Chapter 1 'Is it Neurological?'

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The first step to any neurological evaluation of a veterinary patient, and probably the most common question we are asked by practitioners (in a variety of different ways), is whether the problem facing them is partially or completely neurological. In order to answer this question, it is important to understand the nature of the problem from the point of view of both the animal and the owner, and furthermore to understand what is meant by the question 'Is it neurological?'. For example, when presented with a dog that is showing signs of exercise intolerance, one possible reason may be a neuromuscular disorder, such as myasthenia gravis. However, this dog may present with a completely normal neurological examination, and the clue may be in the presenting clinical signs or medical work-up. Therefore, in such a case the initial answer may have to be 'It might be'. A dog whose problem is intermittent 'episodes' of abnormal behaviour may be having seizures, but might also be suffering from syncope, a compulsive behavioural disorder, or a movement disorder. All of these possibilities may in some way be classified as 'neurological' problems, but with very different aetiologies, treatment possibilities, and prognoses. The goal of this book is to allow practising vets to feel confident that they are approaching potentially neurological problems in a reasonable and evidence-supported way. The first step in this process is learning how to recognise when a particular presentation may be caused by a disease process somewhere within the central nervous system (CNS) or the peripheral nervous system (PNS).

1.1 What Is the Problem?

One of the key skills to be developed in general practice, as well as referral practice, is learning how to control the consultation in order to establish what the client's primary concern is, what they hope to achieve from their visit with you as the veterinarian, and how their expectations match up to their ability and/or

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willingness to afford and allow potential investigations and/or treatments to be performed. This is not an easy skill, especially for the GP vet who may have very limited time in which to carry out the initial consultation. It is, however, key to both ultimate client satisfaction and to providing the most effective service to the animal patient. Without establishing these essential facts, much time can be wasted. In the worst case the client's real concerns may not be addressed at all, meaning that they may leave the practice dissatisfied, perhaps with good reason.

Top tip: Always ask the client directly why they have come to see you today.

Don't make this mistake: Take care not to become side-tracked by a problem which may be very interesting to you, but is possibly chronic and completely unrelated to the reason for the visit!

1.2 Is this Problem Neurological?

There are many possible manifestations of neurological disease, some of which are much easier to recognise as neurological than others. There are also many non-neurological diseases which can mimic a problem involving the nervous system. In this section, we will look at the scope of neurological disease manifestations that the clinician may be presented with and we will aim to provide some clues as to the correct recognition of neurological disorders.

1.3 Neuroanatomy

When attempting to decide whether the problem is neurological, it is important to be aware of the different parts of the nervous system and how disease processes may affect them. Broadly we are concerned with the CNS (the brain and spinal cord) and the PNS (consisting of the peripheral nerves and muscles and the neuromuscular junctions between them). In the brain we can generally distinguish clinical signs referable to the forebrain, the brainstem, and the cerebellum.

The forebrain is known as the prosencephalon, and can be further divided into the telencephalon, which consists of the cerebral hemispheres, and diencephalon, containing the thalamus and the hypothalamus. The group of clinical signs which are commonly caused by lesions affecting the forebrain are sometimes referred to as a prosencephalic syndrome, and include behavioural change, central blindness, and seizure disorders in particular.

The brainstem consists of the midbrain (mesencephalon), the pons (ventral metencephalon), and the medulla (myelencephalon). Disease of the brainstem

also leads to characteristic signs, which can be used to anatomically localise the problem, including proprioceptive deficits and ataxia, sometimes clusters of cranial nerve signs, vestibular syndrome, and mentation change associated with dysfunction of the ascending reticular activating system.

The third major division of the brain is the cerebellum (dorsal metencephalon), and lesions in this region can lead to some of the most recognisable abnormalities in the neurological examination, including hypermetria and intention tremor.

The medulla is contiguous with the spinal cord, which can be divided into a series of segments from which a pair of spinal nerve roots arises, one pair for each segment. For neuroanatomical localisation purposes, the spinal cord segments are grouped together according to their motor function, and whether or not they contain the cell bodies of the nerves which directly supply the skeletal muscles of the limbs (known as lower motor neurons, LMNs). In this regard, the first five cervical spinal segments (C1–C5) contain only the so-called upper motor neurons (UMNs) which run from the gait-generating centres of the cerebral cortex and brainstem to the LMNs innervating the limbs and other structures. Spinal cord lesions affecting segments in this region lead to a characteristic set of neurological examination findings involving UMN effects in all four limbs.

The sixth, seventh, and eighth cervical segments, along with the first two thoracic segments, C6–T2, contain the LMN cell bodies supplying the thoracic limbs, as well as UMNs to the pelvic limbs; lesions here cause a so-called LMN paresis or plegia (paralysis) of thoracic limbs and an UMN paresis/plegia of the pelvic limbs.

Lesions in spinal segments caudal to the second thoracic segment will generally only affect the pelvic limbs, and the division between UMN and LMN here occurs between the third and fourth lumbar segments. Hence, lesions affecting the T3–L3 spinal cord segments lead to UMN paresis of pelvic limbs, whereas lesions caudal to L3 (L4–S3) cause LMN paresis/plegia of the pelvic limbs.

As well as the descending motor tracts within the spinal cord, there are of course ascending sensory tracts including those carrying proprioceptive information from the limbs and trunk; therefore, a spinal cord disorder will usually lead to variable degrees of ataxia and proprioceptive dysfunction, as well as the paresis associated with the loss of motor function.

The final part of the nervous system within which we can make an anatomical localisation consists of the peripheral nerves, neuromuscular junctions, and muscles. Lesions affecting this neuromuscular system tend to lead to more obvious weakness and LMN paresis/plegia affecting all limbs. Therefore, syndromes such as weakness, stiffness, exercise intolerance, and collapse may all arise as a result of disease affecting this PNS.

The neurological examination and neuroanatomical localisation of specific lesions will be explored and explained in more detail in Chapters 3 and 4, but an understanding of the anatomical structures involved in neurological disorders is

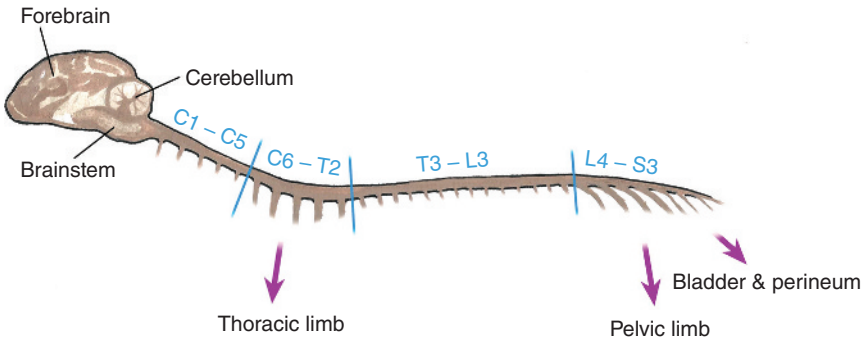

Figure 1.1 Neuroanatomical regions. The aim of the neurological examination is to localise the site of a lesion into the brain, the spinal cord, or peripheral (neuromuscular) regions. Functionally, the brain is separated into the forebrain, brainstem, and cerebellum; the spinal cord into sections containing the segments 1st cervical – 5th cervical (C1–C5), 6th cervical – 2nd thoracic (C6–T2), 3rd thoracic – 3rd lumbar (T3–L3), and 4th lumbar – sacral (L4–S3); and the peripheral nervous system consists of peripheral nerves, with the neuromuscular junctions and muscles also considered as a potential neuroanatomical localisation.

an essential part of the ability to recognise when one is facing a neurological problem (see Figure 1.1).

