### CAUSATIVE AGENTS & GEOGRAPHICAL DISTRIBUTIONS

<table>
<thead>
<tr>
<th>VISCERAL</th>
<th>CUTANEOUS</th>
<th>MUCOCUTANEOUS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Old World:</strong> Africa, Asia, Europe</td>
<td>L. Tropica complex</td>
<td>L. Mexicana Complex &amp; L. Braziliensis Complex</td>
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<tr>
<td>L. Donovan - India, Pakistan, Indonesia, Thailand, Ethiopia, East &amp; Central Africa.</td>
<td>L. Tropica: Big cities of Middle &amp; Far-East, Mediterranean area.</td>
<td>Central &amp; South America</td>
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<tr>
<td>L. Infantum - Mediterranean areas, Middle East &amp; China</td>
<td>L. Major: Central Asia, Middle-East, Africa &amp; Egypt (Sinai, Sohag and Minia).</td>
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<tr>
<td>New World - Americas</td>
<td>L. Aethiopica: Ethiopia and Kenya.</td>
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<tr>
<td>L. Chagasi - Central &amp; South America.</td>
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1. R.E.C viscera: Littoral cells of spleen, Kupffer cells of liver, bone marrow, peyer’s patches & mesenteric L.N.  
2. endothelial cells of kidney (urine).  
3. macrophages of intestinal wall (faeces), and nasal secretions.

<table>
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<tr>
<th>L. tropica - Dogs</th>
<th>L. major - Desert gerbils &amp; rodents</th>
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<tbody>
<tr>
<td>L. aethiopica - Wild rabbits &amp; rodents.</td>
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**Insect Vector** female sand flies - *Phlebotomus / Lutzomyia* Female sand fly of *Phlebotomus* *Lutzomyia* species

**MOI**  
- Bite of infected vector.  
- Blood transfusion/ organ transplantation.  
- Direct in epidemics by nasal secretions.  
- Congenital.  
- Accidental in laboratory.

**Amastigote (Leishman Donovan body):** In RECs all over the human body & reservoir hosts (intracellular in macrophages). Promastigote: In insect vector and culture.

**LIFE CYCLE**

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<th>VISCERAL</th>
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<tr>
<td>Definitive H</td>
<td>Man</td>
<td></td>
</tr>
<tr>
<td>Reservoir</td>
<td>Dogs, rodents, wild &amp; domestic animals.</td>
<td>L. tropica - Dogs</td>
</tr>
<tr>
<td>Insect Vector</td>
<td><strong>female sand flies - Phlebotomus / Lutzomyia</strong></td>
<td><strong>Female sand fly of Phlebotomus</strong></td>
</tr>
<tr>
<td>Infective Stage</td>
<td>Promastigotes in buccal cavity of sand fly</td>
<td>Promastigotes</td>
</tr>
</tbody>
</table>
| MOI | **Bite of infected vector.**  
**Blood transfusion/ organ transplantation.**  
**Direct in epidemics by nasal secretions.**  
**Congenital.**  
**Accidental in laboratory.**  
Amastigote (Leishman Donovan body): In RECs all over the human body & reservoir hosts (intracellular in macrophages). Promastigote: In insect vector and culture. | **Bite of infected sand fly.**  
**Direct contact.**  
**The stable fly (Stomoxys calcitrans).** | **Bite of infected sand fly.**  
**Direct contact.** |

**The vertebrate host is infected with promastigotes when bitten by the vector.**  
**The promastigotes enter circulating macrophages and reproduce as amastigotes.**  
**The vector (a sand fly) ingests macrophages when it ingests blood.**  
**The macrophage dies, the amastigotes are released, and they infect more circulating or fixed macrophages.**  
**The "type" of leishmaniasis (i.e., cutaneous, visceral, etc.) is determined by the primary location of the macrophages that are infected.**

**Vacuole**  
**Remains of axoneme**  
**Nucleus**  
**Kinetoplast (DNA)**  
**14 – 20 µm**  
**Nucleus**  
**Axoneme**  
**Kinetoplast**

