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Ocular Manifestations of Systemic Disease in Cats

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Systemic feline diseases (parasitic, bacterial, fungal, viral, neoplastic, metabolic, vascular, and immune-mediated) are often associated with ocular symptoms. An ocular examination is an important diagnostic tool and should be part of any physical examination. Conversely, cats afflicted with systemic disease require periodic ocular examinations for prognostic information and to prevent vision threatening complications. Typical feline systemic diseases encountered by the practicing clinician are presented with their commonly associated ocular signs.
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Ocular examination is an essential part of a complete physical examination that can aid in the systemic diagnosis of the veterinary patient. The transparent media of the eye can act as a diagnostic window for the clinician. Both the central nervous system and peripheral vasculature can be directly visualized through the clear cornea and lens. Changes in either system can manifest as anomalies within the ocular fundus.[1] The rate of blood flow to the eye is also extremely high[2] which increases the likelihood that the uveal vasculature will come in contact with, and possibly trap, circulating infectious agents and/or metastatic neoplastic cells.[1,3] Ocular immune responses are characterized by a suppression of delayed type hypersensitivity reactions with minimal production of complement-fixating antibodies.[4] This type of response prevents nonspecific ocular tissue damage, but allows various systemic pathogens (fungi, parasites, intracellular bacteria) to evade immunity and persist within the eye.[4] In addition, the unique anatomic and biochemical characteristics of the lens and cornea increase their susceptibility to metabolic disease.[5,6]

This paper is intended to review the ocular manifestations of systemic (parasitic, bacterial, fungal, viral, neoplastic, metabolic, vascular, and immune-mediated) diseases in the feline. The reader is encouraged to read other comprehensive reviews[7-11] of these diseases.

Parasitic Disease

Toxoplasmosis is caused by the coccidial protozoa, *Toxoplasma gondii*, in which the feline is the definitive host.[12] Exposure to *T. gondii* is congenital, via ingestion of sporulated oocysts (sporozytes) within cat feces, or via ingestion of tissue cysts (bradyzoites) within infected carrion.[12] In primary toxoplasmosis, tachyzoites disseminate and replicate within the central nervous system, skeletal muscles, visceral organs, and the eye.[13] Chorioretinitis is the most common ocular manifestation.[7,13] Multifocal gray (hyporeflective) lesions in the tapetal fundus and fluffy white gray lesions in the nontapetal fundus are typically found.[14] Other ocular manifestations include optic neuritis and anterior uveitis.[7,13] Cellular necrosis of ocular tissue may result from intracellular growth of *T. gondii*.[7,15] The role of toxoplasmosis in feline anterior uveitis is not completely understood (Fig. 1).[14]

The parasitic larval stages of dipterous flies (*Cuterebra*) have also been found within the feline orbit (ophthalmomyiasis externa) and globe (ophthalmomyiasis interna).[16] Ocular abnormalities include uveitis, corneal edema, multiple curvilinear tracks within the tapetal and nontapetal fundi, retinal detachment, intraocular hemorrhage, and low grade chorioretinitis.[17,18] *Cuterebra* larvae can also directly penetrate feline sclera causing severe uveitis, fibrin clot formation, and blindness.[16,17] Other neurological signs and blindness can be caused by intracranial migration of these larvae.[19]

Feline demodicosis is caused by parasitic *Demodex cati* and other unnamed *Demodex* sp.[20] This rare disease affects the feline eyelid, periocular area, head, and neck.[21] Variably pruritic lesions with patchy erythema, crusting, scaling, and alopecia are found.[22] Generalized demodicosis is often found in Siamese and Burmese breeds associated with diabetes mellitus, feline leukemia, systemic lupus erythematous, hyperadrenocorticism, or feline immunodeficiency.[23]

Bacterial Disease

Bartonella are fastidious, flea-transmitted, hemotropic, small, curved, Gram-negative bacteria.[24] Human "cat scratch fever" is caused by *B. henselae*.[25] Feline infection with *B. henselae* is

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Figure 1 Toxoplasmosis-induced anterior uveitis in a domestic short hair. There is neovascularization and multifocal inflammatory nodules within the iris. (Image courtesy of Dr. J. Sapienza.)

extremely common. Although 55 to 81% of cats are seropositive, clinical disease is rarely reported.[26] A solitary case of feline unilateral uveitis associated with intraocular antibodies to *Bartonella* has been reported. This cat's uveitis was unaffected by topical or oral steroids, but did respond to oral doxycycline.[26]

Mycobacteria are aerobic, nonspore forming, nonmotile, and acid fast-staining bacteria.[27] Generally mycobacteria cause internal tubercular granulomas (tuberculosis), localized cutaneous nodules (leprosy), or spreading subcutaneous inflammation.[27] In the past, choroidal hemorrhages, subretinal granulomas, and retinal detachments were commonly associated with feline tuberculosis caused by *Mycobacterium bovis*.[28] Today's pasteurization of milk and the culling of *M. bovis* infected cattle have reduced the incidence of feline tuberculosis in the United States. Recently, ocular granulomatous lesions were found in a German cat infected with *M. simiae*. These lesions resolved with antibiotic (enrofloxacin, rifampicin, clarithromycin) therapy.[29]

Fungal Disease

Systemic fungal infections are uncommon in cats.[8,30] The dimorphic saprophytic fungi (*Cryptococcus*, *Histoplasma*, *Blastomyces*, and *Coccidioides*) can act as systemic pathogens.[30] The infective route for these fungi is generally inhalation, but they can also be ingested or inoculated.[30] Fungi can reach the eye hematogenously and then lodge within uveal vessels.[8] It is believed that the fungi must be present within the eye to cause uveitis.[8]

Cryptococcosis occurs worldwide and is the most common systemic fungal infection of cats.[31,32] *Cryptococcus neoformans* is a saprophytic, round, yeast-like fungus (3.5-7 μm in diameter) with the ability to form large capsules.[33] The fungi are commonly found in pigeon droppings, accounting for the high prevalence of cryptococcosis in urban settings.[33]

