A REVIEW ON LEPTOSPIROSIS

Suvarna P. Ningal¹*, Manoj B. Kothule², Nilesh Y. Jadhav², Sagar D.Kadam²,
Yogesh S. Katara², Sandip A. Hapse³

¹V.J.S.M. Institute of Pharmacy for Women, Ale, Tal. Junnar, Dist Pune, Maharashtra, India.
²HSBPVT’s GOI College of Pharmacy, Kashti, Ahmednagar, Maharashtra, India.
³P.D.V.P.F’S College of Pharmacy, Ahmednagar, Maharashtra, India.

ABSTRACT
Leptospirosis is a bacterial disease caused by bacteria from genus of Leptospira. In 1886 Adolf Weil described Leptospirosis as disease entity. Leptospirosis has many different names including: "7-day fever", "harvest fever", "field fever", "canefield fever", "mild fever", "rat catcher's yellows", "Fort Bragg fever", and "pretibial fever". Leptospires are bacteria which can be either pathogenic or saprophytic Leptospirosis are transmitted in humans by contact with soil or water contaminated with urine of certain infected animals like rodents, dog and cattle. This bacteria enters in human body through abrasion in the skin or through conjunctiva. It occurs worldwide but most common areas are tropical and subtropical areas with high rainfall. Mild symptoms include flu, headaches and chill but in severe cases organ failure and bleeding, dengue fever and other haemorrhagic diseases. Leptospirosis can be treated with antibiotics like penicillin G, ampicillin, amoxicillin and Doxycycline. In more severe cases cefotaxime preferred. Most patients can recover completely hence fatality rate is low i.e. 5 to 30%. No human vaccination is available only prevention and treatment is effective.

KEY WORDS: Leptospira, Weil’s disease, Cefotaxime, Saprophytic.

INTRODUCTION¹²³⁴⁵
Leptospirosis is a bacterial disease which causes severe clinical illness in animals and humans. Adolf Weil described leptospirosis as a disease entity in 1886. His name is still attached to a serious form of leptospirosis called Weil's disease. It is caused by bacteria from the genus Leptospira, that thrive directly within hosts (for example dogs and humans) and...
reservoirs (for example rodents), and indirectly within the environment. Leptospira consist of a group of pathogenic leptospires, L.interrogans sensu lato and non-pathogenic leptospires, L.biflexa sensu lato. Leptospirosis is spread to humans by contact with soil or water contaminated with the urine of certain infected wild animals, including cattle, pigs, dogs, and rats. The condition is rare, but people who regularly come in contact with animals, like farmers and veterinarians, are at a higher risk of infection. The spirochete most commonly enters through abrasions in the skin or through the conjunctiva.

Leptospirosis occurs worldwide but is most common in tropical and subtropical areas with high rainfall. Most cases in the U.S. are reported in the Southern and Pacific coastal states, but Hawaii consistently reports more cases than any other state. The infection typically only causes mild flu-like symptoms, including headaches and chills. In severe cases, such as in Weil’s disease, it can lead to organ failure and bleeding, dengue fever and other viral hemorrhagic diseases. Icterus (jaundice). The disease is treated with a course of antibiotics. People with Weil’s disease may need to be admitted to a hospital for extra care while their underlying infection is treated with antibiotics. Symptoms are less common. They are, therefore, often not recognized as a presenting feature of Leptospirosis. The diagnosis is confirmed by laboratory tests, but these are not always available, especially in developing countries. For these reasons, Leptospirosis is overlooked and underreported in many areas of the world. The incubation period in humans is usually 10 days, with a range of 2-30 days.

HISTORY[8]

The disease was first described by Adolf Weil in 1886 when he reported an "acute infectious disease with enlargement of spleen, jaundice, and nephritis. " Leptospira was first observed in 1907 from a post mortem renal tissue slice and in 1916 noted its presence in rats. The mild form of the disease is known as leptospirosis. If the bacteria infect other organs of the body, such as the kidneys, heart, liver, lungs, or brain, it can lead to a more severe disease. This condition is called Weil’s disease.

