Leptospirosis

Background:
- is caused by a spirochaete bacterium called *Leptospira* spp
- More than 200 serovars have been identified within these species. Common pathogenic species are *L. interrogans*, *pomona*, *icterohaemorrhagiae*, *canicola*, and *autumnalis*.
- Primary hosts: rats, mice and moles
- Secondary hosts: wide range of other mammals including dogs, deer, rabbits, hedgehogs, cows, sheep, raccoons, possums, skunks, and certain marine mammals.
- Leptospirosis is transmitted by the urine of an infected animal and is contagious as long as it is still moist.

Mode of transmission
- Contact of skin, especially if abraded, or of mucous membranes with water, moist soil or vegetation contaminated with urine of infected animals
- Direct contact with urine or tissues of infected animals
- Ingestion of foods contaminated with urine of infected rats
- Inhalation of droplet-aerosols of contaminated fluids
- Occupations at risk include veterinarians, slaughterhouse workers, farmers, sewer workers, and people working on derelict buildings.
- The disease is not known to be spread from person to person

Pathophysiology:
Leptospirosis may follow a biphasic course:
- a) **Septicemic phase** (duration: 4 - 7 days): *L. interrogans* dissemination in blood, cerebrospinal fluid (CSF) and most tissues. Clinically it's characterized by extensive vasculitis. Capillary damage (action of leptospiral toxin) is common to all serotypes and during the septicaemic phase, petechial haemorrhages in mucosae are a common expression of this.
- b) **Immune phase** (duration: 10 - 30 days): leptospiroses disapper from blood and CSF, remaining intermittently in the urine. Clinically it's characterized by multissystemic manifestations (interstitial nephritis and tubular necrosis of kidneys; centrilobular necrosis with proliferation of Kupffer cells in liver; edema, vacuolization of myofibrils, and focal necrosis of skeletal muscle).

History:
Incubation period: 2 - 20 days

On the basis of these clinical features, two types of leptospirosis are described:
I. Anicteric leptospirosis
- Almost 90% of patients have this type of illness.
- It is the milder form of the disease.
- Asymptomatic urinary abnormality in the form of mild proteinuria with few casts & cells in the urine. Severe renal involvement in the form of acute renal failure, (which occurs in icteric leptospirosis) is rare.

II. Icteric Leptospirosis: - (Weil’s syndrome)
- It is the severe form of the disease.
- About 5-10% of patients have these type of manifestations
- Is characterized by multissystemic manifestations. An individual patient may have features of one or more organ involvement.
- Vascular and renal dysfunction accompanied by jaundice develop 4-9 days after onset of disease, and jaundice may persist for weeks.

History
- The natural course of leptospirosis falls into 2 distinct phases, septicemic and immune.
During **the first stage**, which lasts about 4-7 days, the patient develops:

- abrupt nature of the onset
- a nonspecific flulike illness of varying severity with:
  - fever
    - remittent fever with chills, it may be moderate to severe.
  - myalgia
    - it is a very characteristic finding in leptospirosis. Calf, abdominal & lumbosacral muscles are very painful & severely tender. This symptom is very useful in differentiating leptospirosis from other diseases causing fever. There is associated increase in serum Creatinine Phosphokinase (C.P.K.) which helps in differentiating leptospirosis from other illnesses.
- conjunctival suffusion
  - there is reddish colouration of conjunctiva. Very useful sign in leptospirosis. Usually bilateral, most marked on palpebral conjunctiva, it may be associated with unilateral or bilateral conjunctival haemorrhage.
- headache
  - usually intense, sometimes throbbing, commonly in frontal region. It is often not relieved by analgesics.

A **brief period of 1-3 days** between the 2 phases, the patient shows some improvement:

- the temperature curve falls and the patient may become afebrile and relatively asymptomatic.