The mode of *Cryptococcus* transmission is unclear but may rely on inhalation of aerosolized basidiospores.[31,33] These spores can then erode the cribriform plate resulting in meningitis.[34] Involvement of the optic nerves results in cryptococcal optic neuritis.[31] Clinical signs of optic neuritis include blindness, or visual problems with either slow pupillary light responses or fixed dilated pupils.[8,30] Cats with optic neuritis have inflamed hyperemic swollen optic nerve heads. The swollen nerves can be associated with increased tortuosity and congestion of the retinal vessels, peripapillary hemorrhages, and/or peripapillary retinal detachments.[31]

The most frequent ocular manifestation of cryptococcosis is chorioretinitis.[35] *Cryptococcus* spores spread to the eye from the nasal cavity via hemological dissemination.[36] The most common ocular lesions are multiple, small, irregular, gray to black, punctate lesions surrounded by an abnormal fundus (Fig. 2). In severe cases, these fundic lesions can progress to retinal detachment.[35] Anterior uveitis, secondary to lesions of the posterior segment, can also occur.[8] Rarer ocular disorders include exophthalmos secondary to retrobulbar abscessation,[22] Horner's syndrome secondary to an aural mass,[37] formation of an anterior chamber granuloma,[38] conjunctival swelling and thickening (or protrusion) of the nictitating membranes,[39] and ocular discharge.[40]

Histoplasmosis is the second most common systemic fungal infection of cats.[30] The etiological agent of American histoplasmosis is the soil-borne, dimorphic fungus *Histoplasma capsulatum*.[41] Most clinical cases occur in the Ohio, Missouri, and Mississippi river valleys and Texas.[42]

The most common ocular manifestation of feline systemic histoplasmosis is granulomatous chorioretinitis.[43,44] Other ocular associations include discharge, blepharospasm, conjunctivitis, chemosis, retinal detachment, and secondary glaucoma.[45] Conjunctival, mucus membrane, and skin granulomas may also develop (Fig. 3).[3]

Blastomycosis is caused by the dimorphic fungus *Blastomyces dermatitidis*.[46] It is found in the Ohio, Missouri, and Mississippi river valleys, as well as Virginia, the Carolinas, and Georgia.[46] A severe pyogranulomatous uveitis is most

Figure 2 Cryptococcosis in the feline fundus. There are multiple small gray lesions (fungal foci surrounded by edema) in the tapetal fundus. (Image courtesy of Dr. D. Wilkie.)

Figure 3 Systemic histoplasmosis in a feline. Hyphema is present in the left eye and a uveitis-induced cataract is present in the right eye. Yellow-pink nodular masses in the left conjunctival sac are histoplasmosis-induced granulomas.

often associated with feline blastomycosis.[46-49] Other ocular manifestations include blindness, chorioretinitis, and anterior uveitis.[49] Blindness can result from ocular or central nervous system involvement. The posterior segment of the eye is more commonly affected than the anterior segment.[49]

Coccidiomycosis is found only in the Southwestern United States, especially in Arizona.[50] In a retrospective study of 48 cats with systemic coccidiomycosis, 6 cats had ocular lesions.[50] The most common ocular manifestation is retinal detachment with concurrent uveitis and iritis. One isolated case of feline coccidiomycosis manifested as an intraocular granuloma with a lens capsule rupture.[51]

The most common feline fungal skin infection (dermatophytosis) affecting the eyelid is caused by *Microsporium canis*.[52] Feline dermatophytosis presents as one or more irregular areas of alopecia with or without scaling.[53] Other lesions occur on the head, pinnae, and paws. Young cats (<1 year of age) and longhaired Persians and Himalayans are predisposed to contracting dermatophytosis.[52]

Viral Disease

The feline immunodeficiency virus (FIV) is most likely transmitted by bites between animals.[54,55] Feral colonies and roaming tomcats show the highest prevalence of infection.[56] The hemological hallmark of FIV infection is a progressive depletion of $CD4^+$ helper T cells, and in advanced stages a loss of $CD8^+$ cells.[57]

The FIV causes ophthalmic disease through direct viral damage of ocular tissues, by initiating secondary immune phenomena, and/or by promoting opportunistic eye infections.[57] The most common ocular manifestations of FIV include anterior uveitis, glaucoma, lens luxation, and pars planitis.[58,59] Pars planitis is characterized by white punctate infiltrates in the anterior vitreous. Histologically, FIV-induced anterior uveitis is characterized by diffuse lymphocytic and/or plasmacytic infiltrates.[57] Inflammation in response to FIV is more commonly associated with the anterior, rather than the posterior ocular segment.[9] Coinfection with FIV also exacerbates ocular manifestations of other pathogens such as *T. gondii*.[60]

Feline leukemia virus (FeLV) is transmitted primarily through saliva where its concentration surpasses that of serum.[61] Viremic cats live and shed virus for several years.[62] Infection eventually leads to malignant transformation or cytopathic depletion of specific lymphocytic/hematopoietic cell populations.[61]

Infection with FeLV can cause infiltrative uveal, conjunctival, orbital, and/or corneal lymphosarcoma.[61] Restricted iris motility is associated with invasion of the anterior uvea by this tumor.[9] Alternatively, dyscoria or anisocoria can stem from the neurological effects of FeLV on the short ciliary nerves.[63,64] In addition, FeLV-induced anemia may lead to secondary retinal hemorrhages.[64,65]

Feline infectious peritonitis (FIP) is a mutated form of the feline corona virus (FECV).[66] This virus systemically replicates within macrophages.[67] The resultant viremia deposits virus-laden macrophages within the endothelium of small blood vessels.[68] In the absence of a strong T cell-mediated immune response, a profound complement-mediated pyogranulomatous vasculitis (effusive FIP) develops. Limited cell-mediated responses slow FIP replication and granuloma formation (noneffusive FIP).[68] Ocular manifestations of FIP are more common in this noneffusive form.[35,69]

Bilateral granulomatous anterior uveitis, accompanied by chorioretinitis, is commonly associated with FIP infection.[35] Virus-laden macrophages damage uveal vasculature allowing the exudation of white blood cells, red blood cells, and/or fibrin into the anterior chamber.[69] Frequently large keratic precipitates and a fibrinous exudate are found within the anterior chamber.[70] Virally induced vasculitis causes perivascular cuffing of the retinal vessels, retinal detachment, and retinal hemorrhage.[71]

Feline herpesvirus-1 (FHV-1) primarily replicates within the conjunctival, nasal, and pharyngeal epithelium.[72] The virus is cytopathic during its replication, destroying the surface epithelia of the conjunctiva, cornea, and nasal passages.[72,73] Primary infection of kittens is associated with upper respiratory and ocular disease.[74] Dendritic ulcers of the corneal epithelium are pathognomonic for FHV-1 infection (Fig.

