Diagnosing Seizure-Like Events: Startling Results of EEG Video Case Studies
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The International League Against Epilepsy (ILAE) defines seizure as the transient occurrence of signs, symptoms or both due to abnormal excessive or synchronous neuronal activity in brain. Although this seems straight forward, there are many events that cause a transient occurrence of signs, symptoms or both that are NOT from abnormal excessive or synchronous neuronal activity in the brain. These events are seizure-like and masquerade as a true epileptic seizure. Without confirming with Electroencephalography (EEG) this events would be falsely classified as seizure. Conversely, abnormal excessive or synchronous neuronal activity in the brain does not always have a detectable transient occurrence of signs, symptoms or both. Thus using observation alone, without EEG, would lead to events being falsely classified as not seizure. The goal of this talk is to provide video and EEG from cases that are seizure-like such in order to improve your ability to detect true epileptic seizure.

Role of EEG
In human medicine EEG is used to discriminate movement disorder, psychogenic events, metabolic disease from true epileptic seizure. EEG is also used to detect subtle or non-convulsive seizure and then evaluate the effectiveness of anti-epileptic drug (AED) therapy. We have EEG in all 4 of our clinics as well as an intramural EEG certification program for our technical staff. The EEG is read with the assistance of an extra-mural physician expert in the interpretation of both human and animal EEG. We perform EEG for the exact same reasons it is performed in human medicine.

Intracranial and extra-cranial activity during seizure
The first step in seizure generation is that a group of neurons synchronizes and depolarizes / repolarizes autonomously and spreads within that hemisphere of the brain due to failure of spatial containment. This hypersynchronous electrical activity then crosses to the other hemisphere capturing the entire brain before eventually being contained, usually within 2 minutes. During the seizure there is excess glutamate release that can lead to temporary neuronal dysfunction.

In the pre-ictal state, as the focus is developing and spreading the patient may experience abnormal visual, auditory, physical, or autonomic nervous system abnormalities manifested as staring off into space, searching a room, restlessness, clingy behavior, fly biting, circling, odd vocalization, a limb becoming stiff or rhythmically moving, elevated heart rate, dilated pupils, salivation, vomiting.

In the ictus or seizure, the focus has captured both cerebral hemispheres and the patient may experience loss of consciousness, collapses, rigidly extend the neck and all 4 limbs. The hypersynchronous or rhythmic nature of the electrical focus can be noted as paddling or all 4 limbs. A failure to control and regulate the breathing can manifest as apnea and paradoxical breathing where the diaphragm and intercostal muscles are not working together. Perturbations in the autonomic nervous system can lead to bradycardia or tachycardia, profuse salivation, urination, defecation, miosis or mydriasis, and piloerection. The post-ictal period results from excitotoxicity and typically lasts 30-30 minutes where the patient emerges from being confused, blind, weak, and side-stepping. If the seizure is not recognized (non-convulsive) or difficult to treat neuronal necrosis and death can result from seizure.

Practical criteria for distinguishing seizure
In a recent paper the inclusion criteria for seizure was when 3 of the 4 of the following were noted.
1. Salivation, urination or defecation
2. Tonic or tonic-clonic posture or movements or rhythmic contractions of facial or appendicular muscles
3. Decreased responsiveness intra-ictally
4. Postictal phase in which abnormal behavior or mental state was noted

Generally episodes that do not have 3 of the 4 criteria are classified as seizure-like and may or may not be manifestation of abnormal electrical activity or true epileptic seizure. There are many episodic expressions of disease or events that are seizure-like but not seizure (Table 1). Therefore using observation alone to detect seizure in these cases would cause a false positive assertion that these event were seizure, delayed diagnosis and treatment of the underlying cause and the needless and potentially harmful application of AED.

Electrical seizure and electrical status epilepticus
As mentioned above a seizure is fundamentally from abnormal excessive or synchronous neuronal activity in the brain. Using EEG, electrographic seizures are defined as ictal discharges consisting of a rhythmic pattern with definitive evolution in frequency,
amplitude and/or morphology persisting for at least 10 seconds. When ictal discharges are present for more than 30 minutes then patient is suffering from electrical status epilepticus.

**Convulsive vs. non-convulsive seizure**

Electrical seizure can occasionally manifest as convulsions (generalized tonic-clonic) with patient flailing on its side, paddling all 4 limbs or holding the limbs, head and neck in rigid extension. A non-convulsive seizure (NCS) is defined as a seizure where there is no overt convulsive movements. Another term used for non-convulsive seizure is complex partial seizure where there is only an acute alteration in consciousness. NCS is more common than convulsive seizure in people and cats, and potentially dogs as well. When an electrical seizure lasts for more than 30 minutes it is almost always non-convulsive and termed non-convulsive status epilepticus (NCSE).

Using observation alone to detect seizure non-convulsive seizure will be missed or falsely negative, AED would not be applied and the patient would be at higher risk for mortality and permanent disability or poor seizure control.

**Retrospective study at Bush Veterinary Neurology Service**

In a recent retrospective of 73 dogs and 13 cats where EEG was performed to evaluate seizure-like events there were many cases of metabolic disease, movement disorders and psychogenic events that appeared as seizure. Many of these cases will be presented during the talk. In this study, 15/86 (17%) had electrographic seizure and 9/86 (10%) had electrographic status epilepticus. Non-convulsive seizure was noted in 13/15 (87%) of these cases and manifested as coma, twitching of the ears or facial muscles, pupil dilation, paroxysmal elevations of temperature or respiratory rate. The incidence of electrical seizure, non-convulsive seizure and non-convulsive status epilepticus in this study mirrored findings in pediatric and adult studies of hospitalized human patients.

Although not statistically significant then in hospital mortality was 40% in the electrical seizure group as compared to 21% in the group without electrical seizure. A higher mortality and disability rate has also been found in humans and independent of the patient’s age or underlying diagnosis. This suggests that electrical seizure detection and treatment can reduce mortality in veterinary patients.

**Predictors of electrical seizure**

Because EEG is rarely available to the veterinary practitioner we examined factors that might predict a patient is experiencing electrical seizure. Cluster seizure, seizure within 8 hours, twitching and a structural brain problem had a trend towards predicting electrical seizure our patient population. Although these factors might raise suspicion for electrical seizure we had many patients in the non-seizure group that looked like they were having seizure. This highlights the necessity of EEG for diagnosing seizure.

One important finding in this study was that cats and younger animals are significantly more likely to have electrical status epileptics and electrical seizure, respectively. Many video examples will be provided within the talk.

**Treating suspect electrical seizure**

In recent human study of 164 patients presenting for convulsive status epilepticus (defined as a seizure lasting more than 5 minutes, 2 seizure without becoming normal between or seizing at presentation) patients were treated with a standard protocol for status epilepticus. Once the convulsive seizure resolved, patients had an EEG and about 50% were found to still have electrical seizure and 14% were in electrical status epilepticus. The mortality rate in the electrical seizure group was 50% an independent of age and underlying diagnosis. This paper also notes that once the EEG was used as the end point for treatment and not observation, outcomes were thought to improve. In the only current veterinary study of a similar population all 10 of the convulsive status epileptic patients were thought to have electrical seizure. This begs the question for veterinary medicine of how and when should we treat without the benefit of EEG.

A general recommendation can be to treat a convulsive seizure patient with AED until there are no signs of twitching or autonomic changes. It is advised to give Levetiracetam 60 mg/kg intravenously and then 10 mg/kg boluses of Phenobarbital every 20 minutes provided the systolic blood pressure is greater or equal to 90 mmHg. A total dose of 50 mg/kg can safely be administered to both dogs and cats.

**Conclusion**

When a patient presents for seizure the veterinarian must ask themselves if the event was a seizure. Falsely identifying events as seizure or failing to recognize non-convulsive seizure will lead to worse outcomes. Although EEG is needed to allow best diagnosis of seizure-like events, a thorough history and examination, considering the list of seizure-like diseases, and being cognizant of varied presentation for non-convulsive seizure can assist in better diagnosis and treatment of seizure-like diseases.
Table 1. Disease processes with seizure-like appearance

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<thead>
<tr>
<th>Disease processes with seizure-like appearance</th>
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<tr>
<td>Atlantoaxial subluxation</td>
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<td>Breed and drug induced dyskinesia / movement disorders</td>
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<td>Cataplexy, narcolepsy, rapid eye movement (REM) sleep disorders</td>
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<td>Cervical muscle spasm</td>
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<td>Chiari-like malformation / syringomyelia</td>
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<td>Encephalitis</td>
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<td>Exercise induced collapse</td>
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<td>Extreme agitation / psychogenic seizure</td>
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<td>Feline hyperesthesia syndrome</td>
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<td>Head bobbing / Tremor syndromes</td>
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<td>Intermittent decerebrate/decerebellate rigidity</td>
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<td>Jaw chomping / fly biting / lip smacking</td>
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<td>Metabolic encephalopathy</td>
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<td>Myoclonus</td>
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<td>Neuromuscular disease</td>
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<td>Psychogenic Non-epileptic Spells / Panic Attacks</td>
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<td>Syncope</td>
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Selected references

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Cuff DE, Bush WW, Williams DC, Stecker MM. Use of continuous electroencephalography for the diagnosis and monitoring of treatment in nonconvulsive status epilepticus. JAVMA 15;244(6):708-14.
A seizure is defined as a transient occurrence of signs, symptoms or both due to abnormal excessive or synchronous neuronal activity. In veterinary medicine, seizure is diagnosed via observations about the patient’s level of awareness, spontaneous muscle movements in the limbs and head as well as autonomic changes. However, a seizure is fundamentally an aberrant electrical event in the brain and therefore best diagnosed using electroencephalography (EEG). In human medicine, EEG is the primary method for distinguishing epileptic seizure from psychogenic seizure, metabolic events or movement disorders. Equally important, EEG is used in seizure patients with altered mentation to detect electrical seizure and assess response to pharmacologic therapy. At our clinic, we have worked with a physician expert in the interpretation of human and animal EEG for over a decade and use EEG for these same purposes. The talk will discuss the characteristics, diagnosis, treatment and prognosis with electrical seizure and non-convulsive status epilepticus in both human and veterinary medicine.

**Seizure terminology**

An electrical seizure is defined as ictal discharges consisting of a rhythmic pattern with definitive evolution in frequency, amplitude and/or morphology persisting for at least 10 seconds. Electrical seizure can occasionally manifest as convulsions (generalized tonic-clonic) with patient flailing on its side, paddling all 4 limbs or holding the limbs, head and neck in rigid extension. A non-convulsive seizure (NCS) is defined as a seizure where there is no overt convulsive movements. Another term used for non-convulsive seizure is complex partial seizure where there is only an acute alteration in consciousness. NCS is more common than convulsive seizure in people and cats, and potentially dogs as well. When an electrical seizure lasts for more than 30 minutes it is almost always non-convulsive and termed non-convulsive status epilepticus (NCSE).

**Seizure frequency and status epilepticus**

Terms to describe seizure frequency from best to worst prognosis include: sporadic seizure, cluster seizure, acute repetitive seizure, convulsive status epilepticus (CSE), non-convulsive status epilepticus (NCSE), refractory status epilepticus (RSE), super-refractory status epilepticus, or malignant status epilepticus. A cluster seizure is 2 or more seizures within 24 hours and acute repetitive seizure is 2 or more seizure within 5-12 hours. When seizures are prolonged and without return to baseline, they are referred to as status epilepticus (SE) with the best studied form being CSE. The original definition of SE was a 30 minute or longer continuous seizure because animal models show neuronal damage and seizure become self-sustaining after 30 minutes. However, the current definition of a SE is a seizure lasting 5 minutes or longer, 2 seizures where the patient is unable to respond to commands or walk between seizures, or when patient is still seizing. This definition has evolved because clinicians no longer want to delay a patient’s entry into a protocol for SE since prompt therapy is required for a good outcome. In human medicine, about 150,000 people are thought to develop CSE per year in the USA. In dogs with idiopathic epilepsy (genetic or unknown cause) the rate of cluster seizure is reported at 41-94% and for CSE 53-69%. These conditions are common and important problems in both veterinary and human medicine.

**Progression from convulsive to non-convulsive status epilepticus**

During CSE treatment with benzodiazepines (BDZ) can be ineffective due to endocytosis and changes to the GABA receptor. In this same period of time the convulsions often stop and the electrical seizure can persist despite no obvious convulsions, which is called non-convulsive status epilepticus (NCSE) (Foreman). Refractory status epilepticus (RSE) is diagnosed when electrical seizure activity persists despite treatment with 2 anti-epileptic drugs (AEDs) at appropriate doses – refractory SE is typically non-convulsive. When RSE persists for greater than 24 hours it is super-refractory SE and when SE returns within 5 days of tapering anesthetic medications used to treat SE, then it is called malignant SE.

**NCSE is clandestine**

As our video cases will demonstrate many of our patients with NCSE appeared to be asleep or comatose. This is common too in people. A paper concludes that many people with NCSE appeared to be sleeping and that “clinical detection of NCSE would not have been possible with routine neurologic evaluations without use of EEG monitoring”. The signs of NCSE can range from mild confusion or disorientation to coma. NCSE should be suspected following a convulsive seizure when there is no improvement in 20 minutes or failure to return to baseline in 60 minutes. Distinguishing NCSE from conditions that mimic seizure can be difficult and about 25% of human patients can have subtle movements that are not from seizure. In human medicine studies have demonstrated some positive symptoms indicative of NCS/NCSE and negative symptoms indicating clinical signs are not from seizure. No such
published criteria exist in veterinary medicine. However, in our population of patients with NCSE we noted subtle twitching of ears or facial muscles, confusion, transient hyperthermia, episodic and unexplained changes in respiratory rates, mydriasis, or coma.

**NCSE frequency in seizure patients**

In veterinary medicine there are a few reports describing electrical seizure or NCSE following treatment of convulsive SE with diazepam and phenobarbital. In one report of ten patients (7 dogs, 3 cats) treated for CSE with anesthetic doses phenobarbital or propofol anesthesia, 100% of the patients had electrical seizure. In 164 human patients at Virginia Commonwealth University treated with their hospital’s typical protocol for CSE, EEG recording after the CSE stopped showed that 48% of the patients had persistent electrical seizure and 14% had NCSE. Another human study showed that about 33% of patients in convulsive status continue to have electrographic seizure after the convulsive seizure had stopped. Generally in human medicine, NCSE is thought to be underdiagnosed and to account for about 30-40% of all SE cases. In an effort to diagnose electrical seizure and NCSE in seizure patient with seizure and an altered mentation we record the routine EEG for about 20-30 minutes, whereas in humans recordings are often done for 1-2 days via continuous monitoring. Using routine EEG we noted 4/11 (36%) of cats and 5/55 (9%) dogs were diagnosed with NCSE and 4/55 (7%) had electrical seizure.

**Pathophysiology with NCSE**

Pathology with CSE is due to both systemic effects from the muscle movement and hyperthermia and the intracranial effects of continuous neuronal firing in the brain with mortality rates of 25- 40% reported in canine patients. NCSE could be thought of as more benign than CSE since there are no obvious muscle movements or systemic effects but, on the other hand, NCSE is typically noted after CSE and represents prolonged and continuous neuronal firing in the brain. Human studies have shown that NCSE is a statistically significant independent predictor of mortality and reduced functional independence separate from age and underlying diagnosis. In other words, when comparing age and diagnoses matched cases, those with NCSE did far worse indicating that NCSE is a pathologic and lethal process.

NCSE cause brain necrosis and facilitates more seizure. The excessive neuronal firing in NCSE generates excess glutamate mediated stimulation of the NMDA receptor, calcium influx and then neuronal cell death. A reduced seizure threshold from the kindling and mirroring phenomenon, structural and cellular reorganization of the hippocampus, selective neurodegeneration and altered cellular expression, and distribution of neurotransmitter and receptor channels can self-sustain the seizure and promote future seizure. This latter phenomenon in people is well known as one study showed 33% of refractory SE will have recurrent seizure within 5 days of tapering an anesthetic medication, a condition referred to as malignant SE (Foreman). In this talk the speaker will describe a 7 year-old Swiss Mountain dog with seizure of unknown cause that had two episodes of NCSE, 30 days apart, where necropsy showed neuronal necrosis. This case demonstrates that NCSE can cause neuronal necrosis and reduce the seizure threshold.

**Mortality with NCSE**

Human studies show that NCSE is an independent predictor of mortality, especially when there is a delay in diagnosis, or longer episodes of NCSE. Mortality rates with CSE in humans is about 30% whereas 50% is a stated mortality rate for NCSE. There are no published veterinary reports regarding the incidence or mortality rates with NCSE, however in our study 2/4 cats and 3/5 dogs or 5/9 (55%) had died within 3 months of their NCSE.

**Treatment of status epilepticus**

The endpoint for treating CSE is cessation of all motor activity, but as noted above, many of these cases will continue to have electrical seizure or NCSE. In human medicine, refractory CSE is treated with anesthetic doses of midazolam, propofol or pentobarbital. There is no clear advantage to any of these agents but surveys of physicians show a preference for barbiturate. EEG defines the endpoint of treatment which includes the reduction or elimination of epileptiform discharges (ED) and/or to establish a burst suppression pattern. Burst suppression is thought to be neuroprotective in NCSE because it hyperpolarizes at least 95% of cortical neurons and conserves on ATP. The necessary duration of burst suppression or whether it is as good or better of an endpoint that eliminating ED is debated in human medicine.

After a benzodiazepine, second line seizure treatment in humans can include Levetiracetam, Valproate and Phenytoin. Levetiracetam had variable response rates (30-79%) as a second line treatment in human NCSE. Levetiracetam has been studied for acute repetitive seizure and SE in veterinary medicine and demonstrated to be more effective than placebo. Furthermore, Levetiracetam is thought to be synergistic with benzodiazepines. Fosphenytoin has also been studied in veterinary medicine in a similar patient population also shown to be much more effective than placebo, however this drug is currently not available and also cost prohibitive. A clinical trial is being proposed in veterinary medicine to study injectable valproate compared to placebo in CSE.
**Recommended seizure treatment**

In our clinic we give 1 mg/kg to 2 mg/kg of valium, IV and 60 mg/kg of Levetiracetam, IV and if patient does not improve in 10-15 minutes then a routine EEG is performed. If epileptiform discharges are noted then boluses of 10 mg/kg of phenobarbital are given until ED abate or burst suppression pattern is noted. We have noted that between 45 mg/kg and 100 mg/kg of phenobarbital is typically required to achieve these endpoints. In a veterinary report of 10 patients with electrical seizure following CSE, burst suppression and/or elimination of ED was a goal and the report concluded this treatment strategy was safe as mechanical ventilation was not required and only treatable hypotension noted as side effects. Without the benefit of EEG, the end point of therapy should be the absence of any subtle twitching of ears or facial muscles, confusion, transient hyperthermia, episodic and unexplained changes in respiratory rates, or mydriasis.

**Conclusion**

Patients presenting after a convulsive seizure or status epilepticus that also exhibit behavioral changes or altered mentation are candidates for having continued electrical seizure and NCSE. EEG is required to prove the diagnosis and ideally to guide therapy. Practically speaking, in seizure patients that remains twitchy or confused following seizure and can’t be referred for EEG, administer 60 mg/kg Levetiracetam and then phenobarbital 8-10 mg/kg boluses every 20-30 minutes to a total dose of 40 mg/kg and blood pressure support if needed. Hopefully the use of veterinary EEG will become more common so patients with CSE can be referred for prompt detection and treatment of NCSE.

**References**


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Idiopathic vs Structural Epilepsy: Clinical Guidelines for Making this Vital Distinction

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Some studies show more than 1 in 20 dogs will suffer from recurrent seizure in their lifetime. When a client presents a recent onset seizure patient they are keenly interested in the diagnosis and prognosis along with best course of action. Some cases will be of unknown or genetic cause (idiopathic) and others will have a specific (structural) cause for the seizure. The diagnostic plan, prognosis and treatment plan can be very different between dogs with an unknown cause for their seizure and dogs with a structural problem (brain tumor, encephalitis, stroke, malformation). Considering the age of onset, breed, weight, historical and neurological exam findings are crucial in estimating the likelihood that there is a structural cause for the seizure. This talk will discuss the current terminology and rationale for grouping seizure by their underlying cause and frequency and then discuss how to make the distinction between structural versus idiopathic epilepsy.

Epilepsy vs. reactive seizure
Epilepsy generally means recurrent seizure, however in humans after just one seizure you can be considered epileptic if the seizure is associated with an enduring alteration of the brain that increases the likelihood of seizure. Reactive seizures occur when the brain is normal but reacting to an extra-cranial toxic or metabolic insult.

Epilepsy terminology
In 1989 the International League Against Epilepsy (ILAE) distinguished 3 etiologies of epilepsy which were then adopted in veterinary medicine. Idiopathic or primary epilepsy is diagnosed if no underlying cause can be determined other than a possible hereditary predisposition. Symptomatic epilepsy is a consequence of an identifiable brain disorder. Cryptogenic (probable symptomatic) epilepsy a heritable cause is not likely and an underlying pathologic change in the brain suspected but not proven. In 2005 these terms for epilepsy were changed by the ILAE to genetic, structural and unknown cause and now these are the terms used in published veterinary literature.

Genetic epilepsy can be diagnosed when the prevalence in a breed exceeds that of the general population. Making this distinction is important because certain breeds may have a particularly severe form of genetic epilepsy. For example in the Border Collie survival from seizure onset is 2 years with a 94% rate of cluster seizure and 53% rate of status epilepticus. Conversely genetic epilepsy in the Lagotto Ramagnolo starts at 6 weeks of age and resolves by 16 weeks of age. Structural epilepsy is diagnosed when there is a physical disruption of the brain from a malformation, infection, inflammation, stroke or brain tumor. Epilepsy of unknown cause is diagnosed when a cause for the seizure has not been determined.

Classification by seizure frequency
Progression of disease and a worse prognosis is often indicated when seizure becomes more frequent. Therefore applying other terms for more frequent or longer seizures is valuable. A cluster seizure is noted there are 2 or more seizure within 24 hours and acute repetitive seizure is 2 or more seizure within 5-12 hours. Status epilepticus (SE) is present when the seizure lasts 5 minutes or longer, 2 seizures where the patient is unable to respond to commands or walk between seizure, or patient having a seizure at presentation. SE may not respond to initial treatment with Benzodiazepine, Phenobarbital and/or Levetiracetam at which time it is called refractory status epilepticus (RSE). In these cases electroencephalography (EEG) often shows continued seizure activity despite few to no physical manifestation of the seizure, a condition called non-convulsive status epilepticus (NCSE). SE and NCSE have an associated 25 and 50% mortality rate in human and veterinary medicine.

Age of onset
A recent study of dogs 7 or older at time of first seizure that had a MRI determined that 79% of dogs had structural epilepsy and 21% had cryptogenic epilepsy (now called seizure of unknown origin). Furthermore when the dogs were 10 or older at seizure onset there was an 87% chance of an abnormal MRI showing a structural cause for the seizure. In the dogs with structural epilepsy, 72% had a brain tumor with stroke and encephalitis being the next most common causes of seizure. At other end of spectrum, dogs younger than 6 months of age are very likely to have a genetic or seizure of unknown cause.

Breed
Genetic epilepsy and epilepsy of unknown cause is the most prevalent diagnosis in dogs between 6 months and 7 years of age. However, within this age group encephalitis in young dogs and prevalent in many small breeds (Pug, Chihuahua, Yorkshire terrier, Maltese, Westie, Dachshund, Miniature poodle, Shih Tzu, others). Therefore in young, small breed dogs encephalitis should be highly
suspected as the cause of seizure, especially when seizure are clustered, progressive over a few weeks to a few months or there are examination or behavioral changes. A recent study showed a statistically higher incidence of brain tumors in the breeds Golden Retriever, Boxers, French Bulldog, Rat Terrier and Boston Terriers. Increasing age and weight were also correlated with higher rates of brain tumor. Therefore in these breeds and dogs > 15 kg, a recent onset seizure when 5 or older should raise a high suspicion for brain tumor.

**Behavior**

In dogs with seizure from structural brain disease the seizure can be the only symptom, however there are often subtle behavioral changes. When these behavioral changes are noted in a seizure patient then this should raise suspicion for a structural brain problem. These include inappropriate defecation, inappropriate urination, not greeting the owners, restless at night, sleeping more in the day, irritability, not playing, and aggression.

**Exam findings**

Seizure is generated from lesions in the forebrain or thalamus. Lesions in this area can cause patients to circle towards the side of the lesion and have contralateral menace and postural deficits. Since strength and gait are generated from the brainstem, a focal forebrain lesion would not be expected to cause weakness or ataxia. If a patient has a unilateral menace deficit with normal pupillary light responses and normal palpebral response then a contralateral forebrain mass lesion should be suspected. Similarly if the gait is normal but there is a unilateral postural deficit (paw flip test, tactile placing, hopping) then a contralateral forebrain lesion should be suspected. Lastly, while in the exam room if a patient circles to only one side then a forebrain lesion is very likely and will be located on the side towards which they are circling. In a recent study of dogs and cats where only neck pain was noted almost 10% had only a focal brain tumor. The presence of neck pain in a seizure patient should suggest there is a structural cause of the seizure. However an abnormal exam is not always noted and about 30% of patients with a mass lesion will have a normal neurological exam.

**Conclusion**

Your client expects a sense of the diagnosis, treatment plan and prognosis when they present with a pet with recent onset seizure. Prior to starting AED or referral for MRI and neurological consultation, you can make an accurate guess as to the diagnosis by considering age, breed, weight, historical findings and then performing a 5 minute neurological examination.

**Selected references**


In the last 10 years my core practice has grown from 1 employee to over a hundred across several locations – our core business is neurology / neurosurgery and advanced imaging (MRI, CT). Additionally, there is an Emergency and Internal Medicine practice in one location and I am part owner in the real estate in several of these locations. We have a centralized, in-house marketing, human resources, accounting, and operational management headed by a CEO that oversees the businesses. The transition from veterinarian to veterinary owner operator (VOO) to being a successful, hands-off owner has fulfilled my business vision but has also been very difficult. The goals of this talk are to share the lessons learned along the way from the innate adversity of veterinary business management and ownership.

One important realization is that the veterinary owner operator (VOO) wears many hats but is always viewed as the owner in every interaction. The VOO is under an intense, invisible spotlight and can compel and inspire their staff to be their best or implode their business. This talk will be divided into the different relationships a VOO has in a given day- VOO – manager, VOO- staff veterinarian, VOO- staff member. Although several “what would you do scenarios” will be presented – it is hoped the participants will bring their own current struggles for us to discuss as a group.

Culture
Defining the vision, mission, and core principles of your practice and then making all decisions centered around these core principles will set the culture. The business goal will be to have a group of like-minded people who understand and are working toward the same goal. Management’s role is to lead by example and correct and coach people when they stray from core principles. One thing I have learned is that when the culture strays at a particular location, everything gets harder and it is expensive. This can take the form of fewer office visits, inadequate follow-up with clients and primary care veterinarians, employee dissatisfaction, and employee turnover. I have found that investing in management pays tremendous dividends and that good management is expensive but bad management is very expensive.

The VOO – manager relationship
Ironically, the biggest hurdle for veterinary business growth is that the VOO is very likely to be the first to stray from the stated core principles and when they do it is devastating to management. This most often takes the form of an owner changing their minds, deviating from a policy, discounting, squeezing in appointments when staff is beyond capacity, or simply not trusting that the manager has good instincts and good ideas. Because the VOO is under an invisible spotlight, any action they take that contradicts a policy or procedure will be felt by the staff 10 fold and devastating to management. This is the key moment in the VOO-manager relationship – the VOO can argue or defend their behavior or simply have the humility to apologize and genuinely try to change their behavior. One way to retain and inspire your manager is to have regularly scheduled meetings where the manager is free to speak of any recent transgressions allowing you to be more self-aware and improve. The absolute key to success as a VOO is to be self-aware and humble – otherwise you will never realize what could have been your team’s full potential. For me personally physical fitness and meditation have allowed me to be more self-aware and find opportunities daily to respond correctly instead of reacting incorrectly.

Recently we gave an award to one of our assistants for up-holding our core principle of integrity because she had the courage to tell the VOO that their behavior in the exam room was inappropriate. I believe I may have contradicted or inadvertently demeaned the assistant – my first reaction could have been to be angry, instead I responded by thinking for a moment and then correctly my behavior.

The VOO – staff veterinarian relationship
Most VOO have obtained their role not because they wanted to be a business owner but because they were exceptional veterinarians that 'needed help’ to meet the demand in their area. The VOO then hires an associate and takes on the roles of owner, manager and often mentor. In this role, humility is again important and also the need to realize that a successful owner and mentor revels in the success of their employee and not their owner ability. Although counter intuitive this should take the form of refusing to see cases on their day off, working more holidays, seeing the more difficult and less lucrative cases, and genuinely wanting their associate to be successful. If you put the associate through the same trials that you remember going through in your career this will likely foster resentment or send the staff veterinarian a mixed message.
Similarly the VOO ability to perform a procedure efficiently, diagnose quickly and accurately, or generate genuine client satisfaction does not matter and holding this as a standard or even as a goal for the associate is unhealthy. The goal for the VOO is to downplay or minimize their ability while striving to develop the employees and celebrate their successes along the way.

One likely limitation of the staff veterinarian as compared to the VOO is the ability to connect with most clients. Often VOO understand that clients are people with animal problems meaning that clients desire a connection to their veterinarian – they want their pet’s problem resolved but they also want to be involved in the plan and feel better after the visit. Veterinary training is very systematic and often associates are generating problem lists and rule-outs plus a plan of attack instead of listening to the client. Veterinarians by nature are very systematic and this can on occasion leave some clients feeling cold or less connected. Since this ability to connect is somewhat innate and can take time to develop, the VOO will need to be careful not to expect too much from an associate. Generally recognizing and optimizing strengths of an associate while not asking them to work solely on their weaknesses will lead to the most success.

VOO – staff member relationships

Whether you like it or not, as a veterinarian and especially as a VOO, you are a manager. Successful management where you optimize an employee’s potential demands a good manager-employee relationship. The responsibility for maintaining and cultivating this relationship is not equally split between the employee and manager, in fact in veterinary medicine about 80% of the responsibility falls on the manager. The veterinarian will need to understand that a disapproving look or comment can be very destructive to this relationship and taking the time to teach, develop the employee skill set, and invest in the employee will inspire the employee to reach their full potential. Once this culture is present in your practice you will no longer have trouble “finding good help”. There is a word of caution however, it is in fact “lonely at the top” and having a manager employee relationship that extends into friendship and beyond the scope of just work will dramatically limit the effectiveness of the manager and will in fact be destructive to that relationship. Therefore, if you want your employee to be successful be friendly and considerate but do not be their friend.

The last point is that the actions of the VOO are always under a magnifying glass, although this is rarely recognized by the VOO. Therefore taking time to teach, investing in an employee and giving them the benefit of the doubt will inspire your team but an expression of frustration or disappointment will devastate them and the team. On bad days this can be difficult but a successful VOO will be always mindful of this relationship and disciplined enough to not to undermine this relationship.

Conclusion

A successful VOO will be mindful of their various relationships and simultaneous roles or hats that they wear within the practice. Although they might think of themselves as simply “seeing a case” they are in fact setting the culture, supporting management, and being a caring owner of the practice at the same time. Being self-aware and humble will be the key to success in this relationship.

References

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Upper vs Lower Motor Neuron: Never Miss Again after this Videocase Presentation
William Bush, VMD, DACVIM
Bush Veterinary Neurology Service
Frederick, MD

The ability to examine a patient and determine where in the body the disease is located is critical to determining the cause, best therapy and prognosis. Weakness is a common presenting complaint and can result from spinal cord (upper motor neuron - UMN) or nerve and muscle disease (lower motor neuron-LMN). Understanding the function of the UMN and LMN system will enhance the accuracy of lesion localization and therefore determination of the diagnostic testing and prognosis. This talk will discuss the function of the UMN and LMN system and then how to assess these systems via examination of a patient’s gait, postural responses, and reflex testing. Secondly we will discuss assessing the cutaneous trunci reflex and for focal pain to assist in lesion localization and honing the list of possible the spinal cord diseases. Lastly we will discuss evaluating the palpebral response and laryngeal / pharyngeal / esophageal function in LMN disease.

Tonic gamma loop mechanism
Muscle tone refers to the intrinsic tension of the muscle when supporting the body against gravity while standing, shifting weight from limb to limb, jumping or performing stairs – but how does this occur? The tonic gamma loop mechanism (TGLM) is intrinsic to the LMN system and understanding TGLM physiology offers insight into how gait is generated and why UMN or LMN disease cause alterations in muscle tone and reflex. When we jump down from a height and our knees start to bend or buckle there is a sudden stretch of the quadriceps muscles and stimulation of stretch receptors (neuromuscular spindle) within these muscles. These receptors then stimulate the sensory portion of the femoral nerve which then directly synapse and stimulates the motor portion (alpha motor neuron) of the femoral nerve. This causes the quadriceps muscle (which is innervated by the femoral nerve) to contract and prevent your knees from buckling. When the patella tendon is artificially simulated with a reflex hammer it fools the body into thinking there is a sudden heavy load on the quadriceps muscle (like jumping down), the TGLM is stimulated and the knee jerks.

Gait generation
As mentioned above, when information from the neuromuscular spindle of the TGLM returns to the spinal cord it directly synapses on the alpha motor neuron or motor portion of the same muscle in which the spindle is located. However, the information also stimulates inhibitory interneurons that then reduce activity or tone in the antagonist muscle group. Therefore when there is contraction of the quadriceps there will be reduced tone in the hamstring or flexor group. The modulation of flexion is performed by the phasic gamma loop or flexor gammas loop. The UMN system acts on the tonic and then phasic gamma loop mechanisms to generate extension and then flexion of the leg by activating this intrinsic reflex mechanisms and therefore generate gait.

UMN lesions influence the TGLM
In our example above, gravity lengthen the quadriceps muscle and stretches the neuromuscular spindle, which then via a direct synaptic connection, stimulates the femoral nerve. This causes contraction of the quadriceps muscle which then causes more stretching of the neuromuscular spindle and more contraction of the quadriceps muscle. This system, if not modulated would lead to dramatic increases in muscle tone and reflex. The UMN system modulates or controls the TGLM and therefore controls muscle tone and reflex. Disease of the UMN lesion can cause increased tone and reflex. Examination of dogs with UMN spinal cord disease often reveals increased tone because there is resistance to flexion of the stifle. This stiffness can also manifest in the protraction phase of the gait and appear as swinging out of the limb (circumduction) or a long-strided gait. Furthermore, brainstem lesion (where the UMN tracts start) can lead to opisthotonus also known as decerebrate rigidity where the head, neck and limbs are held in rigid extension.

Reflex testing
A reflex is something that occurs automatically or spontaneously without influence from the cerebrum whereas a reaction or response requires the unconscious participation of the cerebrum. In reflex testing there is a sensory stimulus that runs into the spinal cord or brainstem and then an immediate spinal cord or brainstem mediated response. For example, stretching the patella tendon with a pleximeter (reflex hammer) causes a sudden, intense stimulation of the stretch receptors within the femoral nerve, in essence simulating what would happen if we jumped down from a large height. Immediately the muscles innervated by the femoral nerve contact and the knee jerks. An absence of reflex often means there is a lesion of the motor or sensory portion of the femoral nerve or severe disease of the quadriceps muscle. If there is an increase in reflex (exaggerated, clonus) then there is a failure of UMN system to control this reflex.
Upper motor neuron system
The UMN system primarily starts in the brainstem. The axons from this collection of neurons run within the white matter of the spinal cord and synapses in the ventral horn of the spinal cord to activate the peripheral nerve (LMN). This system activates the LMN to generate gait and modulates or controls tone and reflex by influencing the tonic gamma loop mechanism. A lesion of the descending or motor component of the UMN system results in paresis (weakness), paralysis, increased reflex and increased muscle tone. A lesion of the ascending or sensory system causes a disordered gait and postural deficits (see below).

Lower motor neuron system
The LMN system starts within the spinal cord where the cell bodies are grouped in the grey matter of the spinal cord within the ventral horn at the intumescence (swelling) located at spinal cord segments C6-T2 and L3-S3. The numbered nerves then run to the brachial or lumbar plexus and then exit as named nerves that will then innervate specific muscles. The LMN generates muscle tone and with a lesion there is weakness, paralysis and loss of muscle tone and reflex. The LMN system also carries sensory information from receptors in the joints and skin into the dorsal horn of the spinal cord and this is eventually relayed via the UMN system to the cerebellum and somatosensory cortex via the spino cerebellar and spinothalamic tract, respectively.

Spinal cord ataxia and postural reactions
A complete lesion of the UMN system causes no movement or paralysis and an increase in muscle tone (spastic paralysis). A partial lesion will cause only weakness or paresis but the movement will be ataxic. Ataxia means disorder. The absence of ascending information reaching the brain can result in a loss of self-reception (proprioception) and consequently spinal cord or proprioceptive ataxia and slow postural reactions. Spinal cord ataxia can take the form of a long-strided gait, the limbs can circumduct, cross midline, and interfere with each other - occasionally causing the patient to trip or fall. In addition the patient might stand on the dorsal surface of the paw or stand with limbs too close, too far apart or with limbs crossed. Besides observation of the gait, testing of the postural reactions (paw flip test, hopping, tactile placing) also assesses the function of the UMN system. The postural reactions will be delayed to absent with an UMN lesion.

LMN lesions
A complete lesion of the LMN system causes paralysis with an absence of muscle tone (flaccid paralysis). An incomplete lesion causes weakness and the patient will have a short-strided or choppy gait as though they are walking on egg shells. Importantly, incomplete LMN lesions do not cause significant disruption of the sensory system. Therefore LMN lesions do not cause ataxia. Furthermore, if the patient’s weight is properly supported the postural reactions will be normal. Please see Table 1.

C6-T2 spinal cord
A lesion that involves the white matter of the spinal cord at C6-T2 will cause UMN signs to the pelvic limbs. The pelvic limbs will have increased tone and reflex, reduced postural reactions, weakness and ataxia. A lesion of the grey matter in this area will generate LMN signs to the thoracic limbs manifested as a short-strided gait, preserved postural reactions and no ataxia, reduced reflex, and neurogenic muscle atrophy. The long-strided, stiff and ataxic gait in the pelvic limbs is much different than the short-strided gait of the thoracic limbs and sometimes referred to as a two engine gait.

T3-L3 spinal cord and the cutaneous trunci reflex
Disease between the two intumescences is called T3-L3 spinal cord disease and results in upper motor neuron disease to the pelvic limbs. The presence of a cut-off or cessation of the cutaneous trunci reflex can indicate the level of the spinal cord lesion. The input for the reflex is stimulation of dorsolateral cutaneous receptors. Once a stimulus is registered the information then ascends in the spinal cord where it synapses motor neurons at the level of spinal cord segment C8 -T2. These nerves form the lateral thoracic nerve that causes contraction of the cutaneous trunci muscle. Functionally a pinch of the skin with hemostats should stimulate contraction of the entire cutaneous trunci muscle along the entire flank of the patient. With a thoracolumbar spinal cord lesion, pinching of the skin behind the lesion will not result in twitching of the skin and thus there appears to be a cut-off of this reflex. A cut-off in the cutaneous trunci reflex indicates the lesion is about 2 vertebral bodies cranial to the cut-off. Furthermore, following surgery movement of the cut-off caudally predicts recovery while movement cranially predicts myelomalacia.

Lumbar intumescence and nerve root disease (lumbosacral syndrome)
Disease of the spinal column or spinal cord/nerve roots from the L5 to S1 vertebrae can generate LMN signs to the pelvic limbs, fecal and urinary incontinence as well as paralysis of the tail. These signs can overlap and be mistaken for osteoarthritis of the hip or stifle. A sciatic lesion can be the cause of an increased patella reflex as a consequence of losing strength and tone to the antagonist of stifle extension, this is called a pseudo-hyperpatella reflex and should not be mistaken for an UMN reflex. A reduction of the patella reflex can help localize lesion to L3-L4 vertebral bodies and would not be expected with disease from L5 – S1 vertebrae. The patella reflex
can be absent in otherwise healthy middle-age and older dogs, presumably from degeneration of the sensory portion of the femoral nerve.

