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Abstract
Systemic diseases can present ocular manifestations. In some cases, the ocular lesions are present along with other generalized lesions characteristic of the disease. In a few cases, however, only ocular lesions are present. The interpretation of these ophthalmologic findings, together with the generalized signs exhibited by the patient, are important in establishing a differential diagnosis and prognosis for the patient. This article reviews selected systemic diseases and their ocular manifestations. A more exhaustive review of the diseases has been already presented.

Disciplines
Medicine and Health Sciences | Ophthalmology | Veterinary Medicine

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Ocular Manifestations of Selected Systemic Diseases

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Systemic diseases can present ocular manifestations. In some cases, the ocular lesions are present along with other generalized lesions characteristic of the disease. In a few cases, however, only ocular lesions are present. The interpretation of these ophthalmologic findings, together with the generalized signs exhibited by the patient, are important in establishing a differential diagnosis and prognosis for the patient. This article reviews selected systemic diseases and their ocular manifestations. A more exhaustive review of these diseases has been already presented.2

Nutritional Diseases
Vitamin A Deficiency
Clinical signs resulting from vitamin A deficiency are rarely seen in dogs and cats. Dogs and cats made deficient by the feeding of experimental diets take several months to show outward ocular signs characteristic of deficiency.

In contrast to the dog and cat, aquarium-raised turtles are very susceptible to vitamin A deficiency. These animals are often raised on very inadequate and restricted diets and exhibit clinical signs characteristic of this deficiency. Vitamin A deficiency in the turtle classically presents with markedly swollen eyelids and closed palpebral fissures (Fig 1). A mucopurulent, tenacious ocular discharge can be present in these animals. The vitamin A deficiency results in epithelial loss from the ductules of the orbital glands. These epithelial cells cause plugging and obstruction of these ducts and the secondary swelling that develops. In addition to the ocular lesions, the animals are lethargic and have a soft shell.

Treatment of vitamin A deficiency in the turtle is very rewarding; subcutaneous or intramuscular injections of vitamin A (1-4,000 IU), repeated every 2 to 3 weeks, will result in slow but dramatic improvement. In addition, oral vitamin A can be given by dipping the food in a vitamin A solution. Animals treated in this manner show regression of the orbital swelling and hardening of the shell. It is important to instruct owners of a proper diet.

Taurine Deficiency
The aminosulfonic acid, taurine, is essential in feline nutrition. Cats are unable to synthesize taurine from dietary precursors and taurine deficiency results in a progressive retinal disease.1 Taurine deficiency in cats is associated with the exclusive feeding of diets based on vegetable protein. These diets are similar to dried dog food and some canned dog and cat foods in that they are deficient in taurine.

The earliest lesions observable on ophthalmoscopy are bilateral focal atrophic areas in the area centralis (Fig 2). With progression of the nutritional deficiency, bilaterally symmetrical, horizontal, band-shaped atrophic lesions

Cardiac Disease
Polycythemia
Congenital hypoxemia
extend along the posterior pole (Fig 3). Animals with this type of retinal lesion do not exhibit any visual deficits and are usually recognized on routine ophthalmoscopic examination. Prolonged deficiency of taurine results in a generalized retinal atrophy (Fig 4) and complete blindness.

When an animal is presented with these classical ophthalmoscopic abnormalities, it is difficult to determine whether an active retinal disease is progressing or whether the disease is arrested. Restoration of a taurine-adequate diet to animals that were previously deficient will arrest the further progression of the retinal abnormality. In animals that have generalized retinal atrophy, however, restoration of vision is not possible and blindness is permanent.

**Cardiovascular and Blood Diseases**

**Polycythemia**

Congenital or acquired hypoxic cardiovascular diseases in animals can result in a secondary polycythemia. In some cases, this is reflected in the eye by the presence of a markedly dilated and engorged retinal vascular tree (Fig 5). The blood vessels are distended and reddened, and retinal exudates, hemorrhages and folds or focal detachments can be readily seen on ophthalmoscopic examination. Recognition of the primary systemic abnormality and its correction, when possible, will frequently correct the retinal vascular problem.

