Leptospirosis

BASIC INFORMATION

DEFINITION
A bacterial disease affecting humans and animals, caused by pathogenic subtypes (serovars) of the aerobic gram-negative filamentous spirochetes, *Leptospira interrogans* and *L. kirschneri*

SYNONYMS
Weil's disease, Stuttgart disease, fall fever

EPIDEMIOLOGY

SPECIES, AGE, SEX
- Dogs: 4-7-year-old males more commonly affected
- Younger dogs are more susceptible to severe disease
- Cats: not clinically affected nor renal carriers; do seroconvert with exposure

GENETICS & BREED PREDISPOSITION: More common in hounds, working dogs, and herding breeds (likely greater exposure risk)

RISK FACTORS
- Suburban or rural environment
- Outdoor exercise areas/activities
- Exposure to wildlife or livestock (maintenance hosts)
- Exposure to moist environments/ standing water or to raw sewage
- Flooding
- Human risk factors: direct contact with domestic animals, environmental exposure (e.g., fisheries, rice fields, water sports), exposure to wild rodents (urban areas of poor sanitation)

CONTAGION & ZOONOSIS
- Readily contagious and zoonotic, typically via exposure to infected urine. When handling patients suspected of having leptospirosis, veterinary personnel and laypersons must use gloves and personal protective equipment to avoid exposure to urine and fomites.
- Leptospirosis is the most widespread zoonosis worldwide, accounting for up to 30% of human cases of acute renal failure in developing countries. Most human infections are asymptomatic or associated with mild, self-limiting flulike symptoms.

GEOGRAPHY AND SEASONALITY
- Worldwide distribution but predominant serovar(s) responsible for disease vary by region. In North America, serovars grippotyphosa, pomona, and bratislava are most common (historically, serovars canicola and icterohaemorrhagiae prior to vaccines targeting them).
- Previously considered a rural disease, leptospirosis is now also urban (rodents) and suburban (wildlife).
- The organisms survive in warm, moist environments, especially water but also mud and soil.
- The incidence of disease is highest in warmer months.

CLINICAL PRESENTATION

DISEASE FORMS/SUBTYPES
- There are at least 8 serovars (*L. interrogans*: autumnalis, bataviae, bratislava, canicola, hardjo, icterohaemorrhagiae, pomona; *L. kirschneri*: grippotyphosa) infectious to dogs and cats, causing variable degrees of renal and liver disease in dogs.
- Most infections are asymptomatic.
- Clinical disease: peracute (rare; sudden death from massive leptospiremia), acute, subacute (common), or chronic (common)
forms

- Some reported variation in tissue tropism and disease severity depending on the infecting serovar and the age and immune status of the host

HISTORY, CHIEF COMPLAINT

- Acute form: younger animals; lethargy, anorexia, shivering, muscle tenderness, vomiting
- Subacute form: lethargy, anorexia, vomiting, polydipsia/polyuria, reluctance to move, lumbar pain, icterus, hemorrhage
- Chronic form: +/- polyuria/polydipsia, icterus, inappetence

PHYSICAL EXAM FINDINGS

- General:
  - Anorexia
  - Lethargy
  - Fever
  - Dehydration +/- progression to hypovolemic shock
  - Injected mucous membranes
  - Conjunctivitis, uveitis
  - Petechial and ecchymotic hemorrhages
  - Nasal discharge
  - Increased lung sounds
  - +/- Abdominal pain, myalgia

- Additional findings vary based on tissue tropism and severity of injury:
  - Most cases show hypovolemia.
  - Manifestations of renal disease are very common.
  - Liver involvement is common; overt signs of liver failure (icterus, hepatic encephalopathy) may be present.
  - Vomiting is common.
  - Diarrhea is very common in experimentally infected puppies, less common in naturally occurring infections (but more common than in other causes of renal failure).
  - Pulmonary disease (labored breathing, cough) is much less common.