3–4 x 2 µm
### VISCERAL LEISHMANIASIS

- Visceral leishmaniasis is an opportunistic disease.
- Immunocompromised status, protein, iron, vitamin A & zinc severity of infection.
- Parasitized macrophages are in small numbers in blood, but are numerous in RECs.
- The amastigotes multiply in fixed macrophages marked hyperplasia and destruction of RECs in the organs.
- In RECs of liver, spleen & LN hepatosplenomegaly & lymphadenopathy.
- BM is heavily infiltrated with parasitized macrophages pancytopenia.
- Parasitized lymphoid macrophages in intestinal mucosa & submucosa ulceration with leishmanial bodies in faeces.
- Urinary tract infiltrated with parasitized macrophages break down of mucosa with leishmanial bodies in urine.
- Naso-pharyngeal affection mucopurulent discharge containing leishmanial bodies.
  - Incubation period: 2-6 ms.
  - A primary lesion at site of infection in infants in Africa in legs & arms (leishmanioma).

### POST-KALA AZAR DERMAL LEISHMANIASIS (PKDL):

- Chronic, progressive, granulomatous, non-ulcerating, hypopigmented nodular cutaneous lesion, 6 ms-5 ys after spontaneous or drug cure (Pentostam).
- Parasites migrate and localized mainly in face, resembling Lupromatous leprosy or disseminated cutaneous leishmaniasis.

### VISCERAL & MUCOCUTANEOUS SPECIFIC TREATMENT

<table>
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<tr>
<th>SYSTEMIC (IV)</th>
<th>ORAL</th>
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<tbody>
<tr>
<td>- Pentavalent antimony compounds: Pentostam (Sodium stibogluconate).</td>
<td>Supportive: - Diet rich in vitamins, iron and liver therapy. - Proper antibiotics. - Blood transfusion.</td>
</tr>
<tr>
<td>- Amphotrocin B.</td>
<td>Local measures: - Surgical excision or scraping (curettage). - Plastic surgery. - Heating of lesion to 50°C with coned infra red rays and freezing therapy using carbon dioxide snow.</td>
</tr>
<tr>
<td>- Interferron gamma &amp; Pentostam-relapse.</td>
<td>- Pentostam is the drug of choice, 2-3 courses may be needed. - If sores are 1-3, treatment is by local infiltration of the drug into the edges of the ulcers. - Resistant cases/ diffuse cutaneous leishmaniasis are treated with pentamidine.</td>
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**Miltefosine:** The first oral drug approved for ttt of leishmaniasis.

- Chemical methods using topical 10% atebrine solution.
- I.D. injection of interferon gamma.
- Cleanliness, secondary infection needs local or systemic antibiotic medication.

### FEVER - IMPORTANT SIGN

- continuous, remittent with a 2x/d rise/irregular.
- due to release of pyrogens by infected macrophages due to:
  - Phagocytosis of amastigotes.
  - Uptake of cellular debris from ruptured parasitized macrophages.

### Types & Causes And Of Anemia In Kala-Azar:

1. Normocytic normochromic anemia:
   - ↑ destruction of RBCs.
   - ↓ erythropoiesis.
   - Autoantibodies to RBCs.
   - Hemorrhage.
   - Alterations in RBCs membrane permeability.
   - Production of haemolysin by the parasites.
2. Macrocytic anemia
   - Due to reticulo-endothelial hyperplasia and fatty infiltration of the liver deficient storage of vitamin B12.
3. Microcytic anemia
   - Due to lack of iron absorption from intestine.
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<th>L. Tropica</th>
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<td>dry oriental sore, Delhi boil/ urban CL</td>
<td>wet sore or rural CL</td>
<td>Chronic diffuse CL</td>
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<tr>
<td>• I.P. up to 6 ms.</td>
<td>I.P. is short; few days or weeks.</td>
<td>It starts as a single lesion that spreads slowly due to proliferation of the parasite.</td>
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<tr>
<td>• Lesion at site of bite (face &amp; hands), single or multiple.</td>
<td>▪ Lesions primarily affect lower limbs.</td>
<td>Whole body is covered with nodules that don’t ulcerate.</td>
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<tr>
<td>• Localized nodule.</td>
<td>▪ Small itchy papules, first dry moist with crust that falls oozing ulcer (wet sore), with raised margin, granulation tissue at the base.</td>
<td>characterized by low humoral and cell-mediated immunity spread of infection.</td>
</tr>
<tr>
<td>• Nodule ulcerates after ms, with sharp cut edges, raised indurated margin &amp; scanty exudate.</td>
<td>▪ The lesion usually ulcerates early and heals rapidly.</td>
<td>It is difficult to treat.</td>
</tr>
<tr>
<td>• The dry ulcers usually heal spontaneously within a year.</td>
<td>▪ 2ry bacterial infection can occur.</td>
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**MUCOCUTANEOUS LEISHMANIASIS**