**Hypertension**

In man, hypertension can present with abnormalities of the retinal vessels. These changes are often anticipated

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**Fig 1**—Vitamin A deficiency in a turtle. Note the markedly swollen eyelids and closed palpebral fissure.

**Fig 2**—In the early stages of the disease (Fig 2), a small hyperreflective lesion is present in the area centralis. This lesion will extend across the posterior pole (Fig 3) and eventually appear as a generalized retinal atrophy (Fig 4).

**Fig 3**—In some cases, this is reflected in the eye by the presence of a markedly dilated and engorged retinal vascular tree (Fig 5). The blood vessels are distended and reddened, and retinal exudates, hemorrhages and folds or focal detachments can be readily seen on ophthalmoscopic examination. Recognition of the primary systemic abnormality and its correction, when possible, will frequently correct the retinal vascular problem.

**Hypertension**

In man, hypertension can present with abnormalities of the retinal vessels. These changes are often anticipated.
since continual monitoring of the patient's blood pressure is easily and routinely performed. In small animals, it is not possible to routinely measure blood pressure. A Doppler technique has been advocated but it appears to be subject to variations. A more reliable method of estimating blood pressure is by femoral artery puncture. This requires, however, a pressure transducer and a recording device, items that are not readily available to most veterinarians.

Acute hypertension, either primary or secondary to renal disease, can result in unilateral or bilateral bullous retinal detachments (Fig 6). If the condition is bilateral, animals are frequently presented with an acute onset of visual loss. Blood pressure elevation of a more chronic nature can result in retinal hemorrhages (Fig 7) or, in some cases, breakdown of the blood ocular barrier anteriorly and low-grade anterior chamber hemorrhages (hyphema). Even with the difficulties in the measurement of blood pressure, the presence of these characteristic ophthalmic lesions should alert the clinician to the possibility of hypertension as their cause.

Animals with these clinical signs should be referred, when possible, to veterinary medical institutions that are capable of diagnosing and treating hypertension. When this is not possible, animals can be treated with methyldopa at a dose of 80 mg/15 kg body weight, qid. Additionally, thiazide diuretics have been valuable in reducing the elevated blood pressure.

Hypertension in small animals is one of the systemic diseases that can present with only ocular manifestations. However, there are cases when the ocular signs are seen in association with renal failure.

*Arteriosonde® 1010, Roche Medical Electronics Div., Cranbury, NJ 08512.
*Aldomet®, Merck Sharpe & Dohme, West Point, PA 19486.
Canine thrombocytopenia. Subconjunctival hemorrhage is seen in the superior bulbar conjunctiva.

Retinal (Fig 9) and intravitreal hemorrhages also occur in coagulation disorders. The former must be differentiated from the retinal hemorrhages that occur in hypertension. As with the subconjunctival and anterior chamber hemorrhages, retinal hemorrhages resorb after correction of the clotting disorder. Intravitreal hemorrhages, on the other hand, cause more severe complications since retraction of the clot can often cause a secondary retinal detachment.

Diabetes Mellitus

The elevated blood sugar that is present in diabetic animals results in the transport and diffusion of this sugar through the semi-permeable capsule of the lens. In the lens, the glucose is converted to a sugar alcohol which cannot diffuse out from the lens. The sugar alcohol is osmotically active and draws water into the lens, thereby causing the osmotic cataract characteristic of diabetes mellitus.

In young diabetic animals, vacuoles can be observed in the equator of the lens after widely dilating the pupil with a mydriatic agent. These vacuoles indicate a progressive ongoing cataractous process. More frequently, however, animals are presented with bilateral cortical to complete cataracts, which are usually mature. Owners frequently state that the process of cataract formation and visual loss has occurred suddenly. A good physical examination and history will often indicate that the animal has concurrent polydipsia and polyuria. A fasting blood sugar will be diagnostic of diabetes mellitus.