The fever then recurs, indicating the onset of **the second stage**.
This stage is called the immune or leptospiruric stage because circulating antibodies may be detected or the organism may be isolated from urine. This stage is characterized by nausea, vomiting, abdominal pain and multisystemic manifestations:

#### Hepatic:

- Jaundice is the most important clinical feature. It may be mild to severe. It starts after 4 to 7 days of illness.
  - Hepatic encephalopathy or death due to hepatic failure is rare.
  - Hepatomegaly & tenderness in right hypochondrium are usually detected.
  - Laboratory investigations show raised level of serum bilirubin (direct) and alkaline phosphatase.
- ALAT & ASAT are either normal or mildly elevated. This helps to differentiate leptospirosis from viral hepatitis where ALAT is markedly elevated and also from alcoholic hepatitis where ASAT is markedly elevated.
- High level of Creatinine Phosphokinase (CPK) is suggestive of Leptospirosis. It is normal in viral hepatitis and alcoholic hepatitis helps in differential diagnosis.

#### Renal:

Renal involvement is almost invariably present in leptospirosis. In severe cases patients have acute renal failure and present with:

- Decreased urine output (oliguria or even anuria)
- Oedema may be present on face and feet.
- Features of uremia like breathlessness, convulsion, delirium and altered level of consciousness may be present in very severe cases.
- The renal dysfunction worsens during the first week to the end of 2nd week, after which it starts improving and complete recovery occurs by the end of the 4th week.
- There is usually no residual renal dysfunction.

#### Pulmonary involvement:

- In mild cases patient will show only cough, chest pain and blood tinged sputum.
- In severe cases patients have:
  - cough, haemoptysis,
  - rapidly increasing breathlessness which may lead to respiratory failure.
On examination, these patients have increased respiratory rate with basal crepitations, which rapidly spread upwards to middle and upper lobes.

- X-ray shows basal and mid zone opacity in severe cases. It may be normal in mild cases.
- The under lying pathology is intra-alveolar haemorrhage.
- The commonest cause of death due to leptospirosis is pulmonary alveolar haemorrhage.

**Haemorrhage:** They occur because of:

- Thrombocytopenia,
- Disseminated Intra-vascular Coagulation (DIC),
- Secondary to liver involvement leading to coagulation factor deficiency.
- Patients may have spontaneous superficial bleeding i.e. petechial, purpura, epistaxis or GIT bleeding. In severe cases ecchymosis or intra-cranial haemorrhage can occur.

**Hypotension Shock:**

- Patient will have hypotension, cold clammy extremities, tachycardia, thready pulse.
- Echocardiography reveals normal systolic function of left ventricle hence hypotension is due to either dehydration or peripheral vasodilatation.

**Arrhythmias:**

- Patient presents with palpitation and syncope & irregular pulse.
- Common arrhythmias seen are supraventricular tachyarrhythmias and various degrees of A.V. blocks.
- Ventricular tachyarrhythmias are infrequent.
- ST Segment depression and T wave inversion may be present in some patients.

### Summary of organs affected in Icteric Leptospirosis

<table>
<thead>
<tr>
<th>Organ</th>
<th>Clinical features</th>
<th>Investigations reveal</th>
</tr>
</thead>
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<tr>
<td>Kidney</td>
<td>Decrease in urine output, features of uremia</td>
<td>pyuria, hematuria, proteinuria, Increase in Serum Creatinine, Increase in Blood Urea</td>
</tr>
<tr>
<td>Liver</td>
<td>Jaundice, hepatomegaly</td>
<td>Increase in Serum Bilirubin with normal or mildly elevated ALAT and ASAT and increased CPK</td>
</tr>
<tr>
<td>Lungs</td>
<td>Cough, haemoptysis, dyspnoea with increase in respiration rate and basal creps</td>
<td>X ray chest shows lower and mid zone opacities.</td>
</tr>
<tr>
<td>Heart</td>
<td>Hypotension, irregular pulse</td>
<td>ECG reveals the type of arrhythmia</td>
</tr>
<tr>
<td>Blood</td>
<td>Bleeding tendencies</td>
<td>Decrease in platelet count</td>
</tr>
<tr>
<td>Brain</td>
<td>Altered consciousness with neck rigidity</td>
<td>CSF shows increase in cells, increase in protein, normal sugar</td>
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### Lab Studies:

- Definitive diagnosis is suggested by isolation of the organism by culture or a positive result on the microscopic agglutination test (MAT).
- Cultures
  - Isolating the organism by culture allows definitive diagnosis.
  - Leptospires may not be detected in the blood until 4 days after the onset of symptoms (7-14 d after exposure). Once the immune system is activated, blood cultures may again become negative. Blood cultures may be negative if drawn too early or too late.
  - Leptospires may be isolated from the urine for several weeks after the initial infection. In some patients, urine cultures may remain positive for months or years after the onset of illness. Positive urine cultures may take up to 8 weeks to grow.
  - Leptospires may be isolated from the CSF within the first 10 days.
- Microscopic agglutination test (MAT).
  - The antibody response does not reach detectable levels until the second week of illness, and it can be affected by treatment.
  - A 4-fold rise in convalescent titers is considered a positive result.
A presumed diagnosis is made by observing an antibody titer of greater than or equal to 1:100 in the MAT in conjunction with symptoms consistent with the disease.

- Macroscopic slide agglutination test
  - This test allows a presumptive diagnosis.
  - This test, which utilizes killed antigen, is useful for screening, but it is not specific.

- Other tests include:
  - an immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA),
  - indirect hemagglutination test,
  - a dark-field examination of blood or urine. The dark-field exam frequently leads to misdiagnosis and should not be used.

- Laboratory studies (general)
  - With mild disease, elevated erythrocyte sedimentation rate and peripheral leukocytosis with a left shift are noted.
  - Aminotransferases may be elevated mildly, up to 200 U/L; serum bilirubin and alkaline phosphatase may also be elevated.
  - Urinalysis
    - Proteinuria may be present.
    - Leukocytes, erythrocytes, hyaline casts, and granular casts may be present in the urinary sediment.
  - Cerebrospinal fluid
    - When CNS becomes involved, polymorphonuclear leukocytes initially predominate and later are replaced by monocytes.
    - CSF protein may be normal or elevated, while glucose levels remain normal.
    - CSF pressure is normal, but a lumbar puncture can relieve the headache.

- Laboratory studies (Weil disease)
  - Patients may exhibit mild thrombocytopenia (as many as 50%), which often is accompanied by renal failure.
  - Azotemia and renal failure are other prominent characteristics.
  - Marked leukocytosis may be present.
  - Prothrombin times may be elevated.
  - Creatine phosphokinase (CPK) is elevated in as many as 50% of patients; acutely, jaundice in Weil disease is associated with very high CPK, but transaminases are elevated only modestly.

**Imaging Studies:**
- In severe disease, a patchy alveolar pattern may be demonstrated on lung radiography, corresponding to alveolar hemorrhage. Most radiographic changes occur in the periphery of the lower lobes.

**Other Tests:**
- Electrocardiographic (ECG) abnormalities are common during the leptospiremic phase of Weil syndrome; in severe cases, congestive heart failure and cardiogenic shock may occur.

**Emergency Department Care:**
- Treatment should be started as soon as possible and may be effective even after the first 4 days of illness onset.
  - Antimicrobial therapy is indicated: the primary therapy is penicillin G. Alternative regimens are ampicillin, amoxicillin, or erythromycin. Several other antibiotics, including cephalosporins, may be useful.
  - Patients with renal failure may require dialysis; renal function is restored in most.
  - Those with Weil syndrome may need transfusions of whole blood and/or platelets.
  - Supportive therapy and careful management of renal, hepatic, hematologic, and CNS complications are important.

**Prognosis:**
- Most patients with leptospirosis recover.
- The highest mortality rates are in elderly patients and in those with Weil syndrome.
• Pregnant women also face a high rate of fetal mortality, as infected women have a higher-than-normal incidence of spontaneous abortion if the infection is acquired in the early months of pregnancy.
• Patients with hepatic dysfunction and renal failure have a good chance of recovering renal and hepatic dysfunction in the long term.