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**CRANIAL NERVE DEFICITS AFFECTING THE PUPIL:
A REVIEW AND CLINICAL CASES.**

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A thesis submitted for the degree of
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SUMMARY

The pupil is an important indicator of the neurological health of the central and peripheral nervous systems (Scagliotti, 1990). Pupil size is determined by the afferent input, i.e. the amount of light illuminating the retina, and the autonomic balance of the parasympathetic and sympathetic nervous systems, as they innervate the reciprocal pupillary constrictor and pupillary dilator muscles respectively, of the iris. The parasympathetic system is dominant and through this efferent arm, light will drive pupillary size; the pupillary light reflex pathway (PLR). The afferent arm of this shares optic fibres with the proximal part of the central visual pathway and evaluation of conscious visual perception, resting pupil size and the response of each pupil to light illuminating the ipsilateral or contralateral eye (direct and consensual PLRs) will aid localisation of any lesion affecting these projections. A series of 36 cases presenting with an abnormality affecting at least one pupil is recorded here, together with the spectrum of associated clinical or neurological signs, the investigations of the cases and, where possible, confirmation of diagnoses. They illustrate the wide spectrum of abnormalities which may affect the pupil in a referral veterinary hospital population.

Although retinal disease, affecting the photoreceptors

or the first order neurons of the central visual pathway, will result in abnormalities in visual acuity and pupil size, such cases are not included in this series - it was limited to cases with neuro-ophthalmological disease. However, a number of cases did have retinal abnormalities obvious on fundoscopy and careful ophthalmoscopy is essential in investigating these cases. Some cases showed fundic evidence of their underlying lesions; cases 3, 4, 6, 7 & 12 with papillitis subsequent to their optic neuritis, case 1 had an obviously hypoplastic optic disc and case 10 had a retinopathy occurring concurrently with the neurological signs reflecting the diffuse granulomatous feline corona virus infection. Cases 3 and 5 developed retinal degeneration subsequent to optic nerve involvement. Some cases, however, had a retinopathy which was presumed not to be associated with the neurological signs, although this could only be an assumption - cases 8, 9 & 11.

A number of cases showed bizarre and aggressive central nervous system involvement which did not appear to respond to any symptomatic therapy; 3, 6, 7, 8, 10, 11, 12, 20 and 23. These ranged from confirmed or assumed inflammatory disease (3, 8, 10, 11, 12 & 20) to unexplained severe widespread cord haemorrhage (23) and confirmed or assumed neoplasia (6 & 7). Other cases had

multifocal signs which could not be explained by a single lesion which remained fairly stable; 5, 13, 15, 16, 18 and case 36 where a space occupying lesion was considered but no progression was documented.

Underlying systemic disease was evident in a number of cases, and, indeed, was the primary reason for presentation; cases 28 and 29 both had coexistent diabetes mellitus and hyperadrenocorticism and Horner's syndrome. Case 14 had diabetes mellitus and an internal ophthalmoplegia. Case 15 had been receiving treatment for lymphoma and developed a facial palsy contralateral to a partial internal and external ophthalmoplegia.

Although many of the cases were readily predictable and logical in the way neurological signs resulted from a distinct lesion, such as otitis media / interna with Horner's syndrome and a facial palsy (cases 31, 32 & 33) or as in cases 21 (cervical disc extrusion), 24 (spinal cord tumour with meningitis) & 25 (thyroid adenocarcinoma), other cases required pharmacological localisation to determine the site of the lesion. To be accurate and informative, pharmacological diagnosis requires a well defined protocol, and this is distinctly lacking in the literature with a huge variation of agents used, concentrations of these agents and time intervals described in determining the level of

involvement in the parasympathetic or sympathetic innervation of the eye. Although in the cases where pharmacological localisation was attempted in this series a standard protocol was followed, and events were carefully timed, a number of problems in interpretation were noted and there was insufficient post mortem follow up to confirm the accuracy of the pharmacological diagnosis. Of note are two cases with parasympathoparesis which completely failed to respond to pilocarpine (cases 17 & 18). Also worthy of mention are some cases of Horner's syndrome which responded rapidly (within 30 seconds) to phenylephrine 10% administration with presumed post-ganglionic (third order neuron) lesions (cases 33, 34, 35 & 36). This reaction, due to denervation supersensitivity to the sympathomimetic agent, was much more rapid and complete than any references in the literature would suggest. However, in another case, case 5, the presumed post-ganglionic sympathoparesis was shown inexplicably on pharmacological testing to be due to a second order lesion.

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GENERAL INTRODUCTION

Neuro-ophthalmology is the study of central or peripheral nervous system disorders which may result in ophthalmic manifestations (Scagliotti, 1980a). It is imperative to have a knowledge of the neuroanatomical pathways concerned in conscious perception of vision, the pupillary light reflex and the general visceral efferent and general somatic efferent innervation of the pupil and the adnexal structures of the eye to enable accurate localisation of lesions from a careful clinical and neurological examination. Pharmacological testing may aid in this localisation with use of agents of known receptor action and effect. This dissertation reviews the veterinary literature and the relevant medical literature on neuro-ophthalmological anatomy, conditions which may effect the projections of these pathways and the pharmacological testing of lesions identified. A series of 36 cases examined by the author at the University of Glasgow Veterinary School which had as at least one of the presenting signs an abnormal pupil are discussed. Five cases were identified to have an optic nerve lesion (cases 1, 2, 3, 4 & 5); four cases had a lesion believed to involve the optic chiasma or the cavernous sinus (cases 6, 7, 8 & 9); eleven cases had oculomotor nerve involvement (cases 10, 11, 12, 8, 13, 14, 15, 16, 17, 18 & 19) and eighteen cases had Horner's syndrome (cases 20, 21, 22, 23, 24, 25, 26, 27, 28, 29,

5, 30, 31, 32, 33, 34, 35 & 36). The associated clinical and neurological examination findings and the investigations are detailed and the cases are discussed with respect to those recorded in the literature.

SECTION A

INTRODUCTION AND LITERATURE REVIEW

This will be divided into the following sections:

- i) a review of neuro-ophthalmological anatomy
- ii) a review of the neurological deficits affecting the pupil
- iii) a review of the pharmacological testing of abnormal pupils.

i) A REVIEW OF NEURO-OPHTHALMOLOGICAL ANATOMY

THE VISUAL PATHWAY

The Retina.

Photoreceptors of the retina synapse with bipolar cells (the first order neurons of the visual pathway) which in turn synapse with ganglion cells; the cell bodies of the neurons of which the optic nerve is composed (Scagliotti, 1980a). The interaction of light with a photoreceptor within the retina is a complex process which ultimately results in an action potential within the optic nerve (Petersen Jones, 1989a). Ganglion cell axons become myelinated as they pass from the nerve fibre layer of the retina into the optic nerve, recognised as the whitish coloration of the optic disc observed by fundoscopy (Pollock, 1979).

The optic nerve.

The optic nerve is cranial nerve II and can be considered to be a tract of the central nervous system rather than a peripheral nerve (De Lahunta, 1973). It is classified as an example of the special somatic afferent system (De Lahunta, 1983a). The retrobulbar part of the optic nerve is formed after axons penetrate the lamina cribrosa lateral and ventral to the posterior pole of the eyeball (Petersen Jones, 1989a). It follows an undulating course to enter the skull through the optic canal of the presphenoid bone. Each optic nerve is

longer than the straight line distance between the optic canal and the posterior pole of the globe to allow for rotation of the eye ball (Pollock, 1979). The optic nerve is surrounded by outer and inner sheaths which are continuous with the dura mater and the pia mater respectively. The space between these two sheaths contains cerebrospinal fluid and is continuous with the subarachnoid space of the central nervous system (Pollock, 1979). The optic nerve is said to be composed of between 128,600 (Stone & Campion, 1978) to over 150,000 axons (Pollock, 1979). The left and right optic nerves eventually converge at the optic chiasma on the rostroventral floor of the calvarium at the base of the diencephalon (Pollock, 1979).

Decussation at the optic chiasma.

In fish and birds with lateral positioning of eyes within the skull, there is a complete crossover of fibres at the optic chiasma to eventually terminate in the contralateral cerebrum (Petersen Jones, 1989a). However, there is a good correlation between more frontal positioning of the eyes, with overlapping visual fields of the two eyes, and percentage of uncrossed fibres (De Lahunta & Cummings, 1967). There are well documented species variations in this: Man: 50% decussation, cats: 65% decussation, dogs: 75% and herbivores: 80 - 90%. (Petersen Jones, 1989a). However,

the situation is even more complex than this. Within the canine species, dolicocephalic breeds of dogs, with the long nose interfering with the nasal field of vision from each eye, there is more decussation compared to brachycephalic breeds where the lack of nose offers a good overlap of vision and a greater proportion of fibres remain ipsilateral in the chiasma (De Lahunta & Cummings, 1967).

The partial decussation results in these mammals possessing binocular vision. In cats, the functional binocular field of view fixating upon a distant object is estimated at $80 - 85^{\circ}$ (Sanderson, 1971). Conjugate eye movements are also developed, enabling both eyes to converge upon the same object at the same time (De Lahunta & Cummings, 1967). These eye movements are known as opticokinetic eye movements; they are independent of head movements, and are more likely to be present in mammals possessing a retinal fovea, such as primates (De Lahunta, 1983b; Hutchison & others, 1984). The fovea is dorsal and temporal to the optic disc (Laties & Sprague, 1966). A less well developed area present in cats and dogs is the area centralis (Scagliotti, 1990).

In general, fibres which do not decussate emanate from the temporal retina. Thus, the visual cortex in the occipital lobe receives fibres from the left or the

right visual fields respectively, each visual field consisting of the nasal retina and the contralateral temporal retina (De Lahunta, 1983b). The naso-temporal division of the retina in the cat, resulting in decussating and non-decussating fibres, has a surprisingly distinct decussation line. In the area centralis, however, there is naso-temporal overlap (Cooper & Pettigrew, 1979). In the Siamese breed, much of the visual pathway is abnormal, suggested to be secondary to the strabismus characteristic of the breed (Hubel & Wiesel, 1971). However, melanin in the retinal pigment epithelium is intimately involved in the regulation of axonal growth from the eye to the brain. Siamese cats, with imperfect albinism, lack pigment in the retinal pigment epithelium and thus this is more likely to be the reason why this breed fails to develop normal central visual pathways (Johnson, 1991). The nasotemporal division of the retina in this breed is disrupted, with a more gradual decussation line, located rather more temporal to the area centralis than is normal (Stone & others, 1978).

Decussating fibres do not take a direct route but rather meander through the chiasma (Petersen Jones, 1989a). However, axons within the optic nerves and the chiasma and subsequent components of the visual pathway are somatotopically arranged representing each point in the

retina (Kay, 1981).

The chiasma is situated rostral to the cavernous sinus (Lewis & others, 1984). The pituitary stalk is in close proximity to the chiasma, although in animals it is directed caudoventrally, away from the chiasma, rather than rostroventrally as in man (Skerrit & others, 1986).

The optic tracts

After traversing the optic chiasma, fibres of the central visual pathway pass contralaterally or ipsilaterally in the optic tracts to the lateral geniculate nuclei (De Lahunta, 1983b). Each optic tract contains fibres from the ipsilateral temporal retina and the contralateral nasal retina, i.e. from the contralateral visual field.

The lateral geniculate nucleus

The second order neurons of the central visual pathway synapse at the lateral geniculate nuclei (LGN). The projection of the retina on the lateral geniculate nucleus is retinotopically organised (Stone & Hansen, 1966). The basic structure of the lateral geniculate nucleus can be considered as trilaminar, with three main laminae, A, A₁ and B (Hayhow, 1958). Two interlaminar zones, responsible for binocular interaction, have overlap of afferents from both eyes

(Sanderson, 1971). These are known as the medial interlaminar nucleus and the central interlaminar nucleus (Laties & Sprague, 1966). Laminae A and B areas receive afferents from the contralateral eye, and lamina A₁ receives fibres projecting from the ipsilateral eye mainly (Sanderson, 1971). Siamese cats, with disruption of central visual pathways, show disordered geniculate lamination to a variable extent (Johnson, 1991).

Optic radiation

Each retinal point terminates in multiple foci in the lateral geniculate nuclei and post-synaptic fibres (the third order neurons of the central visual pathway) project to the occipital lobes (Petersen Jones, 1989a).

The occipital cortex

The occipital cortex is also retinotopically represented (Petersen Jones, 1989a). These areas are divided into functional areas, well identified in primates, although difficult to assess in domestic animals. Area 17 (the striate cortex) is for stationary object vision, areas 18 and 19 (the extrastriate cortex) for panoramic vision for movement, depth and spatial relationship perception (De Lahunta, 1983b) - the extrastriate cortex mainly receives fibres from the medial interlaminar nucleus (Niimi & Sprague, 1970). There is considerable overlap

in the topographical organisation of the geniculo-striate projections (Niimi & Sprague, 1970).

A neuroanatomical representation of the central visual pathway is illustrated in Figure 1.

OPTIC FIBRES

As well as optic fibres projecting to the occipital cortex for conscious perception of vision, other optic fibres relay to other sites at which they synapse (Meikle & Sprague, 1964; Singleton & Peele, 1965). It has been demonstrated electrophysiologically that there are four groups of fibres with successively slower conduction rates, projecting to four different synaptic regions respectively (Bishop & Clare, 1955). The fastest conducting fibres relay to the striate cortex via layer A (A_1 ipsilaterally) of the lateral geniculate nucleus. The next group relays through layer B of the lateral geniculate nucleus to terminate in the lateral nucleus of the thalamus. The third group activates the pretectal area and the fourth the superior colliculus. Optic fibres synapsing at the lateral geniculate nucleus are involved in the pupillary light reflex. Fibres synapsing on cell bodies of the superior (rostral) colliculi are responsible for the coordination of optic reflexes such as the startle or menace reflex, and they project to spinal cord lower motor neurons or the nuclei of cranial

Neuroanatomy of the central visual pathway

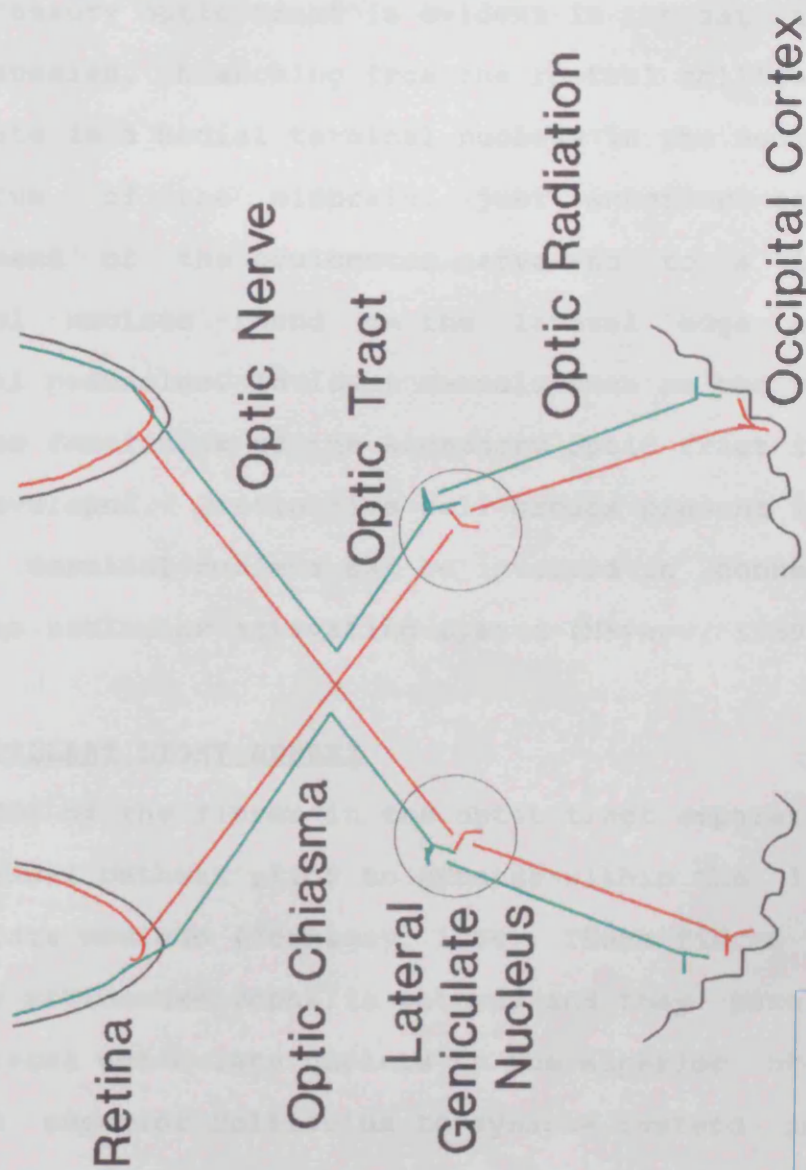


Figure 1

nerves III, IV and VI nerves via the tectospinal and tectobulbar tracts respectively (Kornegay, 1980).

An accessory optic tract is evident in the cat and in other species, branching from the rostral colliculus to terminate in a medial terminal nucleus in the mediobasal tegmentum of the midbrain, just anterior to the attachment of the oculomotor nerve and to a lateral terminal nucleus found on the lateral edge of the cerebral peduncles. In lower mammals such as the rat, an inferior fasciculus of the accessory optic tract is also well developed. Distinctive cell groups present in the medial terminal nucleus may be involved in connections with the reticular activating system (Hayhow, 1959).

THE PUPILLARY LIGHT REFLEX

About 20% of the fibres in the optic tract separate from the visual pathway prior to synapse within the lateral geniculate nucleus (Kornegay, 1980). These fibres travel in the retinomesencephalic pathway and they pass over the lateral geniculate nucleus by the superior brachium of the superior colliculus to synapse instead in the pretectal nuclei or the superior colliculi (De Lahunta, 1973; 1983b; Collins & O'Brien, 1990).

The pretectal nuclei and parasympathetic nuclei

The pretectal nucleus fibres constitute the pupillary

light reflex (photomotor response) pathway. A certain degree of crossing occurs between the two pretectal nuclei (Petersen Jones, 1989a). Most fibres then project caudally to synapse in the rostral part of the contralateral oculomotor nucleus, ventral to the aqueduct at the level of the superior colliculus (De Lahunta, 1973). This part of the oculomotor nucleus is parasympathetic, also known as the Edinger - Westphal Nucleus (Scagliotti, 1980a; Collins & O'Brien, 1990). The nuclei are located in the central grey matter surrounding the mesencephalic aqueduct (Hutchison & others, 1984). A lesser percentage of fibres project to synapse in the ipsilateral parasympathetic nucleus (Scagliotti, 1990). The two parasympathetic nuclei are not obviously separated in the dog (Stromberg, 1979).

The oculomotor nerve and the cavernous sinus

The oculomotor nerve is cranial nerve III and it largely contains general somatic efferent fibres. However, pre-ganglionic general visceral efferent parasympathetic fibres are also carried, with cell bodies in the ipsilateral parasympathetic nucleus and synapse in the ciliary ganglion (Pollock, 1979). Parasympathetic fibres are located medially at the origin of the oculomotor nerve and remain superficial throughout its course (Kerr & Hollowell, 1964). The oculomotor nerve first becomes apparent as it leaves the ventral aspect of the

mesencephalon on the medial aspect of the crus cerebri. The nerve runs laterally then turns rostrally on either side of the hypophyseal stalk and enters the cavernous sinus.

The oculomotor nerve passes through the cavernous sinus, in association with the trochlear nerve (CN IV), the abducens nerve (CN VI) and the ophthalmic branch of the trigeminal nerve (CN V). A large cavernous sinus is present on both sides of the pituitary, connected in the dog by a smaller caudal transverse sinus (Eigenmann & Lubberink, 1985). The cavernous sinus surrounds this suprasellar area and the pituitary fossa. The caudal segment of the internal carotid artery and the meningeal artery are free within the lumen with cranial nerve VI, although cranial nerves III, IV and the ophthalmic branch of the trigeminal nerve (CN V) is in intimate relationship with the cavernous sinus wall (Lewis and others, 1984; Eigenmann & Lubberink, 1985). The trigeminal ganglion is located within the dura mater lateral to the cavernous sinus. The three divisions of the trigeminal nerve arise from this; only the ophthalmic branch penetrates the dura mater to travel in the cavernous sinus, although the maxillary branch passes rostrally within the dura mater of the lateral wall of the cavernous sinus (McClure, 1979).

The oculomotor nerve exits the skull through the orbital fissure with cranial nerves IV, VI and the ophthalmic branch of V. The parasympathetic fibres are located dorsomedial and medial in the oculomotor nerve as it runs rostrally. They are located superficially, just beneath the epineurium, rendering them more susceptible to damage than the somatic efferent oculomotor nerve fibres (Kerr & Hollowell, 1964). Within the orbit, the oculomotor nerve divides into a small dorsal and larger ventral branch. The parasympathetic branch leaves the ventral nerve to enter the ciliary ganglion (Pollock, 1979).

The ciliary ganglion and short ciliary nerves

The ciliary ganglion is located midway between the orbital fissure and the eyeball, closely related to the ventrolateral aspect of the optic nerve (Pollock, 1979). After synapse within the ciliary ganglion, parasympathetic post-ganglionic short ciliary nerves leave the rostral surface of the ganglion and enter the eyeball, innervating the constrictor muscles of the pupil in the iris and the ciliary body. Species variation exists (Collins & O'Brien, 1990). In the dog, between five and eight short ciliary nerves, mixed with post-ganglionic sympathetic fibres and trigeminal ophthalmic sensory nerve fibres, enter the posterior globe (Scagliotti, 1980a). This differs from the

situation in the cat, where only two short ciliary nerves are present. They are only joined by post-ganglionic sympathetic fibres and trigeminal sensory fibres immediately before entering the globe (Scagliotti, 1980a;b). The ciliary nerve supplying the nasal iris is the nasal branch; the malar branch supplies the temporal iris (Scagliotti, 1980a;b).

In man, only about 3% of the parasympathetic fibres within the oculomotor nerve are believed to be pupillomotor; over 90% are to the ciliary muscle for accommodation (Trautmann & Barnett, 1984).

Most fibres of the pupillary light reflex decussate twice, at the chiasma and between the pretectal and the oculomotor parasympathetic nucleus. The pupillary light reflex neuroanatomical projections are diagrammatically illustrated in Figure 2.

SYMPATHETIC INNERVATION OF THE EYE

The sympathetic innervation of the eye is a three neuron pathway of circuitous route. First order neurons (the central fibres) descend from the caudal and lateral parts of the hypothalamus, the tectum and tegmentum (van den Broek, 1987) and project through the brain stem and the lateral funiculus of the cervical cord in the lateral tectotegmentospinal tract (van den Broek, 1987)

THE PUPILLARY LIGHT REFLEX

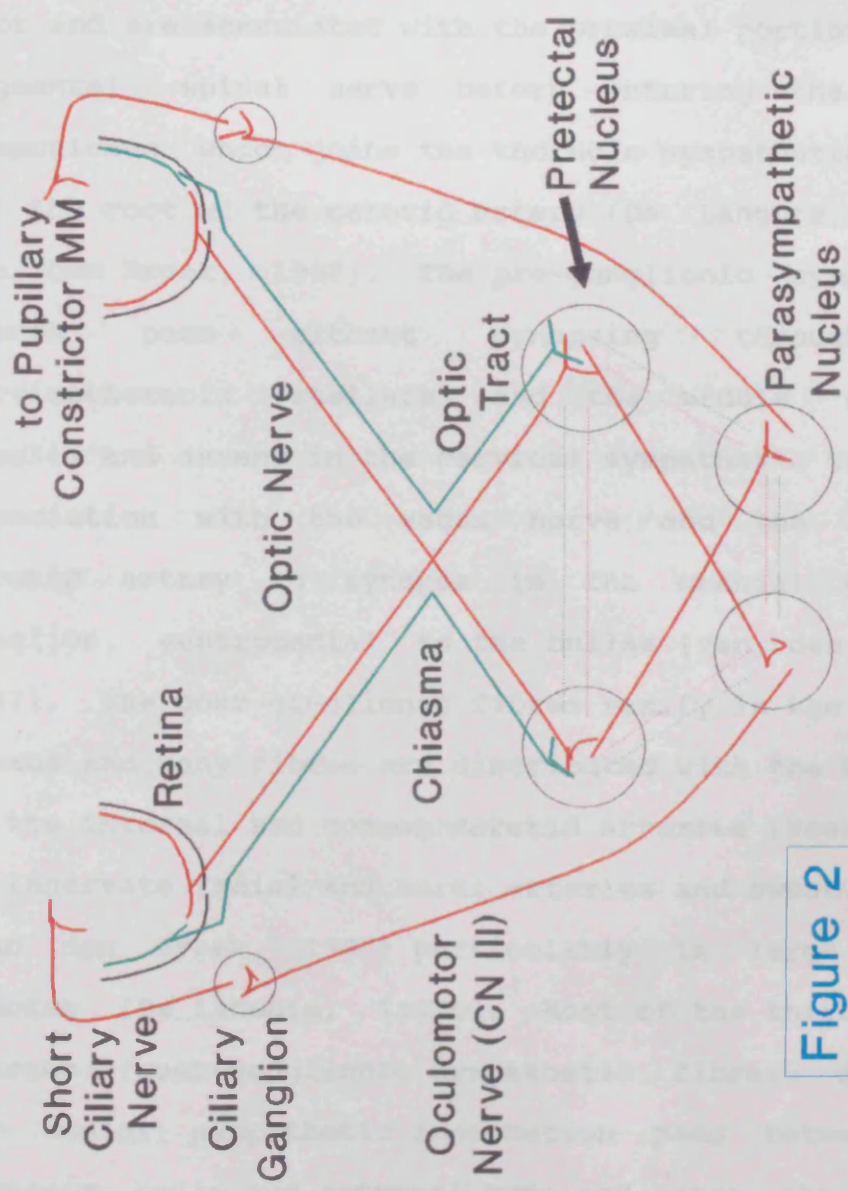


Figure 2

to synapse in the grey matter intermediate horn in thoracic spinal cord segments T1 - T3/4 (Scagliotti, 1980a). Second order neurons (the pre-ganglionic sympathetic fibres) exit the cord through the ventral root and are associated with the proximal portion of the segmental spinal nerve before entering the ramus communicans which joins the thoracic sympathetic trunk at the root of the carotid artery (De Lahunta, 1983c; van den Broek, 1987). The pre-ganglionic sympathetic fibres pass without synapsing through the cervicothoracic (stellate) and the middle cervical ganglia and ascend in the cervical sympathetic trunk in association with the vagus nerve and the internal carotid artery to synapse in the cranial cervical ganglion, ventromedial to the bullae (van den Broek, 1987). The post-ganglionic fibres ramify in the carotid plexus and many fibres are distributed with the branches of the internal and common carotid arteries (Neer, 1984) to innervate facial and aural arteries and sweat glands (van den Broek, 1987) particularly in large animal species (De Lahunta, 1983c). Most of the third order neurons (post-ganglionic sympathetic fibres) destined for ocular sympathetic innervation pass between the tympanic bulla and petrosal bone and enter the middle ear cavity (Barlow & Root, 1949). They eventually join the ventral surface of the trigeminal ganglion and join the ophthalmic branch of the trigeminal nerve (CN V) (De

Lahunta, 1983c). Other fibres enter the tympanic bulla and pass rostrally to also join the trigeminal ganglion and become distributed with the branches of the trigeminal nerve (Barlow & Root, 1949; Petersen Jones, 1989a). Many sympathetic fibres remaining in association with the branches of the internal carotid artery enter the skull through the tympano-occipital fissure and ramify in a sympathetic plexus within the cavernous sinus before joining the ophthalmic branch of the trigeminal nerve (McClure, 1979). After a somewhat variable route to eventually join the ophthalmic branch of the trigeminal nerve, the ocular sympathetic fibres enter the orbit in the nasociliary branch of the ophthalmic division of the trigeminal nerve (McClure, 1979).

Post-ganglionic sympathetic fibres are also supplied to the musculus orbitalis (periorbital smooth muscle), antagonising the retractor bulbi muscle, resulting in globe protrusion (Neer, 1984); smooth muscle of the eyelids, including Muller's muscle (although acknowledgement of the existence of Muller's muscle is controversial in domestic animals (Neer, 1984)); the dilator muscle of the pupil (Neer, 1984); and the smooth muscle present in the third eyelid of the cat (van den Broek, 1987) and possibly also the dog (Neer, 1984).

The neuroanatomy of the sympathetic innervation of the eye is diagrammatically represented in Figure 3.

Sympathetic innervation of the pupil

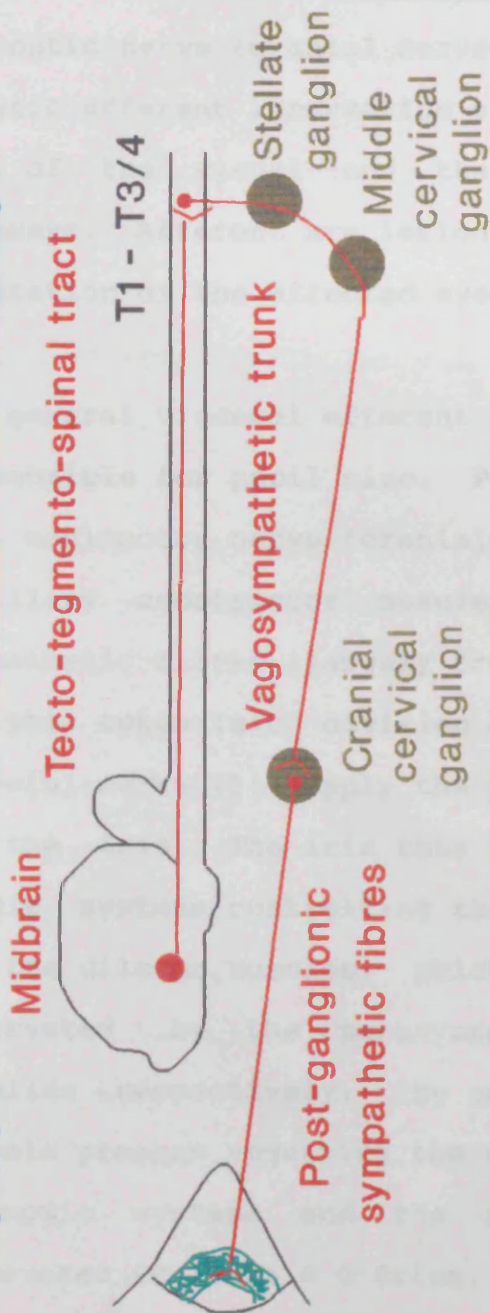


Figure 3

ii) A REVIEW OF NEUROLOGICAL DEFICITS AFFECTING

THE PUPIL

The optic nerve (cranial nerve II) provides the special somatic afferent innervation of the eye and the afferent arm of the visual and the pupillary light reflex pathways. Afferent arm lesions may result in pupillary dilatation of the affected eye.

The general visceral efferent innervation of the eye is responsible for pupil size. Parasympathetic fibres from the oculomotor nerve (cranial nerve III) innervate the pupillary constrictor muscles of the iris and the sympathetic fibres (largely from the long ciliary branch of the ophthalmic division of the trigeminal nerve (cranial nerve V)) supply the pupillary dilator muscles of the iris. The iris thus has two opposing smooth muscle systems controlling the pupil, the constrictor and the dilator muscles, which are antagonistic and are innervated by the parasympathetic and sympathetic supplies respectively. The control of pupil size is a dynamic process requiring the reciprocal actions of both autonomic systems and the respective iris muscles innervated (Collins & O'Brien, 1990), although these are morphologically independent entities (Bistner & others, 1970). The constrictor muscle tends to be stronger and mydriasis is normally passive, with higher centres inhibiting parasympathetic tone. Light thus drives pupil

size through the parasympathetic supply. The sympathetic supply is subordinate (Braund, 1987). Even in constant illumination, minor fluctuations in autonomic activity result in minor alterations in pupil size, called pupillary unrest or hippus (Collins & O'Brien, 1990).

Parasympathetic efferent lesions may result in a dilated pupil and sympathetic lesions in a miotic pupil in the affected eye.

The presence of anisocoria, or unequal pupils, should be regarded as pathological (Thompson & Pilley, 1976). Anisocoria may be subtle, but **distant direct ophthalmoscopy** or the **swinging flashlight test** should detect it (Petersen Jones, 1989a). In investigating a case of anisocoria, it is important to first decide which pupil is abnormal, by assessing whether there is adequate response to light illumination, and whether the anisocoria increases or decreases in light conditions (Thompson & Pilley, 1976). It should then be possible to locate a lesion in the afferent or the efferent systems.

Anisocoria due to ophthalmological causes must be ruled out by careful ophthalmological examination (Neer & Carter, 1987). Iris atrophy can give rise to a dilated pupil (Petersen Jones, 1989a). Uveitis, synechiae, glaucoma and lens luxation usually result in a

constricted pupil (van den Broek, 1987). Dyscorias (misshapen pupils) are almost always due to ophthalmic lesions (Scagliotti, 1980b). Metabolic disease should also be eliminated. Bilateral miosis can be recognised in hepatic encephalopathy or hypocalcaemia (van den Broek, 1987).

