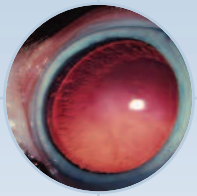

Ocular Manifestations of Endocrine Disease

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ABSTRACT: Small animal patients with endocrinopathies are at risk of developing many ophthalmic conditions resulting from endocrine hormone imbalances. Diabetic animals frequently develop cataracts but can also have numerous other ocular problems, including uveitis, keratopathy, retinopathy, and the effects of lipid derangements and systemic hypertension. Cushing's patients can develop complications from hyperlipidemia and hypertension and sometimes present with corneal disease. Acute blindness from sudden acquired retinal degeneration has been associated with disease of the pituitary–adrenal axis. Growth hormone disturbances can result in the secondary ocular effects of hypertension or of thyroid deficiency (e.g., corneal infiltrates, decreased tear production, neurologic dysfunction). Hyperthyroid animals can present with the ocular manifestations of systemic hypertension. Disorders of calcium homeostasis are unusual, typically manifesting as cataracts in hypocalcemic patients or as metastatic calcification of the ocular tissues.

Endocrine diseases make up a significant percentage of the chronic diseases that veterinarians diagnose and manage. To best treat patients and maintain their quality of life, it is necessary to examine the whole patient and consider all potential clinical manifestations of these diseases and syndromes. Many endocrinopathies have serious ocular signs that may jeopardize quality of life (see box on page 734). This article explores the ophthalmic consequences of common endocrine diseases in small animals, including diabetes mellitus (DM), diseases of the adrenal–pituitary axis, disorders of calcium homeostasis and metabolism, and the highs and lows of thyroid hormone production.

DIABETES MELLITUS

The most well-recognized ophthalmic consequence of an endocrine disorder in dogs is the development of cataracts secondary to DM. However, cataracts are not the only potential ocular complication of this pancreatic endocrine disease. Secondary lens-induced uveitis, poor corneal wound healing, corneal neuropathy, altered lipid metabolism, and retinal lesions are also potential consequences of diabetes in small animals. The devastating chronic complications of DM that are common in humans, particularly diabetic retinopathy, neuropathy, and nephropathy, take 10 to 20 years to develop in humans, so the incidence of complications in small animals is much lower.[1] However, they do occur in some patients, usually as a result of poor glycemic control.

Potential Ophthalmic Manifestations of Endocrinopathies

Diabetes mellitus
- Cataract
  - — Lens-induced uveitis
- Peripheral neuropathy
  - — Decreased corneal sensation
    - - Ulceration
    - - Impaired corneal healing
  - — KCS
  - — Facial nerve palsy
  - — Horner's syndrome
- Hyperlipidemia
  - — Lipemia retinalis
  - — Lipemic aqueous humor
- Retinopathy
- Systemic hypertension
  - — Retinal hemorrhage
  - — Retinal detachment
  - — Hyphema

Hyperadrenocorticism (HAC, Cushing's disease)
- Systemic hypertension
  - — Retinal hemorrhage
  - — Retinal detachment
  - — Hyphema
- Hyperlipidemia
  - — Corneal lipid deposits
  - — Lipemia retinalis
  - — Lipemic aqueous humor
- Pituitary macroadenoma
  - — Blindness
  - — Cranial nerve dysfunction
    - - Oculomotor palsy
    - - Ptosis
- Immunosuppression
  - — Opportunistic infections
    - - Keratitis
    - - Uveitis
    - - Endophthalmitis
- Ectopic calcification
  - — Band keratopathy
    - - Ulceration
    - - Impaired corneal healing
- Facial paralysis
  - — Exposure keratitis
- Exophthalmos
  - — Exposure keratitis
- SARD

Hypoadrenocorticism (Addison's disease)
- Hypercalcemia
  - — Metastatic calcification
    - - Band keratopathy
    - - Deposits in the conjunctiva and elsewhere

Pheochromocytoma
- Mydriasis
- Systemic hypertension
  - — Retinal hemorrhage
  - — Retinal detachment
  - — Hyphema

Acromegaly
- Papilledema
- Systemic hypertension
  - — Retinal hemorrhage
  - — Retinal detachment
  - — Hyphema
- Diabetes (above)

Pituitary dwarfism
- Hypothyroidism (below)

Hypothyroidism
- Hyperlipidemia
  - — Corneal lipid deposits
  - — Lipemic aqueous humor
  - — Lipemia retinalis
- KCS
- Peripheral neuropathy
  - — Facial paralysis
    - - Exposure keratitis
  - — Horner's syndrome
  - — KCS

Hyperthyroidism
- Systemic hypertension
  - — Retinal hemorrhage
  - — Retinal detachment
  - — Hyphema
- Hypercalcemia
  - — Metastatic calcification
    - - Band keratopathy
    - - Deposits in the conjunctiva and elsewhere

