2019 Canine Conference

Proceedings

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2019 CANINE CONFERENCE: Presenters Biographies

Dr. Audrey Cook, DVM, DABVP, DACVIM, DECVIM – Associate Professor. VSCS.

Dr. Audrey Cook obtained her veterinary degree at the University of Edinburgh. She completed an internship in small animal medicine and surgery at North Carolina State University before starting her residency in small animal internal medicine at University of California at Davis. She is board certified through the American College of Veterinary Internal Medicine and the European College of Veterinary Internal Medicine. In addition, she is one of the few internists with additional certification in Feline Practice through the American Board of Veterinary Practitioners.

Dr. Alison B. Diesel, DVM, DACVD – Clinical Assistant Professor. Dr. Alison Diesel is a Clinical Assistant Professor in Texas A&M University. She graduated from Kansas State University College of Veterinary Medicine in 2005 then completed a rotating internship in small animal medicine and surgery at the Veterinary Referral and Emergency Center in Norwalk, Connecticut She worked as an emergency clinician for one year prior to beginning a three-year residency in dermatology at the University of Wisconsin-Madison School of Veterinary Medicine; she became board certified (ACVD) in 2010. She joined the faculty in the fall of 2010 to continue to expand the growing dermatology service and to help guide veterinary students in the management of skin disease in companion animals. Her main research interests lie in feline dermatoses, expanding knowledge of the cutaneous microbiome in companion animals, and methicillin-resistant Staphylococcal skin infections.

Dr. Sarah Hamer, PhD, DVM – Assistant Professor. Dr. Sarah Hamer has been an Assistant Professor at Texas A&M University at the CVM for the past 5 years. She runs a research lab focused on the ecology and epidemiology of zoonotic, wildlife, and vector-borne diseases. Her

PhD in Ecology and DVM degrees are from Michigan State University, and she is a Diplomate in the American College of Veterinary Preventive Medicine. Her research combines field and molecular approaches to study the natural cycles of disease across the landscape in order to identify targets for the protection of human and animal health.

Dr. Johanna Heseltine, MS, DVM- Clinical Assistant Professor. VSCS. Dr. Johanna Heseltine graduated from the University of Saskatchewan and then completed a rotating small animal internship at the University of Prince Edward Island. She completed her Master's degree and small animal internal medicine residency at Virginia Tech and is a Diplomate of the American College of Veterinary Medicine (specialty of small animal internal medicine). She has held faculty and teaching positions at Oklahoma State University and the University of Saskatchewan, respectively. She has also practiced in private specialty clinics in Vancouver, British Columbia and Sugar Land, Texas.

***Dr. Unity Jeffery, VetMB, PhD, DACVP* – Assistant Professor. VTPB.** Dr. Unity graduated from the University of Cambridge and earned her VetMB. Then she earned her Ph.D from Iowa State University. She is currently an assistant professor at Texas A&M University. Her scholarly interests include clinical pathology, diagnostics and treatment for common canine disorders, and veterinary patient safety.

Dr. Jonathan Lidbury, BVMS, MRCVS, PhD, DACVIM, DECVIM-CA- Assistant Professor. VSCS. Dr. Lidbury graduated from University of Glasgow, Scotland. He worked for several years in general and referral practices in the United Kingdom before completing an internship in small animal medicine and surgery at the California Animal Hospital, Los Angeles, California. He then joined the Texas A&M University GI Lab as a PhD student and he started his residency in small animal internal medicine and received his board certification in 2011. His areas of interest include small animal gastroenterology and is

working to develop new non-invasive tests for liver disease in dogs

Dr. Joseph Mankin, DVM, DACVIM, Clinical Associate Professor. Dr. Joseph Mankin received his DVM degree from the University of Tennessee. He completed an internship in small animal medicine at Purdue University, followed by a residency in neurology/neurosurgery at the University of Tennessee. Dr. Mankin is a Diplomate of the American College of Veterinary Internal Medicine (neurology). His special interests include neurology, neurosurgery, and neuroradiology.

Dr. Ashley Saunders, DVM – Associate Professor. Dr. Ashley Saunders is an Associate Professor of Cardiology at Texas A&M University and a native Texan. She is board certified in the specialty of cardiology by the American College of Veterinary Internal Medicine and is a fellow of the Michael E. DeBakey Institute for Comparative Cardiovascular Science and Biomedical Devices. She joined the faculty in the College of Veterinary Medicine and Biomedical Sciences at Texas A&M University in 2005. Dr. Saunders areas of interest include congenital heart disease, interventional cardiology, advanced imaging and innovative teaching. She serves as an editor for the Journal of Veterinary Cardiology and has won multiple teaching awards including the Texas A&M Association of Former Students University-Level Distinguished Achievement Award in Teaching.

Dr. Katie Tolbert, DVM, PhD. Dr. Katie Tolbert completed her veterinary degree and small animal internship at the University of Georgia. She then completed a small animal internal medicine residency and Ph.D. in Comparative Biomedical Sciences at North Carolina State University. Before coming to Texas A&M University as a Clinical Associate Professor, was on faculty at the University of Tennessee, College of Veterinary Medicine and consulted for the TAMU Gastrointestinal Laboratory. Her clinical research program is focused on small animal gastroenterology with a specific interest in the investigation of the efficacy of gastroprotectants and the rationale for their use in the treatment of acid-related disorders, organ failure, neoplasia, and inflammatory diseases in companion animals. Her basic science research program is dedicated to characterizing the pathogenic mechanisms and exploring novel therapies for GI

infections with a particular emphasis on feline *Tritrichomonas foetus* infection. A list of her peer-reviewed publications and grants can be viewed at: orcid.org/0000-0001-8725-9530:

Dr. Andra Voges, DVM- Clinical Associate Professor. VLCS. Dr. Voges graduated from Texas A&M University in 1991. She is a Diplomate of American College of Veterinary Radiology and her areas of interest include clinical radiology, ultrasound and nuclear medicine in small animal and exotic pets, and advanced imaging with 3D software and models.

Dr. Emma Warry, DVM - Clinical Associate Professor. Emma Warry joined the Texas A&M College of Veterinary Medicine & Biomedical Sciences, Department of Small Animal Clinical Sciences as a clinical associate professor of medical oncology in 2018. Dr. Warry obtained her veterinary degree from University of Sydney and went on to complete a residency in medical oncology at Colorado State University, as well as a fellowship in bone marrow transplantation at North Carolina State University. In 2013, she joined the faculty at Ohio State University as a clinical assistant professor and will complete her master's degree in clinical trial design at OSU in 2019.

Dr. Sonya Wesselowski, MS, DVM, DACVIM (Cardiology) - Clinical Assistant Professor. VSCS. Dr. Wesselowski graduated from Kansas State University with her MS and DVM. She then went on to complete an internship at Vet Care Animal Hospital & Referral Center and her residency in cardiology at Virginia Tech University, where she also graduated with another MS degree. Her areas of interest include degenerative mitral valve disease, echocardiographic imaging, and congestive heart failure.

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WHEN SHOULD I SUSPECT GER, HIATAL HERNIA, OR RELATED ESOPHAGEAL DISORDERS?

Katie Tolbert, DVM, PhD, DACVIM
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Esophageal dysmotility is defined by a disruption in the passage of food or liquid from the upper esophageal sphincter to the stomach. There are many causes of esophageal dysmotility including anatomic/structural, neurologic, metabolic, inflammatory, and neoplastic disorders. Thus, diagnosis of specific causes of dysmotility such as gastroesophageal reflux (GER) and hiatal hernia can be challenging. In this presentation, we will use three clinical cases to review a diagnostic and therapeutic approach that can help with the diagnosis of these and other esophageal disorders. A summary of the approach is included below. More detail will be provided in the seminar.

Esophageal dysmotility can be divided into anatomic and functional causes, with anatomic (e.g. structural, inflammatory, and traumatic diseases) being the most common reason for the development of esophageal dysmotility. Thus, evaluation and, if suspected, empirical treatment of anatomic disease such as GER is a reasonable approach for patients where finances are a concern and the patient is presented with stable disease. The signalment, history, and findings on physical examination can help narrow down prioritize a diagnostic approach for animals with esophageal dysmotility. Regurgitation, whether observed or suspected, is a defining feature of esophageal dysmotility. Dysphagia, ptyalism, and odynophagia can also be reported if painful esophageal lesions or concurrent oropharyngeal disease are present. Obtaining a detailed medication and sedation/anesthesia history is important for all animals but is especially important for cats who are more susceptible to drug-induced and sedation-induced esophagitis and esophageal stricture because of their decreased esophageal motility compared to dogs. Dogs, especially brachycephalic breeds, are likely more predisposed to gastroesophageal reflux disease. Sudden onset esophageal dysphagia is more common with reflux esophagitis, esophageal stricture, and esophageal foreign body. These differentials would also be considered if regurgitation immediately followed eating. Chronic and delayed regurgitation are more commonly seen with megaesophagus. Special attention should be paid to the physical and neurologic examination. Animals who are underweight are more likely to have a chronic esophageal disease. The cervical neck including salivary glands and proximal esophagus should be carefully palpated. Patients with inflammation of the salivary glands generally have bilaterally enlarged salivary glands. Patients with vascular ring anomalies may have a palpable enlargement of their proximal esophagus. Patients with esophageal perforation may be lethargic, febrile, and/or have a draining tract or cellulitis in the subcutis of the neck. Regurgitation can also be observed infrequently in dogs with normal esophageal transit but delayed gastric emptying disorders such as gastric stasis or pyloric stenosis. However, abdominal distension secondary to gastric retention and food or water is often present in these patients.

Minimum data base blood work, routine imaging (thoracic and cervical) and swallowing study (unless megaesophagus is identified on radiographs) should be considered as frontline diagnostics for patients with esophageal dysmotility. Additional diagnostics (infectious disease testing, baseline cortisol, acetylcholine receptor autoantibody titer, endoscopy, etc) are pursued when history, physical exam, and frontline diagnostics direct additional testing.

With the exception of cricopharyngeal achalasia and surgically correctable esophageal hernias or tumors, most causes of dysphagia are medically managed. If possible, treatment is directed at the underlying cause (e.g. steroid therapy for addisonian patients, acetylcholinesterase inhibitors for patients with myasthenia gravis, etc). Symptomatic and supportive therapy is provided in the form of nutritional management (food bolus modification based on esophagram findings, upright feeding, frequent small meels, low fat diets, feeding tubes). The use of additional supportive care (i.e. analgesics, acid suppressants, pro-kinetics) is dictated by the patient's clinical signs. These therapies are covered in detail in the seminar on the rational use of gastroprotectants.

RATIONAL USE OF GASTROINTESTINAL PROTECTANTS

Katie Tolbert, DVM, PhD, DACVIM

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Acid Suppressants:

Choices for commercially available acid suppression include histamine-2 receptors antagonists (H2Ras; e.g. famotidine, ranitidine) and proton pump inhibitors (PPIs; e.g. omeprazole, pantoprazole). Although regarded as weak acid suppressants, the H2RAs have some advantages that infrequently warrant their use over PPIs or in addition to PPIs. The H2RAs are maximally effective within hours of administration, have a good safety profile, and, unlike the PPIs, have a bioavailability that is unaffected by food. Unfortunately, prolonged use of famotidine leads to tachyphylaxis, which may occur as soon as the first few days of therapy. These effects appear to be independent of dose or form of administration. Evidence suggests that prolonged famotidine may provide continued symptom relief because of mucosal desensitization but mucosal injury may be ongoing. Thus, H2RAs may be a good treatment for as-needed symptom control, as short-term therapy (e.g., preventative therapy for reflux esophagitis), or for the treatment of nocturnal acid secretion, but are not the preferred treatment for upper gastrointestinal ulceration or erosion (GUE). If H2RAs are the only option, a dose of 1 mg/kg BID is suggested.

Although PPIs can take up to four days to reach peak effect, they are likely as effective as H2RAs on day one of administration. For most causes of GUE, dogs and cats should be treated twice-daily with a PPI (e.g. omeprazole, esomeprazole, pantoprazole) at 1 mg/kg. However, once-daily treatment may be effective for certain causes of GUE such as stress-related mucosal disease. Esomeprazole may be a good choice when once-daily administration is required. In a recent study in a small group of healthy Beagle dogs, esomeprazole administered once-daily provided excellent acid suppression when administered subcutaneously or orally. Moreover, in ongoing studies in the author's laboratory, esomeprazole appears to be a more effective PPI compared to other traditional PPIs in both dogs and cats. A variety of omeprazole formulations (tablet, capsule, reformulated paste, suspension) have been evaluated and demonstrated to be effective in raising the intragastric pH in healthy dog; however, caution is advised in using capsules with enteric-coated PPI granules designed for humans in cats as these might not work as well because of differences in their intestinal pH as compared to dogs and humans. An intravenously administered constant rate infusion of famotidine is efficacious and can be used for short-term therapy in animals with severe GUE or when PPIs are not available. With the exception of adjunctive treatment of ulcerogenic neoplasms, long-term use of acid suppressants is largely discouraged especially in the absence of other risk factors for GI bleeding. Similarly, prophylactic use of acid suppressants in dogs and cats is largely not recommended unless other risk factors, such as mechanical ventilation, coagulopathy, or shock, are present. Prophylactic use of acid suppressants in patients taking NSAIDs is not recommended unless the patient has a previous history of GUE or has an additional risk factor such as critical illness or the concurrent use of other ulcerogenic drugs.

