A VIN Rounds discussion

Update on Leptospirosis

An expert overview of the latest options for diagnosing, treating, and preventing this devastating disease.

Dr. Katherine James: Let’s start this discussion by asking Dr. Lunn to describe how leptospirosis commonly presents in dogs. We’ll also mention some less common manifestations.

Dr. Katharine Lunn: Over the last 10 years, the typical leptospirosis case that we have seen at the University of Wisconsin is a dog in acute renal failure. Case reports from Massachusetts, New York, New Jersey, Michigan, Georgia, and Wisconsin all suggest the same: Acute renal failure is now the most commonly reported presentation of canine leptospirosis. These reports document that the clinical disease is usually due to infection with the serovars grippotyphosa, pomona, or bratislava. Clinical signs usually include anorexia, lethargy, vomiting, fever, stiffness, abdominal pain, polyuria, and polydipsia. Renal failure is the predominant finding in these patients, with a small percentage also showing evidence of liver disease (icterus and elevated liver enzyme activities). Infection with the canicola and icterohaemorrhagiae serovars is much less common now, probably due to vaccination. So we see fewer dogs with classic leptospirosis—a combination of liver and renal failure.

I would also consider leptospirosis in the differential diagnosis of uveitis in dogs. A word of caution: A dog with uveitis at the University of Wisconsin was subsequently found to have leptospirosis. Because the index of suspicion was low (the dog had no other signs), appropriate precautions were not taken. The student managing the case developed clinical signs of leptospirosis, which fortunately were mild. Leptospirosis can also present as polyuria and polydipsia in dogs with no other clinical or biochemical abnormalities. These dogs have isosthenuria or minimally concentrated urine. Leptospirosis serology is now always on my plan for the workup of polyuria and polydipsia in dogs.

Question: What clues help you place leptospirosis higher on your differential list for acute renal failure?

Lunn: The short answer is that it is always on my list for acute renal failure in dogs—the therapy is simple and you can start treating right away while you try to confirm the diagnosis.

Question: Can you see hematuria with leptospirosis?

Lunn: Yes, with severely damaged tubules.

Question: Is there any difference in the clinical manifestation of infection caused by different serovars?

Dr. Carole Bolin: There are some subtle differences between serovars and
between different isolates within a serovar, but in general all the serovars can cause renal failure and liver disease. Consider all the serovars capable of producing a similar clinical picture. While I generally agree with Dr. Lunn’s statements regarding “typical” cases of leptospirosis in dogs, I have seen cases recently that present with a primary picture of liver disease. However, I wholeheartedly agree that almost all dogs with leptospirosis show evidence of renal compromise.

James: In regard to clinical presentation, do you see cats with leptospirosis?

Lunn: Cats certainly are exposed to leptospirosis, and serologic studies indicate that infection occurs. But clinical disease is rare. No specific disease syndromes have been associated with leptospirosis in cats. Because of their lifestyle, I think cats must be innately resistant to the development of clinical disease. Cats in all parts of the world other than the United States are predominantly outdoor creatures, so they are likely to be exposed frequently and may have developed an innate resistance.

Bolin: We have found leptospirosis in some big cats in zoos, but I have never seen a case in a domestic cat.

James: Speaking of lifestyle choices, what types of dogs are more at risk?

Lunn: The most important message is that any dog is at risk if it’s in the wrong place at the wrong time. Some data suggest that male dogs are more at risk, as well as large-breed, rural, and suburban dogs. But small-breed, female, older, urban dogs can certainly get leptospirosis. I think German shepherds are more at risk, based on published case series and on the cases I saw at the University of Wisconsin. Probably at least 10% of the leptospirosis cases at UW involve German shepherds, yet this breed doesn’t make up 10% of the caseload. This may occur because infection is acquired through mucosal surfaces. IgA is involved in mucosal immunity, and some German shepherds have an IgA deficiency.

Question: Do you see increased incidence of leptospirosis during flood years?

Bolin: The incidence almost always increases in wet years.

Question: Do any good regional incidence studies exist?

