

# Abnormalities of Globe Size and Position

### Introduction

It can be a challenge to differentiate between a change in size and a change in position of the eye. An abnormally small eye (microphthalmos) may be confused with a normal-sized eye that is recessed in the orbit (enophthalmos); an enlarged eye (buphthalmos) may have a similar appearance to a normal-sized eye that is anteriorly displaced (exophthalmos). Assessing the size of the palpebral fissure, position of the third eyelid (TEL) and corneal diameter, looking at the eye from different angles, careful comparison with the other eye and concurrent clinical signs are helpful in differentiating between these conditions.

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# CASE STUDY 1

## History

A 12-year-old female neutered domestic shorthaired cat is presented because of a sudden redness in the right eye. The left eye had looked abnormal for several weeks but appeared comfortable. The cat has recently lost weight and is lethargic.

## Questions

1. Describe the abnormalities in Figs. 1.1a, b, and c.
2. What differential diagnoses should be considered for this presentation?
3. What tests could you perform to make the diagnosis?

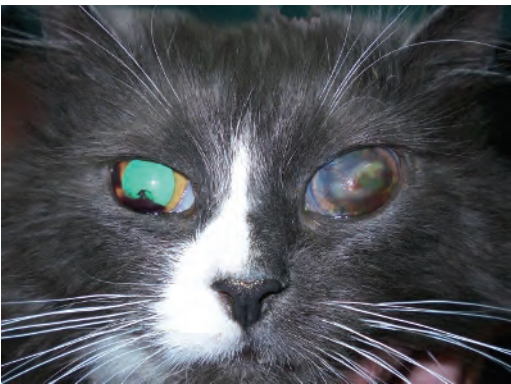
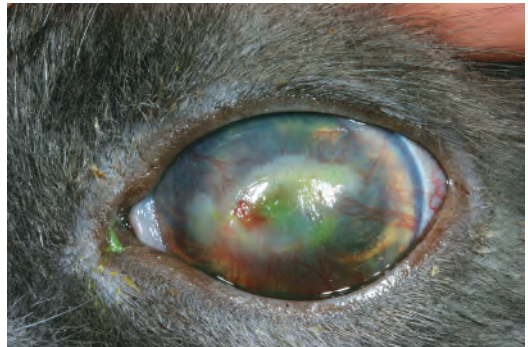
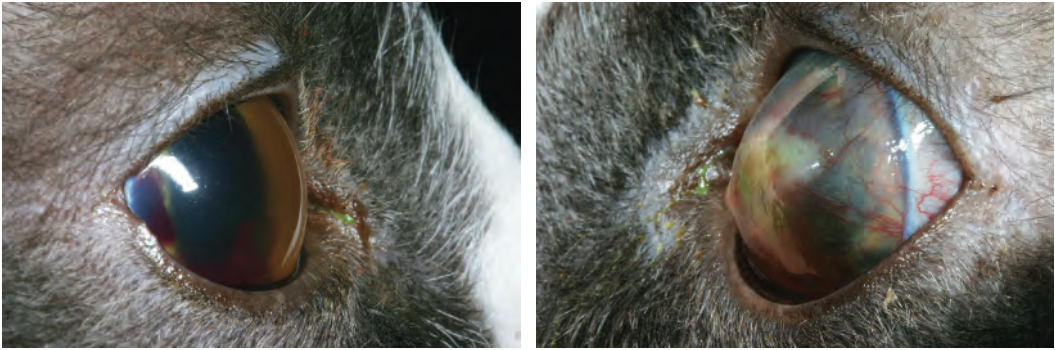


Fig. 1.1a



Fig. 1.1b





**Fig. 1.1c**

## Answers

### 1. What the figures show

**Fig. 1.1a** The left eye appears larger than the right eye; a wide palpebral fissure, increased corneal diameter and clearly visible medial and lateral regions of the limbus are consistent with buphthalmos. There is a generalised corneal opacity which is most dense axially; a tapetal reflection is not visible. In the right eye, the green tapetal reflection is obstructed ventrally by a red/black irregular opacity which appears to be in front of the iris, and there is a similar coloured opacity overlying the iris at the 9 o'clock position. The pupil is moderately dilated.

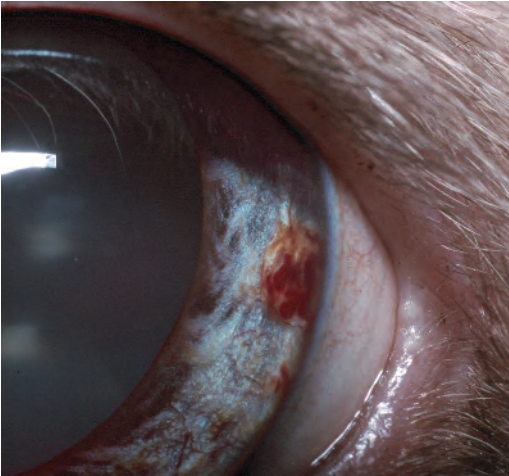
**Fig. 1.1b** In the left eye, the Purkinje images are disrupted. There is generalised corneal vascularisation and a stippled area of fluorescein stain uptake axially. The conjunctival vessels overlying the sclera on the lateral aspect of the globe are congested. The iris is difficult to see well but appears darker (medially) and possibly thickened. In the right eye, there is hyphaema; the regions of the iris that are visible appear normal.

**Fig. 1.1c** Oblique view from the lateral aspect of both eyes. In the left eye there is an irregular contour and anterior protrusion of the cornea (OS > OD). There is increased exposure of the sclera and conjunctiva, and episcleral congestion. The anterior chamber is obliterated by abnormal iris tissue which appears to be displaced anteriorly. In both eyes fluorescein dye is visible on the periocular hair at the medial canthus.

### 2. Differential diagnoses

Given the history and the appearance of the left eye, the following conditions should be considered:

- **Chronic glaucoma** In contrast to the dog, primary glaucoma in the cat is rare, and secondary glaucoma is more common. The most common causes of secondary glaucoma in the cat are chronic idiopathic lymphocytic-plasmacytic uveitis and primary intraocular neoplasia, most notably diffuse iris melanoma. Typical clinical signs include buphthalmos, conjunctival and episcleral congestion, corneal oedema, mydriasis, and impaired or absent vision. Buphthalmos can be difficult to discern in the cat and assessment of the size of the palpebral fissure can be helpful because it becomes wider as the size of the eye increases. Glaucoma in cats is typically insidious in onset and is often difficult to recognise. This is in contrast to canine primary glaucoma which is characterised by peracute pain, episcleral congestion, marked corneal oedema, mydriasis and blindness (*Ch. 6, case 2*).
- **Exophthalmos** Anterior displacement of the globe within the orbit. Common causes of exophthalmos in the cat include orbital neoplasia, orbital cellulitis/abscess and orbital trauma

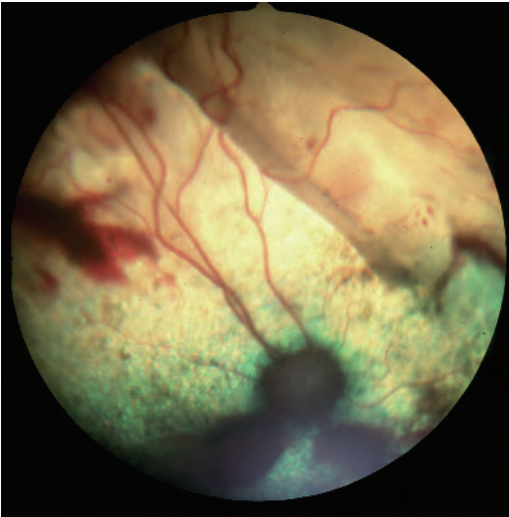


**Fig. 1.1d** Aneurysm within the lateral region of the major arterial circle in the left eye of a cat with systemic hypertension.

