PARASITOLOGY I & II

I. Sporozoa

A. Malaria (Plasmodium – 5 species)

1. **Species:** *falciparum*, *vivax*, *ovale*, *malariae*, *knowlesi*
2. **Diseases:** malaria
3. **Epidemiology:** (listed in descending order of prevalence)
   a) *vivax*: Most prevalent with widest distribution – tropics and subtropics in Asia (Southeast and India), Africa, Central and South America
   b) *falciparum*: Tropics and subtropics Africa and Asia
   c) *ovale*: mostly in tropical and subtropical Africa
   d) *malariae*: same tropical and subtropical areas but less prevalent
   e) *knowlesi*: Malaysia and surrounding countries: Thailand, Singapore, Myanmar, Vietnam and Philippines
4. **Vector:** female anopheles mosquito
5. **Location in Human Host**
   a) Exoerythrocytic phase – sporozoites and schizonts in liver
   b) Erythrocytic phase – trophozoite
5. **Life Cycle**
   a) Stages
      I. Sexual – **Sporogony** in mosquito
      II. Asexual – **Schizogony** in human
Adapted and redrawn from CDC
7. **Pathogenesis** First symptoms associated with rupture of erythrocytic schizont

   a) Fever occurs at time of schizont rupture (RBC lysis) and release of merozoites
   
   b) Anemia due to hemolysis
      
      i. Massive results in hemoglobinuria and renal failure – "blackwater fever"
   
   c) Tissue hypoxia occurs with heavy parasitemia seen in *P. falciparum, knowlesi and rarely with other species*. Hypoxemia in *falciparum* is due to sludging within microcirculation as well as anemia. The organs most likely affected are Brain (cerebral malaria), lung (ARDS-like illness) and kidney
   
   d) Immunopathologic events
      
      i. SIRS – predominately falciparum
      
      ii. Glomerulonephritis – immune complex type seen with *P. malariae*

8. **Clinical manifestations**

   a) Prodrome – flu-like nonspecific illness: headache, muscle pain, anorexia, nausea, vomiting
   
   b) Chills (rigors), fever occur in cycles followed by sweat and exhaustion.

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**Characteristics of Plasmodium species**

<table>
<thead>
<tr>
<th>Species</th>
<th>Cycle Time</th>
<th>RBC Infected</th>
<th>Hepatic Dormancy</th>
<th>Chloroquine Resistance</th>
<th>Other Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. vivax</em></td>
<td>48 hour</td>
<td>Reticulocyte</td>
<td>Yes</td>
<td>Increasing</td>
<td>Schuffner's dots</td>
</tr>
<tr>
<td><em>P. falciparum</em></td>
<td>48 hour</td>
<td>All</td>
<td>No</td>
<td>Widespread</td>
<td>Electron dense knobs, heavy parasitemia</td>
</tr>
<tr>
<td><em>P. ovale</em></td>
<td>48 hour</td>
<td>Reticulocyte</td>
<td>Yes</td>
<td>No</td>
<td>Schuffner's dots</td>
</tr>
<tr>
<td><em>P. malariae</em></td>
<td>72 hour</td>
<td>Mature</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td><em>P. knowlesi</em></td>
<td>24 hour</td>
<td>All</td>
<td>No</td>
<td>No</td>
<td>Heavy parasitemia</td>
</tr>
</tbody>
</table>
c) Frequency of cycles depends on species

d) Other than splenomegaly, no specific physical findings

e) With severe falciparum and sometimes others sepsis, CNS-headache→coma, ARDS and organ failure

9. Diagnosis

a) See parasites in thick and thin blood smears
   i. Distinguish species morphologically

b) Rapid diagnostic tests – immonochromatographic tests on strips

c) PCR

10. Treatment – goal to eliminate the erythrocytic parasites for all species and the persisting hepatic parasites in vivax and ovale

a) Drugs for erythrocytic: chloroquine, mefloquine, quinine/quinidine, antifolates, sulfonamides, tetracycline, halofantrine (lumefantrine), artemisinins (artemether and artesunate) and atovaquone/proguanil (Malarone)
   i. Chloroquine effective for all species except falciparum (highly resistant) and resistant vivax
   ii. Artemisinin-based combination therapy strongly recommended for falciparum malaria
   iii. Severe falciparum – IV quinidine PLUS doxycycline or clindamycin

b) Exoerythrocytic – (vivax and ovale) Primaquine. This is radical cure eliminating the dormant forms in liver.

