As the eye can be examined so readily, it is invaluable to be able to recognise ocular signs that can provide an early, rapid diagnosis and accessible evaluation of therapy success, writes Natasha Mitchell MVB DVophthal MRCVS, Eye Vet Ltd, Crescent Veterinary Clinic, Limerick

Systemic diseases in cats that can affect the eye include infectious (viral, bacterial, protozoal, fungal and parasitic) and non-infectious (cardiovascular, metabolic, neoplastic and nutritional) conditions. In particular, cats presenting with bilateral ocular disease should always be carefully evaluated for such diseases, starting with a thorough clinical examination. The clinician should be familiar with endemic infectious diseases, but with increased movement of pets throughout the world, cats with non-endemic infections can present after travelling.

**INFECTIOUS DISEASES**

**VIRAL INFECTIONS**

Feline herpesvirus-1 (FHV-1) is a very common pathogen causing both upper respiratory tract and ocular disease. Primary infection commonly causes conjunctivitis (see Figure 1). The virus can replicate in the corneal epithelium, causing dendritic ulceration, which is pathognomonic for FHV-1 infection (see Figure 2).

Recrudescent infection occurs in some latently-infected cats. This presents with milder conjunctivitis, dendritic or geographic corneal ulceration, and stromal keratitis. Ocular disease syndromes associated with FHV-1 infection include ophthalmia neonatorum, symblepharon (see Figure 3), proliferative (eosinophilic) keratitis (see Figure 4), keratoconjunctivitis sicca, corneal sequestration (see Figure 5), anterior uveitis and periocular dermatitis (see Figure 6).

Testing for FHV-1 is controversial as the condition is so widespread that the presence of the agent does not give conclusive evidence of the cause of disease, and many tests don’t distinguish vaccine virus from natural virus. Treatment of conjunctivitis due to FHV-1 infection is usually supportive such
as a lubricating eye gel, ideally containing hyaluronate which helps with comfort and goblet cell deficiency. Occasionally topical treatment causes more stress which is counterintuitive. If secondary bacterial infection or corneal ulceration is present, the use of a topical broad spectrum antibiotic is indicated, such as fusidic acid or chloramphenicol. Topical and systemic antiviral medications may be useful with initial infection when there is accompanying upper respiratory tract disease. Systemic famciclovir has been shown to reduce the severity of clinical signs in cats experimentally infected with FHV-1 at a dose of 90mg/kg q8h (Thomasy et al, 2011), but clinical improvement has been at lower doses. However, there is a concern about resistance developing to the drug, and therefore the recommended dose is 90mg/kg twice daily. Oral L-lysine at 500mg PO BID in adults and 250mg BID in kittens is thought to limit FHV-1 replication as this amino acid reduces the uptake of arginine, which the virus needs in order to replicate. However, there is little evidence of its benefits. There is a recent review of treatment options (Maggs and Thomasy, 2016).

Feline coronavirus can result in feline infectious peritonitis (FIP), and ocular manifestations have been reported in 36% of cats with the non-effusive (dry) form (Andrew, 2000). The most common sign is anterior uveitis, as immune-complex deposition in the iridal blood vessels results in the breakdown of the blood ocular barrier. Typically, there are multiple keratic precipitates with fibrinous exudates in the anterior chamber along with iritis (see Figure 7). Chorioretinitis and vasculitis of the retinal vessels may also be seen. Neurological signs may also be present if there is central nervous system (CNS) involvement. The prognosis is poor but symptomatic ocular treatment for uveitis can improve the condition temporarily. Feline leukaemia virus (FeLV) can affect the pupil, as inflammation or tumour infiltration of autonomic nerves controlling pupil size can result in mydriasis (spastic pupil syndrome), or a D-shaped pupil if one of the two short ciliary nerves is affected. FeLV-induced lymphoma may be evident as a focal or more diffuse swelling of the iris (see Figure 8) or with neoplastic changes in the fundus. The virus can cause anaemia or thrombocytopenia, which can also affect the eyes (see later). It can also cause retinal dysplasia in the case of in utero infection.