Coating Agents:

Coating agents include sucralfate and barium. Sucralfate, a polyaluminum sucrose sulfate, forms a protective layer on the proximal GI mucosa. Sucralfate is activated in the presence of an acid to form a gel-like substance that covers areas of denuded epithelium. Sucralfate may also stimulate the production of protective prostaglandins. The results of human studies suggest that sucralfate may be more effective in the adjunctive treatment of duodenal ulcers compared to gastric ulcers. There are very few studies that have evaluated the efficacy of sucralfate in the treatment of GUE in dogs and cats. However, studies investigating the use of sucralfate in the polypharmacy treatment of GUE and mucositis in humans suggest there is a benefit to this practice. Moreover, sucralfate is associated with very few adverse effects aside from constipation. Its use may be discouraged in cats with CKD. Sucralfate does change the pH of the stomach and therefore may interfere with the metabolism of drugs that are dependent on an acidic

gastric pH (e.g. PPIs). It also interferes with drugs affected by the aluminum component of sucralfate (e.g. tetracyclines, ciprofloxacin). Therefore, these drugs should be administered at least two hours before or after sucralfate administration. Sucralfate should not be used as a sole therapy for the treatment of ulcerative disease.

Barium, like sucralfate, is proposed to have mucosal protecting effects and hemostatic properties. Barium enemas are effective for treatment of lower GI bleeding in people. To the author's knowledge, no published studies have evaluated the efficacy of barium in the treatment of dogs and cats with GUE, however, studies in the treatment of rectal bleeding in people and anecdotal information in dogs and cats suggests that it may be an effective adjunct treatment of GUE. The dose recommended for mucosal hemostasis can be occasionally challenging to administer especially in a patient with a history of dysrexia or vomiting. Although barium is inert, aspiration of barium with gastric fluid contents can be fatal. Discontinue barium for at least 24 hours prior to gastrointestinal endoscopy and do not use in animals where GI perforation is suspected.

Prostaglandin Agonists:

The most commonly used prostaglandin agonist in veterinary medicine is misoprostol, a PGE1 analog. By simulating endogenous eicosanoids, misoprostol increases mucosal blood flow and epithelial repair and stimulates mucus and bicarbonate secretion. Despite its mechanism of action, misoprostol is only effective for NSAID-induced injury and has no effect with steroid-associated ulceration. Moreover, there is as surprising lack of studies to support the use of misoprostol in dogs. As mentioned for PPIs, prophylactic use of misoprostol for NSAID-induced GUE is effective but not recommended unless other risk factors are identified. Misoprostol may increase GI and urogenital smooth muscle contractions leading to side effects of cramping, diarrhea, and abortions.

ANTICONVULSANT DRUGS – MAINTENANCE THERAPY

Joseph Mankin, DVM, DACVIM (Neurology)
Texas A&M University

Management of seizures can be a frustrating and time-consuming process. Regardless of the underlying cause, maintenance medications need to be instituted in most cases. The goal of therapy is to control, not cure, the seizures. The typical goal is to have few seizures with minimal drug side effects. Some patient may be able to be maintained at 1-2 seizures a year, while others may be considered a success to have a frequency of 1-2 a month. There are multiple therapeutic options, each with their distinct pros and cons, so drug selection should be based on the individual patient.

Typically, patients are started on an antiepileptic drug (AED) when the patient has 2 or more seizures within 4-6 months. If they have other neurologic abnormalities, it will need to be instituted earlier. If they have epilepsy and their seizures are increasing in frequency, severity, or duration, AED therapy should be started or adjusted. Other criteria for starting medication include an event of status epilepticus or cluster seizures, severe post-ictal signs, or suspicion of a structural lesion based on the neurologic exam.

Owner compliance is key in these cases. It is important to educate them on the risks of stopping an AED abruptly or altering the dose on their own. When owners adjust the medications on their own, it can be difficult to tell if a change in seizure frequency (for better or worse) is due to the medication or due to the cyclic nature of seizure events. It is beneficial to have owners keep a seizure log that includes the duration, frequency, length of post-ictal period, and any medication administered.

When selecting the best AED for the patient, the major things to consider are the cost of the drug, potential side effects, how it is metabolized, the dosing schedule, and how long it takes to reach steady state.

<u>Standard AEDs</u>

- Phenobarbital
    - Dose – 2-4mg/kg
    - It is one of the most commonly used drugs, often instituted as a first line choice but can be an add-on medication. It has a high success rate, being 60-80% effective in IE patients. By definition, to be considered an effective drug there must be a 50% decrease in seizure frequency.
    - You can also load the medication in an emergency situation, and it is easy to continue as a maintenance medication (Dose of 2-3 mg/kg BID). It works by prolonging the opening of Cl channels at GABA receptors, resulting in increased activity of the inhibitory neuron GABA.
    - It takes 2 weeks to achieve steady state at the standard dose, and is effective in 24 hours if loaded.
    - The major side effects of Phenobarbital include elevated liver enzymes, neutropenia, anemia, thrombocytopenia, PU/PD/PP, sedation, ataxia, and rarely superficial necrolytic dermatitis. It is useful in cats, and in general we see fewer side effects when compared to dogs. Phenobarbital has multiple drug interactions, as it can both increase the efficacy of some drugs while decreasing the efficacy of others. It can alter the results of endocrine testing, most commonly including a falsely decreased T4/free T4/TSH. There are also

multiple drugs that can increase/decrease the efficacy of Phenobarbital. Therefore, it is important to look for potential drug interactions on any patient on Phenobarbital.

- Primidone
    - It was the precursor to Phenobarbital, and its anticonvulsant effects come from the phenobarbital metabolite. It is potentially more hepatotoxic to dogs than Phenobarbital. There is debate as whether or not its use is contraindicated in cats, so it must be done with extreme caution. To monitor its efficacy, Phenobarbital levels are checked.

- Potassium Bromide
    - Dose – 20-30 mg/kg/day
    - KBr is the first AED that was used in humans. It is effective as either a sole therapy or as an add-on. Its mechanism of action is poorly understood, but it involves modulation of GABA. It takes 3 months to reach steady state, but it can be loaded over 5 days to achieve therapeutic effect faster (400-500 mg/kg split over 5 days). Typical dosing is 20-30 mg/kg/day or it can be divided to a BID schedule.
    - The major side effects include polyphagia, polydipsia, sedation, ataxia, pancreatitis, and GI signs due to gastric irritation. The sedation seen can be transient, but may last up to 3 weeks. Bromism can occur resulting in muscle pain, proprioceptive deficits, anisocoria, and hyporeflexia. Discontinuation of the drug or induced vomiting in acute cases can bring levels down, as can fluid diuresis.
        - There is a risk of pneumonitis in cats (in one study ~50% developed it), so it is generally avoided in this population.

Newer AEDs

- Zonisamide
    - Dose – 5-10 mg/kg BID
    - Zonisamide (Zonegran) is much more affordable and available now that the generic form is on the market. It works by blocking voltage dependent Ca and Na channels. It is given twice daily, as a single agent or as an add-on AED. By itself, the starting dose is 5mg/kg BID.
        - If the patient is already on Phenobarbital, the dose is 10-12 mg/kg since it can increase the metabolism of Zonisamide. It should reach steady state within approximately 3 days, and was shown to improve seizure control in 80-90% of dogs with poorly controlled epilepsy on other drugs.
    - Side effects are much more uncommon when compared to the first-generation AEDs and include mild sedation, ataxia, rare GI upset, and potentially cause hepatic disease. The drug is a Sulfonamide derivative, so we must monitor for the potential side effects associated with sulfa drugs – KCS and bone marrow suppression. There is limited information about its use in cats, so it is not routinely used. There is risk of using it in pregnant animals, as at high doses there have been reports of cardiomegaly and VSD.

- Levetiracetam
    - Dose – 20mg/kg q8hr
    - Levetiracetam (Keppra) is another of the newer antiepileptics that are used more commonly now that it is available in the generic form. It acts on GABA and glycine gated channels, and it excreted unchanged through the kidneys. It achieves steady state by 1-3 days, and can be loaded in an emergency setting.

    - The main side effects noted are mild sedation and a transient decreased appetite. Dosing is 20 mg/kg TID, which is the drug's major downside. Owner compliance of every 8-hour dosing schedule (not simply morning, evening, prior to bed!) can be very difficult so seizure control may not be as good as we would hope. Phenobarbital does alter the therapeutic levels of Keppra, either increasing or decreasing their values. It has also been shown to be effective in cats.
    - Keppra XR (extended release) is being used much more frequently in humans, and in some veterinary patients. The main advantage is its BID dosing schedule. We do not know how effective it is in our patients at this point, so we do not routinely use it as a sole agent at this point.

- Gabapentin
    - Dose – 15-20 mg/kg TID
    - Gabapentin (Neurontin) is another of the newer AEDs. At a higher dose it is used for its antiepileptic properties, while it is used for neurogenic pain control at a lower dose. It binds to Calcium channels and is excreted unchanged through the kidneys. Side effects include sedation, ataxia, and the "honeymoon effect" – it is effective for only a short time. It also must be given every 8 hours, which makes owner compliance difficult. Due to these issues, it is typically not used as a sole agent.

There are other AEDs that are available, but are not used widely in veterinary medicine for different reasons. Felbamate is cost prohibitive, and there are few dog trials confirming its efficacy. Phenytoin and valproic acid have a short duration of action, so there is not much long-term efficacy. Topiramate is rarely used due to the cost. Pregabalin, the 'more potent' successor of Gabapentin, is also being used, but there is no information in dogs on its effectiveness. Pexion is a newer medication, but has only just been released in the UK so clinical information is lacking at this time. In one study, its efficacy was similar to that of Phenobarbital.

There have been several alterative options to medications for seizure control that have been studied in veterinary medicine. Vagal nerve stimulation was studied in people and in dogs. With this process, stimulation of the vagus can cause desynchronization of cortical neurons. The device is implantable and delivers a repetitive stimulation to the nerve. In people, it decreased seizure frequency by at least 50% in 1/3 of participants. In dogs, there was no significant difference in seizure duration, severity, or frequency noted.
Other alternative modalities such as transcranial magnetic stimulation, ketogenic diet, and allergies have been studied, with their results inconclusive. Surgery is done in people for temporal lobe epilepsy, but we do not attempt this since it is difficult for us to isolate the seizure focus.

When determining what AED to start in a patient, considering the cost, side effects, metabolism, and time to steady state can point you to the best choice for that individual animal. Typically, as with any long-term medication, routine bloodwork should be performed 2 weeks, 1-3 months, and 6 months after starting the medication. We routinely check therapeutic levels for KBr and Phenobarbital, and occasionally check levels for Zonisamide and Keppra. The most important factor in maintenance therapy is owner education, on both the long-term need for the drug as well as proper monitoring.

Is it Orthopedic or Neurologic?

Joseph Mankin, DVM, DACVIM (Neurology)
Texas A&M University

When a patient presents for "being down", there are many reasons that may be the cause. One of the more important differentials is determining if the inability to ambulate normally is due to an orthopedic issue or a neurologic issue. In order to distinguish between the two, it is important to approach all cases with the same pattern of assessment and observation.

Pattern recognition is key in determining whether or not it is neurologic or orthopedic, which puts you on the right track for the proper diagnostics. When watching the animal ambulate, we look to see if it is normal vs abnormal, if there is a lameness vs ataxia, and if there are any postural deficits. Following the gait exam, palpation of the body/spine should be done to look for pain and its origin, followed by reflexes of the limbs. Combination of a good orthopedic and neurologic exam will help determine the cause in many cases.

When watching an animal stand, positioning of the limbs is helpful. In orthopedic disease, the limbs are held under the center of gravity, with normal proprioception. Those animals that have their limbs abducted and away from their center of gravity are more likely to be neurologic in origin.

After a standing exam is done, observation of the gait gives certain clues as well. One aspect to consider is the type of flooring the gait exam is performed on. Slick floors can hinder an animal with orthopedic or neurologic disease, so floors with grip our going outside to the concrete can be beneficial. In addition, when a neurologic patient ambulates on concrete, you may also be able to hear scuffing of the paws which may not be noticeable on a slick floor. Observe the patient at both a walk and a trot, coming towards and away from you as well from both sides. Making the patient circle or go over obstacles will also exacerbate the cause of their abnormal gait.

In orthopedic disease, the gait is regularly irregular. That means that the abnormality is consistently there on every step, and the position of the limb does not vary. Neurologic disease is irregularly irregular. This means that the abnormality may not be present on every step, and the placement of the limbs in space may change as the animal moves. This is a result of abnormal proprioception, or knowledge of where the feet are in space.

Intervertebral disk disease can present with only lameness as the clinical sign. Lateralized disk extrusion can cause impingement of the spinal nerve without concurrent spinal cord compression. This is common in the thoracic limb, and it called a "root signature". The orthopedic exam is normal, but pain is often elicited on neck palpation.

Polyarthritis results in pain and discomfort in the joints of the limbs. There are also joints along the vertebral column, so some patients may have spinal pain as well. Many patients walk slowly and gingerly, and are described as "walking on eggshells". They should maintain normal proprioception and have no ataxia on neurologic exam, and will exhibit pain on flexion of joints during the orthopedic exam. It is diagnosed through joint taps, and it may be infections or immune mediated in origin.

Fibrotic myopathy occurs in German Shepherd dogs, and is overrepresented in young adult males. The onset is slow, and presents as an abnormal pelvic limb gait with a shortened stride that has outward rotation of the hock as the limb is placed back down. It is thought to be due to injury of the gracilis or semitendinosus muscle with subsequent contracture and scar tissue.

Bilateral cranial cruciate ruptures can present with the patient's inability to stand or ambulate. The CCL can rupture concurrently in both stifle's or they may have a chronic tear in one limb and an acute tear in the other. Often they are larger, obese animals that have another concurrent issue such as hyperadrenocorticism or a polyarthropathy.

