Corneal sequestrum in cats: common questions answered

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THE corneal sequestrum is a necrotising, potentially blinding disease of the feline cornea. Continuing on from previous research projects at the Animal Health Trust, a new, but related, project is under way to try to identify the exact aetiology of feline sequestrum formation.

This article introduces studies and provides a brief overview of current knowledge of the condition. Clinical signs routinely seen in practice are described, as well as the different treatment options.

What is a corneal sequestrum?

Corneal sequestrum has also been named corneal mummification, corneal nigrum and corneal necrosis. In general terms, necrosis (from the Greek, nekros, meaning dead) is defined as an irreversible cell death with loss of cell function. The presence of hypoxia and membrane-toxic agents leads to the cessation of oxidative energy production and subsequent increased intracellular lactate levels and pH imbalance. Following irreversible cytological alteration, with lysis of all membrane components, nuclear cell death (karyorrhexis and karyolysis) occurs.

Depending on the tissue involved, and the type of necrosis, the affected area will be surrounded by granulation tissue and will either be demarcated – resulting in an ulcerated bed – or encapsulated.

The corneal sequestrum is a localised stromal lesion devoid of keratocytes, and composed of amorphous collagen bundles that resist enzymatic degradation and neovascularisation. Invasion by inflammatory cells is absent on light microscopy, but has been demonstrated using electron microscopy\(^1\). Conversely, at the periphery of the sequestrum, marked inflammation, bacterial invasion and granulation tissue is frequently present.

The lesion usually involves the anterior stroma. However, involvement of the entire stromal depth can occur. The degree and extension of the sequestrum, inflammatory cell infiltration, oedema and granulation tissue is variable between cases. The sequestrum itself and peripheral margins characteristically show a lack of epithelial attachment (\(Figure~1\))\(^2\).

• Summary
– Localised stromal necrosis.
– Mainly anterior-mid stroma.
– Can penetrate to Descemet’s membrane and can lead to corneal perforation.
– Often surrounded by neovascularisation, granulation tissue and ulceration.
– Also reported in dogs and horses (rare in both).

**What makes the colour?**

The predominant clinical characteristic of feline corneal sequestra is the distinct discolouration. This varies from a light amber stain, with an ill-defined margin, in the early stages of the disease ([Figure 2](#)), to advanced stages, where well-circumscribed black plaques can be observed ([Figure 3](#)).

The origin of this specific discolouration is not fully understood, but electron microscopy studies have demonstrated coccoid bodies or granules[3]. A laboratory analysis of 14 ocular samples ruled out the presence of iron[4], which had been assumed to be the main component[5].

Optical microscopy in bright field mode could distinguish three different zones, demonstrating an increasing amount of black round particles from the transition zone to the inner zone.

The round particles, which comprise varying diameters, were interpreted as melanin particles. In two out of 14 samples, ultraviolet absorbance spectroscopy results were consistent with melanin. Brown-stained lacrimation and mucoid discharge can be seen clinically in many affected cats ([Figures 3](#) and 4). Discolouration of bandage lenses in the affected (3/9 cases), as well as contralateral, eyes (3/6 cases) were also examined in the spectroscopy study[4]. In contrast, in a transmission electron microscopy study, which mainly found apoptotic cell nuclei, the small particles present were interpreted as iron and bacteria[1].

**Summary**

– Unknown, a chromophore, such as melanin is postulated.
– Iron seems unlikely.

**Does the condition only exist in cats?**
Feline corneal sequestrum was first reported by Roberts (1964), and was thought to be a unique disease in cats. However, rare reports of corneal sequestrum also exist in dogs and horses. In contrast to cats, the brown-black discolouration was not a prominent feature in these cases, and concurrent corneal disease – such as recurrent erosion syndrome, acute onset of keratoconjunctivitis sicca (KCS) and equine eosinophilic keratitis – were present.

What is predisposed?

Breed predisposition exists in purebred cats, such as Persian, Burmese, Siamese, Birman, Himalayan and colourpoint cats. However, domestic shorthaired cats that suffer from any chronic corneal irritation can develop a corneal sequestrum. It has been hypothesised that the brachycephalic breeds are over-represented, due to tear film distribution deficits and exposure problems.