Figure 4 Herpesvirus-induced corneal epithelial dendritic ulcers (stained with fluorescein) surrounded by superficial neovascularization and edema. Corneal epithelial dendritic ulcers are considered pathognomonic for the feline herpesvirus.

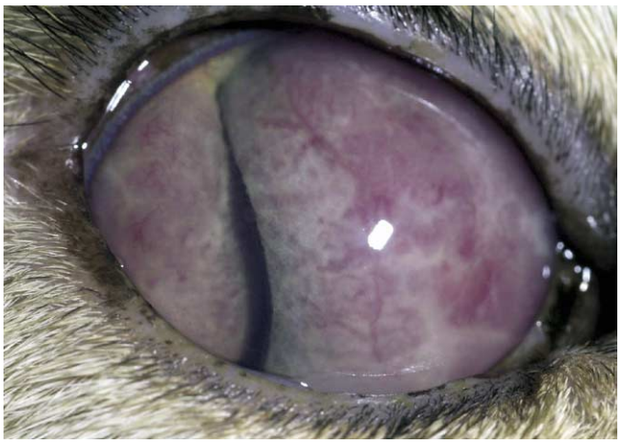

Figure 5 Feline eye with anterior uveal infiltrative lymphosarcoma. The iris is infiltrated and distorted by two pink to red (hyperemic) nodular masses. These masses extend to fill the anterior chamber. (Image courtesy of Dr. A. Metzler.)

4).[75] Secondary bacterial infections within these ulcers may lead to ocular rupture and blindness.[72] The virus can also damage lacrimal duct epithelium resulting in a permanent decrease in tear production.[76]

It is estimated that 80% of cats will become latently infected with FHV-1 and nearly half will experience spontaneous reactivation and shedding of the virus.[76] Reactivation of FHV-1 occurs sporadically and is associated with conjunctivitis, recurrent corneal ulceration, corneal sequestra, stromal keratitis, eosinophilic keratitis, and ulcerative eosinophilic dermatitis.[77-81] Herpesvirus is associated with feline uveitis. Both intraocular anti-FHV-1 antibody production and aqueous humor FHV-1 DNA have been found in cases of feline uveitis not associated with other infectious agents.[82]

Neoplastic Disease

Multicentric lymphoma is the most common metastatic tumor of the feline eye, and ocular anomalies can present the first signs of systemic lymphoma.[10] Typical ocular presentation is a nodular iridal mass (Fig. 5).[10] Other manifestations of ocular lymphoma include uveitis with or without glaucoma, and keratitis.[10] Additional feline tumors that are known to metastasize to the eye include fibrosarcoma,[83] squamous cell carcinoma,[84] mammary adenocarcinoma,[85] uterine adenosarcoma,[86] and adenocarcinomas of undetermined origin.[87]

Pulmonary carcinoma is unusual in its capacity to colonize the vascular endothelium of choroidal retinal arteries.[88] The resultant nonperfused areas of the retina can be viewed ophthalmoscopically.[88,89] These appear as wedge-shaped tan discolorations of the tapetal fundus, with profoundly attenuated retinal vasculature.[88]

Space-occupying orbital masses are usually manifested as exophthalmia.[90] Feline orbital fibrosarcoma is unusual in causing enophthalmos. The tumor causes pressure necrosis of supportive orbital fat.[91] The most common orbital neoplasia of the cat is squamous cell carcinoma invading from periocular areas.[92] Other feline orbital neoplasms include zygomatic osteoma, parosteal osteoma, osteosarcoma, fibrosarcoma, undifferentiated sarcoma, and rhabdomyosarcoma.[92]

Brain tumors can present a variety of ophthalmic signs including blindness, abnormal pupillary light reflexes, changes in vestibular ocular reflexes, and irregular ocular alignment.[63] Acute visual loss can present as the sole sign of a tumor within the optic chiasm of the rostral and cranial brain fossa.[93]

Vascular Disease

The correlation between systemic hypertension and retinal lesions caused by choroidal injury is well established in the feline.[94] Causes of feline hypertension include renal disease, hyperthyroidism, diabetes mellitus, heart disease, anemia, hyperadrenocorticism, hyperaldosteronism, pheochromocytomic cancer, and primary hypertension.[95]

Retinal, choroidal, and optic nerve blood flow is maintained by alternating vascular resistance within precapillary arterioles.[94] Increased blood pressure can cause a breakdown of this autoregulation. Small focal intraretinal periarterial transudates form at sights of collapse and leakage of retinal arterioles. Over time, these areas coalesce and enlarged regions of intraretinal edema appear. As the hypertensive retinopathy advances, a severe disruption of pigmented retinal epithelium leads to subretinal edema, serous retinal detachment, and hemorrhage (Fig. 6).[94] Other associated ocular changes include a narrowing and increased tortuosity of retinal arterioles, papilledema, and optic nerve atrophy.[11,94]

Systolic blood pressures greater then 160[96-98] or 170 mm Hg[95] have been considered diagnostic for hypertension. However, not all cats that have an elevated systolic blood pressure will have signs of hypertensive retinopathy. Monkeys with acute spikes in blood pressure exhibit severe hypertensive retinopathy, whereas those with gradual rises in blood pressure to similar levels do not.[99] Feline vasculature