EPIDEMIOLOGY[3,4,5,8]

Leptospirosis is a worldwide zoonosis disease. Most cases of leptospirosis occur during summer and fall. The disease is more widespread in tropical countries. Direct or indirect contact with urine of infected animal is the major mean by which leptospirosis is transmitted. Annually near about seven to ten million peoples are infected by leptospirosis. The incidence
of leptospirosis in the U.S. overall is 0.05 cases per 100,000 persons, with an incidence of 12.8 cases per 100,000 persons in Hawaii. The frequency of infection is variable because there is considerable geographic variation; in some developing countries, 80% of the population shows serologic evidence of infection. In developing countries, leptospirosis is typically an occupational disease associated with sugarcane workers, farmers and military troops exposed to soil and water contaminated by the urine of infected wild or domestic animals. Infection is usually seen in young adults and is more common in men (male-to-female ratio of 4:1), possibly because of greater participation in high-risk occupations; peak incidence is in men aged 30 to 39 years. Worldwide, about 20% of cases of leptospirosis are thought to be associated with pets or rodents in or around the home. Leptospirosis has been associated with flooding and residents in inner cities where there is contact with rodent and dog urine.

**DISEASE AGENT CHARACTERISTIC**[4, 5, 8, 9]

Leptospira magnified 200 times with dark-field microscope as shown in fig.01.

![Leptospira magnified 200 times with dark-field microscope](image1)

Fig.01: Leptospira magnified 200 times with dark-field microscope.

Scanning electron micrograph of a number of Leptospira sp. bacteria atop a 0.1 μm polycarbonate filter as shown in fig.02.

![Scanning electron micrograph of a number of Leptospira sp. bacteria atop a 0.1 μm polycarbonate filter](image2)

Fig.02: Scanning electron micrograph of a number of Leptospira sp. bacteria atop a 0.1 μm polycarbonate filter.

Family- Leptospiraceae,
Genus- Leptospira,
Order Spirochaetales,
Gram-negative spirochete with internal flagella.
Morphology- Leptospires are corkscrew-shaped bacteria, which differ from other spirochaetes by the presence of end hooks.

Nutritional requirements- The leptospires have relatively simple nutritional requirements; long-chain fatty acids and vitamins B₁ and B₁₂ are to be necessary for growth. When cultivated in media of pH 7.4 at 30°C, their average generation time is about 12 hours. Aeration is required for maximal growth. They can be cultivated in plates containing soft (1 percent) agar medium, in which they form primarily subsurface colonies.

Physicochemical properties- Moist environments with a neutral pH provide suitable conditions for survival of leptospires. They optimally survive for weeks in the environment. These organisms do not survive in freezing conditions. They are killed by dehydration or temperature in excess of 50°C. For disinfection purposes, leptospires are inactivated by 70% ethanol, glutaraldehyde, formaldehyde, detergents and acid. They are also destroyed by moist heat, at 121°C for 15 minutes and by pasteurization.

**STRUCTURE OF LEPTOSPIRA BACTERIA**\[^11,12\]

Model of Leptospiral Membrane Architecture as shown in Fig.03.

![Fig.03: Structure of Leptospira Bacteria.](image)

Model of leptospiral membrane architecture showing the location of outer membrane (OM) components lipopolysaccharide (LPS), the porin, OmpL1, and the lipoproteins LipL41 and LipL36. The endoflagella (EF) are located in the periplasm between the outer and inner membranes. The peptidoglycan cell wall (CW) is associated with the inner membrane (IM).
Inner membrane proteins include penicillin-binding proteins (PBPs) and signal peptidase (SP). The heat-shock protein (GroEL) is located primarily in the cytoplasm.

Leptospiira has the general structural characteristics that distinguish spirochetes from other bacteria. The cell is encased in a three- to five-layer outer membrane. Beneath this outer membrane are the flexible, helical peptidoglycan layer and the cytoplasmic membrane; these encompass the cytoplasmic contents of the cell. The structures surrounded by the outer membrane are collectively called the protoplasmic cylinder. An unusual feature of the spirochetes is the location of the flagella, which lie between the outer membrane and the peptidoglycan layer. They are referred to as periplasmic flagella. The periplasmic flagella are attached to the protoplasmic cylinder subterminally at each end and extend toward the center of the cell. The number of periplasmic flagella per cell varies among the spirochetes. In liquid media, one or both ends are usually hooked. They are too thin to be visible under the ordinary microscope. Dark-field microscopy is most often used to observe leptospires. They do not stain well with aniline dyes.