1.4 Manifestations of Diseases of the Nervous System

Disorders that affect different parts of the nervous system may manifest themselves in a wide variety of ways. In this section, we will briefly look at each of these, with the most important and more common problems being examined in greater detail in Chapter 6. The majority of nervous system disease will result in one or more of the following clinical presentations, some of which can be more easily defined and recognised than others. Where relevant, non-neurological disorders that can mimic or also result in these clinical presentations will also be mentioned:

- seizures
- collapse
- movement disorder/dyskinesia
- mentation change
- behaviour change
- blindness
- deafness
- tremor
- paresis/plegia
- ataxia

- abnormality of head position (head tilt/turn)
- abnormality of eye position or movements
- hypaesthesia
- lameness
- pain
- disorders of micturition/urination.

1.4.1 Seizures

For the purposes of this text, an epileptic seizure will be defined as an acute onset of excessive and hypersynchronous brain activity that results in transient visible motor activity; this description does not allow for so-called 'absence seizures', where a person may become transiently 'absent', since no motor activity is seen in such a seizure. However, such seizures, although they may occur in cats and dogs, are very difficult to diagnose without the help of an electroencephalogram (EEG).

It is rare that an affected animal will seizure during the consultation, so usually we rely on owner description and often video evidence when trying to decide if a problem is truly an epileptic seizure or some kind of seizure mimic. A generalised seizure is normally easily recognisable (see Video 1); the seizure may begin with a focal contraction of, for example, the facial muscles, but this rapidly spreads to cause loss of conscious state and tonic contraction of all the anti-gravity muscles leading to recumbency. There follows a period of tonic and clonic muscle activity causing running-like movements, and there may be vocalising, hypersalivation, jaw champing, and often urination or defecation. The tonic-clonic movements gradually subside and the animal will frequently adopt paddling movements as consciousness returns and attempts are made to stand. There will usually then follow a post-ictal period, which may last for minutes or hours, when the animal may show varying levels of altered behaviour, circling, ataxia, blindness, and other neurological abnormalities.

Focal seizures may involve simple focal muscle twitching, commonly of the orofacial muscles (see Video 2), but may also include more complex patterns of movement and/or behaviour – leading to apparent loss of consciousness and awareness. Such activity can be very difficult to distinguish from obsessive behavioural abnormalities and movement disorders for instance, but there are some key indicators which may be helpful in recognising when a problem is a true focal epileptic seizure (see below). A specific form of focal seizure is the myoclonic seizure, characterised by jerky twitches resembling the dog being fearful of a sudden stimulus, and seen especially in the genetic storage disease of Miniature Wire-haired Dachshunds, Beagles, and Bassett Hounds known as Lafora Disease (see Video 3).

Epilepsy implies a tendency for seizures to recur and can be further classified as 'reactive/metabolic', when there is an extracranial cause, 'structural', when there is an abnormality of brain structure such as an inflammatory or neoplastic lesion, and 'idiopathic', when brain structure is normal.

It is important to try to ascertain whether the abnormal event described by the owner or captured on video is an epileptic seizure or not. This is because the occurrence of true seizures implies a possible prosencephalic or forebrain lesion and dictates a certain path of investigation. The initiation of antiepileptic medication is always a subject for discussion and consideration, since all antiepileptic drugs (AEDs) can have undesirable side-effects, and their use in non-seizure disorders is usually contraindicated.

The description above contains some clues to the features of epileptic seizures that can be used in order to ascertain whether the event described is truly an epileptic seizure or represents a 'seizure mimic'. These include:

1. *Presence of post-ictal signs*. This is common and can include ataxia, blindness, polyphagia, or a temporary character change such as becoming aggressive.
2. *Presence of autonomic signs during the event*. In itself this is not necessarily pathognomonic for an epileptic seizure, but involuntary salivation, urination, and/or defecation is more common in seizure events than syncope, and is rarely observed for movement disorders.
3. *Absence of consciousness during the event*. It can be difficult to be sure about this, especially in mild focal seizures. However, the ability to rouse an animal from the behaviour, as is the case for idiopathic head-bobbing for instance, is an indication that the event is probably not a seizure.
4. *Presence of some form of tonic muscular activity, twitching, or stiffness*.

There are many other causes of paroxysmal transient events, or 'seizure mimics', and these should always be considered when trying to decide whether or not we are dealing with an epileptic seizure. These include:

- *Syncope, which may have a cardiovascular or respiratory cause*. Most cases of syncope result in a flaccid collapse, but this is again not always the case, and there is a significant 'grey zone' of signs seen with seizures and syncope which can make them difficult to distinguish. This is also the case in human medicine, with a significant percentage of people being diagnosed with epilepsy when in fact they are suffering syncopal attacks.
- *Dyskinesia or movement disorder*. These paroxysmal disorders of movement are being increasingly described, often with specific breed associations. Examples include the epileptoid cramping syndrome of Border Terriers (which has been associated with a gluten sensitivity and recently renamed paroxysmal gluten-sensitive dyskinesia, see Video 4) and episodic falling in Cavalier King Charles Spaniels (CKCSs), which has a known genetic mutation associated with it. Although these syndromes are fairly well described, the fact that the CKCS also suffers with idiopathic epilepsy can make this an even more complicated picture in this breed.

- *Behavioural events*. These are often described as obsessive compulsive or OCD behaviours, such as some cases of so-called 'fly-catching'. The latter can also be a focal seizure, and has even been associated with floating bodies within the anterior chamber of the eye, or gastrointestinal pain (see Video 5).
- *Transient vestibular events*. Perhaps associated with transient ischaemic attacks or TIAs.
- *Narcolepsy/cataplexy*. This is a rare condition with a suspected genetic basis in certain breeds, but can look very much like the so-called 'drop seizures' described in humans (see Video 6).
- *Idiopathic generalised tremor syndrome* or so-called 'little white shaker disease' (see Video 7). This is an inflammatory condition of the CNS leading to a generalised tremor. The tremor can wax and wane, worsens with excitement, and is potentially confusable with an animal suffering with a prolonged seizure or status epilepticus, such as may be seen following exposure to certain toxic substances (e.g. aflatoxins or mouldy food).
- *Episodic pain*, such as that associated with some cervical intervertebral disc herniations, may cause episodic, short-lived behavioural and physical changes. The French Bulldog in particular seems prone to such manifestations (see Video 8).
- *Episodic collapse*, which may have a neuromuscular, metabolic, or orthopaedic cause; if recovery is rapid; such events may be mistakenly diagnosed as seizures.
- *Rapid eye movement (*REM*) sleep disorder*. This is a condition where affected dogs may suffer violent episodes of paddling and limb movement during periods of REM sleep (see Video 9). It has recently been shown to have a higher incidence in dogs recovering from tetanus (Shea et al. 2018).

