Leptospira

For Vets

Worms & Germs
Promoting Safe Pet Ownership

General Information

- Leptospires are long, thin, spiral-shaped Gram-negative bacteria which can infect over 160 mammalian species.
- Transmission to humans is most commonly associated with contact with water that has been contaminated with urine of infected wildlife, including rodents. Contact with urine of infected domestic animals can also result in transmission. Among pets, infection is seen most frequently in dogs.
- The nomenclature of the genus *Leptospira* is very complex. Previously, all pathogenic serovars (also called serotypes) of *Leptospira* were classified as *L. interrogans*. This group is still sometimes referred to as *L. interrogans* sensu lato. The genus has since been divided into at least 16 species, including *L. interrogans* sensu stricto. The different species now contain both pathogenic and non-pathogenic serovars.
- *Leptospira interrogans* sensu lato includes more than 200 serovars, which are classified by their surface antigens. Related serovars form serogroups, which do not have a taxonomic basis but are sometimes used to describe the epidemiology of leptospirosis. Many serogroups have the same names as some of the serovars.
- Each pathogenic serovar has one or more reservoir host species, in which infection is typically long-term and subclinical but still results in leptospiruria. This can lead to transmission to incidental hosts in which infection is usually much more severe.

Prevalence & Risk Factors

Leptospirosis (also known as “mud fever” or “fall fever”) is possibly the most widespread zoonotic disease in the world. Leptospirosis is more common during warm, wet weather (e.g. late summer, early fall in temperate climates) and during periods of high rainfall or flooding, when conditions favour survival of leptospires in the environment.

Humans: The incidence of leptospirosis in people in developed countries is generally quite low. Approximately 100-200 cases occur in the USA each year, with about half of these occurring in Hawaii. However, because leptospirosis is not a notifiable disease in most of the USA (and Canada), the number of cases reported may be significantly lower than the number of cases that actually occur.

- Individuals who may have increased exposure to animal urine or water contaminated with animal urine are at increased risk for infection with *Leptospira*. These include veterinarians, animal care personnel, abattoir workers, sewer workers, farmers, rodent control workers, miners, soldiers, gamekeepers, and people who participate in outdoor water sports (e.g. kayaking, swimming).
- Outbreaks associated with exposure to contaminated water sources are more common than disease secondary to transmission of *Leptospira* from dogs or other pets.

Animals: The incidence of leptospirosis in dogs in Canada and the USA has increased significantly in recent years, apparently as a result of spread from wildlife such as raccoons and skunks.

- Exposure to *Leptospira* varies greatly (1-50%) among dogs depending on their location, housing and lifestyle.
- Risk factors that have sometimes been identified for canine leptospirosis (e.g. large, outdoor, working, herding dogs, etc.) likely reflect increased exposure to urine of wild animals and rodents that may carry the infection.
- Dogs kept in crowded, unsanitary conditions are also more likely to be exposed to *Leptospira*.
- Clinical leptospirosis in cats is rare, and seroprevalence is typically 10% or less.
- In developed countries, leptospirosis is more of a concern in livestock (particularly dairy cattle) than in humans.