AFFERENT ARM LESIONS

The anisocoria in unilateral afferent arm lesions such as a retinopathy or an optic nerve lesion is minimal and horizontal pupil diameter difference is $< 1 - 3$ mm (Neer & Carter, 1987). The anisocoria is best identified in uniform subdued lighting and occurs because of a reduced number of action potentials on the affected side (Scagliotti, 1980a). In darkness, both pupils are symmetrical and uniformly dilated (Scagliotti, 1980a). In conditions of bright uniform lighting, the anisocoria due to an afferent arm lesion may not be readily evident, as the pupil of the affected eye constricts due to the consensual pupillary light reflex. The **Cover test** can be useful to identify such a situation. If the normal eye is covered, pupillary dilatation is recognised in the abnormal eye. If the abnormal eye is covered, the pupil in the normal eye remains unchanged in diameter (Petersen Jones, 1989a). The **Marcus Gunn sign** also will aid in identification of a subtle afferent arm lesion. Light directed into the abnormal

eye will result in pupillary dilatation of both eyes. Light directed into the normal eye will result in bilateral pupillary constriction (Scagliotti, 1980a; Collins & O'Brien, 1990).

Vision

A loss of visual acuity is evident with an afferent lesion. Tests to assess visual acuity include the ability to negotiate obstacle courses and to follow objects thrown into the visual field, and intact visual placing and menace reflexes with intact conscious proprioception and facial muscle function (Shell, 1982; Petersen Jones, 1989a). As far as possible in animals, all aspects of the visual fields of both eyes should be tested (Hutchison & others, 1984). Small defects in vision due to focal lesions on the retina or in the central visual pathway are called scotomas (De Lahunta & Cummings, 1967) and are difficult to assess objectively in animals.

The fundus

Afferent arm lesions which are due to a retinopathy are usually differentiated on fundoscopy. Lesions due to a first order neuron afferent lesion and those due to a unilateral extrabulbar optic nerve lesion are only differentiated by electroretinography (Braund & others, 1977).

The optic disc should be carefully examined. Despite very similar fundoscopic appearance, it is important to differentiate between papilloedema, pseudopapilloedema and papillitis (Palmer & others, 1974). Dogs and other domestic animals rarely show papilloedema reflecting the presence of raised intracranial pressure - because, unlike in man, the central optic artery and vein do not pass through the subarachnoid space and so the optic disc does not commonly reflect raised intracranial pressures in these species (Rubin, 1974b). However, when present, bilateral papilloedema is pathognomic of raised intracranial pressure, usually due to cerebral neoplasia (Palmer & others, 1974). Papilloedema as a manifestation of raised intracranial pressure is not associated with blindness (Rubin, 1974b).

It is important to realise that in the dog some degree of myelination of axons can occur prior to entry to the optic nerve head which can give the impression of papilloedema (pseudopapilloedema) (Petersen Jones, 1989a). Most cases of "papilloedema" in the veterinary literature are really papillitis and reflect optic nerve involvement with concurrent associated visual loss (Petersen Jones, 1989a).

Optic nerve disorders

Hypoplastic optic nerves, a congenital abnormality, have

been described in man, cats, rabbits, horses and dogs (Ernest, 1976). A congenital blindness and small optic discs are apparent on fundoscopy (Saunders, 1952; Gelatt & Leipold, 1971; Gelatt, 1973; De Lahunta, 1973; Rubin, 1974a; Ernest, 1976; Shell, 1982).

Optic neuritis is defined as an inflammatory and/or demyelinating optic neuropathy (Nafe & Carter, 1981). It is a syndrome characterised by acute onset amaurosis and dilated pupils unresponsive to light or sluggish pupils (Nafe & Carter, 1981). Concurrent neurological deficits may be present and must be looked for to localise the extent of the lesions involved (Nafe & Carter, 1981). Other neurological signs can subsequently occur (Kay, 1981; Hutchison & others, 1984.) It should be considered to be a bilateral condition, even if not immediately apparent on initial examination. Dogs are more commonly affected than other species (Nafe & Carter, 1981). Possible causes of optic neuritis are canine distemper infection, cryptococcosis, blastomycosis, toxoplasmosis (Nafe & Carter, 1981), infectious rhinotonsillitis, reactions to toxic agents (Fischer & Jones, 1972), reticulosis (granulomatous meningoencephalitis) (Smith & others, 1977), neoplasia (Braund & others, 1977; Kay, 1978), immune-mediated disorders (Kay, 1978) and vitamin A deficiency in rabbits and calves (Fischer & Jones, 1972), although this syndrome also results in

compression of the optic nerve (Petersen Jones, 1989a). A secondary optic neuritis is recognised as a sequel to osteitis due to frontal sinus fungal or bacteriological infection (Kay, 1978).

Traumatic optic neuritis in the horse usually follows blunt trauma to the skull, often in the poll area (Martin & others, 1986), but may be unilateral (Rebhun, 1986). Momentum of the brain in a caudal direction subsequent to skull trauma results in traction of the intracranial portions of the optic nerves, which are fixed at the optic canal. Pathologically, a constricted area of the optic nerve can be recognised, consisting of malacic areas recognised histologically (Martin & others, 1986). Fractures of the optic canal, which are difficult to document radiographically, can be responsible for trauma to the optic nerves (Martin & others, 1986). Immediately after the injury, no abnormality is generally apparent on fundoscopy, although occasionally, haemorrhages of the optic disc are seen (Rebhun, 1986). Optic atrophy can be recognised from about thirty days of the injury, due to slow axonal degeneration from the site of optic nerve trauma (Rebhun, 1986). Attenuation of the retinal vessels may also be detected, either due to concurrent injury of the internal ophthalmic artery, or possibly due to decreased metabolic rate of the inner retina (Martin & others,

1986). Medical therapy, if instituted quickly after the injury, with >1mg/kg dexamethasone, may be successful depending on severity of the lesion (Martin & others, 1986; Rebhun, 1986).

In horses, a neuroretinopathy can be recognised following haemorrhage after trauma, surgery or parturition (Gelatt, 1979). Conspicuous greyish white or yellowish bodies can sometimes be detected on the optic disc soon after onset of blindness in optic neuritis, whatever the aetiology, although it is usually described subsequent to haemorrhage. Histopathologically, these lesions contain dense arrays of glial and phagocytic cells within the internal lamina (Platt & others, 1983).

This must be distinguished from the proliferative optic neuropathy described in older horses, unassociated with demonstrable visual deficit. This may be due to myelin degradation (Platt & others, 1983). Drusen in man is due to accumulation of hyaline and colloid bodies on the optic disc, and is not described in animals (Platt & others, 1983).

Periodic ophthalmia may result in secondary optic atrophy in later stages. In addition, a suppurative optic neuritis, associated with endocarditis (Hatfield & others, 1987) and a granulomatous optic neuritis

secondary to verminous arteritis (Slatter & Huxtable, 1983) have been described. Toxins have also been implicated in the horse (Kelly & Pinsent, 1979).

In man, demyelinating conditions, multiple sclerosis, meningitis, encephalomyelitis, nematode infestations, allergic reactions, drug reactions, ischaemia and many other conditions can result in the clinical syndrome of optic neuritis (Fischer & Jones, 1972).

Optic neuritis may be intra- or extrabulbar. Depending upon the proximity of lesions to the optic disc, changes (papillitis) on fundoscopy may or may not be apparent (Nafe & Carter, 1981). Later in the course of the disease, atrophic changes can be recognised in the disc with increasing pallor (optic atrophy) (Nafe & Carter, 1981). If treatment with glucocorticoids is early and aggressive enough, vision may return, but irreversible damage to fibres may occur (Kay, 1978).

The optic chiasma

Chiasmal lesions are rarer in domestic animals than in man. Pituitary neoplasia in domestic animals rarely affects the visual pathway (De Lahunta, 1973), and such neoplasms must be proportionately larger than those in man (Kay, 1981). This is because the distance between the pituitary gland and the chiasma is proportionately

greater in domestic animals than in man (Kay, 1981). There are also other regional anatomical differences between the species making it less likely for a pituitary neoplasm to affect the chiasma in domestic animals (Skerrit & others, 1986; Sarfaty & others, 1988; Dow & others, 1990). The visual disturbance described in man with pituitary neoplasia involving the chiasma is most commonly a bitemporal hemianopia (Post & Muraszko, 1986), where a midline chiasma lesion affects the decussating fibres from both nasal retinae (De Lahunta & Cummings, 1967). Animals with a complete chiasmal lesion have widely dilated unresponsive pupils and are totally blind (Hutchison & others, 1984). This would be difficult to distinguish from bilateral optic neuritis.

Specification of neoplasia in the region of the optic chiasma depends on the relationship to the sella turcica. Pituitary tumours are initially infrasellar, but craniopharyngiomas can be infra- and extrasellar. Olfactory meningiomas and meningiomas of the tuberculum sellae are suprasellar and meningiomas of the sphenoid ridge are parasellar (Barnett & others, 1967). The mechanism of chiasmal damage may be due to extrinsic tumour pressure, but impairment of the arterial blood supply is also a factor to be considered (Heavner & Dice, 1977). Associated endocrine disturbances may also be recognised (Eigenmann & others, 1983; Eigenmann &

Lubberink, 1985), possibly without neurological deficits. Strong correlation exists between tumour volume and compression or invasion of surrounding nervous tissue and the development of neurological signs (Nelson & others, 1989). Neurological signs recognised with neoplasia in this area include mental depression or stupor as the most frequent sign (Dow & others, 1990), due to interference with the ascending reticular activating system (Allison & others, 1983). Upper motor neuron quadriparesis or circling may result from thalamic involvement (Dow & others, 1990). A positional rotatory nystagmus has been reported (Sarfaty & others, 1988). Behavioural alterations, head pressing, adipsia, anorexia and fluctuations in rectal temperature have been recorded due to hypothalamic involvement (Nelson & others, 1989).

The optic tracts

Visual field deficit suggestive of an optic tract lesion is homonymous hemianopia. Hemianopia literally means that only half normal vision is present. This term implies that one visual field is absent (De Lahunta & Cummings, 1967). For example, with a right sided visual field deficit, the optic nerve fibres from the left temporal retina and the right nasal retina are affected. Such a lesion may be due to a left sided unilateral optic tract lesion, lateral geniculate nucleus lesion,

optic radiation lesion or occipital cortical lesion and is a right homonymous hemianopia (De Lahunta & Cummings, 1967).

The optic tracts are in close proximity to the descending motor tracts. Thus, with hemiparesis, a hemisensory deficit and a homonymous hemianopia are present on one side of the body, a lesion is indicated in the contralateral cerebral hemisphere (Kay, 1981). Such lesions could be due to neoplasia of the thalamus or the hypothalamus, which affects the internal capsule (De Lahunta, 1973). Lesions within the diencephalon, involving the thalamus, hypothalamus, epithalamus or subthalamus could potentially result in endocrine disorders, such as hyperadrenocorticism (Kay, 1981). Involvement of the subventricular regions of the hypothalamus can result in anorexia, due to involvement of appetite control centres (Kay, 1981).

Similarly, a homonymous hemianopia may be detected subsequent to generalised seizure activity. This may be transient, and may or may not be indicative of organic disease (this phenomenon in man is known as Todd's paralysis) (Kay, 1981).

The optic tracts, and other areas of the central visual pathway can be affected by canine distemper virus, which

appears to have a predilection for these areas, resulting in necrosis and inflammation to variable degree (De Lahunta, 1973).

Visual cortical evoked responses can be done in the dog to aid in the diagnosis of visual dysfunction (Howard & Breazile, 1972).

Pupil abnormalities are not detected, despite visual disruption, if the lesion is caudal to the divergence of the axons to the pupillary light reflex, above the synapse in the lateral geniculate nucleus. Rostral to this, a slightly dilated pupil may be evident (De Lahunta & Cummings, 1967), although because of decussating pathways, it may still be possible to have both efferent arms of the pupillary light reflex eventually stimulated (Hutchison & others, 1984; Oliver & Mayhew, 1987).

The lateral geniculate nucleus (LGN).

A homonymous hemianopia may be recognised with a unilateral LGN lesion, without pupillary abnormality.

The optic radiations

Hydrocephalus, because of compromise of the optic radiations as they pass in the lateral wall of the dilated lateral ventricles, may result in bilateral

visual deficit with normal pupils (De Lahunta, 1983c). Other lesions may similarly diffusely affect the optic radiations and the occipital cortex, such as lysosomal storage disorders and vascular lesions (De Lahunta 1983c).

The occipital cortex

Lesions of this area affect vision but have no effect on the pupil. Occipital cortex lesions can result from hypoxic or hypoglycaemic injury or lead poisoning. Visual loss is subsequent to laminar necrosis of related portions of the cerebral cortex, the occipital cortex being particularly sensitive to injury, resulting in blindness (Kay, 1978). Dirofilariasis has been suspected as a cause of ischaemic damage (Braund and others, 1977).

Metabolic disease (such as cirrhosis, hepatitis, renal failure, sepsis, pancreatitis and acidosis) leading to severe cerebral depression can lead to loss in visual acuity (Kay, 1978).

EFFERENT ARM LESIONS

The anisocoria with unilateral efferent lesions tends to be greater in degree than with afferent lesions (Neer & Carter, 1987). The abnormal eye will have a dilated pupil in light conditions (Scagliotti, 1980a).

Vision is unaffected by lesions affecting only the efferent pathway of the pupillary light reflex.

The pretectal nuclei

A complete unilateral lesion affecting the pretectal nucleus would result in the contralateral pupil being dilated. Bilateral destruction of both pretectal nuclei would be unlikely as they are anatomically relatively widely separated. Pinealomas may be rarely responsible for lesions in this area (Hutchison & others 1984).

Parasympathetic (Edinger - Westphal) nuclei

Lesions are rarely unilateral because of the close anatomical relationship of this pair of nuclei. Complete lesions of the nuclei would result in presentation with normal visual function although both pupils would be widely dilated and unresponsive to light shone into either eye (Oliver & Mayhew, 1987). Lesions may be associated with a generalised dysautonomia such as feline dysautonomia (Sharp & others, 1984; Petersen Jones, 1989a).

The oculomotor nerve

Lesions affecting an oculomotor nerve would result in a widely dilated ipsilateral pupil which would be unresponsive to light illumination of either eye (Oliver & Mayhew, 1987). This is known as internal

ophthalmoplegia.

A lesion resulting in complete destruction of the oculomotor nerve would also result in neurological deficits of the extraocular muscles. Denervation of the ventral oblique and the dorsal, medial and ventral rectus muscles results in a lateral strabismus and a largely static globe (Petersen Jones, 1989a). Denervation of the levator palpebrae muscle results in ptosis of the upper lid (Oliver & Mayhew, 1987). This is known as external ophthalmoplegia.

Oculomotor nerve palsy can be idiopathic, known as Adie's or Holmes - Adie's syndrome or idiopathic tonic pupil. In man this is associated with loss or depression of deep tendon reflexes, not reported in the dog. Nonspecific immunological disease has been suspected (Gerding & others, 1986; Ramsay, 1986). The lesion is a post-ganglionic parasympathetic denervation of intraocular and ciliary muscle resulting in a dilated pupil and poor or sluggish pupillary light reflexes in the affected eye (Neer & Carter, 1987). Adie's syndrome is more common in women than men, usually affecting subjects of 20 - 40 years and tends to be slowly progressive. Loss of near vision has also been described, due to paresis of the ciliary body and a failure of accommodation. (Goldfarb & Swan, 1984;

Ramsay, 1986).

Other defects in the parasympathetic innervation of the iris are described in man, including Miller - Fisher's syndrome, alcoholism and oculomotor nerve palsy (Ramsay, 1986).

Thiamine deficiency in cats or inflammatory lesions affecting the midbrain can result in disruption of the parasympathetic innervation of the eye and oculomotor nerve lesions are evident (Braund, 1987). Retrobulbar oculomotor nerve neoplasia has also been described (Petersen Jones, 1989a).

Paralytic mydriasis has been observed with an acutely expanding intracranial mass on the ipsilateral side, assumed to be due to pressure on the oculomotor nerve (Kerr & Hollowell, 1964).

It may be difficult to distinguish the dilated pupils of bilateral optic neuritis from those due to bilateral internal ophthalmoplegia, where visual acuity cannot be assessed. The **cilio-spinal reflex** may be of use here, although it is not a consistent normal finding. The reflex involves noxious stimuli applied to the skin at the back of the neck, which should result in constriction of the pupils, via stimulation of the

oculomotor system (Kay, 1981). Right and left cilio-spinal centres are closely associated in the thoracic spinal cord of the cat (Kerr & Hollowell, 1964). Alternatively, the well known effect of opiates in achieving bilateral miosis can be used to distinguish between these lesions (I.R. Griffiths, personal communication). Morphine is usually used at normal dose rates, which acts on the parasympathetic nuclei causing miosis. This response cannot be recognised in the presence of oculomotor nerve or nuclear lesions.

The cavernous sinus

The oculomotor nerve travels through the cavernous sinus with the trochlear and abducens nerves (cranial nerves IV and VI) and the ophthalmic branch of the trigeminal nerve (cranial nerve V). Cavernous sinus lesions may result in neurological deficits being evident in one or more of these nerves. Cavernous sinus venography can indicate the presence of a space occupying lesion in the cavernous sinus (Griffiths & Lee, 1971; Skerrit & others, 1986) or, where available, computerised tomography and magnetic resonance imaging will image a mass in this area (Collins & O'Brien, 1990). An alternative radiographic diagnosis has been suggested by cisternal access to the subarachnoid space and allowing contrast to run forward (Barr, 1985). Complete ophthalmoplegia is usually associated with cavernous

sinus neoplasms, or metastases (Griffiths & Lee, 1971; Lewis & others, 1984; Murphy & others, 1989; Collins & O'Brien, 1990). Pituitary tumours may extend laterally into the cavernous sinus (Trautmann & Barnett, 1984). The classical **cavernous sinus syndrome** is a combination of trigeminal face pain or anaesthesia and ophthalmoplegia (Trautmann & Barnett, 1984; Fenner, 1989).

Ciliary ganglion and short ciliary nerves

Ciliary ganglion or short ciliary nerve lesions in the dog will show incomplete mydriasis. The pupil is smaller than expected with a parasympathetic lesion because of concurrently disrupted sympathetic post-ganglionic neurons which pass through the ciliary ganglion and enter the globe mixed with the short ciliary nerves (Scagliotti, 1980a). In the cat, however, a ciliary ganglion lesion will not result in concurrent sympathetic denervation (Christensen, 1936). Such lesions are recognised in feline dysautonomia (Sharp & others, 1984). Sympathetic post-ganglionic fibres only join the short ciliary nerves immediately prior to entry to the globe (Scagliotti, 1980a;b). The cat, with the two short ciliary nerves; malar and nasal branches, may have a lesion affecting one of these branches resulting in a D shaped or an inverse D shaped pupil (Scagliotti, 1980a; b).

THE PUPILLARY LIGHT REFLEX (PLR)

Animals under examination for pupillary light responses should be calm and alert, not under the influence of circulating catecholamines (Collins & O'Brien, 1990). The briskness of the pupillary light reflex is proportional to the amount of light entering the eye, and the area of the retina illuminated. It is important to use a pen torch without dying batteries (Scagliotti, 1980b; Collins & O'Brien, 1990). The area centralis, or the fovea, is richer in photoreceptor density, and a stronger direct and consensual pupillary light response will be gained if this area is illuminated (Scagliotti, 1980b).

Most fibres decussate twice, at the chiasma and before the parasympathetic nucleus. In domestic animals, there is inequality in the numbers of crossed and uncrossed fibres (Scagliotti, 1990). Because of this, in domestic animals, the direct and consensual pupillary light responses are not equal, and the direct response is greater. This is known as **contraction anisocoria** or **dynamic anisocoria** (Petersen Jones, 1989a; Collins & O'Brien, 1990). In man, with 50% decussation, direct and consensual responses are equal, and discrepancy would be pathological (Petersen Jones, 1989a). **Alternating contraction anisocoria** is an active illustration of this phenomenon demonstrated by the **swinging flashlight test**

(Scagliotti, 1990).

In general, the pupillary light response is sluggish, with a relatively long latent period after light stimulus to pupillary constriction. This is explained by the multisynaptic pathway involved, and the fact that it is smooth muscle which is ultimately innervated (Scagliotti, 1980b). In the bird, striated muscle is present in the constrictor muscles of the pupil, and the pupillary light reflex is detectably brisker (Scagliotti, 1980b).

Apparent pupillary light areflexia in the horse is usually due to the fact that a light source of inadequate power is being used. The eye in this species is deeply pigmented, including the corpora nigra and the nontapetal fundus, absorbing much light, so that insufficient may reach the retina to result in a reflex (Scagliotti, 1980b).

Animals, including dogs, with no eye pigment, blue irides and no tapetum have a less brisk pupillary light reflex than those with a tapetum. This is because the tapetum results in light being reflected from the tapetum, to rebound back into the photoreceptor zone of the retina. Animals without a tapetum lucidum do not have this double stimulation (Scagliotti, 1980b). This

phenomenon in man is known as the Waardenburg Syndrome.

Supranuclear inhibition of the oculomotor nucleus may be apparent. Animals which are drowsy, approaching a sleep like state, show gradual constriction of their pupils, as higher centres become less active and there is reduced sympathetic activity (Scagliotti, 1980a). Similarly, the pinpoint pupils which can be seen subsequent to cerebral trauma may be indicative of a loss of cerebral inhibition of the oculomotor nucleus, which may be asymmetrical (Kay, 1981).

Pupillary escape is a phenomenon seen on examining the pupillary light responses, characterised by dilatation of a normal pupil after the initial constriction. This is simply due to photoreceptor adaptation (Scagliotti, 1980a), as photoreceptors become hyperpolarised with light (Petersen Jones, 1989a).

With careful examination of both pupils, evaluation of visual acuity and the assessment of direct and consensual pupillary light reflexes, a good estimate of the site of any lesion can be made, as indicated in Figure 4.

HORNER'S SYNDROME (OCULOSYMPATHOPARESIS)

Anisocoria that increases in conditions of low lighting

Figure 4
Localisation of lesions affecting central visual and
pupillary light reflex pathways.

Complete lesion on right side:

Site of lesion	Resting pupils	Vision R. eye	Vision L. eye	PLR; light R. R.	L.	PLR; light L. R.	L.
Retina	Right possibly slightly dilated	Reduced or absent	Normal	Reduced or no response	Reduced or no response	Both pupils constrict.	
Optic Nerve	R. slightly dilated	Absent	Normal	No direct PLR	No consensual PLR	Both pupils constrict	
Chiasma (complete)	Both widely dilated	Absent	Absent	No direct or consensual PLR	No direct or consensual PLR	No direct or consensual PLR	
Optic tract (prior to PLR divergence)	L. possibly slightly dilated (usually normal)	Relatively normal (unless temporal retina tested)	Reduced (except temporal retina)	Constricts (except temporal retina)	Constricts	Reduced constriction (unless temporal)	Reduced constriction
LGN (same findings for optic radiations or occipital cortex complete lesions)	Both normal	Relatively normal (unless temporal retina tested)	Reduced (except temporal retina)	Direct and consensual PLRs intact	Direct and consensual PLRs	Direct and consensual PLRs intact	
Pretectal Nucleus (PTN)	Left possibly slightly dilated	Normal	Normal	Constricts (except temporal)	Constricts	Reduced constriction unless temporal	Reduced constriction
Para-sympathetic nucleus (complete, bilateral)	Both pupils widely dilated	Normal	Normal	No direct or consensual PLR present	No direct or consensual PLR	No direct or consensual PLR present	
Oculomotor nerve (III)	Right pupil widely dilated Left normal	Normal	Normal	No constriction	Constricts	No constriction	Constricts

or in darkness is usually due to Horner's syndrome (Thompson & Pilley, 1976; Neer & Carter, 1987). Loss of sympathetic nerve supply to the eye and periorbital, known as sympathoparesis, or Horner's syndrome, can be due to lesions anywhere along this pathway, and clinical signs are typical of the abolished sympathetic tone (Morgan & Zanotti, 1989). Horner's syndrome was described in 1869 by J.F. Horner (Bistner & others, 1970), but before this by F. Parfour de Petit, in 1827, and Claude Bernard in 1852. It is also known as the Claude - Bernard - Horner's Syndrome (Smith & Mayhew, 1977). A triad of signs are seen in man typically - miosis, ptosis and enophthalmos. A fourth sign is characteristically recognised in domestic animals - third eyelid protrusion.

Abolition of sympathetic tone results in incomplete dilatation of the pupil, especially in conditions of low lighting (Wowk & Olson, 1979), with loss of sympathetic supply to the pupil. Loss of smooth muscle tone in the periorbital smooth muscle results in no antagonism to the retractor bulbi muscle, and enophthalmos results. This passively will result in a narrowed palpebral fissure and third eyelid protrusion. However, domestic animals have smooth muscle present in the third eyelid and the eyelids, and loss of this results in third eyelid protrusion, and narrowing of the palpebral

fissure, with a degree of ptosis (Neer, 1984; van den Broek, 1987; Scagliotti, 1990). It is argued that this is the primary finding in small animals, especially the cat, and that the enophthalmos is only apparent (Scagliotti, 1980b). Loss of sympathetic supply to blood vessels in the area leads to vasodilatation, and this may be appreciated in all species, with palpably warmer pinnae on the affected side (Smith & Mayhew, 1977) or with hyperaemia of conjunctival vessels (Neer, 1984) or the rhinarium (Jones & Studdert, 1975). Cattle may demonstrate reduced sweating of the rhinarium, and sweating is abolished ipsilateral to the sympathoparesis in man also (van den Broek, 1987) whereas horses will sweat markedly on the affected side, especially at the base of the ear (Smith & Mayhew, 1977). This temperature elevation on the affected side is dramatic in the Siamese breed of cat, where reduced melanocyte activity is correlated with increased temperature (Innes, 1973). The dark mask can become lighter on the affected side (Jones & Studdert, 1975).

Another sign which may be detected is a transient reduction in intraocular pressure (Jones & Studdert, 1975), which will amplify any degree of enophthalmos present.

In small animals, miosis is the cardinal sign of

Horner's syndrome (van den Broek, 1987). In a partial sympathoparesis, it may be the only sign (Jones & Studdert, 1975).

In large animals, the miosis may be difficult to discern, and the most consistent sign is ptosis in these species (Smith & Mayhew, 1977).

The **dilatation lag** is a useful test for Horner's Syndrome (Thompson & Pilley, 1976). The Horner's pupil will lag behind the normal pupil in dark-induced mydriasis because of the flaccid dilator muscles.

The site of lesions resulting in Horner's syndrome can be classified according to which of the three neurons in the pathway are affected. The first order neuron is the central one, with cell bodies in the midbrain or hypothalamus, synapsing in the intermediolateral grey matter at T1 - T3/4 of the spinal cord (Petersen Jones, 1989a). Brain stem lesions, presenting with other severe neurological deficits, can result in Horner's syndrome. Neoplasia, infections, trauma and vascular accidents are possible aetiologies (Petersen Jones, 1989a). Other cranial nerve deficits which can be associated with such disease are CN VII, VIII, IX, X, XI and XII (van den Broek, 1987). Cervical lesions could also result in Horner's syndrome if the lateral tectotegmentospinal

tract is disrupted. In practice, high cervical cord disease is rarely responsible for producing Horner's syndrome, although lower cord disease, such as produced by disc extrusion, cervical spondylopathy (Jones & Studdert, 1975), myelitis, fibrocartilaginous embolisation (Greene & Higgins, 1976; De Lahunta & Alexander, 1976) or trauma, may result in Horner's syndrome (Petersen Jones, 1989a; Kern & others, 1989). In higher cervical cord disease, lesions severe enough to destroy the lateral funiculus would be expected to cause respiratory paralysis (De Lahunta & Alexander, 1976).

The second order, or pre-ganglionic, neuron has cell bodies in the intermediolateral cells of the grey matter of T1 - T3/4, and synapses at the cranial cervical ganglion (van den Broek, 1987). It is prone to cervical trauma in the vagosympathetic trunk (Jones & Studdert, 1975; Kneller & others, 1972; Kern & others, 1989), as well as brachial plexus injuries or neoplasia (Fox & Gutnick, 1972; Frye, 1973; Griffiths & others, 1974). Anterior mediastinal neoplasia or haemorrhage may also result in second order Horner's syndrome (Jones & Studdert, 1975; Morgan & Zanotti, 1989; Petersen Jones, 1989a). High thoracic cord disease such as myelitis, trauma or fibrocartilaginous embolism can result in ipsilateral lower motor neuron signs and Horner's

syndrome depending on the extent of the injury to nerve roots or appropriate cord segments.

The third order or post-ganglionic neuron has cell bodies in the cranial cervical ganglion and the neuromuscular junction is in the smooth muscle of the dilator muscles of the pupil (Petersen Jones, 1989a). Middle ear disease, iatrogenic damage during ear cleaning with astringents, neoplasia, retrobulbar lesions or contusion are possible causes of Horner's syndrome (Jones & Studdert, 1975; Carpenter & others, 1987; van den Broek, 1987; Morgan & Zanotti, 1989; Petersen Jones, 1989a). Post-ganglionic lesions are the most commonly diagnosed cause of Horner's syndrome in animals (Morgan & Zanotti, 1989), usually due to otitis media or orbital disease, although in a high percentage of cases, the cause of the post-ganglionic lesion is unknown (Morgan & Zanotti, 1989; Collins & O'Brien, 1990). In man, a local vascular accident is presumed (Maloney & others, 1980).

In long standing lesions in man, heterochromia of the iris has been described (Maloney & others, 1980).

Congenital Horner's syndrome has also been described (Brightman & others, 1977; Maloney & others, 1980). In man, this may be associated with a cataract, and one

case in the veterinary literature has also been reported (van den Broek, 1987).

In many cases, it may not be possible to determine the cause of the Horner's syndrome (Morgan & Zanotti, 1989), although efforts should be made to determine the site of the lesion (van den Broek, 1987). Pharmacological testing is important for this.

If the cause for the Horner's syndrome is transient, both pre- and post-ganglionic lesions can recover, although it may take up to 6 months (Jones & Studdert, 1975). Post-ganglionic or third order lesions are said to carry a more favourable prognosis than pre-ganglionic lesions (Bistner & others, 1970).

Symptomatic topical treatment with sympathomimetic agents has been advocated to transiently resolve clinical signs and to prevent denervation atrophy of the smooth muscle (Collins & O'Brien, 1990).

Differential diagnoses for the components of Horner's syndrome include differential diagnoses for miosis; any painful eye conditions such as corneal ulceration, keratitis, uveitis etc. (van den Broek, 1987). The mechanism by which painful eye conditions result in miosis is known as the **axon or trigeminal reflex**

(Griffiths & Lee, 1971; Scagliotti, 1990). Trigeminal afferent impulses are believed to also travel antidromically to result in impulses terminating on iridal blood vessels resulting in histamine release, mediating miosis (Scagliotti, 1990). Differential diagnosis of ptosis are oculomotor lesions, which can be distinguished by the dilated pupil and oculoparalysis usually seen with a complete oculomotor nerve lesion (van den Broek, 1987). Differential diagnosis of enophthalmos include any painful condition of the eye (van den Broek, 1987).

In man, defects in the sympathetic irideal supply are recognised in vascular headaches, and the syndromes of Guillain - Barré and Miller - Fisher as well as Horner's syndrome (Ramsay, 1986). Simple anisocoria is another differential diagnosis for Horner's syndrome in man, with no known underlying disease process (Thompson & Pilley, 1976).

A **spastic pupil syndrome** is recognised in cats, usually in association with feline leukaemia virus (FeLV) infection. One of the pupils fails to dilate or constrict. Owners will often report a history of abnormal pupil behaviour (possibly intermittent) for some months prior to presentation. The aetiology of this pupillary abnormality is not known (Scagliotti,

1980a; b). Other concurrent viral infections may also be evident (feline infectious peritonitis (FIP), feline immunodeficiency virus (FIV)).

iii) A REVIEW OF THE PHARMACOLOGICAL TESTING OF

ABNORMAL PUPILS

The iris has two reciprocal smooth muscle groups, the pupillary constrictor and the pupillary dilator muscles. These are innervated by the parasympathetic and sympathetic divisions of the autonomic nervous system respectively. The parasympathetic and sympathetic systems peripherally have pre- and post-ganglionic fibres. The post-synaptic receptors at the ganglion of both divisions of the autonomic nervous system are cholinergic (i.e. the normal neurotransmitter is acetylcholine) and nicotinic. The smooth muscle cells innervated by the parasympathetic division have receptors which are also cholinergic, although of the muscarinic subdivision. These receptors can be blocked by atropine, whereas the nicotinic receptors are unaffected by atropine. The pupillary dilator muscle receptors, innervated by the sympathetic division of the autonomic nervous system, have noradrenaline as a neurotransmitter and are consequently described as being adrenergic. Both alpha and beta adrenergic receptors are present in the eye (Tietz & Hall, 1977). Pharmacological testing of the autonomically disordered eye requires a knowledge of these receptor types and the actions of the agents used.