Pain assessment
Diseases of the nerve and muscle (LMN disease) are typically not painful, however many spinal cord diseases are associated with pain. Determining the patient is painful at a specific location can direct diagnostic testing and also hone the list of possible causes of disease – for instance intervertebral disk disease, neoplasia, and diskospondylitis are typically painful whereas ischemic myelopathy (fibrocartilaginous emboli) and acute, non-compressive nucleus pulposus extrusions are often non-painful, especially after the first 24 hours. Neck pain is often suspected when patient spontaneously yelps out but there is no gait or posture deficits, intermittent thoracic limb lameness (root signature), or stiff neck or decreased range of motion is noted. Palpating muscle spasm laterally at level of transverse process, pain with manipulation or ventral process of C6, or resistance to range of motion can also indicate neck pain. Mid-back pain is often suspected with kyphosis, stiffness and when slow to sit or rise. Palpating and applying pressure to dorsal processes while putting pressure / palpating the ventrum and palpating muscle / rib heads at level of transverse process often allow for detection of back pain. Lumbosacral pain is suspected with abnormal tail carriage and when patient is slow to sit and rise. Pain can often be detected with rectal palpation of the lumbosacral junction (or spondylosis at L7-S1), tail extension or by applying pressure to muscle between dorsal process of L7 and S1. Hip extension will not differentiate back from hip pain. However, hip pain can be discerned by slowly elevating the femoral head about 3-5 mm from acetabulum by lifting up on the medial surface of the femur while the patient is in lateral recumbency.

Cranial nerve exam in LMN disease
LMN disease can affect cranial nerves when there is a polymyositis, polyneuropathy, or disease of the neuromuscular junction (Myasthenia gravis). When LMN disease is suspected then a few physical examination maneuvers can be helpful. Firstly listen to the patient’s breathing – a respiratory stridor can indicate weakness of neuromuscular system that abducts the vocal folds. Gagging can indicate pharyngeal weakness or incoordination and misdirection of saliva into the airway. Pneumonia may be present from laryngeal or pharyngeal dysfunction or from megesophagus – listen for a soft, moist cough and carefully auscultation the lungs. Thoracic radiographs are indicated in dogs with suspected LMN disease to assess for megesophagus, aspiration pneumonia and other pathology. Secondly, assess temporalis muscle mass because marked atrophy can indicate a lesion of the mandibular nerve. Lastly, repeated stimulation of the medical canthus of the eye should provoke a prompt and complete blink response – incomplete blinking or an absent blink indicates there is neuromuscular disease.

Table 1. Distinguishing characteristics of UMN and LMN disease

<table>
<thead>
<tr>
<th></th>
<th>UMN</th>
<th>LMN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait Characteristic</td>
<td>Long strides</td>
<td>Short strides</td>
</tr>
<tr>
<td>Ataxia</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Postural Deficit</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Tone &amp; Reflex</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Atrophy</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Spinal Pain</td>
<td>Often</td>
<td>Seldom</td>
</tr>
</tbody>
</table>

References
Braund KG. Clinical Syndromes in Veterinary Neurology. 2nd. St. Louis, MO, Mosby, 1994
The spinal cord connects the brain to the neuromuscular system which is responsible for locomotion and respiration. The spinal cord is protected by a long bony box that is segmented to allow for improved axial movements. The segments of the bony box (vertebrae) are cushioned by the intervertebral disk. The intervertebral disk (IVD) contains a jello-like substance called nucleus pulposus (embryonic notochord) that is wrapped by concentric layers of ligamentous material (annulus fibrosus). The IVD is located below and adjacent to the spinal cord and pathology of the IVD puts the spinal cord at risk for infection, infarction, and compression all of which can lead weakness, paralysis, ataxia, pain, and incontinence.

Role of magnetic resonance imaging (MRI)
MRI characteristics are based on the proton or water content of different tissue allowing for detection of even mild pathology in the soft tissue and to a lesser extent bone. Because MRI directly images the spinal cord it is superior to X-ray based technology like radiography, myelography and CT scanning. MRI consistently demonstrates superior accuracy in the diagnosis of spinal cord disease. Additionally, MRI is better at predicting outcome than assessment of neurological function at presentation. MRI is currently essential to the practice of high quality veterinary neurology.

Hansen type I disk disease
Hansen Type I disease occurs when the degenerated annulus fibrosus loses tensile strength and tears allowing the degenerated, dehydrated nucleus pulposus to extrude or herniate and co-occupy the spinal canal with the spinal cord. The stretching of the meninges, nerve root and annulus fibrosus tear generating pain and the spinal cord compression can cause weakness, paralysis and incontinence. Prognosis and the choice of medical vs. surgical management is made by combining information about the neurological grade and MRI findings. This disease is prevalent in 3-6 year-old dachshunds and many other small breed dogs and 6-9 year-old large breed dogs like the German Shepherd, Rottweiler, Dalmatians and mixed-breeds. Type I disk disease has a very good to excellent prognosis but surgery is often required when there is persistent pain and/or weakness with significant spinal cord compression. Remarkably, in paraplegic dogs with Type I disease that have hemilaminectomy, MRI is a greater predictor of outcome than nociceptive or deep pain status.

Hansen type II disease
Hansen Type II disease is present when there are micro-tears and bulging of the annulus fibrosus and compression of the spinal cord, meninges and nerve roots. The disease is most common in larger breed dogs in the low cervical spine and lumbosacral junction. In the low cervical spine, Type II disk extrusion is an important factor in cervical spondylomyelopathy and is also known by disk associated wobbler’s syndrome (DAWS). In DAWS the outcome with surgery is better than with medical management although there is no significant difference in life expectancy with these 2 treatments. Lumbosacral disk disease can mimic hip or stifle disease but unlike these other conditions, it can lead to urinary or fecal incontinence. Success rates with surgery are generally with LS surgery unless incontinence is already present. Therefore the distinction between lumbosacral Type II disk extrusion and orthopedic disease is an important. Nerve pain (and not orthopedic disease) can be distinguished from orthopedic disease via palpation of lateral muscles just cranial and lateral to the wings of the ilium, between the L7 and S1 dorsal spinous process, ventral surface of L7 and S1 via rectal, or with elevation of the tail. Pain with hip extension can indicate nerve compression or joint pain. However, hip pain can be discerned by slowly elevating the femoral head about 3-5 mm from acetabulum by lifting up on the medial surface of the femur while the patient is laterally recumbent.

Acute non-compressive nucleus pulposus extrusion (ANNPE)
ANNPE is sometimes referred to as Type III disk disease or low volume high velocity disk extrusion. In this disease a small amount of nucleus pulposus (NP) ruptures at a high velocity through a small tear in the dorsal annulus fibrosus leading to edema, malacia, and/or hemorrhage of the spinal cord and epidural fat but minimal to no compression of the spinal cord. ANNPE has a peracute onset and associated with activity or a traumatic event and seen more commonly in medium to large breed, male dogs, especially Labrador retrievers and mixed breeds. About 2/3 of the patients in one study returned to walking and when the T2 weighted cross sectional MRI showed less than 90% of the spinal cord to be affected, 93% of the dogs regained function. Similar to Type I disk disease, the prognosis is more strongly correlated to MRI findings than admission neurological grade or nociceptive status. Many patients have difficulty urinating over the short-term and are treated with phenoxybenzamine or prazosin and diazepam to reduce smooth and skeletal muscle tone, respectively. Urinary catheterization can be a useful way of managing these patients in the first 2-3 days while
the disease improves and the phenoxybenzamine has time to take maximal effect. Monitoring the urinalysis and bacterial culture and sensitivity are advised because the resulting urethral inflammation can frustrate useful urination. Exercise restriction, rehab therapy and pain medication as indicated are hallmarks of therapy. Pain medication in the short term and rehab therapy may improve outcome.

**Fibrocartilaginous emboli (FCE)**

FCE or ischemic myelopathy occur when the NP obstructs blood flow within a spinal cord arteriole leading to necrosis of the spinal cord from loss of blood flow (infarct). The onset and progression of clinical signs are very similar to ANNPE although dogs with FCE are rarely painful. The middle aged Miniature Schnauzer, Shetland sheepdog and Labrador are at higher risk for FCE. The overall recovery rate is about 84% but 100% of dogs will improve if the T2 weighted MRI cross sectional lesion is less than 67% and the length of the lesion is less than 2 vertebral bodies. Despite the fact that the MRI can be normal about 20% of the time, MRI is the most accurate test and the strongest predictor of outcome in dogs with FCE. The same concerns exist for micturition with ANNPE and FCE. Rehab therapy instituted early in disease process may improve recovery rate.

**Diskospondylitis**

Diskospondylitis is an uncommon infectious and therefore inflammatory condition of the intervertebral disk and surrounding bony endplate, soft tissue, and meninges. Increasing age, male, large breed dogs are at higher risk and the Great Dane, Boxer and Labrador are thought to be predisposed to this disease. Pain, lethargy, not eating well and low grade fever are often noted. This can progress to weakness, paralysis and incontinence if there is spinal cord compression from empyema, disk extrusion, fracture or subluxation. Diagnostic evaluation can be frustrating as neutrophilia, monocytosis and hyperglobulinemia are inconsistently elevated – a C reactive protein maybe a sensitive indicator of inflammation from diskospondylitis. Radiographic are often initially normal in this disease, MRI far more sensitive and can help determine degree of spinal cord compression and requirement for surgery. The typical bacteria implicated are *Staphylococcus, Streptococcus, E.Coli* and less commonly the zoonotic agent *Brucella canis* or fungal agents. Antimicrobial therapy is ideally based on a culture from the urine, blood, and/or affected interspace or spinal canal. However, even this combination of testing does not always produce a specific pathogen and sensitivity profile. Empiric therapy often recommended with cephalosporin, fluoroquinolone or/and clindamycin. Pain management is often with NSAIDs, however, despite the concern for immune suppression, the author prefers a tapering course of anti-inflammatory doses of glucocorticoids plus pain modulators. Surgery to decompress the affected spinal cord and nerve roots is often very useful in improving outcome, perhaps by enhancing the delivery of antibiotic to the nervous tissue and surrounding structures. The overall prognosis for this disease is thought to be fair to good with mortality rates of about 30%. Early detection, absence of systemic disease, a better neurological grade, non-fungal and non-*Brucella* cases, and a good response to initial therapy are positive indicators for surviving this disease.

**Conclusion**

Pain, weakness and ataxia are common presenting complaints in veterinary medicine. IVD pathology is commonly implicated as the cause of the clinical signs. A presumptive diagnosis can often be established by considering breed, age of onset, progression but MRI is best test for establishing definitive diagnosis, prognosis and the requirement for surgery.

**Table 1. Clinical features of 5 disk diseases**

<table>
<thead>
<tr>
<th></th>
<th>Type I</th>
<th>Type II</th>
<th>ANNPE</th>
<th>FCE</th>
<th>Diskospondylitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Annulus tear, nucleus pulposus in spinal canal</td>
<td>Annulus bulge, microtears</td>
<td>Small annulus tear, low volume, high velocity</td>
<td>Spinal cord stroke</td>
<td>Infection vertebral endplate, disk, soft tissue</td>
</tr>
<tr>
<td><strong>Signalment</strong></td>
<td>3-6, Chondrodystrophic 6-8, Large Breeds</td>
<td>&gt;6 yrs Large Breeds</td>
<td>6 yrs, medium to large, Lab, Border collie</td>
<td>6 yrs, Sheltie, Schnauzer, Lab</td>
<td>Male, Great Dane, Boxer, Labrador, risk up with age</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Sudden, progressive with periods of rapid progression</td>
<td>Slowly progressive</td>
<td>Peracute, can progress in first 24 hours</td>
<td>Peracute, can progress in first 24 hours</td>
<td>Progressive, wax and wane</td>
</tr>
<tr>
<td><strong>Progress</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Painful</strong></td>
<td>Yes, episodically very painful, muscle spasm</td>
<td>Mild pain, limits mobility</td>
<td>Moderate pain, improves in 24 hours</td>
<td>No</td>
<td>Painful to episodically very painful</td>
</tr>
<tr>
<td>Preferred Location</td>
<td>Neck, TL junction</td>
<td>low neck, low back</td>
<td>Over disk space</td>
<td>Intumescence</td>
<td>C6-7, Mid-thoracic, LS</td>
</tr>
<tr>
<td>--------------------</td>
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<td>----------------</td>
<td>--------------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Signs</td>
<td>Paresis to paralysis</td>
<td>Weak, incontinent, tail down (LS)</td>
<td>Paresis to paralysis, often one side worse</td>
<td>Paresis to paralysis, often one side worse</td>
<td>Painful, sick, weak</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>MRI especially in deep pain negative</td>
<td>MRI</td>
<td>MRI required</td>
<td>MRI required</td>
<td>MRI most sensitive, CRP</td>
</tr>
<tr>
<td>Treating</td>
<td>Surgery often required, exercise restrictions, NSAIDs</td>
<td>Exercise restrictions, surgery, NSAIDs</td>
<td>No surgery, NSAIDs, exercise restrictions</td>
<td>No surgery, NSAIDs, exercise restrictions</td>
<td>Long term antibiotics, surgery, pain meds, NSAID &gt;Steroid</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Dependent on neurological grade and MRI findings but generally good to excellent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**References**

**Type I Disk Disease**


**Type II IVD**


ANNPE / FCE


Cauzinille L, et al. FCE in 75 dogs: clinical findings and factors influencing outcome. *Journ Small Anim Pract* 2003; (44): 76


Diskospondylitis


620
When there are inflammatory cells within the brain, spinal cord or meninges then the terms encephalitis, myelitis, and meningitis are used, respectively. When inflammation is in more than one area the terms are combined like with meningoencephalomyelitis. The inflammation in these cases if most often from a non-infectious, unknown etiology and therefore called meningoencephalomyelitis of unknown etiology (MUE). The signs of the disease are specific to the location of the inflammation and most cases respond well to aggressive immune suppression. This talk discusses the terminology, definition / histopathology, common presentations, treatment and prognosis for different manifestations of non-infectious inflammatory disease within the nervous system.

**Terminology**

MUE is an umbrella term for necrotizing encephalitis (NE) and granulomatous meningoencephalomyelitis (GME). Necrotizing encephalitis implies death of neurons within the brain from inflammation and is further subdivided into Pug dog encephalitis or necrotizing meningoencephalitis (NME) and Yorkshire terrier encephalitis or necrotizing leukoencephalitis (NLE). MUE has replaced these terms since multiple breeds have been identified with these disease and the prognosis, testing and treatment protocols are similar. Steroid responsive meningitis-arteritis (SRMA) is another non-infectious inflammatory disease that typically involves only the meninges – this disease will be discussed separately at end of this talk.

**Definitions and signalments**

NLE was first described in the Yorkshire terrier. NLE is a progressive disease with an acute or chronic onset where there is necrosis of the white matter that with time, can coalesce into cavities or holes in the brain. The grey matter and spinal cord are spared in this disease. The other form of NE, NME first described in the Pug dog has since been noted in many other small breeds like the Maltese, Brussels Griffon, Colon du Tulear, Shih Tzu, and Papillion. NME is typically an acute onset and rapidly progressive disease of the both the grey and white matter of the cerebrum, with only 25 % of cases showing any multifocal or brainstem signs. Because the cerebrum is so commonly affected, seizure is common clinical sign – 94% of Pugs with this disease have seizure. GME is common and may account for up to 25% of canine CNS disease – it is an acute onset, progressive and potentially fatal disease. Unlike NE, the disease can manifest in the cerebrum, brainstem and spinal cord – 8 % of all cases present with only spinal cord signs.

Histopathologically GME is noted most often in the white matter as perivascular infiltrates of rounds cells (plasma cells, lymphocytes and occasionally lymphoblasts) - these can coalesce to form tumors (unlike NE where the lesions coalesce to form cavities within the brain) (SJSR). Female, small breed dogs like the Miniature poodle, Maltese, Dachshund, Westie, and Chihuahua are commonly affected. Most dogs with GME are 4-8 years of age, whereas with NE most dogs are under 4 years of age. The take home point is that MUE should be suspected in small breed under 8 years of age with acute onset of brain and less commonly spinal cord signs.

**Signs of disease with MUE**

The signs of disease are specific to the region of the brain that is involved. Most cases of MUE presents with multifocal clinical representing a mixture of forebrain and brainstem signs which can include altered mentation, visual deficits, central vestibular signs, proprioceptive placing and hopping deficits and seizures. In one report, 8% of cases has only spinal cord signs (weakness, paralysis, ataxia).

**What is the cause of MUE?**

The causes of MUE is thought to be from a genetic predisposition coupled with environmental exposures leading to a pathologic immune response. For instance, the histopathological differences in NE may result from minor differences among breeds, modifying genes, or variations in antigenic exposure. Breed predispositions indicate there is a heritable component to development of MUE. In the Pug, heritability has been proven and a strong association demonstrated between affected dogs with single nucleotide polymorphism within the dog’s leucocyte antigen (DLA) complex II region located on chromosome 12. The authors point out that this same association is made in human multiple sclerosis (MS) patients and that NME in the Pug dog maybe a good model for the less common acute variant forms of MS. Recent work in Maltese with NME show risk loci on chromosome 4 and 15.

MUE has been associated with viral diseases like Borna virus, West Nile, Canine parainfluenza, and Encephalomyocarditis virus, Canine herpes virus-1, Parvovirus, Porcine herpes virus-1, Bunya- and Polyomaviruses. Additionally, DNA from *E. Coli, Mycoplasma canis* and *Bartonella vinsonii subsp berkhoffii* have been identified in sporadic cases of MUE and a recent report shows DNA from *Anaplama phagocytophilum* in 4/23 cases SRMA. These pathogens are not thought to be direct cause of the disease but according to
the “Hit-and-Run Hypothesis” work in tandem with genetic and other environmental factors (vaccination?) to generate an autoimmune response, perhaps through molecular mimicry.

Autoimmune disease is likely in MUE because the CSF and serum of dogs with MUE contain an anti-astrocyte autoantibodies against glial fibrillary acidic protein (GFAP) which is an intermediate filament protein important in astrocyte function. Recent work has shown that the active cellular proliferation is thought to occur within the CNS lesion (and not from a migration from outside the CNS) and is assisted by matrix metalloproteinases (MMPs). MMPs are enzymes necessary for migration of leukocytes into the CNS or CSF and MMP-9 is elevated in some dogs with MUE. Other work by Dr. Mariani has also shown elevations in many interleukins necessary for lymphocyte proliferation and trafficking into tissue. However, to date there is no useful serum or CSF biomarker to assist in the diagnosis or treatment of MUE.

Lastly, since some cases of MUE lesions contain small amount of lymphoblasts and some are truly shown to be lymphoma at the time of histopathology, it is theorized that MUE is a lymphoproliferative disorder with features of both inflammation and neoplasia. Further support for this claim is the marked clinical responses of certain cases to chemotherapy.

MUE diagnosis
An MUE diagnosis is based on clinical suspicion from the signalment and disease progression, and then MRI, CSF and infectious disease testing. It can be difficult ruling-out infection because of inaccurate test results and the fact that there are not tests for all known pathogens. For example, we had a suspected MUE whose necropsy revealed a high burden of an unknown protozoal agent. Complicating things further is not all cases will have an abnormal MRI and between 12-25% of MUE cases will have normal CSF analysis. In cervical spinal cord MUE, MRI of the paraspinal cervical muscles with STIR sequence in MUE is often abnormal (78% sensitivity) and rarely abnormal in normal controls (92% specificity) – because CSF results can be normal in cases of spinal cord MUE about 10% of the time, this sequence is important in suspected cases of cervical and maybe intracranial MUE.

Pursing infectious etiology
When the CSF is abnormal in a MUE cases, less than 10% of cases will have a predominantly neutrophilic CSF analysis. Therefore a neutrophilic pleocytosis should alert clinician to a possible infection rather than MUE. Typical testing when searching for infection could include PCR, serology and rarely cultures for protozoal, rickettsial, fungal, bacterial, and viral diseases. In the Mid-Atlantic region of the USA, we typically test the CSF via PCR for distemper virus, serology for Toxoplasmosis gondii, Neospora caninum and potentially Sarcocystis neurona, and antigen testing for Cryptococcus sp. as well as whole blood PCR testing for vector borne disease. Failure to improve while on antibiotics or a relapse of signs when prednisone is reduced while on antibiotic therapy is often the last step in ruling-out infection and committing to multimodal immune suppressive therapy (see below). Brain biopsy has been reported and occasionally performed in our clinic however, the procedure has risks, costs, may yield false negative or positive results and may not change the course of treatment. A recent paper describing needle guided brain biopsy had 82% of cases achieved a specific diagnosis with a 6% indirect mortality rate and 29% incidence of transient side effects (stupor, seizure, weakness and loss of proprioception).

MUE treatment
Initial testing often reveals inflammation but does not clearly delineate between non-infectious and infectious inflammation. To address a possible infection antimicrobial therapy (clindamycin 15 mg/kg, BID, minocycline 10 mg/kg, BID +/- Fluconazole 10 mg/kg, BID) if often started while waiting for infectious disease test results. Prednisone 0.5 mg/kg, BID is also started and if signs are progressive and severe additional immune suppression could be considered with chemotherapy (Cytosine arabinoside, Lomustine, Procarbazine) and/or immune modulation with (Cyclosporine and less commonly Leflunomide, Azathioprine, or Mycophenolate). Radiation therapy has also been reported to have a positive influence of the disease course with MUE. There are many important and unanswered clinical questions revolving around what is best immunosuppressive protocol and when it is advised to stop therapy.

Steroid alone are insufficient
In a meta-analysis of MUE cases the median survival for dogs treated with corticosteroid plus any other immune suppressant protocol ranged from 240 to 590 days (n=96) compared with corticosteroid alone where range of median survival was 28 to 357 days ( n= 43). A recent retrospective study evaluating different glucocorticoid protocols (no other immune therapy) showed survival times ranging from 2 to 2065 days – and the authors concluded that an 18 week schedule of sole prednisone therapy can be used to treat MUE. However, multiple other authors conclude that treating with immune suppressants other than prednisone will improve control of the immune condition, improve survival times, and improve quality of life for the patient by reducing steroid associated side-effects (polydipsia, polyuria, polyphagia, muscle loss, urinary tract infection, hepatotoxicity, etc.). However, which immune suppressive protocol is best in not known and there is a desperate need for randomized, blinded, controlled, prospective study of MUE to assess current and future therapies that could include (intravenous immunoglobulin, plasma exchange and even anti-viral therapy).
Once remission or improvement is achieved it can be difficult to know when to taper steroid and other immune suppressive therapy. In our experience, tapering medication can lead to relapses with poor outcomes in dogs that had a normal neurological exam. A recent paper showed that follow-up CSF analysis at 3 months can predict relapse and that tapering medication in dogs with an abnormal MRI always lead to relapse. Repeating these tests when they were previously abnormal is advised prior to the tapering or elimination of immune suppressive therapy.

Prognosis
Comparing studies is difficult due to different inclusion criteria, therapy, treatment endpoints, and lack of a prospective, controlled study. There is a recent prospective study of 39 MUE dogs treated with prednisone and then Cytosine arabinoside that provides insight into the prognosis with MUE. 13/39 (33%) died in the first 72 hours and 22/39 (56%) died within the first 52 days and the study had an overall mean survival time of 26 days (range 0-2250 days). The remaining 17 dogs that lived beyond 52 days had survivals that ranged from 562 to 2241 days (median 1616 days). Overall 12/39 (31%) dogs returned to normal and 7/39 (18%) were normal without treatment. These results can best be summarized by saying MUE can have an acute and fatal presentation up to 33% of the time and if alive at 8 weeks then survival time jumps to a median of 4 and ½ years. Among the dogs that survive more than 8 weeks, most return to normal and some can be off medication altogether.

Prognostic indicators
One paper demonstrated that signs of high intracranial pressure (foramen magnum herniation, loss of cerebral sulci) was associated with a higher mortality. Multifocal disease and seizure have been inconsistently reported as negative prognostic indicators in MUE. A recent abstract suggested that focal brainstem disease carried best prognosis in MUE.

Seizure and the role of electroencephalography (EEG) in MUE
Non-convulsive seizure and non-convulsive status epilepticus (NCSE) can be present and only detectable by using EEG. In pediatrics, continuous EEG is used in patients with encephalitis, seizure and altered mentation to identify non-convulsive seizure and non-convulsive status epilepticus. Children with non-convulsive seizure have a poor outcome compared to those with the same diseases without non-convulsive seizure. We have also documented NCSE in MUE and believe that identifying and treating NCSE would improve outcome in MUE cases. NCSE should be highly suspected in MUE patients with seizure as part of the presenting complaint plus altered mentation, twitching of the ears or eyelids, sudden changes in temperature or respiratory rate, or unexplained coma. If referral for EEG is not possible, I recommend treating with Levetiracetam 60 mg/kg, IV and then potentially phenobarbital at doses of 20-40 mg/kg, divided into 6-8 mg/kg boluses until there are no abnormal movements or paroxysmal changes in vital parameters.

Steroid responsive meningitis-arteritis (SRMA)
SRMA is a systemic immune disorder characterized by inflammatory lesions of the meninges and associated arteries. This disease can occur in any breed but the Bernese Mountain Dog, Boxer, Beagle, German Short and Wire Haired pointers, Weimaraner are over-represented. Clinical signs typically start at 10 months of age with a range of 6-18 months, however it has been reported in dogs as old as 7 years of age. Although histopathological changes have been noted in the heart, mediastinum, thyroid and there is an association with immune mediated polyarthritis - the clinical signs are from the meningitis (Webb). Clinical sign include neck pain and lethargy, not eating, and fever. Typical exam findings include stiff neck, short- strided gait, neck and back pain on palpation and spontaneous Yelping-out or with movement. Misdiagnosis can occur because this is a sporadic disease, with non-specific, waving and waning signs that are often initially responsive to antibiotics and NSAID therapy. The diagnosis is made when inflammation is noted on CSF analysis, with most cases having a severe neutrophilic pleocytosis. The major differential diagnosis for these clinical signs is diskospondylitis which would be best identified with MRI.

A peripheral neutrophilia and elevated globulin count are inconsistently findings whereas serum C reactive protein (CRP) is elevated in all cases. CRP is an excellent biomarker for this disease because it drops to normal with resolution of disease and increases with relapse. Serum and CSF IgA concentration are increased indicating this is an immune disease, however IgA is a poor biomarker because it remains elevated, even in remission. Treatment involves high dose steroid therapy and when there is an incomplete response, relapse, or intolerable corticosteroid side effects then other immune modulators can be added-on (Azathioprine, Cyclosporine, Mycophenolate). A chronic form of the disease has been reported where there is weakness and ataxia in all 4 limbs and a mononuclear CSF analysis - it has been suggested this develops from late recognition of the disease or inadequate treatment (premature taper of therapy, too little immune suppression). Most cases return to normal. Relapse can occur in 20-60% of the cases – higher CRP at 4 weeks is associated with multiple relapses. Although treatment durations of up to 20 months have been reported – most cases require about 6-10 months of therapy.

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Conclusion
MUE is common and should be expected in any small breed dog with acute and/or progressive brain or spinal cord signs. Once diagnosed with MUE the prognosis is guarded but might be able to be improved by treating with multiple immune suppressive medications as well as anti-epileptic drugs. A return to normal is certainly possible as well as clinical remission. More study is desperately needed to determine the benefit of different treatment protocols, especially ones where multiple immune suppressive medication are given early in the course of the disease. SRMA is another example of immune mediated disease observed in medium to large breeds at about 10 months of age – if recognized early in the disease course the prognosis is excellent.

References
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Mariani C. Canine meningoencephalitis: what do we know? ACVIM Proceedings 2014
Central vs Peripheral Vestibular Disease: A Matter of Life or Death
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The vestibular system provides information to the brainstem and somatosensory cortex regarding head position, acceleration, and deceleration and provides us with our sense of balance. Clinical signs of dysfunction include side-stepping as though drunk, abnormal head or eye position and spontaneous eye movement. Examination of the patient will allow an assessment of whether the dysfunction is from the nerve and therefore peripheral to the brain or from the brainstem or central. This distinction is critical because central diseases are often life-threatening unless identified and treated, whereas peripheral disease often improves on its own or with minor intervention. There are many causes of peripheral and central vestibular disease but special attention should be given to meningoencephalitis of unknown etiology (MUE) because it is common and often lethal if not treated promptly. This talk will discuss common and distinguishing features of central and peripheral vestibular disease, common causes for diseases in each location and available treatments and prognosis for MUE.

Vestibular anatomy and function
Movement of endolymph over the hair cells of the receptors of the inner ear (semicircular canal, saccule, and utriculus) provides input to the vestibular nerve. The cell bodies for the vestibular nerve are located in 4 paired nuclei located within the brainstem nestled around the fourth ventricle and choroid plexus. The receptor apparatus the detects acceleration, deceleration as well as the static position of the head. There are many outputs from the vestibular nuclei:

1. Vestibular system controls eye position and coordinated movement by synapsing on cranial nerve 3, 4, and 6 via the medial longitudinal fasiculus (MLF). The generation of physiological nystagmus by moving the head left and right is called the vestibulo-ocular reflex. This reflex relies on structures deep within the brainstem and when abnormal and not related to drug therapy, there is an indication of severe brainstem dysfunction.
2. The vestibulospinal tract connects the vestibular nuclei with the nerve and muscle and will increase extensor tone to support the body against gravity during movement
3. Vestibular system has projections via the caudal cerebellar peduncle to the cerebellum which functions to coordinate movement of the eyes, neck, trunk, and limbs in relation to movement of the head as well as static head position.
4. Vestibular influences on the vomiting center in the reticular formation of the brainstem account for the motion sickness often noted in people and possibly in dogs with vestibular dysfunction.
5. There is a conscious awareness or perception of balance and equilibrium and although the pathway is not currently well defined, there is a thalamic relay of information to the somatosensory cortex.

Besides the receptors of the inner ear there are visual and proprioceptive inputs into the vestibular system. Blindfolding a vestibular patient and then lifting them off the floor often increase the sense of poor balance. Also, congenitally blind patients often have spontaneous nystagmus.

Central vs. peripheral vestibular disease
Peripheral vestibular disease has a fairly consistent clinical presentation. A useful tool to think about central disease is that dogs whose clinical signs do not look like they peripheral likely have central disease. Please see Table 1.

Peripheral vestibular disease
Peripheral vestibular disease typically has a sudden onset and can be associated with vomiting at its onset. Patients have rotary or horizontal nystagmus at a rate of 60 beats per minute or greater and a head tilt of about 20 degrees from midline. The nystagmus can change from rotary to horizontal but its fast phase should remain opposite the direction of the head tilt. Persistent weakness and postural deficit are not noted and after a few hours of acclimating these dogs are bright and responsive and able to ambulate. These patients may lean, side-step or rarely roll in the same direction as the head tilt.

The three most common causes of peripheral vestibular disease are infection of the middle ear extending into the inner ear’s bony labyrinth that contains the vestibular receptors (OTMI), the old dog peripheral vestibular or idiopathic vestibular syndrome (dogs typically older than 5, cats of any age), and the low thyroid state, especially when the cholesterol is elevated.

Central vestibular disease
One specific example of central disease is called paradoxical vestibular disease because the signs are different or opposite of what would be expected for peripheral disease. In this syndrome, the lesion is within the brain in the caudal cerebellar peduncle or floculonodular lobe of the cerebellum and the head tilt is opposite the side of the lesion. Some clinical signs of non-peripheral or
central vestibular disease include dull mentation, side-stepping/leaning towards head tilt, sway back and forth, hypermetria, tremors, weakness, non-ambulation, postural deficit, nystagmus at a rate under 60 beats per minute, extreme head tilt, cranial nerve deficits besides those associated with Facial nerve and Horner’s tract (commonly seen with OTMI). Common causes of central vestibular disease include neoplasia like meningioma (larger breeds), meningoencephalitis of unknown etiology (MUE), and infarcts of the cerebellum (larger breeds). Please see Table 2.

**Meningoencephalitis of unknown etiology (MUE)**
MUE is a group of diseases all thought to be immune mediated. Necrotizing disease of the grey matter (NME) and white matter (NLE) and Granulomatous meningoencephalitis (GME) are all examples of MUE. GME has a predisposition for the brainstem and often presents with central vestibular signs and is thought to account for up to 25% of all cases of canine CNS disease. Female, small breed dogs 4-8 years of age are predisposed and the diagnosis is made by a combination of clinical suspicion, MRI, CSF and infectious test results. A recent prospective prospective study of 39 MUE dogs treated with prednisone and then 4 weeks later Cytosine arabinoside provides insight into the prognosis with MUE. 13/39 (33%) died in the first 72 hours and 22/39 (56%) died within the first 52 days and the study had an overall mean survival time of 26 days (range 0-2250 days). In progressive MUE, prompt recognition and treatment with Prednisone 0.5 - 1 mg/kg, BID, plus a chemotherapy (Cytosine arabinoside, Lomustine, Procarbazine) and/or immune modulation with (Cyclosporine and less commonly Leflunomide, Azathioprine, or Mycophenolate) is thought to provide best chance of a return to normal. In that same study, 12/39 (31%) of dogs returned to normal.

**Conclusion**
Vestibular disease is a common presenting complaint and assessing the disease to be central or peripheral provides the owner with the best sense of the appropriate diagnostic plan, treatment and prognosis. Having the image of a typical peripheral case in your mind and comparing all cases against this image can allow for best determination of the likelihood of central disease. Prompt treatment of the diseases that cause central vestibular signs is essential for a good outcome.

<table>
<thead>
<tr>
<th>Observation</th>
<th>Central Disease</th>
<th>Peripheral Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mentation</td>
<td>Dull</td>
<td>Normal</td>
</tr>
<tr>
<td>Gait</td>
<td>Side step opposite head tilt</td>
<td>Side-steps towards side of lesion</td>
</tr>
<tr>
<td></td>
<td>Hypermetria</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Weakness</td>
<td></td>
</tr>
<tr>
<td>Postural Reactions</td>
<td>Delayed or absent</td>
<td>Normal</td>
</tr>
<tr>
<td>Head Tilt</td>
<td>Absent or extreme</td>
<td>20 Degrees</td>
</tr>
<tr>
<td>Cranial Nerve Deficits</td>
<td>Any</td>
<td>+/- Facial, +/- Horner’s tract</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>Vertical or positional (chronic)</td>
<td>Rotary or horizontal</td>
</tr>
<tr>
<td></td>
<td>Fast phase towards lesion</td>
<td>Fast phase away from lesion</td>
</tr>
<tr>
<td></td>
<td>Fewer than 10 beats/second</td>
<td>Greater than 60 beats/minute</td>
</tr>
<tr>
<td>Positional Strabismus</td>
<td>Ventral on side of head tilt</td>
<td>Ventral on side of head tilt</td>
</tr>
<tr>
<td></td>
<td>Dorsal opposite head tilt</td>
<td></td>
</tr>
<tr>
<td>Neck Pain</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Table 2. Categories of disease that cause central or peripheral vestibular disease

<table>
<thead>
<tr>
<th>Category</th>
<th>Central Diseases</th>
<th>Peripheral Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malformation</td>
<td>Rostrocerbellar fluid accumulation, Caudal occipital malformation syndrome (COMS)</td>
<td>Congenital vestibular disease</td>
</tr>
<tr>
<td></td>
<td>Hydrocephalus</td>
<td></td>
</tr>
<tr>
<td>Metabolic</td>
<td>Hypothyroidism (± infarction)</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>Primary intracranial neoplasms, Metastatic neoplasms</td>
<td>Primary aural neoplasia, Vestibular neurofibroma</td>
</tr>
<tr>
<td>Infectious &amp; Inflammatory</td>
<td>Viral: Canine distemper virus, Feline infectious peritonitis, Bacterial: Abscess, Rocky mountain spotted fever, Ehrlichiosis, Bartonellosis, Anaplasmosis, Protozoal: Toxoplasmosis, Neosporosis, Myotic: Cryptococcosis, Blastomycosis, others, Non-infectious (MUE)</td>
<td>Otitis media interna (OMI), Nasal- and otopharyngeal polyps, Idiopathic vestibular disease (vestibular neuronitis)</td>
</tr>
<tr>
<td>Trauma</td>
<td>Brainstem trauma</td>
<td>Inner ear trauma</td>
</tr>
<tr>
<td>Toxic</td>
<td>Metronidazole</td>
<td>Ototoxic drugs (systemic and topical)</td>
</tr>
<tr>
<td>Vascular</td>
<td>Cerebrovascular disease</td>
<td></td>
</tr>
</tbody>
</table>

References
Recognition of pain is perhaps the biggest limitation to treating pain in veterinary practice. The degree and location of the pain can be determined with careful consideration of owner observations in conjunction with the physical examination. Once pain is localized a diagnostic effort should be made to determine the cause of the pain such that it can be treated as specifically. Acute pain is generally easier to manage than chronic pain and in particular neuropathic pain. This talk will discuss the behavioral observations and physical exam techniques to assess the location and degree of pain. Differential diagnoses for spinal pain will be discussed along with tips on diagnoses and treatment. Next we will discuss inflammatory pain (physiologic, nociceptive or acute) and neuropathic pain and implications for pharmacologic and non-pharmacologic treatments.

Pain categories
Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Acute pain (physiologic, nociceptive, and inflammatory) has a sudden onset, dissipates with healing, and is localized and transient – it serves as a protective mechanism to spare an individual tissue damage. Chronic pain however is unrelenting, intense, purposeless and persists long after the recovery from the inciting injury and if often refractory to common analgesic agents. The most severe form of chronic pain is neuropathic pain which occurs when the primary lesion is within the nervous system. Neuropathic pain results from plasticity in the nervous system and is associated with lower quality of life scores and is described in people as burning, lancinating, shooting, tingling, crawling or electrical sensations. Breakthrough pain is an abrupt, short-lived, and intense pain that “breaks through” the around-the-clock analgesics used to control persistent pain. It is common in people and subdivided into incident, idiopathic and incident related.

Pain assessment
Lord Kelvin in 1883 stated the ability to effectively treat pain is dependent on how well pain can be detected and measured. Dogs and cats hide their pain as a protective mechanism such that a dog may still experience pain and wag its tail. Despite this challenge, pain can be localized, characterized and diagnosed with a physical exam and behavioral history. Many of the current pain assessment tools (PATs) in veterinary medicine are adapted from humans and involve questionnaires that determine client-specific outcome measures (CSOM). These have been shown to be a sensitive method for use in the pain management of dogs. Looking at these questionnaires offers insight into what things dogs or cats might do when they are in pain. Please see Table 1.

Physical exam techniques to detect and localize pain
Pain from the cervical vertebral column or neck pain is often suspected when patient spontaneously yelps out and there is no gait or posture deficits, intermittent thoracic limb lameness (root signature), or a stiff neck with decreased range of motion. Palpating muscle spasm laterally at level of transverse process, pain with manipulation or ventral process of C6, or resistance to range of motion can also indicate neck pain. Dog with Caudal Occipital Malformation Syndrome (see below) will often vocalize with firm palpation of dorsal or lateral muscle at level of dorsal process of C2. Pain from thoracic, ribs and lumbar spinal column or mid-back is often suspected with kyphosis, stiffness or when patient is slow to sit or rise. Detection of mid-back pain involves applying pressure to dorsal processes while putting pressure / palpating the ventrum and/or palpating muscle / rib heads at level of transverse process. Lumbosacral or low back pain is suspected with abnormal tail carriage, fecal or urinary incontinence, and when patient is slow to sit and rise. Low back pain can be detected with rectal palpation of the lumbosacral junction (or spondylosis at L7-S1), tail extension and lateral movement, or by applying pressure to muscle between dorsal process of L7 and S1 or muscle just cranial and lateral to ilium. Hip extension will not differentiate back from hip pain. However, hip pain can be discerned by slowly elevating the femoral head about 3-5 mm from acetabulum by lifting up on the medial surface of the femur while the patient is in laterally recumbent. In a patient with mid-back pain testing the cutaneous trunci cut-off can be very useful in determining the level of the lesion (see notes from UMN vs LMN talk).

Neck pain localization and differential diagnoses
Neck pain can come from another location about 25% of the time. When a patient’s pain localizes to the neck it is important to consider the cause of the pain could be only within the head or even the thorax. A recent retrospective of 169 dogs and 9 cats presenting with neck pain showed pathology in only the neck 73% of the time, only the head 9% of the time, head and neck in 17%, and thorax in 1%. We have also diagnosed neck pain with involvement of only the high thoracic spine as well. In this same neck pain retrospective about 50% of the cases suffered from intervertebral disk disease, 20% from neoplasia, 15% from inflammatory disease, 9% from trauma, 3% vascular and 3% malformations. Important points are that if you assume spinal pain is from disk disease then you will be incorrect 50% of the time and that about 10% of the cases of neck pain in this study had a brain tumor.
**Differential diagnoses for spinal pain in small dogs**

The following diseases are diagnosed in mostly but not exclusively small breed dogs. The intervertebral disk (IVD) is located between the vertebral endplates and serves to cushion the vertebrae. In health it consists of a well hydrated nucleus pulposus which is surrounded by concentric rings of collagen called the annulus fibrosis (AF). Type I IVD occurs when the AF completely tears and the dehydrated and often calcified NP extrudes into the spinal canal or intervertebral foramen causing compression and inflammation of the meninges, spinal cord and nerve root. Type II IVD occurs when there is a bulging with microtears of the AF without NP extrusion. Together they are no doubt the most common causes of spinal pain in companion animals. When intractable pain is the only sign of disk disease success rates with surgery are about 98%. Management with pain medication, restricted activity and rehab therapy can also be highly successful. However, as mentioned above, disk disease only accounts for about 50% of the cases of spinal pain. Meningoencephalomyelitis of Unknown Etiology (MUE) is a non-infectious inflammatory condition of the brain, spinal cord and meninges – this disease is common and can present with just spinal cord signs about 10% of the time. MUE is most common in small breed dogs under 8 years of age and responsive to glucocorticoid therapy. The diagnosis is easily confused with IVD without advanced diagnostic testing. MUE can progress to life-threatening intracranial disease especially when not treated with immune suppressive therapy – therefore the veterinarian should be vigilant for progression of signs to include head tilt, depression, and seizure. Glucocorticoids should be avoided for treating spinal pain because it can mask MUE and when compared to NSAIDs is associated with more side-effects, lower quality of life scores and higher recurrence rates of IVD. Caudal Occipital Malformation Syndrome (COMS) or Chiari-Like Malformation occurs when a malformed or hypoplastic occipital bone allows the cerebellum to protrude into the brainstem and high cervical spinal cord often causing fluid build-up within the spinal cord (syringomyelia). The disease is often progressive and best treated with pain modulators +/- surgery. A specific characteristic of this disease is scratching at the side of the head without making contact (phantom scratching). Atlanto-Axial subluxation secondary to an absent or hypoplastic dens and/or associated ligaments can also be seen in young small breed dogs, present as intermittent neck pain and progress to paresis, paralysis, head tilt and death. In our clinic it is not uncommon to find more than of these abnormalities in patients with neck or back pain.

