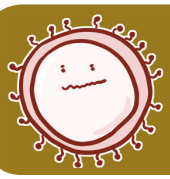

NOTES
HEMATOLOGIC INFECTIONS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

Taxonomy
- *Apicomplexan* phylum protozoa → infectious hematological diseases

Replication/multiplication
- Arthropod transmission

Transmission
- Multiple life cycle stages (host-, vector-dependent)

SIGNS & SYMPTOMS
- See individual infections

DIAGNOSIS

LAB RESULTS
- *Blood smear:* best intra-erythrocyte location diagnosis

TREATMENT
- See individual infections

THIN BLOOD SMEAR FINDINGS OVERVIEW

OBSERVATION	BABESIA	PLASMODIUM
RING APPEARANCE	Pleomorphic common	Monomorphic common
MORPHOLOGY	Ring forms only	Ring forms, schizonts, gametocytes
TETRADS	Present	Absent
ERYTHROCYTE MORPHOLOGY	Normal	Can be normal, unchanged, small, enlarged, fimbriated
ERYTHROCYTE STIPPLING	Absent	Present
EXTRACELLULAR PARASITES	Common	Uncommon

BABESIA

osms.it/babesia

PATHOLOGY & CAUSES

- Malaria-like parasitic infection
  - Ixodes tick transmission
- Phylum *Apicomplexa* (same as *Plasmodium*, *Toxoplasmosis*)
- Common species
  - *Babesia microti* most predominant (northeast, upper midwest United States)
  - *B. duncani* (Western United States)
  - *B. divergens* (Europe)

CAUSES

- *Ixodes scapularis tick:* only recognized vector
  - Same tick transmits *Borrelia burgdorferi* (→ Lyme disease; concurrently infects ⅔ babesiosis-infected individuals) and *Anaplasma phagocytophilum* (→ human granulocytic anaplasmosis; concurrently infects ⅓ babesiosis-infected individuals)
  - Contaminated blood transfusion → rare human-to-human transmission
- Life cycle
  - *Two hosts:* white-footed mouse, Ixodes tick (definitive)
  - Blood meal → *Babesia*-infected tick sporozoites into mouse host → sporozoites directly invade mature mouse erythrocytes → sporogony (asexual reproduction; budding) → in blood, some parasites differentiate into male, female gametes → gametes unite → sporogonic cycle → sporozoites → tick bites human → 1–4 week incubation → sporozoites enter erythrocytes → sporogony
- Sporogony
  - Asynchronous with host → no massive hemolysis (versus malaria)
- Tick's nymph stage is most infectious

RISK FACTORS

- Endemic area resident
- Endemic area travel, especially May–September
- Blood transfusion (last six months)
- Age > 50
- Biologically male
- Asplenia
- Decreased immunity (malignancy, HIV/AIDS infection, immunosuppressive drugs)
- Coinfection with *Borrelia* and/or *Anaplasma*
- Premature birth

COMPLICATIONS

- ↑ occurence in anemic/parasitemic individuals
  - Congestive heart failure
  - Noncardiac pulmonary edema
  - Acute respiratory distress syndrome
  - Splenic infarct
  - Splenic rupture
  - Septic shock
  - Myocardial infarction
  - Disseminated intravascular coagulation
  - Death

SIGNS & SYMPTOMS

- Mostly asymptomatic, may persist undiagnosed months/years
- Blood-stage parasite multiplication → clinical manifestation
- Non-specific flu-like symptoms (misdiagnosis common)
  - Fatigue (gradual onset)
  - Fever, chills, sweats
  - Headache, myalgia, arthralgia
  - Anorexia, nausea
  - Cough

- Severe manifestations include malaria-like illness (fever, fatigue, malaise) + hemolytic anemia manifestation
- *B. microti* case-fatality rate is 5%
- *B. divergens* infections case-fatality rate is 42%
  - Disseminated intravascular coagulation, bleeding diathesis
  - Acute renal failure
  - Cardiopulmonary complications (e.g. hypotension, poor perfusion, pulmonary edema)

