**Leptospirosis**

**Synonyms**
It is known by many names such as Weil’s syndrome, Swamp fever, Mud fever, Autumn fever, Swineherd’s disease, Rice-field fever, Cane-cutter’s fever, Hemorrhagic jaundice, Stuttgart disease, Canicola fever, Red water of calves

**Etiology**
Leptospirosis is caused by various species of Leptospira, a spirochete in the family Leptospiraceae, order Spirochaetales. The classification of this organism is complex. Before 1989, all of the pathogenic isolates belonged to the species Leptospira interrogans, which contained more than 200 serovars in 23 serogroups. More recently, the genus Leptospira has been reclassified into 16 or more species. Pathogenic serovars are now found in the species Leptospira interrogans, L. noguchii, L. santarosai, L. meyeri, L. borgpetersenii, L. kirschneri, L. weilii, L. inadai, L. fainei and L. alexanderi. The new classification system can be confusing because both pathogenic and non-pathogenic serovars and serogroups occur in the same species and a single serovar or serogroup can occur within multiple species. In clinical laboratories, the older serogroup/serovar classification is often still used.

**Geographic Distribution**
Leptospira species are found worldwide; however, the predominant serovars vary by geographic region. The most common serovars in the United States are L.canicola, grippotyphosa, hardjo, icterohaemorrhagiae & pomona.

**Transmission**
Leptospirosis can be transmitted either directly between hosts or indirectly from contaminated the environment. Leptospira spp. can be ingested as contaminated food or water, spread by aerosolized urine or water, or transmitted by direct contact with the skin. The organisms usually enter the body through mucous membranes or abraded skin. They may also penetrate intact skin that has been immersed for a long time in water. Leptospira spp. are excreted in the urine, and can be found in aborted or stillborn fetuses, as well as in normal fetuses or vaginal discharges after calving. They can be isolated from the male reproductive organs. Human cases have rarely been transmitted by breast feeding, from rodent bites, and after laboratory accidents. Leptospira spp. do not multiply outside the host. In the environment, they require high humidity for survival and are killed by dehydration or temperatures greater than 50°C. They can remain viable for a few to many weeks or months in contaminated soil and for several weeks in cattle slurry. They can remain viable in water for several months under laboratory conditions, but do not survive as well in river water under natural conditions. They do not survive in the saline sea water.

**Disinfection**
Leptospira species can be inactivated by 1% sodium hypochlorite, 70% ethanol, glutaraldehyde, formaldehyde, detergents and acid. This organism is sensitive to moist heat (60°C for a minimum of 15 min) and is also killed by pasteurization.

