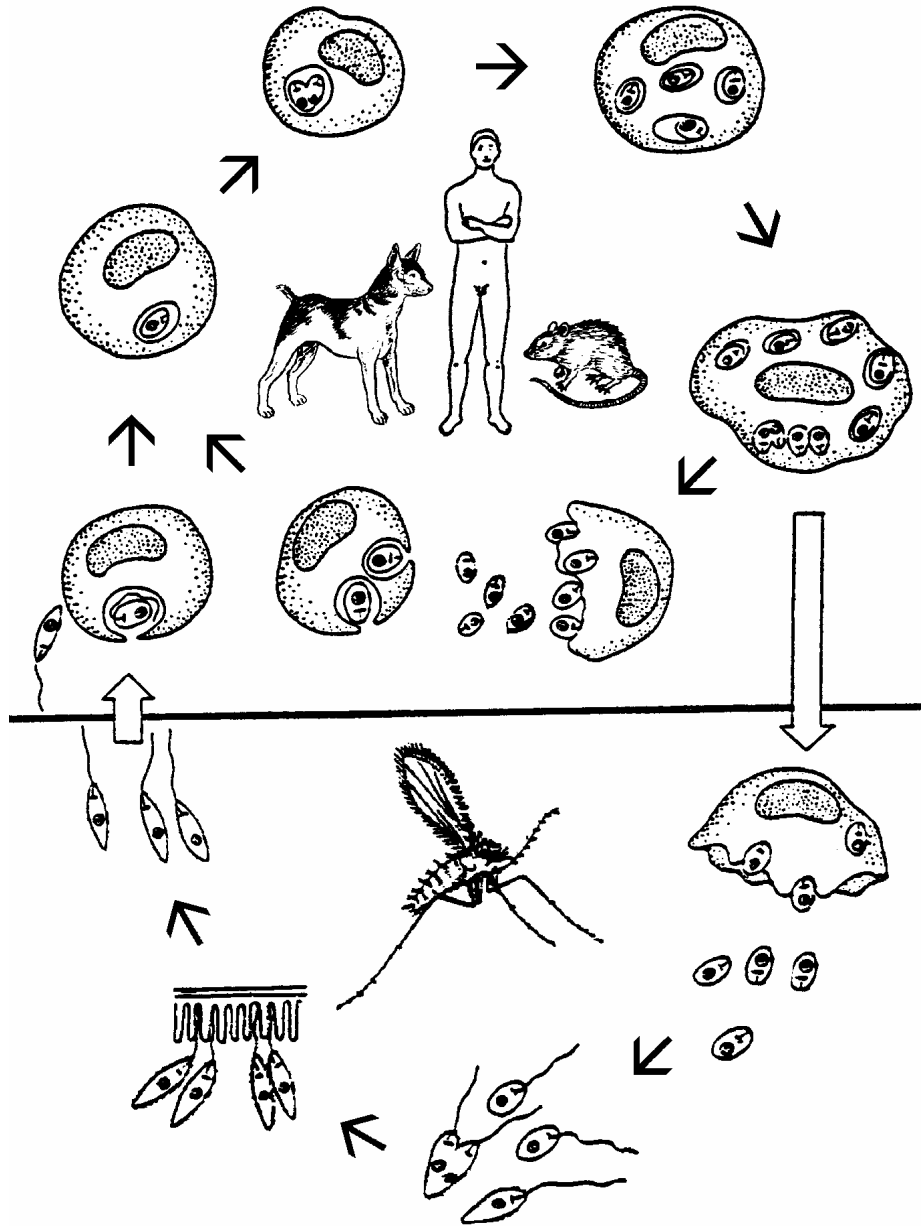


## Leishmania Handout



Leishmania Life Cycle. As the sandfly feeds metacyclic promastigotes are delivered into bite wound of the vertebrate host and phagocytosed by macrophages. The promastigotes convert to amastigotes within the phagolysosome and undergo multiple rounds of binary fission. The infected macrophage lyses and releases the amastigotes which are taken up by other macrophages, thus reinitiating the replicative cycle. Infected macrophages are also ingested by sandfly. Amastigotes are released and convert to promastigotes in the gut of the sandfly and replicate by binary fission. Many of the promastigotes will attach to the epithelium. Their continued replication and migration to the foregut will eventually block the proventriculus, pharynx and proboscis. Biochemical changes in the promastigote surface and slight

morphological changes occur as the parasites stop replicating and develop into infective metacyclic promastigotes.

