

## **Selected Neurologic Diseases**

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Neurologic diseases can be complex in terms of their diagnosis and therapy. On the other hand, through evaluation of the patient, observation of its behavior and performing specific diagnostic tests, a clear clinical picture can be formulated. Acupuncture probably works through its effects upon the nervous system and it is, therefore, reasonable to assume that the nervous system is affected by acupuncture. In fact, acupuncture probably needs an intact nervous system to work. In this course, we will review the signs of neurologic disease and discuss both the TCM and Western diagnoses which may respond to acupuncture. Sample therapies will be provided as a guide in handling patients with neurologic disease. In some cases herbal therapy may be more beneficial, in the long run. However, the information on treatment of neurologic diseases by TCM will be excluded from examination purposes, except where specifically noted.

Whenever looking at a new patient, it is important to determine whether they have a neurologic disease. This can often be determined by observing the patient in its environment, watching its gait and performing some simple tests. A history can also be helpful, since seizures are a sign that the nervous system (cerebral cortex) is involved, even if there are no other signs. Paralysis of a part of the body can certainly indicate neurologic disease. The presence of dysmetria, conscious proprioceptive deficits, tremors, head tilt, and nystagmus are other signs which can be seen with various neurologic diseases. Other signs may be seen, but can be non-specific or occur with non-neurologic diseases, too.

Knowing that the patient has a neurologic disease and where it is located will help determine the likely causes of the problem. Coupled with a TCM diagnosis, the patient can be monitored for progress and the clients informed as to the prognosis and response to therapies initiated. Some acute conditions can still benefit from a Western medical approach in combination with TCM, while some chronic conditions may respond better to TCM. Combining knowledge of both TCM and Western medicine will probably help the patients better than any single approach.

### **Neurologic History & Mechanisms of Disease:**

#### ***The Neurologic History***

Part of the minimum data base for evaluation of any proposed neurologic patient is the neurologic history. Not only can this help describe the type of condition and possible causes of the problem, it can also help confirm that the problem is a neurologic disorder. It can be one of the most important parts of the initial examination, leading to the formation of the appropriate differential diagnosis. The owner's description may lead to determining the exact nature of the problem, how long it has been present and whether the problem has been progressive.

#### **Signalment:**

The signalment includes the species, breed, age, sex and color. While many conditions affect all animals, certain diseases are unique to some species and even to certain breeds of that species. Wobbler's disease is most common in the horse and dog. Moreover, in dogs, it is most often recognized in young Great Danes and older Doberman Pinchers. One would not think of feline leukemia, if treating a dog.

The **age** of the animal can also be important. Younger animals are more prone to congenital problems, infections and toxicities. Older animals are more likely to have degenerative, metabolic, infectious and neoplastic diseases.

The **sex** and **color** of the patient can alter the differential list as well. Hypocalcemia is more common in females around the time parturition. Mammary neoplasia is more common in females, while prostatic disease is most common in male dogs. Blue-eyed, white cats are often congenitally deaf.

### **Specific History:**

The diet, exercise, living conditions (outdoor or indoor), past illnesses, vaccination records, and medications can all be important in developing the differential diagnosis. If the diet is improper, nutritional or secondary metabolic diseases may develop. Animals who lack exercise may hasten the development of degenerative diseases. Having access to other animals and potential trauma from living outside may increase the risk of infectious or traumatic disease. Seizures secondary to canine distemper generally occur after the patient has recovered from the original infection. Lack of preventative medication (such as heartworm prevention) may lead to neurologic symptoms secondary to developing the disease. On the other hand, certain medications may allow manifestation of a previously sub-clinical problem. For example, certain heartworm preventatives can lower the seizure threshold. Treatment with aminoglycoside-antibiotics can lead to disorders of cranial nerve VIII. Occurrence of the disease process following pesticide application or the availability of such pesticides may help determine the nature of intoxication.

### ***Mechanisms of Disease***

The underlying causes for neurologic diseases are similar to those causes for disease within the body in general. The basic mechanisms of neurologic disease are congenital, inflammatory, metabolic, toxic, nutritional, traumatic, vascular, degenerative, neoplastic and idiopathic. (See Table 1) **Congenital** diseases will, for the most part occur in young animals or in older animals who de-compensate for the condition. The most common **metabolic** diseases in small animals are hypoglycemia and hepatoencephalopathy. The most common **nutritional** disease is thiamine deficiency. **Toxicities** in small animals are usually secondary to organophosphate intoxication, lead poisoning or ethylene glycol ingestion. Knowing the basic mechanisms of disease can help identify the cause of the patient's neurologic disease.

**Table 1. Mechanism of Neurologic Disease and Some Common Examples.**

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<b>Congenital Disorders</b>	Hydrocephalus, True Epilepsy, Cerebellar Hypoplasia, Congenital Deafness, Vertebral Column or Neural Tube Defects, Lysosomal Storage Diseases
<b>Inflammatory (Infectious) Disorders</b>	Viral Infection (Canine distemper, Feline infectious peritonitis, Feline leukemia, Panleukopenia, Rabies), Bacterial Infection (meningitis, discospondylitis, Lyme's disease), Fungal Infection (cryptococcosis, aspergillosis), Protozoal Infection (toxoplasmosis, neosporidiosis), Rickettsial Infection (Rocky Mountain spotted fever, ehrlichiosis), Granulomatous Meningoencephalitis, Polyradiculoneuritis, Myasthenia gravis, Polymyositis
<b>Metabolic Disorders</b>	Hypoglycemia, Hepatoencephalopathy, Electrolyte Disturbances (hyper or hypocalcemia), Hypoxia, Hypothyroidism, Osmolality Disturbance, Acid-Base Disturbance
<b>Toxic Disorders</b>	Organophosphates, Lead, Ethylene glycol, Chlorinated hydrocarbons, Aminoglycoside antibiotics
<b>Nutritional Disorders</b>	Thiamine deficiency, Vitamin E deficiency
<b>Traumatic Disorders</b>	Head injury, Spinal Cord injury, Traumatic Disc rupture, Peripheral Nerve injury
<b>Vascular Disorders</b>	Fibrocartilaginous infarction, Septicemia, Vasculitis
<b>Degenerative Disorders</b>	Degenerative myelopathy, Intervertebral disc disease, Cerebellar degeneration
<b>Neoplasia</b>	Gliomas, Astrocytomas, Oligodendrogliomas, Meningiomas, Neurofibromas, Metastatic neoplasia
<b>Idiopathic Disorders</b>	Cranial nerve syndromes, Self-mutilation syndrome, Acquired epilepsy

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Diseases may be symmetrical or asymmetrical. While metabolic, nutritional and toxic disorders are almost always symmetrical, inflammatory, traumatic, vascular and neoplastic diseases are almost always asymmetrical. This can help rule/out certain diseases from the differential. In addition, traumatic and vascular diseases are more commonly acute and non-progressive; whereas inflammatory, degenerative and neoplastic diseases are either acute or chronic, progressive diseases. (See Table 2.)

**Table 2. Onset and Progression of Disease Mechanisms**

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*Acute, Non-progressive*

1. Traumatic Disorders
2. Vascular Disorders

*Acute, Progressive and Symmetrical*

1. Metabolic Disorders
2. Nutritional Disorders
3. Toxic Disorders

*Acute, Progressive and Asymmetrical*

1. Inflammatory (Infectious) Disorders
2. Neoplasia

*Chronic, Progressive and Asymmetrical*

1. Inflammatory (Infectious) Disorders
2. Degenerative Disorders
3. Neoplasia

**Localization of Lesions:**

One of the important aspects of evaluating any neurologic patient is to determine the location of the lesion. Luckily, the function of the nervous system is intimately tied to its structure. As such, when a function is lost, the structure involved is uncovered. Signs of neurologic disease can be divided into those representing diseases above the foramen magnum (head signs) and those below the foramen magnum (spinal cord signs). Head signs include seizures, head tilt, cranial nerve deficits, whole body and head tremors, and ataxia. Spinal cord signs include quadriparesis and paraparesis. The peripheral nervous system shows signs consistent with the distribution of the nerve involved. (See Table 3) Once the disease process is localized, the differential diagnosis can be made and the diagnostic approach determined.

**Table 3. Neurologic Signs and Lesion Location.**

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<i>Neurologic Sign</i>	<i>Location of Lesion</i>
Change in Behavior or Personality	Cerebral Cortex, Thalamus, Hypothalamus
Seizures	Cerebral Cortex, Thalamus, Hypothalamus
Visual Dysfunction	Retina, Optic nerve, Visual pathways, Cerebral Cortex
Signs of Cranial Nerve Dysfunction	
Anisocoria	Sympathetic or Parasympathetic innervation
Strabismus	CN III, CN IV, CN VI
Dropped jaw	CN V
Changed facial sensation	CN V
Paralysis of eyelid, lip or ear	CN VII
Dysphagia	CN IX, CN X
Megaesophagus	CN X
Laryngeal paralysis	CN X, CN XI
Paralysis of tongue	CN XII
Head tilt, circling, nystagmus	CN VIII (vestibular system)
Deafness	CN VIII (auditory system)
Incoordination of the Head and Body	Cerebellum
Paraparesis or Paraplegia	TL Spinal Cord
Paralysis of one Limb	Peripheral nerve

**Ancillary Diagnostic Tests for Neurologic Patients:**

After determining that the patient has a neurologic disease, localizing the disease process, and forming a differential diagnosis, a diagnostic plan can be developed. This will include tests to ascertain the nature of the neurologic disease, but also include tests to evaluate any discrepancies in the physical examination. Some test should be performed on every neurologic patient while other tests must be selected based upon the location of the neurologic lesion or lesions. The former tests are called the minimum data base.

**The Minimum Data Base:**

A **complete blood count** (CBC) including a measure of chronic inflammation such as plasma fibrinogen should be performed on all patients. The presence of polycythemia or anemia, the presence of alterations in plasma proteins and the presence of inflammatory disease or possibility of disseminated intravascular coagulation (DIC) can be assessed, initially, through the CBC. The presence of reduced or elevated white blood cells (WBCs) may indicate infection with viral or bacterial pathogens. Myeloproliferative diseases may produce characteristic changes in the WBC. Increases in circulating nucleated red blood cells (RBCs) may indicate lead poisoning or the presence of hemangiosarcoma.

**Serum chemistry profiles** allow screening for metabolic and toxic conditions which could result in neurologic sequela. Since any disease which effects the body can affect the nervous system, wither directly or indirectly through metabolic intoxication, assessment of the bodies health through screening tests is important in understanding neurologic disease. As will be seen in seizure disorders, the changes reflected in the chemistry profile may help differentiate between an active seizure disease and epilepsy. To this end, the electrolytes (Na, K, Cl, Ca and PO<sub>4</sub>) are important in muscle and nerve strength and reactivity. Assessments of BUN, cholesterol and albumin can help assess liver function. If all of these parameters are low, one should suspect a portosystemic shunt with diminished liver function. Elevations of cholesterol may help suggest endocrine abnormalities such as hypothyroidism or Cushing's disease. Elevated globulins might indicate autoimmune disease or, in the case of cats, the presence of feline infectious peritonitis.

Additional serum chemistries beyond routine screening tests may be indicated based upon the location of the lesion and the nature of the neurologic disease. For example, in seizures, all cases should also have serum cholinesterase levels run (to rule out organophosphate intoxication) and serum bile acid levels determined (to rule out liver dysfunction and as a base-line for possible future examines after anticonvulsant medications have been started). Dogs and cats with muscle pain or weakness may need additional serum muscle enzyme tests and determination of serum T<sub>4</sub>, T<sub>3</sub> and TSH concentrations.

A **urinalysis** can help complete the assessment of the patient's health. Since many neurologic patients exhibit urinary retention or incontinence, this can be important in monitoring for urinary tract infection. Examination for ammonium biurate crystals can help establish

diminished liver function, while the presence of calcium oxalate crystals might confirm ethylene glycol intoxication.

Appropriate **parasite screens** should be performed where indicated. Heartworm infection can result in neurologic and muscular diseases in endemic areas. Heavily parasitized young animals can become anemic or hypoglycemic as a result of the infestation, resulting in seizures or other neurologic conditions.

**Routine radiographs** of the chest and abdomen are indicated where disease is suspected based upon the physical examination. They may also be indicated in animals over 6-8 years of age, even in the absence of overt physical changes. When neoplasia is on the differential, then they are warranted. If the chest or abdomen are riddled with cancer, extensive workup for the concurrent neurologic disease may not be indicated. In addition to abdominal radiography, **abdominal ultrasound** examination may help determine the cause of the problem, even when abdominal radiographs do not show obvious lesions.

### **Other Physical Examinations:**

**Fundoscopy examination** may provide important information about the nervous system, since the retina and optic disc are the only parts of the nervous system which can be directly visualized. With CNS infection, active chorioretinitis might be seen. In the dog, this may mean fungal infection (aspergillosis or cryptococcoses), protozoal infection (toxoplasmosis or neosporidiosis) or canine distemper. In cats, it may lead to the diagnosis of cryptococcoses, toxoplasmosis or viral diseases (FeLV or FIP).

**Otoscopy examination** may help in diagnosing problems in the ears and is especially important in assessing animals with vestibular disease.

### **Specific Neurologic Tests:**

Despite the many different disease processes which can assault the nervous system, there are a limited number of tests which can be used to help make the diagnosis. Many are indicated not matter what the nervous system disorder, while others are indicated for specific neurologic conditions. The include CSF tap and analysis, electroencephalogram (EEG), electromyogram (EMG), brainstem auditory evoked response (BAER), skull or spinal radiographs, myelography and magnetic resonance imaging (MRI). Skillful use of these test will, however, allow for the diagnosis of the majority of neurologic conditions. Definitive diagnosis may be achieved by biopsy techniques, including muscle, nerve or brain biopsies.

The **CSF tap and analysis** is one of the most important tests which can be performed in assessing neurologic disease. It might be contraindicated in cases of recent or ongoing hemorrhage and in cases the intracranial pressure is increased. However, in most cases, it provides direct information about the CNS with minimal risk, being less than that of anesthesia. Evaluation of CSF should include pressure (for cisternal taps), protein determination and cytology. Additional test on CSF might be beneficial in certain diseases, such as acetylcholinesterase levels and 2-D electrophoresis in degenerative myelopathy. In cases where infection is suspected, titers can also be helpful in diagnosing the cause. CSF can be collected from the cisterna magna or the lumbar cistern between L<sub>5</sub> and L<sub>6</sub>. For most animals, a 22 ga

spinal needle is best for achieving the tap, varying in length between 1.5 to 3.5 inches. Allowing the CSF to flow by gravity and collecting into a syringe as it drips from the hub of the needle, one cc of CSF can be collected for every 10 pounds of body weight. To run routine CSF analysis and titers, requires approximately 1.5 cc of CSF. Cytologic examination plays an important part of CSF analysis. Total counts can be useful, but we have found that close inspection of the “reactivity” of the cells on cytology may be more important than the total count. The best method to perform cytology is with the use of a cytocentrifuge. Since the cells deteriorate rapidly in CSF, cytology and cells counts must be performed within 20 minutes of drawing the sample.

The **EEG** tests the outer 3 mm of the cerebral cortex and measures the electrical potentials between scalp electrodes. It can be used to test the forebrain and is an important diagnostic tool for diseases characterized by changes in behavior and seizures. To perform the EEG, the patient is anesthetized for any other neurologic tests which are being performed and, then, the scalp electrodes are inserted and connected to an EEG machine (a filtered, amplifier connected to a recording device). Once the connections are made, the recording is started and the anesthesia is turned off. The EEG is then recorded while the patient recovers from anesthesia. Performing the EEG in this manner induces some artifacts from the effects of anesthesia (however, these are minimized by using the same anesthesia in all patients and becoming familiar with the artifactual changes). On the other hand, it removes artifacts from EMG activity and movements, typical of awake EEG recordings. The normal EEG has fast, low amplitude activity (15-30 Hz and 5-15 : V, respectively). The presence of slow waves (alpha, delta and theta waves) with high amplitude indicates abnormality.

**Electromyographic** examination test the integrity of the lower motor unit. The needle EMG is performed by inserting an exploring electrode into the muscle to examine its intrinsic electrical activity. It is best performed under anesthesia, whereby nerve stimulation studies can also be performed. The presence of fibrillation potentials, fasciculation and bazaar high frequency discharges indicates increased irritability of the muscle membrane, occurring in disorders of the motor neuron, motor nerve, neuromuscular junction or muscle. Based upon the distribution of the EMG changes, the location and nature of the neurologic disorder may be indicated. Since muscle membrane irritability requires time to develop following denervation, the needle EMG may be normal for 5-7 days following acute injury of the motor unit.

Another important part of the EMG is determined by electrical stimulation of peripheral nerves. By stimulating at multiple sites along a motor nerve and recording the latency between the stimulation and the beginning of the compound action potential, the motor nerve conduction velocity can be determined. The distance between the stimulating electrodes at the two sites is divided by the difference between the latencies from the 2 sites to give the motor conduction velocity in meters per second (normal conduction is greater than 50 m/s). In addition to motor conduction velocity, repetitive nerve stimulation can be performed. Normally, the muscle can maintain activity at stimulation rates between 5-10 per second. In myasthenia gravis or sub-acute organophosphate intoxication, there is a decremental response to repetitive stimulation. The F wave is a low-amplitude wave seen several milliseconds following the compound action potential and is thought to be produce by antedromal spread of the stimulation pulse to the cell bodies of the nerve where it results in a secondary pulse traveling down the nerve to the muscle. The H wave is another low-amplitude response several milliseconds after the F wave and

represents stimulation of the sensory fibers in the nerve and subsequent reflexive stimulation of the motor neurons. Both the F wave and H wave may help examine the integrity of the central connections of the peripheral nerves. In addition to motor nerve conduction velocities, sensory nerve conduction can be measured. The sensory nerve is stimulated and a recording electrode placed proximally along the nerve records the passage of the impulse up the nerve. The distance to the recording electrode is divided by the latency of the impulse recording to determine the sensory conduction velocity.

The **BAER** records the electrical activity in the brainstem caused in response to auditory clicks in the ears. The BAER is not affected by sedation or anesthesia, so patients who are fractious can be sedated without affecting the results. The recording is made by placing a ground electrode in the untested ear, a reference electrode in the ear to be tested and a recording electrode over the vertex. The click is introduced in the ear to be tested and the electrical activity generated is averaged to reduce random noise. Generally, 5-7 middle-latency, waves are recorded, representing the transmission of auditory information through the vestibulocochlear nerve, the cochlear nucleus, the nucleus of the trapezoid body, the lemniscal nucleus and caudal colliculus, respectively. The BAER is used most frequently to test young animals for congenital deafness, but may also be used to test the integrity of the brainstem auditory system.

**Neuroradiology and imaging** include routine radiographs of the skull and spinal column. All neuro-imaging techniques are best performed under general anesthesia. Routine radiographs of the skull may reveal fractures, congenital defects, otitis media and interna and obvious neoplasia affecting the osseous structures of the skull. Routine spinal radiographs can help identify fractures, congenital malformations, evidence of degenerative disc disease, discospondylitis and neoplasia of the vertebra. However, many times the effects of the bony changes on routine radiographs do not provide sufficient information about the neural damage without the addition of special imaging techniques.

The most common of these techniques is **myelography**, performed by injecting contrast agent into the subarachnoid space through a spinal needle. Most of the time, the injection is made at the lumbar cistern and the contrast agent (Iohexol 180) is allowed to flow forward to fill the subarachnoid space to beyond the lesion. For diseases in the thoracolumbar region 0.33 cc/kg of body weight is used, while 0.45 cc/kg of body weight is used for cervical disease. It is best to use image-intensification to monitor the flow of the contrast agent and the dosage given adjusted to effect. Since most contrast agents are irritative, most neurologist believe they should not be performed in the face of obvious inflammation of the nervous system. In addition, this irritation can result in seizures upon recovery from anesthesia, another reason not to inject more than necessary to fill the subarachnoid space to the level of C<sub>1</sub>. Giving methylprednisolone immediately following the contrast injection can reduce the incidence of post-myelographic seizure, probably due to helping to maintain intercellular glucose concentrations.

A number of other special imaging techniques have been applied to neuro-imaging including computer assisted tomography (CAT) scans, radioisotopic brain scans, cerebral angiography and ventriculography. Of these, only the **MRI** provides anatomic detail when examining the nervous system. All portions of the CNS can be imaged by MRI. The MRI provides evidence of increased tissue density and fluid accumulation, demonstrates anatomic shifts in CNS structures, and (coupled with contrast studies) demonstrates breaks in the blood-brain barrier. For CNS neoplasia and for lumbosacral stenosis, MRI is the imaging method of

choice.

### **Diagnostic Plans:**

Although the neurologic tests above can help diagnose neurologic disease, not all are indicated for all conditions. For simplicity, the problems of the nervous system can be broken into 1) diseases above the foramen magnum (diseases with head signs), 2) diseases of the spinal column (diseases of quadriplegia or paraplegia) and 3) diseases of the peripheral nerves and muscle.

For diseases of the head, the diagnostic plan includes:

- 1) minimum data base,
- 2) fundoscopic or otoscopic examination,
- 3) CSF tap and analysis,
- 4) skull radiographs,
- 5) EEG or BAER (EMG if cranial neuropathy), and
- 6) MRI or CT scan.

For diseases of the spine, the diagnostic plan includes:

- 1) minimum data base,
- 2) CSF tap and analysis,
- 3) spinal radiographs,
- 4) myelography,
- 5) EMG, and
- 6) MRI or CT scan.