Bolin: We have good data from Michigan indicating that subclinical infection is quite common. We studied the antibody profiles of healthy dogs in Michigan before the introduction of the new vaccine containing grippotyphosa and pomona, and the most common serovars in our area (and likely in the Midwest in general) are grippotyphosa and bratislava, with pomona a distant third.

Question: Does anyone see thrombocytopenia or bleeding tendencies in their canine leptospirosis cases?

Lunn: I have occasionally seen mild thrombocytopenia in some severely affected leptospirosis patients. Platelet counts were not low enough to cause spontaneous bleeding, though.

Diagnosis

James: Let’s talk about diagnosis now. Which laboratory tests are most commonly used to diagnose leptospirosis?

Bolin: The available tests fall into two general categories: tests to detect antibodies against the organism and
tests to detect the presence of the organism itself in tissues or body fluids. Microscopic agglutination is the most commonly used antibody test. It’s available at most state diagnostic labs and some private labs as well. The test measures the serum antibody titer for the various Leptospira serovars. Most labs test dog serum against the serovars bratislava, canicola, grippotyphosa, hardjo, icterohaemorrhagiae, and pomona.

Many labs screen the serum at a dilution of 1:100 and then further test sera that are positive at this titer. So your test results will include a titer for each of the serovars. Most cases of canine leptospirosis are diagnosed on a serology basis. I’m sure you have questions about titer interpretation, but let’s discuss a few more tests first. There are several tests that can be used to detect the organism in blood (during the first week of disease) or urine (after three to five days of illness). These include fluorescent antibody (FA), polymerase chain reaction (PCR), and culture. Different labs perform different tests.

In each case, the best sample to test is urine collected before the patient receives the first dose of antibiotics. After antibiotic therapy begins, the organism is usually difficult or impossible to find in urine samples. Therefore, to get a diagnostic sample, you have to consider a diagnosis of leptospirosis as soon as the dog presents. Culture is the most sensitive test if the samples are handled properly and submitted to a laboratory experienced in performing the procedure. However, the process can take many weeks, so most testing is done by either FA or PCR. With both tests, you need to find a lab with considerable experience and good quality-control procedures. If PCR is used, the PCR test should have been validated in canine urine. If leptospires are detected in the urine, the result is definitive; a negative test result means only that leptospires were not detected—not necessarily that the dog does not have leptospirosis. But neither test can identify the infecting serovar. That can only be done by culture, or indirectly by serology. So my standard recommendation is to submit a urine sample for FA or PCR if the dog has not been treated with antibiotics and to submit a serum specimen for serology.

Question: How sensitive and specific is PCR in diagnosing leptospirosis?

Bolin: It’s best to ask the lab. PCR tests are usually specific—they do not identify other organisms as leptospires. However, the sensitivity varies from 50% to 90% depending on the sample and the lab. In general, PCR and FA tests have about the same sensitivity.

Question: Does the urine have to be collected by cystocentesis or is free catch OK?

Lunn: Cystocentesis is ideal when you are investigating a renal failure case. In addition to looking for leptospirosis, you need a cystocentesis sample for bacterial culture to detect pyelonephritis. Also, when managing a renal failure patient, you’ll probably be placing a urinary catheter, so you can get a good sample that way. If you can only get a voided urine sample, you should still do a urinalysis and even a bacterial culture because quantitative cultures can help you rule out contamination.

Question: Can most labs perform a culture for leptospirosis?

Bolin: Most labs are not able to culture for leptospirosis. You will probably need to call your lab and ask to have the sample sent to another lab. Remember, though, that leptospiral culture results will not help you clinically—the results will be delayed.

Question: How stable are the organisms in the urine sample?

Bolin: For culture, the urine needs to get to a lab within 24 hours. For PCR and FA testing, the sample should be shipped by overnight mail and kept cool but not frozen. It’s best to call your lab and ask for any specific instructions.

