Bulgarian Journal of Veterinary Medicine, 2023, **26**, No 2, 137–150
ISSN 1311-1477; DOI: 10.15547/bjvm.2409

Review

CANINE OPHTHALMIC PATIENTS WITH ENDOCRINE AND METABOLIC DISORDERS – A REVIEW

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Summary

Lapšanská, M., A. Balicka & A. Trbolová, 2023. Canine ophthalmic patients with endocrine and metabolic disorders – a review. *Bulg. J. Vet. Med.,* **26**, No 2, 137–150.

The eye is particularly sensitive to various pathological processes in the body. Ocular changes are often the first symptoms of serious systemic diseases. Due to hormonal and metabolic disturbances in patients with endocrinopathies and metabolic disorders, secondary ophthalmic diseases can occur. Systemic diseases often cause ocular problems in animal and human patients. Early diagnosis of ophthalmic symptoms can help to identify a primary cause, such as endocrinopathies, and start an effective treatment. In some cases, clinical signs of systemic diseases are poorly documented in veterinary ophthalmology. Cataracts, retinopathy, metabolic disorders and systemic hypertension are common problems in animals with diabetes mellitus. Patients with hyperadrenocorticism may develop complications secondary to hyperlipidaemia and hypertension. Acute blindness due to sudden retinal degeneration (SARDS) has been associated with pituitary-adrenal axis disorders. Growth hormone disorders can result in secondary ocular complications due to hypertension (corneal infiltrates, decreased tear production and neurological dysfunction). Animals with hyperthyroidism may have ophthalmic problems associated with systemic hypertension and subsequent retinal bleeding or detachment.

Key words: Cushing's syndrome, dog, metabolism, retinopathy, SARDS

INTRODUCTION

The eye is one of the most complicated organs in the body. Due to transparency of visual axis it is possible to examine its inner segments without the use of invasive methods. It is an important source of information about the health status of the examined individual. Systemic health disorders can be revealed by comprehensive ophthalmological examination. The eye is particularly sensitive to various pathological processes taking place in the body (Cullen & Webb, 2007; Ofri, 2017). Ocular changes can often occur as first signs of systemic disease and can lead to its early diagnosis (Gould & Carter, 2014). The primary cause of the ocular lesion should be always considered. Holistic approach to the patient is valuable when taken into consideration differential diagnosis and individual therapeutic protocols (Cullen & Webb, 2007). Ophthalmic patients often require consultation with in-

ternal specialists focusing on cardiology, nephrology, endocrinology, neurology, oncology, infectology and immunology. Ocular examination should be a part of diagnostic work-up of cases with systemic disorders such as infectious and parasitic, nutritional, vascular, dermatological, immune-mediated and miscellaneous diseases as well as congenital ones (Cullen & Webb, 2007; Gould & Carter, 2014). For instance, in clinical practice systemic hypertension is often diagnosed during ophthalmic examination while clinical signs require additional tests and consultations with other specialists (Gould & Carter, 2014). In this review article the focus is placed on most common metabolic and endocrine disorders that are often primary causes of ophthalmic diseases in veterinary practice.

ENDOCRINE DISORDERS

Diabetes mellitus

Diabetes mellitus (DM) is a well-known disease in small animal practice. According to studies on prevalence, the number of affected dogs is increasing (Guptil *et al.,* 2003). Diabetes mellitus is divided into two subtypes: type I (insulin-dependent diabetes mellitus) and type II (non-insulin-dependent diabetes mellitus). Insulin-dependent diabetes mellitus is the most common form in dogs (Aroch *et al.,* 2012). In this subtype, immune-mediated destruction of pancreatic beta cells (Rucinsky *et al.,* 2010) and insulin deficiency occur, and the process leads to hyperglycaemia. Blood cell alterations via activation of protein kinase C, myo-inositol depletion and sorbitol accumulation may become consequences of persistent hyperglycaemia (Kikkawa, 2000). Obesity, pancreatitis or medication may cause degeneration of beta cells (Nelson, 2005). Many clinical signs of DM result from prolonged hyperglycaemia and glucosuria, such as weight loss, polyuria (PU), polydipsia (PD) and polyphagia (PP) (Behrend *et al.,* 2018). Obesity, pancreatitis, immune-mediated insulinitis (Nelson & Reusch, 2014), and renal and heart diseases have also been associated with diabetes mellitus (Rucinsky *et al.,* 2010). Ocular disorders such as keratoconjunctivitis, Horner's syndrome (Holland, 2007), cataracts and retinopathy are common complications associated with DM (Basher & Roberts, 1995; Muñana, 1995; Good *et al.,* 2003; Cullen *et al.,* 2007; Holland, 2007; Gemensky-Metzler *et al.,* 2014). Some of these problems can lead to patient discomfort or vision loss (Miller & Brines, 2018).