Is feline herpesvirus-1 the major player?

Why the feline cornea seems to have the potential to react differently to chronic insults, resulting in corneal sequestrum, is not known. To what extent a possible feline-specific local metabolic defect and/or primary stromal dystrophy are present has not been the objective of most research studies.

However, several different causal associations between chronic corneal irritation and sequestrum formation have been demonstrated, such as entropion, medial canthal trichiasis, and lagophthalmos.

The tear film quality of affected cats differs from normal cats and decreased lipid levels were found in one study. A further clinical study could not demonstrate abnormal goblet cell numbers, accelerated tear film break-up time or lower Schirmer tear test values.

Possibly the most common predisposing factor is the presence of chronic ulcerative keratitis. Feline herpesvirus-1 (FHV-1) infection is considered to be a major cause of feline corneal ulceration. Analysis of the presence of FHV-1 DNA in corneal sequestra revealed positive results – ranging between 18 per cent to 55 per cent, although 46 per cent FHV-1-positive results were also seen in healthy corneal samples. Interestingly, one study also found Toxoplasma gondii DNA in 44 per cent of sequestrum samples.

Although brachycephalic breeds are predisposed to sequestrum formation, they showed a lower incidence of FHV-1 polymerase chain reaction-positive results, which seems to contradict the supposition that FHV-1 is the only aetiological agent. Topical and subconjunctival steroid application in FHV-1-positive cats is more likely to result in sequestra and stromal keratitis development.

Treatment of non-healing superficial corneal ulceration in cats by debridement and grid keratotomy
increases the risk of sequestrum development, and is ineffective in reducing healing times.\textsuperscript{14}

\textbf{Summary}

– Multifactorial disease, FHV-1 is one factor.

– Predisposing factors include topical corticosteroid application, entropion, lagophthalmos, tear-film deficiency and debridement with grid keratotomy (for non-healing superficial ulcers).

\textbf{What are the typical clinical features?}

The typical clinical appearance in cats, with respect to size, position and intensity of pigmentation, is highly variable. The key feature is discolouration, and depending on the duration and extension of the sequestrum, the appearance can vary from a light brunescence to a black, dense plaque (\textbf{Figures 2} and \textbf{3}).

The necrotic areas are either firmly integrated within the stroma, or possible demarcation of the sequestrum might occur. The central and paracentral cornea is more commonly affected, and conjunctival sequestra are rarely seen.\textsuperscript{15}

Depth assessment of the sequestrum within the cornea, without advanced imaging modalities, such as ultra-high resolution ultrasound biomicroscopy, can be very difficult. Even with slit lamp biomicroscopy, and the benefit of higher magnification (16X), examination may not be conclusive, as the dense, black necrotic stroma obscures deeper layers of the cornea. Clinically, corneal sequestra are described as involving mainly the anterior and mid-stroma. However, full thickness involvement and corneal perforation can be seen (\textbf{Figure 4}).\textsuperscript{2}

Round, small, deep and wellcircumscribed sequestra may be misdiagnosed as corneal foreign bodies. Discomfort is frequently present, as well as secondary bacterial infiltration and deep stromal ulceration. Keratomalacia may also be encountered.

Surrounding neovascularisation is common and, sometimes, marked granulation tissue formation may occur (\textbf{Figure 5}). Mineralisation in conjunction with sequestrum development is rare.\textsuperscript{16}

The age of affected cats ranges from five months to 17 years and no sex predisposition is described. The disease is mainly seen unilaterally, although bilateral involvement at first presentation has been described in one study in six out of 58 cases, of which five cats were Persians. A further seven Persian cats developed a sequestrum in the second eye in the study period of seven years.\textsuperscript{15}

The progression of sequestra is unpredictable, ranging from static sequestra over several years to rapid disease progression within days to weeks. One study that reviewed 64 cases had a range of
one day to two years – with a mean value of 16 weeks\textsuperscript{15}.

