

Bio 54

Lecture I
Leishmania: Structure,
Infection, & Disease

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Leishmania - Background

- 10-15 million infected worldwide, at least 400,000 new cases per year
- Up to 350 million at risk worldwide (range will expand with global warming)
- Diseases caused
 - Cutaneous leishmaniasis
 - Mucocutaneous leishmaniasis
 - Visceral leishmaniasis
- At least 13 species have been identified that can infect humans

Goal for this week

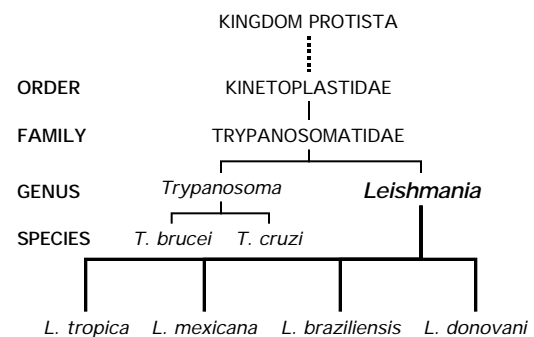
- Understand the Life cycle & Diseases caused by leishmanial parasites
- Molecular Biology & Biochemistry of parasites
- Host Immune responses to infections
- Diagnosis, Treatment & Control

Goal for today's lecture

- Understand the Life cycle & diseases caused by leishmanial parasites
- Understand leishmanial species
- Understand taxonomy of parasites
- Understand parasite ultrastructure
- Diagnosis, Treatment & Control

Today's Class

- Taxonomy
- Life Cycle & Infection
- Parasite Structure
- Disease
- Diagnosis, Treatment & Control



Geographic Distribution of Cutaneous and Mucocutaneous Leishmaniasis



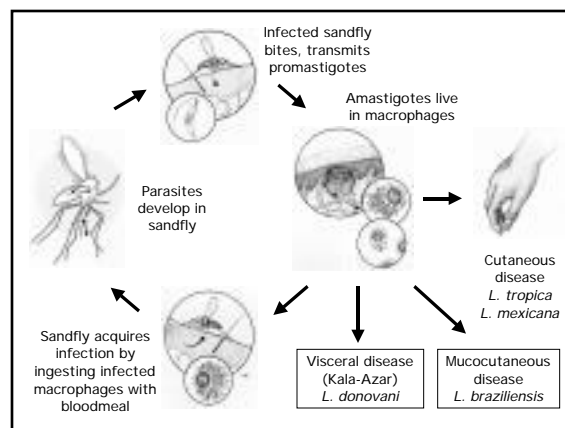
- "Old World": *L. tropica*
- "New World": *L. mexicana*, *L. braziliensis*

Geographic Distribution of Visceral Leishmaniasis



- Typically caused by *L. donovani*

The Life Cycle of *Leishmania*



Mammalian Forms of *Leishmania*



- Promastigotes**
- 15-20 μm in length
 - Flagellated and highly motile
 - Quickly attach to and invade macrophages (within 10-15 minutes)

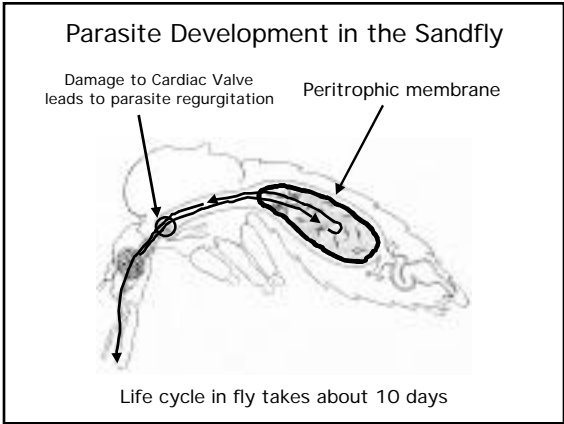


- Amastigotes**
- 2-5 μm in length
 - Reside in the phagolysosome of macrophages (but not other cells)
 - Lack flagellum