For diseases of the peripheral nerves or muscle, the diagnostic plan includes:

- 1) minimum data base,
- 2) EMG,
- 3) special muscle enzymes, and
- 4) muscle and nerve biopsy.

### **Cerebral Disease:**

#### **SEIZURES:**

Seizure disorders make up a significant proportion of referrals to veterinary neurologists. While the number of cats with seizures is less, it is estimated that 1% of the canine population has some form of seizure disorder. Due to the presence of idiopathic (inherited) epilepsy in certain breeds of dogs, the incidence can be as high as 15 to 20% in those breeds. As such, seizure diagnosis and treatment is an important aspect of veterinary neurology.

Any reproducible change in behavior, usually associated with altered consciousness and increased voluntary or involuntary motor tone, can be a seizure. Generally, the seizure represents a paroxysmal, uncontrolled, transient electric discharge from the neurons in the brain. Anatomically, seizures can develop from conditions affecting the forebrain, cranial to the mesencephalon. The presence of a seizure disorder, then, localizes (at least part of) the disease process in the cerebral cortex, thalamus, hypothalamus or mesencephalon. A typical seizure is characterized by a prodromal period (when the animal may recognize that a seizure event is coming and react in a characteristic manner), the ictus (the actual seizure event), the post-ictal phase (which may include pacing, eating or sleeping, but which is characteristic for that patient), and the inter-ictal phase (the period between seizures, where the animal may appear normal). During the seizure (ictus), there is usually a decrease in consciousness followed by increased motor tone including alternative tonic and clonic activity. In addition, autonomic tone increases which can lead to salivation, defecation and urination.

Seizure disorders can be differentiated into epilepsy or active seizure disease. Epilepsy can be inherited (idiopathic) or acquired. As such, epilepsy can be defined as a seizure disorder characterized by an inborn biochemical defect of neurons or by the presence of an old injury, both of which lead to abnormal electrical activity in the brain. The former defines idiopathic epilepsy, while the latter defines acquired epilepsy. In general, epilepsy represents a seizure disorder where the seizure is the disease and treating the seizure treats the disease. On the other hand, active seizure disease is defined as a seizure disorder where the seizure represents only one symptom or manifestation of the true disease process. In this case treating the seizure only treats the symptom, not the disease. The goal of neurologic assessment of patients with seizures is to determine whether the problem is due to epilepsy or secondary to an active seizure disease. The latter condition requires the greatest effort to diagnose and treat, since the active cause must be found and eliminated in order to control the brain abnormality. Failure to do so will eventually result in failure of seizure control. On the other hand, in treating epilepsy, the effort can be concentrated upon controlling the seizure.

### ***Classification of Seizures:***

Seizures are now all considered epilepsy; however, the epilepsies can have different origins and meanings. Idiopathic or inherited epilepsy is now termed primary epilepsy, a generalized and symmetrical seizure disorder usually seen in purebred dogs. Secondary epilepsy includes all forms of seizures that are due to an organic lesion within the brain. Some of these are due to active causes like neoplasia or infection; whereas, other seizures are due to inactive causes resulting from past injury leaving an electrically active area in the brain that causes seizure activity. This latter form is what used to be called acquired epilepsy. The last category is reactive epilepsy which is a seizure disorder caused by systemic metabolic or toxic disorders which result in seizures as a consequence of the systemic problem. The inactive epilepsies (primary and inactive-secondary epilepsy) only require anticonvulsant medications to treat them. On the other hand, the active-secondary and reactive epilepsies require treatment of the primary cause, as well. While the classification of the seizure may not specify the nature of the seizure disorder, it can help narrow the possibilities.

### ***Seizure Diagnosis:***

**Signalment.** The age of the patient is important in assessing the likelihood of the nature of the seizure disorder. Idiopathic epilepsy, in general, has its age of onset between 1 and 3 years of age. In addition, idiopathic epilepsy is most common in purebred dogs and cats. While acquired epilepsy can occur at any age, it usually follows the inciting injury by 6 months to 1 year. As such, acquired epilepsy does not usually begin before the age of 1 year. Since active seizure disease represents concurrent systemic disease, it will occur with greatest frequency at times when animals are most susceptible to disease. These periods are at the extremes of life, when the immune system is less active. As such, active seizure diseases are most common before 1 year of age and after 6 years of age.

**Minimum Data Base.** The minimum data base for seizures is a physical, neurologic and fundoscopic examinations. Initial clinicopathologic examinations include a CBC, Chemistry Profile plus serum cholinesterase and serum bile acid concentrations, and a urinalysis. In some patients, heartworm and internal parasite examinations are needed. Chest and abdominal radiographs are indicated in animals with abnormal physical findings and in patients over 6 years of age. If these tests are normal, a decision to perform ancillary diagnostic test must be made. For seizure evaluation, these include CSF tap and analysis, EEG and MRI examinations.

In idiopathic epilepsy, all of the test results return as normal, since this is an inborn biochemical defect which does not cause abnormalities except during the seizure. In an otherwise healthy purebred dogs between 1 and 3 years of age which have a generalized seizure disorder (or generalized-partial seizure disorder) and no neurologic deficits on examination, the tentative diagnosis of idiopathic epilepsy should be made. The patient should continue to be normal on subsequent examinations. Assuming the patient lives to be an old patient without evidence of neurologic deficits, then the diagnosis was probably correct. In the past, many breeders wished to determine whether the animals had inherited epilepsy. However, epilepsy appears to involve of 6 gene pairs, which make the genetics of epilepsy more complicated than hip dysplasia. As such, I feel it is a disease which we must learn to live with, and treat where appropriate. If a breeder gets an incidence of epilepsy greater than 6%, they are making poor choices. Colony-bred beagles have an incidence of 5.9%, based upon their on breeding decisions.

In both acquired epilepsy and active seizure disease, the neurologic examination will often be abnormal (which distinguish these conditions from idiopathic epilepsy). Often with active seizure disease, the minimum data base will demonstrate the underlying disease process. The minimum data base is normal in acquired epilepsy. However, since certain active seizure diseases are restricted to the CNS, further diagnostic tests are needed to separate these two conditions. The EEG will be abnormal in each, which does not help differentiate the problems, although the EEG will often be more abnormal in active seizure disease. The single most important test is the CSF tap and analysis. Since the injury which results in acquired epilepsy is long healed, the CSF will be normal in that condition. On the other hand, the CSF is usually abnormal in active seizure disease. Finally, MRI can help identify those conditions which do not markedly alter the CSF, yet cause an active seizure disease. The MRI remains normal in acquired epilepsy.

### ***Seizure Treatment:***

When treating active seizure disease, it is necessary to treat the primary disease. If this is successful, the seizure disorder may disappear and not longer need treatment. However, once anticonvulsant medications are started, they should be continued for a minimum of 6 months. If the primary disease is under control and there have been not evidence of continued seizure, the anticonvulsant medications can be withdrawn slowly over 1-2 months. Most of this discussion will focus on the treatment of epilepsy, a disease which is treated by the use of anticonvulsants. The principles of treating the seizures of active seizure disease are consistent with this discussion with the recognition of the above mentioned conditions.

The treatment of epilepsy is limited in dogs and cats due to the relatively few anticonvulsants which have been shown to be effective. In addition, dogs and cats do not develop ketoacidosis on high fat diets, so dietary measures which are effective in human beings are ineffective in animals. Some of the newer anticonvulsants in human beings have toxic side-effects in dogs or cats or do not appear to be effective in controlling seizures in animals.

**Phenobarbital.** Of the available anticonvulsants, the cheapest and most effective in animals is phenobarbital. The dosage in dogs and cats is between 2-4 mg/kg every 12 hours. When treating seizures, it is my experience that it is better to start higher and later reduce the dosage than to use too little, always trying to catch up with the seizure disorder. The goal is to achieve a steady blood level between 20-40 : g/ml. While these values vary slightly between laboratories, most of the methodology to determine serum phenobarbital concentrations is standardize. If you are worried about toxicity, measure the peak concentration by pulling the sample 2 hours after the last dose. If worried about having enough drug to be effective, measure the minimal level by taking the sample just before the last dose. If cost is no factor, measure both and adjust the dosage accordingly. If the peak is high and the valley low, then add a third dose in between. In dogs, unlike human beings, 60% of phenobarbital is bound to plasma proteins and 10% is displacable from the binding sites. As such, phenobarbital concentrations may need adjustment if given with drugs which are known to displace plasma binding, like sulfa drugs.

Phenobarbital is immediately effective, although it takes 3-5 days to reach a stable plasma concentration. During initial medication, phenobarbital will induce hemodilution, due to a steroid-like effect. In addition, many patients experience sedation which will usually diminish within 2 weeks. If the sedation is too severe, the dosage may need to be reduced until the patient develops tolerance to the medication. It is thought that phenobarbital acts through increasing the activity of GABA neurons, the inhibitory neurotransmitter in the CNS. Most neurologists feel that 80% of all seizure disorders can be controlled by phenobarbital, alone.

Phenobarbital generally is safe and well tolerated. It does, however, induce hepatocholestasis and a dose-dependent liver dysfunction. In some cases, this can be a significant problem and require reduction or elimination of the drug. Most of the time, this liver dysfunction will correct upon reduction of phenobarbital. On the other hand, another drug (which I will not speak of here), primidone, can cause a dose-dependent, irreversible liver failure.

**KBr.** Potassium bromide (KBr) is another effective anticonvulsant which has been used in dogs and cats for the past 10 years. It is an old compound and has only recently been re-

discovered as an effective drug. KBr is usually used as an adjunct to phenobarbital therapy. It is believed that KBr will help control 75% of the patients who cannot be controlled with phenobarbital alone. When used with phenobarbital, KBr is dosed once a day at 33 mg/kg. Usually, it is given at night. Since it is not a pharmaceutical, it must be made from chemical grade KBr by a compounding pharmacist. While some people prefer capsules, I find that the liquid formulation works better. It is made as a 250 mg/ml solution and given with food. It has a salty taste which may not be palatable to some patients.

KBr can be added to patients using phenobarbital who have liver dysfunction (since KBr does not have any known liver toxicity). In these cases, the dosage of phenobarbital should be reduced by 50% after the second KBr administration. If this is still effective toward controlling the seizure, the phenobarbital dose can be cut by an additional 50% each month until the dose of phenobarbital is 1/8th of the initial dosage. At this time, I would not go lower. In addition, the serum concentrations of phenobarbital will no longer be of any clinical relevance. Hopefully, this will correct the liver function tests.

In some cases, KBr may need to be used as the sole anticonvulsant. In that case, the dosage is 22 mg/kg every 12 hours. Although the serum half-life is around 27 days, twice a day dosing seems to be more effective when KBr is used alone. Since KBr has a long half-life, blood levels don't reach steady-state for several months. I usually check the level in 1 month, but do not adjust the dosage until a repeat level in 2 months. The goal is to have a serum level between 1200-2000 : g/ml, optimally around 1500 : g/ml. To request this, make sure you ask the laboratory for a quantitative Br level. If the level exceeds 2000 : g/ml, toxicity can develop. This may show up as an increase in the seizures.

It is thought that KBr works by stabilizing the chloride channel, much like the way lithium stabilizes the sodium channels in manic depression. Since the chloride channels are involved in maintaining the "seizure" threshold, KBr appears to work by reducing the likelihood of seizures from developing.

**Diazepam.** Diazepam is a short acting anticonvulsant in dogs and should be limited to stopping a seizure in process. In the cat, however, diazepam is an effective anticonvulsant and can be used as a primary anticonvulsant, given once or twice a day. The usual dosage is between 1-1.5 mg/kg. Recently, intra rectal diazepam has been suggested to help control animals with cluster seizures, whereby the rectal administration might stop the subsequent seizure and can be administered by the client.

**General considerations.** In general, patients with seizures should be fed a balanced diet without extra supplementation. They should avoid chemicals and drugs which could make them more susceptible to seizures, including Heartgard or Heartgard plus, Program, and Advantage. All of these compounds appear to lower the seizure threshold and make seizure disorders more difficult to control. In addition, exposure to organophosphate insecticides should be limited. Interceptor and Filaribits appear to be safe for seizing patients. Of the newer flea control products, Frontline (Top Spot) appears to be safe for dogs with seizure disorders. Revolution may also be safe to control heartworms and other internal and external parasites.

**When to treat.** There are 2 schools of thought. Some feel that with each seizure, the pathway becomes more established and, therefore, more likely to recur. These people feel that early intervention makes ultimate control of seizures more likely. The other school of thought is that anticonvulsants should not be used until the seizure frequency is often enough to determine

whether the anticonvulsant is working. Everyone agrees that they should be begun in cases of severe seizures or when the pattern is of a cluster pattern, when the animal has multiple seizures when they occur (even if the inter-ictal period is long). Since cluster seizures are often severe and eventually life-threatening (and the hardest to control), I usually start with phenobarbital (2 mg/kg BID) and KBr (33 mg/kg SID) right off the bat. Even so, adjustments up and other measures are often needed to help these patients.

**Alternatives.** Sometimes conventional therapy fails. In these cases, alternatives should be investigated. Acupuncture can be effective in some of these cases, if performed by a qualified veterinary acupuncturist. Valerian root, an old anticonvulsant, may work with KBr when phenobarbital cannot be used; however, some studies have found that valerian root is ineffective in dogs. Kava kava, which has several CNS effects which are not clearly understood, does appear to have anticonvulsant actions in dogs. Milk thistle, a natural product, may help protect the liver from toxic damage and has been used to protect the liver from the effects of chemotherapy. It should be investigated as a liver protectant from phenobarbital therapy.

### ***TCM Diagnosis and Treatment:***

Seizures from TCM are either excess or deficiency. There are three of each. The excesses are invasion of pathogens with accumulation of wind, phlegm and heat in the interior or stagnation which is locally excessive.

The wind-phlegm syndrome usually has an acute onset with seizures. The tongue is usually pale or purple with a white greasy coating. The pulse is wiry (liver) and slippery (damp). Treatment principles are to expel phlegm, extinguish the wind, open the orifice and stabilize the seizures. You can use a formula, *Ding Xian Wan*.

The phlegm-fire syndrome also has sudden seizures. (Which probably represents encephalitis-related seizures) There may be agitation, insomnia, or barking at night. There may be constipation or cough. The tongue is red or purple with a yellow, greasy coating. The pulse is rapid (heat), wiry (liver) and slippery (damp). Treatment principles are to clear the liver, drain the heat, transform phlegm and open the orifices. You can use *Di Tan Tang* (herbal equivalent of phenobarbital) and *Long Dan Xie Gan Tang* (*Snake and Dragon*). The former formula stops the seizures and the latter clears the heat, soothes the liver, and moves the damp.

The third form of excess is Blood Stagnation (which probably represents acquired epilepsy). There is a history of head injury. The tongue and pulse are like wind-phlegm. It is the history of previous head injury that accounts for the deference. So treatment principles are the same except that you need to invigorate blood. Use *Ding Xian Wan* and *Tao Hong Si Wu San* (moves blood). You could also use *Di Tan Tang plus Saliva* (*Saliva* is a single herb which is almost the same as *Four Substances*).

The deficiencies represent liver blood, liver and kidney yin and kidney jing deficiencies. Liver Blood deficiency has chronic seizures (like inherited epilepsy) and may have dry or burnt hair and anemia. There may be weakness from loss of stamina (liver sign). Tongue will be pale and dry and the pulse will be weak and thready. The treatment principle is to tonify Qi and Blood and quiet the wind. You can use *Bu Xue Xi Feng San* (build blood and extinguish wind formula) or *Di Tan Tang plus Rehmannia 8* (*Four Substances plus Four Gentlemen*).

Liver and Kidney Yin deficiency also causes chronic seizures, but the nose and mouth

are fry, the tongue is red while the pulse remains weak and thready. The seizures also happen often late afternoon or at night. Treatment principle is to nourish Yin and extinguish wind. you can use *Yang Yin Xi Feng San* or *Di Tan Tang and Left Side Replenished (Zuo Gui Wan)*. You can also use *Tian Ma Gou Teng plus* for this condition.

The final deficiency is for seizures that occur before a year of age due to kidney jing problems. The nose and mouth are often dry. The tongue will be pale or red and the pulse will be weak and thready. The treatment principles is to extinguish the wind and astringe or nourish the kidney jing. Use *Di Tan Tang* or *Tian Ma Gou Teng plus* for the seizures and use *Epimedium Powder* for the Jing issues.

One way to approach all seizures is to use *Di Tan Tang* for the seizure and then add whatever else you need to treat the excess or deficiency. That is a simple approach. Each condition also has acupuncture points that can be used. All can use points to extinguish wind like GB-20 and LI-11. Other points are for the specific excesses or deficiencies. Most of the time you can treat LIV-3 and BL-18 (to tonify the liver), An-Shen and GV17-20 and may want to add ST-40 for phlegm, but then add specific points for the problems you see.

Again, as a classical neurologist, don't put in gold or other beads around the head until you have explained that an MRI might be needed to rule out structural disease. Western medicine is sometimes still better in treating structural disease. You don't want to loose that opportunity.

Sadly, not every seizure case reads the exact book description and you may have to start with what you see initially and adjust as you treat. In addition, sometimes you need to look at the major signs and add the ones on each side of the column (excess or deficiency) to come to the best solution.

## **HYDROCEPHALUS:**

Hydrocephalus is defined as an abnormal accumulation of cerebrospinal fluid (CSF) within the ventricular system of the brain accompanied by a concomitant loss of cerebral white matter or gray matter. This condition is a common neurologic disorder of miniature breed dogs and offers a unique challenge to the clinician for diagnosis and treatment.

### ***Pathophysiology of Hydrocephalus:***

Hydrocephalus develops as a sequel to excessive formation of CSF, to decreased absorption of CSF, or to a loss of cerebral tissue volume. The pathophysiology of the former two conditions is important because these causes of hydrocephalus are likely to respond to CSF shunting procedures. The third condition is not likely to respond to either surgical or medical management.

As a result of excessive fluid accumulation in the ventricular system from increased formation or decreased absorption of CSF, a disequilibrium of forces exists at the ventricular-cerebral interface. Because the ventricular surface is semipermeable, there is a net flux of CSF into the periventricular extracellular fluid compartment. A concomitant decrease must occur in other cranial structures because no "dead space" exists within the cranial cavity. Cerebral vascular structures are most easily compressed, and with increased production of extracellular

fluid from the ventricles, the periventricular white matter's reabsorptive capacity is overloaded. The vasculature of the white matter thereby collapses and leads to the development of periventricular white matter ischemia. Because oligodendroglia are sensitive to ischemic insult, demyelination and ventricular enlargement result. Therefore, early treatment must be given for maximal benefit to the patient.

Some authors have not seen elevated intracranial pressure in dogs with hydrocephalus. In human patients likely to benefit from CSF shunting, however, transient or constantly increased ventricular pressure is common. Although the CSF pressure may be within normal levels in most dogs, increased intracranial pressure does occur in hydrocephalus and may play a significant role in the progression of this disorder. Hydrocephalus in the dog is associated with a higher initial resistance to CSF absorption, but an increased absorptive capacity. The mean rate of CSF formation is also found to be reduced. These findings suggest that canine hydrocephalus would be expected to exhibit low or normal ventricular pressures, but that minor changes in CSF volume would result in pressure increases that could not be normally transmitted or dispersed. Fluctuations in intraventricular pressure, as seen in man, would lead to periods of abnormally high pressures.

### ***Diagnosis:***

The variability of signs of canine hydrocephalus often makes the diagnosis by clinical criteria alone difficult. In young animals in which a dome-shaped calvarium, open fontanelles, and a downcast gaze are also associated with neurologic dysfunction, however, the diagnosis may be easier. Confirmatory laboratory examinations include electroencephalography and radiology.

The electroencephalogram of hydrocephalic dogs is characterized by high-amplitude, slow wave activity. This pattern is accentuated during sleep, but remains abnormal even during the alerting response. Although a correlation does appear to exist between the electroencephalographic changes and the degree of ventricular enlargement, these findings do not correlate with the clinical signs.

Noncontrast radiographs may show some flattening of the gyral impressions upon the calvarium, but such changes are not pathognomonic. Contrast ventriculography with air or radio-opaque contrast agent adequately outlines an enlarged ventricular system. Positive-contrast ventriculography may also provide useful information about CSF circulation patterns and may indicate sites of obstruction to CSF flow. In addition, this technique may be useful in demonstrating shunt patency. Today, computer-assisted tomography (CAT scan) and magnetic resonance imaging (MRI) have replaced most other methods of brain imaging.

Laboratory evaluation of ventricular fluid pressure, volume, and chemical and cellular characteristics may furnish helpful information about the underlying cause of hydrocephalus.

### ***Surgical Correction:***

The decision to place a ventriculoperitoneal shunt should be based upon the progression of clinical signs. The triad of dementia, gait abnormalities, and incontinence is an accurate predictor of responsiveness to shunting procedures in people and can be used in the dog.

The choice of anesthesia should be considered carefully because agents that increase the intracranial pressure may have disastrous consequences. Although isoflurane increases intracranial pressure slightly, this effect can be minimized by hyperventilating the animal for several minutes with oxygen-rich gases prior to the addition of isoflurane to the breathing mixture. Owing to the rapidity with which anesthetic depth can be altered with isoflurane, it is currently the agent of choice.

The animal is positioned in ventral recumbency, and the calvarium, the neck, and the right, dorsolateral body surface to the paralumbar fossa are surgically prepared. The area is draped, preferably with a barrier drape material.

