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**Infectious Disease**

**Canine Leptospirosis**
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Starting in the early 1990s, a resurgence of canine leptospirosis has been observed. The identified leptospiral serovars were atypical and included *Leptospira pomona*, *grippotyphosa*, *autumnalis*, *hardjo*, *bratislava*, and *australis*. In many areas canine leptospirosis remains the top differential diagnosis to consider in dogs presented with acute renal failure (or a close second to nephrotoxins), and affected dogs often require intensive therapy. The goal of this presentation is to review the recent epidemiological and clinical data on canine leptospirosis. Additionally, the elements making this disease a persistent challenge for clinicians and researchers will be discussed.

**Epidemiology**
Leptospires are spirochetes that are transmitted between animals by direct or indirect contact. Exposure to infected urine, ingestion of infected tissues, and bite wounds are probably the most common means of direct transmission in the dog. *Leptospira* can be intermittently detected in the urine of recovered dogs for months to years after infection. Contaminated water sources, food or bedding are causes of indirect transmission.

In North America, most cases of canine leptospirosis occur between July and November. Leptospires survive best in a humid environment at temperatures between 0 and 25°C (32 and 77°F), and a significant correlation between the average rainfall recorded 3 months prior to diagnosis and the number of cases could be identified. Based on experience from several clinical reports, a recrudescence of leptospirosis cases can be expected after intense rainfall and/or floods, especially in the warm season. Male dogs are more likely to develop the disease, probably due to their natural straying behavior. Dogs between 4 and 10 years of age are more frequently affected than puppies one year and younger. Large breed dogs are over-represented in some case series. Additionally, working animals such as herding or hunting dogs are at a greater risk of developing leptospirosis than dogs mainly staying in homes. Contact with livestock appears to be a risk factor for developing positive titers to some leptospiral serovars, while being kept in a fenced yard appears to be protective in some instances. Finally, dogs living in suburban or rural areas are also more likely to come into contact with the infectious agents.

**Pathogenesis**
Leptospires infect their host through intact mucous membranes or skin lesions, and leptospiromia usually develops within days. The incubation period is approximately 1 week but can vary depending on the virulence of the strain and the immunity of the host. The most common targeted organs are kidneys and liver. The lungs can also be affected, probably due to leptospiral vasculitis and focal hemorrhages.

**Clinical Features**
Most dogs have a history of lethargy/depression, vomiting, anorexia prior to presentation. Diarrhea, PU/PD, and reluctance to move may also be mentioned. During the physical exam, either fever or hypothermia may be detected as well as a painful and tense abdomen. Icteric mucous membranes, dehydration, weakness, renomegaly and oculonasal discharge may also be observed. In the last few years, 4 dogs with leptospirosis (*L. australis*) and significant renal involvement were seen at 2 referral centers in Switzerland. These dogs developed intestinal intussusception and 3 of them had to be treated surgically. Intussusception was attributed to the direct effects of leptospiral intestinal wall infection or to an abnormal intestinal motility associated with the uremic syndrome. Complications such as DIC and SIRS may occur due to the high tissue tropism of leptospires, and require aggressive and intensive treatment.

**Diagnosis**
**Clinical-pathological abnormalities**
These may include changes in white blood cells (leucocytosis with neutrophilia and left shift), increases in serum urea, creatinine, phosphorus and bilirubin concentrations as well as increased activities of liver enzymes. Many dogs show changes suggestive of renal and liver involvement, even though impairment of renal function clearly dominates the clinical picture. Some dogs show exclusively abnormal renal function, and others only show signs of liver involvement. Almost all dogs are proteinuric with different levels of magnitude. Urine specific gravity is lower than 1.030 (often isothenuric). Microscopic hematuria is occasionally observed. Increased number of leucocytes and/or epithelial cells, or granulated urinary casts may be seen in the urinary sediment. In a recent study, surviving dogs had lower urinary protein-to-creatinine and albumin-to-creatinine ratios and higher serum albumin concentrations than those that died as a complication of leptospirosis.
Diag nostic imaging
Radiographic findings include renomegaly, and occasionally interstitial to nodular pulmonary infiltrates occurring mostly in the caudodorsal lung fields, and representing focal pulmonary hemorrhages attributed to endothelial damage. Abdominal ultrasound findings are not typical for leptospirosis, but rather for acute to subacute renal and/or liver disease. They include renomegaly, increased cortical echogenicity, mild perirenal fluid accumulation, pyelectasia, and a medullary band of increased echogenicity.

Serologic testing
The standard test for the detection of antibodies against leptospires is the microscopic agglutination test (MAT). This procedure consists of exposing serial dilutions of the patient’s serum to leptospires. The presence of antibodies leads to leptospiral agglutination. The MAT titer corresponds to the highest dilution of the patient’s serum to leptospires. The presence of antibodies results in leptospiral agglutination. Generally, laboratories report titers > 1:100 as positive.

However, a lower limit of >1:400 is usually preferred to rule out the possibility of vaccine-induced titers. Most clinicians prefer to see titers > 1:800 to confirm leptospirosis in dogs with compatible clinical signs. However, false negatives and false positive can occur, and this clinical habit is therefore subject to several caveats:
1. The MAT Titer usually rises within 7-10 days after infection. Because of this lag time, some dogs may be presented with severe, peracute infection and a negative MAT titer.
2. Positive titers only confirm exposure of the animal to leptospiral organisms. This may be enough to make a diagnosis in a dog with typical clinical signs. However, in a study of healthy control dogs and dogs from an intensive care unit without signs suggestive of leptospirosis, many animals had positive titers, some of them even above the 1:800 limit. This was confirmed by a recent publication showing that up to 25% of healthy dogs presented to their veterinarian had titers of 1:200 or above against at least one leptospiral serovar.
3. Some dogs with leptospirosis that were treated early with antibiotics may not develop high antibody titers, or not show a fourfold titer increase. It is not unusual to observe high titers against more than one serovar. In such cases, it is generally assumed that the highest titer identifies the serovar responsible for the infection.

