This parasite include two genus *Leishmania spp.* and *Trypanosoma spp.* They are pathogenic to man and may exist in two or more form in life cycle (Promastigote, Epimastigote, Trypomastigote, Amastigote).

**Leishmania spp**

Include three important *spp.*

1. *Leishmania donovani* (visceral Leishmaniasis)
2. *Leishmania tropica*: (cutaneous Leishmaniasis)
3. *Leishmania braziliensis*: It causes (muco-cutaneous Leishmaniasis) or Espondia

Old word leishmaniasis include *Leishmania donovani & Leishmania tropica*

1-transmitted to human by female sand fly genous phleotomus
2-life cycle pass in two hosts vertebrate & invertebrate
3-in invertebrate host the parasite are extracellular in the gut and transmission via the mouth parts during blood feeding.
Leishmania donovani

Obligate, intracellular parasite of reticuloendothelial cells, predominant in liver, spleen, bone marrow and lymph node of man and other vertebrate host were occurs in amastigote form. Morphologically, found in two forms:

1- Amastigote: Size: 5 by 3\(\mu\)m, Shape: oval to round, Nucleus: One, eccentric. Kinetoplast: Present, Consisting of dot-like blepharoplast, with small axoneme and prabasal body. Flagellum absent


- It causes a disease called Kala-azar or Dum-Dum fever or visceral Leishmaniasis or black fever

**Life cycle**

In man & other vertebrate host, the organism is transmitted by the bite of several species of blood-feeding sand flies (Phlebotomus) ex. *P. argentipes* which carries the promastigote in the anterior gut and pharynx. It gains access to mononuclear phagocytes where it transform into amastigotes and divides until the infected cell ruptures. The released organisms infect other cells.

**Intermediate host**

The sandfly acquires the organisms during the blood meal, the amastigotes transform into flagellate promastigotes and multiply in the gut of vertebrate host (insect) until the anterior gut and pharynx are filled, this event is called the metacyclic stage. By proboscis of sand fly, the metacyclic promastigotes form will enter the skin of man by biting.

**Definitive host**

The promastigotes engulfed by macrophages and change into amastigote in the host after weeks parasitized macrophages are free in blood and carried from the skin to liver, spleen, bone marrow. Parasites multiply inside kupffer's cells till cell rupture, again the amastigote form in blood stream will phagocyted by PMNs and monocytes. Insect will sucking this free amastigote during blood meal and the cycle will repeated.
Pathogenesis

1- *L. donovani* is the causative agent of visceral leishmaniasis, traditionally known as *kala-azar* ("black fever", particularly in India), because of its characteristic symptoms.

2- The disease is highly lethal if not treated properly. The incubation period generally ranges from 3 to 6 months, and in some cases may be over 2 years. In Indian leishmaniasis, incubation can be as short as 10 days.

3- The target cells are those of mononuclear phagocyte system. The two main tissues of infection are spleen and liver. Clinical symptoms include enlargement of spleen, liver (hepato-splenomegaly) and lymph node with fever, malaise, headache, emaciation, and anaemia.

4- heavy skin pigmentation which darkens the physical appearance (the reason for naming "black fever").

5- In a fully developed stage, the patient shows emaciation and anaemia. Where medical facilities are poor, mortality can be as high as 75–95% within 2 years.

6- The disease is often accompanied by complications with dysentery, tuberculosis, septicaemia and even HIV infection.

7- In active kalazar patients the cell-mediated immunity is impaired compare to cutaneous leishmaniasis.

**Lab diagnosis**

1- Parasitological diagnosis:

- Blood film by thick smear to see the amastigote form by using Gimsa stain
needle biopsy/aspiration for lymph node, liver, spleen

Culture of blood or needle biopsy/aspiration to see the promastigote form. NNN agar used as culture media for leishmania it consist of two parts of salt agar and one part defibinated rabbit blood. Media tube consist salt agar and one-third of volume from defibinated rabbit blood and mixing well. The specimen which include the amastigote form will inoculated into water condensation of the medium at 22-25°C. The amastigote form will change to promastigote and rapidly multiplies in the bottom of tube.

