyst, which consists of proteinaceous material and desquamated cells.

Diagnosis

The definitive diagnosis of an CEIC is made through histopathology; however, the presumptive diagnosis is usually based on history and clinical signs alone. A culture or cytology of these inclusion cysts does not reveal any organisms or leukocytes (Whitley and Hamor, 2021). An epithelial inclusion cyst appears as a white to pink or translucent mass with variable corneal vascularization (Cullen and Grahn, 2001) (Figure 13). Cysts usually measure less than 6 mm in diameter, are either single or multiple, and are chronic and painless, but may impair vision (Cullen and Grahn, 2001; Simonazzi et al., 2009; Cassagnes et al., 2020). Included cysts must be distinguished from stromal abscesses (which are usually associated with discomfort), infectious keratitis and corneal neoplasia (Bedford, 1997; Whitley and Hamor, 2021).

Treatment

Depending on the depth of the lesion, treatment can consist of a lamellar or deep keratectomy with or without additional grafting procedures (Campos et al., 2002; Choi et al., 2010; Cassagnes et al., 2020).

YELLOW

Corneal melting

Etiology

Keratomalacia, acute stromal collagenolysis or corneal melting is not a primary disease, but rather a complication of an existing corneal ulcer and can occur at any stage of the healing process (Sanchez, 2014; Whitley and Hamor, 2021). Ulcers can progress to a corneal perforation within hours, making them an ophthalmic emergency (Tsvetanova et al., 2021). Keratomalacia develops when an imbalance between proteinases and proteinase inhibitors occurs, both of which are enzymes found in the cornea and precorneal tear film as contributors to normal tissue maintenance wound healing. Other cells and organisms may

DIFFERENTIALS AND KEY POINTS

- **CORNEAL MELTING** (may appear white or gray in some cases)
  - Often gelatinous or liquefied appearance of the corneal stroma (Figure 15)
  - Infectious until proven otherwise (fungal or bacterial)
  - Always perform cytology and ideally culture and sensitivity testing
  - Often associated with a reflex uveitis leading to miosis and hypopyon
- **CELLULAR INFILTRATE** (may appear white in some cases)
  - Yellow-white corneal plaque with diffuse borders, often infected and associated with ulceration (Figure 16)
  - Accumulation of this infiltrate creates a corneal abscess (Figure 17)
  - Corneal abscesses are typically associated with great discomfort and a severe vascular response

Figure 14. Differential diagnosis and key points of corneal lesions in dogs and cats with a yellow appearance.

equally produce these enzymes including neutrophils, macrophages, keratocytes, as well as some bacterial and fungal species (Matsumoto, 2004). Although not well documented in the veterinary literature, corneal melting can also be caused by sterile inflammation (Whitley and Hamor, 2021). Burns to the cornea, especially caused by alkaline agents can also elicit corneal melting (Baradaran-Rafii et al., 2017).

Diagnosis

In patients with keratomalacia, an opaque white, grey or yellow gelatinous or liquified stroma is pathognomonic (Crispin, 2005; Sanchez, 2014; Maggs, 2016) (Figures 15A and 15B). In a recent retrospective study on canine melting ulcers, the most common bacterial species associated with canine collagenolysis were *Pseudomonas aeruginosa* and β-hemolytic *Streptococcus*. Due to the difference in antibacterial sensitivity between these two species, all dogs with keratomalacia should undergo bacterial cultures and sensitivity testing. Melting corneal ulcers associated with pure *Pseudomonas* infection were significantly more likely to result in globe loss than those associated with other infectious agents (Tsvetanova et al., 2021).

Treatment

Management of melting keratitis usually involves intensive medical treatment initially aiming at arresting stromal destruction using anti-collagenase agents (such as serum, EDTA, N- acetylcysteine, tetracycline, ilomostat) in combination with antimicrobials

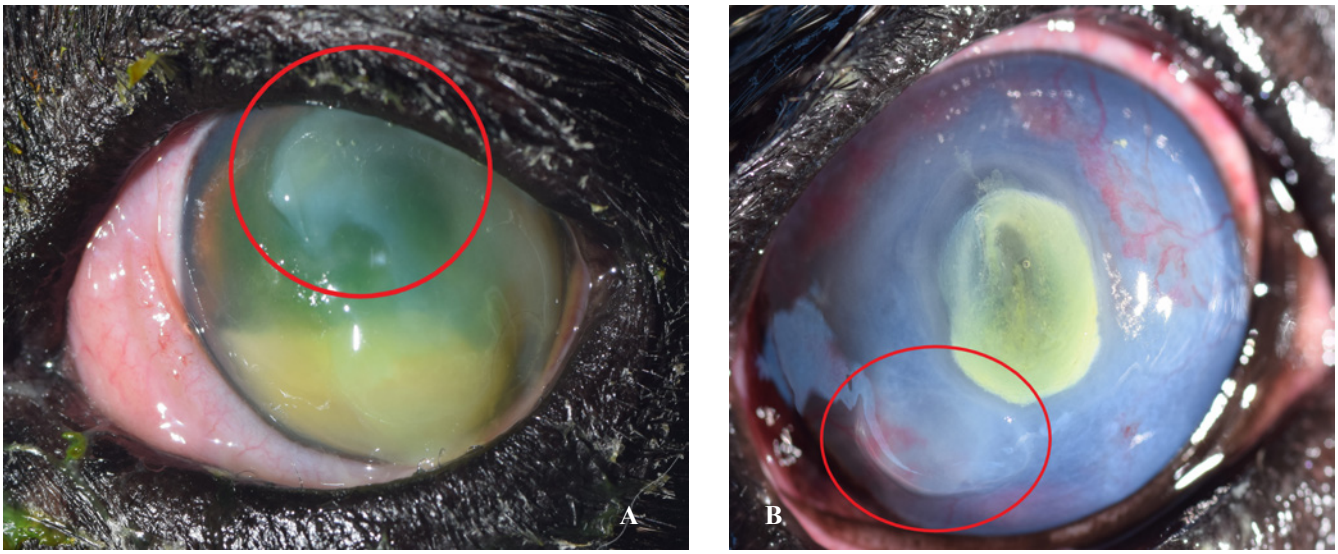

Figure 15. Typical appearance of a melting ulcer in two dogs. A. Melting ulcer in a French Bulldog. Note the hypopyon ventrally which is pus in the anterior chamber. B. Melting ulcer in a great Dane.

