LEISHMANIASIS

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Leishmaniasis

A-Visceral Leishmaniasis (Kala Azar): *Leishmania donovani* complex

In old world

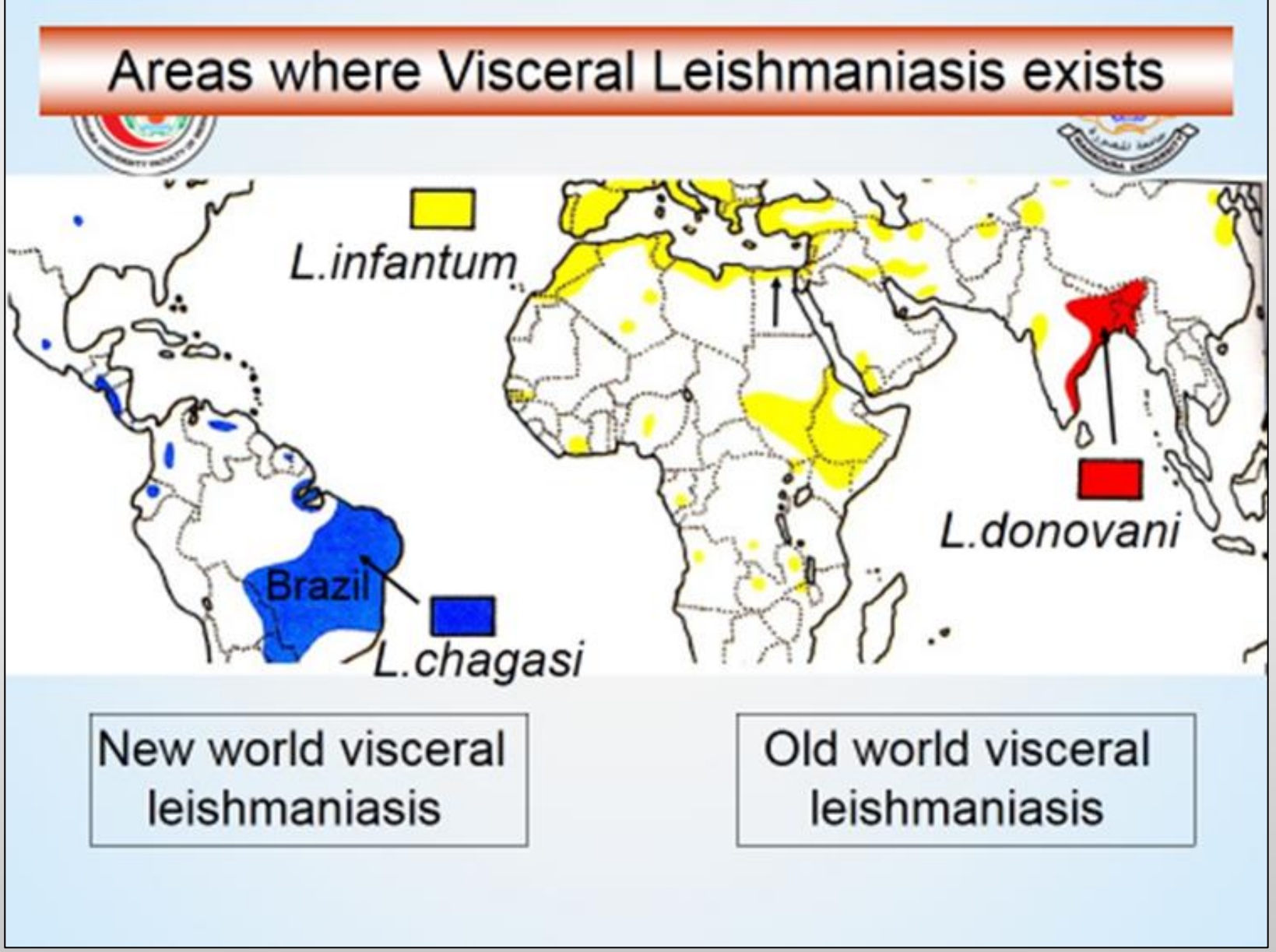
- ***L. donovani***: India, Pakistan, Indonesia, Thailand, Central Africa and Sudan.
- ***L. infantum***: Mediterranean area, Middle East and China.

In new world

- ***L. chagasi***: America (Central and South America).

B- Cutanous Leishmaniasis: In old world: *Leishmania major*

(Old world cutaneous leishmaniasis (**OWCL**)); rural distribution (near desert: Libya, Egypt: Sinai).



Geographical distribution of visceral leishmaniasis

Morphology

Amastigote form:

Shape: ovoid

Size: 2-3µ,

Content: spherical nucleus, kinetoplast: from which arises an intracytoplasmic axoneme (no free flagellum).

Site: In reticuloendothelial cells (RECs)

all over the human body and reservoir host, typically intracellular in macrophages.

