



(Still) an Emerging Infection?

CANINE LEPTOSPIROSIS

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In the United States, outbreaks of leptospirosis among dogs appear rare. The relatively low incidence of cases seen in private practice and lack of a rapid, point-of-care diagnostic test compromise the clinician's ability to define exposure risk and need for routine vaccination among individual animals.

However, studies have highlighted the occurrence of leptospirosis infections and/or exposure with some degree of regularity within many regions of the U.S. and parts of Canada;¹⁻⁶ a number of papers published between 1996 and 2011 highlight that leptospirosis in dogs is *emerging* in the U.S. Considering that canine leptospirosis was first identified in 1899 and has been described in the U.S. for over 100 years, one might ask whether or not canine leptospirosis has, in fact, *arrived*.⁷

RISK ASSESSMENT

Leptospirosis has been referred to as the most widespread zoonotic disease in the world, with infection occurring in numerous species, including dogs. However, assessing risk among individual dogs remains difficult: incidence data on canine leptospirosis is lacking and, in the U.S., mandatory reporting of confirmed cases of human leptospirosis was discontinued in 1994.

Publications citing exposure risk in dogs highlight that approximately 10, of over 200, pathogenic serovars of leptospirosis are capable of infecting dogs worldwide.

- Significant *increases* of canine leptospirosis serovars **Grippityphosa**, **Pomona**, and **Bratislava** have been reported since the early 1990s.^{1,6,8}
- Infections caused by *Leptospira interrogans* serovars **Canicola** and **Icterohaemorrhagiae** have significantly *decreased*; this decline is largely attributed to routine vaccination.

Early reports (before 2000) identified several factors associated with increased risk for canine leptospirosis, and another study identified types of dogs that had significantly increased risk for

Leptospira infection.^{1,3,9} It was *previously believed* that risk was greatest for:

- Dogs > 2 years of age
- Those living in rural, recently urbanized, or wetland (rainfall > 40 inches/year) areas; on farms; or near streams
- Herding, working dogs, and hounds.

However, our understanding of the conventional risk factors for leptospirosis has changed. A 2014 study—in which prevalence and signalment factors for canine leptospirosis were reviewed in 10-year increments—highlights changes that have taken place over the past 40 years, including increased documentation of confirmed infections diagnosed at university teaching hospitals (since the 1990s), with *higher prevalence* in dogs.¹⁰

- Less than 15 pounds body weight
- From the terrier group.

Risk factors that do *not* appear to have changed significantly include:¹⁰

- Dogs > 2 years of age at higher risk for infection than those < 1 year of age
- Increased risk for exposure to wildlife reservoir hosts, likely due to urbanization
- Exposure to standing, contaminated water increases risk for infection.

In contrast to previous reports, the seasonality of canine leptospirosis in the U.S. is not uniform.¹ The highest seropositive rates are reported to occur in the midwestern and northeastern regions of the U.S. from October through December. On the other hand, higher monthly seropositive rates occurred earlier in the calendar year in the south central states (May) and in the southern west coast of California (February).

CLINICAL PRESENTATION

In practice, laboratory testing is the key component to definitively diagnosing leptospirosis. However, the decision whether to treat a dog is typically based on a presumptive diagnosis of leptospirosis following assessment of the patient's history and clinical signs.

In reviewing numerous publications,

it is consistently noted that leptospirosis:

- Is a spirochetal bacterial infection
- Is zoonotic, infecting humans and many species of animals
- Has worldwide distribution
- Is emerging or, at least, re-emerging.

TABLE 1.