Top tip: Seizures can have multiple causes but also have multiple mimics.

Careful observation of video footage, together with accurate history taking, is key to defining whether the presenting problem is truly a seizure.

Ultimately, the only sure way to define a seizure (currently categorised as a Tier 3 level of diagnostic confidence for idiopathic epilepsy) is by making EEG recordings of abnormal brain activity during the abnormal event. Even in specialist referral practice this is rarely an option, and therefore we are usually working at a lower level of confidence.

1.4.2 Collapse

Collapse implies a loss of extensor motor tone, and may be either intermittent or permanent. When an owner describes a problem of collapsing, usually they are referring to episodic collapse, since a permanent collapse is immediately obvious!

Differential diagnoses for intermittent collapse include seizures, syncope, narcolepsy/cataplexy, and metabolic disorders (such as hypoglycaemia). More permanent collapse may be caused by musculoskeletal and orthopaedic problems, inflammatory conditions such as polyarthritis or polymyositis, as well as medical conditions involving weakness, anaemia, or pain. Neurological causes of loss of extensor muscle tone or strength may include brain, spinal cord, and PNS disorders. The neurological examination is therefore key to identifying, firstly, whether the problem is neurological, and then obtaining a correct neuroanatomical localisation.

Care must be taken in interpretation of the findings of the neurological examination in cases of collapse; an animal which is suffering from shock, trauma, or acute pain may well show apparent neurological deficits without any neurological disease or pathology. Examples include animals in shock which apparently have poor proprioception and spinal reflexes, lack of menace response, and even absent deep pain response. Once the shock and pain has been appropriately managed, the neurological abnormalities may disappear.

Top tip: Be careful with interpretation of the neurological examination in severely shocked or traumatised animals.

Don't make this mistake: Diagnosing severe spinal trauma due to apparent loss of deep pain perception post-trauma, especially in cats following a road traffic accident. Once stabilised, the neurological examination may change, indicating a less severe injury.

1.4.3 Movement Disorders

Movement disorders are an increasingly recognised group of conditions which affect many dog breeds. These conditions involve abnormal muscular movements, occasionally episodes of collapse, but no change of consciousness or autonomic signs that may be seen in focal epileptic seizure events (see Video 10). Well-documented examples include episodic falling in CKCSs ('Collapsing Cavaliers'), paroxysmal gluten-sensitive dyskinesia of Border Terriers (epileptoid cramping syndrome or 'Spikes disease', see Video 4), 'Scotty cramp' in Scottish Terriers and 'dancing Dobermann' disease.

Some of these conditions have a known genetic cause, and a specific test may be available (e.g. episodic falling in Cavaliers), but for many there is no specific diagnostic test. Dancing Dobermann disease is suspected to be a polyneuropathy, Spike's disease has been shown to be caused by a hypersensitivity to gluten in the diet, and it may be that some so-called movement disorders are in fact focal seizures.

In all of these conditions, the neurological examination should be normal, and in general all investigations are likely to be unremarkable (with the exception of specific genetic tests for example). The diagnosis is often one of exclusion and pattern recognition, and for many of the conditions there is no specific treatment available.

Further discussion of movement disorders and how they may present in practice can be found in Section 6.2 'Movement Disorders'.

1.4.4 Mentation and Behaviour

Observation and recognition of changes in either behaviour or mentation can be crucial in recognising that one is dealing with a neurological problem. Mentation concerns the level of general alertness and is sometimes referred to as the *level* of mentation (as opposed to the *quality* of mentation, which may be better be understood as behaviour). Mentation levels can be categorised as:

1. *Normal*
2. *Obtundation*. A generalised reduction in level of alertness or interaction with the environment; an animal which appears to show an absence of the usual anxiety and stress associated with a visit to the veterinarian, a lack of normal interaction with the owner, a 'can't be bothered' or 'couldn't care less' attitude. There can clearly be a marked difference between mild and severe obtundation, and milder levels may be variously described as lethargy or depression, although these terms should be used with caution in animal species.
3. *Stupor*. This implies a level of mentation in which the animal is basically asleep or semi-asleep, and only arousable by a noxious stimulus.
4. *Coma*. An animal which is not rousable even by a noxious stimulus.

A change in the level of mentation frequently implies neurological disease; stupor and coma are most commonly seen in moderate to severe brainstem disorders where the ascending reticular activating system is affected. This causes a reduction in sensory input to the cerebral cortex. Forebrain disease may also cause altered mentation, and in particular pituitary macroadenomas can present with obtundation as the only neurological sign.

Focal cerebrocortical lesions more rarely present with obviously altered mentation although larger lesions may, including compulsive pacing or circling behaviour. Animals with generalised encephalopathies, such as those seen in portosystemic shunting for instance, often show an altered level of mentation, sometimes intermittently. Another important observation is that raised intracranial pressure (ICP) can affect mentation, and serial observation and monitoring of mentation level in animals with suspected head trauma or with other reasons for potentially raised ICP (usually as part of the modified Glasgow Coma Scale) is extremely important in allowing recognition of a deteriorating situation/rising ICP.

Top tip: Altered mentation may be the only sign of severe intracranial pathology.

It is also important to be aware that altered mentation can occur as a result of non-neurological disease. Animals which have significant medical disorders,

pyrexia, anaemia, or pain may in some situations show moderate to severe obtundation without any primary neurological disease. As already mentioned, animals which have suffered significant trauma or stress, for example after a road traffic accident, may also show an apparently reduced level of mentation. In these situations, mentation may be expected to improve if the underlying problems are corrected, and this should allow a reduced suspicion of the presence of a primary neurological disorder.

Changes in behaviour or the quality of mentation usually imply involvement of the cerebral cortex. Behavioural changes can be caused by many things, including ageing, stress, change of environment or home situation, metabolic disease, chronic pain, dietary change, etc. Therefore, taking a careful clinical history is crucial in cases where a change of behaviour forms part of the presenting complaint. If a more subtle behavioural change is reported during the history-taking related to the investigation of a problem for which altered behaviour was not immediately apparent, then this may raise the level of suspicion for a possible intracranial disease.

Altered behaviour is less commonly the primary clinical sign reported for neurological disease, possibly due to our relative lack of sensitivity as veterinarians and owners in being able to identify more subtle changes. However, there are occasions when an owner will have recognised a loss of learned behaviour, or a change in demeanour or willingness to play in their pet, and this may be significant. As already stated, neurological disease leading to behavioural change usually implies a prosencephalic lesion and, in such situations, careful performance and interpretation of the neurological examination may identify other abnormalities consistent with a lesion affecting the cerebral cortex.

1.4.5 Blindness

An acute onset of blindness is usually noticed by pet owners, since it may be extremely disorientating for the affected animal, and may lead to behavioural changes as well as more obvious signs such as bumping into objects. It is often the case that vision is lost progressively rather than acutely, but in these situations owners frequently do not notice the more subtle changes brought about in their pet by a reduction in the quality of their vision, and it is only when the problem has progressed to complete or near-complete blindness that the owner becomes aware. When presented with an animal with reduced vision, it is therefore important to question the owner carefully in order to elucidate whether the visual loss may in fact have occurred progressively rather than acutely.