#### CLINICAL SPECTRUM OF DISEASE

- **Cutaneous Leishmaniasis (CL)**

Relatively benign self-healing lesions limited to the skin (aka simple or localized CL). The skin lesions are generally painless and non-pruritic and take weeks to months to heal.

- **Diffuse Cutaneous Leishmaniasis (DCL)**

A rare cutaneous infection with non-ulcerating nodules resembling lepromatous leprosy. The disease is characterized by 'anergy' and the lesions can disseminate over the entire body.

- **Leishmaniasis Recivida**

A hypersensitive dermal response primarily associated with a chronic recurrence of *L. tropica* in the middle east.

- **Mucocutaneous Leishmaniasis (MCL)**

A metastatic spread of infected macrophages to pharyngeal, buccal, or nasal tissues by lymphatic or hematogenous dissemination. Generally refers to the S. American disease called espundia.

- **Visceral Leishmaniasis (VL)**

A generalized infection of the reticuloendothelial system with visceral and bone marrow involvement. Exhibits a high mortality if untreated.

#### Species of *Leishmania* Infecting Humans

Agents of New World cutaneous, mucocutaneous, and diffuse leishmaniasis	Agents of Old World cutaneous, recidivans, and diffuse leishmaniasis	Agents of visceral leishmaniasis
Mexicana Complex  <i>L. mexicana</i> <i>L. amazonensis</i>	<i>L. tropica</i>  <i>L. major</i>	<i>L. donovani</i>  <i>L. infantum*</i>
Braziliensis Complex  <i>L. braziliensis</i> <i>L. panamensis</i> <i>L. guyanensis</i>	<i>L. aethiopica</i>  <i>L. infantum*</i>	<i>L. chagasi**</i>

\*Both visceraltropic and dermatropic strains exist.

\*\**L. chagasi* and *L. infantum* are very similar genetically. *L. chagasi* possibly introduced to New World by Europeans. *L. chagasi* is also associated with an atypical cutaneous disease (nodular lesions).

### Simple (or Localized) Cutaneous Leishmaniasis

- *L. mexicana* complex (chiclero ulcer), *L. tropica* (oriental sore), *L. major*
- chronic ulcerated, papular, or nodular lesion
- the lesion is painless, non-tender, non-pruritic and usually 'clean'
- self-healing, months to years
- sometimes satellite lesions and palpable lymph nodes

### Diffuse Cutaneous Leishmaniasis

- *L. mexicana*, *L. aethiopica*
- scaly, not ulcerated, nodules
- chronic and painless
- numerous parasites in lesions
- seldom heal despite treatment

### Leishmania Recidivans

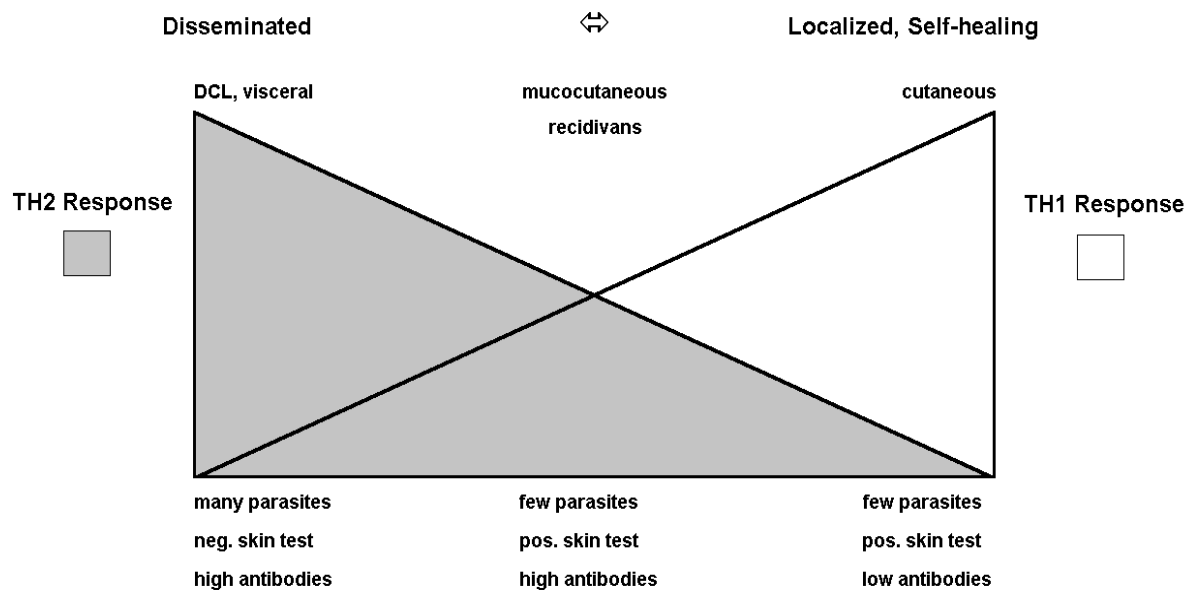
- primarily *L. tropica* (Iran and Iraq)
- chronic recurrence often associated inadequate treatment
- papular lesions or rash
- satellite lesions at margins of healed primary lesion
- not easily cured with treatment

