

Pan American Health Organization

Area of Health Surveillance and Disease Prevention and Control

International Health Regulations/Alert and Response and Epidemic Diseases

Leptospirosis – Fact Sheet

Brief description

Leptospirosis is a zoonotic disease with epidemic potential, especially after a heavy rainfall, caused by a bacterium called *Leptospira*. *Leptospira interrogans* is pathogenic to humans and animals, with more than 200 serologic variants or serovars. Humans usually acquire leptospirosis through direct contact with the urine of infected animals or a urine-contaminated environment. Human-to-human transmission occurs only very rarely. Leptospirosis may present with a wide variety of clinical manifestations, from a mild illness that may progress to a serious and sometimes fatal disease. Its symptoms may mimic many diseases, such as influenza, dengue and other viral haemorrhagic diseases; making the correct diagnosis (clinical and laboratory) at the onset of symptoms is important to prevent severe cases and save lives, primarily in outbreak situations.

:: Reference [WHO](#) (pages V; 1-3; 47-50)

Epidemiological situation

Leptospirosis occurs worldwide but is endemic mainly in countries with humid subtropical and tropical climates. Estimates indicate that there are more than 500,000 cases of leptospirosis each year worldwide. Leptospirosis is a disease of epidemic potential, especially after heavy rainfall or flooding. Cases have been reported in most countries of the Americas and outbreaks have been reported in Brazil, Nicaragua, Guyana and several other Latin American countries. The majority of reported cases have severe manifestations, for which mortality is greater than 10%. The number of human cases is not known precisely due to under- or misdiagnosis. Outbreaks can be associated with floods and hurricanes. Leptospirosis can also be an occupational hazard for people who work outdoors or with animals, such as rice and sugar-cane field workers, farmers, sewer workers, veterinarians, dairy workers, and military personnel. It is also a recreational hazard to those who swim or wade in contaminated water. Leptospirosis is a problem of human and veterinary public health. The numerous *Leptospira* strains can establish infections within a variety of animal hosts that includes rodents, livestock, and other domestic animals while humans serve as incidental hosts. Wild and domestic animals in the carrier state may shed leptospires intermittently for many years or even a lifetime.

:: Reference [WHO](#) (pages 21-22; 37; 81); [WHO\(a\)](#) (pages 9-11); [FAO](#) (pages 30-34; in Spanish)

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Leptospirosis in humans

- *Clinical diagnosis*
 - Typically, the disease presents in four broad clinical categories:
 - I. A mild, influenza-like illness
 - II. Weil's syndrome characterized by jaundice, renal failure, haemorrhage and myocarditis with arrhythmias
 - III. Meningitis/meningoencephalitis
 - IV. Pulmonary haemorrhage with respiratory failure
 - Of the many symptoms the most common clinical features of leptospirosis include fever, headache, myalgia (particularly in the calf muscle), conjunctival suffusion, jaundice, general malaise in addition to other symptoms/signs
 - Incubation period: 5-14 days, with a range of 2-30 days
 - Symptoms are easily confused with other common diseases in the tropics, such as dengue and other hemorrhagic fevers
 - The diagnosis of leptospirosis should be considered in any patient presenting with an abrupt onset of fever, chills, conjunctival suffusion, headache, myalgia and jaundice
 - History of occupational or recreational exposure to infected animals or to an environment potentially contaminated with animal urine

:: Reference [WHO \(pages 5-8; 47-50\)](#)

- *Differential diagnosis*

The following diseases should be considered in the differential diagnosis of leptospirosis: influenza, dengue and dengue hemorrhagic fever, hanta virus infection, yellow fever and other viral hemorrhagic fevers, rickettsiosis, borreliosis, brucellosis, malaria, pyelonephritis, aseptic meningitis, chemical poisoning, food poisoning, typhoid fever and other enteric fevers, viral hepatitis, pyrexia of unknown origin, primary HIV seroconversion, legionnaire's disease, toxoplasmosis, infectious mononucleosis, pharyngitis.