PARASYMPATHETIC LESIONS

An indirect acting parasympathomimetic such as 0.5% **physostigmine** topically applied to the eye will distinguish between pre-ciliary ganglion and post-ciliary ganglion lesions. Rapid pupillary constriction will result if the short ciliary nerves are intact, i.e. with pre-ganglionic or central lesions (De Lahunta, 1983c).

Direct acting parasympathomimetic such as 1% **pilocarpine** topically applied will differentiate between a pre-oculomotor nucleus and post-oculomotor nucleus lesion (De Lahunta, 1983c). A normal pupil will constrict in 20 minutes, whereas a denervated pupil will constrict more quickly, to a greater degree and for a longer duration, but no differentiation is made in the site of the lesion (De Lahunta, 1983c). Supersensitivity to cholinergic agents will be seen with post-ganglionic lesions with topical application of 2.5% **methacholine** or 0.1% **pilocarpine** (Thompson & Pilley, 1976), a concentration which should not cause miosis in the normal eye (Goldfarb & Swan, 1984). The **pilocarpine** preparation is more reliable, as it is a stronger miotic and fewer false negative results are obtained (Goldfarb & Swan, 1984).

Pharmacological blockade resulting in an "atropinic"

mydriasis is a fairly common finding in investigating the dilated pupil unresponsive to light, which fails to constrict after topical pilocarpine. As well as inappropriate medication, it may be due to toxins etc. (Thompson & Pilley, 1976; Scagliotti, 1980b; Collins & O'Brien, 1990).

HORNER'S SYNDROME

Cocaine is useful in confirming the presence of a true Horner's syndrome (Wowk & Olson, 1979; Skarf & Czarnecki, 1982). The action of cocaine is to potentiate or produce adrenergic effects by blocking the transport of catecholamines back into sympathetic post-ganglionic fibres, and is thus one of the original drugs used to test for Horner's syndrome (Bistner & others, 1970). Thus, cocaine will not result in pupillary dilatation in second and third order neuron Horner's syndrome, although some pupillary dilatation may result in first order neuron Horner's syndrome (Bistner & others, 1970). Partial sympathoparesis will result in partial dilatation after topical application of cocaine to the affected eye (Brightman & others, 1977). Between 2 and 5% concentrations of cocaine are the preparations usually described (Bistner & others, 1970), although they are not available in the UK (van den Broek, 1987).

Phenylephrine (phenylephrine) interacts directly with

the adrenergic receptor to produce adrenergic effects, and is thus purely a direct acting sympathomimetic (Bistner & others, 1970). In man, there is significant correlation between sensitivity to topical phenylephrine application and age, with increase in sensitivity of 0.23 mm per decade above 20 years (Ramsay, 1986). The reason for this is believed to be due to gradual age-related degeneration of the sympathetic plexus in the iris, or in diminution of sympathetic neuronal catecholaminergic content. Associated with this is the finding that pupils tend to become more constricted with advancing age (Ramsay, 1986). These factors should be considered when examining domestic animals.

Phenylephrine 10% also aids in nictitating membrane retraction in domestic animals (Laties & Sprague, 1966).

Epinephrine, ephidrine and hydroxyamphetamine act by resulting in the release of noradrenaline from the nerve terminals, thus secondarily producing adrenergic effects (Bistner & others, 1970), thus they are referred to as indirect acting sympathomimetics. Ephidrine but particularly epinephrine also have direct acting effects. Pure indirect acting parasympathomimetic drugs (hydroxyamphetamine 1%) will result in mydriasis with first or second order lesions, but not with post-

ganglionic lesions - the drugs indicate the presence of intact post-ganglionic fibres (Neer, 1984). Hydroxyamphetamine does not distinguish between central (first order) and pre-ganglionic (second order) lesions and will dilate normal pupils as well (Skarf & Czarnecki, 1982). The importance of using hydroxyamphetamine lies in its ability to distinguish post-ganglionic lesions, as no dilatation results with degeneration of nerve terminals (Skarf & Czarnecki, 1982). This is especially important in man, where post-ganglionic lesions are usually benign and associated with vascular headaches, whereas pre-ganglionic lesions or central lesions may be associated with neoplasia (Maloney & others, 1980; Skarf & Czarnecki, 1982).

Unfortunately, hydroxyamphetamine is not available in the UK, nor is ephidrine as sole drug in the preparation.

The degree of supersensitivity to very low doses (0.001%) of epinephrine can distinguish between second and third order lesions (Bistner & others, 1970). Third order neuron lesions will result in pupillary dilatation and loss of anisocoria in 20 minutes, whereas second order lesions take 30 - 40 minutes, and may require 0.01% epinephrine (Morgan & Zanotti, 1989).

Canon's law of denervation supersensitivity is important for the testing of post-ganglionic lesions. When a direct acting sympathomimetic drug is used, the phenomenon of denervation supersensitivity occurs because in the absence of intact post-ganglionic fibres, exogenous drug is not cleared from the post-synaptic space, so more rapid onset and prolonged drug action results (Bistner & others, 1970; Petersen Jones, 1989a). This supersensitivity to phenylephrine correlates well with lack of response to hydroxyamphetamine (Ramsay, 1986). Not all species have the same degree of supersensitivity to adrenergic amines when denervated (Bistner & others, 1970).

Phenylephrine is probably the best drug to use in the UK, as it is more consistently absorbed after topical application to the cornea and conjunctival sac than epinephrine and ephedrine (Bistner & others, 1970). Corneal pathology will interfere with absorption (Petersen Jones, 1989a). A 10% preparation is used, and applied to the affected eye, and the other eye as a control. A normal pupil will dilate in 60 - 90 minutes, first order lesions dilate in 60 - 90 minutes, second order neuron lesions will show mydriasis in 45 minutes, but a third order neuron lesion will become mydriatic very quickly, within 20 minutes (Petersen Jones, 1989a).

Thus, pharmacological testing is a useful diagnostic tool for investigating the autonomically disordered pupil. It must, however, be realised that the neurotransmitter sensitivity of chronically denervated smooth muscle may decrease with time (Ramsay, 1986).

SECTION B

CLINICAL CASES

This will be divided into the following sections:

Materials and methods.

- i) Cases presenting with optic nerve involvement.
- ii) Cases presenting with chiasmal or cavernous sinus involvement.
- iii) Cases presenting with oculomotor nerve involvement.
- iv) Cases presenting with Horner's syndrome.

MATERIALS AND METHODS

The materials and methods detailed are broadly applicable to all the succeeding categories of cases.

Case selection

Thirty six cases were selected which were referred to the University of Glasgow Veterinary School (GUVS) for investigation of a clinical problem which had an abnormal pupil as one of the clinical signs. Most cases were referred by veterinary surgeons to the neurology clinic but in some cases, a neurological problem was identified by another clinician investigating another major system. Cases included are those examined by the author during the period January 1990 - August 1991. Cases were divided into the following divisions:

- i) Cases with optic nerve involvement
- ii) Cases with chiasmal or cavernous sinus involvement
- iii) Cases with oculomotor nerve involvement
- iv) Cases with Horner's syndrome

Historical findings and clinical examination

A full history was obtained from the owner, the referring veterinary surgeon, and/or the primary clinician and relevant details were recorded. All cases received a full clinical examination and only relevant abnormal findings are listed.

Neurological Examination

All cases received a full neurological examination as detailed by Oliver & Mayhew (1987). The animal's mental status and posture was noted. The owner was questioned about any personality or behaviour change. Gait, at a slow walk, was assessed where the animal was ambulatory. Conscious proprioceptive responses and limb motor function were tested by paw position sense, reflex stepping, sway response, visual and tactile placing reflexes, extensor postural thrust, wheelbarrowing, hemiwalking and hopping. Bladder and bowel function were assessed from the history, observation during hospitalisation and by abdominal palpation and attempts to express the bladder and the perineal reflex. Local spinal reflexes were tested, including the panniculus reflex. Muscle bulk and symmetry was assessed by palpation. With the animal in lateral recumbency, muscle tone was evaluated in each limb. The hind limbs were tested for the patella reflex, the gastrocnemius, the cranial tibial and the sciatic myotactic reflexes by percussion with a plexor or the handle of weighty artery forceps. The fore limb myotactic reflexes were assessed for the triceps, biceps and extensor carpi radialis muscles. Pedal reflexes assessed regional areas of sensation in the distal limb and muscle strength of the respective flexor groups in all limbs. The presence/absence of conscious pain perception was

concurrently ascertained.

Visual acuity was assessed from the history, observation of the animal in unfamiliar and cluttered surroundings and testing by dropping objects within the visual field, visual placing reflexes, the menace response and the pupillary light reflexes. Pupil size, the presence or absence of anisocoria, direct and consensual pupillary light reflexes illuminating nasal and temporal retinae, conjunctival appearance, globe position within orbit, position of the membrana nictitans and eyelid appearance were examined to ascertain the presence of any autonomic deficit affecting the globe. As well as distant ophthalmoscopy to evaluate any anisocoria, the fundus was examined. Any abnormality was checked and detailed by an ophthalmologist, Mr. John Mould. Voluntary globe movements and those elicited by changes in head position (oculovestibular reflexes) were assessed to evaluate extraocular motor function. Any constant or positional strabismus or nystagmus was noted. Corneal sensation and the ability to retract the globe were assessed by the corneal reflex. Facial sensation and facial movement was assessed and jaw tone and masticatory muscle bulk and symmetry noted. Head position was checked, and auditory function was evaluated by questioning the owner. Rostral and caudal tongue tactile sensation and movement and the gag reflex were assessed. Laryngeal and cervical

musculature was examined for abnormality by palpation and the owner asked for any historical evidence of dysphagia or dysphonia.

Large animal species, of which a few are included in this series, received a modified neurological examination as described by De Lahunta (1983d).

Abnormal neurological examination findings were recorded and an attempt made to localise the neurological lesion or lesions.

Ancillary investigations

As well as investigating the pupillary lesions which warranted entry into this study, any other clinical or neurological abnormality was fully investigated. All cases received a routine haematological and biochemical evaluation applicable to the species and values compared to reference ranges of GUVS laboratories. Red blood cell count, haematocrit, haemoglobin concentration, mean corpuscular volume, platelet count and total and differential white blood cell count were determined. Small animal routine biochemical analysis included electrolytes: sodium, potassium, calcium, magnesium and phosphate; urea, creatinine, serum alkaline phosphatase (SAP), alanine transferase (ALT), and aspartate transferase (AST) activity, cholesterol, total protein,

albumin and globulin. Cats with evidence of neurological disease were checked for feline leukaemia virus (FeLV), feline immunodeficiency virus (FIV), feline corona virus (FIP) and toxoplasma status. Dogs with suspected multifocal inflammatory disease were checked for serum canine distemper virus antibody and toxoplasma titres, after determining their vaccinal status. Older dogs with neurological disease were checked for hypothyroidism with a resting T_4 initially. If this was < 10 nmol/l, a thyroid stimulating hormone (TSH) test was carried out, injecting 1 - 5 units of TSH intravenously and sampling after 4 hours for T_4 . Dogs showing biochemical evidence of hyperadrenocorticism were tested with a synacthen (ACTH) stimulation test, injecting 0.25mg synacthen intramuscularly and checking cortisol before and after 2 hours. A low dose dexamethasone test was also performed, injecting 0.01 mg/kg dexamethasone intravenously and sampling at 0, 3 and 8 hours for evidence of adrenal suppression.

Urinalysis, for specific gravity, pH, protein content, bilirubinuria, glycosuria, blood pigments, urea concentration and examination of spun deposit for organisms and abnormal cellular debris or crystals was performed where it was felt to be clinically indicated.

Bacteriological culture of urine, blood or other

substances, with determination of organism and antibiotic sensitivity was carried out where bacteriological infection was suspected.

Many of the cases showing neurological signs had cerebrospinal fluid (CSF) obtained, mainly from the cerebellomedullary cistern. This was after general anaesthesia, usually after diazepam premedication and thiopentone or propofol induction, and maintenance with halothane, oxygen and nitrous oxide after intubation. The site was aseptically prepared. A 21G 1.5 inch or a 23G 1 inch needle was used, depending on animal size. The technique used for collection was that described by Duncan and others (1987). The CSF obtained was then assessed for colour and consistency and cell count and total protein content were determined and compared to the reference ranges given by Thomson and others (1990). If the nucleated cell content exceeded $5/\text{mm}^3$, a differential count was obtained after cytopspin. If sufficient CSF could be obtained, it was submitted for canine distemper virus and toxoplasma antibody analysis, and compared to the serum titres. Canine parvovirus titre within the CSF was also checked in these cases, to rule out blood contamination of the CSF.

Radiography was obtained where clinically or neurologically indicated. Thoracic, abdominal, spinal

and skull films were obtained from a number of the cases. Contrast radiography was performed in some of the cases. Myelography where indicated was carried out at the cerebellomedullary cistern immediately after obtaining CSF, and occasionally at the lumbar cistern, when a 20G 3.5 inch or 22G 2 inch spinal needle was used. The contrast medium used was iopamidol (Niopam^R; Merck Ltd.) with concentration of 300mg Iodine/ml, with usual initial dose of 0.2mls/kg. Where angular venography was performed, this was by a radiologist after general anaesthesia, with cannulation of the angular veins and injection of contrast. Meglumine iothalamate (Conray^R 280; May & Baker Ltd.) was used with injection of 1 - 2 mls each side. Jugular veins were occluded during the time of the injection and a dorsoventral skull radiograph obtained immediately after the injection.

Ultrasonography was carried out by the author where this was felt to be clinically indicated. Cases with papilloedema had ocular ultrasonography, done by Professor J.S. Boyd, with a 7.5MHz transducer.

In the cases with suspected middle/inner ear disease, as well as radiographs demonstrating the bullae (intraoral and lateral oblique views), otoscopy was carried out under general anaesthesia to determine the extent of

otitis externa and to obtain samples for cytology and bacteriological culture. Tympanometry was performed as described by Coulter (1987) to determine whether the tympanic membrane was intact, presence of material within the middle ear and innervation of the stapedius muscle by the stapedius reflex. Tympanometry was performed by Dr. C.J.L. Little.

Where facial palsy or neurogenic masticatory muscle atrophy or a more generalised peripheral neuropathy was suspected, electromyography was performed by the author to ascertain the presence and distribution of denervated muscles by recognition of spontaneous electrical activity within these muscles (Bowen, 1987).

The relevant tests are detailed with individual case reports. From the historical, clinical, neurological findings and the results of the ancillary investigations, a definitive diagnosis was made if possible and treated if appropriate. As far as possible, follow-up investigations were carried out. Where there was not a successful outcome, post mortem investigation was carried out where the owners' had granted permission.

Pharmacological testing

Where pupillary lesions were identified and were felt to

be due to autonomic dysfunction, an attempt to confirm and localise this further was made by pharmacological testing. When parasympathoparesis was suspected, pilocarpine drops were instilled into the conjunctival sacs of both eyes. Initially, a 0.1% concentration was used, diluting the 1.0% solution with saline 1:10. If no effect was identified within 30 minutes, two drops of Pilocarpine 1.0% solution (1% Isopto Carpine^R; Alcon Laboratories Ltd.) were instilled into both eyes and the effects assessed and timed. Results were compared with the findings given by Thompson and Pilley (1976) and Neer and Carter (1987).

Where Horner's syndrome was suspected, Phenylephrine 10% drops (Phenylephrine 10% w/v eye drops BPC^R; Richard Daniel & Son Ltd.) were instilled into both eyes and the affect on the abnormal and normal pupils particularly, but also on the membrana nictitans and the palpebral fissure and any enophthalmos present was carefully monitored and timed. The results were compared to the findings given by Petersen Jones (1989a).

B.i) CASES PRESENTING WITH OPTIC NERVE LESIONS

CASE 1: 114825 "Sam"

Signalment: 8 week old male miniature poodle.

Reason for Presentation: Congenital blindness.

Case Summary

This pup was one of a litter of six. After their eyes opened, this pup was observed to be unusually quiet and would bump into things. The pup was well grown and apparently well otherwise. The only abnormality on clinical examination was that the pupils were widely dilated and unresponsive to light and blindness appeared total. Fundoscopy indicated a bluish tapetal fundus of normal vascularity. In the left eye, these vessels converged to a point at which no optic disc could be identified, although a dark shadow in this area, possibly a coloboma, was present. There was an optic disc apparent in the right eye of pink - white colour, although it was abnormally small. Neurological examination was unremarkable for a pup of this age.

Diagnosis

Bilateral optic nerve hypoplasia. As this condition is believed to be inherited in the miniature poodle, a hopeless prognosis was given for the pup and the owner was advised not to repeat this breeding. The pup was

retained by the owner as a pet and re-examined one month later. Fundus photographs were obtained (Figure 5).

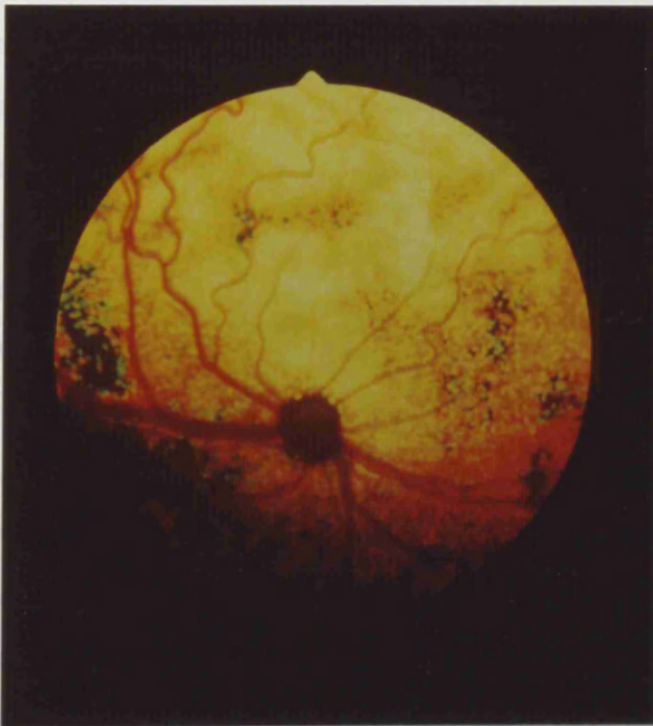


Figure 5. Case 1. 114825. 12 week old male Miniature poodle. Right fundus (top) shows a small hypoplastic optic disc. Left fundus (bottom) without any normal disc apparent at the convergence of the retinal vessels.

CASE 2: 112011 "Rogerio"

Signalment: 16 year old gelding Riding pony.

Reason for presentation: Sudden onset blindness.

Case Summary

This animal was used for show jumping. He was presented because of sudden onset blindness, occurring four days before presentation at GUVS. Prior to this, over the preceding few months, he had unexpectedly refused at several jumps, and the owners suspected a gradual deterioration in visual acuity prior to the complete blindness. The animal was in good condition, and other than a hesitant, slightly hypermetric gait, no other abnormalities of significance were detected on full clinical or neurological examination other than referable to his visual system. Both pupils were widely dilated and unresponsive to light. Visual loss was complete. Haematological, biochemical and endocrinological parameters were all within normal limits. No evidence of active equine herpes virus was present from paired serology titres. There was no evidence of lead poisoning from faecal and plasma blood lead analysis. Fundoscopy was initially unremarkable and optic neuritis was diagnosed and treatment attempted with prednisolone at 1 mg/kg.

No response was seen to treatment so it was tailed off

and terminated. The animal became brighter as he grew accustomed to the visual disability. After one month, fundoscopy showed early evidence of optic atrophy in the right eye, and these changes became more marked as he was followed over a year. At ten months, the first signs of optic atrophy and focal retinal degeneration became apparent in the left eye. At this time, the right eye showed distinct optic atrophy with pallor of the optic disc and marked retinal vessel attenuation. Linear lesions were also apparent in the tapetal and nontapetal fundus probably corresponding to focal retinal degeneration. Fundus photographs are shown in Figure 6.

Although the prognosis for return of vision was hopeless, the horse was maintained due to insurance problems.

Diagnosis

Optic neuritis with secondary progressive retinal degeneration.

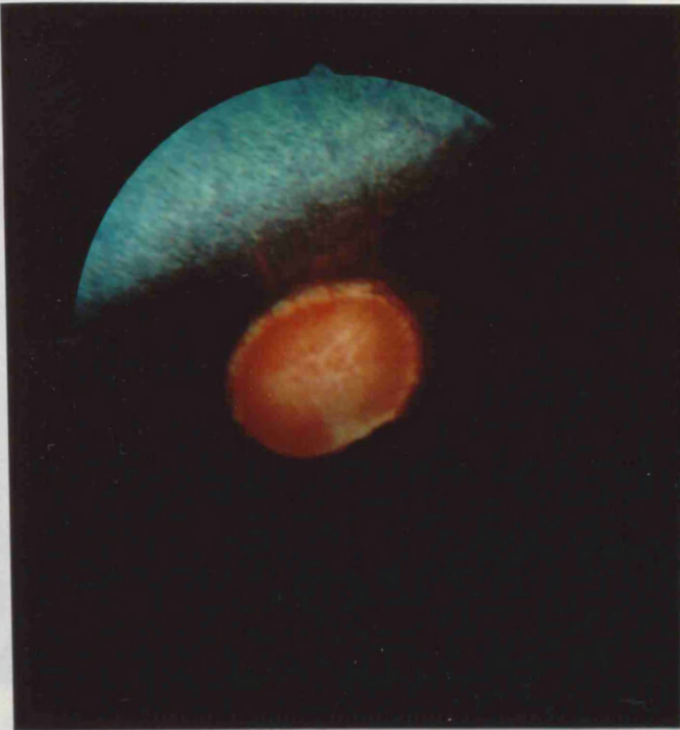
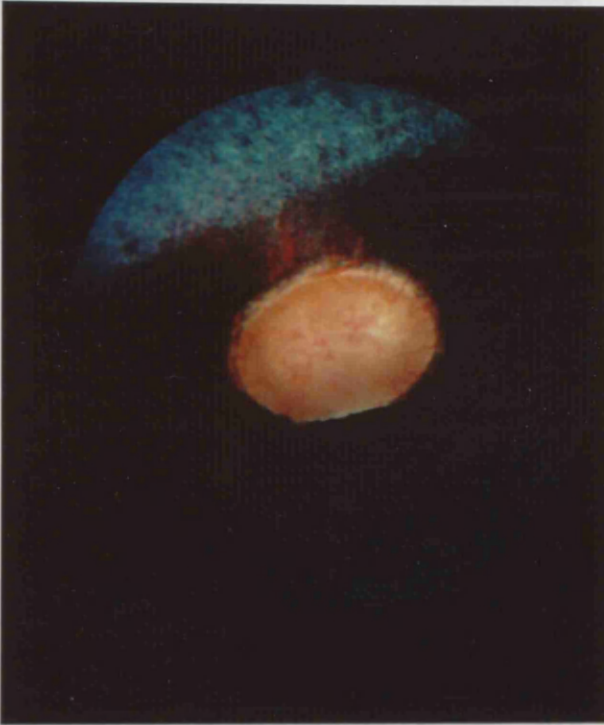


Figure 6. Case 2. 112011. 16 y.o. gelding riding pony. Right fundus (top) after 1 month shows earliest signs of retinal atrophy with slight pallor of the optic disc and decreased retinal vascularity. The left fundus (bottom) appears unremarkable and can be used for comparison.

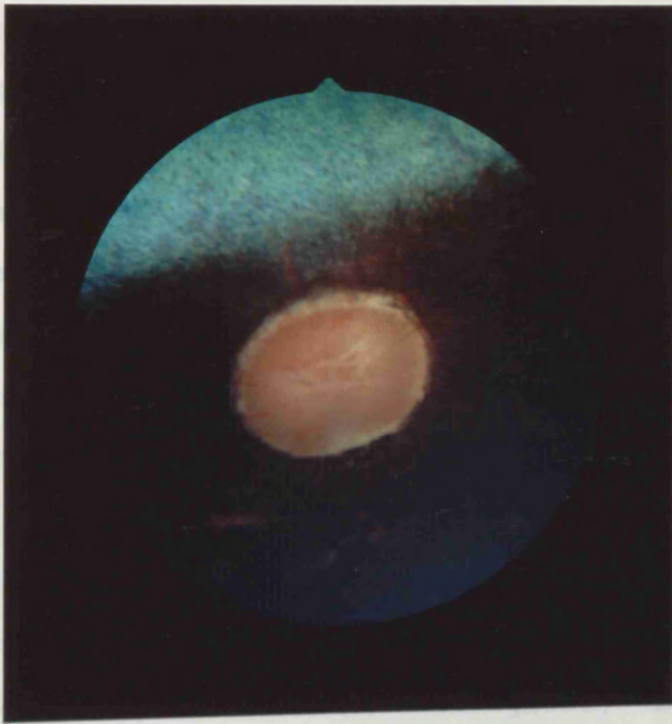
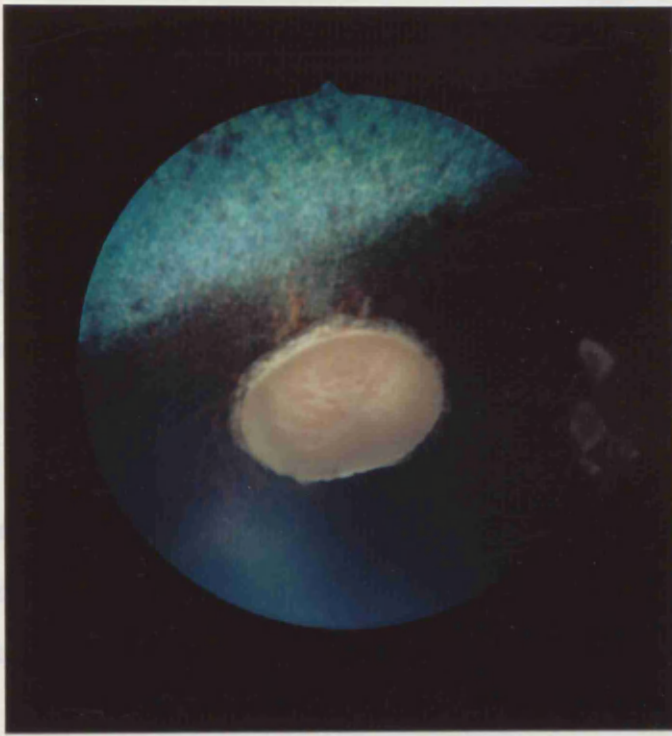


Figure 6 continued. At 10 months, the right optic disc (top) is very pale and there is marked retinal vessel attenuation. The left fundus (bottom) is only now beginning to show initial signs of retinal atrophy although there are some focal retinal degeneration lesions apparent as linear markings in the non-tapetal fundus.

CASE 3: 115472 "Bonnie"

Signalment: 4.7 year old female Cavalier King Charles spaniel.

Reason for presentation: Sudden onset blindness.

Case Summary

Four months prior to presentation at GUVS, this dog had suddenly become totally blind. Some vision returned after treatment with oral glucocorticoids but deteriorated again after therapy terminated. She had also had an episode of cervical pain which responded to steroids although this had not been investigated further. On examination, blindness was total and both pupils were widely dilated (Figure 7a) and direct and consensual pupillary light responses were absent. She had a systolic heart murmur consistent with a diagnosis of mitral endocardiosis and clinical and radiographic evidence of left heart failure with pulmonary oedema. No other significant clinical or neurological abnormalities were evident. Fundoscopy revealed marked bilateral papilloedema (Figure 7b), most obvious in the right eye, which was also apparent on ultrasonography of the eye (Figure 7c). Routine haematological, biochemical and endocrinological investigations were unremarkable. At this stage, bilateral optic neuritis was diagnosed, and prednisolone therapy, starting at 2 mg/kg commenced. Frusemide diuresis adequately controlled her left heart

failure.

One month later, no improvement in the dog's vision had been recognised, although she was coping well with her blindness. Some resolution of the papilloedema was apparent although it was still present in the left eye. There were numerous pigmented patches in the retinas in both eyes, extending from the disc, especially in the left, and there was a band of hyperreflectivity dorsal to the disc in the right eye.

No further treatment was given and the dog was seen six weeks later, now over 6 months since the initial onset of blindness. The owners were now concerned about her as she had lost condition, was listless and lethargic, urinated in inappropriate places and was shedding her haircoat excessively. Leukotrichosis was dramatic on her head and the coat was seborrhoeic and scurfy. Fundoscopy showed marked papilloedema in the left eye and marked asteroid hyalosis in the right eye. The areas of retinal degeneration with pigmentation had progressed in both eyes.

At this stage, the haematological, biochemical and endocrinological (particularly thyroid and adrenal function) tests were repeated as a pituitary lesion affecting the chiasma was suspected. Results were again

unremarkable. Angular venography was performed which identified a filling defect within the rostral cavernous sinus. Cerebrospinal fluid was obtained from the cerebellomedullary cistern. Appearance was unremarkable but analysis was grossly abnormal with a nucleated WBC of $480 / \text{mm}^3$, which were shown to be largely lymphocytes and lymphoblasts on cytopspin, and a protein content of 560 mg/l. The dog was euthanased at this point in view of the hopeless prognosis.

Post mortem examination demonstrated that both optic nerves were thickened especially proximally, most marked on the right (Figure 7d). The lesion was centred around the optic nerves, but extending into the cerebrum cranially and caudally. The optic nerves had a marked mononuclear cell infiltrate (plasma cells, macrophages and lymphocytes) individually and in clumps, often around blood vessels. There was extensive infiltration of tissue between the lateral ventricles. A mild meningitis was also evident. Lymphocytic cuffing and oedema was evident throughout the white matter. These changes were characteristic of granulomatous meningoencephalitis (reticulosis) (Figure 7e).

Diagnosis

Granulomatous meningoencephalitis or reticulosis affecting the visual system.



Figure 7a. Case 3. 115472. 4.7 y.o. Cavalier King Charles Spaniel. The pupils are widely dilated and completely unresponsive to light. Vision is absent.

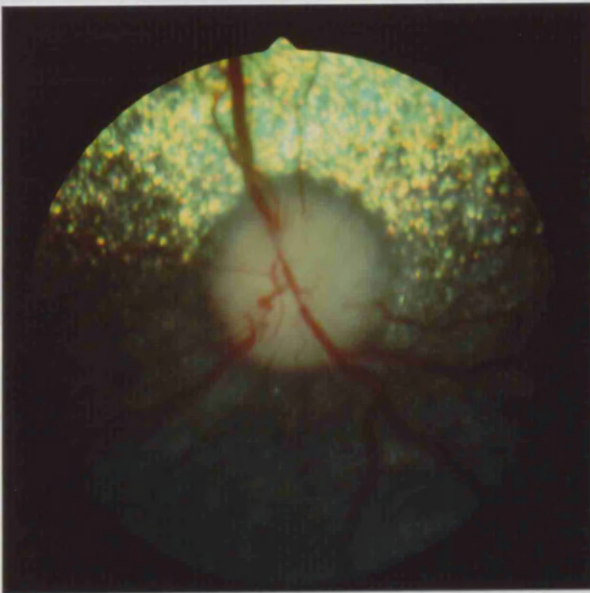
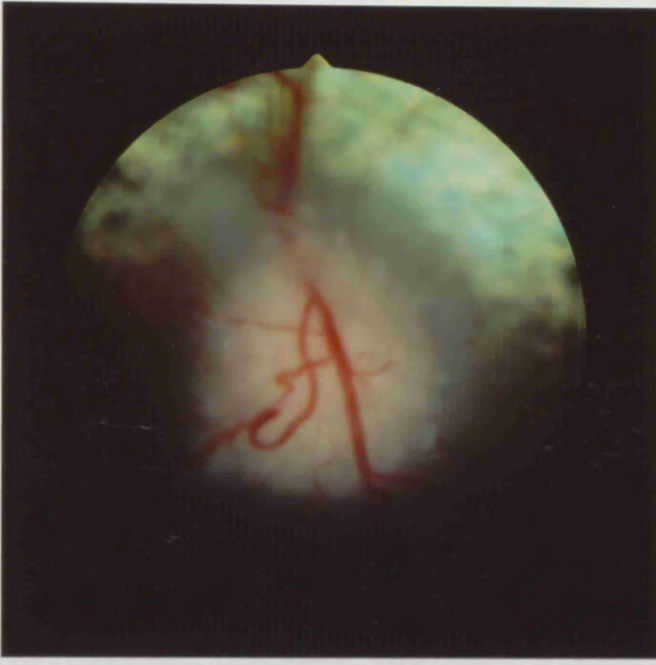


Figure 7b. The optic disc in the right fundus (top) is in focus while the retina is out of focus; consistent with a diagnosis of papilloedema as the disc bulges forwards. This change has resolved (bottom) after 4 days of glucocorticoid therapy.

