Malaria and Babesiosis

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Outlines

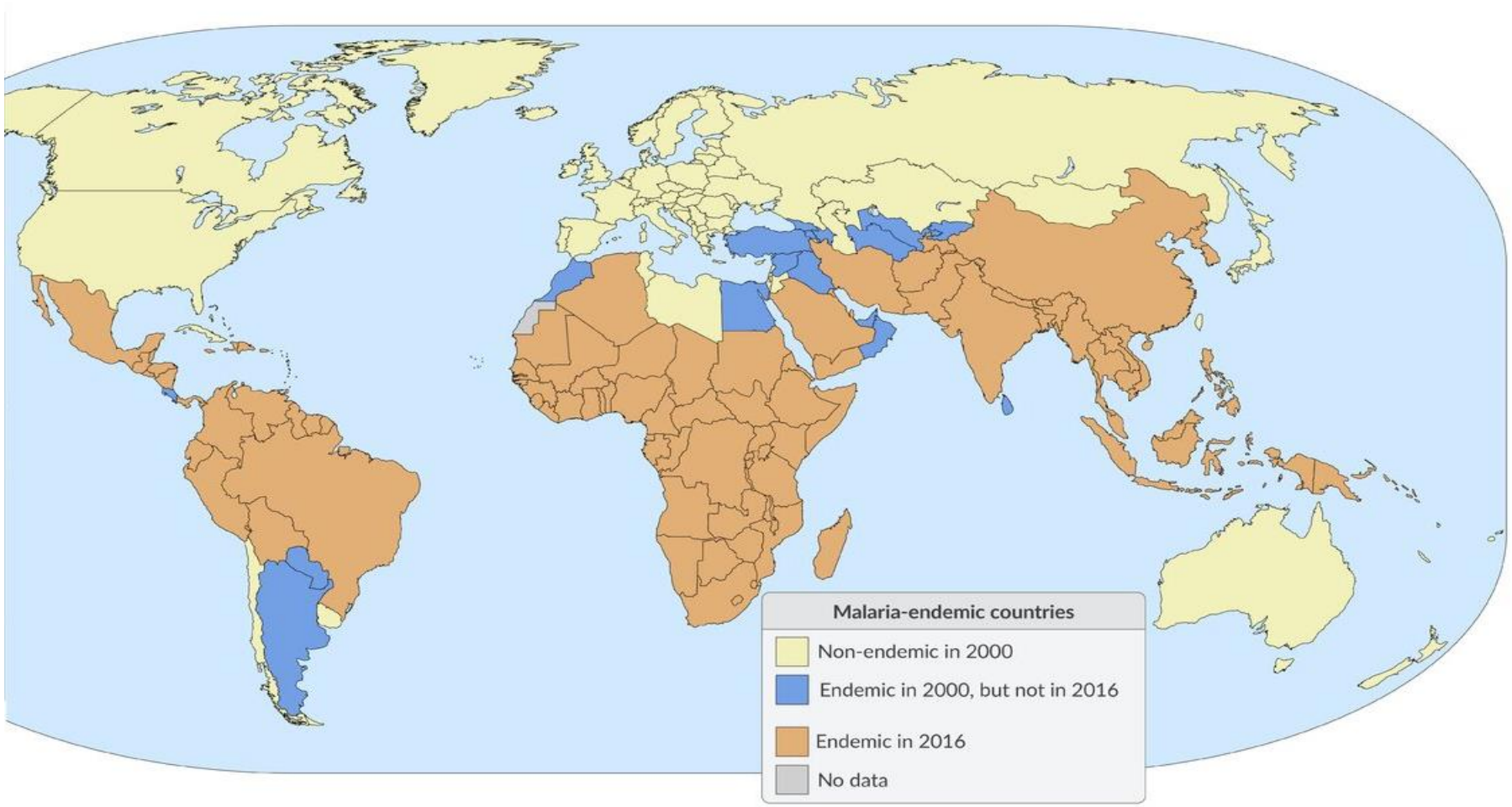
- Malaria:
  - Etiology and life cycle
  - Clinical features
  - Diagnosis, treatment, and prevention
- Babesiosis
  - Etiology
  - Clinical features
  - Diagnosis and treatment

Malaria

Malaria: Introduction

- Malaria is a potentially life-threatening tropical infectious disease caused by Plasmodium parasites, which are transmitted through the bite of an infected female Anopheles mosquito.
- The disease is endemic in tropical and subtropical areas of Africa, Asia, and the Americas.

Malaria: Epidemiology



Data taken from WHO World Malaria Report 2016.

Malaria: Etiology

- Pathogen: ***Plasmodium* genus** (Eukaryotic parasites belonging to the Sporozoa group.
- Carried by Anopheles mosquitoes and transmitted to humans through bites
- Species that affect humans:
  - *P. falciparum*: most common (approximately 70% of cases), and most lethal
  - *P. vivax*: the most common of the less virulent species (causes approximately 20% of cases) and causes milder disease.
  - *P. ovale* and *P. malariae*: less common and cause milder disease.
  - *P. knowlesi*: can cause severe malaria.

Malaria: Etiology- Life cycle of Plasmodium

Asexual development in humans

1. An infected female Anopheles mosquito bites the human and injects sporozoites from its saliva into the blood of the human host.
   - Sporozoites travel through the bloodstream to the liver of the host.
2. In the Liver: sporozoites enter hepatocytes → sporozoites maturate to trophozoites → multiply asexually → schizonts are formed containing thousands of merozoites → release of merozoites into the bloodstream.

- *P. ovale* and *P. vivax* can transform into a dormant stage called hypnozoites that may cause late relapse by reactivating after many months.

Malaria: Etiology- Life cycle of Plasmodium

Asexual development in humans

3. In the Circulatory system (two possible outcomes)

    1. Merozoites enter erythrocytes → maturation to trophozoites → red cell schizonts are formed containing thousands of merozoites → release of merozoites into the bloodstream → penetration of erythrocytes repeated