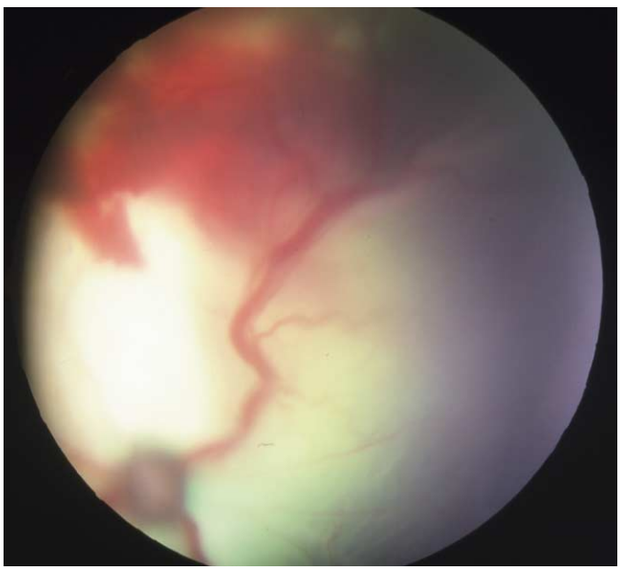

Figure 6 Fundic image of feline hypertensive retinopathy. There is a large subretinal hemorrhage and retinal detachment in the dorsal temporal tapetum. There is a perivascular transudate and increased tortuosity of the retinal vessels. (Image courtesy of Dr. J. Bowersox.)

can similarly accommodate to this gradual increase in blood pressure.[94]

Hyperviscosity syndrome occurs when plasma proteins increase serum viscosity leading to vascular stasis, infarction, thrombosis, tissue injury, and rupture of small blood vessels.[96] Increases in blood viscosity most often occur secondary to increases in IgM or IgA.[100,101] The most common cause of feline hyperviscosity is therefore multiple myeloma.[102,103] Associated ocular lesions include retinal hemorrhage, dilated and tortuous retinal vasculature, retinal detachment, perivascular edema, papilledema, and retinal degeneration.[96]

Retinal hemorrhages are commonly found in anemic cats.[65] As hemoglobin levels fall below 5 g/dL, the supply of oxygen to the vascular endothelium is severely reduced. Endothelial necrosis leads to vascular fragility and secondary leakage.[65] Common causes of feline anemia include *Hemobartonella felis* infection, thrombocytopenia, autoimmune hemolytic anemia, aplastic anemia, lymphoma, and bleeding duodenal ulceration.[65] Ehrlichiosis has also been suspected as a cause of thrombocytopenia and anemia in the cat.[104,105]

Lipemia retinalis describes excessive lipids (triglycerides and triglyceride-rich lipoproteins) within retinal vessels.[106] Hyperlipidemia may impart a pink milky coloration of the retinal vessels that is most easily seen within the nontapetum.[107] Feline hypertriglyceridemia can be caused by postprandial hyperlipidemia, diabetes mellitus, exogenous steroid administration, megestrol acetate administration, nephrotic syndrome, lipoprotein lipase deficiency, and idiopathic hyperchylomicronemia.[106]

Metabolic Disease

Aldose reductase is involved in the formation of secondary cataracts when glucose levels are elevated by diabetes mellitus.[108] Diabetic cataracts do not develop in older cats as the level of aldose reductase within their lenses is reduced when compared with that of dogs.[6] Younger cats (<4 years of age) have elevated levels of aldose reductase.[6] Diabetes mellitus in younger cats is rarely described, and therefore, diabetic feline cataracts are uncommon.[109] Secondary cataracts do occur in the feline secondary to hypocalcemia. Kittens with hyperparathyroidism and secondary hypercalcemia may develop cataracts.[110,111]

Hyperthyroidism can cause systemic hypertension followed by secondary hypertensive retinopathy.[11,95] However, the occurrence of ophthalmic lesions secondary to feline hyperthyroidism is rare. In a retrospective study of 100 hyperthyroid cats, only 3 had active retinal lesions.[112]

Feline nutritional deficiencies in the amino acid taurine result in retinal atrophy after 23 weeks.[113] Though taurine's role in the preservation of feline retinal function is unknown, it is believed that it is involved in the ion fluctuations of the outer retina.[114] Typical lesions of taurine deficiency begin with a granular appearance of the tapetal fundus. This progresses to a hyper-reflective focus in the area centralis. Subsequently, the nasal area of degeneration expands and extends to both sides of the optic disc. Complete retinal atrophy ensues.[115]

Felines with inherited lysosomal storage disorders lack specific catabolic enzymes causing an abnormal accumulation of complex lipids, glycoproteins, or polysaccharides. Those with feline ophthalmic manifestations include mucopolysaccharidosis I and IV, GM1- and GM2-gangliosidosis, and mannosidosis.[5,116-128] The most common associated ocular abnormality is diffuse corneal granular cloudiness.[129] Other manifestations include dark or pale spots in the tapetal fundus[130] and lenticular vacuoles.[119]

Immune-Mediated Diseases

The most common immune-mediated skin disease affecting the feline eyelid is caused by *Pemphigus foliaceous*.[131] *Pemphigus* antigens are heterogeneous (85-260 kD) proteins present in mammalian and avian skin, and are associated with desmosomal and nondesmosomal cell membranes.[132] Desmosome destruction and the resultant loss of intracellular cohesion lead to acantholysis and blister formation within the epidermis. The disease progresses from the face and ears to the foot pads, and becomes generalized within 6 months.[133] The first lesions are erythematous macules that rapidly progress to pustules and then become dry brown crusts.[131]

Ocular hemorrhaging secondary to immune-mediated anemia or thrombocytopenia is uncommon in cats.[134] Feline immune-mediated anemia is associated with hemobartonellosis[135] or neonatal isoerythrolysis.[136] Pure red cell aplasia of the bone marrow is linked to FeLV infection.[137] In rare cases of feline thrombocytopenia hemorrhaging does not even occur with platelet counts as low as 10,000 uL.[134]

Conclusions

Ocular symptoms may be the first sign of a systemic disease.[10,95] Ophthalmic examination associated with routine physical examination will help diagnose systemic problems. Ophthalmic signs must be considered in relation to history, physical examination, and other clinical symptoms. This will determine appropriate ancillary diagnostic testing.

