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## Leptospirosis

### Overview<sup>1, 2, 3, 5, 7</sup>

Leptospirosis is caused by infection with pathogenic spirochetes of the genus *Leptospira*. There are currently 21 named *Leptospira* species, including pathogens, nonpathogenic saprophytes, and species of indeterminate pathogenicity. - It is one of the most widespread zoonotic diseases in the world. After removal from the list of nationally notifiable human conditions in the United States in 1994, it was reinstated beginning in 2013.


Most cases of leptospirosis occur in tropical climates with peak incidence occurring in the rainy season, but cases can occur in other places with a seasonal distribution occurring in the late summer and early fall months in temperate regions. The disease is maintained in nature by chronic renal infection of animals, which excrete the organism in their urine, contaminating the environment. The source of human infection is either by direct or indirect contact with urine or other body fluids (except saliva) from infected animals, infected animal tissues, or more commonly by indirect exposure to *Leptospira* in damp soil or water. *Leptospira* bacteria can survive in damp soil and water for weeks to months. The bacteria can enter the body through skin or mucous membranes (eyes, nose, or mouth), especially if the skin is broken from a cut or scratch. Drinking contaminated water or eating contaminated food can also cause infection.

Animal reservoirs include rodents (particularly rats), swine, cattle, raccoons, and marine mammals, while dogs, horses, and other mammals may become infected and shed bacteria through urine with or without clinical disease. People at highest risk for leptospirosis are those with occupational exposure, such as working in slaughter houses, sewers, mines, agriculture settings, military personnel, veterinarians and animal caretakers. Those with recreational (such as adventure racing and triathlons) or situational (such as during flooding or following heavy rainfall) exposure to contaminated bodies of water are also at increased risk. Human-to-human transmission of *Leptospira* bacteria is very rare.

The incubation period is typically 5 to 14 days with a range of 2 to 30 days.<sup>1, 2</sup> In humans, leptospirosis is most often self-limiting without any clinical signs (in approximately 90% of patients). If disease develops, it can be fatal and presents among four clinical categories:

- Acute febrile illness similar to influenza.
- Weil's syndrome with jaundice, renal failure, hemorrhage, and cardiac complications.
- Meningitis or meningoencephalitis.
- Leptospirosis Associated Pulmonary Hemorrhagic Syndrome.

Clinical illness can be mono- or biphasic.<sup>2</sup> The acute (leptospiemic) phase typically occurs during the first week of illness and is characterized by the abrupt onset of high fever, myalgia, and headache. Other acute symptoms can include nausea, vomiting, abdominal pain, diarrhea, cough, photophobia, chills, and a truncal or pretibial rash. Some patients also have redness (suffusion) of the conjunctiva observed with sclera icterus is a pathognomonic finding for leptospirosis and occurs in about 30% of patients. The second (immune) phase is unresponsive to antibiotics and is characterized by prolonged fever and systemic complications such as jaundice, renal failure, bleeding, respiratory insufficiency, hypotension, myocarditis, meningitis,

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mental confusion and depression. It is estimated that between 5 and 10% of clinical infections progress to severe illness. Case-fatality rates are estimated to be from 5-15% in patients with severe disease, and up to more than 50% in those with pulmonary hemorrhage syndrome. Leptospirosis cases are often under-recognized or mistaken for other diseases (e.g., dengue, malaria, aseptic meningitis, encephalitis, and influenza) due to initial non-specific presentation. During pregnancy, infections can result in fetal death, abortion, stillbirth, or congenital infection. Leptospirosis is treated with antibiotics, such as doxycycline or penicillin, which should be given as early in the course of the disease as suspicion allows.<sup>3</sup> Intravenous antibiotics may be required for persons with more severe symptoms.

The risk of acquiring leptospirosis can be greatly reduced by not swimming or wading in water that might be contaminated with animal urine, or eliminating contact with potentially infected animals. Protective clothing and footwear should be worn by those exposed to contaminated water or soil because of their job or recreational activities.