Acute Leptospirosis: Clinical Signs & Diagnostic Results by Body System

BODY SYSTEM	CLINICAL SIGNS	DIAGNOSTIC RESULTS
Gastrointestinal	Diarrhea Hematemesis Hematochezia Melena Vomiting	
Hematologic	Epistaxis Hematemesis Hematochezia Melena Petechia (mucous membranes, skin)	Anemia Coagulopathy Leukocytosis Thrombocytopenia
Hepatic	Icterus Lethargy Pyrexia	Bilirubinuria Elevated bile acids Hyperbilirubinemia Hyperglobulinemia Hypoalbuminemia Increased liver enzymes
Renal	Anuria Lethargy Oliguria Pyrexia	Glycosuria Granular casts in urine sediment Increased blood urea nitrogen Increased creatinine Urine specific gravity < 1.029

The Diagnostic Results listed for the hepatic and renal body systems typically support **hepatic failure and renal failure**, respectively.

Acute Leptospirosis

The acutely ill patient is typically febrile (39.5°C–40°C; 103.1°F–104°F), lethargic, and may have a history of vomiting and/or diarrhea. Characteristic clinical findings typically support acute-onset renal or, less commonly, hepatic disease (**Table 1**). The spectrum of clinical signs, however, can vary significantly and affect multiple body systems.¹¹⁻¹³ Sudden-onset icterus and/or anuria or oliguria (urine production < 2 mL/kg/H after rehydration) are important findings that support a diagnosis of leptospirosis.

Subacute Leptospirosis

Dogs may also present with more subtle clinical findings consistent with subacute leptospirosis. Signs are variable and may be limited to decreased appetite, diarrhea, lethargy, polydipsia, and vomiting.

Clinicopathologic evidence of renal and/or hepatic failure may be lacking.

Other Clinical Findings

Gastrointestinal. Intestinal intussusception associated with acute enteritis has been reported in dogs with leptospirosis. Pain on abdominal palpation is occasionally reported but the cause is less clearly defined. Pancreatitis and/or acute enteritis may be responsible.

Respiratory. In one study, 35 dogs with leptospirosis presented with severe dyspnea and cough.¹⁴

- Those that presented with severe dyspnea had a significantly greater likelihood of dying from lung injury or euthanasia.
- Radiographic findings included generalized reticulonodular interstitial lung disease and patchy alveolar consolidation.
- Necropsy results revealed acute alveolar and subpleural hemorrhage, but not pneumonia.

Ophthalmic. Uveitis and bulbar conjunctivitis are common clinical manifestations described in humans and horses^{15,16} with leptospirosis but have only occasionally been reported in dogs. The pathogenesis of ocular signs associated with leptospirosis has not been defined but may reflect the fact that the eyes are a portal of entry for spirochete transmission.

Age. While leptospirosis is most commonly diagnosed in dogs > 2 years of age, young dogs with leptospirosis may manifest significantly more severe signs compared with adult dogs.

DIAGNOSTIC TESTING**Microscopic Agglutination Test**

Diagnostic confirmation of leptospirosis is problematic in the clinical setting. The most commonly performed, often-called *standard*, laboratory assay for diagnosis is the microscopic agglutination test (MAT). This serologic test measures antibody (usually IgM) and is intended to provide information on the infecting serogroup.

While reasonably suited for epidemiologic studies, the MAT has significant limitations in practice.

- Patient serum must be sent to a laboratory capable of performing the assay.¹³
- Diagnosis of leptospirosis should be based on results of 2 samples: acute and convalescent—samples are collected 7 to 14 days apart and results must demonstrate a 4-fold or greater increase in the titer to establish positivity.
- Interpreting results based on single-sample testing may be complicated (**Table 2**).

Not surprisingly, pursuing MAT results is somewhat impractical when faced with acutely ill patients in need of immediate treatment. Additionally, establishing the infecting serogroup by MAT results may not be as reliable as once thought: cross-reactivity (molecular mimicry) within the MAT appears to be at least one reason dogs may have “positive” test results for one or more serogroups *not* found in the U.S. (eg, Autumnalis).

Polymerase Chain Reaction

The introduction of polymerase chain reaction (PCR) testing for leptospiral DNA in both blood and urine has some advantages over the MAT (**Table 2**):

- Because the timing of the initial exposure and infection is difficult to determine, simultaneous testing of both blood (reflecting early stage infection) and urine (reflecting a late stage or chronic infection) may enhance diagnostic sensitivity.^{13,17}
- Vaccination does not cause false-positive test results. However:
- Samples must be sent to a laboratory capable of performing PCR.

