POINT OF CARE
Leptospirosis is a complicated disease. Clinical presentations can vary, diagnosis is difficult, and the zoonotic potential is serious.

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CONTINUING EDUCATION

INFECTIOUS DISEASE

Leptospirosis in Dogs

MEET THE AUTHOR

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Leptospirosis is a bacterial infection that has become more and more prevalent in both human and veterinary medicine worldwide. Most mammals are susceptible to infection.[1] As humans expand their environmental footprint, encroachment on wildlife becomes a greater issue, and people, domestic pets, and wild reservoir hosts (e.g., raccoons) cross one another's path more and more often.

ETIOLOGY

Leptospira bacteria are small, thin, flexible, filamentous bacteria known as leptospires or spirochetes. These gram-negative aerobic bacteria measure between 0.1 and 0.2 µm wide and 6 to 12 µm long.[4] They can be stained with the use of carbol fuchsin counterstain and look like fine spirals with hook-shaped ends. These bacteria are highly invasive, partly due to inner periplastic flagella that allow them to swim and crawl around.[4] These flagella are surrounded by a cytoplasmic or protoplasmic cylindrical membrane covered by a double-layered envelope.

Leptospira spp. may be pathogenic or nonpathogenic. For example, *Leptospira biflexa* is saprophytic and nonpathogenic, whereas *Leptospira interrogans* and *Leptospira kirschneri* are among the pathogenic species. More than 250 specific, pathogenic serovars of *L interrogans* have been identified, including those used in current vaccines: canicola, grippotyphosa, icterohaemorrhagiae, and pomona. *L interrogans* has been further classified into antigenically related

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serogroups. Approximately 10 serogroups have been found to cause clinical disease in both dogs and cats.[4] Immunity to *Leptospira* bacteria is serovar specific, but not serogroup specific.

Any serovar within a serogroup can lead to cross-reaction when antibody detection methods are used for diagnosis and serovar identification. Each particular serovar has its preferred host, but this can change over time and geographic location. Preferred hosts include both wild and domestic animals. In nature, serovars are maintained by subclinical infections within wild and domestic reservoirs and domestic hosts.[3,4] These hosts serve as sources of infections and illness for incidental hosts.[4]

EPIDEMIOLOGY

Leptospirosis is believed to be the most widespread zoonotic disease in the world.[1,2,4] Though it can be spread via direct contact, it is most commonly spread via indirect contact with infected urine.[3,4] *Leptospira* spirochetes colonize the brush border of the distal convoluted tubules of the kidney in infected hosts, where they can be intermittently shed into the environment in the urine.[3,4]

Leptospires prefer neutral or slightly alkaline soil and ambient temperatures between 32°F and 77°F (0°C to 25°C).[3,4] Exposure to freezing conditions, dehydration, or ultraviolet radiation markedly decreases their survival time in the environment.[4] Leptospires do not replicate in the environment, even under ideal conditions.[3,4] In aquatic ecosystems, such as stagnant or slow-moving water, they cluster together in colonies and create a biofilm on organic and inorganic objects.[4] There is evidence that leptospires can survive within insects and other invertebrates, although the significance of this fact is not yet known.[4]

Cases of leptospirosis tend to spike in the late summer and fall or, in cooler climates, during rainy winters. Outbreaks tend to follow seasons with abnormally high rainfall or increased flooding.[1,3,4]

Over the past 30 years, the most common antibody reactions have been to serovars other than *L interrogans* canicola and *L interrogans* icterohaemorrhagiae. It is reasonable to assume that vaccination against these serovars has caused their relative decline.[2,3] Other factors may also have led to the emergence of different serovars, such as increased exposure of unnatural hosts (e.g., dogs) in both rural and suburban environments.[1-4]

PATHOGENESIS

Leptospira spirochetes gain access to the host by penetrating intact mucous membranes of the eyes, nose, and mouth or through abraded, scratched, or water-softened skin.[1,3,4] Inside the host, the warm environment inspires transcriptional changes that enhance pathogenicity. Once in the vascular space, the bacteria multiply at an increasing rate. Replication takes place in many tissues, including the kidneys, liver, spleen, central nervous system, eyes, and genital tract,[3,4] and results in leptospiremia.