A blind cat or dog may be reluctant to move around, become ‘clingy’ or fearful in situations where they were previously relaxed and confident, and may even develop obsessive or phobic behaviours. For neuroanatomical evaluation, the important thing to establish is whether the blindness appears peripheral or central. Central blindness implies dysfunction of the central visual pathways and/or visual cortex; this is usually rare in the absence of other signs of intracranial

disease. More commonly, vision may be lost in one eye as a result of a lesion affecting the contralateral visual cortex, but as vision remains normal in the other eye, the owner either may not be aware of the vision loss or may have noticed the animal bumping into objects on only one side. The menace response will be absent in the affected eye, but the pupillary light reflex (PLR) (as well as palpebral reflex and other cranial nerves) are likely to be normal. Use of the so-called 'cotton-ball' test (see Chapter 3) may also help to identify visual loss in one eye.

In general, animals that present as completely or almost completely blind with no other neurological abnormalities, will have lesions affecting either the optic nerves or the eyes themselves. In the case of ocular disease, if there are no grossly obvious abnormalities such as cataracts, then the retina is the region most likely to be affected. A fundic examination should be performed and may reveal evidence of retinal disease or detachment. In the absence of an obvious cause for sudden blindness, then the two conditions which must be considered are sudden acquired retinal degeneration syndrome (SARDS) and optic nerve disease; optic nerve disease can have a number of possible causes (see Section 6.4 'Blindness').

SARDS is a syndrome that usually presents as an apparent acute onset of complete blindness, although careful history taking may reveal evidence that vision has deteriorated over a period of weeks. There is frequently an accompanying history of polyphagia, polydipsia, and polyuria and sometimes behavioural changes. Menace responses are absent bilaterally, and PLRs are reduced although may still be present to some degree. Routine biochemistry can reveal increased alkaline phosphatase and cholesterol, and there is often a high suspicion of hyperadrenocorticism although this is rarely confirmed. Despite the problem being associated with retinal degeneration of an unknown cause, fundic examination is usually normal at least in the early stages. Diagnosis can be made with a high degree of certainty from the history, physical examination, and biochemistry findings, but confirmation requires the presence of a bilaterally abnormal electroretinogram. The prognosis for return of sight is poor, although other systemic signs may improve over time.

The optic nerves can be affected by neoplastic disease that either infiltrates the nerves, such as lymphoma, or that compresses the optic chiasm, such as pituitary macroadenomas. Inflammatory disease affecting the optic nerves is more common and can be either confined to the optic nerves as the condition 'optic neuritis', or present as part of a more generalised inflammatory condition of the CNS (such as meningoencephalitis of unknown origin, MUO). In optic neuritis cases, it is sometimes possible to visualise swollen optic nerve heads during the fundoscopic evaluation. Other neurological abnormalities may be observed in cases with MUO, such as postural reaction deficits or other cranial nerve abnormalities. Cerebrospinal fluid analysis frequently confirms the presence of inflammation.

Top tip: Acute blindness with reduced or absent PLRs and no other physical or neurological abnormalities usually indicates either SARDS or optic neuritis. In both cases, the prognosis is guarded but diagnosis is worth pursuing because some cases of optic neuritis are responsive to immunosuppressive therapy.

1.4.6 Deafness

Deafness is a rare presentation in isolation, but owners may report behavioural changes which could imply that deafness or reduced hearing may be present. Bilateral hearing loss may be very significant to the lifestyle and behaviour of individual animals, and its effects should not be underestimated. Unilateral deafness is more challenging to detect and may be more debilitating than is currently thought as a result of an inability to localise the source of sounds. Deafness is a difficult neurological deficit to confirm clinically, but careful testing may lead to a high index of suspicion. As with other conditions, careful clinical history taking may provide some clues as to the origin of the deafness. Physical examination should obviously include an examination of the external ear canals. Neurological examination may reveal other abnormalities which can give clues as to the origin of the deafness (e.g. vestibular signs, facial nerve paralysis, and Horner syndrome may all be associated with otitis media/interna).

Confirmation of deafness requires electrodiagnostic evaluation through the recording of brainstem auditory evoked responses (BAER). Deafness may be either conductive, associated with abnormalities of conduction of sound waves to the receptors in the inner ear (e.g. accumulation of debris in the external ear canal or fluid accumulation in the tympanic bulla), or sensorineural, associated with a problem in the cochlea of the inner ear or the cochlear nerve itself.

1.4.7 Tremor

Tremor associated with neurological disease can be broadly divided into head tremor and whole-body tremor. Head tremor is most commonly associated with cerebellar disease (see Video 11), when it may be permanent, but tremor often becomes more severe when an affected animal attempts to perform some action involving the head, such as eating or drinking (termed an 'intention tremor'). The tremor may be very mild and subtle, and occasionally has not been appreciated by the owner. If a head tremor is observed in the consultation, then a full neurological examination should be performed, particularly to look for other signs consistent with cerebellar disease.

A slower head 'tremor' known as idiopathic head bobbing is occasionally seen, particularly in young Boxers and English Bulldogs (see Video 12). The cause is unknown, the problem is intermittent, and is generally self-limiting. All investigative and diagnostic tests tend to be normal in affected dogs, and the head-bobbing movements may be vertical ('Yes') or horizontal ('No'). Affected dogs can usually be distracted during an episode; when distracted the head

bobbing will cease, and this can be used to distinguish this paroxysmal occurrence from a focal seizure.

Whole-body tremor is an uncommon presentation, but when seen can be severe and debilitating. The two most common forms of whole-body tremor are that associated with toxin ingestion (particularly tremorgenic mycotoxins found in mouldy food, metaldehyde, chocolate, and some prescription medications) and idiopathic generalised tremor syndrome (see Section 6.2 'Movement Disorders' and Video 7). Tremors resulting from toxicity usually affect the whole body, can be severe and unremitting, do not subside with recumbency, and may occasionally progress to generalised seizures. This is a neurological emergency and requires emergency treatment to prevent hyperthermia and hypoglycaemia. Diagnosis generally relies on thorough history taking and the clinical presentation.

Another type of tremor that may be encountered is orthostatic tremor. This type of tremor predominately affects the limbs in large and giant breed dogs (particularly Great Danes) and is present only when the limbs are weight-bearing (see Video 13). The condition is benign and there is no treatment. Occasionally, a limb tremor may be associated with orthopaedic disease, especially if there is significant muscle atrophy or pain. It can also occur in some older dogs, apparently as part of an ageing process, and this is termed an 'essential' or 'senile' tremor (see Video 14).

There are a few conditions affecting the myelination of axons which present as whole-body tremors in young puppies around 6–8 weeks of age. Breeds that are typically affected include the English Springer Spaniel, Chow, Samoyed, Weimaraner, and Dalmatian.

Top tip: The major differential diagnoses for an acute onset of generalised tremor in an adult dog are toxin ingestion and idiopathic generalised tremor syndrome ('little white shaker' disease); in the former the tremor is persistent and severe, in the latter it may wax and wane and disappears when the dog is at rest.