Hypocalcemia
- Cataracts
- Prolapsed nictitans
- Papilledema, optic neuritis, conjunctivitis, keratitis
- Strabismus, nystagmus, anisocoria

Hypercalcemia
- Metastatic calcification
  - — Band keratopathy
  - — Deposits in the conjunctiva and elsewhere

Cataract formation is the most common ocular complication and the most consistent ocular manifestation of DM in dogs, occurring in 75% of dogs within the first 12 months of the disease.[2] Almost all dogs with diabetes develop cataracts at some point during the course of the disease, so it is crucial to recognize this and appropriately educate clients. Cataracts also occur in diabetic cats but much less frequently than in dogs. The reason for this difference is probably related to the pathogenesis of cataract formation. Cataracts also occur in humans with diabetes but develop much later in the course of the disease and tend to mature at a slower rate.

The avascular lens of the eye is freely permeable to glucose, its main energy source. Glucose enters by diffusion from the surrounding aqueous humor, which is an ultrafiltrate of plasma. Normally, most glucose is then converted to lactic acid via the anaerobic glycolytic pathway. Lactic acid diffuses back out of the lens and into circulation. However, when there is persistent hyperglycemia, the hexokinase enzyme responsible for this conversion becomes saturated. Excess glucose then gets metabolized through the polyol pathway to sorbitol and fructose, which are not freely diffusible.[1] Aldose reductase, the metabolizing enzyme that catalyzes the reduction of glucose to sorbitol, not only has more substrate on which to act but, in the presence of a high glucose concentration, is up-regulated, thereby increasing its activity.[3] Sorbitol and fructose, which are trapped in the lens, act as hydrophilic osmotic agents, drawing water into the lens and causing swelling and rupture of lens fibers, resulting in the lenticular opacities known as *cataracts*. Although it is not specifically known why diabetic cats do not develop cataracts as readily as dogs, it may be related to the fact that aldose reductase activity is significantly lower in older cats than in dogs or cats

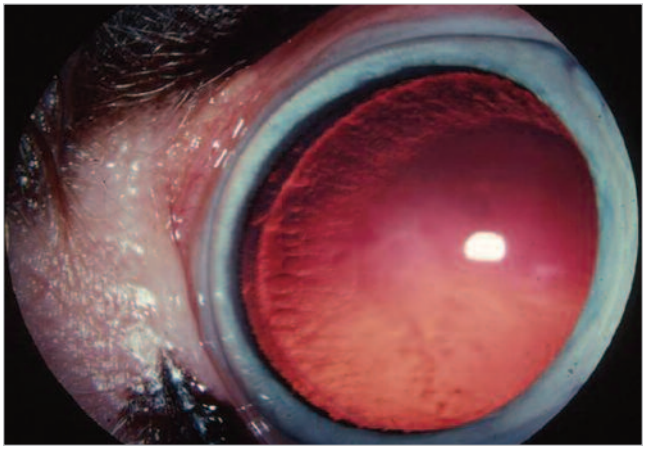

Figure 1. Early, large equatorial vacuoles in the lens of a diabetic patient.

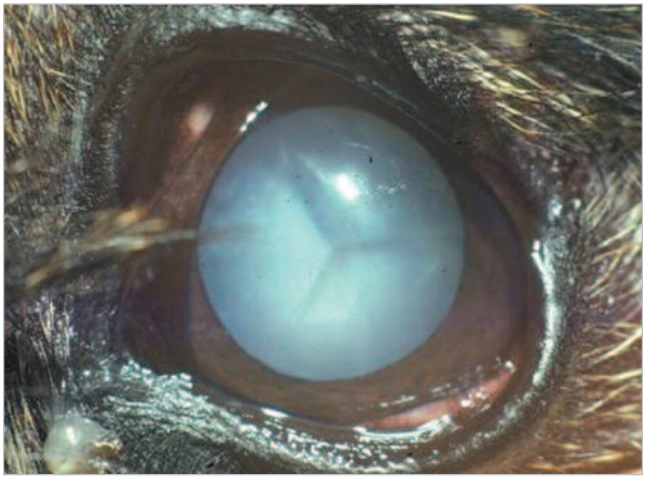

Figure 2. Mature diabetic cataract in a dog.

younger than 4 years of age.[4] Because most cats that develop DM are older than 7 years of age, the infrequency of the development of cataracts in cats may be partly related to lower aldose reductase activity.

In diabetic dogs, cataracts initially develop as vacuoles at the equator of the lens and eventually progress to encompass the entire lens, resulting in fully opaque lenses in both eyes and vision loss (Figures 1 and 2). Because the first changes in the lens occur in the periphery, they are not always readily visible without pharmacologic dilation of the pupil. Therefore, it is advisable to dilate the eyes of newly diagnosed diabetic patients to determine whether cataract formation has begun and to assess progression. The rate at which cataracts mature in diabetic patients is variable and has previously been linked to the degree of glycemic control. Some cataracts may develop slowly over months, while others may progress rapidly, resulting in complete blindness within 1 or 2 weeks. Lens capsule rupture in the equatorial region has even been reported in diabetic dogs. The only treatment for the cataracts is surgical removal. If a client is interested in pursuing surgical removal of cataracts, it is in the best interest of the patient to perform the procedure earlier in the course of the disease because the best surgical outcomes are associated with cases that are addressed before patients develop complications due to long-standing cataracts. Cataract surgery in diabetic dogs has about the same success rate as that in nondiabetic animals.[5]

When cataracts form, there is associated uveitis. This is especially important to know when cataracts form rapidly, which is often the case in diabetic dogs. Lens proteins that leak into the eye from within the lens capsule elicit an inflammatory reaction, which may manifest with various degrees of low intraocular pressure, miosis, aqueous flare and cells, episcleral injection, corneal edema, blepharospasm, and epiphora.[6] Because chronic uveitis can result in secondary glaucoma, vision loss, and ocular pain, intraocular inflammation should be addressed, even if cataract surgery is not pursued. Topical NSAIDs (or steroids in certain cases) and short-acting mydriatics are the mainstays of treatment for lens-induced uveitis. Lifelong therapy is usually required to prevent secondary complications or to decrease their severity.

Systemic hypertension commonly accompanies a variety of endocrine diseases and may have significant ophthalmic consequences, such as ocular hemorrhage and retinal detachment.

The corneal nerves, which are branches of the trigeminal nerve, are critical for eliciting and regulating corneal protective mechanisms (Figure 3). They mediate tear production and eyelid closure and regulate corneal collagen expression and epithelial cell function and integrity.[7] As part of the diffuse neuropathy affect-

Figure 3. Diminished corneal sensation demonstrated with a wisp of cotton contacting the cornea without eliciting a response from the patient.

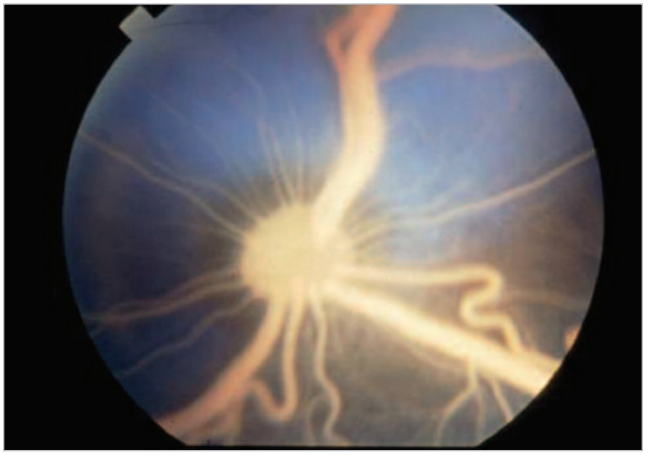

Figure 4. Lipemia retinalis. Most cases are not this pronounced and involve retinal vessels that appear orange.

ing the sensorimotor nervous system of diabetics, corneal sensation may be decreased and result in or complicate recurrent or indolent corneal ulcers.[1,8] With decreased sensation, the patient's response to pain associated with ulcerative keratitis lessens, which may make it harder to diagnose an epithelial defect. These pathologic changes in corneal nerve function are directly related to the degree of glycemic control. Currently, there is no specific treatment for the decreased sensitivity. In certain clinical situations, the decreased sensitivity is especially problematic. For instance, after cataract surgery, patients are generally treated aggressively with topical antiinflammatories, which can complicate, delay, or prevent healing of a corneal ulcer. Also, brachycephalic canine breeds have inherently diminished corneal sensitivity that is exacerbated when these breeds are affected by the neurologic consequences of DM. Therefore, careful vigilance is necessary in treating ulcers in diabetic patients, regardless of whether they have undergone cataract surgery.

Hyperlipidemia is another common problem in diabetic patients, especially if they are untreated or insufficiently regulated. Hypertriglyceridemia results from relative or absolute insulin deficiency associated with a decrease in lipoprotein lipase activity. Hypercholesterolemia also occurs due to increased synthesis and impaired clearance, although this change is often not as significant.[1] In humans, these metabolic alterations are associated with increased risk for atherosclerotic vascular disease, which can be observed as vascular plaque within retinal and choroidal vasculature. Similar vascular complications have been documented in diabetic dogs and cats, albeit infrequently.[9] The more common ocular consequences of hyperlipidemia in small animals include lipemia retinalis and lipid-laden aqueous humor. In patients with lipemia retinalis, retinal vessels appear white or creamy pink, which is reminiscent of blood taken from an animal that has recently eaten a fatty meal (Figure 4). The blood–aqueous barrier usually prevents leakage of large molecules, such as lipoproteins, into the aqueous humor. However, inflammation, such as that associated with uveitis, can alter the permeability of vessels, leading to leakage of these molecules. Lipids then enter the eye and cause the aqueous humor to appear turbid, variably cloudy, and, in some cases, completely opaque (Figure 5). Aside from interfering with vision, the concurrent or resultant uveitis can be exacerbated by lipid and cause further discomfort and damage to the internal structures of the

Diabetic dogs may develop several ophthalmic conditions, including cataracts, corneal changes, intraocular inflammation, and retinal lesions.

eye. Fortunately, most lipid derangements and their ocular manifestations can be improved with treatment and control of diabetes using insulin and dietary therapy as well as treatment of associated uveitis. However, other causes of hyperlipidemia (i.e., hypothyroidism, hyperadrenocorticism [HAC]) should be ruled out, when appropriate, and if good glycemic control does not reduce blood lipid levels, other therapeutic strategies (i.e., administration of essential fatty acids or statin medications) should be considered.

When diabetic retinopathy occurs, it is usually associated with poor or inconsistent glycemic control.[10] The true incidence of diabetic retinopathy is hard to determine because of the high prevalence of cataract formation, especially in dogs, which limits visualization of the characteristic fundic changes. Retinal hemorrhages and microaneurysms are the most common gross findings. The following can be noted on histologic examination: thickened vascular basement membranes, pericyte loss, capillary shunts, and microaneurysms. These changes probably represent ischemic insults due to decreased perfusion.[1] Diabetics have increased blood viscosity, decreased vascular compliance, erythrocyte sludging and aggregation, elevated fibrinogen, and diminished fibrinolysis.[11] In one study, 21% of diabetic dogs had visible retinal hemorrhages and microaneurysms after cataract surgery compared with 0.6% of nondiabetic dogs.[12] The consequences of these pathologic changes on vision are variable but directly correlate to the severity of the condition.

In addition to the retinal changes directly attributed to DM, gross retinal hemorrhages and detachments may be caused by systemic hypertension. The mechanism by which hypertension develops in diabetic patients is unclear; however, impaired lipid metabolism, decreased vascular compliance, glomerular hyperfiltration, and immune-mediated microangiopathy may be contributing or causative factors.[13] The incidence of concurrent diabetes and hypertension in humans is approximately 40% to 80%, and it has been estimated that 46% of diabetic dogs have demonstrable hypertension.[14] Little data are available regarding concurrent diabetes and hypertension in cats.

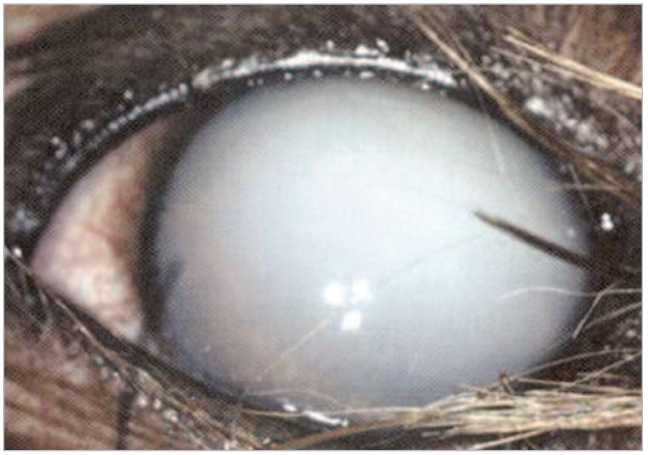

Figure 5. Lipid-laden aqueous humor appears more creamy white than aqueous flare.

PITUITARY–ADRENAL DISEASE

Ocular complications often are not considered among the primary manifestations of HAC in small animals. However, there is actually an extensive list of possible ophthalmic consequences to the excessive levels of corticosteroids present in this disorder. Some possible findings vary, depending on the specific circumstances of the case and the location of the primary causative lesion in the adrenal glands or the pituitary. Conversely, systemic hypertension and its repercussions are common regardless of the site of the primary lesion, as are metabolic changes associated with hyperlipidemia and lipoproteinemia. In addition to its previously discussed lipid-laden aqueous and retinalis, hyperlipidemia occasionally results in cholesterol infiltrates in the cornea of cushingoid patients. Concurrent DM, which occurs in some cases, contributes to the additional risks for cataract development, lens-induced uveitis, and retinal pathology.

Many animals that present with sudden acquired retinal degeneration have systemic clinical signs consistent with those of Cushing's syndrome.

