HEMATOLOGY PARASITES:

The Monsters Within...

Presented by Theresa R. Fruehling, MLS (ASCP), MA (Forensic Psychology)
OBJECTIVES:

- Identify the vector and mode of transmission of each parasites
- Describe the life cycles, symptoms, diagnosis, and treatment methods for:
  - Babesiosis:
    - *Babesia microti*
  - Malaria:
    - *Plasmodium* species:
      - *P. vivax*
      - *P. falciparum*
      - *P. malaria*
      - *P. ovale*
      - *P. knowlesi* *
  - Trypanosomiasis:
    - *Trypanosoma brucei*:
      - *T. brucei rhodesiense*- East African sleeping sickness
      - *T. brucei gambiense*- West African sleeping sickness
  - Schistosomiasis:
    - *Schistosoma* species:
      - *S. mansoni*- Manson’s blood fluke
      - *S. japonicum*- blood fluke
      - *S. haematobium*- bladder fluke
BABESIOSIS: OVERVIEW

• Babesiosis is a tick-borne malaria-like illness caused by *Babesia*- an intraerythrocytic protozoan
• Human babesiosis is infrequent and occurs in limited geographical areas
• These parasites are commonly called piroplasms- pear-shaped forms within infected RBCs
• *Babesia microti*- found only in the United States
• *Babesiosis* is difficult to diagnosis
BABESIOSIS

- Vector: *Ixodes scapularis* (a.k.a *Ixodes dammini*)
  - The black-legged deer tick
  - Specific to the United States
- Transmission:
  - Bite of infected *Ixodes scapularis* (black-legged deer tick)
  - Nymph stage
    - Size of a poppy seed
- Demographics:
  - Endemic to Northeastern Coastal Region of U.S.
    - Cases are more acute and several patients died
  - West Coast
    - Typically subclinical except in splenectomized or immunocompromised patients
BABESIOSIS - LIFE CYCLE

- *Babesia microti* life cycle involves two hosts:
  - Rodent - the white-footed mouse, *Peromyscus leucopus*
  - Tick - genus *Ixodes*

**Life Cycle:**
1. During a blood meal, a *Babesia*-infected tick introduces sporozoites into mouse
2. Sporozoites enter RBCs and undergo asexual reproduction (budding)
3. Parasites differentiate into male and female gametes and wait...
4. To be ingested by an appropriate tick (definitive tick)
5. Gametes unite and undergo a sporogonic cycle resulting in sporozoites.
6. During a blood meal, a *Babesia*-infected tick introduces sporozoites into human host
7. Sporozoites enter RBC (erythrocytes and again undergoes asexual replication (budding).
8. Multiplication of blood-stage parasites is responsible for clinical manifestations of the disease. (Humans are dead-end hosts)
Varying spectrum of symptoms:

- Asymptomatic to severe, life-threatening disease
  - General:
    - Flu-like symptoms:
      - Fever, chills, sweats, headache, body aches, loss of appetite, nausea, or fatigue
    - Hemolytic anemia:
      - Lead to jaundice
      - Dark urine
  - Severe to life-threatening in the following population:
    - Individuals w/o a spleen
    - Immunocompromised due to cancer, lymphoma, HIV/AIDS or other reasons
    - Other serious health conditions (kidney or liver disease)
    - Elderly
BABESIOSIS- ADDITIONAL COMPLICATIONS

• Low/ unstable blood pressure
• Thrombocytopenia
• Disseminated intravascular coagulation (DIC or consumptive coagulopathy)
  • Lead to blood clots and bleeding
• Malfunction of vital organs- kidneys, liver, and lungs
• Death

• Symptoms develop within a week to a few weeks to a few months or longer
BABESIOSIS- DIAGNOSIS

- Identification of trophozoites in peripheral blood.
  - Multiple thick and thin smears
    - Trophozoites appear as small ring forms with multiple rings per RBC
    - Develop into ‘pear-shaped’ cells arranged in pairs or tetrads- ‘Maltese cross’ form
  - Specimens of blood tested by specialized reference laboratories
BABESIOSIS - TREATMENT

• For ill patients, babesiosis usually is treated for at least 7-10 days with a combination of two prescription medications — typically either:
• Atovaquone PLUS Azithromycin;
OR
• Clindamycin PLUS Quinine (this combination is the standard of care for severely ill patients).
The typical daily doses for adults are provided in the table below:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosage (usually treat for at least 7-10 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone</td>
<td>750 mg orally twice a day</td>
</tr>
<tr>
<td>Along with</td>
<td></td>
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<tr>
<td>Azithromycin</td>
<td>On the first day, give a total dose in the range of 500-1000 mg orally; on subsequent days, give a total daily dose in the range of 250-1000 mg</td>
</tr>
</tbody>
</table>

or

<table>
<thead>
<tr>
<th>Clindamycin</th>
<th>600 mg orally 3 times a day or 300-600 mg intravenously 4 times a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>along with</td>
<td></td>
</tr>
<tr>
<td>Quinine</td>
<td>650 mg orally 3 times a day</td>
</tr>
</tbody>
</table>
MALARIA- OVERVIEW