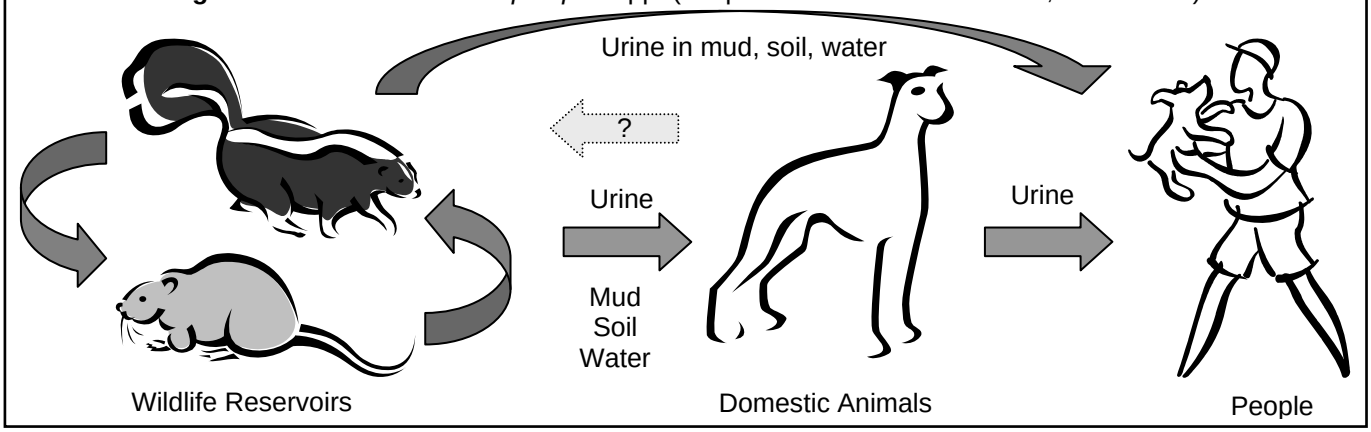
Habitat & Environmental Survival

Leptospires can survive for weeks to months in a warm (0-25°C), wet environment (e.g. urine-soaked soil), particularly in a neutral to alkaline pH, but pathogenic strains generally do not multiply outside a host. The bacteria can only survive for a few hours in the presence of sewage, and they do not survive well in normally concentrated, acidic urine (pH 5.0-5.5). Leptospires are susceptible to most disinfectants, especially iodine-based products.

Transmission of *Leptospira*

- **Indirect transmission** can occur through contact with soil, water, food or bedding that has been contaminated with leptospires, usually from the urine of infected wildlife. Leptospires are adept at burrowing through tissues, therefore transmission can even occur through intact skin that is soft or macerated from moisture, although it is more likely to occur through broken skin or a mucous membrane. Dogs can become infected from simply walking through a puddle in which an infected skunk or raccoon has urinated. People can become infected from swimming in similarly contaminated lakes or ponds.
- **Direct transmission** involves skin or mucous membrane contact with frank urine, venereal discharge or tissues from an infected animal. Because people have such close contact with their pets, this is an important mode of transmission from these animals, although in general it is less common than indirect transmission. The bacteria can occasionally be transmitted by bites, although leptospires are generally not shed in saliva.

Figure 1: Transmission of *Leptospira* spp. (adapted from Brown & Prescott, CMAJ 2008)



Pathogenesis of Leptospirosis

- Once leptospires penetrate the skin or mucous membranes of a host, they enter the bloodstream and begin to multiply rapidly. The bacteria then invade other tissues including the kidney, liver, spleen, central nervous system, eyes and genital tract, and continue to multiply.
- Following development of a humoral immune response, the organisms are cleared from most tissues, but frequently persist in the proximal renal tubules where they are inaccessible to serum antibodies. The bacteria can survive and replicate in this location for weeks or even years in a reservoir host, resulting in leptospiruria.
- Dogs can be persistent (life long) renal carriers of serovar canicola, but this serovar now has a very low prevalence due to widespread canine vaccination. The duration for which dogs may shed other serovars is unknown, but it may be up to at least six weeks.

The mechanisms by which leptospires exert their damaging effects are unclear. The bacteria cause severe vasculitis and endothelial damage, which can lead to coagulation disorders. Damage to the renal tubules commonly leads to renal insufficiency or failure. It is suspected that hepatic necrosis is initially caused by interference with cellular enzyme systems. Chronic active hepatitis and hepatic fibrosis and failure may ensue in some cases. Interstitial pneumonia and pulmonary hemorrhage have both been reported in dogs and humans, but appear to be more common in humans. Myocarditis, pericarditis and cardiac dysrhythmias are also well-recognized sequelae. Although not recognized in dogs, in humans leptospirosis can result in aseptic meningitis, which may be immune-mediated in nature. Acute or chronic recurrent uveitis may occur due to the presence of leptospires in the aqueous humour and/or cross-reactivity of leptospire antibodies with ocular tissues. Although leptospirosis is a relatively commonly reported cause of abortion in cattle and swine, reproductive problems associated with leptospirosis are not commonly reported in other species, including humans, but they can occur.