The leptospires have two periplasmic flagella, one originating at each end of the cell. The free ends of the periplasmic flagella extend toward the center of the cell, but do not overlap as they do in other spirochetes. The basal bodies of Leptospira periplasmic flagella resemble those of Gram-negative bacteria, whereas those of other spirochetes are similar to the basal bodies of Gram-positive bacteria. Leptospira differs from other spirochetes in lacking glycolipids and having diaminopimelic acid rather than ornithine in its peptidoglycan.

**CLASSIFICATION**[^1,^8]

Leptospires are bacteria which can be either pathogenic (i.e. having the potential to cause disease in animals and humans) or saprophytic (i.e. free living and generally considered not to cause disease). Initially, two species of leptospira were recognized, namely pathogenic Leptospira interrogans and saprophytic Leptospira biflexa. Recently, several species of Leptospira have been differentiated on the basis of their DNA-relatedness.

A variety of methods available to classify leptospira like;

1. Genetic analysis.
2. Serological classification.

The genetic classification differs from the serological classification. The sequence of the rrs gene, coding for 16S rRNA, is most commonly used and accepted for studying genetic
relationships. A variety of methods like leptospira spp. based on DNA homology, restriction fragment length polymorphism,, pulsed-field gel electrophoresis, ribotyping, polymerase chain reaction (PCR)-based typing of genetic analysis have become available in the last few years. However, the genetic classification differs from the serological classification.

Current species determination is based on DNA homology. At present about 300 strains have been classified on the basis of DNA homology studies. Species based on genetic analyses are listed together with the sero groups most commonly present in these species. DNA homology methods have the disadvantage that they are too complicated to be suitable for routine performance.

Leptospira are also classified based on their serovar. About 250 pathogenic serovars of Leptospira are recognized. The most prevalent serotypes in the United States are canicola, grippotyphosa, hardjo, icterohaemorrhagiae, and pomona. The diverse sugar composition of the lipopolysaccharide on the surface of the spirochete is responsible for the antigenic difference between serovars. Antigenically related serovars are grouped into 24 sero groups, which are identified using the microscopic agglutination test (MAT). A given sero group is often found in more than one species, suggesting that the LPS genes that determine the serovar are exchanged between species.

DISEASE NAMES[8]
Leptospirosis has many different names including: "7-day fever", "harvest fever", "field fever", "canefield fever", "mild fever", "rat catcher's yellows", "Fort Bragg fever", and "pretibial fever". It has historically been known as "black jaundice" and in Japan it is called "nanukayami fever". Weil's disease or Weil's syndrome is also known as spirochaetosis icterohaemorrhagica.

TRANSMISSION[7]
This disease is caused by an infection with a bacterium from the genus Leptospira. Up to 13 different genetic types of Leptospira may cause disease in humans. The bacteria are typically found in animals, including rodents, farm animals, and dogs. Thus it is transmitted by both wild and domestic animals. The most common animals that spread the disease are rodents.

Human leptospiral infections result primarily from direct or indirect exposure to the urine of infected animals. Other modes of transmission of infection, such as handling infected animal
tissues and ingestion of contaminated food and water, are also possible. The infecting agent is transmitted from one animal carrier to another via direct or indirect contact with urine or other body fluids that contain viable leptospires. Direct transmission occurs via oronasal exposure with infected urine, venereal or placental transfer, bite wounds, or ingestion of infected tissues. Leptospire contact with mucous membranes and abraded skin can also be a method of transmission. Indirect transmission, a very common form of transmission, occurs via handling infected animal tissues, exposure to contaminated sources of water, for example ponds, rivers and water catchment tanks, as well as soil, food. There is some evidence that leptospires can be transmitted to infants through breast-feeding, causing infection. Urine of a patient suffering from leptospirosis should be considered infectious. However, person-to-person transmission is rare.