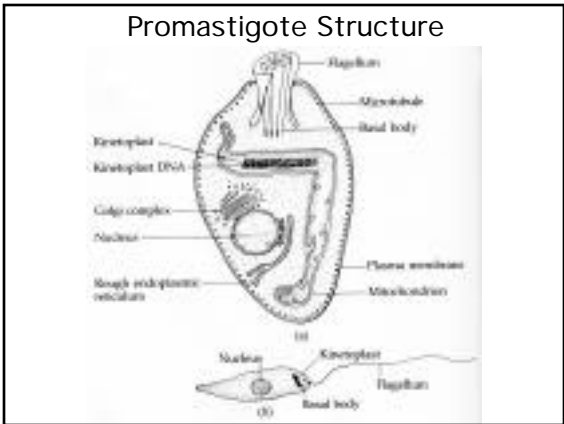
Sandflies (Phlebotomines)



- *Phlebotomus spp.* and *Lutzomyia spp.* transmit *Leishmania*
- Live in moist soil, stone walls, rubbish heaps, etc.
- Only females suck blood
- Adults live about 2 weeks
- Take 2-3 blood meals during lifespan
- Typically feed at night
- Weak fliers ("hop")



- ### Transmission
- Typically from sandfly to human
 - Sandfly may acquire infection from human or reservoir species such as rodents, dogs, primates, etc.
 - Human to Human transmission
 - Contact with material from lesion
 - Blood transfusion
 - Organ or bone marrow transplant
 - Congenital



- ### Important *Leishmania* Surface Molecules
- GP63
 - Activates complement
 - Mediates parasite uptake by macrophages
 - May help protect parasite in phagolysosome by degrading host proteases
 - Lipophosphoglycan (LPG)
 - Activates complement & mediates uptake
 - Inhibits protein kinase C and - galactosidase (lysosomal enzymes)
 - Role in insect stage development

Cutaneous Leishmaniasis

- Typically caused by *L. tropica* or *L. mexicana*
- Also known as "Oriental Sore"
- Typically mild and self-limiting, although scarring occurs
- Once lesions have healed, individuals are immune for life
- In some persons, diffuse cutaneous leishmaniasis develops, which often does not heal spontaneously

Mucocutaneous Leishmaniasis

Destruction of nasal septum by *L. braziliensis*

- Occurs in 3-5% of patients infected with *L. braziliensis*
- Affects the mucocutaneous junctions of the mouth, nose, soft palate, anus, genitalia, etc.
- Leads to disfiguring tissue destruction
- Secondary bacterial infections are common

Visceral Leishmaniasis (Kala-Azar)

- Typically caused by *L. donovani*
- Common in India, first described there by Leishman and Donovan in 1903
- Children have the highest prevalence
- Involves the spleen, liver, and bone marrow
- Leads to intermittent high fever, splenomegaly, anemia, and weakness
- Patient becomes progressively weak and emaciated, and may die if untreated
- Common opportunistic infection in AIDS

Diagnosis

- Direct identification of parasites in tissue samples from skin lesions or organs
- Culturing of parasites from tissue samples
- Leishmanin skin test
 - Not positive early in infection
 - Some infected persons remain anergic
- Agglutination test using promastigotes
- Detection of parasite DNA in samples

Treatment

- Not usually necessary for cutaneous leishmaniasis
- Pentavalent antimonial drugs for mucocutaneous or visceral disease
 - Toxicity
 - Relapse/resistance
- Allopurinol (nucleoside analog)
- Immunotherapy
 - INF- in combination w/ chemotherapy

Prevention & Control

- Vector control
 - Insecticides & repellants
 - Screens and bednets
- Control of reservoir species
- Adjustment of human activity to avoid sandflies at dawn and dusk
- Inoculation with scrapings from lesions
- Vaccination with promastigotes (promising, but not yet!)