c) Chemoprophylaxis given to travelers who will be exposed to malaria – depends on whether traveling to area with chloroquine resistance or not
   i. Chloroquine if sensitive
   ii. Atovaquone/proguanil, mefloquine or doxycycline if resistant

11. Prevention

a) Wide distribution of insecticide impregnated bednets, "residual" indoor spraying of buildings and intermittent preventive treatment of pregnant women and infants has been successful in reducing cases of malaria where it has been employed

b) For travelers: stay indoors at night, use long sleeves and long pants, use insecticide-treated clothing, use mosquito repellants (DEET preferred)
B. Babesiosis

intracellular (intraerythrocytic) sporozoan parasites that resemble plasmodia. Zoonosis affecting deer, cattle, and rodents (field mice, etc.) transmitted by ixodes ticks. These are the same ticks that transmit Borrelia burgdorferi and the geographic range (eastern seaboard, upper Midwest (esp. Wisconsin) is similar. Dual infections (with Lyme) or even triple (with Lyme and Anaplasma) occur Transfusion-related infection also occurs. Babesia is commonest transfusion-related infection in US.

1. Organism Babesia microti in US, other species in Europe
2. Vector: ixodes ticks
3. Reservoir: Small rodents, deer, cattle
4. Life cycle:

5. Epidemiology – range (reservoir, vector, geographic location) same as lyme borreliosis
6. Disease – majority asymptomatic
   a) Incubation 1-4 weeks
   b) Fever
   c) Headache
   d) Fatigue
   e) Hemolytic anemia

c) Vaccines not yet available
f) Prolonged parasitemia with mild illness

g) Immunocompromised (HIV infected, splenectomy)
   I. Severe sepsis

7. Diagnosis
   a) Blood smear
   b) PCR
   c) Serology

8. Treatment
   a) Atovaquone plus azithromycin
   b) Severe – clindamycin plus quinine

C. Toxoplasmosis
   Sporozoan parasite which develop in intestinal cells of cats and other felines. Cysts are passed in cat feces and mature into infective oocysts within few days. Oocysts are ingested by mice and other animals including humans resulting in infection in various tissues, e.g., brain. Cats become infected when they ingest infected animal tissue.

1. Reservoir
   a) Sheep
   b) Pigs
   c) Wild game
   d) Birds
   e) CATS

2. Transmission
   a) Eating inadequately cooked meat containing cysts
   b) Ingestion of oocyst-containing cat feces in food or environment, e.g., sand box, litter box
   c) Vertical intrauterine transmission
   d) Blood transfusion

3. Life cycle
   a) Human ingests cyst (meat) or oocyst (food or environment)
   b) In human, oocysts release sporozoites or cyst is digested releasing tachyzoites. Tachyzoites enter macrophages and are disseminated throughout body
   c) Active form (tachyzoites) are controlled by immune response and form cyst containing dormant organisms (bradyzoites), esp in brain, heart and skeletal muscle
   d) End of life cycle unless human host becomes immunosuppressed and bradyzoites are released from cyst becoming active
4. Clinical Manifestations
   a) **Localized or generalized lymph node enlargement** without symptoms
   b) **Mononucleosis-like illness** with diffuse generalized lymphadenopathy
   c) **Immunocompromised**, esp. AIDS, solid and stem-cell transplant recipients – **encephalitis** (brain infection) myocarditis and other organs (lung and lymphoid tissue)
      i. **Reactivation** of latent infection
   d) **Congenital** – multisystem with prominent CNS involvement
   e) **Chorioretinitis** – often congenital and may be only manifestation

5. Diagnosis
   a) Histology – see cysts and tachyzoites
   b) Serology
      i. IgG and IgM responses measured
      ii. Complex profile used to diagnose infection in pregnancy
   c) PCR

6. Treatment
   a) Pyrimethamine + sulfadiazine
b) Alternative antimicrobials: clindamycin, dapsone, clarithromycin, azithromycin, atovaquone

c) Spiramycin used to treat newly infected pregnant woman to prevent vertical transmission.