**Differential diagnosis for spinal pain in large breed dogs**

The following diseases are diagnosed in mostly but not exclusively large to medium breed dogs. Diskospondylitis is an infection of the intervertebral disk, vertebral endplates and adjacent soft tissues which can enter the spinal canal causing empyema and meningitis. The pain can be from inflammation as well as disk extrusion and pathologic fracture. Male dogs, older dogs and being a Boxer, Great Dane, and Labrador are risk factors for this disease. An intermittent fever, neutrophilia, elevated globulin and radiographic changes are inconsistently present with this disease. MRI and potentially a C reactive protein are most valuable diagnostic aids. Some dogs require anti-microbial therapy for up to a year. The prognosis is fair but improved with early diagnosis. Steroid Responsive Meningitis – Arteritis is an immune disease seen in mostly large dogs (Bernese Mountain Dog, Boxer, Pointer but also the beagle) at about 10 months of age. The signs and biochemical profile closely overlap with diskospondylitis and can include not eating, lethargy, intermittent pain, neck stiffness, and a short-strided gait. Acute Non-Compressive Nucleus Pulposus Extrusion (ANNPE) occurs when during exercise or activity a small amount of NP extrudes at a high velocity through a tear in the AF. Fibrocartilaginous Embolism (FCE) occurs when NP ruptures into the vascular supply and arterial blood flow to the spinal cord. These two disease present very similar clinically in that patients suddenly yelp out and suffer a sudden onset, non-progressive and often asymmetric weakness along with dysuria. Nerve sheath tumors can present as pain alone with muscle atrophy and lameness being noted later in the course of the disease. Vertebral fracture can occur in any size dog and are often suspect based on the history.

**Neuropathic pain**

Neuropathic pain (NP) develops when there is a lesion within the somatosensory system. NP develops when there is physical disruption of the pain pathway which starts with the receptors in the peripheral nerve and ends with the somatosensory cortex. NP results from persistent and exuberant firing of the peripheral pain fibers which then leads to recruitment of silent nociceptors in the periphery (peripheral sensitization), enhanced reactivity or disruption of neurons in the CNS (central sensitization) or imbalance of the endogenous facilitator systems and descending inhibitory systems. Over activity of the spinal cord NMDA receptor is thought to be the key process in generating NP.

In humans, NP results from inadequate recognition and treatment of pain. Furthermore, in humans with NP, the lesion within the nervous system is not always observed (despite having NP) and clinical signs can take more than a year to develop. The abnormal sensations are described as dysaesthesia (spontaneous or evoked unpleasant abnormal sensation like burning or pins and needles), allodynia (pain from stimulus that is normally not painful – light touch might be experienced as an electrical shock), or hyperaesthesia (increased pain response from a normally painful).

**Companion animal examples of neuropathic pain**

One model of NP is thought to occur in the Cavalier King Charles Spaniel where syringomyelia physically disrupts the dorsal horn of the spinal cord leading to increased levels of Substance P and abnormal sensory processing or NP. Affected dogs might be
of laboratory animals. A urine specific gravity, chemistry and CBC are advised prior to anti-inflammatory therapy as the rare dog will have spinal glutamate and substance P receptors. Lastly, COX2 inhibition has been shown to benefit recovery in the brain and spinal cord.

**Ketamine & amantidine**

Ketamine binds the NMDA receptor which prevents central sensitization or wind-up. In humans and veterinary medicine ketamine has been demonstrated to improve analgesia and outcome and reduce requirement for opiates. Ketamine does NOT increase intracranial pressure and has no effect on cerebral blood vessels size when CO2 is controlled. In our neurology clinic all surgical patients are managed peri-operatively with ketamine to improve analgesia and prevent wind-up. A loading dose of 0.5 mg/kg and then a CRI of 0.5 mg/kg/hr can be achieved in a 10 kg patient by placing 60 mg of ketamine in a 1 liter bag in a 10 kg dog – this will achieve a dose of about 10 ug/kg/min when the fluids are run at 10 ml/kg/hr. Some authors suggest doses should be 2-3 times higher than this dose and would likely be very safe.

Amantadine is also a NMDA receptor antagonist and has been shown to be of benefit in a randomized, blind, placebo controlled study as an adjunct to Meloxicam in osteoarthritis. The dose is 3-5 mg/kg once a day and the medication comes in a 10 mg/ml oral syrup or 100 mg tablet.

**Lidocaine**

Systemically administered lidocaine is a sodium channel blocker effective for treating neuropathic pain at doses that do not produce anesthesia or slow cardiac conduction. Lidocaine blocks ectopic afferent neural activity at the NMDA receptor within the dorsal horn and several veterinary studies have shown benefit to lidocaine infusions during anesthesia. A loading dose of 2 mg/kg and then a CRI of 4 mg/kg/hr can be achieved in a 10 kg patient by placing 400 mg in a 1 liter bag 10 ml/kg/hr (surgical fluid rate).

**Amitriptyline**

Tricyclic antidepressants are a recommended first line treatment of neuropathic pain in people. The descending inhibitory system is activated by incoming nociceptive firing and serves to reduce the perception of pain. This system is deficient in neuropathic pain. By blocking the reuptake of serotonin and catecholamine they enhance the activity of the descending inhibitory system. Furthermore, amitriptyline is an NMDA receptor antagonist. The recommended dose of amitriptyline is 1-2 mg/kg, once to twice a day in the dog and 2.5 to 12.5 mg per cat, once a day. The medication is bitter.

**Tramadol**

Although structurally similar to codeine, tramadol is a weak mu opiate agonist and works by inhibiting the reuptake of serotonin and norepinephrine. Therefore it works similar to amitriptyline in that it increases the descending inhibition of pain. Bioavailability in the dog is variable and one study showed that 5 mg/kg, every 6 hours was needed to provide similar serum concentrations to those in people associated with analgesia. However, we use a dose of tramadol of 2-5 mg/kg, 2 to 3 times a day. There is a theoretical concern for serotonin sickness (vomiting, diarrhea, seizures, hyperthermia, hyperesthesia, depression) when tramadol is combined with other therapies that increase serotonin, however we have yet to recognize this condition in our clinic. We have noted mild to moderate sedation with this medication.
Gabapentin
Although an antiepileptic drug, Gabapentin works via several mechanisms to provide pain control and is cornerstone of therapy in our neurology clinic. Gabapentin blocks calcium channels which is important because central sensitization or wind-up is facilitated by the influx of calcium. Gabapentin activates descending noradrenergic systems facilitating the release of NE in the dorsal horn which then binds the alpha-2 receptor and provides analgesia. Gabapentin causes a mild sedation and rarely severe sedation which resolves when drug is stopped. We use 10 mg/kg, 3 times a day in a day and if sedation is absent and pain present then the dose can be increased at 10 mg/kg intervals up to 50 mg/kg per dose. In cats we usually start with 5 mg/kg, twice a day. Gabapentin should be tapered because of the concern for rebound hyperalgesia. When possible, Gabapentin is used prior to spinal surgery and continued beyond when other treatments have been eliminated.

Opiates
Opiates bind receptors both centrally and peripherally to provide analgesia and control anxiety. Peripherally they prevent nociceptive sensitization and prevent neurotransmitter release. Centrally they act in the dorsal horn to modulate input from C- fibers (which mediate secondary pain or the throbbing you feel with ongoing tissue damage) and in the cerebral cortex they blunt the perception of pain. In our clinic we use the mu agonists – fentanyl 2-5 ug/kg/hr as CRI and hydromorphone 0.1 mg/kg, IV or IM. Butorphanol and buprenorphine are partial opioid receptor agonist and used only when there are intolerable side-effects from fentanyl or hydromorphone. We will also use the opiate receptor antagonist, naloxone, to reverse the effects of a mu agonist. For chronic or oral therapy we prescribe codeine, which get metabolized to morphine or much less commonly the fentanyl patch.

Opiates are useful for controlling pain but have several downsides to consider. One, side effects include dysphoria, panting, nausea, not eating, sedation, weakness, and dysuria. This can confound examination and if the clinician assumes changes in exam are from opiate and not from progression of spinal cord or brain disease, then important interventions like surgery and drugs for brain swelling might not be applied. Alternatively a patient might be delivered an inappropriately poor prognosis if the signs of disease are not from the neurological lesion but from the opiate side effects. Secondly, opiates may not be effective for all forms of neuropathic pain because they do not modulate incoming signals from the tactile / proprioceptive fibers that mediate tactile allodynia and opioid receptors in the descending pathway are down-regulated in neuropathic pain. Lastly, although uncommon opiates can generate a hyperalgesic or paradoxical response, physical dependence can develop with chronic use, and individual receptor type difference might mean more than one opiate may need to be used to achieve desired response.

In our clinic we are frequently left to wonder if a patient on opiates is still painful or dysphoric. If we consider it likely that the patient is still painful then we treat dysphoria by adding a CRI of acepromazine 0.01-.01 mg/kg/hr, or dexmedetomidine 1-3 ug/kg/hr . If we suspect dysphoria then we partially or completely reverse opiate with butorphanol 0.3 mg/kg, IV or low dose naloxone 0.01 mg/kg. Another strategy would be to switch opiates – in the patient recovering from surgery we often substitute Tylenol #4 (acetaminophen 325 mg / codeine 60 mg) at a dose of 15 mg/kg acetaminophen and 1-2 mg/kg codeine, 2 to 3 times a day.

Dexmedetomidine
Alpha-2 agonists work in the brainstem to activate the descending inhibitory system by binding a brainstem nucleus called the locus ceruleus. In the spinal cord alpha-2 agonists inhibit incoming peripheral pain signals. Spinally administered alpha-2 agents reverse allodynic and dysesthetic pain in peripheral nerve injury in both rats and people. Dexmedetomidine is use commonly in the control of perioperative pain at doses of 1-3 ug/kg/hr. Pain control is synergistic when used with opiates. Dexmedetomidine is excellent in perioperative setting where a patient on opiate may be either dysphoric from opiate or painful – it has an anxiolytic effect and also reduces or eliminates the dose of opiate needed to control pain.

Anxiolytics
Pain is a conscious or cerebrally recognized phenomenon. The cerebral anticipation of pain causing anxiety or anxiety itself appears to amplify the recognition or experience of pain. Sedation and/or anxiety medication can have a synergistic or useful role in controlling pain. Acepromazine at 1 mg/kg, PO, up to every 6 hours or at bedtime is advised in addition to multimodal pain protocols, especially in beagles with severe neck pain secondary to disk disease. Acepromazine can also be used as a CRI at 0.01 to 0.1 mg/kg/hr for anxiety and dysphoria in the hospital. Trazodone is very popular in our clinic for sedation and anxiety associated with cage confinement or hospitalization and is used at 2.5-5 mg/kg, 2-3 times a day. We have combined trazodone with tramadol without any evidence of serotonin sickness. At these doses seizures have not been noted with either medication. Alprazolam 0.1 mg/kg, PO up to 2 mg, twice a day can also be used for anxiety, however it seems to be less effective than trazodone or acepromazine.

Muscle relaxants
Muscle spasm can be painful and is often associated with processes of the spinal column which are painful, treatment with methocarbamol at 30 mg/kg, 3 times a day and or valium 0.3 -0.5 mg/kg, 3 times a day can be useful for attenuating muscle spasm.

Tylenol and codeine
Acetaminophen is safe and effective when combined with an NSAID or corticosteroid at doses of about 10 mg/kg, twice a day. When needed, as an add-on medication, acetaminophen 300 -325 mg plus codeine 30 mg or codeine 60 mg are administered as Tylenol #3 and Tylenol #4, respectively. The dose of codeine typically starts at 1 mg/kg and can be increased to 2-3 mg/kg. In dogs that are restless at night and potentially painful, the Tylenol #3 or #4 and acepromazine 1 mg/kg combination is effective.
**Acupuncture**

Acupuncture is the stimulating of specific anatomic points in the body to provide a therapeutic or analgesic effect. Placement of needles releases endorphins, serotonin, and NE which can affect the processing of sensory input and amplify the descending inhibitory system. Acupuncture is highly recommended for both acute pain and the treatment of neuropathic pain.

**Rehab therapy / nursing care**

Passive range of motion, hydrotherapy and then controlled exercise plus bladder management are important for optimizing the comfort of neurological patients. These therapies reduce pain from contracture, anxiety, and the discomfort of bladder distension and infection.

**Recommendations**

Whenever a patient presents with pain from a neurological lesion then I advise an anti-inflammatory, gabapentin, and tramadol. If this is insufficient then change the NSAID, add on an opiate and/or acetaminophen. If the patient is suspected of having neuropathic pain or another chronic painful condition then owner is counseled that breakthrough pain is likely and can be treated with hospitalization and a CRI of an opiate plus dexmedetomidine in addition to oral maintenance medications. Prior to surgery these same medications (gabapentin, NSAID, tramadol) are recommended plus ketamine and lidocaine are added to all fluid bags. A fentanyl CRI at 5-10 ug/kg/hr is used for anesthesia and then tapered over the next 2-24 hours post-surgery. Dexmedetomidine is commonly used to reduce the need and side-effects noted with opiates.

**Conclusion**

Veterinarian’s primary responsibility is to recognize and treat pain. Therefore, in every patient and similar to humans, pain should be considered the fifth sign. It should be remembered that nervous system lesions cause severe pain and can transform into a chronic pain syndrome called neuropathic pain. Neuropathic pain is an especially debilitating condition in people and thought to result from inadequate treatment of the initial pain focus. Recognizing, diagnosing, and specifically treating a painful condition plus the use of multi-modal pain protocols are essential to a achieving a good outcome.

**Table 1. Behaviors associated with pain in companion animals**

<table>
<thead>
<tr>
<th>Behaviour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unwilling to jump, slow to more, rise or sit, exercise intolerant, lame, stiff, arched back</td>
</tr>
<tr>
<td>Lethargic, dull, irritable, anxious, fearul, aggressive, aloof, confused, not greeting owner</td>
</tr>
<tr>
<td>Not eating well</td>
</tr>
<tr>
<td>Requires being hand fed to eat well (neck pain)</td>
</tr>
<tr>
<td>Yelping out with movement or spontaneously, crying, groan, scream, quiet</td>
</tr>
<tr>
<td>Squinting</td>
</tr>
<tr>
<td>Panting</td>
</tr>
<tr>
<td>Shaking or trembling</td>
</tr>
<tr>
<td>Chewing, licking, looking, rubbing at specific location or surgical incision</td>
</tr>
<tr>
<td>Crying, flinch, snap, growl, guard or bite in response to touch / being pet</td>
</tr>
</tbody>
</table>

**References**


Mathews K. Neuropathic pain in dogs and cats: if only they could tell us if they hurt. *Vet Clin Small Anim* 2008; 38:1365-1414


Why Dog is Man’s Best Friend: 
Exciting Results of Canine Neurology Clinical Trials

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Despite many significant bench-top findings in laboratory animals there has been little progress in improving clinical outcomes for brain tumors and Status Epilepticus (SE). Veterinary clinical researchers working in tandem with the human research community are making significant progress in fostering a mechanistic understanding of human disease - this effort is called translational medicine. Due to the contributions of dog and their owners we are likely on the brink of significantly better clinical outcomes in both humans and dogs.

Brain tumor
The two most common brain tumor types in canines and people are meningioma and glioma. Each are a serious problem for each species and very similar. Brain tumors in canine have disease courses, clinical manifestations, imaging characteristics, molecular and histopathology and genetic changes that are very similar. The translational value of canine brain tumor research is well recognized resulting in some impressive results from NIH funded clinical trials in the dog.

Glioma
Glioma is a brain tumor arising from the support cells of the brain or glia. Malignant glioma and glioblastoma multiforme in particular represent some of the most biologically aggressive and treatment refractory malignancies in humans and dogs. For humans treated with surgery, radiation and chemotherapy (temozolamide) average survival is 14 months, 2 year survival is seen in 26% and 5 year survival in just 4 %. These abysmal results have not really changed since 1959 despite intensive research. For canine intraxial tumors (all grades of glioma and other tumors) the median survival following radiation, corticosteroids +/- surgery is about 10 months. Dogs are about 3 more times as likely as a human to develop a brain tumor and in each species glioma make up about 1/3 of all brain tumors. Impediments to treating glioma in humans remain failure of the therapy to cross the blood brain barrier, infiltration of disease into the normal brain such that it is hard to know true borders of the tumor, and cellular resistance and heterogeneity.

Meningioma
Meningioma is a brain tumor arising from the arachnoid lining of the brain. They are the most common brain tumor of humans and canine and comprise about 45% of primary canine brain tumors. In people, meningioma are predominantly of a lower grade and surgery is the primary treatment. However about 6000 people per year will have recurrence often due to invasive or malignant (higher grade) disease. Reoperation is often performed but even in low grade disease there is a recurrence rate of 50% by 3 years. Radiation therapy can be effective in lower grade meningioma but has been associated with cognitive deficits, secondary malignancy, and transformation of the tumor to a higher grade neoplasm. More than 40% of canine meningioma are atypical or malignant and tumors in dogs in general 5 to 7 times faster than in people. Surgery for canine meningioma is reported to have a median survival of about 10 months for canine meningioma.

Convection enhanced delivery (CED)
CED is a low-pressure continuous infusion process that occurs over hours to days that can achieve substantial tissue concentrations of macromolecules over a large area of the brain without producing serious injury, increasing intracranial pressure or decreasing blood flow. This technique can be followed with real-time MRI and gadolinium loaded liposomes. Dr. Peter Dickinson at UC Davis’ pioneering research showed CED to be effective and suggested that the canine spontaneous glioma can be a model system for the validation and development of novel therapeutic strategies for human brain tumors. Dr. Simon Platt at UGA is enrolling patients into a funded, canine glioma trial studying the CED of the epidermal growth factor inhibitor Cetuximab. Another proposed clinical trial involves the CED of an Pseudomonal exotoxin coupled to the IL-13 and agonist for the tyrosine kinase receptor Eph2A. Each receptor is overexpressed in high grade glioma in humans and canines but not normal canine brain tissue. A funded study using CED with carboplatin is being performed at UMINN.

Electroporation
Electroporation is performed using electrical pulses in order to reversibly or irreversibly permeabilize the cell membrane. Reversible electroporation safely delivers things like plasmid DNA and viruses through nanopores while irreversible electroporation (IRP) simply leads to cell death. Electroporation can generate heat leading to cell death over a relatively large area, so non-thermal methods are used in the brain. Electrochemotherapy (ECT) occurs when electroporation is combined with chemotherapy to promote delivery across the blood brain barrier. In the rodent glioma model, ECT with bleomycin doubled survival time AND in vitro investigations show that IRP alone has cytotoxic effects on canine, rodent and human glioma cell lines. Dr. John Rossmeisl at Virginia Tech has run a funded clinical trial where canine glioma patients received either stereotactic IRP and placebo or stereotactc IRP and bleomycin. One
patient from our clinic was enrolled and remains disease free two years later. Dr. Rossmeisl has also reported non-thermal irreversible electroporation (N-TIRE) by itself to have reduced the tumor volume in a boxer with a malignant glioma by 75% in 48 hours.

**Brain tumor vaccine**
Surgical biopsies from canine brain tumors can be shipped to the Ohlfest laboratory at UMINN for the production of a vaccine that is then administered intradermally to the patient every 2 weeks for 12 weeks. Funded trials have been performed for both glioma and meningioma. Interim results for surgery plus vaccine +/- IFN gamma for various glioma have shown mean survival for about 8 months. Meningioma vaccine results show a mean survival well over 2 years compared to controls of about 8 months. We have used the UMINN laboratory to prepare vaccine for meningioma and nasal carcinoma with favorable results.

**Human status epilepticus**
Convulsive human status epilepticus (HSE) affects an estimated 152,000 people causing death in 42,000 and leaving the survivors with a lower IQ, lower quality of life and socioeconomic status. Lorazepam and phenytoin have marginal success rates in treating HSE, 67% and 44% respectively, but remain the mainstay of therapy in people. These treatments have potential for respiratory depression and severe sedation (benzodiazepines) and cardiac complications (phenytoin). These drugs are intended for the treatment of chronic epilepsy and are based on clinical studies that are at least 20 years old that were based on research 30 to 80 years old or older. The mechanisms driving HSE are different than chronic epilepsy and therefore adapting drugs designed for chronic epilepsy simply because there is an intravenous formulation seems inadequate. There are many drugs demonstrated in rodents to be highly effective against a broad spectrum of different induced seizures. These drugs are not being developed for HSE because of the relatively smaller market (the drugs will only be used for a short time) and there is not enough safety and preclinical data to warrant a human clinical trial. If there was a more relevant clinical model of SE in the dog then drug companies might develop some of the very promising, ‘rodent proven’ drugs for treatment of the HSE.

**Canine status epilepticus**
Canine status epilepticus (CSE) has many striking similarities to that of HSE. The different seizure types noted in people (simple partial, complex partial, and tonic-clonic) are recognized in dogs. Electroencephalographic (EEG) studies in dogs, including those from our own clinic, have identified interictal and ictal patterns are similar in dogs and people. CSE is a common emergency condition treated in veterinary hospital with 53-59% of dogs with idiopathic or genetic epilepsy experiencing at least one episode of CSE and some experiencing more than 10 episodes. The mean life span of dogs with SE is shorter many veterinary studies and there is a mortality rate of 25% despite being treated with valium and phenobarbital infusions.

**Advantages of canine for the study of HSE**
The similarities between HSE and CSE have provoked researchers to develop the canine as a platform for study of novel drugs for HSE and translating this information into valuable information for researchers and drug companies. Unlike induced disease in rodents, epilepsy in dogs is a natural model and the same mechanism of HSE and drug resistance likely exist in the dog. Separate from generating important preclinical information for people, the other valuable aspect of the canine model is their body size. A dog is about 25% the size of a human but a rodent is 0.025%, this makes it much easier to generate an accurate formula for picking the correct human dose. Furthermore, results of safety and efficacy in the dog are more easily assessed than in a rodent. In particular rodent models fail to predict cognitive, behavioral and neurological side effects like irritability, insomnia, poor balance and cardiac effects like arrhythmia and hypotension. Being able to assess drug side-effect, safety, and efficacy in a clinical trial will make it much easier to generate appropriate approval and interest in human clinical trials.

**CSE clinical trials**
One of the goals of CSE trials was to develop the canine as a platform for study of HSE and to generate a network similar to the Neurological Emergency Treatment Trails (NETT) program in people. The NETT program is funded by NIH and recently reported it’s results “Rapid Anticonvulsant Medications Prior to Arrival Trail (RAMPART) Using Midazolam” ahead of schedule and under budget. Canine trials with Levetiracetam (LEV) and then Fosphenytoin (FOS) have showed that the canine is a useful platform for the study of CSE. This then allowed for the formation of the Canine Neurology Treatment Trail (CNETT) consortium whose focus is to study novel drugs for SE.

In the first trial LEV was used to treat CSE in a randomized, placebo-controlled, double masked study. Dogs were enrolled in the study after having CSE and then if there was further seizure they were given 0.5 mg/kg diazepam and a placebo or LEV (30 mg/kg or 60 mg/kg over 5 minutes). The responder rate defined as dogs with no additional seizure after the study drug was 56% in the LEV group compared to 10% in the placebo group (p=0.057). Furthermore dogs in the placebo group required significantly more boluses of diazepam than the LEV group.
The second study examined FOS in 31 clinical patients (22 in FOS group, 9 in placebo) were enrolled from both university and private specialty practice. There was a significant difference in the 12 hour responder rate with 63% in the FOS group versus 22% in the placebo group having no further seizures after receiving study treatment. This response rate is nearly identical to that seen in HSE with FOS and the authors conclude that this is proof that naturally occurring CSE can be utilized as a translational platform for future studies of novel SE compounds that could economically bridge the laboratory studies in rodent models with human SE trials.

**Conclusion**

Thus far clinical trials in people have failed to produce meaningful progress for the most serious neurological conditions. Utilizing the canine as a clinical model for studying brain tumors and SE should provide vital insight and meaningful advancements in therapy for humans, proving the adage that the dog is man’s best friend.

**Brain tumors references**


Rossmeisl JR. Molecularly Targeted Cytotoxic and Electroporation-Based Therapies for Canine Intracranial glioma. *ACVIM Proceedings*, 2011

Pluhar GE. Canine Brain Tumor Clinical Trials at the University of Minnesota. *ACVIM Proceedings*, 2011

**Status epilepticus references**


Maturity is not a disease

Senior dogs commonly present to veterinarians for primary care and represent approximately one third of the pet dog population. Lifespans are increasing and thus both the percentage and the age of elder dogs may be increasing. Pet owners perceive that most pets, including senior dogs are healthy and do not require a therapeutic food, but they are still left with hundreds of pet foods to choose from. Advice and information recommending the best food is available almost anywhere; from trainers to pet food retailers, from magazines, internet sources and social media. However it is important to remember that there is no established AAFCO nutrient profile for a “senior” life stage, thus the nutrient content of products marketed for senior pets varies widely. This makes it even more critical for the veterinary health care team to play an active role in providing credible nutritional advice, especially for senior dogs that have unique nutritional concerns.

What is old?
The point at which a dog progresses from adult to a senior or geriatric life stage is variable and subjective. Dogs’ life expectancies vary widely depending on breed and body size and aging changes are also variable. They may include loss of senses (hearing or vision), reduced energy requirements and lean body mass as well as a decline in various organ functions. The American Animal Hospital Association Senior Care Guidelines suggest that, with exception of large-breed dogs, most dog breeds reach middle age by 7-8 years of age and should be considered seniors when they reach the last 25% of the predicted life span for their breed. Despite this arbitrary categorization, physiologic changes that occur in middle-aged and senior dogs make them less tolerant of nutritional deficiencies or excesses. Middle aged dogs are “at risk” or more vulnerable to age-related health problems. Middle age may bring an increasing incidence of chronic diseases, many of which can be influenced by nutritional management. Thus a vital component of preventive medical care should include a “senior” screen or health risk assessment for early detection of health problems and adjustments to care to preventing or slow onset of age-related diseases. Every senior health screen should include a thorough nutritional assessment followed by an individualized nutritional recommendation.

Performing a nutritional assessment

Before any diet changes are recommended, a nutritional evaluation should be performed. Each nutritional assessment and recommendation should include 3 components: the patient, the diet and feeding management factors. An accurate diet history is invaluable when assessing of the nutritional health of the patient and will be vital to formulating an individualized diet plan. Understanding the nutritional changes that occur with aging and identifying any changes in the individual patient can help the clinician better match the appropriate food with the patient’s unique needs. The patient, the food and the pet owner’s feeding practices are interrelated and require reassessment. Health and nutritional status are not static especially in senior pets, but rather a dynamic process worthy of continued re-evaluation and treatment modifications to match changing needs of the pet.

Patient assessment

An initial assessment of the patient can be done quickly and utilizes information collected as part of a health assessment: a complete medical and diet history and a thorough physical examination and appropriate lab work (ex, CBC, serum biochemical profile, urinalyses). The nutritional screening process (Table 1) can quickly identify patients with “nutritional” risks. Healthy seniors, (those without identified risks), who are eating a nutritionally balanced diet, have a healthy body weight, body and muscle conditions (BCS, MCS) and are free of significant physical or laboratory abnormalities need no further evaluation at this time. A pet-specific nutrition assessment and recommendation for healthy seniors can be done quickly. Nutritional recommendations should include: the specific name of food that matches the pet’s current nutritional needs, the amount and frequency for feeding and a monitoring plan. In many of these patients, the feeding recommendation involves little or potentially no change, but should include a verification and validation for the owner that the current food and feeding plan meets the pet’s needs, and a documentation of the current feeding plan in the medical record.

If nutritional risk factors or age-related problems are identified, an extended evaluation and management plan is indicated. This in-depth evaluation should address some common age-related diseases that may be influenced by nutritional management (Table 2):

- Weight management-achieve or maintain a healthy body weight
- Osteoarthritis
- Cognitive dysfunction

Diet assessment

A complete diet history is important for evaluating the pet’s current nutritional status. Ideally you would like enough information that you can reproduce the animal’s exact diet (brand and amounts eaten). The diet history should identify all snacks, treats and nutritional
supplements by type and amount. The drug/supplement history should include questions about the use of food to administer medication, as it may comprise to a significant portion of the dog’s intake. Diet history information combined with the patient assessment provides information about the patient’s daily caloric requirements and specific nutrient intake. This nutrient intake should be compared to the patient’s individual needs. For example, and overweight pet with a robust appetite, should not be fed a calorie dense product. Reducing the amount of a high calorie product as a way to limit calorie intake could lead to deficiencies of other essential nutrients and increase hunger or undesirable food-seeking behaviors.

Feeding management assessment

Feeding practices and preferences influence a pet’s intake. Determine whether other pets present competition or limit access to food. Determine whether food is accurately measured, how much/ how often food is offered and how much is eaten. Determine if there have been recent changes to the feeding plan and why, as well how the pet accepted those changes. This information will allow the veterinary team to determine the nutritional adequacy of the current diet, as well as help identify factors that could contribute potential success or problems with adherence to a new recommendation.

Reassessment and modification of treatment plan

Nutritional assessment of geriatric pets is an ongoing process. Dogs experience a variable and wide variety of metabolic changes as they age. It is important to communicate and engage pet owners to create the expectation of continued reassessment and treatment modifications that accommodate the specific changes observed in each individual dog rather than adopting a “geriatric’ protocol. A vigilant monitoring plan allows early detection of problems if they arise and a better opportunity to intervene or modify the pet’s individualized nutritional plan to improve its health. Partner with clients to help ensure success and maintain adherence to the feeding and monitoring goals.

Effects of aging on nutritional needs

Energy

Aging results in changes to both structure and functional of the GI tract. However no studies report clinically relevant differences in nutrient absorption between young adult and geriatric dogs7. Maintenance energy requirement (MER) is defined as the energy required to keep an animal in a “maintenance state”, or maintaining a normal activity. MER caries depending on factors such as breed, health, neuter status and age. As dogs age, MER decreases ~25%, with the greatest decrease at middle age (7 years)8. Loss of lean body muscle (LBM) appears to be the primary factor influencing the reduction in energy requirements9. LBM accounts for about 96% of an animal’s basal energy expenditure 10. Aging dogs are less active which also contributes to reduced LBM and MER. If no adjustments are made to the pet’s energy intake to account for the reduction in LBM, activity and MER, then the senior pet will gain weight and increase the risk for obesity. BCS should be closely monitored in elder dogs to prevent obesity. Unhealthy weight gain exacerbates many age-related conditions. A higher protein to calorie ratio diet would be beneficial to promote ideal weight maintenance in senior pets identified at risk for obesity11. Results from a lifetime study performed in dogs revealed lower disease incidence, later onset of disease and increased life span in calorically restricted animals. Dogs fed a 25% reduction compared to controls lived an average of 13.0 years compared with 11.2 years in the control group12. Thus maintaining energy balance and avoiding unhealthy weight gain should be one of the most important health goals for senior dogs.

Water

Elder humans exhibit decreased thirst and drinking when challenged by fluid deprivation. Although unknown in dogs, a similar response is expected1. Thus water intake should be monitored or ensured when elder dogs are exercising or exposed to hot environments. Senior dogs may also be at risk dehydration if they have subclinical renal insufficiency. When a senior pet’s appetite is good but water intake is suspect, add water to the food to ensure adequate intake and hydration.

Protein

Protein requirements increase with age due to increased protein turnover and reduced protein synthesis13, 14 Healthy senior dogs do not benefit from protein restriction15 and may be harmed by limiting dietary protein16. Protein restriction of seniors could be more detrimental than protein deficiency in younger animals17. A general guideline for estimating daily protein needs is to provide 2.55 gms protein /kg body weight (BW) or ~ 1 gm protein/lb BW.13, 17-19 This level of protein intake should minimize risk of protein deficiency. Senior dogs may need up to 1.5-2 times more than this13. Older dogs also require fewer calories, or less food than younger dogs. Diets for older dogs should not only contain lower calories but a higher percentage of protein or a higher protein:calorie ratio in order to meet the dog’s age-related nutritional needs. Based on the diet history, assure the patient is meeting daily protein needs; ~ 1 gm protein/lb BW minimum. Food with 25 % of the calories from quality protein should meet the needs of most healthy aged dogs and minimize loss of LBM. Assess MCS to monitor LBM.
Nutritional intervention of selected age-related diseases

Although the most common age-related conditions are best managed with a multimodal approach combining nutritional strategies, exercise or environmental enrichment and possible medical management, the discussion will focus on nutritional management.

Overweight/obesity

Hyperadiposity, the most prevalent form of malnutrition, contributes to many of the diseases linked to obesity\(^{21-23}\). Still pets that are overweight go unrecognized or may not have this health concern addressed. Based on the canine lifespan study\(^{12}\) which demonstrated many negative health consequences of overweightedness and benefits of being lean, weight management should remain a top priority for senior pet health. Yet it remains one of the most significant health problems among middle aged and elder dogs. Monitor the pet’s diet, BW, BCS and MCS at each visit. Once excess weight is diagnosed, action should be taken to achieve healthy BW and BCS. Creating a negative energy balance promotes weight loss. This is best achieved by feeding foods with low calorie density, increased protein content and increased nutrient calorie:ratio to assure adequate intake of essential nutrients while restricting calories.

Degenerative joint disease

Osteoarthritis (OA), the most prevalent joint disorder in dogs, affects as many as 20%, and obesity is recognized as a primary risk factor\(^{24}\). Nutritional strategies for OA include the following:

Weight and muscle management

Loss of excess body weight/fat can improve clinical signs of lameness in arthritic dogs\(^{25}\). Strategies to maintain healthy BW, BCS and LBM and prevent sarcopenia should be prioritized for senior dogs. The can be achieved by selecting a complete and balanced diet that meets protein and other nutrients when providing the amount of calories to prevent excess body fat gain. The nutritional goal is to delay onset and prevent progression of OA.

Long chain omeg-3 fatty acids (n-3)

Shows the greatest evidence for synovial anti-inflammatory effects\(^{26,27}\) compared to other nutraceuticals. Marine oils (EPA> DHA)\(^{28}\) are preferred with more effective anti-inflammatory effects compared to shorter chain flax or other plant source n-3 oils. There is no standard accepted dose.

Cognitive dysfunction

As many as 20-68% of middle age to elderly dogs experience cognitive dysfunction or behavioral changes which can manifest in varying degrees of mental decline\(^{29}\). (Table 2). Nutraceuticals may have potential use both in prevention and treatment, but are best when combined with environmental enrichment\(^{30-32}\).

Antioxidants

The brain is especially susceptible to free radical damage and cognitive dysfunction. Multiple studies have shown improved clinical signs of age-related cognitive changes in dogs fed antioxidant-enriched diets or supplements\(^{30-32}\).

Medium chain triglycerides

Supplementation with MCT improved cognitive performance and preserved brain structure of elder dogs. MCT provides an alternate cerebral energy source by way of ketones without restricting dietary carbohydrate or proteins\(^{34,35}\).

Supplements versus enriched diets

One caveat for the use of nutraceutical supplementation is that that they have not been adequately assessed for efficacy, optimal doses or nutrient interactions. When considering whether to select a diet containing the supplement or to prescribe a supplement, consider the nutrient composition of the ‘base diet.’ Assure the base diet meets the macronutrient needs of the patient and determine if it will provide an adequate dose of the intended supplement when fed to meet the energy needs of the pet. If not, it would be prudent to select a more appropriate diet and give the intended dose of supplement.

Table 1. Initial screen: assessing for nutritional risk factors

<table>
<thead>
<tr>
<th>Nutritional Screen for Risk Factors</th>
<th>Require extended evaluation if (✓)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HISTORY OF:</td>
<td></td>
</tr>
<tr>
<td>Treats/snacks/human foods &gt; 10% intake</td>
<td></td>
</tr>
<tr>
<td>Inadequate information/inappropriate feeding/food</td>
<td></td>
</tr>
<tr>
<td>Consuming unconventional diets</td>
<td></td>
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<tr>
<td>Previous/ongoing medical problems</td>
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<tr>
<td>Gastrointestinal signs</td>
<td></td>
</tr>
<tr>
<td>PHYSICAL EXAMINATION:</td>
<td></td>
</tr>
<tr>
<td>Any abnormal BCS (≠5/9 or 3/5)</td>
<td></td>
</tr>
<tr>
<td>Any MCS &lt;3</td>
<td></td>
</tr>
<tr>
<td>Unintentional weight loss OR gain</td>
<td></td>
</tr>
</tbody>
</table>
New medical condition
Poor skin hair coat
Dental disease

Adapted from Table 2, AAHA Nutrition Assessment Guidelines

Table 2. Extended screening: assessing senior dogs for nutritionally relevant age-related factors

<table>
<thead>
<tr>
<th>Extended evaluation: Age-related diseases to evaluate in senior dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abnormal Body Condition</strong> - Is this pet overweight or Underweight?</td>
</tr>
<tr>
<td><strong>Diet</strong> - Is the pet eating appropriate amounts of balanced diet?</td>
</tr>
<tr>
<td>- Assess appetite and intake</td>
</tr>
<tr>
<td>- Assess ability to eat; prehension, mastication swallowing for those underweight &amp;/or poor intake</td>
</tr>
<tr>
<td>- Assess sensory input; smell, vision, palatability of food. Consider palatability enhancer if necessary</td>
</tr>
<tr>
<td><strong>Mobility and access to food and water</strong></td>
</tr>
<tr>
<td>- Is the pet able to walk, access food provided? Able to stand to eat?</td>
</tr>
<tr>
<td>- Other pets or physical limitations impairing access?</td>
</tr>
<tr>
<td>- Mobility and exercise - is the pet’s MCS normal (3/3)?</td>
</tr>
<tr>
<td>- Presence of osteoarthritis, lameness, pain? - play a role in maintenance of comfort, fitness and healthy BCS</td>
</tr>
<tr>
<td>- Activity minimizes sarcopenia</td>
</tr>
<tr>
<td>- Exercise and activity provide mental stimulation and environmental enrichment</td>
</tr>
<tr>
<td><strong>Assess cognitive function</strong></td>
</tr>
<tr>
<td>- Disorientation/confusion - becomes lost or confused, fails to recognize familiar people?</td>
</tr>
<tr>
<td>- Changed interactions with family members? Isolates or seeks attention less often?</td>
</tr>
<tr>
<td>- Change in sleep/activity cycles? Wander or pace, sleep more in day, less at night?</td>
</tr>
<tr>
<td>- Loss of house training (non-medical reasons)</td>
</tr>
</tbody>
</table>

References available upon request


Pet Food Ratings, Rankings, and Recalls: How to Make Sense of it All
Julie Churchill, DVM, PhD, DACVN
University of Minnesota
St. Paul, MN

How to evaluate a pet food and make a diet recommendation
Clients can bombard the veterinarian and veterinary staff with questions about pet food. With almost 5000 different product labels on the market it is inevitable veterinarians will be asked about a product they are not familiar with. Advice and information recommending the best food is readily available almost anywhere; from trainers to pet food retailers, from magazines, internet sources and social media. However these voices can be strongly biased and may compete with the veterinarian healthcare team’s advice. Therefore veterinary professionals need to be competent and confident in evaluating new or less familiar products in order to make nutritional recommendations for their patients and help owners make sound nutritional decisions for their pet.

When evaluating a pet food, the label is a good place to start. All pet food labels must include the following: a guaranteed analysis (% nutrient content as fed), a nutritional adequacy statement according to standards required by the Association of American Feed Control Officials (AAFCO), an ingredient list, food name and type, feeding guideline and manufacturer contact information (Zicker, 2008). A systematic approach to evaluating labels is a useful first step in assessing a product for your patient.