ETIOLOGY AND PATHOPHYSIOLOGY

- Leptospires enter the body by penetrating intact mucous membranes or bruised, abraded, or water-softened skin.
- Leptospiremia (7-10 days) causes dissemination to kidney, liver, spleen, central nervous system, eyes, and genital tract.
- Leptospires can express hemolysin and other factors which cause endothelial damage and vasculitis.
- Renal tubular epithelial-cell colonization occurs in most infected dogs, causing shedding for months to years post infection if not appropriately treated.
- Hepatic disease may result from toxin-induced injury and may be severe; some cases present with acute hepatic dysfunction as the predominant feature. Leptospirosis has been implicated as a cause of chronic hepatitis (serovar grippotyphosa).

DIAGNOSIS

DIAGNOSTIC OVERVIEW

Unexplained fever or signs of renal and/or hepatic insufficiency should prompt consideration of leptospirosis. Diagnosis is multimodal: a serum titer alone is rarely sufficient, and a combination of history (exposure, clinical signs), physical examination, routine blood test results, serologic titers, and organism demonstration (via PCR) all contribute to confirming or refuting the clinical diagnosis.

DIFFERENTIAL DIAGNOSIS

- Other causes of acute renal failure (e.g., toxin, pyelonephritis, heat stroke, shock; see p.31)
- Other causes of vasculitis (e.g., sepsis, rickettsial disease, pancreatitis)
- Other causes of hepatic injury (e.g., bacterial cholangiohepatitis, toxin, sepsis, idiopathic chronic hepatitis)

INITIAL DATABASE

- CBC:
  - Often inflammatory leukogram, with or without a left shift
  - +/- Variable degree of anemia
Thrombocytopenia: a third of cases, mild to moderate (90,000-150,000/mm$^3$), especially if vasculitis or disseminated intravascular coagulation (DIC)

- Serum biochemistry profile:
  - Azotemia and hyperphosphatemia are common.
  - Electrolyte disturbances: hyponatremia, hypochloremia, and hypokalemia
  - Metabolic acidosis
  - +/- Hypoalbuninemia in cases with vasculitis or severe liver dysfunction
  - Liver parameters: increased alanine aminotransferase (ALT), alkaline phosphatase (ALP), and bilirubin usually peak at 6-8 days after the onset of disease.

- Urinalysis:
  - Glucosuria, proteinuria, granular casts, pyuria, and hematuria may be present.
  - Variable specific gravity

- Thoracic radiographs: interstitial, nodular, or patchy alveolar infiltrates with pulmonary involvement or vasculitis

- Abdominal radiography and ultrasonography: +/- enlargement of liver, spleen, kidneys; renal “medullary rim sign” (hyperechoic concentric ring); perinephric effusion

**ADVANCED OR CONFIRMATORY TESTING**

- Microscopic agglutination test (MAT):
  - In animals with compatible clinical signs, the following results are considered diagnostic:
    - Titer > 1:800 in unvaccinated animal
    - Titer > 1:3200 in vaccinated (previous 3-4 months) animal
    - Paired titers 2-4 weeks apart with fourfold increase from first to second titer. Cross-reactivity among serovars is common, and highest serovar’s titer often is not the causative serovar.

- ELISA: used as field tests for human infections
- PCR assays: sensitive and specific; may be positive in early infection before rise in specific antibody detected by MAT or ELISA is present. Current techniques distinguish pathogenic organisms but not serovars.
- Darkfield microscopy: examination of fresh urine for leptospires; low sensitivity (intermittent shedding means frequent false-negative results) and not routinely used
- Bacterial culture: leptospires are difficult to grow in culture; frequent false-negative results; does allow identification of infecting serovar (important epidemiologically)
- Fluorescent antibody techniques: fluid and tissue samples; not widely used
- Histopathologic assessment: lesions nonspecific (lymphoplasmacytic tubulointerstitial nephritis); organisms may be identified using special stains.

**TREATMENT**

**TREATMENT OVERVIEW**

Treatment goals are to treat bacteremia/leptospiremia, maintain renal perfusion and urine output to minimize renal injury, eliminate bacteria to prevent disease progression and shedding to environment, and treat associated conditions (renal failure, hepatic insufficiency, DIC, uveitis).