The most frequently recognised disorder secondary to DM is the cataract. Diabetic cataracts occur in dogs in more than half of the diabetic canine population and in 1% of diabetic humans (Salgado *et al.,* 2000). Cataract development was reported in 75% of dogs in the first 12 months (Beam *et al.,* 1999). According to the study of Davidson (1999), diabetic cataracts developed over 10 days (median value) in Sharpei and brachycephalic dogs after hyperglycaemia. Cataracts can develop over months and in some cases can rapidly progress, resulting in complete blindness due to extremely opaque lenses (Davidson & Nelms, 2013) in one or two weeks (Plummer *et al.,* 2007). The lens is avascular and is freely permeable to glucose. From the surrounding aqueous humour, glucose enters by diffusion. Glucose is converted to lactic acid in the anaerobic glycolytic process. When persistent hyperglycaemia occurs, the hexokinase enzyme, which is responsible for this conversion, becomes saturated. Then, excess glucose is metabolised by the

polyol pathway to fructose and sorbitol. However, fructose and sorbitol are not freely diffusible (Feldman & Nelson, 2004). Aldose reductase is a metabolising enzyme that catalyses the reduction of glucose to sorbitol, whose activity increases at high glucose concentrations (Muirhead & Hothersall, 1995). Sorbitol and fructose trapped in the lens are hydrophilic osmotic agents that draw water into the lens. Consequently, swelled lenses with ruptured fibres become opaque. As a result, lenticular opacities known as cataracts occur (Richter *et al.,* 2002). Based on this pathophysiology, it can be assumed that cataract formation is related to glucose control; however, further research is required.

Patients with DM-related cataracts may be diagnosed with secondary uveitis. While lens capsule leakage occurs, lens proteins elicit an inflammatory response known as lens induced uveitis (LIU). This condition occurs in up to 71% of patients with cataracts (Paulsen *et al.,* 1986). LIU can be split into two groups. Phacolytic LIU occurs when the lens capsule remains intact, and phacoclastic LIU occurs when the lens capsule ruptures (Wilcock & Peiffer, 2016). According to previous studies, rupture of the lens capsule occurs in the equatorial region in patients with DM. The clinical signs of intraocular inflammatory reaction secondary to LIU include blepharospasm, epiphora, episcleral injection, corneal oedema, miosis, low intraocular pressure and aqueous flare and cells (Van der Woerdt *et al.,* 1992).

According to previous studies, 46% of diabetic dogs demonstrate systemic hypertension. Due to systemic hypertension, retinal haemorrhages and detachments can be observed (Struble, 1998; Mclellan & Narfström, 2014). The common fundus lesions observed in dogs with hypertensive chorioretinopathy are: retinal oedema, papilledema, narrowing of the retinal vessels, retinal and vitreal haemorrhages and serous detachment (Villagrasa & Cascales, 2000). Systemic hypertension can be the primal cause of retinal detachment or retinal haemorrhages developed with progression of the disease. Analyses of ocular abnormalites in hypertensive dogs reveled that among 42 dogs diagnosed with increased blood preasure, 40% had retinal haemorrhages while the prevalence of ocular lesions attained 62% (LeBlanc *et al.,* 2011).

Another common disorder associated with DM is diabetic retinopathy (DR), a major cause of blindness in humans (Frank, 1986). In dogs, the mean period from onset of diabetes to the diagnosis of DR is 1.4 years (Landry *et al.,* 2004). Diabetic retinopathy in dogs is characterised by retinal haemorrhages and capillary microaneurysms (Cullen & Webb, 2007; Narfström & Petersen-Jones, 2013). It is difficult to determine the incidence of diabetic retinopathy due to cataract formation (Plummer *et al.,* 2007). To evaluate retinal function, it is necessary to perform complete ophthalmic examination, including electroretinography. This examination helps to detect retinal changes when cataracts affect the examination of the ocular fundus (Ofri, 2017). Changes in retinal function can occur in diabetic patients with and without retinopathies, as they all depend on the severity of changes affecting retinal response (Miranda *et al.,* 2011). According to authors' experience the amplitude of the a-wave and the b-wave during standard stimulation of the mixed rod and cone response was statistically significantly lower in dogs with DM compared to the healthy group of dogs (Lapšanská *et al.,* 2020).

