

Ocular manifestations of systemic disease in cats

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).

Recrudescence 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



Figure 1: A young kitten with symptoms of cat flu due to FHV-1 infection. Apart from the upper respiratory tract signs, there was conjunctivitis and the left eye had corneal oedema due to a corneal ulcer.



Figure 2: Herpetic keratitis in a five-month-old Domestic shorthair with Rose Bengal positive dendritic ulceration (pathognomonic for FHV-1 infection).

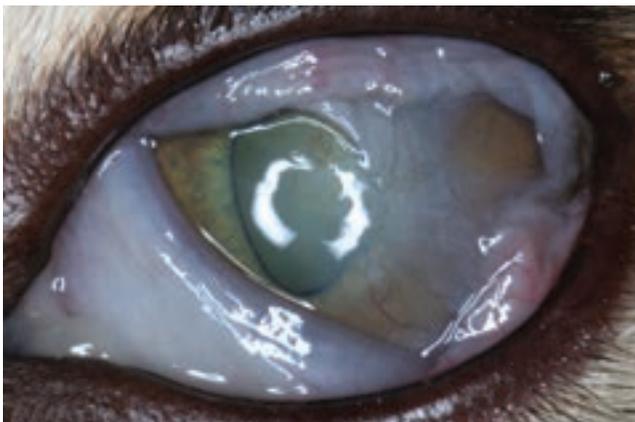


Figure 3: Symblepharon in a two-year-old cat. There is adhesion of conjunctiva to the corneal surface.



Figure 4: Proliferative (eosinophilic) keratitis. There is a thick white plaque on the lateral conjunctiva, lying on a densely neovascularised cornea. Note the single distichium in the upper eyelid.



Figure 5: A focal corneal sequestrum present in the central cornea causing keratitis with neovascularisation, and there is purulent ocular discharge.

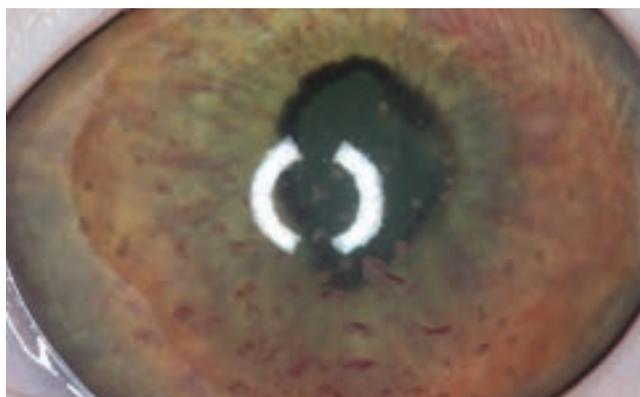


Figure 7: FIP-associated uveitis in a young cat. There are multiple haemorrhagic keratic precipitates, the peripheral iris is thickened and hyperaemic, and there is miosis and ectropion uveae.

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



Figure 6: FHV-1 associated periocular dermatitis bilaterally. Note the left dorsolateral cornea also has a corneal sequestrum.

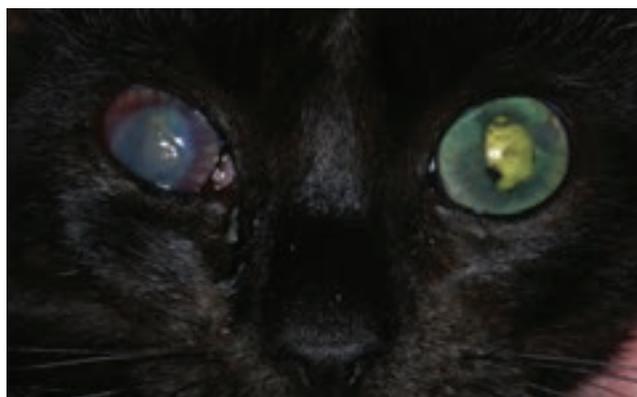


Figure 8: FeLV-associated lymphoma and uveitis. The right eye has corneal ulceration, oedema and neovascularisation. The left eye has cornea cellular infiltrate, miosis and posterior synechiae.

