

Leptospirosis (Weil's disease)

Leptospirosis is a zoonosis, an infection transmitted to humans from animals. It is an infection of worldwide distribution caused by spirochaetes of the genus *Leptospira*, which infect many species of both wild and domestic animals. In humans, the infection most commonly comes from rats.

Aetiology^[1] ^[2]

- Leptospire are naturally aquatic organisms and are found in fresh water, damp soil, vegetation and mud. Flooding may spread the organism because, as water saturates the soil, leptospire pass directly into surface waters.
- The principal source of human infection is the rat but other sources include dogs, cattle, pigs, and other wild animals.
- Infected animals carry the bacteria in their kidneys, often without becoming unwell. They can excrete leptospire in their urine for some time. The spirochaetes are shed from the urine and can survive in the environment for several months in moist, warm conditions.
- Disease is acquired through contact with contaminated water or soil, or through contact with urine or tissues of infected animals.
- Leptospire enter the bloodstream through abraded skin, mucosal membranes or conjunctiva from contaminated water or soil.
- Water-borne transmission has also been documented.
- Infection occurs as two syndromes: anicteric (which is self-limiting, and may present as a flu-like illness) and icteric leptospirosis (a potentially severe condition also known as Weil's disease).
- It seems that an excessive immune response may cause the more severe form of the disease rather than the infection itself, in particular uncontrolled cytokine production^[3] ^[4].

Epidemiology

- Leptospirosis is uncommon in the UK. In 2017 there were 92 cases reported in the UK^[2].
- It is more common in other areas of the world. The World Health Organization (WHO) reports that it affects 0.1 to 1 per 100,000 people living in temperate climates each year, increasing to 10 or more per 100,000 people living in tropical climates. If there is an epidemic, the incidence can soar to 100 or more per 100,000 people. This may not reflect true figures as the disease is under-reported for a number of reasons, including diagnostic difficulty (it is similar to other endemic diseases) and lack of diagnostic facilities in the affected areas.
- It is said to be the most common zoonotic infection in the world^[5].

Risk factors^[6] ^[7]

Certain occupations and recreational activities expose individuals via direct or indirect animal contact.

- Occupational risk from direct animal contact includes farmers, veterinarians, abattoir workers, rodent control workers, butchers and other occupations with animals.
- Occupational risk from indirect animal contact includes sewage workers, miners, military personnel, fish farm workers, septic tank cleaners, plumbers, construction/demolition/building renovation workers and those working with flood relief. Farmers in tropical areas with high rainfall are particularly at risk, as are rice field workers.
- Recreational activities which may involve risk from indirect contact include swimming in open water, rowing, kayaking/canoeing, sailing, windsurfing, caving, fresh water fishing and diving.

Presentation^[8]

Infection may cause no symptoms, a mild flu-like illness, or a more severe illness with jaundice and acute kidney injury (Weil's disease). The majority of infections in humans result in a mild illness or are asymptomatic^[3]. The incubation period is usually 7-12 days but can range from 3-30 days. Onset is usually abrupt.

Clinical features:

- Leptospiral infection often has minimal or no clinical manifestations.
- Of the cases in which fever develops, as many as 90% present as undifferentiated febrile illnesses^[9].
- Many infections are mild with fever, headache, myalgia, anorexia, nausea and vomiting, dry cough and lethargy. Affected patients may not seek medical attention.
- The headache may be severe, and there may be pain behind the eyes and photophobia.
- There is often conjunctival inflammation. There may also be sub-conjunctival haemorrhages and jaundiced sclera.
- Muscle pain and tenderness most often involves the calves and low back.
- Gastrointestinal symptoms may include nausea, vomiting, diarrhoea and abdominal pain. The gallbladder and/or pancreas may be involved.
- The milder anicteric syndrome can recur several days later, in an immune stage during which aseptic meningitis may occur.
- Approximately 10% of those infected become jaundiced (with hepatocellular necrosis) and have a severe and rapidly progressive form of the disease with liver failure and acute kidney injury^[3]. In this severe form, known as Weil's disease, there is often multiple organ failure. The liver, heart, brain and lungs may be involved.
- Purpura, petechiae, epistaxis, minor haemoptysis and other signs of bleeding are common.
- The jaundice appears during days 5–9 of illness and is most intense 4–5 days later, continuing for about one month.
- The lungs are involved in approximately 70% of cases of leptospirosis^[10]. Pulmonary symptoms vary from cough, dyspnoea, and haemoptysis to adult respiratory distress syndrome and massive pulmonary haemorrhage.
- Kidney dysfunction (leptospiral nephropathy) is usual, sometimes with life-threatening acute kidney injury with signs of uraemia and disturbance of consciousness.