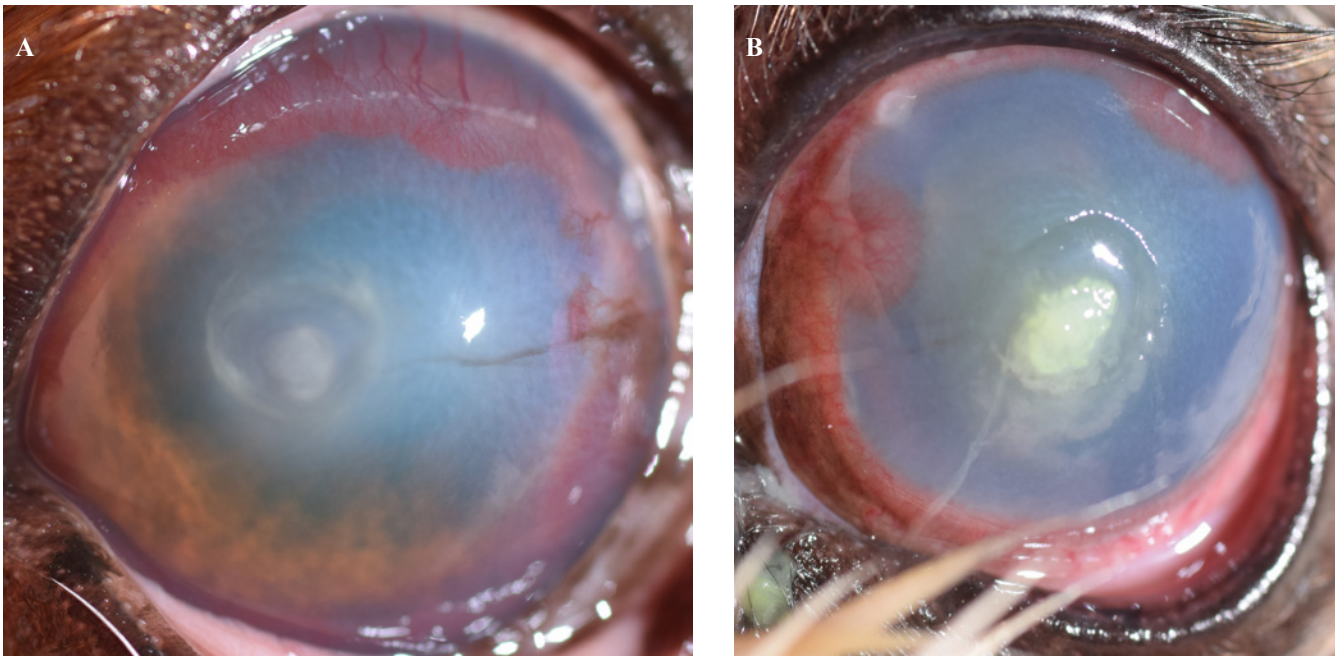

Figure 16A and B. Corneal stromal infiltrate in two dogs. Cytology of both patients included cocci and rods.

and systemic analgesia (Kanao et al., 1993; Perry et al., 1993; Barletta et al., 1996; Conway et al., 2016; Whitley and Hamor, 2021). This damaging process may not stabilize, in which case surgical treatment will be necessary in the form of conjunctival or corneal grafts in order to provide tectonic support (Tsvetanova et al., 2021; Whitley and Hamor, 2021). Corneal crosslinking has also been described as an adjunctive therapy for the treatment of melting keratitis in dogs and cats, but its safety and efficacy need to be confirmed through further research (Famose, 2014; Spiess et al., 2014; Pot et al., 2014; Hellander et al., 2019).

Due to the increased risk of developing stromal collagenolysis in brachycephalic dogs, treating corneal ulcerations in these breeds requires great caution and involves frequent monitoring and addressing underlying conformational issues (Sanchez, 2014).

Cellular infiltrate

Etiology

Inflammatory cell infiltration in the corneal stroma usually consists of a combination of cell debris, necrotic tissue and leucocytes with or without an infectious component (Ledbetter et al., 2006; Maggs, 2016). A corneal abscess is merely a focal accumulation of such a cellular infiltrate surrounded by a zone of reactive inflammation in the superficial or deep stroma Whitley and Hamor, 2021).

Diagnosis

Corneal stromal infiltrate appears as a white, cream or yellow discoloration (Figures 16A and 16B). Regions of cellular infiltrate typically have indistinct borders and are often associated with ulceration or keratomalacia. In all cases, the inflammatory cells originate from the tear film, limbus or uveal tract (Maggs, 2016). A stromal corneal abscess presents as a variably sized, focal, cream to yellow area of stromal corneal discoloration, which is typically associated with intense discomfort as well as an aggressive vascular response (Ollivier et al., 2003; Sherman et al., 2013) (Figure 17). It is best to presume that these infiltrates represent infection until proven otherwise, especially if they appear more greenish yellow (Ledbetter et al., 2006; Maggs, 2016). Cytologic examination along with culture and sensitivity testing should therefore be performed in all cases presenting with corneal stromal infiltrate (Maggs, 2016).

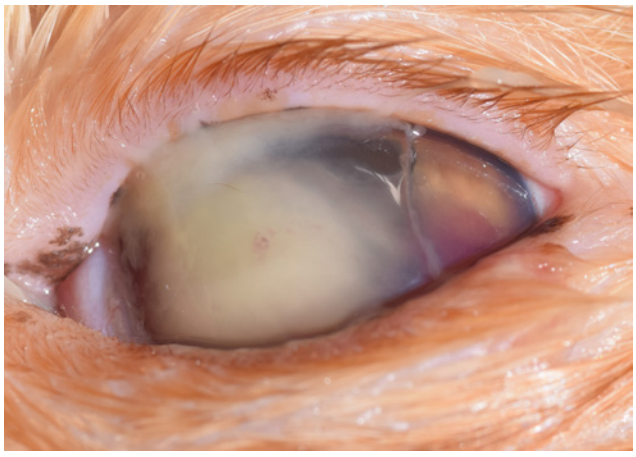

Figure 17. Corneal abscess in the left eye of a cat. Depending on the amount of neutrophils, the lesion can have a more white or yellow appearance.

Treatment

Topical broad-spectrum antibiotics that penetrate intact corneal epithelium (e.g. fluoroquinolones) should be used in combination with topical cycloplegics (e.g. atropine or cyclopentolate) to relieve painful ciliary spasm (Maggs, 2016; Whitley and Hamor, 2021). Release of lytic enzymes from inflammatory cells (especially neutrophils), infectious organisms and keratocytes can be associated with rapid collagenolysis, and therefore, appropriate anti-proteolytic agents should be added if deemed necessary. Curettage of the abscess or a keratectomy followed by placement of a conjunctival graft is also highly effective (Whitley and Hamor, 2021).

The concomitant use of topical and/or systemic nonsteroidal anti-inflammatory therapy may be indicated in some cases. During the healing process, corneas should be monitored closely and frequently and the use of an Elizabethan collar will prevent self-trauma (Ollivier et al., 2003; Sherman et al., 2013).

RED-PINK

Vascularization

Etiology

Corneal vessels occur in response to normal stromal healing or secondary to various chronic pathologic processes. This vascularization may be superficial, deep or a combination of both (Maggs, 2016; Whitley and Hamor, 2021). Exuberant granulation tissue can occur in the face of chronic corneal irritation (e.g. with severe entropion). The owner will often report a strawberry-like or fleshy appearance of the cornea, and it can be mistaken for a corneal tumor (Sanchez, 2014; Sandmeyer et al., 2014) (Figure 19).

Diagnosis

A corneal blood vessel's depth and appearance can often provide insight into the underlying patho-

DIFFERENTIALS AND KEY POINTS

- **VASCULARIZATION**
  - **Superficial**
    - 'Treelike': vessels appear bright red, branching and cross the limbus (Figure 20)
    - Arise from conjunctival vessels
    - Indicate ocular surface disease (e.g. superficial ulcer or chronic irritation)
  - **Deep**
    - 'Hedgelike': vessels appear dark red, straight and do not cross the limbus (Figure 21)
    - Arise from anterior ciliary vessels or less commonly from iridal vessels
    - Indicate deeper corneal or intraocular disease
  - **Granulation tissue**
    - Appears with chronic irritation (e.g. entropion in the shar-pei)
    - Has a fleshy, strawberry-like appearance (Figure 19)
- **CONJUNCTIVALIZATION**
  - Conjunctiva adheres to the cornea, the eyelids or itself (Figure 22)
  - Often in cats with FHV-1 infection
  - Can be seen with chemical burns
- **CELLULAR INFILTRATE**
  - Can be associated with any inflammatory condition e.g. pannus (Figure 23) or systemic histiocytosis (Figure 24)
  - Can be associated with corneal neoplasia (e.g. hemangioma, papilloma, corneal squamous cell carcinoma) (Figure 25)
- **STROMAL HAEMORRHAGE**
  - Uncommon finding, usually in older dogs with systemic diseases (Figure 26)

Figure 18. Differential diagnosis and key points of corneal lesions in dogs and cats with a red/pink appearance.