Animals that have been diagnosed with and treated for diabetes mellitus, before the presence of complete mature cataracts, will usually develop complete mature cataracts during the course of the disease (Fig 10). It appears that the control of the blood sugar, by currently utilized methods, may be inadequate in terms of maintaining normal lens metabolism. Nevertheless, diabetic animals with cataracts can undergo successful cataract surgery once the diabetes is under good medical control. Unlike man, animals do not show the proliferative diabetic retinopathy and associated vision defects, which are common in the human diabetic patient.

Hyperlipemias

The signs of markedly elevated serum lipids and triglycerides can be seen in the eyes of dogs and cats. Lipemia retinalis is the presence of lipid-filled retinal vessels (Fig 11). These appear yellow to orange in color and the contours of the retinal vessels are readily visible. Because of the color
differences in the ocular fundus between the tapetal and the nontapetal zones of the retina, it is important to remember that lipemia retinalis is only visible in the nontapetal areas. It appears that the presence of a dark pigment behind the lipemic vessels enhances the color contrast and permits ready visualization of the lipemic vessels. In contrast, the vessels overlying the tapetal retina in animals with lipemia retinalis appear normal.

Animals with elevations in total serum lipids can also have lipid clots in the anterior chamber. These animals present with low-grade anterior uveitis and corneal edema. On closer examination, the cornea is clear and normal and the apparent edema is the result of a clot of white lipid material within the anterior chamber (Fig 12). Once the low-grade anterior uveitis is brought under control with topical corticosteroids, the lipid clot will rapidly disappear from the anterior chamber.

The diagnosis of hyperlipidemias in animals with either lipemia retinalis and/or lipid clots in the anterior chamber can be confirmed by determination of serum lipids and triglycerides. These are usually elevated several times greater than the maximal normal level. In most of these animals, however, serum cholesterol levels are usually normal. It has been the author's experience that once the diagnosis is confirmed by serum chemistries, correction of the animal's diet to a diet with lower fat content will restore the serum lipid profiles to normal levels. The authors have found that feeding a low-fat diet to dogs will reduce the serum lipids and triglycerides to normal levels.

**Viral Diseases**

**Infectious Canine Hepatitis**

The typical ocular lesions of infectious canine hepatitis are unilateral and bilateral anterior uveitis. The inflammation is so severe that there is widespread destruction of the corneal endothelium, resulting in secondary complete corneal edema. This has been known as blue eye (Fig 13). Approximately 18% to 20% of dogs that survive infection with canine hepatitis virus will develop these ocular lesions in the recovery phase of the disease.

It is more common to observe anterior uveitis and secondary corneal edema in dogs following vaccination with attenuated live canine hepatitis virus. This postvaccination reaction usually develops 9 to 14 days following vaccination and, in idiopathic cases, there is no current evidence to support the St. Louis hypothesis of secondary uveitis with corneal edema as a complication of canine infectious hepatitis (6).

Canine infectious hepatitis can also cause retinal and choroidal retinitis. In contrast to tapetal and nontapetal retinal lesions, retinal involvement secondary to canine infectious hepatitis disease is usually bilateral. The retinal disease is characterized by a circular lesion, often associated with the presence of secondary corneal edema and lesions (Fig 14).

Although it is unusual for the choroid to be involved, it is not uncommon for dogs in which the diagnosis of canine infectious hepatitis is incorrect. In such cases, the retinal lesions are often associated with secondary corneal edema and lesions.

**Systemic Fungal Infections**

Blastomycosis is a fungal infection that can affect the ocular system and is characterized by mycosis of the retina. Mycosis is also common in the cornea and mycosis of the cornea can be associated with secondary corneal edema. Mycosis of the cornea is often associated with secondary corneal edema and lesions.
Canine Distemper

Canine distemper virus has a tropism for the neuroretina where the virus can replicate and cause a multifocal retinal inflammatory lesion. This can be seen in the tapetal and/or nontapetal area (Fig 14) and signs of active retinal inflammation are seen on ophthalmoscopy. Active retinal inflammation can co-exist with acute neurologic disease caused by canine distemper virus. In some cases, the ocular lesions appear to be isolated and no neurologic disease is evident. Following the active inflammatory retinal lesion, ophthalmoscopic examination may reveal the presence of multifocal, inactive, healed retinal inflammatory lesions (Fig 15).