For a complete description of leptospirosis, refer to the following sources:

- *Control of Communicable Diseases Manual (CCDM)*. 20<sup>th</sup> ed. American Public Health Association, 2015.
- American Academy of Pediatrics. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed. 2015.
- *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases: Vol. 2*. 8<sup>th</sup> ed. 2015.
- Council of State and Territorial Epidemiologists. "Public Health Reporting and National Notification for Leptospirosis," 2012. Document 12-ID-02. <http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PS/12-ID-02FINAL.pdf> (11/15).

## **2012 Case Definition – Leptospirosis (*Leptospira Interrogans*)<sup>4</sup>** (11/15)

### ***Clinical Criteria***

An illness characterized by fever, headache, and myalgia, and less frequently by conjunctival suffusion, meningitis, rash, jaundice, or renal insufficiency. Symptoms may be biphasic.

Clinical presentation includes history of fever within the past two weeks and at least two of the following clinical findings: myalgia, headache, jaundice, conjunctival suffusion without purulent discharge, or rash (i.e. maculopapular or petechial); **OR** at least one of the following clinical findings:

- Aseptic meningitis.
- GI symptoms (e.g., abdominal pain, nausea, vomiting, diarrhea).
- Pulmonary complications (e.g., cough, breathlessness, hemoptysis).
- Cardiac arrhythmias, ECG abnormalities.
- Renal insufficiency (e.g., anuria, oliguria).
- Hemorrhage (e.g., intestinal, pulmonary, hematuria, hematemesis).
- Jaundice with acute renal failure.

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### ***Laboratory Criteria for Diagnosis***

Diagnostic testing should be requested for patients in whom there is a high index of suspicion for leptospirosis, based either on signs and symptoms, or on occupational, recreational or vocational exposure to animals or environments contaminated with animal urine.

#### **Supportive:**

- *Leptospira* agglutination titer of  $\geq 200$  but  $< 800$  by Microscopic Agglutination Test (MAT) in one or more serum specimens, **or**
- Demonstration of anti-*Leptospira* antibodies in a clinical specimen by indirect immunofluorescence, **or**
- Demonstration of *Leptospira* in a clinical specimen by darkfield microscopy, **or**
- Detection of IgM antibodies against *Leptospira* in an acute phase serum specimen.

#### **Confirmed:**

- Isolation of *Leptospira* from a clinical specimen, **or**
- Fourfold or greater increase in *Leptospira* agglutination titer between acute- and convalescent-phase serum specimens studied at the same laboratory, **or**
- Demonstration of *Leptospira* in tissue by direct immunofluorescence, **or**
- *Leptospira* agglutination titer of  $\geq 800$  by Microscopic Agglutination Test (MAT) in one or more serum specimens, **or**
- Detection of pathogenic *Leptospira* DNA (e.g., by PCR) from a clinical specimen.

### ***Epidemiologic Linkage***

Involvement in an exposure event (e.g., adventure race, triathlon, flooding) with associated laboratory-confirmed cases.

### ***Case Classification***

#### **Confirmed**

A case with confirmatory laboratory results, as listed above.

#### **Probable**


A clinically compatible case with at least one of the following:

- Involvement in an exposure event (e.g., adventure race, triathlon, flooding) with known associated cases, **or**
- Presumptive laboratory findings, but without confirmatory laboratory evidence of *Leptospira* infection.

## **Information Needed for Investigation**

**Verify the diagnosis.** What laboratory tests were conducted and what were the results? This can be accomplished by referring to the Case Definition, specifically the “**Laboratory Criteria for Diagnosis**” component provided above.