A slightly paramedian incision is made over the surface of the calvarium. The subcutaneous tissue and musculature overlying the bony calvarium is dissected free at approximately half the distance from the lateral canthus of the eye to the occipital protuberance and 1 to 1.5 cm from the midline. At this point, a bur hole sufficient to pass the shunt tubing is made through the skull. In small dogs and cats with a thin calvarium, the skull may be carefully cut away with a sharp scalpel blade. The dura is incised, and a shortened, sharpened mare's catheter is inserted into the ventricular cavity. The ventricular end of the shunt tubing is then introduced through the mare's catheter or through the hole made by the catheter in the cerebral tissue. The length of shunt tubing to be inserted into the ventricle should be determined by the depth required to enter the ventricle with the catheter. The shunt tubing is fixed in place with nonabsorbable suture material passed through a hole in the outer cortical lamina of the calvarium. The muscular layers are apposed around the tubing. Once CSF is noted flowing distally in the shunt tubing, the tubing is clamped to prevent excessive CSF loss.

Alligator forceps are passed subcutaneously through a small skin incision every 9 to 12 cm and are used to pull the distal end of the shunt tubing to the paralumbar fossa. At this point, the peritoneal end of the shunt tubing is bluntly thrust through the body wall and into the peritoneal cavity by grasping it with hemostatic forceps. An additional 15 to 25 cm of shunt tubing should be allowed to lie freely in the peritoneal cavity. The flow of CSF from the tube should be monitored for a few minutes to ensure shunt patency. The skin incisions are closed in a routine manner.

The advent of silicones materials for shunt tubing has greatly improved the success rate for these procedures. Several shunt systems have been described for ventriculoperitoneal shunting employing special valves, pumping devices, and catheter tips. These materials come sterile, but are readily sterilized by ethylene oxide or autoclave. The peritoneal end may be cut to length at the time of operation. Any increase in intraventricular pressure is dissipated through the shunt by the passage of CSF into the peritoneal cavity.

### ***Postoperative Management and Complications:***

Aseptic surgical technique is essential to ensure postoperative success. The routine use of antibiotics is not indicated. If their use is indicated, however, the veterinarian must consider the lack of a normal blood-brain barrier in the choice of an agent. For example, penicillins are known to be epileptogenic and should be used with caution.

The complications associated with the procedure are minimal. In general, these complications can be broken into certain categories: shunt failure due to device failure and

infections secondary to the shunt. In patients with hydrocephalus, the practicality of this system may allow considerable salvage of neurologic tissue.

### **SENILITY:**

As we and our pets age, there is a natural reduction in many biological processes and a loss of tissue structure. This includes the CNS and the cerebral tissues. Neurochemicals change with a general reduction in certain chemical reactions. Neurons are gradually lost from the wear and tear of daily life. Researchers believe Cognitive Dysfunction Syndrome (CDS) is caused by physical and chemical changes that affect the brain function in older dogs; however, in dogs with CDS the signs of confusion or various other behavioral changes are greater than the normal alterations of aging. Most dogs age without the accentuated signs seen in CDS, yet the changes that lead to CDS take place in all dogs to some extent. In one study at the University of California-Davis, 62% of 11- to 16-year-old dogs showed signs in at least one category of CDS. In a pet owner survey, nearly half of dogs age 8 and older showed at least one sign associated with CDS.

### ***Pathophysiology:***

Monoamine oxidase (MAO)s are widely distributed throughout the body and are sub-classified into 2 types, A and B, which differ in their substrate specificity and tissue distribution. MAO plays a role in the catabolism of catecholamines, (dopamine, and, to a lesser extent, norepinephrine and epinephrine) and serotonin. CDS is thought to result in part from reduced catecholaminergic nerve function and decreased dopamine levels in the CNS. The pathogenesis of the development of clinical signs associated with cognitive decline is considered to be partly a result of a decrease in the level of catecholamines in the CNS and deficiencies in neurotransmission. There is also evidence which points to hypothalamic dopamine deficiency playing a role in the pathogenesis of pituitary dependent hyperadrenocorticism in the dog.

In people, numerous studies have indicated that senility and Alzheimer's disease are related to similar changes as occur in CDS. In those human conditions, oxidative free-radicals have been shown to play a key role in causing the pathologic changes seen. Anything which improves cerebral blood flow and enhances cerebral oxygen (cosmic Qi) delivery to the CNS will reduce the rate of progression and improve cognitive function. While people suffer more from cerebral vascular insufficiency than dogs and cats (people get atherosclerosis), animals still respond to the same treatments used in human beings. Recently, it has been suggested that glutamate levels increase in Alzheimer's disease which results in stimulation of specific neural receptors that result in cytotoxic reactions. This glutamate-dependent receptor's effects are blocked by antioxidants.

### ***Diagnosis:***

The diagnosis of CDS is based upon the presentation of the clinical signs in a older patient and ruling out other causes to explain the presence of the condition. A work-up should include a thorough physical and neurological examination. A CBC, chemistry profile and UA

may be helpful in recognizing any additional systemic factors which need therapy or which might contribute to the symptoms. Remember that CDS is a chronic and slowly progressive problem, not one that occurs over-night. Chest and abdominal radiographs and abdominal ultrasound may help look for other complication and diseases which might result in similar symptoms. Perineoplastic signs could mimic signs of CDS and the minimum database helps provide evidence which precludes systemic neoplasia as part of the process. A CSF tap is usually normal with the exception of a possible mild increase in CSF protein. An MRI can be helpful since many of these patients show signs of de novo hydrocephalus from cortical atrophy. If no other signs, except for behavior and the MRI changes are seen, then the tentative diagnosis of CDS is made.

### ***Treatment:***

Anipryl is the first and only drug approved by the FDA for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome. Most dogs are prescribed one tablet each day, preferably in the morning. (Anipryl can be given with food.) It's important to administer every tablet as directed since interruption of therapy could lead to the reappearance of signs.

In studies, pet owners reported that 69 to 75% of dogs improved in at least one clinical sign after one month of Anipryl therapy. Because CDS is a syndrome (a collection of signs), no two dogs will show exactly the same signs. Response to Anipryl may vary from dog to dog.

In the blinded, placebo-controlled study, owners reported that 69% of dogs improved in at least one clinical sign after one month of Anipryl therapy, compared to 52% of placebo-treated dogs. A second open label clinical study revealed that 75% of dogs improved in at least one clinical sign after one month of Anipryl therapy. Some dogs in both studies showed increased improvement for up to three months, indicating that some increased improvement may be seen with continued use. However, onset, duration and magnitude of response varied with individual dogs. In studies, the most common side effects were vomiting, diarrhea or changes in behavior such as hyperactivity and restlessness. Most side effects were mild to moderate.

Based upon IV administration of selegiline to 4 mixed breed female dogs, the plasma elimination half-life was estimated to be  $60 \pm 10$  minutes (mean  $\pm$  SD) and the volume of distribution at steady-state ( $V_{ss}$ ) was estimated to be  $9.4 \pm 1.6$  L/kg (mean  $\pm$  SD). The relatively large  $V_{ss}$  suggests that the selegiline is extensively distributed to body tissues. The absolute bioavailability,  $F$ , of an oral solution was less than 10%.

**Alternative Therapy.** Although Anipryl is recommended for treatment of CDS, I prefer to try other measures before resorting to it for the control of the condition. Aerobic exercise has been shown to improve cognitive function and should not be overlooked as a simple way to improve the pets cerebral functions. Antioxidants can be very useful including vitamin E, vitamin C, Vitamin A (or beta carotene) and selenium should be given. Vitamin E, however, should be given at therapeutic levels which are 50-100 IU/kg. Grape seed extract can be helpful as an antioxidant as well. *Ginkgo biloba* extract (2-4 mg/kg every 8-12 hours) can be very helpful and has been shown to provide long-lasting and effective help in human Alzheimer's patients. Another antioxidant that has been demonstrated in studies to help in senile dementia and Alzheimer's disease is acetylcysteine (25 mg/kg every 8 hours). Compared with vitamin E

and C, acetylcysteine is even more potent as an antioxidant. In addition, coenzyme Q-10, soy lecithin, omega-3-fatty acids, gammalinolenic acid and vitamin B complex can be very useful in helping support CNS function, oxygen utilization, membrane stabilization and neurochemical production. If these measures do not help (and the diagnosis is correct), then Anipryl can be tried.

## **Brainstem Disease:**

### **DISEASES OF MASTICATION:**

The trigeminal nerve give rise to the sensory nerves for the skin and structures of the eye, nose, mouth and face and the motor nerves to the muscles of mastication. It consists of 3 major branches: the ophthalmic nerve which is sensory to the structures of the orbit and skin of the dorsum of the nose; the maxillary nerve which is sensory to the skin of the cheek, side of the nose, muzzle, mucous membrane of the nasopharynx, maxillary sinus, soft and hard palates and the teeth and gingiva of the upper jaw; and , the mandibular nerve which is sensory to the remaining portions of the face and mouth and is motor to the muscles of mastication. Diseases of the trigeminal nerve or the muscles of mastication are not uncommon and must be differentiated from one another.

**Trigeminal neuritis** (an immune disorder affecting the myelinated pathways in the trigeminal nerve) is usually transient, but can present as a significant problem. The cardinal signs of trigeminal neuritis if a dropped jaw with the inability to close the mouth. It affects adult dogs and cats with no breed or sex predilection. It must be differentiated from fracture or subluxation of the temporomandibular joint (evaluated by skull radiographs). On pathologic examination, there is bilateral nonsuppurative neuritis of the trigeminal nerve. As an idiopathic immune-related disorder, the condition will usually improve over 1-3 weeks. On the other hand, methylprednisolone therapy may help reduce the severity of an attack. Additional measures includes the use of antioxidant medications such as vitamin E and C, n-acetylcysteine and ginkgo biloba. These latter measures may help prevent reoccurrence of episodes, which are occasionally seen. Other measures including feeding liquified food and/or introduction of a PEG tubes to support nutrition while the neuritis slowly responses. Some have supported the patients nutrition by placing a wide rubber band around the mouth (which helps close the mouth) while the patient is allowed to eat.

**Masseter and temporalis myositis** is a chronic progressive which presents with acute exacerbations and remissions. It is an auto-immune disease directed at the unique antigenic markers of the muscles innervated by the trigeminal nerve. The cardinal signs of this myositis is the inability to open the jaw, which differentiates it from primary diseases of the trigeminal nerve. In the acute phase, there is elevation of serum muscle enzymes (CPK, AST, LDH and aldolase). On the CBC, there is often an elevation of eosinophils (giving the condition its names, eosinophilic myositis). On the other hand, in the chronic phase, the amount of remaining muscle and, therefore, the amount of inflammation are reduced. The diagnosis can be confirmed on muscle biopsy and determination of serum antibody titers to the 2M antigen. The treatment of acute masseter-temporalis myositis is with immunosuppressive medication. We use oral prednisolone at 1 mg/kg/day divided into 2 or 3 doses for 1-2 weeks, followed by 0.5 mg/kg/day

for 1-3 weeks. There is no evidence to suggest that keeping patients on alternate day steroid therapy between attacks will reduce the chances for progression. Here is another area where using dietary supplements might be useful. In the chronic phase, the jaw may be locked shut. In these cases, it may be necessary to manually open the mouth under anesthesia. This may lead to fracture of the jaw. The hope is that, once the fibrosis is broken, the remaining muscle mass will allow enough function for the patient to be able to feed itself. The jaw must open about 1-1.5 inches for this to happen.

### **FACIAL PARALYSIS:**

The facial nerve exits the brainstem in the cranial medulla and courses out of the calvarium passing near the inner ear (diseases here cause a number of facial nerve problems which have already been discussed). It then travels cranially over the ramus of the mandible to distribute to the muscles of facial expression. Damage of the facial nerve results in decreased movement of the ear, eyelids and buccal muscles. The menace response, palpebral reflex, lip reaction and ear twitch response become decreased to absent. In evaluating the menace response, it is necessary to determine that the animal is visual, either by performing a dazzle response or evaluating the animal's visual behavior. The palpebral reflex should be checked with the corneal reflex, indicating that the problem is not sensory through the trigeminal nerve. The lip retraction can be checked against response to placing a probe gently into the nares. The ear response may be checked by observing the animal's head shaking or pulling the head away. Remember to always check the tear production with the Schirmer's tear test.

Acute unilateral or bilateral facial nerve paralysis may be seen in adult dogs, particularly in the cocker spaniel. There are no other signs of neurologic disease. There is no evidence of otitis on physical, neurologic or radiographic examination. EMG changes (fibrillation potentials and positive sharp waves) are usually present in the muscle innervated by the facial nerve, only. There is no therapy; but, if attention is given to supporting tear production, the animal does not appear to have difficulty living with its deficits. It is felt that this represents an autoimmune disease and immune therapy may be indicated.

### **VESTIBULAR DYSFUNCTION:**

All veterinary species suffer from various forms of vestibular disease. Many of which require only recognition, while others represent significant diagnostic challenges. Although there are a number of diseases which can affect the vestibular system, generally we can break them down anatomically into peripheral and central disorders. With certain exceptions, peripheral diseases bear a better prognosis in most species than central vestibular disease. Partially due to this concern, vestibular diseases represent a large number of neurologic referrals. Often, it is only reassurance that the problem will pass that is necessary. Recognition of when to intervene is as important as when not to.

The **cardinal signs** of unilateral vestibular disease are head tilt, nystagmus (spontaneous abnormal eye movements), circling (toward the lesion in "tight" circles), and incoordination. This is because the vestibular system is an important part of the CNS balance control system. In order for animals to know how they are oriented in space, three neural systems must be

functioning. The vestibular system, through the stimulus-response of the hair cells in the semicircular canals, reacts to angular acceleration and deceleration. The visual system allows the animal to focus on the horizontal and vertical, orienting in space. Finally, gravity is detected by pressure receptors in the skin, orienting the animal on up and down. While the vestibular system is a very important, it requires at least 2 of these orienting systems to function for the animal to negotiate within its environment. This can be important with vestibular disease, since, in acute disease, the nystagmus prevents the eyes from focusing on the horizon, effectively eliminating spacial orientation.

The **anatomic structures** involved in the vestibular system include the hair cells in the saccule and utricle (containing the semicircular canals), the vestibular portion of CN VIII, the vestibular nuclei in the brainstem and the flocculonodular lobe of the cerebellum. The vestibular nuclei send fibers forward in the medial longitudinal fasciculus (MLF) which coordinates ocular movements, projects fibers to the spinal cord as the vestibulospinal tract and descending MLF, projects fibers to the cerebellum, and sends fibers to various structures in the brainstem including the emetic center. Involvement of any of the portions of the vestibular system will result in signs of disfunction. Most lesions result in loss of function and, hence, are ablative in nature. The signs develop due to the imbalance existing between the normal and abnormal sides.

The **nystagmus** seen in vestibular disease can be helpful in localizing the disease process. While horizontal and rotatory nystagmus can be seen with disease anywhere within the vestibular system, vertical and positional nystagmus are almost exclusively seen with central vestibular diseases. Moreover, horizontal nystagmus from peripheral vestibular disease oscillates with the fast-phase away from the direction of the head tilt. With central vestibular disease (particularly of the cerebellum), however, the fast-phase is toward the lesion. So although horizontal and rotatory nystagmus are not specific for peripheral disease, they are compatible with it. Vertical and positional nystagmus suggest the lesion is within the CNS and indicate the need for a thorough neurologic work-up.

Vestibular diseases can be **classified** into three major disease processes: idiopathic vestibular disease, inner ear disease, or central vestibular disease. The former 2 represent common forms of peripheral vestibular disease which need to be separated from each other and from central vestibular disease.

### ***Idiopathic Vestibular Disease:***

All cranial nerves have the potential to develop specific syndromes which are clinically classified as idiopathic disorders. This is probably due to the fact that each cranial nerve represents a unique developmental anatomy from their respective brachial arches. This also gives them an unique antigenic signal allowing very specific immune attack upon them. Idiopathic vestibular disease represents one of this cranial nerve syndromes.

Clinically, idiopathic vestibular disease presents as an acute onset of vestibular signs with severe imbalance, due to its sudden onset and the severe nystagmus which is associated with the onset of the disorder. Since the eyes are unable to fix on the horizon and the vestibular mechanism is defective, there is severe vertigo. This often results in the rolling and rolling described by the owners. This can be mistaken for a seizure, which it is not. During the early phases of idiopathic vestibular disease, the patient often experiences nausea to the point of

frequent vomiting and inappetence. The head tilt will be toward the side of dysfunction and the nystagmus will be horizontal or rotatory with the fast-phase away from the head tilt. If supported, there are no other neurologic deficits and proprioception is normal.

The diagnosis of idiopathic vestibular disease is tentatively made by the presence of acute clinical signs in the absence of other physical findings. The minimum data base include physical examination, otoscopic examination and neurologic examination. The lack of findings (other than the peripheral vestibular signs) supports the diagnosis. The signs of idiopathic vestibular disease are regressive, meaning that they disappear without treatment over time. As such, the fact that the disease is self-limiting is how the final diagnosis is achieved. The nystagmus will usually improve or disappear all together within 3-5 days of the onset. The patient will, then, improve in their imbalance and be more able to function normally. This improvement will continue until minimal deficits will remain. It is possible that there will be a residual head tilt. If the head tilt persists beyond 6 months following the onset of signs, it is likely to permanent.

There is no treatment which will hasten the recovery from idiopathic vestibular disease. Corticosteroids probably do not offer an effective treatment. On the other hand, since idiopathic vestibular disease may represent an immune disease, anti-oxidant steroids (such as Solu Medral) may decrease severe symptoms. During the early phases, anti-vertigo drugs might make the patient more comfortable. Generally, I use diphenhydramine at 2-4 mg/kg every 8 hours as needed. Diphenhydramine is a centrally active anticholinergic, antihistamine which helps reduce vertigo and nausea. Assuming that the regressive course becomes evident, then I monitor the patient periodically for the signs of continued improvement.

Antidotal evidence suggests that idiopathic vestibular disease may represent toxicity to eating certain strains of lizards. Owners often notice the cat with a lizard in its mouth just prior to the onset of clinical signs. However, experimental feeding of the suggested lizard species to cats does not lead to the disease. It is still possible that laboratory conditions do not mimic field conditions. On the other hand, idiopathic vestibular disease occurs in many animals and in animal species where exposure to lizards plays not role in the condition. It is most likely that idiopathic vestibular disease is an immune-related condition affecting the unique antigens presented by the vestibular nerve. It can recur and is often more severe on recurrence.

### ***TCM Diagnosis and Treatment:***

**TCM Pattern:** Idiopathic vestibular disease represents an acute invasion of wind (heat) into the inner ear. This may be secondary to an external pathogen or secondary to internal winds from the liver. Nystagmus is a wind signs affecting the eyes which are under the control of the liver. The liver is directly associated with the external ear via its husband-pair, the gall bladder whose meridian passes the ears several times. The triple heater is also associated with the ear in that its meridian wraps around the ear. The kidney is also important for the neural functions (vestibular and hearing) of the ears and is associated with the ear through its husband-pair, the bladder whose meridian runs just above the ears. In addition, the heart is associated with the ears through its husband-pair, the small intestines, whose meridian ends in front of the ears. Ear problems can result in shen disturbance either by disruption of liver blood or by insult of the heart directly through the small intestine channel.

When wind invades the ear, there are local changes leading to imbalance and abnormal eye movements. This leads to shen disturbance and disrupts qi flow. The disruption of qi flow leads to perversion of stomach qi (probably from over-control of the liver on the stomach) leading to nausea and vomiting. Due to the acute nature, signs are very dramatic, but acupuncture can also be very helpful.

**TCM Treatment Principle:** Clear wind and heat and calm the shen.

**Acupuncture Therapy:** Clear wind and heat (GB-20, LI-4, LI-11, GV-14). Calm the shen (PC-6, HT-7, GV-17, GV-20, GV-21). Local points (TH-18, TH-18, TH-21, SI-19, GB-2, er jian, an shen). Channel points (TH-4, SI-3, BL-66, GB-41, GB-43, LIV-3). Also add constitutional points and points for specific deficiencies or excesses seen.

**TCM Herbal Therapy:** Since this is an acute, regressive disease, no herbal support is likely to be as helpful as acupuncture. Once the signs have begun to clear, any underlying excess or deficiency can be treated appropriately.

### ***Inner Ear Disease:***

Many different problems result in inner ear disease; however, the clinical signs caused by these diseases are similar, indicating the location of the disease rather than the specific cause. These signs are those of peripheral vestibular dysfunction, including head tilt, nystagmus, circling and imbalance. On the other hand, since the diseases which cause inner ear disease are usually slower in evolution, these signs are generally less severe than with idiopathic vestibular disease. In addition to the vestibular signs, there are also varying degrees of facial nerve dysfunction and often Horner's syndrome. Anatomically, the facial nerve and the sympathetic fibers heading to the eye pass near the inner ear in the osseous petrous temporal bone. Damage of these neural structure, in addition to the damage of the vestibular nerve is a hallmark for inner ear disease. It is possible to affect both the facial and vestibular nerves together in the calvarium, but it is rare to see Horner's syndrome from central nervous system disease. As such, Horner's syndrome suggests that the disease in process is in the peripheral C8-T2 nerve roots, the vagosympathetic trunk, the inner ear or within the orbit. When Horner's syndrome is seen in combination with vestibular disease and facial nerve disease, the location must be in the peripheral vestibular system in the region of the osseous petrous temporal bone.

