Article #2

CE

Canine Leptospirosis: Treatment, Prevention, and Zoonosis*

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ABSTRACT:

Treatment of canine leptospirosis has traditionally consisted of a combination of fluid diuresis, antibiotic therapy, and supportive care. However, dogs with renal failure due to acute leptospirosis have reportedly been treated successfully using advanced modalities such as dialysis. Because more cases of canine leptospirosis have recently been associated with previously uncommon serovars (including grippotyphosa, pomona, and bratislava), immunization with vaccines that include these serovars has become necessary. Recent data indicate that the prevalence of human leptospirosis is higher than generally considered. To avoid human exposure and infection, veterinary personnel must maintain strict sanitation when managing cases of canine leptospirosis.

Once canine leptospirosis has been diagnosed, promptly administering appropriate antimicrobial and supportive therapy is imperative. The degree of supportive care required depends on a patient's clinical condition at presentation and the degree of organ involvement. For severe cases of leptospirosis-associated renal failure, aggressive, labor-intensive, and expensive therapies may be required. Treating patients with canine leptospirosis can be rewarding for practitioners if the disease is promptly recognized and managed using appropriate protocols. This article outlines the various treatment aspects associated with canine leptospirosis. In addition, prevention strategies are included, along with information on the zoonotic aspects of this increasingly common disease.

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*A companion article on epidemiology, pathogenesis, and diagnosis was published in the August 2004 issue.

TREATMENT

Antibiotic Therapy

Antibiotics usually reduce fever and leptospiremia within a few hours of administration. Also, they immediately inhibit multiplication of the organism and reduce fatal complications such as renal and hepatic failure.[1] Penicillins and their derivatives are the antibiotics of choice in eliminating leptospiremia, but they do not eliminate the carrier state. Penicillin G (25,000 to 40,000 U/kg IM/SC/IV q12h) or ampicillin (22 mg/kg PO/SC/IV q6–8h) is used initially in most cases, with parenteral routes (i.e., intramuscular, subcutaneous, intravenous) used in vomiting or severely debilitated animals. Because penicillins are eliminated mostly via renal tubules, doses need to be adjusted accordingly in azotemic animals—either the dose should be halved, or the dosage interval doubled.[2] Once the animal has stopped vomiting and oral alimentation has been started, the oral route can be used to administer penicillins for 2 weeks or until azotemia

resolves. Amoxicillin (22 mg/kg PO q8–12h) is recommended because of its superior absorption.[1]

Once penicillin therapy has been completed and azotemia has resolved, other antibiotic classes (i.e., tetracyclines, erythromycin, aminoglycosides, fluoroquinolones) should be administered to eradicate the carrier state. Doxycycline (2.5 to 5 mg/kg PO q12h for 2 weeks) is used most commonly in this situation. Doxycycline can also be used in the initial leptospiremic phase, assuming the animal can tolerate oral medications. The dose does not need to be adjusted in patients with renal failure because the drug is eliminated in the feces.[2] Aminoglycosides should be avoided unless the animal has resumed normal renal function, and urinalyses should be monitored serially to detect renal tubule damage secondary to aminoglycosides.[3] Experimental animal studies have shown that ampicillin and cephalosporins were not effective in eliminating leptospiral organisms from tissues and body fluids, whereas tetracyclines and macrolides such as erythromycin were effective.[4] Table 1 outlines the recommended antibiotics for eliminating both phases (i.e., leptospiremic and renal carrier states) of leptospirosis.

Table 1. Recommended Antibiotics for Eliminating the Leptospiremic and Renal Carrier States[a]

Drug	Dosage[b]
Penicillin G[c]	25,000–40,000 U/kg IM/SC/IV q12h for 14 days
Ampicillin[c]	22 mg/kg PO/SC/IV q6–8h for 14 days
Amoxicillin[c]	22 mg/kg PO q8–12h for 14 days
Doxycycline[d]	5 mg/kg PO/IV q12h for 14 days
Tetracycline	22 mg/kg PO q8h for 14 days
Erythromycin[e]	15–20 mg/kg PO/IV q8–12h for 14 days
Azithromycin[e]	10 mg/kg PO q24h for 5–7 days

[a]Adapted from Greene CE, Miller MA, Brown CA: Leptospirosis, in Greene CE (ed): *Infectious Diseases of the Dog and Cat*. Philadelphia, WB Saunders, 1998, p 274.
[b]Indicates dose per administration at specified interval.
[c]Used for eliminating leptospiremia but are not effective at eliminating the renal carrier state.
[d]Can be used as primary therapy or to clear the renal carrier state.
[e]Efficacy of macrolides for leptospirosis is not well evaluated, although they cover the appropriate spectrum.