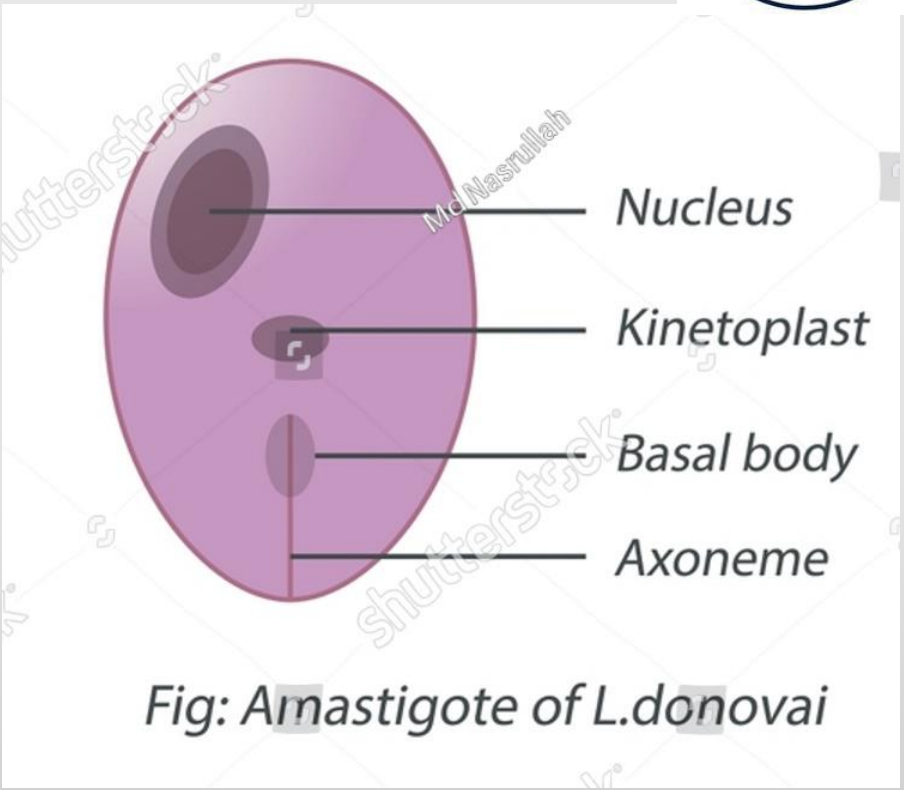
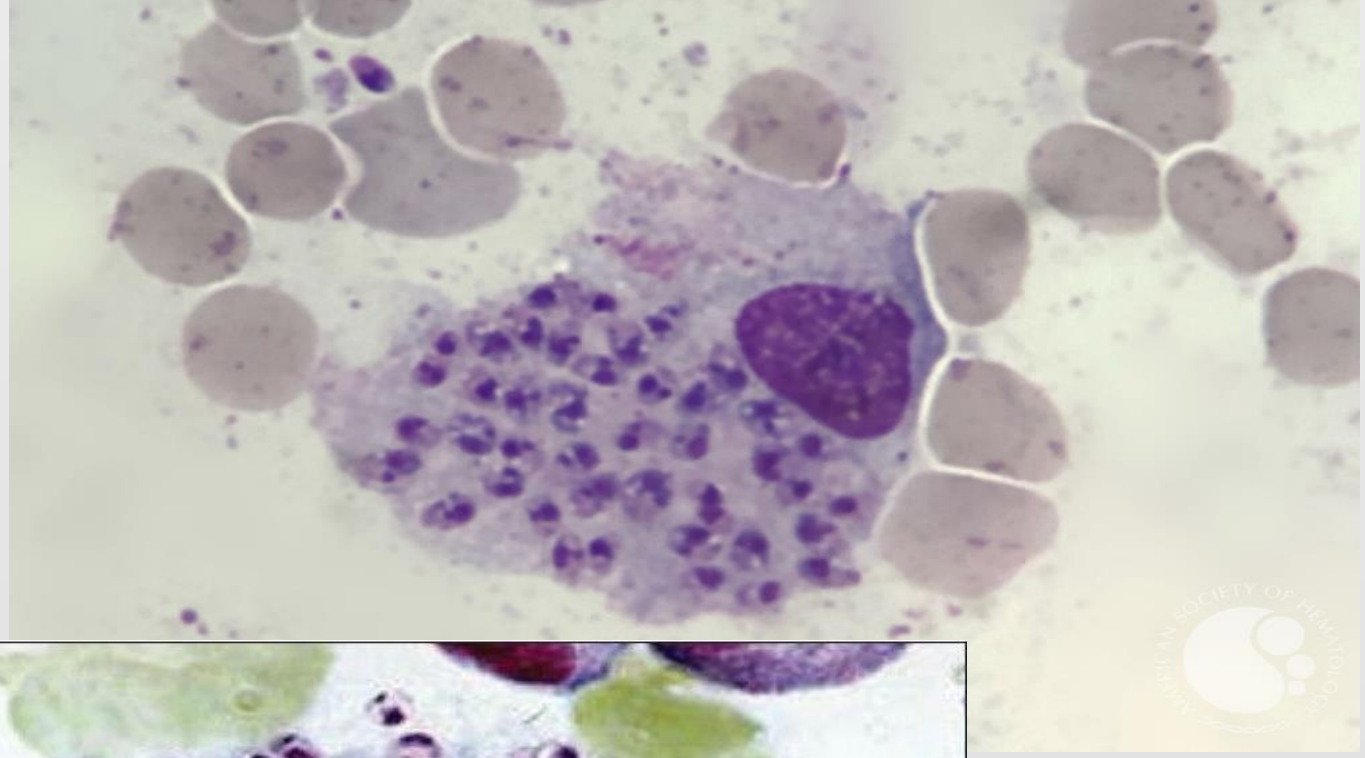
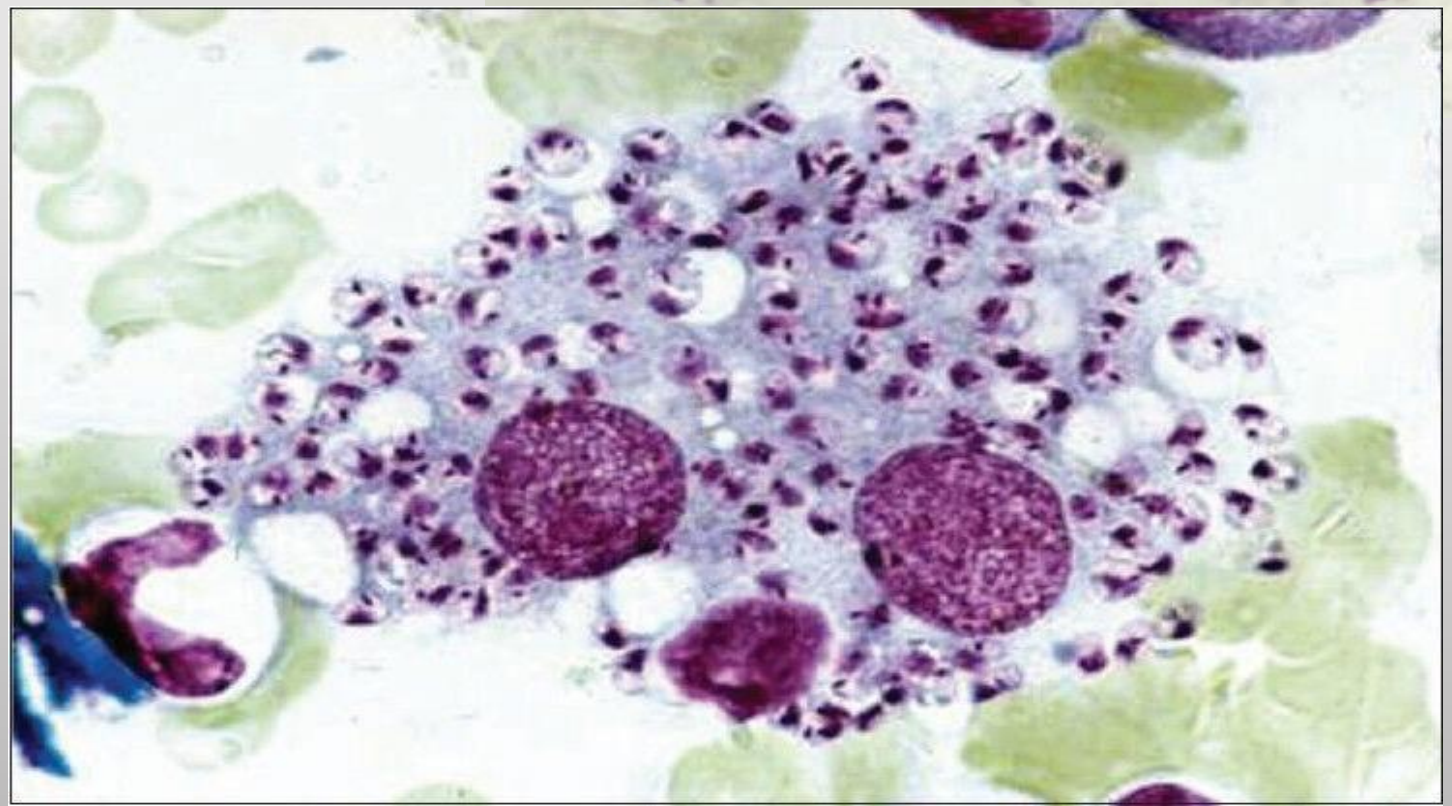