Now, back to titer interpretation. With leptospirosis, this process is more art than science. Generally, titers of 1:100 or lower are considered negative. Dogs that have been vaccinated for leptospirosis will often have antibody titers of >1:100 for several months after vaccination. In general, these titers are ≥1:400 and involve the vaccine serovars. However, antibodies often cross-react. That is, the antibody induced against serovar canicola by vaccination may cross-react (at a lower titer) to serovar bratislava. I pay attention to titers of ≥1:400, even in vaccinated animals. Certainly titers of ≥1:1600 are usually associated with infection rather than vaccination. Generally, the serovar with the highest titer is the infecting serovar. Of course, titers must always be interpreted in the context of clinical and lab data. When the first serum sample is collected early in disease, the titers may be low. In these cases, submission of a second serum sample seven to 10 days later will document rising titers and confirm the diagnosis. However, many dogs have been infected long...
enough by the time they are examined to have diagnostic antibody levels in the first serum sample tested.

James: This is a good spot to test the titer interpretation skills of those of you participating in this VIN Rounds. Please tell us if you think the patient with the following titer results has leptospirosis. And if yes, which serovar is responsible?

Bolin: OK, here are the results:
- bratislava—1:800
- canicola—1:200
- grippotyphosa—1:3200
- hardjo—1:50
- icterohaemorrhagiae—1:100
- pomona—1:800

You all answered the question correctly; good job. The patient does have leptospirosis. And most of you (70%) identified the infecting serovar—grippotyphosa. In this case, the antibodies against serovar grippotyphosa are cross-reacting with the bratislava and pomona antigens.

When testing for this disease, submit your serum samples to laboratories with knowledgeable consultants who can help you interpret test results. A simple positive or negative report is not very helpful, so don’t hesitate to call for help.

Question: How does vaccine immunity interfere with antibody tests?

Dr. Christopher Olsen: Vaccination titers can complicate serology interpretation. It’s important to know which vaccine the dog received. If a dog has been vaccinated only against serovars icterohaemorrhagiae and canicola, then a strong positive titer (e.g. 1:800) against another nonvaccine titer would be significant. We’ve found that vaccine titers generally top out at 1:400 to 1:800 and decrease to 1:100 within about three months.

Question: How long does it take for a titer to be positive relative to the development of clinical signs? (Is it an IgG or IgM test?)

Bolin: A dog usually develops antibodies within 10 to 14 days of infection. So some dogs will have a low titer when they are first presented to the clinic. However, almost all dogs will have a high titer by the time they have shown clinical signs for a week or so. The first antibody response is IgM, then IgG kicks in.

Question: How long do titers from infection remain elevated?

Bolin: When infected dogs have titers of 1:6400 or so, they can be expected to have titers of >1:100 for up to two years after infection.

Treatment

James: Now that we’ve diagnosed the disease, we should talk about treatment. How is leptospirosis treated? What is the prognosis? Are there long-term sequelae?

Lunn: In terms of specific therapy for leptospirosis, we treat the bacteremic phase and eliminate the carrier state. In dogs, we typically use penicillins for the former and doxycycline for the latter. In people, doxycycline eliminates both bacteremia and the carrier state. Ciprofloxacin may do the same. But we don’t know if doxycycline, ciprofloxacin, or other fluoroquinolones eliminate the bacteremic phase in dogs. I use intravenous penicillin G potassium (20,000 U/kg every four to six hours) during the acute illness in dogs because I know it eliminates the bacteremia. Once my patient is eating, I switch to oral doxycycline (5 mg/kg twice daily) for three weeks to eliminate the carrier state. I also use doxy-
cycline for those polyuria and polydipsia cases and for uveitis cases. Intravenous ampicillin (22 mg/kg every six to eight hours) can be used instead of penicillin.

**Bolin:** Keep in mind that if the dog has lots of leptospires in the blood, its symptoms may actually worsen (increased fever, decreased blood pressure, poor CRT, and so on) shortly after you administer the first dose of penicillin. Don’t worry, though; this response means the drug is working. Supportive therapy is all that’s needed.