**Human Infection**
The incubation period in humans is usually 7 days to 12 days, with a range of 2 to 29 days.

**Clinical Signs**
Human infections vary from asymptomatic to severe. Many cases are mild or asymptomatic, and go unrecognized. Some serovars tend to be associated more often with some syndromes (e.g., severe disease is often associated with serovar icterohaemorrhagiae). However, any serovar can cause any type of syndrome. In humans, leptospirosis is usually a biphasic illness. The first phase, called the acute or Leptospiremic phase, usually begins abruptly and lasts approximately a week. This phase is characterized by nonspecific signs including fever, chills, headache and conjunctival suffusion. Myalgia, which typically affects the back, thighs or calves, is often severe. Occasionally, a transient skin rash occurs. Other symptoms may include weakness, photophobia, lymphadenopathy, abdominal pain, nausea, vomiting, a sore throat, cough, chest pain and hemoptyisis. Mental confusion, neck stiffness and other signs of aseptic meningitis have been reported in this phase. Jaundice can be seen in more severe infections. These symptoms last for approximately 4 to 9 days, and then are typically followed by a 1 to 3 day period during which the temperature drops and
the symptoms abate or disappear. The second phase of leptospirosis, called the **Immune phase**, is characterized by the development of anti-Leptospira antibodies, and the excretion of the organisms in the urine. This phase can last up to 30 days or more, but does not develop in all patients. During the immune phase, the patient becomes ill again. Nonspecific symptoms seen in the first stage, such as fever and myalgia, recur but may be less severe than in the first stage of disease. Two forms of disease, **icteric and anicteric**, are seen. Most infections are of the anicteric form. The most important symptoms in this form are associated with aseptic meningitis. A severe headache, stiff neck and other meningeal symptoms occur in approximately half of all patients, and usually last a few days. Occasionally, these signs may be present for up to two weeks. Less common symptoms include cranial nerve palsies, encephalitis, confusion and changes in consciousness. Deaths are rare in the typical anicteric form; however, a syndrome of fatal pulmonary hemorrhage, without jaundice, has recently been reported. The icteric form is more severe. It occurs in 5-10% of all patients, is often rapidly progressive, and may be associated with multiorgan failure. The most commonly involved organ systems are the liver, kidneys and central nervous system. In the icteric form, there may be no period of improvement between the septicemic and immune phases. Jaundice can be severe and may give the skin an orange tone, but it is not usually associated with severe hepatic necrosis. Acute renal failure occurs in 16-40% of cases. Some patients also have pulmonary symptoms, with clinical signs ranging from cough, dyspnea, chest pain, and mild to severe hemoptysis, to adult respiratory distress syndrome. Cardiac involvement can result in congestive heart failure, myocarditis and pericarditis. Hemorrhages may also be seen; epistaxis, petechiae, purpura and ecchymoses are the most common signs, but severe gastro-intestinal bleeding, adrenal or subarachnoid hemorrhage, and pulmonary hemorrhages can occur. Rare complications include stroke, rhabdomyolysis, thrombotic thromboocytopenic purpura, acute acalculous cholecystitis, erythema nodosum, aortic stenosis, Kawasaki syndrome, reactive arthritis, epididymitis, nerve palsy, male hypogonadism, Guillain-Barre’ syndrome and cerebral arteritis. Deaths can occur from kidney failure, cardiac involvement, pulmonary hemorrhage or other serious organ dysfunction. Convalescence from the icteric form may take 1-2 months. Although jaundice can persist for weeks, liver function returns to normal after recovery, and hepatic disease is rarely the cause of death. Most patients also recover kidney function. Anterior uveitis occurs up to a year after recovery in 10% of cases. Most of these patients recover full vision. Iridocyclitis and chorioretinitis can also be complications, and may persist for years. Abortions, fetal death, and rare congenital infections in newborns have been reported. Abortions can occur at any time, including the convalescent period.

**Morbidity and Mortality**

Leptospirosis is thought to be underdiagnosed and underreported since many cases are mild or asymptomatic and self-limiting. The incidence of infection is seasonal, with most cases seen during in the summer and fall in temperate regions. In tropical climates, the peak incidence occurs during the rainy season. Large outbreaks have been seen after floods. Occupational exposure is thought to be responsible for 30-50% of cases. Occupations with a high risk of infection include sewer workers, coal miners, plumbers, farm workers, veterinarians, pet shop owners, abattoir workers, meat handlers, slaughterhouse workers, workers in the fishing industry, and the military. From 8-29% of those who work with livestock have antibodies to Leptospira. Recreational activities that increase the risk of leptospirosis include gardening and water sports such as canoeing, swimming and white-water rafting. Residents of some urban areas are exposed via rat urine. Most cases of leptospirosis are asymptomatic or mild. The overall case fatality rate is 1-5%. The mortality rate varies with the form, and is higher in the elderly. The anicteric form is rarely fatal. The icteric form, which occurs in 5-10% of all patients, has an overall mortality rate of 5-15% and a 54% case fatality rate in severe cases with myocardial involvement. Most patients with kidney failure, hepatic disease or anterior uveitis eventually recover kidney or liver function, and full vision.

