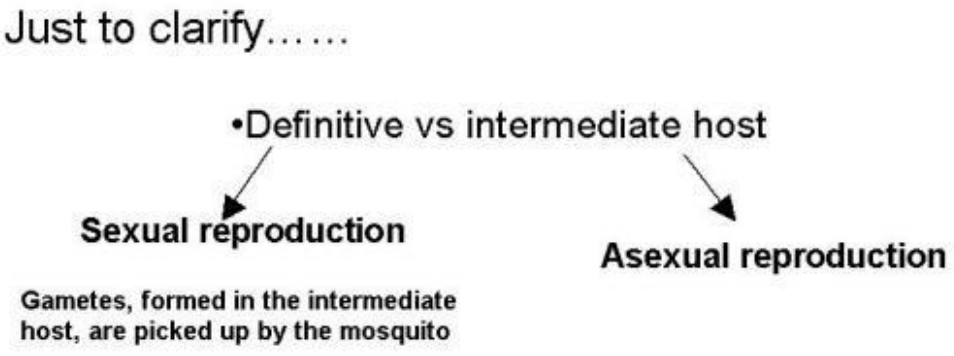
1. Toxoplasmosis - Leishmaniasis: Slide 1



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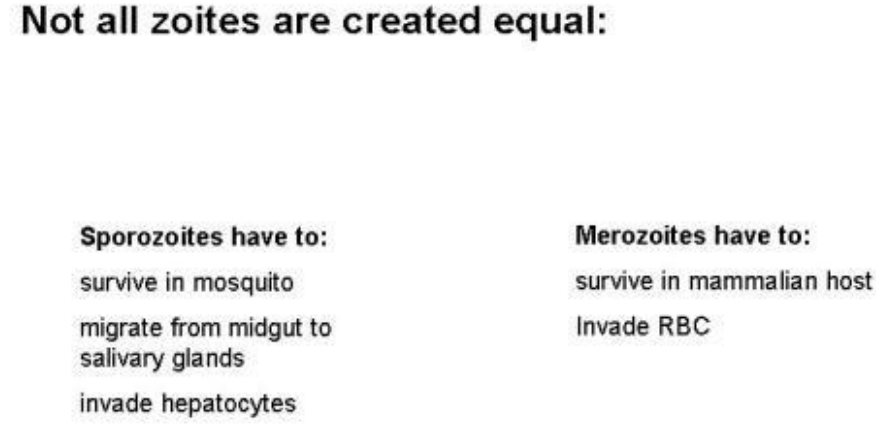
2. Toxoplasmosis - Leishmaniasis: Slide 2



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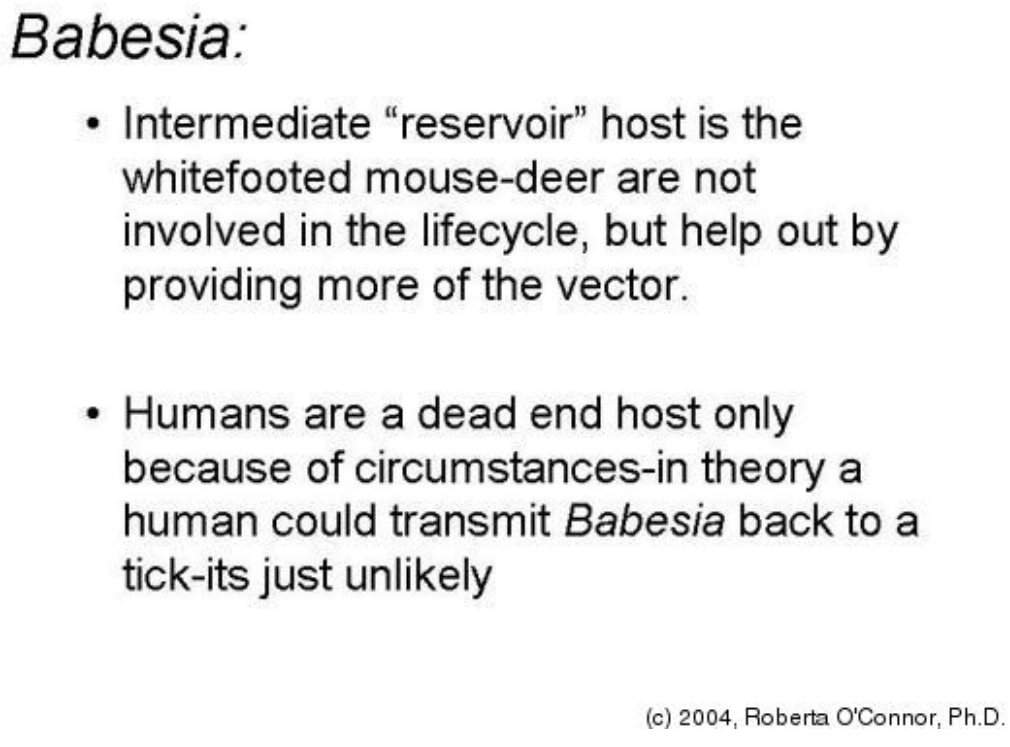
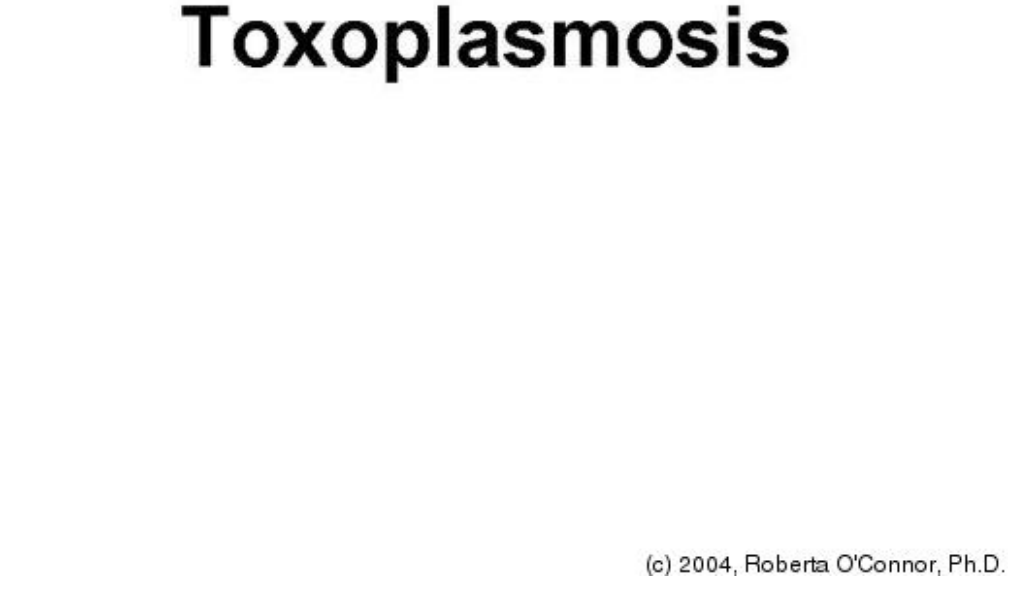
3. Babesia:



4. Toxoplasmosis



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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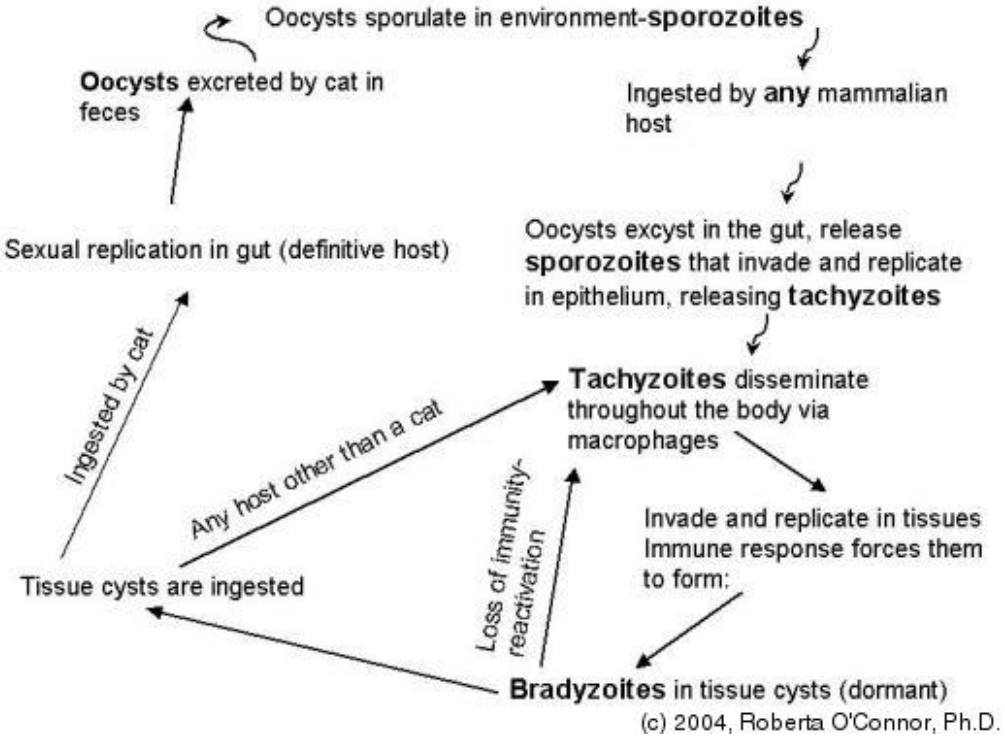
6. Toxoplasmosis - Leishmaniasis: Slide 6



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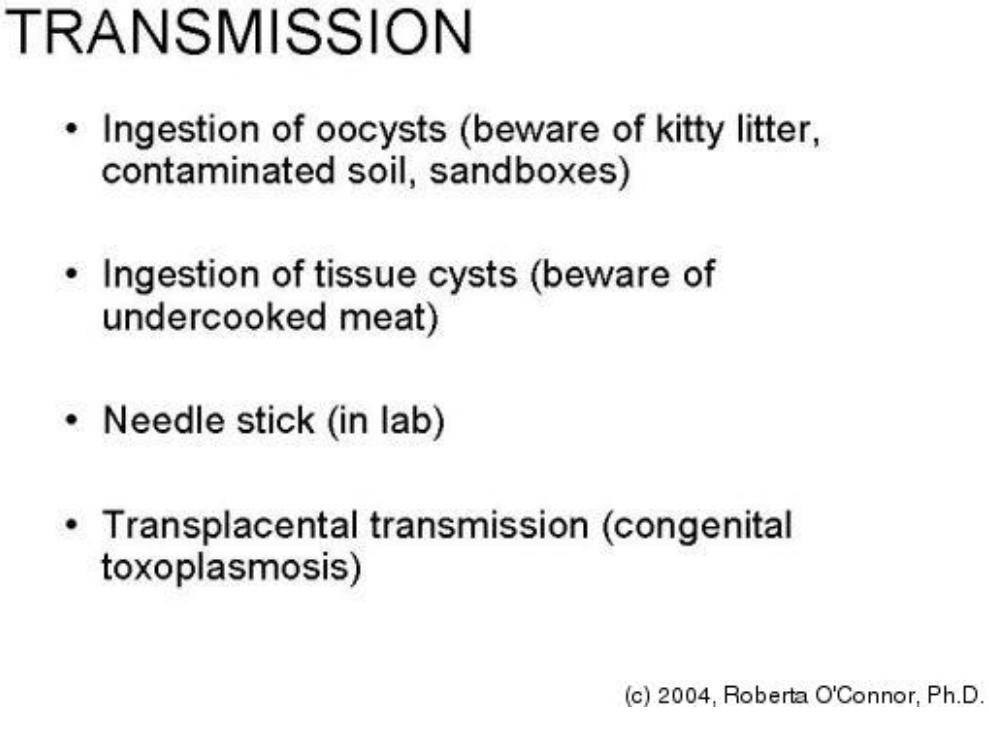
7. Oocysts

8. TRANSMISSION



9. Clinical manifestations:

Clinical manifestations:

- **Immunocompetent:** usually asymptomatic. In small percentage of cases: chills, fever, headache, myalgia, lymphadentitis, 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 sulfamethoxasole (Bactrim-also prevents pneumocystis)
- For sulfa allergies:dapsone plus pyramethamine 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 1st or 2nd 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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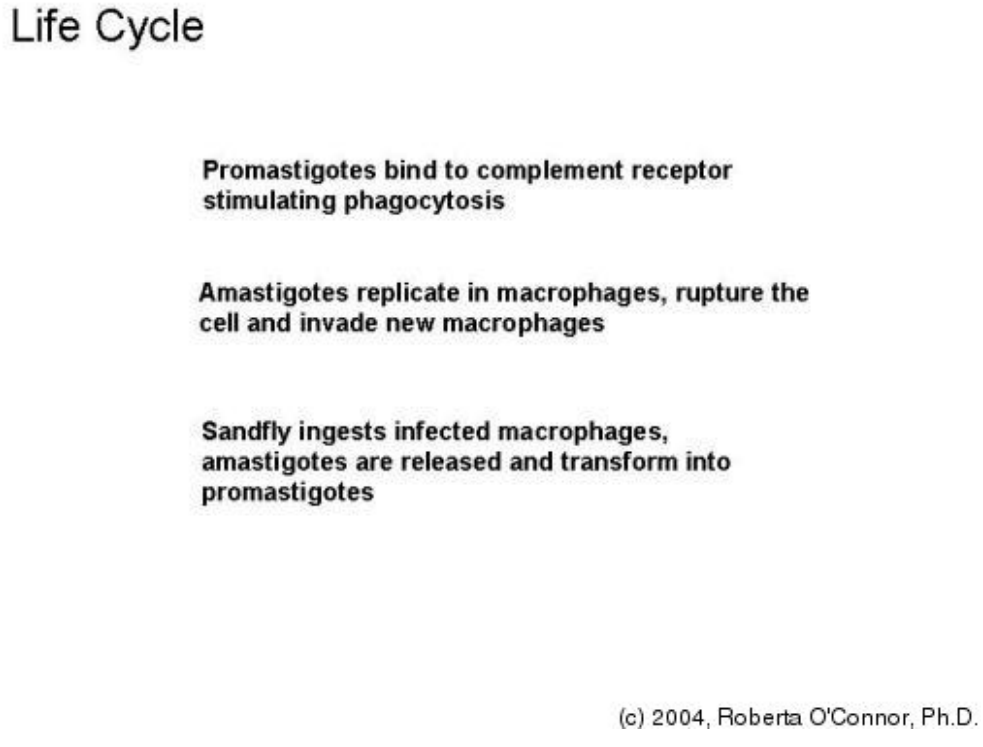
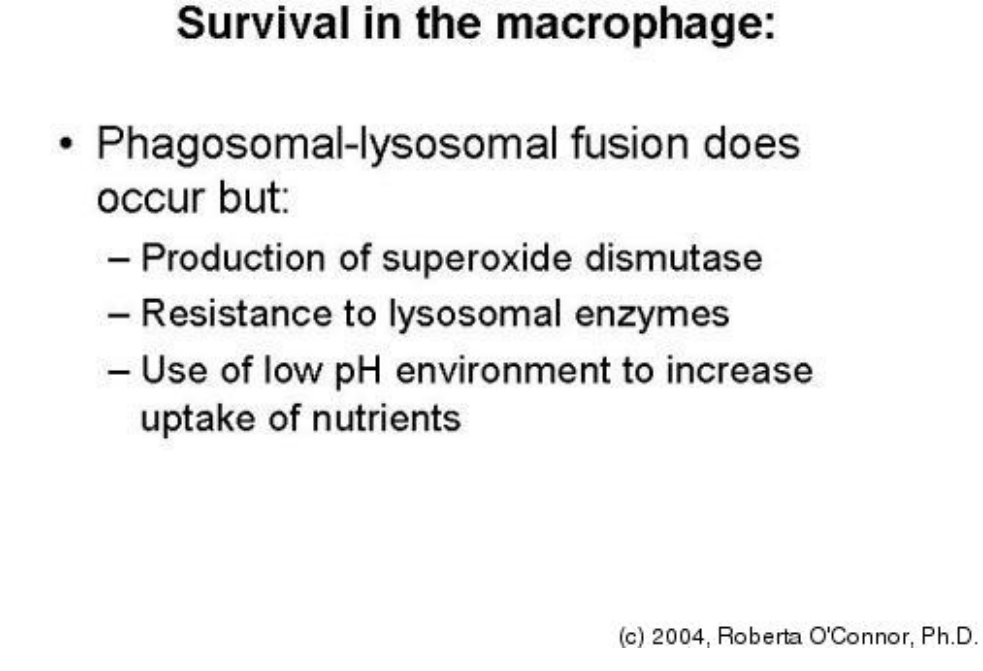
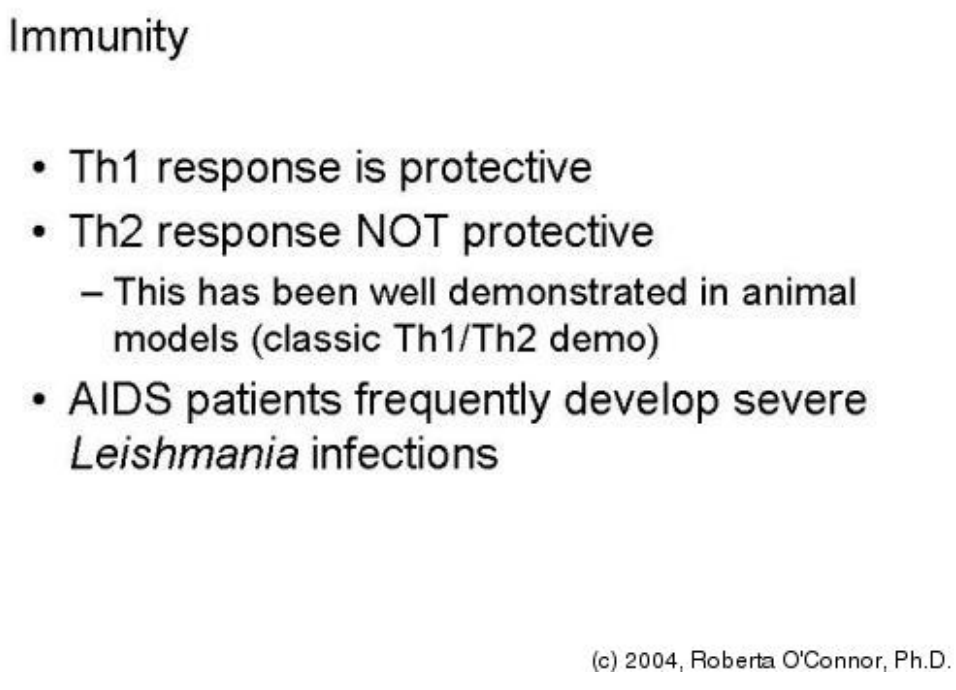
17. Life Cycle



18. Survival in the macrophage:



19. Immunity



20. Clinical manifestations of leishmaniasis:3 disease syndromes...

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 Leismaniasis: Diagnosis

Cutaneous Leismaniasis: 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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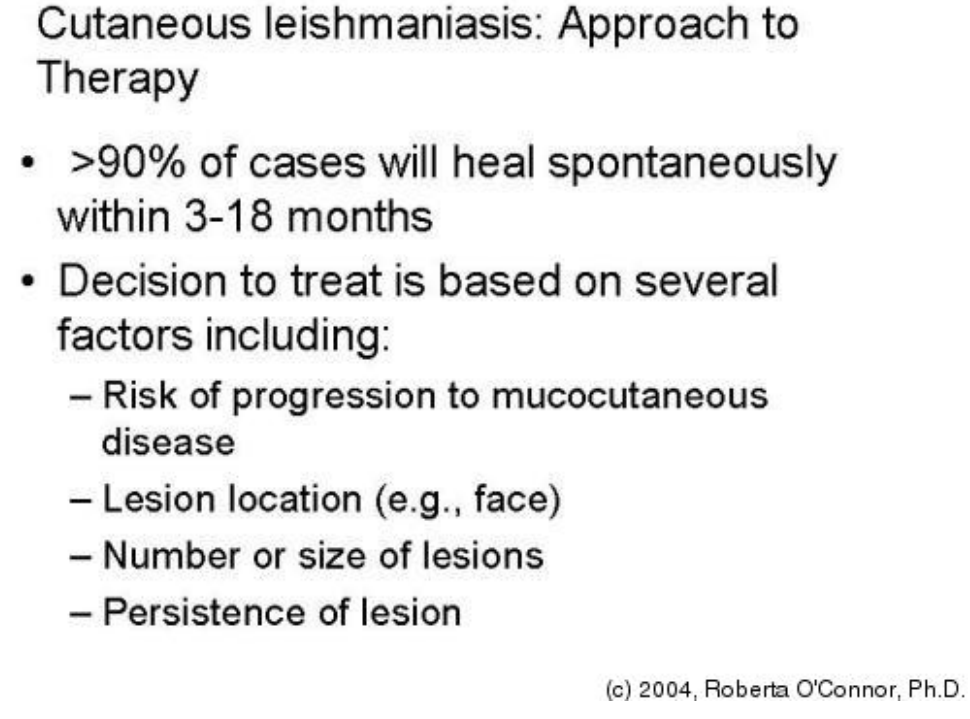
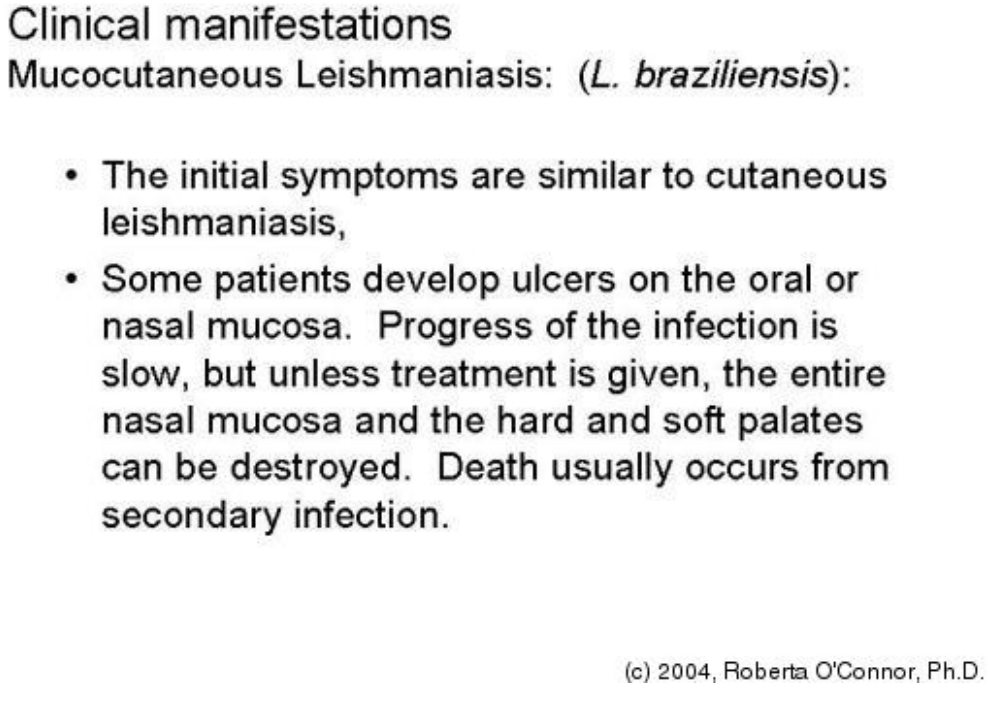
25. Cutaneous leishmaniasis: Approach to Therapy



26. Clinical manifestationsMucocutaneous Leishmaniasis: (L. bra...



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 manifestationsVisceral 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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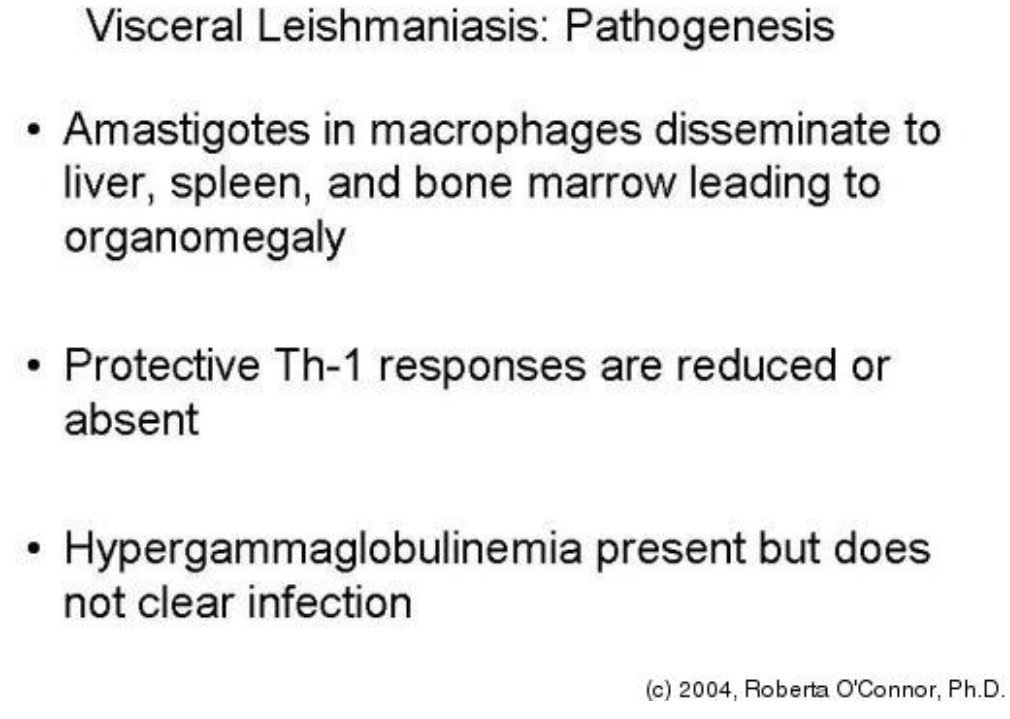
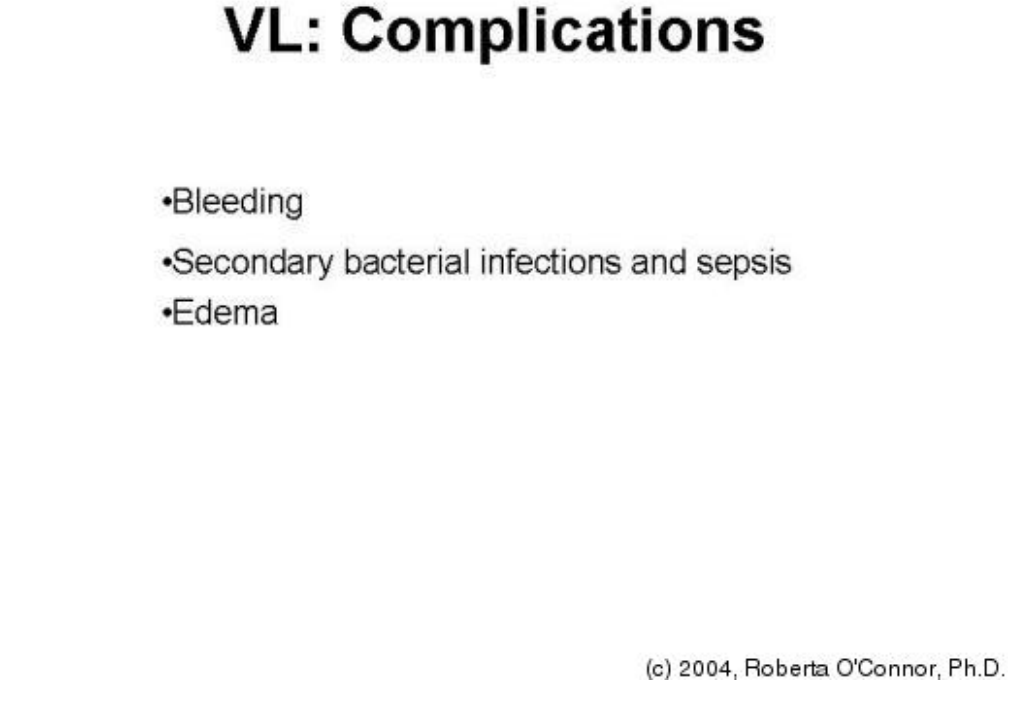
29. Visceral Leishmaniasis: Pathogenesis



30. VL: Complications



31. Clinical manifestationsVisceral 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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