In cases of HAC resulting from a pituitary macroadenoma, blindness may occur due to direct effects of tumor size. As the tumor expands dorsally beyond the confines of the sella turcica, it can compress or invade adjacent structures. However, blindness may also be misdiagnosed due to mental dullness and inappropriate responses to visual stimuli (absent menace response).[1] Ten percent to

20% of dogs with pituitary-dependent HAC have macroadenomas that can result in blindness and/or cranial nerve dysfunction.[15] Humans with pituitary tumors, regardless of whether they have cushingoid signs, occasionally present with third nerve palsy or ptosis as the first or only sign.[16,17] Although it is uncommon for veterinary patients to present early enough for these subtle signs to be the only recognizable signs of HAC, these signs may accompany other, more obvious changes and provide clues as to the likelihood of a primary pituitary lesion.

Because of an overabundance of cortisol, animals with HAC frequently have some degree of immunosuppression. They are, therefore, at risk for infection by a variety of pathogens, many of which frequently target the eye. Infectious agents, particularly fungal organisms, can invade tissues or cause immune-mediated lesions of the posterior uvea and retina (most commonly) and can occasionally affect the anterior uvea or cause a full-blown case of endophthalmitis. In addition, excessive circulating cortisol places patients at risk for ectopic calcification and impaired healing, both of which usually manifest with some degree of keratopathy. When calcium is deposited in the corneal stroma, it may result in ulcerative keratitis or in the opacities classically described as *band keratopathy*, wherein calcium crystals form a horizontal band in the superficial cornea, usually within and along the palpebral fissure.[18] If an ulcer is present over the calcium deposits, it may be possible to remove or prevent the progression or accumulation of crystals with a topical calcium chelator such as EDTA, but this is impossible when the overlying epithelium is intact. The degree of discomfort patients suffer as a result of the corneal deposits and ulcerations can vary. Circulating cortisol also slows corneal healing. When the cornea of a Cushing's patient is injured, it heals less quickly than in a normal animal. Thus, injured or ulcerated tissue in a patient with HAC is at greater risk for progression of injury and for perforation. A protracted period of discomfort is also likely. In addition, Cushing's patients can be affected by facial paralysis or exophthalmos, both of which can result in exposure keratitis and ulceration or exacerbate any corneal disease that is already present.[1]

Primary HAC is rare in cats, as is the naturally occurring disease in humans. Both species are susceptible to all of the ocular signs found in dogs but are specifically prone to hypertension.

Sudden acquired retinal degeneration (SARD), a noninflammatory retinal syndrome with degeneration and loss of photoreceptors, has been loosely associated with HAC because many animals that present with SARD have systemic clinical signs consistent with those of Cushing's syndrome, including polydipsia, polyuria, polyphagia, panting, and anxiety.[19,20] Often, dogs with SARD present with acute, bilateral blindness and initially have normal results from a fundic examination. Vision loss usually occurs in a period of 1 to 2 days but sometimes occurs more gradually, in the course of a few weeks. Electroretinography reveals loss of retinal function (absent waveform), even with a normal-appearing fundus. Over the next few weeks and months, the retina begins to show signs of degeneration, including tapetal hyperreflectivity, blood vessel attenuation, and atrophy of the optic nerve. Eventually, the ophthalmoscopic appearance is consistent with and complementary to the electroretinographic finding of complete lack of retinal function.

Patients with Cushing's disease are particularly susceptible to retinal and corneal pathology secondary to the effects of excessive circulating cortisol.

Many animals with SARD have persistent clinical signs and biochemical abnormalities (elevated alkaline phosphatase, alanine aminotransferase, and cholesterol levels) consistent with excessive glucocorticoid production but may or may not have an elevated serum cortisol level. This raises the question about whether Cushing's syndrome is a cause of SARD, a risk factor for the disease, an associated condition based on some other unknown factor, or a "red herring." It is possible that the adrenal glands or pituitary of SARD patients secretes different substances that could result in clinical signs similar to those found in Cushing's patients. Many sex hormones may have glucocorticoid-like activities. In a recent study[21] that evaluated levels of androstenedione, estradiol, progesterone, 17-OH progesterone, testosterone, pre- and post-stimulation cortisol, and resting adrenocorticotropic hormone levels in 10 dogs with SARD, nine had clinical signs similar to those found with excessive cortisol levels. Nine of the 10 dogs also had elevations in one or more

sex hormones, while five of 10 dogs had elevated cortisol levels after adrenocorticotropic hormone stimulation.[21] Further study of this disease is necessary. At the moment, there is no treatment for the retinal degeneration, and the blindness is permanent.

Adrenal insufficiency, also referred to as *Addison's disease*, does not generally cause ocular problems unless the patient is hypercalcemic. Lesions that form secondary to hypercalcemia are discussed in greater detail in the section titled "Calcium Disorders."