Morphologic changes in DR include pericyte loss, microaneurysm formation, thickening of the vascular basement membrane, capillary closure and loss of smooth muscle cells in the retinal arterioles (Aroch *et al.,* 2012). The pathogenesis of cataract formation has been hypothesised to be the same as that of diabetic retinopathy by aldose reductase-mediated accumulation of sorbitol (Paulsen *et al.,* 1986) within retinal blood vessels (Arden & Sivaprasad, 2012), overproduction of oxidative stress species (Tarr *et al.,* 2013) or activation of the protein kinase C mechanism (Kikkawa, 2000). According to a study, retinal haemorrhages occurred in 21% of diabetic dogs after phacoemulsification, whereas these lesions were present in only 0.6% of nondiabetic dogs (Landry *et al.,* 2004).

In patients affected with tear film disorders, ulcers, secondary infections and polyneuropathies, quality of life changes. Other ocular manifestations of DM in dogs include corneal endothelial cell polymegathism and pleomorphism (Yee *et al.,* 1985), corneal endothelial cell loss (Yee *et al.,* 1985; Datiles *et al.,* 1990), retinal vascular damage (Kador *et al.,* 1990; Landry *et al.,* 2004) and increased susceptibility to keratoconjunctivitis sicca (KCS) (Foote *et al.,* 2019). In dogs affected with DM, significant reductions in tear film production and corneal sensitivity have been reported (Barrera *et al.,* 1992; Briggs *et al.,* 2000; Good *et al.,* 2003; Williams *et al.,* 2007; Woodham-Davies, 2020). Lower corneal sensitivity negatively affects reflex tearing, which results in lower Schirmer tear test values (Miller & Brines, 2018). Dogs with diabetic cataracts had significantly higher corneal touch thresholds than noncataractous dogs and significantly lower Schirmer tear test values than nondiabetic dogs. Due to the reduction in the quality of tear film, the tear film breakup time test becomes significantly lower than that in nondiabetic noncataractous and nondiabetic cataractous dogs (Cullen *et al.,* 2013). The diagnosis of keratoconjunctivitis sicca can be based on reduced tear production, quality of tear film, blepharospasm, mucoid discharge, conjunctival hyperaemia, dull lacklustre appearance of the cornea, corneal ulceration, pigmentation and vascularisation (Kaswan & Salisbury, 1990; Berdoulay *et al.,* 2005; Giuliano, 2013). Peripheral sensorimotor nerves responsible for secretion of lacrimal glands and corneal nerves are affected by diabetic neuropathy. It is characterised by axonal degeneration and segmental demyelination (Unger & Foster, 1992; Módulo *et al.,* 2009). Altered metabolism (Kador & Kinoshita, 1985; Loy *et al.,* 1990; Nathan, 1993) and vascular changes (Jamal, 1990) secondary to the hyperglycaemic state in diabetic patients are possible causes of nerve injury. Elevations in glucose concentration in tears were described in dogs with diabetes mellitus compared with nondiabetic cataractous and nondiabetic noncataractous dogs. According to the study, elevated glucose in tears did not affect conjunctive microbial isolates. Histological examination revealed a reduction in the density of goblet cells in 4 of 7 dogs affected with DM. A similar study revealed epithelial dysplasia and squamous metaplasia in the ventral palpebral conjunctiva in patients with diabetes mellitus (Cullen *et al.,* 2013).

Due to disorders affecting lipid metabolism, such as hyperadrenocorticism, hypothyroidism and DM, secondary hyperlipidaemia has been reported (Barrie *et al.,* 1993). In patients with DM who are not treated or who are insufficiently regulated, occurrence of hyperlipidaemia is a

common problem. Hyperlipidaemia may cause lipaemia retinalis and lipid-laden aqueous humour observed in dogs affected with DM (Miller & Brines, 2018). A relatively uncommon condition observed in older dogs with DM is stromal intracorneal haemorrhage (ICH) (Matas *et al.,* 2011; Violette & Ledbetter, 2016). DM-related ocular changes affect all parts of the eye, causing vision impairment and discomfort (Miller & Brines, 2018).

