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LEPTOSPIROSIS

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Introduction

Leptospirosis is a bacterial zoonotic disease of worldwide significance in many animals and humans caused by infection with antigenically distinct serovars of *Leptospira interrogans sensu lato*. There is some confusion about the classification of leptospires as the serogrouping used in the past overlaps with newer classifications based on genetic methodologies. The important serovars of canine leptospirosis are *icterohaemorrhagiae*, *canicola*, *grippityphosa*, *pomona*, and *bratislava*.

Aetiology

Leptospira organisms are thin, flexible, filamentous bacteria made up of fine spirals with hook-shaped ends. More than 200 different serovars have been identified in the *Leptospira interrogans* complex. Each serovar has a primary host that maintains the organism and contributes to its dissemination in the environment. Although all mammals are susceptible to infection, clinical signs are most severe with non-host adapted serovars.

Pathogenesis

Leptospires can penetrate mucosa or broken skin and can be directly transmitted by contact through urine, venereal routes, placenta, bites, or ingestion of infected tissues. Shedding by infected animals usually occurs via urine. The more common way of transmission is indirect transmission, which occurs through exposure of susceptible animals to a contaminated environment (e.g., soil, food, or bedding). Water contact is the most common means of spread, and habitats with stagnant or slow-moving, warm water favour organism survival.

Once in the host, leptospires begin to multiply entering the circulatory system and organs such as kidneys, liver, spleen, central nervous system, eyes, and genital tract. Organ damage is caused by the replicating leptospires as well as the host's inflammatory response. The extent of damage depends on the virulence of the leptospires and host susceptibility. As serum antibodies increase, the organism is cleared from most tissues, except for the kidneys. Renal colonization occurs in most infected animals, and the organism usually persists in renal tubular epithelial cells for years. Recovered dogs can excrete organisms in their urine intermittently for up to 4 years after infection.

Clinical Signs

The severity of clinical signs depends on the age and immune-competence of the animal, serovar involved, and the virulence and quantity of the acquired bacteria. Dogs under 6 months of age are more susceptible and often show marked hepatic dysfunction.

The majority of leptospiral infections in dogs are sub-clinical. Per-acute leptospiral infections can occur and are characterized by massive leptospiraemia, resulting in shock and often death with few clinical signs. Less severe infections are characterized by fever, anorexia, vomiting, dehydration, and polyuria. Other clinical signs include meningitis, uveitis, abortion, and infertility. Pulmonary changes are associated with pulmonary haemorrhage, most likely due to endothelial damage and vasculitis.

Acute renal failure is common as renal colonization occurs in most infected animals because the organism replicates and persists in renal tubular epithelial cells, even in the presence of neutralizing antibodies. Renal function in some dogs that survive acute infections may return to normal within several weeks or may develop chronic compensated polyuric renal failure.

Leptospirosis can cause profound hepatic dysfunction without major histological changes. The degree of icterus in both canine and human leptospirosis usually corresponds to the severity of hepatic necrosis. In dogs, icterus can also be associated with haemolysis. Chronic active hepatitis and hepatic fibrosis have occasionally been demonstrated as sequelae to serovar *grippityphosa* infection in dogs. The initial hepato-cellular injury and the persistence of the organism in the liver results in altered hepatic circulation and immunologic disturbances that perpetuate the chronic inflammatory response. This process may result in extensive hepatic fibrosis, cirrhosis, and finally hepatic failure.

Disseminated intravascular coagulation may occur rapidly and result in acute endothelial injury and haemorrhagic manifestations. *Leptospira* lipopolysaccharides stimulate neutrophil adherence and platelet activation, which may be involved in inflammatory and coagulatory abnormalities.

Clinical Pathology

On urine analysis bilirubinuria, proteinuria, sometimes glucosuria, and increased numbers of granular casts, leukocytes, and erythrocytes in the sediment may be evident.

Laboratory abnormalities include leukocytosis, thrombocytopenia, azotaemia, electrolyte disturbances, bilirubinaemia, and elevated liver enzyme activity. Coagulation parameters may be altered in severely affected animals.