TABLE 2.
Diagnostic Tests Available to Detect Leptospirosis

TEST	MEASUREMENT	PATIENT SAMPLE ^a	SENSITIVITY & SPECIFICITY
Microscopic Agglutination Test	Antibodies, usually IgM, to infecting <i>Leptospira</i> serogroup	Serum, 2 samples collected 7–14 days apart	<ul style="list-style-type: none"> • <i>False-negative results</i> may occur in acutely infected dogs or due to antibiotic therapy¹³ • <i>False-positive results</i> may occur due to recent leptospirosis vaccination¹³ or cross-reactivity between serogroups
Polymerase Chain Reaction	<i>Leptospira</i> DNA; does not identify infecting <i>Leptospira</i> serogroup	Whole blood, ^b 0.5–2 mL ^c Urine, 2 mL	<ul style="list-style-type: none"> • Not affected by leptospirosis vaccination • <i>False-negative results</i> may occur due to antibiotic therapy
Enzyme-Linked Immunosorbent Assay ^d	Antibodies against LipL32 ^e	Serum, 1 mL	<ul style="list-style-type: none"> • <i>False-positive results</i> may occur due to recent leptospirosis vaccination

a. Always consult individual laboratories before submitting samples to ensure proper sample volume and handling requirements are met.
 b. EDTA, heparinized, or citrated sample; requirements differ based on manufacturer guidelines
 c. Amount required based on manufacturer guidelines
 d. *Leptospira* spp. Antibody by ELISA—Canine (idexx.com)
 e. LipL32 = lipoprotein in outer membrane of pathogenic leptospires

TABLE 3.
Therapeutic Approach to Dogs Infected with *Leptospira*

PATIENT	THERAPEUTIC APPROACH
Severely Affected Dogs	<ul style="list-style-type: none"> • Thorough hematologic and biochemical assessment • In-patient intensive care • Strict adherence to infection control procedures¹²
Dogs with Acute Renal or Hepatic Failure	<ul style="list-style-type: none"> • Intravenous fluid replacement • Indwelling urinary catheter to monitor urine output and collect potentially infectious fluid • Antibiotic therapy
Dogs That Are: <ul style="list-style-type: none"> • Anemic • Profoundly hypoalbuminemic 	<ul style="list-style-type: none"> • Administration of plasma, packed red blood cells, or whole blood

- Antibiotic therapy initiated before sample collection can result in false-negative test results.
- PCR assays do not identify the infecting serogroup.

Antibody by ELISA

In April 2014, a commercial test became available that detects antibodies for a prevalent lipoprotein (LipL32) found in the outer membrane of pathogenic leptospires (Table 2).

- While samples (serum) must be sent to a regional laboratory, enzyme-linked immunosorbent assay (ELISA) is performed daily.
- Results are typically available within 2 to 3 days after sample submission.

- In some dogs, however, recent vaccination may result in false-positive tests.

ELISA technology is commonly used as a point-of-care test in dogs and cats, suggesting that an in-clinic test platform may be available in the near future—availability of a rapid *Leptospira* assay for in-practice use would significantly benefit the profession.

MANAGING INFECTED PATIENTS

Managing any patient known, or suspected, to have leptospirosis is complex. The clinician can be confronted with not only a critically ill patient, but one that is shedding bacteria capable of infecting humans. All individuals involved with handling and treating the patient, including the owner and family, are potentially at risk for exposure.

Table 3 outlines therapeutic

approaches to infected patients.

Diuretic Therapy

Diuretic therapy is essential if evidence of oliguric or anuric renal failure develops and persists after the patient has been adequately resuscitated with IV fluids and maintains normal blood pressure (Table 4, page 90). Intravenous administration of an osmotic diuretic is indicated initially; if this treatment fails, low-dose dopamine is appropriate. Concurrent, parenteral administration of furosemide may be also indicated, if needed to promote urine output.

