Leishmaniasis

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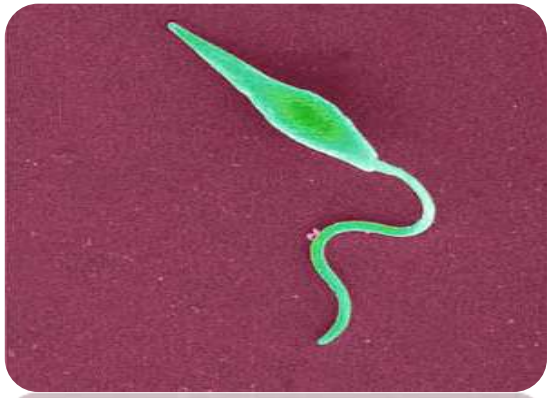


Sir William Leishman

- 1900 – **Sir William Leishman** discovered L. donovani in spleen smears of a soldier who died of fever at **Dum-Dum,** India. The disease was known locally as Dum-Dum fever or kala-azar.

Charles Donovan

- Charles Donovan also recognized these symptoms in other **kala-azar** patients and published his discovery a few weeks after Leishman. After examining the parasite using Leishman's stain, these amastigotes were known as Leishman-Donovan bodies.

Leishmaniasis is Neglected Disease

- Leishmaniasis is a globally important but neglected disease, affecting approximately two million people every year. For most people, infection results in a slow-to-heal skin ulcer. In others, however, the parasite targets the liver, spleen and bone marrow, leading to over 70,000 deaths annually.

The Parasite

- **Phylum** — **Sarcomastigophora**
- **Order** — **Kinetoplastida**
- **Family** — **Trypanosomatidae**
- **Genus** — **Leishmania**

Leishmania Parasites and Diseases

SPECIES	Disease
*Leishmania tropica** *Leishmania major** *Leishmania aethiopica* *Leishmania mexicana*	Cutaneous leishmaniasis
Leishmania braziliensis	Mucocutaneous leishmaniasis
*Leishmania donovani** *Leishmania infantum** *Leishmania chagasi*	Visceral leishmaniasis

* Endemic in Saudi Arabia

Morphology

- **Promastigote**
- **Amastigote**

Flagella

Kinetoplast

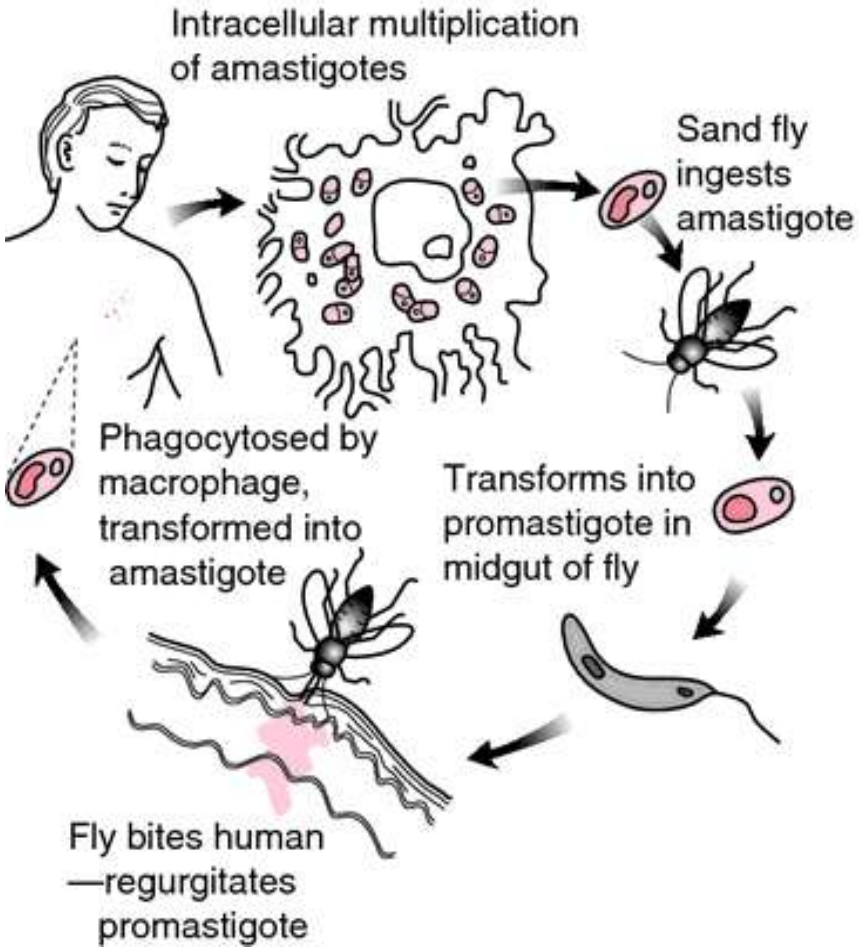
Golgi

Nucleus

Cytoskeleton

Morphology and Life Cycle

- Amastigotes measure 2-3 micrometers, with a large nucleus and Kinetoplast.
- Amastigotes mainly live within cells of the RE system, but have been found in nearly every tissue and fluid of the body.



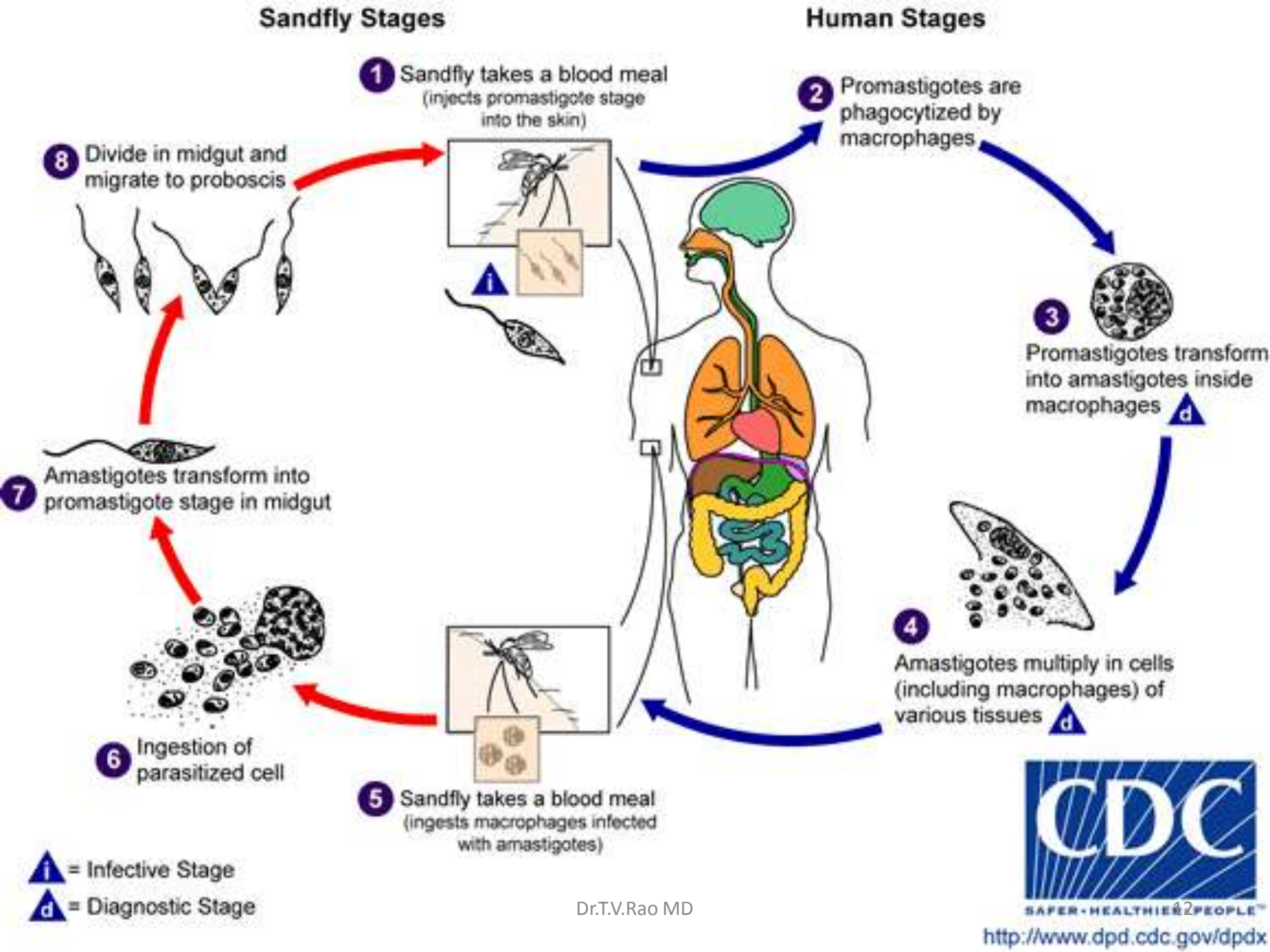
Life cycle

- The organism is transmitted by the bite of several species of blood-feeding **sand flies** (Phlebotomus) which carries the Promastigote in the anterior gut and pharynx. It gains access to mononuclear phagocytes where it transform into Amastigote and divides until the infected cell ruptures.

Sand fly- Vector

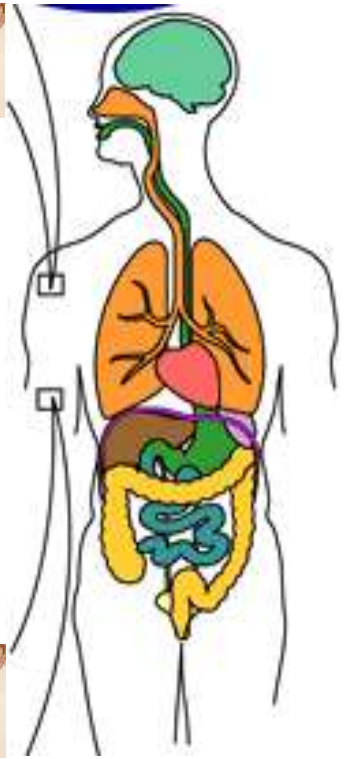
Life cycle

- The released organisms infect other cells. The sand-fly acquires the organisms during the blood meal, the Amastigote transform into flagellate Promastigote and multiply in the gut until the anterior gut and pharynx are packed. Dogs and rodents are common reservoirs.


Sandfly Stages
Human Stages
1 Sandfly takes a blood meal
(injects promastigote stage
into the skin)
2 Promastigotes are
phagocytized by
macrophages
3 Promastigotes transform
into amastigotes inside
macrophages
d
4 Amastigotes multiply in cells
(including macrophages) of
various tissues
d
5 Sandfly takes a blood meal
(ingests macrophages infected
with amastigotes)
6 Ingestion of
parasitized cell
7 Amastigotes transform into
promastigote stage in midgut
8 Divide in midgut and
migrate to proboscis
i = Infective Stage
d = Diagnostic Stage
CDC
SAFER·HEALTHIER·PEOPLE™
http://www.dpd.cdc.gov/dpdx

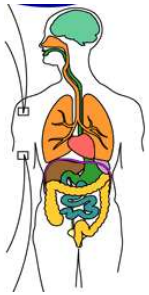
1- Sand-fly bites animal and ingests blood infected with *Leishmania*

2- Sandfly bites human and injects *Leishmania* into skin

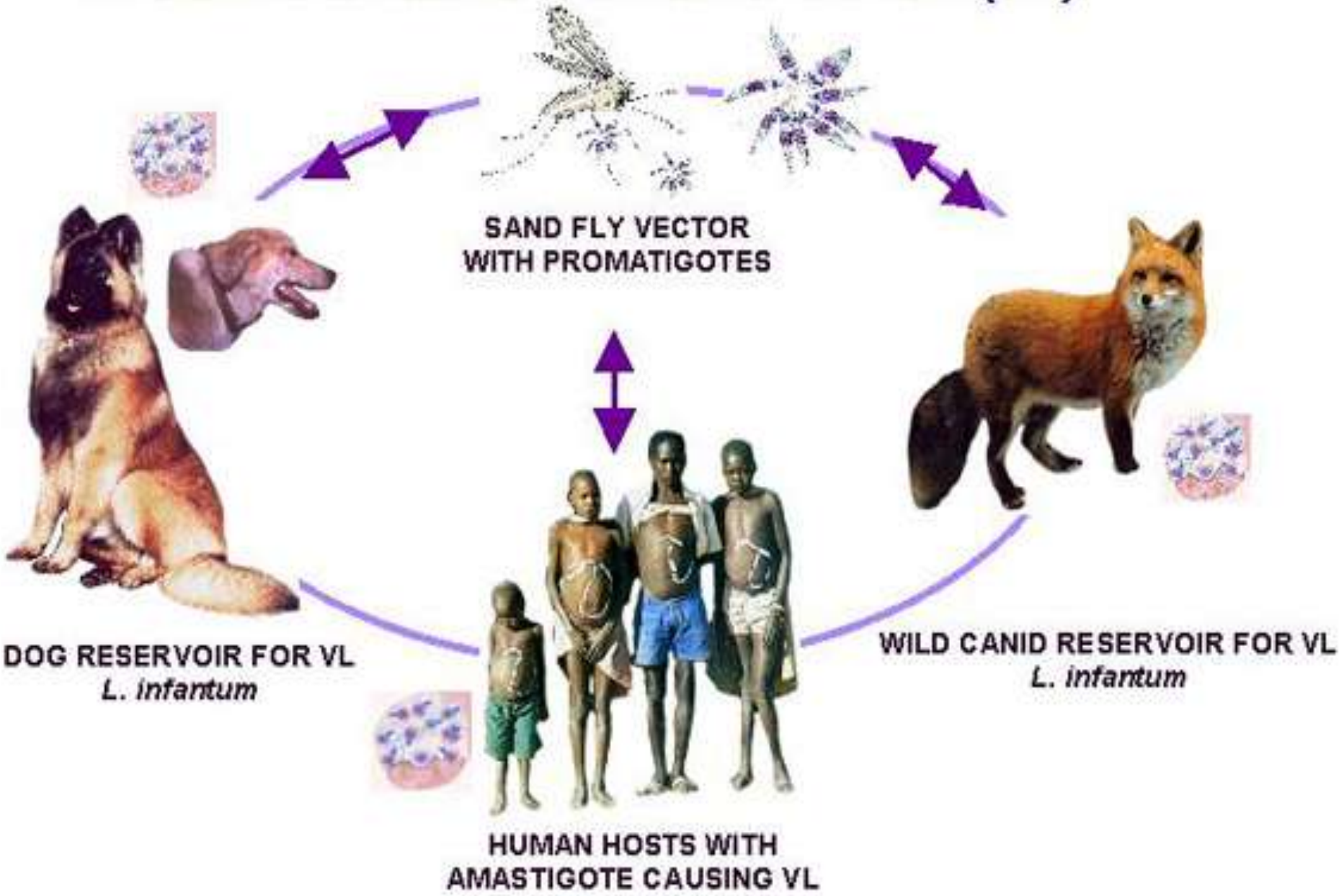


3- Another sandfly bites human and ingests blood infected with *Leishmania*

4- Cycle continues when sandfly bites another human or animal reservoir



LIFE CYCLE OF *LEISHMANIA* CAUSING VISCERAL LEISHMANIASIS (VL)



What is Kala-Azar

- Kala-azar means dark pigmentation which is characteristic of cases of visceral leishmaniasis. It is caused by Leishmania donovani bodies and may be present either in endemic, epidemic or sporadic forms. It is widely prevalent in India in epidemic form in states of **Bihar, Assam and Bengal.** Kala azar found in **East and North Africa** is a disease of young children and young adults, being more common in males as compared to females.

Clinical types of cutaneous leishmaniasis

- **Leishmania major:** Zoonotic cutaneous leishmaniasis: wet lesions with severe reaction
- ***Leishmania tropica*:** Anthropologic cutaneous leishmaniasis: Dry lesions with minimal ulceration

Oriental sore (most common) classical self-limited ulcer

Leishmania species	Host	Clinical features
L. tropica	Dogs	Oriental sore(Baghdad boil)
L. major	Gerbils, desert rodents	Rapid necrosis, wet sores
L. aethiopica	Hyraxes	Solitary facial lesions with satellites

KALA AZAR

- **Leishmaniasis** is a disease caused by protozoan parasites of to the genus Leishmania and is transmitted by the bite of sand fly.
- This disease is also known as kala azar, black fever, sandfly disease, Dum-Dum fever.
- Human infection is caused by about 21 of 30 species that infect mammals. These include the L. donovani complex with three species (L. donovani, L. infantum, and L. chagasi

Cutaneous leishmaniasis

Diffuse cutaneous leishmaniasis

Leishmaniasis recidiva

Uncommon types

- **Diffuse cutaneous leishmaniasis** (DCL):

  Caused by *L. aethiopica*, diffuse nodular non-ulcerating lesions. Low immunity to *Leishmania* antigens, numerous parasites.

- **Leishmaniasis recidiva** (lupoid leishmaniasis):

  Severe immunological reaction to *Leishmania* antigen leading to persistent dry skin lesions, few parasites.

Post Kala-azar Dermal Leishmaniasis

- Post Kala-azar Dermal Leishmaniasis (PKDL) is a condition when Leishmania donovani invades skin cells, resides and develops there and manifests as dermal leisions. Some of the kala-azar cases manifests PKDL after a few years of treatment. Recently it is believed that PKDL may appear without passing through visceral stage.

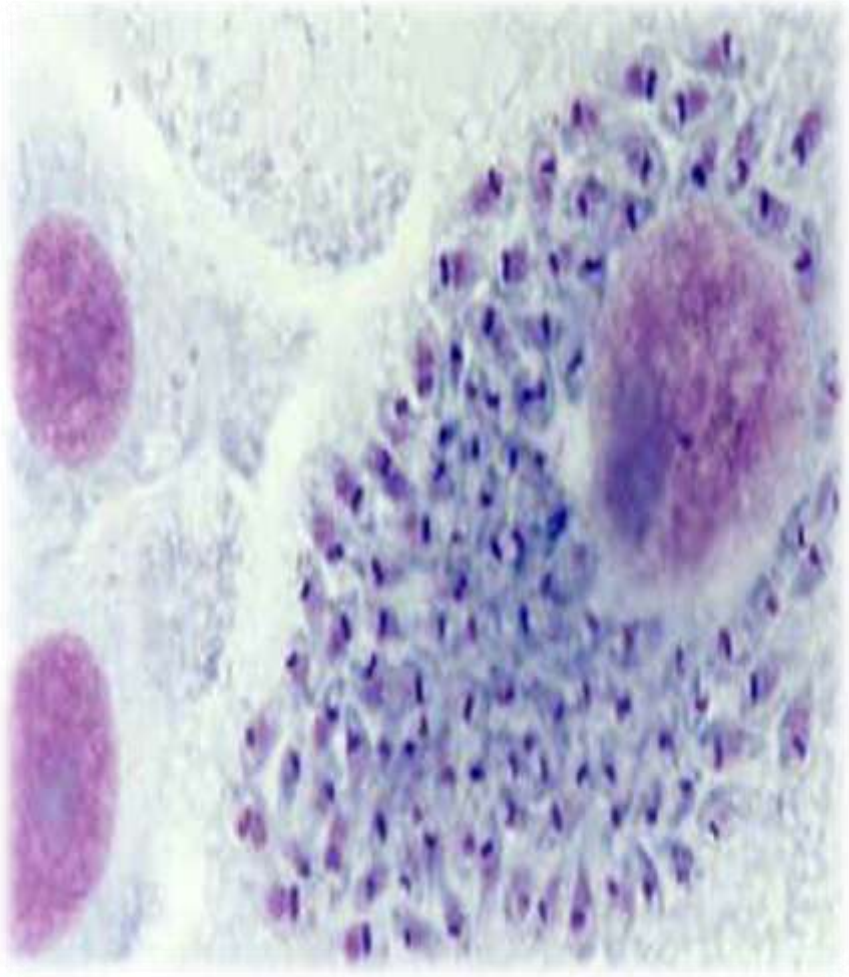
Pathogenesis

- Infections range from asymptomatic to progressive, fully developed kala-azar.
- Incubation period is usually 2 – 4 months.
- Symptoms – Begins with low-grade fever and malaise, followed by progressive wasting, anemia, and protrusion of the abdomen from enlarged liver and spleen.
- Fatal after 2 – 3 years if not treated.
- In acute cases with chills, fevers up to 104 degrees Fahrenheit, and vomiting; death may occur within 6 – 12 months.
- Immediate cause of death is usually an invasion of a secondary pathogen that the body is unable to combat.

Cutaneous leishmaniasis

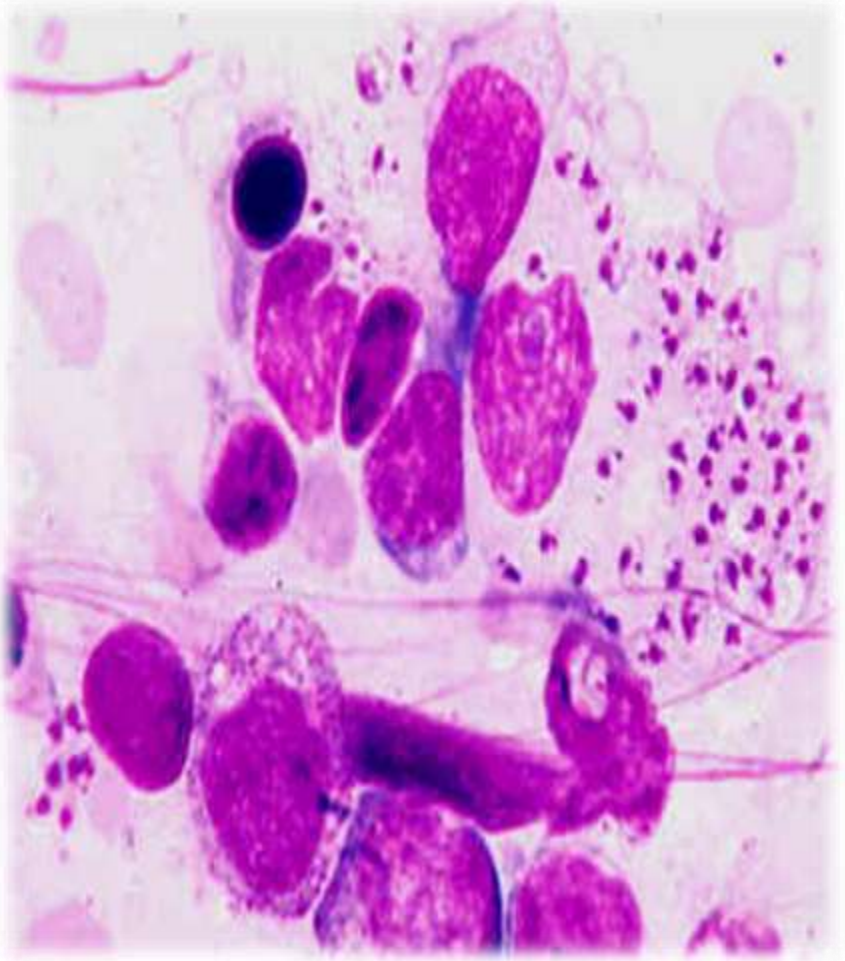
Diagnosis:

- Smear: Giemsa stain – microscopy for LD bodies (Amastigote)
- Biopsy: microscopy for LD bodies or culture in NNN medium for promastigotes



L. donovani bodies

- L. donovani bodies may be demonstrated in buffy coat preparations of blood and bone marrow aspirate. Aspirates taken from enlarged lymph nodes show parasites in 60 percent of cases.



Visceral leishmaniasis

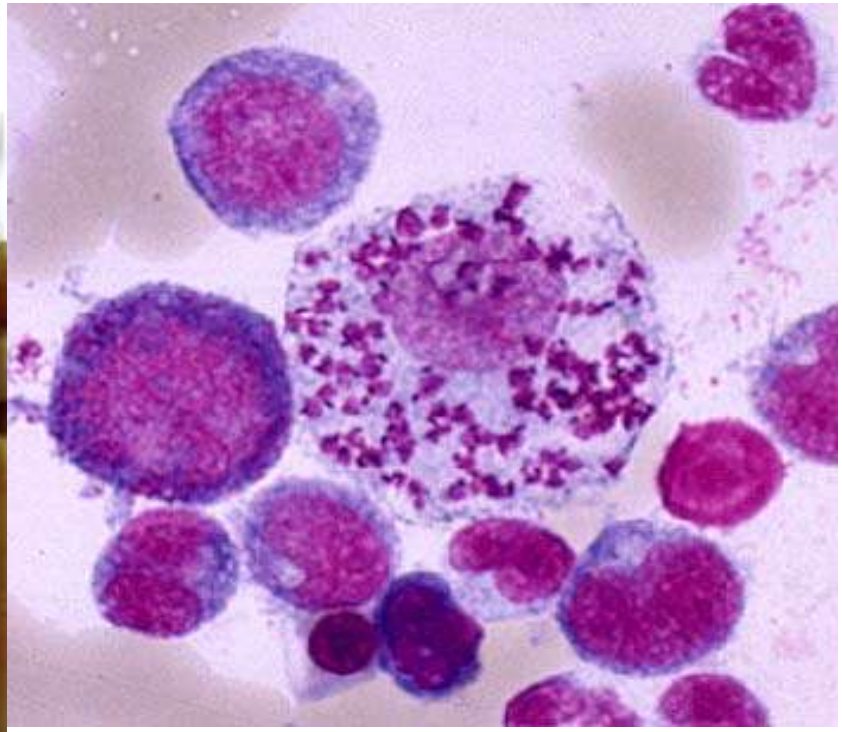
Diagnosis

(1) Parasitological diagnosis: METHOD

Bone marrow aspirate
Splenic aspirate
Lymph node
Tissue biopsy

1. microscopy
2. culture in NNN medium

Bone marrow aspiration

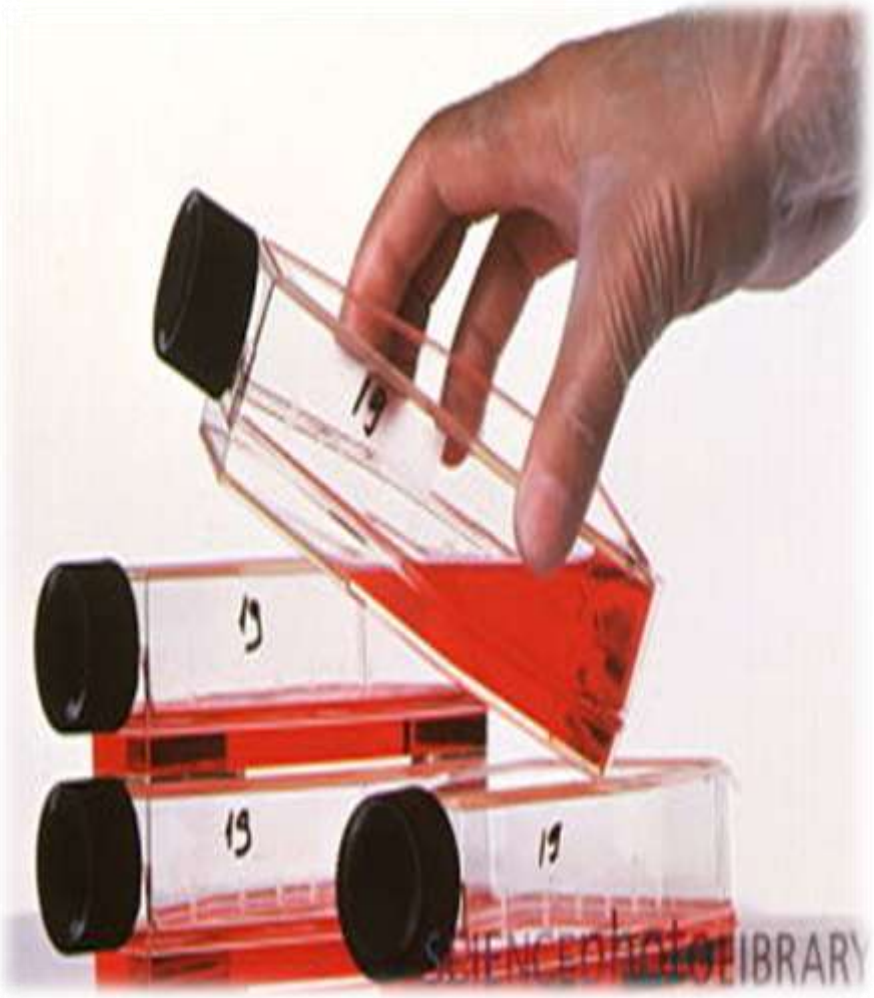


Bone marrow amastigotes

Diagnostic Methods in Leishmaniasis

- Antibody detection. Specific sero diagnostic tests are also employed. Conventional methods include gel diffusion, complement fixation test, indirect haem agglutination test, indirect immuno-fluorescent antibody test (IFAT) and counter immuno electro phoresis. Most of these tests have limited sensitivities and specifies.

Culturing of the Parasite



- Organisms can be cultured in Nicolle-NovyMacneal (NNN media) media from clinical specimens obtained from splenic or bone marrow aspirates.

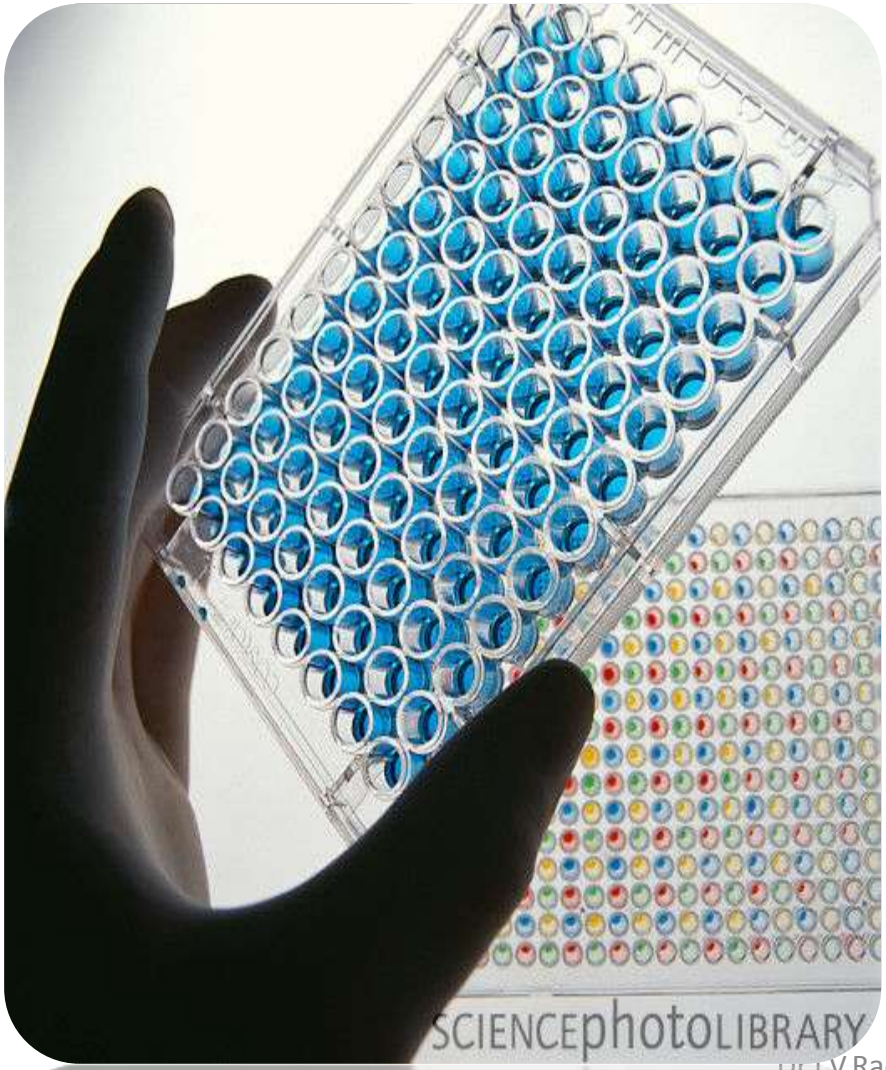
Immunological Diagnosis:

- Specific serologic tests: Direct Agglutination Test (DAT), ELISA, IFAT
- Skin test (leishmanin test) for survey of populations and follow-up after treatment.
- Non specific detection of hypergammaglobulinaem by formaldehyde (formal-gel) test or by electrophoresis.

Direct agglutination test

- Direct agglutination test (DAT) based on agglutination of the trypsenized whole promastigotes is useful in endemic regions. Its sensitivity ranges from 91-100% and specificity from 72 to 100%.

ELISA



- ELISA is an important sero diagnostic tool for leishmaniasis. It is a highly sensitive test and its specificity depends upon the antigen used.

Chromatographic strip test

- A ready to use immuno chromatographic strip test based on rk 39 antigen has been developed as a rapid test for diagnosis of kala azar. An important limitation of this test is the presence of antibodies in healthy controls hailing from endemic regions.

Treatment:

- Pentavalent antimony (Pentostam)
- Amphotericin B

Treatment of complications:

- Anemia
- Bleeding
- Infections etc.

Management of Kala-azar Patients

- It includes both supportive and curative. All patients of Kala azar should preferably be hospitalized. Any infection complicating the disease be treated by use of proper antibiotics. Nutrition must be maintained. Cases with severe anemia may require blood transfusions. Pentavalent antimony compounds are the drug of choice. Sodium antimony gluconate (Pentostam) is the most commonly used drug.

Kala-azar prevention:

- Multipronged approach is needed.
- Sand-flies are extremely sensitive to insecticides & vector control through insecticide spray is very important.
- Mosquito nets or curtains treated with insecticides will keep out the tiny sand-flies.

Kala-azar prevention:

- In endemic areas with zoonotic transmission, infected or stray dogs should be destroyed.
- In areas with anthroponotic transmission, early diagnosis & treatment of human infections, to reduce the reservoir & control epidemics of VL, is extremely important.
- Serology is useful for screening of suspected cases in the field.
- No vaccine is currently available .

- **Programme Created by Dr.T.V.Rao MD for Medical and Paramedical Students in the Developing World**
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