Although canine distemper can cause multifocal retinal inflammation, not all of these lesions can be exclusively attributed to distemper. The veterinary clinician must be aware of this fact in attempts to establish a differential diagnosis for the ongoing disease process.

Systemic Mycoses

Blastomycosis, histoplasmosis, coccidioidomycosis and cryptococcosis are systemic fungal diseases that can have ocular manifestations. The frequency with which a specific fungal infection occurs in the eye depends on the geographic area; in the northeastern United States, cryptococcosis is far more frequently seen than the other systemic mycoses.

Retinal granulomas are the most frequent ocular lesion of cryptococcosis. These granulomas are seen intraretinally and subretinally and can produce large white, elevated lesions in the posterior pole (Fig 16). In cats, as well as dogs, the granulomas can be small in size and scattered in a multifocal manner throughout the entire posterior pole of the eye (Fig 17). Associated with these multiple small intraretinal granulomas, cystic detachments of the retina are seen resulting from subretinal and choroidal granulomas (Fig 18).

Although animals with cryptococcosis can present with...
primary ocular problems, i.e., those seen with optic neuritis and blindness, most animals are presented because of signs of associated neurological or nasal disease. Fundus examination frequently demonstrates retinal granulomas, characteristic of this disease. To confirm the diagnosis, India ink smears of cerebral spinal fluid and/or subretinal aspirates may be necessary. It has been the authors' experience that most affected animals have normal lung fields on radiography and nonspecific changes in the peripheral blood.

**Toxoplasmosis, Feline Infectious Peritonitis and Lymphosarcoma**

Inflammation of the iris and ciliary body (anterior uveitis) can occur in cats associated with a generalized systemic disease. Not all cases of anterior uveitis in this species result from systemic disease but the clinician must be aware that toxoplasmosis, feline infectious peritonitis (FIP) and feline lymphosarcoma can present with ocular lesions.

On the basis of ophthalmologic examination alone, it is not always possible to differentiate clinically among the three diseases in the cat. If the anterior uveitis is mild and iridal distortion has not developed, the three diseases must be considered in the differential diagnosis. When the severity of the anterior uveitis is such that iridal damage, distortion and/or replacement by neoplastic tissue has taken place, feline lymphosarcoma is the most likely diagnosis.

**Toxoplasmosis**

The protozoal organism, *Toxoplasma gondii*, can affect the anterior uvea and the posterior pole of the eye. A low-grade anterior uveitis can be recognized in some affected animals by the presence of aqueous flare and cells, the latter often aggregating as clumps, called keratic precipitates (KPs), in the corneal endothelium (Fig 19). The retina can be selectively infiltrated by the *Toxoplasma* organism, resulting in a multifocal retinochoroiditis. Multiple small retinal granulomas can be found over the tapetal and nontapetal areas. Coalescence of several of these inflammatory foci can occur and result in small localized inflammatory retinal detachments (Fig 20). Inflammatory ocular disease resulting from toxoplasmosis can be restricted to the anterior segment or can affect both anterior and posterior segments.

The diagnosis of toxoplasmosis is based on having a rapidly rising titer, indicative of recent exposure or infection. Since this is a zoonosis, veterinarians and their clients should be counselled about appropriate therapy.

**Feline Infectious Peritonitis**

The clinical signs of pyogranulomatous inflammation found in a feline (Fig 18) can also be seen in the anterior uveitis of cats with FIP. There is a generalized lymphoid hyperplasia in the anterior uvea, and large clumps of lymphocytes, histocytes and plasma cells are often found in the anterior uvea. Retinal granulomas also can be seen in the ocular fundus.

Early inflamed anterior uveitis is often localized to the anterior uvea, and systemic involvement is more common with advanced disease.

Recent cases of FIP, especially those with fluorescein angiography, have had rapidly rising titers. Recent titers are more indicative of disease activity and can be helpful in determining whether a cat is infected. Recent titers are also helpful in determining whether a recent exposure has occurred.