Antibiotic Therapy

Today, most authors recommend doxycycline as the antimicrobial of choice for treatment of leptospirosis in dogs (Table 4, page 90) because it has been shown to rapidly eliminate leptospires from the kidney in experimental infections in dogs.

Options for dogs unable to tolerate doxycycline include (Table 4, page 90):

- Parenteral ampicillin (for dogs unable to tolerate oral medication)
- Oral azithromycin (for dogs that are not vomiting and able to eat).

Duration of treatment in patients with a positive initial response to therapy is generally 2 to 3 weeks. Treatment durations beyond 3 weeks are based on assessment of the individual patient. Use of aminoglycosides is contraindicated, particularly in dogs with concurrent renal impairment.

Prognosis

Renal and hepatic parameters should be monitored when attempting to establish a prognosis. Survival rates of up to 80%

Guidelines to Minimizing Transmission Risk

Public health considerations are primary when managing a dog with leptospirosis, even if the infection is only suspected.

Guidelines for minimizing risk for transmission to humans have recently been reviewed and should be strictly adhered to throughout course of treatment;¹³ at a minimum, follow these recommendations:

1. Minimize patient movement in the hospital.
2. Regularly disinfect the area around patient; a solution of household bleach and water (1:9) is effective for both in-clinic and in-home use.
3. Use floor-level housing, if possible, throughout the treatment period.
4. Minimize number of individuals who handle the affected dog.
5. Create a log-in chart that records the individual treating/handling of the patient and time/date of contact, as part of the medical record.
6. Wear protective clothing, including disposable gloves,

gowns, and masks, whenever treatments are administered and the dog is fed or handled.

7. An indwelling urinary catheter should be used whenever possible to facilitate collection of urine and avoid contamination inside the hospital.
8. Clearly label all samples submitted to a commercial laboratory with a warning for those who will handle tissue, blood, or urine from the patient.
9. Handle all bedding, dishware, and shaved hair as potentially contaminated medical waste.

Dogs discharged from the hospital with oral medication represent a small risk for transmission of spirochetes to humans. Advise owners to:

1. Wear disposable gloves when treating the dog, such as when administering oral medication
2. Clean areas contaminated with urine until the treatment period has been completed.

in dogs are cited, even in patients with renal disease that do not receive dialysis. However, prognosis is significantly worse for dogs that develop pulmonary disease.

PREVENTION & VACCINATION

While vaccination against leptospirosis may be the cornerstone of prevention, dog owners should be aware of measures to mitigate risk for exposure in regions where canine infections have been documented:

- Do not feed pets, including cats, outside because food attracts wildlife that serve as reservoirs for leptospirosis (eg, raccoons)
- Discourage pets, when feasible, from drinking from pools of standing ground water
- Vaccinate all dogs, regardless of breed, likely to swim in lakes/ponds or have contact with wildlife against leptospirosis.

Leptospirosis Vaccination

Leptospirosis vaccination is recommended as a noncore (optional) vaccine.¹⁸ The decision to recommend vaccination should be based on reasonable knowledge of geographic risk, lifestyle factors, and signalment of the individual dog.

Vaccination Against Serovars. With little exception, vaccine serovars are unlikely to provide cross-protection. For this reason, veterinarians recommending leptospirosis vaccination should only administer a 4-way vaccine that includes serogroups Canicola, Icterohaemorrhagiae, Grippotyphosa, and Pomona.^{13,18}

Although still available at this writing, bivalent leptospirosis vaccines, including serogroups Canicola and Icterohaemorrhagiae, are *not* recommended because they are unlikely to induce protective immunity against other infecting serovars.

Note that dogs that receive a 4-way vaccine can still develop leptospirosis. These vaccines do not provide protection against other infecting serovars, such as Bratislava, which have been identified in the U.S. and confirmed in canine infections.