The most common ocular manifestation of systemic disease encountered by the clinician is uveitis. The reader is referred to excellent reviews of feline uveitis diagnostics for further information,[138-140] as well as the feline uveitis review in this issue.

An early diagnosis of systemic disease prompted by ocular examination can aid in the preservation of vision and life of the veterinary patient.

References

1. Peiffer RL Jr: Ocular manifestations of systemic disease. Part I. Dog and cat, in Gelatt KN (ed): Textbook of Veterinary Ophthalmology (ed 1). Philadelphia, Lea & Febiger, 1981, pp 699-723
2. Cioffi GA, Grandstam E, Alm A: Ocular circulation, in Kaufman PL, Alm A (eds): Adler's Physiology of the Eye (ed 10). St. Louis, MO, Mosby, 2003, pp 747-784
3. Peiffer RL Jr., Belkin PV: Ocular manifestations of disseminated histoplasmosis in a cat. Feline Pract 9:24-29, 1979
4. English RV: Regulation of intraocular immune responses. Prog Vet Comp Ophthalmol 2:41-49, 1992
5. Cork LC, Munnell JF, Lorenz MD: The pathology of feline GM2 gangliosidosis. Am J Pathol 90:723-734, 1978
6. Richter M, Guscetti F, Spiess B: Aldose reductase activity and glucose-related opacities in incubated lenses from dogs and cats. Am J Vet Res 63:1591-1597, 2002
7. Davidson MG: Toxoplasmosis. Vet Clin North Am (Small Anim Pract) 30:1051-1062, 2000