**Feline Lymphosarcoma**

Feline lymphosarcoma is a general term for involvement of lymphoid tissue. The disease can involve localized lymph nodes as well as the regional lymph nodes. Cats presenting with FIP may have involvement of feline lymphosarcoma. Low-grade lymphoid involvement of the ocular lymphoid tissue is common in cats with FIP.

Fig 17—Cryptococcosis in a cat. Multiple, small gray retinal granulomas are scattered throughout the tapetal zone in the posterior pole.

Fig 18—Peripheral retina of cat in Fig 17. A large cystic retinal detachment is present peripherally and results from a subretinal granuloma.

Fig 19—Toxoplasmosis in a cat. Anterior uveitis and keratic precipitates (KPs). Multiple KPs are adherent to the corneal endothelium.

Fig 20—Toxoplasmosis in a cat. Keratic precipitates (KPs) are present in the superior corneal endothelium.
Ocular Manifestations

Fig 20—Toxoplasmosis in a cat. Multiple, small gray granulomas are present in the retina at the lower right of the photograph. More superiorly, two cystic retinal detachments are evident.

Fig 21—Feline infectious peritonitis. A pyogranulomatous anterior uveitis obscures the inferonasal iris surface. A large inflammatory nodule is present on the superotemporal pupillary border.

should be aware of the risk attending prolonged medical therapy.

Feline Infectious Peritonitis

The characteristic feature of FIP is a perivascular, pyogranulomatous inflammatory process which can be found in any organ system. In the eye, FIP can manifest as a pyogranulomatous anterior uveitis; the iris is thickened and there is a marked fibrinoid to proteinaceous exudate within the anterior chamber. Inflammatory cells will aggregate and form nodules on the iridal surface as well as forming large coagula of fibrin and inflammatory cells within the anterior chamber (Fig 21). Perivascular inflammatory infiltrates also can occur in the retina and these are visible on ophthalmoscopy. Early in the course of FIP, animals can present with localized ocular disease without any evidence of generalized systemic abnormality. As the disease progresses, the other more classical signs of FIP become evident.

Recent work has identified the etiologic agent of the disease as a virus. Serologic testing using an indirect fluorescent antibody technique can identify those cats that have had previous contact with the virus. Paired serum samples showing a dramatic rise in titer or a single high titer, especially ≥1:400, can support a diagnosis of FIP in cats showing clinical signs. High titers alone do not confirm the diagnosis of FIP disease.

Feline Lymphosarcoma

Feline lymphosarcoma has a multiplicity of organ system involvements. In the eye, the disease can present with localized infiltrates of the orbit, eyelid and conjunctiva, as well as the intraocular structure. Occasionally, animals are presented for a primary ophthalmic problem when, in reality, they are suffering from generalized lymphosarcoma.

Low-grade anterior uveitis can occur in the early stages of feline lymphosarcoma when the anterior uveal tract is involved. The iris appears slightly thickened and inflamed and the animal shows characteristic signs of low-grade anterior uveitis. Solid tumor involvement of the iris can occur in feline lymphosarcoma (Fig 22). Thick, creamy infiltrative neoplastic tissue can distort and/or replace the normal iris architecture. This type of tumor must be differentiated from an amelanotic melanoma of the anterior uvea. Topical steroid treatment of these anterior uveal lymphosarcoma infiltrates will often cause marked regression of the iridal neoplasm (Fig 23). However, recurrence of
the iridal tumor, as well as the development of systemic signs referable to the disease process, will develop.

Although not as common as anterior involvement, the posterior segment of the uveal tract can become affected in feline lymphosarcoma. Diffuse infiltration of the choroid will result in a grayish discoloration to the tapetum, as well as solid retinal detachments. As with any infiltrative disease of the choroid, systemic mycoses must be considered in a differential diagnosis.

**Canine Lymphosarcoma**

Primary ocular involvement is seen less frequently with canine lymphosarcoma than with feline lymphosarcoma. However, since dogs with lymphosarcoma can show ocular disease, it is important to consider lymphosarcoma in the differential diagnosis of any infiltrative anterior uveal inflammatory disease.

