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Topic Overview

In 2023, the American College of Veterinary Internal Medicine published an updated consensus statement on leptospirosis in dogs. This article provides an update on the diagnosis and management of leptospirosis, including new recommendations for annual vaccination of all dogs for leptospirosis—regardless of age, sex, breed, lifestyle, or geographic location—and refined handling precautions for dogs in which leptospirosis is suspected as a differential diagnosis.

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INFECTIOUS DISEASE

An Update on the Diagnosis and Management of Leptospirosis

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Leptospirosis is a globally important zoonotic disease caused by infection with pathogenic serovars of *Leptospira* spirochete bacteria. Although leptospirosis is widely known as a cause of acute kidney injury (AKI) and liver disease in dogs, affected dogs often have multisystemic illness. Despite the availability of effective vaccines, outbreaks in dogs continue to occur throughout the United States, even in more arid and urban regions.^{1,2} Worldwide, this disease is very common in tropical regions, where warm, humid conditions promote survival of the organism in the environment.

In 2023, the American College of Veterinary Internal Medicine (ACVIM) published an updated consensus statement on leptospirosis in dogs.³ This article provides an update on the diagnosis and management of leptospirosis, including recommendations from the 2023 ACVIM consensus statement.

ENVIRONMENTAL FACTORS

Pathogenic *Leptospira* spirochetes circulate between the environment, reservoir hosts (especially rodents), and incidental hosts, which include dogs and humans. Reservoir hosts are

Learning Objectives

- Leptospirosis is a serious multisystemic disease of dogs and humans caused by virulent strains of the spirochete bacteria *Leptospira*.
- Urinary shedding of pathogenic spirochetes by reservoir hosts contaminates the environment, creating a source of infection for new hosts.
- Although leptospirosis is most often manifested as acute kidney injury with or without evidence of cholestatic hepatopathy, other organs can be involved.
- All dogs can develop leptospirosis, and transmission can result from direct exposure to reservoir hosts.
- Because progression to acute kidney injury can occur within 24 to 48 hours, veterinarians should have a high index of suspicion for leptospirosis and consider early treatment.
- A combination of serologic and PCR tests may be needed for definitive diagnosis.
- Current 4-serovar leptospirosis vaccines are effective, have at least a 12-month duration of immunity, and have a safety profile similar to that of other common vaccines. Vaccination is recommended for all dogs.
- Sick dogs should be treated with 2 weeks of doxycycline or parenteral ampicillin. Early referral to a dialysis facility should be considered.



subclinically infected animals that shed spirochetes continuously or intermittently from their renal tubules, where the organisms form a thick biofilm that shields them from immune detection and may be difficult to eliminate with antimicrobials.⁴ Many animal species can act as reservoir hosts, including mammals and poikilotherms, such as reptiles and amphibians⁵; however, the most important reservoir host species contributing to environmental contamination and disease are rodents, especially Norway rats (*Rattus norvegicus*). Globally, approximately 30% of Norway rats are infected with pathogenic leptospires; in tropical regions where resource-poor communities exist, up to 80% may be infected.⁶ Because reservoir hosts do not have clinical disease, they are not considered to have leptospirosis.³

Under suitable conditions, organisms shed into the environment by reservoir hosts can persist and serve as a source of infection for other reservoir hosts and incidental hosts. Optimal survival conditions for leptospires include humidity, temperatures between 0 °C and 30 °C (32 °F to 86 °F), and waterlogged soil; however, spirochetes can survive outside these conditions and can even survive freezing.⁷ Environmental survival is promoted by the formation of biofilm, which may explain the organism's preference for waterlogged soil,⁸ as well as why outbreaks of leptospirosis are often delayed by several months after heavy rainfall or flooding. The seasonality of the disease varies depending on local climatic conditions, especially

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rainfall.⁹ In areas with year-round rainfall, leptospirosis may occur throughout the year.

With increased flooding associated with climate change and population growth, the incidence of leptospirosis in humans and animals is likely to increase.