8. Gionfriddo JR: Feline systemic fungal infections. Vet Clin North Am (Small Anim Pract) 30:1029-1050, 2000
9. Willis AM: Feline leukemia virus and feline immunodeficiency virus. Vet Clin North Am (Small Anim Pract) 30:971-986, 2000
10. Corcoran KA, Peiffer RL Jr, Koch SA: Histopathological features of feline ocular lymphosarcoma: 49 cases (1978-1992). Vet Comp Ophthalmol 5:35-41, 1995
11. Henik RA: Diagnosis and treatment of feline systemic hypertension. Comp Cont Ed Pract Vet 19:163-179, 1997
12. Dubey JP: Toxoplasmosis. J Am Vet Med Assoc 205:1593-1598, 1994
13. Dubey JP, Carpenter JL: Histologically confirmed clinical toxoplasmosis in cats: 100 cases (1952-1990). J Am Vet Med Assoc 203:1556-1566, 1993
14. Davidson MG, English RV: Feline ocular toxoplasmosis. Vet Ophthalmol 1:71-80, 1998
15. Davidson MG, Lappin MR, English RV, et al: A feline model of ocular toxoplasmosis. Invest Ophthalmol Vis Sci 34:3653-3660, 1993
16. Harris BP, Miller PE, Bloss JR, et al: Ophthalmomyiasis interna anterior associated with *Cuterebra* spp in a cat. J Am Vet Med Assoc 216:352-355, 2000
17. Johnson BW, Helper LC, Szajerski ME: Intraocular *Cuterebra* in a cat. J Am Vet Med Assoc 193:829-830, 1988
18. Gwin RM, Merideth R, Martin CL: Ophthalmomyiasis interna posterior in two cats and a dog. J Am Anim Hosp Assoc 20:481-486, 1984
19. McKenzie BE, Lyles DI, Clinkscales JA: Intracerebral migration of *Cuterebra* larva in a kitten. J Am Vet Med Assoc 172:173-175, 1978
20. Chesney CJ: Demodicosis in the cat. J Small Anim Pract 30:689, 1989
21. O'Dair HA, Foster AP: Focal and generalized alopecia. Vet Clin North Am (Small Anim Pract) 25:851-870, 1995
22. Medleau L: Demodicosis in cats. J Am Anim Hosp Assoc 24:85, 1988
23. Stogdale L, Moore DJ: Feline demodicosis. J Am Anim Hosp Assoc 18:427, 1982
24. Breitschwerdt EB, Greene CE: Bartonellosis, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 337-343
25. Anderson B, Lu E, Jones D, et al: Characterization of a 17-kilodalton antigen of *Bartonella henselae* reactive with sera from patients with cat scratch disease. J Clin Microbiol 33:2358-2365, 1995
26. Lappin MR, Black JC: *Bartonella* spp infection as a possible cause of uveitis in a cat. J Am Vet Med Assoc 214:1205-1207, 1999
27. Greene CE, Gunn-Moore DA: Mycobacterial infections, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 313-321
28. Formston C: Retinal detachment and bovine tuberculosis in cats. J Small Anim Pract 35:5-8, 1994
29. Dietrich U, Arnold P, Guscetti F, et al: Ocular manifestation of disseminated *Mycobacterium simiae* infection in a cat. J Small Anim Pract 44:121-125, 2003
30. Davies C, Troy GC: Deep mycotic infections in cats. J Am Anim Hosp Assoc 32:380-391, 1996
31. Wilkinson GT: Feline cryptococcosis: A review and seven case reports. J Small Anim Pract 20:749-768, 1979
32. Pentlarge VW, Martin RA: Treatment of cryptococcosis in three cats, using ketoconazole. J Am Vet Med Assoc 188:536-538, 1986
33. Jacobs GJ, Medleu L: Cryptococcosis, in Greene CE (ed): Infectious Diseases of the Dog and Cat, Philadelphia, WB Saunders, 1998, pp 383-390
34. Malik R, Jacobs G, Love DN: Feline cryptococcosis: New perspectives on aetiology, pathogenesis, diagnosis and clinical management, in August JR (ed): Consultations in Feline Internal Medicine (ed 4). Philadelphia, WB Saunders, 2001, pp 39-50
35. Martin CL, Stiles J: Ocular infections, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 658-672
36. Blouin P, Cello RM: Experimental ocular cryptococcosis. Preliminary studies in cats and mice. Invest Ophthalmol Vis Sci 19:21-30, 1980
37. Noxon JO, Monroe WE, Chinn DR: Ketoconazole therapy in canine and feline cryptococcosis. J Am Anim Hosp Assoc 22:179-183, 1986
38. Gwin RM, Gelatt KN, Hardy R: Ocular cryptococcosis in a cat. J Am Anim Hosp Assoc 13:680-684, 1981
39. Martin CL, Stiles J, Willis M: Ocular adnexal cryptococcosis in a cat. Vet Comp Ophthalmol 6:225-229, 1996
40. Rosenthal JJ, Heidgerd J, Peiffer RL Jr: Ocular and systemic cryptococcosis in a cat. J Am Anim Hosp Assoc 17:307-310, 1981
41. Wolf AM. Histoplasmosis, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 378-383
42. Wolf AM, Belden MN: Feline histoplasmosis: A literature review and retrospective of 20 new cases. J Am Anim Hosp Assoc 20:995-998, 1984
43. Mahaffey E, Gabbert N, Johnson D, et al: Disseminated histoplasmosis in three cats. J Am Anim Hosp Assoc 13:46-51, 1977
44. Gwin RM, Makley TA Jr, Wyman M, et al: Multifocal ocular histoplasmosis in a dog and cat. J Am Vet Med Assoc 176:638-642, 1980
45. Clinkenbeard KD, Wolf AM, Cowell RL, et al: Feline disseminated histoplasmosis. Comp Cont Ed Pract Vet 11:1223-1233, 1989
46. Legendre AM: Blastomycosis, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 371-377
47. Alden CL, Mohan R: Ocular blastomycosis in a cat. J Am Vet Med Assoc 164:527-528, 1974
48. Nasisse MP, van Ee RT, Wright B: Ocular changes in a cat with disseminated blastomycosis. J Am Vet Med Assoc 187:629-631, 1985
49. Miller PE, Miller LM, Schoster JV: Feline blastomycosis: A report of three cases and a literature review (1961 to 1988). J Am Anim Hosp Assoc 26:416-424, 1990
50. Greene RT, Troy GC: Coccidioidomycosis in 48 cats: A retrospective study (1984-1993). J Vet Intern Med 9:86-91, 1995
51. Angell JA, Shively JN, Merideth RE: Ocular coccidiomycosis in a cat. J Am Vet Med Assoc 187:167-169, 1985
52. Moriello KA, DeBoer DJ: Feline dermatophytosis. Recent advances and recommendations for therapy. Vet Clin North Am (Small Anim Pract) 25:901-921, 1995
53. Scott DW, Miller WH, Griffin CE: Fungal skin disease, in Scott DW, Miller WH, Griffin CE (eds): Muller and Kirk's Small Animal Dermatology (ed 5). Philadelphia, WB Saunders, 1995, pp 329-391
54. Pedersen NC, Yamamoto JK, Ishida T, et al: Feline immunodeficiency virus infection. Vet Immunol Immunopathol 21:111-129, 1989
55. Yamamoto JK, Sparger E, Ho EW, et al: Pathogenesis of experimentally induced feline immunodeficiency virus infection in cats. Am J Vet Res 49:1246-1258, 1988
56. Ishida T, Washizu T, Toriyabe K, et al: Feline immunodeficiency virus infection in cats of Japan. J Am Vet Med Assoc 194:221-225, 1989
57. English RV, Nelson P, Johnson CM, et al: Development of clinical disease in cats experimentally infected with feline immunodeficiency virus. J Infect Dis 170:543-552, 1994
58. English RV, Davidson MG, Nasisse MP, et al: Intraocular disease associated with feline immunodeficiency virus infection in cats. J Am Vet Med Assoc 196:1116-1119, 1990
59. Olivero DK, Riis RC, Dutton AG, et al: Feline lens displacement. A retrospective analysis of 345 cases. Prog Vet Comp Ophthalmol 1:239-244, 1991
60. Davidson MG, Rottman JB, English RV, et al: Feline immunodeficiency virus predisposes cats to acute generalized toxoplasmosis. Am J Pathol 143:1486-1497, 1993
61. Hardy WD: Hematopoietic tumors of cats. J Am Anim Hosp Assoc 17:921-940, 1981
62. Cotter SM: Feline viral neoplasia, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 71-83
63. Scagliotti RH: Comparative neuro-ophthalmology, in Gelatt KN (ed): Veterinary Ophthalmology (ed 3). Baltimore, Lippincott Williams & Wilkins, 1999, pp 1307-1400
64. Brightman AH 2nd, Ogilvie GK, Tompkins M: Ocular disease in FeLV-positive cats: 11 cases (1981-1986). J Am Vet Med Assoc 198: 1049-1051, 1991
65. Fischer CA: Retinopathy in anemic cats. J Am Vet Med Assoc 156: 1415-1427, 1970
66. Poland AM, Vennema H, Foley JE, et al: Two related strains of feline infectious peritonitis virus isolated from immunocompromised cats infected with a feline enteric coronavirus. J Clin Microbiol 34:3180-3184, 1996
67. Addie DD, Jarrett O: Feline coronavirus infection, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 58-67

