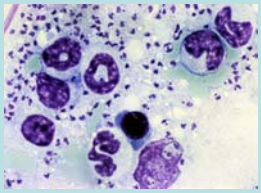
Leishmania spp. and Leishmaniasis

Norma Andrews
Professor, Yale University



Kingdom: **Protista**

Sub-kingdom: **Protozoa**

Phylum: **Sarcomastigophora**

Order: **Kinetoplastida**

Family: **Trypanosomatidae**

Genus: ***Crithidia*** ***Leptomonas*** ***Herpetomonas*** ***Blastocrithidia*** ***Endotrypanum*** ***Rhynchoidomonas*** ***Trypanosoma*** ***Leishmania***

12 million people infected - 350 million at risk

QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture.

Clinical Associations of *Leishmania Sp.*

L. major
L. tropica
L. mexicana

Cutaneous

Clinical Associations of *Leishmania Sp.*

L. braziliensis

Mucocutaneous

Clinical Associations of *Leishmania Sp.*

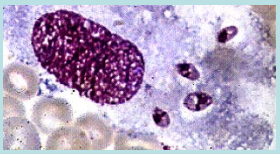
L. donovani
L. infantum
L. chagasi

- **Periodic fever**
- **Severe enlargement of liver and spleen**
- **Weight loss**
- **Anemia**

Visceral

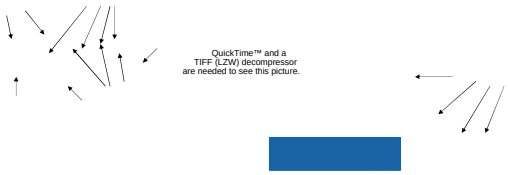
William Boog Leishman
Charles Donovan
1900-1903
Leishman-donovan bodies
in spleen macrophages

Leonard Rogers 1904
Charles Nicolle 1908
Culture of promastigotes revealed existence of extracellular form



John Sinton 1924
Incidence of visceral leishmaniasis in eastern India coincided with distribution of silvery sandfly

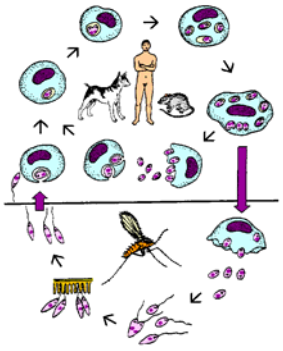
Sandfly species transmitting *Leishmania*



Knowles 1928
***Leishmania* detected in sandflies**

Swaminath 1942
Formal demonstration that sandflies could transmit *Leishmania* to humans

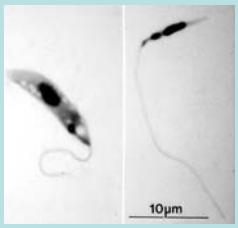
Leishmania Life Cycle



Promastigotes differentiate to complement resistant metacyclic promastigotes in the sand fly midgut

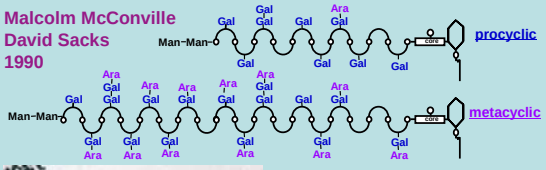
David Sacks 1984-1985

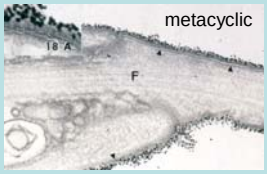
procyclic metacyclic



Differentiation into metacyclics involves LPG coat extension

Malcolm McConville
David Sacks
1990

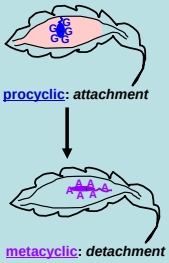




Immunogold surface labeling of *L. major* lipophosphoglycan

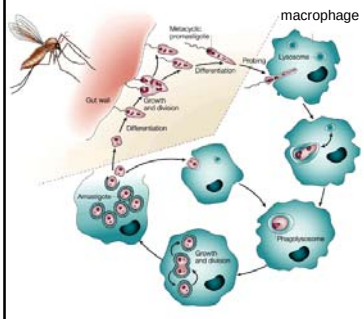
LPG modification promotes infective stage detachment from sandfly midgut

David Sacks 1992

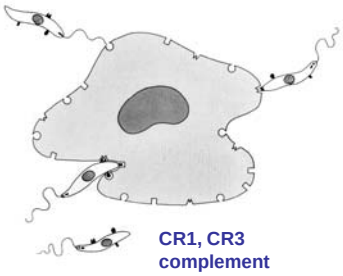


Sandfly vectorial competence for different species of *Leishmania* is associated with LPG polymorphisms

Leishmania Life Cycle



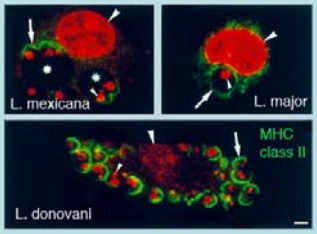
Leishmania invades macrophages by receptor-mediated phagocytosis



CR1, CR3 complement receptors

Leishmania **amastigotes replicate in acidic vacuoles containing lysosomal enzymes and membrane proteins**

Jean Claude Antoine, Pasteur Institute



Control of *Leishmania* transmission is challenging because of difficulties in limiting contact with sandflies

There is a strong need for new drugs with less toxicity