7. Prevention – both primary and secondary in AIDS and transplant patients
   a) Trimethoprim/sulfamethoxazole

D. Cryptosporidiosis
Coccidian protozoan that carries out entire life cycle just within the brush border of intestinal epithelium of host. Spreads as zoonosis from animal reservoirs to humans. Often waterborne but also person-to-person transmission. Causes watery diarrhea. Cryptosporidium parvum responsible for most infections in US

1. Reservoir
   a) Domestic animals
   b) Infected humans.

2. Mode of Transmission
   a) Fecal-oral by ingestion of infectious cysts
   b) Person-to-person (may be sexual)
   c) Waterborne outbreaks – 400,000 in Milwaukee in 1993

3. Life cycle
   a) Ingestion of oocysts
   b) Sporozoite attaches to epithelial surface of GI tract and becomes trophozoite. Several asexual cycles of reproduction occur, but ultimately sexual cycle results in production of oocysts that are passed in feces
4. **Clinical Manifestations**

   a) Incubation 2-10 days

   b) Immunocompetent: watery, large volume diarrhea often with nausea, cramps, vomiting and weight loss. Fever in 1/3. Self limited lasting 2-3 weeks
c) Immunocompromised: severe, relentless watery diarrhea with up to 50 stools per day and very large fluid loss. Can last months to years

5. Diagnosis
   a) Acid-fast staining of cysts in feces
   b) Direct immunofluorescence
   c) PCR (part of the multiplex PCR panel in use at LUMC)
   d) Biopsy

6. Treatment
   a) Antiperistaltic agents
   b) Nitazoxanide MAY be effective
   c) HAART with immune reconstitution is only proven treatment in AIDS

II. Amoebozoa
   A. Amebiasis – Amebae are unicellular microorganisms with simple life cycle. Infective form is the cyst which when digested becomes trophozoite. Divide by binary fission. Motility by extension of pseudopod with movement of remainder of cell in direction of the pseudopod. *Entamoeba histolytica* is the human pathogen. Trophozoites invade and lyse colonic mucosa cells with intense inflammation and necrosis. There are numerous commensal intestinal ameba which must distinguished from *E. histolytica*. Some can be distinguished morphologically but others are morphologically indistinguishable from pathogenic *E. histolytica* (*E. dispar*, *E. moshkovskii*, *E. bangladeshi*). These can be identified with immunological or PCR methods.

   1. Epidemiology
      a) 10% of worlds population
      b) Rare in US (1-2% prevalence)
      c) Fecal-oral transmission with food or waterborne outbreaks
      d) Venereal transmission

   2. Life cycle
   Actively growing, vegetative trophozoites and dormant, highly resistant cysts
   a) Human is host – passes trophozoites and infectious cysts in feces. Asymptomatic pass cysts only
   b) Oral ingestion of cyst (infectious form) from food, water or another person
   c) Cyst digested in stomach and small bowel releasing 4 trophozoites
3. Pathogenesis
   a) Galactose-specific lectin mediates attachment
Mechanisms of Human Disease

I. Affects permeability leading to lysis of epithelial and inflammatory cells

II. Release of neutrophil components contribute to tissue destruction

b) Antibody formation is a marker of a pathogenic strain

4. Pathology

a) Form small mucosal ulcers that are undermined in submucosa – “Flask”