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

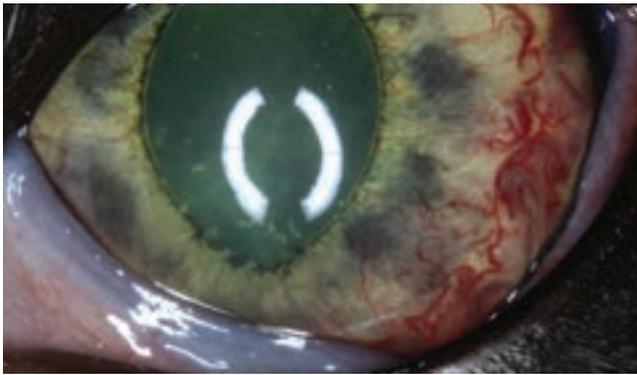


Figure 9: Uveitis in an FIV-positive cat (which may be caused by FIV infection) with conjunctivitis, small keratic precipitates, pronounced iridal hyperaemia and dark nodules within the iris.



Figure 11: Conjunctivitis with chemosis and conjunctival hyperaemia caused by *Chlamydia felis* infection.



Figure 10: Haw's syndrome. Bilateral protrusion of the third eyelid in a cat with diarrhoea.



Figure 12: Mycobacterial blepharitis with thickened and protruding third eyelid and a skin nodule on the upper eyelid.

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 a 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 immunocompromised animals are most commonly affected. There

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Figure 13: Dermatophytosis in the periocular region. *Microsporum canis* was cultured. Courtesy of Rachael Grundon.



Figure 14: Hyphaema due to systemic hypertension. The left eye has blood in the anterior chamber and the right eye has blood in the vitreous chamber. There was bilateral retinal detachment.

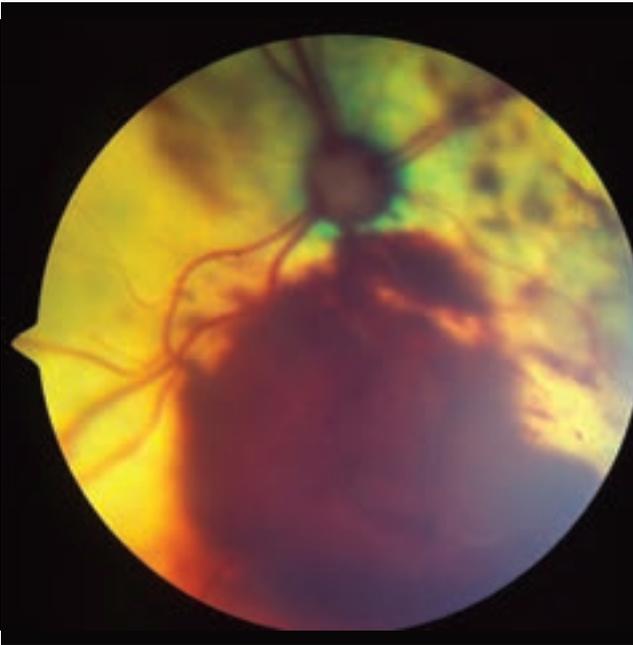


Figure 15: Hypertensive retinopathy. There is ventral subretinal haemorrhage with smaller intraretinal haemorrhages. The blood vessels are out of focus due to retinal oedema.

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*



Figure 16: Dysautonomia. Apart from mydriasis and third eyelid protrusion, there is xerostomia and there was dysphagia.

infection may be self-limiting but could be treated with oral doxycycline for three to four weeks.

Bartonella henselae 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.



Figure 17. Lymphoma in the left eye causing gross thickening and neovascularisation of the iris. Courtesy of James Oliver.

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 chorioretinitis with granulomatous inflammation, anterior uveitis, retinal detachment and optic neuritis. Aspergillosis, blastomycosis, histoplasmosis and coccidiomycosis can cause similar chorioretinal 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 demodicosis is uncommon systemic skin condition that may be caused by infection with *Demodex cati* or *Demodex gatoi*. Localised periocular demodicosis 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 periocular alopecia, folliculitis and ulceration (see Figure 13).