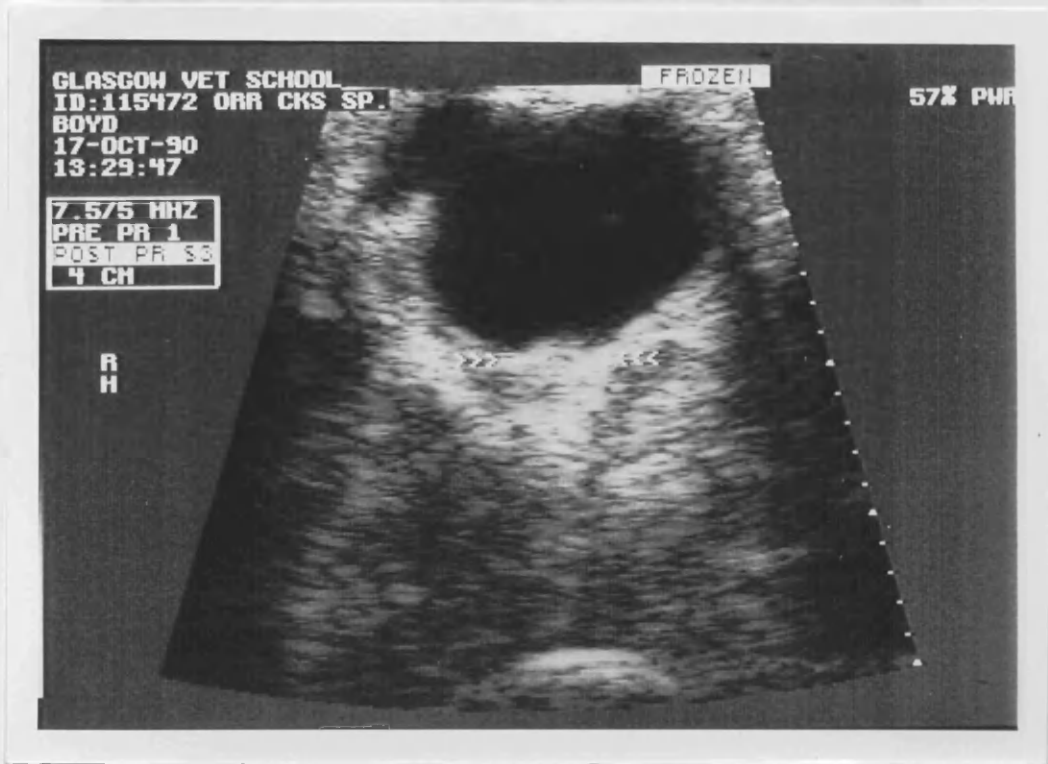


Figure 7c. Ultrasound image from the right eye with horizontal section through the globe indicating the optic disc bulging forwards into the echolucent vitreous (white arrows).

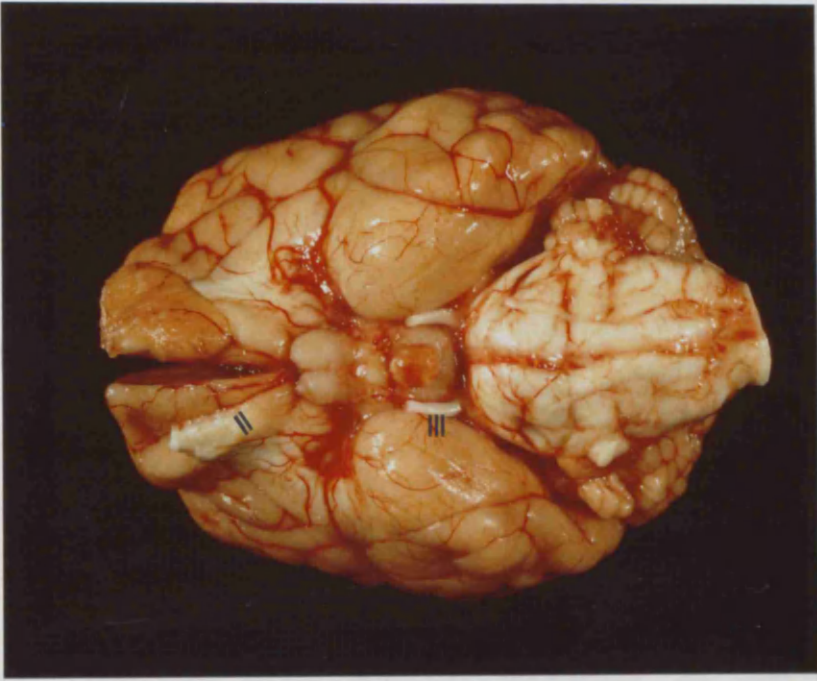


Figure 7d. Ventral view of the brain post mortem showing thickened optic nerves. (II = Optic nerve; III = Oculomotor nerve).

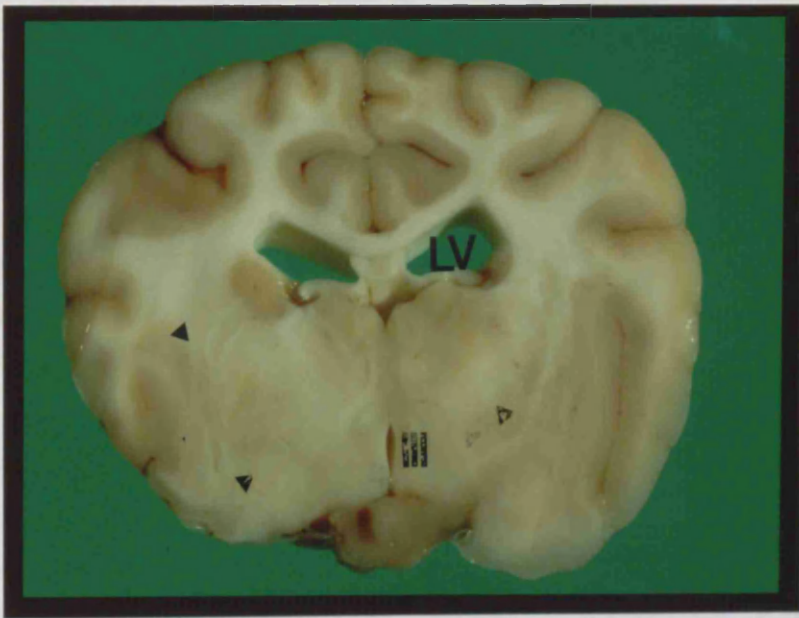


Figure 7d. Transverse section at level of diencephalon showing lesion infiltrating into thalami and cerebrum (arrowed) between third ventricle (III) and lateral ventricles (LV).

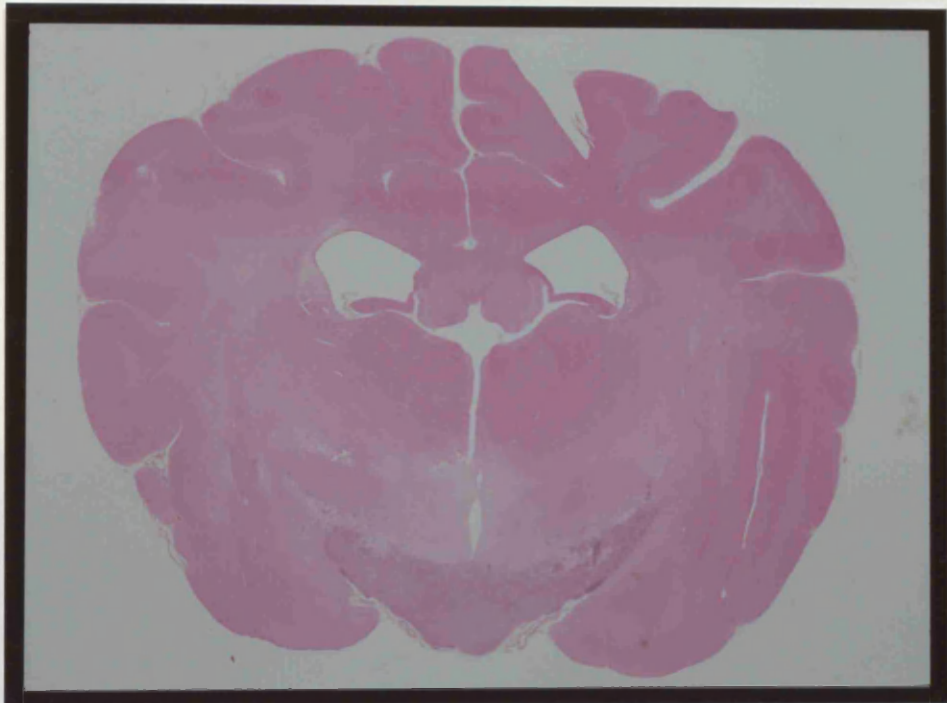


Figure 7e. Transverse section of cerebrum at level of optic chiasma showing base of brain densely infiltrated with mononuclear inflammatory cells.

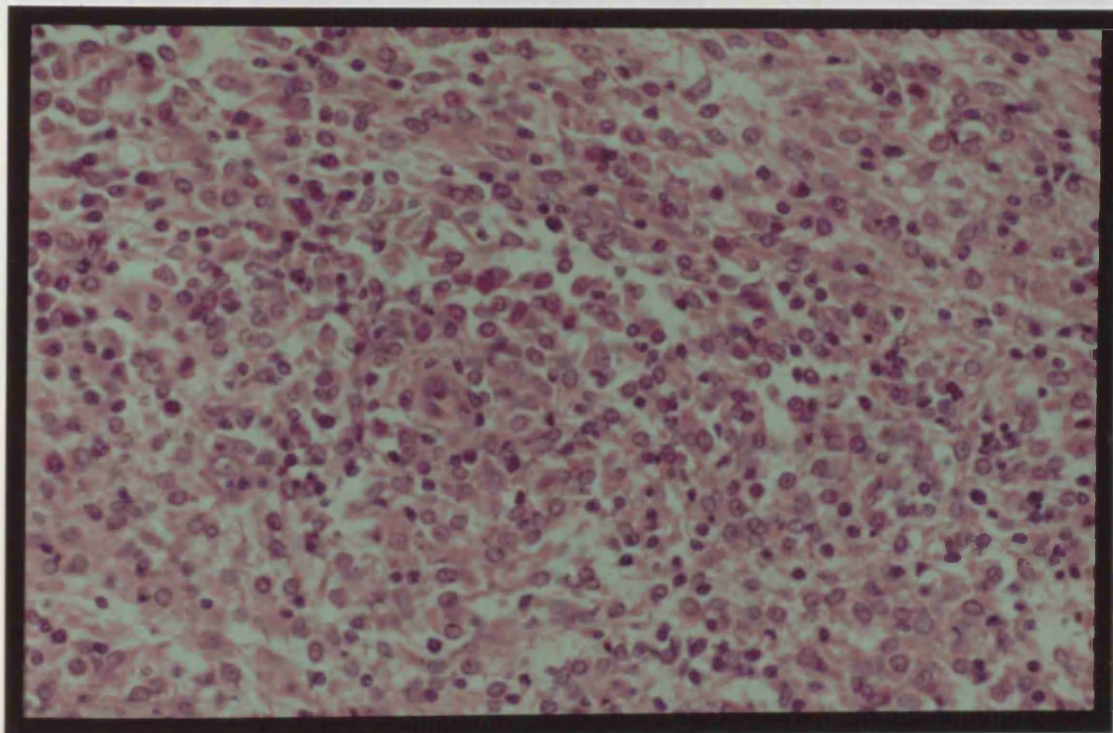


Figure 7e continued. Higher power at chiasma level showing mixed mononuclear inflammatory cell infiltrate. x 40.

PAGE 11 (Continued)

Signalment: 3.5 year old male Jack Russell terrier.
Reason for presentation: Systemic onset blindness.

History: Onset of blindness was insidious, began 4 weeks prior to presentation. Dog had been healthy and active prior to onset of blindness.

Four days prior to presentation of blindness, this dog had

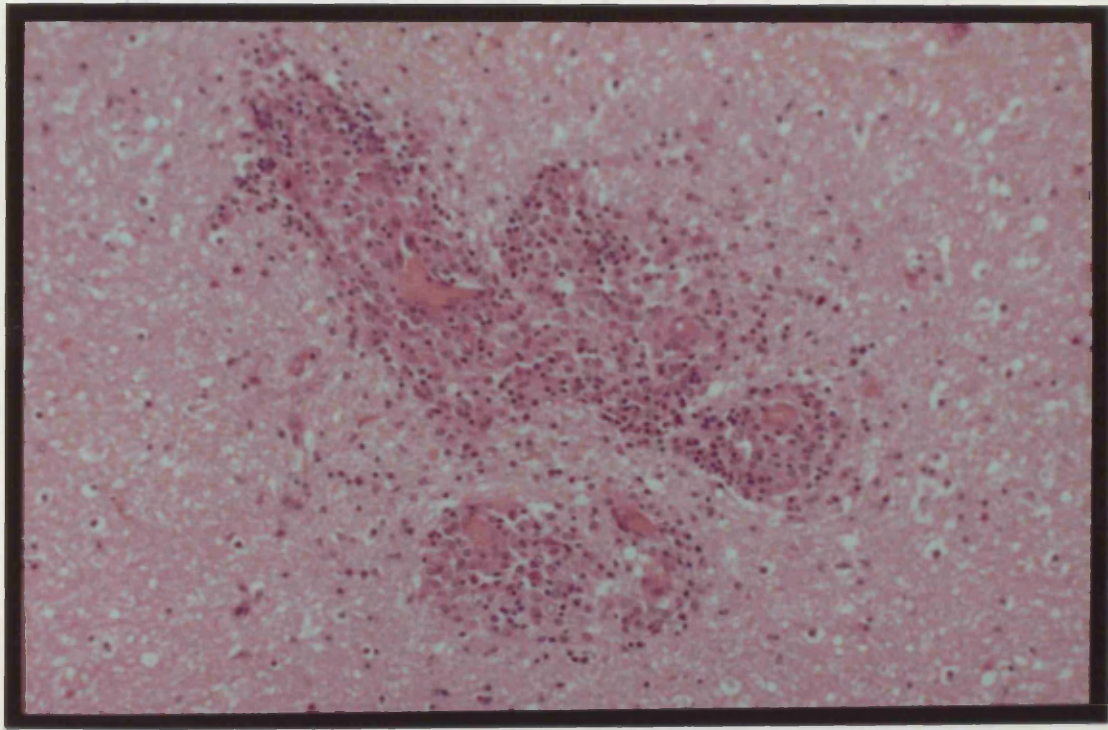


Figure 7e continued. Cuffing of blood vessels at level of chiasma by densely packed lymphoid cells. x 40.

CASE 4: 116606 "Chip"

Signalment: 3.5 year old male Jack Russell terrier.

Reason for presentation: Sudden onset blindness.

Case Summary

Four days prior to presentation to GUVS, this dog had suddenly become blind. He had received vaccinations as a puppy but no booster vaccinations. The dog appeared to be very bright and in good body condition although disorientated by his blindness. No other significant abnormalities were evident on clinical or neurological examination. Both pupils were widely dilated (Figure 8a) and direct and consensual pupillary light responses could not be elicited. Visual loss was total. Fundoscopy demonstrated dramatic bilateral papilloedema with otherwise normal retinas (Figure 8b). Haematological and biochemical screening was unremarkable. A cerebellomedullary cisternal tap revealed CSF fluid to be of unremarkable appearance but was abnormal with 199 nucleated cells/mm³ and a protein content of 280mg/l. Cytospin failed to isolate any cells, so their nature could not be determined. Angular venography was performed in order to identify any mass lesion within the cavernous sinus but was not of diagnostic quality.

Treatment with oral prednisolone commenced but did not result in any clinical improvement. The owner requested

euthanasia and the brain was obtained for post mortem examination. No gross abnormalities were detected, although only the extreme proximal portions of the optic nerves were present. Histopathology revealed a mild meningitis and a very severe perivascular mononuclear cuffing (Figure 8c). This was most marked in the cerebellum. There was also focal demyelination evident in the white matter. Neuronal chromatolysis and degeneration was also evident. Eosinophilic intranuclear inclusion bodies present in some of the glial cells were diagnostic of a distemper encephalitis.

Diagnosis

Distemper virus encephalitis involvement of the visual pathways. Titres to CDV had not been obtained from serum or cerebrospinal fluid.



Figure 8a. Case 4. 116606. 3.5 y.o. M. Jack Russell terrier.

Both pupils are widely dilated, completely unresponsive to light and vision was absent.

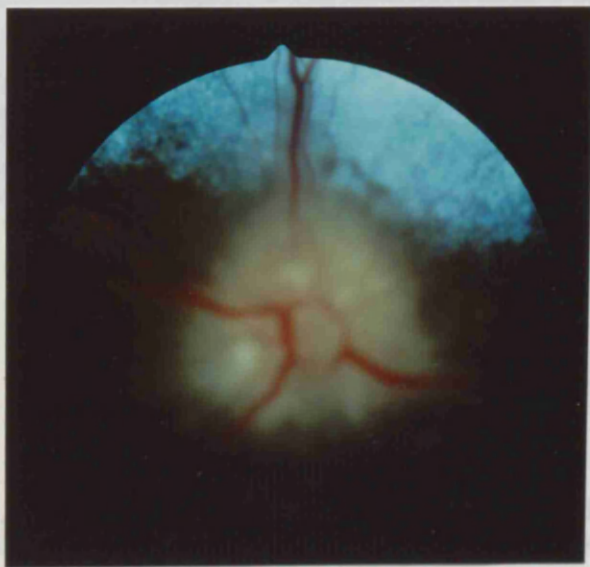


Figure 8b. Fundus photograph from left eye demonstrating papilloedema, with retina in focus and optic disc out of focus.

Subject: 3-year-old female, English Bulldog

History: For presentation. Sudden onset blindness after

being hit by a bicyclist. No trauma to head.

At admission, the dog was blind, disoriented, and

had a severe headache. No vomiting or diarrhea.

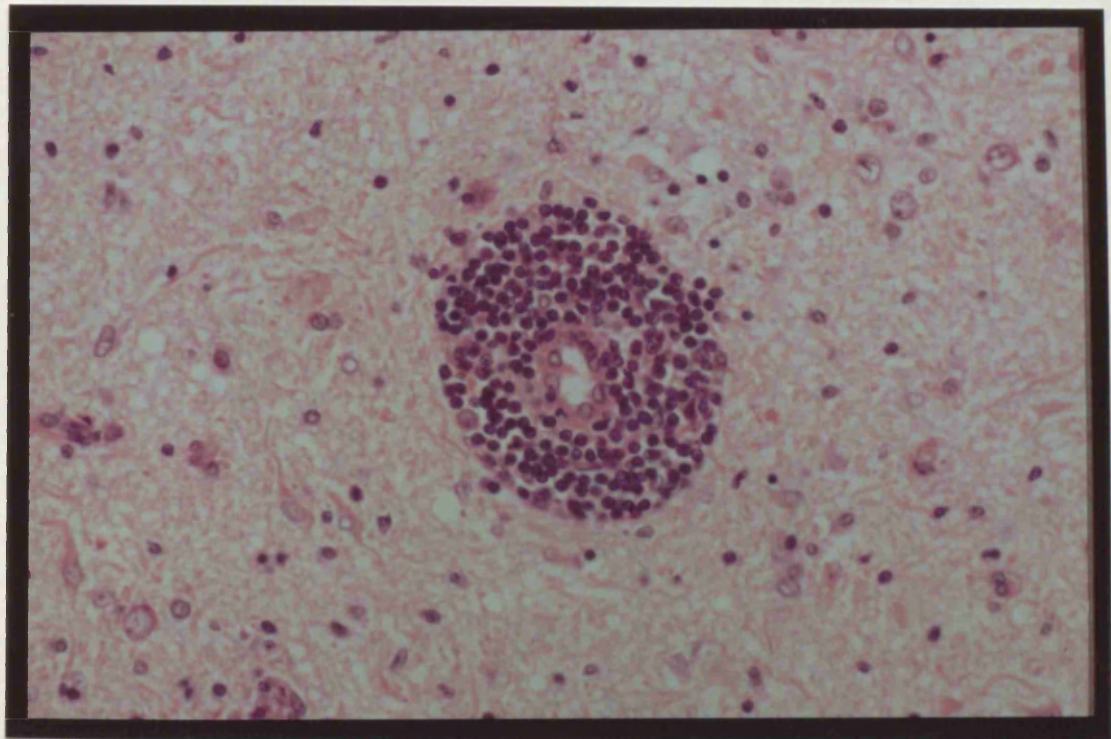


Figure 8c. Section of cerebellum. Cuffing of blood vessel by mononuclear inflammatory cells. x40.

CASE 5: 116314 "Corrie"

Signalment: 9 year old female spayed Rough Collie

Reason for presentation: Sudden onset blindness after being hit by a bicycle.

Case Summary

The accident had occurred three weeks prior to presentation to GUVS after a bicycle had run into her, hitting her head. The right eye was not unduly painful but third eyelid protrusion and scleral haemorrhages were apparent. Some swelling was evident below the eye. The owners felt that she had become completely blind in both eyes after the accident having had normal visual acuity prior to this. The referring veterinary surgeon had treated her with oral antibiotics and topical ophthalmic antibiotic and steroid drops. No improvement was present with her sight although some retraction of her third eyelid had been recognised. On examination, the dog was in good condition but was completely blind. Both pupils were widely dilated, although the right pupil was slightly less dilated. Enophthalmos, protrusion of the third eyelid and ptosis of the upper lid was also apparent affecting her right eye (Figure 9). No pupillary light reflex could be elicited at all. The ciliospinal reflex was normal. Oculovestibular and voluntary eye movements appeared to be normal and no strabismus was evident. No other neurological deficits

were identified. Fundoscopy revealed a normal retina and no papilloedema. Phenylephrine testing resulted in almost complete resolution of the signs of the Horner's syndrome after 40 minutes. Survey radiography of thorax and neck were unremarkable. The dog was treated with oral prednisolone at 1 mg/kg for the possible optic neuritis.

Re-examinations after two and three months failed to demonstrate any return of vision. She was totally blind although was coping better. Both pupils were dilated although the anisocoria and the Horner's syndrome persisted unchanged. No changes were evident on fundus examination on either of these occasions.

This case is also included with the cases with Horner's syndrome (pp 169 - 170).

Diagnosis

The complete blindness suggested either sudden acquired retinal degeneration or optic neuritis (not extending distally enough to result in papilloedema). Horner's syndrome concurrently affected the right eye which pharmacologically appeared to be due to a second order neuron lesion. It did not therefore appear that the same lesion could result in the afferent lesion and the Horner's syndrome. The Horner's syndrome may have

resulted from cervical soft tissue injury. Sudden acquired retinal degeneration in dogs is of unknown aetiology although many cases appear to be associated with pituitary dependent hyperadrenocorticism and is similar to visual paraneoplastic syndrome in man (van der Woerd & others, 1991). No biochemical or endocrinological abnormality was detected in this case.



Figure 9. Case 5. 116314. 9 y.o. F(s) Rough Collie. Both pupils are widely dilated, although the right is incompletely dilated and a narrowed palpebral fissure, enophthalmos and third eyelid protrusion are also apparent in this eye.

C.i) DISCUSSION ABOUT THE CASES PRESENTING WITH

OPTIC NERVE LESIONS

Optic neuritis or optic neuropathy is characterised by a complete and sudden loss of vision with complete pupillary areflexia (Kay, 1981). Optic neuritis is a nonspecific term which may reflect a variety of inflammatory, demyelinating, degenerative or ischaemic conditions affecting the optic nerve between the optic disc and the chiasma (Fischer & Jones, 1972; Nafe & Carter, 1981). Optic neuritis may precede the development of other neurological signs suggesting a diffuse central nervous system inflammatory disease (Fischer & Jones, 1972; Kay, 1981), reflecting the fact that the optic nerves are an extension of the central nervous system and are not peripheral nerves (De Lahunta, 1973). Although cases 3 and 4 did have pathological evidence of more diffuse disease, this involvement had not been recognised prior to euthanasia despite case 3 having historical evidence of cervical pain and showing behavioural disturbances and evidence of malaise.

Primary idiopathic optic neuritis is characterised histologically by a mixed inflammatory cellular infiltrate. It appears to most commonly affect dogs of middle age (Nafe & Carter, 1981). These cases may respond to immunosuppressive doses of steroids if

administered early in the course of the condition (De Lahunta, 1973; Kay, 1981). Causes of optic nerve lesions which must as far as possible be ruled out before a diagnosis of idiopathic optic neuritis is made are distemper, granulomatous meningoencephalitis, toxoplasmosis, mycoses and neoplasia (Fischer & Jones, 1972; Smith & others, 1977; Nafe & Carter, 1981). Such causes were recognised pathologically in cases 3 and 4.

Electroretinography is required to differentiate between retinal lesions such as sudden acquired retinal degeneration (SARD) and bilateral prechiasmal optic neuropathy where there is little to be seen on fundoscopy (Braund & others, 1977; Petersen Jones, 1989b) as may be appreciated from case 5. It was felt with this case that some fundic evidence of retinal degeneration should have been recognised after three months if her visual loss was due to SARD. Her blindness was therefore believed to be due to bilateral optic neuritis, possibly of traumatic origin, although this was not confirmed.

Congenital optic nerve hypoplasia has been described in dogs, cats, horses, rabbits and man (Ernest, 1976). Eyeball size is usually normal. Other congenital ocular defects may concurrently be present (Gelatt & Leipold,

1971). It may be unilateral or bilateral (Gelatt, 1973). If bilateral, many of these animals are said to have a searching nystagmus as well as the widely dilated pupils unresponsive to light and complete blindness (De Lahunta, 1973). The nystagmus was not a feature recognised in the pup described here (case 1). Canine breeds reported to be affected are Collies, Dachshunds, miniature poodles, Beagles and Russian Wolfhounds (Saunders, 1952; Rubin, 1974a). The abnormality appears to be due to hypoplasia and not degeneration (Ernest, 1976). There is no treatment for this condition (Shell, 1982).

Equine optic neuritis has been well described in the literature. Many cases appear to be subsequent to extensive haemorrhage, which is also recognised in man (Gelatt, 1979; Platt & others, 1983). Other cases occur after blunt skull trauma, usually to the poll area, although the pathogenesis of the optic nerve lesion in many of these cases is poorly understood. Martin and others (1986) hypothesised that the trauma results in momentum of the brain in a caudal direction causing a traction injury to the optic nerves as they are fixed rostrally in the optic canal. Therapy with dimethyl sulphoxide (DMSO) and corticosteroids may prevent permanent blindness if treated aggressively immediately after the traumatic incident (Rebhun, 1986). A toxic

aetiology (pyrantel) was suspected in one case reported by Kelly & Pinsent (1979). Suppurative optic neuritis has been recognised in association with endocarditis in one horse (Hatfield & others, 1987). In many horses the aetiology of the optic neuritis can not be determined (Slatter & Huxtable, 1983). In case 2, no preceding trauma, haemorrhage or other incident was recognised. This horse had a history suggesting gradual loss of vision preceding the complete blindness and this is thought to be so with many cases of idiopathic optic neuritis - the difficulty being in detecting subtle visual deficit in most animals (Rubin, 1974c; Nafe & Carter, 1981; Slatter & Huxtable, 1983). Optic atrophy, retinal vessel attenuation and retinal pigmentary disturbances are well recognised with long-standing optic nerve lesions, as seen in case 2, although the reason for these changes is less certain. It has been speculated that they occur due to a reduced metabolic rate of the retina (Martin & others, 1986). In some cases of equine optic neuritis, white masses due to neuroglial proliferation can be seen on and around the optic disc (Platt & others, 1983). These must be distinguished from the condition described as proliferative optic neuropathy seen in old horses not associated with visual deficits (Platt & others, 1983).

Papilloedema as a manifestation of raised intracranial

pressure is not associated with blindness and is uncommon in domestic animals (Rubin, 1974b). "Papilloedema" reflecting optic nerve involvement is more properly called papillitis and is associated with visual loss (Petersen Jones, 1989a), as recognised in cases 3 and 4. The presence or absence of papillitis in optic neuritis results in the syndrome being classified as being intrabulbar or retrobulbar (Nafe & Carter, 1981). If case 5 is a case of optic neuritis, it may be classified as retrobulbar optic neuritis as no abnormality of the optic disc was detected.

Granulomatous meningoencephalitis (GME) or reticulosis has been described as affecting the visual pathways (Neer & Carter, 1987; Braund & others, 1977). It may also result in ocular lesions with choroidoretinitis (Smith & others, 1977) although case 3 appeared to have retinal degeneration secondary to the optic neuritis rather than active inflammation. This case is very similar to the one described by Fischer and Liu (1971).

Canine distemper virus has a predilection for the visual pathways, but usually affects parts of the optic tracts (De Lahunta, 1973; Neer & Carter, 1987). It is one of the most common causes of optic neuritis (Fischer & Jones, 1972) as case 4 illustrates.

In conclusion, it can be seen that a variety of diverse insults may affect the optic nerves resulting in visual loss and widely dilated unresponsive pupils. In many cases, it is not immediately possible to recognise the cause, but later in the course of the disease, appearance of other systemic or neurological signs may help localise and identify the underlying disease. The prognosis for regaining sight is poor or hopeless in most cases.

B.ii) CASES PRESENTING WITH CHIASMAL OR CAVERNOUS SINUS INVOLVEMENT

CASE 6: 112091 "Ealie"

Signalment: 12 year old male castrated Domestic shorthaired cat.

Reason for presentation: Blindness and dilated pupils.

Case Summary

This cat was referred to GUVS after three weeks' history of suspected feline dysautonomia with widely dilated pupils, unresponsive to light. The owner reported sudden onset blindness, marked polydipsia, anorexia, considerable recent weight loss and extreme depression and reluctance to move around. Examination confirmed the cat to be totally blind with widely dilated pupils with no response to light illumination. Both globes were very central and no voluntary or oculovestibular eye movements could be elicited. No nictitating reflex could be elicited although the ophthalmic branch of the trigeminal nerve facial sensory field appeared to be intact. No other neurological deficits were identified. Fundoscopy initially was unremarkable but after three days hospitalisation, papilloedema became evident in his right eye (Figure 10a). Other incidental clinical findings were of otodectes and flea infestations, dental calculus and periodontal disease and a grade III/VI holosystolic heart murmur with point of maximal

intensity on the left heart base. Sinus bradycardia with heart rate of 120 bpm was evident clinically and confirmed by electrocardiography. Radiography and echocardiography (including Doppler) were unremarkable - the murmur was consequently felt to be a flow murmur secondary to the large stroke volume associated with bradycardia.

Haematology demonstrated a mild nonregenerative anaemia with RBC of $5.9 \times 10^9/l$ with numerous schistocytes and abnormal erythrocyte morphology. The animal was not thrombocytopaenic. No clinical or echocardiographic evidence of thromboembolism had been identified or other evidence consistent with disseminated intravascular coagulation (DIC). Biochemistry revealed mild renal dysfunction with a urea of 14.4 mmol/l and creatinine of 171 $\mu\text{mol/l}$. Parameters of liver function and electrolytes were all within reference ranges. Urinalysis consistently indicated a low specific gravity urine of 1.020 but was otherwise unremarkable. He was negative for feline leukaemia virus (FeLV) and *Toxoplasma gondii* and had a zero titre to feline coronavirus (FIP). He was positive for feline immunodeficiency virus (FIV). The cat had a very low resting T4 of 7.5 nmol/l which did not respond to intravenous injection of 1 unit (0.2 units/kg) of thyroid stimulating hormone (TSH) after four hours,

confirming hypothyroidism. He also had a very low resting cortisol in the evening of < 27 nmol/l. This also failed to increase two hours after 125 mcg synacthen (ACTH) injected intramuscularly. As electrolyte parameters were unremarkable, an isolated glucocorticoid hypoadrenocorticism was suspected. During hospitalisation, the cat was markedly polydipsic, drinking 350 - 500 mls per day which was felt to be excessive for the mild renal dysfunction evident. Intravenous fluids rapidly improved the clinical state of the animal and normalised the renal parameters. It was therefore suspected that he concurrently had diabetes insipidus but a water deprivation test was avoided because of the renal dysfunction. Measuring antidiuretic hormone was considered, but required special handling of samples and transport to Bristol so it was not done. The elevation in urea and creatinine may be secondary to diabetes insipidus if the animal was too depressed to physically consume sufficient water.

A bilateral cavernous sinus lesion was suspected from the complete extraocular palsy and a complete chiasmal lesion was suspected from the complete visual loss and widely dilated and unresponsive pupils. He was hypothyroid. The cortisol and synacthen stimulation results with normal Na^+/K^+ ratio indicated a purely glucocorticoid hypoadrenocorticism which may be

recognised with reduced ACTH release (electrolytes are maintained within normal limits by other mechanisms such as the aldosterone system). Diabetes insipidus was suspected. These endocrinological results were suspicious of panhypopituitarism, which may be associated with a possible cavernous sinus / pituitary lesion.

Under general anaesthesia, the pupils did constrict, indicating that the parasympathetic system innervating the pupil was intact. They had not, however, shown any miosis after 0.1 mg/kg morphine injected subcutaneously. Cerebrospinal fluid (CSF) was obtained from the cerebellomedullary cistern. It was abnormal with a nucleated cell content of $39/\text{mm}^3$ and a total protein content of 3320 mg/l. Angular venography was technically very successful but failed to demonstrate a cavernous sinus area, suggesting the presence of a mass lesion causing obliteration of the cavernous sinus (Figure 10b). From the consistently abnormal haematological film, with schistocytosis, it may have been due to a vascular lesion or neoplasm.