Differential diagnosis

The diagnosis of leptospirosis requires a high degree of clinical suspicion because the disease's numerous manifestations can mimic other tropical infections or other nonspecific febrile illnesses, as well as non-infectious diseases – eg, small-vessel vasculitis, systemic lupus erythematosus or malignancies. Always consider leptospirosis in anybody with flu-like symptoms who has been in contact with rat urine via infected water, or who is in contact with cattle or cattle products.

Possible alternative diagnoses to consider will include:

- [Viral hepatitis](#)
- [Meningitis](#)
- [Influenza](#)
- [Malaria](#)
- [Typhoid fever](#)
- [Yellow fever](#)
- [Relapsing fever](#)
- [Scrub typhus](#)
- [Dengue](#)
- [Legionnaires' disease](#)
- [Toxic shock syndrome](#)

Investigations^[8] ^[9]

The initial diagnosis of leptospirosis is based on clinical features, although it is often misdiagnosed.

Isolation of the organism by culture of clinical specimens (blood, CSF, urine) is difficult. Samples need to be taken during the first 7-10 days of the illness as later on the organisms are only intermittently present in the blood. Specific culture medium is required. Initial growth may be slow and it may take up to three months for a positive culture result. Most cases of leptospirosis are diagnosed by serology testing for specific antibodies. Antibodies are present from about 10 days into the illness. This is, however, not ideal as in parts of the world where leptospirosis is most common there may not be the facility for this type of testing, and also a large percentage of these populations may be antibody positive. Recently real-time polymerase chain reaction (PCR) assays have been found more helpful. These can confirm the diagnosis in the early phase of the disease, before antibody titres are at detectable levels, by identifying leptospiral DNA.

Other investigations may reveal:

- Raised ESR.
- FBC: thrombocytopenia, leukocytosis and anaemia.
- LFTs: increased serum bilirubin, alkaline phosphatase (ALP) and transaminases.
- Prolonged prothrombin time (coagulation times may be elevated in patients with hepatic dysfunction and/or disseminated intravascular coagulation).
- Renal function and electrolyte changes where there is acute kidney injury, starting with raised creatinine. Serum amylase levels are raised in acute kidney injury and may also reflect pancreatic involvement.
- Raised creatine kinase (muscle involvement, rhabdomyolysis).
- MSU usually shows sediment and proteinuria. There may be microscopic haematuria.
- CXR: may be normal or show patchy shadowing in alveolar haemorrhage.
- Lumbar puncture: there may be raised CSF pressure and a predominance of lymphocytes and polymorphs

Management^[8]

Most cases of leptospirosis are mild and resolve spontaneously without treatment and indeed often without being identified.

Antibiotic treatment^[11]

Antibiotic treatment is widely used but a Cochrane review found insufficient evidence to recommend for or against the use of antibiotics for leptospirosis. Use of antibiotics for leptospirosis may decrease the duration of clinical illness by two to four days, although this result was not statistically significant. Selection of penicillin, doxycycline, or cephalosporin did not seem to impact on mortality or the duration of fever. It was therefore concluded that the benefit of antibiotic therapy in the treatment of leptospirosis remains unclear, particularly for severe disease^[12].

Antibiotics therefore may not be used for mild cases in low risk people.

- The first-choice of antibiotic in adults who are not critically ill is usually oral doxycycline or azithromycin, starting within 48 hours of illness.
- Oral amoxicillin and ampicillin are also effective in mild-to-moderate infections. Amoxicillin and azithromycin can be used in children and pregnant women.
- Intravenous penicillin G is the drug of choice for severely ill patients who require hospitalisation. Third-generation cephalosporins (eg, cefotaxime, ceftriaxone) are also widely used for intravenous antibiotic treatment for patients with severe leptospirosis.
- Starting antibiotics can lead to a [Jarisch–Herxheimer reaction](#) which may occur in up to 9% of those treated^[13] ^[14].

Other treatments

- Supportive care and treatment of the hypotension, haemorrhage, acute kidney injury and liver failure.
- Intensive care treatment is usually required for those with the severe form of the disease.