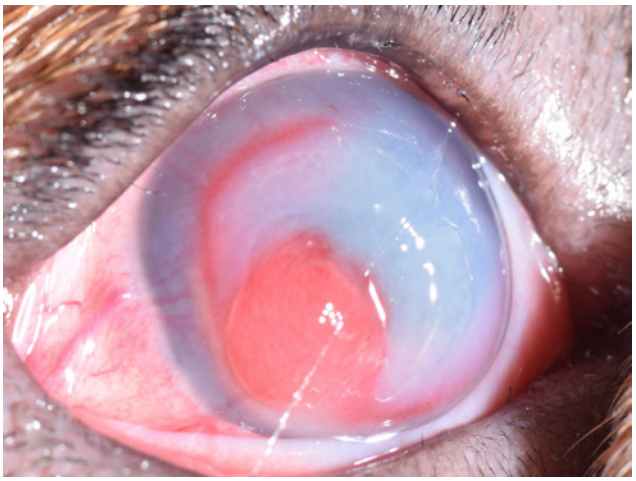

Figure 19. Shar-pei dog with entropion and secondary corneal edema, neovascularization and granulation tissue

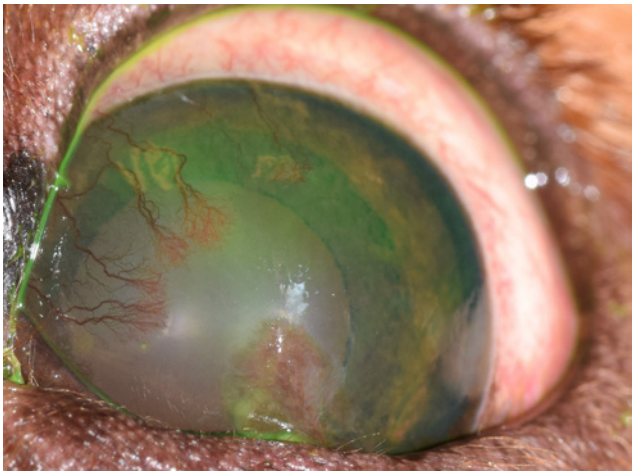

Figure 20. Typical appearance of superficial blood vessels.

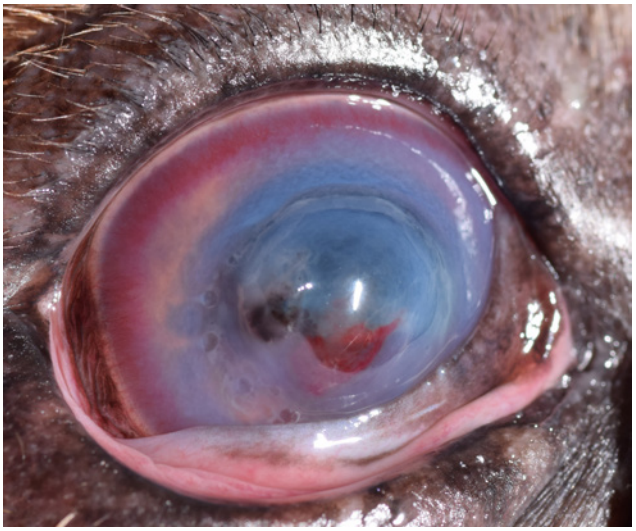

Figure 21. Typical appearance of deep blood vessels that form a 'brush border'. This French bulldog had a melting ulcer with a small corneal perforation that was sealed. There is iris pigment and a stromal hemorrhage present centrally.

logy (Cogan, 1962). Furthermore, they give an idea about the lesions' chronicity, as there is a 4- to-7-day lag period before blood vessels become evident, and then vessels grow across the cornea at approximately 1 mm per day (Maggs, 2016). The superficial corneal vessels are located in the subepithelial and anterior stromal regions and are usually caused by ocular surface disease. They arise from conjunctival vessels and appear 'treelike'. They are bright red, fine, branch repeatedly, and can be observed to cross the limbus (Crispin, 2005; Sanchez, 2014; Maggs, 2016) (Figure 20). Deep corneal vessels on the other hand, are located in the posterior stroma and indicate a deeper corneal or intraocular condition. They usually arise from anterior ciliary vessels. Coalescing vessels can look like clusters of bristles, sometimes referred to as the 'brush border' pattern (Figure 21). Less commonly, deep vascularization may originate from the iris when anterior synechiae are present (Whitley and Hamor, 2021).

Treatment

Although corneal blood vessels may result in deposition of melanin and exacerbate stromal fibrosis, this is often necessary for adequate healing. Topical corticosteroids used to control vascularization during the healing process can be detrimental and are therefore rarely indicated in veterinary ophthalmology (Maggs, 2016). However, some clinicians believe that the judicious use of topical steroids may reduce the formation of vision-obscuring scar tissue in corneal lesions with excessive granulation tissue (e.g. after delayed healing of a SCCED). Animals treated with topical steroids should always be monitored very carefully and a fluorescein test should be performed regularly (Whitley and Hamor, 2021).

Conjunctivalization

Etiology

Symblepharon refers to adhesions of the palpebral, bulbar and/or third eyelid conjunctiva to itself, to the eyelids or to the cornea. This abnormality is commonly encountered in cats as a result of feline herpes virus (FHV-1) infection (Glaze et al., 2021). In dogs, symblepharon is rarely diagnosed but it may develop after trauma, surgery and chemical burns to the cornea and conjunctiva (Singh et al., 2004; Busse et al., 2015). In a case report by Delgado (2012), bilateral canine symblepharon secondary to ophthalmomyiasis externa has been described.

Diagnosis

Clinical signs are determined by the severity and location of the symblepharon, ranging from subtle alterations in conjunctival fornix depth to blinding cor-

neal opacifications (Hartley, 2014). Other symptoms could include a reduced palpebral fissure, a protruded third eyelid, epiphora due to nasolacrimal punctal occlusion and a less distinct junction between the cornea and sclera (Glaze et al., 2021) (Figure 22). The possibility of a chemical burn should be considered in any animal with unexplained acute blepharospasm and severe corneal opacity (Whitley and Hamor, 2021).

Treatment

Symblepharon is not painful and is easier to prevent than to treat (Glaze et al., 2021). Surgical correction is possible, but adhesions may reoccur rapidly due to permanent damage to the limbal stem cells at the time of initial injury (Hartley, 2014; Glaze et al., 2021). Complex procedures to reconstruct the ocular surface and conjunctival fornices have scarcely been reported (Barros et al., 2005; Delgado, 2012; Allbaugh et al., 2017; Glaze et al., 2021), although these are best reserved for patients with impaired vision or altered eyelid function (Gelatt and Brooks, 2011). Intensive nursing of affected patients is needed in order to minimize adhesion formation. Gently separating the conjunctival tissues under topical anesthesia with abundant lubrication is recommended (Hartley, 2014). In case a chemical burn is suspected or confirmed, copious irrigation should immediately be carried out to try and dilute the chemical, remove particulate matter and normalize ocular surface pH (Whitley and Hamor, 2021).

Cellular infiltrate

Cellular infiltrate with a red to pink appearance may be associated with certain inflammatory conditions (e.g. pannus) or systemic histiocytosis) or certain types of neoplasia (e.g. hemangioma, papilloma, corneal squamous cell carcinoma) (Kim et al., 2005; Moore, 2014; Sanchez, 2014; Shank et al., 2018; Whitley and Hamor, 2021) (Figures 23, 24 and 25).

Etiology

Chronic

superficial keratitis (CSK) or pannus is a non-painful, bilateral, progressive, chronic corneal inflammation that potentially could be vision threatening (Bedford and Longstaffe, 1979). While the exact cause in dogs has not been determined yet, current evidence indicates an immune-mediated pathogenesis with a genetic basis (Whitley and Hamor, 2021).

Systemic histiocytosis is a rare disease, most frequently occurring in the Bernese mountain dog (Paterson et al., 1995; Moore, 2014). It is considered a non-neoplastic, generalized histiocytic, proliferative disease and it has been postulated to be an immunoregulatory disorder involving dermal dendritic cells (Affolter and Moore, 2000; Moore, 2014).