:: Reference [WHO \(page 47\)](#)

- *Laboratory testing for confirmation:*

Diagnosis is usually based on serology in conjunction with the clinical presentation and epidemiological data (a history of possible exposure, presence of risk factors). The microscopic agglutination test (MAT) and the enzyme linked immunosorbent assay (ELISA) are two serologic tests used for laboratory diagnosis of leptospirosis. In order to obtain a positive diagnosis using the gold standard MAT, a minimum of two serum samples taken at intervals of about 10 days

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apart, must be compared to observe a four-fold or greater rise in antibody titer. Isolation of leptospire from blood, urine or other clinical materials can be achieved through culture, and detection by polymerase chain reaction (PCR) and immuno staining techniques may be available in some centers. Isolation of leptospire is the only direct and definitive proof of infection. For postmortem diagnosis, in addition to serology and culture, leptospire can be detected in tissues using PCR or immunohistochemical staining, especially by direct immunofluorescence.

:: Reference [WHO](#) (pages 11-16; 69)

▪ *Collection and transportation of samples:*

○ Serology (MAT, ELISA)

MAT

- Sample: Minimum of two clotted blood or serum specimens
- Container: Regular sterile tube
- When to collect sample:
 - First sample: About 10-12 days after the onset of clinical symptoms
 - Second sample: About 10 days after the first sample
- Storage and transportation of samples:
 - In order to separate serum from blood, drawn blood must be stored at room temperature for at least 30 minutes for complete clot formation
 - Serum must be separated from the clotted blood by centrifugation within 60 minutes of sample collection to prevent hemolysis
 - After centrifugation is complete, serum (supernatant) must be decanted using sterile technique into plastic freezing vials
 - Serum should be stored at 4 °C for short term and at -20 °C for long time periods
 - Serum must be transported at 0 °C to 4 °C

:: Reference [WHO](#) (pages 2-3; 9-14; 63-66); [CDC](#) (Appendix 1)

ELISA

- Sample: Clotted blood or serum specimen
- Container: Regular sterile tube
- When to collect sample: Between 6-8 days after the onset of the first clinical symptoms
- Storage and transportation of samples:
 - In order to separate serum from blood, drawn blood must be stored at room temperature for at least 30 minutes for complete clot formation
 - Serum must be separated from the clotted blood by centrifugation within 60 minutes of sample collection to prevent hemolysis

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- After centrifugation is complete, serum (supernatant) must be decanted using sterile technique into plastic freezing vials
- Serum should be stored at 4 °C for short term and at -20 °C for long time periods
- Serum must be transported at 0 °C to 4 °C

:: Reference [WHO \(pages 2-3; 9-14; 66-69\)](#); [CDC \(Appendix 1\)](#)

Culture

- Sample: Blood
- Container: Sterile tube with heparin - blood should be collected using aseptic technique
- When to collect sample: Within the **first 10 days** after the onset of disease (leptospire disappear from the blood after that), and before the administration of antibiotics
- Storage and transportation of samples:
 - Samples for culture should be stored and transported at ambient temperatures, since low temperatures are detrimental to pathogenic leptospire
 - Ideally, blood is inoculated at the bedside into blood culture bottles containing culture medium for *Leptospira*

:: Reference [WHO \(pages 9; 81\)](#)

- Sample: Urine
- Container: Sterile container
- When to collect sample: 7 days after the onset of clinical symptoms
- Storage and transportation of samples: Samples should be inoculated into an appropriate culture medium not more than 2 hours after voiding (leptospire die quickly in urine)

:: Reference [WHO \(pages 9; 81\)](#)

- Sample: Postmortem tissues (e.g. brain, cerebrospinal fluid, aqueous humour, lungs, kidney, liver, pancreas and heart, as well as heart blood, if possible)
- Container: Sterile container or tube containing culture medium
- When to collect sample: Postmortem samples should be collected aseptically and as soon as possible after death; they should also be inoculated into culture medium as soon as possible
- Storage and transportation of samples: Postmortem samples should be stored and transported at +4 °C to prevent the autolysis of cells

:: Reference [WHO \(pages 9-10; 81\)](#)

