

• بِسْمِ اللّٰهِ الرَّحْمٰنِ

الرَّحِیْمِ

• *Cutaneous*

leishmaniasis

• Discuss

- Epidemiology , etiology, lifecycle, transmission
- Pathogenesis
- Clinical features
- Lab diagnosis

- and treatment
- of cutaneous leishmaniasis
- *Leishmania* species
- Kingdom protozoa
- Phylum sarcomastigophora
- Subphylum mastigophora (the flagellates)
- Hemoflagellate
- Leishmania classification
- Infection in humans is caused by ~20 *Leishmania* species (*Leishmania* and *Viannia* subgenera)
- Infection caused by leishmaniasis is called leishmaniasis
- Clinical classification

- Leishmania species are classified into three clinical groups based on site of infection
 - Leishmania that cause infection on the skin called cutaneous leishmaniasis
 - *L. tropica*
 - *L. major*
 - *L. aethiopica*
 - *L. mexicana*
 - Leishmania species that cause infection of both skin and mucous membrane (mucous membranes of the nose, mouth and throat cavities)
 - *L. braziliensis*
 - Leishmania that causes infection of the deep viscera
 - *L. donovani*
- Geographic classification
- Old world leishmaniasis is caused by

- *L. tropica*
- *L. major*
- *L. aethiopica*
- *L. donovani*
- New world leishmaniasis is caused by
 - *L. braziliensis*
 - *L. mexicana*
- History
- The parasite was named in 1903 after the Scottish pathologist William Boog Leishman who observed oval bodies in 1901, while examining pathologic specimens of a spleen from a patient who had died of visceral leishmaniasis.
- Epidemiology

- *Leishmania* currently affects 12 million people in 98 countries. There are ~ 2 million new cases each year
- Transmission
- Transmitted to humans by the bite of ~30 species of sandflies [*Phlebotomus* (Old World) and *Lutzomyia* (New World)]
- The sand fly injects the infective form 'promastigote' in humans
- Morphology
- *Leishmania* exist in two forms:
 - the Amastigote,
 - the intracellular form (cells of reticuloendothelial system) in the vertebrate host. The amastigote, literally means "without a flagellum," (although not totally devoid of it) It is rounded, non-motile form and divides by binary fission

. The amastigote is also called the Leishman-Donovan (LD) body.

– the Promastigote

- The extracellular form in the sandfly. The promastigote, literally the body form with “an anterior flagellum” ; it is motile, and grows by longitudinal binary
Promastigotes can be grown in culture.

- Life cycle
- Pathogenesis
- The pathogenesis involves intracellular survival within the macrophage(safe from the immune response) and formation of a granulomatous reaction
- Clinical features
- Cutaneous leishmaniasis,
 - causes skin lesions. The lesions develop within a few weeks or months of sandfly bite.

- These can change in size and appearance over time.
 - They start out as papules (bumps) or nodules (lumps) and may end up as ulcers (like a volcano, with a raised edge and central crater, the volcano sign) and may get covered with the crust.
 - They are usually painless but can be painful.
 - Some people have swollen regional glands
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- The range of clinical features in cutaneous leishmaniasis parallels patients immunological response to the parasite
 - At one end of the spectrum lies diffuse cutaneous leishmaniasis, , in which there is little cell-

mediated immune response and many lesions and heavy parasitization and at the other end is leishmaniasis recidivans in which there is good immunity and slowly expanding solitary lesion healing at the center with scarce parasites.

- Skin lesions are known by many names oriental sore/baghdad boil/delhi boil etc.
- Cutaneous leishmaniasis
- Mucocutaneous leishmaniasis
- *Mucocutaneous leishmaniasis* refers to a disfiguring sequela of cutaneous leishmaniasis that results from dissemination of parasites from the skin to the nasoro-pharyngeal mucosa

- Progressive ulcerative destruction of naso-oro-pharyngeal mucosa and surrounding tissues in the context of a hyperactive immune response

- Lab diagnosis
- Microscopy
- Culture
- Animal inoculation
- Serology
- PCR
- Skin test

- Specimens
- Cutaneous/ mucocutaneous leishmaniasis
 - Skin biopsy
 - Full thickness punch biopsy specimens at the active border of the lesion

- Needle aspirates
 - Take 0.1 mL of 0.9% saline in a syringe. Insert the needle, into the dermis of the active border. Repeatedly move the needle back and forth under the skin, simultaneously rotating the syringe and applying gentle suction, until pinktinged tissue juice is noted in the hub of the needle
- Visceral leishmaniasis
 - Peripheral blood
 - Bone marrow aspirate
 - Spleen aspirate
- Microscopy
- Smears (skin aspirate, peripheral blood, bone marrow aspirate, spleen aspirate) are stained by Leishman or Giemsa stain and examined under the oil immersion lens. Amastigote forms (LT/LD

bodies) can be seen within macrophages and outside

- Culture
- Novy-McNeal-Nicolle(NNN) medium
 - This is a blood agar slope with overlay of Locke's solution (normal saline+filtered urine) with added antibiotics in screw capped bottles.
 - Incubated at 24 °C for 7 days
 - Promastigote (in clusters) forms grow and can be demonstrated by examining a drop of fluid under microscope after staining
- Animal inoculation
- The clinical specimen material is inoculated in hamsters intraperitoneally and intradermally. The animals are kept at 25 °C. the

parasite is demonstrated in smears from ulcers and spleen.

- Serology
- Specific
 - Antibody detection by ELISA
 - immunochromatographic dipstick testing of fingerstick blood for antibody to rK39 antigens (visceral leishmaniasis)
- Nonspecific
 - NAPIER'S ALDEHYDE TEST: 1ml of clear serum of patient + drop of formalin → shake and kept at room temp → Jellification & opacification within 3 – 30min(POSITIVE)
 - CHOPRA'S ANTIMONY TEST: 0.2ml serum diluted 1 in 10ml distilled water →, Overlaid by 4% urea stibamine → thick flocculent disc within 10 – 15min(POSITIVE)
- Skin test

- MONTENEGRO SKIN TEST---- 0.1ml of killed promastigote antigen intradermally read after 72hrs.
- POSITIVE: dermal leishmania & recovered from kala azar.
NEGATIVE: active case of kala azar
- PCR
- DNA amplification by PCR
- Treatment
- **Any of the following regimens**
- **Visceral Leishmaniasis**
 - Parenteral therapy
 - Pentavalent antimony IV or IM 28 days
 - Amphotericin B
 - Paromomycin for ~21 days
 - Pentamidine IV, IM thrice weekly for ~15–30 doses
 - Oral therapy
 - Miltefosine for 28 days
- **Cutaneous Leishmaniasis**
 - Parenteral therapy

- Pentavalent antimony IV, IM for 10–20 days
- Pentamidine IV, IM for 7 doses
- Amphotericin B
- Oral therapy
 - Fluconazole for 6 weeks
 - Ketoconazole for 28 days
 - Itraconazole for 28 days
 - Miltefosine for 28 days
- **Mucosal Leishmaniasis**
 - Pentavalent antimony IV, IM for 28 days
 - Amphotericin B (deoxycholate) IV
 - Pentamidine IV, IM thrice weekly for 15 doses
- Prevention
- Sand fly control