**Lunn:** The treatment of acute renal failure is a huge subject that we can continue discussing on the VIN boards. Here’s a summary: You need aggressive fluid therapy (for dehydration, maintenance, and ongoing losses) and you need to measure urine output. I recommend an indwelling catheter and closed collection system. Of course, acid-base and electrolyte imbalances can be very problematic for renal failure patients as well. You also need to consider measuring central venous pressure, providing aggressive nutritional support, and maybe monitoring an ECG if you’re using dopamine. Anuria or oliguria should be converted to polyuria with fluids alone, mannitol, or dopamine, and maybe furosemide. Animals in the polyuric phase are trying to heal their kidneys, so it’s critical that you keep up with losses during this phase. These losses can be enormous and should be measured so you can control fluid balance, putting enough in to keep pace with what is coming out. And don’t stop intravenous fluids too soon. If anuria or oliguria persists despite therapy, peritoneal dialysis (or even hemodialysis) will address hyperkalemia and uremia and buy more time for the kidneys to recover. A kidney biopsy at this stage may help you decide if there is any chance of recovery.

**James:** Fifteen years ago, people used to tout biopsy for prognosis in acute renal failure much more than they do now, independent of cause. Although biopsy can provide prognostic information, I think we’re appropriately hesitant to stop the treatment based on biopsy findings. You may not get a representative kidney sample with a couple of throws of a biopsy needle. And, of course, the procedure can be risky.

**Question:** I’m always hesitant to increase intravenous fluid therapy beyond two to three times maintenance levels. But I’ve heard that in these patients, six times maintenance is not unusual. Should you always use an indwelling urinary catheter?

**Lunn:** The catheter is needed to determine losses. Increase fluid administration as much as needed to meet losses, provide maintenance, and rehydrate. On the topic of prognosis, don’t make a decision based on the magnitude of azotemia. If the patient is oliguric or anuric and you can’t reverse that situation, then the prognosis is poor. If the animal is polyuric, just be patient—it may take a long time, but the tubules can heal. Don’t stop intravenous fluids too soon.

Long-term sequelae include chronic renal failure, which can be progressive even if the inciting cause has been eliminated. Some clinicians suggest that leptospirosis can lead to chronic hepatitis. Uveitis can also develop after the initial acute illness.

Here are the take-home messages: Try to get a urine sample before fluid or antibiotic therapy. Assume all dogs with acute renal failure have leptospirosis until proved otherwise. And penicillin is cheap, safe, and effective.

**Bolin:** A second serum sample is often submitted after treatment starts to confirm the diagnosis. But antibody titers can continue to increase during and after successful therapy, or they can slowly decrease. So I don’t put much credence in using titers to monitor therapy.

**Vaccination**

**James:** Let’s discuss vaccination for leptospirosis.

**Lunn:** We may have strong and varied opinions on this, which makes it a good topic for the VIN message boards where we can each give our own position. I think it’s likely that long-term vaccination against canicola and icterohaemorrhagiae has led to the relative rarity of disease caused by these serovars. Despite the fact that immunity is not long-lived, the proportion of immune dogs in developed countries has been sufficient to control disease; dogs rarely get leptospirosis due to the canicola and icterohaemorrhagiae serovars. Therefore, I don’t think we should stop vaccinating against canicola and icterohaemorrhagiae serovars. And now we have the option of vaccinating against serovars pomona.
and grippotyphosa. Should we do it? I think so, as long as we evaluate the known potential risks and discuss them with our clients. Because this is a fairly new vaccine, it may be too early to say how common the side effects are, so we need to be vigilant and try to keep up with any new developments. Like any medical procedure, vaccination has risks and benefits. The client and veterinarian have to weigh these. If the vaccine were 100% safe, I would recommend vaccinating every patient. Acute renal failure due to leptospirosis is devastating. I would not want my dog to experience it. But if side effects are common, then that’s a different story.

**Question:** The earlier leptospirosis vaccines provided short duration of immunity. Is that true for the new vaccine as well?

**Bolin:** The vaccines are designed to prevent disease, not necessarily infection. There’s a reasonable chance that the vaccines provide good protection against disease for a year, and some may protect longer than that; studies are needed to determine the duration of immunity. Less-frequent vaccination is likely to decrease the incidence of hypersensitivity reactions.

**Lunn:** Carole, I’m sometimes asked if a dog should be vaccinated if it has had a documented *Leptospira* infection. Do you recommend this?

**Bolin:** That’s a good question and one for which there is little scientific basis for an answer. So here is what I think. I will try to separate the fact from opinion for you.