CLASSIFICATION

Classification of pathogenic leptospires can be confusing; however, because there are more than 300 pathogenic serovars of *Leptospira* and current vaccines are serovar specific, knowledge of circulating organisms is important.

Pathogenic serovars are grouped into antigenically related serogroups based on their outer lipopolysaccharide antigens. This classification system means that multiple species of *Leptospira* can have the same serovar designation. For example, there is more than 1 serovar of Grippotyphosa (*Leptospira interrogans* serovar Grippotyphosa and *Leptospira kirschneri* serovar Grippotyphosa).^{10,11} Pathogenic leptospires are also grouped as P1 and P2 pathogens, with most disease in humans and animals caused by P1 pathogens, especially *L. interrogans* and *L. kirschneri*.¹⁰ Leptospires can also be classified as sequence types based on genome sequence information.

Although specific serovars and serogroups were previously associated with certain reservoir hosts (such as dogs and *L. interrogans* serovar Canicola), it is increasingly apparent that organisms of the same serogroup can be harbored by multiple reservoir host species.¹²⁻¹⁴ Therefore, a specific reservoir host species cannot be assumed responsible for a leptospirosis outbreak associated with a specific serogroup. Regionally, sequence type associations may be more important.

INFECTION AND CLINICAL DISEASE

Pathogenic leptospires penetrate abraded skin or mucous membranes. Dogs become infected through direct contact with infected urine, ingestion of infected tissues (e.g., predation of rodents or reptiles), or contact with contaminated water or soil.

Once in a host, leptospires multiply rapidly in the bloodstream and tissues. In response, some incidental hosts mount an inflammatory reaction that is responsible for the development of AKI or renal failure,

hepatic injury, and vasculitis. Other organs that can be involved include the pancreas (pancreatitis), gastrointestinal tract (gastroenteritis), eye (uveitis), myocardium (cardiac arrhythmias), and lungs (leptospirosis pulmonary hemorrhage syndrome).³ Clinical manifestations may also depend on the age of the host, host genetic factors, the infectious dose, and the strain of *Leptospira* involved. Serologic surveys suggest that subclinical exposure is widespread and only a small percentage of dogs develop illness after infection.¹⁵

Clinical signs of leptospirosis typically become apparent 2 to 14 days after exposure.³ Pyrexia occurs early in the course of illness and may be rapidly (within 24 to 48 hours) followed by defervescence, with clinical signs of lethargy, anorexia, vomiting, diarrhea, dehydration, abdominal pain, and increased thirst and urination. Reluctance to move (due to myositis) and icterus may also be present. A small percentage of dogs may have ocular complications such as uveitis or petechial retinal hemorrhages.¹⁶ Respiratory distress may result from pulmonary hemorrhage, which can be associated with the development of anemia.¹⁷

Leptospirosis can occur in dogs as young as 11 weeks,^{18,19} in any dog breed, and regardless of geographic location and environment. Dogs in urban regions may be infected following exposure to rodent reservoir hosts, and outbreaks have been described in association with boarding or daycare environments.¹ Over the past decade, diagnosis of leptospirosis in small-breed dogs has increased,²⁰⁻²³ possibly because this population of dogs may remain unvaccinated owing to concerns about adverse reactions to vaccination.

Leptospirosis has also been reported in cats, although they appear to be less susceptible to development of disease than dogs. Cats can act as reservoir hosts, although studies of infection in free-roaming cats have shown a wide variation in the prevalence of seroreactivity and kidney infection.²⁴ In 1 study, only 10% of feral cats from northern California and Texas were seropositive, and no evidence of leptospiruria was detected using PCR assays.²⁵

LABORATORY FINDINGS

In the first 24 to 48 hours of illness, results of a CBC and serum biochemistry panel may be normal or there may be evidence of mild neutrophilia and subtle electrolyte abnormalities. Subsequently, anemia,

leukocytosis due to a neutrophilia with or without increased band neutrophils, monocytosis, lymphopenia, and thrombocytopenia may become apparent on a CBC.³ Serum biochemistry parameters that often emerge are azotemia, hyperphosphatemia, hypoalbuminemia, hyperbilirubinemia, and mild to moderately elevated activities of serum alanine transaminase and alkaline phosphatase. Although hyperkalemia has been reported, normokalemia or hypokalemia are more common due to the effect of *Leptospira* endotoxin on the renal medullary thick ascending limb tubular Na⁺-K⁺-ATPase.²⁶

