LEPTOSPIROSIS: A NEW ERA OF DIAGNOSIS AND PREVENTION

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INTRODUCTION

Leptospirosis is caused by several pathogenic species of the spirochete *Leptospira*. Organisms are transmitted by direct contact with infected urine, bite wounds or predation of infected wildlife, or indirectly, through contact with infected water, soil, food or bedding. Leptospires can survive several weeks in the environment when conditions are optimal, such as where there is a source of water (standing or rapidly moving) and temperatures between 0 and 25°C. The seasonality of the disease is variable depending on local rainfall patterns. In areas with year-round rainfall, the disease may occur throughout the year.

There are hundreds of pathogenic serovars, which are grouped into antigenically-related serogroups. In addition, classification of leptospires is gradually moving from serovar-based classification to genotype-based classification. Each serovar (and more accurately, each genotype) is adapted to a one or more mammalian host species (maintenance hosts). Other hosts act as incidental hosts. Disease in incidental hosts tends to be more severe and the duration of shedding is generally shorter. Maintenance hosts include dogs (Canicola); rats (Icterohaemorrhagiae); small wildlife mammalian species such as voles, skunks, and raccoons (Grippotyphosa); cattle (Hardjo); and mice (Ballum). The prevalence of infection with a serovar/genotype in dogs depends on the degree of contact between the dog population and the maintenance host for that serovar/genotype. In truth, the actual serovars causing disease in dogs worldwide still remain poorly characterized, but recent studies using culture and PCR have begun to shed more light on the true infecting serovars, and what domestic and wildlife reservoir hosts might be infected. Other factors, such as the density of reservoir hosts, the concentration of organisms in their urine, and specific leptospiral strains may also be important in determining whether disease occurs in dogs and humans.

Pathogenic leptospires penetrate abraded skin or mucous membranes and multiply rapidly, causing renal failure, hepatic injury and vasculitis. The disease is multisystemic and may also involve the pancreas (pancreatitis), gastrointestinal tract (gastroenteritis), eye (uveitis) and lungs (leptospiral pulmonary hemorrhage syndrome, or LPHS).

CLINICAL MANIFESTATIONS

Most infections are subclinical. Younger, large breed, outdoor adult dogs are commonly affected, but one study showed an increase in the percentage of small breed dogs diagnosed with leptospirosis between 1970 and 2009 (Lee et al, 2014), possibly because they are less often vaccinated. Younger animals tend to be more severely affected.

Lethargy, anorexia, vomiting, pyrexia, dehydration, abdominal pain and increased thirst and urination are common signs of acute leptospirosis. Reluctance to move due to myositis or pancreatitis; icterus; punctate retinal hemorrhages and uveitis may be noted. Respiratory difficulty may result from

pulmonary hemorrhage, which is often associated with the development of moderate anemia.

LABORATORY FINDINGS

Leukocytosis, thrombocytopenia, azotemia, hypoalbuminemia and mild to moderately elevated liver enzyme activities are common. Although hyperkalemia has been reported, normokalemia or hypokalemia are more common. Urinalysis may reveal isosthenuria, proteinuria, glucosuria and casts. Proteinuria is typically low-level (urine protein:creatinine ratio < 5), in contrast to dogs with Lyme nephritis, which have glomerular disease and higher ratios. Thoracic radiography may reveal a focal or diffuse interstitial to bronchointerstitial pattern; alveolar patterns may represent pulmonary hemorrhage. Hepatomegaly, splenomegaly, renomegaly and/or peritoneal effusion may be evident from abdominal radiography. Hyperechoic renal cortices and mild renal pelvis dilation are occasionally seen on ultrasound.