The signs of facial nerve dysfunction include paresis or paralysis of the muscles of facial expressions (lack of ear movement, lack of blink and lack of buccal muscle reaction on palpation). This leads to deficiency of the vibrissa reaction, decreased to absent menace response and diminished to absent palpebral response. In addition, the facial nerve supplies parasympathetic innervation to the lacrimal gland of the eye. As such, peripheral facial nerve disease can lead to diminished tear production in the eye on the affected side. This can be rather catastrophic in inner ear disease where the facial nerve dysfunction results in the inability to close the eye, while also decreasing tear production. As such, every dog with inner ear disease should have a Schirmer's tear test run on the eyes and appropriate treatment instituted if tear production is deficient.

Horner's syndrome varies among species. In small animals the ocular signs predominate, including myosis, ptosis and enophthalmos. In horses, the signs of Horner's syndrome are expressed primarily as excessive sweating on the affected side of the face. In cattle, there is a lack of sweating on the muzzle of the affected side.

The most common cause of inner ear disease in all species is secondary in inner ear infection. Most of these represent bacterial extension from otitis media which can arise from hematogenous spread from bacteremia or from spread up the eustachian tube to the middle ear. Luckily, these infections, once recognized, can often be successfully treated. Other causes of inner ear disease may not be treatable, including fungal infections and neoplasia. Therefore, it is generally best to "treat-for-the-treatable" when dealing with inner ear disease, using appropriate antibiotic therapy.

The minimum data base for diagnosis of inner ear disease includes physical and neurologic examination, Schirmer's tear test, otoscopic examination (with culture of the external ear canal, if indicated), pharyngeal examination, CBC and urinalysis. If there is evidence of cardiac murmur, then cardiac ultrasound should be performed. Skull radiographs are then necessary to evaluate the degree of change in the osseous structures of the inner ear. This will be helpful in making the diagnosis and in monitoring the response to treatment.

The treatment of bacterial inner ear infection must consider the fact that the disease represent bone infection. As such, the antibiotic must be able to penetrate bone, develop good tissue concentrations (including the blood-ear barrier) and, preferably, be bactericidal in action. Many veterinarians use enrofloxacin as their antibiotic of choice. I find that enrofloxacin is great for treating gram negative infections in the lung, but it may not reach tissue concentrations within neural structures like the inner ear. It needs additional help to do this. Therefore, if I do not use my treatment of choice, I will add a sulfa drug to enrofloxacin to take advantage of the synergistic effect of sulfa drugs. My antibiotic regime of choice is cephalosporins and sulfa drugs (sulfadimethozine) in combination. This meets the criteria for the ideal therapy for inner ear disease. It is excellent in treating gram positive bacteria, which are the most common organisms infecting the inner ear. Since this is a bone infection, the treatment must be continued for 6-8 weeks, minimum. The most common cause of treatment failure is not treating long enough.

### ***TCM Diagnosis and Treatment:***

**TCM Pattern:** Inner ear disease represents a more chronic invasion of wind, heat and damp into the ear. This is usually secondary to an external pathogen or can be secondary to stagnation caused by chronic internal problems. However, unlike idiopathic vestibular disease which is confined to the qi level, inner ear disease is usually deeper and involves the Ying and xue (blood) stages. Overall, the same internal connections and meridians are involved in the disease processes.

When wind and heat invades the ear, causing the initial signs. The heat boils the fluids and leads to the accumulation of damp or phlegm. Alternatively, the qi and blood stagnate leading to local heat which in turn leads to the accumulation of damp.

**TCM Treatment Principle:** Quiet the wind, reduce the heat, disperse the damp, activate

the blood to dissolve stagnation, and calm the shen.

**Acupuncture Therapy:** Clear wind and heat (GB-20, LI-4, LI-11, GV-14, ST-44). Calm the shen (PC-6, HT-7, GV-17, GV-20, GV-21). Eliminate the damp and disperse the phlegm (SP-9, ST-40). Activate the qi and blood (ST-36, Xin shu, SP-10, BL-17). Local points (TH-18, TH-18, TH-21, SI-19, GB-2, er jian, an shen). Channel points (TH-4, SI-3, BL-66, GB-41, GB-43, LIV-3). Also add constitutional points and points for specific deficiencies or excesses seen.

**TCM Herbal Therapy:** Inner ear disease secondary to Damp-Heat shows the tongue is red or purple with a yellow, greasy coating. The pulse is rapid (heat), wiry (liver) and slippery (damp). You can use *Long Dan Xie Gan Tang (Snake and Dragon)* or *Damp-Heat formula (bi xie sheng shi tang)*. The former formula clears the heat, soothes the liver, and moves the damp from the whole body, while the latter is more specific for the skin. If only the ears are involved, you might try *Ear itching formula* which also soothes the liver, clears heat and helps resolve stagnation, but contains an ear transporter (*luo shi teng*).

When the excess is secondary to blood stagnation (associated with swelling, structural disease and pain). The tongue is usually pale or purple with a white greasy coating. The pulse is wiry (liver) and slippery (damp). Treatment principles are to expel phlegm, extinguish the wind, open the orifice and invigorate the blood. Use *Ding Xian Wan* and *Tao Hong Si Wu San* (moves blood).

Once the excess is cleared, then you should look for any underlying deficiencies and treat these until resolved. You may also want to use Ear drop formula to help treat the external signs of ear infection. In addition, you can use a standard approach to treating and maintaining ears using a series of natural products to clean the ears and protect against pathogenic invasion. The general purpose of this procedure is to gently clean the ears, correct their pH to help prevent microorganisms from invading and provide an antibacterial, antifungal, anti-inflammatory agent to clear any existing problems. In the beginning, it may be necessary to use the solutions to clean the ears three times a day. After the problem is under control, daily or biweekly cleansing may be sufficient even in the worst initial cases. This should be used in conjunction with an “Integrative Program” to help improve the animal's ability to heal from the inside, as well.

The initial solutions should be instilled into the ear. The ear can be manipulated to work the solution around in the ear canal. Then, the excess can be wiped away with a cotton ball. Usually, the animal will help by shaking the head. It is not advisable to use cotton swabs in the ear canal, unless specifically instructed to do so by your veterinarian, who has demonstrated the technique for you. Use the solutions in sequence, since this is how they are designed to work. The detergent solution gets rid of wax and debris. The vinegar solution adjusts the pH of the ear to normal. The vitaminE/garlic oil helps treat and prevent infection. It should not be used if the eardrum is ruptured.

#### **Detergent Solution:**

- 1 drop of “free” dishwasher soap
- 8 ounces of water

**Vinegar Solution:**

- 1 ounce apple cider vinegar
- 3 ounces of water

**VitaminE/garlic oil:**

- crush one clove of garlic (use press) into
- 1 ounce of extra virgin olive oil
- let sit overnight at room temperature
- pour oil into dropper container
- add content of a 1000 IU vitamin E capsule
- use 2-3 drops in the ear canals, plus 1-2 on the pinnae

***Central Vestibular Disease:***

Whenever anything else is seen other than the signs above, one must consider the likelihood that the problem is due to central vestibular disease. Additional cranial nerve deficits, proprioceptive deficits and motor deficits indicate brainstem damage affecting the vestibular nuclei and sensor and motor pathways which course through the vestibular region of the brainstem. In addition, the nystagmus seen in central vestibular disease will often be vertical or positional in nature, supporting the location of the disease process within the brainstem or cerebellum. If there is whole body and head tremors, the lesion is likely to be within the flocculonodular lobe of the cerebellum. While diseases which affect the peripheral vestibular system are usually good diseases; that is, diseases which regress without treatment or which respond to appropriate antibiotic therapy, most central vestibular diseases carry a less optimistic prognosis.

The major causes of central vestibular disease are inflammatory/infectious diseases or neoplasia. Organophosphate intoxication, liver disease (with metabolic brainstem degeneration) and thiamine deficiency can occasionally result in central vestibular disease (depending upon the species of animal), but these causes are far less than the inflammatory or neoplastic causes. In dogs, canine distemper virus, granulomatous meningoencephalitis, toxoplasmosis, neosporidiosis, aspergillosis, cryptococcosis, steroid-responsive meningoencephalitis, Lyme's disease, Rocky Mountain spotted fever and ehrlichiosis are the most common inflammatory and infectious diseases recognized. In the cat, FeLV, FIP, and cryptococcosis are the most common infectious diseases. Any of the primary brain tumors can occur in dogs, while only meningiomas are common in cats. Cats who are not eating and stressed can easily develop thiamine deficiency and this should not be overlooked in treating sick cats with vestibular signs.

Diagnosis of central vestibular disease involves the minimal data based for inner ear disease, but must be expanded to include a chemistry profile, a CSF tap and analysis (including species specific titers) and, often, advanced brain-imaging techniques, such as MRI examination. Since CSF cytology is important in assessing central vestibular disease and advanced imaging techniques are needed, central vestibular disease crosses "the referral line", the point in assessing disease which may require the interaction or interpretation of a neurologist.

The treatment and prognosis for central vestibular disease depends upon the cause. In neoplasia, biopsy may help determine whether radioablative surgery might be useful. Unfortunately, the brainstem is not an area amenable to conventional neurosurgery. In small animals, bacterial infections causing central vestibular disease is uncommon. Rickettsial infection is also rare. In cats, cryptococcosis may respond to therapy whether with remission or control of the neurologic signs. In dogs, fungal diseases usually progress in spite vigorous treatment. Toxoplasmosis may be controllable for a period in the dog and treatable in the cat. Canine distemper virus infection may run its course and stop or be chronic and progressive. FeLV and FIP infections are generally, rapidly progressive. Granulomatous meningoencephalitis (GME) will respond temporarily to corticosteroid therapy, but ultimately progress. Steroid-responsive meningoencephalitis can be controlled with medication for long periods in the dog. Finally, organophosphate intoxication and thiamine deficiency may respond to appropriate therapy.

So, while central vestibular disease has many causes, in the absence of specific disease processes, there is limited hope for successful treatment and that hope is often based upon the response of the animal to medical management. The medical management is largely based upon the responsiveness of the disease process to corticosteroids. In other words, there are many causes of central vestibular disease, but often only one treatment approach. If the client understands this, it is possible to treat central vestibular disease without a specific diagnosis, realizing that the response to therapy can suggest whether the disease was “good” or “bad”. The treatment approach that I use when a specific diagnosis cannot be made (either because the patient is too ill to undergo the diagnostic test or the client cannot afford them) is to treat with corticosteroids (usually oral prednisolone) and antibiotics (doxycycline and sulfadimethoxine). The prednisolone will reduce inflammation while the doxycycline can help control bacterial and rickettsial disease while the sulfadimethoxine may help control protozoal infection. I take a more pro-active approach in cats, since toxoplasmosis and cryptococcosis might be treatable. Therefore, I prefer to always perform CSF tap and analysis in cats with central vestibular disease, particularly when they also exhibit active chorioretinitis. I also add parenteral thiamine therapy when treating cats.

We have made important strides in understanding the breadth of central vestibular diseases. There are new promising approaches which may help treat more of the diseases than we have previously been able to treat. New antifungal drugs offer hope in controlling CNS fungal infections. More potent cytotoxic drugs may help diminish the effects of GME in the dog. Computer-Assisted Radioablative surgery offers hope in treating brainstem tumors. On the other hand, we have a long way to go. These new methods are expensive and not always available to every pet owner. We are, however, investigating whether natural medicine might be useful adjunctive therapies in many vestibular diseases. These approaches might reduce the cost and improve the outcome and prognosis for many patients.

### ***TCM Diagnosis and Treatment:***

**TCM Pattern:** Central vestibular diseases like many other problems in the central nervous system can be highly variable as to cause including excess conditions or deficiencies. They can be inflammatory which is most likely secondary to invasion of external pathogens at

the xue level and include wind, heat and damp or wind and cold. Blood stagnation can lead to mass formation and cause central vestibular disease. Liver and kidney yin deficiency and kidney jing deficiency also can lead to central vestibular problems. Therefore, you should identify what you see (tongue and pulse) and treat accordingly. It can also help to know for sure what the Western diagnosis is, since there are TCM herbal approaches that can be used based upon these findings. In fact, I highly encourage traditional veterinarians to seek this information before treating, as well.

**Acupuncture Therapy:** Based upon findings for constitutional issues, 8 principle and Zang-Fu indications.

**TCM Herbal Therapy:** Treat what you find.

**Spinal Cord Disease:**

## **QUADRIPARESIS and QUADRIPLEGIA**

### ***Introduction:***

Quadriparesis (weakness and ataxia of all 4 limbs) and quadriplegia (paralysis of all 4 limbs) are common problems in all animals. Once the neurologist, faced with an animal who has neurologic disease affecting all 4 limbs, has determined that the lesion is below the foramen magnum (meaning a spinal cord or peripheral disease), there are 4 possible anatomic locations for the disease process: 1) if there is UMN disfunction in all 4 legs, the lesion is most likely to be in the spinal cord between C1-C5; 2) if there is LMN disfunction in the fore legs and UMN disfunction to the rear legs, the lesion is severe and involves spinal cord segments C6-T2; 3) if there is UMN disfunction to the rear legs and “root signature” (lameness due to nerve root involvement) in the forelegs, the lesion is mild and affecting spinal cord segments C6-T2; or, 4) if there is LMN disfunction in all 4 limbs, the lesion is due to a diffuse LMN disease.

In developing the differential diagnosis for quadriparesis, the basic mechanisms of disease must be considered along with the signalment and history. Congenital diseases are not uncommon in the cervical spinal column of dogs. These include agenesis of the dens (with resultant atlantoaxial subluxation), blocked vertebra, multiple cartilaginous exostoses, leukoencephalomyelopathy of Rottweilers, and hereditary ataxia of Jack Russell and Smooth-haired Fox terriers. In older animals, degenerative intervertebral disc (IVD) disease, inflammatory meningomyelitis and neoplasia are not uncommon. If the signs are symmetrical, then nutritional, metabolic and toxic diseases must be considered. On the other hand, most asymmetrical diseases can be separated into their most likely causes, which must be included in the differential. These causes are discospondylitis, meningomyelitis, IVD disease and neoplasia.

### ***Diagnostic Approach:***

Like the rest of the nervous system, the neurologic examination is the single most important diagnostic method to localize diseases of the cervical spine, providing an indication from which to

make a tentative differential diagnostic list. On the other hand, localizing diseases in the cervical spinal column to a specific spinal segment can be difficult, since tests like the panniculus response cannot be performed there. Hyperpathia can be difficult to elicit and hyperesthesia is not easily mapped.

The ancillary diagnostic tests for spinal cord disease are similar regardless of the cause and include the minimum data base, spinal radiographs, EMG, CSF tap and analysis, myelography and MRI. The minimum data base will often be normal or may need to be expanded based upon the physical and neurologic examinations. In older patients, routine chest and abdominal radiographs and abdominal ultrasound may help make a diagnosis of the cervical disease or assist in making the prognosis. Spinal radiographs may show signs of degenerative disc disease, congenital malformation, spinal arthritis or discospondylitis. The latter disease being the only disease diagnosis which can be made on plain spinal radiographs. The other diseases will need additional imaging techniques to confirm that they are the source of the problem. In acute diseases, the EMG may not help identify denervation until 5-7 days have past; however, nerve conduction velocity studies may help identify damaged nerves or diffuse LMN disorders. On the other hand, in chronic diseases, the EMG may help to localize the disease process, so that radiographs can concentrate on the lesion. The CSF tap can help determine the presence of inflammation or infection in cervical diseases. The problem of inflammatory myelitis is increasing, making CSF tap and analysis critical in assessing cervical neurologic disease. Even when other neurologic conditions are identified, myelitis may be present. Unfortunately, many patients are treated with corticosteroids before being adequately worked-up for cervical disease. The work-up performed in the face of the steroids may be erroneous. As such, surgical intervention may be performed, only later to discover the cause of neck pain was inflammatory meningomyelitis. Spinal myelography helps to contrast the spinal cord when looking for mass lesions. It can be an extremely valuable diagnostic aid in determining the need for surgical intervention and what surgical approach is best. In cervical vertebral malformation complex, the lesion is dynamic. The only imaging technique which can provide dynamic views is the myelogram. Myelography, therefore, remains the single most important imaging technique for assessing surgical diseases in the cervical spine. When the myelographic data is lacking or when it is not clear what the lesion represents, MRI can add diagnostic detail. MRI may be important in assessing neoplastic disease processes, including nerve root tumors. The sequence of diagnostic tests logically follows the pattern of minimum data base, EMG, spinal radiographs, CSF tap, myelography and, finally, MRI. If an accurate diagnosis is made along the way, the remaining test may not be needed.

### ***Meningomyelitis:***

As stated before, meningomyelitis appears to be on the rise. Twenty years ago, it was rare to diagnose meningomyelitis and most of these were secondary to canine distemper virus with the remainder being due to toxoplasmosis. Today, it is almost impossible to deal with animals with neck pain and not be suspicious of meningomyelitis. For this reason, even with signs of early degenerative disc disease, I do not consider surgery until I have ruled-out meningitis. While some neurologists are unconcerned about performing myelography on patients who have meningomyelitis, most contrast agents are inflammatory by nature. In the face of meningomyelitis, myelography can exacerbate the clinical signs and is, therefore, generally contraindicated in meningomyelitis.

The clinical signs of meningomyelitis are, generally, neck pain and asymmetrical neurologic deficits. The deficits depend upon which pathways are involved in the disease process. The signs are usually progressive, but may develop acutely. In dogs and cats, the causes of meningomyelitis are, in order of likelihood, viral, inflammatory, protozoal, fungal, rickettsial and bacterial diseases. The viral disease most commonly seen in dogs is canine distemper (even in vaccinated dogs). In cats, feline leukemia virus (FeLV), feline infectious peritonitis (FIP) and feline immunodeficiency virus (FIV) are the most common viral infections. Toxoplasmosis can occur in both dogs and cats, while dog also may develop *Neospora caninum* infections. Aspergillosis is not uncommon in dogs, while cryptococcosis is more common in cats. Cats do not appear to have rickettsial diseases, but dogs have been shown to develop meningomyelitis from both ehrlichiosis and Rocky Mountain spotted fever. Titers for these agents should be performed on the serum and/or CSF when presented with meningomyelitis.

The diagnosis is made on CSF tap and analysis. Generally, we approach animals with neck pain and quadriparesis by performing a minimum data base including a CBC, chemistry profile, urinalysis and appropriate radiographs. With the CBC, we run plasma fibrinogen levels. This is a crude estimate of systemic inflammation, but a valuable tool in assessing the potential for meningomyelitis. It may be the only abnormality noted in the CBC. Once the minimal data base is evaluated, we proceed with anesthesia and CSF tap. While this is being processed, spinal radiographs are taken. If the CSF indicates inflammation by increase in cells and protein and the survey radiographs do not demonstrate significant findings, we then treat the inflammation rather than proceed with myelography. Based upon the response to therapy, we reassess the need for further tests. CSF titers are submitted for the relevant infectious agents providing confirmation of the specific disease causing organism. In those cases where a specific disease causing organism can be found, the treatment is adjusted appropriately. When no organism is found, the tentative diagnosis of inflammatory meningomyelitis is made. Many newer forms of meningomyelitis are now recognized including steroid-responsive meningomyelitis. This is usually associated with an increase in blood vessel fragility and may lead to an apparently blood-contaminated CSF tap. On examination, however, there is a marked increase in non-degenerative neutrophils in the CSF.

As in beagles with necrotizing vasculitis (beagle neck pain syndrome), many of patients with steroid-responsive meningomyelitis have elevations in alpha 2 globulins on serum electrophoresis. Steroid-responsive meningomyelitis probably represents a form of vasculitis which results in inflammation in the CNS. Conventional therapy with corticosteroids will not always resolve this condition, since steroids only suppress the symptoms of the disease. Although some dogs recover from this disease following corticosteroid management, many would probably benefit from alternative therapy. Conventional therapy involves giving prednisolone at 1 mg/kg/day in three divided doses. Once the signs resolve (usually within 72 hours), the dosage is reduced to twice a day. This is further reduced to daily medication in the morning and, finally, to alternate day therapy. We find that many patients will benefit from anti-oxidant therapy, including vitamin E, vitamin C and selenium. Additional medications of benefit include omega-3-fatty acids, ginkgo biloba extract and green tea. When pain is present, garlic, ginger and feverfew may help reduce the inflammation without causing additional gastrointestinal signs. Some patients will be relieved by the alternative medication, reducing or replacing the corticosteroid.

### ***Discospondylitis:***

Discospondylitis represents an infection of the vertebrae associated with abscessation of the intervertebral space. It may be secondary to a migrating foreign body; but, often, no specific source of the infections is found. It is thought that, in most cases, there is a hematogenous spread of the infection which isolates into a degenerative disc. Although some cases are associated with vegetative endocarditis, most do not demonstrate a source of infection. It may be that agents enter through inflamed tissues associated with periodontal disease. In cases where there is persistent or intermittent fever, blood cultures may provide information about the infection. This is, however, less common than finding the organism in the urine.