(haematoma, emphysema, fracture, foreign body). Primary malignant neoplasia and abscesses secondary to dental disease are more likely in old cats, whereas head trauma and orbital foreign bodies are more common in young cats (*Ch.12, case 2*).

Given the appearance of the right eye, the following conditions should be considered:

- **Systemic hypertension** Sustained systemic hypertension is commonly associated with ocular manifestations which primarily involve the posterior segment but also affect the anterior segment. Abnormalities in the posterior segment involve the retina, choroid and vitreous humour and appear as retinal oedema and bullae, retinal and intravitreal haemorrhages, retinal detachment and increased tortuosity of the retinal arterioles. Intraocular haemorrhage can occur as a result of haemorrhage from the iris (Fig. 1.1d), ciliary body, retina, and choroid. Extensive hyphaema can lead to the formation of anterior and posterior synechiae and secondary glaucoma.
- **Coagulopathy and platelet disorders** Ocular haemorrhage can be a clinical sign of a coagulopathy or a platelet disorder. Ocular haemorrhage typically occurs when the platelet count is  $<50\,000$  cells/ $\mu\text{l}$ .
- **Uveitis** When there is a breakdown of the blood-aqueous barrier during inflammation, red blood cells can enter the anterior chamber (hyphaema). The blood may form either a homogenous layer in the ventral anterior chamber or a clot, as in this cat.
- **Trauma** Ocular haemorrhage may result from both blunt and penetrating ocular trauma (*Ch. 12, cases 2 and 3*).
- **Pre-iridal fibrovascular membrane (PIFM)** The formation of fibrovascular membranes on the anterior iris is usually a consequence of intraocular inflammation, haemorrhage and/or hypoxia due to the release of vasoactive substances. Hence the formation of PIFMs is common in eyes with chronic uveitis, intraocular haemorrhage, retinal detachment, glaucoma, and neoplasia. The newly formed blood vessels within the membranes are fragile and can cause spontaneous and recurrent hyphaema. PIFMs can extend into the filtration angle and result in secondary glaucoma. Fibrovascular membranes are not restricted to the surface of the iris – they can also form on the retina and optic disc and in the vitreous.
- **Neoplasia (primary or secondary)** Intraocular haemorrhage may occur in eyes affected with primary or secondary neoplasia, either originating from a PIFM or as a result of the direct effect of neoplasia (e.g. adverse effect on clotting function).
- **Congenital anomalies** These include persistent hyaloid artery and persistent hyperplastic primary vitreous, both of which are rare conditions in the cat.



**Fig. 1.1e** Extensive dorsal retinal detachment and multiple retinal haemorrhages throughout the tapetal fundus and ventral to the optic disc.

### 3. Appropriate diagnostic tests

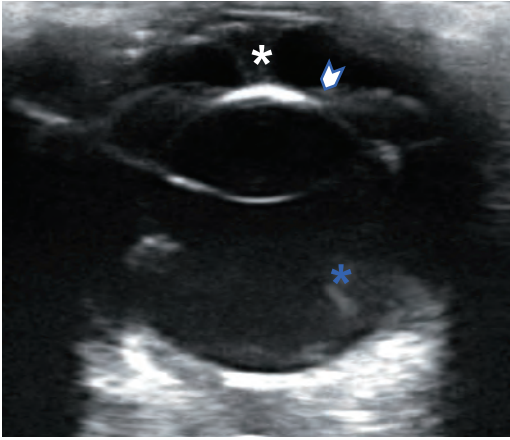
- Ocular reflexes
  - Pupillary light reflex – the left pupil is not visible. Negative consensual OS (from left to right eye); positive direct OD, albeit slow and incomplete.
  - Dazzle reflex – negative OS, positive OD
  - Palpebral reflex – positive OU, OS < OD
  - Corneal reflex – positive OU, OS < OD
- Menace response – negative OS, equivocal OD

In this cat, these results are consistent with blindness, reduced corneal sensation and lagophthalmos in the left eye, and reduced vision in the right eye.

- Examination with a focal light source – in the left eye, slit-lamp biomicroscopy reveals extensive superficial and deep corneal vascularisation, and generalised corneal oedema and fibrosis which is most marked axially.
- Ophthalmoscopy – in the right eye, this reveals an extensive dorsal retinal detachment, most marked within the medial quadrant, and multiple retinal haemorrhages of different sizes throughout the tapetal fundus and ventral to the optic disc (Fig. 1.1e).
- Schirmer tear test – 4 mm/min OS, 10 mm/min OD
- Fluorescein dye – negative staining OD, positive staining in the superficial axial cornea OS. This is indicative of suboptimal ocular surface health in the left eye, most likely because of the lagophthalmos.
- Tonometry – IOP 35 mmHg OS, 20 mmHg OD

There is increased resistance to retropulsion of the left eye; retropulsion of the right eye is normal. The remainder of the ophthalmic examination reveals no additional abnormalities. A general physical examination reveals an underweight body condition and mild dental disease.

The degree of resistance to retropulsion of the eye varies amongst species and between breeds. The normal feline globe is generally retropulsed less than the normal canine globe because of close apposition between the globe and the orbit in the cat. The degree of retropulsion in brachycephalic breeds is less than in other breeds because of the shallow orbit, in both cats and dogs.



**Fig. 1.1f** Horizontal B-mode ultrasound scan (left eye). There is hyperechoic material spanning the anterior chamber (white asterisk) and within the vitreous body (blue asterisk); convex iris leaflets contact the anterior surface of the lens (arrow). In this cat, these changes are consistent with intraocular haemorrhage, anterior synechiae, and iris bombé.

### Further diagnostic tests

- B-mode ocular ultrasound – this is indicated to evaluate the posterior segment when the anterior segment is opaque, and to take measurements. Axial globe length is the distance between the centre of the cornea and the posterior pole.

The ultrasound scan reveals an axial globe length of 22 mm OS and 19 mm OD (within normal limits), which confirms buphthalmos in the left eye. Additional abnormalities in the left eye include hyperechoic material spanning the anterior chamber (consistent with blood, fibrin or anterior synechiae), hyperechoic material within the vitreous (consistent with vitreal degeneration, intravitreal haemorrhage, neoplasm), and convex iris leaflets which contact the anterior lens capsule (consistent with iris bombé, *Ch. 9, case 4*) (Fig. 1.1f).