Though the exact length of time between natural infection and the development of overt illness has not been determined, experimental studies have shown an incubation time of approximately 7 days.[2-4] During incubation, the host produces antibodies and may clear the majority of spirochetes from most organs. Some patients recover completely without treatment and successfully eliminate all bacteria from the body. However, some untreated patients may become persistent carriers and shed the bacteria in their urine.[4] The duration of active shedding has not been determined; it may be dependent on the infecting serovar.[4]

The extent of damage to internal organs is determined by the virulence of the organism and host immunity.[2] Active infection can stimulate neutrophils and platelet activation, which in turn may contribute to inflammatory conditions and coagulation abnormalities. Any pathologic damage that occurs during infection will persist after the infection clears.[4]

In rapid and severe infections, tissue edema and vasculitis may occur.[4] If systemic, endothelial injury and hemorrhagic manifestations such as systemic inflammatory response syndrome (SIRS) associated with sepsis and disseminated intravascular coagulation may result.[3,4] During the acute phase of infection, interstitial nephritis may be noted. Renal inflammation can cause tubular necrosis and hypokalemic, nonoliguric, acute renal injury.[2,4] Acute infections affecting the liver may cause periportal edema, cholestatic hepatitis, and hepatocellular damage.[2,4] Patients with liver involvement suffer from more severe infections and have a higher morbidity and mortality rate.[4]

Infections with the serovars *L interrogans* bratislava and *L interrogans* grippotyphosa have been associated with kidney and liver involvement. *L interrogans* icterohaemorrhagiae and *L interrogans* pomona infections have been implicated with liver involvement. Chronic active hepatitis has been documented as a sequela of infection with *L interrogans* grippotyphosa.

CLINICAL SIGNS

Clinical signs of *Leptospira* infection in dogs vary depending on the patient's age and immunologic status, as well as environmental factors and the virulence of the serovar. Young animals tend to be most severely affected, whereas adult animals that spend a large amount of their time outside and weigh ≥15 kg tend to be more commonly affected. The 2010 ACVIM Small Animal Consensus Statement on Leptospirosis found a correlation between herding dogs and definitive diagnosis.[2]

Infections can be classified as either acute or subacute. Acute infections take hold quickly, generally with an incubation period of >4 days, and have profound consequences. Subacute infections have a longer latency period of 5 to 14 days before clinical signs are seen.

Acute Infection

Dogs suffering from acute leptospirosis can exhibit severe clinical signs. They may be pyrexic (103°F to 104°F [39.5°C to 40.0°C]) and shiver and have muscle tenderness.[4] As the infection progresses, clinical signs tend to become more critical. Protracted vomiting may lead to significant dehydration and even peripheral vascular collapse. If these patients also have coagulopathic deficiencies or vascular injuries, hematemesis, hematochezia, melena, epistaxis, and widespread petechiae may be noted.[2,4] Patients may become tachypneic with rapid and irregular pulses and prolonged capillary refill time. As clinical signs progress, these patients become hypothermic and depressed, and they may succumb to the acute effects of the disease before kidney and/or liver failure has time to develop.[4]

Subacute Infection

Clinical signs of subacute leptospirosis tend to be vague and mild compared with those of acute infection. The most common clinical signs in these patients include vomiting, anorexia, and dehydration.[3,4] Patients may also present with polydipsia and reluctance to move, with possible paraspinal hyperesthesia due to muscular, meningeal, or kidney inflammation.[2,3]

Organ-Specific Clinical Signs

Other clinical signs relate to the organs affected.[2-4]

Weight loss may be due to decreased appetite stemming from visceral inflammation or, in cases of significant azotemia, uremia.[4] These patients can be painful on abdominal palpation.