**POPULATION AT RISK**[^8]

The risk of infection depends on exposure. Risk groups are certain groups of humans in a population that are more likely to be exposed as a result of either occupational or recreational activities.

Risk factors include:

- Occupational exposure -- farmers, ranchers, slaughterhouse workers, trappers, veterinarians, loggers, sewer workers, rice field workers, and military personnel.
- Recreational activities -- fresh water swimming, canoeing, kayaking, and trail biking in warm areas.
- Household exposure -- pet dogs, domesticated livestock, rainwater catchment systems, and infected rodent.

**SYMPTOMS**[^8,10]

Symptoms can take 2 - 26 days (average 10 days) to develop. The symptoms appear after an incubation period of 7–12 days. The first phase (acute or septicemic phase) ends after 3–7 days of illness. The patient is asymptomatic for 3–4 days until the second phase begins with another episode of fever.

The hallmark of the second phase is meningitis.
According to the UK’s National Health Services (NHS), about 90 percent of Leptospirosis infections cause only mild symptoms. Severe infections, which are referred to as Weil’s disease, only occur in about 10 percent of cases.

The symptoms typically occur one to three days after the mild symptoms. Symptoms are shown in Table 01.

Table 01: Symptoms.

<table>
<thead>
<tr>
<th>Mild symptoms include</th>
<th>Severe symptoms include</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Liver damage (causing jaundice)</td>
</tr>
<tr>
<td>Chills</td>
<td>Kidney failure</td>
</tr>
<tr>
<td>Muscle aches</td>
<td>Bleeding</td>
</tr>
<tr>
<td>Headaches</td>
<td>Extreme fatigue,</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Hearing loss</td>
</tr>
<tr>
<td>Cough</td>
<td>Respiratory distress</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>Nausea</td>
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<tr>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Confused mental state</td>
</tr>
<tr>
<td></td>
<td>Drowsiness</td>
</tr>
<tr>
<td></td>
<td>Aggressive behavior</td>
</tr>
<tr>
<td></td>
<td>Seizures and azotemia</td>
</tr>
</tbody>
</table>

Disease severity varies with the infecting serovar. Clinical illness can last for few days to several weeks. The case fatality rate is less than 5% to 30%, most patients recover completely from Leptospirosis only in case at pregnancy causes fetal loss.

**DIAGNOSIS**[^8]

Leptospirosis is difficult to diagnose because the symptoms are very similar to other types of illnesses, such as the flu. Leptospirosis may be under diagnosed because:

(a) The diagnosis is difficult to confirm;
(b) It may be confused with other diseases;
(c) The disease may be mild and not be investigated in the laboratory;

Weil’s disease is easier to diagnose because the symptoms are more severe. A personal history is helpful for a diagnosis. You should tell your doctor if you:

- have recently travelled.
- have participated in water sports.
- have come in contact with a freshwater source.
- have an occupation that involves exposure to animals.
Kidney tissue, revealing the presence of *Leptospira* bacteria as shown in Fig. 04.

![Kidney tissue, revealing the presence of Leptospira bacteria.](image)

**Fig.04 Kidney tissue, using a silver staining technique, revealing the presence of Leptospira bacteria.**

Diagnosis is usually confirmed through blood and urine tests that detect the presence of the leptospira bacteria. Early diagnostic efforts include testing a serum or blood sample serologically with a panel of different strains. Kidney function tests (blood urea nitrogen and creatinine) as well as blood tests for liver functions are performed. Diagnosis of leptospirosis is confirmed with tests such as enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR).

**TREATMENT**

Treatment with effective antibiotics should be initiated as soon as the diagnosis of leptospirosis is suspected and preferably before the fifth day after the onset of illness. 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.

- Antibiotics to treat leptospirosis include, penicillin G, ampicillin, amoxicillin and Doxycycline. In more severe cases cefotaxime or ceftriaxone should be preferred.

- Antibiotics used to reduce fever & bacteria within the bloodstream thus rapidly reduce fatal complications of infection such as liver or kidney failure.

- Glucose and salt solution infusions may be administered.

- Elevations of serum potassium and Serum phosphorus are common and if the potassium or phosphorus level gets too high special measures must be taken.