**Communicability**

Direct person-to-person transmission is very rare. Leptospira organisms are found in the urine during the second (immune) phase of the disease. Most people excrete these bacteria for 60 days or less, but
shedding for months or years have been documented. Other routes of transmission are also very rarely possible.

**Diagnostic Tests**

Leptospirosis can be diagnosed by culture, detection of antigens or nucleic acids, or serology. Serum chemistry values and analysis of the CSF may support the diagnosis. In humans, Leptospira can be isolated from the blood, cerebrospinal fluid or urine. **Culture** can be difficult and may require up to 13 to 26 weeks. Identification of the species, serogroup and serovar level is done by reference laboratories, using genetic and immunologic techniques. Leptospira spp. can also be identified in clinical samples by immunofluorescence and immune histochemical staining, as well as DNA probes and polymerase chain reaction (PCR) techniques. Dark field microscopy can be used but is not specific. Most human cases of leptospirosis are diagnosed by serology. The most commonly used serologic tests are the ELISA and the microscopic agglutination test (MAT), previously known as the agglutination-lysis test. The MAT test is serogroup specific but not serovar specific, and can be complicated by cross reactions. Less commonly used tests include complement fixation, radioimmuno assay, immunofluorescence, counter immune electrophoresis and thin layer immunossay. The macroscopic slide agglutination test (SAT) may be used for a presumptive diagnosis, but is not specific. A high titer with consistent symptoms is suggestive of an acute case, but a rising titer is necessary for a definitive diagnosis. Few serovar specific assays are available in human medicine.

**Treatment**

Severe leptospirosis is treated with antibiotics. The use of antibiotics for the mild form of disease is controversial, and the research is still inconclusive. Antibiotics used in humans include doxycycline, ampicillin, amoxicillin, penicillin and erythromycin. The milder form of Leptospirosis is treated by oral antibiotic given for 7 to 10 days. Doxycycline as 100mg b.i.d is the drug of choice. Ampicillin or Amoxicillin can be given as 500 mg q.i.d. In severe cases, treatment is with intravenous antibiotics. Inj. Benzyl Penicillin 20 lakhs sixth hourly is the first line drug of choice. Inj. Ampicillin 1 g q.i.d or Ceftriaxone 1 g o.d or Cefotaxime 1g t.i.d may also be given with equivalent efficacy. An acute reaction occurs in some patients with in a few hours of starting the antibiotic treatment. This, termed the Jarisch Herxheimer Reaction, is a short-term (a few days to weeks) detoxification reaction in the body. As the body detoxifies the bacterial products, it is not uncommon to experience flu-like symptoms including headache, joint and muscle pain, body aches, sore throat, general malaise, sweating, chills, nausea or other symptoms. This is a normal and even healthy reaction that indicates that the bacteria or other pathogens are being effectively killed off. The biggest problem with this Herxheimer reaction is that people stop taking the medication and thus discontinue the very treatment that is helping to make them better. Supportive treatment and management of complications such as renal failure, hepatic complications, hemorrhages, fluid balance and CNS disturbances may also be necessary.

**Prevention**

The control of infections in livestock and pets reduces the risk of human disease, but the existence of wildlife reservoirs complicates prevention. Rodent control can be important in preventing human infections, particularly in urban areas. Avoidance of contact with contaminated or potentially contaminated water bodies can decrease the risk of infection. Domestic animals should not be allowed to urinate in water that humans contact. Draining wet areas may also decrease the incidence of disease. Food should also be protected from sources of infection. Personal hygiene and protective clothing, proper foot ware are important preventative measures in high risk occupations. Gloves and face shields can help prevent infections when working with infected animals or tissues. Rubber boots can decrease the risk of infection in sewer workers and agricultural workers who may wade in urine-contaminated water. Human vaccines are available for workers in high risk professions in some countries but are not very useful. Immunization is relatively serovar specific, and protects only against the serovar(s) in the vaccine or closely related serovars. Yearly vaccination is required and side effects, including painful swelling, can be seen. Doxycycline has been used for short term prophylaxis.

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