Although a very poor prognosis was given, initial therapy given with intravenous fluids, eltroxin at 50mcg twice daily and prednisolone at 10 mg daily resulted in a good clinical improvement and this was maintained once

the cat was discharged on the oral preparations. Over the following month, he adapted to his visual loss and ate well, putting on weight. His heart rate increased to 170 bpm. He remained extremely polydipsic. After 5 weeks, further increase in thirst and recurrence of depression was reported by the owner. Although the owner was unable to return the cat for further investigations, it was decided to try him on DDAVP (synthetic antidiuretic hormone; ADH) administered into the conjunctival sac. No marked improvement was detected and he returned to GUVS after 7 weeks. He was extremely depressed, dehydrated, bradycardic and the left eye was caked up with dried mucoid ocular discharge. A complete facial paralysis was evident on the left with zero tear flow. The right eye had 15 mm / minute tear flow on the Schirmer test strips. There was no evidence of facial or corneal analgesia. The uraemia had deteriorated with urea of 41.1 mmol/l and creatinine of 528 umol/l. Urine specific gravity was still 1.020. Schistocytosis and abnormal RBC morphology was still evident on haematology. Despite the hopeless prognosis with continued deterioration, the owner requested intensive therapy be tried. After 24 hours of intravenous fluid administration, the renal parameters had returned to normal, appetite returned and the cat was much brighter. Intravenous DDAVP was given at 0.01 mg/kg and the urine specific gravity increased to 1.035, further suggesting

diabetes insipidus was responsible for the dehydration and the renal dysfunction. He was discharged again on the eltroxin, prednisolone and DDAVP conjunctively and artificial tears and antibiotic drops to prevent corneal damage with the left keratoconjunctivitis sicca. Reasonable progress was maintained at home but three weeks later, two and a half months after initial presentation, he represented after two days of trigeminal mandibular nerve palsy with an inability to close his jaw or eat or drink. He was profoundly depressed, bradycardic (90 bpm) and dehydrated. Jaw tone was completely absent. Facial analgesia appeared to be complete on both sides of the face, and facial palsy and KCS was still evident on the left side. Rostral tongue tactile sensation was absent although taste (lemon juice) appeared to be normal. At this stage, the owner gave permission for euthanasia but post mortem permission was not granted.

Diagnosis

It was unfortunate that no post mortem could be performed to explain the bizarre progression of signs in this case. A cavernous sinus mass initially resulted in a chiasmal lesion, deficits in cranial nerves II, III, IV and VI as well as panhypopituitarism. If serial TSH and ACTH tests had been done, the thyroid gland and the adrenal cortex should be stimulated eventually with

secondary lesions. The lesion later appeared to extend to involve the left facial nerve (CN VII) and all three branches of the trigeminal nerve (CN V) bilaterally. Although a vascular lesion was suspected from the haemogram, the appearance was probably too aggressive to be explained by thromboembolism. Bizarre tumours are reported with feline immunodeficiency virus (Hopper & others, 1989) and it may have been a vascular tumour that was present.

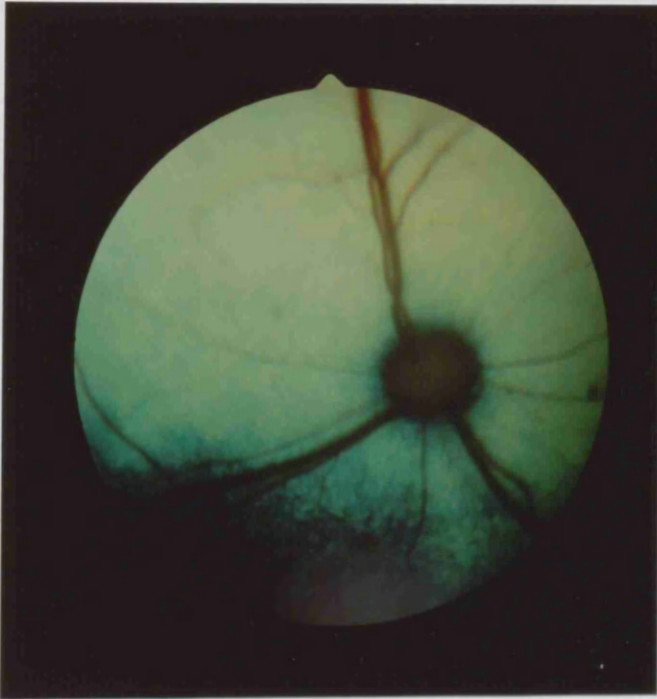


Figure 10a. Case 6. 112091. 12 y.o. M(c) DSH cat.
 Right eye (top) and left eye (bottom) fundus
 photographs. Papilloedema is apparent in the right eye
 (top) as the optic disc is out of focus.



Figure 10b. Angular venogram. The dorsoventral skull radiograph was taken immediately after bolus injection of contrast into both angular veins simultaneously. No cavernous sinus is demonstrable in the area arrowed.

CASE 7: 114696 "Nell"

Signalment: 3.5 year old female Border Collie.

Reason for presentation: Uncoordinated and circling.

Case summary

This case was a working sheep dog and ten days prior to presentation to GUVH she had had diarrhoea which had affected all the dogs on the farm. This had responded to symptomatic treatment but the bitch continued to be dull, lethargic and inappetant. One week prior to presentation, she had aborted pups of about 50 days gestation although it had not previously been known that she was pregnant. She was very depressed and failed to improve with symptomatic treatment and the referring veterinary surgeon performed an exploratory laparotomy with no significant findings although she was spayed at this time. On recovering from her anaesthetic, she was markedly ataxic and circled tightly to her right and she was then referred.

On presentation to GUVH, the dog was very dull, depressed and somnolent. Her gait was fairly normal although she tended to veer to her right side and circled to her right when stressed. A slight right sided head tilt was apparent. Right sided conscious proprioceptive deficits were identified. Vision was absent in her right eye and poor in her left eye, and

appeared to be best from the temporal retina. A positional ventromedial strabismus affecting the left eye was evident. Positional nystagmus, horizontal or vertical, could be elicited in her left eye with fast phase to the left in the horizontal type. The pupil of the right eye was widely dilated and unresponsive to light directed into either eye. The right globe was very central and no voluntary eye movements or oculovestibular movements could be elicited. These movements were very sluggish in the left eye also. A sluggish direct pupillary light reflex could be elicited from the left eye. Corneal ulceration was diffusely present affecting the right eye (Figure 11) and no evidence of corneal, upper lid or medial canthus sensation was present on the right side. No nictitating reflex could be elicited on the right side although the globe could be repulsed. She was bradycardic with sinus bradycardia of 80 bpm on electrocardiography. Papilloedema was evident in her right eye on fundoscopy.

Diffuse brain involvement was suggested by these signs with a predominantly right sided cavernous sinus lesion, and right trigeminal and vestibular involvement. Haematology and biochemistry results were unremarkable. A CSF tap was performed from the cerebellomedullary cistern and demonstrated raised nucleated cell content of 11 WBC/ mm³ and no RBC and a total protein content of

280 mg/l. A diffuse inflammatory lesion such as granulomatous meningoencephalitis was suspected and initial therapy commenced with prednisolone at 2 mg/kg with trimethoprim potentiated sulphonamides as antibiotic cover. This resulted in resolution of the head tilt, nystagmus and strabismus and the dog was much brighter. The right papilloedema continued to be evident and blindness in this eye was complete. After three days, the dog dramatically deteriorated again and became nonambulatory with a marked right sided head tilt. The CSF tap was repeated and on this occasion showed 433 WBC/mm³ and no RBC. The WBC were identified after cytopspin to be neutrophils (70%), lymphocytes (20%) and monocytes (10%). Protein content was 320mg/l. The dog was euthanased.

Post mortem grossly revealed the presence of a tumour extending from the cavernous sinus caudally along the base of the brain, predominantly on the right side. Histopathological determination of the neoplasm is pending.

Diagnosis

It was not felt clinically that neoplasia affecting the cavernous sinus would result in vestibular - like signs, but as post mortem indicated, the caudal extension of the tumour along the base of the brain can result in

this presentation.

Case 7. 114696 "Kerry"

Age: 3.5 year old female soft coated wheaten

Presenting complaint: Blindness.

History: Progressive decrease in visual

function over the last 6 months.

Physical examination: No abnormalities.

The dog was presented to GVS for an ophthalmologic

evaluation because of progressive decrease in visual



Figure 11. Case 7. 114696. 3.5 y.o. F. Border Collie. The dog is depressed and somnolent. The right pupil is widely dilated and unresponsive to light and no globe movements could be elicited in this eye. Diffuse corneal ulceration is apparent in the right eye with positive fluorescein staining (green).

CASE 8: 116877 "Kerry"

Signalment: 12 year old female soft coated wheaten terrier.

Reason for presentation: Blindness.

Case summary

This dog presented to GUVS for an ophthalmological consultation because of progressive decrease in visual acuity over the preceding eight weeks. She had been more thirsty than usual although not by definition polydipsic over the preceding three months. She was also reported to be more lethargic and listless than previously and had an abnormal hind limb gait.

No abnormalities were identified on clinical examination. The dog was totally blind. The gait was abnormal with slightly hypermetric forelimb gait and shuffling hind limb gait occasionally scuffing toes and circumducting her right hind leg. No conscious proprioceptive deficits or abnormalities were detected on testing, however. The abnormal gait was presumed initially to be secondary to her blindness. The right eye was widely dilated and unresponsive to light shone directly or consensually, although pupillary light responses appeared to be intact in her left eye. Narrowed palpebral fissure and ptosis of the upper lid was also evident in the right eye and voluntary and

oculovestibular globe movements were extremely sluggish in this eye, resulting in strabismus or dysconjugate gaze (Figure 12). Fundoscopy in both eyes demonstrated a severe generalised retinal atrophy. In the right eye, a rotation of the expected horizontal line between tapetal and nontapetal fundus was identified, the lateral edge apparently rotated ventrally. Facial sensation was intact and no other neurological deficits were identified. In summary, the initial lesions identified were retinal atrophy and presumably unrelated complete internal and external ophthalmoplegia of the right eye.

Haematology indicated a persistent lymphocytosis of $20 - 30 \times 10^9/l$ although no abnormal cells were identified. Biochemistry indicated an elevated SAP of 667 iu/l and ALT of 262 iu/l. No biochemical evidence of hepatic dysfunction was otherwise present and bile acids were within reference ranges. Thyroid function was unremarkable. A synacthen stimulation test with injection of 250mcg of synacthen intramuscularly was suspicious of hyperadrenocorticism despite the haemogram, with levels of 44 nmol/l resting cortisol increasing to 348 iu/l after 2 hours but a low dose dexamethasone suppression test ruled out this diagnosis. Urine was isosthenuric but otherwise unremarkable. The parasympathetic lesion affecting the right pupil was pharmacologically tested. Miosis was recognised

subsequent to instillation of 1.0% pilocarpine into both eyes, most marked in the right eye, after 40 minutes.

A bone marrow biopsy was performed to rule out a mature lymphocytic leukaemia, and no abnormal cells were identified. CSF analysis from the cerebellomedullary cistern was also unremarkable. As a cavernous sinus lesion may have been responsible for the III, IV and VI cranial nerve deficits, an angular venogram was performed which had some technical difficulties making any findings inconclusive, although it appeared that a filling defect was present on the right side.

The cause of the neuro-ophthalmological abnormality was not determined and no treatment was prescribed. Re-examination after one and two months actually indicated neurological improvement. Although the anisocoria was still evident, a sluggish direct and questionable indirect pupillary light response could be elicited in the right eye and globe movements improved although were still sluggish compared to the left side. The blindness remained complete but the dog was much brighter and livelier. Water consumption remained more than usual for this individual but never became by definition polydipsia.

Three months after initial presentation, the dog was

still bright and well and further neuro-ophthalmological improvement had resulted, with apparently normal voluntary and oculovestibular globe movements in both eyes and less sluggish pupillary light reflexes in the right eye. However, the hind limb ataxia was now marked and the conscious proprioceptive deficits had resulted in excoriation of the dorsum of both paws, particularly the right hind. Forelimb hypermetria was marked but no conscious proprioceptive deficits were evident in these limbs. Spinal reflexes were all unremarkable. The hypermetria may still have been a consequence of the blindness but distinct upper motor neuron lesion deficits were present in the hind limbs particularly the right. No further investigation was pursued; the owner declined myelography and repeat CSF taps but treatment commenced with prednisolone at 2 mg/kg with potentiated sulphonamide antibiotic cover.

Re-examination one month later demonstrated no neurological improvement. The dog remained bright and well although the owner felt the hind limb ataxia continued to slowly deteriorate. However, after this time the lymphocytosis was less marked - with a total WBC of $16.4 \times 10^9/l$; her absolute lymphocyte count was $7.05 \times 10^9/l$. The owners also felt that, despite the steroids, she was less thirsty than previously. The neuro-ophthalmological signs remained unchanged. No

forelimb neurological signs were present at all. No spinal hyperpathia was evident even on vigorous palpation. A separate T3 - L3 lesion was suspected but the owners declined further investigation, in view of the negative findings to date despite previous aggressive investigations and the fact the dog was so well in herself at this time.

Two months later, six months after initial presentation, the dog represented after behavioural signs of pseudocyesis with inappetance and a profuse mucopurulent vaginal discharge. Radiography confirmed the presence of uterine enlargement and ovariohysterectomy confirmed a pyometra. The dog made an uneventful recovery after anaesthesia although the hind limb ataxia appeared much worse.

Diagnosis

This dog at initial presentation had right sided total ophthalmoplegia affecting cranial nerves III, IV and VI and a cavernous sinus lesion was suspected. However, neurological improvement of this lesion was recognised. The retinal atrophy was assumed to be co-incidental to the neurological problems in this dog. A complete external and internal ophthalmoplegia was apparent in the right eye, initially resulting in a static globe and fixed widely dilated pupil. This pupil responded to

pilocarpine but took 40 minutes, by which time the normal pupil had also constricted. The greater degree of miosis in the abnormal pupil after this time suggested a pre-ganglionic or central parasympathoparalysis. This resolved over several months to a residual partial parasympathoparesis of the right pupil. The UMN deficits in the hind limbs are difficult to explain - a brain lesion causing this degree of deficit in the hind limbs should have resulted in some fore limb signs more significant than the high stepping gait. A provisional diagnosis of diffuse inflammatory disease affecting the brain and spinal cord was made. The significance, if any, of the marked persistent lymphocytosis was not determined.

This case is also included in the section of oculomotor nerve presentations (page 121).



Figure 12. Case 8. 116877. 12 y.o. F. soft coated Wheaten terrier. The right pupil is dilated and unresponsive to light. The right palpebral fissure is narrowed with ptosis of the upper lid. Very sluggish globe movements were elicited in the right eye.

CASE 9: 112460

Signalment: 4 year old Aberdeen Angus cow.

Reason for presentation: Blindness.

Case summary

This was one of a 120 cow beef suckler herd from a hill farm in a tick infested area with a bracken problem. She had calved normally five months prior to presentation and was in good condition but one week prior to presentation had suddenly gone blind. She was sold to GUVS for teaching purposes. No abnormal findings were present on clinical, haematological or biochemical investigations, other than complete blindness in both eyes. Both pupils were widely dilated and unresponsive to light. No other neurological deficits were present. Fundoscopy demonstrated a severe and widespread retinal atrophy consistent with a diagnosis of male fern poisoning (Figure 13a). The animal was kept for five months and during this time remained well with good appetite and no further changes in the fundus and no development of neurological signs. She was eventually euthanased and post mortem examination performed. A pituitary abscess was documented with surrounding pressure atrophy of the surrounding bone and compression of the chiasma (Figure 13b). No evidence of skull fractures was present.

Diagnosis

At post mortem examination, the chiasmal involvement from a pituitary abscess could be responsible for the widely dilated pupils with no pupillary light reflexes and total blindness. The retinal degeneration may have been secondary to this, although it was well developed at presentation after just one week of blindness and did not progress. Concurrent male fern poisoning was also possible.

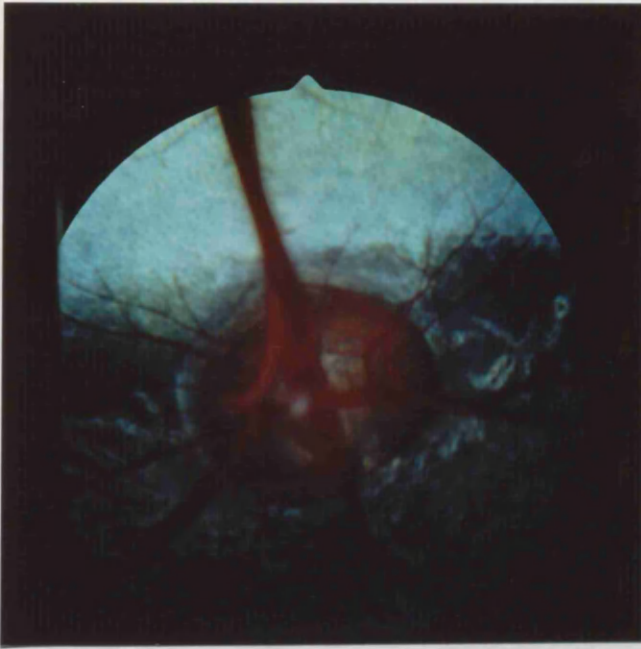
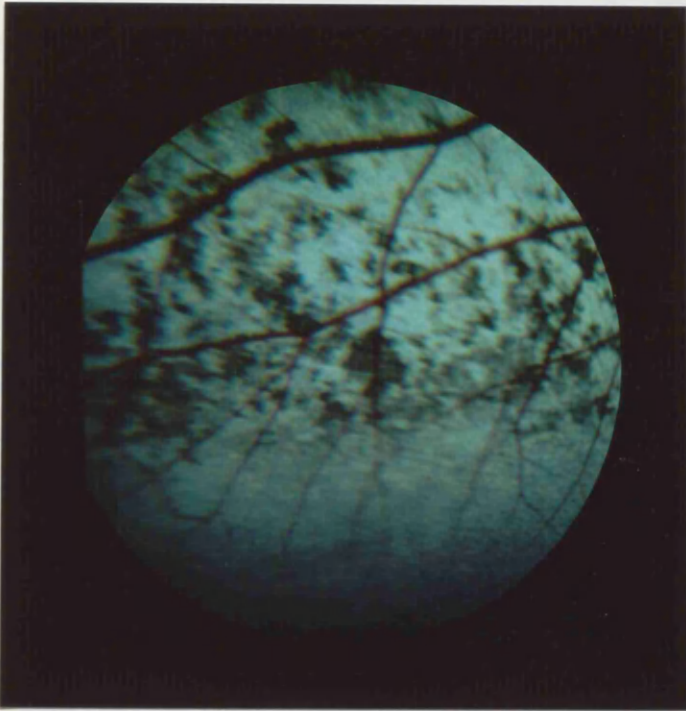


Figure 13a. Case 9. 112460. 4 y.o. Aberdeen Angus cow. Fundus photographs from left eye. A retinopathy is apparent consistent with a diagnosis of male fern poisoning. (See over also).

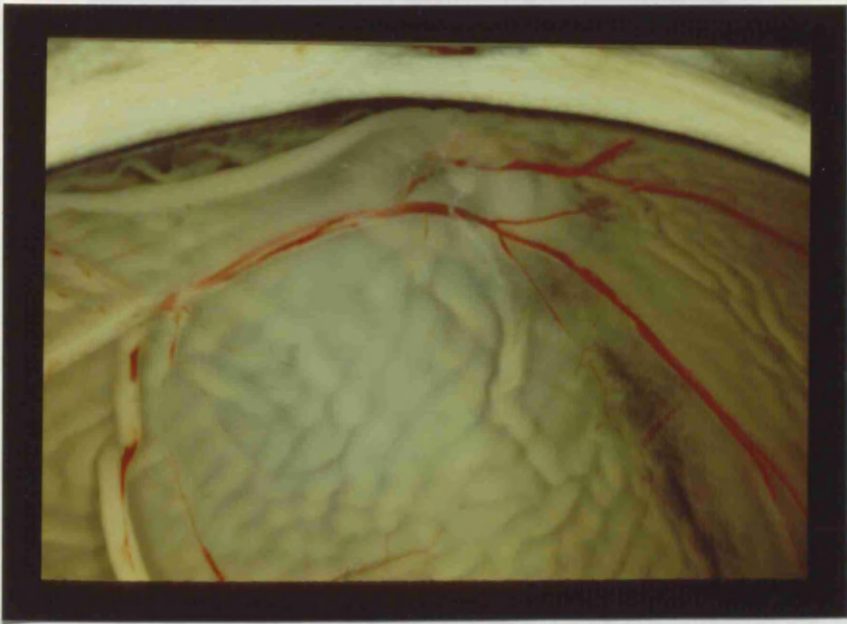
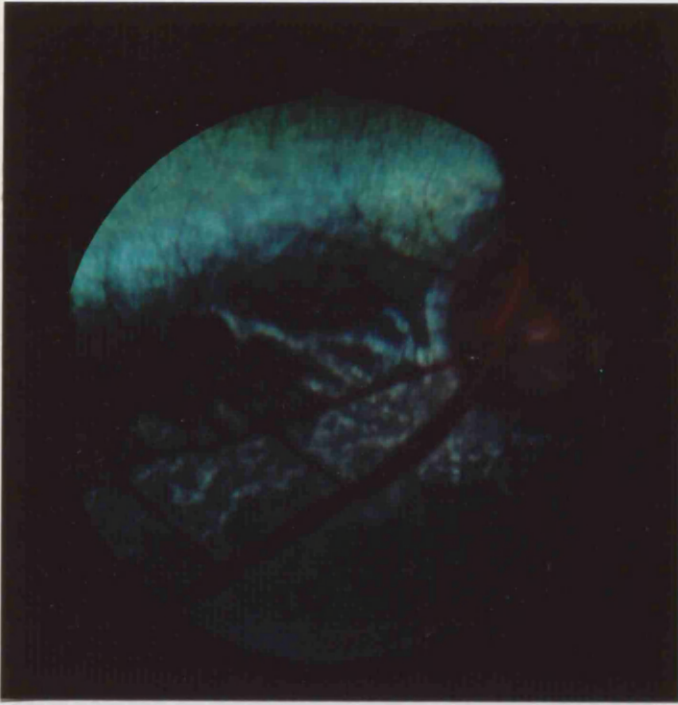


Figure 13a continued. Retinopathy consistent with a diagnosis of male fern poisoning. The bizarre linear lesions and the cobble-stoning appearance can also be appreciated from the post mortem specimen of the globe.



Figure 13b. At post mortem examination, the ventral view of the brain demonstrates the presence of the pituitary abscess and compression of the chiasma.



Figure 13b continued. Dorsal view of the floor of the calvarium showing remains of the pituitary abscess and pressure atrophy of the surrounding bone.

C.ii) DISCUSSION ABOUT CASES PRESENTING WITH CHIASMAL
OR CAVERNOUS SINUS INVOLVEMENT

Three cases presented here showed evidence of cavernous sinus involvement bilaterally (case 6) or unilaterally (cases 7 and 8). One had visual loss probably unassociated with the central nervous system lesion (case 8), one case may have had a separate retinopathy or retinopathy secondary to the chiasmal compressive lesion (case 9) and two cases had evidence of optic nerve or chiasmal involvement associated with the central nervous system lesion (case 6 and case 7). Case 6 did not receive a post mortem examination and case 8 is still alive. Only case 9 was confirmed at necropsy to have a pituitary lesion. This had neurological deficits restricted to the central visual pathway, although this localisation was not recognised in life, due to the gross retinopathy apparent on fundoscopy. Only case 6 had clinical evidence of pituitary dysfunction, manifested as panhypopituitarism. The most common tumours which may result in neurological or endocrinological abnormalities at this site are chromophobe macroadenomas associated with pituitary - dependent hyperadrenocorticism (Capen & others, 1967; El Etreby & others, 1980; Nelson & others, 1989) although no similar cases were documented in this series.

Visual disturbances due to neoplastic invasion or compression of the chiasma are well recognised in man with pituitary neoplasia, usually presenting initially as bitemporal haemianopia (Post & Muraszko, 1986). Pituitary neoplasia is not infrequently recognised in the dog but is not commonly associated with blindness (De Lahunta, 1973) because of regional anatomical differences between the species. If the visual pathway is affected by a pituitary tumour, such neoplasms must be proportionately larger than those in man (Kay, 1981). This is because the distance between the pituitary gland and the chiasma is proportionately greater in domestic animals than in man (Kay, 1981). The pituitary stalk of man is directed rostroventrally, whereas in domestic animals it has more caudoventral direction, away from the chiasma (Skerrit & others, 1986). In addition, the pituitary fossa, or sella turcica, which is a recess in the sphenoid bone, is more shallow in domestic animals than in man. The tuberculum sellae forms the cranial and caudal boundaries to the sella, and dorsally, the diaphragma sella or dorsal sella has a central oval foramen in the dog, not present in man, allowing dorsal expansion of any pituitary lesion into the hypothalamus and thalamus (Sarfaty & others, 1988; Dow & others, 1990). In man, ventrolateral growth of the neoplasm usually occurs (Capen & others, 1967). Neoplasms must extend outwith the pituitary fossa and into the

suprasellar area extending cranially to result in chiasmal lesions in the dog (Kay, 1981; Lewis & others, 1984). Pituitary lesions affecting the visual system have, however, been described in dogs (Griffiths & Lee, 1971; Heavner & Dice, 1977). Most pituitary tumours described in dogs invade dorsally affecting the hypothalamus and thalamus (Allison & others, 1983; Sarfaty & others, 1988). There is a strong correlation between tumour volume, compression or invasion of the surrounding nervous tissue and the development of neurological signs (Nelson & others, 1989).

Neoplasia not of pituitary origin may effect the chiasma. Meningiomas (Barnett & others, 1967; Miller, 1991), an oligodendroglioma (Skerrit & others, 1986) and craniopharyngiomas (Capen & others, 1967) have been described. Comparison of the regional anatomy in the bovine is not well discussed in the literature but the bovine case (case 9) presented here indicates that a pituitary mass lesion, in this case an abscess, can result in chiasmal compression in this species. The chiasma may be affected due to mass lesions compromising vascular supply to this structure rather than direct pressure effects (Heavner & Dice, 1977). Vascular compromise may also result in pituitary dysfunction (Post & Muraszko, 1986). Panhypopituitarism was recognised in the cat (case 6). It has usually been

described secondary to endocrinologically - active neoplasms (e.g. macroadenomas or macroadenocarcinomas responsible for hyperadrenocorticism) (Allison & others, 1983; Barr, 1985; Ferguson & Biery, 1988; Sarfaty & others, 1988) or space occupying lesions (Eigenmann & others, 1983). Failure of secretion of all pituitary hormones is known as Simmond's disease in man (Eigenmann & Lubberink, 1985). The first hormones to be affected are the gonadotrophins and adrenocorticotrophic hormone is usually last (Post & Muraszko, 1986). Antidiuretic hormone insufficiency is said to be rare and due to hypothalamic impairment (Eigenmann & Lubberink, 1985). However, diabetes insipidus has been described in association with mass lesions (Eigenmann & others, 1983; Barr, 1985; Ferguson & Biery, 1988; Sarfaty & others, 1988) and indeed, is stated to be common by Capen and others (1967). It was a major clinical feature in the cat (case 6) resulting in azotaemia.

The cavernous sinus surrounds the suprasellar area and the pituitary (Eigenmann & Lubberink, 1985). Cranial nerves III, IV, VI and the ophthalmic branch of V pass through here with the caudal segment of the internal carotid artery and the meningeal artery (Trautmann & Barnett, 1984). These blood vessels are free within the lumen with cranial nerve VI, although cranial nerves III, IV and the ophthalmic branch of the trigeminal

nerve are in intimate relationship with the cavernous sinus wall (Lewis & others, 1984; Eigenmann & Lubberink, 1985). The close association of the VI nerve and the internal carotid artery is important in man, where carotico-cavernous fistulae are described, usually of traumatic origin (Brosnahan, 1990). Internal carotid artery aneurysms in man may effect any of these cranial nerves as they traverse the cavernous sinus (Trautmann & Barnett, 1984). Sympathetic fibres enter the cavernous sinus initially associated with the internal carotid artery and are distributed to the orbit with the ophthalmic branch of the trigeminal nerve. Thus Horner's syndrome may be recognised with cavernous sinus masses (Lewis & others, 1984; Murphy & others, 1989) although this was not found in the cases reported in this series.

The classical cavernous sinus syndrome involves unilateral or bilateral ophthalmoplegia and trigeminal face pain or anaesthesia (Trautmann & Barnett, 1984). It has been described in cats and possible causes in this species are feline infectious peritonitis, systemic mycoses and lymphoma (Fenner, 1989). Cavernous sinus involvement may be seen with lateral extension of pituitary neoplasms (Trautmann & Barnett, 1984; Post & Muraszko, 1986). Sudden haemorrhage within such a lesion can result in sudden severe headache, visual loss and ophthalmoplegia; a syndrome known as pituitary

apoplexy in man (Trautman & Barnett, 1984). The apparent sudden onset of blindness and associated signs in the cat (case 6) was suggestive of a similar event. Other possible causes of cavernous sinus lesions are squamous cell carcinoma (Murphy & others, 1989), adenocarcinoma (Griffiths & Lee, 1971) and thyroid adenocarcinoma metastases (Lewis & others, 1984).

Cavernous sinus venography can indicate the space occupying lesion in the cavernous sinus (Griffiths & Lee, 1971; Skerit & others, 1986) as indicated in case 6, although the procedure was unsuccessful and therefore uninformative in case 8. Where available, computerised tomography and magnetic resonance imaging are diagnostic (Collins & O'Brien, 1990). An alternative radiographic technique has been suggested by cisternal access to the subarachnoid space and allowing contrast to run forward (Barr, 1985).

The cerebrospinal fluid analysis was useful in the two out of the three cases (6 and 7) where this was done. This is supported by some of the cases reported in the literature (Heavner & Dice, 1977; Sarfaty & others, 1988; Nelson & others, 1989). Cerebrospinal fluid was unremarkable in case 8, however.

Surgical treatment was not contemplated in these cases

although hypophysectomy has been described (Eigenmann & Lubberink, 1985). The cavernous sinuses are not surgically accessible (Fenner, 1989) although surgical exploration in man is advocated to enable pathological determination of the diagnosis (Post & Muraszko, 1986). Palliative radiotherapy has been described (Dow & others, 1990). In the cat with panhypopituitarism (case 6), supportive medical therapy was designed to restore hormonal function.

In case 7, the neurological signs were clinically felt to be too diffuse to suggest neoplasia and yet post mortem diagnosis indicate a mass extending along the base of the brain affecting the right optic nerve, cavernous sinus (mainly right sided) with right cranial nerves III, VI and the ophthalmic branch of V, the thalamus, and the vestibular nuclei of the medulla oblongata. Although it was unfortunate that case 6 did not receive a post mortem examination (especially as no previous reports of panhypopituitarism in cats were discovered in the literature), it is possible that a similar lesion was present in this case. It is odd that cranial nerve VII and other branches of the trigeminal nerve were affected when these structures are not closely associated with the cavernous sinus. The maxillary branch of the trigeminal nerve has been reported as being affected occasionally in man with

cavernous sinus syndrome, although the maxillary and mandibular branches are more caudolateral to the cavernous sinus, anatomically (Lewis & others 1984). However, similar involvement was described in cases reported by Griffiths & Lee (1971), due to an adenocarcinoma affecting the mandibular branch of the trigeminal nerve, and Sarfaty and others (1988) with facial paresis and hypoalgesia in one dog with a pituitary tumour.

Although the pituitary abscess in the bovine (case 9) was clinically unaggressive and was only pathologically found to be causing chiasmal compression without affecting the cavernous sinus, the signs in the other three cases suggested a more aggressive and invasive process with cavernous sinus involvement. This was certainly appreciated with the tumour in case 7 at post mortem and was inferred from case 6 by the neurological progression. Case 8 appeared to have diffuse, fluctuating neurological disease, latterly apparently affecting the spinal cord as well as the cavernous sinus area. The diversity and variable nature of the signs in this case is not suggestive of a mass lesion or neoplasia but may reflect inflammatory disease. The lymphocytosis is difficult to explain and the significance of this finding to the neurological signs is obscure.

B.iii) CASES PRESENTING WITH OCULOMOTOR NERVE LESIONS

As a component of central nervous system disease:

CASE 10: 113766 "Topsy"

Signalment: 12 month old female spayed domestic shorthair cat.

Reason for presentation: Progressive weakness and ataxia.

Case summary

Over the preceding six weeks this cat had progressively deteriorated with signs of weakness and incoordination although these signs were sometimes transient. She was almost totally anorectic and very thin. Examination revealed a subnormal rectal temperature and a mild palpable lymphadenopathy. She was tachypnoeic and hyperpnoeic and widespread adventitious respiratory sounds were detected on auscultation. Neurological examination initially failed to demonstrate any specific neurological deficits other than a general weakness which was initially explained by the general debility of the animal. She was hospitalised for further investigation. During this time, the cat sometimes became confused and disorientated. She was intermittently severely ataxic, falling to either side. Conscious proprioceptive deficits were present, most

marked in the right fore limb. A marked anisocoria developed, which remained constant with a widely dilated right pupil (Figure 14). Vision appeared to be intact, but no direct or consensual pupillary light response could be elicited in the right eye. Oculovestibular and voluntary eye movements were normal and conjugate. No other cranial nerve deficits or signs of dysautonomia were apparent. Fundoscopy was remarkable with a severe inflammatory retinopathy with cobblestone - like areas of tapetal hyperreflectivity and some retinal vessel atrophy. Instillation of pilocarpine 1% drops into both eyes led to miosis of the right pupil and resolution of the anisocoria within 30 minutes.

