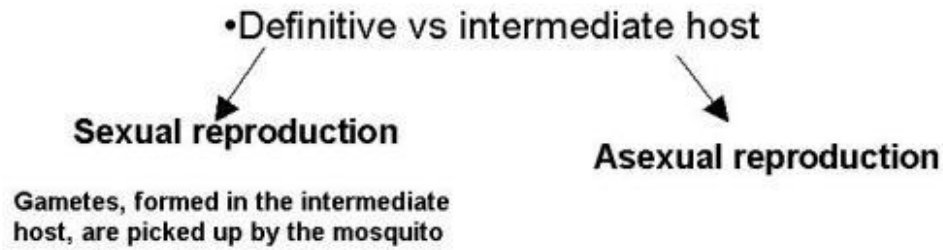


1. Toxoplasmosis - Leishmaniasis: Slide 1

Just to clarify.....



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2. Toxoplasmosis - Leishmaniasis: Slide 2

**Not all zoites are created equal:**

**Sporozoites have to:**

survive in mosquito  
migrate from midgut to salivary glands  
invade hepatocytes

**Merozoites have to:**

survive in mammalian host  
invade RBC

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3. Babesia:

### *Babesia:*

- Intermediate “reservoir” host is the whitefooted mouse-deer are not involved in the lifecycle, but help out by providing more of the vector.
- Humans are a dead end host only because of circumstances-in theory a human could transmit *Babesia* back to a tick-its just unlikely

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4. Toxoplasmosis

# Toxoplasmosis

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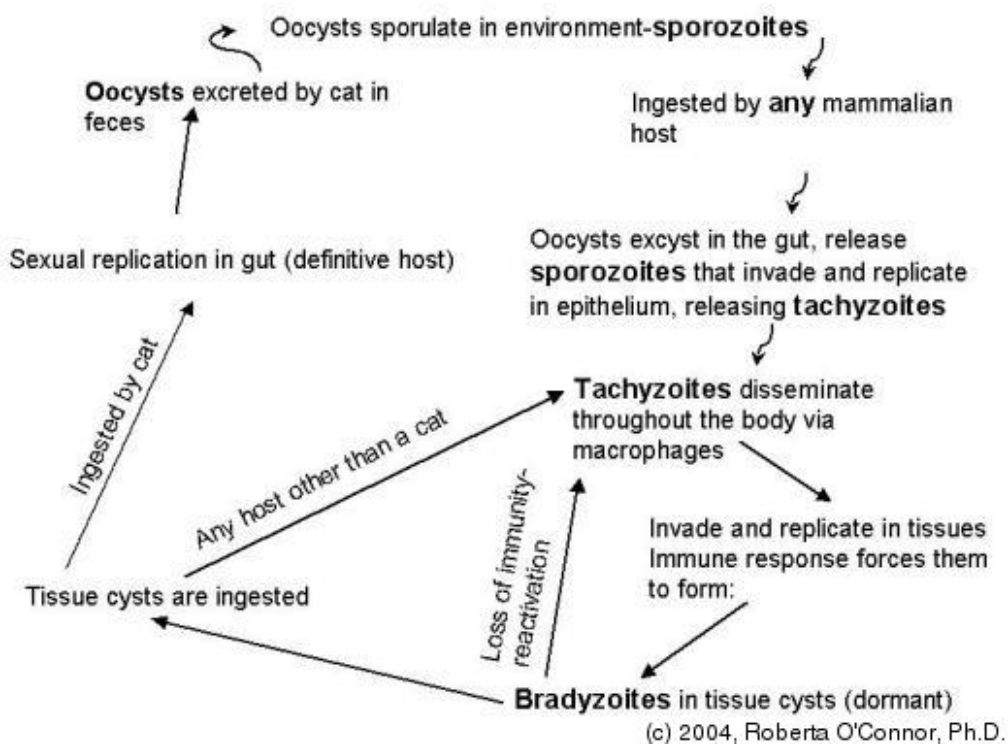
5. In general:

### In general:

- Toxoplasmosis is very common worldwide (anywhere cats can be found)
- Clinical disease is present in only 1% and mostly in the immunocompromised
  - Acute mononucleosis-like illness
  - Congenital infection
  - Activation of brain cysts in the immunocompromised

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6. Toxoplasmosis - Leishmaniasis: Slide 6



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7.

Oocysts

## Oocysts

- Shed by cats
- Excreted for 7-20 days
- Up to 10 million shed/day
- Require 1-5 days in environment to sporulate
- Viable for 16 months in moist soil

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8.

TRANSMISSION

## TRANSMISSION

- Ingestion of oocysts (beware of kitty litter, contaminated soil, sandboxes)
- Ingestion of tissue cysts (beware of undercooked meat)
- Needle stick (in lab)
- Transplacental transmission (congenital toxoplasmosis)

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9. Clinical manifestations:

### Clinical manifestations:

- **Immunocompetent:** usually asymptomatic. In small percentage of cases: chills, fever, headache, myalgia, lymphadenitis, fatigue
- **Immunocompromised:** reactivation of tissue cysts is common (usually from previous infection)
  - Symptoms: headache, confusion, ataxia, retinochoroiditis
  - Diagnostic: lesions on CT scan, *Toxoplasma* specific IgG
- **Congenital toxoplasmosis:** Infection occurs during pregnancy. If infection occurs in the first trimester consequences can be quite severe: retinochoroiditis, encephalitis, and hydrocephalus or microcephaly are common sequelae.
- If infection occurs during the last trimester, the newborn is usually normal but can develop retinochoroiditis later.

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10. Ocular Toxoplasmosis

## OCULAR TOXOPLASMOSIS

- Manifested as retinochoroiditis presenting with unilateral, painless, focally necrotic retinal lesions
- Symptoms include blurred vision, pain, photophobia, scotoma (blind spot), and epiphora
- Prognosis for full visual recovery good with Rx
- Rare complications include glaucoma, blindness

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11.

Diagnosis:

**Diagnosis:**

- **Elevated antibody titer: particularly IgM**
- **Management in pregnancy:**
  - Women with pre-existing titers to *Toxoplasma* have no risk of active toxoplasmosis during pregnancy
  - If seronegative, must be careful not to become infected during pregnancy (gardening)
  - Confirmation of active infection during pregnancy and management are very complicated

**Immunocompromised: IgM not useful:  
diagnosis made on basis of symptoms,  
positive brain scan and anti-*Toxoplasma* IgG**

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12.

Treatment:

**Treatment:**

- CD4 counts below 100: trimethoprim sulfamethoxazole (Bactrim-also prevents pneumocystis)
- For sulfa allergies: dapsone plus pyrimethamine plus folinic acid are substituted (bone marrow suppression can be reduced by the concomitant use of folinic acid), or atovaquone.
- Clindamycin and pyrimethamine is slightly less effective but an adequate alternative.
- Other alternates that are most effective in combination with 1<sup>st</sup> or 2<sup>nd</sup> line drugs include azithromycin, clarithromycin, and atovaquone.
- Corticosteroids may decrease the inflammation of CNS infections in immunocompromised hosts or in retinochoroiditis.

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13.

Leishmaniasis

# Leishmaniasis

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14.

Epidemiology of Leishmaniasis

## Epidemiology of Leishmaniasis

- 2 million new cases in the 88 countries with endemic disease (0.5 million VL; 1.5 CL)
  - About 59,000 deaths in 2001
- Animal reservoirs
  - Dogs
  - Rodents
  - Other small mammals
- Children and young adults most affected
- Risk factors for more severe disease include malnutrition and HIV infection

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15.

Leishmania

## ***Leishmania***

- Protozoa: kinetoplastid (not an apicomplexan)
- In some areas humans are the main host
- In others canines or rodents are reservoirs
- **Vector: sandfly**

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16.

Leishmania Vectors

## ***Leishmania Vectors***

- In the Americas (New World), sandflies of the genus *Lutzomyia* responsible for transmission
- In the "Old World", responsible genus is *Phlebotomus*
- Sandflies breed in cracks in house walls, trash and piles of rubble

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17.

## Life Cycle

### Life Cycle

**Promastigotes bind to complement receptor stimulating phagocytosis**

**Amastigotes replicate in macrophages, rupture the cell and invade new macrophages**

**Sandfly ingests infected macrophages, amastigotes are released and transform into promastigotes**

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18.

## Survival in the macrophage:

### Survival in the macrophage:

- Phagosomal-lysosomal fusion does occur but:
  - Production of superoxide dismutase
  - Resistance to lysosomal enzymes
  - Use of low pH environment to increase uptake of nutrients

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19.

## Immunity

### Immunity

- Th1 response is protective
- Th2 response NOT protective
  - This has been well demonstrated in animal models (classic Th1/Th2 demo)
- AIDS patients frequently develop severe *Leishmania* infections

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20.

Clinical manifestations of leishmaniasis: 3 disease syndromes...

### Clinical manifestations of leishmaniasis: 3 disease syndromes

- Cutaneous leishmaniasis
- Mucocutaneous leishmaniasis
- Visceral leishmaniasis

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21. Cutaneous Leishmaniasis: (*L. major*-“Old World”;, ...

**Cutaneous Leishmaniasis: (*L. major*-“Old World”, *L. mexicana* “New World”)**

- The initial symptom is a small red papule that may itch intensely and grows in size to 2 cm or more and ulcerates (the specific details of the lesion are dependent on the species of *Leishmania*). The lesion usually heals spontaneously with the development of a host cellular immune response
- In some cases the lesions do not heal for one of two reasons (**diffuse cutaneous leishmaniasis**)-Rare
  - ❖ **Anergy:** there is no cellular immune response to the parasite, and the parasite can proliferate indefinitely, forming many lesions.
  - ❖ **Hypersensitivity:** There is a humoral and cellular immune response that cannot control the parasite. The initial lesion heals but peripheral ones continue to form.

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22. Cutaneous Leishmaniasis

**Cutaneous Leishmaniasis**

- Begins as a papule that gradually ulcerates
- Th-1 response leads to scar formation and long lasting immunity

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23. Diffuse Cutaneous Leishmaniasis

## Diffuse Cutaneous Leishmaniasis

- Chronic, progressive, anergic variant wherein large numbers of *Leishmania* migrate to the skin to form numerous nodules
- Caused by *L. aethiopica* and *L. mexicana* complex

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24. Cutaneous Leishmaniasis: Diagnosis

## Cutaneous Leishmaniasis: Diagnosis

- Touch smears or culture of exudates or scrapings yield good results
- Tissue biopsy at active border of lesion
- Geimsa stain

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25. Cutaneous leishmaniasis: Approach to Therapy

### Cutaneous leishmaniasis: Approach to Therapy

- >90% of cases will heal spontaneously within 3-18 months
- Decision to treat is based on several factors including:
  - Risk of progression to mucocutaneous disease
  - Lesion location (e.g., face)
  - Number or size of lesions
  - Persistence of lesion

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26. Clinical manifestations Mucocutaneous Leishmaniasis: (*L. bra...*)

### Clinical manifestations

#### Mucocutaneous Leishmaniasis: (*L. braziliensis*):

- The initial symptoms are similar to cutaneous leishmaniasis,
- Some patients develop ulcers on the oral or nasal mucosa. Progress of the infection is slow, but unless treatment is given, the entire nasal mucosa and the hard and soft palates can be destroyed. Death usually occurs from secondary infection.

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27.

Mucosal Leishmaniasis:

## Mucosal Leishmaniasis:

MCL refractory to therapy:

Cure rates of 10-63% for advanced disease with antimony drugs

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28.

Clinical manifestations Visceral Leishmaniasis: (*L. donovani*...

### Clinical manifestations

#### Visceral Leishmaniasis: (*L. donovani*): Kala-azar

- Parasites are found throughout the body.
- Symptoms
  - initially can be non-specific:
  - abdominal swelling
  - liver and spleen are enlarged,
  - acute onset that mimics an attack of malaria.
  - diarrhea and symptoms resembling typhoid fever.
  - Onset can be insidious with an overall feeling of ill health.

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29. Visceral Leishmaniasis: Pathogenesis

### Visceral Leishmaniasis: Pathogenesis

- Amastigotes in macrophages disseminate to liver, spleen, and bone marrow leading to organomegaly
- Protective Th-1 responses are reduced or absent
- Hypergammaglobulinemia present but does not clear infection

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30. VL: Complications

### VL: Complications

- Bleeding
- Secondary bacterial infections and sepsis
- Edema

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31. Clinical manifestations Visceral Leishmaniasis: (*L. donovani*...

## Clinical manifestations

### Visceral Leishmaniasis: (*L. donovani*): Kala-azar

- **Post-kala-azar dermal leishmaniasis (PKDL)**
  - Rare complication
  - macular, maculopapular, and nodular rash that occurs in patients that have recovered from visceral leishmaniasis and appear well.
  - In some cases these lesions resolve spontaneously, in others treatment is required.

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32. Visceral Leishmaniasis: Diagnosis

## Visceral Leishmaniasis: Diagnosis

- **Definitive diagnosis based on demonstration of amastigotes in tissue**
  - Giemsa stain
- OR
- **Isolation of *Leishmania* in culture**
  - Novy, McNeal, Nicole media
- **Bone marrow aspirate safest**
  - Sensitivity 54-86%
- **Splenic aspirate most sensitive (96-98%)**
  - Risk of bleeding low in experienced hands

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33.

## Treatment

### Treatment

- Pentavalent antimonials: initial therapy
  - Side effects: abdominal pain, nausea, vomiting, headache
- Miltefosine (new) well tolerated, high cure rates can be taken orally-phase IV trials in India
- Amphotericin B (antimony failure)
- Pentamidine (antimony failure-toxic)
- Paromomycin
  - Undergoing phase III trials
- Vaccination...

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34.

## Prevention and Control of Leishmaniasis

### Prevention and Control of Leishmaniasis

- Avoidance of areas where the vector is likely to be found (e.g., within forests)
- Spraying homes with insecticide
  - Effective for endophilic sandflies
- Insecticide-treated bednets
  - Decrease biting rates by 64-100%
- Insecticide-treated curtains
  - Reduce risk of Cutaneous Leishmaniasis

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