DIAGNOSIS

LAB RESULTS

Blood smear

- Wright/Giemsa staining
  - *Thin:* rapid, ↓ microscopy experience required
  - *Thick:* ↑ accurate, ↑ microscopy experience required
  - Pathognomic tetrad "Maltese cross" visible in erythrocyte

Laboratory

- Thrombocytopenia
- Reticulocytosis
- ↓ Hematocrit
- ↓ Hemoglobin
- ↑ Lactate dehydrogenase
- ↓ Haptoglobin
- ↑ Liver function tests
- ↑ Creatinine

Polymerase chain reaction (PCR)

- Speciation (useful for low-level parasitemia)

Serology

- Immunofluorescent antibody testing; species specific

TREATMENT

- *Asymptomatic:* no treatment

MEDICATIONS

- *Symptomatic disease:* azithromycin + atovaquone

OTHER INTERVENTIONS

- Severe disease (parasitemia > 4%)
  - Antimicrobial + exchange transfusion

Prevention

- *Personal:* avoid endemic areas; long pants, shirts minimize exposed skin
- Tick repellant on skin (e.g. DEET)
- Post-exposure tick checks
- No antibiotic prophylaxis

PLASMODIUM SPECIES (MALARIA)

osms.it/malaria

PATHOLOGY & CAUSES

- Anopheles mosquito vector → parasitic hematologic infection
- Four major malarial parasite species
  - *Plasmodium falciparum:* most lethal, most drug-resistant (sub-Saharan Africa)
  - *P. vivax:* widest geographic distribution, relapsing species
  - *P. ovale:* relapsing species (western areas of sub-Saharan Africa)
  - *P. malariae:* AKA 'benign' malaria (mild course)
- *P. knowlesi:* normally infects macaques, recent cause of human malaria cases

CAUSES

- Exoerythrocytic (sporogonic; blood) life cycle stage
  - Blood-stage gametocytes in other host (e.g. human) → female *Anopheles* mosquito blood meal → mosquito multiplication, growth cycle → 10–18 day incubation → sporozoites in mosquito salivary gland → human bite → sporozoite inoculation → hematogenous translocation to liver → rapid hepatic parenchymal cell invasion → parasites undergo exoerythrocytic schizogony (asexual multiplication) → development, multiplication → 7–14 day incubation → merozoite development → invade erythrocytes → symptomatic stage develops → *P. ovale*, *P. vivax* can differentiate into quiescent stage → hypnozoite → can re-enter into schizogony → reemerge to invade erythrocytes
  - Blood stage → malaria symptoms
  - Mosquito vector does not have parasite presence
- Erythrocytic life cycle stage
  - In erythrocytes → parasites can undergo asexual schizogony/ sexual differentiation (necessary for transmission) → gametocytes
- Asexual schizogony
  - Trophozoites (parasite name once inside erythrocyte) digest host cell hemoglobin (amino acids, energy source) → schizont → undergoes mitosis → differentiates into merozoites → erythrocyte rupture → merozoite bloodstream release → fever, malarial symptoms

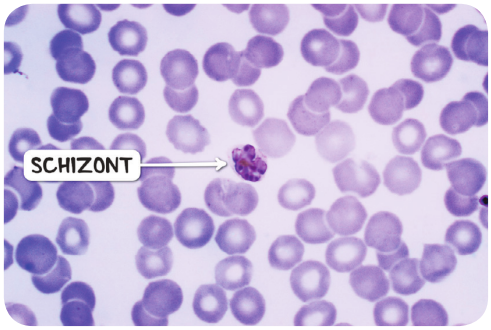

Figure 77.1 A peripheral blood film taken from an individual with *Plasmodium malariae* infection. There is a mature schizont, composed of 6-12 merozoites, contained within a red blood cell.