Symptoms & Signs of Leptospirosis

In humans and animals alike, the majority of leptospiral infections are likely subclinical, or may cause mild, self-limiting flu-like signs including fever, lethargy, and myalgia. The incubation period is typically 5-14 days, but can range from 2-30 days. More severe disease has a wide variety of clinical presentations, and rarely can be fatal.

Humans: Early infection typically presents as fever. This can develop into anicteric or icteric leptospirosis (also called Weil disease). Clinical signs may persist for one week to several months, and are not consistent within nor between serovars. Headache, chills, vomiting, anemia and sometimes skin rash may occur initially. Myalgia may be severe. Respiratory signs can be common, and pulmonary involvement can often be detected radiographically even when respiratory signs are not present. In the second week of illness, aseptic meningitis, uveitis, jaundice and signs of renal disease may develop. The overall mortality rate for leptospirosis varies greatly by region. It may be as low as 1-5% or over 20%. Increased risk of mortality has been associated with dyspnea, oliguria, leukocytosis, repolarization abnormalities on electrocardiograms, and alveolar infiltrates on thoracic radiographs. The list of potential differential diagnoses for leptospirosis in humans is extensive.

Animals: Clinical infection with *Leptospira* in pets is by far most common in dogs, in which the disease may be peracute, acute, subacute or chronic. Disease is more severe in younger animals.

- **Peracute** cases develop massive leptospiremia and die with few premonitory signs.
- **Acute** cases are characterized initially by fever, shivering and muscle tenderness, followed by vomiting, coagulopathy, vascular collapse and shock before renal or hepatic signs are able to develop. Severe gastrointestinal inflammation, which may result in intestinal intussusceptions, has also been reported
- **Subacute** infection is the most commonly recognized clinical syndrome, signs of which include fever, anorexia, vomiting and polyuria/polydypsia, which may lead to oliguric or anuric renal failure. Petechial and ecchymotic hemorrhages may be seen. Hepatic signs (e.g. icterus) are more common in dogs less than six months old. Respiratory signs may be present in 3-20% of cases.
- **Chronic** signs are related to the organs damaged during the primary infection, typically chronic renal failure or chronic active hepatitis. Recurrent uveitis may also occur.

The survival rate for dogs with leptospirosis, if properly treated, ranges from 78% to 88%. Even dogs that required hemodialysis had a survival rate of 86% in one study.

Diagnosis of Leptospirosis

- Hematology, serum biochemistry, urinalysis and abdominal ultrasonography are reflective of the severity and type of primary organ dysfunction (e.g. kidneys, liver, muscle, blood dyscrasias).
- Specific diagnosis based on isolation of leptospires is problematic – the organisms are very difficult to culture *in vitro*, and detection of organisms in body fluids and urine requires dark-field microscopy. This technique is fraught with sensitivity and specificity issues and is no longer a recommended diagnostic for leptospirosis.
- Leptospiruria can be intermittent. Administration of furosemide to a well-hydrated patient may increase recovery of the bacteria, and multiple samples should be collected. In animals, urine samples for culture should be collected by cystocentesis.

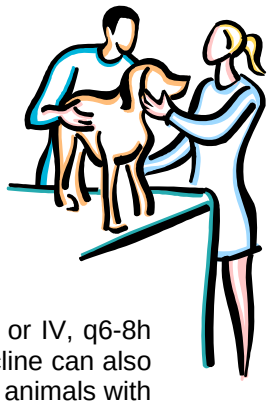
Microscopic agglutination test (MAT): This test remains the gold standard for diagnosis of leptospiral infection in humans and animals. The test is meant to be serogroup-specific, but not serovar-specific. The MAT requires live test strains of the bacteria and dark-field microscopy, so it is only performed by some commercial labs.

- ***In dogs***, diagnosis is typically based on a fourfold rise in specific MAT antibody titre over three weeks, or a single titre of 1:800 or greater. The serogroup with the highest titre is typically considered the infecting strain, but this is very unreliable in acute serum samples because of high cross-reactivity. Titres may be negative during the first 7-10 days of infection, and early antimicrobial therapy decreases the magnitude of the rise in titre. Vaccination rarely causes a specific titre over 1:300; higher vaccine titres rarely persist for over 3 months. Because serovar canicola is host-adapted to dogs, dogs may shed this serovar in their urine without developing a titre over 1:100.