Hepatopathy is cholestatic, and evidence of liver failure (e.g., hypoglycemia, hypocholesterolemia, markedly increased liver enzyme activities) is not typically present. Hepatopathy in the absence of renal failure is rare but has been described in some cases.²⁷

Urinalysis may reveal signs of tubular injury (e.g., isosthenuria, proteinuria, glucosuria, casts). The presence of glucosuria in the absence of hyperglycemia should always raise suspicion for leptospirosis, especially in unvaccinated dogs. Organisms are generally not visible in the urine sediment using routine light microscopy.

IMAGING FINDINGS

Thoracic radiography may reveal a focal, nodular, or diffuse interstitial to bronchointerstitial pattern; patterns may represent pulmonary hemorrhage.³ Occasionally, mild pleural effusion is evident. Because dogs may have radiographic evidence of pulmonary hemorrhage in the absence of respiratory signs, thoracic radiography is recommended for all dogs suspected to have leptospirosis; detection of abnormalities can help raise suspicion for a diagnosis of leptospirosis and guide judicious intravenous fluid therapy to prevent fluid overload with associated pulmonary edema.³

Hepatomegaly, splenomegaly, renomegaly, and/or peritoneal effusion may be evident from abdominal radiography. Hyperechoic renal cortices and mild renal pelvis dilation are occasionally seen with abdominal ultrasonography.³

SPECIFIC DIAGNOSIS

Identification of leptospirosis requires a high degree of clinical suspicion for the disease based on knowledge of the range of possible clinical presentations. Although

TABLE 1 Case Definition for Diagnosis of Leptospirosis in Dogs³

CLINICAL CRITERIA	LABORATORY CRITERIA
Onset of systemic illness within the last 2 weeks, +/- - Gastrointestinal signs - Pulmonary signs - Ocular signs - Oliguria/anuria - Icterus - Hemorrhage AND Two or more of the following: - Neutrophilic leukocytosis, +/- left shift - Thrombocytopenia - Biochemical evidence of acute kidney injury - Biochemical evidence of cholestatic hepatopathy - Biochemical evidence of pancreatitis - Increased creatine kinase - Glucosuria despite normoglycemia - Active urine sediment - Radiographic findings consistent with leptospirosis pulmonary hemorrhage syndrome - Consistent abdominal ultrasonographic findings - Cardiac arrhythmias on electrocardiography or increased serum troponin	Supportive: <i>Leptospira</i> MAT titer of $\geq 1:800$ in 1 or more serum specimens - Detection of IgM antibodies against <i>Leptospira</i> in an acute serum sample - Detection of pathogenic leptospires in urine using a NAAT - Visualization of spirochetes in blood or urine using darkfield microscopy by a <i>Leptospira</i> reference laboratory Confirmatory: - Fourfold or greater increase in <i>Leptospira</i> MAT titer at a single laboratory between acute- and convalescent-phase serum samples - Detection of pathogenic leptospires in blood using a NAAT - Isolation of <i>Leptospira</i> from a clinical specimen by a <i>Leptospira</i> reference laboratory

IgM=immunoglobulin M; MAT=microscopic agglutination test; NAAT=nucleic acid amplification test

leptospirosis has occasionally been documented in dogs vaccinated with 4-serovar vaccines,²⁸ affected dogs are more likely to be unvaccinated, years overdue for vaccination, or vaccinated with 2-serovar vaccines. Thus, other diagnoses are more likely in vaccinated dogs.

Because leptospirosis is an acute illness, the case definition developed by the ACVIM consensus panel for leptospirosis in dogs requires onset of illness within the past 2 weeks (**TABLE 1**).³ Dogs with signs such as chronic polyuria/polydipsia or chronic lethargy do not fall within the case definition and are not likely to have active infection with a pathogenic *Leptospira* species.