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<th>L. Mexicana Complex</th>
<th>L. Braziliensis Complex</th>
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<td>new world CL (Chiclero ulcer)</td>
<td>New world mucocutaneous leishmaniasis (Espundia).</td>
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</table>

- The lesion is usually single & affects the ear causing destruction of the cartilage.
- It occurs in forest workers who collect chicle gum.
  - Multiplication of amastigotes in the skin macrophages formation of papule, nodule and ulcer.
  - The ulcer may be single or multiple, that heals over months to years scar.

Recovery from cutaneous leishmaniasis life-long immunity against the same *Leishmania* species.

- Small painless, itchy nodule, which ulcerates.
- Ulcer heals & mucocutaneous lesions in the face develop after years.
- The mm of nose, mouth pharynx and larynx are affected either by direct extension, or lymphatics.
  1. The ulcers are painful, chronic, destructive & resistant to tt.
  2. Greater deformity (Mutilation)
  3. Erosion of the nasal septum, palate, larynx with loss of voice.
  4. Death may develop from aspiration pneumonia septicemia due to 2ry bacterial infection.

**ESPUNDIA OR MUCOCUTAENOUS LEISHMANIASIS**

- Caused by *L. braziliensis*.
- ~20% of infected patients develop ulcers of the oral and nasal mucosa.
- Progression of the ulceration is slow but steady, ultimately destroying all soft parts of the nose, the lips & soft palate.
**DIAGNOSIS**

**VISCERAL**

1. **M/E:** Detection of amastigotes in smears made from:
   - Peripheral blood.
   - BM puncture.
   - Splenic puncture & liver puncture.
   - Enlarged lymph node aspirate or puncture.
   - Nasopharyngeal secretions, stool & urine.
   - Nodular lesions in PKDL.
   - The smears of body fluids are stained with Leishman, Giemsa/ Wrights stain.
   - H&E stain is used for tissue sections.
   - Amastigotes: inside macrophages in large numbers with little extracellular form.

2. **Culture on NNN medium:** shows promastigotes in the form of rosette grouping, 1-4 weeks.

3. **Animal inoculation:**
   - Intra-peritoneal inoculation of hamster.
   - In +ve cases, amastigotes can be seen in smears from ulcers or nodules at site of inoculation/spleen, weeks post infection.

**INDIRECT**

1. **Immunological diagnosis:**
   Serological tests: Leishmanial antigens prepared from cultures are used to detect anti-leishmanial antibodies using:
   - IFA, IHA, ELISA.
   - Complement fixation test (CFT).
   - Direct agglutination test (DAT).
   - Rapid immunochromatographic dipstick (ICT).

2. **Molecular diagnosis:** It helps in species identification of *Leishmania*.

3. **Blood picture:**
   - CBC: anemia, leucopenia & thrombocytopenia (*Pancytopenia/ Aplastic anemia*).
   - Serum: hypergammaglobulinemia & low albumin level.

**Leishmanin skin test (Montenegro test):**
- It is a delayed hypersensitivity skin test.
- Intradermal 0.1ml of killed promastigotes of *L. donovani*.
- **Positive result:** induration and erythema of ≥ 5 mm after 48-72 hrs.
- **Positive test:** past infection with *Leishmania* as it becomes positive 6-8 weeks after cure.
- The test is negative in active infection and in PKDL due to marked depression of cellular immune response.

**PREVENTION & CONTROL**

- Control of reservoir host & sand flies: destruction of their breeding grounds by DDT (dichloro-diphenyl-trichloroethane).
- Treatment of infected persons & Humans can be protected by using bed nets, window mesh screen (40 meshes / inch²), repellents as dimethyl phthalate, and spraying of insecticides.
- Due to sylvatic and rural nature of the disease, it is difficult to control the source of infection.
- Preventive and control measures are similar to those of visceral leishmaniasis.