Many of the rating systems and pet food reviews are based on judgments about ingredients. With the exception of patients with adverse reactions or primary food allergies, or a traditional Chinese medicine approach, this is often the least useful information provided. Clients also want to prioritize ingredients and much of their information is based on misconceptions. The veterinary team must be careful not to discount client concerns, yet use the opportunity to educate and guide owners in their decision-making about pet foods.

What follows is a suggested approach to assessing labels and pet food products for indicators of a product’s nutritional value and potential impact on pet health.

Suggested in descending order of importance:
Manufacturer contact information
Contact the manufacturer whenever you have questions about a product. This can provide you with valuable information as well as an indication of how willing a company is to work with the veterinary profession. The American Animal Hospital Association (AAHA) (Baldwin 2010) and the World Small Animal Veterinary Association (WSAVA, 2011) Nutritional Assessment Guidelines lists an excellent set of potential questions to ask of manufacturers:

- Do you have a veterinary nutritionist or equivalent on staff and available to answer questions?
- Who formulates the diets and what are their nutritional credentials?
- Which diets are tested using AAFCO feeding trials vs formulation?
- What is the caloric value (per can/cup)?
- Will you provide nutrient analysis and digestibility of your products?
- Describe your quality control measures to assure consistency and quality
- Where are your diets produced and manufactured?
- What kinds of research have been conducted on your products? Where is it published?

Nutritional adequacy
A statement of nutritional adequacy developed by AAFCO is required on all pet food packages. Nutritional adequacy can be met either 1) through animal feeding trials or 2) through formulation tests. Feeding trials are conducted with animals to ensure that nutrients in a given food or line of foods are present in sufficient quantities to promote good health and are bio-available to the animal ensuring the nutrients are digested properly. Formulated products have had nutrient content confirmed by mathematical calculations (adding nutrient content listed in a database of ingredients) or by laboratory testing. The formulation method does not include testing involving animals. Feeding trials allow for an in vivo product evaluation and are preferable to formulations.

Life stage claim
AAFCO requires that foods meet and disclose one of two nutrient profiles based on the pet’s life stage. The “maintenance” life stage nutrient profile is designed to meet the nutritional needs for adult dogs or cats. The “growth and reproduction” nutrient profile is designed to meet the nutritional needs for puppies or kittens as well as pregnant or lactating adults. A product with a nutritional adequacy statement designated to meet ‘all life-stages’ must meet standards for both. Pet foods designed for a single life-stage (i.e. ‘maintenance’ or ‘growth and reproduction’) better match the nutrient profiles for pets of that life stage. Products formulated for “all life stages” may contain excessive amounts of some nutrients, which can result in overfeeding. It is better to feed pets with food designed to match their life stage. It is important to remember that there is no AAFCO defined nutrient profile for senior/geriatric life stage and the nutrient content of products marketed for senior pets can vary widely.
Caloric content disclosure
Because of the prevalence of obesity in pets, caloric disclosure and labeling is essential for veterinarians to assess and counsel clients about purchasing pet foods that meet the energy needs of their pets. Unfortunately, caloric disclosure is not yet required by law and remains optional for manufacturers to include on packaging. Without information on caloric content, pet owners run the risk of over feeding their pets, resulting in obesity and related health problems. Companies that choose to report the caloric content are preferred. Making calorie content readily accessible greatly helps the veterinary team determine a proper food dose when making a nutritional recommendation, and allows consumers to make comparisons between foods and select more appropriate feeding portions.

Ingredients
Evaluation of the ingredient list is often the most controversial aspect when interpreting a label. Evaluating ingredients presents challenges for clients because they are barraged with marketing claims, misinformation and even scare tactics. Evaluation of ingredient lists remains challenging for many veterinary professionals because transparency about ingredients, ingredient sources, and processing methods beyond the minimum of what is legally required is generally difficult to come by in the pet food industry. In addition, the nutrient-based scientific literature is not comprehensive, especially when compared to the research base for human nutrition. Although there is widespread misunderstanding about pet food ingredients, the major ingredients commonly used in pet food (beef, poultry by product, lamb meal etc.) are fairly well regulated and defined by AAFCO. Many fruits, vegetables, and other seemingly healthy ingredients have no AAFCO definition for the ingredient. If an ingredient definition does not exist, AAFCO regulations state that it “shall be identified by the common or usual name.” For example, ‘Apples’ or other fruits may contain seeds, stems, leaves, skins, or pulp. While pulp may contribute nutrients to the food, the generic definition does not clearly exclude any other parts that may not be beneficial to the animal’s health. For all of these reasons, reliance on pet food ingredients as the primary way to assess a pet food product would be a poor indicator of a product’s overall health impact for a pet. As part of the initiative to consider nutrition the 5th vital assessment, a Nutrition reference manual (http://www.everypetevertime.com/docs/en-us/Pet_Nutrition_Ref_Manual.pdf) provides an excellent description of pet food label requirements and clarifications about ingredient definitions.

Nutrition recommendation, a pet-specific process
The final steps of making a nutritional recommendation for a pet food are to use your judgment in evaluating a product and match it closely with life stage, life style and health of the pet. To complete the process, you would continue to monitor the pet’s response to make sure you see the expected results, that the patient maintains optimal health.

Recalls
Sadly, pet food safety issues remain a growing concern. We have become more aware of pet food safety issues, most dramatically evident in 2007 with melamine adulteration of wheat gluten which affected many products and led to renal failure in a number of pets. Most recently, at the time of this writing, at least 3 products have been recalled for aflatoxin contamination, and several more foods or treats with potential salmonella contamination. Pet food safety is now more closely monitored by the FDA, and there are more professional “watch-dogs” sharing information and updates about pet food recall; Veterinary Information Network (VIN), American Veterinary Medical Association (AVMA), and State Veterinary Medical Association etc. There is now a central Food and Drug Administration (FDA) online safety reporting portal for veterinarians and owners to submit reports of concern about pet foods and treats. These can be submitted electronically: http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/default.htm

If the veterinarian has suspicions about the safety of a food, this warrants a thorough diet history. Check the FDA website and contact the pet food manufacturer to alert and confirm your concerns. You will need information from the product label, so advise client to keep the label with the food until the bag is completely consumed.

References
FDA Animal and veterinary safety reporting portal (2010), http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/default.htm
Zicker, S. Evaluating pet foods: how confident are you when you recommend a commercial pet food?” Topics in Companion Animal Medicine. 23 (3).121-126, 2008.
Evidence based medicine (EBM)
The concept of EBM represents a major but largely untested advance when making clinical decisions to determine patient care. The conceptual model for this suggests that the best clinical decisions are made when high quality evidence from controlled studies, clinical expertise and patient/client preferences overlap.

High quality research refers to clinically relevant research from patient centered clinical trials. Clinical expertise refers to the use of clinical skills to identify each patient’s unique health condition, reach a diagnosis and consider the risks and benefits of potential intervention. A quality of evidence grading scale has been developed:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence from one or more properly designed randomized controlled clinical studies performed in clinical patients of the target species</td>
</tr>
<tr>
<td>II</td>
<td>Evidence from properly designed randomized controlled studies performed using animals of the target species with spontaneous disease in a lab setting or research colony of animals</td>
</tr>
<tr>
<td>III</td>
<td>Evidence from appropriately controlled study without randomization, appropriate cohort or case control design using acceptable models of disease or simulations in target species; dramatic result from uncontrolled study or case series</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence from studies conducted in other species, report of expert committee, descriptive study, case report, or pathophysiologic justification or opinion of expert based on clinical experience</td>
</tr>
</tbody>
</table>

Although there is a paucity of grade I evidence in much of veterinary medicine, the focus of nutritional research is to evaluate effectiveness of treatment including veterinary therapeutic diets. In the absence of evidence, patients must eat.

Using the circle of nutrition to make a nutrition recommendation, a pet-specific process
In addition to assessing the patient (species, lifestage health or disease) the diet must be assessed to assure that it first and foremost meets the needs of the patient and is appropriate for managing disease. The owner and environment must be taken into consideration and to complete the process, monitor the pet’s response to make sure it achieves the expected results. If not, reassess and begin the process again. There are many options for therapeutic diets and it can be difficult deciding which, if any product to use.

Comparing therapeutic veterinary diets-using information from a product guide
(adapted and used with permission from CA Buffington and http://vet.osu.edu/vmc/nutrition-support-service)
Look for tables containing some nutrient parameters of the therapeutic veterinary foods. The diets are classified as veterinary foods because they are to be used only under veterinary supervision. Commercially available foods also may be appropriate for some of the conditions listed (as described where appropriate in the tables). The tables are based on the most commonly recognized nutrient modifications for a particular disease. This format was chosen because veterinarians commonly make the diagnosis, decide on necessary nutrient modifications, then choose the most appropriate diet for their particular patient. Some foods are used for more conditions than are mentioned in the tables.

The data in the tables can be used to compare the nutrient content of different diets and, to compare nutrient content of a diet with the nutrient needs of a patient:
To compare diets

a. of similar moisture content and energy density, one can use the amount of nutrient per unit as fed - AAFCO regulations require that minimum percentages of protein and fat, and maximums for moisture and fiber, be reported on all pet foods.

b. of differing moisture content (e.g., dry vs. canned) and similar energy density, one can use the amount of nutrient per unit dry matter. For example, a dry diet containing 20% protein and 9% water (=91% dry matter) on an as fed basis contains 20/91 * 100 = 22% protein on a dry matter basis, whereas a canned diet containing 5% protein and 77% water (=23% dry matter) on an as fed basis contains 5/23 * 100 = 22% protein on a dry matter basis.

c. of differing energy density (e.g., high vs. low fat), one can use the amount of nutrient per 100 kcal - For example, a diet containing 25% protein and 7% fat on a dry matter basis contains 8 grams of protein per 100 kcal, whereas a diet containing 25% protein and 21% fat on a dry matter basis contains only 5 grams of protein per 100 kcal. The therapeutic (prescription) diets report information this way.

To compare nutrient content of a diet with the nutrient needs of a patient, use the amount per unit body weight per day - because many veterinary foods contain restricted amounts of some nutrients, one must compare the number of grams of nutrient in the amount of food consumed with the needs of the animal to ensure that deficiencies are avoided. This is of practical concern for protein and sodium. For example, the minimum protein intake to sustain protein reserves in dogs is approximately 2.55 gms protein /kg body weight (BW) or ~ 1 gm protein/pound BW per day. If a dog with advanced renal failure consumes 20 kcal per pound body weight per day, the diet would need to contain at least 5 grams per 100 kcal to provide enough protein to meet the dog’s needs. If the dog consumed 30 kcal per pound body weight per day, only 3.3 grams protein per 100 kcal diet would be necessary.

Because diet therapy for a number of diseases consists of restriction of nutrient intake, and because many patients with nutrient-sensitive diseases are older and don’t eat much, the risk of nutrient deficiencies must be considered. This is particularly true when the therapy is anticipated to continue for months or years. For these reasons, estimates of daily minimum intakes of some essential nutrients (amount per pound body weight) for adult, average-sized pets are presented below:

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dog</th>
<th>Cat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>10 kcal</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>10 ml</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>1 gm (2.55gm/kg BW)</td>
<td>2 gm (~ 5 gm/kg BW)</td>
</tr>
<tr>
<td>Sodium</td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>Phosphorus</td>
<td>20 mg</td>
<td></td>
</tr>
</tbody>
</table>

Veterinary foods often are sold as containing "high" or "low" levels of some nutrients. Currently, no generally accepted definition of these terms exists. My own definitions, many extrapolated from humans, follow:

**Definition of "high" and "low" nutrient densities**

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Dog</th>
<th>Cat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low calorie</td>
<td>&lt; 3 kcal/gm dry matter</td>
<td>&lt; 3 kcal/gm dry matter</td>
</tr>
<tr>
<td>High calorie</td>
<td>&gt;4.5 kcal/gm dry matter</td>
<td>&gt;4.5 kcal/gm dry matter</td>
</tr>
<tr>
<td>Low protein</td>
<td>&lt;5 gm/100 kcal</td>
<td>&lt;7 gm/100 kcal</td>
</tr>
<tr>
<td>High protein</td>
<td>&gt;8 gm/100 kcal</td>
<td>&gt;10 gm/100 kcal</td>
</tr>
<tr>
<td>Low fat</td>
<td>&lt;2.5 gm/100 kcal</td>
<td>&lt;3 gm/100 kcal</td>
</tr>
<tr>
<td>High fat</td>
<td>&gt;5 gm/100 kcal</td>
<td>&gt;5 gm/100 kcal</td>
</tr>
<tr>
<td>Low fiber</td>
<td>&lt;0.25 gm/100 kcal</td>
<td>&lt;0.25 gm/100 kcal</td>
</tr>
<tr>
<td>High fiber</td>
<td>&gt;1.5 gm/100 kcal</td>
<td>&gt;1.5 gm/100 kcal</td>
</tr>
<tr>
<td>Low sodium</td>
<td>&lt;100 mg/100 kcal</td>
<td>&lt;100 mg/100 kcal</td>
</tr>
</tbody>
</table>

**General feeding suggestions: Remember, It is may be better for a patient to eat some of the "wrong" diet than none of the "right" diet!**

1. Introduce diet gradually, **once the patient’s condition is improving**, to avoid creating a learned aversion, which is the association of an adverse stimulus with a novel diet. If one intends to feed a particular diet long-term, it should be introduced when the patient is feeling better so it is associated with feelings of improving health.

2. Amount- use the "Energy needs of sedentary dogs and cats” graph for initial guidelines, or offer ~20 kcal per pound body weight per day to cats and most dogs (~10 kcal/pound if > ~100 pounds), adjusting intake as necessary to maintain a moderate body condition.

3. Follow instructions in the section entitled "treating inappetence" when patient food intake falls below the above intake estimates.
The remainder of this discussion will use cases of commonly used veterinary therapeutic diets to evaluate evidence in the context of patients.

References
Buffington CA. The Ohio State University Veterinary Medical Center Nutrition Support Service website. Accessed March 2014:
http://vet.osu.edu/vmc/nutrition-support-service
Integrate Nutrition in Preventative Care: 
The 5th Vital Assessment
Julie Churchill, DVM, PhD, DACVN
University of Minnesota
St. Paul, MN

Food matters
The idea that great or even ‘optimal’ nutrition positively influences an animal’s health is fairly well accepted by pet owners and veterinary professionals alike. Increasingly, the public is asking the veterinarian to serve as a resource for nutritional advice for their pets, and nutrition is playing a bigger role in clinical practice. Several recent publications have helped to include nutrition as a standard of care; the American Animal Hospital Association-American Veterinary Medical Association jointly introduced the first (AAHA-AVMA) Preventative Healthcare Guidelines (2011), and the AAHA Nutritional Assessment Guidelines (Baldwin, 2010). The AAHA Nutritional Assessment Guidelines outline the goals of providing better:

- Awareness of the importance of nutritional assessment of dogs and cats.
- Guidelines for nutritional evaluation of animals to promote optimal health and response to disease.
- Evidence and tools to support recommendations.

In 2011 the World Small Animal Veterinary Association (WSAVA) followed suit with a similar document of Guidelines for nutritional assessment. WSAVA promoted a global initiative to standardize the process to include nutritional assessments as the “fifth” vital sign (temperature, pulse, respiration, pain assessment, and nutritional assessment) to be included as a standard of care when performing physical examinations and histories for all small animals. Together these documents endorse the incorporation of nutritional assessments into regular patient care as critical for maintaining animal health and optimizing response to disease. Incorporating nutrition standards in the care of small animal patients will help develop a partnership between owner, veterinary healthcare team and lead to healthier pets.

Every pet, every time
Incorporating the AAHA/WSAVA Nutritional Assessment Guidelines doesn’t need to be time consuming or complex for most patients, but it does need to be specific to that individual pet. The assessment process can be quickly incorporated into the routine history and physical examination portion of every appointment. In the course of obtaining the history and performing the exam, each patient is screened for nutritional risk factors, established by the pet’s breed, life stage and life style, body weight and condition, health history, and underlying comorbidities, medications and diet.

The nutritional screening process can be used to quickly eliminate or identify patients with ‘nutritional’ risks. Patients who are healthy have a normal body weight, normal body and muscle condition (BCS, MCS) and are free of any other abnormal historical or physical exam findings. Making a pet-specific nutrition recommendation for these healthy patients can be done quickly, by recommending the amount and type of a high quality food that matches the pet’s nutritional life stage requirements. In many of these patients, it involves little or no change, but a verification and documentation of the current feeding plan.

Pets should be considered to have nutritional risk factors when any of the following are present:

- Abnormal BCS (or MCS)
- Snacks, treats or table foods > 10% of total Calories
- Specific life stage considerations; especially at the time of spay or neuter
- Unconventional diet
- Systemic or dental disease
- Gastrointestinal signs
- Poor skin condition or hair coat
- Inadequate or inappropriate housing

When any of these findings are discovered by the nutritional screening process, it raises the index of suspicion for a nutrition-related problem. Discovery of nutritional risk factors also identifies an opportunity for further evaluation and the potential for nutrition to play an increased role in improving the pet’s health. When any of the above risk factors are identified, an extended nutritional evaluation is likely indicated. The importance of the extended evaluation increases as the number or severity of risk factors increases. The extended nutrition evaluation would include a more in-depth diet history and assessment of the pet’s diet.

Practicing great nutrition
The Pet Nutrition Alliance (PNA; www.petnutritionalliance.org) was created to help raise awareness about the importance of proper pet nutrition, and the value of nutritional assessments for every pet, every time. The PNA is developing a set of practical tools for the entire veterinary healthcare team to assist them in implementing these nutritional guidelines for every pet. One of the first tools, AAHA Tips for Implementing Nutrition as a Vital Assessment in Your Practice can be downloaded from the Pet Nutrition Alliance.
website resource section. Recent evidence suggests this process is most successful when the veterinary team develops easy protocols for each team member to follow.

Now is the time for the veterinary healthcare team to reclaim the role of nutrition counselor. Matching a diet with the proper species and life stage nutritional requirements can help prevent diet-associated diseases. Modifying a food to better meet an animal’s needs or intolerances allows diet to play an important role in the therapeutic management of the disease. Clients are seeking information about how diet can improve the health of their pets. When veterinary professionals don’t meet this need, clients seek less reliable sources for dietary information. Veterinarians may lose the opportunity to improve patient health and provide high quality preventative care. When the veterinary team makes individualized nutrition part of the every pets visit, they not only meet the needs of the patient but strengthen the relationship with their clients.

References
To Cook or not to Cook!
Quagmires and Controversies of “Natural Diets”
Julie Churchill, DVM, PhD, DACVN
University of Minnesota
St. Paul, MN

People have passion about their pets and feeding is an essential component of and caring for them. Clients want the very best for their pets and nutrition plays a big role in keeping pets healthy. Nutrition is also an important part of the human-animal bond, because there is no better way to nurture pets than by feeding them well. As we become more aware of the role great nutrition can impact human health, owners consider many of the same factors when choosing foods for their dog or cat. In the past 15 years, there has been increasing interest in finding more “natural” alternatives to feeding pets. This increased even more since 2007 with the recall involving melamine adulteration of pet foods. In an effort to choose more “natural,” potentially safer foods for their dogs, many owners are feeding or considering feeding unconventional diets such as home cooked or raw food diets.

Home preparation of less conventional diets either raw or cooked, remains a controversial subject among veterinarians, nutritionists, trainers, breeders and pet owners. Why does this controversy persist when everyone shares the same goal; to feed their pet best diet? There are pros and cons to consider with every feeding recommendation. This discussion will examine the evidence behind the recommendations, including nutritional goals, evaluation of resources, indications or contraindications for considering an alternative to conventional commercial pet food. The nutrition reference manual offers discussion points to have with clients about unconventional diets (http://www.everypeteverytime.com/docs/en-us/Pet_Nutrition_Ref_Manual.pdf).

Home cooked diets
When a client wants to prepare food for their pet it is important to understand their reasons. Once you understand the goals of the client you can partner with them to find the best fit for them and their pet which may or may not be a home cooked diet. Often clients are seeking control in selecting the ingredients in order to provide high quality or organic, additive or preservative-free. Other reasons for wanting to prepare foods at home include diagnostic or elimination diets to detect food allergies, management of multiple diseases for which there is no commercially available therapeutic diet, or end stage care for inappetant patients with terminal disease.

Because most nutritional problems do not cause noticeable physical or laboratory abnormalities until the nutritional imbalance has been present for months or years, the link to diet can be hard to identify. The appearance of a glossy coat and a happy dog can mislead people into thinking all is well. Truthfully, many pets can tolerate nutritional imbalance quite well and even flourish, for a while. This is in part because dogs are very resilient and can do well as long as they get basic nutrients. However, a nutritional imbalance that is tolerable is not the optimal care that pet owners are striving for when they choose to feed homemade or raw diets. Although some were close, not a single homemade diet evaluated by the Nutrition Support Service at the University of Minnesota Veterinary Medical Center in the past 10 years was truly complete and balanced. Formulating complete and balanced diets is not simple. Verify the nutrition credentials and training of people advocating unconventional diets and select a recipe that has been formulated by a veterinary nutritionist. Guidelines have been published to help practitioners make a quick assessment of an existing typical home made recipe for clients (Remillard and Crane 2010, Appendix 1). Homemade diets for patients with medical problems should always be formulated by a veterinary nutritionist specifically for the individual patient after careful nutritional assessment of the patient.

Raw diets
The lines are blurring regarding raw food diets. In the 1990’s and early 2000 several books were published (Billinghurst 1993, Volhard 2000, Schultze 1999) advocating the feeding of raw and meaty bones. More recently there has been an increase in the number of commercially available raw meat diets. There are abundant health and nutritional claims that raw foods offer superior nutrition, and maintain the enzymes needed for healthy digestion. There is no nutritional advantage gained by feeding raw meat, bones and/ or eggs. A healthy animal has sufficient enzymes within its own digestive tract to fully utilize the nutrients from their food. The cooking process can alter digestibility and some vitamin levels to a slight degree. However cooking will not cause significant nutrient loss that would make a complete and balanced diet nutritionally deficient. There has been a growing body of literature reporting health risks associated with bacterial contamination (salmonella and e. coli spp) of raw meat based diets, both home prepared and commercially prepared raw foods. To date there is no evidence for health benefits of raw foods, and public health (AAHA position statement 2012).

There are newer commercial raw pet food products that process the food by freezing, freeze drying or high pressure pasteurization (HPP). Each of these processes may reduce the risk of bacterial and parasitic contamination to some degree; however it does not eliminate it (Weese et al, 2005). As yet, there are no regulations specifically defining ‘raw’. Should a food undergoing HPP still be considered raw. Several of these newer products do not comply with label regulations and some do not describe safe handling practices on the label (Mehlenbacher, 2012).
The goal behind feeding homemade or raw foods is certainly laudable, the desire to do the very best for pets. Excellent communication skills will be paramount when discussing this issue with owners so that you can focus on shared goals—; the optimal health of the animal and minimizing health risks. It is important to partner with the client to find the best approach for feeding a healthy choice for their pets. Helpful tools to use in your discussion may be the raw protein diet policy by the Delta Society, an organization promoting the human–animal connection with the mission to improve health.


**Tips for discussing unconventional diets with pet owners**

a. Obtain a thorough diet history to include treats, snacks and human foods. Also include any foods used to administer medication. If 90% or more of the intake is composed of a good quality complete and balanced product it is unlikely to adversely affect the nutritional balance for healthy adult (non-reproducing) pets. Pets are higher risk if treats or additional food exceed 10% of the diet and should not contain potentially harmful foods such as chocolate, grapes, raisins, or onions.

b. Identify and discuss the reason for the owner’s selection of unconventional foods and their concerns about changing the diet. This can focus your discussion to address their concerns.

c. Use empathy and care when discussing foods, presenting evidence based facts and be aware of determining an owners “readiness to change”.

**References**


Mehlenbacher S et al., Availability, brands, labeling and salmonella contamination of raw pet food in minneapolis/st paul area. Zoonosis and public health, 2012 59(7) 513–520.


Schultz K, The ultimate diet; Natural nutrition for dogs and cats. Carlsbad: Hay House 1999


**Appendix 1. (Hand 2010)**

Guidelines* to assess a homemade recipe:

**Do five food groups appear in the recipe?**

- a carbohydrate/fiber source
- a protein source, preferably animal origin
- a source of macro minerals, particularly calcium
- a multi-vitamin and trace mineral source

**Is the carbohydrate source a cooked cereal and present in equal or higher quantity than meat?**

- Carbohydrate :protein ratio 1:1 in cats and 2:1 to 3:1 in dogs

**What is the type and quantity of the primary protein source?**

- Protein content of various mammalian and avian skeletal muscle tissues is generally equivalent
- For amino acid balance, provide some liver as part of the meat portion once a week

**Is the animal protein source lean or fatty?**

- If the protein source is “lean”, an additional fat source is required, at least 2% of the formula for dogs and 5% of the formula for cats

**Is a source of calcium and other minerals provided****** (most often neglected item)**

- Most home made formulas require a specific calcium supplement
- Use calcium carbonate (0.5 g. per 5 kg BW) when the protein portion is equal to or is greater than the carbohydrate portion
- Use calcium and phosphorus supplement (dicalcium phosphate or bone meal) when the protein fraction is less than the carbohydrate fraction

**Is a source of vitamins and other micronutrients provided?**

- Supplements providing vitamins, trace minerals, fatty acids and taurine should always be provided
- these guidelines for healthy adult (“maintenance” life stage) animals.
There are many references for home cooked diets for pets. They all have pros and cons. Check the nutrition credentials of the author, and use some of the above guidelines to make an assessment of the recipes.

Other resources for complete and balanced homemade diets are: acvn.org for a list of nutritionists available for consultation and www.BalanceIT.com and www.petdiets.com for formulated recipes by veterinary nutritionists.
Client Conversations:
Keeping Clients through Nutritional Questions

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We are all familiar with the ‘good news’ about preventive care: it saves lives, improves health and quality of life. Nutrition is an integral and essential component of providing optimal preventive health care for pets. Yet the bad news is that many veterinary patients are not receiving the preventive care they deserve. Recent studies document a decline in preventive veterinary care. Veterinary professionals tend to view following their recommendations or “compliance”, especially when it comes to nutrition, as the responsibility of the client. A common misconception is that clients heedlessly ignore the veterinary team’s recommendations, but in reality there are many factors contributing to non-compliance. Employing great communication skills can be a key way in which the veterinary team can take active and important role in helping clients care for their pets. This will support clients’ understanding, trust and remembering the nutritional care plan, thus improving compliance, adherence and ultimately the pet’s care.

Veterinarian professionals may lack concrete tools to assess the clients’ understanding, receptiveness or readiness for change. Through carefully worded questions when taking a medical and diet history, the veterinary professional can identify the client’s receptiveness and readiness for change. Based on this knowledge, they can better identify the appropriate way and time to implement a nutritional plan. If a client is not yet ready, they can instead help clients explore obstacles and overcome barriers to sustainable change. For example, the best predictors of adherence to a weight loss program are the veterinary professional’s interviewing skills and qualities of the veterinary-client interaction. In order to improve adherence, it is essential to establish an atmosphere of trust and demonstrate concern for both the patient and the client's well-being.

The American Animal Hospital Association (AAHA) has developed a practical acronym for veterinary staff to use to remember techniques to increase client compliance. The CRAFT formula: Compliance = Recommendation, Acceptance, and Follow Through. Compliance is thought to be optimal once the veterinary team member has made a specific recommendation to the client; the client accepts the recommendation and follows through with the care plan. CRAFT depends on the abilities of the veterinary staff to communicate effectively with the client using an intentional approach to communication known as ‘relationship-centered’ care. This style of communication and care has been associated with improved adherence. Using relationship centered communication, the veterinary professional shares information with the client in ways that they understand what is happening with their pet and share in decision-making.

Recommendation
The Nutritional recommendation should provide the client with specific, concise recommendation and a rationale describing the benefits for the pet. The selection should provide complete and balanced nutrition, be acceptable to the owner, enjoyed by the pet and maintain stable and healthy ideal body weight to prevent many health risks.

The way the recommendation is delivered is also important. Below are some tips to making a clear recommendation:

- Avoid distractions from the conversation. Discuss in the exam room, rather than a noisy lobby.
- Organize the recommendation: specific brand, amount, frequency, monitoring plan.
- Give information is short pieces if information and check for understanding by the client.
- Use lay person language.
- Use ‘props’ such as pet food labels, portion sizes, measuring cups etc.
- Summarize the discussion to repeat important points.
- Provide written instructions to go home.

Definitions
Compliance
The extent to which a pet receives a treatment, screening or procedure in accordance with accepted veterinary health care practices. Compliance involves both veterinary staff performing and recommending this treatment, screening or care, as well as client follow through.

Adherence
The extent to which patients take medications prescribed, involving the pet owner in: filling/refilling prescriptions; administering correct dose; timing and use and completing the prescribed course. Adherence is generally a term applied to medication rather than recommendations for wellness checks or diagnostic screenings.

AAHA 2009
Acceptance
When the client receives the recommendation and understands and agrees to the plan, this is ‘acceptance’. Although this step seems dependent only on the client, the veterinary team can significantly influence client acceptance by:

- Observing the client for verbal/nonverbal cues of non-acceptance.
- Acknowledging these signs and invite concerns or worries they might have. “it seems like you may be worried about changing foods, can you tell me about your thoughts?”
- Active listening through verbal and nonverbal cues (maintain eye contact, allow pauses for clients to speak, encourage them to ‘go on”).

Follow through
Non-compliance most often happens due to a failure of follow through. It is very important even after the client has left the veterinary clinic to receive support from the veterinary team to follow through with the agreed upon plan. Veterinary clients may find it difficult to remember all that is said during the consultation. There are a variety of ways to support clients and follow through after the client and pet return home:

- Provide written instructions that include
  - trouble shooting ideas or adverse events to watch for
  - ways to contact you if they have questions.
- Schedule recheck appointments before the client leaves the clinic
- Verify contact information and ask for preferred choice of reminder contact
- Call/email client to check in 2-3 days after the visit to see if there are challenges to following the treatment plan
- Use a reminder system to assist with follow up appointments

Team approach
The veterinary support staff plays a vital role in all parts of CRAFT and it is important that all members share a consistent message. Review the clinic protocol at staff meetings, and periodically evaluate/refine the protocol. There are helpful resources available for team training. Suggestions and resources for incorporating nutrition in the care of each patient is available at:

[www.everypeteverytime.com](http://www.everypeteverytime.com)

The partnership for Healthy Pets Initiative ([http://www.partnersforhealthypets.org](http://www.partnersforhealthypets.org)) has the goal of helping veterinary professionals gain the tools needed to insure a healthy, long life for the pet and to communicate the importance of preventive care for the lifelong health of the patient. There are tools and resources available specifically aimed at improving communication skills; "words that work” ([http://www.partnersforhealthypets.org/communications.aspx](http://www.partnersforhealthypets.org/communications.aspx))

Check-in

- Client fills out nutrition history/update form
- Weigh in
- Front desk staff places nutrition history/update form in patient’s records

Exam room

- Veterinary technician records history using nutrition history form to help ask questions and initiate discussion
- Veterinarian performs a physical exam and nutritional assessment, makes a specific nutrition recommendation and documents the recommendation in patient’s records
- Veterinary technician asks client if there are any questions and reinforces the recommendation, dispenses tools (measuring cups, literature about nutrition, information packet) and sends patient home with an information packet even if they don’t purchase recommended food

Check out

- Front desk staff asks client again if there are any questions, dispenses food and reinforces recommendation, schedules a callback in 2-7 days if recommendation is for a new food and enters reminder code for re-purchase of food two weeks before food will run out

Techniques of using relationship-centered communication to develop a health care plan.

Explore the clients’ perspective
Check in with the client to get their specific concerns, beliefs, goals and expectations, to better understand the client’s perceived value of each treatment option. For example: “Ms Gray, there are several great food choices that will meet Spike’s needs. What are your concerns about what he is eating now? What are your biggest goals for feeding Spike?
Share veterinary thinking
When appropriate, discuss your findings and reasoning out loud. This shows the client your ‘work’ and allows them to follow the thought process or problems you face and can encourage their input. For example: “we wanted a food Spike really enjoyed, but he is only eating a small amount yet gained almost 15% in the last month”……”yes, it’s such a little amount and he’s still always hungry and started stealing food from the kids. Is there anything we can do?”

Encourage the client to participate
Let the client help with suggestions or solutions that work for them. “Maybe a different food would help, and I can have the kids put food away when they finish snacks”.

Incorporate the client’s individual concerns. Partner in care
Relate the treatment choice to a concern or comment the client made so they make the connection between care and benefit.

“You mention you want Spike to enjoy his meals, but unhealthy weight gain is related to many health risks and a shorter lifespan. We can try some foods that are really tasty, higher in protein and lower in calories so he can eat more food and feel more satisfied.”

Recommended reading
Be a change agent- move your clients from thinking to doing to successfully manage the weight of their pet

Over the past decade there have been many efforts in the veterinary profession to increase awareness about pet obesity. Yet obesity continues to be one of the most common diseases affecting dogs and cats (Association for pet obesity prevention 2012). In spite of increased awareness of obesity by pet owners, the discussion about weight loss remains a common and frustrating aspect of small animal practice. This conversation can be sensitive and recommendations frequently go unheeded. Before this lack of success in helping pets achieve and maintain healthy weight leads you to ignore this disease, consider it an opportunity to try another way to help these patients. In spite of the evidence that obesity negatively influences health, wellbeing and even life span (Kealy et al. 2002, Pibot 2006), veterinary professionals still struggle to influence clients to begin or adhere to a weight loss program for their pets. One reason for this may be that the veterinary team lacks concrete tools to assess the clients’ readiness for change. Through carefully worded questions when taking a medical and diet history, the veterinary professional can identify their client’s receptiveness and readiness for change. Based on the client’s readiness, the health professional can better identify the appropriate time to implement a nutritional plan. If a client is not yet ready, they can instead help clients explore obstacles and overcome barriers to sustainable change.

Three essential elements should be present to make a weight loss program successful 1) owner commitment 2) individualized weight loss plan 3) regular reassessment. Careful attention to assure each component is present not only contributes to successful weight loss of the patient but also increases satisfaction of both the client and veterinary team.

Establish owner commitment
Assess the client’s readiness for change. If they are ready to act, proceed with your nutritional plan. If not, employ ways to move them from thinking (contemplation) to doing (action).

Individualize the weight loss plan
Partner with clients to make the weight loss plan patient-specific; a plan that works for the client and meets the nutritional needs of the pet. A careful and complete diet history (food and treat types, amounts, schedule etc) reveals important information about how the family relates to the pet through food and often provides insight about potential challenges the client will face (Michel 2009). The diet history also reveals information about the pet’s nutritional status which is often imbalanced from additional treats and human foods added to commercial products. Because of individual variation in energy needs of pets, the diet history serves as an invaluable diagnostic tool. An accurate diet history provides information about current caloric intake which then serves as a more precise starting point for the food dose calculation (start at 75-80% of current intake) (Perea 2010).

3. Regularly reassess
Initially biweekly follow-up will help support clients, assure a healthy rate of loss (0.5-1.5% body weight per week) and provide early detection of potential relapses so the weight loss plan can be adjusted or the clients redirected before excessive weight gain occurs and frustration becomes another barrier to success.

Great communication skills are as essential as clinical skills (physical examination and technical skills) for achieving success in helping clients with weight loss programs for their pets. A useful resource for communicating about this and other nutrition topics is available online through partners for healthy pets, http://www.partnersforhealthypets.org/communications.aspx. Often the most frustrating cases are those where there is a mismatch of expectations between the client and the veterinary professionals. An appreciation of the client’s level of motivation for weight loss allows us to tailor our interventions and can help reduce our frustration with clients that do not adhere to the weight loss program.

Key challenges to consider include:

- Do busy veterinary professionals have time to discuss feeding and lifestyle issues with clients in a manner that will be effective?
- When recommending changes in feeding and lifestyle, how can adherence to a weight loss program be increased?

The best predictors of adherence to a weight loss program are the veterinary professional's interviewing skills and qualities of the veterinary-client interaction. (Morrissey JK and Voiland B 2007) In order to improve adherence, it is essential to establish an atmosphere of trust and demonstrate concern for both the patient and the client's well-being. It is also important to understand how behavior change takes place (Abood 2007).

Psychologists have developed several models that help guide our understanding of how humans make changes in behavior to improve health. The “stages of change” model, also known as the transtheoretical model (TTM), developed by James Prochaska (Shumaker, et al 2009 and colleagues), can be used to assess the client’s readiness to change their behavior (Buffington 2004). Using this model can help the veterinary professional better understand the change process and provide useful strategies to customize their recommendations to the client. TTM helps us better partner with our client and patient to provide an individualized plan to best suit the client's needs.
their needs. Implementing a weight loss plan when the client is ready to act on this advice will improve the success and be a more efficient use of time.

**Step 1: Identify the stage of change**
The 5 stages of change and characteristic attributes of clients:

1. **Precontemplation**—the person has no intention of taking action in the next 6 months. These clients might commonly be referred to as resistant, unmotivated or unaware, but clearly, they are not ready to change. In reality, it is often our intervention programs that have not been ready for them.

2. **Contemplation**—the person is aware of pros and cons of changing and *intends* to change in next 6 months. They may be stuck “thinking about it”, intending to change “soon”.

3. **Preparation**—the person plans to take action in the next month. Clients may have recognized the problem and sought advice already from books or online or by talking to a pet store employee, trainer or veterinary professional. Recruit these people for action-oriented programs.

4. **Action**—the person has taken action that is significant enough to result in a reduction of risks for disease. For example, the client may have reduced treats or selected a different pet food. However, the change would not be considered a significant action unless it reduced calories by at least 10% and provided complete and balanced nutrition. Veterinary professionals can help refine the plan to achieve healthy weight loss.

5. **Maintenance**—the individual continues action to prevent relapse.

**Step 2: Understand the change process**
By understanding the stages of change the health professional can adapt their communication to meet the stage of the client. If a client is in one of the early stages, it isn’t the time to try and implement a weight loss plan for this pet. It’s equally important that we don’t ignore this patient’s obesity. Don’t give up. These patients warrant a monitoring plan. It may take time and several visits to establish rapport and build the trust necessary to move the client along to the next stage, hopefully closer to being ready to “take action” and implement a weight loss program for their pet and ultimately take steps to improve their health (see table).

**Step 3: Select a stage-appropriate intervention**
The failure of many weight loss programs are often because of a mismatch between the type of intervention and the client's readiness to change. Many traditional programs are action-oriented while the majority of clients are not in the action stage. See the table for examples of communication tools to identify the client’s stage of change and how to communicate best to match the client’s readiness. When a partnership is formed with the client you create an environment that supports change. By understanding the stages of change the veterinarian can help move the client from thinking to doing. Selecting the right intervention at the right time for the right client can tremendously improve the clinical outcome. Successfully managing obesity can change a frustrating problem to a rewarding one. The pet achieves greater health, an improved quality of life and pet owners become loyal clients because they have been active partners in the healthcare plan.

**References**
Association for pet obesity prevention(2012), http://www.petobesityprevention.com/
Lymphoma is one of the most commonly diagnosed cancers in dogs, cats and people. Canine lymphoma bears similarity to the non-Hodgkin’s lymphomas (NHL) in humans and both exhibit similar responses to treatment with chemotherapy. Lymphoma is very difficult to cure and a leading cause of cancer death in dogs and people. Despite many efforts over the last 20-30 years, outcomes in canine patients have not significantly improved over those achieved with CHOP-based chemotherapy protocols (cyclophosphamide, doxorubicin, vincristine, and prednisone). These chemotherapy protocols have extended both the longevity and quality of life in dogs with lymphoma but novel strategies are needed to increase survival times. This presentation will cover a general review of lymphoma and recent advances that hold promise for the future.

Diagnosis and diagnostic advances

Lymphomas are a diverse group of cancers arising from lymphoid cells. There are greater than 30 types of canine lymphoma described that differ in anatomic, histologic and immunophenotypic (T vs. B cell) classification. These different types of lymphoma can vary in their biologic behavior and prognosis; however, further studies are currently needed to correlate the various categories of disease with clinical outcome. The majority of canine lymphomas are intermediate or high grade and are generally characterized as being biologically aggressive and rapidly progressing. Indolent lymphomas may progress more slowly and dogs may experience long-term survival with limited or no therapy; however, indolent lymphomas represent a small percentage of lymphoma in dogs. Diagnosis of lymphoma is achieved via cytology or biopsy. While not performed in every case, the following diagnostics may be helpful to establish a diagnosis of lymphoma or to further characterize the tumor.

**Immunophenotyping (cytology, histopathology, or flow cytometry)**

Using antibodies against specific cell surface markers (ex. B cell CD 79a/CD20, T cell CD3/CD4/CD8), this test is primarily used to determine if the lymphoma is B or T cell in origin. However, it can also be helpful to support a diagnosis of lymphoma by documenting a homogenous population of the same immunophenotype within a tissue.

