Neurologic diseases are seen almost entirely as dysfunction rather than observable structural abnormalities. Neural function can be altered by disease of neural or surrounding tissues (vertebrae, skull, meninges etc), or by metabolic abnormalities or toxins without primary neural disease.

The likely causes of neurologic abnormalities should be considered prior to undertaking any ancillary diagnostic tests.
When confronted with any clinical abnormality it is useful to consider all the possible underlying causes. The DAMNIT (V) list can be useful (alternatively VITAMIN D)

D - degenerative
A - anomalous (developmental, congenital or inherited)
M - metabolic
N - neoplastic, nutritional
I - inflammatory, infectious, ischaemic (and other Vascular), idiopathic,iatrogenic
T - trauma, toxic

Think about what you are looking for prior to looking. As with all diagnostic processes the big picture should be looked at first (a differential diagnosis list drawn up) and narrowed based on signalment, likelihood of a particular diagnosis and the results of selected diagnostic tests or possible treatments. Depending on the severity of neurologic deficits and the likely differential diagnoses further diagnostic tests or treatment can be recommended. In most cases it is not possible to definitively differentiate between possible causes just based on neurologic findings. Haematology, biochemistry profile, serology, advanced imaging (MRI or in some cases CT) and CSF analysis may be required to arrive at a more definitive diagnosis. A definitive diagnosis may not be possible without histologic examination (pre or post mortem) and treatment in many cases is instituted on best guess (most likely).

The expense and invasiveness of diagnostic tests should also be considered and the decision to pursue particular diagnostic tests (eg CSF collection, advanced imaging) made based on likely information gained (ie is it going to change the way I manage this case) vs potential risks. The prognosis associated with various neurologic diseases should also be considered prior to embarking on often expensive diagnostic testing. But all diagnostic options and possible treatments should be presented to owners.

Despite many neurologic syndromes presenting with severe and often distressing clinical signs it is often the most acute and severe neurologic diseases that have the best prognosis. Early investigation and / or appropriate treatment is also very important and empiric treatment and “seeing how things go” may result in further neurologic deterioration that is irreversible - this is especially true of compressive spinal cord disease (acute IV disc extrusion) and of inflammatory CNS disease. However some
diseases present with very typical neurologic signs (pattern recognition here) and may be treated on index of suspicion without further diagnostic tests. Some diseases require extensive and possibly surgical treatment and others require no treatment but nursing and time (which may be weeks to months).

Signalment: Some diseases are more likely to occur in some breeds and in animals of a certain age however almost any disease can be seen in any breed of any age. Neoplasia is more common in dogs 7 years of age and older however brain tumours can be seen in dogs < 2 years of age. GME is more commonly seen in toy and terrier breeds however it is the most common cause of inflammatory disease of the brain and spinal cord in dogs of all breeds and ages (where distemper is unlikely). Metabolic disease eg hepatic encephalopathy is most commonly seen in young dogs with portosystemic shunts however PSS s may not be recognized until dogs are much older (even >10 years of age). CVAs are more common in older dogs but may be seen in young active dogs with no underlying predisposing cause established. Acute IV disc extrusion is most commonly seen in chondrodystrophoid breeds but can be seen in kelpies or Dobermans. Discospondylitis is most commonly seen in medium to large breed dogs >1 year of age but can be seen in dogs less than a year of age.

History
- Presenting complaint
  - onset (acute, subacute, chronic) days, weeks, months, years.
  - Progression (static, worsening, improving)
  - Any pain associated with clinical signs
- Physical exam
  - Complete neurologic exam – multifocal disease process?
  - There are typical cases and not so typical cases

Neurologic abnormalities may be associated with diseases of other organ systems or generalized disease. Coagulopathy (rodenticide toxicity, IMTP etc) may result in subarachnoid, ventricular or parenchymal haemorrhage. Neoplasia may be associated with metastasis to brain, spinal cord, vertebrae or skull. Systemic infection may result in bacteremia, and endocarditis may cause septic embolism in the brain. Cardiomyopathy may result in aortic/femoral/brachial or cerebral thromboembolism. Metabolic encephalopathy and/or neuropathy may result from liver, renal, adrenal or thyroid disease and hypoglycemia associated with insulinoma.