1.4.8 Paresis/Plegia

Paresis can be defined as a reduced ability to initiate or maintain motor activity. It may manifest as a reduced ability to support weight (LMN paresis) or a reduced ability to generate gait (UMN paresis). Plegia is defined as an absence of voluntary movement (i.e. paralysis). A plegic animal usually indicates that severe CNS injury has occurred, either at the level of the brainstem or neck for tetraplegia or caudal to the T2 spinal segment for paraplegia. Paraplegia, involving only the pelvic limbs, is far more common than tetraplegia, partly because any lesion in the CNS that is capable of causing tetraplegia may be accompanied by other severe effects which may include respiratory failure and death. When an animal is presented in such a condition, particularly if there is a history of possible or

definite trauma, great care should be taken when moving the patient in case there is instability of the vertebral column and the potential for further spinal cord damage.

In an animal that is plegic (and only in these animals), it is necessary to include the testing of so-called 'deep pain perception' (DPP), which is the ability of the animal to recognise a noxious stimulus applied to the deep structures of the foot or toe (see Chapter 3). The loss of DPP is a poor prognostic indicator in many situations, since the sensory fibres that convey this information are carried in many tracts which are located deep within the spinal cord. Their loss may therefore indicate spinal cord damage at the deepest level. However, DPP is *not* likely to be lost in animals which have less severe spinal cord injury and remain paretic; testing for DPP therefore need not be performed in such animals.

The neurological examination is critical to being able to localise the likely anatomical location of any lesion causing paresis or plegia. This particularly includes an understanding of the spinal reflexes. It is still a common mistake to interpret the presence of a normal pedal withdrawal reflex as an indicator that DPP is present, and this can lead to overly optimistic prognosis being given to owners of animals with severe spinal cord injury (see Chapter 3 and Video 15).

Don't make this mistake: In paralysed animals, make sure you understand the difference between testing spinal reflexes and testing for deep pain perception (see Chapter 3).

Disorders affecting the PNS can present as a relatively acute onset of tetraplegia or severe tetraparesis. In this situation, the differentiation from a spinal cord lesion can usually be made by the fact that the neurological deficits cannot be explained by a single, focal CNS lesion as the spinal reflexes are reduced in all limbs. The major differentials for acute onset severe tetraparesis/tetraplegia localising to the PNS are acute canine polyradiculoneuritis, fulminant myasthenia gravis, and botulism.

Milder forms of paresis may be much more difficult to identify and a degree of paresis affecting one or more limbs may be the only sign of a neurological problem. Close observation of gait, including retrospective and slow-motion video analysis, may be helpful in identifying a reduction in the quality of movement. UMN paresis occurs when the control or initiation of movement is affected by a lesion that is affecting either the gait-generating regions of the cerebral cortex or brainstem or the spinal cord pathways containing the UMNs descending to synapse with the LMNs in the brachial or lumbosacral plexi. UMN paresis may lead to a long-strided gait, toe dragging, and postural reaction deficits, but the affected limbs retain normal spinal reflexes and are not weak. LMN paresis, by contrast, causes a paresis like that seen in PNS diseases, characterised by weakness, an inability to support weight, and a short-strided, choppy gait. For

lesions affecting the C6–T2 spinal cord segments, this can lead to the so-called 'two-engine' gait, with short, choppy thoracic limbs and long-striding, ataxic pelvic limbs.

Paraparesis can be misinterpreted as bilateral pelvic limb lameness of orthopaedic origin, and vice versa. Some conditions, such as hip dysplasia and bilateral cranial cruciate ligament disease, can present in a very similar way to a paraparesis caused by a spinal cord disorder. A knowledge of orthopaedic disease and a familiarity with basic orthopaedic examination is therefore important for the neurologist to avoid unnecessary investigative procedures resulting from a failure to recognise potential orthopaedic problems. Testing of postural reactions may allow recognition of a genuine neurological problem, but significant orthopaedic disease involving pain and a reluctance to bear weight may also complicate the interpretation of postural reaction testing. When in doubt, it may be wise to consult the opinion of an orthopaedic surgeon in these cases before assuming a neurological problem.

Don't make this mistake: An acute onset of bilateral cranial cruciate ligament failure can appear surprisingly similar to an acute T3–L3 myelopathy!

1.4.9 Ataxia

Ataxia is frequently, but not always, associated with paresis. Ataxia implies some disorder of coordination of movement, and there are three recognisable forms of ataxia that each suggest a lesion involving different parts of the nervous system. The observation of ataxia is highly suggestive of a neurological problem. However, as for paresis, some non-neurological problems can mimic ataxia if they significantly interfere with an animal's gait (e.g. bilateral cruciate ligament disease). The hallmark of ataxia is an unpredictability of limb placement, which is usually different to the predictable gait abnormalities observed in cases with lameness or orthopaedic disease.

The form of ataxia that is most commonly associated with paresis is a general proprioceptive ataxia (or 'spinal' ataxia, see Video 16). This occurs when a lesion disrupts the proprioceptive pathways in the spinal cord or brainstem, and is invariably therefore seen in conjunction with paresis. It may be symmetric or asymmetric, depending on the precise location of the lesion and, as for paresis, may affect all limbs or just the pelvic limbs. Attempting to differentiating between ataxia and paresis for lesions affecting the brain or spinal cord is neither necessary nor particularly useful; the most important thing is being able to recognise mild forms of either, which may give a clue to the possibility of a neurological condition as opposed to, for instance, an orthopaedic problem.

Lesions affecting the vestibular system result in a vestibular ataxia. This has a different quality to general proprioceptive ataxia, being caused in part by a loss of extensor muscle tone on the side of the lesion due to a reduction in the level of activity in the ipsilateral vestibulospinal tracts. This leads to a tendency

to collapse or fall towards the affected side, and sometimes tight circling towards that side; there is also a loss of balance associated with the vestibular disturbance, which increases the tendency to fall or lurch towards the affected side (see Video 17).

The third form of ataxia is caused by lesions of the cerebellum, resulting in a cerebellar ataxia (see Video 18). The cerebellum is intimately involved in the coordination of gait and movement, receiving proprioceptive information from the limbs and body, as well as from the vestibular system; this involves feedback loops with the gait-generating centres of the forebrain and brainstem, as well as having a significant inhibitory function on the vestibular nuclei of the brainstem. All of this explains the signs seen with cerebellar disease, including the intention tremor described above, the classical hypermetric gait, and the potential for vestibular signs. The gait of a dog with a cerebellar lesion may therefore have qualities of both vestibular and cerebellar ataxia, sometimes termed 'cerebellovestibular ataxia'. The hypermetria seen in cerebellar ataxia can affect all limbs but may also be confined to one side of the body, or even just one limb, depending on the precise location of the lesion. The other confusing aspect of cerebellar disorders, which can cause problems when trying to decide if the neurological deficits can be explained by a single lesion, is its involvement with the vestibular system; because the cerebellum receives some direct input from the peripheral vestibular system bilaterally, some cerebellar lesions will cause vestibular signs (such as a head tilt) on the same side as the lesion (ipsilateral). However, since the cerebellum itself has a primarily inhibitory influence on the vestibular nuclei of the brainstem, cerebellar lesions in specific locations may result in a so-called paradoxical vestibular syndrome, where the vestibular signs would suggest a lesion on the opposite side of the body to that of the actual lesion (see Chapter 4 and Section 6.8 'Cerebellar Dysfunction' for a fuller explanation, and Video 19). If this is not appreciated, then it may lead to the incorrect assumption that there must be a multifocal localisation, potentially suggesting a different set of differential diagnoses to a problem explained by a single (focal) lesion.