Pheochromocytomas are catecholamine-secreting tumors of the adrenal medulla. The catecholamines exert a direct effect on α_1-adrenergic receptors on radial iris muscle (dilator), resulting in mydriasis, which is usually episodic. Other ocular signs, when present, are usually the result of systemic hypertension. Acute blindness occurs in 5% to 8% of cases and is usually due to retinal detachment. Ocular hemorrhage (retinal hemorrhage, hyphema) occurs in 10% to 15% of cases.[1]

GROWTH HORMONE DISORDERS

Acromegaly is usually due to a functional adenoma of somatotropic cells in the pars distalis of the pituitary and is generally considered a disease of cats.[22] It is unusual in dogs, and when it occurs, it is usually induced by progesterone, either in older, intact, cycling female dogs or dogs with a history of long-term progestin administration.[23] The clinical signs are due to chronic excessive secretion of growth hormone. Potential ocular signs include neoplasia-induced papilledema (noninflammatory swelling of the optic nerve head), blindness (rarely; usually with larger pituitary lesions), and signs secondary to DM (which is invariably present in acromegalic cats), along with systemic hypertension.[1] Hypertension is variably present and occurs frequently secondary to the cardiovascular effects in cats with concurrent renal insufficiency.[1]

Pituitary dwarfism results from a congenital deficiency of growth hormone. It is most common in German shepherds, in which it is inherited in a simple, autosomal recessive pattern.[24] It also occurs occasionally in the weimaraner, Eskimo spitz, and Karelian bear dog and rarely in cats. Clinical signs are due to both the primary deficiency of growth hormone and the secondary deficiency of insulin-like growth factor 1 and other hormones.[25] The growth rate of affected animals slows at 2 to 3 months of age, causing them to appear stunted and persistently juvenile. Ocular signs are nonspecific and attributable to secondary hypothyroidism, which is observed in most cases and results from a deficiency of thyroid-stimulating hormone.

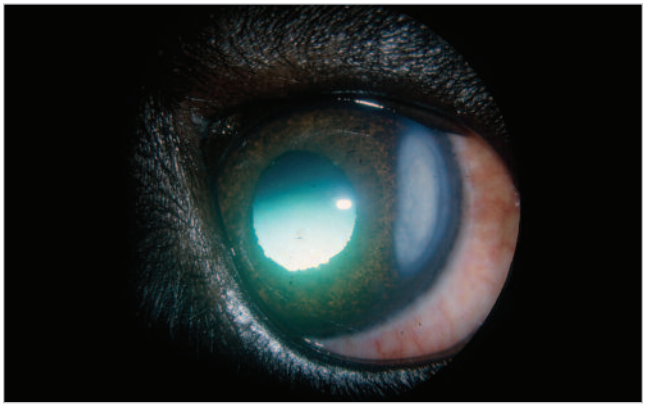

Figure 6. Lipid infiltrates in the cornea of a hypothyroid dog.

THYROID DISEASE

Hypothyroidism may be primary, secondary, tertiary, congenital, or acquired (iodine deficiency is rare), but the underlying disorder in all cases is a decreased level of circulating thyroid hormones. This is a fairly common condition in dogs, but cats are very rarely affected. Ocular signs are uncommon and usually secondary to hyperlipidemia or hyperlipoproteinemia.[1] However, there are other potential ocular consequences of hypothyroidism, including those due to neurologic dysfunction.

Thyroid deficiencies can result in significant ocular surface disease and may also be associated with anterior segment changes.

Corneal lipid deposits and infiltrates or lipid-laden aqueous humor and its associated uveitis are the most common metabolic consequences of hypothyroidism. Arcus lipoides corneae is most common in hypothyroid German shepherds and appears as an opaque ring of crystalline lipid deposits along and within the peripheral cornea near the corneoscleral limbus[1,26] (Figure 6).

Figure 7. Facial paralysis in a dog.

Figure 8. A cat with Horner's syndrome exhibiting miosis, ptosis, enophthalmos, and protrusion of the nictitating membrane.

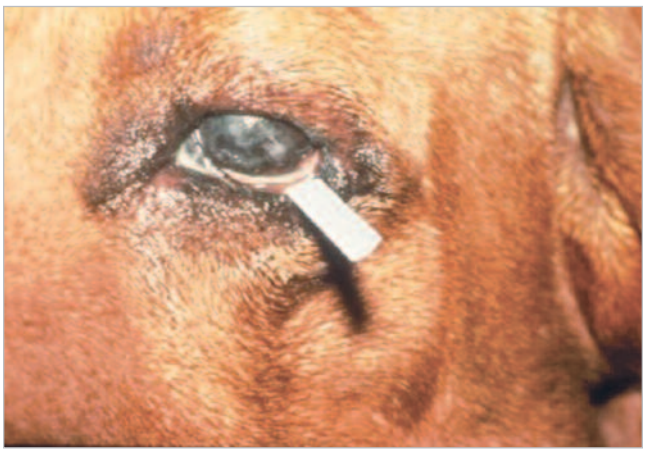

Figure 9. A severe case of KCS.