Other serologic tests: Tests have been developed that are easier to perform, can detect antibody (IgM) titres earlier in infection and potentially differentiate vaccine and disease-induced titres. These include enzyme-linked immunosorbent assays (ELISAs), latex agglutination test (LAT), macroscopic slide agglutination test (MSAT) and indirect hemagglutination assay (IHA). Most were developed for use in humans and are not widely available for animal testing. The primary problem with these tests remains low sensitivity during the first week of illness.

Polymerase chain reaction (PCR): This methodology can detect leptospiral DNA in clinical samples before serologic tests can confirm infection, and is available from some labs for both human and animal testing. However, additional research is needed to determine the diagnostic sensitivity and reliability in animals, as leptospires can occasionally be found in the tissues and urine of normal dogs. Thus far, PCR is primarily used for outbreak investigations in humans due to the technical demands of performing the test.

Treatment of Leptospirosis



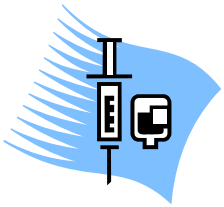
Animals:

- Standard therapy should be employed for the animal's condition based on the body systems involved and the severity of signs, and may include intravenous fluids, plasma, blood transfusion, gastroprotectants, and diuretics.
- Specific therapy for leptospirosis consists of antimicrobial therapy. It is very important to administer antimicrobials as early as possible to reduce leptospiremia and avoid further organ damage.
  - Penicillins are the antimicrobials of choice initially (e.g. ampicillin 22 mg/kg PO, SC or IV, q6-8h for 2 weeks in both dogs and cats), but will not clear the renal carrier state. Doxycycline can also be used in dogs (5 mg/kg PO or IV, q12h for 2 weeks), and may be advantageous in animals with marked renal dysfunction but minimal hepatic dysfunction, as it is primarily excreted in the feces.
  - Options for antimicrobial therapy that can be used to clear the renal carrier state include doxycycline, tetracycline, and macrolides (e.g. erythromycin) at standard doses, although the latter have not been well studied. Aminogylcosides are very effective for clearing the renal carrier state, but they should only be given to animals with normal renal function test results. Chloramphenicol and sulfonamides are ineffective for clearing leptospires from the tissues. Fluoroquinolones have been variably effective when used in experimental models.
- ***All animals with leptospiruria***, regardless of clinical presentation, should be treated with antimicrobials due to the associated public health risk. Once an animal begins treatment, viable organisms should not be shed in the urine, but shedding of viable organisms may recur if antimicrobial therapy is withdrawn before renal colonization is completely eliminated.

Humans:

As in animals, initial therapy in humans must be tailored to the severity of the patient's condition and organ systems involved. Specific treatment is based on antimicrobial therapy. Prophylactic antimicrobial therapy has been used in individuals at short-term, high-risk for exposure, but such therapy is generally not recommended due to concerns of developing antimicrobial resistance. Pregnant women who have been exposed to *Leptospira* are at risk of abortion; prophylactic antimicrobial therapy should therefore be considered in these cases.

Vaccination



Currently the most prevalent serovars of *Leptospira* found in dogs in North America include grippotyphosa, pomona, bratislava and perhaps, though it has not been confirmed, autumnalis. Previously the most common serovars were canicola and icterohemorrhagiae. There are currently vaccines available for dogs for serovars canicola and icterohemorrhagiae, grippotyphosa and pomona, and tetravalent vaccines for all four of these serovars. The vaccines do not provide cross-protection to other serogroups. Newer vaccines are effective at reducing renal colonization and shedding as well as clinical disease, but no vaccine is 100% effective. Older vaccines were whole-cell bacterins, which tended to be quite allergenic, but the newer subunit vaccines that have been produced are less problematic in this regard. A primary series of three injections 2-3 weeks apart is recommended. Because immunity tends to wane over time, for dogs at increased risk of exposure, annual vaccination is recommended. Leptospiral vaccines for humans are not available in North America.