A complete blood count and biochemistry profile are indicated in most animals that present with clinical signs of brain, spinal cord or motor unit disease.

Clinical signs of metabolic abnormality are generally symmetric and diffuse however different neuronal populations may have different sensitivities to metabolic derangement for example cortical blindness is most common sign seen as a result of hypoxia (eg as a result of anaesthetic accident). However some may produce focal (but usually symmetric neurologic abnormalities eg thiamine deficiency in small animals often causes acute onset of bilateral central vestibular signs.

Cerebral energy requirements are the highest of all body tissues with glucose the primary energy source. Cerebral metabolic systems have a limited ability to utilise glycogen and ketoacids. Normal CNS neuronal activity relies on a stable extracellular environment with a constant source of glucose and O2, is controlled with respect to osmotic, ionic and acid-base balance and is safe guarded from potential toxins. Most metabolic encephalopathies alter consciousness- with
confusion, altered behaviour, delirium, obtundation, stupor, coma seen. Abnormal pupillary light reflexes, abnormal pupil size (miosis or mydriasis), gait abnormalities, abnormal respiratory patterns, seizures may also be seen. Blindness is common. Hypoglycemic and hypoxic animals may be extremely anxious and/or weak. Hypocalcemic small animals are often apprehensive, restless and show muscle fasciculations. Cows with hypocalcaemia are weak. Ptyalism (salivation) is commonly seen associated with hepatic encephalopathy especially in cats.

Generally there are no abnormalities on physical examination or on haematology or biochemistry profile in many dogs with meningoencephalitis (infectious or immune mediated) and many affected cats (with the exception of FIP). Pyrexia may be seen but is uncommon. Bacterial infections (empyema or brain abscess associated with penetrating wounds or foreign bodies, or extension from middle ear or orbit) and septic embolism or bacteremia may or may not be associated with a peripheral increase in WBC count or any other evidence of acute or chronic infection (monocytosis/reduced platelet number etc) in all species.

Inflammatory diseases of the CNS can affect the brain, meninges and/or the spinal cord. Most disease processes causing meningitis also cause an associated encephalitis and/or myelitis in animals. Typically animals with CNS inflammatory disease present with an acute onset of multifocal CNS signs (brain or spinal) and hyperaesthesia (cervical or thoracolumbar). However a more chronic progressive history (months or in some cases years) is seen in many cases and in a study of inflammatory disease in dogs two thirds presented with focal neurologic signs. Animals with meningitis often have severe neck pain, hunched posture and show reluctance to move and a stiff stilted gait. Non infectious and presumed immune mediated forms of meningoencephalomyelitis (GME, NME, MUA) are much more common in dogs than infectious causes. Infectious causes are more common in cats, horses cattle etc.

Serologic tests for specific viral, fungal and protozoal diseases can be useful in the diagnosis of specific infections.

Imaging - Radiography
Neoplasia may be metastatic. Thoracic radiographs or CT are indicated in animals with intracranial disease that are 7 years of age or older or in any animal where metastatic tumour is suspected. Abdominal ultrasound may also be considered in older dogs especially those breeds with a higher incidence of abdominal tumours such as haemangiosarcoma (German Shepherds, Australian Cattle dogs etc).

Imaging is only useful if the causative lesion is within the field of view that is imaged. Neuroanatomic localisation of neurologic deficits is therefore important. However localisation may be difficult and all areas that may cause the neurologic abnormalities should be considered. Spinal radiographs will only show vertebral abnormalities and are not predictive in most cases of spinal cord lesions. Extensive spondylosis on radiographs is rarely associated with spinal cord compression and neurologic deficit. Narrowing of an IV disc space is poorly correlated with IV disc extrusion and spinal cord compression. Further imaging (myelography, CT and myelography or MRI) is required in most cases to determine spinal cord lesions (exception - fractures, vertebral instability, discospondylitis and large vertebral tumours causing osteolysis or excessive mineralization).
With suspected spinal cord disease, once a lesion is localised to a particular region of the spinal cord the relationship of the spinal cord to the surrounding vertebra has to be considered when planning any imaging. Not all spinal cord segments are contained within the vertebra of the same number. In the cervical region there are 7 vertebrae and 8 spinal cord segments. Generally each vertebra contains the spinal segment one number higher. Therefore lesions as far cranial as C4-C5 vertebrae may cause LMN deficits in the thoracic limbs (contain spinal cord segments C6).