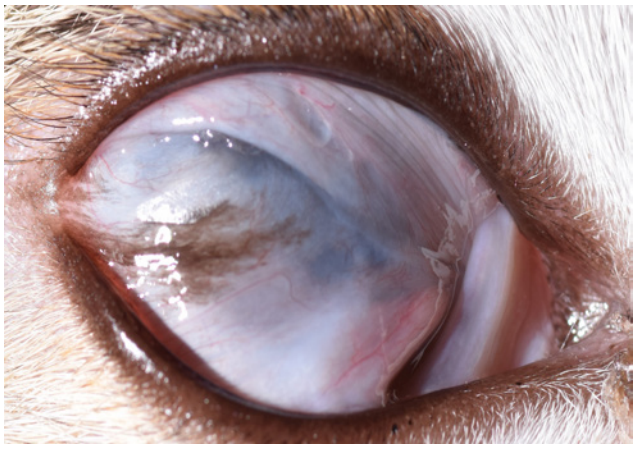

Figure 22. Severe symblepharon formation in a kitten secondary to a presumed herpes virus infection.

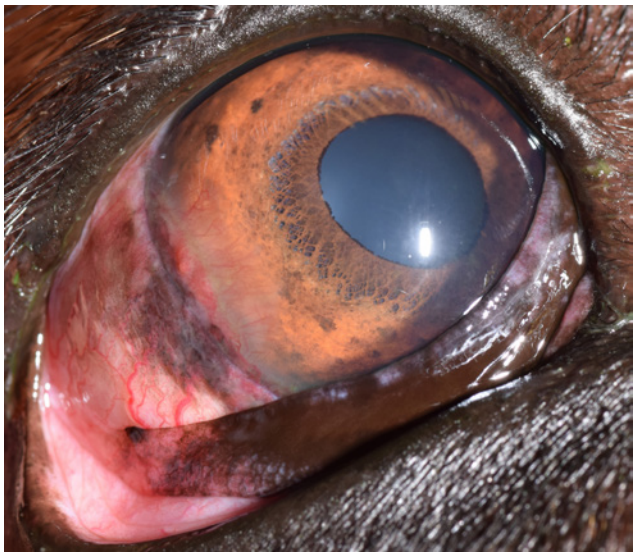

Figure 23. Lymphocytic-plasmacytic infiltrate in a German shepherd dog with pannus. Note also the infiltration and discoloration of the leading edge of the third eyelid (plasmoma).

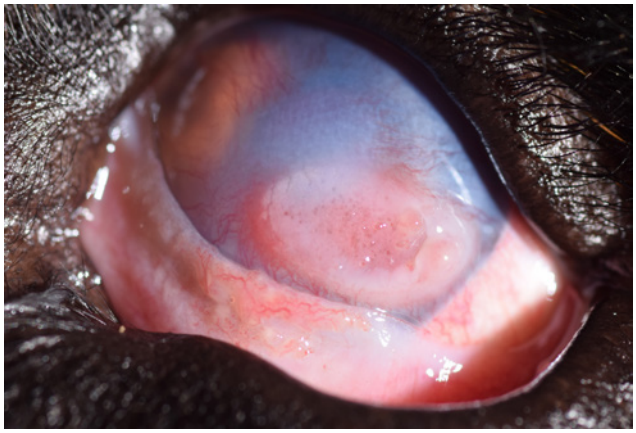

Figure 24. Corneal edema, neovascularization and cellular infiltrate in the left eye of an eight-year-old Bernese Mountain dog with systemic histiocytosis.

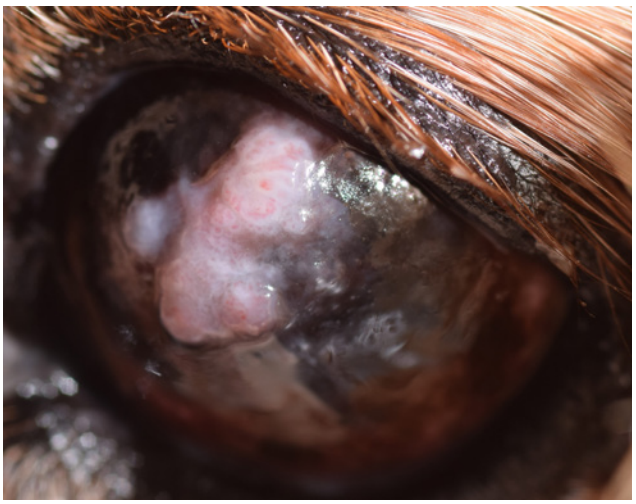

Figure 25. Left eye of an eleven-year-old English cocker spaniel with chronic KCS. This raised, white-to-pink mass was presumed to be a corneal squamous cell carcinoma.

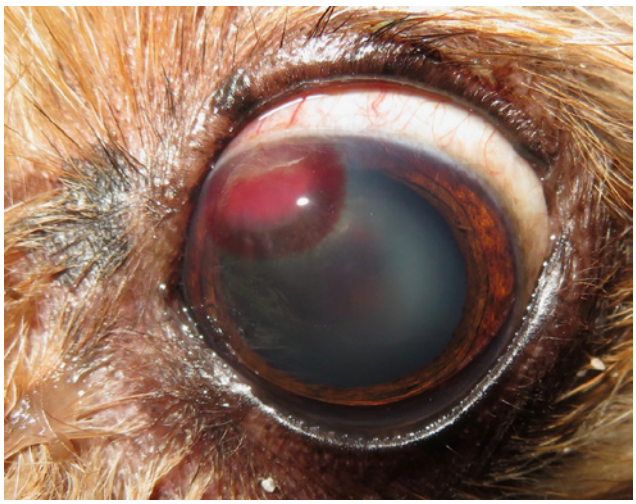

Figure 26. Intracorneal stromal hemorrhage in a dog (Photo courtesy of H. Appelboam).

Diagnosis

Breeds predisposed to this disorder include German shepherds, greyhounds, Belgian Tervuren and Malinois, but it can affect any dog and should never be discounted as a diagnosis simply because the patient does not belong to one of the commonly affected breeds (Maggs, 2016). Plasma cells and lymphocytes infiltrate the superficial stroma in the early stages (Figure 23) and as the disease progresses, melanocytes, histiocytes and fibrocytes equally enter the cornea with associated edema and neovascularization. It tends to develop in the temporal paralimbal cornea and may progress to other regions with chronicity (Sanchez, 2014).

Treatment

There is no cure for CSK, and owners should be advised that it requires a lifelong therapy and that the severity and prognosis depend on a number of factors, including age of onset, altitude and geographic location (Whitley and Hamor, 2021). In most cases, CSK can be managed medically with topical immunemodulating agents such as ciclosporin or corticosteroids. Topical ciclosporin is usually considered the long-term treatment of choice. However, both may initially be used in combination (Sanchez, 2014; Whitley and Hamor, 2021). As the condition may be triggered or exacerbated by UV light, owners should be advised that clinical signs may worsen during summer (Maggs, 2016).

The treatment of systemic histiocytosis often consists of immunosuppressive doses of corticosteroids and other immunomodulatory agents such as cyclosporine A or leflunomide, (Affolter and Moore, 2000). It is possible, however, for severe lesions to persist and to fail to respond to therapy (Whitley and Hamor, 2021).

Stromal hemorrhage

Etiology

A condition known as intracorneal stromal hemorrhage (ICH) has rarely been described in older dogs (Matas et al., 2012). This corneal abnormality usually occurs in one eye with no predilection for the right versus the left. Despite the lack of a definitive underlying cause, corneal vascularization may be prerequisite for its development (Matas et al., 2012; Violette and Ledbetter, 2017). In one retrospective study, ICH was associated with other ocular conditions in 91% of cases, including KCS, cataract and corneal ulcers. Additionally, 59% of dogs had underlying systemic diseases with diabetes mellitus, hyperadrenocorticism, hypothyroidism, and systemic hypertension being the most common (Violette and Ledbetter, 2017).