- Laboratory tests – results of routine haematology, biochemistry (including electrolytes), urine analysis and thyroid function are consistent with chronic renal failure.
- Systemic blood pressure measurement – indirect assessment with a Doppler sphygmomanometer (ultrasonic detection device) reveals a systolic blood pressure of 220 mmHg (upper limit for systolic blood pressure in the cat is 160–170 mmHg).

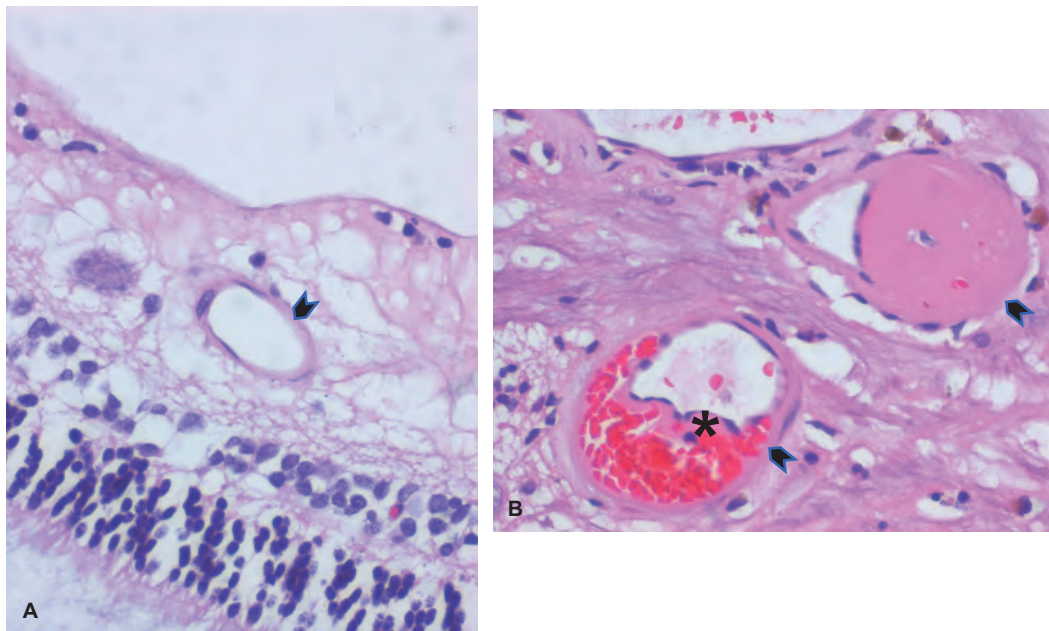
### Diagnosis

Based on the information available, a diagnosis of systemic hypertension is made. The ocular manifestations are hyphaema and hypertensive retinopathy in the right eye, and glaucoma secondary to intraocular haemorrhage in the left eye.

### Treatment

The preferred first-line treatment for feline systemic hypertension is amlodipine besylate (a calcium channel blocker) at a dose of 0.625–1.25 mg *per os* q24 hours. The aim of treatment is to lower the systolic blood pressure to a safe range, i.e.  $\leq 160$ –170 mmHg. Some cats need more frequent dosing (amlodipine besylate q12 hours) and others require the addition of benazepril to become normotensive. Adverse effects of amlodipine besylate are uncommon but include azotaemia, lethargy, hypokalaemia, reflex tachycardia and weight loss.

Symptomatic treatment for hyphaema can be considered with topical corticosteroid therapy, e.g. 1% prednisolone acetate q8–12 hours. Enucleation of the left eye in this cat is indicated because of pain, irreversible blindness and to prevent complications arising from progressive corneal disease.



**Fig. 1.1g** (A) H&E section of a normal feline retina demonstrating a normal retinal arteriole (arrow) ( $\times 200$ ). (B) H&E section of the detached retina in this hypertensive cat demonstrating two abnormal retinal arterioles (arrows) ( $\times 400$ ). The arteriolar walls are diffusely expanded by a bright pink homogenous matrix. This is referred to as hyalinisation and results from the leakage of plasma products into the vessel wall secondary to endothelial damage. Note the haemorrhage dissecting the vessel wall (asterisk) and the perivascular haemorrhage. Thickening of the vessel walls has resulted in extreme narrowing of the blood vessel lumens which are now barely visible; this degree of narrowing could result in ischaemic injury. The histopathological diagnosis is retinal and choroidal hyalinising arteriosclerosis with intraocular haemorrhage characteristic of hypertensive retinopathy. Reproduced with permission from EJ Scurrall.

A transconjunctival procedure is performed. In addition to the clinical findings, ocular histopathology reveals retinal detachment and confirms the clinical diagnosis of glaucoma secondary to extensive intraocular haemorrhage caused by the systemic hypertension (Fig. 1.1g).

Repeated thorough physical and ophthalmic examinations as well as blood pressure measurements are recommended, e.g. every 3–6 months.

All enucleated globes should be submitted for ocular histopathology. For routine diagnostic purposes, fixation of the globe in 10% formalin is generally appropriate, although confirmation with the chosen laboratory is recommended. Prior to fixation, as much excess extraocular tissue as possible should be removed, and the optic nerve should be left as long as possible.

## Prognosis

The prognosis is good for retinal detachment secondary to systemic hypertension in that most retinas reattach if antihypertensive therapy is successful at lowering the blood pressure sufficiently. The prognosis for vision is variable because it depends on the extent and duration of retinal detachment

prior to treatment, as well as the severity of any associated haemorrhage. There is evidence to suggest that the feline retina begins to degenerate within the first week of detachment. However, most cats only present when they are severely visually impaired or blind, by which stage both eyes are affected. The retinal pathology is often chronic in the eye that is affected first but is only noted when the fellow eye develops significant disease. Even if vision is not restored, continued treatment of the systemic hypertension is imperative to minimise progressive disease of other target organs (brain, heart, kidney).

## **Discussion**

Systemic hypertension is a relatively common disease in cats older than 10 years and is usually associated with chronic renal failure, and less frequently, with hyperthyroidism and Conn's syndrome. As the eye is a target organ for hypertensive damage, the most common reason for presentation is acute blindness secondary to retinal detachment. Neurological deficits may be present and are generally the result of cerebrovascular disease. Prolonged hypertension initially leads to arteriolar vasoconstriction, manifested as narrowing and increased tortuosity of the retinal arterioles, and finally to compromise of the vascular integrity. This in turn leads to intraocular haemorrhage as well as retinal oedema and an accumulation of serous fluid which separates the neurosensory retina from the underlying retinal pigment epithelium. The ocular changes progress over several months and early diagnosis of 'at risk' cats is important in preventing blindness. Ideally any geriatric cat should have an annual blood pressure assessment together with a complete ocular examination including fundic examination. Cats with e.g. renal disease or hyperthyroidism should be monitored particularly closely.

## **Further reading**

See Appendix 2.