Hyperadrenocorticism

Hyperadrenocorticism (HAC), known as Cushing's syndrome, is a common endocrinopathy in dogs and is described as glucocorticoid excess. HAC can be caused by adrenocorticotropic hormone (ACTH)-secreting neoplastic or hyperplastic pituitary gland (pituitary-dependent HAC) or a cortisol-secreting adrenocortical tumour. The third cause may be iatrogenic, caused by chronic excessive glucocorticoid therapy (Aroch *et al.*, 2012). Ocular manifestations of HAC are considered secondary consequences. Due to the presence of excessive levels of corticosteroids, many ophthalmic consequences can be observed. The findings depend on the location of the primary lesion in the pituitary or adrenal glands. Metabolic changes associated with hyperlipidaemia, lipoproteinemia and systemic hypertension are common regardless of the site of the primary lesion (Plummer *et al.,* 2007). Hyperlipidaemia can occasionally result in cholesterol infiltrates in the cornea in the Golden retriever (Samson & Blunden, 2010). Canine patients with Cushing's syndrome may have concurrent diabetes mellitus (Aroch *et al., 2012*). In cases where DM occurs in patients with HAC, there is a risk of cataract formation, LIU and retinopathies. Pituitary-dependent HAC in canine patients may include macroadenomas that can result in blindness or cranial nerve dysfunction. This condition has been described in 10 to 20% of dogs with HAC. In dogs with pituitary macroadenoma secondary to HAC, vision impairment depends on the stage of advancement of the tumour (Duesberg *et al.,* 1995).

Cushing's patients are at risk of developing corneal calcification, KCS, cataracts, lesions associated with systemic hypertension, lipaemia retinalis or lipids in the aqueous humour. (Lorenz, 1982; Ward *et al.,* 1989; Williams *et al.,* 2007; Cullen *et al.,* 2013). Additionally, corneal healing may be affected by circulating cortisol (Plummer *et al.,* 2007).

In most dogs affected by sudden retinal degeneration (SARDS), vision loss is associated with clinical signs such as weight gain, anxiety, panting, PP, PU and PD (Mattson, 1992; Holt *et al.,* 1999). Additional laboratory abnormalities observed in SARDS cases include neutrophilia, lymphopaenia, elevated serum alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase or cholesterol as well as reduced urine specific gravity and proteinuria. These changes are consistent with those seen in certain endocrinopathies, such as hyperadrenocorticism (Vainisi *et al.,* 1983; 1985; Acland *et al.,* 1984; Acland & Aguirre, 1986; Van der Woerdt *et al.,* 1991; Mattson *et al.,* 1992; O'Toole *et al.,* 1992; Abrams *et al.,* 2001; Gilmour *et al.,* 2006; Braus *et al.,* 2008; Montgomery *et al.,* 2008; Carter *et al.,* 2009). Approximately 20% of dogs with SARDS are diagnosed with typical hyperadrenocorticism (Acland *et al.,* 1984; Vainisi *et al.,* 1985; Acland & Aguirre 1986; Van der Woerdt *et al.,* 1991; Mattson *et al.,* 1992; Holt *et al.,* 1999). Although the clinical signs resolve in dogs with SARDS, blindness remains

irreversible. In cases affected by Cushing's syndrome, eventual clinical signs regress after therapy (Acland *et al.,* 1984; Acland & Aguirre, 1986; Van der Woerdt *et al.,* 1991; Mattson *et al.,* 1992; Holt *et al.,* 1999; Carter *et al.,* 2009). According to reports, the development of SARDS in dogs with pre-existing hyperadrenocorticism was observed (O'Toole *et al.,* 1992; Cabrera Blatter *et al.,* 2012). Due to hyperadrenocorticism in middle-aged to old dogs, the relationship between hyperadrenocorticism and SARDS remains controversial. Other studies suggest that sudden vision loss as a physiologic response to stress is present in patients with atypical hyperadrenocorticism (Vainisi *et al.,* 1983; 1985; Acland *et al.,* 1984; Acland & Aguirre, 1986; Chastain *et al.,* 1986; Mattson *et al.,* 1992; Holt *et al.,* 1999).

Immunosuppression is commonly observed in patients with HAC. These patients are at risk of developing immune-mediated lesions often caused by fungal organisms. Ocular manifestations include endophthalmitis, lesions on the posterior uvea and retinal changes. Ulcerative keratitis or opacities described as band keratopathy can arise when calcium is deposited in the cornea (Ward, 1989; Samson & Blunden, 2010). Additionally, in patients with HAC, delayed corneal healing, facial paralysis and exophthalmos can be observed (Anoop *et al.,* 2020). Retinal and corneal pathology secondary to excessive circulating cortisol often occurs in patients with hyperadrenocorticism (Plummer *et al.,* 2007).