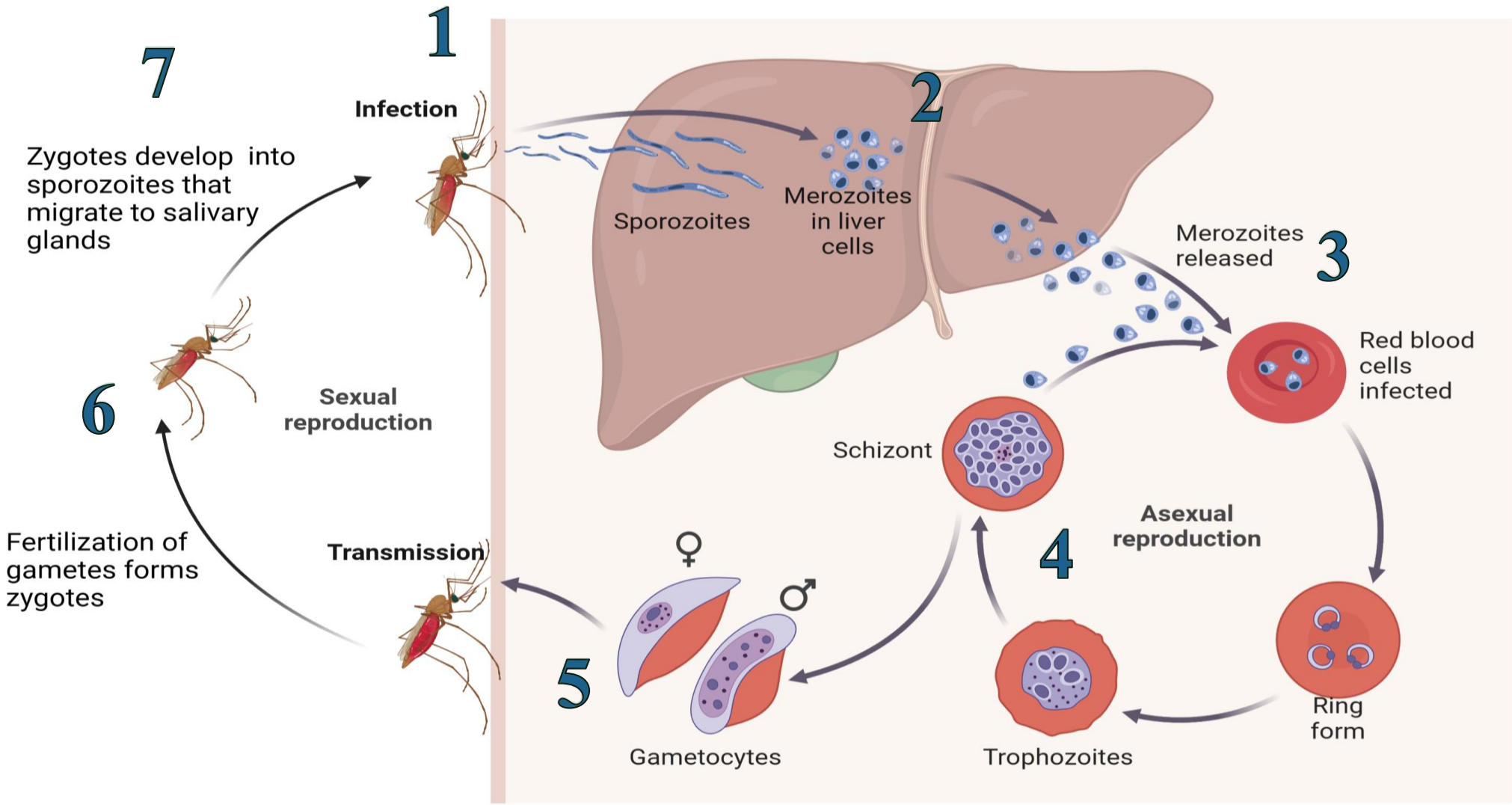
    2. Merozoites enter erythrocytes → differentiation into gametocytes (male or female)

Malaria: Etiology- Life cycle of Plasmodium

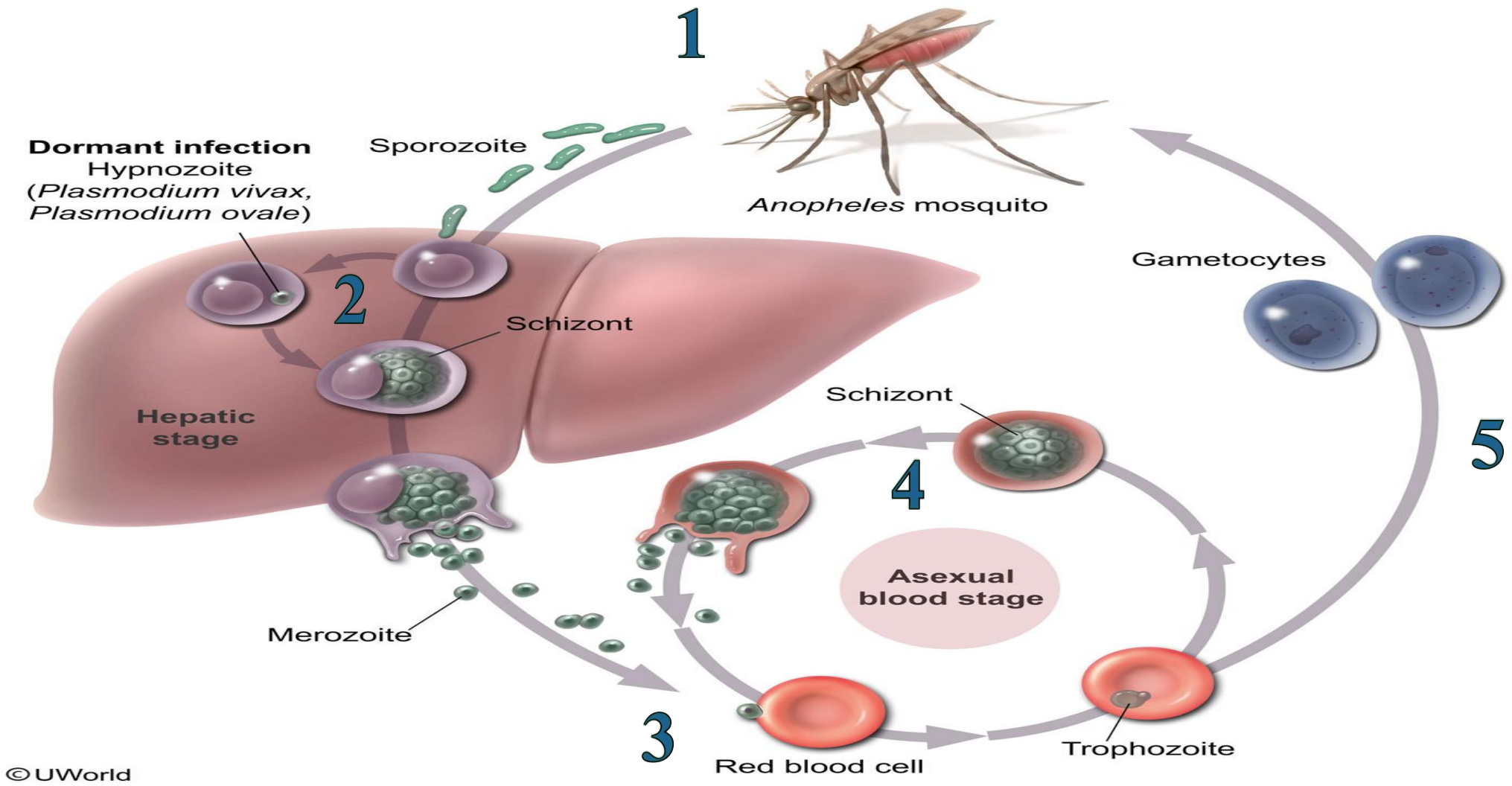
Sexual development in female *Anopheles* mosquito

- A mosquito bites an infected human and ingests gametocytes → gametocytes mature within the mosquito intestines → sporozoites are formed and these migrate to the salivary glands → transmission of sporozoites to humans via mosquito bite