• Genus- Plasmodium
• Approx. 156 species identified; 4 of which are considered true parasites of humans and one zoonotic malaria which has infected humans
• The four true human parasites are: P. falciparum; P. vivax; P. ovale; and P. malariae
• Zoonotic species: P. knowlesi
• Anopheles mosquito are responsible for the transmission of malaria. In the United States (prior to elimination) the three species responsible were: Anopheles quadrimaculatus in the east, Anopheles freeborni in the west, and Anopheles pseudopunctipennis along the U.S./ Mexico border. They are back thus a risk does exist that malaria could be reintroduced.
PLASMODIUM LIFE CYCLE

Mosquito Stages

1. Ruptured oocyst
2. Release of sporozoites

Sporogonic Cycle

3. Oocyst
4. Ookinete
5. Macrogametocyte
6. Microgametocyte entering macrogametocyte
7. Exflagellated microgametocyte

Human Liver Stages

8. Mosquito takes a blood meal (injects sporozoites)
9. Infected liver cell

Exo-erythrocytic Cycle

10. Ruptured schizont
11. Schizont

Human Blood Stages

12. Mosquito takes a blood meal (ingests gametocytes)
13. Immature trophozoite (ring stage)
14. Mature trophozoite

Erythrocytic Cycle

15. Ruptured schizont
16. Schizont
17. Gametocytes
18. Gametocytes

P. falciparum
P. vivax
P. ovale
P. malariae
PLASMODIUM FALCIPARUM

- Deadliest form of Malaria
- Invades RBCs of all ages
- Physiologic changes RBC- “knobby” appearance; RBC’s more likely to clump or clog small blood vessels.
  - Clogs in the brain lead to cerebral malaria
- Multiples rapidly in the blood leading to severe anemia.
- Severity related to immune status:
  - Most severe in children; pregnant women & non-immune population (i.e. travelers, foreign workers)
- Distribution: Tropical and subtropical areas.
- Treatment- Chloroquinine & Quinine & others (Cocktail recommended)
  - Non-immune status- Admit to ICU; aggressively monitor
PLASMODIUM VIVAX

- Most prevalent form of human malaria (80% of cases)
- 300 million cases per year
- Dormant stage in liver:
  - Relapse: months up to 4 years later
  - Dormant form - hypnozoites
- Invade reticulocytes
- Distribution: Asia, Latin American, and in some parts of Africa
- Decrease occurrences of relapse by treating with primaquine after 1st attack
PLASMODIUM OVALE

- Biologically and morphologically similar to P. vivax
- Can infect individuals who are negative for the Duffy blood group (sub-Saharan Africa)
- Lay dormant in the liver for several months to 4 years.
- P. ovale is more prevalent in most of Africa than P. vivax
- Distribution: mainly Africa (especially West Africa) and the islands of the western Pacific.
- Dx: P. vivax v. P. ovale:
  - Thin Giemsa smear (per 500 RBC):
    - P. vivax - 12-24 merozites
    - P. ovale - 6-14 merozites
PLASMODIUM MALARIAE

• Only human malaria parasite that has a quartan cycle
  • 3-day cycle
  • The three other species have a tertian, two-day cycle

• If untreated can lead to a long-lasting chronic infection
  • Some cases lifetime

• Chronically infected patients have serious complications:
  • Nephrotic syndrome

• Distribution: Worldwide
PLASMODIUM KNOWLESI

- Zoonotic malaria
- Natural pathogen of long-tailed and pig-tailed macaques.
- 24-hour replication cycle
  - Rapidly progress from an uncomplicated infection to a severe infection
  - Fatalities have been reported.
SYMPTOMS

• Variable:
  • Sudden/ severe illness
  • Non-specific symptoms- malaise; headache; myalgias; fever; severe anemia

MOVES TO

• Cyclic fevers- duration 6-10 days
  • Severe/ extreme cycles
    • Cold- shivering, feeling cold
    • Hot- fever, headache. Vomiting (best time to draw blood)
    • Sweating stage- sweating; return to normal; exhaustion
  • Cycles vary from daily to every other day to every 3rd day
**P. falciparum**
- RBC: Normal size; Maurer’s dots or clefts rarely seen
- Trophozoites:
  - Ring forms extremely small (1/5 RBC). Double nuclei are common; multiple rings per RBC. Applique forms on RBCs
- Schizonts:
  - Not normally seen. 24 + merozoites are characteristic
- Gametocytes:
  - Crescent/banana-shaped forms. Micro forms stain lighter than macro forms
- Special Features:
  - Ratio of infected RBC to normal is high. Asexual cycle lasts 48 hrs.