Organism identification
The direct identification of leptospires in the urine is best performed using PCR. Bacterial isolation and culture as well as dark-field microscopy are difficult and require a fully equipped in-house microbiological laboratory. Antibiotic therapy started prior to urine sampling makes it impossible to isolate leptospires. PCR is a sensitive method to confirm the presence of leptospiiral DNA in body fluids including urine, however it does not allow reliable identification of serovars. Using PCR it was shown that 8% of animals from a group of 500 dogs seen at a veterinary teaching hospital excreted leptospires in the urine. Only 10% of the shedding dogs had clinical signs of leptospirosis, and PCR detected leptospiral DNA in 3 out of 4 of these infected dogs. All other PCR-positive dogs were either healthy or had unrelated illnesses. Dogs can excrete L. canicola for months to years after they recover from infection, however it is not clear how long urinary excretion continues in dogs infected with other serovars. This study showed that leptospires can be present in the urine from a large number of dogs without clinical signs of leptospirosis. This is comparable to the finding of positive MAT titers in dogs without clinical evidence of leptospirosis, and suggests that only a small proportion of dogs exposed to leptospires eventually develop a clinically relevant infection.

In a recent case series from 2 referral centers in New York State, L. grippotyphosa was the most frequently detected serovar, followed by L. pomona, and L. autumnalis. L. bratislava was also reported to be frequent in other studies. L. pomona was more likely to be associated with marked azotemia and hyperphosphatemia, thrombocytopenia, and vomiting. Dogs with highest MAT titers against L. pomona were less likely to be discharged from the hospital than those infected with other serovars (only 50% left the hospital compared to 80-100% of dogs infected with other serovars). In other reports, L. pomona caused predominantly liver disease. However, the differentiation of clinical and clinicopathological changes caused by specific serovars has been a source of disagreement between the different published case series. This is probably due to the uncertain correlation between MAT results and those of urine culture or PCR. Finally, dogs < 6 months old appear to develop liver disease more frequently than renal disease.

Therapy
In canine leptospirosis, renal and liver failures are potentially reversible and should be treated as early and aggressively as possible. The affected dogs are treated symptomatically with antiemetics and gastric protectants, and particular attention is paid to adequate urine production after the animals have been properly rehydrated. The placement of a sterile urinary catheter can be helpful in assessing urine production as well as containing potentially infective waste. Urine production < 2 ml/kg/hr in an adequately hydrated dog indicates oliguria and must be treated aggressively. In animals that are not fluid overloaded, mannitol is
Infectious Disease

usually considered the treatment of choice. It is initially given as a bolus, (0.5 g/kg over 30-60 min) and then followed as a constant rate infusion (1-2 mg/kg/min) if urine production responds appropriately. Alternatively, furosemide can also be administered. It is initially given as a bolus (2-4 mg/kg) and then followed as a constant rate infusion (0.25 - 1 mg/kg/hour) if urine production increases appropriately. Urine production should be followed closely and over-hydration of the patient avoided. Antibiotic therapy is usually given in 2 phases: ampicillin or amoxicillin can be administered parenterally (20-25 mg/kg i.v. TID) during the initial, critical phase. It is important to note that the kidneys clear these drugs and blood concentrations can become inappropriately high in patients with renal dysfunction. A common method of adjusting these antibiotic dosages is to multiply the normal dose by 1/serum creatinine. When the dogs are recovered, doxycycline (10 mg/kg p.o. daily in 1 or 2 doses) is the antibiotic of choice and is prescribed for a minimum of 3 weeks to prevent persistent renal shedding. The prognosis of canine leptospirosis is fair; depending on the case series, between 50 and 90% of dogs can be discharged from the hospital after a stay of up to 7-10 days. Oliguric/anuric renal failure is a strong negative prognostic factor in most reports. However, dogs affected with this complication do benefit from hemodialysis or continuous renal replacement therapy. Both procedures may significantly decrease mortality, and are currently available in many teaching hospitals and large referral centers.

Prevention
Currently, the mainstay of prophylaxis consists of vaccination of dogs at risk with a bacterin containing the 4 main serovars (canicola, icterohemorrhagiae, grippotyphosa and pomona). It is not known if this vaccine causes cross-protective immunity against other serovars such as autumnalis, bratislava and australis. In kennels in which leptospirosis is a problem, the environment must be optimized to avoid risk factors.

Zoonotic potential
Urine from dogs with leptospirosis can infect people if it comes in contact with mucous membranes or skin lesions. In industrial countries, most infections in humans are associated with occupational exposure to infected wildlife or domestic animal hosts, or practice of water sports activities. Although urinary excretion of leptospires ceases shortly after administration of systemic antibiotics, it is recommended to take precautionary measures with hospitalized infected dogs to avoid contamination of the staff. Latex gloves (and long sleeve shirts) should be worn when handling these dogs in the initial phase of treatment. Disinfection of contaminated areas should be done with goggles and face masks. It is important to remember that healthy dogs excreting leptospires in the urine represent a higher risk for human infection.

Selected references
Available on request from the author