Lumbosacral disease occurs due to spinal nerve compression at the level of L7 to S1. It may be due to either protrusion of the LS disk or due to narrowing of the L7 foramina secondary to bony changes. Patients can present with reluctance to walk if both limbs are affected, or they may present with lameness in only one limb. Pain is elicited on palpation of the LS region, on lifting the tail, and may also be present on rectal exam. Diagnosis is made through advanced imaging, either CT or MRI of the region.

To determine if something is neurologic or orthopedic in origin, you must break down the gait exam and look for the position and movement. Observing the patient walk towards you, away from you, and from the side are key in determining if the abnormality is regular or irregular. In orthopedic disease, speeding up the animal to a trot may help in identifying the lameness. With neurologic disease, walking slower may exacerbate the abnormality. Subsequent orthopedic and neurologic exams will help determine the cause, as well as a thorough history.

DIAGNOSING AND MANAGING RECURRENT OTITIS IN DOGS

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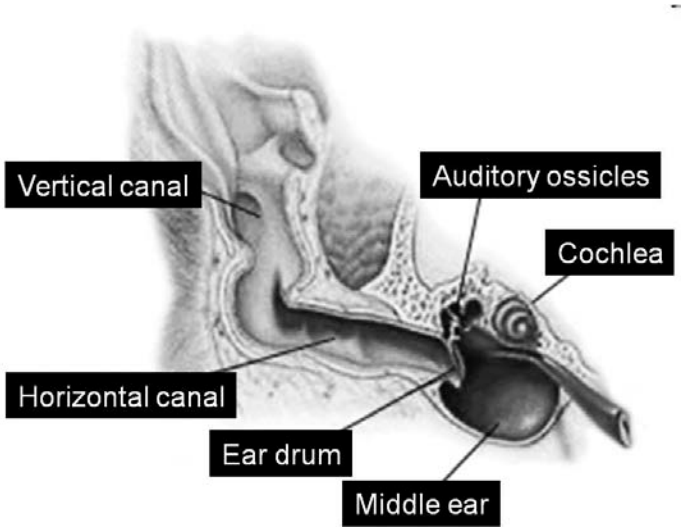
Ear disease tends to be one of the more frustrating conditions to manage for many veterinary practitioners. Likewise, it is a frustrating and wearisome problem for owners of pets with chronic or recurrent ear problems. For many patients, however, much of the recurrent nature of the disease can be managed or even prevented from winding up as a case of end-stage ear disease no longer amenable to medical treatments. In this presentation, we will review different reasons for the development of otitis. Reasons for recurrence of ear infections will also be discussed along with strategies for treating and managing the patient with chronic otitis. Indications for continued medical management vs. surgical intervention will also be presented. The goal of the presentation is to make ear disease less of a headache for the client, the patient, and the veterinarian by developing successful management strategies and techniques for disease intervention.



Why ear disease develops and/or persists

When it comes to ear disease, determining the underlying reason for infection/discomfort development and persistence is one of the most important pieces of the puzzle. This information will help guide long-term treatment recommendations and management practices in those patients with chronic or recurrent ear problems. Since otitis externa is a manifestation of skin disease, obtaining a complete dermatologic history is imperative to developing the rule out list of underlying etiologies.

Several factors can contribute to the development of otitis externa. These factors can be divided into three categories: predisposing causes, primary causes, and perpetuating causes. Predisposing factors themselves are insufficient to cause otitis externa however they make the patient more susceptible to the development of ear disease when a primary cause is present. Primary causes on their own directly result in clinical signs of otitis. Perpetuating causes are secondary factors which result from primary causes and contribute to the persistence of ear disease. Unless these factors are sufficiently addressed, they can hinder resolution even in the face of adequate primary/predisposing cause management.

PREDISPOSING CAUSES	PRIMARY CAUSES	PERPETUATING CAUSES
Conformation • **Pendulous pinnae** • **Normally "stenotic" canals** • **Excess hair** • **Excess glandular tissue**	**Parasites** • *Otodectes* • *Demodex* • Ticks	**Bacteria** • Cocci o *Staphylococcus* spp. o *Streptococcus* spp. o *Enterococcus* spp. • Rods o *Pseudomonas* spp. o *Proteus* spp. o *E. coli* o *Corynebacterium* spp.
Moisture • **Swimming** • **Bathing** • **Humid environmental region**	**Allergic disease** • Cutaneous adverse reaction to food (CARF; food allergy) • Atopic dermatitis	**Yeast** • *Malassezia* spp. • *Candida* spp.
Excess cerumen production	**Cornification defects** • Primary seborrhea • Facial dermatitis of Persians and Himalayans	**Ongoing ear canal pathology** • Failure of epithelial migration • Edema • Glandular hyperplasia • Folding • Stenosis • Fibrosis • Calcification/ossification
Iatrogenic and owner errors • **Inappropriate treatment** • **Excessive ear flushing** • **Overtreatment** • **Undertreatment** • **Trauma from cotton swabs**	**Foreign body** • Grass awns • Small toys • Wax concretion • Hair plug • Inspissated medication	**Otitis media** • Result of chronic otitis externa • Ascending infection • Primary secretory otitis media (PSOM)
	Mass • Neoplasia • Polyp • Cyst • Granuloma	
	Endocrinopathy	

• Hypothyroidism • Hyperadrenocorticism
Autoimmune/immune-mediated disease • Pemphigus foliaceus • Systemic lupus erythematosus (SLE) • Juvenile cellulitis ("puppy strangles")
Trauma

Managing "easy" chronic otitis externa

When ear disease starts to become more than very occasional or infrequent, it is imperative to determine the underlying primary cause contributing to the problem. History and other dermatologic abnormalities can provide clues as to the most likely diagnosis. Patients that are frequently pruritic for example, either ears alone or ears and skin, are likely to be suffering from allergic disease. While atopic dermatitis is the most likely allergic cause, cutaneous adverse food reaction (CAFR, food allergy) should also be considered. This is especially true for the patient with only pruritic ears (not skin) or an "ears and rears" distribution of pruritus. With food allergy, dietary manipulation alone may sufficiently control otitis externa. In patients with atopic dermatitis however, I have found that more often than not, these patients still require maintenance ear care even if the rest of their allergic disease is under fairly good control. Typically, this involves routine cleaning with an appropriate ear cleaner (no more than twice weekly) and application of a steroid-only ear drop (e.g. Synotic®). In patients where ear disease is fairly mild, they may be able to be maintained on cleaning alone.

Cocker spaniels and other spaniel breeds are another story altogether. These dogs are prone to the development of primary seborrhea which contributes to their propensity of perpetuating canal pathology. What may start as excess cerumen production can progress into glandular hyperplasia, failure of normal epithelial migration, and resultant "cauliflower ear" which will become end-stage, non-responsive to medical management if left untreated. Although this genetic defect cannot be cured, this progression can be prevented by initiating maintenance ear care early in the process. Routine cleaning with a ceruminolytic agent (typically two or three times weekly) can help maintain a more "normal" ear environment by removing excess cerumen, assisting in epithelial migration and removal of debris. It would not be wrong, in my opinion, to discuss ear care maintenance at the first puppy visit in Cocker spaniels and other breeds prone to ear disease. While cleaning may not need to be performed as frequently (perhaps once every two weeks), starting the process of ear care at an early age can help train both the patient and the client before problems develop.

The key point in managing the chronic otitis patient: do not treat the ears just when disease is present. Establishing a maintenance care plan can decrease the frequency and severity of infections if and when they do recur. Failing to do so will result in relapse without question.

Managing "not-so-easy" chronic otitis

And here is where the headache sets in… One of the most frustrating conditions for many practitioners is the patient with chronic otitis that is not amenable to treatments prescribed. These are typically patients with underlying primary conditions which have not been sufficiently addressed and/or have developed secondary bacterial otitis externa and/or media. These chronic, recurrent or "smoldering" infections are frustrating to deal with and can become essentially impossible to resolve with medical management alone. In some of these cases, surgery is the only option left for resolution.

There is typically at least one of three reasons for why these infections recur or persist: occlusion in the canal (e.g. swelling, stenosis, mass) that prevents medication from getting in and debris/infection from getting out, the presence of resistant organisms, and/or concurrent middle ear disease. When presented with the recurrent/persistent ear infection, it is important to determine which of the three variables is/are present and contributing to the disease.

APPROACH TO MRSP SKIN INFECTIONS

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Staphylococcus spp. bacteria are Gram-positive, facultative anaerobic organisms that are part of the normal cutaneous and mucosal microflora of mammals and birds. Since the initiation of antibiotic use in modern medicine, these bacteria have evolved and developed resistance mechanisms in response to antimicrobial pressure and use. Methicillin was first introduced in 1959 for the use in treatment of penicillin-resistant staphylococcal infections. Two years later in 1961, the first case of methicillin-resistant *Staphylococcus aureus* (MRSA) was reported. The incidence of MRSA has since escalated within the human population.

Since the early to mid-1970s, there have been numerous cases of infections due to MRSA isolated from various domestic animal species. MRSA infection has been diagnosed in cattle, horses, pigs, dogs, cats, guinea pigs, and rabbits as well as individual reports of more exotic species such as a parrot, bat, and turtle. Although it is still considered to be fairly uncommon, there has been an increase in reports of MRSA particularly in small animals and horses over the past decade. As well, isolation of other methicillin-resistant *Staphylococcus* (MRS) spp. such as *S. pseudintermedius* and coagulase-negative *Staphylococcus* spp. (e.g. *S. schleiferi*) have been reported with increasing frequency in companion animal species. Although previously thought to be non-pathogenic, these coagulase negative *Staphylococcus* species can also cause skin infections in dogs and cats.

Recently, a consensus statement was released by the World Association for Veterinary Dermatology (WAVD) to highlight the current recommendations for diagnosing, treating, and preventing these resistant skin infections in small animal patients. Summary of the findings are discussed during this presentation.

Reference

The Clinical Consensus Guidelines of the World Association of Veterinary Dermatology for the recommendations for approaching methicillin-resistant staphylococcal (MRS) infections in small animals may be found in the free-press article available online:

Morris DO, Loeffler A, Davis MF, Guardabassi L, Weese JS. Recommendations for approaches to methicillin-resistant staphylococcal infections of small animals: diagnosis, therapeutic considerations and preventative measures. *Veterinary Dermatology* 2017; 28: 304-e69.

Summary of the Clinical Consensus Guidelines

(Excerpted from the Clinical Consensus Guidelines of the WAVD for the recommendations for approaching methicillin-resistant staphylococcal (MRS) infections in small animals)

1. *Staphylococcus pseudintermedius, S. schleiferi* (including the coagulase-negative variant) and *S. aureus* are the primary pathogens encountered in small animal dermatology practice. Clinical isolates of all three species commonly express methicillin resistance and multidrug resistance.

2. In addition, several other species of coagulase-negative *Staphylococcus* (CoNS) have been reported to cause skin and soft tissue infections, and the pathogenic role of a CoNS must be deduced by the clinician on a case-by-case basis.

3. The pathogenic potential of any CoNS isolate obtained from a secondary skin lesion or a contaminated body site should be interpreted in light of the clinical disease process (urgency, co-

morbidities, risk for adverse reactions to specific antibacterial drugs) and with respect to any other pathogenic species of bacteria that may be co-isolated with it.

4. Minimum reporting by microbiology laboratories should include complete speciation of staphylococci – regardless of tube coagulase status – and an antibiogram for all cultured isolates.

5. Topical therapy, using antibacterial agents and biocides with proven anti-staphylococcal efficacy, is the recommended treatment modality for any surface or superficial pyoderma involving MRS; particularly those with localized lesions, and for otitis and superficial wound infections.

6. Topical therapy should be used as the sole on-animal antibacterial treatment for surface and superficial infections whenever the pet and owner can be expected to be compliant.

7. Geographical differences exist in the availability and licensure of antimicrobial drugs for use in animals. Judicious use decisions need to take into account regional prescribing recommendations in veterinary and human medicine.

8. Empirical drug selection for systemic therapy is always contraindicated when a MRS infection is suspected based on historical factors, due to the high prevalence of multidrug resistance within these strains.

9. A restriction-of-use policy should apply to glycopeptides (vancomycin, teicoplanin, telavancin) linezolid (oxazolidinon), anti-MRSA cephalosporins and potentially new compounds that may be approved in the future for treatment of multidrug resistant pathogens of people.

10. There is little evidence for a difference of outcome between MRS and methicillin susceptible *Staphylococcus* infections in animals, and the prognosis for MRS skin infections in pets if good, depending on the underlying cause and co-morbidities.

11. There is currently not enough evidence to recommend routine decolonization of MRS carrier animals.

12. Molecular strain typing methods are research tools used to investigate the epidemiology and ecology of certain outbreak situations of MRS. However, the clinical value of strain typing largely depends on the organism's population structure, the typing method(s) used and the goals of investigation. Strain typing rarely has impact on patient- or clinic-level management.

13. Hand hygiene (proper washing/drying and use of alcohol-based hand sanitizers) is the mainstay of personal responsibility for infection control. No data exists regarding optimal personal protective equipment practices for handling animals infected with MRS. However, the use of some degree of enhanced precautions to reduce contamination of clothing and skin is reasonable. Typically, this would consist of a gown or dedicated laboratory coat and disposable gloves.

14. In contemporary veterinary practices, routing cleaning and disinfection protocols are cornerstones of hospital infection control. MRS are susceptible to commonly used disinfectants. Protocols should be designed to reduce or eliminate pathogenic burdens in the environment and on equipment. These protocols must be communicated clearly (and often) to the hospital team and practiced correctly and consistently.

15. Transmission of MRS by infected pets to other individuals in the home or community is known to occur, but data to guide recommendations are incomplete. In lieu of such data, it is reasonable to restrict animals from contact situations until treatment has started and a clinical response is evident. In the home, this could include social distancing from "at risk" individuals and enhanced hygienic measures for the occupants of the environment.

