Leptospirosis (Weil's Disease)

Leptospirosis is an infection of worldwide distribution caused by spirochaetes of the genus *Leptospira*, which infect many species of both wild and domestic animals.[1]

- Leptospires 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, leptospires pass directly into surface waters.[1]
- 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 leptospires 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.
- They enter the bloodstream through abraded skin or the mucosa from contaminated water or soil.
- Water-borne transmission has also been documented.
- Infection occurs as two syndromes: anicteric (which is self-limiting) and icteric leptospirosis (Weil's disease).

**Epidemiology**

- Leptospirosis is uncommon in the UK with an incidence in England and Wales of about 1 case per million of the population each year.[1]
- Reported to be the most widespread zoonosis in the world (having an incidence greater in tropical areas than in temperate regions).[2]
- However, the reported incidence seems to be underestimated, especially in countries located in the temperate climatic zone.[3]
- A large proportion of the population is antibody-positive in areas such as rural Belize and Vietnam. Leptospirosis is a significant human disease in eastern and southern Europe, Australia and New Zealand.

**Risk factors**[1]

- Occupational risk factors include sewage workers, farmers, veterinarians, abattoir workers, rodent control workers, and other occupations with animals.
- Recreational risk factors include taking part in activities which expose them to natural water, including canals, ponds or rivers, or who have contact with rats.
- Activities in freshwater that can increase the risk include swimming (including participating in triathlons), sailing, water skiing and wind surfing.
- Travelling abroad - eg, swimming in contaminated water.

**Presentation**

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 incubation period is usually 7-21 days but can range from 2-30 days. Onset is usually abrupt.
- Many infections are mild with fever, headache, myalgia, anorexia, nausea and vomiting, dry cough and lethargy. Affected patients may not seek medical attention.
- The anicteric form may cause pneumonitis, arthritis, orchitis, cholecystitis, myocarditis, coronary arteritis, aortitis, aseptic meningitis and uveitis.
The flu-like illness may resolve without treatment but, in some cases, an immune phase follows with a return of fever, jaundice, red eyes, abdominal pain, diarrhoea, or a rash. In more severe cases, there may be organ failure (eg, the kidneys) or meningitis.

- 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.\(^4\)
- 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.
- The jaundice appears during days 5-9 of illness and is most intense 4-5 days later, continuing for about one month.
- Purpura, petechiae, epistaxis, minor haemoptysis and other signs of bleeding are common.
- Other symptoms include fever, vomiting, abdominal pain, skin rashes, conjunctival haemorrhage, and uveitis. There is often a severe headache, retro-orbital pain, and photophobia. A severe myalgia (lower back, and legs) is common. Leptospirosis may present as aseptic meningitis.
- The lungs are involved in approximately 70% of cases of leptospirosis.\(^5\) Pulmonary symptoms vary from cough, dyspnoea, and haemoptysis to adult respiratory distress syndrome and massive pulmonary haemorrhage.
- Hepatomegaly.
- 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.\(^2\)

Possible alternative diagnoses to consider will include:

- Viral hepatitis
- Meningitis
- Influenza
- Malaria
- Typhoid fever
- Yellow fever
- Relapsing fever
- Scrub typhus
- Dengue fever
- Legionnaires' disease
- Toxic shock syndrome

**Investigations**

The initial diagnosis of leptospirosis is based on clinical features. Initial blood tests may show raised ESR, peripheral leukocytosis, variable degrees of cytopenias, mildly increased aminotransferases and increased serum bilirubin and alkaline phosphatase (ALP).\(^2\)

Isolation of the organism by culture of clinical specimens (blood, CSF, urine) during the first 7-10 days of the illness is difficult, requires longer than 16 weeks because initial growth may be slow and has a low sensitivity and specificity. Most cases of leptospirosis are diagnosed by serology testing.\(^2\)

- LFTs: increased serum bilirubin, transaminases.
- Prolonged prothrombin time (coagulation times may be elevated in patients with hepatic dysfunction and/or disseminated intravascular coagulation).
- FBC: thrombocytopenia, leucocytosis and anaemia.
- Renal function and electrolytes (acute kidney injury); serum amylase levels are raised in acute kidney injury.
- Raised creatine kinase (muscle involvement, rhabdomyolysis).
- MSU usually shows sediment and proteinuria.
- CXR: may be normal or show patchy shadowing in alveolar haemorrhage.
Serology. Diagnosis is usually performed by serology; enzyme-linked immunosorbent assay and the microscopic agglutination tests are the laboratory methods generally used. Limitation of serology is that antibodies are lacking at the acute phase of the disease. In recent years, several real-time polymerase chain reaction assays have been described. These can confirm the diagnosis in the early phase of the disease, before antibody titres are at detectable levels.

Management

Antibiotic treatment

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.

- First-choice drug is oral doxycycline, starting within 48 hours of illness (starting antibiotics can lead to a Jarisch-Herxheimer reaction).
- Oral amoxicillin, ampicillin and doxycycline are effective in mild-to-moderate infections.
- Intravenous penicillin G is the drug of choice for severely ill patients.
- Third-generation cephalosporins (e.g., cefotaxime, ceftriaxone are now widely used for intravenous antibiotic treatment for patients with severe leptospirosis.

Other treatments

- Supportive care and treatment of the hypotension, haemorrhage, acute kidney injury and liver failure.
- 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 pulmonary haemorrhage, thrombocytopenia and acute kidney injury.
- Vitamin K should be administered for hypoprothrombinaemia.
- Immunity to leptospirosis is incomplete and so patients should be advised to adopt lifestyle changes to avoid re-exposure if possible.

Complications

Acute kidney injury is one of the most common complications of severe leptospirosis. 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, with profuse lung haemorrhage. Hepatic dysfunction is usually mild and reversible. Variable degrees of thrombocytopenia have been reported with leptospirosis.

- Spontaneous abortion in pregnant women.
- Acute kidney injury.
- Thrombocytopenia.
- Liver failure.
- Disseminated intravascular coagulation.
- Gastrointestinal haemorrhage.
- Pulmonary haemorrhage.
- 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.
- Congestive heart failure is rare but nonspecific ECG changes are common.
Prognosis

The vast majority of leptospiral infections are self-limiting. However, Weil's disease has a mortality rate of 5-10%. Important causes of death include acute kidney injury, cardiopulmonary failure and widespread haemorrhage.\[^2\]\ Two 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.
- Leptospirosis with jaundice is fatal in 5-15%. Death is often caused by gastrointestinal and pulmonary haemorrhage, acute kidney injury and adult respiratory distress syndrome.
- Infection in pregnant women may be grave leading to severe fetal and maternal morbidity and mortality.\[^10\]
- Mortality is increased in the elderly.
- After infection, immunity develops against the infecting strain, but this may not fully protect against infection with unrelated strains.

Prevention\[^1\]

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 informing persons of the risk involved in recreational water activities.\[^2\]

- 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.
- Reduce rodent populations - eg, by clearing rubbish and preventing rodent access into buildings.
- 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 capsize drill 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.

Further reading & references

1. Leptospirosis; Public Health England

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