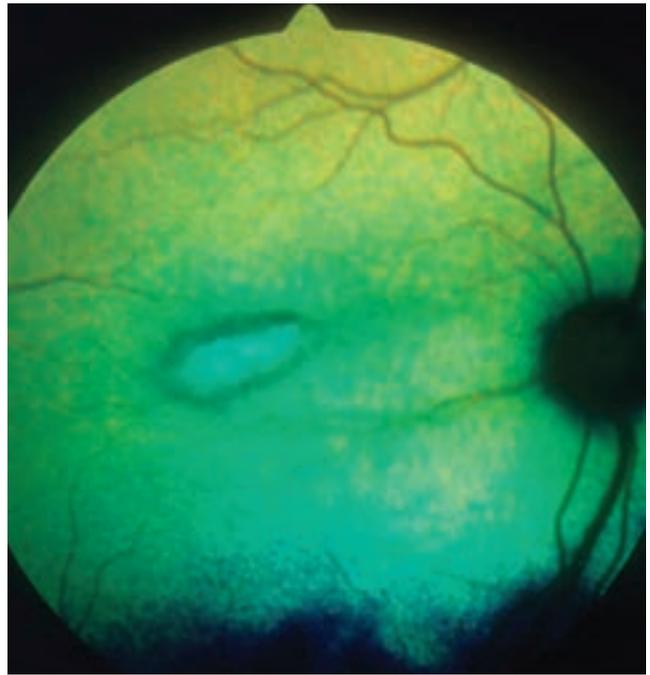


Figure 18: Taurine deficiency retinopathy (feline central retinal degeneration). A well-defined region of tapetal hyperreflectivity is present within the area centralis, dorsolateral to the optic nerve head. Courtesy of Animal Health Trust.

Microsporium canis is the most commonly identified pathogen on fungal culture (~98%). Treatment involves clipping the periocular hair, systemic itraconazole, or careful application of topical enilconazole or miconazole solutions.

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

condition is not longstanding.

Anaemia, when profound, can cause pale, narrowed retinal vasculature and, less commonly, retinal haemorrhage. The most common cause of, anaemia is inflammatory disease, caused by a variety of chronic infections, inflammation and neoplasia. Aplastic anaemia can be caused by infections with FIV, FeLV, feline infectious peritonitis (FIP), toxoplasmosis, ehrlichiosis, parvovirus. It can also arise due to chronic kidney disease and starvation. Thrombocytopenia or thrombocytopathy are not very common in cats, but may be associated with FIV, FeLV and neoplasia. It may present with petechiae/small haemorrhages of the conjunctiva or of the retina, with hyphaema in severe cases.

Hyperviscosity syndrome occurs when the serum protein content is very high. It is most commonly associated with neoplasia such as multiple myeloma, lymphoma, chronic lymphocytic leukemia or plasmacytoma. It can also arise with FIP. Ocular symptoms include dilated and congested tortuous retinal vessels, bullous retinal detachment and hyphaema. Diagnosis is achieved by measuring serum viscosity and protein electrophoresis. Hyperlipidaemia occurs when there are elevated fasting serum triglycerides or cholesterol. The lipoproteins may be visible within the retinal vessels which are white in colour and appear wider than normal. It is most commonly associated with prolonged oestrogenic acetate or corticosteroid treatment but may also occur with diabetes mellitus and secondary hyperlipidaemia.

METABOLIC DISEASES

Diabetes mellitus rarely causes cataracts in cats because of a very low activity of aldose reductase in the feline lens. Diabetic retinopathy is also very uncommon, with some reported cases possibly due to undiagnosed systemic hypertension. Corneal sensitivity can be reduced, which may lead to impaired corneal healing and a predisposition for corneal ulcer formation. Tear-film breakup time can be lower in diabetic cats, and qualitative tear-film deficiency could lead to premature evaporation of the tear film and further confound corneal healing.

Hyperthyroidism can cause systemic hypertension, which can present with retinopathy, as already discussed.

Dysautonomia (Key-Gaskell syndrome) arises from widespread parasympathetic and sympathetic dysfunction, including the supply to the eye and adnexa. Systemic signs include dehydration, xerostomia, urinary retention and gastrointestinal signs including constipation. Ocular signs are bilateral and include unresponsive mydriasis, reduced tear production and nictitans protrusion (see Figure 16). The cause of feline dysautonomia is unknown. Treatment involves supportive therapy but the prognosis is poor.

NEOPLASIC DISEASES

Lymphoma is the most common metastatic tumour to the eye. It may be associated with FIV or FeLV infection. FeLV can directly induce neoplasia whereas FIV indirectly results in neoplasia due to its immunosuppressive effects, with co-infection further increasing the risk. The incidence of 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. Aqueocentesis 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

Feline Ophthalmology – The Manual. 2015. Natasha Mitchell and James Oliver. Grupo Asis. ISBN 978-84-16315-11-6

BSAVA Manual of Canine and Feline Ophthalmology 2014. Third edition. Edited by David Gould and Gillian McLellan. ISBN 978-1-905319-42-8

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READER QUESTIONS AND ANSWERS

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

ANSWERS: 1: C; 2: A; 3: D; 4: A; 5: C; 6: B; 7: D; 8: B; 9: D; 10: A; 11: A