16. Screening of clinical normal animals for carriage of MRS – regardless of the setting – rarely leads to clear and justifiable actions. Screening of humans leads to issues of confidentiality, and testing of clinic personnel (especially is not clearly voluntary and anonymous) could lead to a host of legal problems for clinic management. Testing of healthy individuals, particularly humans, should be a rare event that is based on a specific need and with a clear plan to act on results.

"Go to" treatment and management recommendations for MRS skin infections

The strategy we have found to be most effective for treating the patient with MRS skin infections is to initiate a therapy plan incorporating aggressive topical management. As antibiotic choices become more and more limited, or are limited to those antibiotics with more severe side effects (e.g. every practitioner's nightmare of the Staph infection susceptible to ONLY amikacin and rifampin), the importance of aggressive topical therapy becomes even more important. Aggressive topical therapy generally involves the recommendation of VERY frequent bathing (at least every other day if not daily) and/or the use of antiseptic sprays or other leave-on formulations (e.g. mousse). Using the "more potent" antiseptic shampoos (e.g. higher concentrations of chlorhexidine +/- Triz EDTA, sodium hypochloritie) is typically recommended for patients with resistant infections. Frequent laundering of the infected pets bedding is important as well to address recontamination. These items should be washed separately from other human clothing. Other recommendations for owners and care takers include:

- Keeping young and immunocompromised people away from the infected pet
- Washing hands or using alcohol based hand sanitizers after contacting the infected pet
- Making sure all antibiotics prescribed are completely finished and making sure recheck examinations happen in a timely fashion
- Regularly picking up infected pet's stool and/or cleaning the litter box frequently
- Wear gloves when treating the infected pet topically
- Keep draining wounds covered
- Do not allow the infected pet to lick the face or wounds of people
- Do not share the same bed as the infected pet
- Do not share towels or linens with the infected pet
- Do not allow the infected pet to serve as a "therapy animal" or attend social activities (e.g. puppy class, doggy day care) until the infection has been cleared

APPROACH TO THE ASYMPTOMATIC DOG WITH INCREASED LIVER ENZYMES

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Introduction

Increased serum liver enzyme activities, especially alkaline phosphatase (ALP) activities, are commonly identified in dogs. These increases represent a diagnostic challenge to clinicians for a number of reasons. Firstly, sometimes increased serum liver enzymes activities occur due to primary hepatobiliary disease and other times they can occur secondary to extrahepatic disease. This may be because tissues other than the liver also produce these enzymes. Additionally, the liver plays a major role in the metabolism and the excretion of drugs, as well as exogenous and endogenous toxins. The liver is perfused by the portal circulation, whereby a large proportion of its blood supply comes from the splanchnic circulation via the portal vein. Consequently, the liver is susceptible to injury caused by a variety of toxins, diseases in other parts of the body, as well as ischemia. Thirdly, sometimes increased liver enzyme activities can occur due to benign processes, such as hepatic nodular hyperplasia or can be due to conditions that are progressive and require early intervention to have an optimal outcome, such as chronic hepatitis. This can make it difficult for clinicians to know how aggressive to be when working up these dogs. Performing extensive diagnostic evaluation, including invasive tests such liver biopsy, is costly causing some clients to be reluctant or unable to proceed. Sometimes in-depth evaluation of dogs with increased serum liver enzyme activities is not required. For example, when there are mild increases in ALP activity.

Hepatic enzymology

Alanine aminotransferase (ALT) is found primarily in the cytosol of hepatocytes. ALT is released when the cell membrane permeability of the hepatocytes increases or if there is hepatocyte necrosis. Although this enzyme is found in a variety of tissues, increased serum ALT activities are considered to be relatively liver specific. The exception to this is that rarely ALT activity can increase in patients with severe muscle injury. Alanine aminotransferase is considered to be a sensitive marker of liver injury. Aspartate aminotransferase (AST) is found in the mitochondria and cytosol of hepatocytes. The cytosolic fraction is released when the cell membrane permeability of the hepatocytes increases or if there is hepatocyte necrosis, whereas the mitochondrial fraction is only released when there is necrosis. Increases in AST generally parallel those in ALT but muscle disease can cause an increase in serum AST activity. Because of this, AST is considered less liver specific than ALT.

The hepatic, bone, and steroid induced ALP isoenzymes can all contribute to serum ALP activity in dogs. In the liver, this enzyme is bound to the membranes of the hepatocytes that form the bile canaliculi and the sinusoidal membranes. When there is cholestasis, this membrane bound ALP is released into the circulation and the synthesis of this enzyme is induced. Alkaline phosphatase is therefore considered to be a sensitive marker of cholestasis in dogs. Because of the two non-hepatic isoenzymes mentioned above, ALP is not liver specific. Serum ALP activities can be increased when there is increased osteoblast activity e.g. growing dogs or dogs with osteolytic disease e.g. osteosarcoma. Synthesis of the steroid induced ALP isoenzyme is induced by both exogenous and endogenous glucocorticoids. It is also important to note that increased serum ALP activities have been reported in a family of apparently healthy Siberian Huskies and also in some apparently healthy Scottish Terriers. Vacuolar hepatopathy due to excess adrenal production of androgens is suspected to be the cause in the latter. Gamma-glutamyltransferase (GGT) is an enzyme that is found bound to the hepatocytes that comprise the bile canaliculi and bile ducts. Increases in serum GGT activity generally parallel those in ALP as both are considered to be relatively sensitive markers of cholestasis. In general increases in GGT are considered to be less sensitive but more specific for the presence of hepatobiliary disease than those of ALP.

Initial patient evaluation

There are many causes of increased liver enzymes activities, so it very important for clinicians to go from a list of all the possible causes to a list of all the causes that are “probable for that patient on that

day". Information collected during history taking and physical examination is often very helpful when doing this. The patient's signalment can help refine the differential list. For example, very young dogs are more likely to suffer from congenital conditions, e.g., congenital portosystemic shunts (CPSS) or certain infectious diseases, e.g. infectious hepatitis than neoplasia or inflammatory conditions, e.g. chronic hepatitis. Some breeds, i.e. Bedlington terriers, Skye terriers, West Highland white terriers, Dalmatians, and Labradors are predisposed to copper associated chronic hepatitis. Doberman pinchers and Cocker spaniels are predisposed to idiopathic chronic hepatitis. The breeds of dog predisposed to CPSS include the Maltese terrier, Yorkshire terrier, Havanese terrier, pug, and miniature schnauzer. Increased serum liver enzyme activities are more concerning in these breeds. When taking a history, it is very important to ask specifically about exposure to hepatotoxins such as cycads, blue green algae, amanita mushrooms, aflatoxins, heavy metals, xylitol, or chlorinated compounds. A variety of drugs can also be hepatotoxic, these include: ketoconazole, various antimicrobial agents, azathioprine, carprofen, lomustine, acetaminophen, ketoconazole, mitotane, and phenobarbital. It is important to specifically ask about any herbal remedies that the dog is receiving as many of these have been reported to be hepatotoxic, including: herbal teas, pennyroyal oil, and comfrey. Ascertaining the dog's vaccination history is also worthwhile as leptospirosis and canine adenovirus-1 can cause hepatic injury. Early in the course of liver disease dogs may not have any clinical signs. The earliest clinical signs seen in dogs with liver disease are often non-specific and include: vomiting, diarrhea, weight-loss, polyuria/polydipsia, and hyporexia. More liver specific signs such as icterus, ascites, and encephalopathy occur in late in the progression of chronic hepatitis. When any of these clinical signs are present, they warrant further investigation in an attempt to determine their cause. Certain historical findings may be relevant because they are suggestive of an extrahepatic disease that can cause increased liver enzyme activities. For example, polyphagia is consistent with diabetes mellitus or hyperadrenocorticism. Physical examination findings consistent with hepatobiliary disease include: icterus, ascites, poor body condition, stunted growth, hepatomegaly, or signs of hepatic encephalopathy. It is important to emphasize that dogs with hepatobiliary disease do not always display clinical signs or have abnormal findings on physical examination. Physical examination may also reveal findings that are suggestive of extrahepatic disease. For example, bilateral symmetrical alopecia is consistent with hypothyroidism or hyperadrenocorticism.

Routine laboratory testing

Other changes on a serum biochemistry panel can provide important clues as to the cause of increased serum liver enzyme activities. When serum concentrations of albumin, cholesterol, glucose, and urea are below the lower limit of the reference interval or towards the lower limit of the reference interval, and/or when the serum bilirubin concentration is above the higher limit of the reference interval, this is consistent with decreased hepatic function. It is important to remember that these changes are not specific for hepatobiliary disease. For example, the serum bilirubin concentration may also be increased when there is hemolysis. Additionally, due to the large hepatic functional reserve capacity, liver disease must be severe before these changes are seen. Patterns of serum liver enzymes activities can be suggestive of certain pathologies. For example, during cholestasis the serum activity of ALP is dramatically increased and is higher relative to that of ALT. There may also be evidence of extrahepatic diseases. Analysis of a complete blood count can suggest inflammatory conditions, rule out hemolysis, and if microcytosis is present this is consistent with portosystemic shunting (or iron deficiency). Urine specific gravity can be decreased in patients with hepatic insufficiency or portosystemic shunts. Excessive bilirubinuria in dogs implies hemolytic or hepatobiliary disease. Urate urolithiasis seems to be more common in patients with portosystemic shunts than those with other types of hepatic dysfunction. However, it should be noted that urate crystalluria is not specific for hepatobiliary disease.

When do you recommend further diagnostic testing?

Every case is different so it is difficult to make universal recommendations. However, I can offer the following general guidance:

- If there are clinical findings or other laboratory test results that are suggestive of primary hepatobiliary disease, further diagnostic testing should be pursued.
- If there are clinical findings or laboratory tests results that suggest the extrahepatic diseases that can lead to increased liver enzyme activities, further diagnostic evaluation to identify their cause is needed.
- If serum liver enzymes activities (ALP or ALT) are severely (three times greater the upper limit of the reference interval) or persistently increased (greater than twice the upper limit of the reference for more than 3 to 4 weeks), further diagnostic evaluation is needed.
- As ALT is more liver specific than ALP, increases in serum ALT activity are more concerning than increases in ALP
- If none of these conditions apply then it is reasonable to wait and recheck the serum liver enzymes at a later date.

Further diagnostic testing

The utility of plain abdominal radiographs for diagnosing hepatobiliary disease is limited and they rarely lead to a definitive diagnosis. However, they can be used to assess the hepatic size and to rule out certain extrahepatic diseases. Abdominal ultrasound is more useful than radiology for evaluating the hepatic parenchyma and the biliary tract. It is also sometimes possible to diagnose portosystemic shunts using this modality. However, unless a disease is characterized by architectural changes of the hepatobiliary system, a definitive diagnosis cannot be made with ultrasound examination. It is also important to remember that dogs with severe liver disease may not have any changes on abdominal ultrasound examination. Despite this limitation, when primary hepatic disease is suspected, abdominal ultrasound is usually performed prior to liver biopsy.

Measurement of plasma ammonia and paired preprandial and postprandial bile acids are sensitive tests for portosystemic shunting and one of these tests should be performed when this is suspected. However, because of the hepatic functional reserve capacity, these tests are not as sensitive for detecting hepatic insufficiency in the absence of shunting and normal results do not rule out severe liver disease.

In selected cases, hepatic cytology is useful as it can lead to a definitive diagnosis of certain diseases and can be highly suggestive for the presence of others. Indications for performing hepatic cytology are a suspicion that a round cell tumor is present, when infectious agents, for example *Histoplasma capsulatum* are suspected, and when hepatic masses are observed on abdominal ultrasound.

To make a definitive diagnosis of primary hepatic disease liver biopsy is often required. Prior to doing this the patient's risk of hemorrhage should be assessed by measuring prothrombin and activated partial thromboplastin time, ideally measuring serum fibrinogen concentration, performing a platelet count, and performing a buccal mucosal bleeding time. Liver biopsy techniques in dogs include: percutaneous needle biopsy, laparoscopic biopsy, and surgical biopsy. No matter which technique is chosen, it is important to collect multiple biopsies as well as to save a specimen for copper quantification and another for bacterial culture. When in doubt, if there is a suspicion of primary hepatic disease it is better to biopsy rather than to delay biopsy until the dog is in end-stage liver failure, at which point treatment is unlikely to be effective.

When should I biopsy the liver?

Every case is different but I can offer the following general guidelines:

- Hepatic biopsy is indicated when a hepatic mass has been diagnosed and a diagnosis has not been made based on cytology
- Hepatic biopsy is indicated when the serum ALT activity has been greater than twice the upper limit of the reference interval for more than 3 to 4 weeks and extrahepatic disease is unlikely to be the cause.
- Hepatic biopsy should be considered when there are multiple acquired portosystemic shunts. Acquired shunts suggest that there is hepatic parenchymal disease e.g. chronic hepatitis, which

requires biopsy to be definitively diagnosed. However, acquired portosystemic shunts occur late in the course of disease and are irreversible. Consequently, the prognosis for these dogs is poorer so some clients may not wish to proceed. They can also occur due to prehepatic portal hypertension e.g. due to portal vein thrombosis.

CANINE IMMUNE-MEDIATED HEMOLYTIC ANEMIA

Johanna Heseltine, DVM, MS, DACVIM

The destruction of red blood cells (RBCs) coated with immunoglobulins, complement, or both causes hemolysis. Intravascular hemolysis results when activation of complement results in formation of membrane attack complexes, and extravascular hemolysis results when antibodies attach to RBC membrane causing phagocytosis by macrophages. IMHA can occur in any breed, males, and females. Young to middle-aged dogs are typically affected, but dogs 4 months to 13 years of age have been reported.