68. McReynolds C, Macy D: Feline infectious peritonitis. Part 1. Etiology and diagnosis. Compend Cont Educ Pract Vet 19:1007-1016, 1997
69. Andrew SE: Feline infectious peritonitis. Vet Clin North Am (Small Anim Pract) 30:987-1000, 2000
70. Glaze MB, Gelatt KN: Feline ophthalmology, in Gelatt KN (ed): Veterinary Ophthalmology (ed 3). Baltimore, Lippincott Williams & Wilkins, 1999, pp 997-1052
71. Doherty MJ: Ocular manifestations of feline infectious peritonitis. J Am Vet Med Assoc 159:417-424, 1971
72. Stiles J: Feline herpesvirus. Vet Clin North Am (Small Anim Pract) 30:1001-1014, 2000
73. Nasisse MP, Weigler BJ: The diagnosis of feline herpes infection. Vet Comp Ophthalmol 7:44-51, 1997
74. Gaskell R, Dawson S: Feline respiratory disease, in Greene CE (ed): Infectious Diseases of the Dog and Cat (ed 2). Philadelphia, WB Saunders, 1998, pp 97-106
75. Nasisse MP, Guy JS, Davidson MG, et al: Experimental ocular herpesvirus infection in the cat. Sites of virus replication, clinical features and effects of corticosteroid administration. Invest Ophthalmol Vis Sci 30:1758-1768, 1989
76. Nasisse MP: Manifestations, diagnosis and treatment of ocular herpes infection in the cat. Comp Cont Ed Pract Vet 4:962-970, 1982
77. Stiles J, Bienzle D, Render JA, et al: Use of nested polymerase chain reaction (PCR) for detection of retroviruses from formalin-fixed, paraffin-embedded uveal melanomas in cats. Vet Ophthalmol 2:113-116, 1999
78. Nasisse MP, Glover TL, Moore CP, et al: Detection of feline herpesvirus 1 DNA in corneas of cats with eosinophilic keratitis or corneal sequestration. Am J Vet Res 59:856-858, 1998
79. Munson L, Wack R, Duncan M, et al: Chronic eosinophilic dermatitis associated with persistent feline herpesvirus infection in cheetahs (*Acinonyx jubatus*). Vet Pathol 41:170-176, 2004
80. Hargis AM, Ginn PE, Mansell JEL, et al: Ulcerative facial and nasal dermatitis and stomatitis in cats associated with feline herpesvirus 1. Vet Dermatol 10:267-274, 1999
81. Nasisse MP, English RV, Tompkins MB, et al: Immunologic, histologic, and virologic features of herpesvirus-induced stromal keratitis in cats. Am J Vet Res 56:51-55, 1995
82. Maggs DJ, Lappin MR, Nasisse MP: Detection of feline herpesvirus-specific antibodies and DNA in aqueous humor from cats with or without uveitis. Am J Vet Res 60:932-936, 1999
83. Fulton LM, Bromberg NM, Goldschmidt MA: Soft tissue fibrosarcoma with intraocular metastasis in the cat. Prog Vet Comp Ophthalmol 1:129-132, 1991
84. Hayden DW: Squamous cell carcinoma in a cat with intraocular and orbital metastases. Vet Pathol 13:332-336, 1976
85. West CS, Wolf ED, Vainisi SJ: Intraocular metastasis of mammary adenocarcinoma in a cat. J Am Anim Hosp Assoc 15:725-728, 1979
86. Bellhorn RW: Secondary ocular adenocarcinoma in three dogs and a cat. J Am Vet Med Assoc 160:302-307, 1972
87. Murphy CJ, Canton DC, Bellhorn RW, et al: Disseminated adenocarcinoma with ocular involvement in a cat. J Am Vet Med Assoc 195: 488-491, 1989
88. Cassotis NJ, Dubielzig RR, Gilger BC, et al: Angioinvasive pulmonary carcinoma with posterior segment metastasis in four cats. Vet Ophthalmol 2:125-131, 1999
89. Hamilton HB, Severin GA, Nold J: Pulmonary squamous cell carcinoma with intraocular metastasis in a cat. J Am Vet Med Assoc 185: 307-309, 1984
90. Williams LW, Gelatt KN, Gwin RM: Ophthalmic neoplasms in the cat. J Am Anim Hosp Assoc 17:999-1008, 1981
91. Pentlarge VW, Powell-Johnson G, Martin CL, et al: Orbital neoplasia with enophthalmos in a cat. J Am Vet Med Assoc 195:1249-1251, 1989
92. Gilger BC, McLaughlin SA, Whitley RD, et al: Orbital neoplasms in cats: 21 cases (1974-1990). J Am Vet Med Assoc 201:1083-1086, 1992
93. Davidson MG, Nasisse MP, Breitschwerdt EB, et al: Acute blindness associated with intracranial tumors in dogs and cats: Eight cases (1984-1989). J Am Vet Med Assoc 199:755-758, 1991
94. Crispin SM, Mould JR: Systemic hypertensive disease and the feline fundus. Vet Ophthalmol 4:131-140, 2001
95. Maggio F, DeFrancesco TC, Atkins CE, et al: Ocular lesions associated with systemic hypertension in cats: 69 cases (1985-1998). J Am Vet Med Assoc 217:695-702, 2000
96. Lane IF, Roberts SM, Lappin MR: Ocular manifestations of vascular disease: Hypertension, hyperviscosity and hyperlipidemia. J Am Anim Hosp Assoc 29:28-36, 1993
97. Littman MP: Spontaneous systemic hypertension in 24 cats. J Vet Intern Med 8:79-86, 1994
98. Stiles J, Polzin DJ, Bistner SI: The prevalence of retinopathy in cats with systemic hypertension and chronic renal failure or hyperthyroidism. J Am Anim Hosp Assoc 30:564-572, 1994
99. Hayreh SS, Servais GE, Virdi PS, et al: Fundus lesions in malignant hypertension. III. Arterial blood pressure, biochemical, and fundus changes. Ophthalmology 93:45-59, 1986
100. Hawkins EC, Feldman BF, Blanchard PC: Immunoglobulin A myeloma in a cat with pleural effusion and serum hyperviscosity. J Am Vet Med Assoc 188:876-878, 1986
101. MacEwen EG, Hurvitz AI: Diagnosis and management of monoclonal gammopathies. Vet Clin North Am 7:119-132, 1977
102. Hribernik TN, Barta O, Gaunt SD, et al: Serum hyperviscosity syndrome associated with IgG myeloma in a cat. J Am Vet Med Assoc 181:169-170, 1982
103. Forrester SD, Greco DS, Relford RL: Serum hyperviscosity syndrome associated with multiple myeloma in two cats. J Am Vet Med Assoc 200:79-82, 1992
104. Peavy GM, Holland CJ, Dutta SK, et al: Suspected ehrlichial infection in five cats from a household. J Am Vet Med Assoc 210:231-234, 1997
105. Breitschwerdt EB, Abrams-Ogg AC, Lappin MR, et al: Molecular evidence supporting *Ehrlichia canis*-like infection in cats. J Vet Intern Med 16:642-649, 2002
106. Crispin SM: Ocular manifestations of hyperlipoproteinaemia. J Small Anim Pract 34:500-506, 1993
107. Wyman M, McKissck GA: Lipemia retinalis in the dog and cat: Case reports. J Am Anim Hosp Assoc 9:288-291, 1973
108. Basher AW, Roberts SM: Ocular manifestations of diabetes mellitus: Diabetic cataracts in dogs. Vet Clin North Am (Small Anim Pract) 25:661-676, 1995
109. Thoresen SI, Bjerkas E, Aleksandersen M, et al: Diabetes mellitus and bilateral cataracts in a kitten. J Feline Med Surg 4:115-122, 2002
110. Bassett JR: Hypocalcemia and hyperphosphatemia due to primary hypoparathyroidism in a six-month-old kitten. J Am Anim Hosp Assoc 34:503-7, 1998
111. Stiles J: Cataracts in a kitten with nutritional secondary hyperparathyroidism. Prog Vet Comp Ophthalmol 1:296-298, 1991
112. van der Woerdt A, Peterson ME: Prevalence of ocular abnormalities in cats with hyperthyroidism. J Vet Intern Med 14:202-203, 2000
113. Schmidt SY, Berson EL, Hayes KC: Retinal degeneration in cats fed casein. I. Taurine deficiency. Invest Ophthalmol 15:47-52, 1976
114. Schmidt SY, Berson EL, Watson G, et al: Retinal degeneration in cats fed casein. III. Taurine deficiency and ERG amplitudes. Invest Ophthalmol Vis Sci 16:673-678, 1977
115. Hayes KC, Carey RE, Schmidt SY: Retinal degeneration associated with taurine deficiency in the cat. Science 188:949-951, 1975
116. Burditt LJ, Chotai K, Hirani S, et al: Biochemical studies on a case of feline mannosidosis. Biochem J 189:467-473, 1980
117. Vandevelde M, Fankhauser R, Bichsel P, et al: Hereditary neurovisceral mannosidosis associated with alpha-mannosidase deficiency in a family of Persian cats. Acta Neuropathol (Berl) 58:64-68, 1982
118. Jezyk PF, Haskins ME, Newman LR: Alpha-mannosidosis in a Persian cat. J Am Vet Med Assoc 189:1483-1485, 1986
119. Cummings JF, Wood PA, de Lahunta A, et al: The clinical and pathologic heterogeneity of feline alpha-mannosidosis. J Vet Intern Med 2:163-170, 1988
120. Cowell KR, Jezyk PF, Haskins ME, et al: Mucopolysaccharidosis in a cat. J Am Vet Med Assoc 169:334-339, 1976
121. Jezyk PF, Haskins ME, Patterson DF, et al: Mucopolysaccharidosis in a cat with arylsulfatase B deficiency: A model of Maroteaux-Lamy syndrome. Science 198:834-836, 1977
122. Vine DT, McGovern MM, Haskins ME, et al: Feline mucopolysaccharidosis VI: Purification and characterization of the resident arylsulfatase B activity. Am J Hum Genet 33:916-927, 1981
123. Aguirre G, Stramm L, Haskins M: Feline mucopolysaccharidosis VI: General ocular and pigment epithelial pathology. Invest Ophthalmol Vis Sci 24:991-1007, 1983