Top tip: Learn to recognise the three common forms of ataxia, as this provides a short cut to lesion localisation and assists with forming the list of differential diagnoses.

Don't make this mistake: Remember, pure cerebellar lesions may cause variable hypermetria, and either ipsilateral or contralateral vestibular signs.

1.4.10 Abnormalities of Head Position and Eyeball Position and Movement

1. Head tilt

Rotation of the head about the long axis of the body is known as a head tilt and is typically associated with disorders of the vestibular system or cerebellum (see above). The head is rotated so that the affected side is down relative to the midline,

such that the ear on the affected side lies at a lower level than that of the unaffected side (see Figure 1.2). This is indicative of a reduction in the influence of the vestibular system on the affected side. This also explains the so-called paradoxical head tilt seen with certain unilateral cerebellar lesions, where the head is tilted in the opposite way due to relative increase in influence of the vestibular system on the affected side brought about by a loss of inhibitory input from the cerebellum.

2. Head turn

Some unilateral forebrain lesions can cause a phenomenon known as a head turn. This occurs when the head remains level about its central long axis, but is turned to right or left, usually towards the affected side. It may also be associated with compulsive circling in the same direction and is thought to be caused by the loss of sensory input being perceived from the contralateral environment (i.e. the animal turns and circles towards the side from which it still perceives sensory information).

Figure 1.2 A Cavalier King Charles Spaniel with a left head tilt associated with a left peripheral vestibular syndrome caused by otitis media/interna.

3. Strabismus

This indicates an abnormal position of one or both eyes and may be either static or positional. In a static strabismus, the eye is permanently positioned incorrectly, and this indicates a lesion affecting either the extraocular muscles or one or more of the cranial nerves supplying them (III, IV, or VI, see Chapter 3). The direction of the strabismus is governed by the precise loss of muscle function. A bilateral ventrolateral strabismus (so-called 'sunset sign') is seen in certain cases of severe hydrocephalus, and is thought to occur as a result of either changes in skull morphology or pressure on the oculomotor nuclei in the midbrain.

Positional strabismus occurs when an eye moves into an abnormal position only when the head position is changed. When there is a suspicion of vestibular syndrome it is necessary to elevate the head so that the affected animal is looking directly up at the observer. In this position, the eye on the affected side often assumes an abnormal ventrolateral position. This occurs due to loss of the ability to determine the new correct position of the eye when the head has been moved (see Section 6.7 'Vestibular Syndrome' for a fuller explanation).

4. Nystagmus

This is the phenomenon of rapid involuntary eye movements. Physiological nystagmus is seen in response to head movement, and is a normal phenomenon requiring the vestibular system and extraocular muscles to all be functioning normally (see Chapter 3). Pathological nystagmus occurs most commonly when there is an imbalance between the two sides of the vestibular system. This usually implies a unilateral vestibular lesion, and in this situation the movements are commonly described as a jerk nystagmus, with fast and slow phases in opposite directions. The direction of the movements may be horizontal, rotatory, and occasionally vertical. When it is possible to define the direction of each phase, the slow phase of movement tends to be directed towards the side of the vestibular lesion (see Video 20).

Pendular nystagmus is seen in some oriental cat breeds, especially Siamese cats. Affected animals show rhythmic, usually horizontal, eye movements at rest, with no fast or slow phase. This is considered normal in these cats, and does not appear to affect their quality of life. It is thought to occur as a result of an abnormal degree of crossing over of optic nerve fibres at the optic chiasm during embryological development (see Video 21).

Top tip: Be prepared to move an affected animal's head into abnormal positions to induce nystagmus or strabismus when there is a suspicion of vestibular disease; any abnormality of eye position or movement which occurs when the head is at rest is likely to be pathological and usually indicative of vestibular dysfunction.

Don't make this mistake: Pendular nystagmus can be a 'normal' phenomenon in certain pedigree oriental cats and is not always an indicator of vestibular disease.

1.4.11 Reduced Sensation (Hypaesthesia)

The skin is supplied with sensory receptors that are sensitive to pressure and deformation (mechanoreceptors), heat (thermoreceptors), and pain (nociceptors). These are relatively specific and respond only to the source of energy for which they are adapted. Each spinal cord segment receives information from sensory neurons that enter via the dorsal horn from a region of skin known as the dermatome. Along most of the trunk, this information is carried in cutaneous nerves which arise in a largely segmental fashion and form an important part of the cutaneous trunci reflex (see Chapter 3). Skin sensation in the limbs is transmitted via sensory neurons carried in the major peripheral nerves of the limb, most of which are mixed nerves carrying both motor and sensory fibres. In the limbs, much of the skin is supplied by more than one peripheral nerve. The area of skin supplied by a single nerve is divided into overlap zones around the edges; the specific regions in the centre supplied by just that nerve are known as autonomous zones (see Figure 1.3). A knowledge of these zones is important to allow for the identification of damage to individual spinal nerves or segments, for instance in the case of brachial or lumbosacral plexus injury.

Skin sensation from the face and head is carried largely within the different branches of the trigeminal nerve (V), including from the surface of the cornea. Identification of hypaesthesia on one side of the face can be indicative of a trigeminal neuropathy, sometimes in the absence of other signs. The only exception is the skin of the outer (concave) surface of the pinna, which is supplied by the auricular branch of the facial nerve (VII).

Loss of sensation from the inner medial surface of the nose (nasal planum sensation) may be useful in recognising the presence of a focal forebrain lesion. Touching the nasal planum induces a conscious reaction in the normal dog or cat, and lesions either of the ipsilateral trigeminal nerve or of the contralateral forebrain may lead to a loss of this response (see Chapter 3).

1.4.12 Lameness

Lameness represents a reluctance to bear weight on a limb. Lameness resulting from neurological disease (neurogenic lameness) can be very difficult to distinguish from orthopaedic lameness. Monoparesis may also appear very similar to a true lameness in many cases. Clues to the lameness having a neurogenic origin may include rapid muscle atrophy, reduced proprioception, toe dragging, and reduced spinal reflexes (particularly the pedal withdrawal reflex). However, in many cases electrodiagnostic testing and imaging are required for certainty of diagnosis. Neurogenic lameness can arise from a variety of causes, such as a lateralised disc herniation, peripheral nerve sheath tumour, neuritis, nerve trauma, and degenerative lumbosacral stenosis (DLSS).