## CASE STUDY 2

### History

A 9-month-old male Labrador Retriever is presented because both eyes have looked different for several months. There has been no evidence of ocular discomfort and the dog catches balls well. The dog has received his primary vaccination course and routine anthelmintic treatment and is reported to be clinically well.

### Questions

1. Describe the abnormalities and pertinent normal features in Figs. 1.2a and b.
2. What differential diagnoses should be considered for this presentation?
3. What tests could you perform to make the diagnosis?



Fig. 1.2a



Fig. 1.2b Right eye has received a topical mydriatic agent (tropicamide).

## Answers

### 1. What the figures show

**Fig. 1.2a** Left eye – is normal and shows an iris colour variation consisting of a mid brown outer zone and a dark brown pupillary zone. Right eye – has a small palpebral fissure; there is protrusion of the TEL. The pupil is small which creates a subtle anisocoria (OD < OS). The iris is slightly dark compared to the left eye. A tapetal reflection is not visible.

**Fig 1.2b** Both eyes are shown – the right pupil has been artificially dilated with tropicamide. Right eye – there is a structure which comprises multiple strands of iris tissue. The strands originate from the iris collarette and join at a single focal point. A cataract is present, resulting in leukocoria (white pupil).

### 2. Differential diagnoses

Given the history and appearance of the right eye, the following conditions should be considered:

- **Microphthalmos** This is a congenital anomaly in which the eye is abnormally small and deeply set within the orbit and has a range of concurrent defects including persistent pupillary membrane (PPM) remnants, cataract, retinal dysplasia, staphyloma, and nystagmus.
- **Nanophthalmos** A congenital anomaly in which the eye is abnormally small but otherwise normal.
- **Phthisis bulbi** Acquired end-stage atrophy of the eye following severe inflammation, ocular trauma or glaucoma. Typical features include an absence of visible signs of inflammation, an opaque cornea which prevents intraocular examination and marked hypotony (Fig. 1.2c).
- **Enophthalmos** An eye that is recessed in the orbit, causes of which include:
  - **Pain** Stimulation of the ophthalmic branch of the trigeminal nerve results in globe retraction by the retractor bulbi muscle which leads to enophthalmos and passive TEL protrusion. Conditions such as entropion and corneal ulceration often cause enophthalmos secondary to ocular surface pain. Ocular surface pain is also manifested by blepharospasm and increased lacrimation (*Ch. 5*).
  - **Horner's syndrome** Interruption of the sympathetic innervation of the eye, eyelids and orbital smooth muscle resulting in miosis, anisocoria, ptosis, narrow palpebral fissure, enophthalmos, and TEL protrusion (*Ch. 10, case 1*).
  - **Reduced volume of orbital tissue** This can arise because of dehydration, weight loss (reduction in orbital fat) or fibrosis of orbital tissues following orbital inflammation or surgery.



**Fig. 1.2c** Phthisis bulbi secondary to chronic uveitis in the right eye of a Tibetan Terrier. Note the third eyelid protrusion, increased scleral show, absence of external signs of inflammation, and diffuse corneal fibrosis.

### 3. Appropriate diagnostic tests

- Ocular reflexes
  - Pupillary light reflex – positive direct and consensual OU
  - Dazzle reflex – positive OU
- Menace response – positive OS, negative OD

In this dog, these results are consistent with absent vision but some retinal and optic nerve function in the right eye.

- Examination with a focal light source – in the right eye, slit-lamp biomicroscopy shows that the structure originating at the iris collarette converges at a focal point on the anterior lens capsule, consistent with a PPM.
- Tonometry – IOP 15 mmHg OU
- B-mode ocular ultrasound – this is indicated to evaluate the posterior segment when the anterior segment is opaque, and to take measurements. Axial globe length is the distance between the centre of the cornea and the posterior pole. Axial lens length is the distance between the centre of the anterior and posterior lens capsules.

The ultrasound reveals an axial globe length of 20.8 mm OS (within normal limits) and 18.5 mm OD, which confirms microphthalmos in the right eye (Fig. 1.2d). The right lens is hyperechoic and slightly smaller than the left lens (axial length 7.1 mm compared to 7.3 mm, both within normal limits); the hyperechogenicity is consistent with a cataract.

There is no change in the appearance or apparent comfort level of the right eye following the application of topical anaesthetic eye drops, which rules out enophthalmos because of ocular surface pain. The position of the TEL in the right eye does not change following the application of topical 1% phenylephrine, which makes Horner's syndrome an unlikely cause of the TEL protrusion (*Ch. 10, case 1*). The remainder of the ophthalmic examination reveals no additional abnormalities and a general physical examination is unremarkable.

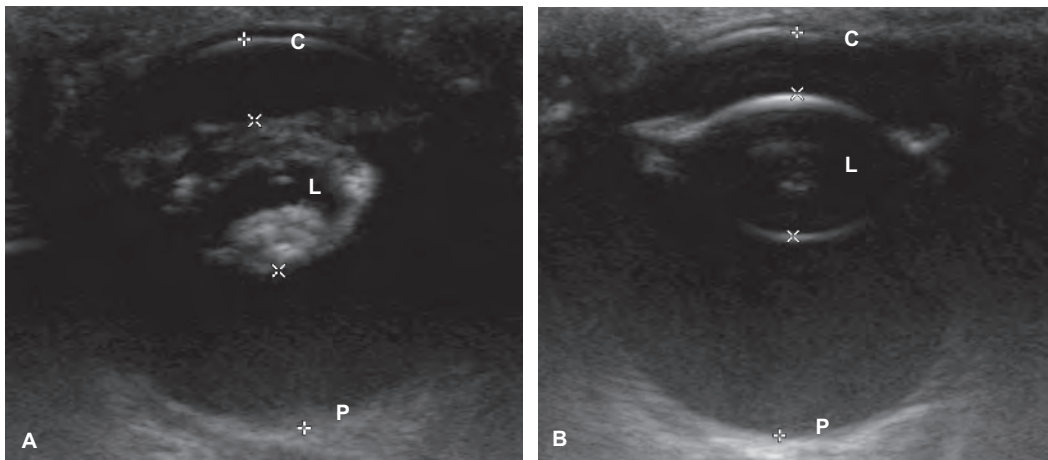
A single drop of a topical anaesthetic will anaesthetise the ocular surface (conjunctiva and cornea) within approximately 10 s. Anaesthesia lasts for about 45 min in the normal dog eye (25 min in the cat). The depth and duration of anaesthesia can be increased by the repeat application of the topical anaesthetic, e.g. one drop applied twice over one minute. The application of a topical anaesthetic can be a simple way of differentiating surface ocular pain from pain caused by intraocular or orbital disease.

## Diagnosis

Based on the information available, a diagnosis of microphthalmos in the right eye is made.