**Establish the extent of the illness.** Determine if household members, travelling companions, co-workers, or other close contacts are, or have been ill. Are there any other persons with a similar illness that may require medical evaluation? Obtain demographic, clinical and laboratory information on the case from the attending physician, hospital, and/or

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laboratory. Obtain the other epidemiological information necessary to complete the [Disease Case Report](#) (CD-1) and the [Leptospirosis Case Investigation Report](#). The information may be obtained from the patient or a knowledgeable family member. *NOTE: Leptospirosis is generally treated with antibiotics, which is most effective when started as early in the course of the disease as suspicion allows.<sup>3</sup> The clinical course of illness is highly variable with a case fatality rate of 1 to 5%.<sup>7</sup>*

**Determine the source of the infection:** Establish the occupation of the case since this information may help narrow the search for the route of exposure. Are other co-workers at risk? Shared activities or exposures should be investigated for cases among families and friends. Identify possible routes of exposure in the 30 days prior to illness. Did the patient report:

1. Contact with animals?
2. Contact with untreated water?
3. Reside in housing with evidence of rodents?
4. Travel? Obtain the date of departure, destinations, length of stay, routes, activities, or other details that would identify the date and location of infection.
5. Ingestion of untreated water?
6. Exposure to flooding or heavy rainfall?
7. Recreational activities such as boating, hiking, hunting, etc?


*COMMENT: Infections generally occur following occupational or recreational exposure to water or soil contaminated with urine from infected animals. Sometimes the source of infection cannot be identified.*

**Provide leptospirosis information to persons at risk for infection and the general public as needed.** Efforts should be made to promote leptospirosis awareness and persons at risk should be provided prevention information. A "[Leptospirosis Fact Sheet](#)" is available from the Centers for Disease Control and Prevention for distribution, and a "[Leptospirosis Fast Facts](#) sheet" is available from the Center for Food Security & Public Health, Iowa State University.

Adventure race participants should also be aware of the potential risk of exposure to leptospirosis in unfamiliar environments where water may be contaminated with urine from infected animals, or the bacteria may be found in damp soil, vegetation and mud. Additional information on [Adventure Racing and Leptospirosis](#) may be found on CDC's website.

To help prevent leptospirosis in pets, get your pet vaccinated. The vaccine does not provide 100% protection because there are many different species (types) of leptospires and the current pet vaccine does not provide immunity against all species. However, the vaccine is an important prevention strategy. For additional pet prevention information, see [CDC's Prevention in Pets](#) website. Leptospirosis vaccines are also available for certain livestock. Seek the advice of your veterinarian on the use of these vaccines. *NOTE: These vaccines help to prevent disease severity but may not completely prevent infection.*

**Leptospirosis Surveillance.** Leptospirosis was reinstated as a nationally notifiable disease in January 2013. It is estimated that 100-200 leptospirosis cases are identified annually in the United States. Currently, about 50% of the cases occur in Hawaii. Data collected from leptospirosis surveillance is used to monitor trends and identify areas of risk. Furthermore, public health surveillance can enhance healthcare provider awareness of leptospirosis and

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characterize persons or geographic areas in which additional efforts are needed to raise awareness and reduce disease incidence.

Review WebSurv to determine whether there have been other leptospirosis cases related by person, place, or time. If yes, every effort should be made to identify the source.

### **Notification**

Immediately contact the [District Communicable Disease Coordinator](#), or the [Senior Epidemiology Specialist for the District](#), or the Missouri Department of Health and Senior Services (MDHSS) – Bureau of Communicable Disease Control and Prevention (BCDCP), phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7) if an outbreak\* of leptospirosis is suspected.

- If a case(s) is associated with a child care center, BCDCP or the local public health agency (LPHA) will contact the BEHS, phone (573) 751-6095, Fax (573) 526-7377 and the Section for Child Care Regulation, phone (573) 751-2450, Fax (573) 526-5345.
- If a case(s) is associated with a long-term care facility, BCDCP or the LPHA will contact the Section for Long Term Care Regulation, phone (573) 526-8524, Fax (573) 751-8493.
- If a case is associated with a hospital, hospital-based long-term care facility, or ambulatory surgical center BCDCP or the LPHA will contact the Bureau of Health Services Regulation phone (573) 751-6303, Fax (573) 526-3621.
- Contact the Department of Natural Resources, Public Drinking Water Branch, at (573) 751-1187, Fax (573) 751-3110 if cases are associated with a public water supply, or BEHS, phone (573) 751-6095, Fax (573) 526-7377, if cases are associated with a private water supply.