• **Summary**

– Typical discolouration: light brown to black in the central and paracentral cornea.

– Associated superficial ulceration and discomfort is commonly seen.

– Size, depth and progression varies.

– Often accompanied by granulation tissue and neovascularisation.

– Purebred cats, such as the Persian, may be predisposed for bilateral involvement.

**Is surgical intervention always required and how long can I wait?**

The prognosis is unpredictable in cases where surgical intervention is not an option. Spontaneous healing, with demarcation of the sequestered stroma, is seen as unlikely\textsuperscript{17}. Histopathologically, the corneal epithelium can undermine the sequestrum, causing a demarcation and, potentially, sloughing of the lesion\textsuperscript{2}. However, this variant of the healing process can take months (during which the cat is in discomfort), is rare, and bears the risk of corneal perforation.

In a review of 80 cases, only six eyes were treated medically, of which no follow-up data was available\textsuperscript{15}.

Generally, an early surgical approach will minimise surgical intervention and anterior stromal involvement, necessitating a superficial keratectomy only. Placement of a soft contact lens postoperatively will provide analgesia for the first few days after surgery.

Superficial keratectomy without additional conjunctival pedicle flap placement did not reveal significantly higher recurrence rates in one study, and is an appropriate technique for anterior stromal to midstromal involvement\textsuperscript{15}. An additional conjunctival pedicle flap is indicated where deep stromal necrosis is present and a deep keratectomy cannot be avoided, or the necrotic area cannot be completely excised\textsuperscript{18}.

• **Summary**

– Spontaneous healing with topical treatment is unlikely.

– An early surgical approach will reduce the surgical complexity and costs, and increase the likelihood of complete and safe excision with reduced scarring.
– Corneal surgery should be undertaken by those who are equipped for intraocular surgery, as the extension of the sequestrum is not predictable.

**What types of surgical procedure exist?**

The feline cornea is 592±80µm (approximately 0.5mm to 0.7mm) thick, and given that with stromal healing the cornea is unlikely to regain the preoperative thickness, accurate keratectomy should be performed under high magnification and with adequate illumination (operating microscope) to allow precise excision of the affected area and protect healthy corneal stroma.

For the keratectomy, the affected area is ideally demarcated by a set-depth knife or beaver blade. The corneal stroma is then excised by lamellar excision using a crescent-bevelled lamellar dissection knife, ideally until healthy cornea can be appreciated (Figure 6).

A conjunctival pedicle flap is indicated in cases of deep involvement, and where more than half of the corneal thickness needs to be excised. If the conjunctival pedicle flap is accurately prepared and positioned, longterm clearance of the integrated conjunctiva can be expected and the visual outcome can be seen as satisfactory (Figure 7).

Recurrence rates appear to be increased after pedicle sectioning, therefore it is worthwhile to leave the pedicle in place – especially in purebreds, such as Persian cats, and in cases of incomplete excision (Figure 8).

Corneoconjunctival transposition, performed in 17 cases with affected areas ranging between 1.0mm to 10mm, showed excellent cosmesis, functional vision and no recurrences in a follow-up period of one month to seven years.

Amniotic membrane transplantation after lamellar keratectomy was used with satisfactory results. However, case selection should exclude those with deep stromal keratectomy without neovascularisation.

Lamellar corneal allograft or heterograft (canine corneal tissue) was placed in the keratectomy bed in six Persian cats’ eyes with promising results, with a follow-up period of four to 30 months. One case report described the use of a heterologous–penetrating keratoplasty in a cat with satisfactory results 16 months post-surgery.

In conclusion, even though integrated thin conjunctival flaps often have a good visual outcome, corneoconjunctival transposition, and lamellar and penetrating keratoplasty show promising results.

**• Summary**

– Lamellar keratectomy in anterior stromal necrosis.
– Additionally, conjunctival pedicle flap in mid to deepstromal keratectomy.

– Corneoconjunctival transposition may be suitable, with good results in cosmesis and general vision.

– Lamellar/penetrating keratoplasty also show promising results.

References