Supportive Care

The degree of supportive care required for animals with leptospirosis depends on the severity of the infection and degree of dehydration, renal compromise, and general health before infection. In severely affected patients, dehydration and shock can ensue, requiring more aggressive care. Vomiting and diarrhea can cause severe electrolyte abnormalities and acidosis that require treatment with intravenous crystalloid solutions. If oliguria or anuria develops, diuresis should be attempted using aggressive fluid diuresis with isotonic fluids plus osmotic diuretics (such as mannitol or 10% dextrose solutions) with or without furosemide.[5] Dopamine and other dopaminergic agents may be considered, as well.[5] Placing a jugular catheter is usually recommended to allow frequent blood sampling, high-dose fluid therapy, and measurement of central venous pressures. In severe cases, indwelling urinary catheters may be required to precisely measure urine output. Antiemetics and gastric protectants (i.e., H_2-receptor blockers, sucralfate) may be used in selected cases based on clinical signs and degree of uremia.[6] During treatment, enteric nutrition should be implemented as soon as possible through either oral (preferably) or tube (i.e., esophagostomy, nasoesophageal, or gastric) feeding as allowed by the patient; however, animals with protracted vomiting may require partial or total parenteral nutrition as dictated by the animal's clinical status and duration of anorexia.

Successful therapy for leptospirosis requires early recognition and treatment with diuresis and appropriate antimicrobials for both the leptospiremic and carrier phases of the disease.

In animals that do not respond adequately to fluid and pharmacologic diuresis (i.e., urine output less than 2 ml/kg/hr), more aggressive therapies may be required. Adin and Cowgill[7] reviewed 36 dogs treated either conservatively (i.e., medical management alone) or with

Table 2. Leptospirosis Vaccines

Vaccine	Serovars Included	Manufacturer
Duramune Max 5-CvK/4L Duramune Max 5/4L LeptoVax 4	Grippotyphosa Pomona Icterohaemorrhagiae Canicola	Fort Dodge Animal Health Fort Dodge, IA 50501 Phone: 1-800-477-1365
Duramune LGP	Grippotyphosa Pomona	Fort Dodge Animal Health Fort Dodge, IA 50501 Phone: 1-800-477-1365
Performer-7	Icterohaemorrhagiae Canicola	AgriLabs St. Louis, MO 64503 Phone: 1-800-542-8916
Champion Protector Canine 7-Way	Icterohaemorrhagiae	AgriLabs St. Louis, MO 64503 Phone: 1-800-542-8916
Canine 7-Way	Icterohaemorrhagiae Canicola	Durvet Animal Health Products Blue Springs, MO 64013 Phone: 1-800-821-5570
Commander 7L Adenomune 7L	Icterohaemorrhagiae Canicola	BioCor Animal Health Omaha, NE 68134 Phone: 1-800-441-7480
Progard-7 with CPV Strain 154 Progard-8 with CPV Strain 154	Icterohaemorrhagiae Canicola	Intervet Millsboro, DE 19966 Phone: 1-800-441-8272
Galaxy DA2PPvL + Cv	Icterohaemorrhagiae Canicola	Schering-Plough Animal Health Union, NJ 07083 Phone: 1-800-224-5318
Vanguard 5/L	Icterohaemorrhagiae Canicola	Pfizer Animal Health Exton, PA 19341 Phone: 1-800-366-5288

hemodialysis. Treatment choice was based on severity of azotemia and whether the dogs were oliguric. The prognosis for dogs with mild to moderate azotemia was good with conservative management, whereas treatment with hemodialysis appeared to improve the prognosis for dogs with severe azotemia.[7] Hemodialysis as a treatment for leptospirosis is limited by its sparse availability to most veterinary practitioners. Its use in dogs and cats has been described elsewhere.[8] Although not reported in studies on treating leptospirosis specifically, peritoneal dialysis is another possible therapeutic option if a facility has the technical support necessary to successfully perform this procedure.