\*An outbreak is defined as the occurrence in a community or region, illness(es) similar in nature, clearly in excess of normal expectancy and derived from a common or a propagated source.

### **Control Measures**


A human vaccine for leptospirosis is currently not available in the United States. There are several steps you can take to help prevent getting leptospirosis. These include:

- See a veterinarian to get vaccines for your pets and livestock that can protect against this disease.
- Avoid contact with animal urine or body fluids, especially if there are any cuts or abrasion of the skin.
- Do not swim in, walk in, or swallow water that may contain animal urine.
- Wear protective clothing and footwear near soil or water that may be contaminated with animal urine.

For high-risk groups with short-term exposure, prophylaxis may be considered with doxycycline. Vector (rodent) control options should be evaluated, particularly in *Leptospira*-endemic areas. To prevent human infections, increasing awareness through education and outreach is important. Providing information about safe swimming practices and potential exposures is key. For pet or livestock owners, providing information about vaccination options may be helpful.

For control of illness in a hospitalized patient, observe standard blood and body fluid isolation precautions. Person-to-person transmission of leptospirosis is rare. Leptospirosis is treated with



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antibiotics, such as doxycycline or penicillin, which should be given early in the course of the disease. Intravenous antibiotics may be required for persons with more severe symptoms. Persons with symptoms suggestive of leptospirosis should contact a health care provider.<sup>7</sup>

### **Laboratory Procedures**

Testing for leptospirosis is available through commercial clinical laboratories. Since the early clinical presentation and routine laboratory results are non-specific for this disease, clinical suspicion and specific diagnostic testing are important. *NOTE: Treatment should be initiated early, without waiting for confirmatory test results; if leptospirosis is suspected.*<sup>8</sup> *Serologic tests are helpful when positive but may have poor sensitivity during the first week of illness. Signs and symptoms of early leptospirosis are generally nonspecific.*<sup>3</sup>

Laboratory tests for diagnosis include:

- *Leptospira* agglutination titer by Microscopic Agglutination Test (MAT) in one or more serum specimens:
  - Supportive:  $\geq 200$  but  $< 800$
  - Confirmed:  $>800$ .
- Fourfold or greater increase in *Leptospira* agglutination titer between acute and convalescent serum specimens studied at the same laboratory.
- Demonstration of anti-*Leptospira* antibodies in a clinical specimen by indirect immunofluorescence.
- Detection of IgM antibodies against *Leptospira* in an acute serum specimen.
- Demonstration of *Leptospira* in a clinical specimen by darkfield microscopy.
- Isolation of *Leptospira* from a clinical specimen.
- Detection of pathogenic *Leptospira* DNA (e.g., by PCR) from a clinical specimen.

The Zoonoses and Select Agent Laboratory (ZSAL) of the Bacterial Special Pathogens Branch (BSPB) of CDC provides reference testing for leptospirosis. **IMPORTANT:** *All of Missouri's results will be sent to MDHSS. Healthcare providers are asked to notify the state health department of any submissions to ZSAL by calling the Missouri State Public Health Laboratory (573 751-3334) and/or the MDHSS – BCDCP at 573-751-6113.* For information on ZSAL shipping and reference activities, see the following web site:


[http://www.cdc.gov/ncezid/dhcpp/bacterial\\_special/zoonoses\\_lab.html](http://www.cdc.gov/ncezid/dhcpp/bacterial_special/zoonoses_lab.html).

### **Reporting Requirements**

Leptospirosis is a Category III reportable disease and shall be reported to the [local public health agency](#) or to MDHSS within three (3) days of first knowledge or suspicion, by telephone, facsimile, or other rapid communication.