**Flow cytometry**

This test allows immunophenotyping of cells in suspension (blood, effusions, and aspirates of LNs or organs). Flow cytometry can also provide information regarding cell size and expression of other CD molecules that may correlate with prognostic information.

**PARR (PCR for antigen receptor rearrangement)**

Theoretically, a malignant cell population should be derived from expansion of a single clone. PARR amplifies the variable regions of the T cell receptor or Immunoglobulin (Ig) receptor gene to detect the presence of clonal lymphocyte populations. When it is not possible to differentiate between malignant and benign lymphocytes based on cytology or histopathology alone, PARR may be helpful to confirm a diagnosis (especially useful when the lymphocyte population is heterogeneous). PARR can be used to detect minimal residual disease but investigations are ongoing to determine if this is a useful clinical marker of early recurrence.

**Proteomics (ex. PetScreen)**

Proteomics analyzes the protein components of a cell, which may be used to identify cancer specific markers. Preliminary studies have been performed in canine lymphoma but clinical application is limited at this time.

Staging

Lymphoma is considered a systemic disease and most dogs are presented in advanced stages (III to IV). Ideally, the extent of disease is determined after diagnosis as a baseline for treatment monitoring. However, the degree of staging necessary is controversial. The completeness of staging in any given case is often dictated by 1) how a diagnostic test affects treatment plan, 2) how it affects client’s decision making and 3) how it affects patient prognosis. A thorough physical exam, CBC, serum chemistry profile, and urinalysis are indicated for every patient to obtain vital information regarding organ and bone marrow function before starting treatment with chemotherapy. Additionally, information regarding prognostic factors (hypercalcemia, anemia) may be obtained. Further diagnostics to consider include thoracic radiographs and abdominal radiographs/ ultrasound. These imaging studies are non-invasive and may provide information regarding areas of significant disease burden (such as mediastinal or sublumbar lymph nodes). This can be important information when monitoring for lymphoma relapse. In the author’s practice, abdominal ultrasound is also highly recommended for any dog with clinical signs attributable to the GI tract in order to rule out involvement, and thoracic radiographs/echocardiogram are recommended for any dog predisposed to heart disease. The value of a bone marrow aspirate in the face of a normal CBC is questionable and rarely pursued in the author’s practice.
PET/CT (positron emission tomography/ computed tomography)
PET/CT combines functional and anatomical imaging to allow detection of metabolic or proliferative activity throughout the body. PET/CT is currently the standard of care for monitoring and predicting response to therapy in people with lymphoma. PET/CT has also shown promise for evaluating response to chemotherapy and predicting relapse in dogs with lymphoma.

Standard treatment options
Multiagent chemotherapy is the mainstay of treatment for lymphoma. For intermediate to high grade lymphomas, CHOP-based protocols are typically advised as first line therapy and provide the best response rates (80-95%) and treatment outcomes. At this time, long term maintenance chemotherapy does not appear to improve remission times. Additionally, dogs that do not receive maintenance therapy appear to be more likely to achieve a second remission following relapse. Several studies suggest that inclusion of L-asparaginase in the protocol does not significantly improve outcome (remission rates or duration of remission). In the author’s practice, the decision to use L-asparaginase is made on a case-by-case basis and typically reserved for particular situations (ex. sick patient, cytopenic, rescue, etc.). Individual response and remission durations vary depending on prognostic factors. Overall median survival times are 12-14 months with approximately 20-25% of dogs alive at 2 years. Alternative protocols are offered if clients need less costly or more convenient options.

Rescue chemotherapy is associated with lower response rates and shorter remission times. Chemotherapy agents that are commonly used in the rescue setting include lomustine (CCNU), doxorubicin, mitoxantrone, MOPP (mustargen, vincristine, procarbazine and prednisone), actinomycin-D, and dacarbazine (DTIC).

Novel treatment options
Monoclonal Antibodies (Mab): Outcome improvements in people with non-Hodgkin’s lymphoma have been due in large part to Mab therapies such as rituximab (anti-CD20 antibody used to treat B-cell lymphomas). However, rituximab is not effective in dogs. Currently, clinical studies are ongoing to evaluate two conditionally approved monoclonal antibodies (Aratana Therapeutics) for use in the treatment of canine lymphoma. These promising canine-specific antibodies are directed against CD20 (AT-004) for B-cell lymphoma and CD52 (AT-005) for T-cell lymphoma.

Bone marrow/ stem cell transplantation
Ablative total body irradiation and/or chemotherapy combined with bone marrow or stem cell transplantation is available for dogs with lymphoma. However, these treatments are not widely accessible, are costly, and are associated with increased morbidity in dogs undergoing treatment. While these treatments present a potential for increased cure rates, results of a large number of treated cases have yet to be reported.

Adoptive T cell therapy
Expanded autologous T cells infused after CHOP chemotherapy has been shown to significantly improve overall and disease free survival in a small number of dogs with B cell lymphoma. While quite promising, this therapy is currently available to client-owned dogs only through clinical trials.

Prognosis
Widely accepted negative prognostic factors include T cell immunophenotype (for multicentric lymphoma), substage b (sick), prior treatment with prednisone, and certain anatomic sites (cranial mediastinal involvement, primary diffuse cutaneous, GI, hepatosplenic, and primary CNS). Recently, it has been shown that B-cell lymphomas expressing low levels of class II MHC or lower than normal levels of B5 antigen also had a poorer prognosis. Presence of anemia is also associated with a worse prognosis. Alternatively, it appears that dogs with indolent lymphoma experience prolonged survival times.
Mast Cell Tumors: The Good, the Bad, and the Ugly

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This presentation will cover a general review of canine mast cell tumors (MCTs) and the range of biologic and clinical behavior seen with this tumor. Using case examples, we will concentrate on best practice for diagnosis, staging, and treatment as well as a practical, patient-focused approach to considering options and choosing a treatment plan.

Mast cell tumors are one of the most common cutaneous tumors in the dog. Biologic behavior is variable and clinical outcome is best predicted by histologic grade. Grade I tumors are usually well differentiated, rarely metastasize and are associated with an excellent outcome. Grade II tumors are locally invasive, may spread to local lymph nodes, and uncommonly spread throughout the body. A population of intermediate grade (Patnaik grade II) MCTs appear to follow a more malignant course, spreading locally and to distant sites. Additional factors are often considered in attempt to predict the behavior of grade II tumors. Grade III tumors are usually anaplastic and locally aggressive, with a high rate of metastasis. These tumors are not cured typically, but many dogs can have extended remissions if tumors are caught early and treated aggressively. In practice, deciphering which MCTs will behave aggressively can be difficult, making prognosis and optimal treatment challenging to predict. Consideration of a number of clinical (tumor size, clinical signs, etc.) and histologic factors (mitotic index, c-kit, etc.) can be used to help the clinician best present to and guide clients through a wide range of diagnostic and treatment options.

Diagnosis and staging

In most cases, MCTs can be easily diagnosed via fine needle aspirate and cytology with the rapid hematologic-type stains used in most practices. A small percentage of MCTs may have poorly staining granules, in which case a Wright-Giemsa or toluidine blue stain may be necessary. If histopathology is required for diagnosis, careful consideration of tumor location, size, and clinical factors is needed to plan for biopsy. When possible, wide excisional biopsy is preferred and incisional biopsy is uncommonly pursued in the author’s practice.

Staging is important in the clinical evaluation of canine MCT patients; however, what constitutes adequate staging is controversial. In select cases, an extensive work-up may not be necessary. Generally speaking, a minimum database (complete blood count serum biochemistry profile) and regional lymph node cytology are recommended for all dogs with MCT. These diagnostics are typically inexpensive and quick to perform and are likely sufficient for cases where the tumor is amenable to wide surgical excision and no negative prognostic factors are present. Histologic assessment of a regional lymph node may be required for definitive diagnosis of regional metastasis if cytology is suspicious but not definitive for metastatic disease. If the tumor is in an undesirable surgical location or if negative prognostic factors exist, further staging with abdominal ultrasound is advised. Abdominal ultrasound is non-invasive and allows evaluation of spleen, liver, and intra-abdominal lymph nodes for metastatic disease. Fine needle aspirate of the spleen and liver are always advised if the organs look abnormal. Several studies have suggested that FNA of the spleen and liver is warranted in the case of clinically or histopathologically aggressive disease even if they appear normal on ultrasound. In the author’s practice, splenic aspirate is strongly advised for any high grade II or III tumor or in the case of concerning clinical behavior (see prognostic factors). Thoracic radiographs rarely reveal metastasis. However, it is reasonable to pursue this as a pre-anesthetic screening and to rule out other unrelated disease processes prior to a surgical procedure. Bone marrow aspirate is rarely indicated.

Prognostic factors

Grade

Histologic grade is considered the most consistent prognostic factor available for canine MCT but should be interpreted in light of other prognostic factors when making treatment decisions. Histopathologic grading is complicated by interobserver variation among pathologists. Currently, two forms of grading are reported in clinical practice. The most commonly utilized grading system is the Patnaik grading system (low- grade I, intermediate- grade II, high- grade III). More recently, a 2-tier histologic grading system (low, high) has been introduced for canine MCTs. The second system was developed in an attempt to compensate for some of the weaknesses of the Patnaik system. However, further validation is needed to determine if this is truly better at predicting behavior and clinical outcome.
Proliferation indices
Mitotic index (MI) is a strong predictor of overall survival in dogs. Using a cutoff of 5/10 high powered fields, dogs with a low MI (<5) had a median survival time of 80 months compared to 3 months for dogs with a high MI (>5). It is advisable that any tumor with a high MI is staged and treated as an aggressive MCT in practice.

Other markers of proliferation that have been evaluated include Ki67 (a protein in the nucleus that correlates with cell proliferation), AGNORs (argyrophilic nucleolar organizer regions), and PCNA. These require the use of special stains and are often included in the MCT prognostic panel. Interpretation of this panel can often be confusing for clinicians. At this point, it appears that Ki67 is most useful clinically as a prognostic factor for intermediate grade tumors to help predict expected survival times when the clinical picture remains confusing based on other factors.

C-Kit
KIT (a receptor tyrosine kinase) dysregulation has been implicated in the pathogenesis of MCT development and evaluated as a prognostic factor. While KIT staining patterns (cytoplasmic localization) may be associated with dysregulation and prognosis, clinical application of this as a prognostic factor remains challenging. Alternatively, the presence of c-kit activating mutations is strongly associated with a higher rate of local recurrence, metastasis, and death from disease and should be considered a poor prognostic indicator.

Tumor location
Some tumor locations may differ in behavior and prognosis. Subcutaneous tumors may have a better prognosis. Mucous membrane sites, subungual, and visceral tumors are associated with a worse prognosis. Conjunctival tumors and those of the eyelid margin may be an exception with studies showing prolonged survival after surgery alone. Perioral and muzzle MCTs have an increased risk of locoregional metastasis yet prolonged median survival times despite the higher rate of lymph node metastasis. Scrotal and preputial tumors may be associated with a worse prognosis but this remains controversial.

Clinical stage
Higher stage disease is associated with a worse prognosis. The effect of lymph node metastasis on outcome may be dependent on grade of the primary tumor and how the lymph node is treated. Thus, clinical judgment is important. Multiple tumors may not negatively affect prognosis.

Other factors
Local recurrence, systemic and local clinical signs, growth rate, and tumor size have all been correlated with prognosis and should be considered in the overall evaluation of a patient’s tumor.

Treatment options
Primary therapy
Wide surgical excision is the primary treatment of choice for tumors localized to the skin and subcutaneous tissues. Adequate tissue margins may be related to grade; however, grade is often unknown prior to therapy. At least 2-3 cm lateral margins and one tissue plane deep is generally recommended; 2 cm margins are likely adequate for grade I and II tumors. One study found no local recurrence at 2 years for primarily low to intermediate grade tumors removed with a lateral histologic margin of >10 mm and a deep histologic margin of >4 mm. However, histologic margin size may not accurately reflect margin size at surgery. Histopathology is advised for every tumor to determine grade and evaluate margins. The majority of low and intermediate grade tumors are cured with adequate surgical excision. Occasionally, external beam radiation therapy (RT) may be used as a primary treatment in cases of non-resectable tumors. Approaching the dog with multiple mast cell tumors can be challenging and primary therapy should be considered on a case by case basis.

Adjuvant local therapy
Adjuvant local therapy should be discussed with pet owners when adequate margins cannot be achieved due to location or histologic assessment reveals incomplete or narrow excision. Unfortunately, confusion exists regarding which tumors require additional treatment due to varied reports of local recurrence rate in incompletely and narrowly resected tumors (ranging anywhere from about 12-60%). When local therapy is being considered, grade, proliferation indices and c-kit status may be helpful in determining which cases would benefit. The implication of regrowth based on location may also play a factor in discussion with owners regarding the importance of adjuvant therapy. Standard of care options include primary re-excision and radiation therapy, both of which have been found to reduce local recurrence rates and increase survival times. MCTs are radiosensitive and 75-96% of dogs will have a local cure with adjuvant radiation therapy. An alternative option is electrochemotherapy (when available) which shows initial promise in improving local control for incompletely removed tumors.

Systemic therapy
Chemotherapy or tyrosine kinase inhibitors (TKIs) should be offered following excision of tumors in dogs with poor prognostic indicators (grade III, high mitotic index, metastasis, poor location, etc.). High grade and metastatic mast cell tumors are unlikely to be cured, but adjuvant therapy may improve disease free intervals and survival times. Vinblastine and lomustine are commonly used traditional chemotherapy agents. Response rates range from 11-64% when used against bulky disease; however, chemotherapy is more
successful against microscopic disease. A variety of chemotherapy protocols exist. A combination vinblastine/prednisone protocol is preferred as a first-line protocol for adjuvant therapy in the author’s practice (weekly therapy for 4 treatments and then biweekly therapy for 4 treatments). If the initial vinblastine dose is well tolerated (2 mg/m2), dose escalations (increases of 0.25 mg/m2 at a time up to 3.5 mg/m2) should be considered in an attempt to improve efficacy. Lomustine (CCNU) is typically dosed every 2-3 weeks and requires close monitoring due to potential for myelosuppression and hepatotoxicity. Denamarin is recommended as supportive therapy for any dog treated with lomustine. Paclitaxel (Paccal Vet) has also recently been evaluated and appears to be safe and clinically effective for gross disease (complete or partial response 59%). However, the role of this agent in the adjuvant setting has not yet been defined. Metronomic chlorambucil may also be a consideration in cases where dogs have failed other therapies or a lower cost alternative is desired.

Toceranib phosphate (Palladia) and masitinib (Kinavet) are orally administered TKIs that have efficacy against gross disease. While these drugs can be considered as adjuvant treatment, there is no data currently to define the efficacy of TKIs alone in the adjuvant setting. In the author’s practice, toceranib is discussed as an option for primary adjuvant therapy in cases when an owner declines intravenous treatment for their pet or subsequent to traditional chemotherapy when the presence of a c-kit mutation is known. In the treatment of bulky disease, Toceranib has a response rate of about 40% (~60% if stable disease is included). While dogs with KIT mutations were more likely to have a response than those without (69% vs. 37%), routine testing prior to toceranib therapy is probably not indicated for bulky disease as tumor response will guide therapy. Adverse effects include GI toxicity, mild to moderate leukopenia, and occasional muscle pain or mild PLN. Tolerability of toceranib improves when doses lower than the label dosage are used (2.5-2.75 mg/kg EOD or M,W,F). Combination of toceranib with vinblastine chemotherapy and palliative radiation therapy has also been studied.

Masitinib is conditionally approved for the treatment of nonresectable grade II or III cutaneous MCTs as a first-line therapy. Treatment with masitinib (12.5 mg/kg daily) has been shown to improve time to progression and survival rates at 12 and 24 months for dogs harboring activating c-kit mutations. Thus, this drug can provide the potential for long-term disease stabilization in some dogs. Adverse effects include mild GI toxicity, mild myelosuppression, occasionally PLN, and rarely hemolytic anemia. An appropriate monitoring schedule is important when treatment with oral TKIs is employed. When significant adverse effects are noted, treatment is typically discontinued for a period of time. In the author’s experience, it can often be restarted at a lower dose.

**Ancillary therapy**

Histamine blockers (H1 and H2) are indicated for cases when gross disease is present, either preoperatively or in the palliative setting for nonresectable masses/ metastatic disease. Diphenhydramine (2 mg/kg BID-TID) and famotidine (0.5 mg/kg QD-BID) are common choices.

Clinical management of mast cell tumors can be challenging due to the wide range of biologic behavior. Although many cases are cured with adequate local therapy, the use of prognostic indicators discussed can help guide the clinician in determining which tumors are more likely to behave aggressively, and thus, become life-threatening for the dog. When clear poor prognostic factors exist, complete staging and adjuvant therapy is strongly advised. However, uncertainty regarding prognosis may remain in some cases despite our best efforts to define tumor behavior. This highlights the importance of owner education and clinical judgment in selecting appropriate diagnostic and therapeutic options.
Transitional cell and prostate carcinoma continue to be problematic diseases in our canine patients. Tumors are often locally advanced at diagnosis and the location of disease frequently limits surgical options and results in dysuria or obstruction of the urinary tract. Additionally, as advancements in primary tumor control are made, the rate and impact of distant metastases becomes greater. Despite these challenges, treatment options are available that may afford dogs improved quality of life and extended survival time.

Transitional cell carcinoma (TCC) is the most common tumor of the urinary bladder and affects tens of thousands of dogs each year. Risk factors for development of TCC include both heritable genetic factors and environmental exposures. Breeds at an increased risk of developing TCC include Scottish Terriers Eskimo dogs, Shetland Sheepdogs, West Highland White Terriers, Keeshonds, Samoyeds, and Beagles. Owners of such breeds should be educated on the risk of TCC and informed of concerning clinical signs related to the urinary tract. Prostatic cancer may be either TCC or prostatic carcinoma (PC). Prostatic carcinomas are less common, representing less than 1% of canine tumors. The etiology of prostatic carcinoma is unknown although high grade prostatic intraepithelial neoplasia (PIN) has been detected in dogs with and without prostatic carcinoma. Breeds at an increased risk include Bouvier des Flandres, Doberman pinscher, Shetland sheepdog, Scottish terrier, beagle, miniature poodle, German shorthaired pointer, Airedale, and Norwegian elkhound. The risk of both TCC and prostatic adenocarcinoma may be increased in neutered dogs. Both TCC and prostatic carcinoma are of particular interest due to similarities between dogs and humans and the potential for translation of research between species.

Presentation and diagnosis
Dogs with both TCC and prostate carcinoma commonly present with hematuria, stranguria and pollakyuria. In addition, tenesmus and dyschezia may occur secondary to prostate tumors or enlarged regional lymph nodes. Since these tumors predispose dogs to bacterial infections of the urinary tract, temporary improvement or resolution of clinical signs may occur with antibiotic therapy. When evaluating dogs with signs related to the urinary tract, neoplasia should be considered and further investigation pursued if no bacterial infection is present, response to therapy is transient or incomplete, or if the breed is at high risk for TCC or prostatic carcinoma. Clinical signs of local invasion and distant metastatic disease may also be present.

Evaluation of dogs with suspected TCC or prostate carcinoma often begins with a thorough physical examination including a rectal exam, urinalysis, and imaging of the abdomen. Thickening and/or a mass of the bladder wall or urinary tract or an enlarged, irregular prostate increases suspicion for TCC or prostatic carcinoma, respectively. Finding abnormal epithelial cells in urine also increases suspicion. Cytology may be able to provide a diagnosis of carcinoma. However, histopathology is ultimately needed for definitive diagnosis. Samples may be obtained via surgical routes, cystoscopy, traumatic catheterization, FNA or prostatic wash depending on tumor type. Tumor seeding is a risk of percutaneous biopsy/FNA. Samples may be obtained from the primary tumor or metastatic lesions. The value of urine antigen testing for TCC has limited value due to false-positive results.

Staging
Canine TCC is most commonly located in the trigone region of the urinary bladder. Urethral involvement occurs in 56% of dogs and prostatic involvement occurs in 29% of male dogs. Almost 80% are invading the bladder wall (T2) and 20% invade nearby organs (T3). Metastasis is present in about 20% of patients at diagnosis but more than half of dogs at death. Canine prostatic tumors are both locally invasive and have a high rate of regional and distant metastasis (~80%). Lymph node and lungs are the most common sites but skeletal metastasis (especially lumbar vertebrae and pelvis) occurs in 22-42% of patients. Staging should include CBC, serum chemistry profile, urinalysis and culture, thoracic radiographs, abdominal radiographs and/or abdominal ultrasound, +/- urinary tract imaging. Abdominal ultrasound is most often employed to monitor tumor response; however, a standardized protocol is often necessary for this to be accurate.

Treatment
Systemic medical therapy
The mainstay of TCC and prostate carcinoma treatment is systemic medical therapy with chemotherapy, COX inhibitors, and a combination of these. The goal of therapy is remission or disease stabilization and improvement in clinical signs. The typical chemotherapy drugs employed are generally well tolerated and include mitoxantrone, vinblastine, gemcitabine, and platinum agents. Doxorubicin and metronomic chlorambucil have also been investigated for TCC. The best outcomes are seen when COX inhibitors (such as piroxicam) are combined with chemotherapy agents. Mitoxantrone is most commonly used as a first line agent in the author’s practice; vinblastine is also commonly used for TCC. However, many drugs are often employed sequentially throughout the disease...
course guided by tumor and clinical response as well as tolerability of therapy. With combination therapy for TCC, survival times can extend beyond a year with good quality of life. When chemotherapy is declined piroxicam used as a sole agent can provide palliation of clinical signs and a median survival time of about 6-8 months. In cases where piroxicam is not well tolerated, evidence supports deracoxib as a reasonable alternative. For prostate carcinoma, evidence supports a survival benefit with piroxicam or carprofen (~7 vs. 1 month) whereas the benefit of systemic chemotherapy is less clear.

Treatment of secondary urinary tract infections should be guided by culture and sensitivity results to minimize antibacterial resistance.

**Surgery**

Curative intent surgery has a limited role in dogs with TCC due to the typical trigonal location, extensive bladder wall invasion, multifocal lesions, or the presence of metastatic disease. It may be indicated for cytoreduction when small tumors are located away from the trigone; however, it is unclear if cytoreductive surgery augments the benefit of adjuvant therapy. Transurethral approaches (tumor removal via cystoscopy) including laser ablation are possible but less beneficial in canine patients compared to humans since disease is rarely superficial. The benefit of including this type of therapy in a multi-modal approach is unknown but may be considered in select cases when owners are highly motivated. Surgery is also generally palliative for prostatic carcinoma and prostatectomy or electrosurgical transurethral resection is generally recommended only for dogs with early stage disease. Importantly, complications are common and survival benefit is limited; careful case selection is necessary.

Palliative surgical procedures to maintain urine flow are possible for both tumors and include prepubic cystotomy catheters and placement of urethral stents. Placement of urethral stents is preferred since there are no external components or owner maintenance. Complications can occur and the median survival time after stent placement is limited (about 1-2 months) but owners are generally satisfied with the outcome.

**Radiation therapy**

The use of radiation therapy (RT) to treat TCC and prostate carcinoma is challenging due to change in bladder location and shape. Because of this, large fields are needed and complications in surrounding normal tissues are common. Advances in RT technology (IM-IGRT/ SRT) may allow more targeted and controlled delivery to local disease and preliminary information shows promise for increased survival times when combined with chemotherapy and NSAIDs. Currently, the benefit of adding coarse-fraction external beam RT to systemic therapy is questionable but there may be a place for palliation of urinary tract obstruction or clinical signs relating to local disease or skeletal metastases in select cases.

**Intravesicular therapy for TCC**

Partial remission and stable disease have been documented in dogs treated with chemotherapy delivered directly into the bladder. Significant systemic absorption occurred in some dogs and response was not superior to systemic therapy. However, this treatment may be considered for select cases or dogs that have failed other therapies.

**Emerging therapies**

New strategies currently under investigation include folate targeted therapy, a bladder cancer specific peptide (PLZ4) targeted therapy, and demethylating agents.
Osteosarcoma (OS) is the most common primary bone tumor of dogs, accounting for approximately 85% of malignancies arising in the skeleton. It is a high grade, biologically aggressive neoplasm of mesenchymal origin that closely parallels human OS. It is estimated that 10,000 dogs per year develop OS in the United States. The peak incidence of canine OS occurs primarily in middle-aged to older animals, with a median age of 7 years; although, a bimodal age distribution is reported with a second small peak at 18 to 24 months. Approximately 75% of OS occurs in the appendicular skeleton. Analogous to humans, the metaphysis of long bones is the most common primary location, with the forelimbs affected twice as commonly as the rear limbs. The most frequent anatomical sites are the distal radius (35%) and proximal humerus (18%) followed by the distal femur, proximal tibia, and distal tibia. Osteosarcoma is typically a cancer of large and giant breed dogs with only 5% of tumors occurring in dogs weighing less than 15 kilograms, the majority of which originate in the axial skeleton. The precise etiology of canine OS is unknown; however, likely include genetic predispositions, exposure to ionizing radiation and sustained microtrauma (e.g., repetitive weight bearing stresses, metallic implants) as possible risk factors in dogs for OS development.

Current local therapies
The local effects of OS which result in excessive and pathologic bone resorption have a significant impact on patient mobility and quality of life, and thus, addressing the primary tumor is one of the major goals of OS therapy. Effective local therapy for canine OS necessitates the removal or killing of malignant osteoblasts and various treatment modalities have been employed to this end. The following discussion will focus on the benefits and limitations of current local therapies for canine OS.

Surgery
Surgical resection of the primary tumor followed by either a platinum- or doxorubicin-based chemotherapy protocol generally results in the longest median survival times, with a median survival time approximately 275-300 days. For appendicular OS, surgical options include amputation or limb-sparing procedures. High amputation of the affected limb is the standard local treatment, and most dogs function well after this procedure, retaining good mobility and quality of life. An advantage of amputation is that it usually ensures complete local tumor removal. However, in cases where severe preexisting conditions exist, such as obesity, orthopedic or neurological disease, limb amputation may not be a viable option.

In select cases, a limb-sparing surgery may be an alternative to amputation, in which the affected bone is resected and replaced by a normal bone allograft, metal endoprosthesis, or other less common methods. Overall, outcome has been acceptable following limb salvage, with approximately 80% of dogs experiencing good to excellent limb function; however, even in the hands of the most experienced surgeons, there remains a risk for relatively high rates of local complications including recurrent disease, construct failure, and post-operative infection.

Local palliative strategies
Standard-of-care therapy, defined as the treatment option that results in the longest median survival times, is surgical resection of the primary tumor followed by 3 to 6 cycles of either a platinum- or doxorubicin-based chemotherapy protocol. Unfortunately, not all dogs with OS are considered good candidates for amputation, and alternative palliative treatment options for controlling bone pain should be considered. Reported survival times for canine patients treated with palliative intent therapy ranges from 3 to 10 months. With the commercial boom of pharmacologic pain medications approved for use in dogs and cats, the general practitioner is now offered a plethora of novel analgesics that may provide some moderate relief for chronic osteolytic pain associated with appendicular OS. In addition to the administration of conventional nonsteroidal anti-inflammatory drugs (NSAIDs) or the application of transdermal opioids, newer analgesics such as tramadol and gabapentin may also alleviate cancer-related pain.

Palliative radiation therapy (RT)
Palliative RT is effective for the management of malignant bone pain, and typically involves administering coarse fractions of 8 to 10 Gy of megavoltage irradiation, in 3 treatments at 0, 7 and 21 days. Palliative RT reportedly improves limb function and quality of life in about 75% of patients, and for a median of 2-3 months duration. The concurrent administration of systemic chemotherapy along with palliative RT appears to enhance analgesic response rates and durations, and should be highly recommended.

Radiopharmaceuticals
The use of a therapeutic radionuclide called \(^{153}\)Samarium-EDTMP has been described for both appendicular and axial OS in dogs, and provided pain relief in many treated patients. By means of delivery concentrated radiation doses to the site of active bone remodeling, \(^{153}\)Samarium-EDTMP administration is capable of providing significant and meaningful palliation of bone pain in dogs suffering from appendicular OS. \(^{153}\)Samarium-EDTMP therapy is well tolerated and alleviates osteolytic bone pain in the majority of dogs treated. Side effects associated with treatment include transient decreases in platelet and white blood cell counts.
**Stereotactic radiosurgery (SRS)**

Radiosurgery involves the precise delivery of a single large dose of radiation to a designated tumor target, and has been used for the treatment of brain tumors, as well as, appendicular OS. The use of SRS in dogs with OS can provide pain alleviation, long-term local tumor control and improvement in limb function. Similar to palliative radiation therapy, combining systemic chemotherapy with SRS appears to enhance response rates and durations.

**Aminobisphosphonates**

The pharmaceutical use of aminobisphosphonates is accepted for the treatment of neoplastic bone disorders in human cancer patients. At low concentrations aminobisphosphonates inhibit bone resorption without inhibiting the process of bone mineralization. This results in stabilization and even enhancement of bone mineral density. Bisphosphonates directly inhibit bone resorption by binding to hydroxyapatite crystals, as well as inducing osteoclast apoptosis. In part, pain associated with bone cancers is a direct consequence of malignant bone resorption. Therefore, inhibiting pathologic bone resorption with aminobisphosphonates would theoretically decrease the likelihood of pathologic fracture, as well as alleviate intense bone pain.

Aminobisphosphonates are synthetic analogs of inorganic pyrophosphate (PPi) that were initially utilized in the detergent industry as demineralizing agents, and then for diagnostic purposes in bone scanning, based on their ability to adsorb to bone mineral. The pharmaceutical use of aminobisphosphonates has now gained wide acceptance in human non-neoplastic bone disorders such as osteoporosis and Paget’s disease. In the last decade, aminobisphosphonates have been intensely investigated as novel antineoplastic agents. Currently, several aminobisphosphonates have demonstrated efficacy for treatment of tumor-induced hypercalcemia, multiple myeloma, and metastatic bone diseases.

The effective treatment of bone disorders by aminobisphosphonates is attributed to their differential effect on bone resorption and bone mineralization. At low concentrations aminobisphosphonates inhibit bone resorption without inhibiting the process of bone mineralization. This results in stabilization and even enhancement of bone mineral density. Aminobisphosphonates directly inhibit bone resorption by binding to hydroxyapatite crystals. Once incorporated into the hydroxyapatite matrix of bone, aminobisphosphonates inhibit further calcium and phosphorous mineral dissolution. Perhaps more importantly, aminobisphosphonates impede osteoclast activity and induce osteoclast apoptosis; both mechanisms result in inhibition of bone resorption.

**Systemic therapies**

Chemotherapy agents that have demonstrated efficacy in the treatment of OS include the platinum agents and doxorubicin. While chemotherapy is primarily used in the management of canine OS for the purpose of delaying onset of metastasis, it may also be employed in local therapy as a pretreatment to amputation or limb salvage. In veterinary medicine, studies that evaluated dogs receiving intra-arterial (IA) cisplatin prior to limb spare surgery found that cisplatin IA with or without radiation therapy induced a significantly greater percent tumor necrosis when compared with dogs receiving no pretreatment, and that percent tumor necrosis was strongly predictive of local tumor control.
Hemangiosarcoma (HSA) is a malignant neoplasm which originates from vascular endothelium and accounts for 0.3-2% of all canine cancers. Large breed dogs such as German Shepherd Dogs, Golden Retrievers, and Labrador Retrievers are over represented with a median age at diagnosis of 9-10 years. Most frequently affected primary sites of HSA in these patients include the spleen, skin, and heart (right atrium and auricle). Other less common sites include the liver, lungs, kidney, muscle, oral cavity, bone, and the urinary bladder. Clinical signs can be nonspecific or consist of acute weakness or collapse with corresponding abdominal distension, tachycardia, tachypnea, pale mucus membranes, and weak pulses. These clinical signs are often secondary to acute blood loss into the peritoneal or pericardial cavity.

Standard of care treatment for HSA depends primarily on tumor location but in large part consists of surgery followed by chemotherapy. The chemotherapeutic agent of choice for HSA is Doxorubicin. For strictly dermal HSA, chemotherapy is not necessary following complete surgical removal with adequate margins. However, for the remaining HSA locations surgery alone affords the patient with a median survival time of less than 2 months. Even with the addition of chemotherapy, the majority of patients will succumb to their disease within 4-8 months. Death is usually secondary to metastatic disease via hematogenous spread to the pulmonary parenchyma and intraabdominal dissemination primarily, but also to the skin, bones, and brain.

Pathology and natural behavior
Malignant endothelium serves as the underlying pathology of HSA, and hence HSA can involve any organ requiring nutrition and oxygen via blood circulation. Often dogs presenting for visceral organ HSA will present with signs associated with acute tumor rupture and resultant hemorrhage and hypovolemic shock. Symptomology reflects the hemodynamic instability of these acutely bleeding patients and include lethargy, weakness, collapse, anorexia, mucous membrane pallor, delayed capillary refill time, tachycardia, tachypnea, cardiac arrhythmias, and poor pulse quality. In circumstances where the patient does not experience a life-threatening hemorrhage event, clinical symptoms might recur and take on an episodic pattern. With primary splenic or hepatic HSA, tumor rupture results in abdominal distention and a noticeable fluid wave secondary to hemorrhagic effusion. With primary cardiac HSA, muffled heart sounds, venous congestion, and signs compatible with cardiac tamponade may be noted. Primary subcutaneous and intramuscular HSA, typically occur as large, firm or fluctuant masses. Overlying skin may be ecchymotic and ulcerated.

Diagnosis and staging
Presumptive diagnosis of HSA can be made based upon multiple clinical and physical findings, as well as patient signalment. However, baseline diagnostics which should be considered in any patient with presumed HSA might include the following:

- Complete blood count
  - Anemia: secondary to hemorrhage
  - Schistocytes: red blood cell morphology
  - Thrombocytopenia: immune mediated destruction, splenic sequestration, severe hemorrhage, and/or disseminated intravascular coagulopathy (DIC)
  - Neutrophilic leukocytosis

- Serum chemistry panel
  - Hypoproteinemia: secondary to blood loss
  - Liver enzyme elevations: involvement of hepatic parenchyma
  - Hypoglycemia: rare paraneoplastic syndrome

- Coagulation panel
  - Elevations in clotting times: disseminated intravascular coagulation
  - Defects in both primary and secondary coagulation cascades

- Thoracic radiography
  - Evaluation of overt lung metastases
  - Cardiac involvement with globoid cardiac silhouette
    - Pericardial effusion

- Echocardiography
  - Evaluation of right auricle or atrial mass effects
  - ECG might demonstrate ventricular arrhythmias and electrical alternans

- Abdominal ultrasound
- Evaluate primary abdominal tumor involvement, as well as regional metastases within the visceral organs residing within the peritoneal cavity

- Cytology
  - Considered insensitive for diagnosis given poorly exfoliative nature of sarcomas

- Biopsy
  - Required for definitive diagnosis
  - Diagnostic and therapeutic

**Canine hemangiosarcoma treatment options**

Due to the devastating prognosis for HSA, multiple new therapies outside the realm of surgery and standard doxorubicin administration have been devised and evaluated. These include various alternative chemotherapeutic protocols, intracavitary chemotherapy administration, immune modulation, matrix metalloproteinase inhibitors, antiangiogenic therapy, and tumor vaccines.

Combination chemotherapy protocols with doxorubicin, cyclophosphamide and vincristine (VAC) or doxorubicin and cyclophosphamide (AC) have been evaluated. Unfortunately, the addition of these chemotherapeutic agents to standard treatment with doxorubicin afforded no significant increase in survival times with median survival times of 172 and 179 days respectively. A dose intensified doxorubicin protocol has also been evaluated with doxorubicin being administered every 2 weeks instead of every 3 weeks, however median survival time was not statistically different from that of standard treatment methods. Intraperitoneal administration of liposome encapsulated doxorubicin has been evaluated as the abdomen is a main site of progression of disease and thus it is logical to treat them with a drug that due to its liposome encapsulation and pegylated nature should have a longer half-life in the plasma. Unfortunately, again survival times did not vary significantly from those previously reported.

Tumors require angiogenesis for growth and thus anti-angiogenic drugs have been and are currently being heavily investigated for the use in a multitude of tumors. Minocycline, an antiangiogenic metalloproteinase agent with anticollagenase activity, was evaluated in combination with doxorubicin and cyclophosphamide for treatment of dogs with hemangiosarcoma. Regrettably, the addition of this drug revealed no significant survival advantage with an all too familiar median survival time of 170 days. Additionally continuous low dose chemotherapy with the combination of etoposide, cyclophosphamide, and piroxicam was evaluated in 9 dogs diagnosed with stage II splenic HSA. The goal of this study was to see if this combination of drugs, which targets the tumor neovasculature itself, would improve survival times in contrast to traditional therapy. Survival times of the dogs in this study were comparable to other previously established studies and known survival times.

Immune modulation via administration of a liposome-encapsulated muramyl tripeptide-phosphatidylethanolamine (L-MTP-PE), a synthetic derivative of a component of bacterial cell walls, in combination with chemotherapy afforded the longest survival times of all above novel treatment options. L-MTP-PE activates macrophages and monocytes leading to increased tumoricidal activity. While the survival time of dogs treated with this therapy (277 days) is the longest seen in the literature, there were an equivalent number of dogs with stage I as compared with stage II and this likely biased the results. Further study with a larger sample size of stage II HSA would be interesting but, studies have not been pursued further due to the lack of availability of this product to the veterinary community at this time, due to high cost and limited supply.

As immune modulation seems to be one of limited treatment options which may improve overall survival times in dogs with hemangiosarcoma, a vaccine prepared from lysates of allogeneic canine HSA cell lines was evaluated in 28 dogs. Vaccines were given intraperitoneally once per week for 5 weeks then once monthly for three additional treatments. The vaccine was often given in combination with standard doxorubicin doses. Of the 6 dogs evaluated for antibody production, all 6 mounted a strong response to the vaccine and side effects were minimal. No statistically significant improvement in survival time was seen.
The nasal cavity is comprised of various cell types which provide secretory and structural functions. As such, the malignant transformation of cells within the nasal passage often gives rise to tumors of epithelial or mesenchymal origin. Primary tumors of the nasal cavity account for approximately 1-2% of all neoplasms in dogs. In the majority of cases, nasal neoplasms are histologically malignant and are capable of regionally invasive and expansive growth patterns which invade into the nasal passages, frontal sinuses, and cranial vault cavity. With lower frequency, nasal tumors can eventually spread to regional and distant sites, which include the draining lymph nodes and lungs, respectively. Histologically, carcinomas are more common than sarcomas, and account for 60% to 78% of all nasal tumors. In the majority of descriptive studies, adenocarcinoma was most common (45%) histologic subtype, followed by squamous cell carcinoma (20%), chondrosarcoma (14%), undifferentiated or anaplastic carcinoma (11%), and unspecified carcinoma (10%). Nasal tumors are less commonly diagnosed in felines than dogs, but nonetheless are malignant in greater than 90% of affected cats. Lymphoma and carcinoma are the most common types of nasal tumor diagnosed in cats.

Pathology and clinical symptoms
Nasal tumors are characterized by rapid and progressive local tissue invasion, but a low metastatic rate. Humane euthanasia of dogs diagnosed with nasal tumors is the result of local tumor progression rather than development of metastatic disease. Although the incidence of regional and distant metastases for nasal tumors is relatively low (less than 30%), the histologic subtype may influence both localized and metastatic behaviors. Carcinomas may be subcategorized as being less or more aggressive. In general, highly undifferentiated and anaplastic carcinomas, as well as squamous cell carcinomas, prove more difficult to treat in dogs. Consequently, dogs suffering from anaplastic carcinoma or squamous cell carcinoma generally survive for shorter periods of time in comparison with dogs diagnosed with nasal adenocarcinoma. Median survival time of dogs with aggressive carcinomas and less aggressive carcinomas has been reported to be 7.2 and 11.9 months, respectively. Nasal tumors arising from mesenchymal origin, in particular chondrosarcoma appear to be less aggressive, with dogs achieving median survival durations approaching 2 years.

Given their growth within the nasal passage, many dogs remain asymptomatic for many months until tumor burden is substantial and occludes airflow or erodes through bone and blood vessels. The most common clinical signs seen in animals with nasal tumors include epistaxis, facial asymmetry, non-hemorrhagic nasal discharge, and sneezing. Physical examination findings may include stertorous breathing, enlarged mandibular lymph nodes, neurologic signs, decreased retropulsion of the eye(s), exophthalmus, ocular discharge resulting from nasolacrimal duct obstruction, and overt facial bone deformation. Although the presence of facial deformity is highly suggestive of a cancerous process, other differential diagnoses should include fungal or bacterial rhinitis, foreign body, trauma, developmental abnormalities, and dental pathology. Epistaxis is a common clinical sign in dogs and cats diagnosed with nasal tumors. The majority of dogs (~85%) with nasal neoplasia will manifest with frank hemorrhagic or serosanguinous nasal discharge, which correlates with a poorer prognosis.