Fact: Immunity is serovar-specific. Dogs infected with grippotyphosa are likely to be immune against that serovar, maybe for life. But these dogs are fully susceptible to infection with other serovars. The cross-reacting antibody is not cross protective.

Fact: Dogs recently infected with leptospirosis often have very high titers against one or more serovars.

Opinion: Therefore, with a concern for hypersensitivity reactions, I hesitate to recommend that a dog be vaccinated with a vaccine containing the serovar it was infected with. So, if a dog had serovar grippotyphosa, I’d suggest that it receive the canicola-icterohaemorrhagiae vaccine. But it should not receive a product containing grippotyphosa until the next year.

I am certainly open to disagreements on this approach. Chris or Kathy, are you telling folks anything different on this issue?

**Olsen:** Infection with the actual organism provides the best immunity, and I see no reason to doubt this with leptospirosis. So I agree that it isn’t necessary to revaccinate immediately with the infecting strain. In fact, it may not ever be necessary to revaccinate against the infecting serovar.

**Shedding and carrier states**

**James:** Let’s talk about shedding for a moment. How long do dogs shed the organism in their urine? Does antibiotic therapy prevent urinary shedding?

**Bolin:** Good studies have not been performed in dogs. Consequently, I base my opinion on extrapolation from excellent data available for other species. In general, dogs are important reservoir hosts only for serovar canicola. As reservoir hosts, dogs can shed this organism for months to years after infection, making canicola infection a serious potential problem. The dog does not serve as an important host for the other serovars—that is, bratislava, pomona, and grippotyphosa. In general, infected dogs shed these organisms in their
urine for a relatively short time: days to a couple of weeks. Some dogs shed serovar icterohaemorrhagiae for a few months. It’s clear that appropriate antibiotic therapy will decrease or eliminate the shedding of live, infectious leptospires in urine. Therefore, it’s quite unlikely that dogs will shed leptospires in their urine after a course of appropriate therapy. However, dogs infected with serovar canicola may not be cured by a routine course of antibiotics—a small percentage of them may shed after the antibiotics are withdrawn.

**Question:** Can vaccinated animals still be carriers?

**Bolin:** Yes, but this is usually a problem only with canicola infections. Dogs tend to shed this serovar for a long time even if they’ve been vaccinated.

**James:** If one dog is diagnosed with leptospirosis, should you treat the other dogs in that household?

**Lunn:** Yes. People working in a location where infection has occurred, such as in the military or a medical environment, are treated prophylactically with doxycycline. So if one dog in a household becomes infected (presumably from the environment), then the other dogs are likely exposed to leptospires in that same environment. And if the sick dog survives and comes home, that pet may initially contribute to environmental contamination. I would use doxycycline in these pets.

**Leptospirosis in humans**

**James:** Perhaps this is a good time to switch gears slightly. Chris is going to talk about leptospirosis in people. Let’s start this discussion with how leptospirosis presents clinically in people.

**Olsen:** There are two clinical forms of leptospirosis in people. The first and most common form (affecting about 90% of patients) begins with a period of febrile illness that lasts about a week. During this time, people most commonly have fever, chills, headache, and muscle pain. This may be the end of it, or these people may develop a second period of fever and headaches associated with meningitis. They may also experience changes in mental state, along with the neck pain and nausea often associated with meningitis. The development of meningitis in people is interesting because we don’t typically diagnose this condition in our domestic animal patients with leptospirosis.

The other major form of leptospirosis in people is a serious condition called Weil’s disease or icteric leptospirosis. As the name suggests, these patients suffer from liver involvement; this form of the disease is most similar to the classic acute liver disease seen in dogs with serovar icterohaemorrhagiae infection. These people may progress to disseminated intravascular coagulation because of both liver failure and vasculitis initiating coagulopathy. In addition, people may experience renal impairment, as well as ocular involvement and skin rashes. Unfortunately, the mortality rate with this form of leptospirosis in people can be up to 10%, even with the aggressive medical therapy available today.

**Question:** Can vaccinated animals still provide good protection against disease for a year, and some may protect longer than that.

**Question:** So the meningitis in people isn’t serious? It’s curable?

**Olsen:** Any case of meningitis is scary, but in most cases patients recover relatively uneventfully. People may be left with neurologic sequelae, though.