**ACUTE GENERAL TREATMENT**

- Penicillins: antimicrobial of choice for bacteremic phase (crystalline [transparent] formulations for IV use)
  - Penicillin sodium, 20,000 IU/kg IV q 4 h; or
  - Ampicillin, 22 mg/kg IV or PO q 8 h; or
  - Amoxicillin, 22 mg/kg IV or PO q 8 h
- Intravenous fluid therapy to replace deficits (vomiting, polyuria, decreased intake) and initial management of renal injury: target is rapid rehydration without volume overload (see p. 31)
- Adjunctive management of organ dysfunction and other consequences of infection as indicated for individual case (see Acute Renal Failure, p. 31; Acute Liver Injury; Disseminated Intravascular Coagulation p. 315; Vasculitis; Sepsis p. 1014)

**CHRONIC TREATMENT**

Doxycycline, 5 mg/kg PO q 12 h for 2 weeks to eliminate leptospires from tissues, eliminate renal shedding

**RECOMMENDED MONITORING**

- Serum electrolyte levels, renal and hepatic parameters: to assess response to treatment or disease progression and to tailor therapy
Hypertension may occur, requiring modification of treatment (see p. 1068).
Urine output monitoring is essential in patients with acute renal failure.
Monitor for development of complications (DIC, respiratory failure).

PROGNOSIS AND OUTCOME

- Survival rates for patients with clinical leptospirosis: 70%-85%
- Patients with acute renal failure are frequently oliguric to anuric and may require dialysis.
- Survivors may have persisting/chronic kidney (common) or liver dysfunction.

PEARLS & CONSIDERATIONS

COMMENTS

- Leptospirosis should be considered as a differential in any case of acute renal failure, fever of unknown origin, vasculitis, and/or acute or chronic liver disease in a dog.
- Due to the zoonotic potential of *Leptospira* pathogens, extreme caution should be used when handling suspected leptospirosis cases (dogs with acute febrile disease, especially with evidence of acute renal or liver disease).
- Human physicians are often unfamiliar with leptospirosis and its zoonotic potential.
- Intensive early therapy is important both for the patient's benefit and to reduce the risk of transmission to humans and other animals (empirical penicillin therapy in leptospirosis suspects while awaiting confirmatory test results).
- Leptospirosis is a reportable disease in many U.S. states; contact regional authorities.

PREVENTION

- Vaccination: whole-cell killed bacterin and subunit vaccines exist; vary in duration of immunity (6-13 months) and which serovars are included; prevent clinical disease and development of carrier state; most protect against icterohaemorrhagiae and canicola, newer vaccines include pomona and grippotyphosa.
- Vaccine protection is serovar specific: no cross-protection against nonvaccine serovars.
- Adverse reactions have been reported with disproportionate frequency with whole-cell leptospirosis vaccines; patients with a history of intolerance should either not receive the vaccine or be premedicated with antihistamines (e.g., diphenhydramine, 2 mg/kg IM) and glucocorticoids (e.g., dexamethasone, 0.2 mg/kg IM) 15-30 minutes before vaccination.
- Rodent control, avoidance of contact with reservoir hosts, and proper sanitation/drainage are also important.

TECHNICIAN TIPS

- Leptospirosis can be transmitted from infected animals to humans. To prevent exposure of people and other animals to the disease, strict protective measures should be used in handling animals, their bedding, and all laboratory samples. Use of hoses to clean cages of infected animals may result in generation of aerosols that can spread the organisms to people and other animals, and seed building surfaces with bacteria. Goggles, masks, and gloves should be worn to prevent exposure via mucous membranes (eyes, nose, mouth) and skin.
- Leptospirosis patients or suspects should be isolated from other patients and their movement restricted (patient remains in assigned cage unless absolutely necessary). If moved, patients should be transported by gurney or portable carrier that can be thoroughly disinfected.

CLIENT EDUCATION

- Leptospirosis can be transmitted to people, principally through direct or indirect contact with urine.
- Owners should be advised to contact their family physician for recommendations following exposure to an infected pet.
- Dogs should be supervised to prevent direct exposure to wildlife and should not be allowed to play in/drink from pools of stagnant water.

SUGGESTED READING


AUTHOR: MARCELLA D. RIDGWAY

EDITOR: DOUGLASS K. MACINTIRE