Malaria: Etiology- Life cycle of Plasmodium

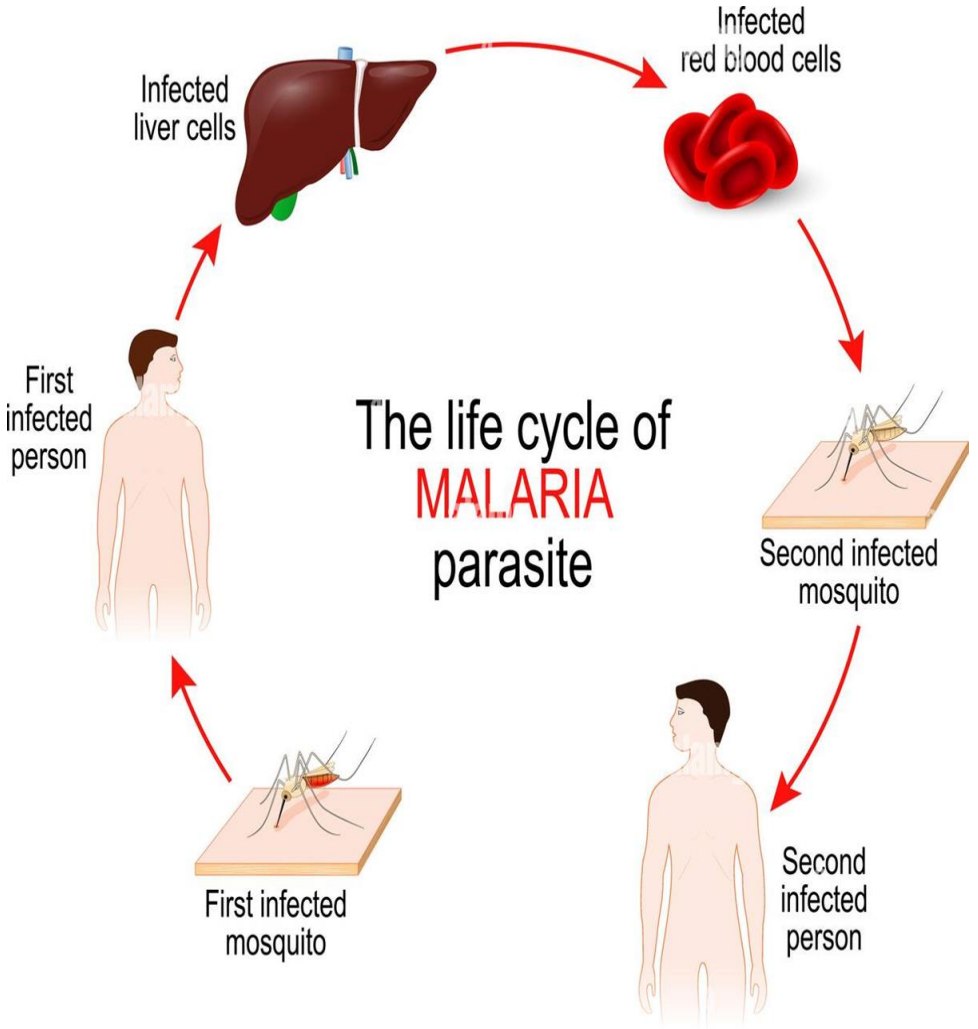


Malaria: Etiology- Life cycle of Plasmodium

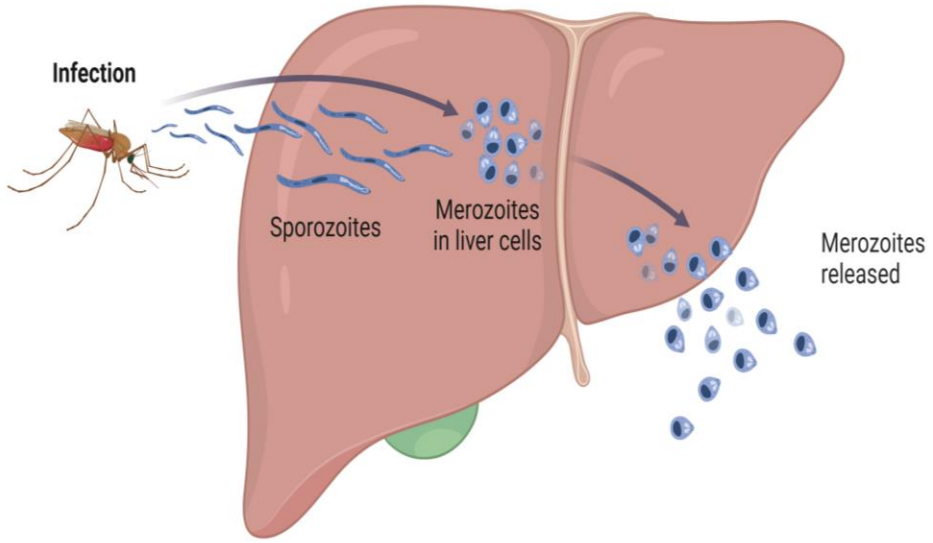


Malaria: Mode of Transmission

1. **Vector-Borne**: **Primary Mode**: Through bites from infected female *Anopheles* mosquitoes.
2. **Blood Transfusion: Risk**: Transmission from infected donor blood.
3. **Organ Transplant: Occurrence**: Rare transmission through infected donated organs.