The primary complaint in discospondylitis is pain at the site of infection. In severe cases, quadriplegia and anorexia may be present with cervical discospondylitis. The diagnosis is confirmed by routine spinal radiographs showing characteristic lysis and sclerosis of the adjacent endplates of the vertebrae. This is one of the few neurologic conditions where the diagnosis can be made on routine radiographic examination. The minimum data base includes a CBC (with a marker of inflammation such as the plasma fibrinogen level), urinalysis (with culture), fecal examination, *Brucella canis* titer, and spinal radiographs. Chest radiographs and echocardiography may be indicated if there is a heart murmur. Since the radiography changes may not occur until 2-3 weeks from the start of clinical signs, repeat radiographic examination is indicated when discospondylitis is high on the differential list. The CBC may reflect changes consistent with infection (including neutrophilia) or be normal. One of the important monitors is the marker of inflammation. We use fibrinogen, since it is easy and inexpensive to run. When the fibrinogen levels are elevated, this is a good indicator of a disease with much tissue reaction. On the other hand, when the fibrinogen is low, I am particularly concerned about the possibility of fungal disease. In the latter case, I usually perform a routine chest radiograph looking for discospondylitic-like lesions between the sternabrae. When lesions are also present between the sternabrae, most often fungal infection is the cause of the discospondylitis lesions.

The causative agents are bacteria (*Staphylococcus*, *Streptococcus* and *Corynebacterium* are the most common, although *Brucella* can be occasionally be seen as a cause), parasitic (*Spirocerca lupi* in thoracic discospondylitis), and fungal (*Aspergillus* and *Nocardia*). As such, the treatment and prognosis vary depending upon the organism causing the infection. Parasitic infections are rare except in the Southwestern US and usually represent advanced cases of parasitism. *Brucella canis* infection is not uncommon, but much less so than the other bacterial causes. When *Brucella* appears to be the cause, antibiotic therapy must take this into account (usually, I use doxycycline). Fungal infections with *Aspergillus* do not respond well to antifungal drugs. Recently, there have been reports of controlling the infection for extended period using itraconazole. I use raw garlic in hopes that it will help control the problem.

By in large, the most common causes of discospondylitis are secondary to bacteria which can be treated using a combination of sulfa drugs (sulfadimethoxine, 15 mg/kg every 12 hours) and either cephalosporins (22 mg/kg every 8-12 hours) or enrofloxacin (5-7.5 mg/kg every 12 hours). I prefer the former combination and treat the infection for a minimum of 6-8 weeks. Radiographic repair usually lags behind remission of the infection; however, following the response to therapy and continuing therapy beyond the time of radiographic quiescence seem the best policy. In cases which do not respond, the urine should be reexamined and abdominal ultrasound of the kidneys performed, looking for evidence that fungal disease was the real cause. Rarely, the infection will result in bony compression or instability requiring surgical intervention. Most often, spinal cord compression is

the result of soft tissue inflammation which subsides quickly with appropriate antibiotic therapy.

### ***Cervical Vertebral Malformation Complex:***

Wobbler's disease occurs in young and old animals. In young animals, it appears to be secondary to inherited malformation and mis-articulation of the cervical vertebrae which is accentuated by high protein diets. In older animals, it appears to be secondary to chronic degenerative disc disease. Although other large breeds can be affected, it is said to be a disease of young Great Danes and old Doberman Pinchers. When a Doberman Pincher presents with signs of rear leg ataxia with "root signature" in the forelegs, there is a high probability that the dog has Wobbler's disease.

The onset of clinical signs can be acute or slow and insidious. There is evidence of ataxia in all four limbs with the pelvic limbs being more affected. There will be both conscious and unconscious proprioceptive dysfunction with a wide-based stance in the rear legs. The forelegs may show a stiff and stilted gait with atrophy or fasciculations of the deltoideus, biceps and infra- and supraspinatus muscles. There is usually some degree of neck pain on palpation and neck manipulations. One sign of this is a reluctance to hop medially with the forelegs.

The diagnosis can be suspected on survey radiographs of the neck, looking for narrowed IVD spaces and sclerosis of the demi-facets. CSF analysis is usually within normal limits, although a small number of cases will show a mild increase in cells (4-10 cells/: 1) and protein (25-35 mg/ml). EMG can help confirm the location and the denervation of the muscles with fasciculations. The diagnosis is confirmed on myelography, which shows evidence of IVD protrusion and the presence of ligamentous or bony intrusion into the neural canal. Since CVM represents a dynamic lesion, myelography with mildly flexed and extended views is the diagnostic technique of choice. It is also important to take a "lazy" lateral view, since stretching the neck can reduce the lesion so as to overlook it. If the lesion is alleviated with flexion and accentuated on extension, the problem is partially due to ligamentous hypertrophy. On the other hand, if flexion and extension do not affect the lesion, it is probably secondary to IVD protrusion. I feel that a single lesion is better than multiple ones. Further, an IVD protrusion is less problematic than one with ligamentous hypertrophy.

The treatment of CVM is surgery. In cases where surgery is not possible (patient has complications or is elderly), medical management with prednisolone and diazepam may provide temporary relief. However, in the absence of compelling reasons not to perform surgery, surgical decompression is needed. There are several surgical techniques available to treat Wobbler's disease including dorsal laminectomy, ventral slot and ventral slot with distraction (by various means). In cases of multiple lesions, dorsal laminectomy was the method of choice, in the past. Dorsal laminectomy has risks and the success rate is the lowest of methods for correcting CVM. In qualified hands, it is still a good technique. The overall success is around 75% with a 20-25% morbidity and a 5-10% mortality. Large breeds do not tolerate dorsal laminectomy well. Ventral slot is excellent for IVD protrusion, but increases compression from ligamentous hypertrophy. In simple IVD protrusion, ventral slot has a 90-95% success rate with a 5% morbidity and <1% mortality. The morbidity and mortality increase for ventral slots when ligamentous hypertrophy is present. When ligamentous hypertrophy is present, ventral slot alone is generally inadequate to correct the problem. A number of techniques have been described to perform a ventral slot and

maintain distraction across the IVD space. These methods include various implants from Harrington rods to screws (or pins) and methylmethacrylate. The method we use is a modified “screw and washer” technique. The washer we use is a polypropylene ring made from the end of an endotracheal tube. This is packed with bone graft and the screw stabilizes the implant while fusion takes place. In this method, the “slot” is performed by discectomy without removing the endplates. It is my belief that fusion is the goal of CVM surgery and this is best done in distraction. Another popular method (which I do not believe provides adequate fusion) is to inject methylmethacrylate between the vertebrae at the ventral slot site. This can be used as a salvage procedure.

Following surgery, the patient should be kept quite for 30 days and supported with a neck brace and bandage. After the first month, the activity level is gradually returned to normal. Depending upon the severity of the initial damage, most patients will improve, reaching 80% of their recovery in the first 3 months. There is a potential for the “domino” effect, whereby the IVD on either side of the surgery site will develop problems in 6 months to 2 years following the initial correction. I find that this is more often when the beginnings of CVM were present in the beginning. We now are much more aggressive than in the past, fixing multiple lesions from the start.

## **PARAPARESIS AND PARAPLEGIA**

### ***Introduction:***

Paraparesis (weakness in the rear limbs) and paraplegia (paralysis of the rear limbs) unaccompanied by signs of additional CNS disturbance suggests that the disease is located caudal to T2. If the rear limb reflexes are intact, the lesion is between T2 and L3. If the rear leg reflexes are diminished to absent, the lesion is between L4 and S2. This can be refined further in that lesions between L4 and L5 result in loss of femoral nerve function, manifested as a decrease in the patellar tendon reflex and inability to support weight in the rear legs. Lesions between L6 and S2 result in sciatic nerve dysfunction, reducing rear leg withdrawal, cranial tibialis muscle, gastrocnemius muscle and sciatic nerve reflexes.

The differential diagnosis of paraparesis and paraplegia include a number of congenital diseases, including vertebral malformations, various spinal cord malformations, multiple cartilaginous exostoses, lysosomal storage diseases, and breed-specific disorders. Other disorders are similar to those which affect the cervical spinal cord including meningomyelitis (from various causes), degenerative disc disease, spinal cord trauma, fibrocartilaginous infarction, and neoplasia. In some breeds, the differential also includes degenerative myelopathy.

### ***Diagnostic Approach:***

The neurologic assessment of patients with rear leg problems helps to confirm that the disease is neurologic in nature and its location. Weakness can indicate neurologic disease, muscle disease or systemic illness. On the other hand, reproducible deficits in proprioception usually is indicative of neurologic disease, whether knuckling, stumbling or falling or conscious proprioceptive deficits or dysmetria of unconscious proprioceptive dysfunction. When deciding whether a rear leg lameness is secondary to orthopedic or neurologic disease, examination of proprioceptive function can help make the differentiation.

Unlike cervical disease, there are several neurologic tests which can assist in lesion localization with TL disease. If the lesion is between T2 and L3, Schiff-Sherrington syndrome may be seen. Also, between T2 and L4 is the panniculus response, where superficial stimulation of the skin over the back results in stimulation of intraspinal pain pathways with the resultant contraction of the latisimus dorsi muscle. Due to the overlap of sensory dermatomes, the panniculus response will be absent 1-2 segments caudal to the lesion. Hyperpathia on deep palpation will be present at the cranial edge of the lesion and hyperesthesia will be evident on pin prick of the skin at the cranial and caudal edges of the lesion. By locating hyperpathia and hyperesthesia and demonstrating the loss of the panniculus response 1-2 segments caudally, the lesion is found.

The ancillary diagnostic tests for TL spinal disease are identical to those for cervical disease with the exception that lumbar CSF should be obtained in most instances. Since the flow of CSF is from cranial to caudal, lumbar CSF more accurately represents changes within the TL spinal column. This is usually obtained by carefully passing a needle into the subarachnoid space between L5-L6 or L4-L5.

### ***Thoracolumbar IVD Disease:***

Intervertebral disc (IVD) disease is a surgical disease. Now, that has been said I will attempt to explain the disease and why surgery is the treatment of choice. Not only is IVD disease a common problem, it is one which I personally like, since it is one neurologic disease which can be cured. IVD disease can occur as a protrusion of the IVD (Hansen's Type 2 IVD) with the dorsal annulus still covering the disc material or as a herniation of the nucleus pulposus into the neural canal (Hansen's Type 1 IVD). The former is most common in non-chondrodystrophic animals (straight-legged dogs) and occurs as a result of age-related changes in the IVD. As animals age, the water content of the IVD diminishes and the collagen content increases (similar to nuclear sclerosis of the eye). This results in a decrease in the IVD elasticity, leading to degeneration of the annulus fibrosis and protrusion of the IVD. Depending upon the location, this can result in spinal cord or nerve root compression and development neurologic signs. The onset of signs increases with age, peaking around 8-10 years of age. This type of IVD protrusion is uncommon before 5-6 years of age.

On the other hand, chondrodystrophic breeds of dogs are prone to the development of IVD herniation early in life. In these breeds (including dachshunds, beagles, Pekinese, miniature poodles, cocker spaniels, Pomeranians and basset hounds), there is a metaplasia of the nucleus pulposus whereby the normal collagen fibers of the nucleus are replaced by hyaline fibers. The hyaline fibers are less elastic than collagen fibers leading to degeneration of the annulus fibrosis. The hyaline fibers during this degenerative process calcify, creating further inelasticity. Due to the fact that the annulus fibrosis is thinnest dorsally toward the spinal cord, the least line of resistance for the degeneration and breakdown of the annulus is toward the spinal cord. Ultimately, the annulus ruptures allowing the herniation of the degenerative nucleus into the neural canal, compressing the spinal cord. Not only does the IVD material compress the spinal cord, but the degenerative material is irritative in nature. The presence of the herniated material in the epidural space causes inflammation, furthering the swelling associated with the herniation.

Almost all chondrodystrophic dogs will show some degree of IVD degeneration within a year of age. The earliest I have seen clinical IVD herniation in these dogs is at 7 months. Usually the onset is between 2-3 years of age with the peak incidence being between 4-6 years of age. There

are 26 IVD is dogs, ant one of which can herniate. However, IVD herniation is less common in the upper thoracic region due to the conjugal ligament which connects the rib heads and reinforces the dorsal annulus in that area. Of the remaining spinal column regions, 20% of IVD herniations occur in the cervical region (C2-C7) with 80% of these at C2-3. In the thoracolumbar spinal column, 80% of the IVD herniations occur with 67-75% of these occurring at T12-13 or T13-L1. The incidence rapidly dissipates cranially and caudally from the TL junction. The incidence between T1 and T9 is less than 0.5%. From L4 caudally, each disc has an incidence of around 2.5%. Cervical IVD herniation will cause quadriparesis (or quadriplegia) while TL IVD herniations result in paraparesis to paraplegia.

In addition to location, the dynamic factor dictates the severity of clinical signs. The amount of traumatic force imparted by a small amount of material traveling rapidly is greater than a larger amount going slow. In the worst case, this means then time for intervention is also quiet short. In most cases of IVD disease, definitive treatment must be started before 24 hours in order to achieve the greatest success. In some cases, this time is shorter. Unfortunately, delaying treatment to see the outcome may preclude success. We treat severe IVD disease as a medical and surgical emergency. In patients with complete motor and sensory paralysis, the patient should be treated for acute spinal injury and be immediately referred to a center who can diagnose and definitively treat the problem. In patients who are paralyzed but retain deep pain, then it is possible to treat them for acute spinal injury and observe them for signs of improvement. If they are worse or no better within 24 hours, they then constitute an emergency referral. On the other hand, it is best to refer these patients at the outset. In patients with mild paresis or mere back pain, they can be worked-up for the rule/out and referred if they do not make improvements in 5-7 days. These later patients may benefit from surgical intervention, but might also recover from the current IVD herniation with medical management. They are still surgical candidates upon recovery, to prevent future IVD disease.

Medical management of IVD disease consists of absolute rest for a minimum of 30 days or 3 weeks beyond return to clinical normalcy. This confinement must be in a cage no more than 2.5 x 1.5 times the animal's body length. An airline carrier is ideal. Many patients will benefit from corticosteroid management during the initiation of treatment. I think this should only be done under direct veterinary supervision. If the patient feels better and then becomes active before healing has occur, they are at great risk to get worse. We see this outcome commonly. It could be prevented in many cases, with absolute confinement of the patient. Owners do not always comply, allowing their pet to worsen. For that reason, I prefer to treat these patients in the hospital for the first 5-7 days, going home without medication, only confinement. I would give 30 mg/kg of methylprednisolone (Solu Medral or Solu Delta Cortef) IV, initially; followed by 15 mg/kg every 8 hours for the first 24 hours. Then, I give oral prednisolone at 1 mg/kg/day in 2 divided doses for 5 days. If more steroids are needed, I give 0.5 mg/kg every other day in the morning. During steroid medication, it is necessary to protect against steroid-gastritis. I use misoprostol (50-100 : g) every 12 hours until using alternate day steroids. Many patients feel better with muscle relaxants. I prefer diazepam at 0.25-0.5 mg/kg every 8 hours. Once the animal has recovered and has been normal without medication for 3 weeks, prophylactic IVD fenestration can be performed. It is felt that 60% of patients with moderate to mild IVD disease will recover with medical management. On the other hand, 50-80% of these patients will experience additional IVD disease at the same or other site during their lives. Clinically, I usually see recurrence of IVD disease in patients without

prophylactic fenestration every 6 months to a year.

As such, I prefer the surgical approach, decompression to treat the acute disease combined with fenestration to prevent future problems. Fenestration is a statistical game, removing the nuclear material (and creating fibrosis within the disc for additional support) so that the chance of IVD herniation at the fenestrated site is lessened. Fenestration does not remove material from the neural canal, laminectomy is needed for that. In the neck, fenestration of C2-C6 reduces the likelihood of future herniation by 99% in that region (.99 x .2, overall). In the TL region, fenestration of T11-L3 reduces the chances by 95% in that region (.92 x .8, overall). By combining cervical and TL fenestration, the overall chances of recurrent IVD disease is reduced by 93%. While not all patients read the same statistical books, generally this will eliminate future IVD disease. If decompression is need for the patient to recover, fenestration can be performed to prevent recurrence. In cases where fenestration has not been done, the patient remains at risk for recurrent IVD disease.

The diagnosis of IVD disease is made with radiographs and myelography. Since many cases present with acute signs, EMG does not offer assistance. In some cases, CSF analysis helps rule/out meningomyelitis, but myelography is what determines the extend and surgical approach of choice. In most cases, this will be hemilaminectomy. Myelography helps to confirm the side upon which to perform the laminectomy. Scout radiographs may demonstrate the presence of degenerative disc disease by revealing calcified nuclear material. The site of herniation may show collapse of the IVD space, wedging of the IVD space, collapse of the demi-facets and the presence of calcified material in the neural canal. Coupled with the neurologic examination, this may be enough to determine the need for surgical intervention. When there is doubt about the location or the radiographic changes do not fit the neurologic findings, myelography is needed. Myelography will also help rule/out other diseases which might cause spinal cord compression, such as neoplasia.

Beyond treatment and surgical fenestration, it is possible that certain dietary supplements would benefit chondrodystrophic patients to prevent IVD disease or to facilitate their recovery upon IVD herniation. Tofu (rich in soy lecithin) may aid in spinal cord myelination. Antioxidants like vitamin E, vitamin C and ginkgo biloba may help prevent degeneration and, certainly, appear to help protect the spinal cord from the results on spinal cord injury. Vitamin E and C must be given prior to the damage, while ginkgo biloba may be as effective as methylprednisolone in treating the injury once it has happened. Our current understanding of spinal cord damage suggests that antioxidants may work by sparing spinal cord function, while the steroid receptor may help protect spinal cord architecture. As such, methylprednisolone, which contains both the antioxidant effect and steroid receptor effect, is currently the best medication for the treatment of brain and spinal cord injury.

### ***Fibrocartilaginous Infarction:***

Even though animals do not suffer from to the same degree of vascular disease as human beings, infarction of the spinal cord with fibrocartilaginous material is not uncommon. It occurs in any breed of dogs, but is most common in large breeds, such as Great Danes, Labrador retrievers and German Shepherds. Although both arteries and veins can be affected, most commonly it is the venous system of the spinal cord which is obstructed, leading to a hemorrhagic infarction. It is believed that herniation of the nucleus pulposus takes place either into the vertebral body or the venous sinuses within the spinal column. Since the vertebral body represents a vascular space communicating with the spinal venous system, the material gains access to the spinal veins. These

veins do not have valves, allowing the fibrocartilaginous material to flow up and down the spinal column. When intra-thoracic pressure increases, this material can be back-flushed into small penetrating spinal cord veins. When the intra-thoracic pressure returns to normal, the veins collapse trapping the material and leading to excessive venous pressure upstream to the occlusion. The venules rupture leading to a hemorrhagic infarction. The pattern of infarction usually affects a quadrant of the spinal cord, although initial signs may affect more of the spinal pathways from inflammation and spinal cord swelling. The infarction can occur anywhere along the spinal cord, but the causal cervical and mid- to lower lumbar spinal cord segments appear to be most frequently involved.

The presence of spinal cord infarction should be suspected whenever a patient presents with acute onset of paresis or paralysis which is markedly asymmetrical and there is no evidence of hyperpathia. Vascular disease is generally acute and non-progressive. In addition, the spinal cord contains pain pathways, but no pain receptors. As such, strict diseases within the spinal cord without meningeal involvement are usually not painful. Most of the other diagnostic tests will be within normal limits. Occasionally, there will be evidence of hemorrhage on CSF analysis. Spinal radiographs, do not demonstrate the disease, but may reveal other evidence of spinal column degeneration. Myelography will be normal or demonstrate mild intramedullary swelling. In a small number of cases (where the vascular occlusion is secondary to a systemic disease), the minimum data base will show evidence of the systemic disease.

The treatment of spinal cord infarction is that for acute spinal cord injury, using methylprednisolone at 30 mg/kg initially. This is followed by 15 mg/kg every 8 hours for the first 24-48 hours. Then, oral prednisolone is begun at 0.5 mg /kg every 12 hours for 5 days. I continue prednisolone at 0.5 mg/kg every other day, in the morning, for up to another 2 weeks. Many cases will improve dramatically within the first week, although they will still improve over several months. If there has been no improvement in the first week, re-examination and additional tests may be indicated. Since usually only a quadrant of the spinal cord is affected, the patient will improve most on the unaffected side. Reorganization will usually allow these patients to function adequately. Spinal cord infarction from fibrocartilaginous material is a sporadic problem and, usually, does not reoccur.

### ***Lumbosacral Stenosis:***

The cauda equina is less frequently the site of neurologic dysfunction than the cervical or thoracolumbar spine in small animals; however, it is not uncommon to see the condition in large breeds of dogs. Disease of the low lumbar spine has a pronounced effect in that several nerves controlling locomotion, fecal and urinary continence, and sensation to the hind quarters can be involved simultaneously or individually. Therefore, the syndrome of cauda equina compression can result in diverse symptoms and is often difficult to diagnose. In order to understand diagnosis and treatment of the problem better, this discussion reviews the anatomic features, pathomechanics, diagnostic aids, and treatment of this syndrome.

### ***Anatomic Features:***

The cauda equina is a leash of nerve roots of the low lumbar spine. These nerve roots

descend from their spinal cord segment origins to their site of emergence from the spinal canal. Early in the development of the embryo, the spinal nerves leave the spinal cord at right angles to exit at the respective foramina. As the embryo continues to develop, the spinal cord ceases to grow before the vertebral column. It is because of this differential growth of the two structures that the spinal cord of the dog extends only to the level of the fifth or sixth lumbar vertebra. Thus, the spinal nerves of the mature dog have to course obliquely and caudally to exit at the respective foramina.