Thoracic radiographic findings were consistent with a widespread pneumonia with a diffuse infiltrate affecting all lung lobes. Haematology demonstrated a raised WBC of $18.0 \times 10^9/l$, mainly affecting the neutrophils but no other abnormalities. Biochemical screens were unremarkable. The cat was negative for FeLV, FIV and *Toxoplasma gondii*. However, a very high titre to feline corona virus was identified (1280) and the "dry" or granulomatous form of Feline Infectious Peritonitis (FIP) was diagnosed. In view of the hopeless prognosis and the rapidly deteriorating course, the cat was euthanased. Post mortem permission was not granted.

Diagnosis

FIP resulting in encephalitis was believed to be responsible for the confusion and ataxia. The retinopathy was also probably due to FIP. Involvement of the parasympathetic innervation of the right eye was identified. The pharmacological testing with pilocarpine suggested that there was a central, possibly parasympathetic oculomotor nuclear, lesion.



Figure 14. Case 10. 113766. 12 month old F(s) DSH cat. The cat was very dull and depressed and had been fed liquidised food. The right pupil was widely dilated and unresponsive to light.

CASE 11: 105576 "Christie"

Signalment: 6 year old female Shetland sheepdog.

Reason for presentation: Seizures.

Case summary

This dog had progressive loss of vision over the preceding several years and had been seen two years previously at GUVS by an ophthalmologist who diagnosed central progressive retinal atrophy (CPRA). She had adapted to being almost totally blind. Six weeks, four weeks and one week prior to presentation at GUVS, she had had severe tonic-clonic generalised seizures, occurring when the dog was apparently bright and alert and often when on a walk. She had also recently had an oestrous cycle.

Examination showed the dog to be in good condition with a mitral systolic murmur consistent with a diagnosis of endocardiosis but no signs of heart failure. The dog was completely blind and fundoscopy demonstrated a number of yellow pigmented areas scattered throughout the retinae as islands. These findings were suggestive of either CPRA or a post - inflammatory retinopathy.

A number of abnormalities were evident on neurological examination, although localised to the cranial nerves. Vision and pupillary light responses were absent in both

eyes, and both pupils were widely dilated. These findings were presumed to be due to the retinopathy. However, a narrowed palpebral fissure and a ptosis of the upper lid was evident in the right eye (Figure 15). The right globe was central and stationary within the orbit and no voluntary or oculovestibular eye movements could be elicited in this eye despite being present in the left eye. A positional strabismus could consequently be elicited and the gaze was frequently disconjugate. Facial and corneal sensation appeared to be intact but no nictitating reflex could be elicited from the right eye. No rotation of the globe was apparent on fundoscopy.

Severe atrophy of the masticatory muscles was present on the right side. Electromyography demonstrated spontaneous electrical activity from these muscles and also from the muscles on the left hand side, despite no obvious atrophy. No other evidence of denervation was demonstrated in the limbs.

A 1% pilocarpine solution was instilled into both eyes. Both pupils constricted within 20 minutes, although an anisocoria resulted, with more miosis occurring on the right side.

Cerebrospinal fluid (CSF) analysis obtained by a

cerebellomedullary cistern tap was unremarkable in cell and protein content. Insufficient sample was present to check canine distemper virus or toxoplasma titres. Haematological, biochemical and endocrine parameters were all within normal limits. The serum titre to canine distemper virus was consistent with vaccination status. A high titre to *Toxoplasma gondii* of 250 units by the Sabin Feldman dye test was identified and Toxoplasmosis was therefore thought to be responsible for the diffuse neurological disease in this dog.

This dog was treated with pyrimethamine (Daraprim^R) and trimethoprim potentiated sulphonamide. Phenobarbitone was used to control the seizures. No neurological improvement was identified and the seizures became more frequent, clustered and more severe. Three weeks later, the animal represented very depressed, circling to the right with left sided conscious proprioceptive deficits in the limbs. Prior to this, the owners had reported a left - sided head tilt although this was not evident at this presentation. However, a constant horizontal nystagmus with fast phase to the right side was present affecting the left eye although the right eye remained central and stationary. The signs appeared to partially resolve with diazepam and she returned home. Another serum sample submitted for toxoplasma titre was this time negative. Several days later, the dog went into

status epilepticus and the owners opted for euthanasia carried out by the referring veterinary surgeon at the home and the body was not available for post mortem examination. This happened before the receipt of the toxoplasma result and before steroid therapy could be contemplated.

Diagnosis

Toxoplasma gondii was initially believed to be responsible for the diffuse neurological disease in this animal. Cerebral involvement was inferred from the seizures. The circling to the right with left sided conscious proprioceptive deficits were felt to reflect a right cerebral lesion also. The history of left sided head tilt, the nystagmus and possibly the left sided conscious proprioceptive deficits indicated left vestibular involvement. Asymmetrical although bilateral trigeminal (mandibular) involvement and a right sided complete oculomotor palsy and abducens palsy was also evident. Although the parasympathetic oculomotor nerve lesion is difficult to prove in an animal with visual deficits, the apparent hypersensitivity to pilocarpine appeared to support the suspicion of this lesion. The later negative titre to *Toxoplasma* was confusing, and the laboratory reported the initial result to be given in error. It may be that this dog had some other diffuse inflammatory disease such as granulomatous

meningoencephalitis (GME). It was unfortunate that steroid therapy had been avoided in the belief that the animal had toxoplasmosis.



Figure 15. Case 11. 195576. 6 y.o. F. Shetland sheepdog. The dog was totally blind because of a retinopathy assumed to be unrelated to the neurological signs. The right eye had a narrowed palpebral fissure and ptosis of the upper lid. The right globe was static within the orbit. Right masticatory muscle atrophy was marked.

CASE 12: 113090 "Jill"

Signalment: 11 year old female spayed Collie cross.

Reason for presentation: Acute ocular pain.

Case summary

This dog presented to GUVS as an ophthalmological emergency after 24 hours of apparent left ocular pain, bumping into objects, pyrexia, depression and inappetance. The owner reported that she had been knuckling on her left fore leg also. On examination, no visual deficits were apparent. She was depressed with a rectal temperature of 104⁰F. Her left pupil was fixed and dilated and unresponsive to light into either eye. No other neurological deficits were identified but the dog resented opening its jaw, and a retrobulbar abscess was suspected. Examination under anaesthesia was, however, unremarkable and treatment with antibiotics commenced. Haematology indicated a slightly raised WBC of $13.2 \times 10^9/l$ but no other abnormality. Biochemistry was unremarkable.

The dog continued improving and the owners were pleased with progress when she was re-examined after two weeks. On this occasion, the left pupil was still fixed and dilated although no visual deficit was apparent in either eye. Direct and consensual pupillary light responses were absent in the left eye and present in the

right eye. Ocular movements were sluggish in the left eye and a lateral strabismus was evident. A ptosis was present of the left upper lid. No other neurological deficits were present although the owner felt her visual acuity had recently deteriorated. Fundoscopy was unremarkable. A partial left sided oculomotor nerve palsy was diagnosed. Haematology, biochemistry and endocrine screen was unremarkable. A CSF tap was obtained from the cerebellomedullary cistern which showed 22 nucleated cells/mm³ and several RBCs, most of which were normal lymphocytes with occasional neutrophils on cytopspin. The protein content was 240mg/l. No significant titre to canine distemper virus or to toxoplasma was evident in the CSF. The dog was monitored monthly without any treatment.

For a further three months, no further neurological improvement or obvious deterioration was evident, although the owners continued to report reduced visual acuity, not evident on testing. She continued to occasionally knuckle on her left fore but conscious proprioceptive deficits or other neurological abnormality could not be demonstrated on testing.

After this time, however, she represented as she was dull and depressed and the owners felt she was vague and confused at home. This was confirmed on examination. She

held her left fore paw in abnormal positions, and conscious proprioceptive deficits were evident. Paresis was not a feature. She had a slight right - sided head tilt. The left oculomotor palsy was still present. Vision appeared to be normal in her left eye but she was completely blind in her right eye and papilloedema was evident on ophthalmoscopy. Oculovestibular movements were normal in the right eye but the left eye had become very central and no globe movement could be elicited. Facial and corneal sensation was intact bilaterally, and both globes were retracted with the nictitating reflex. In summary, it appeared that this animal had diffuse disease affecting the central nervous system with right optic neuritis, complete oculomotor nerve palsy of the left eye, right sided cerebral involvement with head tilt, contralateral conscious proprioceptive deficits and behavioural disturbances.

Haematology, biochemistry and endocrine parameters were re-checked. A mild leukopaenia with WBC of $4.1 \times 10^9/l$ and nonregenerative anaemia with RBC of $4.91 \times 10^{12}/l$ and profound lymphopaenia of $0.31 \times 10^9/l$ was identified. A titre to canine distemper virus was consistent with vaccination status and no serum titre to toxoplasma was present. CSF analysis was repeated but was unremarkable with 0 WBC, 0 RBC and a protein content of 80mg/l. Despite this, a diffuse inflammatory

encephalitis was suspected and treatment commenced with 2 mg/kg prednisolone with potentiated sulphonamide as antibiotic cover.

Re-examination after 2 weeks indicated a good response on the high dose of steroids but deterioration as the dose was reduced. She was ataxic on all four limbs, most marked on the left, although was not demonstrably paretic. A right - sided head tilt was still apparent. The neuro-ophthalmological signs were as previously although papilloedema was no longer evident in the right eye. High doses but alternate day steroid therapy continued. The owners failed to turn up for a re-examination appointment and when contacted by telephone were in some distress as the dog had been found dead one morning shortly after this last consultation, some five months after initial presentation. She had been buried in the garden, so post mortem follow up was not possible.

Diagnosis

Diffuse central nervous system involvement was present in this dog of undetermined aetiology affecting the left oculomotor nerve and the right optic nerve as well as probable involvement of the right cerebrum.

CASE 8: 116877 "Kerry"

Signalment: 12 year old female soft coated wheaten terrier.

Reason for presentation: Blindness.

Case summary

See pages 93 - 98, where this case is included with cases showing presumed cavernous sinus involvement. A right complete oculomotor nerve palsy, initially associated with a trochlear and abducens nerve palsy was present. Neuro-ophthalmological status improved, leaving a residual partial parasympathetic and somatic oculomotor paresis, and presumed spinal cord involvement developed.

Pilocarpine 1% administration into both eyes resulted in bilateral miosis, more profound on the right, after 40 minutes. This suggested a central parasympathoparalysis.

CASE 13: 117388

Signalment: 4 month old female Texel x Charolais lamb.

Reason for presentation: Circling.

Case summary

The farmer found this lamb to have an abnormal head carriage and a tendency to circle. His veterinary surgeon diagnosed a space occupying lesion and it was referred to GUVS. The lamb was in good condition, eating and drinking normally. She was bright, alert and responsive but tended to circle tightly to the right particularly when frightened. She held her head turned to the right and also had a slight right - sided head tilt (Figure 16a). Apart from the tendency to circle, the gait was not particularly abnormal, although mild conscious proprioceptive deficits were identified in the right limbs. The left eye was abnormal (Figure 16b). It appeared to be exophthalmic although could be easily repulsed into the orbit. The pupil was widely dilated and unresponsive to light illuminating either eye. Vision in both eyes appeared to be normal. The globe was very central and no voluntary or elicited globe movements could be elicited in any direction. The animal was able to blink with this eye but the nictitating reflex was absent although facial and corneal sensation was intact. No evidence of globe rotation within the orbit was identified. The right eye was normal. The lamb

had a bizarre appearance, with the head turn and tilt to the right, she tended to position herself to fixate a person within the visual field of the left abnormal eye.

Haematology, biochemistry, fundoscopy and CSF analysis was all unremarkable. Pilocarpine 0.1% drops instilled into both eyes and miosis had resulted within 20 minutes demonstrating a supersensitivity to the drug (Figure 16c).

No improvement or deterioration were seen over several weeks observation. No treatment was given. The lamb remained very well in herself. She was sacrificed and a full post mortem examination performed. No gross abnormalities were detectable. Histopathology results are pending.

Diagnosis

The right - sided circling, head turn and head tilt and mild conscious proprioceptive deficits and the apparent left - sided exophthalmos and deficits in cranial nerves III and VI and the apparent post-ganglionic parasympathetic oculomotor nerve lesion were all difficult to interpret with a single space occupying lesion and none was identified on gross post mortem.



Figure 16a. Case 13. 117388. 4 month old F. Texel / Charolais X lamb.

The lamb was bright, alert and responsive. She tended to circle to the right and her head was turned to the right and a slight right head tilt was apparent. The left eye was exophthalmic with a static globe and a widely dilated pupil unresponsive to light with intact visual perception.



Figure 16b. The left eye is shown with the widely dilated pupil (top). 20 minutes after instillation of 2 drops of 0.1% pilocarpine solution, the pupil constricted well (bottom), demonstrating supersensitivity to this agent.

Associated with systemic disease:

CASE 14: 117056 "Lella"

Signalment: 11 year old female Jack Russell terrier.

Reason for presentation: Diabetes mellitus.

Case summary

This dog had been polyuric and polydipsic over three months preceding presentation to GUVS. Latterly, she had lost weight and was lethargic. Examination showed her to be still obese with palpable hepatomegaly. She had early partial cortical cataracts with no visual impairment. The left eye was widely dilated and unresponsive to light directed into either eye but direct and consensual pupillary light reflexes were present in the right eye. No deficits in oculovestibular movements or any other abnormality on full neurological examination were detected. Fundoscopy was unremarkable other than the cataracts. Haematology indicated a mild nonregenerative anaemia. Hyperglycaemia, hyper-cholesterolaemia and elevated liver enzymes were evident on the biochemistry screen and glycosuria was also present. These findings were consistent with a diagnosis of diabetes mellitus. The parasympathetic lesion affecting the pupil of the left eye was pharmacologically tested. Pilocarpine at 0.1% concentration did not have a detectable effect. However, 1.0% resulted in pupillary constriction in both eyes after 45 minutes although the left eye constricted

slightly more than the normal eye.

The dog was stabilised with insulin during hospitalisation and spayed, which led to a reduction in her insulin requirement. Once discharged, the owners coped well with her daily injections and management and she remains four months after initial stabilisation. However, the left pupil remains unchanged and is still widely dilated.

Diagnosis

Diabetes mellitus with a parasympathetic oculomotor lesion in the left eye of this dog. Whether the pupil lesion is associated with the endocrinopathy is unknown. The result of the pilocarpine testing suggested a central parasympathetic lesion.

CASE 15: 111692 "Rimsky"

Signalment: 7 year old male Cavalier King Charles spaniel.

Reason for presentation: Lymphoma and heart failure.

Case summary

This dog had been under treatment at GUVS over the preceding 20 months for multicentric lymphoma. He had received epirubicin initially but latterly had been in remission on prednisolone. Two months prior to this presentation, he had shown signs of left heart failure although had not been investigated further and this had been managed with frusemide.

The owners were concerned about the dog because of increasing breathlessness and respiratory distress. On examination, he showed signs of severe myocardial failure and pulmonary oedema. Echocardiography demonstrated greatly reduced left ventricular contractility and mild mitral regurgitation consistent with dilated cardiomyopathy and minimal valvular endocardiosis changes. This was believed to be a consequence of the epirubicin therapy which is known to be cardiotoxic. The dog also had biochemical evidence of renal dysfunction, assumed to be prerenal and therapy was started with digoxin and hydralazine with continued diuresis.

The dog was observed to have a widely dilated left pupil which was totally unresponsive to light although direct and indirect pupillary light reflexes were intact in the right eye. Visual acuity appeared to be normal. There was also a ptosis of the upper lid and markedly reduced globe movements, although the dog could abduct his gaze with this eye. The right eye showed normal oculovestibular movements although was unable to blink. Saliva was drooling from this side of his mouth and a complete right sided facial palsy was evident (Figure 17). This appeared to be from proximal to the lacrimal branch as tear production was reduced in the right eye (Schirmer tear test strips read 7 mm / minute in the right eye and 12 mm / minute flow in the left eye). Bilateral masticatory muscle atrophy was also evident although this was presumed to be associated with the cachetic state rather than to a trigeminal nerve lesion, although neurogenic atrophy was not ruled out by electromyography.

The parasympathetic component of the left oculomotor lesion was pharmacologically tested. Pilocarpine at 0.1% had no detectable effect on either pupil but at 1.0% it resulted in pupillary constriction after 20 minutes.

The dog did not improve and the owners opted for euthanasia but post mortem permission was not granted.

Diagnosis

As well as lymphoma in remission, a presumed drug-induced dilated cardiomyopathy and prerenal azotaemia, this dog had a facial (VII) nerve palsy on the right side and an oculomotor (III) nerve palsy on the left. A single space occupying lesion could not explain these findings. Epirubicin is not known to be associated with peripheral neuropathies, unlike the vinca alkaloids (McLeod & Walsh, 1984). The relationship between the lymphoma and therapy and the neuropathies is uncertain. As a post mortem was not carried out in this dog, the aetiology of the III and contralateral VII peripheral neuropathy is mere conjecture, but may be related to the primary disease or the chemotherapy.

FIELD other clinical nerve involvement:

CASE 15: 111692, 7 y.o. M.

Signalment: 7 year old female spayed Cocker spaniel.

Reason for presentation: Chronic ocular irritation.



Figure 17. Case 15. 111692. 7 y.o. M. Cavalier King Charles Spaniel.

The left eye shows a widely dilated pupil, unresponsive to light, and ptosis of the upper lid and narrowed palpebral fissure. Globe movements were reduced. A right sided facial palsy was apparent on neurological testing.

With other cranial nerve involvement:

CASE 16: 115475 "Corrie"

Signalment: 9 year old female spayed Cocker spaniel.

Reason for presentation: Chronic ocular irritation.

Case summary

This dog had a chronic pruritic skin problem, chronic otitis externa and chronic conjunctivitis, epiphora and periorbital irritation all of which had been treated symptomatically by the veterinary surgeon. Latterly, the ocular irritation had increased and the dog was referred for an ophthalmological consultation. On examination, the dog had widely opened eyes with an inability to blink and widely dilated pupils completely unresponsive to light although vision was normal. Periocular hair loss and staining due to chronic epiphora, mucopurulent ocular discharge and generalised skin and ear involvement were evident. Entropion of the upper lids and trichiasis appeared to be responsible for much of the ocular pathology and a healed corneal ulcer was present, affecting the left eye. The fundus was unremarkable. Globe movements were unremarkable. Complete facial palsy was evident with normal facial sensation (Figure 18). Tear production was normal, indeed excessive, in both eyes. No other abnormalities on clinical or full neurological examination were evident. Haematological, biochemical and

endocrinological screening were unremarkable. Pilocarpine 1.0% concentration resulted in symmetrical miosis after 30 minutes.

The dog received eyelid surgery and was re-examined one month later. Great improvement in the ocular irritation was evident although the neurological deficits remained unchanged. The dog was not adversely affected by them.

Diagnosis

Bilateral facial (VII) nerve and bilateral parasympathetic oculomotor (III) palsies. No single anatomical site could explain involvement of these lesions, and a cranial polyneuropathy was diagnosed.

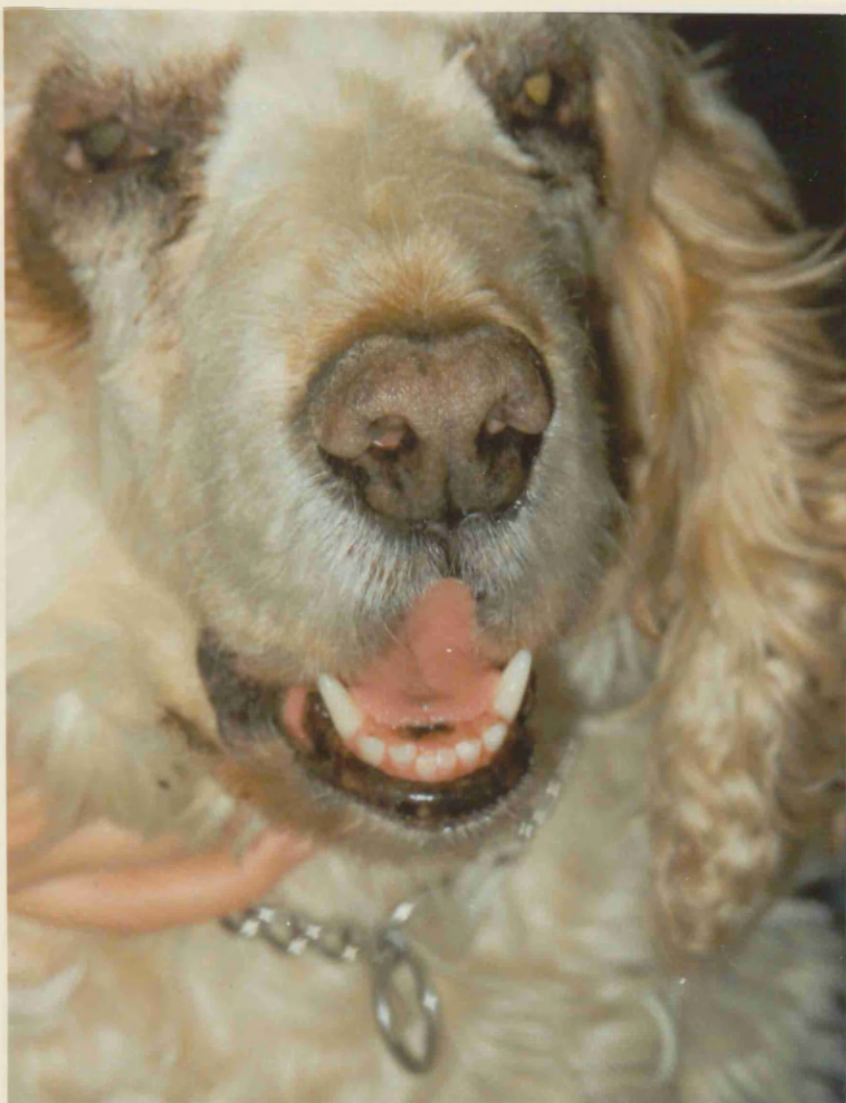


Figure 18. Case 16. 115475. 9 y.o. F(s) Cocker Spaniel. Periorbital irritation and epiphora are evident. Both pupils were widely dilated and unresponsive to light although vision was normal. Bilateral facial palsy was also present with an inability to blink and drooping upper lips.

Isolated oculomotor nerve lesions:

CASE 17: 117057 "McGinty"

Signalment: 12 year old male Labrador x Jack Russell terrier.

Reason for presentation: "Cloudy" eyes.

Case summary

One month preceding presentation, the owners observed that this dog's eyes appeared to be cloudy. The referring veterinary surgeon identified bilateral mydriasis and an ophthalmological consultation was requested. On examination, both pupils were widely dilated and unresponsive to light shone into either eye. Vision was normal. Globe movements were unremarkable. Nuclear sclerosis was marked in both lenses and this, in association with the mydriasis, was responsible for the cloudiness observed by the owner (Figure 19). The left lens was subluxated medially and a vitreal pigmented cyst was identified on fundoscopy. No retinal lesions were apparent otherwise, nor was there raised intraocular pressure. No other abnormality was identified on full neurological examination.

Haematological, biochemical and endocrinological parameters were all within normal reference ranges. Pharmacological testing of the parasympathetic lesion was done but no detectable response was seen with 0.1%

or 1.0% concentrations even after 60 minutes.

The dog had a lendeotomy of the abnormal left subluxated lens. The surgery was difficult and a disappointing cosmetic result was present when re-examined one month later with iridal adhesions to the limbus incision site, distorting the pupillary margin. Both pupils were still widely dilated and no response to light was detectable.

Diagnosis

Bilateral parasympathetic lesion of the oculomotor nerves. The pilocarpine testing suggested that both parasympathetic lesions were central or pre-ganglionic.



Figure 19. Case 17. 117057. 12 y.o. M. Jack Russell terrier cross Labrador. Both pupils were widely dilated and unresponsive to light although vision was normal. Nuclear sclerosis can be seen especially in the right eye. The subluxation of the lens in the left eye can also be recognised in this photograph which has caught the tapetal reflection.

CASE 18: 116387 "Mitzie"

Signalment: 8 year old female miniature Poodle.

Reason for presentation: Seizure.

Case summary

Four days prior to presentation at GUVS, this dog had a full tonic-clonic generalised seizure while sleeping. Veterinary attention was immediately sought but the dog had recovered by the time she was examined. However, both pupils were observed to be widely dilated and unresponsive to light and the dog was referred to GUVS.

On examination, the dog was thin but very bright and alert. No other seizure episodes had been noted. Clinical examination revealed a systolic heart murmur consistent with valvular endocardiosis but no signs of heart failure and severe dental calculus and periodontal disease. Both pupils were widely dilated, the left more than the right. Scleral haemorrhages were present in both eyes but no other signs of haemorrhage was found on the body. The dog's vision was normal. The left pupil failed to respond to light but a weak and sluggish direct and controversial indirect pupillary light reflex could be elicited in the right eye. No other neurological defects were identified.

Pharmacological testing of the pupillary lesions with

1.0% pilocarpine failed to elicit any detectable response by either pupil even after 60 minutes. Haematology, biochemistry coagulation and endocrine screening were all unremarkable. Re-examination after one month indicated that the scleral haemorrhages had resolved and no other seizure episodes or coagulopathy episodes had been reported. The dog remained very well although the parasympathoparesis remained unchanged in both pupils.

Diagnosis

Bilateral parasympathoparesis of both pupils, the left completely and the right partially affected. Asymmetrical involvement of the parasympathetic oculomotor nucleus (Edinger-Westphal nucleus) may be involved. Mesencephalic lesions are not associated with seizures. The lack of response to pilocarpine was peculiar.

CASE 19: 116780 "Tiga"

Signalment: 7 year old female Staffordshire bull terrier.

Reason for presentation: Painful eye.

Case summary

One week prior to presentation, this dog had collided with a tree and the right eye had been painful and of abnormal appearance since then. The dog was very active and excitable. The right eye appeared red and inflamed and a ptosis of the upper lid was apparent, causing narrowing of the palpebral fissure (Figure 20). The pupil was widely dilated and very slow and incomplete direct and indirect pupillary light reflexes although these were brisk in the left eye and vision was intact in both eyes. A dorsolateral strabismus of the right globe was evident and ocular movements were sluggish except laterally. No abnormal findings were identified on fundoscopy and a complete neurological examination was unremarkable. Haematology indicated a raised WBC of $17.4 \times 10^9/l$ and biochemical analysis showed an elevated AST of 588 iu/l with normal hepatic function and other muscle enzymes were not assayed. Endocrine parameters were all within normal limits.

The dog was treated with oral antibiotics and a topical antibiotic/cortisone ophthalmic preparation. This

quickly resulted in less ocular discomfort and re-examination one month after the injury indicated some improvement in extraocular muscle function and pupillary light response although not complete resolution of the lesion.

Diagnosis

A partial parasympathetic and somatic motor efferent oculomotor nerve lesion was apparent in this eye presumed to be secondary to trauma.

COLLECTION OF CASES OF STRABISMUS

Eleven cases were seen where a dilated pupil consistent with a diagnosis of a parasympathetic resulting from oculomotor nerve involvement was one of the presenting signs. Eight of these were unilateral. Four affected the right eye and four the left.



Figure 20. Case 19. 116780 7 y.o. F. Staffordshire Bull Terrier.

The right eye was red with scleral haemorrhages. The pupil was dilated with sluggish response to light. A dorsolateral strabismus of the right globe and reduced globe movements were apparent, except laterally.

C.iii) DISCUSSION ABOUT CASES PRESENTING WITH OCULOMOTOR NERVE INVOLVEMENT

Eleven cases were seen where a dilated pupil consistent with a diagnosis of a parasympathoparesis resulting from oculomotor nerve involvement was one of the presenting signs. Eight of these cases were unilateral; four affecting the right pupil (cases 10, 11, 8 & 19), four the left pupil (cases 12, 13, 14, and 15) and three cases were bilateral (cases 16, 17 & 18). Five of these (cases 10, 11, 12, 8 & 13) had concurrent signs of central nervous system involvement distant to the oculomotor system. Two cases had concurrent systemic disease (case 14 with diabetes mellitus and case 15 with lymphoma). Two cases had facial (VII) nerve involvement also (case 15, with facial palsy contralateral to the oculomotor nerve parasympathoparesis and general somatic efferent involvement and case 16 with bilateral facial palsy and bilateral isolated parasympathoparesis). Two cases also had a retinopathy (cases 11 and 8) which preceded the development of diffuse central nervous system involvement which was assumed to be unrelated to the neurological disease. Case 19 had a partial unilateral complete oculomotor nerve paresis which may have occurred subsequent to trauma. The seizure episode preceding presentation of case 18 may also have resulted in traumatic aetiology of the asymmetrical but bilateral parasympathoparesis, as the scleral haemorrhages

suggested. Case 17 had no known traumatic incident but had bilateral parasympathoparesis and a subluxated lens in one eye.

Anisocoria is described in the cat associated with feline leukaemia virus infection. This may be due to a dilated pupil (Shell, 1990), although is usually due to a moderately constricted pupil which fails to dilate under dark conditions (Neer & Carter, 1987). Feline immunodeficiency virus is also reported to result in dilated pupils and other neurological signs in some cases (Hopper & others, 1989). This cat (case 10) had a dilated pupil unresponsive to light and pharmacologically was consistent with a parasympathoparesis. Feline dysautonomia, not related to known infectious agents, also frequently presents with parasympathoparesis of the pupils, usually bilaterally, as well as other signs of autonomic dysfunction (Sharp & others, 1984). This cat did not have any other sign of dysautonomia. Canine dysautonomia has also been reported (Pollin & Sullivan, 1986; Schrauwen and others, 1991) but none of the canine cases reported here had other signs of autonomic dysfunction. Feline Corona Virus is known to cause a nonsuppurative meningitis and ependymitis which may effect the mesencephalic aqueduct (Fenner, 1989) which is how the parasympathetic nucleus of the oculomotor nerve of this cat may have become

affected.

A variety of infectious, inflammatory, vascular or neoplastic processes can affect the oculomotor nerve (Shell, 1982). In man, there is a large group of ocular palsies where no cause can be determined (Trautmann & Barnett, 1984). Head trauma and neoplasia are also common causes of palsies in man (Trautmann & Barnett, 1984). Oculomotor palsy may be a false localising sign with raised intracranial pressure with the brain stem displaced downwards (Trautmann & Barnett, 1984). The parasympathetic fibres alone may be affected as they are medially and superficially located on the oculomotor trunk (Kerr & Hollowell, 1964) where they are susceptible to nerve compression with midbrain swelling (De Lahunta, 1983b; Shell, 1990). Retrobulbar neoplasia may be responsible for the ophthalmoplegia (Neer & Carter, 1987). No case of neoplasia was confirmed as being the cause of the oculomotor palsy in any of these cases but it was certainly initially suspected in cases 11, 12, and 8. It is unfortunate that these cases, so challenging from a diagnostic point of view, did not receive postmortem investigation. In cases 10, 11, 12, 8, & 13, it was felt that diffuse inflammatory disease was present to result in the diverse and bizarre presentations and courses of these cases.

Abnormal pupillary responses are frequently reported in insulin - dependent diabetes mellitus in man, but these usually involve reduced pupillary size and reduced hippus (Thomas & Eliasson, 1984). The small pupillary diameter with sluggish response to light is known as the Argyll Robertson pupil and is the most common form of diabetic autonomic neuropathy occurring in man (Smith & others, 1978). This abnormality is believed to be due to involvement of the pupillomotor fibres of the oculomotor nerve not necessarily with significant peripheral neuropathy otherwise (Friedmann & others, 1967). Isolated or multiple palsies of the nerves to the external ocular muscles are also recognised but the parasympathetic fibres are usually unaffected (Goldstein & Cogan, 1960; Thomas & Eliasson, 1984; Trautmann & Barnett, 1984). The oculomotor palsies in these cases are believed to be due to demyelination subsequent to focal ischaemia (Asbury & others, 1970).

Lymphoma in man can result in cranial nerve involvement, usually by direct invasion or compression and the third and seventh nerves are commonly affected (McLeod & Walsh, 1984). Although nonmetastatic peripheral neuropathies have been described in man, reports have not referred to cranial nerve involvement (McLeod & Walsh, 1984). The cause of the cranial nerve involvement in case 15 was not determined.