DIAGNOSIS OF IMHA

Signs of Immune-Mediated Destruction

In an anemic dog, diagnosis of IMHA begins with evidence of immune-mediated destruction of RBCs. Spherocytes result from removal of a portion of the RBC membrane by macrophages. Finding greater than 3-5 spherocytes per high-powered field supports a diagnosis of IMHA, although non-immune causes (such as zinc toxicity or envenomation) should be excluded. Blood smears should be prepared prior to blood transfusion and submitted to a clinical pathologist for confirmation. Blood smears are also evaluated for RBC clumping, in which case, a saline agglutination test should be performed by adding 1 drop of EDTA blood to 4 drops of saline on a slide and evaluating for agglutination (antibody-mediated clumping of RBCs). If agglutination is absent, a direct antiglobulin (or Coombs) test or flow cytometry to detect anti-erythrocyte antibodies can help support the diagnosis. Other evidence of hemolysis also helps to confirm the diagnosis and includes hyperbilirubinemia (not due to hepatobiliary disease or sepsis), hemoglobinemia, hemoglobinuria, and RBC ghosts.

Patient History

Relevant information includes travel, vaccination and drug history, and the potential for toxin ingestion. Clinical signs of IMHA are due to severe anemia and hypoxia and may be acute or chronic. Common signs include anorexia, lethargy, collapse, vomiting, diarrhea, and discolored urine. Physical examination typically reveals pale mucous membrane and sometimes icterus, fever, tachypnea, and tachycardia. Erythrophagocytosis may cause splenomegaly, sometimes with hepatomegaly. A soft systolic heart murmur may result from anemia.

Evaluation of the CBC

Most IMHA dogs have a PCV <20%. In 70% of patients, the anemia is regenerative. A corrected reticulocyte percentage is determined as: (reticulocyte %) x (patient's PCV ÷ a normal PCV). A corrected value of >2% indicates regeneration. Absolute reticulocyte counts >100,000/uL represent a regenerative response. The anemia may be non-regenerative if there has been inadequate time for regeneration (<2-3 days) or if the immune process is directed against RBC precursors in bone marrow. Polychromatophils will result in an increase in MCV and a decrease in MCHC. Blood smears should be evaluated for spherocytes and/or agglutination. RBC parasites are rarely seen. A platelet count should be assessed, as 50-70% of dogs with IMHA have concurrent thrombocytopenia (from concurrent immune-mediated thrombocytopenia or disseminated intravascular coagulation). A mild to marked neutrophilia, often with a left shift and toxic change, is commonly present.

Biochemistry Panel

Elevated liver enzymes and hyperbilirubinemia (from extravascular hemolysis) or hemoglobinemia (from intravascular hemolysis) are common. Hyperbilirubinemia may be absent with mild or chronic hemolysis, as the hepatic pathways are not overwhelmed. Biochemical changes may indicate abnormalities of other body systems.

Additional Testing

A coagulation panel (PT, PTT, fibrinogen, and D-dimers) may provide additional indicators of DIC. Abdominal radiographs should be taken to rule out zinc foreign bodies. *Babesia* spp. can trigger IMHA, so PCR and titers are recommended. Certain infections (heartworm, *Bartonella* spp., and *Leishmania* spp.) can cause positive Coombs test results, so testing is indicated in endemic regions. Urinalysis completes the data base and urine culture may be warranted prior to immunosuppression. Cancer screening via thoracic radiographs and abdominal ultrasound is reasonable. A fecal flotation may be performed.

IMHA can be associative vs. non-associative, indicating that a comorbidity is present without implying a causal relationship. This replaces the traditional classification of primary vs. secondary.

SUPPORTIVE THERAPY

Intravenous fluids maintain adequate perfusion and normalize acid-base status. Most patients require hospitalization for aggressive supportive therapy. The most important goal of supportive therapy is adequate tissue oxygenation, and packed RBCs are the ideal product for transfusion. The need for transfusion is based on clinical signs including tachypnea, dyspnea, and tachycardia; however, most patients with a PCV <12-15% will require a transfusion. The volume given can be calculated as: (90) x (body weight in kg) x (desired PCV/PCV of donor blood product). Generally, a target PCV of 25-30% is used. Dogs with any history of transfusion >5 days prior must be crossmatched because of the potential for a life-threatening transfusion reaction. Some patients require multiple transfusions.

GLUCOCORTICOIDS

Prednisone, prednisolone, and/or dexamethasone are the mainstay of therapy for IMHA. Common side effects include polyuria (which may result in incontinence), polydipsia, polyphagia, and panting. More serious side effects that may develop include secondary infections and gastrointestinal ulceration. Abrupt tapering or discontinuation of glucocorticoid therapy may result in relapse of IMHA and/or signs of hypoadrenocorticism.

SECOND IMMUNOSUPPRESSIVE MEDICATION

Modified cyclosporine, mycophenolate mofetil, or azathioprine may be selected as a second line drug. The additional cost and the potential for side effects should be considered. A second line drug is initiated with glucocorticoids (not instead of glucocorticoids) and may be started from the outset of treatment in patients with severe or life-threatening disease, when the PCV drops by ≥5% in a 24-hour period, or if the dog is expected to have severe adverse effects from the glucocorticoid. The benefits of second-line immunosuppression have not been proven, but this remains the standard approach at our hospital. Alternatively, a second drug may be added if transfusions are required after more than 7 days of glucocorticoid therapy. Administering ≥3 immunosuppressive drugs concurrently increases the risk of sepsis and is avoided whenever possible.

ANTITHROMBOTICS

Antithrombotic therapy is indicated unless the platelet count is <50,000/uL. The ACVIM consensus statement recommends preferential use of anticoagulants to decrease the risk of thromboembolism. However, anti-Xa monitoring is recommended and is not readily accessible to practitioners. PTT can be measured (target 1.5-2 x baseline) but only to detect an increased risk of bleeding. For these reasons, clopidogrel remains a common choice, although its action is as an anti-platelet drug. Antithrombotic therapy is continued until the patient is in remission and no longer receiving prednisone (or for ≥6 months for dogs that remain on prednisone life-long).

PROGNOSIS

The prognosis for canine IMHA is guarded. Prognostic factors have not been consistently identified. In a 2015 study, 74% of dogs survived until discharge and 67% were alive at 1 month. Thromboembolic complications are the most common cause of death. A complete response may take weeks to months, and some patients require life-long treatment. Relapses are reported in 11-15% of cases.

TAPERING MEDICATION

PCV should be closely monitored initially, usually at least daily. Once the PCV stabilizes, monitoring may be performed weekly. PCV should be evaluated prior to any adjustment in medication dosage. When the PCV has remained over 30% and is stable for 2 weeks, the dose of prednisone may be tapered by 25%. (If a second immunosuppressive agent is being given, the prednisone dose may be reduced by 25-50%.) The dose of the second immunosuppressive drug is not changed. Provided the PCV remains stable and >30% and the patient's other parameters are stable, the dose of prednisone may be decreased by 25% every 3 weeks. In addition to monitoring PCV, evaluation for spherocytes, agglutination, and hyperbilirubinemia should be performed periodically.

Glucocorticoids		
Prednisone or prednisolone	For dogs <25 kg: 2 mg/kg/day PO For dogs >25 kg: 50-60 mg/m^2/day PO	
Dexamethasone	0.2-0.4 mg/kg/day IV	May be used instead of oral prednisone if patient is inappetent
Second Line Immunosuppressive Medications		
Cyclosporine	5 mg/kg PO q12h	Use only microemulsified formulations Therapeutic drug monitoring is available Best absorbed on an empty stomach, but giving with food may lessen GI upset GI upset, especially vomiting, is common Freezing capsules may decrease GI signs Gingival hyperplasia may develop Associated with higher risk of opportunistic infections Metabolized by the cytochrome P-450 enzyme system Hepatotoxicity is uncommon but liver enzymes should be monitored q2-3 months
Mycophenolate mofetil	8-12 mg/kg PO q12h	May cause GI upset including hemorrhagic diarrhea Monitor CBC q2-3 weeks x 1 month and then q2-3 months Do NOT give with azathioprine
Azathioprine	2 mg/kg or 50 mg/m^2 PO q24h	Dosing is reduced to q48h after 2-3 weeks May cause mild GI upset that is often self-limiting May cause myelosuppression or hepatotoxicity. Monitor CBC and liver enzymes q2 weeks x 2 months and then monthly thereafter Do NOT give with mycophenolate

Antithrombotics		
Clopidogrel	Consider loading dose of up to 10 mg/kg PO once; then 2-4 mg/kg PO q24h	
Unfractionated heparin	100 U/kg IV bolus then 900 U/kg/24 hr IV *or* 150-300 U/kg SC q6h	Monitor anti-Xa activity to adjust dose
Dalteparin	150-175 U/kg SC q8h	Monitor anti-Xa activity to adjust dose
Enoxaparin	0.8-1.0 mg/kg SC q6-8h	Monitor anti-Xa activity to adjust dose
Rivaroxaban	1-2 mg/kg PO q24h	

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CANINE SCHISTOSOMIASIS

Johanna Heseltine, DVM, MS, DACVIM

Canine schistosomiasis is caused by infection with *Heterobilharzia americana.* Most infections are reported in the Gulf Coast states, but some cases have been reported in south Atlantic states and rarely from the Midwest. Natural hosts include wild and domestic dogs, raccoons, and a few other mammals. The lifecycle also involves freshwater snails. Dogs are infected when wading or swimming in contaminated fresh water; infective cercariae penetrate the dog's skin. Cercariae migrate through the lungs and liver, where they mature into adult worms. Adult worms travel through the mesenteric veins, where they lay eggs. Eggs penetrate the mesenteric vein and intestinal wall and can be passed in stool. Eggs can migrate to many organs resulting in granulomatous disease, with large and small intestine, liver, abdominal lymph nodes, and pancreas commonly involved. The average prepatent period in experimental infections is 84 days. The clinical presentation and severity of infection depends on the number of mature flukes, the location of the eggs, and the amount of subsequent inflammation, and/or hypercalcemia. Failure to diagnose schistosomiasis can result in inappropriate treatment, unnecessary client cost, poor patient outcomes, and death. With diagnosis and treatment, canine schistosomiasis can be a curable disease.

In Texas, this is not a rare disease. Common clinical signs reported with *Heterobilharzia* infection in dogs include lethargy, weight loss, hyporexia, vomiting, and diarrhea. Infected dogs may have a poor body condition. Fever may also be noted. Early in the infection, dogs may have a papular rash or a cough, but these signs may be overlooked. Traditionally, recommendations were to test dogs with diarrhea. Now, recommendations have been extended to include testing dogs with weight loss, gastrointestinal disease, liver disease, and hypercalcemia.

Diagnosis

Common clinicopathological abnormalities include hyperglobulinemia, hypoalbuminemia, eosinophilia, and anemia. Liver enzymes may or may not be elevated. Hypercalcemia is present in approximately 30-50% of cases. Changes on abdominal imaging reflect sites of organ involvement; however, imaging may be normal. Routine fecal flotation will not detect the infection. A fecal polymerase chain reaction (PCR) can be performed through the Texas A&M GI Laboratory. Testing of loose stool is recommended and 1 gram of fresh feces should be submitted. The diagnosis can be made by fecal saline sedimentation exam. It is recommended to test 2-3 fecal samples from different days because shedding of eggs into the feces is intermittent. Some cases are diagnosed based on histopathology of infected tissues, including endoscopic intestinal biopsies. Multiple dogs in a household may be infected, so it is recommended that all dogs be tested and treated.

Gastrointestinal tract involvement

Diarrhea is common in dogs with *Heterobilharzia* infection. Eggs can reside in the mucosa, submucosa, or muscularis and induce a hypersensitivity response. Clinical signs may be consistent with small bowel diarrhea, large bowel diarrhea (particularly blood and/or mucous), or both. Signs may be intermittent or persistent. Melena may be present. Some affected dogs have thickened intestinal loops. Radiographs may be normal or occasionally show severe mineralization of the stomach or intestinal wall, either due to dystrophic calcification or a very large numbers of mineralized eggs. On ultrasound, finding linear areas of mineralization in the submucosa or muscularis layers of the intestine (and sometimes in the liver) should prompt testing for *Heterobilharzia.* Abdominal lymph nodes may be enlarged (reactive or infected). Intussusception secondary to intestinal infection has been reported. Some cases have been diagnosed based on endoscopic biopsies, but fecal testing is generally performed prior to endoscopy. Lesions are characterized as diffuse to multifocal enterocolitis with intralesional eggs that may be mineralized or partially mineralized. In addition to causing acute or chronic diarrhea, *Heterobilharzia* infection results in a protein-losing enteropathy in some dogs.

Differential diagnoses that may be considered for dogs with diarrhea include histoplasmosis, pythiosis, other parasites, neoplasia, intussusception, breed-related ulcerative colitis, or inflammatory bowel disease. Differentials for a chronic protein-losing enteropathy include histoplasmosis, pythiosis, hookworms, lymphangiectasia, intestinal neoplasia, inflammatory bowel disease, breed-related enteropathies, or chronic intussusception.

Pancreatic involvement

Based on histopathology, granulomatous, fibrosing pancreatitis is present in some infected dogs.

Hepatic involvement

Infected dogs may have a hyperechoic liver on ultrasound. Mineralized eggs in the liver may be visible as hyperechoic foci in the hepatic parenchyma. Lesions are primarily periportal because of route of parasite migration (eggs are deposited in the mesenteric veins and then carried into portal circulation of the liver, where they lodge in small hepatic veins). Histopathology shows granulomatous inflammation, typically with intralesional eggs. Periportal fibrosis may result, causing decreased portal blood flow and portal hypertension. This may lead to liver dysfunction or failure.