The lumbar cord segments (L4 Caudal 5) lie in the vertebral canal of the L3 - L5 vertebrae in most dogs. The spinal cord ends at L6 vertebra in most dogs and L7 in cats.

The cauda equina (lumbar, sacral and caudal nerve roots) lies in the vertebral canal from L5 vertebra caudally and nerve roots exit at the intervertebral foramina caudal to the vertebra they are named after, eg. spinal nerve L7 exits at the L7-S1 intervertebral foramen.

Lesions of the cauda equina result in the same clinical signs as lesions of the spinal cord segments from which the nerves arise (L6 - Cd5). In other words LMN signs in the pelvic limbs can be due to a vertebral lesion anywhere caudal to L3. This needs to be considered when any imaging is undertaken in animals suspected of having cauda equina lesions.

When undertaking any diagnostic tests in animals with neurologic abnormalities imaging of the entire spinal segment (and in some cases caudal brainstem) that could account for an animals neurologic deficits should be done (radiographs, CT, myelography or MRI) for example radiographs or CT of the spine from at least C5 - sacrum should be taken in animals presenting with hind limb neurologic abnormalities. HL abnormalities only are common in animals with caudal cervical or cranial thoracic lesions. Poorly positioned radiographs or radiographs that don’t include all of the area that may cause the neurologic abnormalities are a waste of time and owners money.

For spinal radiographs:
- **GA required for necessary positioning unless trauma or vertebral instability known /suspected**
- **survey radiographs should be taken of all of spine enclosing the spinal cord segments that may be affected (that would account for the neurologic signs seen) that is the whole spine in animals with cervical signs and to the level of C4 in animals with T3-L3 signs**
- **Cranial lesions may mask more caudal lesions**
Skull radiographs are of little value in assessing animals with clinical signs indicative of brain disease; however, tumours and some infective processes of the skull, nasal cavity and middle ear may extend intracranially causing neurologic signs without any other clinical signs and radiographs may show evidence of osteolysis, proliferative bone or abnormal soft tissue densities. Increased bone density and thickening (hyperostosis) of the overlying calvarium may be evident on skull radiographs of cats with meningiomas.

Computed tomography (CT) is very useful in assessing vertebral diseases and IV disc extrusion.

- Is a radiographic technique
- Transverse images are visualised
- Images can be obtained rapidly
- May require subarachnoid injection of contrast to delineate spinal cord—less contrast required than myelography
- Is the imaging technique of choice for bony lesions and more sensitive than conventional radiographs in determining osteolysis, mineralisation and soft tissue delineation.

Computed Tomography (CT) is much less sensitive in evaluating the brain especially in evaluating caudal fossa lesions (beam hardening artifact). “Mass effect” deviation of the falx or disruption of normal brain anatomy may be seen on CT and lesions may be visible after the administration of contrast however detail provided by MR is vastly superior. Contrast enhancement may (or may not) be seen with neoplastic, inflammatory, infectious or vascular disease.

Computerised tomography (CT) is a better imaging technique than MRI for evaluation of bony lesions of the skull.

Magnetic Resonance Imaging (MRI) is the most sensitive imaging technique in evaluating the CNS. MRI will identify structural abnormalities such as congenital malformations and shifts in brain mass (e.g., potential brain herniation, midline shifts associated with expanding mass lesions), and will demonstrate mass lesions and soft tissue changes associated with vascular and inflammatory disease. Higher strength magnets (1.0T, 1.5T) allow better imaging of inflammatory lesions than low strength magnet MRI. There is however no “definitive” MRI picture and inflammatory, infectious, vascular or neoplastic lesions may be indistinguishable on imaging however many lesions have highly suggestive MRI appearances. Different imaging sequences—T1, T2, FLAIR, STIR, gradient echo and diffusion sequences are all used to highlight different tissues (fluid, fat, blood, white matter, grey matter). Intensity of each tissue on imaging depends on the sequence used. Administration of a paramagnetic agent (contrast) is used primarily to highlight tumours. Meningeal enhancement may be evident in inflammatory or infectious disease. Multifocal lesions however are most typical of inflammatory disease. Focal granulomatous lesions may have a very similar appearance to neoplasms and infarctive lesions.