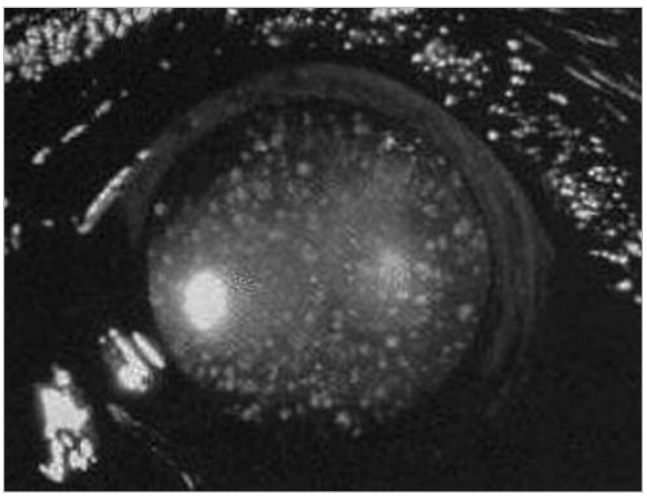

Figure 10. Hypocalcemic cataracts in a dog.

Treatment is aimed at the primary cause of the disorder, but if the lesion is superficial, the opacity can be removed by keratectomy.

Specific details of the pathogenesis and initiation of facial paralysis and other peripheral neuropathies associated with hypothyroidism are not well described. Facial nerve paralysis can initiate or exacerbate difficulties with corneal exposure and subsequent keratitis (Figure 7). Horner's syndrome, in which patients present with miosis, ptosis, enophthalmos, and protrusion of the third eyelid, may also be present in some cases[27] (Figure 8). Although usually nonpainful for the patient, Horner's syndrome can be quite disconcerting to the owner. These neurologic changes most likely result from hypothyroid-induced segmental demyelination and axonopathy.

Keratoconjunctivitis sicca (KCS), which is commonly referred to as *dry eye*, can also facilitate exposure and secondary keratitis (Figure 9). When hypothyroidism and KCS occur in the same patient, it is most likely attributable to an immune-mediated process affecting the thyroid and lacrimal glands.[28,29] Treatment should consist of tear replacement and lacrimogenic therapy, as would be instituted to treat primary KCS, and thyroid supplementation. Occasionally, KCS can result from peripheral neuropathy affecting innervation of the lacrimal gland and may even accompany facial paralysis. Lubrication is the most important aspect of therapy in these cases, particularly because affected patients cannot blink or produce an adequate amount of tears.

The most predictable ophthalmic manifestations of hyperthyroidism are those associated with systemic

hypertension (see box on this page). Hyperthyroidism is common in older cats and results from an intrinsic disorder of the thyroid gland. Although systemic blood pressure is elevated to a systolic pressure above 160 mm Hg in 87% of hyperthyroid cats, ocular signs are relatively uncommon.[30] Retinopathy with detachments, subretinal effusion, edema, and hemorrhage and subsequent degeneration are the typical ophthalmic findings, frequently with a history of acute loss of vision.[31,32] In a study of 69 cats with hypertensive retinopathy, only five were hyperthyroid.[31] Another survey of 100 hyperthyroid cats and 30 normotensive controls reported that no ophthalmologic abnormalities were more common in hyperthyroid cats compared with euthyroid cats and only two hyperthyroid cats had ophthalmic signs of hypertensive retinopathy.[33]

Dogs rarely develop hyperthyroidism. When it does occur, it is usually due to a functional malignant neoplastic process of the thyroid.[1] No data regarding the ophthalmic signs of hyperthyroidism in dogs are available, but mechanisms and pathology similar to those that affect cats are possible. Some dogs with hyperthyroidism could also have ophthalmic signs due to hypercalcemia.

CALCIUM DISORDERS

Hypocalcemia can be caused by a number of conditions, including primary hypoparathyroidism, renal failure, pancreatitis, eclampsia, and C-cell (thyroid parafollicular cell) tumors, that result in excess secretion of calcitonin.[1] Of the many potential ocular signs, cataracts are the most characteristic and have a classic appearance (Figure 10). They typically appear bilaterally as multifocal, punctate to linear, white opacities in the anterior and posterior subcapsular and cortical regions of the lens.[34–36] It is believed that the opacities are the result of a hypocalcemic derangement of the active cation transport mechanism of the lens epithelium, which leads to osmotic imbalance and swelling and rupture of lens fibers.[35,36] A survey of hypocalcemic dogs revealed that 12 of 37 (32%) developed cataracts.[1] In a similar study, two of five (40%)