DLSS is a common condition with a variety of causes in which the nerves of the cauda equina are variably compressed by adjacent structures at the level of the lumbosacral disc and intervertebral foraminae. These structures include the

intervertebral disc, bony structures, such as the articular facets, pedicle, and arch of the sacrum, and other soft tissue structures, including the interarcuate ligament and joint capsules. Because of the different functions supplied by the nerves of the cauda equina at this level, the presentations associated with DLSS can be variable and also similar to orthopaedic diseases such as hip dysplasia. Unilateral lameness may occur if there is significant foraminal stenosis leading to compression of the L7 nerve root which exits the vertebral canal at this level. Bilateral lameness, paresis, and stiffness, as well as pain, are also commonly seen. Ataxia is usually mild or non-existent in these cases.

1.4.13 Pain (Hyperaesthesia)

Pain can be very severe in neurological disease and may be the only presenting sign in some conditions. Pain is defined as the conscious awareness of a noxious stimulus, and requires a conscious response to stimulation of nociceptors. Detecting, interpreting, and localising the source of pain, even when one is reasonably certain it is present, can be a challenge. In some conditions, the pain may be focal but so severe that the animal responds to palpation in multiple regions of the body. At other times, multiple regions of the body may be genuinely painful, but this again may make the examination difficult to interpret.

In the authors' experience, when an animal presents with a history of crying or screaming in pain, a neurological cause should always be considered. There are very few conditions which will induce this reaction in an animal. Orthopaedic conditions, even including fractures, will rarely cause an animal to vocalise unless a peripheral nerve is involved in the fracture site. Visceral pain can be severe, but affected animals usually become dull and depressed rather than vocalise. The pain associated with mechanically pinching or stretching a peripheral nerve is extreme and acute, and is often associated with specific or sudden movements; this history should therefore lead to a high index of suspicion for a neurogenic origin.

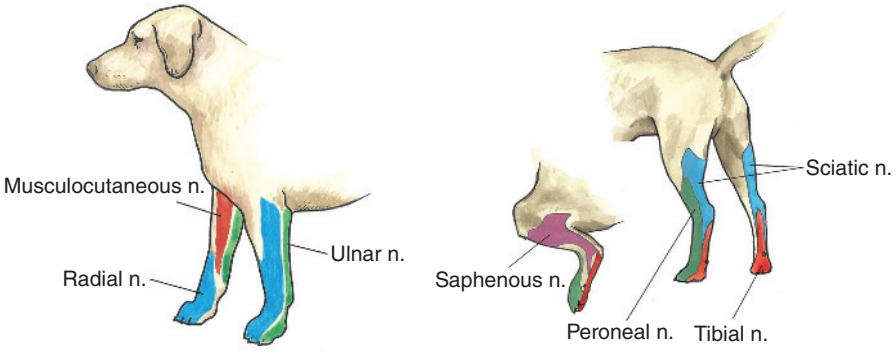

Figure 1.3 The cutaneous autonomous zones of the distal parts of the thoracic limb and the distal parts of the pelvic limb. A knowledge of these zones may assist the clinician in determining which peripheral nerves may be involved in a traumatic injury for instance.

Other potential sources of severe neurogenic pain include inflammation of the meninges, as seen in conditions such as steroid responsive meningitis arteritis (SRMA), stretching of the meninges and/or compression of the nerve roots in intervertebral disc herniation, atlantoaxial instability, certain spinal neoplastic conditions, and inflammation/infection of the intervertebral disc in discospondylitis. The nerves of the cauda equina and tail can be the source of severe pain associated with DLSS or other compressive or inflammatory lesions. In these situations, the presenting signs can be limited to behavioural change or extreme reluctance to lift the tail. An animal presenting with severe pain when defecating may have tail-base pain, which can be associated with intervertebral disc disease at this level. Severe inflammation of the epidural fat and meninges, such as in epidural empyema, may also cause severe pain.

Certain intraparenchymal spinal cord conditions such as syringohydromyelia can present with signs of intermittent crying in pain. In this situation, there appears to be an association with larger lesions and those affecting the dorsolateral horns of the spinal cord. In susceptible breeds, this diagnosis should be considered in an animal presenting with pain only.

When faced with a potentially painful animal, the physical examination becomes crucial in trying to locate the source of the pain, but as already stated this can easily be misinterpreted or misleading. Great care should be taken, and the examination initially performed gently and with minimal movements of head and/or limbs. The amount of movement and pressure applied by palpation can then gradually be increased. If a potentially painful region is identified (e.g. in the thoracolumbar region), the examination should focus on other parts of the body before returning to the suspected region in order to try to elucidate if this is really the source of the pain. Even with this approach, mistakes will be made!

Top tip: Always look for a neurogenic cause when presented with an animal with a history of vocalising in pain.

Don't make this mistake: Be prepared to repeat imaging when an animal remains persistently in pain and a cause of the pain has not been found. Non-displaced vertebral fractures can be missed!

1.4.14 Disorders of Micturition

The ability to pass urine can be affected by many neurological problems, although rarely in isolation. Spinal cord lesions (myelopathies), particularly severe lesions associated with intervertebral disc extrusion, are commonly associated with problems of micturition, and the anatomical level of the myelopathy dictates the nature of the dysfunction. It is necessary to have an understanding of the innervation of the bladder and urethral sphincters in order to appreciate why this is the case.

The bladder is innervated by the pelvic nerve which arises from the sacral spinal cord segments. This provides motor (parasympathetic) innervation to the smooth muscle of the detrusor as well as carrying sensory information from stretch receptors in the bladder wall. The external urethral sphincter (striated muscle) is supplied by the pudendal nerve arising also from S1–S3 spinal cord segments. This is also motor to the anal sphincter and carries sensory information from the perineum. These LMNs receive modulation from the UMNs arising from the micturition centre in the medulla (see Figure 1.4). Problems affecting the spinal cord segments cranial to S1 usually lead to a so-called UMN bladder, whereas problems caudal to L7 normally lead to a LMN bladder.

In the UMN bladder, loss of modulation of the LMNs leads to an increase in tone in both detrusor and external urethral sphincter. The result is a bladder which over-fills to the point at which the pressure from inside the bladder is enough to force leakage through the spastic urethral sphincter. The detrusor muscle can be stretched and, if not treated, irreversible detrusor muscle damage can occur, and this leads to irreversible incontinence.

In the LMN bladder, damage to the LMNs supplying both the detrusor and sphincter muscles leads to a flaccid bladder and sphincter, so that urine leaks out easily and the bladder remains small and flaccid. Lesions that cause this type of presentation usually also cause loss of anal tone, loss of perineal sensation, and,