Hypercalcemia

Hypercalcemia occurs in 30-50% of infected dogs. Hypercalcemia may cause polyuria-polydipsia or clinical signs of renal failure. Total calcium may be severely elevated. Hypercalcemia of granulomatous disease is due to overproduction of calcitriol by activated macrophages; this is the proposed mechanism of hypercalcemia in canine schistosomiasis. Some reported cases have low PTH concentrations, while others have high PTH. Dystrophic mineralization of many tissues may result. Hypercalcemia may cause in renal failure, which may be the primary reason the patient presents. Hypercalcemia does not resolve until infected dogs are treated with praziquantel.

Differential diagnoses for hypercalcemia include hypercalcemia of malignancy from lymphoma or other cancers, cholecalciferol toxicity, primary hyperparathyroidism, and other granulomatous diseases.

Other renal disease

In addition to dystrophic mineralization, granulomatous inflammation due to *Heterobilharzia* eggs in the renal parenchyma and immune complex glomerulonephritis (protein-losing nephropathy) may occur in infected dogs.

Subclinical Disease

Some dogs have presented for other medical conditions and are incidentally diagnosed with schistosomiasis during evaluation or at necropsy.

Treatment

Praziquantel (25 mg/kg PO q8h for 2 days) and/or fenbendazole (40 mg/kg q24h for 10 days) is used to treat infection. Use of compounded praziquantel may be considered due to the cost of the high-dose protocol that is required. Treatment may result in a cure, resolution of clinical signs, or may be ineffective. In reported cases, it is difficult to distinguish between treatment failure and repeated infection. Severe fibrosis, particularly in dogs with liver failure, is likely associated with a poor prognosis. Follow-up testing 4 weeks post-treatment is recommended and re-treatment may be necessary.

Other symptomatic or supportive therapies should be provided as needed. Patients with severe hypercalcemia require urgent care, which may include intravenous fluid therapy with 0.9% sodium chloride, glucocorticoids, judicious use of furosemide, and possibly other therapies, such as bisphosphonates. However, hypercalcemia does not resolve without praziquantel treatment (36-48 hours post-treatment). Clinical signs suspected to be the result of rapid die-off of the parasite have been described anecdotally, and concurrent administration of an anti-inflammatory dose of prednisone during initial therapy has been suggested.

Multiple dogs in a household can be infected, and testing of all potentially infected dogs is recommended. To prevent re-infection, contact with contaminated fresh water sources should be avoided.

Conclusion

Schistosomiasis is an important parasitic infection in dogs in the Gulf Coast states, but should also be considered in dogs in certain other geographic locations, and in dogs that have been transported from endemic regions. Infection results in a broad range of presentations that may be acute or chronic, asymptomatic to fatal. *Heterobilharzia* eggs are not detected by routine fecal flotation, so directed testing via fecal sedimentation exam or fecal PCR testing should be performed. Early recognition and treatment is important.

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AM I MISSING IT? ATYPICAL ADDISON'S

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Introduction

Dogs with 'classic' hypoadrenocorticism (HOC; aka Addison's disease) manifest clinical signs reflecting deficiencies in both cortisol and aldosterone. These patients are relatively easily identified, often based on predictable electrolyte derangements. However, we are now increasingly recognizing a subset of dogs with hypoadrenocorticism but normal electrolyte status. Clinical signs in these patients reflect hypocortisolemia only, and are often subtle and insidious. This condition is referred to as glucocorticoid deficient HOC (GDHOC) or 'atypical' Addison's disease.

Adrenal gland physiology

The adrenal gland consists of a capsule, an outer cortex and an inner medulla. The cortex is subdivided into three sections, based primarily on physiologic function. These sections are the zona glomerulosa, the zona fasciculata and the zona reticularis; they secrete mineralocorticoids (aldosterone), glucocorticoids (cortisol) and sex hormones (androgens and estrogens) respectively.

The function of the adrenal gland is complex, and various hormonal influences play an important role in the release of the various steroid hormones. Adrenocorticotrophic hormone (ACTH) is need for the release of glucocorticoids, whilst angiotensin II is the primary trigger for the release of aldosterone. Hyperkalemia also triggers aldosterone release. The natriuretic peptides suppress aldosterone release.

There are three main mechanisms for adrenal insufficiency, i.e. HOC. The most important is the primary type, in which a pathological process (most often, an immune-mediated attack) results in destruction of the adrenal cortex. Over 90% of the tissue must be lost before clinical signs are noted. In some patients, the attack appears to be initially directed against the zona fasciculata; the glomerulosa is spared and the ability to secrete aldosterone is preserved. However, a recent study of dogs with all forms of HOC indicated that many dogs with so-called AHOC and normal serum electrolytes had substantially subnormal aldosterone production. It is unclear how these dogs manage to maintain normal electrolyte levels; clearly, other mechanism (likely renal?) must play a key role in this process. Secondary HOC describes patients with pituitary dysfunction and compromised ACTH release. In this disorder, the adrenal glands are not directly injured, and continue to make mineralocorticoids. Iatrogenic HOC occurs in patients on adrenolytic therapy (such as mitotane), and adrenal hormone inhibitors (such as trilostane). It also occurs following the abrupt withdrawal of long-term exogenous glucocorticoids.

Patients with AHOC may have primary or secondary HOC. They can be reliably categorized by measurement of endogenous ACTH concentrations; dogs with primary HOC have high levels and those with secondary HOC have subnormal concentrations. Determining the type of AHOC may be useful from a prognostic viewpoint, although it does not impact short-term therapeutic decisions.

Cortisol is a remarkably important hormone: it influences most body systems and has a profound effect on many metabolic processes. Glucocorticoid receptors are expressed by most tissues, and the full effects of cortisol are still incompletely understood. Under normal circumstances, secretion is increased at times of physical or psychological stress, in response to increased ACTH released by the pituitary. Adequate amounts of cortisol are needed for gluconeogenesis, smooth muscle function, gastrointestinal (GI) health, hepatic function (including albumin synthesis) and adequate food intake.

Clinical signs and findings

AHOC can affect any age or breed of dog, but the classic signalment is a middle-aged female. Certain breeds (e.g. Portuguese water dog, West Highland white terrier, black standard poodle) are genetically predisposed to HOC.

The signs of hypocortisolemia are vague and non-specific, which is why so many patients with AHOC are initially misdiagnosed. In addition, the manifestations often wax and wane, and owners may report periods of apparent improvement. The most prevalent complaints include hyporexia or complete

anorexia, along with changes in stool consistency. Some patients will vomit or manifest abdominal discomfort. Lethargy and depression are also frequently noted.

Occasionally, more severe signs are reported. Hypoglycemia may result in exercise-induced collapse or seizures; a reversible megaesophagus may cause regurgitation; gastrointestinal hemorrhage with melena and hematemesis may occur.

The signs of hypocortisolemia are often exacerbated by stressful events, such as boarding, grooming, or surgery. Any patient with an episodic illness which appears to be triggered by stress should be evaluated carefully for AHOC. In addition, dramatic improvements are noted if glucocorticoids are administered, followed by a quick decline when therapy is discontinued.

Laboratory evaluation

The complete blood count is usually within normal limits. The "normal" CBC is in fact a useful clue, as dogs with AHOC are unable to mount a stress response with the expected white cell pattern (i.e., neutrophilia, lymphopenia, monocytosis, eosinopenia). Some patients may be mildly anemic, due to GI loss and depressed erythropoiesis. A relative eosinophilia (meaning >500 eosinophils/µl in a sick dog) is commonly noted and is a very useful flag for HOC.

The serum biochemical profile often shows some changes, but they are generally mild. It is often helpful to look back to previous lab work for the patient, as 'normal' parameters may still be substantially different. For example, the serum albumin and cholesterol may have dropped 30% but still be within the published ranges. Hypoalbuminemia, hypocholesterolemia and hypoglycemia may be present, and may cause concerns about hepatic function.

GI hemorrhage is a common problem in dogs with AHOC and can be severe. This will increase the BUN concentration, as the blood becomes a high protein 'meal'. Serum creatinine levels are unchanged, so the BUN: Creatinine ratio is often > 20.

Serum electrolytes are within normal limits. The urine analysis is also unremarkable, with evidence of acceptable renal concentrating ability.

Imaging studies

Megaesophagus is a rare complication of hypocortisolemia and may be noted on survey radiographic images. A skilled ultrasonographer may note small adrenal glands or a change in echogenicity.

When to consider AHOC

I consider the possibility of AHOC for every non-specific GI case, particularly if my initial bloodwork is relatively unexciting or suggests a protein-losing enteropathy (low albumin and cholesterol) or GI bleeding. Essentially every GI case is screened for this before I pursue endoscopy or other more invasive or expensive testing. It is also reasonable to add AHOC to the list of differential diagnoses for dogs with acute hemorrhagic diarrhea syndrome (AHDS; formerly hemorrhagic gastroenteritis) as GI bleeding is often associated with cortisol deficiency and can be substantial. AHOC is also worth considering in dogs with esophageal dysfunction or hypoglycemia.

Diagnosis

Patients can be inexpensively screened for AHOC by measuring a resting (baseline) cortisol concentration. This can be added to a standard reference lab serum or plasma biochemical profile at little extra cost, or if you routinely send serum to the Texas A&M GI Lab for folate/cobalamin/PLI testing, you can add a cortisol to this request. I personally do not have a lot of confidence with in-house systems for cortisol measurement, so would strongly suggest using a reference lab for this.

Dogs with HOC always have a resting cortisol concentration below 2.0 µg/dl, so the diagnosis can be confidently discounted if the resting cortisol is > 2.0 µg/dl. Bear in mind however than many synthetic glucocorticoids will cross react with standard ‘cortisol’ assays, so the recent administration of a drug such as prednisone will push the baseline cortisol value above this threshold. Although the 2.0 µg/dl value is an extremely sensitive screening test for HOC, it lacks specificity, and over 20% of dogs with

non-adrenal disease will fall below this value. A single, low resting cortisol measurement is not enough to diagnose HOC and confirmatory testing is needed.

The gold standard test for the diagnosis of HOC is the ACTH stimulation test. A baseline serum sample is collected, and then the patient is injected with a dose of synthetic ACTH. Cosyntropin (Cortrosyn®) is recommended, as the compounded gels may have unpredictable activity. The dose of Cortrosyn is 5 µg/kg IV or IM, or 1 µg/kg IV. One vial can be divided aseptically into small aliquots (e.g., 20 or 50 µg) and frozen at -20ºC in plastic syringes for up to 6 months without appreciable loss of potency. The maximum dose is 250 µg, even in dogs > 50 kg. A second serum sample is collected 60 minutes later.

Patients with healthy adrenal glands will respond robustly, with a post-ACTH stim cortisol concentration > 5 µg/dl (over 10 µg/dl is usual in dogs with non-adrenal disease). Most dogs with AHOC have a 'flat-line' response, with both pre-and post cortisol concentrations < 1.0 µg/dl. If a subnormal response is noted (i.e. a post-cortisol that is higher than baseline but <5 µg/dl), the possibility of iatrogenic HOC should be considered. The patient history usually identifies dogs with this disorder, but occasionally topical medications are overlooked and can confuse the issue. We may also see a subnormal response in dogs with secondary HOC; prolonged ACTH deficiency results in atrophy of the zona fasciculata but some response may occur with exogenous ACTH.

Dexamethasone does not cross react with the cortisol assay, so this can be administered without impacting the post-ACTH cortisol measurement (although it will depress the baseline value). Ideally, all steroids should be withheld for at least 24 hours before any adrenal function tests are performed.

Dogs with primary AHOC can be diagnosed on the basis of the cortisol:ACTH ratio (CAR). This number is much lower in dogs with HOC than normal dogs. However, this test is not routinely used as it will fail to identify dogs with secondary HOC and requires careful sample handling.

In order to differentiate between primary and secondary AHOC, a sample of EDTA plasma can be collected prior to administration of cosyntropin for measurement of endogenous ACTH levels. This hormone is very labile, so careful sample handling (chilled plastic EDTA tubes; spun and the plasma harvested and frozen ASAP) or the use of special EDTA tubes with a preservative (aprotinin; available from most reference labs) is necessary. High endogenous ACTH concentrations indicate primary AHOC, whilst low levels support a diagnosis of secondary.

Therapy

Glucocorticoids should be provided as soon as all adrenal testing is completed. If the patient is unwilling to eat, parenteral steroids should be provided. Prednisolone sodium succinate (5 mg/kg IV) is an ideal choice. Dexamethasone (0.1 – 0.2 mg/kg) is also acceptable and is less expensive and more readily available. This dose is equivalent to 10-20 times normal physiologic levels of cortisol, so it is certainly adequate. Some older publications suggest much higher doses for dogs with HOC, but there is no supporting data and side effects are more likely. Dexamethasone is particularly tough on the GI tract and high doses may result in substantial ulceration and compromise.

As soon as the patient is eating, oral glucocorticoids can be started. In general, it is assumed that physiologic replacement doses of prednisone are around 0.1 mg/kg, once daily. This may be more than some giant breeds need. However, patients are under substantial stress at the time of diagnosis, so higher doses (up to 0.5 mg/kg twice daily) are warranted. The dose can then be slowly tapered down over the next 2-3 weeks. Higher doses should be given before, during and after any perceived stress, such as boarding or surgery.

Additional therapies may be necessary at the time of diagnosis. Fluid support is rarely needed but may improve well-being in severely compromised patients or those with hypoglycemia. GI protectants and antacids may be necessary, and occasional patient may need a transfusion following severe GI hemorrhage.

Monitoring

An undetermined proportion of dogs with primary AHOC are eventually unable to maintain normal serum sodium concentrations and/or become hyperkalemic. In my experience, this occurs in less than 50% of cases. Consequently, regular (q3 months) checks of serum electrolytes and renal parameters are indicated for the first year. If routine lab work shows patterns associated with cortisol excess, such as elevated ALP activity or hypercholesterolemia, the prednisone dose should be reduced. Similarly, excessively dilute urine may be a sign of over supplementation.