Idiopathic dilated pupils (tonic pupil) (Adie's syndrome) is well recognised in man and has been reported in the dog (Goldfarb & Swann, 1984; Gerding & others, 1986). In man, the idiopathic syndrome usually affects young women (Gittinger & Asdourian, 1988) and is usually associated with the loss of deep tendon reflexes (Goldfarb & Swann, 1984; Collins & O'Brien, 1990) although this has not been reported in the dog or in any of the cases recorded here. Post-ganglionic denervation of the intraocular muscles, including the ciliary muscles is present, leading to supersensitivity to very dilute (0.1% and 0.3%) pilocarpine solutions (Goldfarb & Swann, 1984; Gerding & others, 1986; Neer & Carter, 1987). The cause of the condition is unknown but appears to be due to a degeneration of the ciliary ganglion (Gerding & others, 1986). None of the cases reported here really fit with a diagnosis of idiopathic tonic pupils as case 16 had concurrent bilateral facial nerve palsies, case 17 had unilateral lens pathology, case 18 was preceded by a seizure and case 19 was preceded by probable traumatic damage to the somatic efferent as well as the parasympathetic component of the oculomotor nerve. Cases 17 and 18 failed to respond to pilocarpine 1%. Local ocular disorders are a potential cause of a tonic pupil (Gittinger & Asdourian, 1988) and this may explain the pupillary abnormalities evident in cases 16, 17, 18 & 19.

Pharmacological testing with pilocarpine was carried out in nine of the cases. Only the sheep (case 13) responded to the 0.1% concentration, indicating supersensitivity to the drug consistent with a post-ganglionic lesion (Thompson & Pilley, 1976; Neer & Carter, 1987). Most cases responded to the pilocarpine 1.0% after 20 - 40 minutes. Two cases (17 and 18) failed to respond to pilocarpine at 0.1% or 1.0% even after 60 minutes. De Lahunta (1983b) describes pharmacological testing with pilocarpine as a 2.0% solution (Scagliotti, 1980a; b; Neer & Carter, 1987). First and second order neuron (pre- and post-ganglionic) lesions should respond more quickly, more completely and for longer than a normal pupil. This was certainly recognised in those cases with a unilateral lesion (cases 10, 11, 8, 13, 14 & 15) where the testing was performed. The failure of response in cases 17 and 18 to respond to the 1.0% pilocarpine may be because of the more dilute concentration than that recommended (Scagliotti, 1980a; b; De Lahunta, 1983b) or because of an atropinic influence (pharmacological blockade) or unrecognised iridal disease (Neer & Carter, 1987). The fact that a more dilute concentration was used may have explained the longer time interval before miosis was evident in these cases, whereas a normal pupil should show miosis within 20 minutes after application of 2.0% pilocarpine (Scagliotti, 1980a; b; De Lahunta, 1983b; Neer & Carter,

1987). However, other references document the use of 1.0% pilocarpine (Thompson & Pilley, 1976; Shell, 1982; Ramsay, 1986). Pilocarpine is not believed to differentiate between first order (pre-ganglionic) and second order (post-ganglionic or ciliary ganglion / short ciliary nerve lesions). Physostigmine 0.5% as an indirect acting parasympathomimetic drug, will confirm the presence of pre-ganglionic lesions (Scagliotti, 1980a; b; De Lahunta, 1983b; Neer & Carter, 1987) but unfortunately this drug was not available. Not all parasympathetically denervated tonic pupils demonstrate supersensitivity to pilocarpine (Ramsay, 1986) particularly if the lesions are partial or if they have been long-standing. This may explain the disappointing results obtained from the pharmacological testing in some of these cases.

B.iv) CASES PRESENTING WITH HORNER'S SYNDROME

Ia) With First Order Neuron Lesions (Brain)

CASE 20: 114578 "Eilidh"

Signalment: 8 year old female spayed Weimaraner.

Reason for Presentation: Incoordination and seizure.

Case Summary

This dog had been seen at GUVS one year prior to this investigation, when she was investigated for marked cervical pain. A myelitis had been the diagnosis of exclusion after radiography, myelography and CSF analysis, and good response had been obtained with prednisolone therapy. She had been on no treatment for ten months until two weeks prior to representation at GUVS, when odd episodes of apparent pain were followed with incoordination and falling to her right side. The owner felt the dog was abnormally depressed and lethargic. One tonic-clonic seizure occurred ten days prior to GUVS presentation. The referring veterinary surgeon described a transient right - sided head tilt and right - sided facial palsy lasting for just one day, one week prior to presentation. She had been treated with betamethasone, and some improvement had been reported by the owner.

On examination, the dog appeared bright and alert, although she somewhat compulsively paced around the room, usually circling to her left. She had a low head carriage and some cervical pain could be elicited on ventroflexing her neck further. She also demonstrated right - sided conscious proprioceptive deficits, scuffing her right fore particularly. The dorsolateral aspect of her right hind was excoriated and both hind limbs appeared to be ataxic. A right - sided hemiparesis was also evident on attempting to hemiwalk her or to hop her on these limbs. The left limbs appeared to be normal on observing the gait and on neurological examination. The right eye was abnormal with enophthalmos, ptosis, third eyelid protrusion and subtle miosis. She failed to demonstrate a gag reflex and the owner had reported a change in her bark; it had become higher pitched and hoarse. Haematology and biochemistry samples were unremarkable. Toxoplasmosis and CDV had been ruled out at initial presentation and were not rechecked. CSF sampling from the cerebellomedullary cistern was repeated despite having been on glucocorticoid therapy. There were 6 nucleated cells, none of which was abnormal, and the total protein content was 340 mg/l which was slightly elevated.

A diffuse inflammatory lesion was suspected, with cerebral involvement (seizure) and brain stem

involvement (CN IX, X deficits apparent on neurological examination, and the referring veterinarian suggested transient CN VII and VIII lesions). The cervical pain may have reflected cervical meningomyelitis or solely unlocalised meningeal pain. Continuing glucocorticoid therapy was advised, with further monitoring of her progress. Over the following ten days, she improved slowly, but then had a severe seizure. During the postictal phase, gastric dilatation and volvulus was diagnosed and corrected with a laparotomy by the referring veterinary surgeon. She survived the surgery well but showed a complete right - sided hemiplegia the following day and was euthanased by the referring veterinary surgeon without a post mortem.

Diagnosis

The Horner's syndrome was believed to be associated with a brain stem or a cervical inflammatory meningoencephalomyelitis. However, pharmacological testing was not done in this case to confirm the initial presumption that this was a first order neuron lesion. Ocular sympathoparesis may alternatively have been due to damage of the cranial cervical ganglion at the synapse of the second and third order neuron lesions ventromedial to the tympanic bulla; an area associated with the proximal portions of cranial nerves IX, X, XI and XII (van den Broek, 1987).

Ib) With First Order Neuron Lesions (Spinal Cord)

CASE 21: 114598 "Sparky"

Signalment: 6 year old Male Jack Russell Terrier.

Reason for Presentation: Cervical pain.

Case Summary:

The dog had shown several episodes of extreme cervical pain for two weeks prior to presentation. He was obviously in pain when examined, held up his left foreleg and was extremely reluctant to move and was aggressive when encouraged to do so. Muscle atrophy was evident over the left infraspinatus and supraspinatus muscles and muscle fasciculations were present in his neck. Anisocoria was present with miosis of his left pupil, although no other neurological deficits were present. Phenylephrine 10% drops were instilled into both eyes leading to partial resolution of the anisocoria after 40 minutes. Subsequent to general anaesthesia, radiography and myelography of the cervical spine was performed. Calcified intervertebral discs were present at C2C3, C5C6 and C6C7. The disc space at C5C6 was narrowed (Figure 21) and myelography confirmed the presence of cord compression at this site. The dog went on to surgery in the same anaesthetic and all disc spaces were fenestrated. Subsequent to surgery, the dog no longer appeared to be in pain and complete resolution

of the anisocoria was evident.

Diagnosis

This dog had a C5C6 cervical disc extrusion (Hansen type I) resulting in lateralisation evidenced by the root signature and the first order Horner's syndrome present on the left side due to involvement of the tectotegmentospinal tract.

CASE 21. 114598. 6 y.o. M. Jack Russell Terrier

Signalment: 42 month old male terrier cross.

Reason for Presentation: Inappetence subsequent to a road traffic accident.

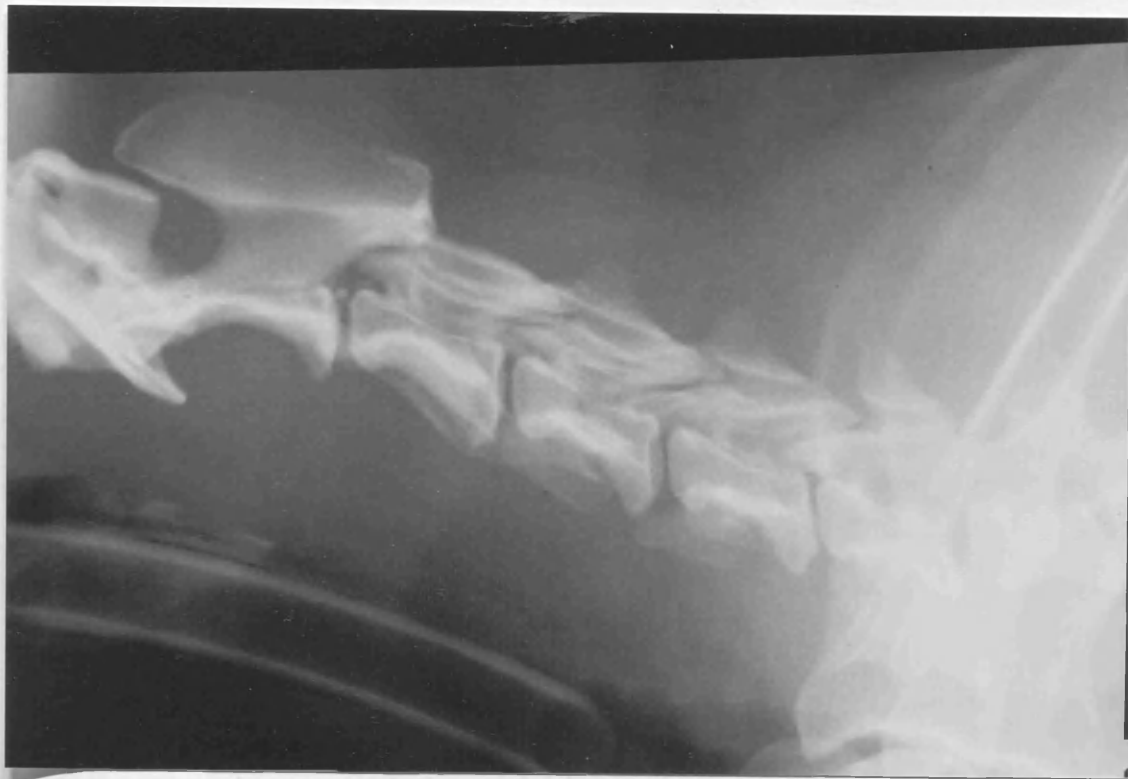


Figure 21. Case 21. 114598. 6 y.o. M. Jack Russell Terrier.

Plain radiograph of the lateral cervical spine obtained under general anaesthesia. Calcified intervertebral discs are present at C2C3, C5C6 and C6C7. The C5C6 disc space is narrowed with calcified disc material within the canal. Cervical disc extrusion was diagnosed at this site.

CASE 22: 111330 "Scamper"

Signalment: 11 month old Male Collie Cross.

Reason for Presentation: Quadriparesis subsequent to a road traffic accident.

Case Summary

This dog was examined ten days after a road traffic accident after being hospitalised by the referring veterinary surgeon in which time considerable improvement had been recognised in his neurological status although the owners requested a second opinion about his prognosis. On examination, the dog was very bright and alert although non-ambulatory. Multiple healing abrasions were present. He was severely quadriparetic, which was worse on his left side. He was able to hemiwalk on his right side with support. Muscle tone was increased in all four limbs, more marked on the left side. A body torsion to the left side was present and he preferred to lie on his right side. Urinary retention was present and his bladder was difficult to express, requiring catheterisation. The left limbs were palpably warmer than the right limbs. The left eye had a miotic pupil, was enophthalmic with a narrowed palpebral fissure and third eyelid protrusion and ptosis of the upper lid was also recognised. Instillation of Phenylephrine 10% drops into both eyes resulted in partial although not complete resolution of his

anisocoria after 40 minutes. After sedation, radiographs were obtained of his cervical spine. No bony abnormality was detected and further investigation was not done as it was decided to manage the dog conservatively. After two further weeks of cage resting, the dog was ambulatory and able to urinate voluntarily although a marked left - sided hemiparesis and the Horner's syndrome were still evident. He was discharged and re-examination one month later demonstrated further improvement in ambulation, although left - sided hemiparesis and conscious proprioceptive deficits were still evident. The Horner's syndrome had resolved. A letter from the owners after a further two months described the dog as being entirely normal again although a neurological examination was not performed.

Diagnosis

A C1 - C5 lesion was present after a traumatic incident resulting in asymmetrical mainly left sided quadriparesis. Involvement of the tectotegmentospinal tract resulted in sympathoparesis of the left side of his body, affecting vasomotor tone and the eye.

CASE 23: 113780 "Megan"

Signalment: A $2\frac{1}{2}$ year old Female Labrador Retriever.

Reason for presentation: Quadriplegia.

Case Summary

Two weeks prior to presentation at GUVS, this dog had been reported to be unwell with pyrexia, lethargy and inappetance but without obvious clinical signs evident to the referring veterinary surgeon. Some improvement was seen with antibiotic therapy, but one week later, she was found, under a bed, suddenly completely quadriplegic. No neurological deficits had been evident to the owner prior to this. She was hospitalised at the referring veterinary surgeons premises, treated with high doses of glucocorticoids and referred when no neurological improvement had been evident. Considerable weight loss was reported over this time. On examination, the dog was in very poor body condition and markedly depressed. No significant clinical abnormality was present apart from the neurological examination. She was completely non-ambulatory. Considerable neurogenic muscle atrophy was present in both forelimbs, particularly affecting the right side, involving the supraspinatus, infraspinatus and biceps muscles. Muscle tone was reduced in both forelimbs, and the withdrawal reflex was absent in her right fore although deep pain perception was intact. The withdrawal reflex was weak in

the left fore. Muscle tone, local reflexes and pain perception appeared to be normal in the hind limbs and some residual voluntary movement of her left hip was apparent. Her hind limbs appeared to be palpably warmer than her fore limbs. Urinary retention and overflow was present. The right pupil was miotic but no other signs of ocular sympathoparesis were identified.

Routine haematology and biochemistry samples were obtained which demonstrated a raised WBC with neutrophilia and left shift ($19.5 \times 10^9/l$ with 84.5% neutrophils). Raised SAP and ALT was presumed to result from the glucocorticoid therapy she had been receiving. Serum CDV titre of 512 was unremarkable for a dog which was fully vaccinated. A Sabin Feldman dye test titre to **Toxoplasma gondii** of 65 units was of dubious significance. CSF obtained from the cerebellomedullary cistern was xanthochromic and analysis demonstrated 11 nucleated cells/ mm^3 which were shown on cytopspin to be lymphocytes, macrophages and occasional neutrophils with numerous degenerate RBCs. The protein content was 240 mg/l. No titre to CDV or toxoplasmosis was evident in the CSF.

Subsequent to general anaesthesia, plain radiographs of the cervical spine were obtained which were unremarkable. Myelography demonstrated dramatic cord

swelling between C4 - C7, with cord deviation and attenuation ventrally and dorsally (Figure 22) and with medial deviation of the right column over C4 then cord swelling caudal to this on the ventrodorsal view. Electromyography confirmed the presence of neurogenic atrophy in the forelimbs with evidence of spontaneous electrical activity. The dog was treated with 2 mg/kg of prednisolone; a higher dose than had been initially prescribed.

The CSF analysis and myelography was repeated four days later, when no neurological improvement had been recognised. The CSF appeared to be less xanthochromic and the cord less swollen although the appearance of a right - sided extradural mass at C4 was still present. Lumbar myelography was not done.

The dog over the next 5 days remained very dull and no neurological improvement was evident at all. She was euthanased 15 days after onset of the quadriplegia.

Post mortem investigation was dramatic. Cord haemorrhage was profound and affected the entire length of the cord, intradurally, intramedullary and extradurally, affecting C1 - C3, C4 - T2 and L2 caudally. T3 - L2 appeared grossly normal. An organising blood clot on the right

side of C4 was responsible for the apparent extradural mass evidenced on myelography. Histopathology failed to identify any cause for the spinal haemorrhage, although the haemorrhage was responsible for the compressive changes recognised by coarse white matter vacuolation, particularly marked at the C4 segment of the cord (Figure 22b).

Diagnosis

From the neurological examination, it was felt that a C6C7 lesion was present resulting in cord compression and affecting the tectotegmentospinal tracts resulting in sympathoparesis of the right eye and the peripheral vasodilatation manifested as palpable appreciation of increased warmth of the hind limbs. The myelographic findings appeared to support this diagnosis although the full extent of the cord involvement was not apparent until post mortem. The Horner's syndrome may in fact have been due to haemorrhage affecting the T1 nerve roots, although no panniculus cut off or other evidence of a T1 lesion had been evident neurologically. Phenylephrine testing had not been done in this case.



Figure 22. Case 23. 113780. 2.5 y.o. F. Labrador. Lateral radiograph of cervico-thoracic spine with myelogram from cerebellomedullary cistern. The cord appeared swollen from C4 - C7 and the ventral column appears to split at C7, suggesting a ventral intradural extramedullary mass at this site.



Figure 22 continued. Ventro-dorsal radiograph of caudal cervical spine with myelogram showing medial deviation of the right column over C4, suggesting an extradural right sided mass at this site. The "masses" were extra- and intradural haemorrhages.

CASE 154-11220-2007

Signalment: A 5-year-old male dog, mixed breed, owner reported.

History: The dog was found dead in the yard, approximately 100 yards from the house.

Physical Exam: The dog was found dead.

Cause of Death

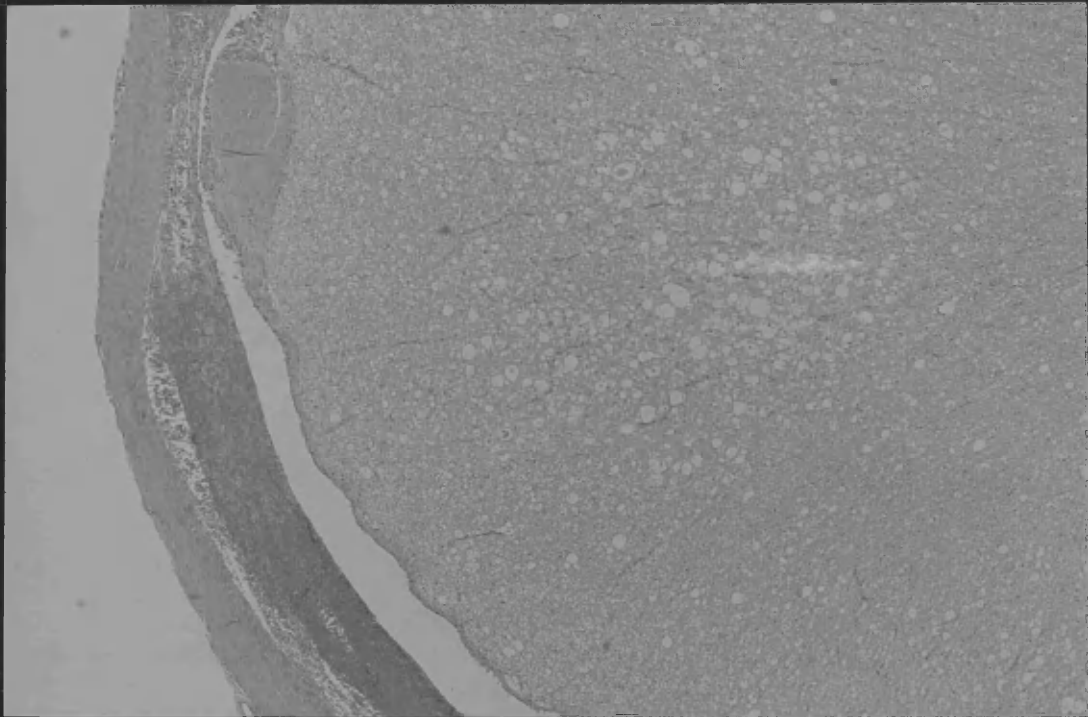


Figure 22b. Section of cervical spinal cord at level of C4 showing subdural haemorrhage and coarse vacuolation of the white matter as a consequence of the cord compression caused by the haemorrhage. x10.

CASE 24: 113260 "Meg"

Signalment: A 6 year old Female Gordon Setter.

Reason for presentation: Paraparesis progressing to paraplegia and back pain.

Case Summary

Five days prior to presentation to GUVS, this dog had appeared to be uncoordinated on her hind legs. She appeared to be in pain, and the pain and the neurological signs deteriorated until she was completely paraplegic with urinary retention and overflow. On examination, the dog was in good body condition, although completely paraplegic. She had difficulty in rising from lateral recumbency, but once helped up, had no difficulty moving on her front limbs. Muscle tone was increased in the hind limbs and spinal reflexes were brisk although no voluntary movement was present. Deep pain perception was present in the hind limbs. The bladder was a normal size but difficult to express. Abnormal tail wag reflexes could be elicited by abdominal palpation. A high panniculus reflex cut off was apparent bilaterally, estimated to correspond to the caudal border of the T6 dermatome. Marked spinal hyperpathia was present at this site also. No difference in temperature of the limbs was detected. The left pupil was miotic although no other abnormality of the left eye was detected.

After general anaesthesia, plain radiographs of the caudal cervical and thoracic spine were obtained which were unremarkable. Myelography, from cerebellomedullary and lumbar cisternal sites, demonstrated divergence and thinning of ventral and dorsal dye columns over T5T6 on the lateral view and an abrupt termination of the left column and thinning and lateral deviation of the right column on the ventrodorsal view. CSF analysis was performed from the cerebellomedullary (CMC) and lumbar (LUM) cisterns:

	CMC	LUM
Nucleated cells / mm ³ :	4	5
Protein content (mg/l):	190	800

In addition, the sample obtained from the lumbar cistern appeared slightly xanthochromic. The marked elevation in the protein levels caudal to a compressive site, at the lumbar cistern, reflects CSF flow (Thomson & others, 1990).

The dog was euthanased with the provisional diagnosis of a spinal cord tumour. Gross pathology demonstrated a 3 cm grey - white mass within the spinal canal at the level of T5 - T6. The mass filled most of the right side of the canal, and the cord was severely compressed. The mass was extradural, and extended through the right

intervertebral foramen of T5T6, here apparently attached to the nerve sheath. Areas of discolouration was present in the cord anterior and caudal to this mass. Histopathology of this mass was diagnostic of a neurofibroma. Anterior and caudal to the lesion, the cord had areas of focal haemorrhage and an irregular meningitis, extending around nerve roots. The meningitis was extending far enough cranially to affect T1.

Diagnosis

A neurofibroma resulting in high thoracic cord compression associated with a meningitis extending cranially to affect T1 which was the probable cause of the Horner's syndrome. Phenylephrine testing was not performed in this case, as the other neurological signs isolated the lesion. The tumour itself was too caudal to directly result in Horner's syndrome.

II) With Second Order Neuron Lesions

IIa) Associated with a Cervical Lesion

CASE 25: 117009 "Domino"

Signalment: 12 year old male Dalmation.

Reason for Presentation: Abnormal appearance to right eye and cervical mass.

Case Summary

This case initially presented to the veterinary surgeon with an abnormal appearance to the right eye. Horner's syndrome was diagnosed which was felt to be related to the chronic otitis externa. No neurological improvement was seen with glucocorticoid therapy and topical ear preparations, and then he represented as he had difficulty swallowing. A painless cervical mass was then detected and the dog was referred for further evaluation. Clinical examination showed the dog to be in good condition with a firm, poorly - mobile lobulated mass of about 15 x 15 cm within the ventral cervical area. The right eye was enophthalmic with ptosis, narrowed palpebral fissure and a miotic pupil. Application of Phenylephrine 10% resulted in resolution of the anisocoria and partial resolution of the other signs of ocular sympathoparesis after 30 minutes. No other neurological deficits were evident and

the dog had no history of a change in bark, but there was a history of dysphagia. Haematology was unremarkable although biochemistry demonstrated elevated liver enzymes (SAP = 1193 iu/l; ALT = 256 iu/l). Total T4 was not, however, assayed. A needle aspirate of the mass demonstrated epithelial type cells many with bizarre and multiple nuclei and frequent mitotic figures.

The owners were advised that the mass lesion, probably a thyroid carcinoma, was probably responsible for the Horner's syndrome and they opted for euthanasia. Immediately after this was achieved, prior to the body being submitted for cremation, the mass was removed. Normal thyroid glands were not found. The mass appeared to have infiltrated the right vagosympathetic trunk, which was thickened, and the oesophagus. Histopathology of the mass confirmed it to be a thyroid carcinoma.

Diagnosis

Thyroid carcinoma with involvement of the right vagosympathetic trunk resulting in second order Horner's syndrome.

CASE 26: 116171 "Lugsby"

Signalment: Two year old female spayed Domestic Shorthair cat.

Reason for Presentation: Dyspnoea.

Case Summary

This cat was admitted to investigate the cause of its dyspnoea. It was found to have a nasopharyngeal polyp which was removed by traction. Histopathology confirmed that it was a polyp. Subsequent to this surgery, the cat could no longer miaow and had miosis, ptosis, enophthalmos, protrusion of the membrana nictitans and narrowed palpebral fissure evident in her right eye (Figure 23). Phenylephrine 10% instillation into both eyes resulted in resolution of the anisocoria after 30 minutes. Neurological examination did not demonstrate any other neurological lesions. The gag reflex was intact and the cat was bright and alert and no dysphagia was apparent. No further investigation was carried out and the cat was discharged. Re-examination one week later demonstrated slight return of a hoarse miaow and partial resolution of the Horner's syndrome. One month later, the miaow had returned to normal and only a slight anisocoria was evident.

Diagnosis

It was presumed that the polyp removal by traction had

also resulted in some neuropraxic injury of the vagosympathetic trunk on the right side. This was, however, difficult to explain anatomically.

Significant clinical signs were observed.

Reason for presentation: Symptoms of unknown origin.

CASE SUMMARY

Prior to presentation, the cat had had a 2 week



right pupil associated with miosis and ptosis (Figure 23a). Phenylephrine 1% testing resulted in resolution of the anisocoria within 30 minutes after instillation (Figure 23b).

Hematology was unremarkable and urinalysis was unremarkable.

Figure 23. Case 26. 116171. 2 y.o. F(s) DSH cat.

The miaow was lost and Horner's syndrome was evident in the right eye, with miosis, ptosis, narrowed palpebral fissure, apparent enophthalmos and third eyelid protrusion.

Significant antibody titre to Lyme disease was found from a tick infested area. Initial treatment consisted of oral oxytetracycline and she rapidly improved.

CASE 27: 116242 "Lisa"

Signalment: 11 month old female Weimaraner.

Reason for Presentation: Pyrexia of unknown origin.

Case Summary

Prior to presentation, this dog had had a 2 week duration of fluctuating pyrexia (102° - 105° F), malaise and inappetance. These signs had immediately followed her first oestrous. She had been treated with subcutaneous injections of cephalexin and intramuscular injections of flunixin by her referring veterinary surgeon. This had resulted in considerable multiple injection reactions in her neck which were painful on palpation. She was pyrexia on presentation to GUVS but no other major clinical abnormalities were identified. Neurological examination showed that she had a miotic right pupil associated with ipsilateral mild ptosis (Figure 26a). Phenylephrine 10% testing resulted in resolution of the anisocoria within 30 minutes after instillation (Figure 26b).

Haematology was suggestive of infection with an elevated WBC of $30.3 \times 10^9/l$ with 84% neutrophils showing a left shift. Liver enzymes were slightly elevated. She had a significant antibody titre to Lyme disease and was from a tick infested area. Initial treatment consisted of oral oxytetracycline and she rapidly improved.

She was seen about one month later, when the anisocoria was very subtle, and her cervical muscles had recovered. However, she was pyrexia and unwell again. At this time, she had a mucoid vaginal discharge and cystic endometrial hyperplasia was suspected, and ovariohysterectomy was performed. Her reproductive tract was abnormal and subsequent lymphocyte culture demonstrated that she was an XX/XY intersex. Three months later, no further pyrexia episodes had occurred and the dog was very well and no neurological deficits were identified.

Diagnosis

Horner's syndrome in this case was believed to be due to a second order neuron lesion, suggested by the pharmacological testing, presumably due to the reactions to the multiple injections into her neck.



Figure 24a. Case 27. 116242. 11 month old F. Weimaraner. Horner's syndrome was present in the right eye, with miosis, narrowed palpebral fissure, ptosis, apparent enophthalmos and third eyelid protrusion.



Figure 24b. The anisocoria has resolved and the third eyelid retracted within 30 minutes of administering Phenylephrine 10% into both eyes.

IIb) Associated with an Endocrinopathy

CASE 28: 113498 "Heidi"

Signalment: 10 year old female spayed Labrador Retriever.

Reason for Presentation: Unstable diabetes mellitus. Red droopy left eye.

Case Summary

This dog was presented because of a huge requirement for insulin and lack of glycaemic control. In addition, two weeks prior to presentation, the owners had observed an abnormality affecting her left eye which they described as being red and droopy. This had been treated by the referring veterinary surgeon with an ophthalmic antibiotic preparation. On examination, the dog was obese, with a marked lordosis and pendulous abdomen. She was poorly muscled and reluctant to exercise. Bilateral cortical cataracts were present. She had a narrowed palpebral fissure, gross protrusion of her membrana nictitans, ptosis of the upper lid, conjunctival congestion and a miotic pupil affecting her left eye. Further investigation demonstrated that as well as diabetes mellitus, she had pituitary dependent hyperadrenocorticism. Phenylephrine 10% testing demonstrated complete resolution of the anisocoria and partial resolution of the third eyelid protrusion and

ptosis within 30 minutes after administration.

No other neurological deficits were present on testing, although no electrodiagnostic testing had been done to confirm the absence of peripheral neuropathy.

Treatment with opDDD for the hyperadrenocorticism over two months resulted in reduced insulin requirement and improvement of her polyuria / polydipsia, after two months of stabilisation. Gradual resolution of the Horner's syndrome was apparent and four months after presentation, it was no longer present.

The dog was carefully monitored over the next few months, and six months after initial presentation to GUVS, similar signs of Horner's syndrome became apparent, now in her right eye. This resolved after phenylephrine 10% administration 20 minutes after administration of the drops into both eyes. No signs of further endocrine instability were apparent to explain this. The right sided ocular sympathoparesis also resolved after six weeks.

Diagnosis

As well as the diabetes mellitus and hyperadrenocorticism in this case, Horner's syndrome, which pharmacologically was believed to be due to a

second order neuron lesion, was sequentially apparent in both eyes.

CASE 29: 116318 "Tim"

Signalment: 6 year old male Labrador Retriever.

Reason for presentation: Unstable diabetes mellitus and hyperadrenocorticism.

Case Summary

This dog had been investigated six months previously at GUVS for unstable diabetes mellitus when it was found that he also had pituitary dependent hyperadrenocorticism. He was treated with intermediate - acting insulin and opDDD. He was never well controlled, as the owners did not lead a particularly regular lifestyle and the dog either had a fussy appetite and refused to eat or scavenged, making glycaemic control difficult.

He was represented with increased thirst and an abnormal appearance to his right eye. On investigation, narrowed palpebral fissure, miosis, ptosis and protrusion of his third eyelid was evident (Figure 25). Phenylephrine 10% testing resulted in resolution of the sympathoparesis of his right eye after 35 minutes. Further investigation showed him to be ketotic and that the hyperadrenocorticism was also unstable, with no longer a "flat line" synacthen stimulation test. The insulin and opDDD doses were titrated and increased further. Six weeks after the onset of Horner's syndrome

in his right eye, no change with this lesion was documented. No other abnormality was detected on neurological examination although a peripheral neuropathy was not ruled out by electromyography or nerve conduction studies.

Diagnosis

In this case, from pharmacological testing, Horner's syndrome with a second order neuron lesion was apparent, with the diabetes mellitus and hyperadrenocorticism.



Figure 25. Case 29. 116318. 6 y.o. M. Labrador. Horner's syndrome is present affecting the right eye with miosis, ptosis, narrowed palpebral fissure, apparent enophthalmos and protrusion of the third eyelid.

IIc) Idiopathic or Unknown Cause

CASE 5: 116314 "Corrie"

Signalment: 9 year old female spayed Rough Collie.

Reason for Presentation: Sudden onset blindness after being hit by a bicycle.

Case Summary

Case details are given on pp 73 - 75, as it also was believed that this case had bilateral optic nerve involvement as well as a right sided Horner's syndrome. Phenylephrine 10% administration into both eyes resulted in mydriasis occurring to a greater extent in the right eye than the left eye after 40 minutes.

Diagnosis

The complete blindness suggested either sudden acquired retinal degeneration or optic neuritis (not extending distally enough to result in papilloedema). A second order Horner's syndrome was also present, which did not seem to be due to the same lesion as the visual loss but may have resulted from cervical trauma.

