Clinical Presentation

Leptospirosis infection is widespread and prevalent, affecting all mammals. The persistence of this Gram-negative spirochete is associated with its ability to infect and be spread by many far-ranging species including rats, raccoon, cattle, marine mammals, and dogs. These species can act as reservoirs, transmitting and spreading the infection to people. Infection in the dog and people is usually caused by exposure to infected water or urine, and it is presumed that dogs that spend more time outdoors would be at greater risk. Surprisingly, an evaluation of signalment changes over time revealed that small breed dogs (< 15 pounds) were the MOST likely to be diagnosed with infection in the decade from 2000-2009. Cats rarely become infected. Veterinary professionals are at risk for exposure because of their increased exposure to ill family pets and farm animals.

Before 1960, leptospirosis cases were described as causing acute and chronic hepatopathy, nephropathy and hemorrhagic diathesis. This observation led to the foundational vaccinations that are administered to protect against the most common serovars Leptospira interrogans and gryppotyphosa. Additional serovars have been identified and vaccine serums have been updated, however a dog is not protected against all serovars or infection with routine vaccination alone.

Leptospirosis is considered when there are clinical signs of an acute interstitial nephritis (inappropriately reduced urine concentration, renal enzyme elevation pyuria, glucosuria), renal tubular necrosis (cylindruria), cholestatic hepatitis (elevated AST and ALP with or without elevated ALT and bilirubin), and unexplained pneumonitis. When present, proteinuria is generally mild, since damage is primarily targeted to the tubular as opposed to the glomerular segment. Therefore, leptospirosis is NOT a differential for protein-losing nephropathy. Statistically, primary hepatopathy in the absence of azotemia is uncommon (10-15% of cases in one study). Endotheliitis is another aspect of leptospirosis that can manifest in systemic inflammation and a coagulopathy including thrombocytopenia.

Since it takes up to 2 weeks (if paired antibody titers are being compared) to determine if leptospirosis is likely, the patient must be treated for and personnel must be protected from infection when leptospirosis is on the differential list. Therefore, any case of diagnosed acute kidney injury or acute hepatitis, and possibly pneumonitis, should be treated for leptospirosis pending diagnosis.

Therapy is focused on symptomatic treatment for organ dysfunction, systemic inflammatory response syndrome and antimicrobial administration against leptospiremia and leptospiriuria. Early nutritional support and analgesia are also recommended. Fluid therapy can be complicated since severely affected animals will have a combination of increased capillary permeability, decreased plasma colloid osmotic pressure, and increased hydrostatic pressure that can result in severe tissue edema. Close monitoring of the patient's tolerance to fluids involves frequent examination for signs of edema, comparing fluid volumes administered to fluids lost, urine output, packed cell volume, and body weight. Arterial hypertension can be managed with injectable or oral calcium channel blockers, and may increase urine output in relatively oliguric states. Dialysis is indicated with severe volume overload, refractory azotemia, and/or severe hyperkalemia in conjunction with olig-, an-uria.

Doxycycline or penicillins are reported clear organisms in the acute phase. Injectable preparations are preferred since most cases present because they are ill, and gastrointestinal absorption may be unpredictable. Injectable penicillins (amoxicillin or ampicillin 22 mg/kg q8h) are generally less expensive than injectable doxycycline (5 mg/kg q12h), so they tend to be the drug of choice. Based on studies in hamsters, it is believed that leptospiriuria is eliminated after 24h of therapy with penicillins, and that doxycycline for at least 5 days is
needed to clear tissue infection. The ACVIM Consensus Statement on Leptospirosis recommends a 3-4-week course of doxycycline. (Sykes JE, et al. J Vet Intern Med 2011) During the recovery phase, antihypertensive medication and renal support with subcutaneous fluids may be necessary. Chronic therapy is determined based on the extent of recovery.

Diagnosis
Specific testing options for leptospirosis include tissue culture, dark field microscopy, polymerase chain reaction (PCR), microscopic agglutination titer (MAT), and a new IgM immunochromatographic test from Zoetis (WITNESS® Lepto; Kodjo A, et al. Biomed Res Int 2016. Epub 2016 Mar 24). Culture is nearly never recommended, as *Leptospira* are a fastidious organism that are difficult to culture, and handling poses potential risks to laboratory staff. Culture could be considered as part of tissue evaluation (with PCR) in post mortem exams. Darkfield microscopy, similarly, is of little clinical utility, requires specialized equipment, has limited sensitivity based on urinary shedding patterns of the organisms, and involves handling viable (and hence zoonotic) organisms.

PCR can effectively identify very low levels of Leptospiral DNA, but the sensitivity and specificity of the test depend on having organism DNA within the collected sample, and yield may be low if the patient has received antimicrobials. PCR should always be run on paired blood and urine samples, as leptospiremia and leptospiuria can be intermittent, and occur at different points during infection. PCR can NOT rule out leptospirosis, however it is not affected by vaccination.