There is no need to repeat an ACTH stim test in a dog with AHOC, as the results will never change. The only exception to this rule would be a dog with iatrogenic AHOC following therapy for hyperadrenocorticism.

Summary

AHOC is an uncommon but interesting disorder. A high index of suspicion is necessary for a timely diagnosis, but the response to therapy is rapid and gratifying. Many patients are initially treated for GI or hepatic problems as the disease may mimic other disorders. A baseline serum cortisol concentration should be performed in any patient with a history or laboratory data consistent with hypocortisolemia.

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MINIMALLY INVASIVE MANAGEMENT OF UROLITHIASIS

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Advances in interventional radiology and endoscopy have revolutionized our options regarding the management of urolithiasis. Many patients can be treated without the need for invasive surgery, and practitioners need to understand what is available, and which dogs are suitable candidates. The recommendations discussed here are based on the ACVIM Consensus on canine and feline urolithiasis (available on-line). The Consensus statement also covers prevention strategies (not reviewed here).

Treatment of lower urinary tract (bladder and urethra) uroliths

Struvite (magnesium ammonium phosphate) stones and calcium oxalate (CaOx) stones are routinely found in the lower urinary system; both are radiopaque and cannot be distinguished on standard imaging modalities. In a dog with alkaline urine and a concurrent urease-producing urinary tract infection (UTI; usually *Proteus or Staph spp*), it is reasonable to assume that any stones have a struvite component. In the absence of these circumstances, assume a radiopaque stone is CaOx. Both urate and cysteine are also a possibility but are usually radiolucent (or barely visible).

Medical dissolution is generally the best option for struvite stones, and usually takes 4-6 weeks. Urate and cysteine stones may also be dissolved (see ACVIM Consensus). Removal should be considered for any stone(s) that are causing clinical discomfort or may be likely to lodge in the urethra. A traditional cystotomy is certainly an option, but other methods should be considered (voiding hydropulsion, endoscopic retrieval, lithotripsy, percutaneous cystolithotomy). Urethral surgery for the management of uroliths should always be regarded as an option of last resort, as complications are common and can be very problematic. Always determine the nature of the stone(s) so that appropriate preventative methods can be initiated.

- **Voiding hydropulsion**

This is a low-tech option for stone removal, but is only a suitable choice for a minority of patients. First, the stones must be small enough to pass through the urethra; stone size can be estimated from imaging studies, but it can be hard to predict urethral size in both male and female dogs. Bear in mind that 1 mm = 3 French, so a 3 mm stone will not pass through a urethra that can barely accommodate an 8 Fr urinary catheter. The bladder wall must be healthy, as considerable pressure is used to 'spit out' the stones.

The patient must be anesthetized and intubated; this cannot be done successfully under sedation. A urinary catheter (red rubber) is placed and used to fill the bladder with sterile saline. Expect to instill about 10 ml/kg to achieve adequate distention. The bladder must be easily palpable through the abdominal wall. The patient is then held up so that the urethra is essentially vertical and kept in that position for about 1 minute while the urinary catheter is backed down into the urethra. Pressure is maintained by pinching the prepuce or occluding the urethral papilla. In a carefully coordinated effort, the U-cath is withdrawn and the urinary bladder is expressed.

In my opinion, this is a great option for small, slim, female dog. It is very challenging in larger dogs as holding them up is problematic, and it can be difficult to effectively compress the bladder. Some transient hematuria is common, but most dogs recover very quickly. Risks include bladder rupture (very unlikely) or urethral obstruction from a large or irregular stone.

- **Endoscopic retrieval**

Small stones (see caveats described above) can be captured and removed using a basket device through a cystoscope. Urethral size is the limitation (our male flexible scope is >8 Fr in diameter).

- **Lithotripsy**

A Ho-YAG laser can be used to fragment stones; the pieces are then usually expelled using hydropulsion or retrieved using a basket. This process is quite tedious, and is not a good option in patients with more than 3-4 cystoliths. A very large single stone is also a poor option as it takes so long to break the stone in to suitable fragments. Risks include damage to the bladder (very unlikely) or entrapment of a stone fragment in the urethra.

Lithotripsy is an excellent option for patients with a stone wedged in the urethra, as such stones can usually be fragmented and removed. There is some risk of damage to the urethra, but this appears to be uncommon. Certainly, lithotripsy of urethral stones is a superior option to a urethrostomy/urethrotomy.

- **Percutaneous cystolithotomy (PCCL)**

This is my preferred option for dogs with multiple stones that are too large for voiding hydropulsion. The bladder is initially filled and then a small ventral abdominal incision is made over the apex. The bladder is brought up to the body wall and secured with stay sutures. A screw-in trocar is inserted in to the apex and a rigid scope is used to retrieve stones. Tiny stones and sand can be flushed retrograde and removed. The scope is used to confirm stone removal. This procedure causes much less damage to the bladder than a traditional cystotomy. However, as the abdomen cannot be lavaged, this is not a suitable option for a patient with a UTI. Previous cystotomies can also complicate things, due to adhesions and limitations in bladder mobility. In our clinic, PCCL is more expensive than a standard cystotomy as use of the endoscopic equipment adds substantial cost.

Treatment of upper urinary tract (kidney and ureter) uroliths

As a general rule, there is no reason to intervene in patients with non-problematic nephroliths. The only exception to this rule is struvite nephrolithiasis, in which case medical dissolution should be attempted.

Problematic nephroliths include those associated with pain, recurrent infection, outflow obstruction (of the kidney itself), or renal parenchymal compression. If the goal is removal of the stone(s), endoscopic nephrolithotomy or extracorporeal shock wave lithotripsy are indicated. Neither procedure is available at TAMU; we recommend referral to the AMC in NY for endoscopic nephrolithotomy.

Ureteral obstruction is (fortunately) much more common than the problematic nephrolith, and can be managed by the TAMU team using novel methods (ureteral stenting, subcutaneous ureteral bypass [SUB]). Obstruction should be assumed in every patient with hydronephrosis (even if minimal) and ureteral dilation. As a good rule of thumb, assume obstruction if the renal pelvis is >7mm, but do not rule this possibility out on the basis of renal pelvis size alone. Also, failure to find a urolith does not rule out ureteral obstruction, as patients may have ureteral strictures or blood stones.

On occasion, a ureteral stone may be encouraged to move to the bladder with medical therapy (fluids, +/- mannitol, tamsulosin, amitriptyline). It is therefore reasonable to try 48 hours of medical management prior to intervention, although care should be taken to avoid iatrogenic fluid overload.

It is hard to predict renal recovery in dogs with ureteral obstruction, particularly if this is partial and not acute. We do know that time matters, based on experimental studies in dogs with complete obstruction. Four days of obstruction was shown to result in a 7% decrease in GFR; 7 days resulted in a 22% decrease, and after 2 weeks of complete obstruction, GFR in that kidney was down by >50%. Three weeks of obstruction resulted in >85% loss of functionality.

- **Ureteral stents**

These stents are made of soft, flexible plastic, and are positioned with one end in the renal pelvis and the other in the urinary bladder. Both ends of the stent are fenestrated, so urine can flow through and around the stent. A ‘pigtail’ at either end keeps the stent in place, although migration can occur in either direction. Ureteral stents are removable, although encrustation can occur and make this impossible. The stents themselves are made in various sizes and lengths and are relatively inexpensive. Placement requires general anesthesia. Cystoscopic placement is ideal and is the standard approach for a female >4 kg (this size rule is variable, and will depend on urethral diameter and size of available rigid cystoscopes). In

males, it is very difficult to direct a guidewire up the ureter using a flexible scope, so the trigone must be accessed via cystotomy or a minimally invasive, fluoroscopic and US guided, perineal approach. In essence, the boy dog is temporarily made in to a girl. This is fairly straightforward in a male >25 kg and heals quickly by secondary intention. Fluoroscopy is always needed for ureteral stent placement. This option has essentially eclipsed ureteral surgery (ureterotomy or implantation) in animals and people with obstruction, and is associated with much better outcomes, both short and long-term. In normal ureters, the presence of a stent causes a rapid (3 weeks) and substantial (3-6x) dilation of the ureter; this can allow a stone to passively move into the urinary bladder.

Ureteral stents are very well tolerated in dogs and the vast majority are unaware of the pigtail in the urinary bladder. Complications may arise during placement, including ureteral perforation (usually managed with the stent itself), and there are occasions in which the guidewire cannot get past the obstruction and placement is simply not possible. Stent migration is also a concern. Ideally, a ureteral stent is removed when the problem is addressed but this is not always possible (e.g., patients with an embedded stone). Stents left in place for prolonged periods can become encrusted with mineral material and lose their flexibility. If the renal pigtail becomes rigid, the stent cannot be removed. Chronic infection seems to hasten encrustation.

Owners must be made aware that a stent will not prevent further stone formation and long-term management will be necessary in those patients. In all cases, we recommend regular US examinations (≈3 months) to check placement and collection of urine for analysis culture. Stents can be removed endoscopically in almost all cases (when appropriate) using a rigid or flexible scope.

- **Subcutaneous ureteral bypass device (the SUB)**

The SUB is an option for a dog with a complete ureteral obstruction which cannot be overcome with a guidewire and a stent. We would also consider a ureterotomy, with stone removal and subsequent stent placement in such a case.

Essentially, a locking-loop catheter is placed in the renal pelvis and connected to a subcutaneous port. This carries the urine to the bladder via a second tube, which is secured in the bladder apex. A full laparotomy (sternum to pubis) is needed to access the kidney and urinary bladder, and to secure the tubing appropriately. Outcomes with the SUB are impressive and the recovery times are relatively short. Regular flushing of the system is necessary to maintain patency, so clients must be prepared to return periodically. The SUB should be regarded as a permanent implant; all the component parts can be replaced if necessary, but the device is expected to stay in the animal for the rest of its life.

SUB devices are vulnerable to obstruction, more so than ureteral stents. Obstruction can occur in the post-operative period if any of the tubing kinks; there are methods to reduce this risk, but patient movement can result in problems as the tubing settles itself within the abdominal cavity. Hemorrhage can occur during placement of the renal tubing, resulting in substantial hematuria or blockage of the fenestrations by a clot within the renal pelvis. Obstruction can also occur later due to encrustation, stone migration or infection.

A urine sample can be collected via the subcutaneous port only, using special (Huber) needles. The skin overlying the port must be clipped and prepared aseptically first. It is essential that the operator wears sterile gloves etc. to prevent contamination of the system.

Owners need to understand that the SUB device will require regular checking and must be flushed on a routine basis. We flush them before discharge (≈2 days post placement), one week later, one month later and then every 3 months. Our biggest concerns are obstruction due to encrustation or infection. It is very hard to eradicate infection from a SUB as biofilm lets bacteria persist despite sustained therapy. It is recommended that the system be flushed with a chelator (T-FloLoc, Norfolk Vet Products, Skokie, IL) to reduce the risk of infection and encrustation. Owners also need to be aware that we cannot predict renal recovery; they need to accept the risks of a major surgery and substantial cost without any guarantee of a positive outcome.

Summary

Novel devices and methods now provide us with effective options for patients with urethral and ureteral obstructions or other issues. These approaches require specialized training and equipment but are become more and more accessible. First-opinion practitioners play a key role in identifying suitable candidates and supporting them both before and after intervention.

Recommended reading

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CHAGAS DISEASE: FREQUENTLY ASKED QUESTIONS

Ashley B. Saunders, DVM, DACVIM (Cardiology); Sarah A. Hamer, MS, PhD, DVM, DACVPM (Epi)
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This session will provide updated information for frequently asked questions pertaining to the epidemiology, transmission and prevention, diagnostic testing and medical therapy of Chagas Disease in dogs. Responses from conference attendees will be incorporated in the discussion with Drs. Saunders and Hamer.

OVERVIEW

Trypanosoma cruzi is a protozoal organism transmitted through feces of Triatomine insect vectors from the Reduviidae family, also known as cone-nose or kissing bugs. The disease is endemic in Latin America, and infected vectors have been identified across the southern half of the United States. The kissing bug vectors typically feed at night and are attracted to light. The infectious stage of the parasite is passed in insect feces, which can infect hosts upon contact. Alternately, transmission can occur when a host eats an infected insect. Within the host, the trypomastigotes enter and invade host cells where they become amastigotes and result in various degrees of myocarditis and fibrosis. The acute stage of the disease is characterized by inflammation that often goes undetected or can be associated with fever, lethargy, lymphadenopathy, and arrhythmias. The chronic stage is characterized by fibrosis and clinical signs, if they develop, are related to tissue damage that results in arrhythmias, cardiomyopathy (dilated cardiomyopathy phenotype), heart failure, and sudden death.

CLINICAL PRESENTATION AND DIAGNOSIS

Characteristic clinical problems include arrhythmias (ventricular, sinus node dysfunction, atrioventricular block), cardiomegaly, ventricular dysfunction, and heart failure. Physical examination findings support the presence of heart disease but are not specific for Chagas disease. Abnormal findings could include tachycardia, arrhythmias, abnormal pulse rhythm and quality, tachypnea or dyspnea, murmur, and ascites. Lymphadenopathy has been documented as well.

Antemortem testing is usually based on antibody detection, most commonly thought the indirect fluorescent antibody (IFA) test. Antibody-positive hosts are interpreted as currently infected because self-cure is not common. PCR of blood may detect circulating parasite during acute infections, but negative results are not uncommon in infected/seropositive dogs, especially chronic infections. Echocardiography and ECG aid in characterization of the heart disease in a dog with a positive IFA test. After death, histopathology of tissues, especially cardiac tissue, may show amastigotes although it is not uncommon that chronically infected dogs will show lymphoplasmacytic inflammation and fibrosis without apparent amastigotes.

