

- A disease of the reticuloendothelial system
- caused by kinetoplastid protozoa of the genus *Leishmania*.
- infect humans and have animal reservoirs
- transmitted by sandflies belonging to the genera **Phlebotomus** in the Old World and **Lutzomyia** in the New World.
- assume the **amastigote** form in **mammalian** hosts and the **promastigote** form in **insect** vectors.

* **LEISHMANIA**

* Species of *Leishmania* cannot be differentiated by examination of amastigotes or promastigotes.

* clinical forms

* Cutaneous

* Mucocutaneous

* visceral diseases

* **LEISHMANIA**

- **Cutaneous Leishmaniasis or Old World cutaneous leishmaniasis (oriental sore)**
 - southern Europe, northern and eastern Africa, the Middle East, Iran, Afghanistan, India, and southern Russia.
 - caused by:
 - *Leishmania tropica*
 - *Leishmania major*
 - *Leishmania aethiopica*
 - *Leishmania donovani*
 - *Leishmania infantum*

* **LEISHMANIA**

- * L. tropica
 - * urban or dry ulcer
- * L. major.
 - * rural or wet ulcer
- * Ulcers develop on an exposed area of the body and heal spontaneously.
- * Infection produces long-lasting immunity.

* **LEISHMANIA**

* *L. aethiopica*

- more aggressive cutaneous infection
- in some individuals, they metastasizes to produce mucosal lesions or diffuse cutaneous leishmaniasis, the latter of which is characterized by multiple skin nodules resembling lepromatous leprosy.

* LEISHMANIA

* Cutaneous leishmaniasis of the New World

* caused by:

- * *Leishmania mexicana*
- * *Leishmania braziliensis*
- * *Leishmania amazonensis*
- * *Leishmania venezuelensis*
- * *Leishmania garnhami*
- * *Leishmania pifanoi*
- * *Leishmania peruviana*
- * *Leishmania panamensis*
- * *Leishmania guyanensis*

* **LEISHMANIA**

Leishmania spp.

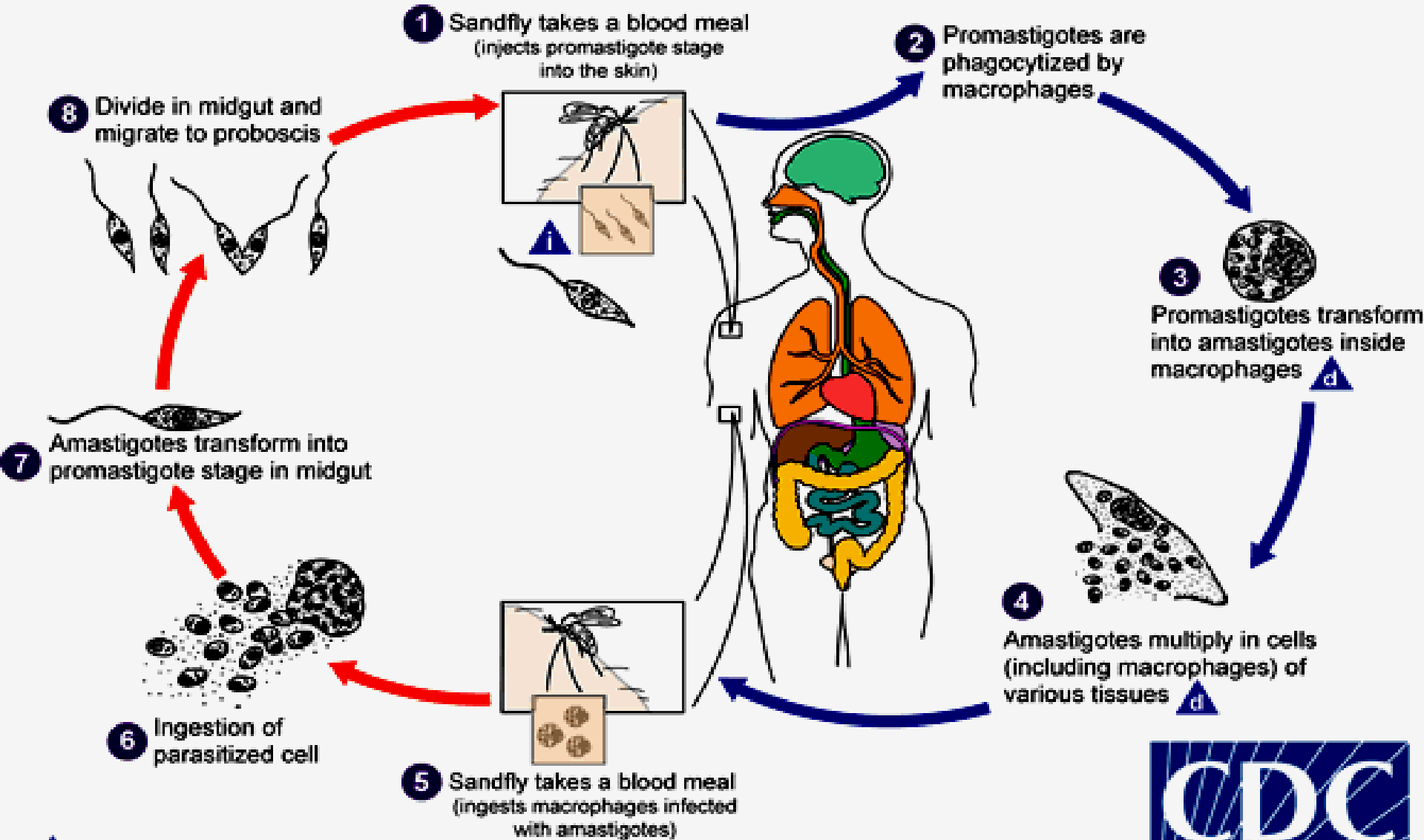
- ✓ Heteroxenous, blood flagellates
- ✓ Cause Leishmaniasis; Kala-azar
- ✓ **Vector**: Female sandflies (30 species of *Phlebotomus* and *Lutzomyia*) in inter-tropical and temperate regions