124. Stramm L, Haskins M, Desnick RJ, et al: Disease expression in cultured pigment epithelium. Feline mucopolysaccharidosis VI. Invest Ophthalmol Vis Sci 26:182-192, 1985
125. Blakemore WF: GM1-gangliosidosis in a cat. J Comp Pathol 82:179-185, 1972
126. Neuwelt EA, Johnson WG, Blank NK, et al: Characterization of a new model of GM2-gangliosidosis (Sandhoff's disease) in Korat cats. J Clin Invest 76:482-490, 1985
127. Barker CG, Blakemore WF, Dell A, et al: GM1 gangliosidosis (type 1) in a cat. Biochem J 235:151-8, 1986
128. Nowakowski RW, Thompson JN, Baker HJ: Diagnosis of feline GM1 gangliosidosis by enzyme assay of cultured conjunctival cells. Invest Ophthalmol Vis Sci 29:487-490, 1988
129. Cork LC, Munnell JF, Lorenz MD, et al: GM2 ganglioside lysosomal storage disease in cats with beta-hexosaminidase deficiency. Science 196:1014-1017, 1977
130. Murray JA, Blakemore WF, Barnett KC: Ocular lesions in cats with GM1-gangliosidosis with visceral involvement. J Small Anim Pract 18:1-10, 1977
131. Sousa CA: Exudative, crusting, and scaling dermatoses. Vet Clin North Am (Small Anim Pract) 25:813-831, 1995
132. Manning TO: Pemphigus diseases in the feline: Seven case reports and discussion. J Am Anim Hosp Assoc 18:433, 1982
133. Scott DW, Miller WH, Griffin CE: Immunological skin diseases, in Scott DW, Miller WH, Griffin CE (eds): Muller and Kirk's Small Animal Dermatology (ed 5). Philadelphia, WB Saunders, 1995, pp 484-626
134. Weiser MG: Erythrocyte responses and disorders, in Ettinger SJ, Feldman EC (eds): Texbook of Veterinary Internal Medicine, Vol 2 (ed 4). Philadelphia, WB Saunders, 1995, pp 1864-1891
135. Carney HC, England JJ: Feline hemobartonellosis. Vet Clin North Am (Small Anim Pract) 23:79-90, 1993
136. Cain GR, Suzuki Y: Presumptive neonatal isoerythrolysis in cats. J Am Vet Med Assoc 187:46-48, 1985
137. Shelton GH, Linenberger ML: Hematologic abnormalities associated with retroviral infections in the cat. Semin Vet Med Surg (Small Anim) 10:220-233, 1995
138. Powell CC, Lappin MR: Diagnosis and treatment of feline uveitis. Comp Cont Ed Pract Vet 23:258-269, 2001
139. Powell CC, Lappin MR: Causes of feline uveitis. Comp Cont Ed Pract Vet 23:128-141, 2001
140. van der Woerdt A: Management of intraocular inflammatory disease. Clin Tech Small Anim Pract 16:58-61, 2001