### Mucocutaneous Leishmaniasis

- primarily *L. braziliensis* (espudias)
- two stages
  - simple skin lesion
  - 2° mucosal involvement
- can occur long after primary lesion (up to 16 years)
- frequently in naso-pharyngeal mucosae
- metastasis via blood or lymphatic systems
- variable types and sizes of lesions
  - chronic and painless

## Visceral Leishmaniasis

- *L. donovani* (Kala Azar), *L. infantum*, *L. chagasi*
- incubation period of 10 days to years (generally 2-6 months)
- amastigotes in reticuloendothelial system (RES) of spleen, liver, bone marrow, and lymph nodes
- fever, malaise, weakness
- wasting despite good appetite
- spleno- and hepatomegaly, enlarged lymph nodes and tonsils
- depressed hemopoiesis (anemia, leucopenia, thrombocytopenia)
  - immunocompromised
  - petechial hemorrhages in gums, lips, gut
- inadequate treatment can result in dermal manifestations



### Diagnosis of CL, MCL, and DCL

- suspected because of:
  - ◆ geographical presence of parasite
  - ◆ history of sandfly bite
  
  - ◆ chronic, painless, 'clean' ulcer
  - ◆ chronic, painless naso-pharyngeal lesions (destruction of nasal septum)
  - ◆ chronic nodular lesions
  
- demonstration of parasite
  - ◆ amastigotes in scrapings or aspirates
  - ◆ culture of promastigotes
  - ◆ inoculation into hamsters
  
- delayed hypersensitivity skin test (Montenegro)
  
- serology (?)

### VL DIAGNOSIS

- suspected because of:
  - ◆ geographical presence of parasite
  - ◆ history of sandfly bite
  - ◆ prolonged fever, spleno-megaly, hepatomegaly, anemia, leukopenia, hyperglobulinemia
  
- demonstration of amastigote in bone marrow aspirate
  
- serological tests
  - ◆ direct agglutination test
  - ◆ ELISA ('dipstick') with recombinant 39 kDa antigen

### TREATMENT

- pentavalent antimonials (eg., glucantime, pentostan)
  - ◆ 20 mg/kg/day for 15-20 days
- pentamidine (for Sb<sup>5+</sup> failures)
- Amphotericin B
  - ◆ 0.25-1 mg/kg/day

### CONTROL

- avoid sandfly bites
- bed nets
- insecticide in domiciliary and peridomiciliary transmission
- destruction of dog reservoir
- 'tropica vaccine'
  - ◆ historical inoculation in 'covered areas'
  - ◆ risk of recidiva or VL

### EPIDEMIOLOGICAL ASPECTS

- New World Dermal
  - ◆ zoonosis (reservoir without lesions)
  - ◆ human infection acquired by entering forest (eg., occupational, recreational)
- Old World Dermal
  - ◆ urban--dog reservoir
  - ◆ rural--rodent reservoir
- Visceral
  - ◆ *L. donovani* (India): human-fly-human transmission
  - ◆ *L. donovani* (Africa): rodent reservoir
  - ◆ dog (usually with lesions) is potential reservoir in other species