Fig: Amastigote of L.donovai

Leishmania amastigotes

inside macrophage





Morphology

Promastigote form:

Shape: fusiform (spindle-shaped)

Size: 4×12µ,

Content: central vesicular nucleus, anterior free flagellum, anterior kinetoplast (no undulating membrane).

Site: In insect vector and culture.

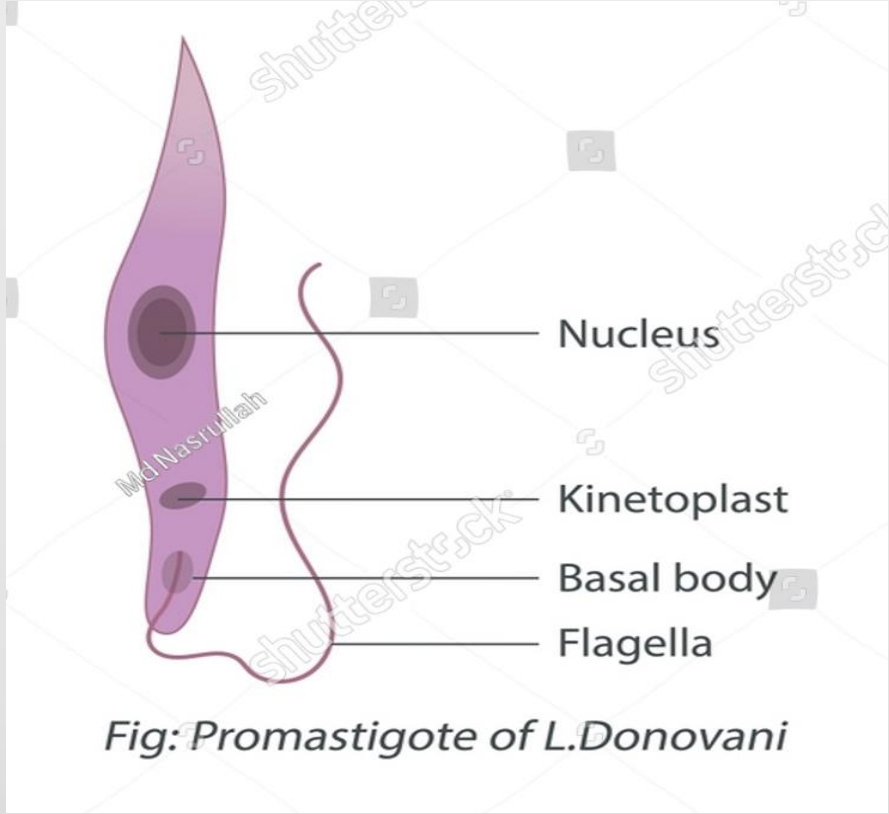
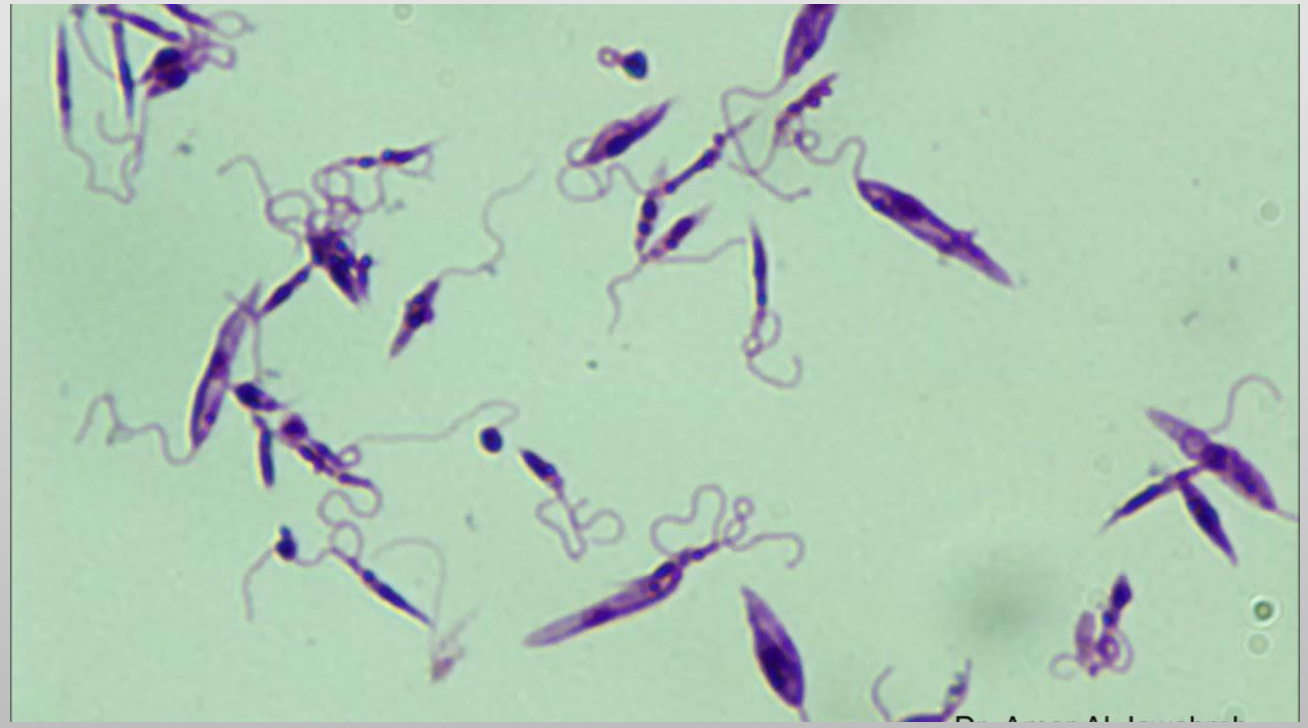
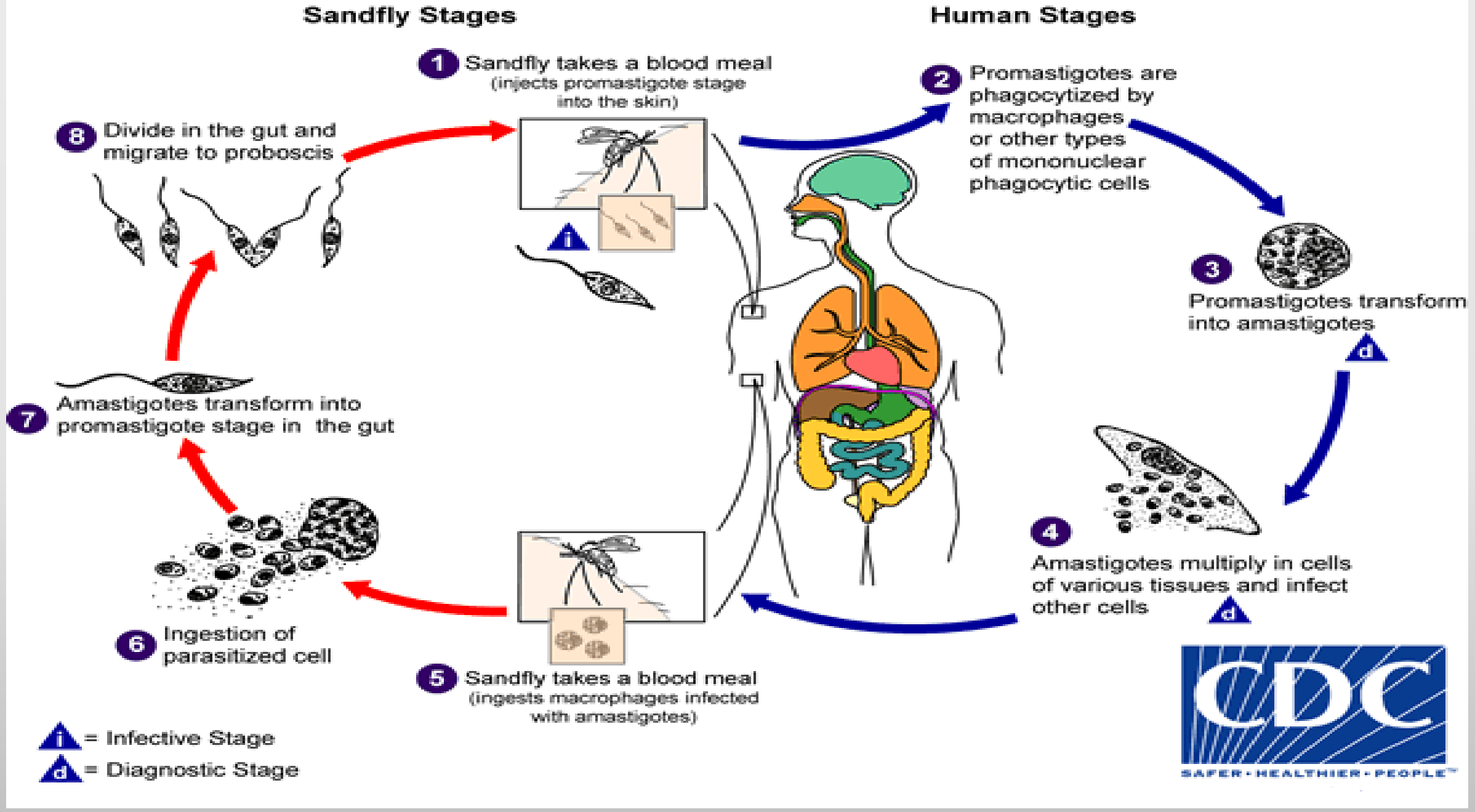