Nerves included in the cauda equina are L7, S1 to 3, and coccygeal nerves 1 to 5. The L6, L7, and S1 nerve roots contribute fibers to the sciatic nerve. The pudendal nerve, which innervates the perineum, is composed of the S1 and S2 nerve roots. The pelvic nerve, which carries parasympathetic fibers to the bowel and bladder, is composed of fibers from S2 and S3. The tail is innervated by the nerve roots originating from the coccygeal segments. The cauda equina is enclosed within the spinal canal whose boundaries are (1) dorsally, the lamina of the vertebrae, ligamentum flavum, and articular facets; (2) laterally, the pedicles of the vertebrae and ligamentum flavum; and (3) ventrally, the body of the vertebrae, dorsal longitudinal ligament, and the annulus fibrosus. The cross section of the spinal canal is triangular in shape, and the facets form lateral recesses in which nerves lie just prior to their exit through the foramina.

The intervertebral foramina form short restricting canals for exit of spinal nerves and blood vessels to and from the spinal canal. Articular facets, ligamentum flavum, pedicles, vertebral bodies, and intervertebral disks make up the boundaries of the foramina. In the sacrum, the nerves exit through the foramina in the bone. Deformities and injuries, whether congenital or acquired, of any of these structures comprising the canal or foramina may result in attenuation of the cauda equina and structures in the intervertebral foramina.

### ***Causes of Compression:***

Attenuation of the cauda equina may have several causes. Neoplasia, infection (discospondylitis), acute disk extrusion, spondylosis, trauma, or congenital spinal stenosis are among the lesions that may attenuate the cauda equina and may cause neurologic dysfunction. Infectious processes such as discospondylitis may be of bacterial or, less frequently, of fungal origin. The source of these infections may be systemic or may be spread from local wounds in the area, such as from tail docking and bite wounds over and around the dorsum of the pelvis. The subsequent inflammatory, destructive, and proliferative processes may cause instability as well as nerve root compression.

Although neoplasia is not commonly the cause of cauda equina compression, chondrosarcomas, osteosarcomas, and metastatic choroid plexus carcinoma of the lumbosacral spine have been reported. Trauma from various causes can result in fracture dislocations of the lumbosacral spine.

Other than the aforementioned etiologic factors, spinal stenosis can be either acquired or congenital. Acquired forms of lumbar spinal stenosis can be caused by primary degenerative spondylosis (multifocal), focal spondylosis secondary to or associated with degenerative disk disease, spondylolytic spondylolisthesis, or pseudospondylolisthesis. These changes basically result from instability of one or more segments of the lumbar spine. In an effort to afford stability, the body responds to the proliferative changes in several structures (that is, thickened lamina, pedicles, facets, and ligaments). In veterinary medicine, some of the causes of acquired stenosis have been

documented.

Congenital stenosis can be subdivided into those episodes that occur in dogs with achondroplasia and those considered to be idiopathic. Whatever the cause, congenital stenosis is characterized by a shortening of the pedicles, thickened and sclerotic apposition of the lamina and articular processes, infolding and hypertrophy of the ligamentum flavum adjoining the lamina, and sclerotic and bulbous articular facets that bulge into the dorsal half of the canal. The most common sites of involvement in dogs are the L6-L7 and L7-S1 spinal cord segments. Idiopathic lumbar spinal stenosis does not usually manifest itself until middle or late age. In these patients, the bony changes are present at birth with further attenuation, as evidenced by a thickened ligamentum flavum, occurring later in life and resulting in clinical signs.

Spinal stenosis not only causes mechanical compression of the dural tube and nerve roots, but also produces intermittent ischemia of the nerve roots. Dilation of the vessels of the nerve roots and spinal cord occurs subsequent to the increased demand imposed on neural function during exercise. The nerve roots and associated vessels, being abnormally confined by the stenosed canal or intervertebral foramen, are further attenuated when exercise is induced. The subsequent overall increased diameter of the nerve roots, confined by the stenotic canal, reduces the effective blood flow to roots and causes an ischemic phenomenon.

Ischemia produces root pain and subsequent reflex pain (paresthesias, dysesthesias) to the part innervated by that nerve(s). Various states of paresis may also be associated with the ischemic and pressure phenomena. In each instance, early in the course of the disease, the referred pain or paresis is intermittent and is associated with exercise. The severity of pain or paresis progresses with increased stenosis, which is associated with degenerative disease of the ligamentous and bony structure of the stenotic canal. In the latter instance, the pain or paresis may be persistent. Therefore, adequate historical information is mandatory to establish the initial intermittency of the deficits. Signs referable to the extremities, tail, bowel or bladder function, and genitals have been reported.

### ***Diagnosis of Compression:***

Animals presented to the veterinarian with stenosis of the cauda equina usually exhibit intermittent lameness, fecal or urinary incontinence, or paresthesias and dysesthesias, such as evidenced by tail biting, leg biting, genital licking, conscious proprioception deficits, and motor weakness. These animals all have lumbosacral pain. The lameness is usually related to dysfunction of the nerve roots comprising the sciatic nerve, whereas fecal and urinary incontinence are the result of attenuation of the S2 and S3 nerve roots.

Paresthesias are unpleasant sensory disturbances that often manifest as referred pain (lameness) or in various forms of self-mutilation of the tail, leg, or extremity. More often than not, dogs are treated for various obscure dermatologic problems. Dysesthesias are even less pleasant sensory disturbances enhanced by manipulation of the affected part by the clinician. Each condition has been demonstrated in previous literature.

The cauda equina is unique because a large number of nerve roots are contained in a small area (L6 through S3). A single lesion can involve several nerves and may result in one or all of the aforementioned signs. Thus, the presenting symptoms are often bizarre and mimic other problems, such as orthopedic disorders, anal sacculitis, and tail-head dermatitis. In order to arrive at a correct

diagnosis, a general examination of the entire animal and an orthopedic examination of the hind limbs should be performed first.

Once the more common causes are ruled out, a critical neurologic examination is indicated, including an evaluation of conscious proprioception, motor function, reflexes, sensory status, anal tone, and state of continence (from the patient's medical history). Most important, the clinician must manipulate the lumbosacral spine to establish the presence or absence of pain. This finding was the most consistent on all reported cases.

Electromyographic studies have also been used to localize the lesions to specific nerves and segments in animals with this syndrome. Whenever facilities are available, this tool can provide useful information to support a diagnosis. In our experience, however, confirmation with such studies is not the rule.

Having established historical and clinical neurologic signs referable to the cauda equina, plain radiographs, taken when the patient is under general anesthesia, are indicated to evaluate potential existing disease of the lumbosacral spine. Neoplasia, fractures, congenital lesions, herniated disks, spondylosis, discospondylitis, and lumbosacral stenosis can often be confirmed by radiographic means alone. In numerous cases of congenital stenosis, however, little if any bony pathologic tissue may be demonstrated. Myelographic studies in this area are of little value because it is often difficult to obtain an adequate dye column this far caudally. Intraosseous venography may be of value in some patients; however, it does not permit adequate study of the dorsal aspect of the canal. Consideration should be given to epidural dye studies. CT scans and MRI scans offer the best method to accurately examine the cauda equina and to determine the extent of involvement of the various anatomic structures in the disease process. They do not allow dynamic studies which can be done with other radiographic techniques, but dynamic studies are not often needed.

### ***Surgical Treatment of Compression:***

In patients demonstrating neurologic dysfunction of the cauda equina, several factors should be considered in deciding the optimal mode of therapy:

1. **Duration and severity of the dysfunction.** An animal with mild proprioceptive deficits of short duration (1 to 2 days) has a better prognosis than an animal with no sensation to the hind quarters.

2. **Etiologic factors.** Neoplastic processes, such as osteogenic sarcoma, may offer a poor prognosis. Congenital stenosis and some other disorders offer a good prognosis if a surgical procedure is performed early in the course of the disease. Discospondylitis responds, in our experience, most favorably to analgesics, muscle relaxants, and antibiotics. Patients that respond poorly are candidates for surgical treatment, culture, and biopsy.

3. **Economics and aftercare.** Especially in the case of traumatic luxations or fractures of the area, surgical decompression, stabilization, and aftercare are costly and time-consuming. If the patient's owners are unwilling or unable to make financial commitments or fail to understand their role in postoperative care, surgical treatment is not warranted.

It should be remembered that each case is to be evaluated on an individual basis; not all are clear cut with regard to prognosis, and individual decisions must be made.

Surgical exposure of the cauda equina is best accomplished by laminectomy, facetectomy, and foraminotomy. The epiaxial musculature is subperiosteally elevated and is retracted laterally.

The dorsal spinous processes are removed with a rongeur. The dorsal lamina is removed with a rongeur or a high-speed bur. In cases of congenital stenosis, a thickened ligamentum flavum may be encountered. The ligament can be resected using a No. 11 Bard-Parker scalpel blade. The extent of the laminectomy should continue cranially and caudally until the dural contents are free of compression. Laterally, the facets must be removed, effecting a foraminotomy and subsequently decompressing the nerve roots. Biopsy specimens can be taken in cases of suspected neoplasia or infection. Curettage and culture of the interspace in cases of discospondylitis can be accomplished by working lateral to the sheath of nerves. Prior to closure, the spine is evaluated for stability. Rarely is instability a feature in patients with stenosis of the spinal canal. If the spine is unstable, the technique used in the repair of spinal fractures can be employed. The wound is copiously lavaged with normothermic saline solution. A free graft of fat is taken from the subcutaneous tissue near the incision and is placed over the laminectomy site to effectively decrease scar formation. The lumbosacral fascia is closed on the midline with 2-0 or 3-0 monofilament nylon suture material. The remainder of the closure is routine.

### ***Postoperative Care:***

As with all surgical cases, proper postoperative care is essential to obtain satisfactory results. Strict rest and confinement should be enforced especially in active dogs for 4 to 8 weeks. In dogs that are unable to ambulate, straw bedding helps to prevent decubitus ulcers and urine burns, and bladder expressions or intermittent catheterization and assisted fecal evacuation may be indicated to prevent adverse sequella.

### ***Degenerative Myelopathy of German Shepherd Dogs:***

#### ***Introduction:***

Degenerative Myelopathy (DM) was first described as a specific degenerative neurologic disease in 1973. Since then, much has been done to understand the processes involved in the disease and into the treatment of DM. Hopefully, this will help you understand the problem and to explain further the steps that can be taken to help dogs afflicted with DM.

The age at onset is 5 to 14 years, which corresponds to the third to sixth decades of human life. Although a few cases have been reported in other large breeds of dogs, the disease appears with relative frequency only in the German Shepherd breed, suggesting that there is a genetic predisposition for German Shepherd dogs (GSD) in developing DM. The work presented here and by others on the nature of DM has been performed in the German Shepherd breed. Care must be taken in extrapolating this information to other breeds of dogs. It is currently not known whether the exact condition exists in other breeds of dogs. Many dogs may experience a spinal cord disease (myelopathy) which is chronic and progressive (degenerative); but, unless they are caused by the same immune-related disease which characterizes DM of GSD, the treatments described herein may be ineffectual. The breeds for which there is data to suggest that they also suffer from DM of GSD are the Belgium Shepherd, Old English Sheep Dog, Rhodesian Ridgeback, Weimaraner and, probably, Great Pyrenees. Confirmation of the diagnosis is important in other breeds before assuming that they have DM of GSD.

Diagnosis of DM is made by a history of progressive spinal ataxia and weakness that may have a waxing and waning course or be steadily progressive. This is supported by the neurologic findings of a diffuse thoracolumbar spinal cord dysfunction. Clinical pathologic examinations are generally normal except for an elevated cerebral spinal fluid (CSF) protein in the lumbar cistern. Electromyographic (EMG) examination reveals no lower motor unit disease, supporting the localization of the disease process in the white matter pathways of the spinal cord. Spinal cord evoked potentials recorded during the EMG do show changes which help determine the presence of spinal cord disease. Radiographs of the spinal column including myelography are normal (other than old age changes) in uncomplicated DM. Unfortunately, myelography can be associated with worsening of clinical signs and carries some degree of risk for certain patients.

Dogs afflicted with DM have depressed lymphocyte blastogenesis to plant mitogens. The depression of their cell mediated immune responses correlates with the clinical stage and severity of the disease. Furthermore, this suppression has been shown to be due to the genesis of a circulating suppressor cell. Some dogs with DM exhibit antigen-binding cells specific to canine myelin basic protein. Immunoglobulins have been shown to be bound within lesions within the spinal cords of dogs with DM. These patients also show increased circulating immune-complexes in their sera. The antigens in these immune-complexes have been examined and appear to be markers of inflammation as they have been found to exist in patients who have other inflammatory diseases of the central nervous system. 2-Dimensional electrophoresis of CSF proteins indicates that the elevated proteins in the CSF of DM patients represent changes which are related to inflammation. While these changes are not specific for DM, the other conditions in which the inflammatory proteins have been found in CSF can be differentiated by clinical signs. The 2-dimensional electrophoresis of CSF proteins appears to be one of the most specific change seen in DM. Recently, we have found that CSF levels of the enzyme, acetylcholinesterase, are elevated in patients with DM. Again, this occurs in other forms of central nervous system inflammation in dogs. However, when combined with the history, neurologic signs, CSF protein concentration and EMG, the elevated CSF acetylcholinesterase level helps confirm the diagnosis. This allows the inclusion of DM in the diagnosis, even if other problems are uncovered during the examination.

The gross pathologic examination of dogs with DM generally is not contributory toward the diagnosis. The striking features being the reduction of rear limb and caudal axial musculature. The microscopic neural tissue lesions consist of widespread demyelination of the spinal cord, with the greatest concentration of lesions in the thoracolumbar spinal cord region. In severely involved areas, there is also a reduced number of axons, an increased number of astroglial cells and an increased density of small vascular elements. In the thoracic spinal cord, nearly all funiculi are vacuolated. Similar lesions are occasionally seen scattered throughout the white matter of the brains from some dogs, as well. Many patients have evidence of plasma cell infiltrates in the kidneys on throughout the gastrointestinal tract, providing a hint to the underlying immune disorder causing DM.

During the past two decades, we, at the University of Florida, have provided important new insights into the pathoetiology of DM. The release of antigens during the disease process could explain the immune deficits seen in DM and suggests that processing these immune-complexes by circulating macrophages leads to the development of the circulating suppressor cells that were previously noted. This provides a logical explanation for the presence of immune abnormalities in GSD with DM. Electrophoresis of immune-complexes demonstrates that the proteins present are inflammatory proteins which increase in inflammatory diseases of the dog nervous system. It is

hoped that working with the antigens present in the immune-complexes will lead to a major breakthrough in our understanding of DM and that this also could lead to an early serodiagnostic test for the condition. However, the development of a serodiagnostic test will await the availability of antibodies specific to unique markers within the inflammatory proteins of DM dog immune-complexes.

While the cause of the altered immune system is not known, what is increasingly clear is that DM is caused by an autoimmune disease attacking the nervous systems of patients, leading to progressive neural tissue damage. In many respects, DM is similar to what has been discovered about the pathogenesis of Multiple Sclerosis in human beings. In fact, based upon new data concerning the pathology of MS, we can now say with some degree of certainty that DM is MS in dogs. We believe that, due to some triggering factor, immune-complexes circulate. These immune-complexes lead to endothelial cell damage in the vessels of the CNS. Subsequently, fibrin is deposited in the perivascular spaces. When this degrades (point of action of aminocaproic acid), inflammatory cells are stimulated to migrate into the lesions. The inflammatory cells release prostaglandins and cytokines (point of action of vitamin E and C) which leads to the activation of tissue enzymes and the formation of oxygen free-radicals (point of action of acetylcysteine) which, in turn, leads to tissue damage. Treatment of DM of GSD, which we recommend, is directed at these pathologic processes.

### ***Integrative Medical Approach to Treatment:***

The treatment of DM involves four basic approaches:

- 1) exercise
- 2) dietary supplementation
- 3) medication
- 4) other supportive measures

### ***Rationale:***

Degenerative Myelopathy is an autoimmune disease whereby the patient's own immune system attacks their central nervous system. This immune attack leads to loss of myelin (insulation around nerve fibers) and axons (nerve fibers). While it begins and is most severe within the thoracolumbar (middle back) spinal cord, DM also affects other areas of the central nervous system including the brain stem and sub-cortical white matter. The cause of this autoimmune disease is not known, but there are probably genetic, environmental and toxic factors which eventually lead to its development. Conventional medicine has little to offer patients with DM. On the other hand, use of exercise, certain vitamins and selected drugs have delayed or prevented progression of DM in many afflicted dogs. While these treatment modalities have been directed at suppression of the clinical signs, little has been done to prevent the development of this autoimmune disease.

The purpose of this paper is to provide a rationale for treatment of German Shepherd dogs afflicted with DM with dietary alternatives and certain dietary supplements, hoping to prevent or correct the immune dysfunction which leads to the development of DM. Most of the suggestions presented here have been extrapolated from the human disease most similar to DM in dogs, Multiple Sclerosis, or its animal model, experimental allergic encephalitis. Additional information about the

integrative treatment of MS can be found on Dr. Weil's web page (<http://www.drweil.com>). Dr. Weil teaches integrative medicine at the University of Arizona's Medical School.

### ***Exercise:***

The importance of regular aerobic exercise in the prevention of chronic degenerative diseases should not be overlooked. Many studies in human beings have demonstrated improved muscle performance, memory and cerebral blood flow in patients who undertake aerobic exercise. Many of the goals of treatment in DM are obtainable through regular exercise. Two forms of exercise seem the most useful: walking and swimming. Both have their merits and they may not be exclusive. A number of owners have reported that swimming assists dogs beyond the exercise of mere walking. Swimming generally increases muscle tone and allows movement without stress on joints. Walking, on the other hand, helps build strength, since gravity is involved. In older patients, particularly those with arthritis, gradually building the exercise program is important. In addition, allowing a day of rest between heavy workouts can help the patient recover faster from the exercise. A good general reference of exercise physiology and exercise programs is a book by Jeff Galloway: *Galloway's Book on Running*, Shelter Publications, Inc., Bolinas, CA, 1984.

Exercise is extremely important in maintaining the well being of affected dogs, maximizing muscle tone and maintaining good circulation and conditioning. This is best achieved by an increasing schedule of alternative day exercise. Running loose on the owner's property is not adequate; regular periods of programmed continuous exercise are the most important. It is equally important that the patient with DM be allowed to rest on the day when exercise is not programmed. This will allow strained muscles and tendons to heal and increase the build up of muscle strength. The dogs do not have to be confined, only that they are not encouraged to do strenuous exercise on the "off" day. I recommend starting with 5-10 minutes of walking or swimming every other day for 2 weeks. Then, increase the length of exercise time to a goal of 30 minutes twice a week and a long walk of 1 hour once a week. If your dog already exceeds this limits, that is fine. However, remember to provide a day of easier exercise between vigorous workouts. This is particularly important as the patient gets older. If the patient exhibits muscle or joint stiffness on the day following vigorous exercise, try ginger, garlic, mustard and feverfew to reduce inflammation. Alternately, carprofen (Rimadyl 2 mg/kg twice a day) or acetaminophen (5 mg/kg up to 3 times a day) may help make the patient more comfortable. Many DM patients have remained functional because of exercise alone. We use to think that hospitalization was harmful to patients. We now know it is the lack of exercise which is harmful. Make sure your pet gets their exercise if they are hospitalized or kenneled for any period of time.

### ***Supplementation:***

#### **Dietary Considerations:**

Dietary and dietary supplement management of DM has not received great attention. We, and others, have long sense recommended certain dietary additives do in part to deficient levels of certain vitamins in dogs afflicted with DM, yet dietary supplementation has not resulted in more than mild reduction in the rate of progression of the clinical signs. On the other hand, diet may have

a powerful influence on the development of chronic degenerative diseases and new information suggests that dietary regulation might play a more significant role in the progression and development of diseases like MS. Elimination of toxins from pre-processed food may assist in preventing a number of immune-related disorders. The current treatment of DM is designed to suppress the immune disease, but does nothing to correct the immune alterations which led to the disease state. Diet might help in correcting this defect and allow the immune system in DM dogs to stabilize. The principles of dietary therapy are outlined here, including a "home-made" diet. For those who cannot "cook" for their dog, the basic diet should be supplemented with the additional ingredients list below. It is best to choose a dog food which is close in protein content and is as "natural" as possible. Wild dogs were not meat eaters. They ate bodies, including intestinal contents (often laden with plants and plant materials). Dogs have evolved so that eating animal fats and protein do not cause them to suffer the same problems as human beings when eating these sources of saturated fats. Even so, dogs probably suffer from the same causes of dietary and environmental intoxication which affects human beings.

The basic diet and its components have been checked for balance. In addition to the basic components, we are adding vitamins, minerals and natural herb supplements for which no specific requirement is known or at levels which are to provide a specific pharmacologic effect. Again, we recommend those compounds which scientific evidence supports their efficacy. Used according to the following formula, the diet and compounds should not do any harm and have the potential to do good. By cooking for your dog, you can select healthy products which do not have preservatives and additives which might be harmful. In addition, you have the option to use organically grown foods. If the dietary approach is successful, DM patients may not need to use other medications to prevent further deterioration. It is also possible that this diet might prevent the development of DM in dogs who are presently healthy. These hypotheses will be evident in the future, if they remain true.