Diagnosis

Stromal hemorrhage is noted as light to dark red, focal, well-demarcated areas of free blood, typically seen in close proximity to corneal vascularization (Figure 26). The nasal quadrant is most commonly affected, but it can occur in any part. Affected patients should, at the very least, have a complete physical examination and undergo a systemic blood work-up, particularly if other systemic clinical signs are present (Violette and Ledbetter, 2017).

Treatment

In many cases, ICH resolves spontaneously over time with or without the use of specific topical treatments (Donnenfeld et al., 1991; Matas et al., 2012).

DIFFERENTIALS AND KEY POINTS

- **EPITHELIAL DYSFUNCTION**
  - Usually focal & mild
  - Typically caused by ulcers (Figure 28)
  - Fluorescein currently or recently retained
- **ENDOTHELIAL DYSFUNCTION**
  - Usually diffuse & marked
  - Fluorescein usually not retained
  - Can have a cobblestone appearance
  - Primary
    - **Endothelial dystrophy**
      - Present in certain breeds from a young age (e.g. Chihuahua) (Figure 29)
      - Results from abnormal dystrophic endothelial cells
      - Uncommon finding
    - **Senile endothelial degeneration**
      - Present in older dogs of all breeds and is usually bilateral (Figure 30)
      - The cornea is easily affected by non-healing superficial ulcers (Figure 31)
      - Common finding
  - Secondary
    - **Glaucoma** (Figure 32)
    - **Anterior uveitis** (Figure 33)
    - **Persistent pupillary membranes iris-cornea** (Figure 34)
    - **Mechanical trauma** (e.g. intraocular mass, iatrogenic or anterior lens luxation) (Figure 35)
    - **Endothelitis** (post-vaccination, 'blue-eye') (Figure 36)
- **ASSOCIATED WITH NEOVASCULARIZATION**

Figure 27. Differential diagnosis and key points of corneal lesions in dogs and cats with a blue appearance.

BLUE

Corneal edema

Etiology

Corneal edema is indicative of corneal damage, and stromal edema can result from injuries to the anterior epithelium, the posterior endothelium or the stroma itself. As a result of stromal edema, the cornea swells and becomes thicker, compromising its optical properties (Crispin, 2005; Whitley and Hamor, 2021). The corneal endothelium forms a monolayer immediately posterior to Descemet's membrane, lining the anterior chamber. This layer is the major contributor to corneal transparency due to its build-in pump system that moves ions and therefore water from the corneal stroma into the aqueous humor (Maggs, 2016; Whitley and Hamor, 2021). Endothelial cells are postmitotic in adult animals with a limited regenerative capacity (Gwin et al., 1982a). A lesser but critical role is played by the epithelium by preventing water from the tear film from entering the corneal stroma (Maggs, 2016).

Focal corneal edema related to an epithelial dysfunction is usually associated with ulceration (Figure 28). Endothelial abnormalities leading to corneal edema can be primary or secondary. Primary endothelial dystrophy results in spontaneous, progressive corneal edema due to abnormal dystrophic endothelial cells (Cooley and Dice 1990; Thomasy et al., 2016). This

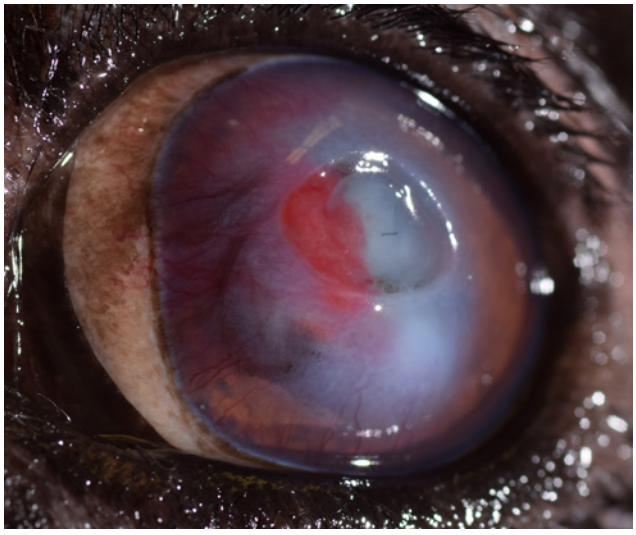

Figure 28. Midstromal corneal ulcer in a French bulldog with associated corneal edema and neovascularization.

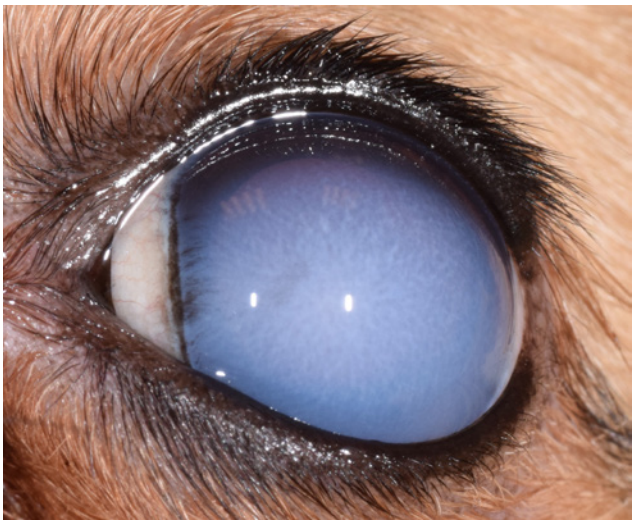

Figure 29. Left eye of a six-month-old Chihuahua with corneal dystrophy. Both eyes were symmetrically affected.

is relatively uncommon in dogs and is most prevalent in younger dogs of certain breeds (e.g. Boston terrier, Chihuahua, and dachshund) (Martin and Dice, 1982; Sanchez, 2014) (Figure 29). On the contrary, age-related endothelial degeneration occurs because of gradual decompensation of the ability of the corneal endothelium to actively pump water out of the corneal stroma. It is commonly diagnosed in older dogs and can occur in any breed (Bayley et al., 2019) (Figure 30). The chronic edema reduces the cornea's healing capacity and non-healing ulcers are a common associated finding (Sanchez, 2014; Whitley and Hamor, 2021) (Figure 31). Secondary endothelial dysfunction may result from a variety of other ocular problems including glaucoma (Figures 32A and 32B), anterior uveitis (Figure 33), persistent pupillary membranes between the iris and corneal endothelium (Figure 34), mechanical trauma caused by e.g. an anterior lens luxation (Figure 35) and inflammation of the endothelium that can occur secondary to an Adenovirus vaccination or infection (Figure 36) (Roberts and Bistner, 1968; Gwin et al., 1982a; Gwin et al., 1982b; Blogg, 1983; Gwin et al., 1983; Yee et al., 1985; Macdonald et al., 1987; Gagnon et al., 1997; Sanchez, 2014; Maggs, 2016; Whitley and Hamor, 2021).

When the corneal epithelium and stroma are severely edematous, small vesicles or bullae may form, which may coalesce to form larger bullae. This is known as bullous keratopathy. These bullae may rupture and result in corneal ulceration, which is painful (Sanchez, 2014; Maggs, 2016; Whitley and Hamor, 2021).

Diagnosis

Irrespective of the cause and whether originated from epithelial or endothelial cell loss, corneal edema appears hazy blue and has indistinct borders. In all cases presenting with signs of corneal edema, a thorough and complete ophthalmic examination is indicated (Maggs, 2016). Corneal edema may appear focal (e.g. following superficial ulceration or anterior lens luxation) or diffuse (e.g. following a chemical burn or endothelial degeneration) (Crispin, 2005; Whitley and Hamor, 2021). Cornea's affected by corneal endothelial dystrophy or degeneration are usually not painful nor inflamed and have a normal IOP. In contrast, if an animal is presenting with glaucoma, anterior uveitis or anterior lens luxation, the eye is painful and inflamed and usually accompanied by an abnormal IOP (Maggs, 2016).