Diagnosis and staging
Presumptive diagnosis of nasal passage cancer can be made based upon multiple clinical and physical findings, as well as patient signalment. However, baseline diagnostics which should be considered in any patient with presumed nasal tumor might include the following:

- Complete blood count
  - Anemia: secondary to hemorrhage
    - Uncommon to have severe blood loss
- Serum chemistry panel
  - Usually unremarkable
- Coagulation panel and buccal mucosal bleeding time
  - Rule out systemic coagulopathy for epistaxis
- Systemic blood pressure and fundoscopic examination
  - Rule out systemic hypertension for epistaxis
- Regional lymph node aspiration and cytology
  - Determine if malignant population of cells have regionally spread to dependent lymph node (uncommon)
- Thoracic radiography
  - Determine if malignant population of cells have distantly metastases to the pulmonary parenchyma (uncommon)
• **Skull radiography**
  - Evaluate for asymmetry
    - Filling defect on affected side, contrary to findings with fungal rhinitis (lysis)
    - Insensitive measure for identifying nasal pathology
• **Computed tomography**
  - Identification of mass effect
  - Identification of associated bony lysis and proliferation
  - Highly sensitive imaging modality for detecting nasal pathology
• **Cytology**
  - Feasibility is dependent upon location of primary tumor and ability to sample with needle
• **Biopsy**
  - Preferred method of definitive diagnosis
  - Several different methodologies for sample retrieval
    - Blind intranasal sample collection with forceps or curette
    - Rhinoscopic assisted biopsy (space and visual constraints)
    - Otoscopic transilluminator guided biopsy for rostral lesions
    - Open rhinotomy biopsy (not generally performed, high morbidity)
    - Hydropulsion with nasal flushing and dislodgment of tissue fragments

**Nasal tumor treatment options**

**Radiation therapy**
The delivery of ionizing radiation with megavoltage therapy machines have been used for curative intent and palliative therapy for nasal tumors. Radiation therapy has the advantage of treating the entire nasal cavity, including bone, and its use has been associated with the greatest improvement in survival when compared to non-radiation treatment options. Despite the inability to cure the majority of dogs treated with radiation therapy, many patients enjoy relatively long durations of local disease control, improved clinical symptoms, and increased quality of life scores.

**Definitive treatment**
Radiation therapy with curative intent has been previously described as a sole treatment option of nasal tumors in dogs. Conventional protocols require the administration of small fractions (3-4.2 Gy) repeatedly (10-19 treatments) on a daily or every other day basis for a total radiation dosage of 40 to 57 Gy. With the advancement in radiation technologies, it has become possible to “sculp” the radiation field to the contours of tumors within the nasal passages, thereby minimizing adverse effects to surrounding normal tissues. Advanced radiation units which allow for conformal targeting of tumor tissues include stereotactic radiosurgery and intensity-modulated radiation therapy. The use of stereotactic radiosurgery and intensity-modulated radiation therapy have not definitively proven improvements in survival time for treated patients, however, their remarkable precision with depositing radiation lessens undesirable acute and late radiation side effects, thereby attenuating unnecessary patient treatment-related morbidity.

**Radiation therapy with surgery**
Some debate exists over the utility of combining radiation therapy with surgical resection for the management of canine nasal tumors. For the majority of patients diagnosed with nasal cancer, cytoreductive surgery is not deemed possible or favorable for improved outcome, given the highly invasive properties of nasal tumors and the confined anatomic region of involvement. The vast majority of studies do not demonstrate any added benefit when surgery is combined with radiation therapy for the localized management of nasal tumors. However, in patients with small and ventrally confined nasal tumors which can be surgically approached through the soft palate, the combination of radiation therapy with surgery might be an option which improves overall disease control durations without and unacceptable increase in patient morbidity.

**Radiation therapy with chemotherapy**
Systemic chemotherapy has been classically indicated for the treatment of disseminated metastatic disease. However, the achievement of high local concentrations within the primary tumor microenvironment may allow for systemic chemotherapy to exert direct anticancer activities, which may contribute to the localized control of various cancers, including nasal tumors. However, given the paramount role of ionizing radiation for the management of nasal tumors, the inclusion of systemic chemotherapy for the treatment of nasal cancer has been as a radiosensitizer, rather than a direct cytotoxic agent. Various small descriptive studies have been conducted in veterinary medicine to support the potential benefit of combining radiation therapy with a radiosensitizing chemotherapeutic agent such as cisplatin or carboplatin. Collectively, the anecdotal evidence would suggest the feasibility of combining platinum agents with radiation therapy, without unacceptable toxicity; however, historical studies have been inadequately designed to determine if any therapeutic benefit is achieved with this rational combination approach.
Palliative radiation therapy

The goal of palliative radiation therapy is to reduce tumor burden and improve quality of life. Most commonly, palliative radiation protocols deliver large fractions of radiation (6-8 Gy fractions) once to twice weekly for a total of 4-6 treatments. This palliative dosing strategy typically ameliorates clinical symptoms associated with disease, however is insufficient to dramatically reduce tumor burden for prolonged periods of time.
Plasma Cell Tumors:
The Interesting Cancer
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The plasma cell is of lymphoid lineage and specifically a terminally differentiated B-lymphocyte. Based upon its origin, plasma cells have the capacity to produce immunoglobulins, which under physiologic conditions preserve immune competence and protect the host organism from extracellular pathogens. Like any normal cell, malignant transformation can occur and give rise to a cancerous population of plasma cells. There are a number of disease conditions comprised of malignant plasma cells and include multiple myeloma (MM), solitary osseous plasmacytoma (SOP), extramedullary plasmacytoma, and in felines a syndrome known as myeloma-related disorder in which cancerous plasma cells infiltrate visceral organs.

In dogs and cats, the cause of plasma cell cancers is largely undetermined; however, given the role of plasma cells in mucosal immunity, there has been some speculation that chronic antigen stimulation might promote the development of these malignancies. Anecdotally, there is some support for this speculation would be the common anatomic regions affected by plasma cell tumors including the interdigital regions, oral cavity, and gastrointestinal tract, which are systems commonly in contact with environmental antigens. Multiple myeloma is the most common plasma cell malignancies to cause systemic signs of illness, and will be the focus of this review.

Pathology and natural behavior

Clonal origin plasma cell proliferating systemically (usually within multiple bone marrow sites) producing immunoglobulin. Neoplastic cell of origin is the terminally differentiated B-lymphocyte (plasma cell), which normal function is to produce specific immunoglobulin to recognize pathogenic antigens (neutralization, agglutination, and opsonization).

Physical appearance of the cells varies markedly between patients (can be very bizarre). Immunoglobulin produced in excess (a.k.a. M component or paraprotein), usually complete immunoglobulin but sometimes just a portion of the molecule (light chains only = Bence Jones protein, heavy chains only = heavy chain disease). Remember that fully function immunoglobulin is a heterodimer (2 light chains binding with 2 heavy chains).

The M component is usually IgG or IgA. If the M component is IgM, it is called macroglobulinemia or Waldenstrom’s macroglobulinemia. Cryoglobulins are paraproteins that precipitate at temperatures <37º C, causing cutaneous lesions in extremities (colder areas). The M component can cause multiple problems for the patient. Infection is a major problem, and arises because excessive production of the paraprotein inhibits production of normal immunoglobulin, patients are considered to be ‘immunologic cripples’. Hyperviscosity syndrome arises secondary to the massive amounts of paraprotein present. The severity of the serum hyperviscosity is related to the type, size, shape and concentration of the M component. Hyperviscosity necessitates increased perfusion pressure to maintain vascular flow and also causes hypervolemia both of which increase the cardiac workload and can cause cardiomegaly. Combine this with myocardial hypoxia secondary to poor vascular perfusion and heart failure may result. Neurologic abnormalities including lethargy, ataxia and seizures occur because of poor perfusion. Bleeding problems (hemorrhagic diathesis) occur in about 1/3 of dogs with myeloma.

Bleeding may be caused by M-components 1) inhibiting platelet aggregation and release of activating factors 2) adsorbing minor clotting proteins 3) generating abnormal fibrin polymerization 4) producing a functional decrease in calcium. Thrombocytopenia will play a role in bleeding also. Renal failure can be caused by the high protein content in the glomerular filtrate, as a consequence of tubular obstruction by proteinaceous casts, amyloidosis, ascending pyelonephritis, tumor infiltration, and decreased perfusion secondary to hyperviscosity. Retinal lesions are another sequelae of hyperviscosity. Changes include dilated and tortuous retinal vessels and retinal hemorrhages.
History and physical examination

Animals may present with nonspecific signs of weakness, PU/PD, pain, lethargy, or inappetance. More specific signs include epistaxis and gingival bleeding or signs due to a compressive lesion or fracture. Rarely, dogs will present with neurologic signs. PE is often nonspecific, try to localize pain if possible (palpate along limbs and spine).

- CBC may reveal anemia (secondary to either anemia of chronic disease, blood loss, or red blood cell destruction secondary to high serum viscosity, or myelophthisis).
  - Neutropenia and thrombocytopenia will be seen first if myelophthisis is present.
  - Thrombocytopenia may also be immune-mediated.
- Serum chemistry will show hyperglobulinemia (> 90%) and hypercalcemia (15 - 20%). Renal failure is seen in 33-50% of dogs (secondary to poor perfusion).
- Serum electrophoresis should be performed to characterize the globulinemia as monoclonal or polyclonal.
- Urine can be evaluated for Bence-Jones proteins. This requires heat precipitation or electrophoresis, as commercial urine dipstick methods will not detect these proteins.
- Bone marrow aspirate reveals > 10% infiltration of plasma cells.
- Survey skeletal radiographs evaluating specifically for osteolytic (punched out) lesions. Sites most commonly affected include the vertebral bodies, ribs, pelvis, skull and proximal long bones.
  - Biopsy or fine needle aspirate of osteolytic lesions may be needed for diagnosis.
- Demonstration of two or more of the following strongly supports the diagnosis:
  1. Bone marrow plasmacytosis
  2. Presence of osteolytic bone lesions (No osteoproliferation)
  3. Hyperglobulinemia with monoclonal gammopathy
  4. Bence-Jones proteinuria

Prognostic factors

Negative prognostic factors are somewhat intuitive and include:

- Hypercalcemia
- Bence-Jones proteinuria
- Extensive osteolytic bone lesions
- Renal Failure
- Severe hyperviscosity

Treatments options and long term prognosis

- Fluid therapy
  - Intravenous fluid therapy is often needed initially to correct dehydration, improve cardiovascular status, and manage hypercalcemia and azotemia. Treatment with isotonic saline solution is preferred over other fluids in the initial management of hypercalcemic patients.
- Antibiotics
  - Antibiotic therapy may be needed to treat concurrent infections, such as urinary tract infection or bacterial pyoderma, as these can progress to life-threatening infections if left untreated.
- Palliative radiation
  - Neoplastic plasma cells are sensitive to irradiation, and radiation therapy is a highly effective palliative treatment for MM since it can relieve discomfort and quickly decrease the tumor burden. Indications for radiation therapy include painful bone lesions, spinal cord compression, pathologic fracture (after fracture stabilization), or a large soft tissue mass.
- Bisphosphonates
  - Bisphosphonates, such as pamidronate, may be useful in managing hypercalcemia as well as decreasing osteoclastic bone resorption and bone pain. The recommended dose of pamidronate is 1 to 2 mg/kg given intravenously in dogs and, anecdotally, 1 mg/kg given intravenously in cats every 21 to 28 days. Prior to administration, evaluate renal function; dilute the pamidronate in saline solution (amount based on the size of the patient) and administer as a slow infusion over two hours to minimize renal toxicities.
Aminobisphosphonates are an essential component of therapy for MM in people, and their use is associated with significantly reduced skeletal-related events and improved survival in some studies.

- **Analgesics**
  - Dogs and cats with MM may experience moderate to severe pain; treating for this pain is a priority. Pain may be relieved by treating the underlying cancer and providing various analgesic therapies and supportive care.

- **Chemotherapy**
  - Although a cure is unlikely, MM can be a rewarding disease to treat since chemotherapy can greatly extend the quality and duration of life. The chemotherapy drugs most often used are alkylating agents, usually melphalan, combined with corticosteroids. However, eventual relapse during therapy is anticipated.
  - The overall response rate for dogs treated with melphalan and prednisone chemotherapy is 92%, with 43% of dogs achieving a complete response and 49% achieving a partial response. The median survival time of dogs treated with this drug combination is 540 days, which is significantly longer than the survival time of 220 days in dogs treated with prednisone alone.
Glucoma is a complicated and often frustrating cause of vision loss in small animals. The pathogenesis of glaucoma is only partially understood, however the end result is loss of retinal ganglion cell function, axonal destruction in the optic nerve, and vision loss. Because clinical signs of glaucoma have been described in humans without overt increases in intraocular pressure (IOP), and because optic nerve microcirculation and retinal ganglion cell function impairment have been observed before elevations in IOP in Beagle dogs with hereditary glaucoma, elevated IOP is now considered a ‘risk factor’ for glaucoma, not the primary cause. Moreover, glaucoma is considered to be a group of many diseases (rather than one single disease) with a common outcome.

Normal aqueous humor dynamics involves the production of aqueous humor by the nonpigmented epithelial cells of the ciliary body (via active transport, passive diffusion and ultrafiltration), with concurrent drainage from the globe via multiple mechanisms. In the dog and cat, most aqueous humor exits the eye through the iridocorneal angle and trabecular meshwork (‘conventional outflow’), with a smaller volume exiting the globe through uveoscleral vasculature (“unconventional outflow”). To maintain a stable intraocular pressure, the rate of drainage must match the rate of aqueous humor formation. Diurnal variations in intraocular pressure have been observed in most species studied, and in the dog, intraocular pressure tends to decrease mildly with age. A ‘normal’ intraocular pressure in any given patient depends on multiple variables but intraocular pressures in excess of 25-30mmHg in the dog and cat are generally concerning.

Accurate evaluation of intraocular pressure can be difficult due to patient noncompliance or a multitude of other factors. Patient positioning, increased jugular pressure, tonometer used, excessive eyelid manipulation during measurements, corneal thickness and cleanliness of the tonometer have all been identified as factors contributing to erroneous IOP estimation.

In the dog, glaucoma is most commonly diagnosed as a primary disease. Abnormalities in iridocorneal anatomy can be observed on biomicroscopic evaluation (gonioscopy). These visible abnormalities are considered to be linked to microscopic abnormalities in the conventional drainage system as a whole. Dogs with abnormally appearing iridocorneal angles (excessively narrow or closed) are considered ‘goniodysgenic’, and are at risk of bilateral glaucoma in their lifetimes. Primary glaucomas have been classified as either ‘open angle’ or ‘closed angle’ in both human and veterinary medicine. Open angle glaucoma is most common in humans while in the dog the lion’s share of cases are closed angle. The difference is clinically significant, as open angle glaucomas are generally chronic, milder (increases in IOP of a few points are considered significant), and more responsive to medical therapy, while closed angle glaucoma as observed in the dog is generally associated with an acute, marked increase in IOP that is accompanied by pain and acute vision loss. It is also significant in that due to availability of funding, the majority of pharmacologic studies evaluating anti-glaucoma drugs are based on treatment of open angle glaucomas (including veterinary studies, in which a rare colony of Beagles with open angle glaucoma is the target of most pharmacologic medical research). In the cat, a rare form of glaucoma known as Feline Aqueous Humor Misdirection Syndrome (FAHMS) has been described in which changes in the anterior vitreous face result in aqueous humor accumulation in the vitreal chamber (rather than the anterior chamber), resulting in progressive anterior chamber shallowing and elevations in intraocular pressure. Most feline glaucomas, however, are secondary to chronic intraocular inflammation and can be especially difficult to treat given the dearth of effective anti-glaucoma medications in this species.

Common causes of secondary glaucoma include uveitis, intraocular hemorrhage, intraocular surgery, lens instability, retinal detachment, and intraocular neoplasia. The pathogenesis of the secondary glaucomas usually involves either pre-iridal fibrovascular membrane (PIFVM) development (in the cases of uveitis, intraocular hemorrhage, intraocular surgery, lens instability, retinal detachment and occasionally neoplasia), direct obstruction of the conventional outflow system (also in the case of lens instability and neoplasia), or both. PIFVMs develop over the anterior or posterior surface of the iris and grow anteriorly to occlude the iridocorneal angle. There is to date no known treatment available to prevent the development of these membranes in eyes at risk.

Commonly applied medical therapies for glaucoma are outlined below.

### Osmotic agents

Osmotic agents are commonly used in emergency management of glaucoma due to rapid efficacy. They are administered systemically and distributed to extracellular fluids (ie plasma), increasing plasma osmolality. When plasma osmolality exceeds that of the intraocular fluid, water diffuses from the aqueous and vitreous humor down-gradient to plasma, essentially dehydrating the vitreal and aqueous chambers. Mannitol is administered IV at dosages ranging from 1-2 g/kg over 30 minutes. The reduction in IOP generally begins within 30 minutes-1 hour with effects lasting from 6-10 hours. Mannitol is not metabolized and therefore can be administered to diabetic patients. It should be administered through a filter given its propensity to form crystals. Glycerin is easy to administer, inexpensive and does not require intravenous access or special storage. It is administered orally at a dosage of 1-2 g/kg. A reduction in IOP should be observed within an hour of administration and can last as long as 10 hours. Administration may result in vomiting.
Glycerin should NOT be administered to diabetics, as it is metabolized to glucose and will result in hyperglycemia. **Isosorbide** can be administered orally like glycerin but unlike glycerin, will not result in hyperglycemia. The recommended dosage in dogs is 1-1.5 g/kg; efficacy in one report was similar to that of glycerin. Use of hyperosmotic agents is contraindicated in uveitic eyes due to the increased permeability of inflamed eyes. They should not be administered with fluids (and water should be withheld for ~2 hours post-administration). Due to the expected increase in intravascular volume associated with these agents, hyperosmotics should not be administered in patients with significant cardiovascular disease.

**Carbonic anhydrase inhibitors (CAIs)**

Carbonic anhydrase inhibitors inhibit formation of bicarbonate in the ciliary body that is necessary for production of aqueous humor. Commonly used topical agents include dorzolamide (Trusopt®) and brinzolamide (Azopt®). Oral CAIs include methazolamide and acetazolamide. Dorzolamide is available as a generic and is fairly cost effective. Topical CAIs can be administered 2-3 times daily. Maximum efficacy may take 4-5 days to achieve but decreased aqueous humor production occurs within 30 minutes – a few hours of dosing. The topical CAIs can be used in dogs and cats and are effective in both species. They can be used in all types of glaucoma, have no effect on pupil size, and do not contribute to intraocular inflammation. Dorzolamide is available as a combination drug with timolol (Cosopt®), which is now available as a generic. The efficacy of topical CAIs has been shown to be of equal efficacy to that of systemic CAIs. Methazolamide is dosed at 2-5mg/kg PO q12h and is available as a 50mg tablet. Acetazolamide is available as 125mg and 500mg tablets. The recommended dosage is 4-8mg/kg PO q8-12 hours. Commonly reported side effects of systemic CAIs include PU/PD, GI upset and panting (to compensate for metabolic acidosis). Systemic CAIs should not be used in patients with respiratory compromise. Cats appear to be more susceptible to metabolic acidosis and therefore systemic CAIs should be used with extreme caution in this species.

**Beta-blockers**

Beta blockers are very effective for reduction of IOP in humans and are the most commonly prescribed class of drugs for the treatment of glaucoma in people. Timolol is the most widely used of these medications in both human and veterinary medicine, but other topical beta blockers are available, including levobunolol, betaxolol, metipranolol and carteolol. Beta blockers reduce IOP by decreasing aqueous humor production but the exact mechanism of this effect is not completely understood. In the dog and cat their efficacy is considered relatively poor and bradycardia and mild (bilateral) miosis associated with their use has been documented. Their use in equine glaucoma appears more promising. In veterinary medicine, timolol 0.5% is administered twice daily. Use with caution in patients with cardiovascular disease.

**Prostaglandin analogs**

The prostaglandin analogs appear to be the most effective drugs in the treatment of canine glaucoma. These drugs increase aqueous outflow (with no effect on aqueous production). The mechanism of action is mediated through binding to prostanoid FP receptors. In the dog and human, activation of the prostanoid FP receptor results in increased uveoscleral outflow (ie unconventional outflow) through remodeling of the ciliary body musculature. Increased conventional outflow also occurs through morphological changes in the trabecular meshwork. The most commonly prescribed prostaglandin analog in veterinary medicine is latanoprost (Xalatan®), which is now available as a generic. The efficacy of topical CAIs has been shown to be of equal efficacy to that of systemic CAIs. Methazolamide is dosed at 2-5mg/kg PO q12h and is available as a 50mg tablet. Acetazolamide is available as 125mg and 500mg tablets. The recommended dosage is 4-8mg/kg PO q8-12 hours. Commonly reported side effects of systemic CAIs include PU/PD, GI upset and panting (to compensate for metabolic acidosis). Systemic CAIs should not be used in patients with respiratory compromise. Cats appear to be more susceptible to metabolic acidosis and therefore systemic CAIs should be used with extreme caution in this species.

**Other classes**

Other, less commonly utilized anti-glaucoma drug classes include the cholinergic agonists (pilocarpine, carbachol, demecarium bromide, echothiophate iodide), adrenergic agonists (dipivefrin), and alpha2-adrenergic agonists (apraclonidine, brimonidine). Due to associated local side effects, lack of availability and/or systemic side effects, they are seldom used.

**Surgical therapy**

The recommended surgical options often depend on whether vision is considered salvageable. Surgical options for the visual eye consist of laser ciliary body destruction and gonioimplants.

**Endolaser cyclophotocoagulation (ECP)**

ECP is a relatively new surgical option. A diode laser is used to target the pigmented tissue of the ciliary body, thereby destroying the adjacent nonpigmented epithelium. The advantage of this procedure is that the laser is built into an endoscopic probe, allowing for localization and direct treatment of the ciliary processes with little bystander damage. Because the laser energy is likely to induce cataract development the process is often combined with phacoemulsification. No studies evaluating the long term efficacy of this surgery have been published, however preliminary results are promising.

**Transscleral cyclophotocoagulation (TSCPC)**
TSCPC involves laser ablation of the ciliary body, similarly to ECP. Both Nd:YAG and diode lasers have been utilized. The main difference between TSCPC and ECP is that TSCPC does not involve direct visualization of the ciliary body. Rather, external landmarks are used to position the laser probe over the external surface of the eye and the laser energy is directed through the sclera. Possible post-operative complications include excessive intraocular inflammation (with the potential to induce retinal detachment), cataract development, hyphema, and, as with any glaucoma surgery short of enucleation or evisceration, uncontrolled intraocular pressure. One retrospective study quoted a ~50% success rate in terms of IOP control with a ~20% success rate in terms of vision 1 year post-treatment. Immediate post-operative spikes in IOP are common and can result in post-operative vision loss.

**Gonioimplants/valves**

Gonioimplants facilitate drainage of aqueous humor through a tubing system implanted directly into the anterior chamber. Both valved and nonvalved implants exist. Valved systems allow for egress of aqueous humor at intraocular pressures >12mmHg, while nonvalved systems are limited only by resistance of the tubing itself. Although these shunt systems are generally efficacious in the short term, post-operative uveitis with fibrin development and valve occlusion, requiring intracameral tissue plasminogen activator administration, is relatively common. The long term efficacy of shunts is limited by avascular bleb development, in which an avascular fibrotic capsule develops around the base of the device. This fibrosis is observed so commonly that gonioimplant failure is generally considered inevitable, and implant placement is often combined with a cyclodestructive procedure to provide more long term control of IOP.

Eyes that have lost vision are most commonly treated with one of the following surgeries to improve quality of life by controlling pain related to elevated IOP.

**Enucleation**

Enucleation is probably the most commonly performed ‘surgery of comfort’ for glaucoma. Possible post-operative complications include hemorrhage, post-operative fistulas or mucocele development caused by incomplete removal of conjunctival, caruncular or third eyelid glandular tissue, and, rarely, orbital emphysema. In the cat, the optic nerve is relatively short and excessive traction on the enucleated globe must be avoided during surgery to prevent damage to the optic chiasm and contralateral blindness.

**Cyclocryothermy**

Cyclocryothermy allows for reduction in IOP without loss of the globe. This procedure is generally reserved for the canine and has a reported ~80% success rate. Either nitrous gas or liquid nitrogen can be used. Using external landmarks to estimate the site of probe placement, the cryotherapy is applied externally. The ‘cryodose’ applied depends on the pre-operative intraocular pressure. The biggest advantage is that the surgery is noninvasive; post-operative therapy generally involves anti-inflammatories (often continued for life). Disadvantages include the potential for persistently elevated IOP, cataract development, hyphema, retinal detachment and globe phthisis.

**Chemical ciliary body ablation**

Pharmacologic ablation of the ciliary body can be performed with gentamicin, or, as more recently described, cidofovir. Gentamicin is cytotoxic to both the ciliary body and retina and therefore should never be used in a visual eye. Even in blind eyes, however, this procedure should be used with caution as retrospective pathologic studies have reported an increased incidence of intraocular tumor development post-operatively. The outcome of this procedure is also the least predictable of the cyclodestructive procedures, with published reports citing a ~65% success rate. Other possible post-operative complications include cataract development, retinal detachment, hyphema, chronic uveitis and phthisis. Intravitreal gentamicin should NOT be administered to patients with renal compromise, as the drug is detectable in plasma post-operatively.

**Evisceration and Intrascleral prosthesis (ISP)**

ISP surgery involves creating a 180 degree limbal incision at the corneoscleral junction, removal of all intraocular contents, and replacement of these contents with a silicone intraocular prosthetic. The advantages of ISP include complete resolution of glaucoma and maintenance of a ‘cosmetic’ globe. Disadvantages include the potential for recurrent corneal ulcerations due to decreased corneal sensitivity (caused both by historical glaucoma and transection of corneal nerves intraoperatively) and the potential for KCS. ISPs should generally be avoided in eyes with underlying intraocular neoplasia, pre-operative keratitis or KCS.

Unfortunately, glaucoma remains a disease with no effective ‘cure’, and although primary glaucoma often presents initially as a unilateral process, most ‘at-risk’ dogs will develop glaucoma in the contralateral eye within 1 year of diagnosis. Initiating prophylactic anti-glaucoma treatment in the normotensive eye has been shown to delay the onset of glaucoma in a dog at risk by as much as 18 months. Client education and early intervention can delay vision loss and improve quality of life for your patients.

References

How to Approach the Squinty Cat
Micki Armour, VMD, DACVO
Eye Care for Animals
Leesburg, VA

There are many potential pathogens that can lead to ocular irritation in cats; of note are Chlamyphila felis, Calicivirus, Mycoplasma, and Feline herpesvirus 1 (FHV1). Of these pathogens, FHV1 is by far the most incriminated when it comes to chronic and recrudescent conjunctivitis, blepharitis, and keratitis.

Chlamyphila felis
The most common ocular sign associated with Chlamyphila felis is chemosis. There are 2 morphologic forms of C. felis: the elementary body, which is an extracellular infectious form, insensitive to antibiotics, and the reticulate body, which is the intracellular form that leads to cellular damage. The reticulate form is sensitive to antibiotics. Transmission of C. felis is generally thought to be via aerosolization, direct contact, or contracted via fomites. Incubation is 3-5 days, and C. felis is shed for approximately 60 days after inoculation. Clinical signs include chemosis, hyperemia, serous discharge and blepharospasm. Cats less than 1 year are most likely to become infected; cats greater than 5 are fairly resistant. Chalmydophila infections tend to follow a chronic course, that typically begins with unilateral clinical signs that then can include the contralateral eye. The clinical signs typically resolve in a few weeks, although mild conjunctivitis can persist for months.

In a study (Vet Record, 1994) comparing 6 otherwise healthy to 6 FIV positive cats experimentally infected with C. Felis, clinical signs in control cats resolved within a mean of 109 days post-infection, while in FIV infected cats clinical signs persisted beyond 200 days.

Cytology of the intracytoplasmic reticulate bodies days 3-14 post-inoculation has poor sensitivity and specificity; false positives are common. PCR and serology after day 32 of inoculation are possible diagnostic tools. However, cell culture is considered the gold standard for the identification of C. felis. Cats vaccinated prior to conjunctival and nasal infections developed milder ocular and URI signs than unvaccinated cats, with a shorter shedding period. However, the vaccine doesn’t prevent infection or clinical signs, and can be associated with fever, lethargy, anorexia and lameness following vaccination.

Therapeutic options for the treatment of C. felis include doxycycline, azithromycin and clavamoc. Doxycycline appears to be the most efficacious for C. felis with clinical improvement in as few as 2 days.

Calicivirus
Calicivirus is a single stranded non-enveloped RNA virus, transmitted via aerosols or fomites. The virus typically incubates for 2-3 days, and results in acute respiratory tract signs, including glossal ulceration. It also results in polyarthritis and conjunctivitis in cats. It is generally considered a self-limiting disease process, which appears to resolve in 7-10 days. Topical antivirals do not appear to be effective as all of our topical antivirals target DNA, not RNA. Calicivirus also does not result in latent infections.

Calicivirus is diagnosed via cell culture, scrapings of respiratory or conjunctival secretions, immunohistochemical stainin, and electron biomicroscopy. Prevention is via the modified live or killed vaccine.

Mycoplasma
Mycoplasma felis and M. gatae are two isolates that are also incriminated in ocular irritation. Mycoplasma spp. Have questionable clinical significance because they have been isolated from clinically normal cats and have resulted in variable conjunctivitis when administered experimentally. In addition, the disease process has not been replicated when cats were experimentally infected.

Diagnosis is via culture, cytology (noting the epithelial cytoplasmic basophilic inclusion bodies), and PCR (which has the highest sensitivity and specificity). Topical antibiotics have resulted in resolution of ocular clinical signs.

Feline herpesvirus 1 (FHV1)
Feline herpesvirus 1 is an enveloped alphaherpesvirus known for its notorious chronic tissue latency. It is environmentally very fragile, and only lives 12-18 hours outside of a host. It is transmitted via direct contact or aerosolization, and infects the oral, nasal, and conjunctival surfaces. Like all herpesviruses, FHV1 is highly species specific. Its seroprevalence within the feline population has been reported as high as 97%.

Feline herpesvirus 1 infects the epithelial cells lining the respiratory tract, conjunctiva and corneal epithelium. The replicating virus results in cytolysis and causes inflammatory-mediated cell damage 4-6 days following exposure. Of note, it also established latency in the trigeminal ganglia, and can chronically and repeatedly travel to the eye via anterograde axonal transport, spontaneously shedding virus particles.

Maternal antibody protection wanes 8-12 weeks following birth. Although the course of the disease process can be self-limiting (10-20 days), it can result in severe ocular signs, including hyperemia, blepharospasm, chemosis, serous to purulent ocular discharge,
corneal ulceration and keratitis, and fibrinocellular exudate. Dendritic corneal ulcers are pathognomonic for this disease process. It is often associated with a concurrent upper respiratory tract infection.

Cytology is often unrewarding, as it is likely only useful in primary infections and inclusion bodies are rare. Histopathology reveals epithelial necrosis 4 days following infection with a neutrophilic infiltrate, fibrosis and scarring. Viral detection is best performed via PCR using a dry cotton swab and performing a standard volume PCR assay. Virus isolation, fluorescent antibody, serum neutralizing antibody and ELISA testing have also been documented to detect FHV1. Prevention is difficult due to the high seroprevalence of FHV1, although vaccination may help protect against future disease episodes.

The contraindication of corticosteroids and FHV1 has been documented in the literature. Steroids have been associated with persistent and progressive corneal ulceration, neovascularization, prolonged viral shedding, corneal sequesta formation, calcific band keratopathy, and decreased tear production. Also, secondary bacterial infections may complicate viral flare-ups, and warrant the use of concurrent antibiotic therapy.

Topical and systemic antiviral therapy is often warranted. Potential antiviral therapeutic options include trifluridine, idoxuridine, vidarabine, cidofovir, acyclovir and famciclovir. Other therapies include the utilization of interferon, lysine and mucinomimetics.

Feline herpesvirus 1 may be associated with other disease processes, including eosinophilic conjunctivitis and keratitis, corneal sequestrum formation and dendritic dermatitis.

References
Managing the Bug-Eyed Dog
Susan Keil, DVM, MS, DACVO
Keil Veterinary Ophthalmology
Lenexa, KS

A significant percentage of an ophthalmologist’s weekly caseload is devoted to this subset of dogs. The goal of this lecture is to review factors to help you manage the ocular health of the brachycephalic individuals (Pug, Shih Tzu, Lhasa Apso, Boston, Japanese Chin, Pekingese).

Educate your clients
- Special needs – use caution around dogs (including play), do not allow to hang out of car windows, recommend harness over collar (tugging increases ocular pressure), monitor if they sleep with their eyes (think about lubricating every night throughout life), no cage drying (hand dry)
- Grooming – start grooming very early (as a puppy, getting used to the noises, the table and routine of a groomer), allowing handling of face, utilize both reward and reprimand, need REGULAR grooming appointments
- Annual exams – take extra time on the eyes, always do a Schirmer tear test, look at lid apposition, evaluate corneal clarity, check nasal hair status
- Teach client when to reach out for help –
  - If the eye is red, but not painful
  - If the eye is red and painful
  - If the eye is red, painful, and getting worse
  - Meaning – call with any concern lasting over 24-28 hours!

**Great questions to help you determine severity over the phone = is the eye open or squinting/closed?**

Goals for the primary care veterinarian
- Reduce chronic pain
- Recheck frequently
- Identify and appropriately treat all ulcers, especially infected situations
- Identify and refer descemetoceles and full-thickness corneal ruptures
- Reduce the numbers of visually impaired and blind eyes
- Reduce the numbers of enucleations
- Extra attention for monocular bug-eyed patients – evaluate more than once annually if needed

Anatomy & physiology

Skull anatomy
- dolichocephalic
- mesaticephalic
- brachycephalic

Eyelids
- folds of thin skin continuous with facial skin with the free edges forming lateral / medial canthi
- palpebral fissure is the opening between the lids
- provide obvious physical protection
- contain meibomian glands which produce meibum (outer tear film (TF) layer) to reduce evaporation
- contain conjunctival goblet cells which produce mucin (inner TF layer) to attach TF to the cornea
- distributes tear film around cornea
- removes debris
- these dogs have a shallow orbit combined with both a large globe and a large palpebral fissure

Blinking
- upper lid provides more movement and protection than the lower lid
- 10-20 per minute with 85% being yoked blinks and up to 66% being incomplete in brachycephalics closure
  - CN VII – orbicularis oculi
  - CN VII – corrugator superciliii
  - CN III – levator palpebral superioris

Cornea
- nerve sensitivity a MAJOR protector – often lost with years, microtraumas, chronic disease
• rapid blink and globe retraction with nictitans prolapse is a basic protective reflex which is very challenged in these dogs
• Cochet-Bonnet esthesiometer is an instrument which detects corneal sensitivity; brachycephalics
• have the least corneal sensitivity of all breeds; additionally, the central zone is the least sensitive which is also the most anatomically exposed region

Reflexes
• corneal
  o afferent arm – ophthalmic and maxillary of the trigeminal (V)
  o efferent arm – facial (VII)
• palpebral
  o afferent arm – ophthalmic of trigeminal (V)
  o efferent arm – facial (VII)
• menace
  o afferent arm - retinal rods / cones and optic (II)
  o efferent arm – facial (VII)

The annual exam
Evaluation of the blink response: Is it complete?
• Touch all four canthi – scrutinize! If not blinking completely, need to be lubricating life long!
  o viscous, before bed, in am, more often?
  o need a permanent canthoplasty?

Quantitative assessment of the tear film: Measure aqueous layer with the Schirmer Tear Test (STT)
• Do for a full 60 seconds (often 15 mm / 30 sec and 17 mm / 60 secs)
• Do every year! May need to do more often!
• Very under utilized for the red-eye exam!!
  o 15 mm / 60 seconds is not adequate for a 1.5 year old Pug that cannot blink
  o Start immunomodulators if not adequate!
    ▪ Cyclosporine (Optimmune (0.2%), compounded 1 or 2% in aqueous or oils)
    ▪ Tacrolimus (0.03% compounded in aqueous or oils, 0.5%)

Qualitative assessment of the tear film
• Tear film breakup time (TFBUT) – evaluates the integrity of the mucin layer
  o use rose Bengal dye
  o normal is a dry spot on the cornea @ 20 seconds
  o can be very challenging cases / very uncommon
  o need to lubricate constantly / not a specific therapy

Trichiasis: normal eyelid hair from normal follicle that deviates to contact the cornea/conjunctiva
• Nasal
  • Caruncular – small, pink, globe-like nodule at medial canthus
    o Shih Tzu, Lhasa Apso
    o wick tear, but do not poke
  • Treatment: +/-resection, cryoepilation, manual epilation (temporary, will grow in more stiff)
  • May not require treatment

Trichomegaly: abnormally long normal eyelash
• Clinically not a problem – does not require treatment, can complicate ocular hygiene
  • Cocker, Shih Tzu, Lhasa

Nasal fold trichiasis
• Pug, Pekingese
• Treatment: surgical resection if causing chronic irritation
  o evaluate from the front and sides with eyes looking forward and moving right/left to determine if bothering the corneas
  o closely look at corneal pigment and fibroses patterns to see if they match

Distichia / districhiasis: normal cilia from an abnormal spot
• Grow from the meibomian gland duct
  o distichia are modified hair follicles following the path of least resistance out the duct
• May cause no problems (Cockers!)
- May be very problematic
  - Location, numbers, and combination of other surface disease are all factors
- May cause problems in the future
  - if in doubt, take it out!
  - if going under anesthesia for something else, remove if possible even if non-clinical
- Treatment: cryoepilation (liquid nitrogen, nitrous oxide)
  - tedious, boring, and may be very time consuming
  - lid splitting and electrolysis not recommended
  - small individual cryo units possible for very small numbers of hairs

**Ectopic cilia: normal cilia from the meibomian gland but erupting through the palpebral conjunctiva**
- Not following the path of least resistance down the meibomian gland
- Very painful!
- Typically located from 10 to 2 o’clock on the superior lid (had one inferior case)
- Can be very challenging to locate sometimes (need magnification–slit lamp, operating scope)
- Think young dog with superficial ulcer that keeps coming back
  - these are NOT refractory
- Treatment: en bloc excision with magnification and cryo treatment
  - Eyelid swollen but instantly dog’s comfort much improved

**Entropion: inward rolling of part or all of the eyelid margin causing hair-bearing skin to chronically rub on the cornea / conjunctiva**
- Always clinically significant
- A function of lid laxity
- Mild (little inversion and loose contact with ocular surface) cases – epiphora, low-grade
  - discomfort, excessive lacrimation
- Moderate to severe cases cause constant trigeminal irritation, resulting in constant pain,
  - secondary inflammation and ulceration/descemetoceles, self-trauma;
  - with chronicity pigmentation, scarring, vascularization, blindness result.
- Treatment: surgery
  - very undertreated condition
  - consistently hear how more active, energetic, engaging the dogs are after corrected

**Ectropion: outward rolling of the eyelid margin causing conjunctival tissue to be exposed and lagophthalmos may occur**
- Lower eyelid typically involved
- A function of lid laxity
- May see cicatricial eversion of the upper lid
- Typically not clinically significant – especially in brachycephalics
  - exposure of the conjunctiva may lead to low-grade conjunctivitis and predispose to epiphora and pre-corneal tear film deficiency

**Euryblepharon = Macroblepharon = abnormally large palpebral fissure**
- Required feature in many breeds
- Two different clinical presentations
  - brachycephalics obtain exophthalmos through a shortened maxilla and shallow orbit with Euryblepharon resulting from protrusion of the globe forward through the fissure
  - other types have an excessive eyelid length and the palpebral fissure is poorly supported by the globe
  - both types have a disturbance of the tear film dynamics and possible surface disease
- Treatment: may benefit medial / lateral canthoplasty

**Lagophthalmos: inability for a complete blink to occur**
- Treatment: may benefit from medial / lateral canthoplasty

**Corneal clarity: pigment, vessels, edema, fibrosis**
- For all these corneal changes, identifying the underlying disease important
  - KCS, trichiasis, Lagophthalmos, entropion, multi-factorial situation

**The management plan**
1. Encourage regular grooming with a groomer that can trim around the face safely and thoroughly
2. Practice / acclimate dog to getting drops and ointments
3. Annual, semi-annual, quarterly exams
4. Patient age and owner goals factor into both the short and long term plans
5. Require more aggressive integration of surgical treatments than for non-brachycephalic dogs
6. Be less tolerant of “mild” situations than for non-brachycephalic dogs
7. Life long medical requirements: lubricants before bed, constant corneal needs
8. No set protocol – modify for each patient
9. Often under treated for our convenience
10. More clients willing / wanting to do more

Medical management
Topical non-steroids (NSAIDs)
- Flurbiprofen
- Ketorolac
- Diclofenac

Topical steroid
- Prednisolone acetate 1%: penetrates better
- Dexamethasone 0.1%
- NeoPolyDexamethasone 0.1%: do you need this combined with an antibiotic?