## Treatment

No treatment is indicated for the majority of eyes affected with microphthalmos. In a small number of dogs, recurrent conjunctivitis may develop because of poor tear drainage and/or entropion because of poor eyelid-to-globe apposition. Conjunctivitis is usually managed conservatively with topical lubricant and antibiotic therapy; entropion should be surgically corrected. Congenital cataract associated with microphthalmos is typically non-progressive, and cataract removal in a



**Fig.1.2d** Horizontal B-mode ultrasound scan. (A) Right eye – axial globe length 18.5 mm, axial lens length 7.1 mm; hyperechoic lens. This is consistent with microphthalmos and cataract. (B) Left eye – axial globe length 20.8 mm, axial lens length 7.3 mm. C, cornea; L, lens; P, posterior limit of globe; 'x' and '+' represent points of measurement for the axial length of lens and globe respectively.

microphthalmic eye is associated with an increased risk of complications. Cataract removal is not considered in this dog because vision in the left eye is considered to be normal.

### Prognosis

Most microphthalmic eyes remain stable as the associated ocular abnormalities are typically non-progressive. The prognosis for the right eye is therefore considered to be good.

### Discussion

Microphthalmos is described in many species and in many different dog breeds. Although typically unilateral it may be bilateral but not necessarily symmetrical. Abnormalities range from mild to severe and vision may be normal, reduced or absent. In addition, microphthalmic eyes commonly have clinically insignificant iris hypoplasia seen as miosis (because of hypoplasia of the iris dilator muscle) and a darkened iris, as in this dog. Miosis and darkening of the iris can also occur with anterior uveitis and should be ruled out on the basis of other clinical signs (*Ch. 7, case 1, Fig. 7.1e*). Although the cause of microphthalmos is often unknown, a heritable basis is described in several dog breeds including the Dobermann Pinscher, Miniature Schnauzer, English Cocker Spaniel and the Australian Shepherd. Animals with reduced pigment (melanin) in the body (subalbinism) are also commonly affected, e.g. merle collies. Regardless of the severity of the defect, affected animals should not be used for breeding.

### Further reading

See Appendix 2.

## CASE STUDY 3

### History

A 5-year-old male neutered Weimaraner is presented with a two-day history of a prominent red eye, reduced appetite and lethargy. The dog has received routine vaccinations and anthelmintic treatment.

### Questions

1. Describe the abnormalities and pertinent normal features in Figs. 1.3a and b.
2. What differential diagnoses should be considered for this presentation?
3. What tests could you perform to make the diagnosis?

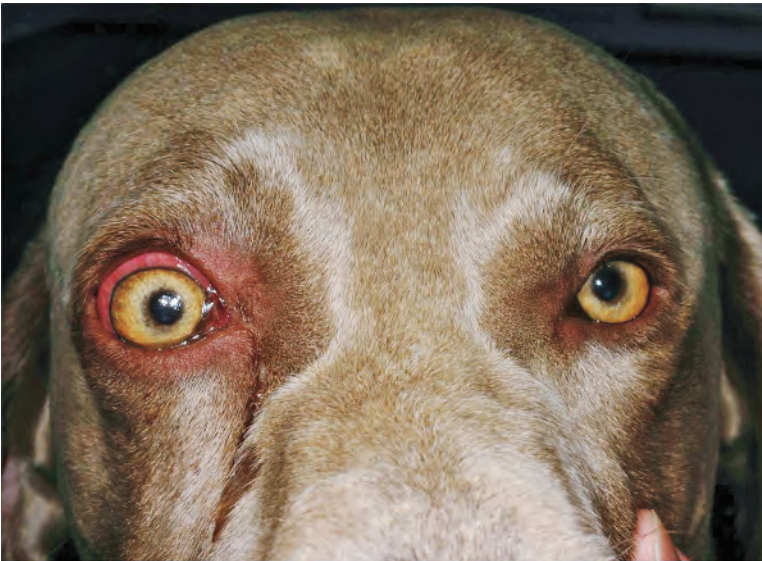


Fig. 1.3a

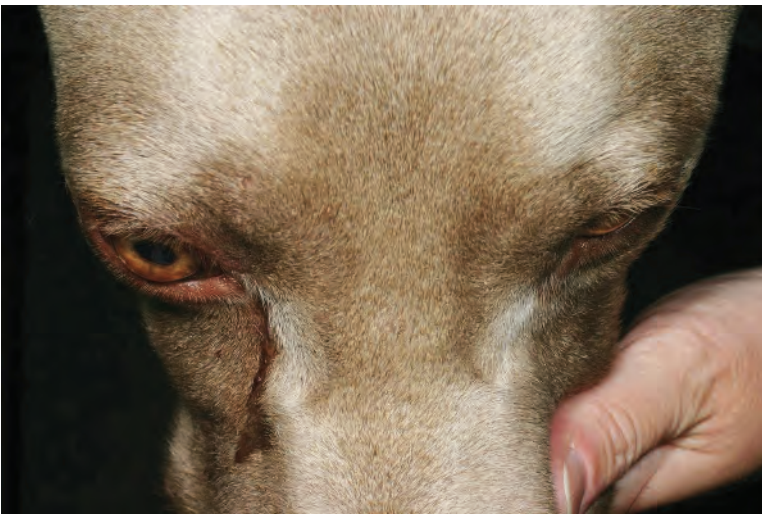


Fig. 1.3b

## Answers

### 1. What the figures show

**Fig. 1.3a** Both eyes are shown, the left eye is normal. Right eye – there is marked periocular swelling, erythema of the upper and lower eyelid skin and a widened palpebral fissure (OD > OS). The Purkinje images are disrupted and displaced. There is epiphora, TEL protrusion and hyperaemia of the bulbar conjunctiva.

**Fig. 1.3b** Aerial view of both eyes. Right eye – there is an obvious anterior displacement of the eye; this appears as a larger visible surface area of cornea when compared to the left eye. The periocular swelling ventral to the eye is more evident with this view.

### 2. Differential diagnoses

Given the appearance of the right eye, the clinical diagnosis is exophthalmos. The following conditions should be considered:

- **Orbital neoplasia** This can be primary (60–70% of tumours) or secondary, arising from adjacent structures or metastasis from distant sites. Orbital neoplasia is more likely in older dogs (mean age 9.5 years) and is characterised by a slowly progressive unilateral exophthalmos with variable degrees of strabismus. Affected dogs are typically but not exclusively non-painful. Indentation of the caudal globe can be seen on fundic examination and with some imaging modalities (ultrasonography, MRI and CT).
- **Orbital cellulitis/abscess** This is most common in young dogs (mean age 4 years) and is characterised by acute onset unilateral exophthalmos, and pain on opening the mouth and palpation of the globe and periocular region. Associated clinical signs include an ipsilateral swelling of the oral mucosa caudal to the last upper premolar, pyrexia, anorexia and neutrophilia. The cause of the cellulitis/abscess is not always identified but includes an orbital foreign body, dental problem or from haematogenous spread.
- **Myositis**
  - **Extraocular polymyositis (EOM)** Inflammation of the extraocular muscles causes bilateral but not necessarily symmetrical ocular signs including exophthalmos, strabismus and impaired globe movement. EOM has been described in several breeds but is most commonly seen in the Golden Retriever (*case 4, this chapter*).
  - **Masticatory/eosinophilic myositis** Acute inflammation of the masticatory muscles (masseter, temporal, pterygoid and digastric muscles) causes anorexia, pyrexia, and bilateral exophthalmos. Chronic disease results in fibrosis of the masticatory muscles and can lead to enophthalmos, entropion, TEL protrusion, and impaired vision.
- **Trauma**
  - **Orbital haematoma** This occurs most commonly following proptosis as a result of severe trauma, e.g. road traffic accident, and is often associated with subconjunctival haemorrhage and lagophthalmos.
  - **Orbital emphysema** This can arise as a complication of enucleation, especially in brachycephalic breeds, as well as from fractures involving the frontal sinus.
  - **Proptosis** This term describes the sudden forward displacement of the eye with subsequent entrapment behind the eyelids (*Ch. 12, case 1*).
  - **Orbital fractures** Fractures of the frontal, temporal and zygomatic bone can result in exophthalmos or enophthalmos, strabismus, orbital and periocular haemorrhage, pain, and facial asymmetry.
- **Abnormalities of the zygomatic salivary gland** Neoplasia, inflammation of the zygomatic salivary gland (sialoadenitis) or leakage of saliva can cause exophthalmos. There is often a history