I. Dysentery – severe coalescent ulcer disease

II. Ameboma – tumor-like mass of granulation tissue

b) Metastatic spread to liver, pleura, pericardium, lung and brain

5. Clinical Manifestations

a) Abdominal pain, cramping, diarrhea which may be bloody

b) Dysentery – fever, tenesmus, frequent bloody stools, severe abdominal pain

c) Extraintestinal

I. Liver abscess – fever and pain

II. Pleural – pleuritic pain, cough

III. Pericarditis

6. Diagnosis

a) Trophozoites and cysts in stained stool or DFA

b) Stool antigen testing

c) Imaging for extraintestinal

d) Serology

e) PCR specific for pathogenic strains and part of the multiplex PCR panel in use at LUMC

7. Treatment

a) Invasive: metronidazole, tinidazole, nitazoxanide

b) Luminal (cysts): iodoquinol, paromomycin, diloxanide furoate

B. Free Living Amoebae – Three genera of amoebae, *Acanthamoeba, Naegleria* and *Balamuthia* can cause encephalitis in man. *Naegleria fowleri* causes acute amebic encephalitis. Swimming in contaminated water results in invasion of nasal mucosa with extension to brain. Course is rapid with very high mortality. *Acanthamoeba* encephalitis occurs in immunocompromised with unknown mechanism of transmission. *Acanthamoeba* can also cause eye infection associated with trauma and contaminated contact lens solutions. *Balamuthia* has been isolated from soil and dust and has caused rare but fatal encephalitis in
immunocompromised. Two organ-transplant clusters of *Balamuthia* were reported by the CDC in 2010.

**III. FLAGLLATES – INTESTINAL AND UROGENITAL**

**A. *Giardia duodenalis (G. lamblia)*** *Giardia* is an intestinal flagellate with trophozoite and an infective cyst form that causes water, food and sexually transmitted diarrhea.

1. **Morphology**
   a) Trophozoite – sting ray shape, “Popeye”
      i. 2 nuclei
      ii. 4 pairs flagella
      iii. Sucking disc
   b) Cyst
      i. Oval
      ii. Clear cyst wall with four nuclei
      iii. Survives in cold water – 2 months

2. **Epidemiology**
   a) World wide including cosmopolitan distribution
      i. Source is contaminated food or water
      ii. Highest in areas with poor sanitation
   b) Rural water
      i. “wilderness” – wells or municipal water supply
      ii. rivers and other surface water
      iii. Animal reservoir: beavers, muskrats, sheep, cattle, dog, cat
   c) Person to person
      i. Day care
      ii. Sexual

3. **Life cycle**
4. Pathogenesis
   
   a) Trophozoite attach to intestinal villi by sucking disc
   
   b) Biopsy – flattening of microvilli and inflammation, no necrosis
   
   c) Diarrhea is malabsorption type

5. Clinical manifestations
   
   a) Asymptomatic 1/3 – 2/3
   
   b) Foul-smelling, watery diarrhea, abdominal cramps, flatulence, steatorrhea
   
   c) May become chronic or relapse

6. Diagnosis
a) Microscopic examination of stool for cysts and trophozoites,
   I. Multiple samples may be required
   II. Direct fluorescence
b) Stool antigen
c) PCR included in multiplex PCR panel at LUMC
7. Treatment
   a) Tinidazole, nitazoxanide, metronidazole

### Other Intestinal Protozoa

<table>
<thead>
<tr>
<th>Name</th>
<th>Type</th>
<th>Source</th>
<th>Reservoir</th>
<th>Illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balantidium coli</td>
<td>Ciliate</td>
<td>Water</td>
<td>Swine, monkeys</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Cystoispora belli</td>
<td>Coccidian</td>
<td>Food, water, person</td>
<td>Human</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Cyclospora cayetanensis</td>
<td>Coccidian</td>
<td>Water, food</td>
<td>Reptiles, birds, mammals</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Microsporidiosis</td>
<td>?</td>
<td>Many invertebrate, vertebrate hosts</td>
<td></td>
<td>Diarrhea, Encephalitis, Eye infections</td>
</tr>
</tbody>
</table>