Currently available specific diagnostic tests for diagnosis of leptospirosis in North America include the microscopic agglutination test (MAT), in-clinic serologic assays that detect immunoglobulin G (IgG) (SNAP Lepto; IDEXX, idexx.com) or immunoglobulin M (IgM) (WITNESS Lepto; Zoetis, zoetisus.com), and nucleic acid amplification tests (usually PCR-based assays).^{3,29} Examination of urine specimens using darkfield microscopy can also be used for diagnosis, but this technique requires expertise and a darkfield microscope and lacks sensitivity. Growth of leptospires in culture requires expertise and special media and may require several weeks of incubation. Use of multiple types of media and inoculation of media patient-side may increase the chance of successful isolation, but culture is mostly used as a research tool.

Microscopic Agglutination Test

The reference standard test for diagnosis of leptospirosis is seroconversion using the MAT.²⁹ In the MAT, serial twofold dilutions of patient serum are reacted with a battery of live pathogenic leptospiral serovars. The serum dilution that causes 50% of spirochetes to agglutinate using darkfield microscopy is reported to the clinician as the titer to the respective serovar tested. Multiple serovars are included to increase the chance of antibody detection to any single serovar. Most veterinary diagnostic laboratories that perform the MAT offer a panel of 6 or 7 different serovars.³⁰

The serovar with the highest titer is not necessarily the serovar causing infection. This is due to: (1) paradoxical serologic cross-reactivity, in which noninfecting serovars used in the panel are associated with higher titers than the infecting serovar; (2) the possibility that the infecting serovar is not in the panel, and all positive titers represent cross-reactions to noninfecting serovars; and (3) the possibility that even higher titers could be observed should another serovar be added to the panel.³

Titers are often negative in the first week of illness due to the short incubation period and delay in antibody production. Low-positive or negative titers after at least 1 week of illness make leptospirosis less likely. Positive titers early in the course of an illness may reflect previous subclinical infection (or vaccination for

leptospirosis, should a vaccinated dog be tested) and are not diagnostic. Demonstration of a fourfold rise in titer is required over a 1- to 2-week interval.³ The results can also vary among laboratories; therefore, the same laboratory should be used for acute and convalescent testing.

In-Clinic Serologic Assays

In-clinic serologic assays yield qualitative (positive or negative) results and are useful for rapid assessment for the presence or absence of antibodies.³¹ Importantly, because these are antibody tests, a positive result does not imply infection and a negative result does not rule out infection. Should these kits yield negative results, the clinician should consider whether it may be too early for the animal to have developed antibodies (as can occur with the MAT). A second test can be performed 1 week later to see if the animal seroconverts.

The SNAP Lepto assay detects IgG; therefore, it may provide positive results in dogs with previous subclinical exposure or dogs that have been vaccinated for leptospirosis. For example, a leptospirosis-vaccinated dog with AKI secondary to ibuprofen toxicity may have a positive SNAP Lepto test result.

The WITNESS Lepto test detects IgM, and studies performed to date suggest that positive results with this assay strongly support a diagnosis of leptospirosis in dogs not recently vaccinated for leptospirosis with consistent clinical signs (specificity > 97%).^{32,33} Clinicians should consider reflex testing with the MAT to obtain a quantitative titer if positive results are obtained with in-clinic serologic tests, followed by convalescent serology 1 to 2 weeks later to document a change in titer.³

PCR Assays

Increasingly, PCR is being recognized as a promising tool for diagnosis of leptospirosis, especially in the first week of illness when antibody tests yield weak positive or negative results and antimicrobials have not yet been administered. However, sensitivity and specificity may vary geographically depending on the serovars present and their shedding patterns. Current assays may not detect some strains of *Leptospira* (such as those belonging to the P2 pathogens). Sensitivity may also be higher very early in the course of illness and in dogs that have not received any treatment with antimicrobials.

Because organisms are present in the blood in the first week of illness before appearing in the urine, both blood and urine specimens should be submitted to increase the chance of a positive result. Negative results do not rule out leptospirosis because organisms can be shed intermittently and in very low numbers. Positive results have been detected in the urine of some healthy dogs, especially those that are free-roaming, from kennels, or in shelters (acting as reservoir hosts).