of trauma with the non-neoplastic conditions. Oral examination may reveal distension of the zygomatic papilla.

- **Vascular anomalies** Orbital varices and arteriovenous fistulas are rare congenital anomalies that may cause pulsating or intermittent exophthalmos.

### 3. Appropriate diagnostic tests

- Ocular reflexes
  - Pupillary light reflex – positive direct and consensual OS, negative direct and consensual OD
  - Dazzle reflex – positive OS, negative OD
  - Palpebral reflex – positive OU but reduced OD
  - Vestibulo-ocular reflex – positive OU but reduced OD
- Menace response – positive OS, equivocal OD

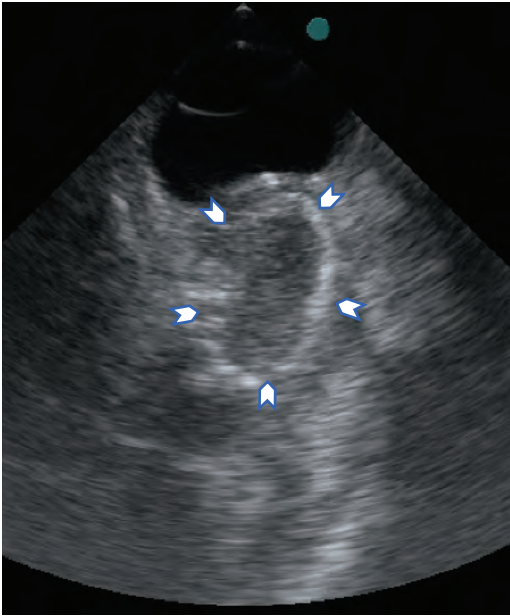
In this dog, these results are consistent with blindness, absent retinal and optic nerve function, reduced ocular motility and lagophthalmos in the right eye.

- Ophthalmoscopy – this reveals an extensive area of hyporeflexivity in the tapetal fundus in the right eye, and no abnormalities in the left eye.
- Fluorescein dye
  - Staining – negative OS, positive diffuse stippling of the axial cornea OD. This is indicative of suboptimal ocular surface health in the right eye, most likely because of the lagophthalmos.
  - Jones test (fluorescein dye passage test) – positive OS, negative OD. This is consistent with reduced tear drainage on the right side because of compression of the nasolacrimal punctum by anterior displacement of the globe.
- Tonometry – IOP 18 mmHg OS, 27 mmHg OD. In the absence of other signs of glaucoma (e.g. mydriasis), the elevated IOP in the right eye is consistent with increased intraorbital pressure causing ocular hypertension rather than glaucoma.
- Luedde or Hertel exophthalmometer – an instrument specifically designed to measure the distance between the cornea and the lateral orbital ligament. It is not routinely used in veterinary ophthalmology. Examination from an aerial perspective confirms that the right eye is displaced anteriorly (Fig. 1.3b).

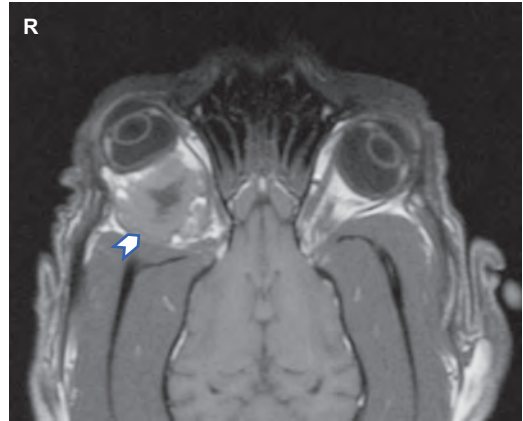
On further examination there is pain and increased resistance to retropulsion of the right eye; retropulsion of the left eye is normal. There is pain when the mouth is opened but no intraoral abnormalities are observed. A general physical examination is otherwise unremarkable except for mild bilateral mandibular lymphadenopathy.

### Further diagnostic tests

- Laboratory tests – routine haematology, biochemistry and urine analysis are unremarkable
- Imaging
  - B-mode ocular and orbital ultrasound – this is indicated to evaluate the retrobulbar space and the orbit. It reveals a hypoechoic oval mass with a hyperechoic rim within the retrobulbar space of the right eye. The mass is causing marked indentation of the posterior aspect of the globe which is consistent with the fundoscopic findings (Fig. 1.3c).
  - Abdominal ultrasonography – unremarkable
  - Thoracic radiography – unremarkable
  - MRI – this is performed to evaluate the full extent of the orbital lesion and to determine if surgical management is possible. The dorsal T1 image confirms the presence of the retrobulbar mass identified on the ultrasound examination. The mass is isointense to brain tissue, has a hypointense core, and indents the posterior aspect of the globe (Fig. 1.3d).



**Fig. 1.3c** Horizontal B-mode ultrasound scan (right eye). A hypochoic oval mass (arrows) within the retrobulbar space indents the posterior aspect of the eye.



**Fig. 1.3d** MRI scan (dorsal T1 image). A large retrobulbar mass (arrow) indents the posterior aspect of the eye. Reproduced with permission from R Dennis, Animal Health Trust.

- Fine-needle aspiration (FNA) for bacteriology and cytology – under general anaesthesia and with ultrasound guidance, an FNA of the retrobulbar mass (via an intraoral approach) and the right mandibular lymph node is performed. Cytological examination reveals a monomorphic population of large neoplastic lymphocytes in both the orbit and lymph node (Fig. 1.3e). There is no growth on bacterial culture.