### B. TRICHOMONAS VAGINALIS

Cause of sexually transmitted vaginitis. Men are usually asymptomatic

1. Morphology
   a) Oval shaped
   b) Axostyle
   c) 4 flagella
   d) Undulating membrane
2. Epidemiology
   a) Prevalence in developed countries: 20% women, 2-10% men
   b) Spread by sexual intercourse
   c) Nonvenereal transmission is rare

3. Pathogenesis
   a) Damages squamous epithelium of female genital tract
      i. Neutrophilic inflammatory reaction
      ii. Petechial hemorrhages
   b) Virulence not defined
   c) Associated with preterm birth

4. Clinical Manifestations
   a) Vaginal discharge, itching, burning, vaginal erythema, dysuria
   b) Rare dysuria in men

5. Diagnosis
   a) Wet mount of discharge – see motile organisms
   b) Urinalysis
   c) Both of the above tests are being replaced by nucleic acid amplification test (NAAT ideal when combined with gonorrhea and chlamydia)
   d) Culture

6. Treatment
   a) Tinidazole – single dose
   b) Metronidazole – single dose or seven day course
IV. INTRODUCTION TO BLOOD AND TISSUE FLAGELLATES

1. Genera
   a) Leishmania
   b) Trypanosoma

2. Life cycles: involve two hosts
   a) Man – definitive host
   b) Blood sucking arthropod – intermediate host

3. Vectors
   a) Sand flies (Phlebotomus, Lutzomyia) - Leishmania
   b) Tsetse fly (Glossina) – African trypanosomiasis
   c) Triatomid bug – American trypanosimiasis

4. Morphology
   a) Insect – promastigote and epimastigote in gut
   b) Mammal (man) – trypomastigotes free in blood, amastigotes are intracellular form

5. Epidemiology
   a) Leishmania – Asia, Middle East, Africa, Central and South America
   b) T. burcei gambiense and rhodesiense – Africa
   c) T. cruzi – Western hemisphere (Central and South America)

B. LEISHMANIASIS
1. Organisms

With the availability of PCR for diagnosis, there are at least 23 species of Leishmania that are pathogenic for man. Current treatment regimens are species specific so that PCR diagnosis is now considered necessary for treatment. A current species classification will be discussed in the lecture. Older classifications shown in the table below separate species endemic in the “old world” (Middle East, Africa, India) from those endemic in the “new world” (Central and South America). The syndromes are classified as cutaneous, mucocutaneous and visceral.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Manifestation</th>
<th>Reservoir</th>
<th>Vector</th>
<th>Unique Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. tropica</em></td>
<td>Localized cutaneous Leishmaniasis</td>
<td>Rural-gerbil, rodents Urban-dog</td>
<td>Sandfly</td>
<td>Localized chronic ulcer</td>
</tr>
<tr>
<td><em>L. braziliensis</em></td>
<td>Mucocutaneous Leishmaniasis</td>
<td>Forest rodents</td>
<td>Sandfly</td>
<td>Ulcer, metastatic to mouth, nose, perineum</td>
</tr>
<tr>
<td><em>L. donovani</em></td>
<td>Disseminated visceral Leishmaniasis</td>
<td>Africa-rodents. Eurasia, Latin America-dog India-human</td>
<td>Sandfly</td>
<td>Bloodstream dissemination to liver, spleen, bone marrow, lymph nodes, small bowel, skin</td>
</tr>
</tbody>
</table>

90% of visceral infections occur in India, Bangladesh, Nepal, Sudan, Ethiopia and Brazil
90% of cutaneous infections occur in Afghanistan, Algeria, Iran, Saudi Arabia, Syria, Brazil, Columbia, Peru and Bolivia