Hypothyroidism

Canine hypothyroidism is a common endocrinopathy. It occurs in 0.2% of dogs and is extremely rare in cats. Hypothyroidism leads to decreased production of thyroxine (T_4) and triiodothyronine (T_3). The disease can be caused by thyroid gland disorder (primary hypothyroidism), a pituitary disorder leading to thyrotropin deficiency (secondary hypothyroidism), or hypothalamic disorder leading to deficiency of thyrotropin-releasing hormone (THR) (tertiary hypothyroidism) (Aroch *et al.,* 2012). According to a study, hypertriglyceridaemia was diagnosed in 88% of dogs, and hypercholesterolaemia – in 78% of dogs with hypothyroidism (Dixon *et al.,* 1999). Ocular signs are rare but usually secondary to hyperlipoproteinaemia or lipidaemia (Feldman & Nelson, 2004) and may lead to lipid dystrophy (corneal lipidosis) with secondary ulceration and uveitis (Scott-Moncrieff, 2007). In German Shepherd dogs with hyperthyroidism, secondary *arcus lipidosis corneae* can be observed, which is a form of metabolic corneal dystrophy that manifests with opaque rings of crystalline lipid deposits along the peripheral cornea (Crispin, 1988; Feldman & Nelson, 2004). Hyperlipidaemia can also cause lipid effusion in the aqueous humour and lipaemia retinalis with retinal bleeding (Landry *et al.,* 2004; LeBlanc *et al.,* 2011) and detachment (Crispin & Barnett, 1978; Kern & Riis, 1980). Lipid abnormalities are usually resolved while treating hypothyroidism (Rogers *et al.,* 1975). Glaucoma has been reported as a secondary consequence of hypothyroidism. Concurrent KCS has been reported in 20% of patients affected with hypothyroidism (Aroch *et al.,* 2012). The association with KCS is probably indirect and results from multiple glandular, immune-mediated inflammation events (Gosselin *et al.,* 1981; Peruccio, 1982). Other potential consequences include those due to neurological dysfunction (Plummer *et al.,* 2007). In patients with hypothyroidism, a variety of neurologic signs, such as cranial nerve dys-

function of vestibular disease (e.g., facial nerve paresis/paralysis, strabismus, nystagmus) (Vitale & Olby, 2007; Rushton *et al.,* 2013; Utsugi *et al.,* 2014), and Horner's syndrome can occur (Kern *et al.,* 1989; De Lahunta *et al.,* 2014). The pathogenesis and clinical signs of facial paralysis in cases of hypothyroidism require further research.

There are also less common endocrine diseases, such as Addison's disease, pituitary dwarfism and acromegaly, which may lead to vision impairment. Addison's disease, known as hypoadrenocorticism, is very rare in dogs (Anoop *et al.,* 2020). Its ocular manifestation is associated with secondary hypercalcaemia (Plummer *et al.,* 2007). Growth hormone disorders are common in cats but very rare in dogs (Anoop *et al.,* 2020). Pituitary dwarfism is characterised by congenital deficiencies in growth hormones. It is common in German Shephard dogs and occasionally occurs in Eskimo Spitz, Weimaraner and Karelian Bear dogs (Eigenmann *et al.,* 1984). Ocular signs associated with pituitary dwarfism are nonspecific and attributable to secondary hypothyroidism (Plummer *et al.,* 2007). Potential ocular signs of acromegaly include blindness and neoplasia-included papilledema. Other ocular signs may present secondary to DM and hypertension (Plummer, 2007; Nelson & Reusch, 2014).