Petechial and ecchymotic hemorrhage may indicate vasculitis-associated thrombocytopenia or, in more severely affected cases, the onset of disseminated intravascular coagulation (DIC). In these cases, fresh-frozen plasma or fresh whole blood transfusions may be used with concurrent parenteral heparin injections for ongoing DIC.[1]

Recovery from leptospirosis involves resolution of azotemia and other associated electrolyte, metabolic, and biochemical abnormalities. Dogs that recover from leptospirosis may have permanent renal insufficiency that requires life-long therapy for chronic renal failure (e.g., dietary modifications, phosphate binding). However, clinical recovery is usually complete, requiring no life-long therapy. Regardless, all recovered patients should be monitored closely for at least 6 to 12 months after therapy for development of or complications associated with chronic renal failure (i.e., hypertension, gastrointestinal ulceration, vomiting, hypokalemia, hyperphosphatemia).[9]

PREVENTION AND VACCINATION

Preventing leptospirosis involves eliminating the carrier state. However, subclinically affected animals and wild animal reservoirs continue to harbor and shed the organism. Strict kennel sanitation, rodent control, and strict isolation of infected animals are all appropriate to decrease exposure to and the spread of leptospirosis in endemic areas. Because leptospires are typically very labile organisms, most disinfectants, including bleach, povidone–iodine, and chlorhexidine, are usually very effective in controlling leptospirosis.

Bivalent bacterins containing the serovars canicola and icterohaemorrhagiae have been available and in relatively widespread use since the mid-1980s (Table 2). However, these vaccines are not cross-protective against other serovars, including pomona, grippotyphosa, bataviae, hardjo, and bratislava. Thus documented infec-

tions with the serovars canicola and icterohaemorrhagiae have decreased, while the prevalence of infection involving other serovars has increased during that time span.[9–16] Canine vaccination with these bacterins induces an IgG titer that subsides in about 3 months.[17] IgG antibodies are primarily responsible for protection and are produced for at least 1 year after the third vaccination in dogs.[1,17] A recent study supported this protection in dogs repeatedly challenged with the serovars icterohaemorrhagiae and canicola up to 1 year after vaccination.[18] Based on these results, two initial vaccinations 3 weeks apart followed by annual revaccination was recommended. It should be noted, however, that these dogs were challenged with either serovar icterohaemorrhagiae or canicola. Thus these results may not apply equally to all leptospirosis bacterins. Andre-Fontaine et al[19] recently revealed inconsistent protection in vaccinated puppies against challenge to leptospirosis regarding leptospiremia and development of the renal carrier state. One limitation of this study, however, was the sole use of serovar canicola as the challenge bacterium. Only bivalent bacterins were evaluated in this study.

Anaphylactic reactions (manifested as facial edema, pruritus, hypotension, or dyspnea) may be noted when administering leptospirosis vaccines. A previous allergic reaction to a combination booster in any dog is probably enhanced by *Leptospira* bacterins, which should be eliminated or administered cautiously in subsequent vaccinations.[20] Likewise, their use should be avoided in miniature dachshunds, which have a high rate of allergic reactions.

New vaccines (Duramune Max 5/4L and LeptoVax 4, Fort Dodge Animal Health) that include serovars canicola, icterohaemorrhagiae, pomona, and grippotyphosa recently became available. A bivalent vaccine with these new serovars is also available to supplement existing vaccination regimens. However, clinical studies documenting their efficacy against experimental or natural infections with the serovars pomona and grippotyphosa have not been reported in the veterinary literature. For further information on canine vaccines and vaccination

Human Leptospirosis[a]

Symptoms

Fever	Jaundice
Headache	Anemia
Chills	Rash (occasional)
Muscle aches	Incubation: 2–29 days
Vomiting	

Sequelae

Kidney damage	Respiratory distress
Meningitis	Fatality rate: 1%–5%
Liver failure	

Groups at Risk

Farm workers	Travelers to the tropics
Sewer/mine workers	People participating in freshwater sports in tropical and temperate climates
Slaughterhouse workers	
Veterinarians	
Animal caretakers	

Incidence

The incidence of leptospirosis appears to be on the rise. One hundred to 200 cases are identified annually in the United States (more than 50% occur in Hawaii). Leptospirosis is not nationally reportable, although numerous states have a reporting system. Although the incidence in the United States is low, leptospirosis is considered the most widespread zoonotic disease in the world.

Prevention

Improved sanitation	Disinfecting contaminated areas
Early treatment with antibiotics	Handwashing

[a]Adapted from The Centers for Disease Control and Prevention: *Leptospirosis*. Available at www.cdc.gov/ncidod/dbmd/diseaseinfo/leptospirosis_g.htm; accessed July 2004.

protocols, see the American Animal Hospital Association canine vaccination guidelines and recommendations.[21]

ZOONOSIS

Immunization against leptospirosis has been effective in reducing the prevalence and severity of canine leptospirosis, but it does not prevent the carrier state, which potentially increases the risk of zoonosis.[1] Most human infections occur in persons involved in water sports[22,23] and other outdoor recreational activities[24] (see box on page 704). However, recent studies have revealed that the incidence of leptospirosis in US cities is remarkably high.[25] Increased contact of dogs and humans with some of the primary nondomestic hosts (e.g., skunks, opossums, raccoons) has likely contributed to the increased incidence of leptospirosis in these urban environments.