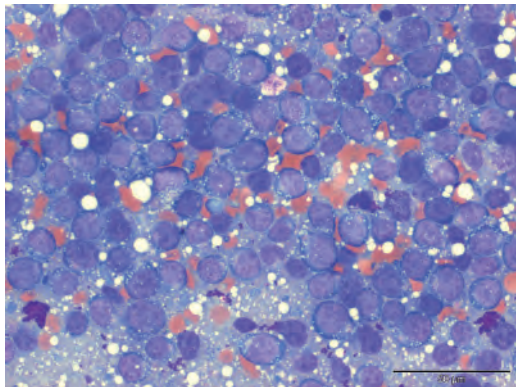
There is a close association between the soft tissue floor of the orbit, and the maxilla and the mandible. With some orbital disorders, opening of the mouth can result in discomfort because the coronoid process of the ramus of the mandible presses on the soft tissue floor of the orbit. Careful inspection of the oral mucosa caudal to the last upper premolar on the affected side (conscious or under general anaesthesia) to look for abnormalities such as redness or swelling is important in the evaluation of suspected orbital conditions.

## Diagnosis

Based on the information available, a diagnosis of orbital lymphoma on the right side is made.

## Treatment

The treatment of exophthalmos depends on the underlying cause. Clinical staging is indicated in cases of lymphoma and typically includes a complete blood count, biochemistry, urinalysis, diagnostic imaging (abdominal and thoracic), and, if indicated, bone marrow evaluation and immunophenotyping. The reader is referred to appropriate sources for further information.



**Fig. 1.3e** Orbital FNA depicting neoplastic lymphocytes. Wright's Giemsa stain. Bar = 50  $\mu$ m. Reproduced with permission from EJ Scurrell.

Non-specific therapy for exophthalmos includes a topical lubricant to minimise the risk of corneal ulceration because of exposure. Many topical lubricants are commercially available – a paraffin-based, bland ophthalmic ointment applied generously q4–6 hours is appropriate. Placement of a temporary tarsorrhaphy (eyelid sutures that partially or completely close the palpebral fissure) is an alternative means of protecting the ocular surface until the exophthalmos improves or resolves. This can be performed whilst the animal is under general anaesthesia for imaging.

### Prognosis

In this dog the prognosis for the rapid resolution of the exophthalmos is good if there is a satisfactory response to chemotherapy. The exophthalmos should improve within several days and/or resolve during the first 1–2 weeks of treatment. However, prolonged or severe exophthalmos can result in corneal ulceration and blindness because of optic nerve damage.

Most preferred chemotherapy protocols will result in an 80–90% rate of clinical remission, with median survival times of 12 months. Approximately 25% of affected dogs survive longer than two years.

### Discussion

Most orbital space-occupying lesions are neoplastic in the dog. Orbital neoplasia usually causes a slowly progressive, non-painful exophthalmos, in contrast to the acute onset, painful exophthalmos typical of an inflammatory process. However, orbital lymphoma can mimic inflammation because it often has an acute onset and can be painful. Diagnostic imaging is always indicated for a thorough evaluation of exophthalmos. Orbital ultrasound is relatively simple and inexpensive to perform but the interpretation of orbital scans is often challenging, even for an experienced ultrasonographer. Plain skull radiography is only helpful if there is bony involvement. MRI and CT can provide further information about the nature and extent of the orbital lesion which can then facilitate accurate planning of orbital surgery (if indicated).

### Further reading

See Appendix 2.

## CASE STUDY 4

### History

A 1-year-old female Miniature Shorthaired Dachsund is presented with a five-day history of 'bulging eyes'. The dog has received routine vaccinations and regular anthelmintic treatment, and is reported to be otherwise clinically well.

### Questions

1. Describe the abnormalities and pertinent normal features in Fig. 1.4a.
2. What differential diagnoses should be considered for this presentation?
3. What tests could you perform to make the diagnosis?



**Fig. 1.4a** Reproduced with permission from EA Giuliano.

## Answers

### 1. What the figure shows

**Fig. 1.4a** The left and right eyes are similar except for the presence of a scant mucoid discharge in the left eye. There is a startled expression and symmetrical exotropia, i.e. a divergent strabismus or lateral deviation. Evidence of exotropia includes an increase in the amount of visible sclera on the medial aspect of the globe and the abnormal position of the Purkinje images (see Fig. 1.4b for comparison). The exotropia has resulted in misalignment between the camera flash and the visual axis and as a result a tapetal reflection is not visible. There is a mild exophthalmos with associated widening of the palpebral fissure and exposure of the sclera on the dorsal and ventral aspects of the eye. The TEL is in a normal position. The pupil size is appropriate for the ambient lighting.

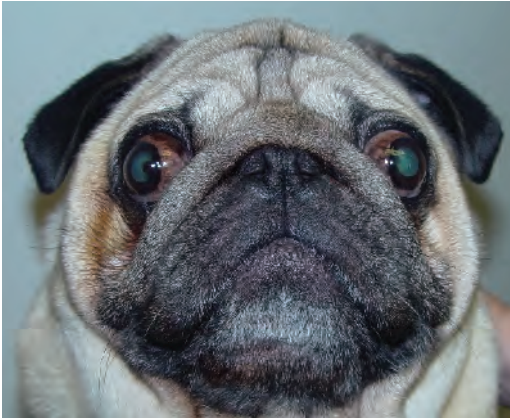
### 2. Differential diagnoses

Given the history and the appearance of both eyes, the following conditions should be considered:

- **EOM** An acute inflammatory process confined to the extraocular muscles (excluding the retractor bulbi). EOM is characterised by bilateral exophthalmos and strabismus and a classic startled expression; TEL protrusion, pain and visible signs of inflammation are absent. Although there is an idiopathic predisposition for the young female Golden Retriever, EOM has been described in many dog breeds.
- **Masticatory muscle myositis (MMM)** An acute inflammatory process involving the muscles of mastication (masseter, temporal, pterygoid and digastric muscles). MMM is characterised by bilateral exophthalmos, TEL protrusion and congestion of the conjunctival and episcleral vessels. Concurrent non-ocular signs are more often the reason for presentation and include lethargy, pyrexia, and anorexia, the latter primarily because of jaw pain. Jaw pain results from pressure applied by the ramus of the mandible on the swollen soft tissue floor of the orbit when the mouth is opened. The masticatory muscles are often visibly swollen and painful when palpated. Haematological and biochemical abnormalities include a leukocytosis, eosinophilia and elevated creatinine phosphokinase. The masticatory muscles are composed of unique type 2M myofibre, for which specific autoantibodies can be identified. The serum 2M antibody test and immunocytochemical staining on muscle tissue are important diagnostic tests for MMM. Chronic or severe disease leads to fibrosis of the muscles and subsequent enophthalmos, entropion, TEL protrusion, impaired vision and trismus.
- **Physiological exotropia and exophthalmos** The optical axes are offset by approximately 20° in a rostralateral direction in the normal dog, resulting in good binocular vision and dorsomedial positioning of the Purkinje images. The position of the optical axes and the depth of the orbit depends on skull shape – brachycephalic breeds have a tendency for mild bilateral exotropia and exophthalmos that is within normal limits for the breed type (Fig. 1.4b).
- **Orbital lymphoma** Lymphoma can present as acute onset, unilateral or bilateral orbital disease – the clinical signs mimic an inflammatory rather than a neoplastic process. With the exception of lymphoma, orbital neoplasia is more typically unilateral, non-painful and slowly progressive in nature (*case 3, this chapter*).
- **Abnormalities of the zygomatic salivary gland** Neoplasia, inflammation of the zygomatic salivary gland (sialoadenitis) or leakage of saliva can cause exophthalmos. There is often a history of trauma with the non-neoplastic conditions. Oral examination may reveal distension of the zygomatic papilla.