**James:** Perhaps next we can talk about how people become infected with *Leptospira* organisms.

**Olsen:** People are infected primarily through mucosal contact with the organism, either via the conjunctival, oral, or respiratory mucous membranes. The *Leptospira* organisms can penetrate through intact mucosa, so you don’t need cuts or lesions.

Leptospirosis is in many ways a classic zoonosis, because the organism is exclusively maintained in nature through infection of animals. These include not only our domestic animals (dogs, pigs, and cattle), but also a variety of wild animals (especially rats in developing countries). However, peo-
ple in the general population don’t typically contract the organism from infected animals. The most common mechanism of infection is indirect through contact with contaminated water or soil. The organism survives quite well for weeks to months in stagnant warm water. People who get infected include campers, those recreating in contaminated lake water, and people occupationally exposed to water, such as sewer workers.

But veterinarians, technicians, clients (both dog owners and farm clients), slaughterhouse workers, and so on are occupationally at risk through direct contact with infected animals, especially their urine. The renal tubules are persistently infected; animals shed the organism in their urine for months or longer. So we need to be particularly careful in handling urine and, in livestock species, reproductive tract fluids.

James: Let’s ask the group another question. How many of you are implementing leptospirosis prevention procedures with your hospital staff when dogs present with acute renal failure?

Bolin: In looking at your answers, it appears that about one-third of you are taking the necessary precautions and consider this an important issue. Chris, can you address what veterinarians, staff, and clients need to do when working with a potentially infected dog?

Olsen: An infected animal doesn’t have to pose a serious risk if basic precautions are taken. The most important step is to avoid exposing mucosal or abraded skin to urine. If owners need to clean up urine spills at home, they should wear gloves and then disinfect the area with detergent.

In the clinic environment, I recommend that technicians treat all canine urine samples as potentially contaminated because dogs can be infected and shed the organism in the urine without showing clinical signs. Consequently, when performing urinalysis, technicians should wear gloves and safety glasses. If you have a dog known to be infected, add a surgical mask to prevent droplet contact with the respiratory tract. This may seem excessive, but it’s important.

Another issue is cleaning runs. The kennel staff should definitely wear gloves, masks, and safety goggles because they’re potentially aerosolizing the organism when they spray the runs. They may balk at first, but after they get used to it, it will become second nature. Each practice should have an occupational safety plan in place.

Bolin: The plan should inform everyone of the risks and stipulate what employees should do if they think they’ve been exposed. If a potential exposure has occurred, they may consider having a serum sample collected for a baseline titer which can be compared to later titers if they become ill. It’s important that clients or staff who may have been exposed explain to their physicians what they have been exposed to. Most physicians have never seen a case of leptospirosis.

Lunn: With acute renal failure cases, an indwelling catheter and a closed collection system really help in handling contaminated urine. All our renal failure cases have a big red card on the cage reading “leptospirosis suspect” and listing precautions that should be taken.

Bolin: This organism is very sensitive to environmental conditions. When it dries or freezes, it dies. It’s also very sensitive to soaps and almost any disinfectant will kill it quickly.

Question: How do you recommend disposing of the urine?

Olsen: You can put the waste urine down the sink because the sewage treatment system will kill the bacteria. However, you might want to mix the urine with disinfectant to reduce contamination in the sink and the infectivity of anything that splashes up.

Question: Do you worry about contamination of grass or dirt?

Bolin: Outside runs and grassy areas do become contaminated. The organism can survive for some time under the right conditions. However, ultraviolet light will kill the bug, and the combination of drying, normal cleaning procedures, and UV light will disinfect runs. So the best thing to do is let these areas dry thoroughly and let the sunshine do the rest.

Question: Is vaccination available for people in high-risk professions?

Bolin: In some countries, people at high risk are vaccinated. No human vaccine is available or needed in the United States because of safety concerns with the available vaccines and because the overall risk of disease is low.

James: I want to thank everyone for participating in this VIN Rounds. And a special thanks to Fort Dodge Animal Health for sponsoring this educational event. We’ll see you on the VIN message boards.

References