Respiratory manifestations of leptospirosis can present in a variety of ways. Most commonly, dyspnea and coughing may arise with interstitial pneumonia. Conjunctivitis, rhinitis, and tonsillitis can be seen with

GLOSSARY

Direct Contact Transmission Transmission of disease via physical contact of an infected individual and a susceptible individual

Indirect Contact Transmission Transmission of disease via contact with infective material

Reservoir Host Infected definitive host that can act as a source of infection for other animals

Serogroup Group of serovars that share common antigens

Serovar Distinct variation within a species of bacteria or virus

Clinical signs of subacute leptospirosis tend to be vague and mild compared with those of acute infection. The most common clinical signs in these patients include vomiting, anorexia, and dehydration.[3,4]

respiratory tract involvement.[2] There are European reports of leptospirosis pulmonary hemorrhage syndrome (LPHS).[2] LPHS is characterized by intra-alveolar hemorrhage and edema and can affect both human and canine patients.[2]

Complications due to acute kidney injury (AKI) can be seen in laboratory results (see **DIAGNOSIS**). In these cases, the kidneys may be normal to slightly enlarged on palpation.[3,4] The clinician may elicit pain on palpation as well. As AKI progresses, urine output decreases from normal to oliguria and, in severe cases, anuria.[4] If patients can be supported through the subacute phase of infection, kidney function may return to normal in approximately 2 to 3 weeks.[4] If kidney function does not return to normal, compensated polyuric kidney failure may develop.

Human medical literature has shown pancreatitis to be a sequela of leptospirosis.[2] It is reasonable to use this as an explanation for veterinary patients that continue to suffer from vomiting, diarrhea, and abdominal pain after clinical azotemia has resolved.

Patients that are severely affected by infection may also have cardiac manifestations.[4] Cardiac disturbances can be detected during a thorough physical examination. Auscultation of an irregular heart rhythm can be confirmed with an electrocardiogram and/or echocardiogram. Most arrhythmias tend to be ventricular tachycardias and are believed to be due to myocardial damage.[2]

Uveitis (inflammation of the middle tissue layer of the eye) can be seen with leptospirosis.[2-4]

Leptospirosis has been implicated in spontaneous abortions in horses, cows, and pigs.[3] *L interrogans* batavia has been implicated in spontaneous abortions in dogs.[3]

DIAGNOSIS

Because many of the clinical signs associated with leptospirosis are vague, it is prudent to begin diagnostics by obtaining a minimum database. Results of laboratory tests will elucidate which organs are being targeted by the leptospiral infection.

Physical Examination

Patients should be fully examined not only when they are admitted to the hospital but also at the beginning and end of every shift. In addition to a complete physical examination, careful abdominal palpation in patients with suspected leptospirosis can yield a wealth of information. Gentle palpation may reveal hepatomegaly, renomegaly, and/or splenomegaly, all of which can help guide diagnostics and therapy. Abdominal palpation should be performed during each patient evaluation, as well as when clinical signs change. For example, patients that develop vomiting and diarrhea with scant defecation may have an intussusception, which may be felt during abdominal palpation.

Minimum Database

Complete blood count results may reveal leukocytosis with or without a left shift.[2-4] The degree of leukocytosis depends on the stage and severity of infection.[3] Many patients have a mild nonregenerative anemia that can be attributed to an inflammatory state or decreased erythrocyte production due to kidney failure.[2,3]

Serum biochemistry panel results reveal most patients to be azotemic to varying degrees at the first examination.[2-4] Hypoalbuminemia may be detected and can be attributed to decreased production, proteinuria, or SIRS.[3] Depending on the severity of hypoalbuminemia, hypocalcemia may be noted, caused by serum calcium binding to serum proteins, predominantly albumin. Hyperglobulinemia can be attributed to chronic immune stimulation due to prolonged infection and/or dehydration.[3]

As liver dysfunction progresses to liver failure, hypoglycemia will be noted. The degree of liver damage can be determined by elevations in alanine aminotransferase, aspartate aminotransferase, lactate, and alkaline phosphatase.[2-4] Elevations in amylase and lipase can be attributed to hepatocellular damage and damage to the gastrointestinal cells that line the small intestine.[3] Elevations in creatine kinase can be seen with muscle inflammation and should be self-limiting.[2,4]

Gastrointestinal function and kidney efficiency play a significant role in electrolyte homeostasis. Changes in electrolyte values often correlate to the severity of dysfunction of these systems. Patients with terminal oliguric kidney failure will have marked hyperkalemia on laboratory results.