TREATMENT

Left untreated, progression to irreversible renal failure can occur within days; therefore, treatment is indicated pending the results of specific diagnostic testing. Antimicrobials recommended for specific treatment of leptospirosis in dogs are intravenous penicillin derivatives or doxycycline. Doxycycline is the first choice, based on research using a hamster model of infection that showed doxycycline to be most effective for eliminating organisms from the renal tubules.³⁴ However, other evidence to support this choice in dogs is lacking.

If parenteral doxycycline is not available or vomiting precludes administration of oral doxycycline, ampicillin is recommended (20 mg/kg IV q6h to q8h, adjusting dose down if severe azotemia is present) until vomiting has resolved.³ As soon as tolerated, a 2-week course of doxycycline (5 mg/kg PO q12h) should be administered, irrespective of the number of days the pet has previously received other antibiotics.

Supportive therapy is also indicated for organ dysfunction (e.g., IV fluids, proton pump inhibitors, antihypertensives, antiemetics, phosphate binders, packed red blood cells). Early enteral nutrition with a highly digestible, normal- to high-protein diet is indicated.³ In general, kidney diets are not appropriate for dogs with leptospirosis as they tend to be high in fat, which has the potential to exacerbate gastroenteritis or pancreatitis. If hydration has been properly addressed through fluid therapy and there is persistent anuria or oliguria, progressive azotemia, and evidence of overhydration, early referral for continuous renal replacement therapy may be the difference between complete recovery and death due to renal failure.³

PREVENTION

Because all dogs are at risk of leptospirosis—regardless of age, breed, sex, geographic location, lifestyle, or time



of year—and because current 4-serovar vaccines have been shown to be safe and efficacious, the ACVIM consensus statement recommends that all dogs be vaccinated for leptospirosis.³ Because the duration of immunity for leptospirosis vaccines requires them to be administered annually, this represents a significant shift from current practices of vaccinating dogs every 3 years with core vaccines. Veterinarians should recommend that all dogs return for vaccination with leptospirosis vaccines annually; the distemper-adenovirus-parvovirus-parainfluenza (DAPP) combination vaccine should continue to be administered every 3 years according to guidelines from the AAHA and WSAVA.^{23,35} The ACVIM consensus panel also recommends that boarding and daycare environments require vaccination for leptospirosis and that vaccination protocols in shelters include leptospirosis vaccines.³

Historically, bacterin vaccines were associated with a higher rate of adverse effects than attenuated live vaccines; however, recent studies suggest that owing to new vaccine technology, currently available leptospirosis vaccines have an adverse effect profile similar to that of the DAPP combination vaccine, even in small-breed dogs.³⁶ In North America, vaccines that contain serovars Canicola, Icterohaemorrhagiae, Pomona, and Grippotyphosa are in widespread use. The vaccines are generally safe and efficacious, and studies suggest they provide a minimum of 1 year of immunity.³⁷⁻³⁹ Vaccination of dogs with 4-serovar vaccines has been associated with reduction in the prevalence of disease in dogs worldwide,⁴⁰ although disease can still occasionally occur in vaccinated dogs (usually caused by serovars that are not included in the vaccine).

Vaccination against pathogenic leptospires is strongly recommended even for small-breed dogs that live in urban areas as infection can follow direct or indirect exposure to rodents. Control of rodent exposure and minimizing access to livestock and wildlife can also prevent infection.

PUBLIC HEALTH RISK

Leptospirosis represents a quintessential One Health problem due to the circulation of pathogenic spirochetes between the environment, reservoir hosts, and incidental hosts. Although most documented cases of human leptospirosis in North America result from recreational activities that involve water (rather than

contact with diseased dogs), leptospirosis remains an important zoonosis. Rare reports of leptospirosis in humans following exposure to infected dogs exist,⁴¹ but unambiguous proof of transmission has been lacking, and prospective investigations of human disease in circumstances where exposure to diseased dogs is likely have failed to reveal any evidence of human infection or disease.^{42,43} Human leptospirosis is typically a “flu-like illness” but in some cases may be associated with vomiting, diarrhea, shock, jaundice, renal failure, pneumonia, meningitis, or abortion.