- ✓ **Transmission -**
 - Inoculation by the vector
 - some reports of transmission by blood transfusions and contaminated needles
 - rarely spread from mother to baby

Sandfly Stages

Human Stages



Types Of Leishmaniasis

Visceral Leishmaniasis/Kala-azar (Bangladesh, Brazil, India, Nepal and Sudan)

Cutaneous Leishmaniasis (Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria)

Mucocutaneous Leishmaniasis (Central Mexico, Northern Argentina, Bolivia, Brazil and Peru)

Post Kala-azar dermal Leishmaniasis (Endemic to India and the Sudan)

- recurrence of **Kala-azar** that may appear on the skin of affected individuals up to 20 years after being partially treated, untreated or even in those considered adequately treated.

Leishmania donovani

- Visceral Leishmaniasis
- aka Kala-azar/black disease
 - Dum-dum fever
- Most severe form, fatal if non-treated
- Irregular bouts of fever
- Substantial weight loss
- Swelling of the spleen and liver
- Anemia



1. Indian Kala-azar

- infects humans but may be transmitted experimentally to dogs
- a disease of adults
- transmitted by *Phlebotomus argentipes*

2. Chinese Kala-azar

- Northern China
- affects children
- develops in dogs
- transmitted by *Phlebotomus chinensis*

3. Mediterranean Kala-azar

- tropical Africa, Southern Europe, Greece
- Affects very young children
- develops in dogs
- Transmitted by *Phlebotomus perniciosus* and *Phlebotomus major*

4. Sudanese Kala-azar

- similar to Indian strain
- infects adults; does not infect dogs
- Outbreaks occur unpredictable
- Transmitted by *P. orientalis*

5. South American Kala-azar

- From Venezuela to Northern Argentina
- Affects all ages
- Reservoir hosts are dogs
- Transmitted by *Lutzomyia flaviscutellata* and *L. intermedium*

Leishmania tropica



- Cutaneous leishmaniasis
- aka Chiclero ulcer, tropical sore, oriental sore
- Common form
- Parasite invades the reticuloendothelial system and causes cutaneous lesions

4. “Uta”

- Occurs in the mountains of Peru
- Skin lesions occur
- No mucous membrane invasion

5. Chiclero ulcer

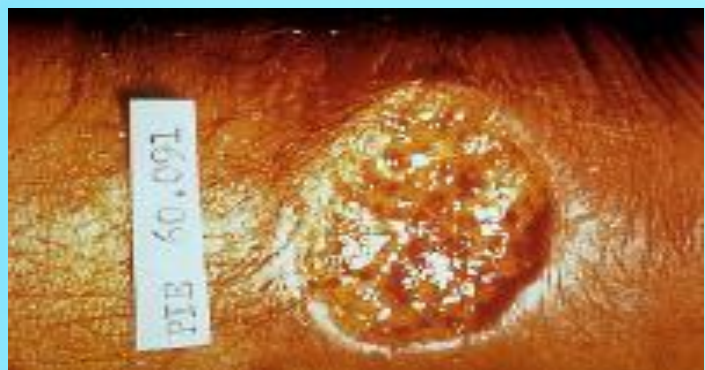
- *L. tropica mexicana*
- Southern Mexico and Guatemala
- Small skin lesions
- Cause disfigurement of the ear
- chronic condition lasting for several years



Leishmania braziliense

- Mucocutaneous leishmaniasis
- Endemic to Brazilian rainforests
- Partial or total mutilation of the mucous membranes in the nose, mouth, and throat cavities – degeneration of cartilaginous and soft tissue
- “Espundia”
- Death may result from secondary infection of respiratory complications





Epidemiology

- **Endemic in 88 countries on 5 continents—Africa, Asia, Europe, N. America and S. America**
- **350M people at risk; 12M people are affected by Leishmaniasis**
- **1.5-2M new cases of Leishmaniasis estimated to occur annually**
- **500,000 new cases of VL which occur annually**

Diagnosis, Detection and Surveillance

Visceral Leishmaniasis - combining clinical signs with parasitological or serological tests (rapid diagnostic tests and others)

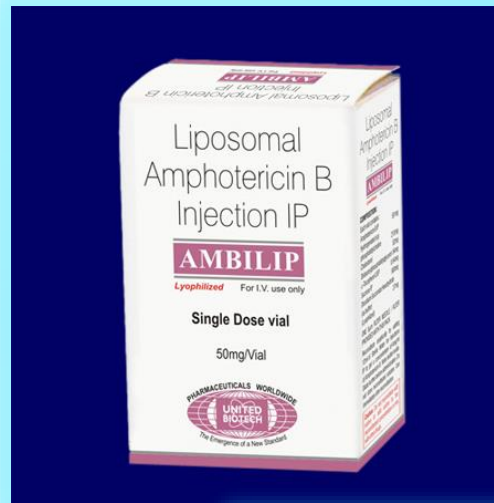
Cutaneous - clinical manifestation with parasitological tests confirm the diagnosis

Cutaneous and Mucocutaneous - serological tests have limited value

- PCR
- ELISA, IFA or direct agglutination for increased levels of serum igG

Treatment

- liposomal amphotericin-B



- Miltefosine (approval by the Indian and German Regulatory Authorities (2002))



- Paromomycin



Alternative Treatments

- ✓ Pentamidine
- ✓ Allopurinol
- ✓ Ketoconazole
- ✓ Interferon Gamma
- ✓ BCG
- ✓ Rifampin
- ✓ Dapsone
- ✓ Clotrimazole
- ✓ Cautery/Excision
- ✓ Shiraz cream

- * *L. mexicana*
 - earlobe (chiclero ulcer)
 - self-limiting, and are not known to metastasize to the mucosa.
- * *L. mexicana* and *L. amazonensis* may produce diffuse cutaneous lesions similar to those produced by *L. aethiopica*.

* **LEISHMANIA**

- * L. Peruviana
 - * western slopes of the Peruvian Andes
 - * causes an infection called **uta**, a benign cutaneous lesion that occurs predominantly in children.
- * L. peruviana
 - * acquired usually at home
 - * main reservoirs are domestic dogs.

* **LEISHMANIA**

- Mucocutaneous Leishmaniasis (**espundia**)
 - L. braziliensis and related species
 - produce typical cutaneous lesions that generally are more aggressive, last longer, and often disseminate to mucous membranes, especially in the nasal, oral, or pharyngeal areas.
- In these locations, they may produce disfiguring lesions secondary to erosion of soft tissues and cartilage.
- L. braziliensis is distributed in Mexico and Central and South America.

* **LEISHMANIA**

- Visceral Leishmaniasis / Visceral leishmaniasis of the Old World
 - occurs sporadically over a wide geographic area
 - L. donovani or by L. infantum.
- L. donovani
 - predominates in Africa, India, and Asia
- L. infantum
 - predominates in the Mediterranean region and the Middle East, although overlapping ranges occur.

 **LEISHMANIA**

- New World visceral leishmaniasis
 - L. chagasi
 - occurs sporadically throughout Central and South America.
- * The infection is usually benign and often subclinical
- * young children and malnourished individuals, have marked involvement of the viscera, especially liver, spleen, bone marrow, and lymph nodes.

* **LEISHMANIA**

- *The infection is called **kala-azar** in India, in reference to the darkening of the skin.
- *Also is an opportunistic infection in individuals with concurrent human immunodeficiency virus (HIV), and the condition responds poorly to therapy in such circumstances.

* **LEISHMANIA**

* Diagnosis:

- * visualization of amastigotes in smears, imprints, or biopsies, or by growth of promastigotes in culture.
- * In **integumentary leishmaniasis**, the border of the most active lesion should be biopsied, and the fresh biopsy should be used to make imprints.

* **LEISHMANIA**

- * A smear should be prepared by making a 2-3-mm incision at the border of the ulcer and recovering small amounts of tissue from the cut surfaces with the scalpel blade.
- * Both the imprint and the smear should be treated with Giemsa stain.

* **LEISHMANIA**

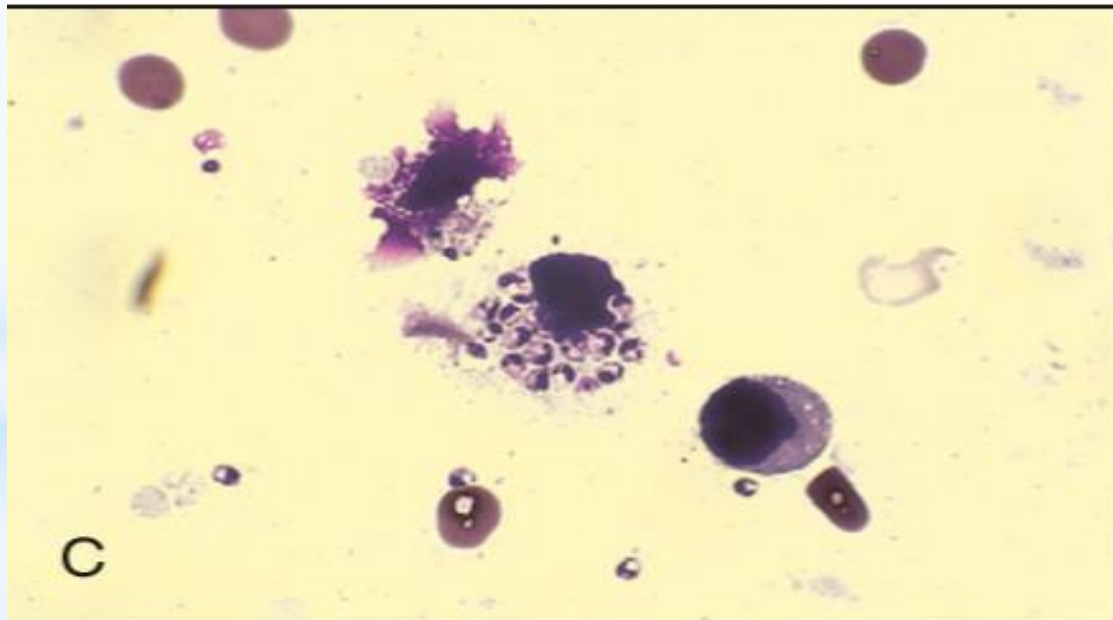
- * Specimens that may be submitted when visceral leishmaniasis is suspected include:
 - * Buffy coat preparations
 - * lymph node and bone marrow aspirates
 - * spleen and liver biopsies.

* **LEISHMANIA**

- culture
 - desirable because it is more sensitive
 - allows determination of the species or subspecies, to help in clinical management of the patient.
- Biopsy or aspirate specimens collected aseptically are cultured in **Novy-MacNeal-Nicolle medium** or in **Schneider's Drosophila medium supplemented with fetal calf serum.**
- Cultures usually begin to show promastigotes in 2-5 days but should be held for 4 weeks.

* **LEISHMANIA**

- Amastigotes found in imprints, smears, and tissue sections are recognized by their size (2-4 μm) and the presence of delicate cytoplasm, a nucleus, and a kinetoplast (see Fig. 62-6, C).



NIA

- * Amastigotes must be differentiated from other intracellular organisms, including yeast cells of *Histoplasma capsulatum* and trophozoites of *Toxoplasma gondii*.
- * *Leishmania* spp. have a kinetoplast and do not have a cell wall.
- * In contrast, *Histoplasma* lack the kinetoplast, and the cell wall stains with periodic acid-Schiff (PAS) and methenamine silver stains.

* LEISHMANIA