Urinalysis results tend to be characterized by glucosuria and proteinuria with or without granular casts, and isosthenuria.[2-4] These results can all be attributed to acute renal tubular injury. Other urinalysis results include elevated urine protein:creatinine ratio and the presence of leukocytes. Leptospires cannot be seen in urine without special staining and darkfield microscopy.[2,4]

Imaging

Plain film radiographs can show thoracic abnormalities in patients suffering from respiratory manifestations. Thoracic radiographs of these patients may show interstitial, nodular, or patchy alveolar lung patterns.[2-4] Abdominal radiographs may show hepatomegaly, renomegaly, and splenomegaly.[2-4]

Abdominal ultrasonography may reveal scant free abdominal fluid, most noticeably around the kidneys; renomegaly; pyelectasia; and brightly echogenic kidneys, potentially with a medullary band of echogenicity.[2-4] These findings of "bright kidneys" and a band of brightness are not pathognomonic for leptospirosis, but they help prove that edema of the kidneys is present.[2-4]

Other Tests

Specific and standard tests for leptospirosis include the microscopic agglutination test (MAT), polymerase chain reaction (PCR) testing, darkfield microscopy, indirect immunofluorescence assay (IFA), bacterial culture, and histopathology. The MAT tests for *Leptospira*-specific antibodies, whereas the other tests demonstrate the presence of the organism itself.

Microscopic Agglutination Test

The MAT is the gold standard when testing for leptospirosis.[2,4] For this test, the patient's serum is sent to a referral laboratory, where it is combined with live leptospires. The determination of which serogroups to include depends on the geographic location of the patient. After a specific incubation period, the solution is evaluated using darkfield microscopy. The reported result is the lowest dilution of patient serum and live bacteria in which ≥50% of the organisms remain agglutinated. Agglutination indicates an immune response to *Leptospira* bacteria.

While the MAT is the gold standard test, it has several limitations. Although it can indicate whether a patient has been exposed to a particular serogroup, it cannot identify a specific serovar owing to significant cross-reactivity.[3,4] This test can also have false-positive results in patients that have been vaccinated against leptospirosis within the previous 3 months and false-negative results if the serogroup to which the patient was exposed was not included in testing.[2-4] Patients that are being tested within 7 days of exposure may have not had adequate time to produce sufficient quantities of antibodies, and therefore may also have false-negative results.

To circumvent the limitations of the MAT, paired titer testing is recommended.

Paired Titer Test

To circumvent the limitations of the MAT, paired titer testing is recommended. To perform paired testing, the initial (acute) sample should be gathered on admission to the hospital and the subsequent sample (convalescent) obtained 7 to 14 days later.[3,4] A MAT result showing at least a fourfold increase proves recent infection. However, titer increase may be stunted due to appropriate antibiotic therapy.

Polymerase Chain Reaction Test

In the past several years, testing for leptospirosis has begun to include PCR testing. PCR testing detects and amplifies any bacterial DNA contained within a

When submitting samples for PCR testing, it is advised to submit blood samples if the exposure was within 7 to 10 days and to submit urine samples for exposures outside of this range.[3]

sample, and therefore can be performed on a variety of samples, including blood, tissue, and urine. PCR testing is similar to the MAT in that it cannot differentiate between serovars;[3] however, PCR is not affected by recent vaccination.