The index of suspicion for Chagas disease increases in dogs from an endemic location or when abnormalities characteristic of the disease are identified in an atypical breed (ie. a non-Doberman Pinscher with arrhythmias and DCM phenotype).

Consider testing:

- A dog that originated, has traveled to, or is currently living in an area where kissing bugs have been found and Chagas disease has been reported (more common in southern states)
- Dog with arrhythmias, dilated cardiomyopathy phenotype, and congestive heart failure (Doberman or atypical breed)
- Dog whose mother, littermate, or housemate (dog or cat) has been diagnosed with Chagas disease

MANAGEMENT AND PROGNOSIS

Currently, management of infected dogs is directed at controlling the cardiac effects of the disease. For ventricular arrhythmias, antiarrhythmic therapy options include parenteral lidocaine or oral atenolol, sotalol, or mexilitine. Sotalol or amiodarone can be effective for more complex arrhythmias (supraventricular and ventricular) with careful monitoring for adverse effects. For atrioventricular block

or sinus node dysfunction resulting in bradycardia, weakness, or collapse, pacemaker implantation may be indicated. Standard supportive therapy for congestive heart failure secondary to myocardial dysfunction should be instituted as indicated and would include oxygen supplementation if dyspneic, pimobendan as a positive inotrope, diuretic therapy with furosemide and spironolactone, and abdominocentesis if ascites is present and compromising breathing or patient comfort. Arrhythmias and heart failure typically require long-term management for the remainder of the life of the dog.

Information about the course of the disease in asymptomatic naturally-infected dogs is limited. Approximately 30% of asymptomatic infected humans develop clinical Chagas disease. In the asymptomatic patient (dog or human), routine recheck evaluations are advised to monitor for development of clinical heart disease.

Anti-trypanosomal medications used specifically to treat the parasitic organism (e.g., benznidazole, nifurtimox, amiodarone/itraconazole) do not currently have consistently proven efficacy for curing the disease in dogs or preventing the chronic fibrosis and myocardial dysfunction that often develops. Further investigation into optimal timing and dose of administration of these medications may help improve the long-term clinical course of the disease. Many anti-trypanosomal medications have not been readily available in North America. Veterinarians can contact the Centers for Disease Control and Prevention in Atlanta, Georgia, (www.cdc.gov/parasites/chagas) for the most up-to-date information regarding current recommendations as well as availability of anti-protozoal drug therapy for both dogs and humans.

CONTROL AND PREVENTION

If a dog is diagnosed with Chagas disease, the other dogs in the household or litter should be tested for the infection as well. Vector control is an important component of managing the disease. The insects are attracted to lights and often feed at night. Dogs housed outdoors are more likely to encounter the insect vectors. Wildlife reservoirs in North America include wood rats, raccoons, opossums, and armadillos. Eliminate woodpiles, wood rat nesting sites, and other brushy areas that can serve as breeding areas for the insect vectors.

SUGGESTED READING

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When to Blame the Heart: Differentiating Between Cardiac and Respiratory Disease in Dogs

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In dogs presenting with respiratory clinical signs, differentiation between congestive heart failure (CHF) and pulmonary hypertension (PH) and/or primary respiratory disease can be difficult. In particular, left-sided CHF and PH are two clinical scenarios that are easily confused, as their clinical presentations are very similar. Several distinctions on physical examination and screening diagnostics may allow a veterinarian to more strongly suspect one condition over the other.

On physical examination, dogs with acute left-sided CHF are expected to develop a sinus tachycardia as a compensatory mechanism of the sympathetic nervous system meant to address poor cardiac output. If a dyspneic dog has a normal heart rate or a preserved sinus arrhythmia (indicating a predominance of vagal tone), active CHF becomes very unlikely. Similarly, dogs with acute left-sided CHF are expected to have a heart murmur (often loud) if the etiology of their CHF is chronic mitral valve disease (CVD). If a heart murmur is absent, CHF secondary to CVD should no longer be a differential. If a heart murmur is appreciated, but the point of maximal intensity is on the right side of the chest, pulmonary hypertension may be more likely. It is important to note that the auscultation of pulmonary crackles is not specific for pulmonary edema and may be a more prominent finding in dogs with chronic airway disease or idiopathic pulmonary fibrosis. Additionally, dogs with pulmonary hypertension may have split or loud S2 heart sounds and jugular pulses appreciated on their physical examination, both of which would not be expected in typical cases of left-sided CHF.

Thoracic radiographs are the diagnostic test of choice to confirm the presence of pulmonary edema due to CHF. In cases of pulmonary hypertension, thoracic radiographs can be supportive of the diagnosis but not confirmatory. When considering the likelihood of left-sided CHF it is extremely important to confirm the presence of radiographic left atrial enlargement, as dilation of this chamber is nearly always identified by the time CHF develops. The exception to this rule is acute rupture of a chordae tendinae leading to massive mitral regurgitation and acute CHF before chronic remodeling and dilation of the left heart can occur. Congestion of pulmonary veins may also be appreciated in acute CHF patients but is not always present, especially if initial doses of furosemide are administered prior to obtaining thoracic radiographs. Typical distribution of cardiogenic pulmonary edema is perihilar and caudal (particularly right caudal lung fields in early cases). In pulmonary hypertension cases, evidence of right ventricular and/or right atrial enlargement, main pulmonary artery dilation, tortuous and/or dilated lobar pulmonary arteries and various pulmonary infiltrates may be appreciated.

Echocardiography is the standard, non-invasive method used to diagnose PH in veterinary medicine. Secondary remodeling that can develop as a result of PH includes right ventricular concentric hypertrophy (with or without dilation), right atrial enlargement, dilation of the main pulmonary artery, and flattening of the interventricular septum (indicative of suprasystemic right ventricular pressures). If tricuspid regurgitation is present, measurement of the regurgitation velocity can be performed with Doppler modalities to estimate systolic pulmonary artery pressures, with dogs measuring between 31-50 mmHg considered to have mild PH, dogs measuring 51-79 mmHg considered to have moderate PH, and dogs that measure at or above 80 mmHg considered to have severe PH.

In dogs with acute left-sided CHF, echocardiography can be used to definitively diagnose any underlying cardiac disease and to assess chamber size and systolic function. From a rapid clinical assessment standpoint, fast scans aimed at evaluating left atrial size are the most meaningful when determining whether left-sided CHF is likely to blame in a dog with respiratory compromise. The left atrial to aortic root ratio is

commonly used to assess left atrial size from short axis views at the level of the heart base. If left atrial size is normal, CHF is very unlikely.

Treatment for PH is aimed at initial stabilization with oxygen (a potent pulmonary arterial vasodilator). mild sedation (butorphanol at a dose of 0.2 mg/kg IV or IM is commonly used), and the administration of phosphodiesterase-5 inhibitors such as sildenafil (1-2 mg/kg PO BID-TID) or tadalafil (1 mg/kg PO SID). Pimobendan may provide some additional pulmonary vasodilation and can be especially useful in cases with right ventricular failure. It is also important to work PH patients up for any underlying diseases that triggered their PH. If identified, any underlying triggers should be medically addressed.

Another common clinical scenario that leads to treatment dilemmas in small breed dogs is the clinical history of cough in a patient with both CVD and collapsing airway disease. These two diseases are commonly present in the same patient population, with both diseases having the potential to trigger worsening cough with disease progression. A history of worsening cough alone does not provide enough information to direct adjustments in therapy. From a history standpoint, clients who have been trained to monitor sleeping respiratory rates in the home environment can often help to elucidate whether a worsening cough is likely due to the onset or worsening of CHF or an exacerbation of collapsing airway disease, simply based on the presence or absence of elevated respiratory rates at home. If needed, empiric therapy decisions can be made based on in-home respiratory rate data alone. Several phone applications are available for clients interested in charting their dog's respiratory rate data. This data can then be shared with veterinarians providing care to their pet.

Ideally, thoracic radiographs are obtained in patients with worsening cough who have a history of both CVD and collapsing airway disease. This allows for confirmation of the presence or absence of pulmonary edema and provides a practitioner with more confidence in adjustment of the treatment protocol. In difficult to manage cases, focused echocardiograms aimed at estimating left-sided filling pressures may catch cases that are on the brink of tipping into overt CHF that do not yet have obvious radiographic pulmonary edema.

Therapy for these patients should be aimed at optimizing treatment for both of their existing diseases. Chronic mitral valve disease dogs should be prescribed Pimobendan if they have developed dilation of the left atrium and left ventricle (ACVIM stage B2). If active CHF is appreciated, diuretics should be initiated or up-titrated based on clinical history. Cough suppressants can be administered if no active CHF is appreciated and are often required to manage cough in advanced cases. Advocating for weight loss (if indicated), switching from collars to harnesses, and avoiding excitement triggers should all be considered as well. In some cases, even if active pulmonary edema is not appreciated, the initiation of an ACE-inhibitor and/or a low dose of furosemide may be considered in an effort to decrease left atrial size and thus decrease pressure on the weakened mainstem bronchi. Clients should be advised that in this type of case, complete elimination of all cough is very unlikely. The treatment goal is instead aimed at decreasing the cough to a level that does not impair quality of life for either the pet or the client.

Why is This Dog in Respiratory Distress?

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Canine Conference August 2019

Causes of respiratory distress are many, but can typically be categorized by their cause into one of these categories: pleural, pulmonary, upper airway or other. Patient clinical history is important in evaluating for respiratory distress and should include the following: onset, duration, trauma, toxin exposures, history of cardiac disease, etc. Diagnostics to assess respiratory distress beyond the physical exam include sonographic and radiographic studies of the thorax and cervical/pharyngeal regions, which can be used to narrow the differentials of the cause of respiratory distress into one of these categories.

Thoracic ultrasound in the distressed patient can be used to evaluate for the presence or absence of pleural effusion, pneumothorax and peripheral lung disease. Radiographs of the pharyngeal/cervical region are helpful in accessing the upper airways and thoracic radiographs will be used to evaluate the thoracic structures, which will include the heart, lungs and pleural space, as well assess the diaphragm and body wall.

Pleural disease:

Pneumothorax is presence of air in the pleural space on radiographs or ultrasound. On ultrasound, this is seen as a lack of glide sign. Pleural effusion can be identified on ultrasound as anechoic to echogenic fluid between the lung lobes and chest wall and has many causes and we will limit today's discussion to diagnosing the presence or absence of effusion with minimal discussion of the various causes, as the differential list varies with the type of effusion. A pleurocentesis is typically needed to determine fluid type. Pleural effusion on radiographs will be identified as increased opacity in the pleural space with retraction of the lung lobes from the chest wall and thickening/widening of the pleural fissures. Pleural mass can present with respiratory distress, which is typically progressive symptoms but can be acute if results in acute pleural effusion.

Pulmonary changes:

Pulmonary changes typically result in increased opacity of the lung caused by tissue or fluid in the lung which interferes with oxygen exchange. The opacity should be described to include the pattern and distribution, as this will assist in narrowing the differential list. Pulmonary patterns include bronchial, alveolar and interstitial or a combination. The distribution should be described as focal, multifocal, diffuse, patchy, symmetric, and/or asymmetric. Diseases which cause pulmonary infiltrates include infectious, inflammatory, neoplastic, hemorrhagic and edematous (cardiogenic or noncardiogenic) processes.

Bronchial patterns are typically associated with allergic, eosinophilic or inflammatory processes and typically related allergic, parasitic or inflammatory conditions.

Alveolar pulmonary disease differentials include those processes that will cause fluid or tissue to flood the alveoli, and include edema, pneumonia, hemorrhage and neoplasia. Cardiogenic edema is typically perihilar and most severe in caudal dorsal lung; this can be symmetric or asymmetric, and frequently most severe in right caudal lobe. Look for pulmonary venous congestion and enlarged left heart with cardiogenic pulmonary edema. Noncardiogenic edema is typically caudal dorsal distribution and most severe peripherally (airway obstructive processes) or diffuse and patchy (vascular leakage processes). Bronchopneumonia or aspiration pneumonia is typically most severe in t he cranial and ventral lung lobes. If it is a systemic infectious process, the distribution will be diffuse and patchy. Hemorrhage will have a distribution related to the cause. If caused by trauma it will be at the site of trauma and/or opposite side (contrecoup type effect) or diffuse or patchy with a coagulopathy. Neoplasia can cause a focal mass or less commonly a diffuse pattern. Most common location for primary lung tumor is caudal dorsal lung, but can occur anywhere.

The list of processes that result in interstitial lung disease is extensive, and includes processes that cause both alveolar or bronchial disease and often the difference between an alveolar pattern and interstitial pattern is just the severity of the disease. Look at the distribution of the interstitial pattern to create differential list.

Upper airway conditions:

Airway obstructive processes can result in respiratory distress and include processes affecting the nasal passages, pharynx, larynx, trachea and bronchi. To evaluate the nasal cavity, you would need full nasal series radiographs or CT and this is beyond this talk. A lateral view of the pharynx /larynx is helpful to evaluate for pharyngeal disease and ensure patent airway. VD view may not be very helpful unless there is a mass, as the pharynx/larynx will be obscured by the spine. Look for masses or soft tissues opacities in the pharynx or trachea, including polyps, granulomas, neoplasia and foreign bodies. Chondromalacia and pharyngeal, tracheal or bronchial collapse will result in narrowing of the airway and can cause respiratory distress.

Other causes:

Other causes of respiratory distress can be related to the cardiovascular system (congestive left heart failure, right sided congestive heart failure), pulmonary arterial hypertension, pulmonary thromboembolism, neuromuscular disease and systemic diseases (including feline hyperthyroidism). These process will not be included in this lecture, but should be considered in cases in which you have excluded pleural, pulmonary and upper airway disease causes of respiratory distress.