Hypertensive Retinopathy

Retinal changes associated with systemic hypertension include hemorrhages, edema, and detachments, especially with subretinal effusions and retinal degeneration (Figure A). These changes often occur acutely and bilaterally, and patients often present with blindness. Pathologic changes can result from increased hydrostatic pressures, especially in the choroidal vasculature, subsequent to increased systemic blood pressures. Treatment is aimed at lowering blood pressure and addressing the primary disease that is causing the hypertension. The prognosis is directly related to the severity of the pathologic changes and the response to therapy. Detached portions of retina may reattach once blood pressure has normalized, and some vision may be restored. However, if the retina has been detached for a long time, the chances of regaining vision are reduced because of retinal degeneration that occurs subsequent to the retina's displacement and subsequent inadequate nutrition. The retinal photoreceptors can tolerate detachment for only a limited period before their death ensues; then, any vision changes are irreversible. Any hemorrhages that occur will likely result in focal scarring of the fundus and disruption and death of the involved photoreceptors. This may result in the formation of scotomas (blind spots) that may or may not be clinically relevant to the animal's vision. The treatment aims are to address the initiating endocrine disorder and directly treat the elevated blood pressure as soon as possible using systemic antihypertensive agents.

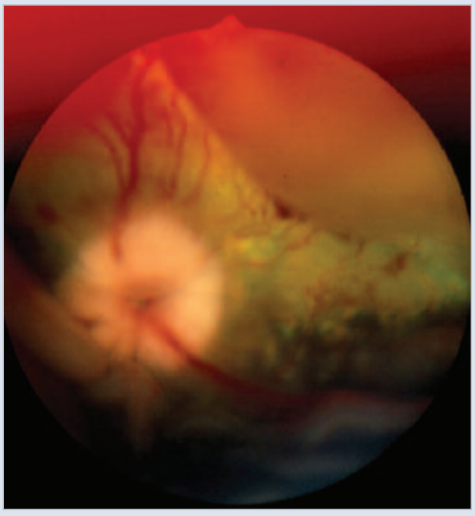

Figure A. Hypertensive retinal changes, including retinal detachment, edema, papilledema, and small hemorrhages, in a dog.

If, due to hypertensive forces, a blood vessel anywhere in the eye tears or bleeds, resulting in free blood within the anterior or posterior chambers or segments of the eye, secondary inflammation can occur. Therefore, hyphema must be treated as uveitis because the body reacts to having erythrocytes within the eye, as they are not normally present outside of blood vessels. Occasionally, hemorrhage can occur within the iris, possibly resulting in a more traditionally appearing uveitis, with flare, miosis, and iridic swelling. When anterior uveitis is present, administration of topical antiinflammatory drugs is necessary. Posterior uveitis requires systemic antiinflammatory drugs.

cats with hypocalcemia had cataracts.[1] Development of hypocalcemic cataracts is related to serum and aqueous humor calcium levels rather than duration of disease.[35] Successful treatment for hypocalcemia halts the progression of cataracts but does not reverse changes that have already occurred.[34,37] Other ocular signs of hypocalcemia may include prolapsed nictitans (particularly in cats), papilledema, optic neuritis, conjunctivitis, keratitis, blepharospasm, loss of eyelashes, strabismus, nystagmus, and anisocoria. The mechanism behind the development of these pathologic changes is not completely understood.

Conversely, when a patient's serum calcium concentration exceeds established normal levels and hypercalcemia occurs, primary hyperparathyroidism, hypercalcemia of malignancy, hypoadrenocorticism, vitamin D toxicity, osteoclastic disease, granulomatous disease, renal failure, or hyperthyroidism may be the underlying cause.[1] Idiopathic hypercalcemia can have similar clinical findings. Metastatic calcification, including band keratopathy and conjunctival deposits of calcium, can occur in ocular and orbital tissues in addition to more traditional locations, such as the skin, lungs, or renal pelvices.[38] It is also important to consider contributing problems, such as those associated with renal failure and hyperthyroidism (e.g., hypertension), which may not be directly attributable to the elevated calcium concentration but may result in ocular abnormalities.

The many potential ophthalmic manifestations of endocrine disorders in small animal patients are as diverse as the diseases they represent. Reactions of the eye to hormonal imbalances parallel the endocrine mechanisms of the body in that a complex set of interactions is required to maintain stable, normal function. Thus, any response of the eye to insults or stimuli, whether external or intrinsic, tends to induce other responses and changes not unlike those that occur with endocrinopathies. For example, a cataract can induce uveitis, possibly resulting in glaucoma or decreased tear production, which can worsen an exposure problem and lead to an ulcer. When ophthalmic disease is directly or indirectly caused by an endocrine disorder, treatment of the ocular signs is invariably aimed at or facilitated by treatment or control of the underlying systemic disease. It is essential for practitioners to be aware of the potential ocular consequences of endocrinopathies so that potentially painful or vision-threatening problems can be addressed early, thereby preventing more serious complications.

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