**P. malariae**
- RBC: Normal size. No dots or clefts
- Trophozoites:
  - EARLY: similar to vivax; staining is deeper and the cytoplasm of the ring is broader. Double rings are rare
  - MATURE: forms a ribbon or band
- Schizonts:
  - More than 12 merozoites are rarely seen. Arranged in rosettes; pigment is abundant and coarse often in aggregates w/in the center of the rosettes.
- Gametocytes:
  - RBCs not enlarged. Resemble P.vivax; pigment is more abundant and tends to be coarse and unevenly distributed compared to vivax.
- Special Features:
  - Asexual cycle 72 hours

**P. vivax**
- RBC: Enlarged and pale; Schuffner’s dots usually prominent
- Trophozoites:
  - EARLY: ring relatively large (1/3 RBC). Rings with 2 nuclei or cells with 2 or 3 rings may be seen.
  - MATURE: Ameboid, with delicate pseudopodia that flow to fill the entire red blood cell.
- Schizonts:
  - 12-24 merozoites; pigment fine grained and inconspicuous
- Gametocytes:
  - Round to oval and almost completely fill RBC. Large chromatin mass. Pigment is coarse and evenly distributed.
- Special Features:
  - Asexual cycle 48 hours
• *Trypanosoma brucei*:
  • *T. brucei rhodesiense* - East African sleeping sickness
  • *T. brucei gambiense* - West African sleeping sickness
    • Morphologically indistinguishable
    • Geographically separate and cause distinct disease patterns in humans.

• *Trypanosoma cruzi*:
  • American trypanosomiasis, Chagas disease
Symptoms and Pathology

• **First stage:** Chance at site of bite

• **Second stage (hemolymphatic)** - fever, lymphadenopathy, and pruritus

• **Third stage (meningoencephalitic)** - invades the central nervous system, causing headaches, somnolence, abnormal behavior, and lead to loss of consciousness, coma, and death.

• *T. brucei rhodesiense* - symptoms are more acute; emerge within a few weeks and patients deteriorate rapidly.

• *T. brucei gambiense* - Patients maybe infected for years without obvious symptoms

• Can cross the placenta and infect the fetus - abortion or perinatal death
TRANSMISSION, DISTRIBUTION, DIAGNOSIS, AND TREATMENT

• Transmission - Tsetse fly

• Distribution -
  • *T. brucei gambiense* - found in large areas of western and central Africa
  • *T. brucei rhodesiense* - found in isolated areas of eastern and southeastern Africa (10% of cases)

• Diagnosis -
  • Microscopic observation in chancre fluid, lymph node aspirates, blood, bone marrow, or in the late stages of infection cerebral spinal fluid

• Treatment -
  • Started immediately; based on patient’s symptoms and laboratory results. The drug regimen depends on the infecting species and the stage of infection.
TRYPANOSOMA LIFE CYCLE

Tsetse fly Stages
1. Tsetse fly takes a blood meal (injects metacyclic trypomastigotes)
2. Injected metacyclic trypomastigotes transform into bloodstream trypomastigotes, which are carried to other sites.

Human Stages
3. Trypomastigotes multiply by binary fission in various body fluids, e.g., blood, lymph, and spinal fluid.
4. Trypomastigotes in blood
5. Tsetse fly takes a blood meal (bloodstream trypomastigotes are ingested)
7. Procyclic trypomastigotes leave the midgut and transform into epimastigotes.
8. Epimastigotes multiply in salivary gland. They transform into metacyclic trypomastigotes.

Icons:
= Infective Stage
= Diagnostic Stage

http://www.dpd.cdc.gov/dpdx
• **Disease**- American trypanosomiasis, Chagas disease

• **Symptoms & Pathology**-
  - **First stage** - a local lesion can appear at the site of the bite
  - **Acute phase** - usually asymptomatic, but can have fever, anorexia, lymphadenopathy, mild hepatosplenomegaly, and myocarditis. Resolve within 2 to 3 months into an asymptomatic chronic stage
  - **Chronic Phase (Chagas Disease)** - May occur years or decades after initial infection. Its manifestations include cardiomyopathy (the most serious); pathologies of the digestive tract - megaesophagus and megacolon; and weight loss. Chronic Chagas disease and its complications can be fatal.