2-Non Specific Lab. Test

Blood Count: Normally, total leucocyte count is 3000/µl, during disease the count reach to 1000/µl or less also decrease in erythrocytes number reveals pancytopenia.

- Haemoglobin estimation
- Serum protein estimation: It will be raised reveal to albumin:globulin ratio (IgG High).

3-Molecular method: using DNA probes, PCR

4-Immunological test using ELISA, Monoclonal antibody

5-Animal inoculation

6-Leishmania (Montenegro) test
	a test used in the diagnosis of cutaneous leishmaniasis, in which killed suspension promastigotes antigens containing 6-10 million of this form per ml of 5% phenol salin injected intradermally. A positive reaction is indicated by the appearance of a erythema in 48 to 72 hours the test become positive 6-8 weeks after cure from kala-azar because the cell mediated immunity is low and lack delay hypersensitivity in active disease.

Post kala-azar dermal Leishmaniasis (PKDL)

It is skin lesion may appear 2-10 years after successful therapy for visceral Leishmaniasis caused by L. donovani in India. It is caused by the reversal of L. donovani from viscerotropic to dermatotropic. These lesions are soft, painless, granulomatous of varying size.

Leishmania tropica

It causes a disease called Dry or urban cutaneous Leishmaniasis or oriental sore or Baghdad boil or Old world cutaneous Leishmaniasis or tropica sore. Morphological and life cycle resemble to Leishmania donovani has two form amastigote in man & promastigote in sandfly.

life cycle also similar in both except that in man amastigote form resides in reticuloendothelial cells in skin not viscera causing cutaneous Leishmaniasis & the sandfly is P. sergenti.
Pathogenesis

- by direct inoculation of promastigotes through bite or itching the skin, it will transformed into amastigote

- cutaneous lesions develop causing chronic infective granuloma with fibrosis.

- after proliferation of amastigote, it will infiltrate the lymphocytes and plasma cells causing delay hypersensitivity skin reaction.

- during 1-2 years the ulceration will occur. This ulcer may heal alone leaving scar.

- the sores spread on the face and extremities, oriental sores may enlargement of draining lymph nodes.

Lab. Diagnosis

- Puncture of the esore edge then stained with Gimsa will allow to see the amastigotes inside macrophage.

- aspiration from the ulcer can culture it in NNN media or Hockmeyer’s medium

- Leishmania skin test: injection (killed promastigotes of Leishmania tropica in 0.5% phenol salin) show delayed hypersensitive response.

Treatment
<table>
<thead>
<tr>
<th>Leishmaniosis</th>
<th>Causative organism</th>
<th>Clinical manifestations</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visceral leishmaniosis</td>
<td><em>L. d. donovani</em></td>
<td>VL with rare cases of post kala-azar CL</td>
<td>China, India, Iran, Sudan, Kenya, Ethiopia, Mediterranean basin</td>
</tr>
<tr>
<td></td>
<td><em>L. d. infantum</em></td>
<td>VL or CL depending on strain</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>L. d. chagasi</em></td>
<td>VL and some atypical CL</td>
<td>Brazil, Columbia, Venezuela, Argentina</td>
</tr>
<tr>
<td>Cutaneous leishmaniosis</td>
<td><em>L. tropica</em></td>
<td>CL (dry) and rare cases of recidiva</td>
<td>Mediterranean basin, Afghanistan, Middle East, W &amp; N Africa, Kenya, Ethiopia</td>
</tr>
<tr>
<td></td>
<td><em>L. major</em></td>
<td>CL (wet)</td>
<td></td>
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<tr>
<td></td>
<td><em>L. aethiopica</em></td>
<td>CL and rare cases of DCL</td>
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<tr>
<td></td>
<td><em>L. mexicana</em></td>
<td>CL and rare cases of MCL and DCL</td>
<td>Central America &amp; Amazon basin</td>
</tr>
<tr>
<td>Mucocutaneous leishmaniosis</td>
<td><em>L. braziliensis</em></td>
<td>CL with some cases developing MCL later</td>
<td>Brazil, Peru, Ecuador, Venezuela, Columbia</td>
</tr>
<tr>
<td></td>
<td>complex</td>
<td></td>
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