2. Life cycle includes sandfly feeding on infected person
Mechanisms of Human Disease

Friday, January 4, 2019 8:30 and 9:30 AM

J. Paul O’Keefe, MD

3. Pathogenesis

a) Fly injects promastigotes which are opsonized by complement
b) Taken up by macrophages; multiply intracellularly
c) Cell ruptures releasing amastigotes to fly or to infect monocytes/macrophages
d) Vigorous cellular response controls infection, OR
e) Failure of immune response allows circulation and dissemination to other organs despite antibody response
4. Clinical Manifestations
   a) Localized cutaneous leishmaniasis (*L. tropica, L. major, L. mexicana, L guyanensis, others*)
      
      i. Skin lesion (papule) on extremities, face weeks to months after bite
      
      ii. Becomes painless ulcer that resolves over 3-12 months
   
   b) Mucocutaneous leishmaniasis (*L. braziliensis*)
      
      i. Local lesion 1 to 4 weeks after bite enlarges or heals
      
      ii. Metastatic destructive lesions of nose, mouth, perineum
   c) Diffuse Cutaneous Leishmaniasis
      
      i. Disseminates from localized cutaneous in persons with defects in cell mediated immunity, e.g., HIV infection
   d) Visceral leishmaniasis (*L. donovani, L. infantum*)
      
      i. Weeks to months after bite – fever
      
      ii. Diarrhea, lymphadenopathy, massive splenomegaly
      
      iii. Anemia, thrombocytopenia, leukopenia
      
      iv. Weakness and emaciation
   e) Post-kala-azar dermal leishmaniasis (PKDL)

5. Diagnosis
   a) Localized
      
      i. biopsy or smear-see amastigotes
      
      ii. Culture, antigen or PCR
   b) Visceral
      
      i. Aspirates of bone marrow, liver, spleen, lymph node
      
      ii. PCR
   c) PCR important for species identification directing therapy

6. Treatment
   a) Current treatments based on accurate PCR based identification
   b) Many cutaneous are self limiting
   c) Topical for some cutaneous: 15% paromomycin/12% methylbenzethonium chloride ointment, intralesional antimonials, cryotherapy
   d) Other cutaneous – require systemic treatments as visceral
e) Visceral – Liposomal amphotericin b, Miltefosine, Antimonials

C. African trypanosomiasis Cause chronic systemic illness with prominent CNS involvement. There are two distinct forms of the disease caused by *T. brucei rhodesiense* and *T. brucei gambiense*

<table>
<thead>
<tr>
<th>African Trypanosomiasis</th>
<th>Species</th>
<th>Geographical area</th>
<th>Reservoir</th>
<th>Vector</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>T. brucei gambiense</em></td>
<td>Saharan W. Africa</td>
<td>Human</td>
<td>Glossina (tsetse)</td>
</tr>
<tr>
<td></td>
<td><em>T. brucei rhodesiense</em></td>
<td>Savannas E. Africa</td>
<td>Antelop, domestic animals</td>
<td>Glossina (tsetse)</td>
</tr>
</tbody>
</table>

Ongoing epidemic in Africa from coast to coast.
*T. brucei gambiense* widely found in West and Central Africa
*T. brucei rhodesiense* in small areas of East/Southeast Africa

1. Life cycle
   a) Fly ingests trypomastigotes with blood meal which develop in midgut. Migrate to salivary gland and become epimastigote. Transformed to trypomastigote that is infectious
   b) Fly inoculates parasite with saliva during blood meal. Trypomastigotes multiply and invade bloodstream. Then localize in lymph nodes, heart and CNS
   c) Fly infected with blood meal
2. Pathogenesis

   a) Localize in small blood vessels of heart and CNS causing endothelial proliferation and localized vasculitis. Inflammation may be immune mediated

   b) Parasite can alter antigenic structure of surface glycoprotein allowing it to evade the immune response and reemerge in the blood.

   c) Results in hemorrhage and demyelinating panencephalitis

3. Clinical Manifestations

   a) First stage two weeks after bite (before CNS involvement)

      i. Ulcer (chancre) at site of fly bite
      ii. Fever, myalgias
      iii. Lymphadenopathy

         i. Tbg: Posterior cervical – Winterbottom sign

         ii. Tbr: Other sites depending on location of bite

   b) Second stage after CNS involvement
Mechanisms of Human Disease

I. Headache, impaired mentation progressing to coma
II. Tbg-chronic, slow psychomotor impairment→coma
III. Tbr-more acute with rapid progression (<1 year) heart failure, coma