### 3. Appropriate diagnostic tests

- Ocular reflexes



**Fig. 1.4b** Bilateral breed-related exotropia, exophthalmos and macropalpebral fissure in an adult Pug. Reproduced with permission from DJ Gould.

- Pupillary light reflex – direct and consensual positive OU
- Dazzle reflex – positive OU
- Palpebral reflex – positive OU
- Vestibulo-ocular reflex – positive but reduced OU
- Vision assessment
  - Menace response – positive OU
  - Visual placing and tracking reflexes – positive OU

In this dog, these results are consistent with reduced ocular motility in both eyes.

- Tonometry – IOP 26mmHg OU. In the absence of signs of glaucoma (e.g. mydriasis, corneal oedema, episcleral congestion, pain), the mildly elevated IOP is consistent with increased intra-orbital pressure causing ocular hypertension.

There is mild resistance to retropulsion of both eyes but no obvious pain. The remainder of the ophthalmic examination reveals no additional abnormalities and a general physical examination is unremarkable.

#### **Further diagnostic tests**

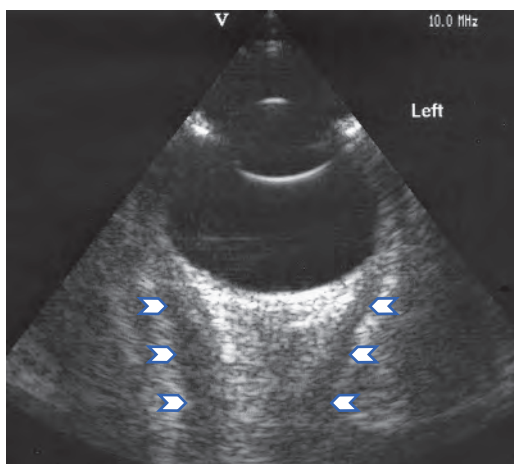
- Forced duction test – this test helps to differentiate mechanical restriction from a neurological disorder in an eye with reduced motility. It can be performed in a conscious (active forced duction) or unconscious, anaesthetised animal (passive forced duction).

A passive forced duction test is performed in this dog. Each eye in turn is grasped with fine rat-toothed forceps close to the limbus and is moved only partially in all directions. This is a positive result which excludes a neurological problem and suggests that the reduced vestibulo-ocular reflex is the result of a restrictive (mechanical) problem.

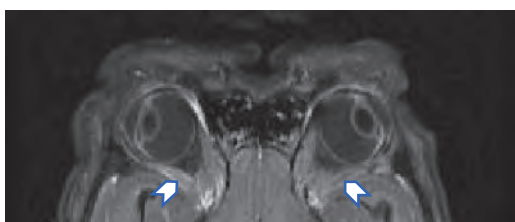
- Laboratory tests – routine haematology, biochemistry and urine analysis are recommended prior to starting treatment; the results are unremarkable.
- B-mode ocular ultrasound – this reveals thickening of the extraocular muscles in both eyes, and associated enlargement of the retrobulbar cone (Fig. 1.4c).
- Orbital MRI – this confirms marked thickening of the extraocular muscles and reveals contrast enhancement consistent with inflammation (Fig. 1.4d).

#### **Diagnosis**

Based on the information available, a diagnosis of bilateral extraocular polymyositis is made.



**Fig. 1.4c** Horizontal B-mode ultrasound scan. Marked thickening of the extraocular muscles of the left eye (arrows). Reproduced with permission from R Dennis, Animal Health Trust.



**Fig. 1.4d** MRI image (dorsal T1 post contrast). Marked thickening and enhancement of the extraocular muscles of both eyes (arrows). Reproduced with permission from R Dennis, Animal Health Trust.

## Treatment

The mainstay of treatment for EOM is systemic corticosteroid therapy at immunosuppressive doses. Prednisolone, 1.1 mg/kg q12 hours for three weeks, is recommended (Ramsey *et al.*, 1995). The prednisolone can then be tapered over several weeks. Adjunctive therapy with azathioprine may need to be considered in patients that cannot tolerate the side-effects of corticosteroid therapy or become refractory to prednisolone therapy alone. Alternative immunomodulatory therapy with oral cyclophosphamide alone, and a combination of oxytetracycline and niacinamide have also been reported for this condition.

## Prognosis

With early accurate diagnosis and appropriate treatment, the prognosis for EOM is generally good and clinical signs usually resolve. However, recurrence is common and is reported to be as high as 80%, with 10% of dogs experiencing multiple recurrences (Ramsey *et al.*, 1995). Recurrence was found to be most likely if the initial dose of prednisolone was reduced before the end of the recommended three-week period. A small number of dogs require low-dose, long-term therapy to maintain remission.

## Discussion

EOM is an idiopathic inflammatory condition that probably has an immune-mediated component; this assumption is based on the pattern of muscle involvement, histopathological features and response to treatment. A common history of a non-specific stressor (e.g. a stay in boarding kennels, surgery, oestrus) prior to the onset of clinical signs has been noted in some cases.

The startled facial expression is virtually pathognomic for EOM and the diagnosis can usually be made from the characteristic clinical appearance alone. In addition to the clinical signs described above, less common clinical signs include conjunctival hyperaemia, chemosis, fundic changes and visual impairment. The lack of TEL protrusion in this condition is especially noteworthy as this is in contrast to most orbital disease in dogs (*case 3, this chapter*). Advanced imaging in the form of ocular and orbital ultrasonography, CT and MRI helps localise the abnormality and confirm the diagnosis. Ultrasonography, although quick and relatively inexpensive to perform, does not necessarily provide precise information about the nature of the problem and the tissues involved. Although MMM can also cause bilateral exophthalmos, the clinical presentation is very different to that for EOM (see earlier). The clinical differences between these two myopathies arise from the fact that the muscle groups have different embryological origins. The type 2M myofibre is unique to the masticatory muscles and can be identified with serology (2M autoantibodies) and immunocytochemistry on frozen muscle sections; the masticatory muscles are easy to biopsy as they are large and readily accessible (Melmed *et al.*, 2004). Although the extraocular muscles can be biopsied, the procedure is challenging and is generally unnecessary as histopathology of the muscles is non-specific (myonecrosis with a mononuclear infiltrate) and type 2M fibres are not present. Serology and muscle biopsy are therefore useful diagnostic tests to confirm the diagnosis of MMM but are not indicated for EOM.

### References and further reading

- Melmed C, Shelton GD, Bergman R, Barton C. (2004) Masticatory muscle myositis: pathogenesis, diagnosis and treatment. *Compend Contin Ed.*, 590–605.
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- Williams DL (2008) Extraocular myositis in dogs. *Vet Clin North Am: Small Animal Pract*, 38, 347–59.

See Appendix 2.