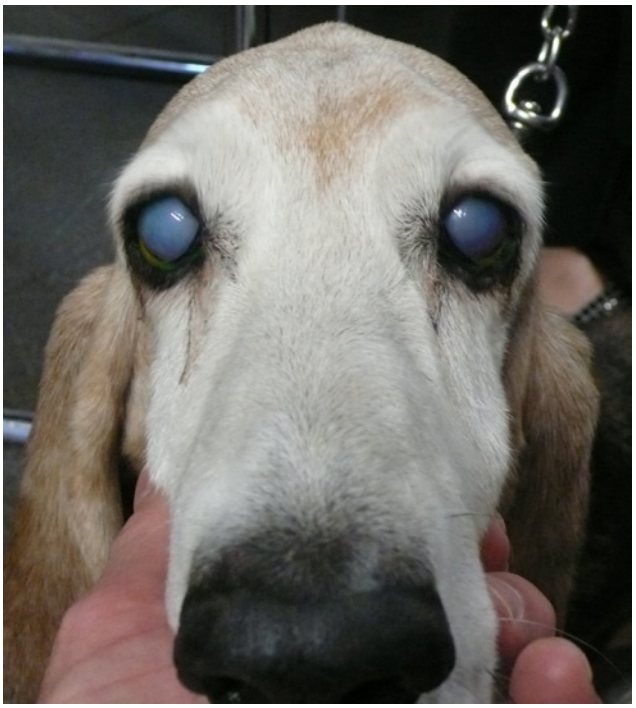

Figure 30. A thirteen-year-old bassett hound with bilateral senile endothelial degeneration (Photo courtesy of P. Hansen).

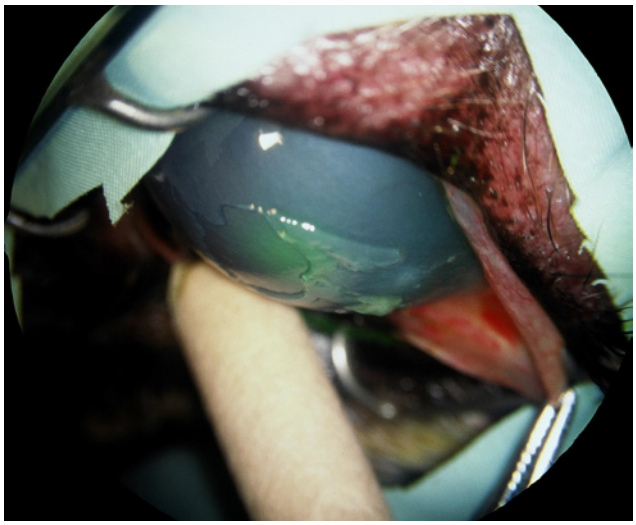

Figure 31. Superficial, non-healing ulcer in a dog with senile endothelial degeneration (Photocourtesy of P. Hansen).

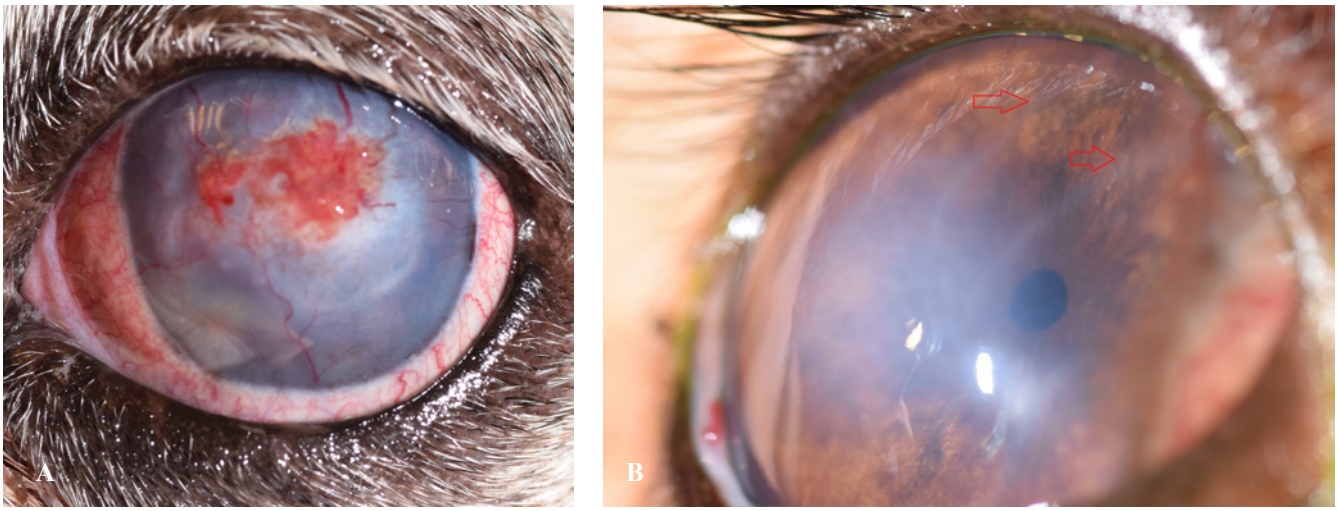

Figure 32. Left eye of a thirteen-year-old French bulldog with chronic primary glaucoma. A. Note the episcleral injection, the diffuse corneal edema, neovascularization and granulation tissue secondary to a healing indolent ulcer. B. Haab striae in a dog with chronic primary glaucoma. Note the small pinpoint pupil secondary to latanoprost instillation.

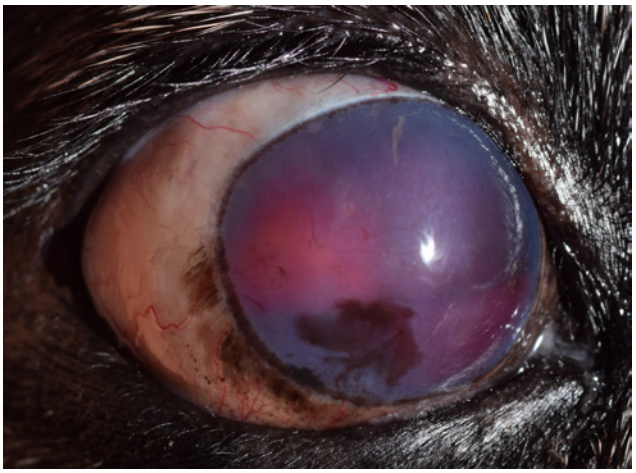

Figure 33. Right eye of a nine-year-old French bulldog with anterior exsudative uveitis. Note the intense diffuse corneal edema and hyphema. This dog had end-stage primary glaucoma and developed the uveitis secondary to an intravitreal Gentamycine injection.

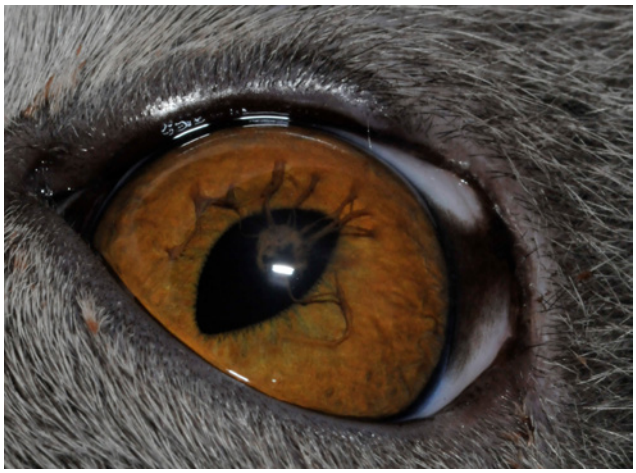

Figure 34. Left eye of a kitten with a persistent pupillary membrane (PPM) from the iris to the corneal endothelium (Photo courtesy of P. Hansen).