4. Diagnosis
   a) Blood smear, smears from lymph node aspirates, CSF
      I. See trypomastigotes
   b) Serology – rapid card test in field CATT
   c) PCR in specialized labs only

5. Treatment
   a) First stage
      I. Tbg – pentamidine
      II. Tbr – Suramin
   b) Second stage
      I. Tbg – Eflornithine with or without Nifurtimox
      II. Tbr – Melarsoprol

B. AMERICAN TRYPANOSOMIASIS Infection with Trypanosoma cruzi, commonly referred to as Chagas’ disease, can cause an acute systemic illness and chronic heart, esophagus and colon involvement.

<table>
<thead>
<tr>
<th>American Trypanosomiasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Species</strong></td>
</tr>
<tr>
<td><em>T. cruzi</em></td>
</tr>
</tbody>
</table>

1. Epidemiology
   a) 15-20 million people in Central and South America infected with 50,000 deaths annually
   b) Zoonotic reservoirs and vectors in southern US but transmission is rare due to lack of human dwellings which support vector (Reduviid bug) habitat
   c) Carriers in US have resulted in donor to recipient infection in transplant patients.
I. Donor screening implemented

2. Life cycle
   a) Reduviid bug lives in cracks of mud walls or thatch in roofs of rural dwellings
   b) Nocturnal bug bites, often on face, and defecates organisms in area of bite
   c) Organisms rubbed into open wound and enter blood as trypomastigotes
   d) Trypomastigotes enter cardiac, skeletal, and smooth muscle and glial cells, transform into amastigote stage and multiply disrupting cell
   e) Invade adjacent cells and multiply or transform to trypomastigotes and are released to circulating blood
   f) Ingested by reduviid bug

3. Pathogenesis
   a) Chagoma due to local inflammation
   b) Disseminate and organ invasion including CNS
      I. Acute febrile illness
      II. Heart, skeletal muscle, smooth muscle, glial nerve cells
      III. Adhere – adhesin surface protein to host fibronectin
IV. Cell ruptures with intense inflammation
   
   c) Immune destruction of parasite terminates the process
   
   d) Affects blood vessels, muscle, conduction and nerve tissue in heart as well as nerve and smooth muscle in esophagus and colon

4. Clinical manifestations
   
   a) Chagoma (Romaña sign if around eye)
   
   b) Acute illness: fever, rash, splenomegaly, lymphadenopathy, edema
      
      I. May be fatal
   
   c) Chronic illness develops in 20-30% of chronic infected
      
      I. Heart disease – cardiomegaly and failure, arrhythmia
      
      II. Megaesophagus
      
      III. Megacolon
      
      IV. AIDS – severe CNS manifestations

5. Diagnosis
   
   a) Blood smear – see trypomastigotes
      
      I. Difficult to find after acute infection
   
   b) Xenodiagnosis
   
   c) Serology – recommended by CDC
   
   d) PCR

6. Treatment
   
   a) Nifurtimox, Benznidazole

II. UNCLASSIFIED ORGANISM (Fungus)

A. PNEUMOCYSTIS JIROVCEII
   
   1. Reservoir:
      
      a) normal flora of man
   
   2. Encounter:
      
      a) probably air-borne for initial exposure.
      
      b) Disease either from primary infection OR reactivation of quiescent old infection
   
   3. Life Cycle:
      
      a) ribosomal RNA homologies indicate that it is a **fungus**, not a protozoa.
      
      Cysts → Sporozoites → Trophozoites → Cysts
4. Clinical Manifestations:
   a) **Interstitial pneumonia** in immunocompromised hosts, esp. AIDS patients.
   b) Diagnosis made by demonstration of the organism in open lung biopsies or bronchoalveolar lavage fluids.
      i. Silver stain
      ii. Direct fluorescence antibody stain
      iii. PCR may be overly sensitive
   c) Chemoprophylaxis and/or treatment:
      i. Trimethoprim/sulfamethoxazole or pentamidine
      ii. Other drugs effective