**Basic diet:** (based upon 1 serving size for 30-50 pounds body weight)

- 2 oz Boneless Pork Center Loin Chop (boiled, baked or fried in olive oil)
- 4 oz Tofu (soybean curd)
- 8 oz Long Grain Brown Rice (3 oz cooked in 6 oz water)
- 2 tsp Extra Virgin Olive Oil
- ¼ cup Molasses or Honey
- 2 Whole Carrots (boiled and then cut up)
- 1 cup Spinach (cooked)
- 4 Tbs Green Bell Pepper (chopped and steamed)
- 4 Broccoli Spears (boiled and then cut up)

This diet (1 serving for 30-50 pounds body weight) provides approximately 1160-1460 calories per serving. You can substitute poultry meats, beef and lamb for the pork chop. This will alter the composition slightly, mainly by added additional fat. The weight of meat is based upon boneless weight. Most of the items can be prepared in a microwave. Based upon your dogs body weight, you will need to make more or less. For example, if your dog weighs 80 pounds, multiply all the ingredients by 1.5 (can be as high as 2.5 times, though), keeping their relative proportions. This is a starting point. You can also make this portion of the diet in advance, aliquot it into

appropriate quantities and freeze it for later use. Just before feeding time, remove the diet from the freezer and thaw in hot (or boiling) water or microwave to defrost. To complete the diet, add (amount per serving) before serving:

- 1 tsp Dry Ground Ginger
- 2 Raw Garlic Cloves (crushed)
- ½ tsp Dry Mustard
- 1 tsp Bone Meal

Using the above diet, approximately 1 serving equals 1 can of commercial dog food. The exact requirements for your dog can be approximated by substituting the diet on that basis. You should weigh your dog each week, if losing weight, increase the amount of the diet given. If gaining weight, cut back on the amount given. Eventually, the correct amount will be clear. The reason why the amount has such a broad range in that ideas about the daily caloric requirements vary. Since many German Shepherds have sensitive stomachs, it may be wise to phase in the new diet by mixing it with their existing food until they have adapted. Start by mixing the diet with their existing food in equal amounts. After 1 week increase the diet to 75% of their food. After another week, switch completely over to the diet. This diet is balanced and high in most of the vitamins and minerals which your dog will need. Any shortcomings will be corrected with the supplements given below as part of the treatment.

*Note:* The general purpose of the diet is to provide excellent quality of ingredients with protein coming from Soybean curd (tofu). Tofu contains many valuable flavonoids and other ingredients which promote health. If you decide to use a commercial food, you may want to use a Soybean Concentrate which contains these ingredients, but lacks the extra protein. Alternatively, you can add tofu to the diet (5-6 oz/day) and add honey or molasses to it (¼ cup) to make it taste better. Reduce the commercial diet by 25-33% and monitor your dogs weight, reducing or increasing the commercial diet accordingly. The addition of raw garlic is to provide garlic's anti-inflammatory action and (since it is raw) to provide an antibiotic action. Raw garlic is anti-bacterial and anti-fungal. This action is lost when garlic is cooked or dried. Dry ginger is also a good anti-inflammatory. Together with garlic, dry ginger can replace the need for aspirin-like (NSAID) drugs. Fresh ginger or pickled ginger are also good anti-emetic compounds, calming the stomach. Mustard provides ingredients which support improved digestion and bowel function. So, raw garlic, dry ginger (occasionally using fresh or pickled ginger) and dry mustard should be added to the food, even if it is commercial. These will not unbalance the commercial food, providing important drug properties without the side-effects of "non-natural" drugs. Using the vegetables, the diet also provides many nutrient and vitamins which are not found in commercial dog food. If commercial dog food is given, giving extra Soy Concentrate, Soy Lecithin and Beta-Carotene to the diet will improve the commercial food. They are not needed, if you feed the above diet. The diet provides a balanced, moderate protein and fat diet which is high in many essential nutrients. The only commercial food which fulfills many of the goals is Nature's Recipe Canine Vegetarian Diet, available from many specialty pet supply stores.

### **Supplements (dietary):**

Vitamins:

**B-Complex:** B vitamins are water soluble and any excess amount will be eliminated through the urine. They may help in neural regeneration and are something which should be given to dogs. No dog should die while having cheap urine. In DM, there is altered absorption of some B vitamins and supplementation can correct this. If your dog is healthy, then give high potency B-complex (containing approximately 50 mg of most of the B components). If your dog has DM, give stress formula B-complex containing 100 mg of most of the B components.

**Yeast:** Nutritional yeast, in powder or flake form, is a good source of the B-complex vitamins, trace minerals, and some protein. It is not expensive. A heaping tablespoon of yeast will color your dog's urine yellow (owing to its content of riboflavin). You may sprinkle it on the diet, as an alternative to giving your dog a B-complex pill. However, it may be more difficult to be sure you are giving the right dose. Try 1-2 T with eat meal.

Antioxidants:

**Vitamin E:** Vitamin E is an important nutrient which has been shown to have a number of physiologic and pharmacologic effects. It is a potent antioxidant and reduces fat oxidation and increases the production of HDL cholesterol. At higher doses it also reduces cyclooxygenase and lipooxygenases activities, decreasing production of prostaglandins and leukotrienes. As such, it is a potent anti-inflammatory drug. It will reduce platelet function and prolong the bleeding time slightly in healthy individuals. There is no known side-effects to vitamin E at levels less than 4000-6000 IU per day (except in cats, where levels >400 IU/day might create hepatolipidosis). This drug slows the progression of DM and corrects for low serum and tissue levels. In DM, there does appear to be a deficient absorption and tissue-binding protein which accounts for the low serum and tissue concentrations of vitamin E. I recommend that vitamin E be given to all German Shepherd dogs. For GSD under 2 years of age, give 400 IU of vitamin E daily. For GSD over 2 years of age, give 800 IU of vitamin E daily. If your dog develops DM, then the dose of vitamin E should be increased to 2000 IU daily.

**Vitamin C:** Vitamin C works with vitamin E and helps regenerate vitamin E, potentiating its antioxidant effect. Vitamin C supplementation does no harm, since the excess is excreted through the kidney. While dogs produce vitamin C in their bodies (unlike human beings, pigs and guinea pigs who must have it in their diet), under stress or disease, they may need vitamin C in excess of their manufacturing capacity. In excessive dose, vitamin C can cause flatulence and diarrhea. This intestinal tolerance level varies among dogs, but is generally around 3000 mg per day in an adult GSD. I recommend this be given to all GSD. For GSD under 2 years of age, give 250 mg vitamin C twice a day. For GSD over 2 years of age, give 500 mg of vitamin C twice a day. If your dog develops DM, then increase the vitamin C to 1000 mg twice a day unless this level causes diarrhea.

**Selenium:** Selenium is an important mineral which has antioxidant properties similar to vitamin E. Vitamin E can replace the requirement for selenium in the body, but selenium cannot substitute for vitamin E. In addition, selenium does not cross the blood-brain barrier like vitamin E. On the

other hand, selenium may help allow vitamin E to be more effective. Many plant sources are low in selenium and supplementation may be important. Selenium can create toxicity if given at too high a level; therefore, never give more than 200 : g of selenium per day in large dogs nor more than 100 : g per day to small dogs. Below these levels, selenium should be safe. I recommend giving selenium to GSD. For GSD under 2 years of age, give 100 : g of selenium daily. For GSD over 2 years of age, give 200 : g of selenium daily.

Membrane stabilizers:

**Omega-3 fatty acids:** Omega-3 fatty acids like EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) are the constituents of fish oils that act as anti-inflammatory agents and may be worth trying if your dog has an autoimmune disorder or arthritis. Many versions of these substances are on the shelves of health-food stores, from salmon oil to capsules of concentrated EPA. However, eating some cooked salmon or sardines may have benefits over capsular forms of the fish oils. Alternatively, you can give ground flax seeds, flax oil, or hemp oil as a dietary supplement; rather than fish oils. These materials will reduce platelet function for a brief period in dogs, but it seems that dogs compensate for this within about 8 weeks. Omega-3 fatty acids replace the 2-series fatty acids over time. As such, cellular stimulation produces 3-series prostaglandins and thromboxanes. The latter does not cause inflammation and reduce blood flow like the 2-series thromboxanes. I recommend all dogs receive a 1000 mg of fish oil capsule, 1 T ground flax seeds or eat 2 sardines every day.

**Gammalinolenic acid:** Borage oil, evening primrose oil or black currant oil, are natural sources of gammalinolenic acid, a fatty acid which is hard to get in the diet. GLA is an effective anti-inflammatory agent with none of the side effects of anti-inflammatory drugs. It also promotes healthy growth of skin, hair, and nails. It may be good for skin conditions, arthritis, and autoimmune disorders. It takes six to eight weeks to see changes after adding GLA to the diet. I recommend all dogs receive 500 mg of GLA twice a day, either as borage oil, evening primrose oil or as black currant oil.

**Soybean Lecithin:** Lecithin is a fat-like substance found in the cells of the body. It may combat atherosclerosis, improve memory, and fight Alzheimer's disease in human beings. However, there is no scientific evidence to support these claims. On the other hand, lecithin is harmless. It is not necessary as a supplement unless your dog has DM and you elect not to use the diet proposed above. (There is plenty of soybean lecithin in the tofu.) If you decide to use commercial dog food, add 1-2 tsp of soybean lecithin granules to the food at each feeding.

**Coenzyme Q:** Coenzyme Q also called Co-Q-10, is a natural substance that assists in oxidative metabolism. It may improve the utilization of oxygen at the cellular level, and patients with heart, muscle and nerve problems may find it worth trying in doses of 30-100 milligrams a day. Some human beings report that it increases their aerobic endurance. Coenzyme Q is harmless, but not cheap. It is probably not worth supplementing your dog with Coenzyme Q, if it is healthy. However, since DM patients suffer from nervous system problems, muscle wasting and need aerobic endurance, I recommend giving DM patients 100 mg Coenzyme Q daily.

Tonic herbs (natural remedies):

**Ginkgo leaves:** One tonic I recommend is an herbal preparation made from the leaves of the ginkgo tree (*Ginkgo bilboa*). Recently extracts of ginkgo leaves have attracted much attention from researchers because of their ability to increase blood flow to the brain. You can buy capsules of these extracts in most health-food stores, although different brands vary considerably in their content of active ingredients (ginkgocides). Ginkgo is nontoxic. For DM dogs, give 1 capsule twice a day.

**Ginseng:** (males only) Two species of ginseng are available: Oriental ginseng (*Panax ginseng*) and American ginseng (*Panax quinquefolium*). Both are full of compounds (ginsenosides) that work on the pituitary-adrenal axis, increasing resistance to stress and affecting metabolism, skin and muscle tone, and hormonal balance. Oriental ginseng is more of a stimulant and can raise blood pressure in some people, so I recommend using only the American species for dogs. Ginseng probably has little to offer young dogs, but may provide an increase in vitality to an older one. I recommend using 1 capsule of American ginseng once or twice a day in male dogs over 6 years of age. (Obviously, this includes male GSD who have DM!)

**Dong quai:** (females only) Dong quai is a Chinese herbal remedy made from the root of *Angelica sinensis*, a large plant in the carrot family. It is often called "female ginseng," because it is a general tonic for women and the female reproductive system in much the same way that ginseng acts as a tonic for men and the male reproductive system. Dong quai is available in the form of encapsulated extracts. It is a good general remedy for female dogs who lack energy. I recommend using 1 capsule of dong quai once or twice a day for female dogs over 5 years of the age.

**Green tea:** Green tea is a good general tonic and has some cholesterol lowering effects. It also contains theophylline which can help boost energy. It is available as a capsular extract or you can make green tea and add it to the diet. I recommend 1 capsule (or cup) twice a day for DM dogs.

**Grape seed extract:** A great deal of recent evidence supports the value of grape seed extract in reducing free radicals and decreasing the chances of developing chronic diseases. It is best to use standardized extracts. Alternatively, your dog can drink 1 cup of "purple" grape juice or eat 5-6 red grapes (peel and seeds included) a day. The dose of the extract is 1 capsule (50 mg) daily for DM dogs.

**Siberian Ginseng:** Siberian ginseng is derived from the root of a large, spiny shrub (*Eleutherococcus senticosus*) found in Siberia and northern China. It is a relative of true ginseng, but has entirely different properties. Siberian ginseng has "adaptogenic" properties and reduces physiologic responses to stress. Scientific investigations suggest it increases physical performance and endurance and improves immune function. For dogs with DM, given 1 capsule twice a day.

**Bromelain/Curcumin:** Bromelain is an extract of pineapple stems which has the property of decreasing circulating immune-complexes. As such, there is no Western medicine which is its equal. Since many of the complications and the direct initiation of the immune damage may be caused by the elevated immune-complexes in DM, bromelain may be an important key in helping to control

the progression of DM. Curcumin (the yellow pigment of turmeric plants) is a potent anti-inflammatory agent. Bromelain and curcumin have a synergistic effect whereby they assist the absorption of each other from the gastrointestinal tract, increasing their potency. As such, they should be given together. Many health food stores carry combinations of bromelain and curcumin. For dogs with DM, give 400-500 mg of bromelain with 500-400 mg of curcumin twice a day. (Curcumin is found in low concentrations in the spices turmeric and yellow mustard. As such, it is possible to replace the "capsule" form by adding 1-2 Tbs of turmeric and 1-2 tsp of dry yellow mustard to the diet.)

**Feverfew:** Feverfew is a natural NSAID compound without the side-effects of prescription drugs. It can be used in dogs with pain or arthritis to help reduce inflammation and discomfort. I do not recommend it for routine use; but, if your dog has pain from arthritis, give 1 capsule every 8-12 hours as needed. You can use this for 5 days out of the week, safely.

*Note:* WestLab Pharmacy has developed a palatable vitamin/mineral/herb product (Antiox-Q) which contains bovine cartilage, coenzyme Q, vitamin E, GLA, omega fatty acids, selenium, ginkgo, bromelain, curcumin, olive oil and B complex. This product contains the correct dosage of these compounds and only needs the addition of vitamin C, the ginsengs, green tea and grape seed to be complete. They may be contacted at 1-(800)-4WESTLA [1-(352)-373-8111, locally].

### **Medication:**

Over the last 2 decades, we have found 2 medications which appear to prevent progression or result in clinical remission of DM in many (up to 80%) of the patients. These medications are aminocaproic acid (EACA) and n-acetylcysteine (NAC). We recommend giving EACA as a solution, using the generic product. This product, while designed for injection, can be mixed with chicken broth to provide a palatable solution for oral usage. We mix 2 parts of aminocaproic acid solution (250 mg/ml) with 1 part chicken broth and give 3 ml of this mixture orally every 8 hours. In our experience, this mixture has been equally, if not more, effective to the tablet form of EACA. Besides, the solution is much less expensive than the tablets. The generic form of EACA solution can be obtained from American Regent, 1-(800) 645-1706 (outside of NY). The generic drug from American Regent may be obtained through prescription with the help from a local pharmacy. An alternative source for EACA is to have a compounding pharmacy make the solution from chemical grade EACA. One such pharmacy is WestLab Pharmacy in Gainesville, FL. They can be reached at 1-(800) 4WESTLA [1-(352) 373-8111, locally] and can mail the medication and bill the client directly. The only side effects that have been attributed to EACA have been occasional gastrointestinal irritation. This presents a problem only in a few patients, usually who have pre-existing GI problems that the medication might exaggerate. A local pharmacist can help in determining whether any additional drugs might be contra-indicated or lead to possible drug-interactions with the recommended therapy. The only known interaction is with estrogen compounds; but, only in high doses.

Acetylcysteine is a potent anti-oxidant which has powerful neuroprotective effects. We give 75 mg/kg divided in 3 doses a day for 2 weeks. Then, we give the 3 doses every other day. The N-acetylcysteine comes as a 20% solution and must be diluted with chicken broth (or other

compatible substitute) to 5%. Otherwise, it will cause stomach upset. This new treatment is expensive unless purchased through compounding pharmacies. Again, WestLab Pharmacy has this product and can send it to clients upon veterinary prescription. Using N-acetylcysteine at the above dosing does not appear to have side-effects. It can produce vomiting and may increase the bleeding time. The GI upset is likely due to the sodium content of the pharmaceutical product, which requires high concentration of base to buffer to pH 7.4. By reducing the pH during preparation, WestLab's product does not have as many side-effects. Giving fresh ginger 30 minutes before and giving the NAC with food (or on a full stomach) often reduces this effect.

The combination of aminocaproic acid, N-acetylcysteine, dietary supplements and exercise is the best treatment we have been able to discover to date. It corrects those aspects of the immune dysfunction which we can treat, based upon our belief that DM is an immune-mediated inflammatory disease. We always hope that all patients will respond to our treatment protocol. Unfortunately, it does not work in all cases; however, this combined treatment has been up to 80% effective in patients diagnosed at the University of Florida. The chances of successful treatment are improved if the therapy is begun early in the course of DM rather than later. A response to the drugs should be evident within the first 7-10 days. There is no other medications that we have found to provide any real benefits in the long term treatment of DM. Further information about other treatments may be found in Current Therapy X, pages 830-833 and in Vet. Clin. Nor. Am. 22:965-971, 1992.

### **Other Supportive Measures:**

Heartworm medication:

Since the monthly heartworm medications (Heartgard, Heartgard plus and Interceptor) increase immune responsiveness, we do not recommend using these products. Instead, we recommend plain diethylcarbamazine (DEC or Filaribits) which must be given daily. I do not recommend Filaribits plus (some dogs experience liver problems using it). If your dog is currently taking a monthly heartworm preventative, you must give one last dose and start the daily medication the next day. This is because the medications work at different points in the heartworm "life-cycle". Revolution, which is a new topical heartworm preventative, does not alter the immune response like the other monthly products. As such, Revolution should be safe to use in DM to control internal (and external) parasites.

Flea prevention:

Many of the old and new flea product can cause problems when certain neurologic conditions are present. As such, we recommend using boron, pyrethrums and Precor as the main control methods. Of the new medications, Frontline Spray and Revolution may be safe to use.

Acupuncture:

The traditional Chinese art of insertion of needles into various specific points of the body (with injection of small amounts of fluid or electrical stimulation) has been shown to provide

analgesia and relief from acute and chronic pain. This has the advantage of having none of the side-effects of analgesic drugs. In addition, acupuncture can do no harm. In DM, acupuncture alone slows the condition, but does not stop the progress. On the other hand, DM patients who have concurrent arthritis may benefit from acupuncture therapy.

#### Dietary Cartilage:

In many cases of degenerative joint disease with arthritis, recent studies have suggested that glycosaminoglycans and chondroitin sulfate may help reduce pain and inflammation from osteoarthritis, assisting in the healing process. While these products are available through health-food stores or a pharmaceutical medication through your veterinarian, you can give these to your dog directly by giving cooked cartilage. Sources of dietary cartilage would include cooked and "de-bone" chicken wings or using cooked spare ribs as the meat source in the diet. Why pay for cartilage products if it can be gotten for free in the dietary source. Some people taught the benefits of shark cartilage, but there are no scientific studies to support these claims. (It is also ecologically unsound to kill sharks to harvest their cartilage.) On the other hand, increase dietary cartilage can do no harm, particularly in the face of arthritis. In DM patients with arthritis, I recommend 1-2 grams of dietary cartilage with each meal. Another alternative is bovine gelatin (Knox gelatin or Knox Nutrajoint) which can be added to the food (1-2 packages per feeding). In some dogs, using glucosamine/chondroitin sulfate complex will be beneficial in controlling joint pain and stimulating healing; however, dietary cartilage has these compounds along with other important ingredients. Forms of glucosamine/chondroitin sulfate complex are available at health food store. (These are cheaper than products available from your veterinarian and may work as well) I recommend around 1200 mg of glucosamine and 1500 mg of chondroitin sulfate daily, if other forms of cartilage are not available.

#### Stress Reduction:

DM progresses at different rates and "stress" plays a role in its advancement. Minimizing stressful situations is important where possible. While anesthesia does not appear to cause problems with DM; in the past, even minor invasive surgical procedures can result in a marked increase in clinical signs of DM. Unfortunately, the worsening caused by surgical stress can be irreversible. Due to the advent of N-acetylcysteine therapy and being more attentive to the continued exercise of hospitalized DM patients, we now have been successful in performing many surgical procedures in these dogs. These have included cervical and thoracolumbar disc surgery and total hip replacement. Before aggressive surgeries are considered, it is best to determine that the patient's neurologic status is stable. Post-operative physical therapy remains crucial in getting patients on their feet quickly.

*Note:* If your dog already has DM, you should consider treatment with the above natural products and more traditional aminocaproic acid and acetylcysteine medications. Use the aminocaproic acid and acetylcysteine for the first 2 months of therapy and then see if they can be withdrawn (without signs of deterioration). If so, then continue with the natural approach from that point on.

#### **Lower Motor Neuron Disorders:**

### ***Introduction:***

One of the causes of acute quadriparesis or quadriplegia is that of diffuse lower motor neuronal (LMN) dysfunction, resulting in diminished to absent reflexes in all 4 legs. In this instance the immediate differential diagnosis must include acute polyradiculoneuropathy, Coral snake envenomation, tick paralysis, and botulism. Other causes which normally result in normal reflexes with progressive weakness on exercise include polymyositis, myasthenia gravis, and sub-acute organophosphate (OP) intoxication. The nature of these diseases are that they affect some portion of the lower motor unit. Polyradiculoneuropathy affects the myelinated fibers of the motor nerves. Coral snake envenomation, tick paralysis and botulism result from toxins which alter the release of acetylcholine at the neuromuscular junction. Myasthenia gravis and sub-acute OP intoxication alter the release or responsiveness of the neuromuscular junction to acetylcholine on repeated neural activity. Polymyositis directly affects the muscle. The former conditions result in flaccid paralysis, while the latter ones result in weakness, stiffness and collapse on exercise. Coral snakes are limited in their distribution and it should be considered in cases of LMN disease in areas where they are endemic. The ticks which are associated with tick paralysis vary and are present throughout the world. Tick paralysis appears to be seasonal, but can occur at any time. Botulism can occur from food poisoning or from alterations in the intestinal flora. Dogs are fairly resistant to botulinum toxin, but intoxication is occasionally seen.