DIAGNOSIS

Identification of leptospirosis requires a high clinical suspicion for the disease. Currently available diagnostic tests include PCR, serology using the *microscopic agglutination test (MAT)*, and in-clinic serologic assays that detect IgG/IgM (SNAP Lepto, IDEXX Laboratories), or IgM (WITNESS Lepto, Zoetis). In the *MAT,* respective titers are provided for each of several different serovars in order to increase the chance of antibody detection. The MAT does not accurately predict the infecting serovar, and therefore *should not* be used for this purpose. Titers with any serologic test may be negative in the first week of illness. Positive titers early in the course of an illness may reflect residual post-vaccination titers or prior subclinical infection. *Demonstration of a fourfold rise in titer is required over a 1-2 week interval*. *In acutely ill dogs (< 1 week of illness), it is the author's opinion that leptospirosis serology should only be performed in a paired fashion or not at all, because of the limited utility of a single positive titer, regardless of its magnitude.* Postvaccinal titers against Icterohaemorrhagiae, Canicola, Grippotyphosa and Pomona occasionally rise as high as 1:6400 for a few months after vaccination, and these can interfere with interpretation. Use of a laboratory with a high level of quality control is recommended, or a laboratory that participates in the International Leptospirosis Society's proficiency testing scheme.

In-clinic serologic assays are useful for screening dogs for the presence or absence of antibodies. Should these kits yield negative results, it may be too early for the animal to have developed antibodies (as can occur with the MAT). Another test should be performed one week later to see if the animal seroconverts. The IDEXX assay detects IgG and IgM, and the WITNESS test detects IgM. Should these kits yield positive results, then the clinician should consider whether previous vaccination has occurred. Previous subclinical exposure should also be considered as a reason for positive results. Although the WITNESS test is less likely to be influenced by previous exposure or vaccination, some dogs can still be positive several weeks after vaccination. Clinicians should consider reflex testing with MAT in order to obtain a quantitative titer if positive results occur using in-clinic serologic tests, followed by convalescent serology 1-2 weeks later in order to document a change in titer. Additional clinical validation of these assays in different

regions of the United States would be helpful to confirm their sensitivity and specificity.

The sensitivity and specificity of PCR may vary geographically depending on the serovars present and shedding patterns that occur for those serovars. The sensitivity may also be higher very early in the course of illness and in dogs that have not received any treatment with antimicrobials. PCR assays are best performed on blood AND urine concurrently because urinary shedding begins 10 days after the onset of infection.

TREATMENT

Treatment involves use of parenteral penicillin derivatives for leptospiremia, such as ampicillin (20 mg/kg IV q6-8h, adjusting dose down if severe azotemia is present) for up to 14 days or as long as the patient is vomiting. Teatment should then be changed to doxycycline (5 mg/kg PO q12h) for 2 weeks, in order to eliminate the carrier phase. Supportive therapy is also indicated for acute renal failure. The use of hemodialysis can improve survival in dogs with severe renal failure.

PREVENTION

In North America, vaccines are available for serovars Canicola, Icterohaemorrhagiae, Pomona and Grippotyphosa. The vaccines are safe and efficacious and several recent studies indicate they provide a 1-year duration of immunity.

Although it was prevalent when the two-way (Canicola and Icterohaemorrhagiae) vaccines were in widespread use, vaccine failure appears to be rare with the current 4-serovar vaccines (Hennebelle et al, 2013). With improvement in vaccines, the incidence of adverse reactions appear to be approaching those of distemper-hepatitis-parvovirus vaccines, even in small breed dogs. Vaccination against pathogenic leptospires is strongly recommended for dogs living in areas where leptospirosis occurs (ie. throughout the US), and are recommended even for small breed dogs that are confined to urban backyards, because of the possibility of infection as a result of rodent exposure. Minimizing access to rodents, farm animals and other wild animals also should help to prevent infection.

PUBLIC HEALTH RISK

Leptospirosis remains an important zoonosis, although most documented human leptospirosis in North America results from recreational activities that involve water, rather than contact with dogs. There are anecdotal reports of leptospirosis in staff that work in veterinary hospitals. Warnings should be placed on cages, and gloves should be worn while handling these dogs. At the author's hospital, contact precautions are lifted after 72 hours of specific antimicrobial therapy.

References available upon request