Feline immunodeficiency virus (FIV) causes ocular signs in some infected cats. The most common signs are mild chronic conjunctivitis and, in a few cases, anterior uveitis (see Figure 9). Intermediate uveitis (pars planitis) has been associated with FIV infection and presents as an accumulation of white blood cells (mainly plasma cells) in the anterior vitreous (termed ‘snow-banking’). Anisocoria with mydriasis, possibly related to CNS disease, has been reported. FIV-positive cats have a higher rate of B-cell lymphoma, which may occur in the uvea. FIV
infection predisposes cats to opportunistic infections such as Toxoplasma gondii, which may also cause uveitis. Feline calicivirus (FCV) is a common cause of upper respiratory disease. Typical systemic signs of infection include fever, rhinitis, oral mucosal ulcerations and chronic stomatitis. In the past it was thought to be only associated with mild conjunctivitis, but, more recently, it is thought to cause more significant ocular surface disease, especially conjunctival ulceration. Laboratory diagnosis is made by virus isolation or by polymerase chain reaction (PCR). FCV is an ribonucleic acid (RNA) virus, and therefore cannot be effectively treated with antiviral medications that inhibit DNA synthesis, such as those used to treat FHV-1. The use of topical broad spectrum antibiotics is always advisable to reduce complications associated with secondary bacterial infection. Topical or systemic nonsteroidal anti-inflammatory drugs (NSAIDs) could be considered when inflammation is severe or prolonged.

Tora-like virus has been implicated in causing Haw's syndrome. In this condition, bilateral nictitans protrusion occurs, and there may also be symptoms of diarrhoea or gastroenteritis (see Figure 10). It is thought to occur due to a reduction in sympathetic tone. It is self-limiting but may continue for several weeks.

Feline panleucopenia infection, in utero, can result in retinal dysplasia and optic nerve hypoplasia. Affected kittens may also have cerebellar hypoplasia and generalised immunosuppression. Feline poxvirus infection is fairly uncommon, but usually begins by affecting the face and paws before spreading to the rest of the body. Kittens and immuno-compromised animals are most commonly affected.
is no specific treatment and most animals will recover with supportive therapy alone.

BACTERIAL INFECTIONS

Chlamydophila/C felis is an important cause of conjunctivitis in cats, and most typically causes bilateral pronounced chemosis and a mucopurulent or purulent ocular discharge (see Figure 11). Treatment is with oral doxycycline at 10mg/kg once daily for three weeks (and up to six weeks). Doxycycline can cause reflux oesophagitis with resultant stricture formation, and, therefore, water or food should follow tablet administration. It is recommended to treat in-contact cats as it is highly infectious and also to remove a potential latent carrier state as it may be sequestered in the urogenital and gastrointestinal tracts.

Mycoplasma felis has been reported to cause conjunctivitis, chemosis, follicle and pseudomembrane formation, but it has also been isolated from clinically normal cats. Mycoplasma infection may be self-limiting but could be treated with oral doxycycline for three to four weeks.

Bartonella henselaeis is transmitted by fleas and causes cat scratch fever in people. There is some debate about whether it can cause uveitis in cats, but it has been isolated in some cases without being the proven cause of disease (Stiles, 2011). Other ocular signs include blepharitis, conjunctivitis, keratitis, and chorioretinitis. Suggested treatment is with oral doxycycline for several weeks (six to 12 weeks), in combination with an oral fluoroquinolone. Azithromycin has been used but the organism can become resistant to it.

Mycobacteria species infections can cause several different ocular signs. These include blepharitis, conjunctivitis, keratitis and uveitis (see Figure 12). Systemic signs may include bronchopneumonia, pulmonary nodules, fever and cough. Diagnosis can be made from cytological aspirates and impression smears with acid-fast stain. A tissue sample should be divided in four: one sample preserved in formalin for histopathology; one quarter left unfixed for bacterial culture; and two frozen, unfixed samples, which could be sent for further investigation depending on the initial results. PCR can be done on fixed samples. There are zoonotic implications, even with the biopsy samples. Treatment is with surgical removal of small skin nodules and prolonged multiple antibiotic therapy (for six to nine months). There is a better prognosis for feline leprosy but a poor prognosis for tuberculosis and opportunistic (nontuberculous) mycobacterial infections. Euthanasia is sometimes carried out in preference to treatment for public health reasons.
PROTOZOAL INFECTIONS
Toxoplasma gondii can present with systemic signs such as anorexia, fever, hepatitis, myositis, pneumonia, diarrhoea and neurological dysfunction; and with ocular signs such as anterior and/or posterior uveitis. Cats with active ocular disease may have concurrent FIV infection. Diagnosis is made by serology, and treatment includes topical and oral steroids along with oral clindamycin (25mg/kg every 12 hours for 21-30 days). Uveitis may become recurrent.