METABOLIC DISORDERS

Hyperlipidaemia

Hyperlipidaemia is an excess of blood lipids. Although primary (hereditary) and secondary hyperlipidaemias have been described in canine patients, secondary hyperlipidaemia occurs more often. In dogs affected with DM, hypothyroidism, HAC (Rogers *et al.,* 1975; Rogers, 1977; Whitney, 1992; Bauer, 2004; Feldman & Nelson, 2004; Johnson, 2005), pancreatitis, cholestasis, glomerulonephropathy or, in the case of a high-fat diet, secondary hyperlipidaemia can be observed (Aroch *et al.,* 2012). According to one study, 14% of the canine population has been diagnosed with hyperlipidaemia. In affected dogs, secondary ocular manifestations of systemic disease can be observed, including corneal lipid keratopathy, corneal opacities (Crispin, 1993), lipaemia of the ocular blood vessels and lipid infiltration of the globe, which were most frequently observed in the cornea or uvea. As a result of secondary uveitis, lipids may also be observed in the anterior chamber of the eye. Abnormal accumulation of lipoproteins in the anterior chamber occurs rarely in ophthalmic patients. It has been described in human medicine and there are several reports regarding dogs (Olin *et al.,* 1976; Sottiaux, 1999). In this cases this characteristic lipid-laden aqueous flare creates opacity to the aqueous humour. This opacity is also known as lipemic aqueous, lipid aqueous and lipemic uveitis (LU) (Olin *et al.,* 1976; Halenda & Moore, 1998; *Klein et al.,* 2011). Although it has been hypothesised that both disruption of the blood aqueous humour barrier and hyperlipidaemia has to develop to cause lipemic uveitis, in some cases it has been considered that LU can occur in dogs with hyperlipidaemia without blood-aqueous barrier breakdown (Hendrix, 2013). Detection of lipoproteins in the aqueous humour occurs only in affected cases (Mahley & Weisgraber, 1974; Olin *et al.,* 1976) when increase in serum cholesterol concentration (hypercholesterolaemia), serum triglyceride concentration (hypertriglyceridaemia), or both is diagnosed (Bauer, 1995). Miniature Schnauzers, Beagles, and Shetland

Sheepdogs are the breeds most commonly affected with primary hyperlipidaemia (Bauer, 1995; Sato *et al.,* 2000). Secondary hyperlipidaemia occurs when lipid metabolism is affected, like in cases with diabetes mellitus, hyperadrenocorticism, and hypothyroidism (Barrie *et al.,* 1993; De Marco *et al.,* 2017). Similarly, atherosclerosis that is associated with diabetes mellitus and hypothyroidism, may be a cause of increased permeability of the uveal vessels and in consequence LU (Liu *et al.,* 1986; Sottiaux, 1999; Hess *et al.,* 2003). Development of LU and its stages depends on the patients' natural predisposition. Lipemic uveitis has been also reported as a postoperative complication after phacoemulsification in canine patients (Klein *et al.,* 2011). Visible changes, such as pink conjunctiva and retinal blood vessels, may be observed when hyperlipidaemia is associated with hypertriglyceridaemia (Aroch *et al.,* 2012).

Ionic disturbances

Endocrinopathies are frequently associated with calcium disorders. Primary hypoparathyroidism, pancreatitis, eclampsia, renal failure and C-cell (thyroid parafollicular cell) tumours can cause hypocalcaemia (Fledman & Neslson, 2004). Bilateral cataract formation with opacities in anterior and posterior subcapsular and cortical regions of the lens can occur (Koregay & Greece, 1980). The development of other possible ophthalmic changes is not completely understood. Due to hypocalcaemia, blepharospasm, loss of eyelashes, strabismus, nystagmus, anisocoria, conjunctivitis, keratitis, papilledema and optic neuritis can be observed (Plummer *et al.,* 2007).

Hypoadrenocorticism, primary hyperparathyroidism, hyperthyroidism, hypercalcaemia of malignancy, osteoclastic disease, renal failure, granulomatous disease or vitamin D toxicity may be underlying causes for the development of hypercalcaemia (Fledman & Nelsom, 2004). Hypercalcaemia is defined as an increase in calcium levels above a physiological norm. Deposits of calcium can occur in conjunctiva and orbital tissue (Aurbach, 1985). The development of band keratopathy and metastatic calcification has also been described in dogs diagnosed with hypercalcaemia (Anoop *et al.,* 2020). However, in some cases affected by specific ocular abnormalities, elevated calcium concentrations have not been diagnosed, so contributing problems should be taken into consideration.

CONCLUSION

Many ophthalmic conditions are secondary to endocrine and hormonal imbalances. It is important to diagnose the primary cause of ocular changes in canine patients early and to consider the eventual presence of endocrinopathies. Early initiation of therapy is an important factor in stopping the development of the disease and the increasing risk of persistent ocular changes, including vision impairment.

ACKNOWLEDGEMENTS

The study was supported by the project VEGA 1/0479/18.

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Paper received 23.11.2020; accepted for publication 09.02.2021

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