Fig: Promastigote of L.Donovani

Leishmania promastigotes





Life cycle of *Leishmania donovani*

Life cycle of Visceral Leishmaniasis

Habitat: *Leishmania* amastigotes live intracellular in **macrophages** of reticuloendothelial (**R.E.S.**) tissue, especially spleen, liver, bone marrow, intestinal mucosa and mesenteric lymph nodes.

Definitive host: Man

Reservoir host: Dogs, rodents, wild and domestic animals.

Insect vector: **Female sand flies** of the genus ***Phelebotomus*** in the old world, and ***Lutzomyia*** in the new world.

Infective stage: *Leishmania* promastigotes in female sand fly gut.

Mode of infection:

1-Regurgitation of **promastigotes** into bite wound of infected sand fly.

2- Rare modes: (by **amastigotes**):

(a) Blood transfusion.

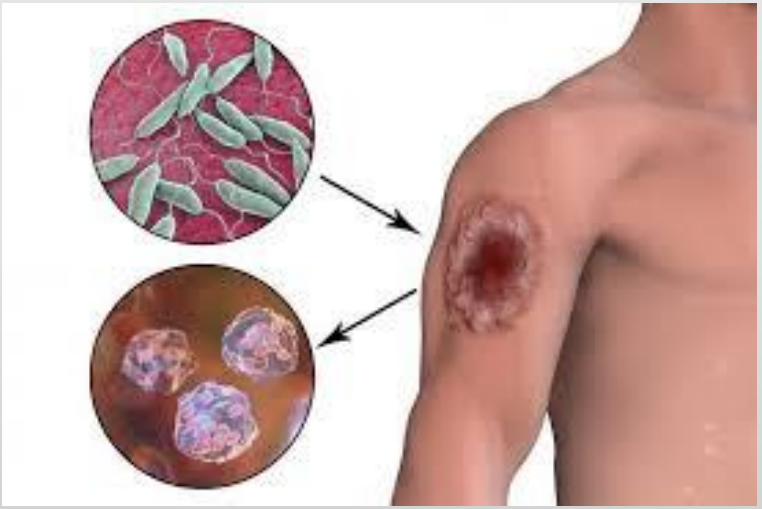
(b) Transplacental.

(c) Accidental laboratory wound.

(d) Mechanical by blood sucking flies.

Life cycle of Cutanous Leishmaniasis

Habitat: *Leishmania* amastigotes inhabits the **RECs** of **skin;** the amastigotes reside and multiply in the RECs of the **skin**, without invasion of blood or internal organs.



Definitive host: Man.

Reservoir host: Desert gerbils and rodents.

Insect vector: **Female sand flies** of the genus ***Phelebotomus.***

Infective stage: *Leishmania* promastigotes in female sand fly gut.

Mode of infection:

1. Bite of infected sand fly.
2. Direct contact.
3. The **stable fly** may transmit the organisms mechanically from an **open ulcer** or through unbroken skin.

A- Visceral Leishmaniasis

A- Visceral Leishmaniasis (Kala Azar):

➢Definition:

Visceral Leishmaniasis (Kala Azar): A chronic and potentially fatal parasitic disease of the viscera RECs (particularly the liver, spleen, bone marrow and lymph nodes) due to infection by *Leishmania* parasite. Also known as Kala-azar.

Pathogenesis

- **Amastigotes** multiply in macrophages → (rupture + reinvasion) → compensatory and reactive **hyperplasia** and **destruction** of R.E.Cs.
- **Macrophages** as kupffer cells of liver, littoral cells of spleen, peyer's patches of intestine, bone marrow and lymph nodes.

- **Multiplication of amastigotes in the RECs** of liver, spleen and lymph nodes → hepatosplenomegaly and lymphadenopathy
- The bone marrow → pancytopenia
- Lymphoid macrophage cells in intestinal submucosa → ulceration and dysenteric symptoms, with leishmanial bodies (amastigotes) in faeces.
- Urinary tract: kidneys, pelvis and urinary bladder → break down of mucosa with leishmanial bodies escape in urine.
- Naso-pharyngeal affection → mucopurulent discharge containing leishmanial bodies.