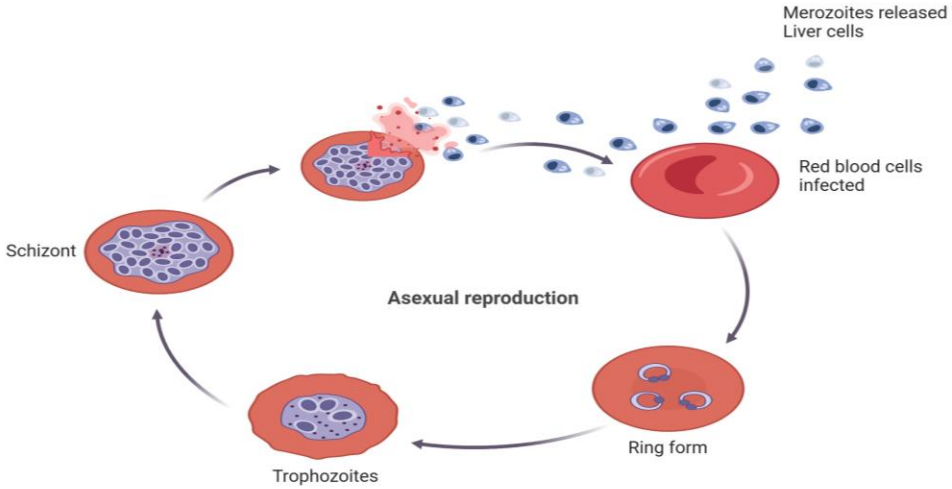


Malaria: Clinical Features- Exoerythrocytic or Liver stage



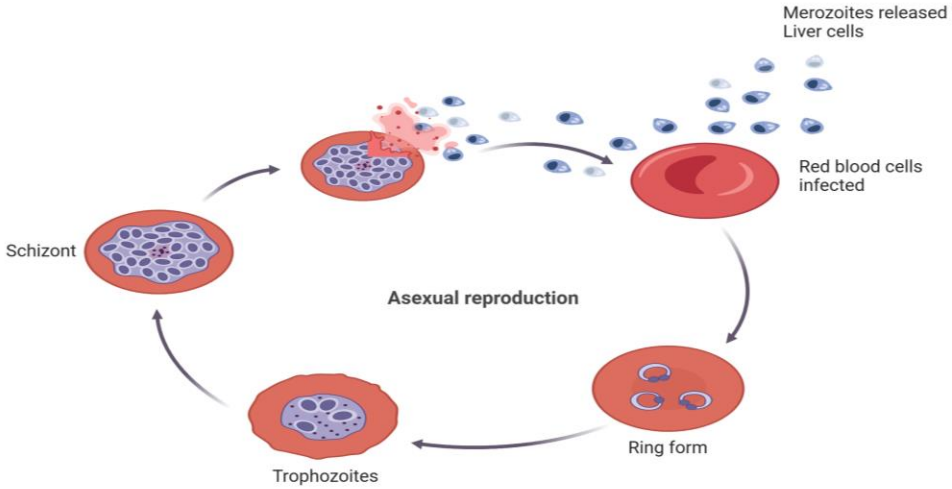
- Incubation period: 7-30 days.
- Exoerythrocytic stage: generally asymptomatic
  - In *P. vivax* and *P. ovale*, the exoerythrocytic phase can persist for months to years as the parasites form dormant hypnozoites in the liver.
  - For *P. malariae*, *P. knowlesi*, and *P. falciparum*, the duration of this stage is typically 1-2 weeks, during which sporozoites undergo asexual multiplication in hepatocytes, resulting in the production of merozoites.

Malaria: Clinical Features- Erythrocytic stage



1. Paroxysm of fever (Fever spikes):
   - **High fever**: Fever spikes occurring at **regular intervals**
   - Due to synchronous rupture of a large number of infected-RBCs and liberation of merozoites with malarial pigment and toxin into the circulation.
   - RBC rupture (lysis) causes a release of inflammatory cytokines → causing fever spikes.

Malaria: Clinical Features- Erythrocytic stage (Cont. 1)



Fever patterns of different plasmodium species:

Species	Disease	Fever spikes
P. vivax *P. ovale*	Tertian malaria (usually less severe)	Every 48 hours
P. malariae	Quartan malaria (usually less severe)	Every 72 hours
P. knowlesi	Quotidian malaria	Every 24 hours
P. falciparum	Falciparum malaria (most severe form; also known as malignant tertian malaria)	Irregular

Malaria: Plasmodium Species & Fever Cycles - Easy Mnemonic

"**F**ast **O**wls **V**isit **M**ad **K**angaroo Daily "

- Fast → *P. falciparum* (Speed & danger& Irregular fever)

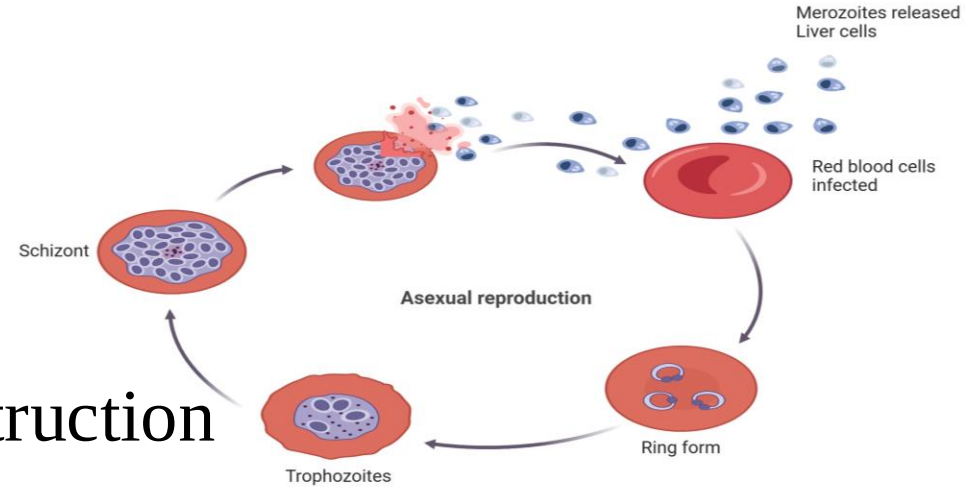
- Owls → *P. ovale*

- Visit → *P. vivax* *(Relapses = keeps coming back)*

- Mad → *P. malariae* *(Slow but stubborn, 72h fever)*

- Kangaroo → *P. knowlesi* *(Daily fever, jumps around)*

Malaria: Clinical Features- Erythrocytic stage (Cont. 2)



2. Haemolytic anaemia- repeated RBCs destruction

Cause

- ✓ Fatigue
- ✓ Weakness
- ✓ Headache
- ✓ Dizziness
- ✓ Jaundice
- ✓ Splenomegaly

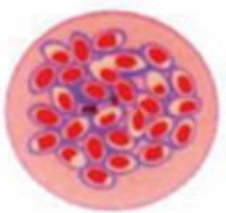
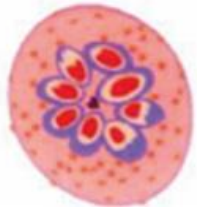
Malaria: Clinical Features-
Erythrocytic stage- *P. falciparum* Specific Features

P. falciparum is the most virulent among other plasmodium species due to several factors:

1. High Parasitemia Levels: Parasitemia refers to the percentage of RBCs that are infected with the malaria parasite. This extremely high level is attributed to:

- Rapid Multiplication: each infected RBC can produce up to 32 new merozoites, compared to fewer in other species.
- Wide Range of Infectable RBCs: *P. falciparum* can infect RBCs at any stage of their development → more extensive and rapid increase in the number of infected cells.

Malaria: Clinical Features-
Erythrocytic stage- *P. falciparum* Specific Features

	Mature schizonts	Targeted RBCs	
P. falciparum		All ages	
P. ovale		Young RBCs	
p. vivax		Young RBCs	
p. malariae		Old RBCs	

High Parasitemia

Levels:

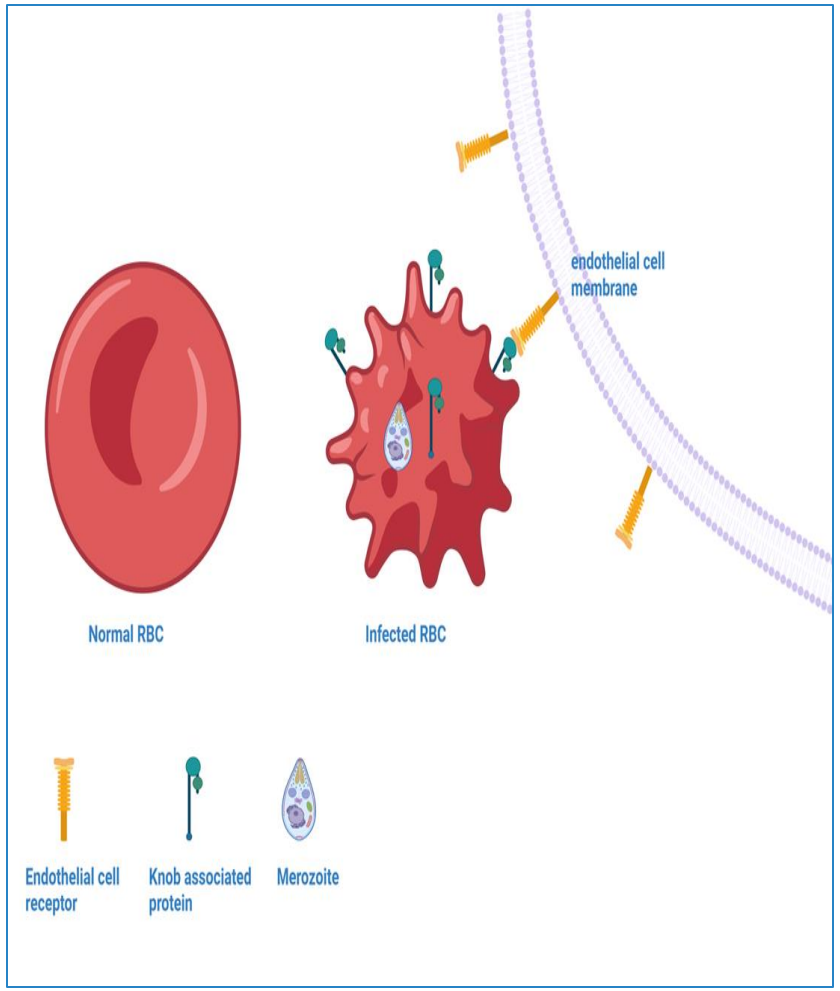
- Rapid Multiplication
- Invade RBCs of all ages

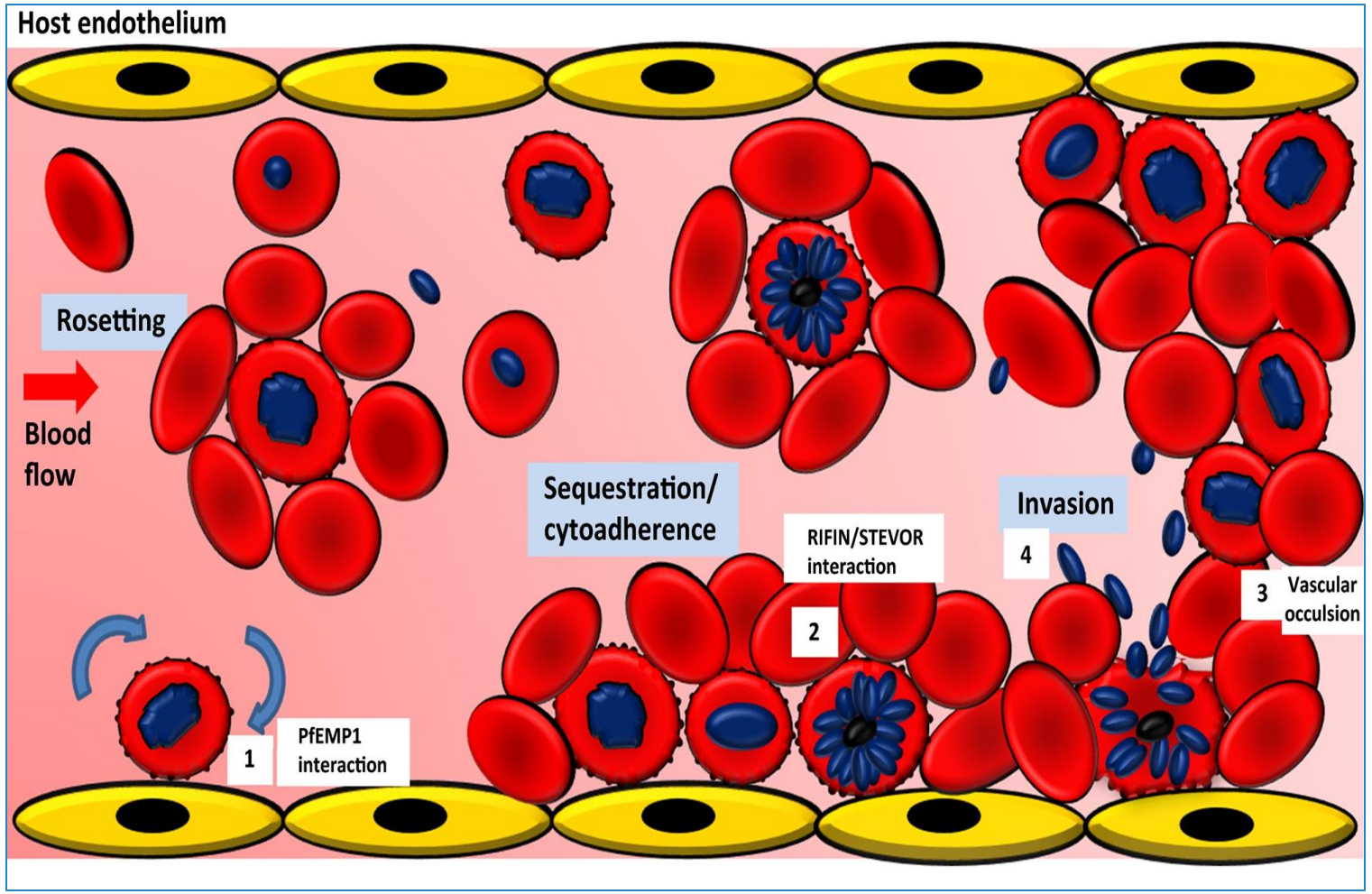
Malaria: Clinical Features-
Erythrocytic stage- *P. falciparum* Specific Features

2. The adhesion phenomena: refer to the ability of infected red blood cells (RBCs) to adhere to endothelial cells lining the blood vessels, as well as to uninfected RBCs.

   - *P. falciparum* goal: to avoid splenic clearance and evade the immune system.
   - Mechanism: iRBCs express proteins on their surface, which facilitate adherence to the vascular endothelium and sequestering in capillary beds of organs that are less dangerous than the spleen.
   - Consequences on host: Vascular occlusion → Reduced blood flow → tissue hypoxia and organ dysfunction.

Malaria: Clinical Features-
Erythrocytic stage- *P. falciparum* Specific Features





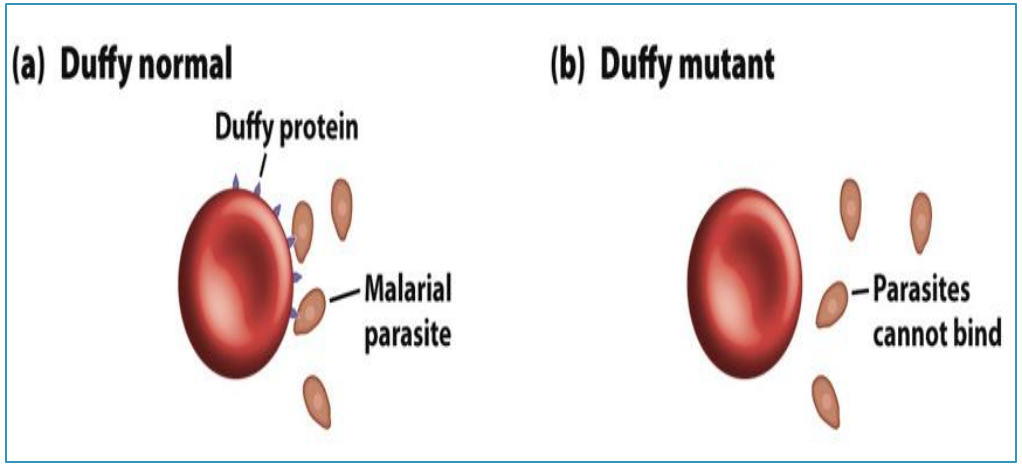
Malaria: Clinical Features-
Erythrocytic stage- *P. falciparum* Specific Features

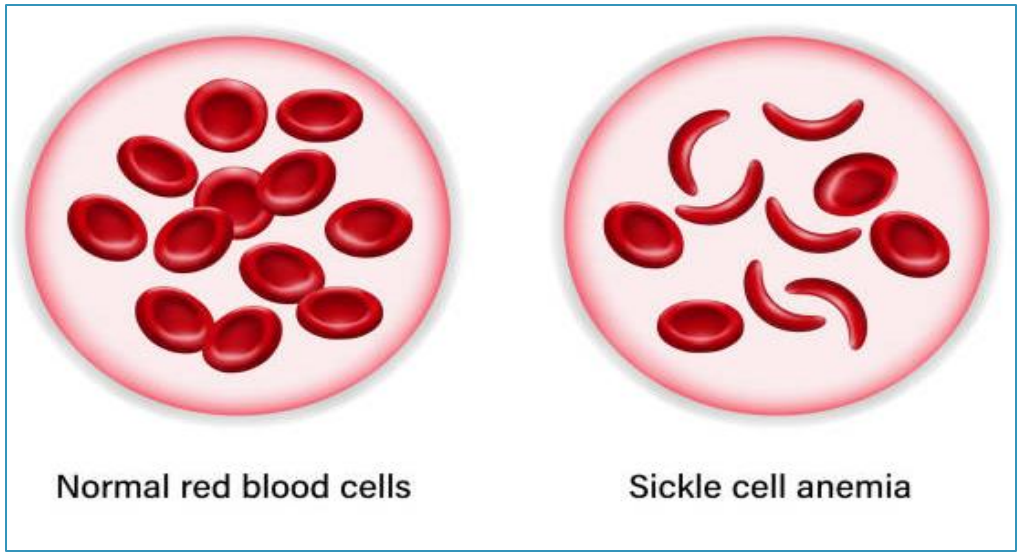
Disease	Causes
Adhesion phenomena (pernicious syndrome)	iRBCs obstruct blood flow to organs like the brain, kidneys, and lungs leading to multiple organ failure
Algid malaria	vascular obstruction leads to reduced blood flow and profound shock or collapse
Cerebral malaria	iRBCs adhere to cerebral capillaries, leading to obstruction of blood flow and inflammation.
Gastrointestinal malaria	vascular obstruction exacerbated by the inflammation caused by iRBCs cytoadherence and the release of inflammatory cytokines.

Malaria: Partial resistance against malaria

Host factors play a significant role in susceptibility and disease severity:

- RBC antigens: Absence of the Duffy antigen provides protection against *P. vivax* malaria.
- Some RBC diseases confer partial protection against malaria:
  - Sickle cell anemia
  - Thalassemia (reduced parasite multiplication)



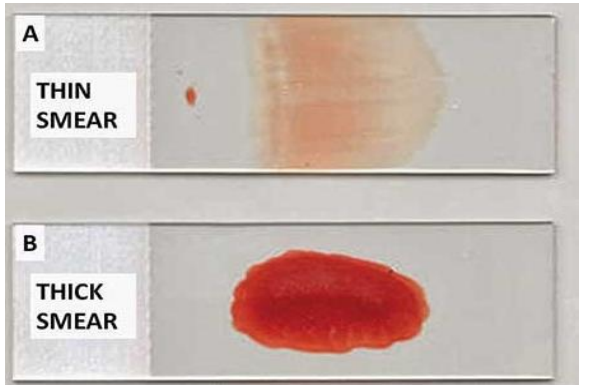


Malaria: Diagnosis

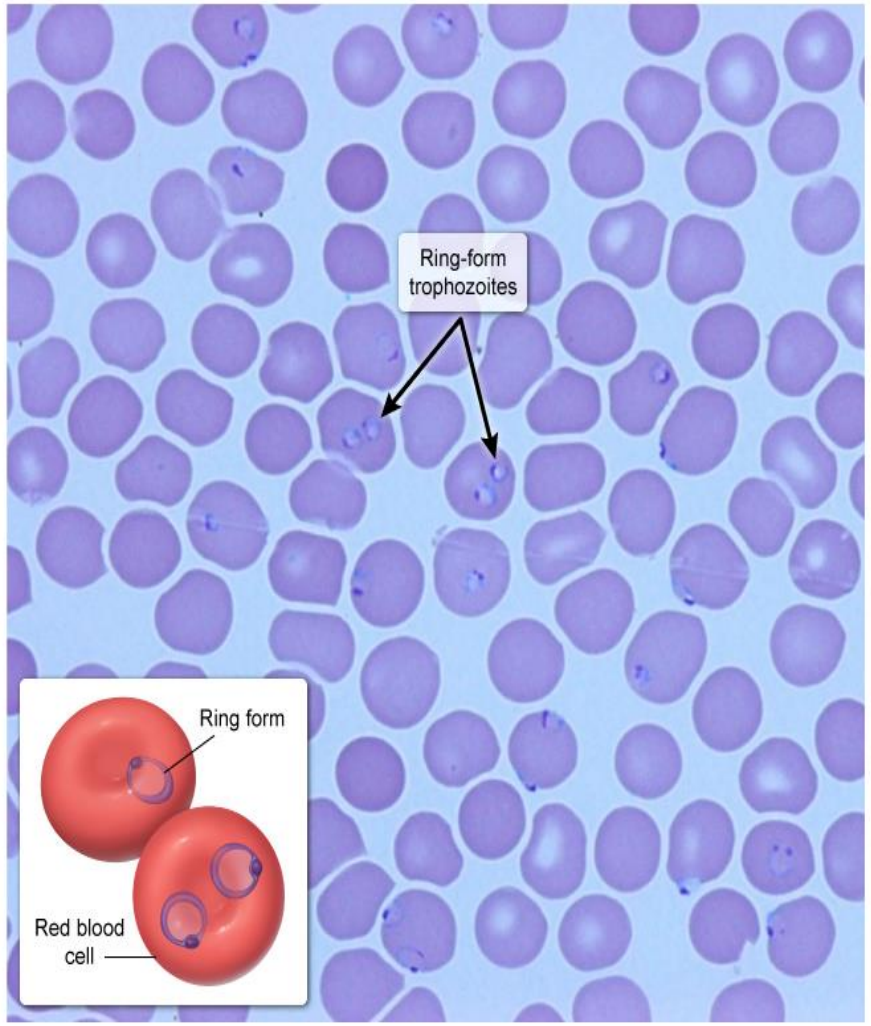
1. History and physical exam
   - Residence or travel to an endemic region
   - Evaluate for signs of severe malaria.
2. Routine laboratory studies: anemia (decreased haemoglobin and haematocrit), increased reticulocyte counts, thrombocytopenia

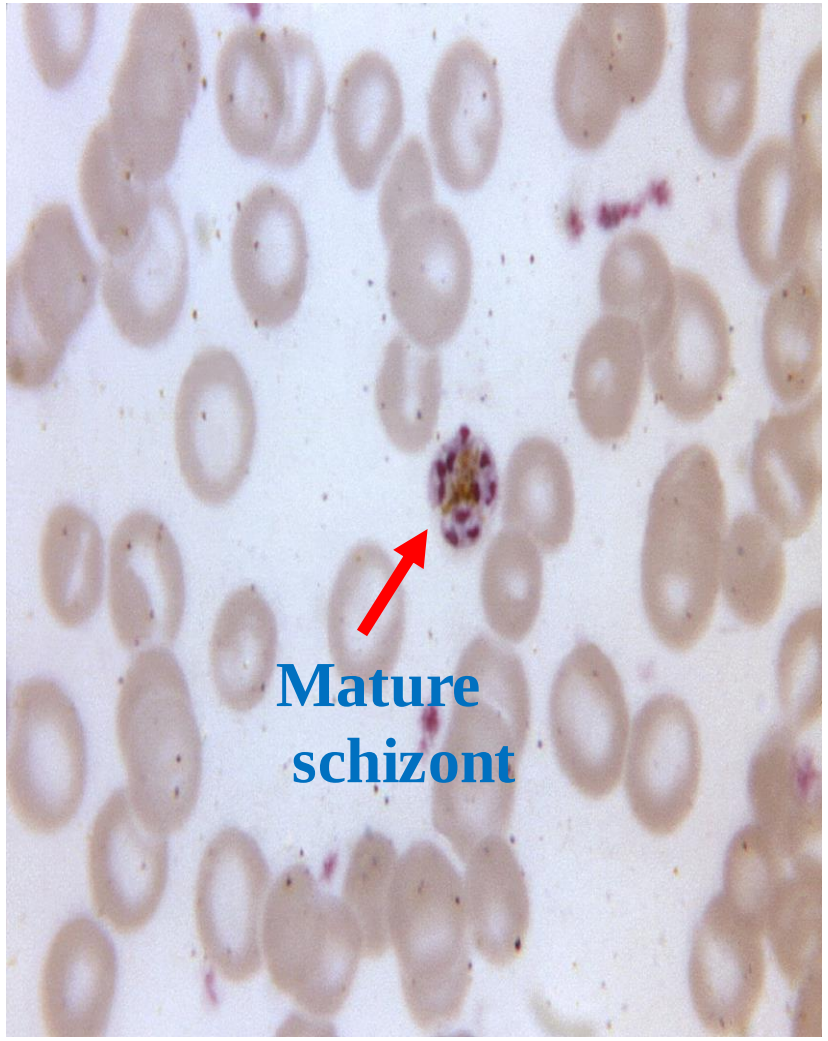
Malaria: Diagnosis

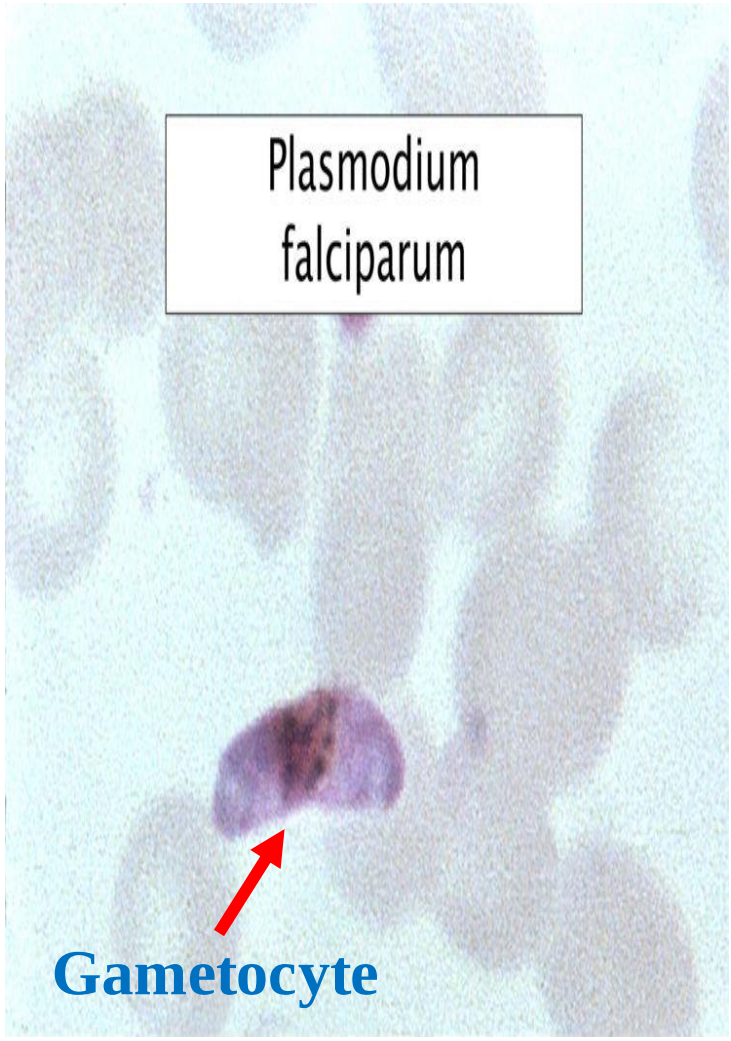
3. Blood smear: gold standard test allows for visualization of parasites within RBCs via microscopy to confirm malaria diagnosis
   - Thick blood smear: high sensitivity; best initial test.
   - Thin blood smear: lower sensitivity, high specificity; confirmatory test
   - Findings: Trophozoite ring within RBCs, Schizont containing merozoites, Gametocytes in peripheral blood.
4. Antigen detection test: detects specific malaria antigens (more rapid but less sensitive)



Malaria: Diagnosis



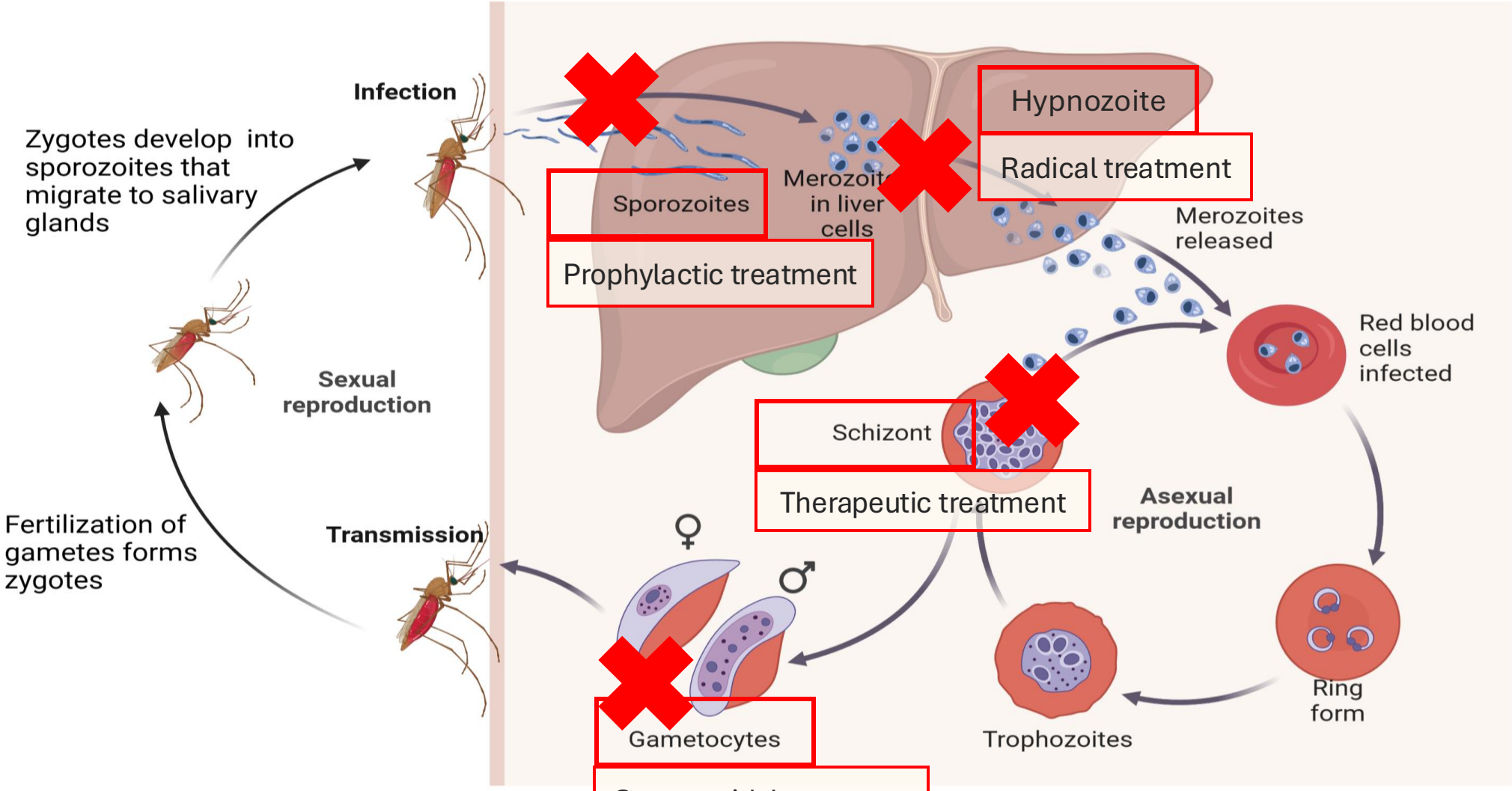




Malaria: Treatment

- All confirmed cases of malaria must be reported.
- Most cases of uncomplicated malaria resolve with treatment
- Treat with antimalarial drugs:
  - Avoid the same drug for treatment if it was already used for prophylaxis.
  - Chloroquine or hydroxychloroquine for sensitive species
  - Doxycycline for areas resistant to Chloroquine
  - Use primaquine for hypnozoites if *P. vivax* or *P. ovale* are identified.

Malaria: Treatment- Treatment Stages



Malaria: Prevention

- Mosquito bite prevention
  - Long-sleeved clothes
  - Insect repellent
  - Mosquito nets

- Malaria prophylaxis:
  - Medications need to be initiated before traveling to endemic regions, e.g., tropical Africa, Asia, and Central/South America

Malaria Song

 Make a simple rhyming song to remember malaria facts:

"Mosquito bites at night, fever’s in sight…
Falciparum’s mean, the worst we’ve seen…
Vivax and ovale, they play the long game…
Hiding in the liver, they won’t go away!
Get Primaquine fast, clear them away…
No more relapses, keep them away!

 Tip: Music is a powerful memory booster!

Question1

- Which Plasmodium species causes the most severe form of malaria?

A. *P. malariae*
B. *P. falciparum*
C. *P. vivax*
D. *P. knowlesi*
E. *P. ovale*

Question 2

- *Which Plasmodium species can relapse due to liver-stage hypnozoites?*

A. *P. malariae*

B. *P. falciparum*

C. *P. vivax and P. ovale*

D. *P. berghei*

E. *P. knowlesi*

USMLE Question 1

- A 34-year-old man comes to the emergency department due to **recurrent fever**, chills, and excessive sweating. The symptoms began a few days ago and seem to recur every 48 hours. The patient recently returned from a trip to Latin America. Temperature is 38.6 C.
- Physical examination is otherwise normal.
- Laboratory studies are notable for anaemia and thrombocytopenia. A blood smear with Giemsa staining demonstrates red blood cell inclusions. Chloroquine and primaquine are prescribed. The addition of primaquine to the treatment regimen is most likely to have which of the following effects?

Prevent disease relapse

USMLE Question 2

- A 2-week-old girl is brought to her primary care provider for a routine visit. Newborn screening results from haemoglobin electrophoresis show signs of sickle cell anaemia.
- The patient's mother has sickle cell trait, and a maternal cousin has sickle cell anaemia. Which of the following is most likely true about this patient?

She has relative protection from Plasmodium falciparum

Babesiosis

Babesiosis

- Babesiosis is an infection caused by a protozoa belonging to the genus, Babesia. The protozoa replicate within host erythrocytes. Lysis of erythrocytes and the body's immune response result in clinical symptoms.
- Pathogen: Babesia species
- Vector: deer tick (Ixodes scapularis)
- Transmission:
  - Tick bite (most common)
  - Exposure to infected blood, i.e, transfusions, organ transplantation, perinatal

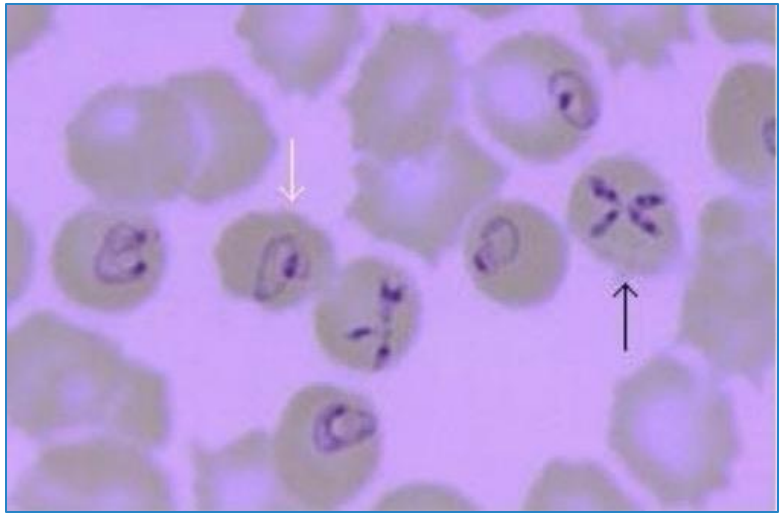
Babesiosis: Clinical features

Patients usually present with a flu-like illness and jaundice. In severe cases, organ damage may occur.

Babesiosis has no disease-specific distinguishing clinical features.

- Fever and other flu-like symptoms
- Anorexia
- Nonproductive cough
- Dark urine, jaundice from haemolytic anaemia
- Mild splenomegaly and/or hepatomegaly
- Gastrointestinal symptoms (e.g., nausea, vomiting, abdominal pain)

Babesiosis: Diagnostics



Supportive laboratory findings:

- CBC: ↓ hematocrit, thrombocytopenia, ↑ reticulocyte count

Diagnostic confirmation:

- The diagnosis is confirmed by peripheral blood smear showing Babesia as intraerythrocytic rings and/or Maltese cross
- Detection of Babesia DNA on a blood sample (e.g., PCR)

Babesiosis: Treatment

- Antibiotic regimens:
  - Atovaquone PLUS azithromycin
- Exchange transfusion: consider for patients with parasitemia > 10% and/or severe disease


THANK YOU


WARNING
NO QUESTIONS ALLOWED