Leishmania infection in cats is uncommon, but has been reported in Portugal, Spain, Italy, France, Greece, Israel, Palestine and Brazil. Ocular signs have been reported in one third of affected cats and can include blepharitis, conjunctivitis and anterior uveitis progressing to panophthalmitis (Pennisi et al, 2015). Treatment is with systemic pentavalent antimonials, such as allopurinol (10-20mg/kg once or twice daily) long-term.

FUNGAL INFECTIONS
Fungal infections are not very common in cats in Europe, and are more common in immunosuppressed individuals. Cryptococcus is the most commonly reported infection and it can cause choriorretinitis with granulomatous inflammation, anterior uveitis, retinal detachment and optic neuritis. Aspergillosis, blastomycosis, histoplasmosis and coccidiomycosis can cause similar choriorretinal lesions. Cytology or histopathology samples are used to diagnose the mycoses. Antifungal therapy can be achieved with systemic amphotericin B, ketoconazole, fluconazole or itraconazole, which are fungistatic rather than fungicidal.

PARASITIC INFECTIONS
Feline demodecosis is uncommon systemic skin condition that may be caused by infection with Demodex cati or Demodex gatoi. Localised periorcular demodecosis can occur and is usually self-limiting. If treatment is necessary, lime sulphur or amitraz solution can be carefully applied to the eyelids, avoiding any contact with the ocular surface. Feline scabies is caused by Notoedres cati and this is also uncommon. If the mite is identified in a skin scrape from the affected eyelid, treatment with topical selamectin is advised. Dermatophytosis causes facial and periorcular alopecia, folliculitis and ulceration (see Figure 13).

NON-INFECTIOUS DISEASES
CARDIOVASCULAR DISEASES
With many of these conditions, successful treatment of any identifiable underlying cause is associated with resolution of the ocular signs.

Systemic hypertension is one of the most common causes of blindness and of retinal detachment in geriatric cats. It may be idiopathic, or secondary to chronic kidney disease, hyperthyroidism or hyperaldosteronism (Conn’s syndrome). Ventricular hypertrophy may be present, but more likely as a result of, rather than a cause of, systemic hypertension. Sustained systolic blood pressure above 170mmHg compromises vascular integrity causing ischaemic necrosis and results in increased vascular permeability. Ocular symptoms include blindness, hyphaema, multiple serous bullous retinal detachment with intra- and pre-retinal hemorrhages and vitreal hemorrhage (see Figures 14 and 15). Treatment of systemic hypertension involves treatment of the primary cause, if identified, as well as antihypertensive medications. Amlodipine is a calcium channel blocker (CCB) and is considered the treatment of choice at a dose of 0.625-1.25mg orally once daily (Elliott et al, 2001). An angiotensin converting enzyme (ACE) inhibitor, such as benazepril, or angiotensin-receptor blocker (ARB,) such as telmisartan, may be added if there is inadequate response to treatment. Lowering the blood pressure usually leads to retinal reattachment, with the chance of some vision recovery if the
FeLV infection has reduced because of vaccination, yet the incidence of lymphoma in older cats is increasing. Ocular signs include uveitis, and there may be fleshy pink intraocular masses (see Figure 17). Secondary glaucoma is a common complication due to obstruction of the aqueous humour outflow pathways. Aquouecentesis may be considered for cytology of aqueous fluid aspirates as the tumour is exfoliative and therefore, relatively easy to detect (Linn-Pearl et al, 2015). Ocular signs may precede systemic signs. Metastasis of carcinomas is also seen regularly in cats. Angioinvasive pulmonary carcinoma can metastasise to the eye, skeletal muscle and bone (it is sometimes referred to as ‘feline lung-digit syndrome’). In the eye, it causes quite a characteristic ischaemic chorioretinopathy, with multiple wedge-shaped tan-coloured areas (Goldfinch & Argyle, 2012). Other rare metastatic tumours to the eye include mammary and intrauterine adenocarcinoma, haemangioma and squamous cell carcinoma (SCC). As already mentioned, multiple myeloma causes ocular signs due to hyperviscosity syndrome.