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▪ *Treatment:*

- Initiate antibiotic therapy as soon as possible (preferably before the fifth day after the onset of illness) for suspected cases
- Less severe cases can be treated with oral antibiotics such as amoxicillin, ampicillin, doxycycline or erythromycin; third-generation cephalosporins (ceftriaxone and cefotaxime) and quinolone antibiotics also appear to be effective
- Severe cases (icterohaemorrhagic and/or pulmonary) of leptospirosis should be treated with high doses of intravenous penicillin (1.5 million U/IV every 6 hours), or ceftriaxone (1g/IV per day), or ampicillin (1g/IV every 6 hours), for 7 days. Hospitalization and supportive care with strict attention to fluid and electrolyte balance is also necessary. Peritoneal or haemodialysis is indicated in renal failure
- Jarisch-Herxheimer reactions may occur after penicillin treatment
- Clinicians should never wait for the results of laboratory tests before starting treatment with antibiotics because serological tests do not become positive until about a week after the onset of illness, and cultures may not become positive for several weeks
- Prophylaxis: During high-risk situations, a doctor may prescribe doxycycline 200mg/by mouth once a week as prophylaxis to specific groups, while the risk of infection remains

:: Reference [WHO \(pages 6-7\)](#); [OPS \(page 112; in Spanish\)](#); [APHA \(pages 306-309\)](#)

Intersectoral coordination and control measures

Measures for intervention and control of leptospirosis require the coordination of the public health, animal health and environmental authorities. The approach differs depending if there is an outbreak due to a natural disaster (flooding or heavy rainfall) that results in many human leptospirosis cases or if the situation concerns an endemic area where sporadic transmission occurs.

In the event of natural disasters it is important to save lives by providing timely medical care at the local level for suspected cases. A thorough field investigation is also required to identify which animal species are the source of infection, as well as survey the area to better understand the disease and possible prevention and control measures.

Given the large number of pathogenic serovars, numerous potential sources of infection, and variety of transmission conditions, the control of leptospirosis will involve a complex strategy that will depend on the local conditions. Raising awareness of the risk areas, risk groups for infection, as well as local drivers is essential when considering preventive measures.

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- *Intervention at the source of infection (reservoir host/carrier):*
 - Determine what animal species are the infection sources and direct control measures to target to the local reservoir
 - Separate animal reservoirs from human dwellings through fences and screens
 - Control animal hygiene and perform surveillance using serological diagnosis on a subset of the animal population
 - Immunize dogs and livestock annually
 - Establish rodent control (poisoning, trapping, avoiding access to food and drinking water, separation of human habitation)
 - Removing litter and maintaining cleanliness in the areas surrounding human dwellings; motivating people to not leave open food containers
 - Maintain cleanliness of areas surrounding human dwellings through the removal of litter and by motivating people to not leave open food containers

- *Intervention at the transmission route*
 - Risk of infection is minimized by avoiding contact with animal urine, infected animals or a contaminated environment
 - Transmission can be prevented by: wearing protective clothing; covering skin abrasions with waterproof dressings; washing or showering after exposure to urine splashes and contaminated soil or water; washing and cleaning wounds; developing awareness of potential risks and methods of preventing and minimizing exposure; providing clean drinking-water; avoiding bodies of water known or suspected to be contaminated (pools, rivers, lakes); establishing standard safety procedures for laboratories; introducing good herd management; disinfecting contaminated areas if feasible

- *Intervention at the level of the human host*
 - Raising awareness in the general population and at-risk groups; providing antibiotic prophylaxis in specific cases; providing immunization in countries where vaccines are available; educating physicians and the community; disseminating outbreak control information through press releases, radio and television announcements

:: Reference [WHO \(pages 23-24; 37-40\)](#)

- *Laboratory testing for confirmation in animals*
 - Serological testing (MAT, ELISA) is the laboratory method most frequently used to confirm clinical diagnosis, to determine herd prevalence and to conduct epidemiological studies

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- The microscopic agglutination test (MAT), the standard serological test, is used to diagnose individual animals and herds. The MAT is very useful for diagnosing acute infection in animals: a positive result is indicated by a four-fold or greater rise in antibody titer in paired acute and convalescent serum samples. To obtain useful information from a herd of animals, at least ten animals, or 10% of the herd, whichever is greater, should be tested and the vaccination history of the animals documented (tissue culture and body fluids included)
- The enzyme-linked immunosorbent assay (ELISA) can also be useful for detection of antibodies against leptospire. Numerous assays have been developed and are primarily used for the detection of recent infections. Animals that have been vaccinated against the serovar of interest may be positive in some ELISA, thus complicating interpretation of the results.