As a Nationally Notifiable Condition, all confirmed and probable cases are a **STANDARD** report to CDC. MDHSS will submit these reports to the CDC by electronic case notification (WebSurv) within the next reporting cycle.

1. For confirmed and probable cases, complete a "[Disease Case Report](#)" (CD-1) and a "[Leptospirosis Case Investigation Report](#)" (CDC 52.98).


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2. Entry of the completed CD-1 into WebSurv negates the need for the paper CD-1 to be forwarded to the District Health Office.
3. Send the completed “Leptospirosis Case Investigation Report” to the [District Health Office](#).
4. MDHSS will report to CDC following the above reporting criteria (see box).
5. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the [District Communicable Disease Coordinator](#). This can be accomplished by completing the [Missouri Outbreak Surveillance Report](#) (CD-51).
6. If an outbreak is associated with food, person-to-person transmission, environmental contamination, animal contact, or indeterminate/other/unknown etiology, a [National Outbreak Reporting System – Foodborne Disease Transmission, Person-to-Person Disease Transmission, Animal Contact](#) form (CDC 52.13) is to be completed and submitted to the District Health Office at the conclusion of the outbreak.
7. If an outbreak is associated with the consumption or use of water for drinking, or with ingestion, contact, or inhalation of recreational water, a [National Outbreak Reporting System - Waterborne Disease Transmission](#) form (CDC 52.12) is to be completed and submitted to the District Health Office at the conclusion of the outbreak.
8. Within 90 days of the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

## References

1. American Public Health Association. *Leptospirosis (Weil’s disease, canicola fever, hemorrhagic jaundice, mud fever, canefield fever, swineherd disease, rat urine disease)*. Galloway R, Guerra M, Shadomy S In: Heymann, D (ed.), *Control of Communicable Diseases Manual*. 20<sup>th</sup> ed. Washington, DC: American Public Health Association; 2015: 348-353.
2. American Academy of Pediatrics. *Leptospirosis*. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30<sup>th</sup> ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015: 510-513.
3. Elsevier Inc. *Leptospira Species (Leptospirosis)*. Haake DA, Levett PN In: Bennett JE, Dolin R, Blaser MJ eds. *Mandell, Douglas, and Bennett’s Principles and Practices of Infectious Diseases: Vol. 2*. 8<sup>th</sup> ed. 2015: 2714-2720.
4. Centers for Disease Control and Prevention’s (CDC) National Notifiable Diseases Surveillance System (NNDSS) and Case Definitions. <http://wwwn.cdc.gov/nndss/> (10/15).
5. Council of State and Territorial Epidemiologists. “Public Health Reporting and National Notification for Leptospirosis,” 2012. Document 12-ID-02. <http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PS/12-ID-02FINAL.pdf> (11/15).
6. The Center for Food Security and Public Health, Iowa State University, College of Veterinary Medicine, Ames, IA. *Home; Animal Disease Information; Fast Facts Disease Summary*. [http://www.cfsph.iastate.edu/FastFacts/pdfs/leptospirosis\\_F.pdf](http://www.cfsph.iastate.edu/FastFacts/pdfs/leptospirosis_F.pdf) (11/15).



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7. Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases, Division of Vector-borne Diseases. *Leptospirosis*. <http://www.cdc.gov/leptospirosis/> (11/15).
8. Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases, Division of Global Migration and Quarantine. *Leptospirosis*. *CDC Traveler's Health*. <http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/leptospirosis> (11/15).

### **Other Sources of Information**

1. Merck & Co., Inc. *Overview of Leptospirosis*. Kahn CM, Line S eds. Online: *The Merck Veterinary Manual, Professional Version*. 10<sup>th</sup> ed. Whitehouse Station, NJ; 2010. <http://www.merckvetmanual.com/mvm/index.jsp> (search "leptospirosis" on 11/15).
2. Medscape. "Leptospirosis". <http://www.emedicine.com/ped/topic1298.htm> (11/15).