NUTRITIONAL DISEASES

Taurine deficiency is the most common nutritional deficiency to cause ocular disease, manifesting as feline central retinal degeneration. Taurine is an essential amino acid in the cat and a dietary intake of at least 500ppm is required to prevent retinal and cardiac disease – where taurine levels and requirements are highest. Deficiency causes retinal degeneration that begins as a dull, granular appearance to the area centralis region, which then develops into a hyperreflective area dorsolateral (see Figure 18), and later, dorsomedial to the optic nerve head, which gradually progresses to an overall diffuse retinal degeneration and poor vision. Plasma taurine concentrations can be measured and values less than 40nmol/ml are considered as diagnostic of deficiency. With adequate dietary supplementation, the progression of the disease can be halted, but the pre-existing signs cannot be reversed. The heart should also be evaluated. Thiamine deficiency is uncommon although can arise in anorexic cats or those fed exclusively on raw fish-based diets. It causes neuro-ophthalmic abnormalities along with ataxia, cervical ventroflexion and seizures. Mydriasis, papilloedema and neovascularisation of the optic nerve head have been reported. Serum thiamine concentration can be measured, and supplementation of deficient cats with a vitamin B complex containing thiamine can improve clinical signs.

CONCLUSION

Being aware of a wide variety of systemic conditions that can affect the eye is important. The next step is to apply that knowledge with a logical approach, pulling it all together to reach a list of differential diagnoses for the presenting signs such as periocular dermatitis, uveitis and retinal haemorrhages.

FURTHER READING

Maggs DJ, Thomasy SM. A review of antiviral drugs and other compounds with activity against feline herpesvirus type 1. Veterinary Ophthalmology 2016
Stiles J. Bartonellosis in cats: a role in uveitis? Veterinary Ophthalmology 2011; 14: 9-14

1. OCULAR SIGNS OF THIAMINE DEFICIENCY INCLUDE:
A A dull, granular appearance to the area centralis region of the retina
B Uveitis
C Mydriasis and neovascularisation of the optic nerve head
D Blindness

2. AQUEOCENTESIS IS A USEFUL TEST FOR THE DIAGNOSIS OF:
A Lymphoma
B Mycobacterial uveitis
C FIP
D Leishmaniasis

3. EOSINOPHILIC (PROLIFERATIVE) KERATITIS IS SOMETIMES ASSOCIATED WITH INFECTION WITH:
A FIV
B FeLV
C FIP
D FHV-1

4. BLEPHARITIS MAY BE A SIGN OF SYSTEMIC INFECTION WITH:
A Mycobacteria spp
B Toxoplasma gondii
C Feline panleucopenia virus
D Feline calicivirus

5. THE MOST COMMON OCULAR SIGN OF FIP IS:
A Blepharitis
B Conjunctivitis
C Uveitis
D Retinal detachment

6. THE MOST COMMON CAUSE OF RETINAL DETACHMENT IN OLDER CATS IS:
A Anaemic retinopathy
B Systemic hypertension
C Hyperlipidaemia
D Thrombocytopenia

7. OCULAR SIGNS OF DYSAUTONOMIA INCLUDE:
A Miosis
B Epiphora
C Uveitis
D Third eyelid protrusion

8. WHICH OF THE FOLLOWING CONDITIONS HAS NOT BEEN FOUND ASSOCIATED WITH FELINE HERPESVIRUS-1 INFECTIONS?
A Periorbital dermatitis
B Optic neuritis
C Uveitis
D Corneal sequestrum

9. WHICH OF THE FOLLOWING CONDITIONS HAS BEEN FOUND ASSOCIATED WITH FELINE LEUKAEMIA VIRUS INFECTION?
A D-shaped pupil
B Uveitis
C Retinal dysplasia
D Periorbital dermatitis

10. WHICH OF THE FOLLOWING CONDITIONS HAS NOT BEEN FOUND ASSOCIATED WITH FELINE IMMUNODEFICIENCY INFECTION?
A Corneal sequestrum
B Anisocoria with mydriasis
C Uveitis
D Pars planitis

11. WHICH OF THE FOLLOWING CONDITIONS HAS NOT BEEN FOUND ASSOCIATED WITH INTRAOCULAR LYMPHOMA?
A Pars planitis
B Uveitis
C Glaucoma
D Pink iridal masses