When submitting samples for PCR testing, it is advised to submit blood samples if the exposure was within 7 to 10 days and to submit urine samples for exposures outside of this range.[3] While PCR testing is not affected by vaccination status, it can be affected by antibiotic use; therefore, all samples should be submitted prior to the start of treatment.

In-Clinic Tests

Two in-clinic tests are available for leptospirosis: Witness Lepto (**zoetisus.com**) and SNAP Lepto Test (**idexx.com**). Both use the enzyme-linked immunosorbent assay technology.[5,6] The Witness test detects leptospiral antibodies (either IgG or IgM),[6] whereas the SNAP test detects LipL32, a leptospiral-specific lipoprotein.[5] Both tests can be affected by vaccination status as well as insufficient time to mount a response to exposure.[5,6] Despite these shortcomings, they provide the veterinary staff the opportunity to use appropriate personal protective equipment to prevent the spread of this zoonotic disease.

Leptospires are challenging to grow in culture. This fact, coupled with the low sensitivity and frequent false-negative results associated with bacterial culture, means that culture and sensitivity testing is rarely used.[7]

TREATMENT

Treatment for patients with leptospirosis depends on the severity of the infection. Additional considerations are warranted for patients with hepatic or renal involvement.

The mainstay of treatment for leptospirosis is antibiotic therapy. Upon administration, antibiotics immediately inhibit multiplication and replication of the organism, thereby rapidly decreasing the chances of fatal complications. Penicillins, such as penicillin sodium, or aminopenicillins, such as ampicillin, are used during the initial phases of treatment. Once leptospiremia has been cleared, a transition to a tetracycline, such as doxycycline, may ease the treatment burden for the owner.

As patients are being treated with antibiotic therapies, other general treatments should not be halted. Supportive therapy for the complications of leptospirosis, such as dehydration and electrolyte imbalances, should be instituted and maintained as long as the patient's status dictates.

Patients that are nauseous, hyporexic, or vomiting may benefit from antiemetic therapy such as maropitant or ondansetron.

Animals must eat to heal. This includes patients that are in the hospital being treated for leptospirosis. If patients are not willing to eat on their own, they may be enticed to do so. Options to encourage patients to eat include high-calorie commercial therapeutic recovery diets. If these diets are not readily accepted, offer whatever the patient will eat, as it is more important for the patient to eat while hospitalized. The use of appetite stimulants may be considered for patients that are still reluctant to eat. However, it is in the patient's best interest to place a feeding tube as soon as possible.

Patients that have been hyporexic or anorexic for up to 3 days should have a feeding tube placed. Nasogastric (NG) or nasoesophageal (NE) tube placement can be done quickly and with minimal sedation. An alternative to the NG or NE tube is the esophagostomy tube (E-tube). E-tubes can be left in place for a longer period of time than NG or NE tubes, and the patient can be discharged from the hospital with the E-tube in place. The downside of E-tube placement is the need for anesthesia.

BOX 1

Surface Cleaning Agents Effective Against Spirochetes[3]

- Iodine-based disinfectant
- Accelerated hydrogen peroxide
- 1:1 bleach solution

Feeding tubes allow enteral feeding while bypassing the patient's unwillingness to eat. E-tubes can also be used to deliver oral medications.

PREVENTION

In Patients

Vaccines against leptospirosis have been available since the 1970s. The immunity gained from the vaccine is serovar specific, and therefore gives no cross-immunity.[3] The bivalent vaccine provides immunity against the canicola and icterohaemorrhagiae serovars.[1,3] The quadrivalent vaccine covers the canicola, icterohaemorrhagiae, grippotyphosa, and pomona serovars.[3,4] These vaccinations are given initially as a 2-part series with the injections administered 2 to 4 weeks apart. Boosters are given every 6 to 12 months or more frequently, depending on the risk factor of the individual patient.[3,4]

Keeping pets from accessing areas frequented by reservoir hosts and away from areas where confirmed or suspected patients with leptospirosis urinate helps prevent infection or reinfection.[3]

In the hospital, leptospirosis patients should be housed away from other patients, especially those with incompetent immune systems.[3] Ideally, thorough cleaning with an agent that can kill spirochetes should be used anywhere these patients have walked (**BOX 1**).[3] Alternatively, leptospirosis patients can be placed on a gurney during transport through the hospital, which prevents accidental urination in an area that is frequented by veterinary staff or animals.