Retrobulbar injury has been described causing Horner's syndrome in association with other cranial nerve deficits, usually parasympathetic III and optic nerve lesions (Neer, 1984). Despite the appropriate history in

this case, the pharmacological testing appeared to suggest that this dog did not have a post-ganglionic lesion but one affecting the second order neurons. No identifiable contusion or skin lesions were evident around the neck or elsewhere in this dog, however.

CASE 30: 116782 "Muffin"

Signalment: 9 year old Female Labrador Retriever.

Case presentation: Abnormal appearance of right eye.

Case Summary

One month prior to presentation to GUVS, an abnormal appearance had been observed affecting her right eye, which the referring veterinary surgeon diagnosed as being Horner's syndrome. She was in her third trimester of pregnancy at this time and she whelped uneventfully several days prior to presentation at GUVS. On examination, the bitch was in excellent condition, lactating heavily, and had miosis, third eyelid protrusion, enophthalmos, ptosis and narrowed palpebral fissure affecting her right eye. No other neurological deficits were evident. Phenylephrine 10% testing demonstrated resolution of most of the signs of the sympathoparesis within 40 minutes after application of the drops. Radiography of the thorax and the soft tissue structures of the neck was unremarkable. Telephone follow up with the owner three months after presentation documented that these signs had resolved after several weeks.

Diagnosis

A second order Horner's syndrome was diagnosed, although its cause was not determined.

III) With Third Order Neuron (Post-ganglionic) lesions

IIIIa) Associated with Otitis Media / Interna

CASE 31: 112964 "Benji"

Signalment: 13 month old Male Cocker Spaniel

Reason for presentation: Left sided head tilt and quidding food from the left cheek.

Case Summary

This dog had a long-standing history of otitis externa. Four months preceding initial presentation, he had the first of several general anaesthetics to allow flushing of the external ear canals. Subsequently, he was observed to have a head tilt to the left side. This was not improved by a variety of systemic and topical antibiotic preparations or further cleanings under anaesthesia. The left tympanic membrane was observed to be ruptured. The dogs general state deteriorated and he became pyrexia, was inappetent, developed a left sided facial paralysis and resented his mouth being opened.

Initial investigation at GUVS showed the dog to have a left sided head tilt, a ventrolateral strabismus of his left eye, constant horizontal nystagmus with fast phase to the right, left unilateral facial palsy, extreme discomfort on opening his jaw, otitis externa, pyrexia,

hyperpnoea, tachypnoea, frequent productive coughing and adventitious respiratory sounds on auscultation. Haematology samples supported the diagnosis of systemic infection, with a WBC of $16.1 \times 10^9/l$ with a neutrophilia. Thoracic radiography confirmed he had bronchopneumonia. Prior to further investigation, he was discharged on antibiotics to clear this infection. One month later, he was re-examined at GUVS. In the intervening period, after a slight improvement, he had returned to the referring veterinary surgeon as he had become head shy and showed episodic but extreme pain when opening his mouth. He was given steroid therapy which resulted in neurological deterioration. The head tilt worsened, the dog became ataxic and kept falling to the left and the nystagmus recurred. Re-examination at GUVS showed that the dog still had the left sided facial palsy and the Horner's syndrome. The bronchopneumonia appeared to have cleared. The dog still resented opening his jaw and there was pain on palpation of his left bulla / temporomandibular joint area. There also appeared to be a greater bony mass in this area compared to the right side. Although he was ataxic and tended to fall, no paresis or conscious proprioceptive deficits could be identified in any limbs. He was bright and alert on this occasion. A Schirmer tear test in both eyes demonstrated flow of 12 mm / minute in the right eye and 8 mm / minute in the left, showing slightly

reduced tear production from the left lacrimal gland. Haematology continued to show a slightly raised WBC of $14.4 \times 10^9/l$ with a mature neutrophilia. Biochemistry results were unremarkable.

Under general anaesthesia, radiographs of the skull were obtained. Intraoral and lateral oblique views demonstrated the bullae. The left bulla wall was grossly thickened with soft tissue density within the bulla. New ragged bone formation was evident around the bulla, the jugular process and the temporomandibular joint in this area (Figure 26).

Tympanometry demonstrated that both tympanic membranes were intact but the left middle ear was fluid filled. The stapedius reflex was intact.

CSF analysis was abnormal from the cerebellomedullary cistern. There were 94 nucleated cells / mm^3 , which cytopspin showed to be due to 34% neutrophils, 55% lymphocytes and 11% monocytes. Protein content was 2080 mg/l. These findings suggested an inflammatory lesion.

Blood culture revealed the presence of **Staphylococcus intermedius** and non-haemolytic **E. coli**. Urine and CSF culture were negative.

The dog was treated with large doses of cephalalexin and continued to improve. He began to cope better with his facial palsy. However, he represented on month later, with recurrence of the neurological signs and was off colour again. Blood culture was still positive for **Staph. intermedius** and haematology showed a raised WBC again. He still had dramatic raised WBC and protein in his CSF. The radiographic appearance was similar to previously. His antibiotic was changed to flucloxacillin, as a drug indicated for resistant staphylococcal infections. Its use in man is indicated where osteomyelitis and meningitis is a clinical problem.

Re-examination on monthly occasions continued to show no resolution of the bony and soft tissue abnormality around his bulla although the TMJ pain was controlled. Blood cultures were consistently negative while the dog was on the flucloxacillin. The head tilt continued to be feature although the other signs of vestibular disease had resolved. Facial palsy and Horner's syndrome continued to be present, although the Horner's syndrome had resolved to the extent it was only manifest as an anisocoria. Consistently raised WBC and protein was identified in his CSF although he never demonstrated any signs of clinically evident central nervous system disease. Five months after initial presentation, he

showed signs of malaise again, despite being on continued antibiotics and a mucoid ocular discharge. Schirmer tear test strips now showed no tear flow whatsoever in either eye. Artificial tears (Isopto^R plain) were prescribed. The cause of the keratoconjunctivitis sicca was not determined. Since it was bilateral, it did not appear to be due to the left sided facial palsy. At this time, his antibiotic was changed to cefuroxime (Zinnat^R) and two weeks later, when the dogs condition had improved again, a ventral bulla osteotomy was performed on the left side. Much inspissated caseous material was curetted out. This material and much of the new bone was submitted for bacteriological culture, which resulted in isolation of a mixed population of **Staphylococcus**, **Streptococcus** and **E.coli**. This was sensitive to a variety of antibiotics although the cefuroxime was continued.

One month later (7 months after initial presentation to GUVS), the dog was bright and alert; he was still on antibiotics. A marked head tilt was evident, as was the facial palsy and miosis of the left pupil and facial palsy. His blood culture was negative, and the CSF sample showed less evidence of inflammatory disease, with 0 nucleated cells and, although the protein content was still 500 mg/l, this was considerably lower than previously.

The antibiotics were continued for a further month and then stopped. The owners reported a continued head tilt and left sided facial palsy and partial Horner's syndrome but the dog remained very well even off antibiotics. This was still the case 1 year later, although intermittent topical antibiotic treatment was required for otitis externa.

Diagnosis

Bilateral otitis externa with invasive ear cleaning possibly being responsible for ruptured tympanic membrane on the left side, causing otitis media and interna and facial nerve and sympathetic post-ganglionic fibres to the eye becoming involved. The tympanic membrane was, however, intact by the time tympanometry was performed, which is not uncommon. Osteomyelitis and ascending infection was believed to be responsible for the evidence of meningoencephalitis based on CSF analysis, although without neurological signs suggesting this. The CSF analysis was not, however, typical of a septic meningoencephalitis.



Figure 26. Case 31. 112964. 13 month old M. Cocker Spaniel.

Radiograph obtained from intraoral rostro-caudal skull view demonstrating tympanic bullae with opacification of the left bulla.



Figure 26 continued. A right lateral oblique (top) and left lateral oblique (bottom) radiograph of the skull demonstrating the tympanic bulla. The right is normal. The left shows opacification and periosteal new bone formation around the bulla and the jugular process.

CASE 32: 114239 "Dawn"

Signalment: 8 year old female spayed Cocker Spaniel.

Reason for Presentation: Head tilt, loss of balance and quidding food.

Case Summary

This dog had had a life time of external ear disease and two years prior to presentation had had a bilateral vertical canal ablation which the owners felt improved her problem considerably. Eight weeks prior to presentation she had had elective dental treatment and the right upper carnassial tooth had been removed. Six weeks prior to presentation, the dog suddenly became ataxic and was falling to her right side and had a right - sided head tilt. The referring veterinary surgeon had treated her with antibiotics and glucocorticoids and a slow improvement was seen until three weeks prior to GUVS presentation when she was observed to be dropping food and drooling from her right cheek.

Examination showed the dog to be very bright and alert but with a slight head tilt to the right. A mucopurulent ocular discharge was present affecting her right eye and right nares, causing noisy respiration. There was facial paralysis on the right side, with saliva drooling from the right cheek. The right eye was enophthalmic with protrusion of the third eyelid, ptosis of the upper lid

and miosis of the pupil. Schirmer tear test strips showed tear flow to be absent in the right eye and 7 mm/minute in the left eye. No deficits in oculovestibular or voluntary eye movements were identified and the dog did not have any strabismus or nystagmus, even with variation of her head position. No paresis or neurological deficits were present in the limbs and the dog no longer appeared to be ataxic.

Under general anaesthesia, skull radiographs were obtained to demonstrate the bullae - no bony abnormality was detected and both bullae appeared to have normal thin walls and were air filled. Radiograph of the jaw failed to demonstrate any abnormality from where the extracted tooth had been.

Tympanometry was attempted but was not successful due to the degree of stenosis of both remaining horizontal canals. Otoscopy revealed both tympanic membranes to be apparently intact. Bacteriological culture of the material within the horizontal canals isolated *Pseudomonas* bilaterally, sensitive to gentamicin. This drug was prescribed topically.

CSF analysis from a cerebellomedullary cisternal site was unremarkable.

The dog was discharged on clavulonate potentiated amoxycillin (Synulox^R) as well as the topical aural antibiotic and artificial tears (Isopto^R plain).

Re-examination one month later showed some neurological improvement. The head tilt was no longer evident. A partial blink could be seen on the menace reflex to her right eye. Anisocoria with miosis of the right pupil and slight protrusion of the third eyelid was still evident. The dog was coping better with eating and no longer drooled food or saliva. Telephone follow up two months later revealed that the dog still had slight Horner's syndrome and still could not blink normally although she was coping well.

Diagnosis

Otitis externa presumably leading to otitis media / interna and involvement of the facial nerve and the sympathetic post-ganglionic fibres to the orbit.

CASE 33: 114002 "William"

Signalment: 6 year old male English Springer Spaniel.

Reason for presentation: Chronic otitis externa and recent development of a facial droop on his right side. Weak hind limbs.

Case Summary

This dog had chronic recurrent otitis externa although signs usually resolved with topical treatment. He had never had any invasive ear flushing. He had a road traffic accident 2 years prior to presentation to GUVS and was left with severe osteoarthritis and gross restriction of range of movement of his left elbow after repair of a severely comminuted left humeral fracture. He was also stiff on his hind limbs, and this was of most concern to the owner and the referring veterinary surgeon. Examination revealed evidence of osteoarthritis of all joints in both hind limbs, supported by radiography. Asymmetry of his face was evident with a facial droop and an inability to blink on the right side, with saliva drooling. There was also a narrowed palpebral fissure on the right side with protrusion of the third eyelid, enophthalmos and miosis of the right pupil. No head tilt was evident. No other neurological deficits could be isolated.

Phenylephrine 10% testing confirmed that the Horner's

syndrome was due to a post-ganglionic lesion, with resolution of the miosis and most of the other signs within 30 seconds of administering the drops. Schirmer tear test strips confirmed normal tear production from both lacrimal glands.

Under general anaesthesia, otoscopy demonstrated that both ear canals were full of wax and debris, and both horizontal and vertical canals were inflamed. The right tympanic membrane did not appear to be intact. Tympanometry confirmed the lack of an intact tympanic membrane on the right and a normal tympanogram was obtained on the left. The stapedius reflex was bilaterally intact. Samples were submitted for bacteriology and pathogenic **Staphylococci** and beta haemolytic **Streptococci** were isolated, with broad spectrum of sensitivity to most antibiotics.

Radiographs were obtained of the tympanic bullae. Soft tissue opacification was evident within the right bulla but no bony abnormality was detected.

CSF analysis from the cerebellomedullary cistern was unremarkable.

The dog was discharged on a one month course of clavulonate potentiated amoxycillin (Synulox^R), topical

antibiotic drops for his ears (Surolan^R) and phenylbutazone. Telephone follow up after one month described the dog as having some partial return of facial function and the dog had improved his gait on the nonsteroidal anti-inflammatory drugs. The owner was pleased with his progress.

Diagnosis

Otitis externa resulting in perforation of the tympanic membrane and otitis media, affecting the facial nerve and the sympathetic post-ganglionic fibres to the eye. There was no evidence of otitis interna, with no head tilt and no proximal branches of the facial nerve being affected, as the lacrimal gland innervation (major petrosal branch) and the branch responsible for the stapedius reflex (stapedius branch) appear to be intact.

IIIB) Idiopathic

CASE 34: 113466 "Dileas"

Signalment: 8 year old male Golden Retriever.

Reason for Presentation: Apparent sudden onset facial droop affecting vision.

Case Summary

Two months prior to presentation to GUVS, the owners described an apparently sudden onset lateral protrusion of the third eyelids, marked ptosis of both upper lids and both lower lids causing conjunctival exposure and bilateral enophthalmos all resulting in the cornea being obscured making it difficult for the dog to see. The conjunctiva appeared congested and he had been treated by the referring veterinary surgeon with topical ophthalmic antibiotic as a case of conjunctivitis, with no discernable change in his condition. The dog was well otherwise, bright, alert and responsive, and no other neurological deficits were identified. The owner described him as "choking up" occasionally when being exercised although no dysphonia or dysphagia was identified. No palpable atrophy was present affecting the laryngeal muscles. The gag reflex was intact and a cough could easily be elicited upon tracheal palpation. He also had no inspiratory stridor and his exercise tolerance was good.

The findings were suggestive of a bilateral Horner's syndrome, although, because it was bilateral, no anisocoria could be detected even under variable lighting conditions. Instillation of 10% phenylephrine into both eyes resulted in dramatic improvement within 30 seconds. The third eyelids appeared to retract, the ptosis and enophthalmos appeared to lessen and both pupils dilated equally. The conjunctiva became less red and congested also. These changes resulted in the globes being revealed and the dog's vision consequently improved.

The dog was screened for endocrine and metabolic problems. All results were within reference ranges and the cause of the Horner's syndrome was never ascertained. The dog was treated with Phenylephrine 10% drops to aid his vision and to improve his cosmetic appearance. Re-examination after one month still demonstrated Horner's syndrome although it was less profound, and the owner no longer needed to apply the drops. Telephone follow up after a further four months revealed that in the owner's opinion, complete resolution had not been achieved but that the dog was fine. The choking up episodes had stopped after about one month.

The dog represented to GUVS after 15 months, after the

referring veterinary surgeon had been treating him for a liver problem. Liver enzymes, especially Alkaline Phosphatase, were very high, suggesting biliary obstruction. Ultrasonography revealed multiple anechoic areas within the hepatic substance, consistent with neoplasia or metastases, possibly haemangiosarcoma. At this time, although the dog still had a droopy facial appearance, not uncharacteristic of the breed, no neurological deficits or evidence of Horner's syndrome were identified. The owner's opted to keep the dog at home for as long as he was comfortable.

Diagnosis

Idiopathic bilateral post-ganglionic Horner's syndrome. The history suggested some involvement of the laryngeal innervation although this could not be identified neurologically. These lesions resolved over the following months although the dog then developed hepatic neoplasia, presumed to be unassociated with the previous problem.

CASE 35: 113572 "Jason"

Signalment: 8 year old male Labrador Retriever.

Reason for Presentation: Narrowing of the right palpebral fissure.

Case Summary

The dog had idiopathic epilepsy from when he was two years old, with clusters of seizures occurring approximately every six months. Treatment for epilepsy was rather unconventional and he received primadone (Mysoline^R) as the owner felt was necessary. No deterioration had been observed in this condition. Five weeks prior to presentation to GUVS, the owner observed a "narrowing" of the dog's right eye, which he felt became more prominent when the dog was excited. The referring veterinary surgeon had diagnosed Horner's syndrome and had prescribed oral prednisolone and topical neomycin / hydrocortisone drops which had not affected the condition.

Examination showed the dog to be obese but with no other significant clinical abnormalities. The right eye had a miotic pupil, protrusion of the third eyelid, ptosis of the upper lid, enophthalmos and a narrowed palpebral fissure. Conjunctival congestion was also evident as the conjunctiva was redder than in the contralateral eye. No other neurological deficits were identified.

Phenylephrine 10% administration resulted in complete resolution of the anisocoria and the conjunctival redness and improvement in the enophthalmos and third eyelid protrusion rapidly (20 seconds) after administration into both eyes.

Haematology was abnormal with a panleukopaenia being evident. Total WBC was $2.3 \times 10^9/l$ with 77% neutrophils, 2% lymphocytes, 2% monocytes and 7% eosinophils. Red cell parameters and platelet counts were within reference ranges. The biochemistry sample was lipaemic and liver enzymes were elevated (SAP = 928 iu/l; ALT = 389 iu/l; AST = 112 iu/l). No signs of liver failure were present on the screen and the dog showed no systemic signs of illness or polyuria / polydipsia. Resting cortisol and T4 was within reference ranges. The raised liver enzymes may be due to a fatty liver, primadone or prednisolone administration.

The referring veterinary surgeon repeated the blood samples a month later. The WBC parameters returned to normal although the liver enzymes were still elevated. At this time, they reported partial resolution in the Horner's syndrome, with anisocoria and slight protrusion of the third eyelid. The dog was lost to follow up after this time.

Diagnosis

Idiopathic post-ganglionic Horner's syndrome.

CASE 36: 113781 "Jay"

Signalment: 7 year old male Golden Retriever.

Reason for Presentation: Previous masticatory muscle atrophy and then drooping of the left eye.

Case Summary

Two months prior to referral to GUVS, the dog had been taken to the referring veterinary surgeon because of increasing prominence of his occipital crest and asymmetry of the temporal muscles. An idiopathic trigeminal neuritis, mainly left sided, was diagnosed and the dog had no further problems or treatment until Horner's syndrome was suddenly observed affecting his left eye, two days prior to presentation.

The dog was well muscled and in good condition. Considerable muscle atrophy of the temporal and masseter muscles was evident on the left side. Miosis, enophthalmos, protrusion of the third eyelid, narrowed palpebral fissure and conjunctival congestion were all evident affecting the left eye (Figure 27). These features were not believed to be due to the globe sinking secondary to muscle wasting, as this would not result in anisocoria. Facial sensation and movement appeared to be intact and jaw tone appeared to be normal. No difficulty eating was reported. No other neurological deficits were identified. Phenylephrine

10% testing resulted in virtually complete resolution of all the signs of sympathoparesis within 20 seconds after administration of drops into both eyes.

The dog had a mild, waxy otitis externa but tympanometry and radiography after general anaesthesia failed to identify any middle or inner ear disease. Electromyography demonstrated spontaneous electrical activity in all masticatory muscles, including the right side. There was no evidence of denervation of the tongue, laryngeal or pharyngeal muscles, although all the interosseous muscles of the limbs, the coccygeal and the perianal muscles did show evidence of denervation, despite no clinical evidence of a peripheral neuropathy. These changes may be associated with a polyradiculoneuritis which can concurrently affect the trigeminal nerve.

Full haematology, biochemistry and endocrine screen was obtained which failed to show any abnormality.

The owner declined to attend a re-examination consultation, although he reported that the dog was doing well one month after initial presentation, with a less abnormal appearance of his eye.

Diagnosis

This dog showed evidence of bilateral neurogenic atrophy of his masticatory muscles, with a trigeminal nerve somatic efferent lesion, mainly affecting the left side. Trigeminal nerve sensation appeared to be intact. He also had a post-ganglionic Horner's syndrome affecting his left eye. He may have had a generalised peripheral polyneuropathy or polyradiculoneuritis, from the electrodiagnostic results. Although no other signs were identified, it was unfortunate it could not be followed up further.



Figure 27. Case 36. 113781. 7 y.o. M. Golden Retriever. Bilateral, mainly left sided masticatory muscle atrophy is present. Horner's syndrome is apparent in the left eye with miosis, ptosis, narrowed palpebral fissure, apparent enophthalmos and third eyelid protrusion.

C.iv) DISCUSSION ABOUT CASES RESULTING IN

HORNER'S SYNDROME

Eighteen cases were seen where Horner's syndrome was one of the clinical signs evident. Seventeen cases were dogs and one case was a cat. In sixteen cases the lesion was unilateral, affecting the right side in 11 cases (61.1%) and the left eye in 5 cases (27.8%). Of the cases showing bilateral involvement (11.1%), one case was bilateral at initial presentation (case 34), another sequentially developed left and then right - sided involvement (case 28). Of the 17 dogs, 9 were male and 8 were female. Labrador Retrievers were overrepresented, with 5 cases. Two cases were Golden Retrievers and 2 were Cocker Spaniels and 2 were Weimaraners. Five cases (27.8%) appeared to predominantly affect the first order neurons. One was assumed to be due to diffuse CNS inflammatory disease (case 20). One was as a result of a cervical disc extrusion (case 21). One was as a result of cervical cord trauma subsequent to a road traffic accident (case 22) and another due to unexplained spinal cord haemorrhage (case 23). One case was due to spinal cord neoplasia (case 24). Ocular sympathoparesis believed to be due to second order neuron lesions occurred in 7 cases (38.9%). The vagosympathetic trunk appeared to be affected in three cases: one due to a thyroid adenocarcinoma (case 25), one due to multiple injection reactions (case 27) and one due to iatrogenic

damage associated with polyp removal (case 26). Two cases with concurrent diabetes mellitus and hyperadrenocorticism also had a second order neuron lesion affecting the sympathetic innervation of the eye, suggested on pharmacological testing; cases 28 and 29. In a further two cases, the cause of the second order neuron lesion could not be accurately identified, in case 30, late in gestation and case 5, after a preceding traumatic incident. Third order neuron lesions, or post-ganglionic lesions of the oculosympathetic pathway were evident clinically or pharmacologically in 6 cases (33.3%). Otitis media / interna and associated facial palsy was responsible for 3 cases (16.67%) of Horner's syndrome affecting the post-ganglionic fibres (cases 31, 32 and 33). One other case was of unknown cause but associated with a trigeminal neuropathy (case 36). Two cases were idiopathic but pharmacologically appeared to affect the post-ganglionic fibres (cases 34; with a simultaneously bilateral condition and case 35, which also had idiopathic epilepsy).

Summary table of cases of Horner's syndrome

Unknown cause "idiopathic"	27.78%	(Cases 5,30,34,35,36)
Otitis media /interna	16.67%	(Cases 31,32,33)
Iatrogenic	11.1%	(Cases 26,27)
Associated with endocrinopathy	11.1%	(Cases 28,29)
CNS inflammatory disease	5.5%	(Case 20)
Cervical disc	5.5%	(Case 21)
RTA trauma	5.5%	(Case 22)
Spinal cord neoplasia	5.5%	(Case 23)
Spinal cord haemorrhage	5.5%	(Case 24)
Thyroid carcinoma	5.5%	(Case 25)

The sympathetic component of the general visceral efferent innervation of the eye follows a circuitous route. This series of 18 cases of Horner's syndrome well - illustrates the huge diversity of presenting signs reflecting the many anatomical sites at which a lesion may affect the sympathetic innervation of the eye.

The tectotegmentospinal tracts are laterally located with the other visceral efferent upper motor neuron supply within the brain stem and the spinal cord (De Lahunta, 1983c). From the neurological signs, the localisation of the Horner's syndrome in case 20 was not determined, but multifocal probably inflammatory disease was suspected. Cervical spinal lesions resulting in Horner's syndrome are usually severe (Petersen Jones, 1989b) as in case 23 with complete quadriplegia, but it is interesting to note that lateralised lesions may result in Horner's syndrome with minimal other signs of cervical cord compressive disease such as in case 21 with nerve root signature or a resolving asymmetric quadriparesis such as in case 22. Vascular lesions are said to be the most common cause of lateralised cervical lesions resulting in Horner's syndrome (Neer, 1984) such as with fibrocartilaginous embolism (Greene & Higgins, 1976; De Lahunta & Alexander, 1976). The aetiology of the cord haemorrhage in case 23 even at post mortem was a matter of speculation. Trauma (Frye, 1973) and

cervical disc disease are also described as being associated with Horner's syndrome (Jones & Studdert, 1975; van den Broek, 1987) as recognised in cases 21 & 22. It is also interesting to note that a couple of these cases also showed evidence of sympathetic denervation of blood vessels ipsilateral and caudal to the lesion, manifested as a vasodilatation of peripheral arterioles resulting in a palpable hyperthermia recognised in cases 22 and 23.

In case 24, the Horner's syndrome appeared to result from a cranially - extending meningitis affecting the ventral nerve roots of the cranial thoracic segments, rather than from direct tumour involvement. Thus, the proximal axons of the second order neurons, rather than the first order neurons themselves, may have been affected in this case causing an ipsilateral Horner's syndrome; it is unfortunate pharmacological testing had not been carried out in this case to attempt to distinguish between a first and second order neuron lesion. Proximal axons of second order neurons have also been described as being affected with brachial plexus avulsion injuries, although no such cases are represented here - probably as it was a referral population of animals being investigated rather than a first opinion series. Griffiths and others (1974) described partial Horner's syndrome in 10 out of 18

cases presented for traumatic brachial plexus avulsion. The fact that the sympathoparesis was partial in this situation was explained by the fact that only the T1 nerve root is affected by the avulsion and not the more caudal segments. However, in case 24 with the cranial extension of the meningitis, it appeared that T1 - T4 was equally affected. From the cases described here, cases 21 and 23 also had a partial Horner's syndrome manifested by an ipsilateral miotic pupil alone, and in cases 20 and 22 although other signs of Horner's syndrome were present, these were subtle. It appears that the more proximal the lesion in the anatomical pathway of the sympathetic innervation of the orbit, the more subtle the signs are of sympathoparesis.

The brachial plexus, including second order (pre-ganglionic) oculosympathetic fibres, may also be affected by neoplasia such as lymphoma and Horner's syndrome as has been described in association with such a lesion (Fox & Gutnick, 1972). Neoplasia or trauma affecting the thoracic inlet or anterior mediastinum may also affect the proximal axons of the second order neurons (Jones & Studdert, 1975; De Lahunta, 1983c; Morgan & Zanotti, 1989). In man, undetected malignancy responsible for development of Horner's syndrome is usually at the pulmonary apex, often associated with pain in the ipsilateral arm (Pancoast's syndrome)

(Gittinger & Asdourian, 1988).

The vagosympathetic trunk is fairly vulnerable within the soft tissue structures of the neck and trauma such as bite wounds is commonly reported in the literature as a cause of Horner's syndrome (Jones & Studdert, 1975; van den Broek, 1987). It may also be affected by neoplasia such as the thyroid carcinoma reported in case 25 here and suggested by Neer (1984) and De Lahunta (1983c). Iatrogenic trauma to the vagosympathetic trunk resulting in Horner's syndrome has been described during cervical surgery (van den Broek, 1987) and after carotid artery catheterisation in a number of cats (Kneller and others, 1972). In case 27 reported here, it appeared that the cervical sympathetic trunk was affected due to multiple injection reactions.

Case 5 is similar to the case described by Wowk and Olson (1979) where head trauma and a painful eye preceded the development of Horner's syndrome although pharmacological testing demonstrated the lesion to be due to a second order neuron lesion in their case and case 5.

In the large series of Horner's syndrome described in dogs and cats by Kern and others (1989), nine animals had unilateral Horner's syndrome in association with

hypothyroidism. Horner's syndrome is not, however, a common neuropathy described in hypothyroid humans. None of the cases reported here were hypothyroid, although they were checked for this. Two of the cases (28 & 29) did have evidence of concurrent diabetes mellitus and hyperadrenocorticism. The relationship between the endocrinopathy and development of Horner's syndrome is uncertain. No other examples of diabetes mellitus or hyperadrenocorticism in association with Horner's syndrome were found by the author in the literature. In man, diabetes mellitus is associated with pupillary abnormalities, usually a small pupil diameter and a sluggish response to light (the Argyll Robertson pupil) (Smith & others, 1978). Horner's syndrome is not a common finding with diabetic neuropathy in man, however.

Case 30 developed an apparent second order neuron lesion of the oculosympathetic innervation of the eye resulting in Horner's syndrome for which a cause could not be identified, although it initially occurred late in gestation. Other "idiopathic" second order Horner's syndromes are also described in the literature (Morgan & Zanotti, 1989).

One of the most common causes of Horner's syndrome in the cases reported here is the involvement of the sympathetic post-ganglionic fibres in syndromes of

otitis media / interna such as in cases 31, 32 and 33. This has also been the case described by Scagliotti (1980a; b) and Collins and O'Brien (1990). Onset in case 31 appeared to be associated with invasive ear cleaning, which is also suggested by Morgan & Zanotti (1989).

One dog in the series described by Kern and others (1989) was epileptic as was case 35 described here, although whether these observations are significant or not is uncertain. It is most unlikely the Horner's syndrome, which pharmacologically appeared to be due to a post-ganglionic lesion, and the seizure focus are caused by the same lesion.

Case 36 had Horner's syndrome occurring after neurogenic masticatory muscle atrophy secondary to a presumed trigeminal neuritis. Horner's syndrome has been reported as occurring with idiopathic trigeminal neuritis (De Lahunta, 1983c; Shell, 1990) or with space occupying or inflammatory lesions of the cavernous sinus or paratrigeminal region (Lewis & others, 1984; Murphy & others, 1989). It is difficult to imagine how a single space occupying lesion could result in purely somatic efferent involvement of the trigeminal (mandibular) nerve with oculosympathoparesis when it is considered that the sympathetic fibres are in the ophthalmic branch of the trigeminal nerve, and no deficits in facial or

corneal sensation were identified in this case. No evidence of any of the trigeminal nerve branches sensory field impairment was identified at all. Bilateral trigeminal nerve paralysis and bilateral Horner's syndrome has also been described in association with an aleukaemic myelomonocytic neoplasia which was found at autopsy to affect each trigeminal nerve and ganglion as well as other organs (Carpenter and others, 1987). However, in this reported case, trigeminal sensory deficits were also identified.

There are a large number of Horner's syndrome cases reported here where I was unable to identify a known cause. This is consistent with previous reports in animals. Undetermined causes of Horner's syndrome are reported in 37% of cases reported by van den Broek (1987), 54.5% of dogs by Morgan and Zanotti (1989) and 50% of dogs and 42% of cats by Kern and others (1989). Similar unidentified causes of Horner's syndrome occur in man also, where it is proposed that a local vascular event is responsible (Maloney and others, 1980; Gittinger & Asdourian, 1988) although this is unlikely in animals where primary vascular disease is rare. Undetected malignancy is another frequent cause of first or second order neuron lesions in man (Maloney and others, 1980) and this must be of concern in animals, in particular case 36 reported here. However, most

idiopathic Horner's syndrome cases described in the literature have not been associated with significant complications or mortality but often have shown spontaneous recovery (Morgan & Zanotti, 1989). It appears that genuine spontaneous idiopathic Horner's syndrome does occur in animals, but this should not preclude the importance of investigating as far as possible the localisation of the lesion and any associated abnormality.

Careful investigations will tend to localise the site of the lesion affecting the sympathetic innervation to the eye resulting in Horner's syndrome in most cases, even if the cause of the lesion cannot be ascertained, as illustrated in the series described here. In some cases, clinical and careful neurological examination may identify the site of the lesion. However, pharmacological differentiation of the lesion to first, second and third order neuron lesions is useful where other signs are absent. Many different drugs and protocols have been described in the literature. Because of availability, in this study, it was decided to use phenylephrine 10% solution alone, following the protocol given by Petersen Jones (1989a). Reports of the use of phenylephrine and the interpretation of results are extremely variable in the literature (Neer, 1984; Kern & others, 1989; Petersen Jones, 1989a). The

specificity and accuracy of phenylephidine testing could not be commented on in these cases, where few cases were verified at post mortem and this was also the case in the series described by Kern and others (1989). It appears, however, in cases with complete Horner's syndrome, results of application of phenylephidine were very much quicker than 20 minutes, and in the cases reported here believed to be due to third order neuron lesions, the denervation supersensitivity was so marked, resolution of the anisocoria and the other signs were recognised within 20 - 30 seconds in cases 33, 34, 35 and 36. However, in case 30, where results indicated the presence of a second order neuron lesion, it would have been expected that retrobulbar trauma would have been responsible for the sympathoparesis from the history. More work, like that performed by Bistner and others (1970) with epinephrine, is required to document to accuracy and specificity of phenylephidine as localisation aid.

Case 34 was prescribed phenylephidine 10% to improve cosmetic appearance and aid vision. However it may be argued that continued use of the drug in anticipation of neuronal regeneration may prevent disuse atrophy of the smooth muscle (Wowk & Olson, 1979). Neuronal regeneration is said to occur within 1 - 6 months if at all (Wowk & Olson, 1979).

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