- *P. malariae*
  - Low-level persistence possible for decades without diagnosis, treatment
- *P. vivax*
  - Prefers erythrocytes with Duffy blood group antigen (rare in persons from West and Central Africa); prefers reticulocytes but will also invade mature erythrocytes
- Others preferentially invade mature erythrocytes

- *P. falciparum*
  - Develop 'knobs' on infected erythrocytes in late trophozoite stage → parasitized erythrocytes adhere to capillary endothelium → various organ sequestration (notably brain) → cerebral malaria
- Most malaria deaths
  - Children < five years old in high-transmission areas

CYCLIC FEVER PATTERNS OF PLASMODIUM SPECIES

PLASMODIUM SPECIES	CYCLIC FEVER PATTERNS
P. VIVAX	48 hours
P. OVALE	48 hours
P. MALARIAE	72 hours
P. FALCIPARUM	Irregular
P. KNOWLESI	24 hours

RISK FACTORS

- Poor rural populations in endemic areas
- Proximity to standing water
  - Larvae breeding site (e.g. agriculture, irrigation ditches)
- Travel in endemic areas
- Blood transfusion (last six months)
- Lack of insect repellant, chemoprophylaxis, personal protective measures (long pants, shirts, mosquito nets)
- Duffy blood group antigen-positive individuals

Protective factors

- *P. falciparum protection:* sickle cell trait (heterozygotes)
- *P. vivax:* Duffy blood group antigen-negative individuals

COMPLICATIONS

- Coma
- Seizure
- Severe anemia
- Acute renal failure
  - Acute tubular necrosis secondary to hypoperfusion, hypovolemia
- Acute respiratory distress syndrome
- Shock
- Septicemia

SIGNS & SYMPTOMS

- Febrile paroxysm (hallmark feature)
  - 10–12 hours of intense rigors, chills → high fever, profuse diaphoresis
  - Febrile seizure potential
- Non-specific complaints
  - Headache, malaise, myalgia, arthralgia
- Abdominal pain, diarrhea, vomiting
- Possibly remarkably asymptomatic between episodes
- *P. falciparum* cerebral effects
  - Significant morbidity, mortality (delirium, confusion, seizures → declining mental status → coma → death)
- Parasitemia, cytokine disturbance → hypotension, metabolic acidosis, hypoglycemia
- Anemia (high parasitemia → more pronounced)
- Sequestration, red blood cell destruction by spleen → hypersplenism

DIAGNOSIS

LAB RESULTS

Giemsa stain blood smear

- *Thin:* rapid, ↓ microscopy experience required
- *Thick:* ↑ accurate, ↑ microscopy experience required
- *P. falciparum:* red blood cells contain multiple parasites, ring forms, lack of schizonts
- Banana-shaped gametocyte form

Rapid diagnostic test

- 15–20 minute results
- *Histidine-rich protein 2:* detects *P. falciparum*

PCR

- Supportive laboratory results (nondiagnostic)
  - Normocytic hemolytic anemia
  - Thrombocytopenia

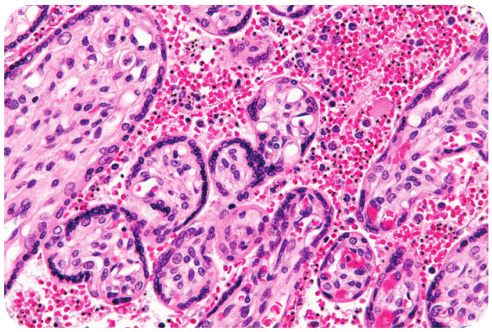

Figure 77.2 A histological section of the placenta from an individual infected with malaria. The numerous black dots within the red blood cells are malaria organisms.

TREATMENT

MEDICATIONS

- Severe malaria
  - Quinidine + doxycycline/tetracycline/clindamycin/artesunate (test for G6PD deficiency)
- Uncomplicated malaria
  - *Chloroquine-sensitive strain:* chloroquine phosphate/hydroxychloroquine (blocks Plasmodium heme polymerase)
  - *Chloroquine-resistant strain:* atovaquone-proguanil, mefloquine, artesunate, quinine-based regimens
- *P. ovale, P. vivax:* + primaquine for hypnozoite (test for G6PD deficiency)

OTHER INTERVENTIONS

Prevention

- Chemoprophylaxis
- Avoid outdoors (dusk/dawn)
- Reduce exposed skin (long pants, shirts)
- Bed netting/mosquito nets
- Insect repellent (DEET 30–50%)