In Staff

Because leptospirosis is a zoonotic disease, all protective measures should be taken when handling patients, their bedding, and laboratory samples. Cleaning contaminated bedding from leptospirosis patients requires only normal laundering.[3] Despite this, all contaminated laundry should be clearly marked as such to alert all staff to take proper precautions. Contaminated surfaces require cleaning with one of the agents listed in **BOX 1**.

Staff members should wear complete personal protective equipment—gloves, face shields, goggles, and gowns—at all times while handling these patients, as well as cleaning up after them. Staff members who are immunocompromised, pregnant, or trying to become pregnant, or who are not fully trained to deal with patients with zoonotic diseases should be barred from working with leptospirosis patients.

To protect the entire veterinary team as best as possible, a high level of suspicion for leptospirosis should be made clear for all patients presenting with acute kidney injury, acute kidney failure, and acute-on-chronic kidney failure.

In Owners

Zoonotic diseases are quite serious and can pose a great danger to the general public if proper precautions are not taken. Thorough client education should be provided at every instance to ensure the safety of the household. Important topics to discuss include proper hygiene and handwashing techniques, safe handling of inappropriate elimination, and how to launder bedding and blankets effectively. **TVN**

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CONTINUING EDUCATION

Leptospirosis in Dogs

LEARNING OBJECTIVES

After reading this article, the veterinary nurse will understand the causes and diagnosis of leptospirosis, as well as the treatment and supportive care of patients with leptospirosis. When leprospirosis is treated early and aggressively, the chances for recovery are good. The reader will understand the precautionary measures that are taken when handling patients with leptospirosis.

TOPIC OVERVIEW

This article provides an overview of the etiology and pathogenesis of the *Leptospira* bacteria. It also details the clinical signs for dogs with leptospirosis. The article outlines the clinical examinations and tools used in making the diagnosis and how to manage the treatment of patients with leptospirosis. The article examines the protective measures that should be taken by staff and clients.

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1. **Which of the following is a species of *Leptospira*?**
   a. interrogans
   b. icterohaemorrhagiae
   c. canicola
   d. pneumonia

2. **How many pathogenic *Leptospira* serovars have been identified?**
   a. <50
   b. 51–150
   c. 151–200
   d. >250

3. **Leptospirosis is most commonly spread via _____ transmission.**
   a. airborne
   b. direct contact
   c. indirect contact
   d. vector

4. **Patients with acute leptospirosis infections most commonly present with clinical signs that include:**
   a. vomiting, anorexia, dehydration
   b. polyphagia, polydipsia, polyuria
   c. epistaxis, hematemesis, hematochezia
   d. intermittent joint swelling and lameness

5. **Which *Leptospira* serovar has been implicated in spontaneous abortions in dogs?**
   a. icterohaemorrhagiae
   b. canicola
   c. batavia
   d. grippotyphosa

6. **Which of the following is not a common laboratory finding in patients with leptospirosis?**
   a. glucosuria
   b. leukocytosis with or without a left shift
   c. hyperglycemia
   d. azotemia

7. **Which test is the gold standard for diagnosing leptospirosis?**
   a. microscopic agglutination test (MAT)
   b. polymerase chain reaction (PCR)
   c. immunofluorescence assay (IFA)
   d. histopathology

8. **Which of the following treatments is most important for clearing infection with *Leptospira*?**
   a. IV fluids
   b. antibiotics
   c. antiemetics
   d. appetite stimulants

9. **True or false: Leptospirosis is a zoonotic disease.**
   a. True
   b. False

10. **Personal protective equipment that is recommended to be worn while interacting with leptospirosis patients includes:**
    a. gowns
    b. goggles
    c. gloves
    d. all of the above