Infection Control

Hand Hygiene: Hands should be thoroughly washed with soap and water after handling any pet, or after coming in direct or indirect contact with an animal's urine, feces or other body fluids.

Precautions for Infected Animals:

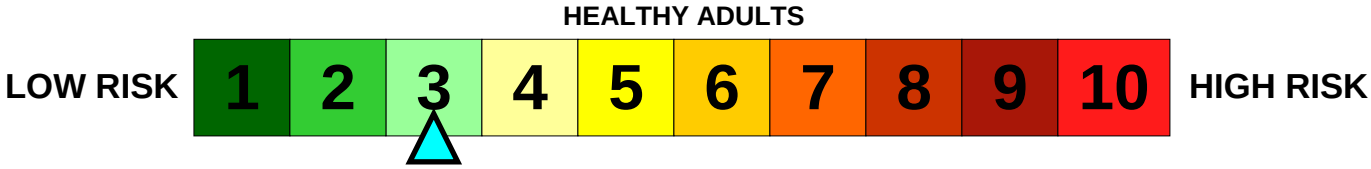
- Isolate any animal suspected or known to be infected with *Leptospira*, and use barrier precautions when handling the animal (e.g. gloves, gown, over boots).
    - Contain urine using a closed collection system or absorbent, disposable cage pads. Do not allow the animal to urinate in an area where other animals or people normally go.
- Wear latex gloves and a face mask when handling urine samples or any item that may be contaminated with urine and that may present a splash hazard.
- Contaminated areas and equipment should be washed with detergent, treated with a standard disinfectant, and dried thoroughly. Avoid high pressure hosing of any area until it has been disinfected.
- Wear a facemask and goggles when hosing potentially contaminated kennels or areas.
- Even though most dogs stop shedding viable leptospires in their urine after a few days of antimicrobial therapy, they should remain in isolation while in hospital until the treatment course is complete.
- The owner should disinfect any surface/area of the house that may have been contaminated with the animal's urine, and anyone who had recent contact with the animal should consult a physician if he or she has concerns, particularly if the person is pregnant.

General Precautions:

- Where possible, control rodent/wildlife populations (outside and inside) that can harbour and spread *Leptospira*.
- Prevent build up of stagnant water, particularly in areas where animals (wild or domestic) may urinate.
- Other mammalian pets (e.g. guinea pigs, hamsters, rats, mice) can also be infected by leptospires. To prevent leptospirosis and leptospiruria in these pets, prevent exposure to urine from other animals that may be infected.
    - Do not allow the pet to roam loose in the house, as it may come in contact with an area where another pet or wild rodents have urinated.
    - Keep the pet in a secure enclosure that prevents escape and also prevents wild rodents from getting in.
- Do not drink untreated water from open water sources such as lakes and ponds.

Zoonotic Disease Risk

The zoonotic disease risk to the general population posed by *Leptospira* in dogs is:



Individuals with compromised immune systems (e.g. HIV/AIDS, transplant and cancer patients) are more susceptible to many kinds of infections, including those which may be transmitted by pets. Patients with HIV/AIDS are at risk of developing particularly severe infection if they are exposed to *Leptospira*, although in general they respond well to treatment if it is provided promptly. While these individuals are not advised to get rid of their pets, precautions, as outlined above, should be taken to reduce the frequency of contacts that could result in pathogen transmission, as well as the ability of infectious agents to survive in the household. **Women who are pregnant** should take similar precautions to avoid being exposed to leptospires.

- Dogs should be vaccinated regularly with a multivalent vaccine, and can be screened for infection if necessary.
- Cats should be kept indoors to prevent exposure to leptospires, as well as other zoonotic pathogens.

Infants and Young Children are more likely than adults to extensively handle animals if given the opportunity, more likely to touch their faces or mouths, and less likely to wash their hands after handling an animal. Children may "snuggle" with pets such as dogs and cats; this very close contact can increase the risk of disease transmission.

- Young children should be supervised when playing with animals, and an adult should ensure that they wash their hands afterwards, and especially prior to handling food. Older children should be taught to do the same.

For these groups, the zoonotic disease risk posed by *Leptospira* in dogs is likely: