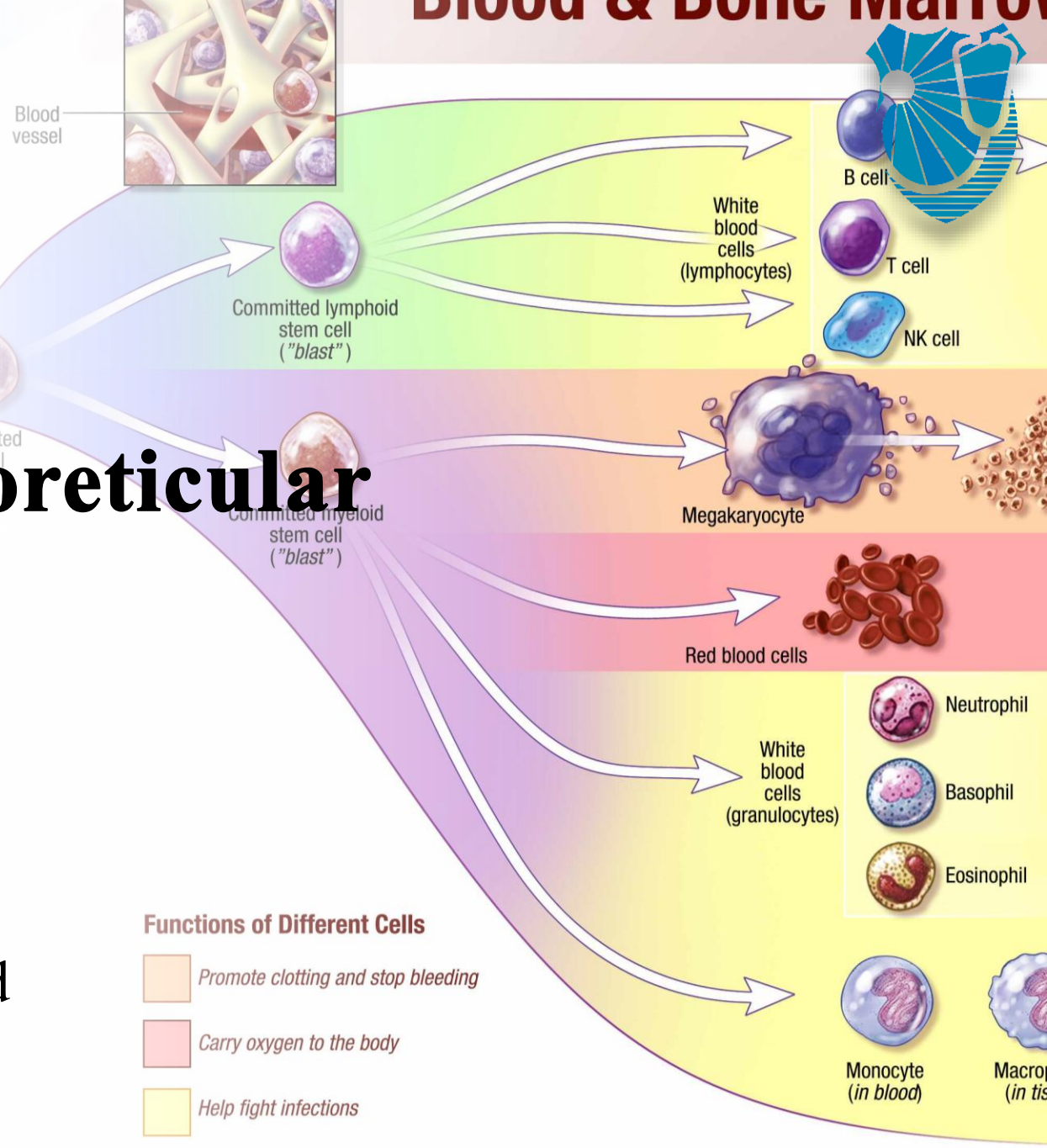
Overview of the Hematopoietic & Lymphoreticular Infections

University of Jordan

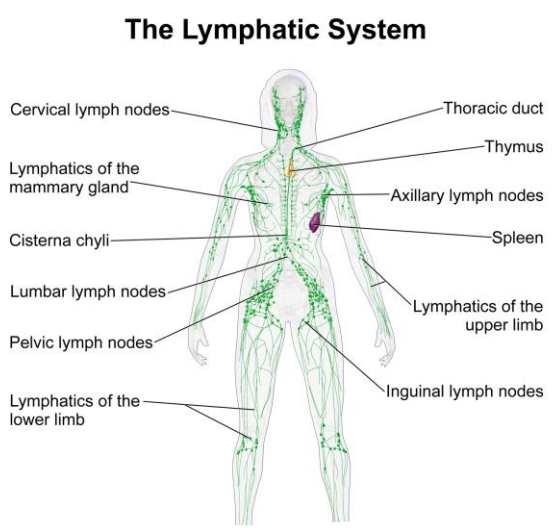
Malik Sallam, M.D., Ph.D.

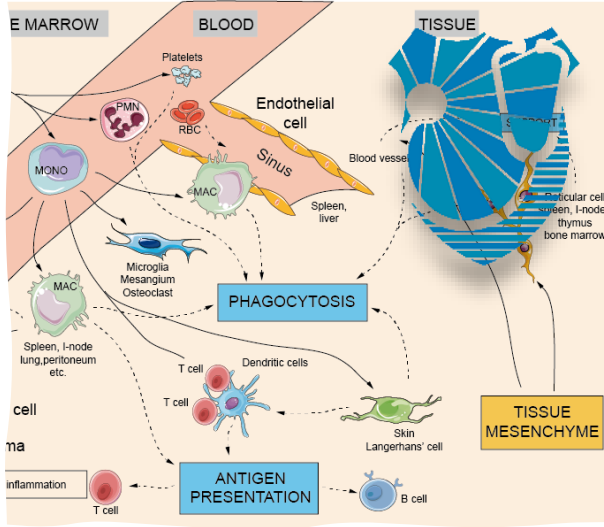
School of Medicine

Department of Pathology, Microbiology and Forensic Medicine

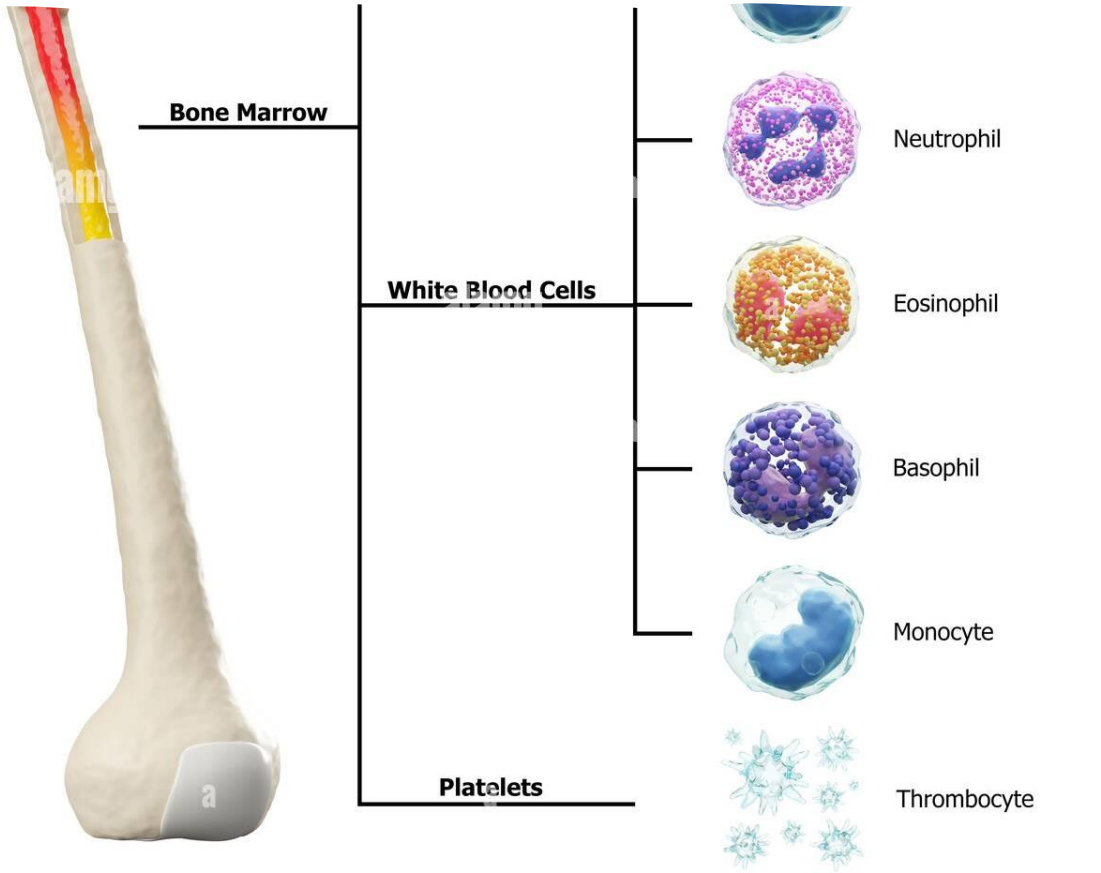


Cells, tissues, and organs of the HLRS





- Hematopoietic system: Bone marrow, Thymus, Other organs (spleen, lymph nodes, liver in fetus) support blood/immune cell production.
- Lymphoid system: Lymph nodes, Spleen, MALT
- Mononuclear phagocyte system (reticuloendothelial system; RES)







Clinical presentation of HLRS infections

The HLRS shares similar components. So, HLRS infections often present with similar signs/symptoms:

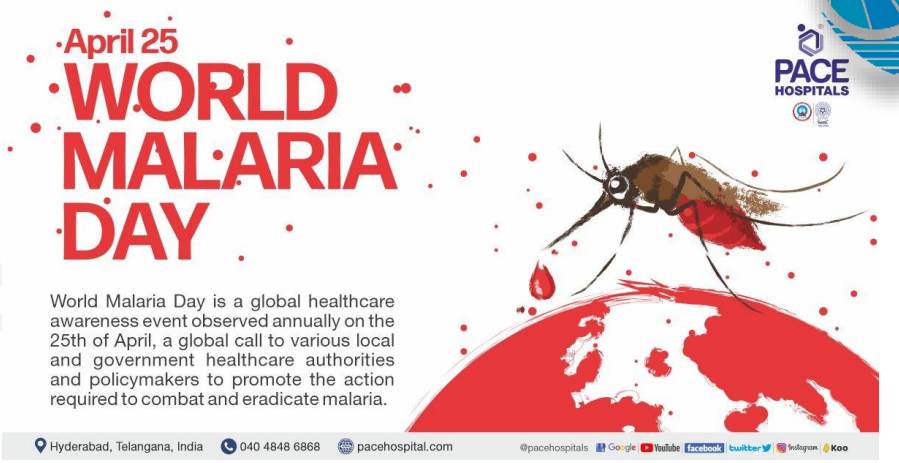
- Splenomegaly
- Hepatomegaly
- Fever (recurring or constant)
- Malaise
- Anorexia
- Lymphadenopathy (regional or generalized)

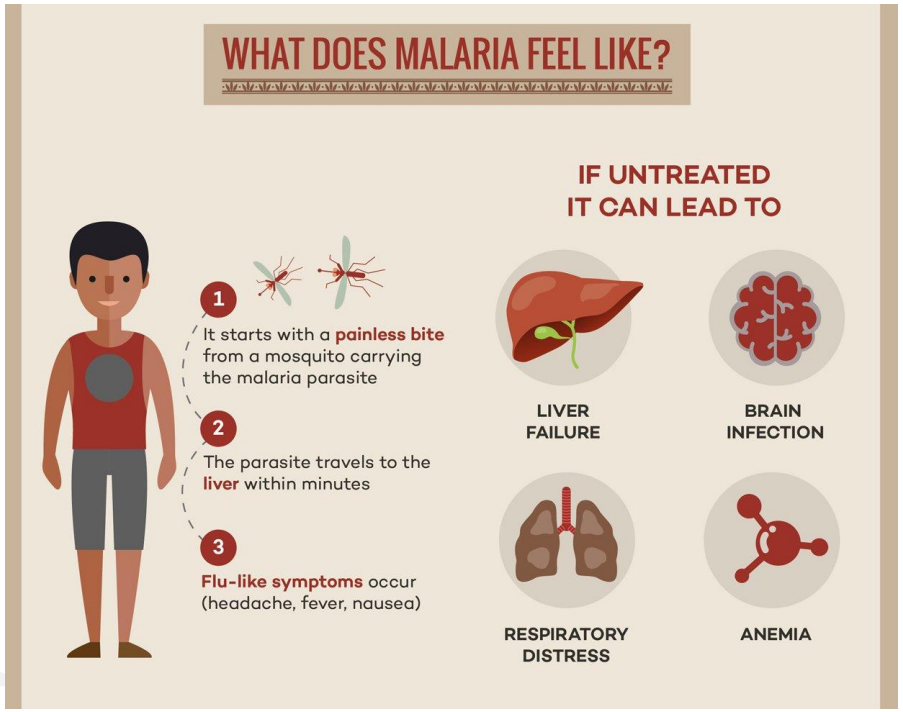
Overview of the HLRS infections by etiology and types of cells infected

Cells	Disease	Infectious etiology
Erythrocytes	Malaria Babesiosis	*Plasmodium* *Babesia*
Lymphocytes	HIV infection/AIDS Infectious mononucleosis-like Adult T-cell leukemia/lymphoma Primary effusion lymphoma Typhoid fever	HIV-1, HIV-2 EBV, CMV, others HTLV-1 HHV-8 *Salmonella typhi*
Phagocytes	Brucellosis Tularemia Q fever Cat scratch disease	*Brucella* *Francisella* *Coxiella* *Bartonella*

Malaria – Overview

- Malaria is one of the big three infectious diseases along with HIV infection/AIDS and tuberculosis.
- Malaria is caused by *Plasmodium* parasites, primarily transmitted to humans through the bites of infected Anopheles mosquitoes.
- Of the five Plasmodium species capable of infecting humans (*P. falciparum, P. malariae, P. ovale, P. vivax, and P. knowlesi*), *P. falciparum* is responsible for the majority of severe malaria cases and fatalities.





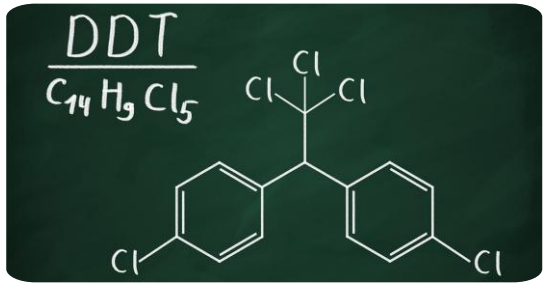
Malaria – Epidemiology

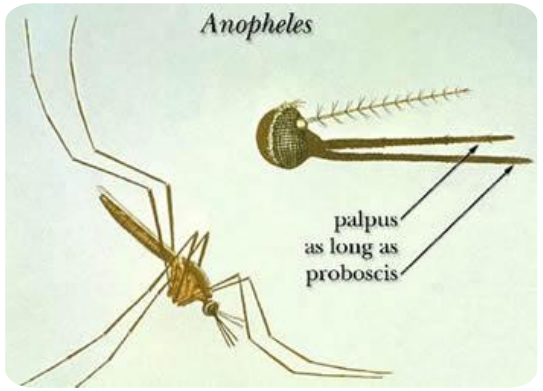
Transmission & Vector:

- Malaria is transmitted by Anopheles mosquitoes.
- Vector control methods like DDT spraying and insecticide-treated nets have reduced transmission, but mosquito resistance to insecticides is a growing problem.

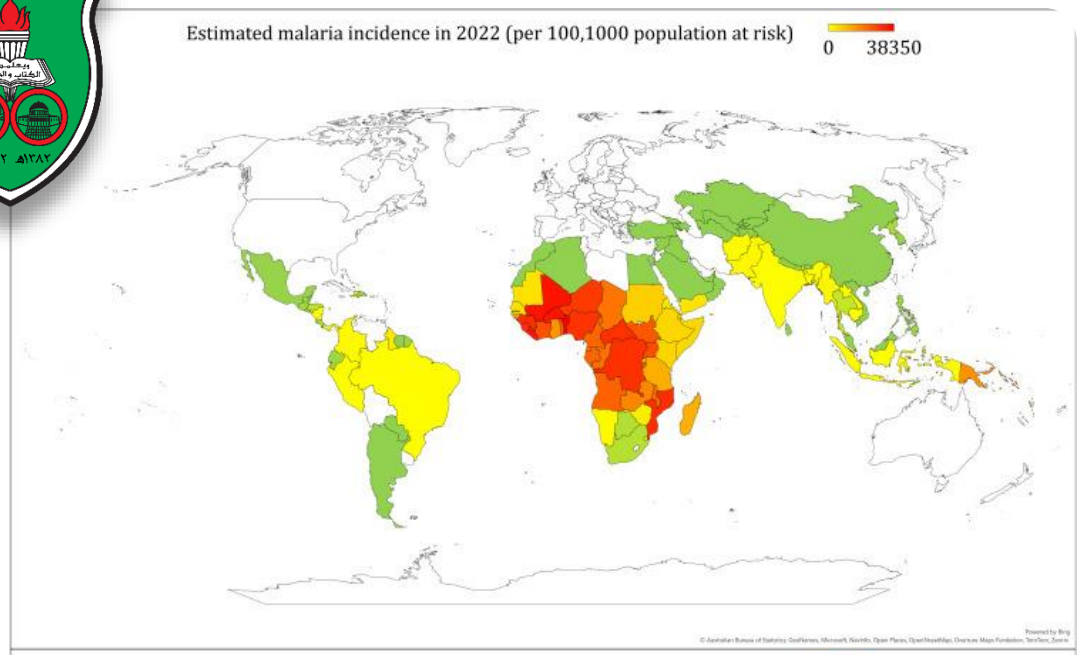


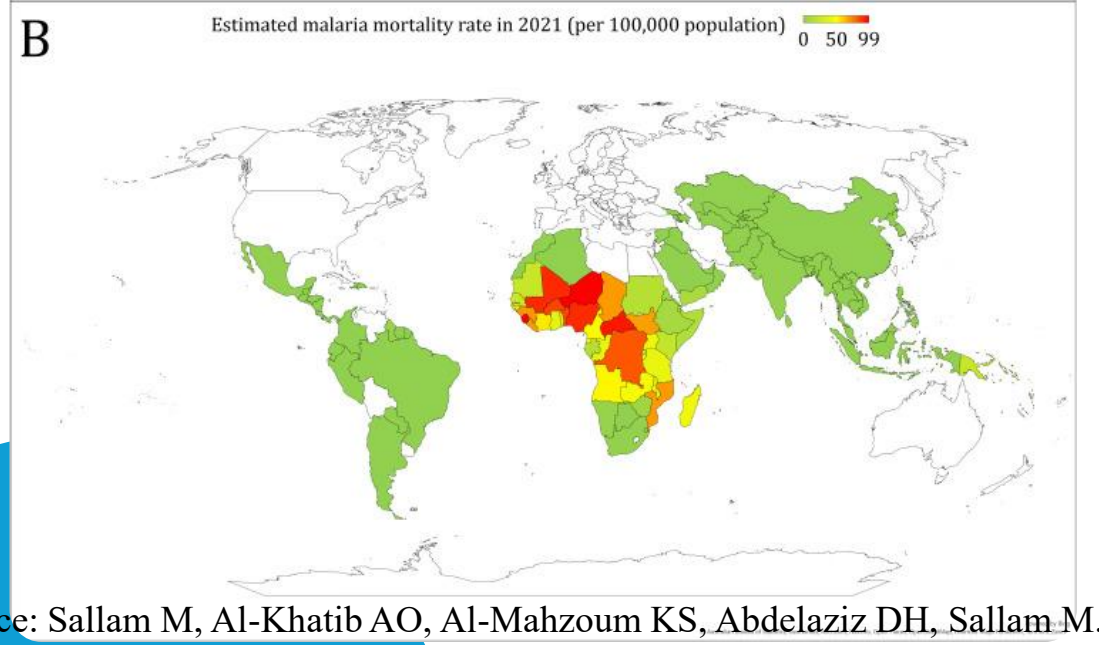






Malaria – Epidemiology

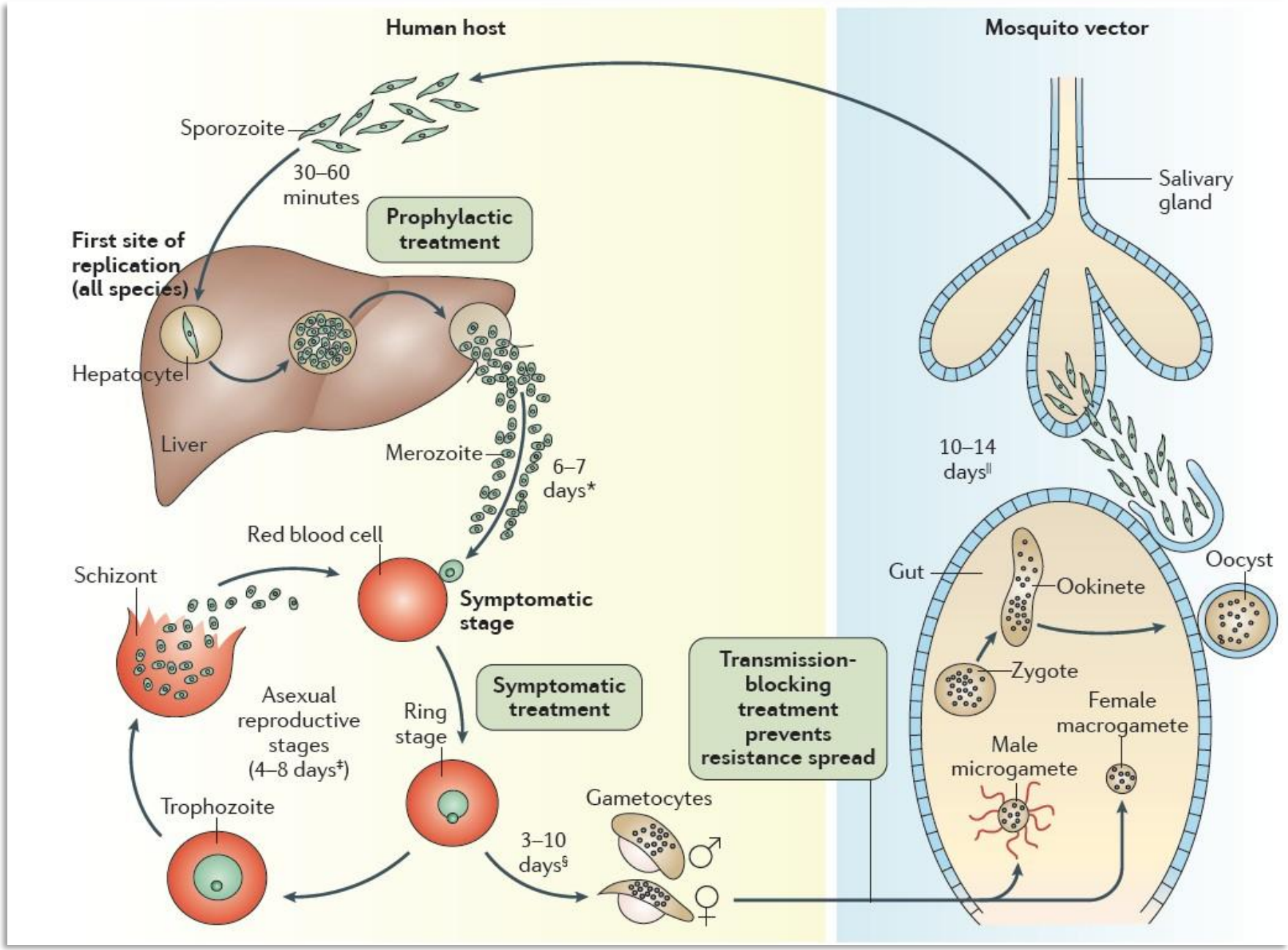




- *Plasmodium falciparum* causes most severe cases and deaths, especially in sub-Saharan Africa.
- *P. vivax* dominates in Southeast Asia, Ethiopia, and South America and can remain dormant in the liver as hypnozoites.
- *P. ovale* (West Africa, Asia), *P. malariae* (worldwide, mild infections), and zoonotic P. *knowlesi* (from primates, can cause severe disease).

Source: Sallam M, Al-Khatib AO, Al-Mahzoum KS, Abdelaziz DH, Sallam M. Current Developments in Malaria Vaccination: A Concise Review on Implementation, Challenges, and Future Directions. Clin Pharmacol. 2025 Apr 1;17:29-47.

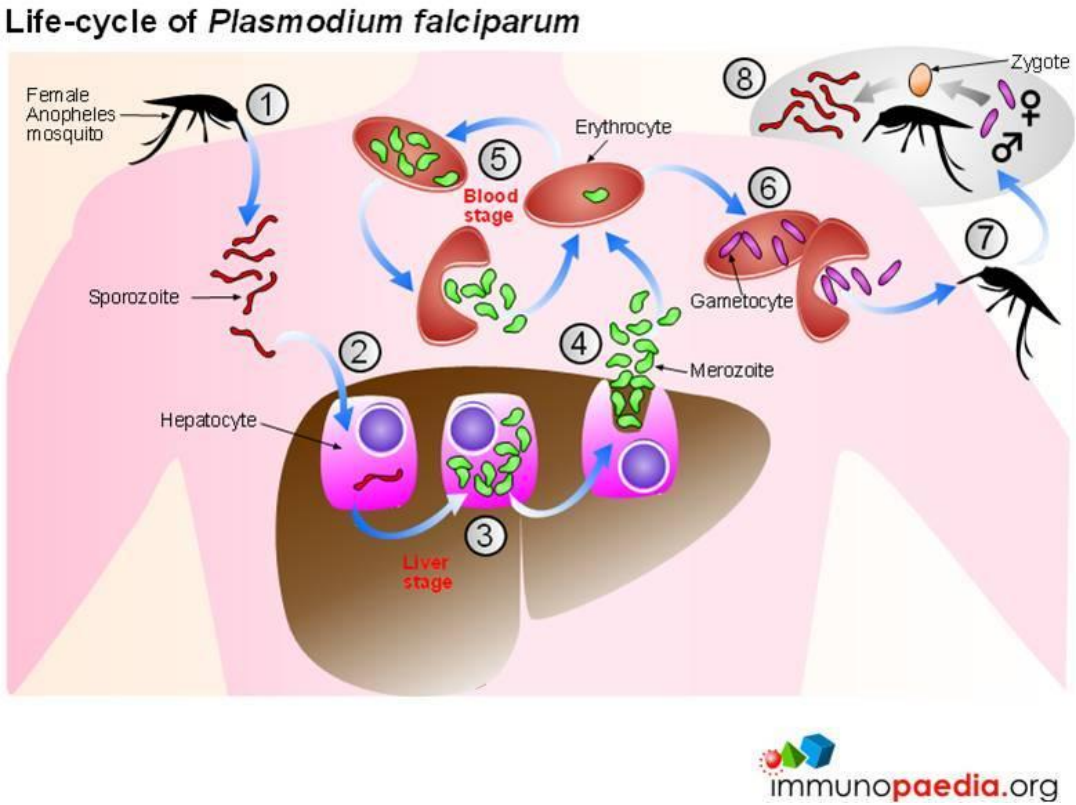
Plasmodium – Life cycle



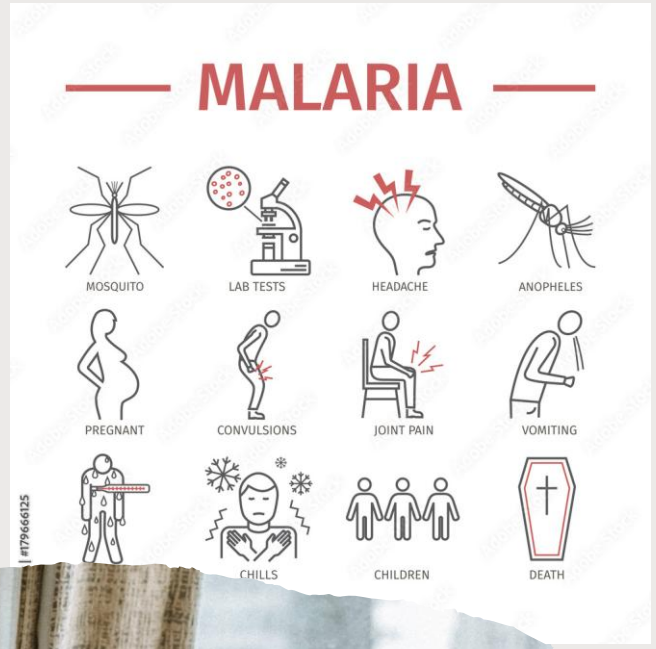
Source: Phillips MA, Burrows JN, Manyando C, van Huijsduijnen RH, Van Voorhis WC, Wells TNC. Malaria. Nat Rev Dis Primers. 2017 Aug 3;3:17050. doi: 10.1038/nrdp.2017.50. PMID: 28770814.

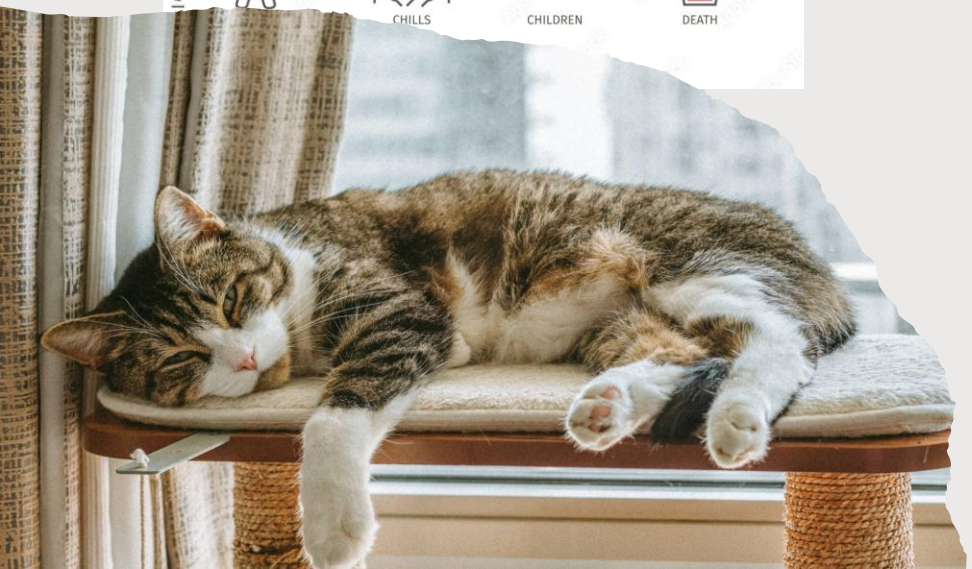
Malaria – Pathophysiology

- Transmission: Female Anopheles mosquito injects **sporozoites** during blood meal. **Sporozoites** travel to liver within 60 minutes
- **Liver stage:** Sporozoites invade hepatocytes, multiply and release **merozoites** into bloodstream
- **Blood stage: Merozoites** infect RBCs, feed on hemoglobin and develop into **trophozoites** that evolve into **schizonts** that cause RBC lysis
- Some form **gametocytes** that infect the next mosquito



Malaria – Pathophysiology





- Hemolysis & inflammation: Free heme leads to endothelial activation which result in fever and systemic symptoms
- TNF-α and IFN-γ cause immune cell activation, suppressed hematopoiesis, anemia
- Organ effects: **Splenomegaly, hepatomegaly**
- Hypnozoites: Dormant liver stage in *P. vivax* and *P. ovale* which can result in relapses months to years later
- Severe malaria: High parasitemia (≥5%) resulting in **cerebral malaria** and multi-organ damage
- Intracellular digestion of hemoglobin by parasites forms hemozoin and makes the membrane less deformable, which results in hemolysis or splenic clearance

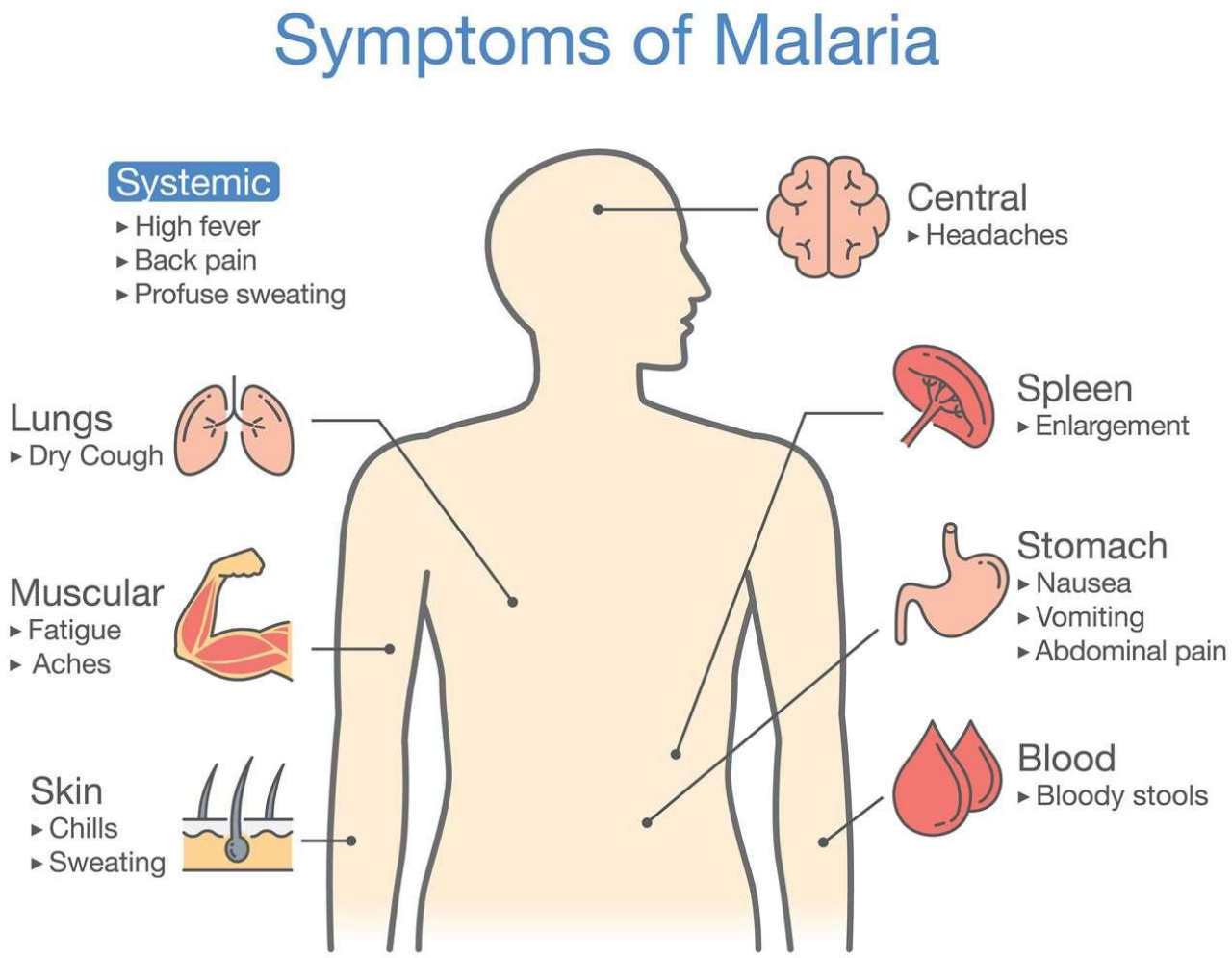
Malaria – Clinical Manifestations

Early: Fever, headache, lethargy, vomiting, abdominal pain malaise, GI symptoms, muscle aches

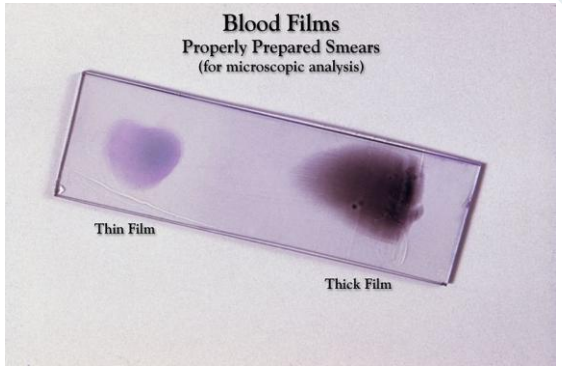
Severe: Jaundice, confusion, seizures, dark urine

Common signs: Hepatomegaly, splenomegaly, severe anemia

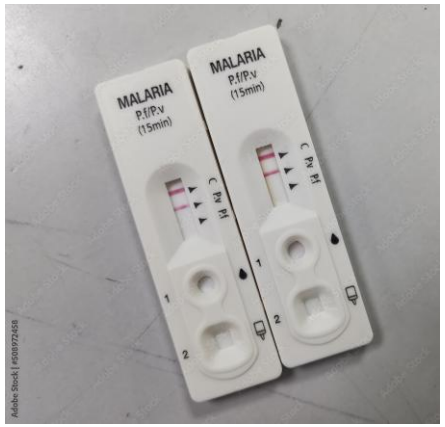
Pregnancy risks: Maternal anemia, miscarriage, stillbirth, low birth weight



Malaria – Diagnosis



- Initial evaluation: CBC, metabolic panel, coagulation panel, blood culture, urinalysis
- Key lab findings
  - Thrombocytopenia: 60–70% of cases
  - Anemia: more severe in *P. falciparum*
  - Liver & kidney involvement: elevated bilirubin, electrolyte imbalance, proteinuria
- The gold standard lab diagnosis is through thick & thin blood smears to identify parasite species & parasitemia
- Other tests: Rapid Diagnostic Tests (RDTs) to antigens; PCR: detects low-level parasitemia, good for speciation



Malaria – Management

- Schizonticidal drugs and supportive care.
- Admission for high-risk patients to monitor dosing and parasitemia trends.
- ICU care for cerebral malaria, respiratory distress, or shock.
- **Medications:**
  - Chloroquine / Hydroxychloroquine: Targets RBC stage, raises parasite pH
  - Primaquine: Clears liver hypnozoites (*P. vivax*, *P. ovale*). Contraindicated in pregnancy & G6PD deficiency
  - Artemisinin-based therapy: Active against all stages.
  - Atovaquone-Proguanil: Blocks parasite mitochondria, works in blood & liver stages



Malaria – Prevention



- Insecticide-treated bed nets and indoor spraying; Prompt diagnosis and treatment with effective anti-malarials; Surveillance for drug resistance and mosquito behavior changes; Community engagement and education.
- Malaria Vaccines: RTS,S/AS01 (Mosquirix):First malaria vaccine approved (2021).~47% efficacy at 12 months, wanes to 34% at 30 months without booster. Oxford R21/Matrix-M: Higher antigen-to-adjuvant ratio, promising improved immunity.

Babesiosis – Overview

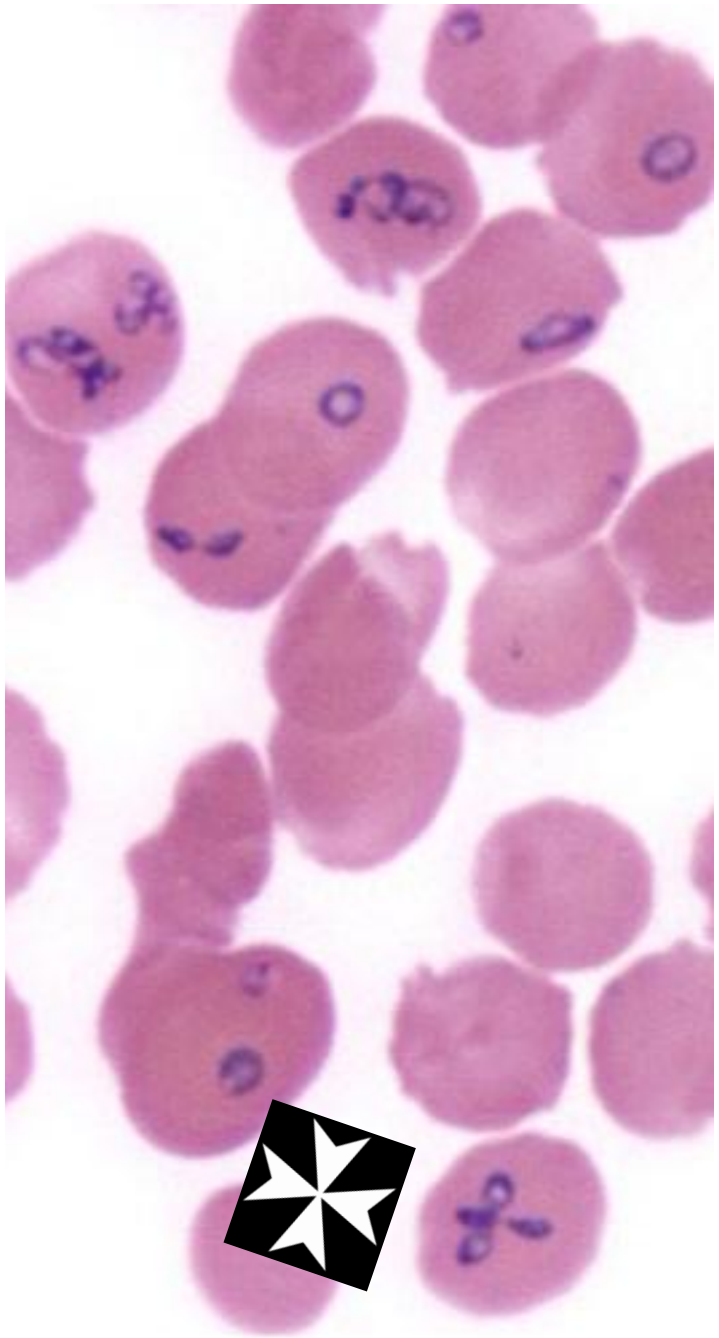




- Tick-borne parasitic infection caused by *Babesia* species that infects RBCs.
- Transmission: *Ixodes* tick. Other routes: blood transfusion, transplacental transmission. Reservoirs: white-footed mouse, birds (primary); deer sustain tick population. Humans are accidental/dead-end hosts.
- Epidemiology: Seasonal: late spring to early fall.
- Risk groups: Immunocompromised, elderly, HIV/AIDS, neonates.
- Pathophysiology: Tick must feed 36-72 hours to transmit sporozoites. Sporozoites infect RBC and multiply to become merozoites that rupture RBC and infect others. Spleen clears infected RBCs.

Babesiosis

- Clinical features: Asymptomatic in up to 50%. Mild illness: fever, chills, sweats, fatigue, malaise, headache, hepatosplenomegaly. Severe disease: multi-organ failure, ARDS, renal failure, DIC, splenic rupture.
- Diagnosis: Peripheral blood smear showing ring forms that may mimic *Plasmodium*.
- Maltese cross (tetrads) is a classic finding. PCR: more sensitive, confirms diagnosis. Labs: anemia, high LDH, thrombocytopenia, high BUN/creatinine, high LFTs.
- Treatment: atovaquone, azithromycin, clindamycin, RBC exchange transfusion if parasitemia ≥10% or organ dysfunction.



Thanks for listening!