MRI of the spinal cord

- does not require subarachnoid injection to visualise the spinal cord
- dense bone images poorly
- abnormalities within the spinal cord are better identified
- field of view is limited—neuroanatomic diagnosis important
- imaging time is longer and less accessible
CSF analysis and an increase in WBC counts has in the past been the diagnostic test of choice to evaluate inflammatory CNS diseases and for a long time was the only diagnostic test available to evaluate intracranial diseases. Advanced brain imaging is often used in preference to CSF analysis as often gives more information on the cause of brain and/or spinal cord disease. In most cases CSF analysis does not provide a definitive diagnosis but can be one of the pieces of a puzzle when trying to establish a likely diagnosis in cases of spinal or intracranial disease. **CSF analysis is indicated if inflammatory disease of the central nervous system is suspected, information cannot be obtained in a different way (eg serology) and collection of CSF is not a significant risk to the animal.** CSF analysis may be indicated in animals with clinical signs of diffuse or multifocal brain disease (when metabolic causes have been ruled out) and is indicated in cases of diffuse or multifocal spinal disease or spinal pain (cervical or thoracolumbar). CSF analysis will determine whether inflammation is present but only if inflammation involves the meninges, ependymal lining or tissue close to CSF pathways. With the exception of cryptococcal meningoencephalomyelitis infective organisms are rarely seen or cultured in CSF and tumour cells (with the exception of some cases of CNS lymphoma) are rarely seen. Non-specific CSF abnormalities are commonly seen in vascular, traumatic, degenerative, neoplastic and inflammatory CNS conditions.

**CSF collection is not without risk and the benefits and risks should be weighed before recommending this procedure.** Significant risk is associated with the collection of CSF in animals with increased intracranial pressure (ICP) where brain herniation, either of the cerebral hemisphere/s under the tentorium cerebelli or herniation of the cerebellum through the foramen magnum, is a possible sequela. CSF collection is also risky in animals with severe brain disease with or without increased intracranial pressure where changes in cerebral perfusion associated with anaesthesia and lack of normal brain autoregulatory responses may result in further deterioration in neurologic status. Unfortunately these are often the animals where CSF analysis is of most value. Clinical signs associated with increased ICP include obtundation, stupor, panting, headpressing bradycardia and increased systemic blood pressure. Some animals with increased intracranial pressure will not have any obvious clinical signs.

CSF analysis can be an important part of evaluating animals with spinal cord disease especially those with multifocal or diffuse spinal cord signs.

**Damage to neural structures (spinal cord or medulla oblongata) is also a risk with cisternal CSF collection,** especially in small animals or in animals with obstruction to CSF flow at the level of the cerebellomedullary cistern. The majority of dogs with GME are small and may be of breeds with cranio-cervical junction abnormalities such as Chiari like malformation.

**Cells in CSF deteriorate rapidly and CSF should be examined within 1 - 2 hours of collection especially samples with low cell and protein content.** If the CSF cannot be examined for a cell count and a concentrating technique performed to enable a differential cell count within several hours of collection there may not be not much to be gained by collecting CSF. If CSF cannot be examined quickly a cell count can be done using a haemocytometer in house and cell preservation may be extended to 24-48 hours by the addition of autologous serum to the remainder of the sample and refrigeration. Dr Jim Sutherland (ex VPS/IDEXX) recommended submitting a CSF sample with 10% added serum (one drop of serum to 9 drops of CSF or measure in an insulin syringe). Serum should be collected from the patient prior to CSF collection and make sure lab is aware serum has been added to sample. An additional sample (at least 0.1 mL) without added serum should be submitted for biochemistry. **CSF may be collected from the cerebellomedullary cistern or the lumbar subarachnoid space in most animals.** Sufficient CSF can be collected from the lumbar subarachnoid space (L5-L6 or L4-L5) in most dogs and cats. Techniques for these procedures have been described
in many texts. Lumbar CSF collection takes practice and is easier in smaller dogs (and most cats) than larger dogs. Blood contamination of the CSF sample is more likely with lumbar collection and in some cases collection at this site is not possible.