- The use of steroids in patients with leptospirosis has not been well established. However, some reports have shown beneficial effects of glucocorticoids in severe leptospirosis with acute kidney injury and pulmonary haemorrhage but use is controversial.
- Vitamin K is administered for hypoprothrombinaemia.
- Mechanical ventilation may be required where there is pulmonary involvement.
- Immunity to leptospirosis is incomplete and so patients should be advised to adopt lifestyle changes to avoid re-exposure if possible.

Complications

These can include:

- [Acute kidney injury](#). This is one of the most common complications of severe leptospirosis.
- [Thrombocytopenia](#).
- [Liver failure](#). Hepatic dysfunction in most patients, however, is mild and reversible.
- [Disseminated intravascular coagulation](#).
- Gastrointestinal haemorrhage.
- Pulmonary haemorrhage. A particularly serious type of lung involvement (severe pulmonary haemorrhagic syndrome) is a major cause of death in patients with Weil's disease in developing countries.
- [Rhabdomyolysis](#).
- Eye problems – eg, chronic or recurrent [uveitis](#), iridocyclitis, chorioretinitis.
- [Adult respiratory distress syndrome](#).
- [Hypotension](#). Vascular collapse may develop abruptly and can be fatal in the absence of aggressive supportive care.
- Cerebrovascular accident, [subarachnoid haemorrhage](#), cerebral arteritis.

- [Kawasaki disease.](#)
- [Erythema nodosum.](#)
- [Myocarditis.](#)
- Pericarditis
- Coronary arteritis and aortitis.
- Congestive heart failure is rare but nonspecific ECG changes are common.
- [Spontaneous abortion in pregnant women.](#)

Prognosis^[8]

The vast majority of leptospiral infections are self-limiting. However, Weil's disease has a mortality rate of up to 22% in developing countries and around 5% in the UK^[7]. Important causes of death include acute kidney injury, cardiopulmonary failure and widespread haemorrhage. One to three people in England and Wales die every year from leptospirosis^[1].

- Leptospirosis is usually self-limiting. Most cases recover fully within two to six weeks but some may take up to three months.
- Liver and renal dysfunction are usually reversible, with resolution over a period of 1-2 months.
- Death is often caused by gastrointestinal and pulmonary haemorrhage, acute kidney injury and adult respiratory distress syndrome.
- Factors associated with poor prognosis include altered mental status, oliguria, acute kidney injury, respiratory involvement, hypotension and arrhythmia.
- Severe pulmonary hemorrhage syndrome due to extensive alveolar haemorrhage has a fatality rate of over 50%.
- Infection in pregnant women may be grave leading to severe fetal and maternal morbidity and mortality^[15].
- Mortality increases with age.

- After infection, immunity develops against the infecting strain, but this may not fully protect against infection with unrelated strains.

Prevention ^[1] ^[7]

- Public health measures to prevent and reduce leptospirosis include identification of contaminated water sources, rodent control, prohibition of swimming in waters where risk of infection is high and raising risk awareness for those involved in recreational water activities. Reducing rodent populations reduces risk – eg, by clearing rubbish and preventing rodent access into buildings.
- There is no available human vaccine effective against leptospirosis.
- For people who may be at high risk for short periods (eg, occupational risk, high-risk water sports activities in known endemic areas or living or working in areas after natural disasters), taking doxycycline (200 mg weekly) may be effective.
- Immunisation of animals with *Leptospira* vaccines: an animal vaccine is available, and immunising and treating infected animals is worthwhile.
- The risk of infection can be greatly reduced by not swimming or wading in water that might be contaminated with animal urine.

- If there is contact with fresh, surface waters (eg, canals, ponds or rivers) or with rats then advise the person to:
 - If swimming, minimise the swallowing of water.
 - Cover cuts, scratches or sores with a waterproof plaster and thoroughly clean any cuts or abrasions caused during the water activity.
 - Wear appropriate protective clothing, gloves or protective footwear.
 - Wash or shower promptly after water sports.
 - Avoid capsizing or rolling in stagnant or slow-moving water.
 - Wear thick gloves when handling rats.
 - Wash hands after any contact with natural water or after handling any animal, and again before eating.

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Authored by:	Peer Reviewed by: Dr Hannah Gronow, MBACP	
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