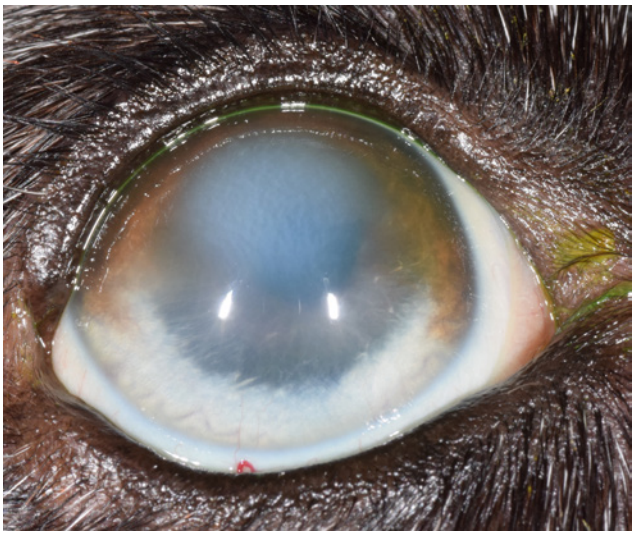

Figure 35. Right eye of a seven-year-old border collie that had an anterior lens luxation. Note the focal, circular area of corneal edema.

Figure 36. Kitten with bilateral endothelitis of unknown origin (Photo courtesy of P. Hansen).

Treatment

The inciting cause will dictate the most appropriate treatment and its purpose (Whitley and Hamor, 2021). For example, the primary goal of treating severe corneal edema related to endothelial dystrophy or degeneration is to relieve ocular pain caused by ruptured epithelial bullae (Giannikaki et al., 2020). Corneal edema is reversible if the underlying cause is dealt with timely and sufficient endothelial cell function remains (Maggs, 2016). However, in progressive conditions such as senile endothelial degeneration, corneal clearing is limited and therapy is focused on controlling the disease rather than curing it (Whitley and Hamor, 2021). Anecdotally, it is thought that inflammation can accompany the degeneration and Doxycycline with or without topical anti-inflammatory drops are sometimes added to the initial treatment regimen with variable results (direct communication with P. Hansen).

BROWN/BLACK

Pigment

Etiology

Corneal pigmentation can be a nonspecific response to various irritating stimuli. Some brachycephalic breeds (e.g. pug, shih-tzu, Pekingese) appear prone to more marked and rapid corneal pigmentation (Labelle et al., 2013) (Figure 38). The stimulus may be mechanical (e.g. entropion), secondary to corneal exposure (e.g. lagophthalmos) or immune-mediated (e.g. chronic superficial keratitis) (Roberts, 1954; Slatter et al., 1977; Van der Woerdt, 2004) (Figure 39). Corneal pigmentation may also develop as a consequence of wound-healing or when concomitant aqueous tear film deficiencies are present, such as KCS (Kaswan et al., 1989; Stiles et al., 1995) (Figure 40).

Epithelial and anterior stromal melanin originates from proliferation and centripetal migration of melanocytes that are normally confined to the limbus (Maggs, 2016). Less commonly, endothelial pigment is noted, and may be associated with intraocular diseases, such as rupture of anterior uveal cysts (Figure 41), anterior synechiae and extension of anterior uveal or limbal melanocytomas (Sanchez, 2014) (Figure 42). Ocular melanosis, as typically seen in Cairn terriers usually affects the perilimbal sclera (Petersen-Jones et al., 2008), although one case with stage 3 ocular melanosis has been shown to have pigment lining a part of the ventral corneal endothelium (Petersen-Jones et al., 2007).

Lastly, in a recent study by Sanches et al. (2020), progressive retrocorneal pigment has been described. This is a slowly progressive pigmentary lesion on the endothelium of older dogs that could possibly impact vision. This abnormality is often an incidental finding that causes minimal discomfort. The exact pathogenesis of this abnormality is yet to be determined and histological studies of affected eyes are therefore warranted (Sanchez et al., 2020).

DIFFERENTIALS AND KEY POINTS

- **MELANIN DEPOSITION**
  - **Superficial**
    - Often present in brachycephalic breeds due to a combination of abnormalities (Figure 38)
    - Can be linked to any form of chronic keratitis e.g. pannus (Figure 39) or delayed wound healing
    - Often in association with KCS (Figure 40)
    - If severe can lead to impaired vision
  - **Endothelial**
    - Often circular with ruptured iris cysts (Figure 41)
    - Can be seen idiopathically in older dogs

- **FELINE CORNEAL SEQUESTRUM** (Figure 43)
  - Light to dark brown pigmented, well-demarcated lesion
  - Often in brachycephalic breeds
  - Often associated with chronic corneal irritation e.g. entropion
  - Possible association with FHV-1
  - Can be ulcerated
  - Can be treated with a superficial keratectomy with or without a grafting procedure

Figure 37. Differential diagnosis and key points of corneal lesions in dogs and cats with a brown/black appearance.

Diagnosis

Clinically, it can be recognized by its dark brown to black coloration and very distinct borders (Maggs, 2016). The term 'pigmentary keratitis' is often used to specifically describe superficial corneal pigment (SCP) in brachycephalic dogs. The use of this term has been justified by a recent study, in which the association of SCP with microscopic evidence of inflammation has been demonstrated (Vallone et al., 2017). Corneal pigmentation is a clinical sign, not a diagnosis (Labelle et al., 2013) and a complete ophthalmic examination is warranted in every patient presenting for this problem to identify underlying conditions. Other signs of active keratitis, such as corneal vascularization, stromal inflammatory cell infiltration, and granulation tissue formation, usually accompany pigment cell migration (Whitley and Hamor, 2021). A slit-lamp biomicroscope is paramount to distinguish epithelial and stromal pigment from its endothelial counterpart (Featherstone and Heinrich, 2021).

Treatment

The treatment and prognosis of corneal pigment will depend on the inciting cause. Corneal melanosis itself is not normally treated unless it is rapidly progressive in susceptible breeds (e.g. pugs) or interferes with vision. Current treatment options for pigmentary keratitis are directed at halting the progression of pigmentation and correcting the inciting cause (Maggs, 2016). In brachycephalic breeds, a combination of surgical procedures, which usually includes correction of lower medial eyelid entropion, and lateral or medial canthoplasty, will often prevent disease progression (Yi et al., 2006). Application of beta radiation or cryotherapy has also been used, but the overall success rate is unknown (Azoulay et al., 2014; Whitley and Hamor, 2021). The use of superficial keratectomy has been reported, however, frequent pigment recurrence and corneal scarring generally limits its success (Whitley and Hamor, 2021).

Topical agents, such as corticosteroids, cyclosporine and tacrolimus, have been administered in the treatment of pigmentary keratitis but their clinical efficacy is still debated (Nell et al., 2005). Corneal dermoids are usually surgically managed via superficial keratectomy (Whitley and Hamor, 2021). Regardless of its cause, endothelial pigment is left untreated in dogs (Sanchez et al., 2020; Hendrix, 2021).

Feline corneal sequestrum

Etiology

A corneal sequestrum is a condition characterized by necrosis of the cornea that has mainly been described in cats (Morgan, 1994) but has also been reported sporadically in dogs (Bouhanna et al., 2008; Dubin et al., 2013). Sequestra may affect all corneal

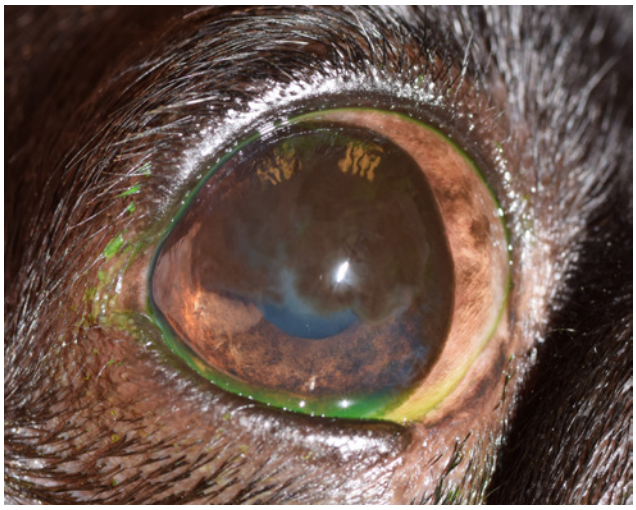

Figure 38. Right eye of a five-year-old pug with severe corneal pigmentation.

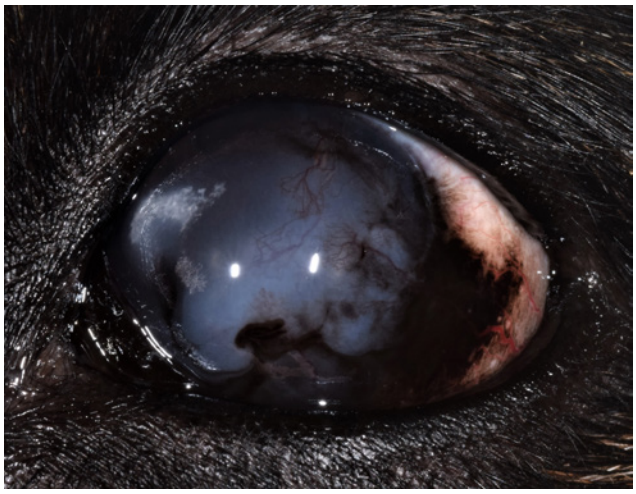

Figure 39. Left eye of a seven-year-old German shepherd with severe pannus. Note the lateral neovascularization and associated pigment, diffuse corneal edema, and medially there is white mineral deposition, presumably lipid.

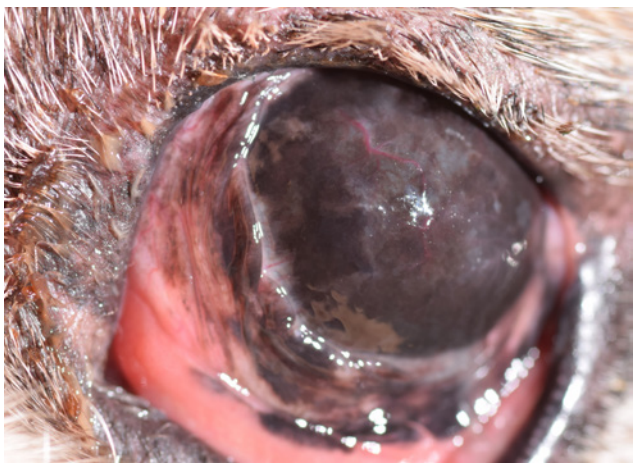

Figure 40. Left eye of a ten-year-old English cocker spaniel with chronic and severe KCS with secondary corneal neovascularization and pigmentation.

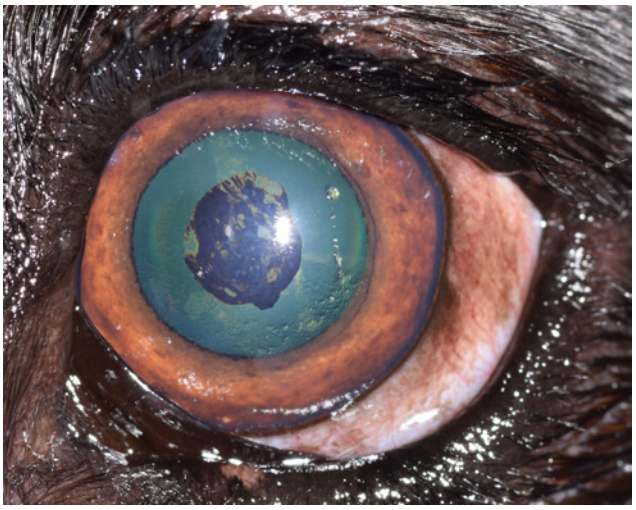

Figure 41. Left eye of a twelve-year-old Labrador retriever with endothelial pigment due to a ruptured iris cyst.

Figure 42. Right eye of a six-year-old French bulldog with an epibulbar melanoma. Note how the pigment invaded the dorsal corneal endothelium.

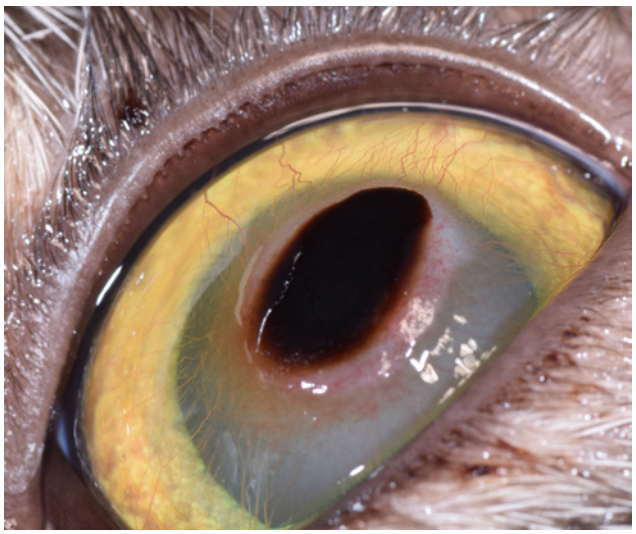

Figure 43. Typical appearance of a corneal sequestrum in a cat.

layers and can result in corneal perforation if not treated adequately (Ragozzino et al. 2012, Laguna et al. 2015).

Although the etiology is still unknown (Featherstone et al., 2004; Cullen et al., 2005), contributing conditions have been documented, suggesting that this pathology could be associated with FHV-1, chronic corneal irritation (e.g. entropion) or iatrogenic corneal trauma (Featherstone et al., 2004; Laguna et al., 2015; Glaze et al., 2021). Ultimately, the cause of stromal discoloration remains debated (Glaze et al., 2021).

Diagnosis

Diagnosis of corneal sequestrum is based on the characteristic clinical appearance (Multari et al., 2021). A sequestrum appears as a diffuse or well-demarcated pigmented lesion, varying from a faint brown color to an opaque dark opacity (Graham et al., 2017) (Figure 43). The brachycephalic breed is overrepresented (Laguna et al. 2015; Graham et al. 2017) and in one study, the Persian had a prevalence rate of 71.5% (Multari et al., 2021).

Treatment

Treatment must address causative factors as well as the sequestrum itself. For example, partial permanent tarsorrhaphy or correction of medial entropion may reduce corneal exposure and irritation and reduce the recurrence rate in brachycephalics (Glaze et al., 2021). In most cases, surgical techniques are used to manage the discomfort and restore the structural integrity of the corneal stroma (Andrew et al. 2001, Graham et al. 2017). Over the past decades, numerous grafting techniques have been reported in association with a lamellar or full-thickness keratectomy (Blogg et al., 1989; Townsend et al., 2008; Laguna et al., 2015; Yang et al., 2019). However, a consensus does not exist regarding choice of surgical procedure as a great variety of lesion size and depth are encountered (Michel et al., 2021).

The sequestrum sometimes sloughs without the need for surgical intervention, but this is an extremely protracted and painful process, which can result in corneal perforation and is usually not recommended (Maggs, 2016; Glaze et al., 2021). Manual removal of sequestra should never be attempted, as some lesions extend to Descemet's membrane with possible secondary corneal perforation (Maggs, 2016).

REFERENCES

For the complete reference list, contact the authors.