Any animal with acute renal failure should be treated as a suspected leptospirosis patient. Warnings should be placed on cages, gloves should be worn while handling presumably or definitively infected dogs, and a disinfectant should be used to clean areas soiled with urine. Owners should be warned that, without specific treatment, leptospires may be shed in the urine for months despite clinical recovery. Contact precautions can be lifted after 48 hours of specific antimicrobial therapy.³ One modeling study demonstrated that where populations of humans, rodents, and domestic/stray dogs intermingle, vaccination of dogs may reduce risk of human infection from rodents.⁴⁴

SUMMARY

Leptospirosis is a disease that threatens the health of companion dogs in both urban and rural areas worldwide. Pathogenic leptospires circulate between reservoir hosts, especially rodents, and the environment. Exposure of incidental hosts leads to multisystemic disease, especially manifested by evidence of AKI. Many different serovars, defined by their outer lipopolysaccharide antigens, can cause disease in dogs, and outbreaks continue to occur in dogs despite the widespread availability of effective vaccines. Recent outbreaks have been associated with boarding kennel environments. Diagnosis of leptospirosis relies on use of a combination of PCR and acute and convalescent serologic testing. Current vaccines provide serovar-specific protection; however, leptospirosis is rarely reported in dogs that have been vaccinated with 4-serovar vaccines. Because all dogs are at risk of leptospirosis—regardless of age, breed, sex, geographic location, lifestyle, or time of year—and because current 4-serovar vaccines have been shown to be safe and efficacious, it is recommended that all dogs be vaccinated annually for leptospirosis. **TVP**



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CE QUIZ QUESTIONS

1. Which of the following reservoir hosts is considered the most important for maintenance of pathogenic leptospires worldwide?
 - a. Cattle
 - b. Dogs
 - c. Rats
 - d. Mice
 - e. Horses
2. Which antimicrobial treatment approach is preferred (if tolerated) for sick dogs with leptospirosis?
 - a. Ampicillin 22 mg/kg IV q6h, transitioning to oral doxycycline for 2 weeks when vomiting stops
 - b. Doxycycline 5 mg/kg IV or PO q12h for a total of 2 weeks
 - c. Doxycycline 5 mg/kg IV or PO q12h for 4 weeks
 - d. Enrofloxacin 5 mg/kg IV or PO q24h for 2 weeks
 - e. Clindamycin 10 mg/kg IV q8h, transitioning to oral doxycycline for 2 weeks when vomiting stops
3. Which of the following statements about vaccination for leptospirosis is false?
 - a. Newer leptospirosis vaccines provide protection regardless of the identity of circulating serovars.
 - b. All dogs should be vaccinated annually for leptospirosis, regardless of age, breed, sex, lifestyle, or geographic location.
 - c. Leptospirosis vaccination should be commenced in puppies as soon as label recommendations permit.
 - d. Current leptospirosis vaccination should be required for boarding/daycare admission.
 - e. Current leptospirosis vaccines appear to protect dogs from disease and have adverse reaction rates similar to those of distemper-adenovirus-parvovirus-parainfluenza vaccines.
4. Which of the following clinical findings, when present in association with biochemical evidence of acute kidney injury, should raise suspicion for leptospirosis?
 - a. Thrombocytopenia
 - b. Ultrasonographic evidence of pancreatitis
 - c. Glucosuria in the absence of hyperglycemia
 - d. Increased activity of serum creatine kinase
 - e. Any of the above
5. For how long should contact handling precautions be adhered to in a dog with suspected leptospirosis?
 - a. Until an alternative diagnosis has been identified or leptospirosis has been ruled out
 - b. Until appropriate antimicrobials have been administered for 48 hours
 - c. Until appropriate antimicrobials have been administered for 72 hours
 - d. Precautions are no longer recommended because dogs with leptospirosis are unlikely to transmit infection to humans