- A ventilator may be used to assist with breathing.
• Peritoneal dialysis may be required if kidneys are not functioning properly.

• Corticosteroids administration in gradually reduced doses (e.g., prednisolone) during 7–10 days in cases of severe haemorrhagic effects.

**PROGNOSIS**[^4,5]
During treatments the animal must be carefully monitored within the hospital and following treatment as an outpatient. If the symptoms are severe and debilitating, the prognosis may be critical and involve mortality.

**PREVENTION**[^1,2,3,4,5,6]
Prevention and control can take place in the form of interventions,
(a) At the infection source.
(b) At the route of transmission between the infection source and the human host.
(c) At the level of the human host.
The following are some recommended precautions to prevent leptospirosis.

**Pet exposure**
• Pet owners are encouraged to wash their hands after cleaning pets, washing the animal or disposing of things that is contaminated with urine.
• Any cut to skin and abrasions should cover with waterproof dressings if their pet is infected.
• Pet owners should avoid their children to play in the areas where the animals are placed.
• Animal vaccination and eradication of rodents. No human vaccination is available.
• Pet owners should not leave food and water outside so that animal will not attract to their.

**Occupational exposure**
• Farmers should prevent contact with rodents, wild animals and other livestock, which could potentially be infected.
• Cleaning, disinfection and drying of areas where healthy animals are exposed.
• Farmers should discuss the possibility of vaccination and antibiotic use with their veterinarian to prevent and minimize outbreaks in their livestock.
• Farmers should minimize exposure of livestock to contaminated water by avoiding urine drainage into water sources.
• People working in animal husbandry should wear protective clothing and wounds covered
with waterproof dressings to reduce the chance of infection.

- Veterinarians may want to consider pre- or post-exposure prophylaxis if they will be working with infected animals.
- Pet shop owners should wear rubber gloves when cleaning up animal waste, especially that of dogs, and especially that of any animal that appears ill.

Recreational exposure

- Eco and adventure tourists should protect exposed skin, eyes and mucous membranes as much as possible during primary and secondary contact with recreational water in tropical areas.
- Eco adventure tourists should be discussed pre-exposure prophylaxis with their health care provider if they will be participating in high-risk activities.
- The public should avoid swimming and boating in freshwater that could be influenced by recent heavy rains or flooding and that could receive drainage from agricultural areas.

Interventions At The Level Of The Human Host

- Raising awareness: People need to understand the disease and, if possible, how to avoid risks, rising awareness.
- Antibiotic prophylaxis: Treatment with antibiotics immediately after diagnosis of infection.
- Immunization: Vaccines are available for animals, but vaccination only prevents clinical symptoms, and may not prevent infection. Vaccines may produce side-effects and are available only in certain countries.

- Educational method

1. Physician education and update: Information on the symptoms of leptospirosis, risk factors, diagnostic testing and therapeutic strategies should be regularly disseminated to licensed physicians and health care providers.

2. Community education: community education is related with identification of risk factors, the prevention of illness, and reducing the duration of illness and its severity. Various methods can be used for community education like, Brochures, videotape, Display boards, tee-shirts, brightly colored warning signs.

CONCLUSIONS
The leptospira bacteria found worldwide. Leptospirosis is a bacterial disease caused by bacteria from the genus Leptospira, that thrive directly within hosts which cause severe clinical illness in animals and humans. The bacteria are typically found in animals, including rodents, farm animals, and dogs. Leptospirosis is spread to humans by contact with soil or water contaminated with the urine of certain infected wild animals, including cattle, pigs, dogs, and rats. The infection typically only causes mild flu-like symptoms, including headaches and chills. In severe cases, such as in Weil’s disease, it can lead to organ failure and bleeding, dengue fever and other viral hemorrhagic diseases. Icterus (jaundice). Leptospirosis can be treated with antibiotics like penicillin G, ampicillin, amoxicillin and Doxycycline. In more severe cases cefotaxime preferred. Glucose and salt solution infusions may be administered.

Prevention and control can take place in the form of interventions, at the infection source, at the route of transmission between the infection source and the human host; at the level of the human host also care should be taken while handling the pet animals like their cleaning and personal hygiene etc.

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