Administration. When administering leptospirosis vaccine to dogs, 2 initial doses, 2 to 4 weeks apart, are required to immunize. Do not administer the first of the initial 2 doses before 12 weeks of age because maternally derived antibody can interfere with this dose.¹⁸

TABLE 4.

Drugs Commonly Used in Treatment of Leptospirosis

DRUG	DOSAGE
Diuresis for Renal Failure	
10% to 20% Glucose ^a	5 mL/kg IV administered over 30–60 min
Mannitol (20%)	0.5–1 g/kg IV bolus administered slowly
Dopamine	2.5–5 mcg/kg/min IV CRI
Furosemide (2 options)	0.5–2 mg/kg IV bolus, followed by 0.2–2 mg/kg/H IV CRI
	2 mg/kg IV bolus: <ul style="list-style-type: none"> • If diuresis begins within 30 min, repeat as needed • If initial dose does not result in diuresis, may increase dose to 4–6 mg/kg IV at hourly intervals
Antibiotics for Leptospire	
Doxycycline	5 mg/kg IV or PO Q 12 H for 2–3 weeks ^b
Ampicillin	20 mg/kg IV Q 6 H
Azithromycin	5 mg/kg PO Q 24 H

a. Due to hyperosmolality, ideally through a central venous catheter

b. Longer treatment periods likely required for severely infected dogs

Despite earlier recommendations that leptospirosis vaccine should be administered to dogs at 6-month intervals, current recommendations stipulate that dogs be revaccinated annually as long as the risk for exposure is sustained.

Duration of Immunity. Product detail sheets of individual leptospirosis vaccines should be reviewed for data pertaining to duration of immunity (1 year or longer) and claims citing the extent to which the vaccine has been shown to prevent infection and shedding.

It should also be noted that postvaccination antibody titers are not a reliable index of immunity. Vaccine-induced *Leptospira* titers characteristically decline to “negative” levels within 3 to 4 months postvaccination in dogs, yet challenge studies reflect that most vaccines provide protection for 1 year.^{13,19}

Vaccine Reactions

Anecdotal concerns expressed by practicing veterinarians cite a high incidence of acute (within hours), postvaccinal adverse reactions, particularly angioedema involving the ears and muzzle. While it is likely that acute vaccine-associated adverse reactions are predominantly associated with inactivated (killed) vaccines, the sensitizing proteins causing acute type-1 hypersensitivity reactions are unknown.

It has also been cited that acute-onset adverse reactions are more likely to occur in small breed dogs < 10 kg in body weight, especially when multiple vaccines are administered at the same appointment.¹⁸ However, the practice of arbitrarily reducing vaccine volume (ie, administering 0.5 mL of a 1-mL dose) when inoculating small dogs is strongly discouraged. Doing so may result in failure of adequate immunization.

IN SUMMARY

The emergence of infecting serovars Grippityphosa and Pomona within North America highlights the infection risk for leptospirosis and justifies use of a multivalent (4-way) vaccine in dogs at risk for exposure.

The challenge for veterinarians is determining which individual dogs should be vaccinated based on reasonable risk for exposure, which is especially important considering that risk factors appear to be changing and potentially putting a larger portion of pet dogs at risk. Infection risk appears to be significantly higher among small dogs (< 15 kg) and terrier breeds, which strongly argues against the decision to avoid vaccination.

ELISA = enzyme-linked immunosorbent assay; MAT = microscopic agglutination test; PCR = polymerase chain reaction

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Leptospirosis in Cats

Reported seropositivity rate for leptospirosis in cats is typically less than 10%.¹² Clinical disease associated with leptospirosis in cats appears to be rare, suggesting that cats may be naturally more resistant to clinical manifestations following infection. However, a recent study finds that *Leptospira* seropositivity, based on PCR testing, was significantly higher in cats with kidney disease compared with healthy cats.²⁰ Results suggest that cats are not only susceptible to infection and intermittent urinary shedding (for months), but leptospirosis infection may represent an underdiagnosed cause of feline kidney disease.²⁰



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