### ***Diagnostic Approach:***

The diagnosis of motor unit disease requires looking for systemic illness, ruling out obvious vertebral disease and identifying the specific changes of the disease. This includes many of the test employed in looking for cervical and TL disease, including CSF tap and analysis. On the other hand, serum muscle enzyme levels (CPK, AST, LDH and aldolase concentrations) should be run. In some cases, pre- and post-exercise levels of CPK and lactate can help confirm the diagnosis. In addition, serum cholinesterase levels are needed to evaluate the potential for OP intoxication. The most important aspect of the examination are EMG studies, including needle EMG, nerve conduction velocities and repetitive nerve stimulation. Muscle and/or nerve biopsy may allow histopathologic diagnosis, muscle immunohistology, fiber typing and enzyme measurements. In cases of suspected myasthenia gravis, response to edrophonium HCl, a short acting anticholinergic drug, can be used. Edrophonium given intravenously at 0.1-0.2 mg/kg can produce dramatic improvements in muscle strength in 1-2 minutes in patients in myasthenic crisis or who is exercise intolerant. On the other hand, it can worsen the signs of OP intoxication. For this reason, I prefer to perform edrophonium testing under anesthesia during the EMG procedure.

### **POLYMYOSITIS:**

Idiopathic polymyositis is a diffuse inflammation of the skeletal muscles. An autoimmune process is suspected, in most cases. Hypergammaglobulinemia, positive titers for serum antinuclear antibody (ANA), and elevations of circulating anti-muscle antibodies (also demonstrable by indirect immunohistology) have been found in many cases. There is generalized

weakness which worsens on exercise. These patients also have a stiff stilted gait, lameness and pain on muscle palpation. Occasionally, generalized loss of skeletal muscle mass is evident. Megaesophagus may be present with regurgitation and aspiration pneumonia.

The main features on examination are the stiff, stilted gait. Neurologic examination (in a quiet room) is often within normal limits, except for possible muscle pain on palpation. Other signs relate to the presence of aspiration pneumonia, including fever and listlessness. During the acute phase, muscle enzymes will be elevated. The diagnosis is supported by the findings of an abnormal needle EMG with normal nerve conduction velocities. There is occasionally a decremental response on repetitive nerve stimulation. Muscle biopsy will confirm the diagnosis.

The treatment of polymyositis is with immunosuppressive doses of corticosteroids. Cases with aspiration pneumonia have a poor prognosis, since treatment with immunosuppressive drugs cannot be initiated. In those cases where corticosteroids are effective, monitoring the CPK may be useful in determining the course of therapy. If the CPK decline to normal for 1 month, the steroid medication can be stopped. The prognosis is generally good if esophageal, pharyngeal and laryngeal muscles are not severely affected. The megaesophagus may resolve with therapy or be permanent.

Recently, (probably due to a more aggressive approach to muscle disease including biopsy and special staining procedures) many additional muscle diseases which present similarly to polymyositis have been uncovered. Lipid-storage myopathy is one of these. These patients present with stiff, stilted painful gaits with tremendous pain on muscle palpation. Histopathology reveals increases in mitochondrial lipids on special (oil red O) stains. These patients may respond dramatically to coenzyme Q-10 and l-carnitine supplementation.

### **MYASTHENIA GRAVIS:**

Myasthenia gravis has been considered a rare disease; however, the adult-onset form seems to be on the rise. Whether this represents improvements in diagnostic criteria and methodology or a real increase in the condition remains unsure. On the other hand, this may represent an increase, similar to that for other immune-related diseases. It has been reported in young dogs (juvenile form) and adult dogs and cats. The juvenile form represents a genetic problem where there are too few acetylcholine receptors at the neuromuscular junction. The adult form represents an auto-immune disease where there is the production of antibodies against the acetylcholine receptor, demonstrated by elevations in circulating anti-receptor antibodies. With either the juvenile form or the adult form, myasthenia represent a functional deficiency of sustainable release of acetylcholine from the pre-synaptic neuron at the neuromuscular junction. This distinguishes myasthenia from the myasthenic-like disease of OP intoxication.

The disease can be seen in any adult dog or cat, the young adult German Shepherd dog being overly represented. There may be an inciting febrile episode, but often no inciting cause is found. Animals present with weakness and exercise intolerance. There may be changes in bark, difficulty in swallowing and prehending food. Regurgitation and megaesophagus may be present. Some cases present in a myasthenic crises where the animal has collapsed and is unable to rise. At this time, there may be muscle flaccidity.

In uncomplicated myasthenia gravis (those without pulmonary pathology from aspiration pneumonia), the animal demonstrates progressive weakness on movement which improves with

rest. Mild cases may be difficult to differentiate from animals with polymyositis. Except when in a myasthenic crisis, neurologic assessment is usually normal. The diagnosis is suspected by demonstration of a normal needle EMG, normal nerve conduction velocities and decremental response to repetitive nerve stimulation. (We normally stimulate at 10/second, recording the first 9 stimulations. An abnormal response is when the 4th and 9th waves are <85% of the initial wave) Confirmation of the diagnosis is made by demonstrating elevated serum anti-acetylcholine receptor antibodies (>0.06 ng/ml). Additional confirmation can be made by positive response to edrophonium HCl either in the conscious animal or during the EMG procedure. (Remember the OP intoxication can look like myasthenia. I, therefore, do not give edrophonium until I have checked serum cholinesterase levels.)

The treatment of myasthenia is to suppress the production of antibodies and to increase acetylcholinergic function. The former is usually done by the administration of prednisolone at 1-2 mg/kg/day. The dose is reduced while monitoring the serum anti-receptor antibody levels. The latter is done by giving pyridostigmine at 10-60 mg twice a day (depending upon the size of the patient). During a myasthenic crisis, intramuscular injections of neostigmine (0.5-2.5 mg) may be given in cats and dogs. The prognosis is guarded. In uncomplicated cases, the signs may resolve and go into remission. In cases with aspiration pneumonia, the prognosis is usually poor. Recently, immunotherapy has offered new hope in treating refractory cases. By inoculation of patients with purified anti-receptor antibodies, they produce anti-idiotypic antibodies which can help control their altered immunity. Since this may be a disorder which is developed in response to environmental intoxication with resultant failure of the healing process, dietary supplementation and antioxidant support may help prevent this disease.

### **ORGANOPHOSPHATE INTOXICATION:**

Acute, subacute and chronic forms of organophosphate intoxication occur. The chronic form is due to a dying-back neuropathy which occurs relatively infrequently and was caused by older forms of organophosphates no longer in use. Treatment of the acute and subacute forms of organophosphate intoxication will be discussed here.

In the acute syndrome, the main signs are associated with muscarinic receptor over stimulation, including salivation, vomiting, diarrhea and tachycardia. Central cholinergic receptor over stimulation results in hyperexcitability, body tremors and seizure activity. The muscarinic signs are best treated with atropine (0.04 mg/kg IV or SQ), which blocks the muscarinic receptor overstimulation. The central cholinergic signs may be treated with diazepam (0.5-1.0 mg/kg IV), if necessary to stop seizure discharges. The seizures can be controlled further with pentobarbital (1 mg/kg IV) and/or phenobarbital (1-2 mg/kg IV). Additional therapy for acute organophosphate intoxication (in the dog, only), within the first 24 hours, should include the use of pralidoxime chloride (2-PAM, 20 mg/kg IV, IM or SQ) in order to bind any free organophosphate in the blood stream and aid in the elimination of the intoxicant. Following the initial 24 hours, the organophosphate compound will already be irreversibly bound to acetylcholinesterase and 2-PAM may not be beneficial. To maintain the control over the muscarinic receptor overstimulation and to prevent the development of signs of subacute organophosphate intoxication, continued treatment of acute organophosphate intoxication should include diphenhydramine (Benadryl) orally (1-4 mg/kg) every 8 hours for, at least, 21 days of

total therapy. Continued use of atropine in combination with diphenhydramine is not recommended, since overt sedation can result. One initial dose of atropine followed by diphenhydramine for maintenance is sufficient to minimize the signs of acute organophosphate intoxication.

The clinical signs of subacute organophosphate intoxication include muscle weakness, exercise intolerance, bradycardia, central depression, acute dystonia and central vestibular signs and are secondary to diminished nicotinic and central cholinergic receptor function. Since the muscarinic receptor rapidly develops tolerance, the muscarinic signs of acute organophosphate intoxication decrease, and the signs of nicotinic receptor paralysis dominate. Nicotinic receptor paralysis may be delayed in development for 7-10 days after exposure and are much more likely to occur following high or repeated exposure to organophosphate. Anti-muscarinic drugs and 2-PAM are ineffective in treating these signs. Diphenhydramine will stabilize the nicotinic receptor and improve the clinical signs. In subacute organophosphate intoxication, nicotinic paralysis often results in a decremental response seen following repetitive nerve stimulation, producing a myasthenic-like syndrome. This decremental response is worsened by edrophonium HCl, but resolves following diphenhydramine therapy. The mental depression caused by central cholinergic receptor dysfunction and acute dystonia improve with diphenhydramine treatment, as well. Treatment with diphenhydramine should be started IV or IM medication (IM only in the cat) at 4 mg/kg every 4-6 hours. Parenteral therapy should continue until there is improvement in clinical signs, usually by 24-72 hours. Then, oral diphenhydramine is continued at 4 mg/kg every 8 hours. In small and large dogs, sedation may occur at this dosage. Reducing the dose of diphenhydramine to 1-2 mg/kg may be necessary in these patients. Oral diphenhydramine should be continued for, at least, 3 weeks, or until the acetylcholinesterase enzyme has been replaced. While it may require a number of weeks for the plasma cholinesterase to return to normal levels, the functional pool (approximately 20% of the total) usually returns within 3 weeks. This method of therapy for the subacute organophosphate disorders has been highly successful except where the intoxication is extreme. While the exact mechanism of action of diphenhydramine is not known, it is an antihistamine with anticholinergic properties. It is useful as a central anticholinergic, reducing cholinergic activation. While it does not block nicotinic receptor activity, diphenhydramine appears to prevent nicotinic receptor overstimulation. Over the past 10 years, diphenhydramine has been used successfully to reduce the morbidity and mortality of subacute organophosphate intoxication in the dog and cat.

### **Peripheral Nerve Injury:**

#### ***Incidence: Frequent***

The most common cause of monoplegia is injury to a nerve plexus or peripheral nerve. The traumatic insult produces immediate neurologic deficits, which either improve or stay the same over time.

Neurapraxia is a transient loss of nerve function following injury, with no resultant nerve degeneration. Neurapraxia is analogous to concussion in the brain and spinal shock in the spinal cord, and is a physiologic dysfunction of the nerve. Because neurapraxia has a better prognosis than does structural damage, the two must be differentiated. The duration of neurapraxia in

animals is unknown, but in man it is thought to last from 3 to 12 weeks. Serial neurologic examinations and EMG can be used to differentiate neurapraxia from neurotmesis and aid in forming an accurate prognosis for recovery of function.

Neurotmesis is the complete severance of a nerve. The nerve function is never recovered unless surgical repair is performed. Axonotmesis is a rupture or severance of axons within a nerve but with the supporting structures of the nerve spared. Ruptured axons may regenerate and eventually reinnervate the muscles.

Most nerve injuries are caused by stretching, direct blows, excessive pressure, or injections and are a combination of neurapraxia and axonotmesis. Associated local hemorrhage and edema also contribute to the loss of nerve function.

When the axon is ruptured, the portion detached from the cell body completely degenerates, a process referred to as Wallerian degeneration. The portion still attached to the cell body may degenerate toward the cell body one or two nodes of Ranvier. After about 1 week, regeneration begins. Distally, the axon and myelin degenerate but the Schwann cells proliferate to form a neurolemmal tube through which regrowing axons can find their way back to the appropriate muscle to reinnervate it. The rate of axon growth is about 1 to 4 mm per day, or an average of 1 inch a month. The distance an axon can regrow is limited by continual shrinking of the neurolemmal tube. Function is also inhibited by fibrosis of denervated muscles fibers, which occurs after time.

The closer the nerve injury is to the muscle it must reinnervate, the better the prognosis for anatomic contact and reinnervation of muscle before fibrosis occurs. Any injury over 12 inch from a muscle will probably be unable to make anatomic contact with the muscle before the neurolemmal tube closes. If anatomic contact can be made, the neurolemmal tube may be so small that proper myelination of the new axons is impossible. Slow axonal conduction time and muscle fibrosis severely retard function. When an injury can be localized to a certain portion of the nerve, the distance from the injury to the muscle to be reinnervated may be measured and time for regeneration may be estimated using the 1 inch per month as a guide. The minimal recovery time is usually several months.

Positive waves and fibrillation potentials are seen in denervated muscles 5 to 7 days following the nerve injury. The presence of motor unit action potentials (MUAP) indicate that some axons are still intact, even though no function may be found on the neurologic examination.

Nerve stimulation and the ability to elicit an evoked response indicate that some axons within the nerve are still intact. The amplitude of the evoked response may be a guide to the prognosis for recovery. A small amplitude, between 100 to 200 : V, indicates a poorer prognosis than a 1,000 to 5,000 : V or greater response. Serial evaluations of motor nerve conduction velocities may aid in determining the prognosis. If the initial motor nerve conduction velocity is slow and remains slow, the prognosis is poorer than if the initial motor nerve conduction velocity is slow and returns to normal. A severed nerve responds to electric stimulation distal to the site of injury for about 72 hours, but loses the response to electric stimulation immediately proximal to the site of injury. With brachial plexus avulsions, it is often difficult to place the electrode proximal to the lesion site; therefore, if there is no response to electric stimulation distal to the injury site 72 hours or more after the trauma, the nerve most likely is not intact.

Serial examinations, noting improvement in voluntary movements, sensory levels, spinal

reflexes, and serial EMG studies, are the greatest aids in determining an accurate prognosis for peripheral nerve injuries.

### ***Therapy:***

If the nerve has intact axons following an injury, if the distance that the ruptured axons have to regenerate is not prohibitive, and if the owner is willing to make the commitment for daily nursing care, then a physical therapy program may be outlined. Most physical therapy programs combine heat, massage, and joint manipulation to keep the circulation in the limb as good as possible to prevent stasis and local hypoxia, which contribute further to muscle atrophy and fibrosis. Joints develop tendon contractures because of the decrease in tendon movements. The carpus and tarsus are often the last joints to be reinnervated, so they commonly contract and the animal walks on the dorsum of the paw. The elbow joint may also become contracted in a flexed position in brachial plexus injuries that spare the musculocutaneous nerve. The limb is often carried flexed at the elbow; the tendons contract and hold it in this position.

Hot towels may be placed around the denervated limb and the muscles massaged or a whirlpool of warm water used to increase circulation to the muscles. A regimen of 15 minutes twice daily is preferred. Then the affected carpus, tarsus, or elbow should be stretched in extension twice daily for 10 to 15 minutes to keep the tendons supple. A spoon splint may be applied to keep the digits, carpus, or tarsus extended and to aid the animal in using the limb without these joints collapsing. The splint should be placed on the limb for only a few hours a day between physical therapy sessions, as it restricts circulation to the muscles. The splint should be removed overnight.

The animal may drag the dorsum of the paw on the ground or rough surface and because of the loss of sensation may develop severe abrasions. The lesions can become infected and osteomyelitis of the digits can result. A protective stocking or boot should be placed over the digits to prevent abrasions. If abrasions occur, they should be kept clean and treated with topical antibiotics and further protection provided. The animal should be kept from licking the wounds, as this only further abrades the denervated skin.

During certain stages of the regeneration period, the animal may begin to mutilate the paw. This may be caused by a regeneration of sensory nerves and a tingling or itching sensation. This period is usually transient, but can be very frustrating to the owner and veterinarian, as the animal may produce severe lesions by selfmutilation, regardless of attempts to bandage and protect the foot. Elizabethan collars, muzzles, wire-mesh foot guards, and leather boots are among the many things that have been tried in individual cases. Prednisone 1 mg/kg orally divided every 12 hours, then reduced by half every 3 to 5 days may be tried during this period, but often has little effect.

The overall prognosis for most nerve injuries depends on the severity of the injury, how much of the dysfunction is caused by neurapraxia, and how much by axonotmesis, how far the injury occurs from the muscles denervated by it and on the owner's commitment to provide months of physical therapy.

If no change has occurred over 1 month or if there is no response to electric stimulation, surgical exploration of the nerve may be made for possible repair if the distance from the nerve injury to the muscles the nerve needs to innervate is less than 5 to 6 inches. Peripheral nerve

surgery techniques are well described elsewhere.

If electromyography is not available, serial neurologic examinations should be performed over several months. If there has been no change for several months and surgical repair is impossible, then surgery for joint fusion or tendon transplants of the carpus or tarsus may be considered. Amputation of the limb is a last resort, considered only when no improvement occurs after several months of critical evaluation.

### **BRACHIAL PLEXUS AVULSION:**

#### ***Incidence: Frequent***

A common neurologic injury from trauma (such as being hit by a car) is that of brachial plexus avulsion. The brachial plexus is susceptible to injuries that produce abduction of the thoracic limb from the body wall or a direct blow to the lateral surface of the scapula. The cardinal signs of brachial plexus avulsion are a monoplegia of one front leg, Horner's syndrome on the affected side, lack of panniculus response on the side of the lesion and a Babinski's sign in the ipsilateral rear leg. The nerve roots are stretched or torn from their origin by this trauma, since the meningeal coverings of the nerve roots are thinner than those in the peripheral nerve. The epineurium of the peripheral nerve is contiguous with the dural mater, providing extra support to the peripheral nerves. In cases where the nerve roots have been torn, recovery is unlikely without new experimental surgical techniques.

The diagnosis may be confirmed by EMG examination in 5-7 days. The evidence of denervation will be evident. If there is no nerve conduction 72 hours after the injury, then avulsion is most likely.

Treatment is with time, physical therapy and protection from injury. If there is no problem with the leg, then amputation is not warranted until, at least, 6 months of time has past. On the other hand, if the leg gets infected or troubles the patient, amputation may help the patient. Serial neurologic assessments and EMG examinations may help determine the ultimate prognosis. Some patients experience "tingling" of the foot as healing occurs. These patients can attack the foot causing considerable self-mutilation, even months after the initial injury.

### **RADIAL NERVE INJURY:**

#### ***Incidence: Frequent***

Radial nerve injury alone may occur with fractures of the first rib or the humerus. With the distal radial nerve injuries, the animal may bear weight on the limb because of the ability to extend and fix the elbow, but stands knuckled over at the carpus because of the inability to actively extend the carpus or digits.

The radial nerve may be stimulated electrically on the lateral aspect of the humerus, and recordings taken from extensor muscles to determine whether the nerve is intact. The nerve should be explored and repaired surgically if there is evidence that it is severed.

### **SCIATIC NERVE INJURY:**

### ***Incidence: Frequent***

Sciatic nerve injury is commonly associated with fractures of the ilium or proximal femur. The nerve is commonly traumatized by retraction during hip and proximal femur surgery and by improper intramuscular injections into the semimembranosus and semitendinosus muscles. The sciatic nerve may be electrically stimulated at the lateral proximal femur and at the stifle, and recordings taken from the various extensor and flexor muscles to determine nerve integrity. If the nerve is severed and the site of injury is known, surgical exploration and repair may be indicated. Proximal sciatic nerve injuries in larger dogs have a poor prognosis if the nerve is severed, because of the distance the nerve must regenerate for reinnervation of distal musculature.

### **POLYNEUROPATHY:**

The most common polyneuropathy seen in dogs is acute polyradiculopathy. This disorder is also referred to as "coonhound paralysis" since a great number of hounds developed an ascending flaccid paralysis following contact with raccoons. This suggests that there are a number of inciting causes of polyradiculopathy in dogs, including something present in the bite of the raccoon. Other patients experience similar syndromes following rabies vaccination. It is probable that the inciting cause causes a cross-reactivity with the neural antigens in the nerve roots, leading to demyelination and the clinical signs.

This disorder can affect any age, breed or sex of dog or cat, although the condition is rare before the age of 6 months. The onset of signs begins as rear leg weakness which rapidly ascends over 24-48 hours until the animal is quadriplegic. Occasionally, the condition can start in the fore legs and then progress to quadriplegia. Physical examination is usually within normal limits (an old raccoon bite might be apparent in hounds). Usually, there are no cranial nerve signs; however, in severe cases, the bark may be altered, swallowing impaired and facial nerve signs be evident. In some cases, respiration is impaired necessitating respiratory support.

The diagnosis is supported by finding mild elevation of CSF protein, particularly from lumbar spinal tap. The EMG reveals denervation potentials (fibrillation potentials and positive sharp waves). The motor conduction velocity is usually slower (< 50 M/sec), particularly later in the course of the disease.

There is no specific treatment for polyradiculopathy. Corticosteroid therapy may reduce the recovery time, but have not been shown to reduce the time to reach maximal severity nor the eventual severity of the disease. Recent evidence, support a role of antioxidant steroids (methylprednisolone) in reducing clinical signs. When respiratory depression is evident, this may be helpful in treating the patient. The clinical course is variable and may last from a few days to several weeks. In some cases, there are permanent neurologic deficits. Recovered animals may have the condition reoccur. Recurrences are often more severe than the initial incident. Some cases become chronic in nature, requiring more aggressive medication in hopes of controlling the problem. I have found that many of these patients respond better to antioxidant therapy with drugs like acetylcysteine or ginkgo biloba than to steroid medication alone.