• **Transmission** - contamination of skin lesions with feces of the reduviid (triatomid, kissing) bug. Can also be transmitted through blood transfusions, transplacentally and in laboratory accidents.

• **Distribution** - Central and South America (Mainly Brazil)
  - Has been found in wild and domestic animals in the southern U.S. (Texas, California); however infections among U.S. residents are very rare.

• **Diagnosis** - Microscopic examination of fresh anticoagulated blood, or its buffy coat, for motile parasites and examination of thin and thick Giemsa stains, or inoculation, or xenodiagnoses.

• **Treatment** - Effective if started during the acute phase of the disease. For chronic Chagas disease, treatment involves only managing the symptoms.
Trypanosomiasis, American (Chagas disease)  
(Trypanosoma cruzi)

**Triatomine Bug Stages**
1. Metacyclic trypomastigotes in hindgut
2. Multiply in midgut
3. Epimastigotes in midgut
4. Triatomine bug takes a blood meal (trypomastigotes ingested)
5. = Infective Stage
6. = Diagnostic Stage

**Human Stages**
1. Metacyclic trypomastigotes penetrate various cells at bite wound site. Inside cells they transform into amastigotes.
2. Amastigotes multiply by binary fission in cells of infected tissues.
3. Trypomastigotes can infect other cells and transform into intracellular amastigotes in new infection sites. Clinical manifestations can result from this infective cycle.
4. Intracellular amastigotes transform into trypomastigotes, then burst out of the cell and enter the bloodstream.

**Common Names**
- triatomine bugs
- reduviid bugs
- assassin bugs
- kissing bugs
- Cone-nosed bugs

**Genera**
- Triatoma
- Rhodnius
- Panstrongyulus
SCHISTOSOMA SPECIES - THE BLOOD FLUKES

• Schistosoma Species:
  • *S. mansoni* - Manson’s blood fluke
  • *S. japonicum* - blood fluke
  • *S. haematobium* - bladder fluke

• What sets them apart from other flukes?
  • Separate male and female adults
    • Live together as a pair
  • Do not invade host tissue; instead they live within the abdominal blood vessels
  • Have only one intermediate host - the snail.
    • Cercariae that are released from the snail directly penetrate human skin - no other host is needed.
SYMPTOMS & PATHOLOGY

• Many infections are asymptomatic

• Acute schistosomiasis may occur weeks after the initial infection
  • Especially S. mansoni and S. japonicum

• Symptoms:
  • Fever, cough, abdominal pain, diarrhea, hepatosplenomegaly, and eosinophilia.
  • Occasionally central nervous system lesions occur
  • Continuing infection: granulomatous reactions and fibrosis in the affected organs, may result in-
    • Colonic polyposis with bloody diarrhea (S. mansoni mostly); portal hypertension with hematemesis and splenomegaly (S. mansoni, S. japonicum); cystitis and ureteritis (S. haematobium) with hematuria can progress to bladder cancer; pulmonary hypertension (S. mansoni, S. japonicum, and rarely S. haematobium); glomerulonephritis; and central nervous system lesions.
TRANSMISSION; DISTRIBUTION; DIAGNOSIS; AND TREATMENT

• Transmission-
  • Contact with water contaminated with human feces or urine

• Distribution-
  • *S. mansoni* - parts of South America and the Caribbean, Africa, and the Middle East
  • *S. haematobium* - Africa and the Middle East
  • *S. japonicum* - Far East

  *Schistosomiasis ranks second behind malaria as a cause of serious worldwide morbidity and mortality, and it is spreading and increasing because of recent new water-control projects that have provided increased snail breeding areas.*

• Diagnosis-
  • *S. mansoni* and *S. japonicum* - observation of eggs in feces or in rectal biopsies
  • *S. haematobium* - observation of eggs in urine

• Treatment-
  • Praziquantel
DIAGNOSIS: THE EGGS

Schistosoma japonicum
Schistosoma mekongi
Schistosoma haematobium
Schistosoma intercalatum
Schistosoma mansoni
LIFE CYCLE

1. Infective Stage
2. Diagnostic Stage

Sporocysts in snail
(succesive generations)

3. Miracidia penetrate snail tissue

4. Eggs hatch releasing miracidia

5. Cercariae released by snail into water and free-swimming

6. Cercariae penetrate skin

7. Cercariae lose tails during penetration and become schistosomulae

8. Circulation

9. Migrate to portal blood in liver and mature into adults

10. Paired adult worms migrate to:

   A. mesenteric venules of bowel/rectum (laying eggs that circulate to the liver and shed in stools)

   B. venous plexus of bladder

   C. S. mansoni

   D. S. japonicum

   E. S. haematobium
THE MONSTERS
QUESTIONS??