:: Reference: [OIE \(pages 251-255\)](#)

▪ *Laboratory testing to identify circulating strains*

- Typing of isolates may give an indication of the sources of infection and reservoirs, and thus determine the choice of methods for eventual prevention and control
- A method that allows rapid typing of the most common isolates can be used to identify strains circulating in an area. Typing of uncommon and unusual strains should be sent to a reference center
- Whatever typing method is used, comparison with reference strains will be needed. Local isolates may exhibit unique characteristics which differ from those of reference strains. Observation of differences between reference strains and local isolates is important, both from an epidemiological perspective and in defining the particular features that will enable local strains to be identified

:: Reference [WHO \(pages 19-20\)](#)

▪ *Identification of the agent and collection of samples in animals:*

- Leptospire in the internal organs and body fluids of clinically infected animals gives a definitive diagnosis of acute clinical disease. In the case of a fetus, leptospire in the above indicate chronic infection of the mother
- Leptospire in the kidney, urine or genital tract of animals without clinical signs help determine the animal's chronic carrier state
- The identification of leptospire in the blood and milk of animals showing clinical signs is considered to be diagnostic. Isolation of leptospire from blood is not always successful because of the transient nature of bacteremia and the fact that it is not always accompanied by clinical signs. Identification of leptospire in blood is further diminished when the animal has been treated with antibiotics
- The demonstration of leptospiral infection in organs taken at necropsy is diagnostic. If the animal has lived long enough or has been treated with antibiotics (thus making

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- it more difficult to identify leptospire in necrotic organs), then immunohistochemistry can be particularly useful in identifying residual leptospiral antigen
- Failing to demonstrate leptospire in the urine of an animal does not rule out the possibility of the animal being a chronic renal carrier

:: Reference: [OIE \(pages 251-255\)](#)

Communication and education

- Both the medical community and the general public need to be informed of the risk of the disease, especially after a hurricane or flood since leptospirosis outbreaks are very common. For this reason there are risk communication guidelines (WHO: Outbreak Communication Planning Guide)
- Physicians and health care providers should be informed about the symptoms of leptospirosis, risk factors, diagnostic testing and therapeutic strategies
- Widespread community education can greatly assist in the identification of risk factors, prevention of illness, and reduction of the duration of the disease and its severity through early recognition of suspicious symptoms

:: Reference [WHO \(pages 39-40\)](#)

References and links for Leptospirosis

:: WHO: Human Leptospirosis: Guidance for Diagnosis, Surveillance and Control:

http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=19120&Itemid=2518&lang=en

:: WHO(a): Report of the First Meeting of the Leptospirosis Burden Epidemiology Reference Group:

http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=19162&Itemid=2518&lang=en

:: WHO(b): Report of the Second Meeting of the Leptospirosis Burden Epidemiology Reference Group:

http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=19163&Itemid=2518&lang=en

:: FAO: Zoonosis en los sistemas de producción animal de las áreas urbanas y periurbanas de América Latina:

http://www.fao.org/AG/AGAInfo/resources/en/publications/sector_discuss/PP_Nr2_Final.pdf

:: OIE: Leptospirosis Manual:

http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.09_LEPTO.pdf

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:: WHO(c): World Health Organization Outbreak Communication Planning Guide:
http://www.searo.who.int/LinkFiles/CDS_WHO_Outbreak_Comm_Planning_Guide.pdf

:: PAHO: Rodents in Disasters: http://www.paho.org/english/dd/ped/te_rdes.htm

:: OPS. Tratamiento de las Enfermedades Infecciosas 2011-2012, 5ª ed. Washington, D.C. OPS. 2011.

:: American Public Health Association (APHA). Control of Communicable Diseases Manual: 18th Edition. Washington D.C.: APHA; 2004.

:: CDC: Emergency Preparedness and Response - Information for Clinical and Laboratory Support for Diagnosis, Management and Treatment of Leptospirosis in the Aftermath of a Disaster: <http://www.bt.cdc.gov/disasters/disease/leptoclin.asp>