

General Information

- Leptospire 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 leptospiuria. 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 leptospire 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.

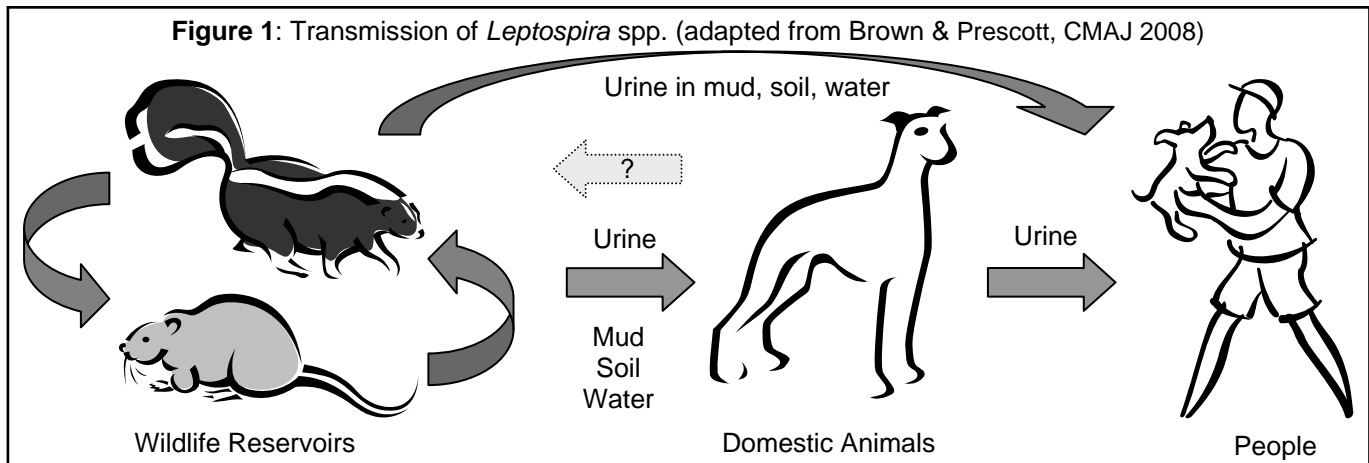
Habitat & Environmental Survival

Leptospire 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). Leptospire 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.



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 leptospiuria.
- 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's 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. Meningitis is more common in children less than 14 years old than in adults. The overall mortality rate for leptospirosis varies greatly by region. It may be as low as 1-5% or over 20%. The mortality rate for anicteric disease is very low. 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 fulminant, acute, subacute or chronic. The more acute forms are typically characterized by complications of vasculitis and coagulopathies resulting in shock and sudden death. Subacute and chronic forms are typically characterized by signs of renal or hepatic failure. Recurrent uveitis may also occur in some cases. The survival rate for dogs with leptospirosis, if properly treated, ranges from 78% to 88%.



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 leptospire 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.



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. The serogroup with the highest titre is typically considered the infecting strain, but in dogs this is not reliable.

Other serologic tests: Tests have been developed that are easier to perform and can detect antibody (IgM) titres earlier in infection than the MAT. These include enzyme-linked immunosorbent assays (ELISAs), latex agglutination tests (LAT), macroscopic slide agglutination test (MSAT) and an indirect hemagglutination assay (IHA). 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. Thus far, PCR is primarily used for outbreak investigations in humans due to the technical demands of performing the test.

Treatment of Leptospirosis

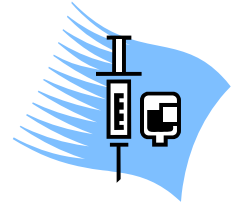


Humans: As in animals, initial therapy in humans must be tailored to the severity of the patient's condition and organ systems involved. Although antimicrobial therapy is currently recommended for treatment of acute human leptospirosis, over the years there has been some debate as to whether or not antimicrobial therapy is effective in these cases. Penicillins have traditionally been used as the first line treatment, but ceftriaxone has been shown to be an effective alternative and has the advantage of being administered only once a day and can be given IM or IV. Doxycycline and cefotaxime have also been shown to be reasonable alternative treatments in one open-label clinical trial. Doxycycline has been used prophylactically 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 some risk of miscarriage; 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 autumnalis. Previously the most common serovars were canicola and icterohemorrhagiae. There are currently vaccines available for dogs for serovars canicola, icterohemorrhagiae, grippotyphosa, and pomona. Newer vaccines are effective at reducing renal colonization and shedding as well as clinical disease, but no vaccine is 100% effective. 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 body fluids.

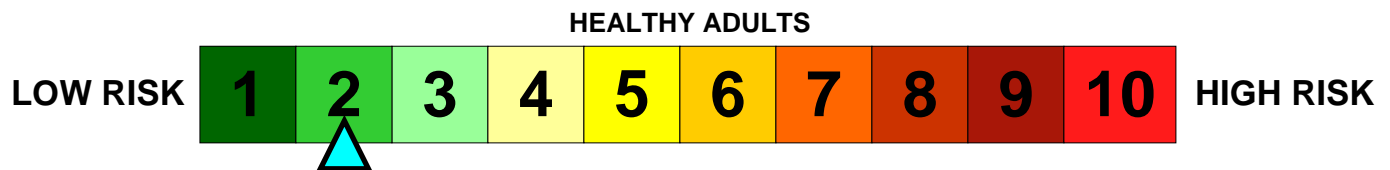
Infected Pets: Once a dog is being treated with an appropriate antimicrobial to help clear the renal carrier state, viable organisms should no longer be shed in the urine. Nonetheless, the animal's urine should be treated as potentially infectious until treatment is complete. If the treatment course is not completed in its entirety, the animal may begin to shed live bacteria in its urine once again. Clean up urine using a household disinfectant or bleach.

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.
- Keep other mammalian pets (e.g. guinea pigs, hamsters, rats, mice) in a secure enclosure that prevents escape and also prevents wild rodents from getting in. Do not allow the pet to roam loose in the house.
- 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:

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:

