Blood & Tissue Protozoa – The Hemoflagellates

- A. Introduction
 - 1. The family Trypanosomatidae, (includes hemoflagellates) contain only two genera that parasitize humans.
 - a. Genus *Leishmania* are always intracellular, principally in cells of the reticuloendothelial system.
 - b. Genus *Trypanosoma* contains members that may be found both in the circulating blood and intracellularly in cardiac muscle. African blood; American cardiac muscle.
 - 2. In all probability, the hemoflagellates were originally parasites of insects. They are transmitted by insects, and in them undergo a developmental cycle (the arthropod serves as intermediate host).
 - a. "Old World" leishmaniasis transmitted by the bite of various species of sandflies of the genus *Phlebotomus*.
 - b. South American leishmaniasis carried by *Lutzomyia* spp. sandflies.
 - c. American trypanosomiasis transmitted by reduviid bugs; transmission occurs when infective feces of the bug contaminates the wound made by the insect's bite or an abrasion of the skin.
 - d. African trypanosomiasis transmitted by *Glossina spp.* tsetse flies.
 - 3. No cyst stage
 - 4. Red blood Must know transmission and disease names
- B. Trypanosoma brucei







Trypanosoma b. gambiense

- 1. Two subspecies: *rhodesiense* & *gambiense*
- 2. Transmission Life cycles are essentially identical.
 - a. Rhodesian form primarily an animal pathogen, this is a zoonosis which reservoirs in wild grazing animals of East Africa. Parasite progresses rapidly into the central nervous system when occasionally transmitted to humans by *Glossina morsitans* species of tsetse flies.
 - b. Gambian form transmitted by *Glossina palpalis* group of tsetse fly. Although pathogenic in humans, an asymptomatic reservoir can be found in domestic pigs.

- 3. T. brucei rhodesiense & T. brucei gambiense
 - a. Transmission by bite of tsetse fly. Organisms are in the salivary glands of the fly.
 - b. Site of infection organisms multiply in blood early in disease; later in lymph nodes and in the CNS.
 - c. Disease febrile episodes, night sweats, malaise, headache; enlarged cervical lymph nodes "Winterbottom's sign"; final stages- uncontrolled desire to sleep thus the common name "sleeping sickness."
 - d. Diagnosis examine wet mounts of aspirates from chancre (insect bite sight), or blood (buffy coat) for presence of trypanosomes (numbers of organisms peak during fever spikes).
 - e. Morphology Epimastigote is the developmental form in flies; trypomastigote is the infective stage. It is present in the salivary gland of the fly and is the stage seen in the human bloodstream.
- B. Trypanosoma cruzi





Trypanosoma cruzi trypomastigote

Trypanosoma cruzi amastigotes

- 1. Distinctly different form of genus *Trypanosoma* than that associated with African sleeping sickness.
- 2. Disease American trypanosomiasis. Chagas' disease.
- 3. Transmission Metacyclic trypomastigote in reduviid bug feces is introduced through the skin following the bug's bite. Ingestion of the bug is also a mode of infection.
- 4. Trypomastigote and epimastigote (amastigote stage) forms may be found in human tissue & blood the amastigote is a tissue stage; trypomastigote is blood stage; the epimastigote is the developmental stage in the bug.
- 5. Morphology the trypomastigote has a characteristic "U" or "C" shape with an undulating membrane and anteriorly extending flagellum; the amastigote is oval to suboval, averages 3 to 5 microns in diameter and contains a nucleus and rod-shaped kinetoplast.
- 6. Pathogenesis acute phase shortly after infection (1-4 month's duration; chronic phase decades long. Edema of eyelids (Romana's sign). Fever, headache, malaise, myalgia, megacolon, megaesophagus. Cardiac manifestations.
- 7. Reservoir hosts many animals- dogs, opossums, cat, armadillos, etc.

- 8. Epidemiology notes: Limited geographic range most prevalent in South America especially Brazil, Argentina, Uruguay, Chile, and Venezuela. Has been found in Central America, and in a few immigrants or travelers in the Southwest. Five cases have been confirmed in Texas; one in California. There is great concern about transfusion-induced cases in the blood banking industry.
- D. Genus *Leishmania*



Leishmania lesion (cutaneous)



Leishmania amastigotes in tissue

- 1. Four pathogenic species.
- 2. Speciation based on clinical symptoms and manifestations.
- 3. Transmission by bite of infected sandfly.
- 4. Western Hemisphere (New World) sand fly genus: *Lutzomyia*. Rest of the world:

sand fly genus: Phlebotomus

- 5. Complex life cycle.
- 6. Diagnosis finding amastigotes in lesions; clinical signs/symptoms determine "differential" diagnosis.
- 7. Leishmania tropica Mediterranean basin, India, Middle East, Asia & Africa.
 - a. Disease -- Old World cutaneous leishmaniasis; "Baghdad boil", "Oriental sore". A viscerotropic form of this organism is thought to be one cause of the "Desert Storm" syndrome.
 - b. Moist ulcers associated with *L. tropica major* Incubation period of several weeks to months is followed by rapid development of weeping ulcers that heal within 6 months.
 - c. Dry ulcers associated with *L. tropica minor* Incubation period may last for several years before appearance of slowly developing ulcer that is covered with a scaly crust that may take years to heal. Ulcers resemble those produced by the New World form, although this is a different species *L. mexicana* complex.
 - d. Healing of lesions of cutaneous leishmaniasis signifies cell-mediated, species-specific, lifelong immunity. Secondary bacterial infections represent significant complications of the ulcer site. These can advance into diffuse cutaneous leishmaniasis in persons with inadequate cellular

immunity.

- e. Diagnosis identification of intracellular amastigotes in macrophages from active lesions.
- 8. Leishmania mexicana
 - a. Similar to *L. tropica* in that it causes cutaneous leishmaniasis. Found in Central America, Mexico, & Texas.
 - b. Disease New World cutaneous leishmaniasis, chiclero ulcer. Probably the form being detected in Texas.
 - c. Diagnosis identification of amastigotes at periphery of lesion. Organism exists in healthy tissue; necrotic area at center of lesion contains bacteria, few if any organisms.
- 9. Leishmania braziliensis
 - a. Disease Mucocutaneous leishmaniasis, espundia.
 - b. Disfigurement erosion of oral, nasal structures. Organism spread via bloodstream to other areas, especially the mucous membranes and cartilaginous areas of the nasal and oral structures. Erosion and disfigurement of these areas was called "espundia" in native cultures.
- 10. Leishmania donovani
 - a. Disease visceral leishmaniasis, kala-azar. Kala-azar is Hindi for "black fever" a symptom of hyperpigmentation of hands, feet & abdomen.
 - b. Pathogenesis Traditionally the viscerotropic form, skin lesion seldom noticed; in reticuloendothelial system, organisms multiply; extensive hyperplasia of parasitized tissue impairs function of organs. Patients die from acute infections, or from a wide variety of secondary infections. Asymptomatic and long-term chronic infections exist also.
- II. Blood & Tissue Protozoa the Coccidia & Others
 - A. Introduction
 - 1. A number of species parasitize humans: *Isospora, Sarcocystis, Cryptosporidium,* & *Toxoplasma*
 - 2. Have complex life cycles most have 2-host life cycle.
 - 3. Schizogony asexual binary fission.
 - 4. Sporogony -sexual reproduction
 - 5. Diagnostic stages are often difficult to locate. They are easily overlooked due to their nearly transparent appearance. Permanently stained smears not helpful. Acid fast and giemsa stains are more often used. Oocysts do not stain with iodine.

B. Toxoplasma gondii



Toxoplasma gondii trophozoites

- 1. Definitive host felines, domestic cat is most important.
- 2. Human infections are due to accidental ingestion of the infective oocyst from cat feces in kitty litter, etc.; also from ingestion of trophozoites and pseudocysts in undercooked or uncooked meat from a variety of animals; the organism has been isolated from mother's milk; congenital transmission has been documented in cases where infection of the mother occurs during pregnancy.
- 3. Infections are usually asymptomatic this results in large numbers of infected persons (estimated 25% or more of the population); the immune system keeps infections in check; immunosuppression (HIV, etc.) results in fulminating infection.
- 4. Very dangerous in pregnant women the organism can cross the placental barrier and infect the fetus. Result can range from asymptomatic infection to microcephaly, hydrocephaly, or stillborn fetus.
- 5. Diagnosis isolation of organism is difficult; best diagnosed via serological techniques.
- B. Babesia



Babesia sp. rings in red blood cells



Babesia sp. "maltese cross" (arrow)

- 1. Introduction a widespread zoonosis, babesiosis is transmitted via the bite of infected hard ticks. Most cases in USA currently are diagnosed in northeast; the condition can be fatal in splenectomized patients.
- 2. Definitive hosts sexual reproduction takes place in ticks. Asexual reproduction takes place in a variety of mammalian hosts.
- 3. Multiplies within red blood cells; can be confused with malaria ring forms, especially those of *Plasmodium falciparum*. *Babesia* rings are more pyriform (tear-shaped); multiplication gives rise to pairs and tetrads resembling a "maltese"

cross". No pigment is formed (digestion of hemoglobin to hematin).

- 4. Pathology very similar to malaria, but without synchronization of paroxysms. Hemolysis is common, resulting in anemia and jaundice. Severe cases progress to renal failure, hypotension, coma and death.
- 5. Disease name babesiosis, piroplasmosis. "Piro" from "pyro"- Latin for "fire". Because the disease is fever (fire) inducing. The "piroplasms" are a group of fever-inducing organisms or infections. Malaria is a piroplasm also.
- C. Pneumocystis carinii



Pneumocystis carinii cysts in lung tissue



P. carinii cysts (silver stain)

- 1. Pathology Cause of "Interstitial Plasma-Cell Pneumonia," a highly fatal complication of AIDS. The organism and infection are widespread, similar to toxoplasmosis. Classically an infection of the lungs, the alveolar spaces fill with a foamy exudate. The infection has been shown to disseminate to other organ systems in AIDS patients.
- 2. Classification of the organism and its life cycle are uncertain. It has been classified as a fungus as well as a parasite. It is generally accepted that the infection is "airborne," especially prevalent in crowded populations.
- 3. Very common in AIDS patients, and as with toxoplasmosis, parasites formerly held in check are freed to multiply unchecked concurrent with immunosuppression.
- 4. Diagnosis identification of cysts (containing 8 trophozoites) or free trophozoite forms in lung exudates. Various stains are used: methenamine silver demonstrates the cyst wall, but not the trophozoites (yeast & fungi demonstrate similar staining characteristics); Giemsa stains trophozoites but not the cyst wall. Sputum is acceptable in AIDS patients; open lung biopsy, bronchio-alviolar lavage (BAL), or transbronchial biopsy are preferred in other patients.