Because infectious organisms can persist in the renal tubules in chronically infected dogs, immunized dogs have been shown to excrete infectious leptospires for prolonged periods of time.[26] Contaminated urine is highly infectious to both humans and other susceptible animal species. Thus gloves should be worn when handling or treating dogs with suspected leptospirosis and all excretions should be disposed of in appropriate medical waste containers. Strict kennel sanitation (i.e., gloves, face masks) should be used when cleaning contaminated housing. All dogs with suspected leptospirosis should be physically isolated from other animals, as well. In the future, polymerase chain reaction may be a suitable tool to identify shedders earlier, thus decreasing exposure of kennel personnel and other dogs to infective organisms.[27]

Leptospirosis in humans is likely underdiagnosed because it presents with typical flu-like signs. However, progression to fulminant hepatic and renal failure is possible, culminating in death in the most severe untreated cases.[25] Alternative diagnoses are initially made in up to 60% to 70% of patients ultimately found to have leptospirosis.[28] Thus potentially exposed persons with symptoms of leptospirosis should notify their physician of possible exposure to avoid delaying appropriate therapy or necessary diagnostics.

For more on leptospirosis, see Industry Insights on page 709.

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1. The least appropriate antibiotic to use in eliminating the renal carrier state of leptospirosis is

a. enrofloxacin.
b. erythromycin.
c. amoxicillin.
d. doxycycline.
e. ciprofloxacin.

2. Which leptospira serovar is not included in most available vaccines?

a. icterohaemorrhagiae
b. canicola
c. pomona
d. grippotyphosa
e. bratislava

3. Which treatment is contraindicated in animals with severe acute leptospirosis?

a. hemodialysis
b. parenteral ampicillin
c. fresh-frozen plasma transfusion
d. isotonic fluid diuresis
e. none of the above

4. Which statement regarding zoonotic aspects of leptospirosis is incorrect?

a. Immunization against leptospirosis does not prevent the carrier state.
b. Immunized dogs can excrete infectious leptospires for prolonged periods.
c. Contaminated urine is rarely infectious in immunocompetent humans.

d. Leptospirosis in humans is likely underdiagnosed by physicians.
e. Leptospirosis in humans can occasionally be fatal if untreated.

5. Which statement regarding antibiotic therapy for leptospirosis is incorrect?
a. Penicillins are eliminated mostly via the feces.
b. Oral antibiotics can be used when treating leptospirosis.
c. Using antibiotics can reduce fatal complications such as renal failure.
d. Doxycycline is eliminated primarily in the feces.
e. Using aminoglycosides requires significant monitoring in patients with reduced renal function.

6. Which statement regarding supportive therapy for leptospirosis is correct?
a. Hemodialysis is readily available to practicing veterinarians.
b. Peritoneal dialysis is not an option in treating leptospirosis.
c. All dogs with leptospirosis require hemodialysis.
d. Enteric nutrition should be implemented as soon as possible in the disease course.
e. Jugular catheterization is of little use in patients with leptospirosis.

7. Which statement regarding recovery from leptospirosis is incorrect?
a. Dogs that recover may have permanent renal insufficiency.
b. Clinical recovery from leptospirosis is usually complete.
c. Recovery includes resolution of azotemia and electrolyte abnormalities.
d. All surviving patients should be monitored for complications associated with chronic renal failure.
e. none of the above

8. Which of the following is contraindicated in preventing leptospirosis?
a. rodent control
b. isolation of infected animals
c. strict kennel sanitation
d. vaccination
e. none of the above

9. Which statement regarding leptospirosis vaccination is correct?
a. IgA antibodies are primarily responsible for protection.
b. Serovars included in bivalent vaccines are cross-protective against serovars not included in the vaccines.
c. Anaphylaxis is not seen with leptospirosis vaccine administration.
d. The IgG titer induced by leptospirosis vaccination subsides within 3 months.
e. Various vaccination studies have revealed consistent protection against experimental challenge with leptospirosis.

10. Which statement regarding human infection with leptospirosis is incorrect?
a. Most infections occur in persons involved in water sports.
b. The incidence of human leptospirosis in US cities is remarkably low.
c. Gloves should be worn when handling infected urine.
d. Infected humans typically present with flu-like symptoms.
e. Progression to fulminant hepatic and renal failure is possible.