MAT is currently considered the gold standard test for leptospirosis, with the greatest limitation being that seroconversion can lag up to 1-2 weeks behind clinical infection. Zoetis has developed a rapid in-clinic test (WITNESS® Lepto) for IgM against *Leptospira* antigen that appears able to accurately identify infection earlier than the MAT. This test will hopefully be approved for use in the US within the year. While many studies focus on specific serovars with relation to vaccination, clinical outcome, etc., it is important to note that the magnitude of MAT titer results do not accurately identify the infecting serovar. Recent vaccination can result in false positive results for both MAT and WITNESS®. Testing of post-vaccinal dogs using the WITNESS® test resulted in false positive results for 24% of dogs 12 weeks after; all dogs tested negative at 26 weeks post-vaccination.

Our recommendation is that paired PCR be offered for any case with acute presentation of illness suggestive of leptospirosis. If the PCR is negative and a definitive diagnosis is not identified (effectively replacing leptospirosis as the working diagnosis), MAT should be evaluated 10-14 days after the earliest documented sign of illness. As the WITNESS® test rolls out in the US, we will get a better sense of how to incorporate it into clinical practice. Presumably, positive results should be followed up with MAT titers, and until we know exactly how early during infection this test can detect illness, negative results should not be assumed to definitively rule OUT leptospirosis.

Although cats have rarely been identified as developing seropositivity and/or being PCR positive for *Leptospira* in blood or urine, the significance of this is unknown, as clinical leptospirosis is not recognized in cats.

Nursing Care
Nursing care plays a large role in managing patients suspected of being and diagnosed as being positive for leptospirosis. It involves barrier protection, minimizing exposure to urine, monitoring urine output and signs of fluid overload, as well as waste disposal, laundry protocol, and transport for these cases.

All patients suspected of having leptospirosis should be housed away from other animals. In our hospital, we place them in a local isolation cage as opposed to the isolation room, since the danger of disease transmission is primarily though the urine and blood, which can be contained. A tape barrier is placed around the kennel to alert staff of their isolated status. The taped off area is approximately the width of the kennel and deep enough to allow staff to bring the patient out of the cage and work on them within the taped off area. It is very important that all staff adhere to strict isolation protocol and when handling the patient wear gloves,
gown/body suit, shoe covers, and, preferably, a face shield. We hang signs on the patient’s cage to provide a short synopsis of what leptospirosis is, and what personal protective equipment is required.

Individual bags for waste and soiled laundry hang right by the cage. Isolation laundry protocol includes washing all laundry separate from general laundry with a bleach and detergent regimen. A sign is placed on the washer indicating it's an isolation load.

Very often leptospirosis patients have some degree of acute kidney injury which can cause increased urination. Frequent cage cleaning and patient hygiene, as well as changing the bedding is necessary if they do not have a urinary catheter in place. To avoid accidental contact with infected urine, a towel should be first used to soak up the urine, then disinfectant sprayed onto a second towel to wipe up the remaining urine. Spraying disinfectant directly onto the soiled area is avoided as it may cause the urine to splash and increase the risk of transmission. If the patient can walk and control their urine, they may need orders for walks outside Q2-4hrs. They should be walked or carried through the area of least traffic within the hospital. A designated area should be set up outside where other hospitalized patients and neighborhood pets do not have access. If a designated area is not available or the patient is recumbent, then placement of a urinary catheter is recommended. This will minimize transmission of disease, keep the patient clean and dry, and provide the opportunity to monitor urine output should urine output acutely declines. Isolation measures are kept in place for at least 48 hours after initiation of treatment with penicillins or doxycycline.

As previously discussed, leptospirosis patients with acute kidney injury will be at risk for hypertension and fluid overload. Signs of fluid intolerance to monitor for include a serous nasal discharge, chemosis, peripheral edema, increased respiratory rate, increased respiratory effort, which may indicate pulmonary edema. Frequent monitoring is needed to detect early signs of fluid overload.

Special considerations with phlebotomy include the potential for decreased clotting factors in patients with hepatic involvement, and many have thrombocytopenia. Jugular venipuncture should be avoided in these patients. Peripheral veins such as the lateral saphenous may be a preferred venipuncture site, and the most experienced person should perform the blood draw. If a patient has specific instructions for phlebotomy they should be clearly labeled on the treatment sheet and discussed with staff coming on shift.

Other important nursing care factors in the treatment of leptospirosis patients include providing nutrition, recumbency care (rotating sides and performing passive range of motion exercises), and accurate treatment sheet orders and transcription. Finally, should a test convey a finding suggestive of leptospirosis infection, every staff member and the clients should be informed of the results, and advised to discuss their specific health situation with their own physician.

We hope to see you at our next event on Saturday, April 22nd!

Lakeshore’s 9th Annual Swing Into Summer Symposium
at the North Shore Event Centre (Previously called Radisson North Shore)