CSF should be collected into a plain sterile container (no clot activator). Some laboratories prefer an EDTA sample as well for cytology. Unless the protein content of CSF is very high CSF will not clot in a plain tube.

Normal CSF is clear and colourless. If the cell count is high (>500 per uL) the CSF may be cloudy. Bloody CSF usually occurs as a result of iatrogenic contamination. Xanthrochromia and erythrophagocytosis on cytology is indicative of pathologic haemorrhage.

**Normal CSF contains no RBCs and <6 WBC per uL. Normally only small mononuclear cells (lymphocytes) are seen in CSF.** Some blood contamination does not significantly alter the CSF WBC count. A rough guide is to allow 1 WBC for every 500 RBCs counted, however if CSF is heavily contaminated the WBC count of the CSF will be significantly altered by peripheral blood WBCs.

The total WBC count is often not a good indicator of either the underlying cause or the severity of the disease process. Very high cell counts can be seen in animals with very treatable diseases and normal CSF cell counts may be seen in animals with severe and life threatening diseases. Unfortunately the type of WBCs seen are not always a reliable indicator either of the underlying cause.

A predominantly neutrophilic CSF is seen in both bacterial and immune-mediated meningoencephalitides. It may also be seen associated with neoplasia and FIP. A predominantly lymphocytic pleocytosis can be seen in inflammatory, infectious and neoplastic conditions especially GME, viral encephalitis and lymphoma. A mixed pleocytosis can be seen in vascular or traumatic CNS conditions as well as inflammatory, infectious and neoplastic disease. The WBC count can vary from <10 cells to > 10,000 cells in many of these conditions. A predominantly eosinophilic pleocytosis (>60%) associated with a moderate to marked elevation in WBC count (>100) is almost pathognomonic in NSW and QLD for parasitic meningoencephalomyelitis associated with angiostrongylus infection. Neoplastic cells are occasionally seen in CSF.

**Protein quantitation** is also important in CSF analysis. Normal CSF contains albumin which is capable of crossing the blood/CSF barrier and the protein content is generally <0.3 g/L in a cisternal sample and <0.45-0.5g/L in a lumbar sample. Normal levels may vary from lab to lab. Elevation in CSF protein content is seen in many conditions and may be due to a breakdown of the normal blood/CSF or brain/CSF barrier and leakage of protein from the blood and interstitial fluid into the CSF (CNS malacia or inflammation associated with trauma, vascular abnormalities, tumour, inflammation etc). Total protein may also be elevated due to local production of immunoglobulins. Significant blood contamination of CSF samples will alter the CSF protein level.

CSF protein may be markedly elevated in cats with FIP (>5.0g/L). CSF with a very high protein content may be viscous, difficult to collect and may clot.

**CSF should be examined carefully for infectious organisms** especially yeasts (cryptococcus sp). CSF should be cultured (bacterial aerobic and anaerobic and possibly fungal) if an infectious cause is suspected or if organisms are seen on cytology. **CSF culture often fails to yield any growth despite organisms being visualised and a negative culture does not rule out an infectious cause.**
The conclusion from a retrospective study of CNS inflammatory disease in dogs was that a specific diagnosis was not obtainable in at least one third of cases despite extensive ancillary tests including CSF analysis. "Typical" case presentations accounted for less than half of cases of meningoencephalomyelitis. In cats, results of a retrospective study of cases with an inflammatory CSF a specific diagnosis was not possible in one third of cases and 53% of cats survived less than one year.

Brain biopsy or histology post mortem often provides the only way of making a definitive diagnosis. Gross examination of brain or spinal cord often does not reveal any abnormalities in even in animals with severe disease. Whole brain if possible and spinal cord (representative samples) should be fixed in formalin for at least several days prior to processing. Collection of fresh neural tissue (may be frozen) is also important in evaluation of infectious diseases and laboratories should be consulted prior to collection and submission of samples.