Immunomodulators
- Cyclosporine
  - Optimmune 0.2% ointment
  - 1%, 2% compounded solution
    - aqueous
    - oils (coconut, sunflower, safflower, vegetable, other)
      - The OILS may irritate – not the drug – switch to aqueous
- Tacrolimus
  - 0.03%, 0.5%
    - aqueous
    - oils (coconut, sunflower, safflower, vegetable, other)
    - determine if patient annoyed or actually irritated by oil
    - oils have a longer contact time (providing lubrication)

Artificial tear products
- For aqueous deficiencies
  - 0.3% hydroxypropyl methylcellulose: Genteal, Tears Naturale, Bion Tears
  - 1% carboxymethylcellulose: Refresh Liquigel, Celluvisc
  - hydroxypropyl gel forming matrix: Systane
  - 0.3% hyaluronate: I-drop
- For lipid deficiencies
  - Caster oil, glycerin, polysorbate-80: Refresh endura
  - Mineral oil, polysorbate -80: Soothe emollient drops
- For mucin deficiency
  - 1% carboxymethylcellulose: Refresh Liquigel / celluvisc
  - hydroxylpropyl gel forming matrix: Systane ultra
- Gels
  - 0.3% hydroxypropyl methylcellulose: Genteal Gel
  - 1.5% carboxymethylcellulose: Tears again Night and Day gels
- Ointments
  - Petrolatum, mineral oil: Refresh PM, Tears Naturale PM, Lacrilube
Disorders of the Lens
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A. Crystalline anatomy: The lens is transparent, avascular, and biconvex to support the jobs of refraction and image focusing on the retina. Because the lens is avascular, the aqueous humor provides nourishment and waste removal. Uveitis alters lens metabolism. The hyaloid and pupillary membranes provide the vascular network during embryogenesis.

A. Lens regions
- Nuclear: central 80%
- Cortical: surrounds nucleus – anterior, posterior, equatorial
- Capsular: epithelial cell membrane semipermeable for nutrition & metabolic waste
- Y-sutures: capsule epithelial cells under the anterior lens capsule
  - replicate and migrate anterior & posterior to form new fibers
  - these tips join at the Y-sutures.
- Regular arrangement of fibers is responsible for the lens transparency
- A cataract is a change in the fiber arrangement.
- New fibers result in increased lens density as the lens is restricted in size (~ 6 yrs)

B. Congenital anomalies
- May be solitary or multiple ocular disorders
- Variations in shape, location, size, and transparency occur
- Etiologies during embryogenesis: toxic, inherited, nutritional, traumatic, infectious.
  - microphakia, posterior lenticonus, coloboma, cataract, retinal dysplasia, microphthalmia, PPMs, persistent tunica vasculosa lentis
- Suspicious of congenital problems:
  - perform a complete bilateral exam after dilation
  - remove individuals from breeding programs
  - follow affected animals, monitoring for cataract & glaucoma
  - cataract surgery may be an options +/- IOL.
  - do have an increased risk of glaucoma and retinal detachments.

C. Cataracts
- Opacity of the lens/capsule regardless of size
- Two common etiologies are inherited (congenital or acquired) and diabetes mellitus
- 50% of diabetics will develop cataracts in 6 months; 80% in 1.3 years.
- trauma, uveitis, electric shock, radiation, nutritional deficiencies less common.
- classifications:
  - age (congenital vs. developmental)
  - cause
  - location (capsular, cortical, nuclear, equatorial vs axial)
  - severity
    - incipient does not affect vision significantly (<10%)
    - immature (vision compromise but not complete)
    - mature (obscures image completely)
    - hypermature (volume reduces to lens protein liquefaction)
    - Morgagnian (hypermature cataract undergoing substantial resorption where the cortex liquefies and the nuclear drops (uncommon, Cocker / Bichon)
- feline: not by diabetes, commonly occur secondary to uveitis, inherited possible
- diabetic intumescent cataract:
  - aldose reductase enzyme catalyzes the reduction of glucose to intracellular sorbitol
  - sorbitol causes an osmotic shift, leading to significant swelling and fiber disruption
  - equatorial vacuoles (bubbles) progress to fiber swelling and rupture,
  - complete opacification, and Y-suture clefting.
• diabetic cataracts may develop in just days.
  o spontaneous lens capsule ruptures may occur due to the rapid osmotic lens swelling
  o (rapid forming genetic cataracts may also do this)
  o this situation is both a medical and surgical emergency.

A referral is recommended for ALL patients, even if the client is not interested in surgery. Many of these cases have lens-induced uveitis (LIU). LIU needs therapy. The goals are to prevent tertiary glaucoma and avoid shutting the door of surgical opportunity.

D. Lens induced uveitis: up to 71% of mature, intumescent, hypermature cataracts have LIU
1. Phacolytic: uveal inflammatory response occurring secondary to lens proteins leaking through an intact lens capsule, resulting in lens shrinkage/capsule wrinkling.
2. Phacoclastic: spillage of lens proteins into the eye after the capsule ruptures

E. Cataract management and surgery
Should surgery be performed? This depends on numerous factors, such as the degree of visual impairment and the goals and finances of the client. Age is not a disease, but often a factor in client decision as is patient general health. Diabetics are over 50% of my surgery cases. They do not need to be completely regulated prior to surgery. Often, surgery often needs to be performed quickly to help eliminate LIU. The patients are significantly more active and engaged after surgery, I believe helping to maintain weight and regulation. Diabetics do well under anesthesia. All surgery patients, but particularly the diabetics, look and act 3-4 years younger.

There is currently no medical therapy for cataracts that has any clinical benefit for vision restoration. Do not fall prey to various dietary and holistic “cures” such as NuVet, Can-CTM, N-Acetyl-Carnosine. Proper nutrition may play a role in prevention, but once a cataract, always a cataract. Mature, intumescent, and hypermature cataracts increases risk of LIU, secondary glaucoma, instability, retinal detachment, capsule opacification.

Prompt referral is imperative to ensure the best ocular management and postoperative results. Some clients are unwilling or unable to visit an ophthalmologist. Recommendation in these cases is to monitor for both uveitis and glaucoma, use a topical anti-inflammatory (+/- atropine to control LIU), and monitor tear production.

Cataract surgery has improved dramatically over the past decades due to many improvements: phacoemulsification techniques, viscoelastic agents, intraocular lenses, anti-inflammatory drugs.

Successful outcomes also dictated by surgeon skill / experience, appropriate patient selection, meticulous attention to detail, and diligent post op treatment and monitoring. The surgery is very rewarding, a significant financial investment and a large time investment. Pre-op requirements: complete general and ocular exam, electroretinogram, ocular ultrasound, gonioscopy, appropriate pre-op blood work, +/- dental, +/- urine culture

If surgery is not performed, continue to monitor indefinitely. Complications w/out surgery include uveitis, glaucoma, luxation, and retinal detachment. Lim, et all 2011 found 20% of cases without medical or surgical therapy had a poor outcome (pain, aforementioned complications, enucleation, evisceration).

Unoperated eyes have a higher percentage of eventual glaucoma (20%) then operated (8%).

Uncommonly younger dogs may have spontaneous resorption and regain aphakic vision (Cocker, Bichon). Sooner is always better than later when referring / performing surgery. Topical NSAIDS / steroid may be required until no longer leaking protein. Exams recommended every 6 to 8 months for mature, hypermature, intumescent cataracts once stable.

Phacoemulsification and intraocular lens (IOL) implantation is the standard of care.

Extensive training and equipment required. Surgical success recorded as 85-92%. It is important to get LIU controlled prior to surgery. Bilateral typical at one surgery due to reduced cost, one anesthesia, one post op recovery, and one two week post surgery requirement for owner. Typically, 10-14 days of harness walk only, Elizabethan collars, and many meds. Rechecks at least at 1 day, 1 week, 1 month, 3 months, 6 months, annual.

The post-op management by a primary care veterinarian would include menace, PLR, STT measurement, IOP (with definite caution immediately post op, especially with Schiotz and even Tonopen) as well as examine anterior and posterior segment. Annual exams are recommend with an ophthalmologist to look for early complications. Some patients require low dose life long topical medications.

F. Lens instability
Primary (genetic) luxations - think all terrier breed, Shar Pei, cattle dog, Brittany, Border Collie, mini bull. There is of ten asymmetric bilateral disease. There are some genetic tests available for this autosomal recessive disorder.

Secondary luxations – glaucoma, hypermature cataracts, chronic LIU
• Clinical signs: aphakic crescent, phacodenesis (lens tremble), iridodenesis (iris tremble), vitreous in anterior chamber, corneal edema, lens in the wrong position (anterior / posterior / subluxated)
• Case evaluation: measure IOP, assess function (dazzle, menace, PLR), and determine lens location.
Anterior luxations are considered emergencies if the eye is functioning (perform intracapsular cataract extraction (ICCE) but not an ER case if negative function (enucleation, evisceration). Contraindicated are the topical miotic agents (Latanoprost, pilocarpine, demecarium bromide). Utilize carbonic anhydrase inhibitors (CAI), beta blocker, and osmotic agents.

Posterior luxations are not emergency situations but a referral is recommended to assess both eyes and discuss long term goals, options, and medications. Topical miotics may be used to trap lens/lower IOP. Removing a subluxated lens is debatable. The conservative approach is to use a topical miotic. The surgical approach is an ICCE. Increased complications include retinal detachments and glaucoma.

G. Trauma
Both blunt and sharp trauma can result in significant damage, blindness, and globe loss. Penetrating sharp items (barb wire, cat claws, metal objects) may penetrated the anterior lens capsule (ALC), causing a cataract and phacoclastic uveitis. This requires a prompt referral for corneal repair and cataract surgery. Blunt damage (ball, kick), may also result in cataract, uveitis, luxation, glaucoma and retinal detachment (sometimes years later). Utilize topical NSAIDS and antibiotics (and often atropine) until an ophthalmology examination.
Equine Recurrent Uveitis
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General information
- ERU is the most common cause of equine blindness, affecting 8-25% of US horses.
- An Essay on the Disease of the Eye of the Horse (1818) described a “specific inflammation”
- aka – periodic ophthalmia, moon blindness (Vegetius / 4th century AD – cyclic nature)
- other causes of uveitis include trauma, surgery, corneal disease
- ERU has an initial acute uveitis separated by recurrences at variable time intervals
- Etiology is not understood – genetic, infectious, environment, multi-factorial?
  o is understood to be a dysregulated immune response
    - responsive to steroids  b. unresponsive to antibiotics  c. inflammatory recurrences
- Of the affected horses, 1-2% has clinical disease considered vision threatening
- High cost to the equine community
- Still cannot be cured and may be difficult to manage
- Peak age of presentation 4-6 years with no gender preference
- May be either unilateral or bilateral
- If a patient goes two years without a flare-up, the risk of future flare-ups is greatly reduced

Uveal tract anatomy
- Anterior uvea: iris and ciliary body (pars plicata and pars plana)
- Posterior uvea: choroid
- Blood ocular barrier (BOB) = blood aqueous barrier (BAB) and the blood retinal barrier (BRB)

Uveitis pathophysiology
- Uveal tract inflammation >> vascular congestion >> increased vascular permeability >>
  - BOB breakdown >> leakage of blood / cells, fibrin, protein into the aqueous humor >> visible as aqueous flare, hyphema, hypopyon

Histology
In the acute phase, the iris and ciliary body (CB) are first infiltrated by the neutrophil (hypopyon), then lymphocytes, plasma cells, and macrophages invade resulting in exudates of protein and fibrin in the anterior chamber (retina typically spared initially)

In the chronic phase, lymphocytes continue to infiltrate the iris and CB resulting in nodules. T lymphocytes predominate with a high % of CD4+; blood vessel walls and the ciliary processes thicken; with continued disease, all ocular structures are damaged histologically.

ERU clinical classifications
Disease stage
- acute: actively painful, obvious intraocular inflammation
- quiescent: inactive; comfortable without visible active intraocular inflammation, but research has shown that even in stages of quiescence there remains active inflammation
- end stage: clinical signs include chorioretinal scarring ((butterfly lesion = wing-shaped hypopigmentation nasal and temporal to optic nerve head) and small, circular focal depigmentation with central hyperpigmentation in the non-tapetal region), blindness, phthisis bulbi, mature / hypermature cataracts, synechia, retinal detachments

Inflammation location
- anterior segment: clinical signs include pain, epiphora, conjunctival hyperemia, corneal edema, aqueous flare, miosis, limbal neovascularization (often deep / short), corneal ulcers, keratic precipitates, hyphema, hypopyon, iris color change (rubeiosis or dullness caused by inflammation / edema), hypotony (5-15 mmHg), anterior / posterior synechia, can see calcific hand keratopathy with chronicity
- posterior segment: involves choroid, vitreous, retina with anterior uveitis signs absent to very mild; clinical signs include vitreal cloudiness & opacities, retinal detachments, peripapillary chorioretinal scarring, difficulty in assessing fundus; affects warm bloods, European horses, draft breeds; least common type
- both segments (panuveitis): see a combination of anterior & posterior disease changes
Type of recurrence
- classic: typical presentation of acute followed by quiescent phase, shorter periods between flares, increasing severity with flare-ups; affects many breeds; sequelae include glaucoma, synchiae, lens luxation, cataract, retinal detachment, optic nerve atrophy, blindness, phthisis bulbi
- insidious: chronic, persistent low-grade inflammation; acute stages often not noticed and not painful; gradual cataract formation, retinal degeneration, blindness; affects mainly Appaloosa and draft breeds; difficult for the owner to note a problem until progression is too late; thought to be a distinct disease from classic ERU

ERU pathogenesis hypotheses
Infectious antigen or agent in the uveal tract or vitreous after initial uveitis
- molecular mimicry
Persistence of immune-competent sensitized T-cells in the uveal tract
- autogenerative T cell reaction against retinal proteins which leads to continued destruction of intraocular tissues
Deposition of immune complexes

ERU immunology
T cells (CD4+ with Th1-phenotype) are the main infiltrating cells
- invade the iris and retina
- form characteristic iris follicles
- goal is to adjust treatment approach to specifically target T cell inflammation rather than general inflammation

The T cells target retinal autoantigens
- S-Ag (S-antigen), IRBP (interphotoreceptor-retinoid binding protein), MDH (malate dehydrogenase), CRALBP (cellular retinaldehyde binding protein)

Horses carrying the gene coding for the MHC class I haplotype ELA-A9 are more susceptible in developing ERU
- 41% of warmblood horses with ERU carried this gene

ERU diagnostics
- Complete ophthalmic exam
- Complete general physical
- CBC/Profile +/- Lepto serology

ERU in the Appaloosa breed
- 8x more likely to develop uveitis and 4x more likely to develop blindness vs all other breeds
- Insidious form!
Duration and age of onset are challenging to document
Two specific genetic markers have been identified in Appaloosa uveitis
- MHC Class I and II markers (Kaese et al, 2008)
  - many human diseases linked to MHC alleles
  - MHC microsatellite association with Appaloosa ERU
    - Ume011 and EqMHC1
- does melanin play a role in immune dysfunction
  - is melanin linked to the predisposition of immune system dysfunction?
  - is the lack of melanin a primary factor in development of the disease?
Coat color / pattern IS a factor with the disease
- affected horses have an overall light coat pattern with focal darker spots
- affected horses show annual coat color changes, often tending to lighten with age
- non-affected horses tend to have a dark coat with a blanket

IEOC 2009 conference lecture by AE Dwyer
- New York study of 160 horses over 11 years with uveitis
  - 26% (42 horses) were Appaloosa
  - 74% (118 horses) were other breeds
- Seroreactivity to L. Pomona
  - 62% were seropositive
  - study population divided into four groups
    - Appaloosa that were seropositive (14)
    - Appaloosa that were seronegative (28)
    - other breeds that were seropositive (86)
- other breeds that were seronegative (32)
- Horses presenting with bilateral disease

**Leptospirosis**
- Smallest spirochete bacteria that is motile and able to enter hosts (wounds, mucous membranes)
- Aquatic unicellular organism in rivers, lakes, sewage
- Principle reservoirs: deer, swine, rats, cattle, possum
- Organism multiplies in the kidneys and shed in the urine
- Horses infected by drinking contaminated water with cases most commonly seen in rainy seasons
- Clinical signs: fever, icterus, anemia, anorexia, transient depression
- Organisms localize in the renal tubules, genital tracts, and anterior / posterior ocular segments
- Two most common serovars incriminated in disease are L. interrogans pomona and grippotyphosa
- First reported in Ithaca, NY, 1947, with horses developing ERU 18-24 months later
- Lepto may have helped initiate ERU in some cases, but did not factor into the recurrences
- To date, the exact mechanism of interaction between the horse’s immune system and the organism is not understood

**ERU treatment**

**Goals**
- Control pain
- Preserve vision
- Reduce inflammation

**Decrease inflammation**
- Systemic NSAID / corticosteroid
  - flunixin meglumine***
    - use this first!!!
    - dose: 1 mg / kg PO, IV every 12 to 36 hours (depends on disease stage) reducing to 0.5 mg/kg PO every 12 to 36 hours
    - risk: long term concern of gastric and renal toxicity
    - Gastrogard recommended at preventative dosing (1/4 tube daily)
  - phenylbutazone
    - at consult often stopping this drug and starting flunixin*
    - dose: 4.4 mg/kg PO, IV every 12 to 36 hours (depends on disease stage)
    - risk: long term concern of gastric and renal toxicity
  - aspirin
  - dexamethasone (Azium)
    - potent anti-inflammatory
    - dose: 5-20 mg/day PO or 2.5 mg/day IM
    - risk: frequent side effects including laminitis and GI concerns; use with caution and as a last resort; taper off dose, alter management (decrease stresses / confinement, increase forage, decrease starches)
  - prednisone
    - potent anti-inflammatory
    - dose: 100-300 mg/day PO, IM
    - risk: see dexamethasone
- Topical NSAID / corticosteroid
  - pred acetate 1%***, dexamethasone 0.1%**
    - potent, excellent penetration, dose frequency depends on stage of disease hourly to weekly
    - risk: predisposes to corneal fungal disease
  - diclofenac 0.1%, flurbiprofen 0.03%, ketorolac
    - good penetration, dose frequency depends on stage of disease hourly to weekly
    - risk: decreases corneal epithelialization
      - remember = NSAIDs are not 100% safe
- Ocular injections
  - subconjunctival triamcinolone
    - potent anti-inflammatory
• dose: 1-2 mg providing 7-10 day duration
  • risk: cannot remove!; severe predisposition for bacterial or fungal keratitis
    o intravitreal gentocin
      • being utilized if patient demonstrating seropositivity to Leptospira
      • dose 4 mg
      • efficacy not proven, but clinical improvement noted in certain cases
    o intravitreal
  • Surgical cyclosporine suprachoroidal implants
    o suppresses T-cells
    o provides a slow release of CsA over 2-3 years
    o essential to control uveitis BEFORE surgery**
    o cases need to be referred earlier in general to have this option more accessible
    o surgery for visual eyes only (expense / general anesthesia)

Reduce discomfort and synechia
• Mydriatic cycloplegic
  o atropine 1%
    • minimize synechia and provide pain relief
    • dose depends on stage of disease (TID to every 72 hours)
    • predispose to colic / decrease gut motility (overstressed)

ERU management
• Optimize systemic health
  o maintain good nutrition, regular activity, and regular fecal egg counts / deworming schedule
• Decrease risk of injury
  o keep enclosures safe
• Minimize inflammatory stimuli
  o wear a fly mask! (uv light flies, wind, other antigens)
  o routine hoof and dental care
  o control rodents, environmental insects
  o bedding type
• Keep up to date with vaccinations

Blind ERU horses
• Review expectations – be realistic, acknowledging each situation different
• Encourage the horse owner to start training and acclimation for blindness early, before vision is lost
• Most horses will eventually loose monocular or binocular vision
• Most horses will adapt, but this period can vary between weeks to months
• Euthanasia may be elected for individual situation (expense, horse not adapting, safety, etc)
• Find a calm companion (horse, mini, goat) and decrease stressors (wind, noise)
• Keep the horse’s daily routine very regular
• Really utilize other senses – sound, tactile
• Teach verbal cues
• ”Proof” the pasture
• BlindHorses.org is a good source of advice
• Realize that being blind +/- phthisis bulbi does not mean the patient is pain-free!
  o really assess this situation if you have chronic epiphora
• Enucleation may be needed to eliminate all discomfort
Equine Fungal Keratitis
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Anatomy
- Dimensions: 30 – 34 mm horizontal and 23 – 26.5 mm vertical limbus to limbus
  - 780 micrometers thick centrally; thicker at the periphery
- Histologically three layers with a pre-corneal tear film
- Lipophilic superficial epithelium: 8-12 layers of nonkeratinized squam, wing, and basal cells
- Hydrophilic stroma: 90% of thickness being 75 – 80% water
- Lipophilic deep endothelium: single layer, basement membrane of which is Descemet’s

Physiology
- Nutrition:
  - Oxygen – tear film, atmosphere, slight from aqueous humor and limbal blood vessels
  - Glucose, amino acids, vitamins from the aqueous humor, slight from tears and blood vessels
- Microflora:
  - Primarily gram positive and fungal organisms with some gram negative
- Innervation: the cornea is highly sensitive, with innervation via the ophthalmic branch of CN V

Prevalence
- Regionally frequent (humid climates, warm months)
- Regional species variability

Clinical appearance
- Superficial keratomycosis
  - Microerosion: multifocal subepithelial whitish opacities, pain / secondary reflex uveitis
  - Superficial ulceration: more severe, defined epithelial loss, pain / secondary uveitis
  - Plaque formation (“cake-frosting” look): white-yellow necrotic stromal plaque with ulceration
- Stromal ulcerative keratomycosis*: most common, 50-80% of cases, severe pain / anterior uveitis
  - Corneal furrowing: rapidly occurs at any time, curvilinear region of stromal loss at ulcer edge
  - Melting
  - Perforation
- Stromal abscess

Differential diagnoses
- Cytology, cultures (bacterial / fungal), PCR
  - Be prepared to repeat cytology +/- culture at second, third, fourth exams!
- Trauma / foreign bodies
- Infiltrative ulcerative disease
- Mixed fungal / bacterial infection (20-35% of infectious cases)
- Calcific band keratopathy
- Corneal degeneration
- Corneal neoplasia

Pathogenesis
- Loss of the epithelium allows ocular surface and environmental fungal organisms to adhere, invade, colonize, and infect the stroma
- Protease production by epithelial cells, fungi, stromal fibroblasts, and inflammatory cells triggers extensive keratomalacia
- Fungal organisms known to inhibit in vitro angiogenesis
- Deep stromal disease is perpetuated by the fungal affinity for the glycosaminoglycans near the Descemet’s membrane

Predisposing factors
- Topical antibiotics
Healthy gram positive microflora which produce balanced antifungal and antibacterial substances shift to gram negative in corneal ulcers

Antibiotic use can exacerbate this use

- Topical steroids
- Alteration in corneal biofilm

**Medical treatment**

The multiple goals are to attack the fungus and secondary bacterial infection, as well as manage corneal destruction, ocular pain, and secondary anterior uveitis

- Placement of a subpalpebral lavage tube
  - Think about formulation of medications you are dispensing – ointments do not go through a tube
  - Must be placed properly

**Antifungal medication**

Most drugs are fungistatic because of the inability to achieve adequate concentrations in the presence of an intact corneal epithelium

- If the epithelium is lost, the drug concentration increases
- High frequency administration is required to increase the drug concentration
- Clinical experience – too much too fast increases risk of a melt down??
  - this possibly results in clinical deterioration
    - intense inflammatory reaction
  - weigh this risk against stage of primary disease

**Therapeutic debridement**

- debulks organism and increases drug penetration
- Treat two weeks past the resolution of clinical signs***

**Antifungal classes (three)**

**Polyenes**

- preferentially bind to ergosterol (fungi cell membrane sterol)
- increases membrane permeability, leakage, oxidative damage
- broad spectrum
- good efficacy against filamentous and yeast fungi
- best for ulcerative disease
- start at every 2-4 hours, then taper
- Natamycin 5% suspension
  - only commercially available ophthalmic antifungal
- Amphotericin B: increased epithelial toxicity vs Natamycin

**Azoles**

- preferentially binds to fungal enzyme in cytochrome P450 system
- inhibits ergosterol synthesis, increases membrane permeability, alters fungi cell enzyme systems
- start at every 2-4 hours, then taper
- Imidazoles
  - Miconazole topical 1%
    - good penetration through intact epithelium
    - subconjunctival 1% - 5 to 10 mg q 24 to 48 hours
  - Ketoconazole topical 1%: best for ulcers, poorest efficacy of azoles

**Triazoles**

- Voriconazole topical 1%
  - good penetration through intact epithelium
  - refrigerate
  - systemic 3 mg / kg PO q 12 hours
  - good intraocular penetration with or without inflammation
  - more limited spectrum than other azoles
- Itraconazole 1% in 30% DMSO suspension
  - good penetration through intact epithelium
  - systemic 1.5 mg / kg IV q 24 hrs; 5.0 mg / kg PO q 24 hrs
  - poor intraocular penetration
  - if using PO, suggested to use IV solution as capsules have highly variable absorption
• Fluconazole topical 0.2%
  o poorer efficacy vs other azoles against filamentous sp. & yeast
  o systemic 14 mg / kg PO once, then 5 mg / kg PO q 24 hrs
  o good intraocular penetration with or without inflammation
  o more limited spectrum than other azoles
• Nucleoside analogs = Flucytosine: enzymatically altered within the fungal cell to the cytotoxic principal fluorouracil
• Other antifungal treatments
  o Silver sulfadiazine 1% ointment
    ▪ topical q 8 to 12 to 24 hrs
    ▪ metal ions bind microbial DNA and inhibit synthesis
• DILUTE Povidone – iodine solution
  o topical q 8 to 12 to 24 hours
  o germicide

Topical antibiotics
• Targeted therapy is ideal
• Prophylactic if primary organism is not identified
• May require more than one antibiotic
  o space frequency appropriately
• Gram negative: Ofloxacin, ciprofloxacin, aminoglycosides, chloramphenicol (not Pseudomonas)
• Gram positive: chloramphenicol, mofloxacin, Cefazolin / AT, neomycin, bacitracin
• Topical mydriatic / cycloplegic: 1% atropine
  o Reduces risk of posterior synechia and secondary glaucoma
  o Degree of mydriasis correlates with severity of cycloplegia
    ▪ more severe uveitis will require more frequent treatments
• Systemic NSAIDs
  o Flunixin meglumine (1.1 mg / kg) PO or IV q 12 hours
  o Taper dose with control of disease
    -typically tapered too soon
• Topical antiproteases
  o Autologous serum: serine protease entrapment
  o EDTA 0.2%: Ca / Zn chelation of MMPs
  o Tetracyclines: Ca / Zn chelation of MMPs (may also be administered oral)
  o N-Acetylcysteine 5-10%: Ca / Zn chelation of MMPs
• Systemic steroids
  o Not recommended due to increase systemic and ocular risks
• Omeprazole (Gastrogard)
  o Preventative dose: 2 mg / kg PO daily
  o Treatment dose: 4 mg / kg PO daily
• Oral / parenteral antibiotics
  o Penetration of drug into tear film, cornea, and anterior chamber unknown
  o Corneal inflammation and neovascularization may increase drug delivery
  o TMS, Potassium Penicillin, Gentocin
  o Doxycycline
    ▪ antibiotic
    ▪ anti-inflammatory
    ▪ anticollagenolytic
• Subconjunctival medications: simply not ideal
  o Limited area
  o Unpredictable drug bioavailability; often need BID – TID to achieve therapeutic levels
  o Incited inflammatory response

Surgical treatment
Utilize this option when medical therapy was delayed or is ineffective
Goals

- Remove infectious organisms and inflammatory cells
- Bring in structural support
- Bring in an immediate blood supply
  - protease inhibitors
  - growth factors
  - fibroblasts

Indications

- Ulcers with $>/=50\%$ stromal loss
- Ulcers with $<50\%$ stromal loss but associated with progressive malacia
- Descemetocele
- Corneal perforation / iris prolapse
- Monitor degree of uveitis

Procedures

- Conjunctival grafts (pedicle, bipedicle, free island, hood, bridge, 360 degree)
- Lamellar corneal grafts (corneoscleral or corneoconjunctival transposition; posterior lamellar (PLK) or deep lamellar endothelial keratoplasty (DLEK), penetrating keratoplasty) $+/-$
- conjunctival grafting
- Natural (autologous cornea, amnion) or synthetic / biosynthetic tissue (A-Cell, Biosys) graft

Medical treatment as indicated above after surgery

Prognosis

- Infection, corneal digestion, and associated inflammation must be controlled
- These cases are a huge financial, time, and emotional commitment
- Client education and constant client support by the veterinary team is key
- The use of the subpalpebral lavage system cannot be overemphasized
- Treatment is often very prolonged (weeks (3) to months (4)) and costly
- Vision: 50-90\% of cases
- Globe retention: 70-95\% of cases
Evidence-Based Approach to Cranial Cruciate Repair Surgery
Jennifer Wardlaw, DVM, MS, DACVS
Gateway Veterinary Surgery
St. Louis, MO

Current research and literature will be reviewed to encourage the audience to update and make their own decisions regarding this multi-million dollar problem in our small animal patients. This lecture gets to the heart of which procedures are the best in skilled surgeons’ hands for our canine patients.

Cranial cruciate ligament rupture is a common cause of hindlimb lameness in dogs and is seen in cats as well. Patients can be managed without surgery with exercise restrictions, body weight management and pain medications. However, a better prognosis is achieved when the patients are less than 15 kg. Also, the presence of a meniscal tear or concurrent patellar luxation makes medical management less successful.

When surgical stabilization is opted for, the veterinarian is faced with a plethora of options. The key is to find the balance of what the surgeon is comfortable with and what the best option is for the patient. If the best possible option is chosen by the veterinarian but they do not have the training or experience to perform the procedure correctly, the potential complications can be disastrous. The fact that several options are available to address the same surgical problem indicates that no one procedure is perfect for all cases and all situations. Being current on the options and the data published is necessary to make the most educated decisions for your patients.

There are innumerable intraarticular repair methods in the literature and the theory behind these is the basis for human ACL repair. However, due to the degenerative nature of CCLR in dogs, these techniques have fallen out of favor. Intracapsular techniques are degraded by the inflammatory mediators seen in stifles with osteoarthritis (OA). The result is an unstable surgical repair and a lower level of function due to lameness with progressive OA. Long term outcomes with intracapsular repair are not as good as extracapsular techniques. However, if this is the procedure you are most comfortable with, and the owner will not accept referral to a surgeon, than this may be the “best” option for that patient.

The original extracapsular prosthetic stabilization has gone through many revisions and adjustments since its inception in 1966. The current technique is usually a lateral circumf fabellar-tibial suture. Bone anchors can be used on the femur instead of around the fabella if preferred. The tibial suture is typically passed through a tibial bone tunnel located at the level of the long digital extensor tendon groove. Sutures can be tied or crimped. Nylon leader, monofilament or braided sutures are currently used, while stainless steel is no longer recommended due to cycling failure. The type of knot thrown can affect structural strength of some suture materials. For instance a surgeon’s throw may weaken knot security, but a square knot where the first throw is clamped to maintain tension while the rest of the knot is tied has not shown to weaken a number of suture materials. Crimps are available for use with specific prosthetic materials but are not interchangeable with sizes or types of sutures. Crimp placement requires addition equipment and slippage is found to occur in 8% of cases. However crimp placement has less elongation and more stiffness than a clamped square knot. The loop configuration of the prosthetic material has also been shown to influence performance. But in most cases, the tension of the suture is not conserved for longer than six to eight weeks after surgery. Most commonly the strength is lost through elongation or rupture. Despite positive clinical results, these techniques do not achieve normalization of stifte biomechanics to the cruciate deficient stifle and may not be the best option especially for large or overweight dogs.

Isometry and a stiffer prosthesis are the potential benefits of the TightRope CCL®. The FiberTape (Arthrex Vet Systems) used in the system has shown significantly greater stiffness and ultimate load to failure forces. However this puts the joint at risk if the prosthesis is over-tightened or if poor isometry is created with inaccurate bone tunnels. In a recent study the TightRope CCL® resulted in outcomes similar to that of the TPLO (Tibial Plateau Leveling Osteotomy). A multicenter study has shown 94% of dogs having good to excellent outcomes with a 9% major complication rate including implant failure, infection, and meniscal tear.

The TPLO surgery has historically been promoted for use in active large breed dogs or dogs with excessive tibial plateau slope. Several studies have found similar results six months postoperatively when comparing the extracapsular suture and the TPLO. However, the extracapsular dogs tended to be lighter and begin physical rehabilitation earlier than the TPLO group. It is possible that larger dogs treated with a lateral suture may have had a worse outcome. Clinically the TPLO dogs are believed to bear more weight sooner while the extracapsular dogs hold the leg up for 1-2 weeks. The TPLO surgery involves specialized equipment and is described as having a steep learning curve. Utilizing arthroscopy or a mini-arthrotomy is proposed to minimize patient discomfort over the arthrotomy used with the lateral suture technique. Complication rates with the TPLO are lower with unilateral or staged procedures ranging from 12-21%. A less specialized version of the TPLO is the Cranial Closing Wedge (CCW) which also lessens the tibial slope to negate tibial thrust, but also alters the mechanical axis of the tibia with a forward shift. This changes the biomechanics of the tibia and may change weight distribution on the menisci. The technique utilizes a saw but does not require a specialized bone plate. It can be combined with the TPLO in cases with excessive (greater than 30°) tibial slope.

The Tibial Tuberosity Advancement (TTA) is a newer procedure that eliminates cranial tibial thrust. The mechanics place the patellar tendon force perpendicular to the weight-bearing force through the stifle. A bone graft appears to be beneficial for speeding
the healing of the boney defect created. Specialized equipment is required but the procedure is technically less challenging and perhaps faster than the TPLO. Long term studies show similarities between the TPLO and TTA, although the TTA appears to take longer to heal the osteotomy and cannot be used in cases with excessive tibial slope. Implant designs are still changing with regards to fork design and available cage sizes for advancement. The overall complication rate for TTA ranges from 25-59%, including minor complications.

All of the osteotomy techniques require strict confinement while the bone heals. This may be a deciding factor between techniques in ill mannered dogs or outdoor-only animals. While physical rehabilitation is started early in all dogs, the postoperative care for the osteotomy dogs can be weeks to month longer than the lateral suture technique. However, early return to function is vital for joint health, and to rebuild muscle mass and regain lost bone density. Service or therapy dogs who are kept in a controlled manner will likely benefit from the quick return to weight bearing of the osteotomy procedures, with their daily activities being as controlled and calm as most rehabilitation programs.

The existence of so many variations on the same surgical problem has shown no concrete superior method for treating our veterinary patients exists to date. Research is ongoing to illustrate the pros and cons of the newer techniques to determine the best options. Kinematic and objective controlled multi-center prospective trials are needed. But patient needs and variation in fibrosis, activity level, meniscal damage and age along with owner financial constraints will all play into the decision of the “right” treatment modality.
Surgical Options for Repairing Luxating Patellas
Jennifer Wardlaw, DVM, MS, DACVS
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Soft tissue and orthopedic procedures are both needed to correct luxating patellas. The intricate details of both will be discussed with focus on anatomy and accuracy. Postoperative care and physical rehabilitation will also be discussed.

Patellar luxation can be congenital or traumatic. Congenital is typically the presentation for small and toy breed dogs. Although some large breed dogs can have it as well. It is typically bilateral, with medial being the most common side of the luxation. Often times one side may be more severe than the other side. Traumatic patellar luxation is typically unilateral in nature and tends to be laterally luxated.

The patella is a sesamoid bone in quadriceps mechanism and uses the straight patellar tendon to insert on the tibial tuberosity. Although the true pathogenesis is unknown, it may result from abnormal hip conformation, angle of inclination, or coxa vara. Any of these components that cause a malalignment of the quadriceps mechanism, can lead to patella luxation. After the patella has been luxated is leads to secondary changes to the limb including medial displacement of the quadriceps, lateral bowing of the femur, torsion of the distal femur, shallow trochlear groove, stifle instability and medial displacement of the tibial tuberosity.

Clinical signs are very suggestive of the disease with an intermittent lameness or “hopping”. Animals may also have a crouched stance or “bowlegged” appearance. Lameness often increases as degenerative joint disease develops. Diagnosis is based on clinical signs and physical examination. However, radiographs are needed of the entire hindlimb to assess for torsional deformity, hip conformation and other orthopedic issues as well. Radiographs will show the displacement of the patella on the craniocaudal view. Shyline views can also be used to assess the trochlear groove. Documentation of secondary arthritis is also important for prognostic goals following surgery.

The patella luxation grading system is currently used to help elicit when surgery is needed and judge the level of surgery needed to correct the limb abnormality.

Grade 1
- Intermittent luxation
- Patella can be manually luxated, but reduces spontaneously
- Rarely lame, occasionally skip
- Minimal medial tibial rotation

Grade 2
- Frequent luxation
- Patella luxates with stifle manipulation, reduces spontaneously with rotation of the tibia
- Lameness varies- occasional skip to weight bearing lameness
- Medial tibial rotation- up to 30°

Grade 3
- Patella is luxated but it can be reduced, reluxates
- Chronic lameness of varying severity
- Medial tibial rotation of 30° to 60°
- Moderate angular and torsional deformities

Grade 4
- Patella is luxated continually and cannot be manually reduced
- Limb is carried or the animal moves in a crouched stance
- Medial tibial rotation of 60° to 90°
- Marked angular and torsional deformities

Surgical repair goals are to realign the extensor apparatus, normalize the forces acting on the physes/cartilage and stabilize the patella in the trochlear groove. Soft tissue reconstruction is helpful, but not a surgical solution to this orthopedic condition by itself. More commonly used soft tissue procedures include; Imbrication of the lateral retinacular fascia, Patellar and tibial anti-rotational sutures, Medial release (desmotomy). Bone reconstruction is far more successful and should be the cornerstone of any patellar luxation surgery. Orthopedic corrections can include; Tibial tuberosity transposition, Trochleoplasty techniques, Corrective osteotomies of femur / tibia. The goal of surgery is to improve limb function in dogs with lameness. Surgery does not prevent the progression of OA.
Reluxation is common with up to 48% reluxation in one study. However relaxation is usually mild (grade 1), and clinical signs may be minimal, negating the need for further surgery.
Managing Hip Dysplasia in Young Dogs
Jennifer Wardlaw, DVM, MS, DACVS
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St. Louis, MO

At birth most hips are normal. The femoral head and neck are cartilaginous and begin forming bone by endochondral ossification. Joint congruence and stability are dependent on periarticular soft tissues. This congruency and stability is critical for normal joint development. Disparity in the development can happen with any boney part of the joint or soft tissue including muscles, ligaments and the joint capsule. The skeleton develops rapidly and small problems can rapidly lead to a chain reaction of disease. If the hip joint is lax or unstable it leads to poor joint congruence which causes subluxation and further abnormal hip development. A dog may have normal hips at birth but through genetics, nutritional or environmental factors, develops hip dysplasia (HD).

Nutritional influences such as a high plane of nutrition or imbalance can lead to HD. A high plane of nutrition affects growth rate and can lead to rapid bone growth and weight gain. This can over-load the soft tissue support and has been shown to increase the frequency and severity of HD. Studies have shown a faster than average weight gain may lead to HD, even with exercise restriction. A dietary electrolyte imbalance may affect the synovial fluid. A low dietary anion gap (sodium + potassium –chloride) results in less subluxation while excess may increase synovial fluid amount and joint laxity. This may be due to surface tension and hydrostatic pressure.

Pay special attention to “at risk” puppies during initial examination is a key component to managing these patients. Asking pertinent questions about their normal activity, keeping them lean and on a balanced diet to avoid adverse nutritional influences are key. In puppies that are large or giant breeds, or have known familial histories perform an Ortolani and Barden exam. Also consider switching off puppy formulas at 6 months to slow the rate of growth. You may also want to consider prophylactic management.

A radiographic diagnosis of HD is more difficult in younger dogs but can be performed with various techniques. The hip extended view is used by the Orthopedic Foundation for Animals (OFA), and the Norberg Angle. Distraction radiography is used in the PennHIP Program and Dorsolateral subluxation techniques. The OFA scale does not require special equipment but identifies OA and is not a sensitive method to detect early or mild laxity. You can also not certify with OFA until they are 2 years of age making it a difficult screening test for puppies unless they are severely affected. PennHIP requires certification to submit films as well as sedation or anesthesia of the patients. You need three mandatory radiographs. The distraction index is calculated off the percent of the femoral head that is luxated out of the acetabulum. A distraction index of greater than 0.3 is considered disease susceptible, but breed variation of measurements exist. This modality has been shown to be statistically predictable at 16 weeks of age.