Infiltration of the iris and ciliary body results in the accumulation within the anterior chamber of the coagulum of neoplastic white blood cells (hypopyon) (Fig 24). Although hypopyon is seen with other anterior uveitides, as well as with deep interstitial keratitis, the presence of hypopyon should suggest that lymphosarcoma be considered in a differential diagnosis. In animals undergoing chemotherapy for lymphosarcoma, the hypopyon appears to reflect very closely the responsiveness of the neoplasm to the drugs used, that is, in the remission stages of the disease, the hypopyon gradually clears and disappears from the anterior chamber, while in the recurrence stages of the disease, the hypopyon will return. Hyphema (Fig 25) is another common sign of animals with ocular lymphosarcoma. The blood can be clotted or nonclotted. The type of hyphema developing in these animals must be differentiated from that occurring with hypertension and clotting disorders.

**REFERENCES**


ARTICLE #6 REVIEW QUESTIONS

The article you have read qualifies for ½ hour of Continuing Education Credit from the University of Pennsylvania School of Veterinary Medicine. For your reference, record your answers on this page, and then transfer them to the registration form inserted in the back of The Compendium.

1. Ocular signs of toxoplasmosis, FIP and feline lymphosarcoma easily differentiate these diseases.
   a. true
   b. false

2. Which is not correct concerning taurine metabolism and utilization in the cat?
   a. Cats are unable to synthesize taurine from dietary precursors.
   b. Dried dog foods as well as some canned dog and cat foods are deficient in taurine.
   c. Although cats may show no visual deficits early in the deficiency, prolonged deficiency of taurine results in a generalized retinal atrophy and complete blindness.
   d. Animals that have become blind from the deficiency can have vision restored if a taurine-adequate diet is begun.

3. Keratic precipitates (KPs) are
   a. aggregates of cells and fibrin deposited on the corneal endothelium.
   b. lipid deposits just below the corneal epithelium.
   c. small clumps of blood vessels invading the cornea from the limbus.
   d. mineralized areas in the corneal stroma.

4. Which is not true concerning the ocular postvaccination reaction encountered with attenuated live canine hepatitis virus?
   a. Ocular reactions are only rarely encountered.
   b. Anterior uveitis and secondary corneal edema causes the blue eye appearance.
   c. Very few cases clear spontaneously in 1 to 2 weeks.
   d. The postvaccination reaction usually develops 9 to 14 days following vaccination.

5. Lipemia retinalis is only visible ophthalmoscopically in the nontapetal fundus.
   a. true
   b. false

6. The most probable cause of multifocal, inactive, healed retinal inflammatory lesions in a 4-year-old dog would be
   a. a traumatic head injury early in the dog's life.
   b. canine distemper virus infection at a young age.
   c. active autoimmune disease.
   d. a postvaccinal reaction to canine hepatitis.

7. FIP infections in cats
   a. rarely demonstrate ocular lesions.
   b. can be manifested in the eye as a pyogranulomatous uveitis, with iris thickening and fibrinoid exudate within the anterior chamber.
   c. are confirmed by high antibody titers, alone, using the indirect fluorescent antibody technique.

8. Retinal granulomas that may appear white and elevated are the most frequent ocular lesions of cryptococcosis.
   a. true
   b. false

9. The cataracts frequently seen in diabetic animals
   a. are due to the accumulation of an osmotically active sugar alcohol drawing water into the lens.
   b. characteristically involve only the posterior capsule of the lens.
   c. characteristically involve only the anterior capsule of the lens.
   d. are not amenable to cataract surgery.

10. Which is not true concerning hypertension in animals?
    a. Problems with measuring blood pressure make the diagnosis difficult.
    b. Acute hypertension, either primary or secondary to renal disease, can result in unilateral or bilateral bullous retinal detachments.
    c. A Doppler technique has recently been used in blood pressure measurements of cats and dogs with great reliability.
    d. Methyldopa has been used in treating animals known to be hypertensive.