➢ Clinical manifestations of Kala azar:

1. **fever**: intermittent (40c, 2 peaks in one day, twice-daily rise).
2. **Enlarged** liver, spleen, lymph nodes (hepatosplenomegaly + generalized lymphadenopathy).
3. **Pancytopenia**: (aplastic anaemia + leucopenia + thrombocytopenia).
4. **GIT:** Diarrhoea or dysentery (ulceration of intestinal mucosa).
5. Normocytic normochromic **anemia** is a significant feature of kala-azar with hemoglobin levels of 5-10 g/dl.

Types and causes of anemia in Kala-azar:

a. Normocytic normochromic anemia:

- Increased sequestration and destruction of RBCs due to hyperspleenism.
- Decreased erythropoiesis due infiltration of bone marrow by parasitized macrophages.
- Alterations in RBCs membrane permeability.
- Autoantibodies to red cells may cause hemolysis.
- Hemorrhage.
- Production of haemolysin by the parasites.

b. Macrocytic anemia: Due to reticuloendothelial hyperplasia and fatty infiltration of the liver leading to deficient storage of vitamin B12.

c. Microcytic anemia: Due to lack of iron absorption from intestine.

6. Post kala-azar dermal leishmaniasis (PKDL):

- It appears after spontaneous or drug cure (Pentostam) of kala-azar (6 months - 5 ys).
- It is common in the Indian and African type of kala-azar.
- It is due to migration of the parasites from viscera to the skin.
- The **skin lesions** (**diffuse depigmented nodules**) are chronic, progressive and painless hypopigmented macules, erythematous patches, or yellowish pink non-ulcerative granulomatous nodules.
- It is localized in the outer surface of the body mostly the face especially on nose, chin, cheeks, lips, forehead and ears, resembling Lepromatous leprosy or disseminated cutaneous leishmaniasis.

Post kala-azar dermal leishmaniasis (PKDL)

➢Diagnosis:

I. **Clinical:** Any case, in an endemic area, with fever of more than 2 weeks, splenomegaly and/or weight loss is suspected of having kala azar

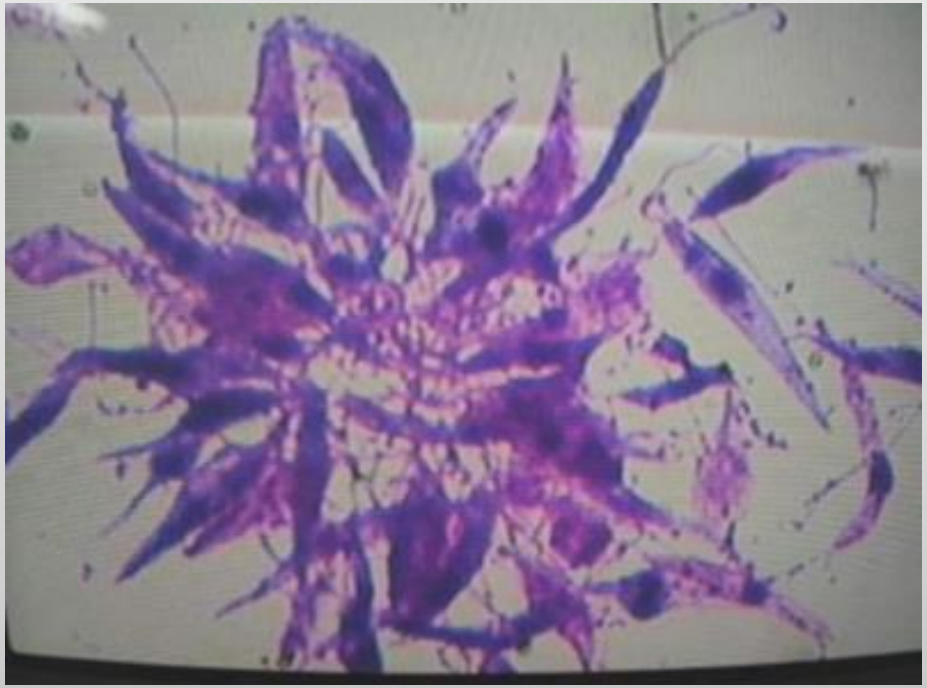
II. **Laboratory:**

1- Microscopy: Detection of amastigotes in smears:

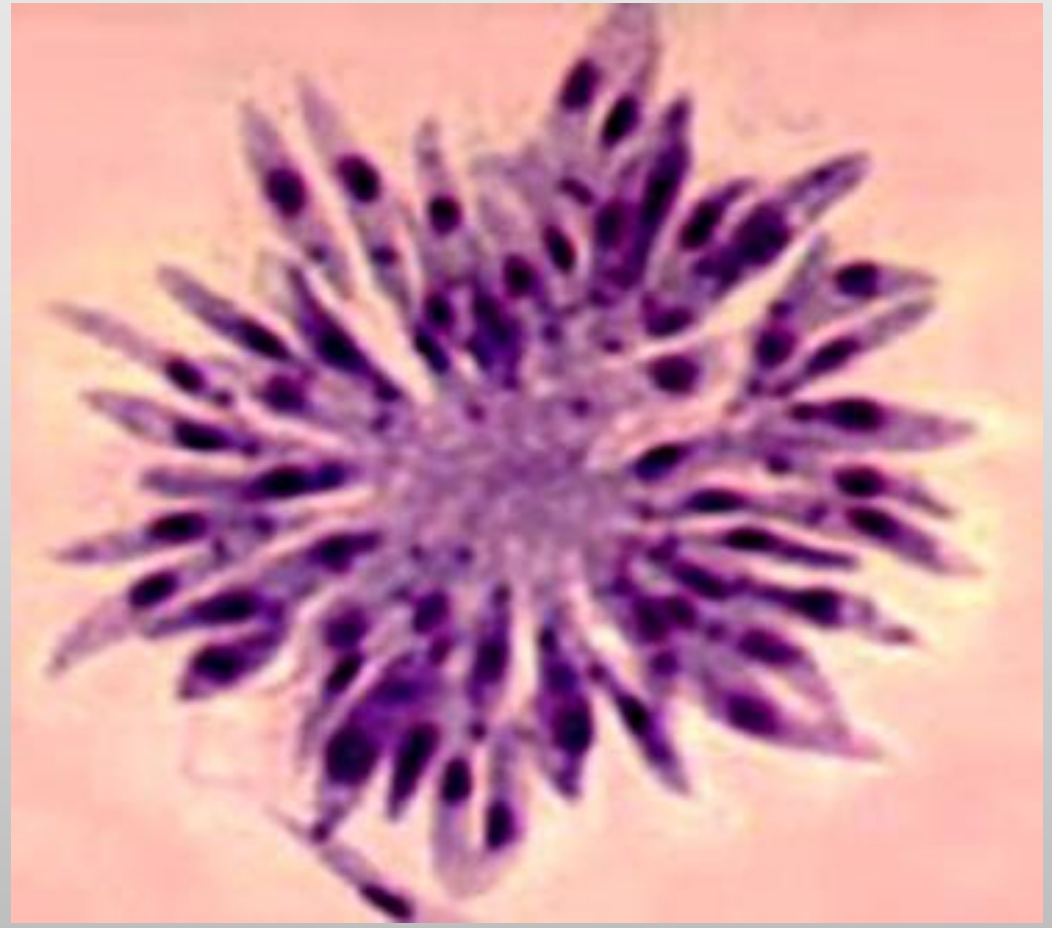
- Peripheral blood by thick film or buffy coat smears
- Bone marrow puncture (sternal or iliac crest).
- Enlarged lymph node aspirate or puncture.
- Nasopharyngeal secretions.
- urine
- Splenic puncture (spleen pulp).
- Liver puncture.
- Nodular lesions in PKDL.
- stool

2. Culture: Materials are cultured on NNN medium.

Promastigotes in the form of rosette grouping of parasites can be detected 1-4 weeks after cultivation.



Promastigotes forming a rosette



3. Animal inoculation: Intra-peritoneal inoculation of golden hamster by aspirated specimens. In positive cases, the amastigotes can be seen in smears taken from ulcers or nodules at site of inoculation or from the spleen, weeks post infection.

4. Immunological diagnosis:

a. **Serolodiagnosis:** Specific leishmanial antigens prepared from cultures are used to detect **anti-leishmanial antibodies** using some tests as: IFA, IHA, ELISA, CFT, DAT, and ICT.

b. Leishmanin skin test (Montenegro test): It is a delayed hypersensitivity skin test.

- A 0.1ml of killed promastigotes of *L. donovani* is injected intradermal.

- Positive result is indicated by an induration and erythema of 5 mm or more after 48-72 hours.

- Positive test **indicates** past infection with Leishmania parasites as it becomes positive 6-8 weeks after cure. The test is negative in active infection due to marked depression of cellular immune response and in PKDL.

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

6. Blood picture:

- Complete blood count shows normocytic normochromic anemia, leucopenia and thrombocytopenia.

➢Treatment of Visceral Leishmaniasis:

1. Supportive treatment:

- Diet rich in vitamins, iron and liver therapy.
- Antibiotics for secondary bacterial infection.
- Correction of pancytopenia.

2. Specific treatment:

a. Systemic therapy (parenteral,

- **Pentostam:** IM injection or IV, and therapy continues for 28–30 days till smear microscopy is negative.

b. Systemic therapy (oral)

- **Miltefosine:** It is the first oral drug approved for treatment of leishmaniasis.

➢ Prevention and control:

1. Control of **sand flies vector** by destruction of their breeding grounds near human habitations and by the use of insecticides.

2. Eradication of **reservoir hosts** will reduce the sources of infection.

3. **Personal protection** using wire screens, repellents & mosquito nets.

4. Treatment of **infected persons**.

B- Cutanous Leishmaniasis

Pathogenesis

Cutaneous leishmaniasis is characterized by:

1. Multiplication of amastigotes in the **skin macrophages** leading to formation of papule, nodule and ulcer.

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

➢ Clinical manifestations of Cutanous Leishmaniasis:

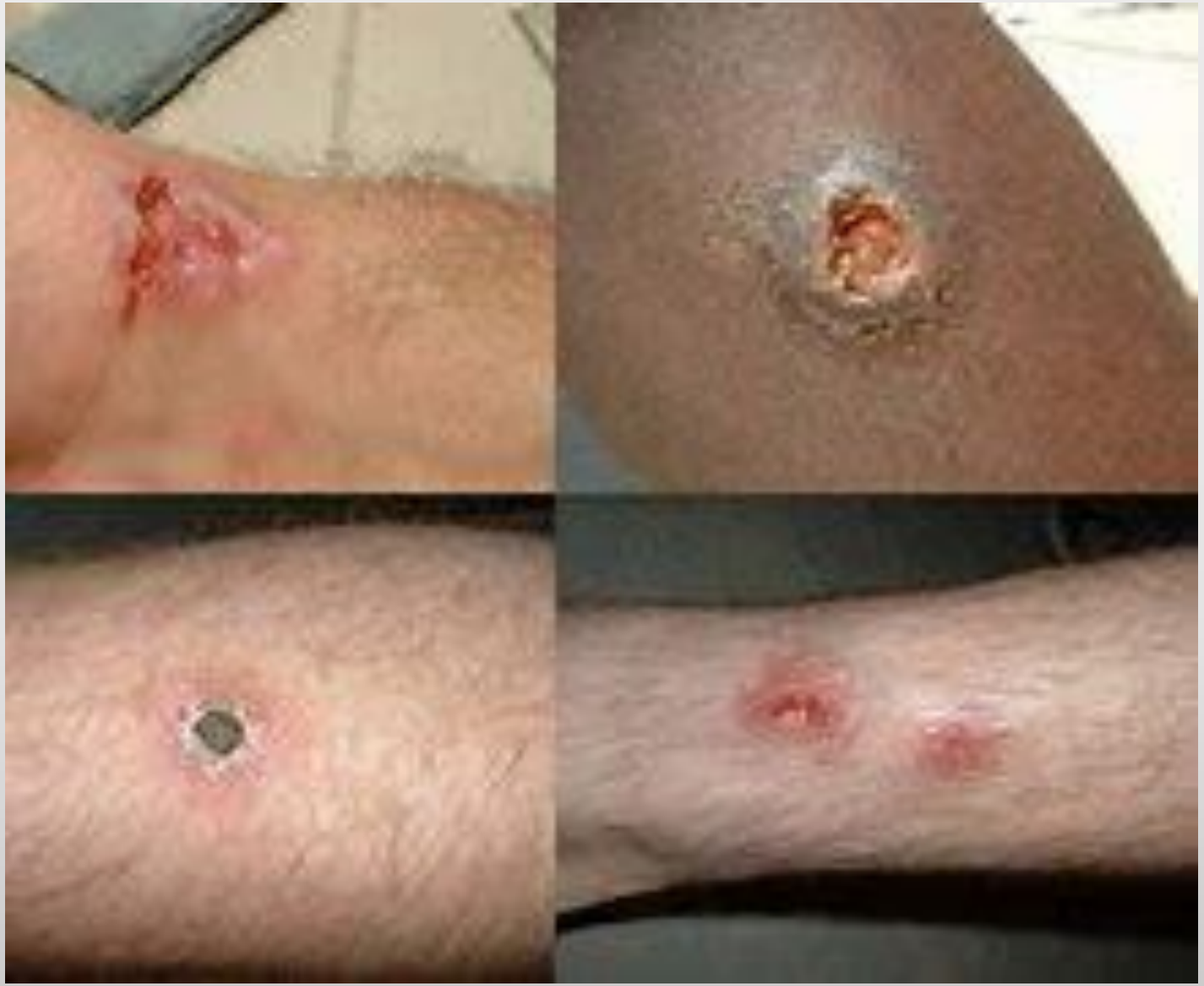
- ***Wet (moist) sore:*** The incubation period is short, few days or weeks.

- The lesion usually affects the **lower limbs.**

- It starts as small itchy **papules**, at first dry, then becomes moist, thick and brown, forming **crusts** which fall leaving shallow oozing **ulcers** with raised margin, granulation tissue at the base and seropurulent **exudates**.

- Ulceration occurs very early and heals more rapidly (3-6 ms).

- Secondary bacterial infection usually occurs.



Cutaneous leishmaniasis; Wet (moist) sore

➢Diagnosis:

I. **Clinical:** Any case, in an endemic area.

II. **Laboratory:**

1- Microscopy: Detection of amastigotes in smears:

- aspirated or scraped from the edge of the lesion.
- Biopsy of skin lesion.

2. Culture: Materials are cultured on NNN medium to detect Promastigotes in the form of rosette grouping of parasites.

3. Animal inoculation: inoculation of mice by aspirated specimens. In positive cases, the amastigotes can be seen in smears taken from ulcers.

4. Immunological diagnosis:

- **Serodiagnosis:** These are of limited value in the diagnosis of cutaneous leishmaniasis as the patient has **no** detectable level of circulating antibodies.

b. Leishmanin skin test (Montenegro test):

It is helpful, becomes **positive** few days after infection.

Disadvantage: remains positive after cure for years (does not indicate active infection).

➢Treatment of cutanous Leishmaniasis:

1. Local measures:

- Surgical excision especially in single lesions.
- Scraping (curettage).
- Plastic surgery for scars or disfiguring nodules.
- Local heating of lesion by infra-red rays or freezing therapy by carbon dioxide.
- Local injection of 10% atebrine solution.
- I.D. injection of interferon gamma around lesions promotes healing of ulcers.
- Cleanliness to prevent secondary bacterial infection.

2. Systemic treatment: (parenteral)

- **Pentostam** is the drug of choice.
- I.M. + Local around the lesion edge
- If the sores are **1-3 in number**, treatment may be facilitated by local infiltration of the drug into the edges of the ulcers.

MCQ 1: What is the habitat of *Leishmania donovani*?

a. Intracellular in macrophages of reticuloendothelial tissue

b. Intracellular in macrophages of skin

c. Extracellular in interstitial fluids

d. Intracellular in red blood cells

e. Intracellular inside epithelial cells

MCQ 2: Which clinical manifestation is characteristic for diagnosis of Visceral Leishmaniasis?

a. Hepatosplenomegaly

b. Intermittent twice-daily rise fever

c. Generalized lymphadenopathy

d. Pancytopenia

e. Dysentery

Discussion & Feedback

10 minutes