Once you have a diagnosis or have decided for early prevention, time is one your side since you caught it early. Medical management is 80% successful and is clinically more helpful the earlier you begin. Weight control or reduction is the cornerstone to minimize the stress of the growing active joints. A regulated exercise program should be utilized but not overdone. OA disease modifying agents or nutraceuticals can be started early. Physical rehabilitation can be tailored for a puppy and includes homework for owners that promote not only joint health but obedience and training. NSAIDs can safely be used in puppies after 2 months if pain is an issue. The key to conservative treatment or prevention of HD is the multimodal approach. Controlled exercise programs should be designed for the active playful puppy. Consider postponing strict training until they are at least 6 months of age. Excessive force even on normal joints can cause OA. Agility, flyball, sporting and rescue training should be “walk through” training to get the idea and the motions without the force. Exercise is good in moderation and will help reduce obesity as well as maintain a good range of motion. Low impact exercise can be used liberally including swimming, walking, obedience class and leash training. Studies have shown that even with radiographic evidence at a young age of HD, weight control and leash walking can dramatically increase the range of motion, exercise tolerance and long-term function for years.

Nutraceuticals have been shown to be the most beneficial in offsetting OA when given before the inflammation starts, meaning preemptively when we suspect disease. Since they have minimal if any side effects and the potential for a large impact, it is easy to prescribe them to owners who are willing. Nutraceuticals have been called disease modifying agents, disease modifying osteoarthritic drugs, supplements, additive and vitamins. The key to understanding the options are to realize the FDA does not regulate these products for efficacy or quality. It is vital you find a company you like, believe in and has research to support their products and claims. If you are using a product and not seeing results, then try a new source. Some options work better for certain cases, but generally speaking when added to a well balanced multimodal approach can make a big difference with regards to patient comfort and cartilage health. Most contain glucosamine and chondroitin sulfate in various forms. It is reported that they are absorbed by the GI tract, become incorporated into joint tissues, and provide the necessary precursors to maintain cartilage health and decrease inflammation. Anecdotal reports, in vitro studies, and published clinical trials indicate that these agents are effective in treating OA.

Glucosamine is an amino-monosaccharide nutrient that has exhibited no toxicity even at high oral doses. It is a precursor to the disaccharide unit of glycosaminoglycans, which comprise the proteoglycan ground substance of articular cartilage. Studies using radiolabeled compounds in man and animals have shown that 87% of orally administered glucosamine is absorbed. Glucosamine acts
by providing the regulatory stimulus and raw materials for synthesis of glycosaminoglycans. Since chondrocytes obtain preformed glucosamine from the circulation (or synthesize it from glucose and amino acids), adequate glucosamine levels in the body are essential for synthesis of glycosaminoglycans in cartilage. Glucosamine is also used directly for the production of hyaluronic acid by synoviocytes.

In vitro biochemical and pharmacological studies indicate that the administration of glucosamine normalizes cartilage metabolism and stimulates the synthesis of proteoglycans. In one study, glucosamine stimulated synthesis of glycosaminoglycans, proteoglycan and collagen, suggesting it not only provides raw material for their production, but may actually up-regulate synthesis. The effects of glucosamine sulfate on human chondrocyte gene expression was also evaluated, assessing its effects on type II collagen, fibronectin and proteoglycans in normal adult chondrocytes. Glucosamine modulated the expression of cartilage proteoglycans, decreased stromelysin mRNA levels in osteoarthritic chondrocytes, and preserved the constitutive expression of type II collagen and fibronectin in both normal and osteoarthritic chondrocytes.

Chondroitin Sulfate (CS) is a long chain polymer of a repeating disaccharide unit. It is the predominant glycosaminoglycan found in articular cartilage and can be purified from bovine, whale, and shark cartilage sources. Bioavailability studies in rats, dogs and humans have shown 70% absorption of CS following oral administration. Studies in rats and humans using radiolabeled CS have shown that CS does reach synovial fluid and articular cartilage.

When human articular chondrocytes were cultivated in clusters in the presence of CS, proteoglycan levels were significantly increased and collagenolytic activity was decreased. A similar study indicated that CS competitively inhibited degradative enzymes of proteoglycans in cartilage and synovium. In a study of rabbits with chymopapain-induced stifle arthritis, proteoglycan depletion was reduced by the administration of CS.

Clinical trials in humans have also found CS to be effective in reducing the symptoms of OA. In a placebo-controlled, double-blinded study of 120 patients with OA of the knees and hips, treatment with CS resulted in significant improvements in pain-scale scores and pain-function index. In another study of 42 patients with knee OA, CS treatment significantly reduced pain and increased joint mobility. Bone and joint metabolism (as assessed by various biochemical markers) also stabilized in the patients treated with CS while remaining abnormal in patients receiving a placebo. Hyaluronic concentrations and viscosity were increased, and collagenolytic activity was decreased, in the synovial fluid of OA patients treated with CS for 10 days. These clinical trials indicate that CS has a positive effect in controlling the symptoms associated with OA. Combinations of glucosamine and chondroitin sulfate are commonly used and it has been reported that these agents work synergistically.

Dasuquin® (Nutramax Laboratories, Inc.) is a joint nutraceutical marketed for management of OA in dogs and cats. It is a combination of glucosamine, chondroitin sulfate, decaffeinated tea polyphenols, and avocado/soybean unsaponifiables (ASU). Tea polyphenols may have a positive effect on cartilage health and provide oxidative balance in the body. ASU, which are biologically active lipids, have been shown to be more effective than chondroitin sulfate in inhibiting the expression of certain OA mediators responsible for cartilage breakdown. In in vitro studies, ASU has been shown to decrease the expression of COX-2 enzyme, TNF-α, IL-1β, and PGE2 in chondrocytes. It was also shown to stimulate synthesis of cartilage matrix by increasing levels of TGF-β. A 2007 study found that dogs given ASU for 3 months had elevated levels of TGF-β in their synovial fluid compared to control dogs. The combination of ASU with glucosamine and chondroitin sulfate decreased the expression of numerous pro-inflammatory mediators, including TNF-α, IL-1β, and INOS. This decrease in pro-inflammatory mediators seen with Dasuquin® (Cosequin® with ASU) is greater than that seen with Cosequin® alone. In an in vivo study of the effects of Cosequin® on cartilage metabolism in dogs, serum samples were collected after treatment with Cosequin® and tested for circulating glycosaminoglycan content. Median serum glycosaminoglycan levels were significantly increased in treated dogs. When normal calf cartilage segments were exposed to the serum from the treated dogs, the biosynthetic activity of chondrocytes was significantly increased and proteolytic degradation of the cartilage segments cultured in serum was reduced. In vitro studies at the Nutramax laboratories also demonstrated the beneficial effect of Dasuquin® on chondrocytes from different species including equine, camelid, canine, feline and bovine. Dasuquin® inhibited the production of inflammatory mediators and signaling molecules in the inflammatory cascade.

Omega acid supplementation was discovered when dermatologic patients were experiencing relief from their OA. Maintaining a high content of the long chain omega-3 fatty acids EPA, and DHA is the key with this nutraceutical. Short chain omega-3s compete with omega-6s for conversion to long chain fatty acids and then for uptake into cell membranes. Omega-3s and omega-6s have different effects on the inflammatory response. Omega-6 arachidonic acid is the precursor to more pro-inflammatory mediators. While omega-3 EPA is a precursor to less potent inflammatory mediators. Omega-3s are readily available from several companies for veterinary as well as human products. Pet foods that contain them must be kept in a sealed bag for less than 30 days or they dry out. Fish oils will also help lubricate the skin and shine the coat. For large breed dogs I follow the human label recommendation for full grown dogs or half the dose for puppies. If you overdose the oils, they can have soft stool or diarrhea and should decrease the dose.

Some other options that are developing for easy oral administration include green-lipped mussel, methyl-sulfonyl-methane, duralactin and S-adenyl-L-methionine. Less research or anecdotal evidence exists for these but is continually being developed.
The use of joint nutraceuticals in dogs prior to the development of OA is controversial. No controlled studies have been reported that document the efficacy of nutraceuticals in preventing the development of OA. However, because of their reported effects on improving cartilage matrix and reducing levels of inflammatory mediators within the joint, many clinicians have advocated the prophylactic use of joint nutraceuticals, particularly in athletic and large dogs that might be susceptible to joint injury. Additional research is needed to confirm the value of prophylactic use of joint nutraceuticals.

There are also surgical options to diminish the signs of OA in puppies that have HD. The two surgical options are Juvenile Pubic Symphysiodesis (JPS) and Triple Pelvic Osteotomy (TPO). JPS is a simple procedure performed on puppies 12 to 20 weeks of age. But the optimal results are achieved on puppies less than 16 weeks old. Please note that this age is before the PennHIP certification age. The procedure fuses the pubic symphysis with electrocautery via a ventral midline incision. There are no implants and, with proper protection of the urethra and depth to avoid the colon, very few potential side effects. Electrocautery is used every 2-3 mm along the symphysis to cause thermal necrosis and premature closure. The pelvis continues to grow in all other planes while being static at the pubis, resulting in ventroversion of the acetabulum. This procedure is not readily detectable on OFA and PennHIP films and should therefore only be performed on animals that will be sterilized to avoid certifying or breeding falsely represented hip conformation. The TPO is typically performed on dogs less than 10-12 months of age without radiographic signs of OA. It is used to correct hip laxity. Three osteotomies are made on the pubis, ischium and ilium to allow reorientation of the acetabulum. Then an angled plate is placed on the ilium to secure the weight bearing axis for boney healing. The forced manual ventroversion increases dorsal coverage of the femoral head and reduces the formation of OA by improving joint stability and congruence. However bilateral surgery is not performed due to high complication rates and surgeries should be staged at least 4 weeks apart. Potential complications include a narrowed pelvic canal, sciatic neuropraxia, implant failure and an abnormal gait. Lameness improves in 92% of dogs and the progression of OA appears to be slowed with this procedure. The JPS and TPO procedures have similar effects on hip conformation, although neither eliminate laxity or completely cure HD. They can arrest or limit the progression of HD in mild to moderate cases. Both of these preventative surgeries require early puppy screening and counseling of owners about potential benefits and expected outcomes.
At birth the hips are normal. The femoral head and neck are cartilaginous and begin forming bone by endochondral ossification. Joint congruence and stability are dependent on periarticular soft tissues. This congruence and stability is critical for normal joint development. Disparity in the development can happen with any boney part of the joint or soft tissue including muscles, ligaments and the joint capsule. The skeleton develops rapidly and small problems can rapidly lead to a chain reaction of disease. If the hip joint is lax or unstable it leads to poor joint congruence which causes subluxation and further abnormal hip development. A dog may have normal hips at birth but through genetics, nutritional or environmental factors, develops hip dysplasia (HD).

A presumptive diagnosis of HD can often be made based on clinical signs or physical examination. Palpating for crepitus, a luxated hip or performing the Ortolani and Barden maneuvers can all help make a correct diagnosis of HD. A radiographic diagnosis of HD is more easily made in older dogs. The hip extended view is used by the Orthopedic Foundation for Animals (OFA), and the Norberg Angle. Distraction radiography is used in the Penn HIP Program and Dorsolateral subluxation techniques. The OFA scale does not require special equipment but identifies OA yet is not a sensitive method to detect early or mild laxity.

Medical management is 80% successful and is clinically more helpful the earlier you begin. Weight control or reduction is the cornerstone to minimize the stress diseased joints. A regulated exercise program should be utilized but not overdone. OA disease modifying agents or nutraceuticals can be started early. The key to conservative treatment of HD is the multimodal approach. Excessive force even on normal joints can cause OA. Exercise is good in moderation and will help reduce obesity as well as maintain a good range of motion and comfort.

Weight loss is the easiest and perhaps most beneficial part of a multimodal approach to OA. Minimizing the work the diseased joints have to contend with should be paramount to any regime. Dogs with OA should be kept on the thin side of normal. With proper weight management, many dogs are able to stop taking pain medications until much later in the disease process. Commercially available diets are geared towards weight loss as well as joint comfort. Diets should be low calorie and low in protein while providing an otherwise balanced nutritional plane. Having truthful conversations about treats and table scraps should be geared to reveal honest habits. Caloric responsibility should be encouraged and adjustments made to account for the dogs’ favorite treats or foods. Exercise is also important to maintain a good range of motion and weight level. Minimizing concussive forces like stairs, jumping, climbing, running, and horse play should be minimized while still maintaining a good quality of life. Encourage leash walks, swimming and pay close attention to what activities make them sorer afterwards. While we don’t want to lock our patients in a box or take away their quality of life, easing their burden is important for their joints. If they love to play fetch on the weekends, make their owners aware that that will be a painful time and they should premedicate or otherwise adjust the protocol for their pet. Having thick warm bedding should also be encouraged to help aching joints. If an overweight animal prefers the hard, cold floor, suggest placing a fan near the orthopedic bed to encourage usage.

NSAIDs are readily available and widely used for OA in dogs. The important thing is to find a drug that works well for each patient and to make the owners aware of potential side effects. If one stops working for a patient, try switching to a different one. When switching NSAIDs, a wash out period of at least two half-lives is recommended. NSAIDs can be used for painful flare ups, around times of increased activity, or later in the disease, for daily maintenance pain relief. For patients with NSAID sensitivities or for patients needing additional pain medication there are other options as well. Tramadol is a synthetic mu opiod with a wide safety margin. It can be given several times a day which make it ideal for use around exercise or physical rehabilitation periods. I typically use 5 mg/kg up to 4 times daily. Gabapentin is a GABA analogue design to treat epilepsy but is widely used for neuropathic pain and OA in people. The most common side effect appears to be sedation. An accepted canine dose is 5-10 mg/kg 2-3 times daily. Acetaminophen with codeine is an additional option for OA management. Due to the limited pill size it is often times easier to dose than tramadol in larger patients. Since it is not considered a COX1 or COX2 drug, side effects should be minimal when used concurrently with NSAIDs, but should still be considered. This drug is dosed off the codeine at 1-2 mg/kg three times daily.

Nutraceuticals have been shown to be the most beneficial in offsetting OA when given before the inflammation starts, meaning preemptively when we suspect disease. Since they have minimal if any side effects and the potential for a large impact, it is easy to prescribe them to owners who are willing. Nutraceuticals have been called disease modifying agents, disease modifying osteoarthritic drugs, supplements, additives and vitamins. The key to understanding the options are to realize the FDA does not regulate these products for efficacy or quality. It is vital you find a company you like, believe in and has research to support their products and claims. If you are using a product and not seeing results, then try a new source. Some options work better for certain cases, but generally speaking when added to a well balanced multimodal approach can make a big difference with regards to patient comfort and cartilage health. Most contain glucosamine and chondroitin sulfate in various forms. It is reported that they are absorbed by the GI
tract, become incorporated into joint tissues, and provide the necessary precursors to maintain cartilage health and decrease inflammation. Anecdotal reports, in vitro studies, and published clinical trials indicate that these agents are effective in treating OA.

Physical rehabilitation for muscle mass, range of motion and comfort are a huge component to managing an older dog with arthritis. Passive range of motion with stretching and massage can help aid in comfort while bathing the articular cartilage with nutrients from the synovial fluid. Increasing awareness with bedding, stairs, and household routines will help minimize concussive activities. While implementing therapeutic exercises during regular walks can increase muscle mass and range of motion, especially extension. Focus on increasing comfort while optimizing rear weight distribution through regular, motivated exercise.

If medical management is not an option or is not working for your patient, there are two salvage procedures; Total Hip Arthroplasty (THA) and Femoral head and neck ostectomy (FHO). THA is indicated for large and giant breed dogs but is available in sizes for small dogs and cats. Unilateral replacement is adequate for 80% of dogs. The procedure is technically challenging and expensive. There are cemented and cementless systems with templates and modular designs for a custom fit. The prognosis for a pain-free function is 95% having a good to excellent outcome. Potential complications include infection, luxation, fracture, sciatic neuropaxia or implant loosening. FHO is used to preserve limb function in severe OA when medical management is ineffective or when a THA has unrepairable complications. It is typically performed in small dogs and cats but can be used for larger dogs when THA is not feasible. It is less expensive and easier to perform than a THA. The prognosis is good in smaller patients but much better if muscle atrophy is not severe. Postoperative physical therapy is important to achieve a flexible pseudoarthrosis.
Coxofemoral luxation is the most commonly luxated joint in dogs, accounting for 90% of all luxations. It is usually the result of trauma or severe hip dysplasia with 78% being craniodorsally luxated. The primary stabilizers of the hip joint are the joint capsule and the ligament of the head of the femur also known as the round ligament for the teres ligament. The secondary stabilizers are the periartricular muscles, such as the gluteals and the hydrostatic pressure. In immature dogs, capital physeal fracture may result from hip trauma and dogs less than 11 months are twice as likely to fracture as they are to luxate their hips.

Diagnosis of hip luxation can be made with a history of trauma, physical examination, radiographs, but should also be focused on identifying other traumatic injuries. Physical examination of an acute luxation may show non-weight bearing lameness with external rotation of the femur and adduction of the limb. More chronic luxations may show some weight bearing. Palpation may reveal swelling in the hip region. Coxofemoral luxation may be identified palpably by placing a thumb in the ischiatic notch (between the greater trochanter and the ischiatic tuberosity) and externally rotating the femur. If the femoral head is normally seated within the acetabulum, the thumb will be displaced from the ischiatic notch with external rotation of the femur. However, if the femoral head is luxated, the clinician’s thumb is not displaced when the femur is rotated. The integrity of the coxofemoral joint may also be evaluated by palpation of the craniodorsal border of the ilium, the greater trochanter, and the ischiatic tuberosity. When the hip is reduced, the greater trochanter is positioned distal to the axis of a line drawn between the craniodorsal border of the ilium and the ischiatic tuberosity, and it is positioned markedly closer to the ischiatic tuberosity than the craniodorsal border of the ilium. With a craniodorsal luxation, the greater trochanter is equidistant from both points. With ventral and caudoventral luxations, the greater trochanter is displaced medially, and hip adduction and internal rotation may be constrained by entrapment of the femoral head within the obturator foramen.

Reduction and stabilization of the coxofemoral joint is preferred in most cases and may be accomplished using closed or open techniques. Conservative treatment can be tolerated in some cats in which, without reduction, a pseudoarthrosis may develop between the luxated femoral head and the caudal portion of the ilium, allowing limited, pain-free function. However, reduction and stabilization of the joint is recommended in cats that fail to bear weight on the limb within 4 to 5 days of injury, and in all dogs with coxofemoral luxation. In most cases, closed reduction of the coxofemoral luxation is attempted first. Although closed reduction is unsuccessful in many cases, attempted closed reduction before open surgical reduction does not appear to alter the long-term prognosis. However, initial open (surgical) reduction is indicated if acetabular or femoral head fractures are present, the joint relaxates after radiographically confirmed closed reduction, concurrent injuries require immediate return of hip function, or the luxation is chronic and visual evaluation of the cartilage is necessary. After closed reduction of a craniodorsal hip luxation, a non–weight bearing sling (Ehmer sling or figure of eight bandage) is typically applied to the hindlimb to maintain reduction. The Ehmer sling flexes the hip joint and abducts and internally rotates the femur to position the femoral head within the acetabulum. After closed reduction of a ventral luxation, hobbles may be placed on the hindlimbs (at the hocks or stifles) to prevent limb abduction and maintain joint reduction. However, many ventral luxations are managed successfully without hobbles. In a report of 14 dogs with caudoventral hip luxation, 80% returned to normal gait and function after closed reduction alone.

Insertion of an ischioilial pin (DeVita pin) has been described to stabilize the hip joint after closed reduction. A Steinmann pin is placed through a stab incision ventral to the ischium, is passed cranially over the femoral head, and is embedded into the wing of the ilium. Typically, the pin is allowed to remain in place for 2 to 4 weeks, with exercise restricted for an additional 2 to 4 weeks following removal. A study of 21 dogs with craniodorsal coxofemoral luxation demonstrated that reduction was maintained in 73% of dogs treated with ischioiliial pinning; however, the complication rate was 32%. Complications reported with ischioiliial pinning include pin migration, relaxation, sciatic nerve injury, damage to the femoral head, and joint sepsis. External fixation (both rigid and flexible) has been described for maintaining joint stability after closed reduction. No published studies have described the long-term outcome associated with the use of external fixation for hip joint stabilization.

Open reduction of coxofemoral luxations allows exploration of the joint, removal of hematoma and soft tissues entrapped within the acetabulum, and application of internal stabilization. The success rate after open reduction and stabilization (≈85%) is significantly greater than after closed reduction. Various techniques are used alone or in combination to stabilize the joint while the joint capsule and periartricular soft tissues heal. Techniques described for open reduction and stabilization are numerous and include capsulorrhaphy, ischioiliial pinning, prosthetic capsule technique, transposition of the greater trochanter, transarticular pinning, toggle rod stabilization, fascia lata loop stabilization, extra-articular iliofemoral suture placement, transposition of the sacrotuberous ligament, femoral head and neck excision arthroplasty, triple pelvic osteotomy, and total hip arthroplasty. Success rates of 83% to 90% have been reported with use of the capsulorrhaphy technique. However, in many cases, the joint capsule is too severely damaged to permit adequate closure.
The prosthetic capsule technique is performed if the joint capsule is damaged or avulsed from the acetabulum, two bone screws or bone anchors are placed in the dorsal acetabular rim to serve as anchor points for suture attachment. The prosthetic capsule technique is reported to prevent reluxation in 66% to 100% of cases. Excellent or good outcomes were noted in 65% to 67% of dogs; 18% had mild lameness and 18% had severe lameness.

Osteotomy of the greater trochanter can improve exposure to the joint for other open reduction techniques. The greater trochanter is reattached with a tension band wire fixation or a lag screw. Trochanteric transposition alone prevented reluxation in 84% of patients in one report. Toggle rod stabilization allows early use of the limb after surgery, which may be necessary if injury to the opposite hindlimb or forelimbs are present. Although toggle rod fixation is often used as a single technique, this method of repair may be augmented by capsulorrhaphy if a midsubstance tear of the capsule occurs, or by the prosthetic capsule technique if the capsule is avulsed from the acetabular rim or femoral neck. If a dorsal open approach was used, the greater trochanter is transposed or reattached to its original position using tension band wire fixation. Toggle rod relaxation rate is less than 11%, with 81% of dogs exhibiting little or no long-term lameness, when commercial toggles are used.

An extra-articular iliofemoral suturing technique has been described for stabilization of hip luxation in dogs and cats. A hole is drilled from lateral to medial in the ilium just cranial to the acetabulum. A second hole is drilled from caudal to cranial through the femur just distal to the insertion of the gluteal muscles at the base of the greater trochanter. The suture is then passed from cranial to caudal through the hole in the femur, and from caudal to cranial beneath the insertion of the gluteal muscles on the greater trochanter and tied. An alternative method of placing the suture, which avoids the need to drill holes in the ilium and femur, has been described, in which the suture is anchored cranially in the tendon of origin of the psoas minor muscle and caudally to the tendon of insertion of the middle gluteal muscle. A report of 14 dogs described no reluxations and nor complications with dogs bearing weight 1 to 10 days postoperatively. Lameness persisted for an average of 20 days.

Surgical removal of the femoral head and neck is indicated for the treatment of recurrent hip luxation, concurrent severe fractures of the acetabulum or femoral head and neck, and coxofemoral osteoarthritis. Femoral head and neck excision should be considered if closed and open techniques are unsuccessful, if severe femoral head damage is present and total hip replacement is not an option for the patient or client, or if the client wishes to avoid the possibility of reluxation and additional surgery. Excision arthroplasty is also used by some surgeons as a primary treatment for hip luxation in cats because the procedure typically leads to full return of function.

Triple pelvic osteotomy has been described for management of craniodorsal coxofemoral luxation; it provides stability by rotating the acetabulum laterally to provide greater coverage of the femoral head. This technique has been used primarily for recurrent luxations, for dogs with hip dysplasia, and for coxofemoral luxation after total hip replacement. Hip replacement arthroplasty may be used in cases of chronic reluxation, severe osteoarthritis, or damage to the femoral head.

Postoperative care for most patients with coxofemoral luxation should include confinement and restricted activity for 4 to 6 weeks to allow soft tissue healing. After closed reduction of a coxofemoral luxation, the limb is typically placed in a non–weight-bearing sling (Ehmer or figure of eight) for 7 to 14 days, and the patient is monitored closely for complications. However, many internal stabilization techniques can be used without external coaptation, allowing early postoperative use of the surgically treated limb if necessary. Patients should be monitored closely for clinical signs of reluxation, including lameness, hip pain, and reduced function. Serial radiographic evaluation of the joint is warranted to confirm reduction, monitor for implant complications, and assess the development of osteoarthritis. Medical management to preserve healthy articular cartilage should be instituted because development of arthritis is a common complication after hip luxation. Initiating OA management should be early to achieve the most benefit. Nutraceuticals, anti-inflammatory drugs and physical rehabilitation should be considered to promote an early return to function and maintenance of joint health when an arthroplasty is not performed. Hip arthroplasty, either hip replacement or femoral head ostectomy, require specific postoperative care and exercise regimes.

The prognosis after coxofemoral luxation is fair to good if reduction and stability are achieved soon after injury. A long-term study (8 to 156 months’ follow-up) of 64 dogs treated for coxofemoral luxation using various techniques, including closed reduction and bandaging, extracapsular suture stabilization, toggle rod stabilization, DeVita pinning, and femoral head and neck excision arthroplasty, found that 62% showed no lameness and 20% were severely lame. Palpation of the hip joint revealed crepitus in 32% of dogs and pain in 48% of dogs. In all, 92% of dogs were found to have normal range of motion in the affected hip joint. Investigators also reported that the presence of concomitant injuries and treatment delayed for longer than 3 days did not result in a worse prognosis. Osteoarthritis of the hip joint progresses in 55% to 62% of patients after coxofemoral luxation and was more pronounced in heavier dogs.
A fairly recent study* showed that 32% of dogs referred to a surgeon for hip dysplasia treatment had, in fact, a torn ACL. Indeed, differentiating between a torn cruciate ligament and hip dysplasia can be tricky if not frustrating. Let's review the differences between the two conditions.

**Cranial cruciate ligament tear**

Severity of lameness depends on the severity of ligament disruption.
- In stable partial tears, lameness can be subtle and noted only after periods of strenuous activity.
- In complete tears, lameness will initially be severe and non weight-bearing. Then, moderate to severe weight-bearing lameness will occur.
- In obvious cases, of course, a positive cranial drawer and a tibial thrust are the keys to diagnosing a cranial cruciate rupture. But what to do in less obvious cases?
- Examination reveals various degrees of stifle pain with flexion and extension, variable crepitus, and possibly clicking associated with a meniscal tear.
- In partial tears, a pain response is elicited when the joint is in full extension. In chronic cases, muscle atrophy is notable and periarticular fibrosis (medial buttress) is evident on the medial side of the stifle. Medial buttress is almost pathognomonic for a cranial cruciate rupture. The only other condition that can present with medial buttress is a medial collateral ligament tear, which is usually seen with a deranged stifle, not a simple lameness.
- Joint effusion is also a key finding: it can be palpated on the medial and lateral aspect of the patellar tendon.
- Affected dogs have an abnormal "sit test," i.e. they sit with the affected leg extending out to the side, rather than sitting squarely (which they will do even with hip dysplasia). This is critical step in the evaluation. See below how this Lab does not want to flex his left knee.

In a partial tear, the cranial drawer may or may not be present. A sedated exam is needed to confirm the findings. MANY patients who don't seem to have a drawer while awake, suddenly have one once they are sedated and relaxed.
- Radiographs are warranted in all cases to document stifle arthritis, to confirm pathology in challenging cases of partial tears, and to rule out other disorders (occasionally, we find a tumor).
- The earliest and most consistent finding is the loss of infra-patellar fat pad shadow by a soft tissue opacity in the lateral view. This is consistent with effusion.
- Caudal displacement of fat density located caudal to the joint capsule by a soft tissue opacity is also consistent with synovial distention.
- In many cases, you can "see" the cranial tibial thrust on an X-ray. See below how subluxated the knee is.
- Another consistent finding is osteophyte and/or enthesiophyte formation in the region of femoral trochlear ridges, tibial plateau, and at the base and apex of the patella.
- Rupture of the contralateral cruciate ligament occurs in 37%-48% of dogs within 6-17 months of the initial diagnosis. However, rupture can be bilateral on presentation, often times giving them a “neurologic” crouched walk.

**Hip dysplasia**

Hip dysplasia causes joint inflammation and secondary osteoarthritis, which lead to variable degrees of pain. Clinical signs can vary from slight discomfort to severe acute or chronic pain. Although the disease onset has a linear progression over time, it can be divided into two forms.
- The juvenile form typically affects dogs between 5 and 12 months of age. They present with unilateral or bilateral hind limb lameness, bunny hopping, and difficulty rising after rest, reluctance to walk, run, jump, or climb stairs, exercise intolerance, and pain on hip extension.
- These clinical signs are the result of joint laxity.
The chronic form of hip dysplasia has a highly variable onset of clinical signs in old dogs. Pain is most often related to DJD and has a more chronic presentation. Clinical signs are similar to the juvenile form. Pain is elicited most notably during hip extension.

As the disease progresses, crepitus can be palpated with range of motion. A sedated exam followed by orthogonal radiographs will further support the diagnosis.

Hip dysplasia dogs have a normal "sit test," i.e. they sit with both legs flexed symmetrically.

**Hip and knee**

Of course, both conditions can be present at the same time. In the study mentioned above, 32% of dogs referred to a surgeon for hip dysplasia treatment had, in fact, a torn cranial cruciate ligament. Interestingly, 94% of those dogs with a cruciate tear had concurrent radiographic signs of hip dysplasia.

It is imperative to do a thorough orthopedic and neurologic exam to accurately localize the clinical signs to avoid inappropriate diagnosis and treatment.

My absolute best advice? If in doubt, repeat your entire exam under sedation. Let's go over the 7 magic benefits of sedation:

1. Sedation allows you to check for cranial drawer, tibial thrust, Barden and Ortolani sign.
2. Under light sedation, you may still notice a pain response: increased respiratory rate or pulling on the leg.
3. Under heavy sedation, total relaxation allows you much better joint evaluation.
4. Sedation allows you to tap the knee (arthrocentesis), which is an invaluable test.

Crudely, normal fluid = clear, tiny amount and viscous. Abnormal fluid = yellowish, large amount and watery.

1. Sedation allows you to "block" a joint, with lidocaine and/or steroids.
2. Sedation enables you to take X-rays in a perfect position (knee = TPLO position, with a quarter in the picture; hip = OFA style) without fighting or causing pain.
3. Sedation allows you to focus and take your time without fighting with your patient and alienating your technicians.

**Reference**

How to Lower Infection Rates in Orthopedic Surgeries
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The normal incidence of clean surgical wound infections is 0-4.4%. Keeping your hospital and staff under good surveillance will help minimize nosocomial infections. Washing hands between patients, using soap for at least 20 seconds and using care when taking rectal temperatures to clean equipment and hand will help. The main sources of surgical infection come from the OR, the surgical team, instruments, but mostly the patient’s endogenous flora.

Antibiotics should be considered for surgeries over two hours, ones with implants, or if there is a break in asepsis. If the animal has been on an appropriate antibiotic for a few days prior to surgery, perioperative antibiotics are not needed. For orthopedic procedures indicating the need for antibiotics, *Staphylococci spp.* are the most common skin flora we encounter. Therefore, most orthopedic surgeons choose cefazolin or similar antibiotics. However, good surgical technique is the best prevention of infection and when a break in asepsis occurs it should be repaired appropriately. Not every patient and every surgery needs antibiotics and the potential downsides or complications should be weighed against the risk with need for perioperative drugs. Typically perioperative antibiotics are given at induction or 30 minutes before the skin incision, then every 90 minutes. The first dose should not be given until cultures are obtained, if they are indicated.

Anesthesia reduces a patient’s resistance to infection. Propofol has been associated with higher postoperative infections, and sepsis. It should be used with aseptic technique and promptly disposed of to avoid contamination. Maintaining a patient’s blood pressure and body temperature will help their immune system fight infection. Warming tables, circulating water blankets and Bair Huggers should be considered. Bair Hugger’s have been shown to grow bacteria in their hoses and may increase wound colonies, although data is conflicting. Most surgeons prefer to turn on the Bair Hugger after the patient is completely draped to avoid this potential issue.

Controlling the surgical environment will limit bacteria significantly. Disinfection of equipment should be routine and frequent. Traffic should be minimized, the door closed and laminar flow should create 15 air exchanges per hour. Laminar flow decreased room bacteria by 61% and wound bacteria by 92%. Proper surgical attire should be fresh scrubs, caps that cover all hair and masks that are soft with pleated fabric. Shoe covers may help with sanitation but are not necessary.

Patient preparation should include getting rid of fleas if present, bathing if dirty (dry completely afterwards), walking outside to eliminate or expressing the bladder. Shaving should be performed while surgical scrubs are protected with a lab coat, in the prep area. The surgical clip should be performed with a 40 blade, against the grain, at least two clipper blades from the proposed incision. Hair should be removed with a vacuum. Care must be taken not to cause razor burn by keeping clipper blades clean, sharp and well lubricated. Clipper cleaning should be performed after every surgical prep case. A rectal purse string should also be considered for pelvic limb procedures.

The surgical site is prepared with a rough prep in the preparation area, and then a final sterile prep in the surgical suite. The skin cannot be sterilized, but the number of bacteria can be significantly reduced. The “ideal” method is elusive but several options exist. Povidone-iodine (PI) is cheap, has a broad spectrum, but will stain fur, and is inactivated by organic debris. Chlorhexidine (Chlorhex) has good activity in organic debris, good residual activity, broad spectrum, low tissue toxicity except mucous membranes and does not stain clothing. Rinsing agents are commonly used but not necessary. 70% Isopropol alcohol is antibacterial, dries quickly but is flammable and may cool the patient. Sterile saline is non-flammable but has not antimicrobial activity.

A 3 minute chlorhex scrub was shown to be equivalent to a 10 minute PI scrub in one study with no difference in infection rates. Another study agreed that both scrubs work, but the Chlorhex with saline had a better residual activity than Chlorhex and alcohol. Alcohol rinse after iodine helps release the iodine activity, but decreases the residual activity as well. If an alcohol rinse is used, the surgical site should then be painted or sprayed with betadine.

The surgical site prep is performed next in the surgical suite. It is ideally performed with sterile gloves, with sterile gauze and prep basin with ‘new’ surgical scrub. If a rinsing agent is not used, dry gauze can be used to remove the scrub detergent. Good technique should be used for the sterile scrub to not contaminate the surgical site during the scrubbing. It should be noted that one step 70% PI solution was as efficacious as alternating with alcohol and is much simpler. Additionally paint-only or spray-only seems efficacious as well. One study indicated that applying antiseptic with gauze versus sterile gloves did not make a difference as long as the proper agent and contact time were used.

Surgeon prep with surgical scrub offers the same multitude of scrub solutions. PI and chlorhex have the same pros and cons for the surgeon’s hands as they did for the patient’s leg. However, the World Health Organization and scientific evidence support the use of hydro-alcoholic rubs for presurgical hand scrubs. If your hands are free of gross contamination, these methods are less abrasive and less likely to cause bacterial proliferation on microabrasions from the scrub sponge. Two such solutions are Avagard (1% chlorhax,
61% alcohol) and Sterilium (80% alcohol). Numerous studies compare the two solutions, but both work very well and the choice is
surgeon preference.

Strict aseptic technique should be followed once in surgery. Surgeons should stand properly to avoid contamination, surgical
supplies should be handled properly, opened properly and their sterility confirmed. Sterile saline for lavage should be poured from a
fresh unopened bottle with care to avoid splashing on the instrument tray. Traffic around the room should be minimized. It is
everyone’s responsibility in the room to monitor for a break in asepsis and make the surgeon aware if such a break occurs. When in
doubt, change it out.

Surgical drapes should be resistant to penetration, strike-through and movement. Four quarter drapes are used at the primary layer
and may be adhesive or towel clamps applied. Once the foot is captured with sterile vetwrap, a full length patient drape should be
used to cover the entire patient. Clamps on the patient drape should not penetrate both layers of drapes. A stockinette or ioban on the
incision may be used but are not necessary. However, some sort of sterile water impermeable layer must be applied over the sterile
vetwrap due to its porosity. All cables, hoses etc. should be secured with a non-penetrating clamp as well.

Disposable gowns decrease contamination rate. Hemostasis, minimizing tissue trauma, good aseptic technique and speed are all
important for the surgeon to be mindful of. Infection rate doubles with every hour of surgery. Braided suture should be kept off the
skin during handling. Gloves should be checked regularly for holes and remain tight on the hands and fingertips. Wearing double
gloves or orthopedic gloves will decrease the chance of exposed hands. 84% of glove defects occur in procedures over an hour long
and individuals were not able to accurately predict a defect. Overall glove defects occurred in 23% of cases and were more likely to
occur in orthopedic cases.

Surgical closure can be performed with staples for speed or suture for cost savings. A couple of studies contradict whether staples
versus sutures are better for closure on TPLOs and extracapsular surgeries. But notably, one retrospective study showed no increased
benefit of antibiotic impregnated suture for preventing infection with TPLOs. This may indicate there is not a need for these more
expensive sutures in clean procedures.

After surgery patients should have their bladder expressed or emptied to avoid eliminating on the surgical site, body temperature
should be brought back to normal. Clean bedding with spill resistant water bowls should be maintained throughout the hospital stay.
Postsurgical site infections in dogs and cats can be minimized with these proactive precautionary steps.
Laser therapy is Light Amplification by the Stimulated Emission of Radiation (LASER). Lasers are classified into four levels depending on their potential to harm tissue. Class 1 is a laser pointer used in lectures or at a grocery store while an example of a Class 4 laser would be a surgical cutting laser. Class 3 and 4s are used for low level laser therapy or physical rehabilitation. They are advocated for many things but mostly for wound healing and pain relief.

Laser therapy cause cellular oxygen production by photons being absorbed into the mitochondria. This in turn causes a proton gradient across the cell and mitochondrial membrane. The gradients result in increased cell permeability. Laser therapy also stimulates the production of ATP, thereby stimulating DNA production. Also laser therapy increases cellular metabolism and growth. This accelerates tissue repair and cell growth in tendons, ligaments and muscles.

There are also indications in human and rodent models that laser therapy may block pain transmission through conduction latencies and selectively inhibit nociceptive neuronal activities. It may also increase endorphins. For this reason laser therapy is being used for muscle trigger points and acupuncture, called acupressure.

Laser therapy is advocated in wound healing due to its ability to stimulate fibroblasts and speed collagen production to repair tissues. It appears to accelerate angiogenesis and neovascularization. Laser is used on edema because it causes vasodilation and improves lymphatic drainage. It appears laser therapy may help with surgical incisions, open wounds and burns. The goal of wound laser therapy is to increase blood circulation, stimulate the reduction of hemoglobin, then stimulate both the reduction and immediate re-oxygenation of cytochrome c oxidase. This is the normal metabolic, wound healing process, just trying to speed it up with laser therapy.

Lasers emit energy, or joules, at a certain wavelength. This wavelength determines how deep the laser will penetrate into the tissue. The power, or watts, of a laser is the rate or speed at which it can deliver the desired energy to the tissues. There are many different lasers with different penetrating wavelengths, but the energy density or dose for square of centimeter of tissue is the critical data point. Not only does the laser light need to fully penetrate the area we want, but it needs to bring the right level of energy to the tissue. Based on the size of the tissue or area we are treating (cm2) is how we determine the total dosage (J/cm2). The power of your laser will determine if that takes you 10 seconds or 10 minutes to accomplish that treatment dose. Research is still ongoing for determining whether continuous wave, or pulsed wave lasers are better, if daily or every other day protocols are superior and what the ideal dosage is for a condition. So given all the variables in laser company styles, format and protocols, it is of paramount importance that we discuss energy density and dosages in the same concise language so we can communicate appropriately; Joules per centimeter squared.

We do know that the minimum dosage in humans to achieve a photochemical response to laser therapy is 5 J/cm2. We also know there are contraindications to laser therapy; active hemorrhage, local steroids, pregnancy, cancer, heart disease, photosensitive medications.

There are limited studies looking at laser therapy, but many are in progress. Once human study should an improvement in pain relief for 2 months and up to 1 year after a two week protocol. A canine study showed similar results with weekly sessions for four to six weeks showing 70% of patients showing some improvement in arthritic pain and gait abnormalities.

The difference between commercially available laser units lie solely in the wavelength, power density, pulse modulation and aesthetics. The goal is to stimulate the cell, and ultimately the body, to perform its natural functions, but at an enhanced rate.