Diagnosis

The diagnosis is based on a combination of clinical signs, clinical pathology changes, and use of the microscopic agglutination test (MAT). Establishment

of a diagnosis is important, as animals can serve as reservoirs and thus pose potential zoonotic risks.

The specific diagnosis of leptospirosis can be accomplished by several techniques:

Serology

Serological tests using MAT, immunofluorescent assays, or enzyme-linked immunosorbent assay (ELISA) are all available. The problem, however, in the interpretation of antibody test results is the high prevalence of sub-clinical infections and the persistence of antibodies. In addition, leptospiral vaccines induce antibodies; therefore the presence of antibodies in itself does not necessarily reflect disease. High titres or a 4-fold increase in paired sera increases the sensitivity of the diagnosis.

Direct visualization

Visualisation of leptospires can be done in fresh urine by dark-field microscopy, tissue sections, air-dried smears, and immunofluorescence and immunohistochemical staining techniques.

Culture

Leptospires are difficult to culture and may take weeks to months to grow. They can be cultured from blood, urine, or CSF using special liquid, semisolid, or solid culture media. As they are fastidious organisms sampling should always be done prior to any antimicrobial therapy.

PCR

PCR not only allows a diagnosis but also identification of specific serovars. PCR can be used to detect leptospires in blood, CSF, aqueous humor, and urine.

Treatment

Antimicrobial therapy is essential to terminate the bacteraemia with treatment being divided into two stages: the first stage is to inhibit multiplication of the organism and reduce fatal complications of infection, whereas the second stage is to eliminate the carrier state.

Penicillin (such as ampicillin or amoxicillin) and its derivatives are the antibiotics of choice for terminating leptospiraemia. These drugs prevent shedding and transmission of the organism within 24 hours of therapy. They do not, however, clear renal infections or eliminate the carrier state and chronic shedding.

Drugs that are effective in eliminating the carrier state include doxycycline, tetracyclines, aminoglycosides, or the newer erythromycin derivatives. In

animals with only mild clinical signs, doxycycline can be used for both initial and elimination therapy.

Supportive therapy depends on the severity of the clinical signs, whether renal or hepatic dysfunction is present, and presence of other complicating factors.

Prevention

Vaccination against *icterohaemorrhagiae* and *canicola* infection has been widely used, and has reduced the prevalence of highly virulent forms of illness. However, these vaccines are not cross-protective against the serovars responsible for most of the current infections in dogs. More recent vaccines contain the *grippotyphosa* and *pomona* strains, either as bivalent or quadrivalent products with the other two strains. The use of multi-strain vaccines will likely reduce disease prevalence. All dogs should receive at least three injections in the primary vaccination series, followed yearly and possible biannual vaccinations.

As wild animal reservoirs and sub-clinically affected domestic animals continue to harbour and shed organisms, control of rodents in kennels, maintenance of environmental conditions to discourage bacterial survival, and isolation of infected animals are important steps in preventing the spread of disease. As complete control of shedding by wild animal reservoirs is impossible, vaccination of dogs in endemic areas is essential.

Leptospirosis in Cats

The prevalence of clinical illness is low in cats, despite the presence of leptospiral antibodies in the feline population and the exposure of cats to leptospire excreted by wildlife. Serovars *canicola*, *grippotyphosa*, and *pomona* have been isolated from cats. Outdoor cats have the highest antibody titres and transmission from rodents is most likely. Although cats develop antibodies after exposure, they appear to be less susceptible than dogs to both spontaneous and experimental infection. Clinical signs are usually mild or not apparent, despite the presence of leptospiraemia and leptospiuria and histological evidence of renal and hepatic inflammation.

Public Health Considerations

Urine from infected dogs can cause disease in humans when it comes in contact with mucosal surfaces or a break in the epidermal barrier. Latex gloves are necessary when urine or urine-contaminated items are handled, and face masks and goggles should be worn when contaminated kennel areas are hosed down. Urine-contaminated areas should be cleaned with dry paper first to avoid dilution of urine, then washed with detergent and treated with iodophor disinfectants, to which the organism is susceptible. All dogs known to be or suspected of shedding should be treated with doxycycline.