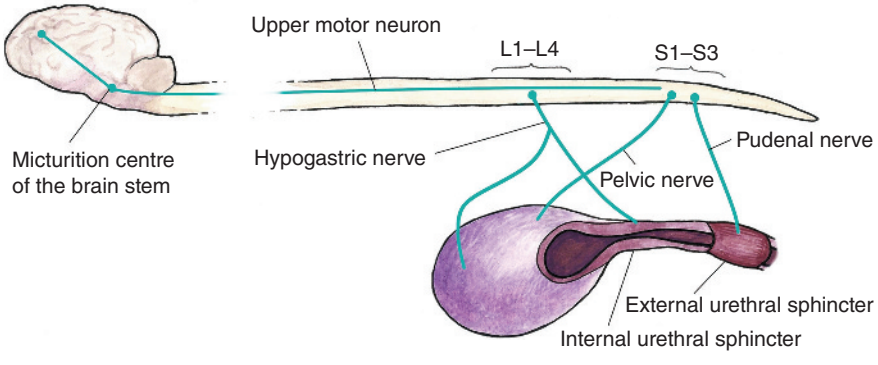

Figure 1.4 The innervation of the urinary tract. The bladder detrusor muscle is innervated mainly by the pelvic nerve (parasympathetic supply) originating in the sacral spinal cord segments (S1–S3), but also by the sympathetic nervous system via the hypogastric nerve, which originates in the lumbar spine. The pelvic nerve carries both motor fibres responsible for contraction of the detrusor muscle in micturition and sensory fibres responsible for detecting bladder wall stretching. In young animals, there is a simple reflex arc involving these fibres, meaning the bladder empties when it is full; in older animals, higher centres in the brainstem and forebrain lead to voluntary control of micturition and the possibility of 'toilet-training'. The external urethral sphincter is a skeletal muscle sphincter innervated by the pudendal nerve, arising from the sacral spinal cord (S1–S3); this nerve also receives upper motor neuron input, as well as carrying sensory information back from the sphincter. The internal urethral sphincter is a smooth muscle thickening of the urethral wall innervated by the sympathetic fibres of the hypogastric nerve.

sometimes, loss of tail function. The prognosis for return to function with this type of injury may be more guarded than for an UMN lesion. A common presentation of LMN bladder that does not always behave in this way is the so-called 'tail-pull' injury seen in cats, when a traumatic incident results in fracture/luxation of sacral or caudal vertebrae. In this situation, the bladder often becomes over-full, as in the UMN bladder, and is difficult to express. This is believed to result from on-going innervation of the internal urethral smooth muscle sphincter by the hypogastric (sympathetic) nerve which arises from more cranially in the lumbar spine. Interestingly, this phenomenon is rarely seen in dogs with fractures of the sacrum for instance.

Reflex dyssynergia is a disorder of micturition where the coordination between contraction of the detrusor muscle and relaxation of the urethral sphincters is lost. This leads to an inability to empty the bladder; the usual presentation is of an over-full bladder with no urethral obstruction and a history of straining and sometimes urine leakage or dripping. The cause of this problem is unknown, and treatment can be challenging.

1.5 Summary

It is clear that diseases of the nervous system may present in a wide variety of different ways, and this presents the first challenge to their diagnosis and treatment. Once it has been decided that a problem is likely to have a neurological origin, the next step is to use the neurological examination to decide where the lesion may be located within the CNS or PNS. It is only at this stage that further investigations should be planned. In the following chapters we shall attempt to present a logical and methodical approach to neurological disease, which should enable the practitioner to develop a good differential diagnosis list when faced with such problems. We also attempt to give sensible, practical advice to owners of animals affected by neurological conditions.

Bibliography

Amin, U. and Benbadis, S.R. (2019). The role of EEG in the erroneous diagnosis of epilepsy. *J. Clin. Neurophysiol.* 36: 294–297.

Añor, S. (2014). Acute lower motor neuron tetraparesis. *Vet. Clin. North Am. Small Anim. Pract.* 44: 1201–1222.

De Risio, L., Bhatti, S., Muñana, K. et al. (2015). International veterinary epilepsy task force consensus proposal: diagnostic approach to epilepsy in dogs. *BMC Vet. Res.* 11: 148.

De Strobel, F., Paluš, V., Vettorato, E., and Cherubini, G.B. (2019). Cervical hyperaesthesia in dogs: an epidemiological retrospective study of 185 cases. *J. Small Anim. Pract.* 60 (7): 404–410.

Díaz Espiñeira, M.M., Viehoff, F.W., and Nickel, R.F. (1998). Idiopathic detrusor-urethral dyssynergia in dogs: a retrospective analysis of 22 cases. *J. Small Anim. Pract.* 39: 264–270.

Forman, O.P., Penderis, J., Hartley, C. et al. (2012). Parallel mapping and simultaneous sequencing reveals deletions in BCAN and FAM83H associated with discrete inherited disorders in a domestic dog breed. *PLoS Genet.* 8: e1002462. https://doi.org/10.1371/journal.pgen.1002462 .Epub 2012 Jan 12.

Ives, E.J., MacKillop, E., and Olby, N.J. (2018). Saccadic oscillations in 4 dogs and 1 cat. *J. Vet. Intern. Med.* 32: 1392–1396.

Jeffery, N.D., Barker, A.K., Hu, H.Z. et al. (2016). Factors associated with recovery from paraplegia in dogs with loss of pain perception in the pelvic limbs following intervertebral disk herniation. *J. Am. Vet. Med. Assoc.* 248: 386–394.

Kitchell, R.L., Whalen, L.R., Bailey, C.S., and Lohse, C.L. (1980). Electrophysiologic studies of cutaneous nerves of the thoracic limb of the dog. *Am. J. Vet. Res.* 41: 61–76.

Komáromy, A.M., Abrams, K.L., Heckenlively, J.R. et al. (2016). Sudden acquired retinal degeneration syndrome (SARDS) – a review and proposed strategies toward a better understanding of pathogenesis, early diagnosis, and therapy. *Vet. Ophthalmol.* 19: 319–331.

Lowrie, M. and Garosi, L. (2016). Classification of involuntary movements in dogs: tremors and twitches. *Vet. J.* 214: 109–116.

Lowrie, M. and Garosi, L. (2017). Classification of involuntary movements in dogs: paroxysmal dyskinesias. *Vet. J.* 220: 65–71.

Lowrie, M., Garden, O.A., Hadjivassiliou, M. et al. (2018). Characterization of paroxysmal gluten-sensitive dyskinesia in border terriers using serological markers. *J. Vet. Intern. Med.* 32: 775–781.

Meeson, R. and Corr, S. (2011). Management of pelvic trauma: neurological damage, urinary tract disruption and pelvic fractures. *J. Feline Med. Surg.* 13: 347–361.

Platt, S.R., Radaelli, S.T., and McDonnell, J.J. (2001). The prognostic value of the modified Glasgow Coma Scale in head trauma in dogs. *J. Vet. Intern. Med.* 15: 581–584.

Rusbridge, C., Stringer, F., and Knowler, S.P. (2018). Clinical application of diagnostic imaging of Chiari-like malformation and syringomyelia. *Front. Vet. Sci.* 5: 280.

Shea, A., Hatch, A., De Risio, L. et al. (2018). Association between clinically probable REM sleep behavior disorder and tetanus in dogs. *J. Vet. Intern. Med.* 32 (6): 2029–2036.

Smith, S.M., Westermeyer, H.D., Mariani, C.L. et al. (2018). Optic neuritis in dogs: 96 cases (1983–2016). *Vet. Ophthalmol.* 21: 442–451.

Tipold, A. and Schatzberg, S.J. (2010). An update on steroid responsive meningitis-arteritis. *J. Small Anim. Pract.* 51: 150–154.

Walmsley, G.L., Herrtage, M.E., Dennis, R. et al. (2006). The relationship between clinical signs and brain herniation associated with rostrotentorial mass lesions in the dog. *Vet. J.* 172: 258–264.