

Malaria and Babesiosis

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Outlines

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

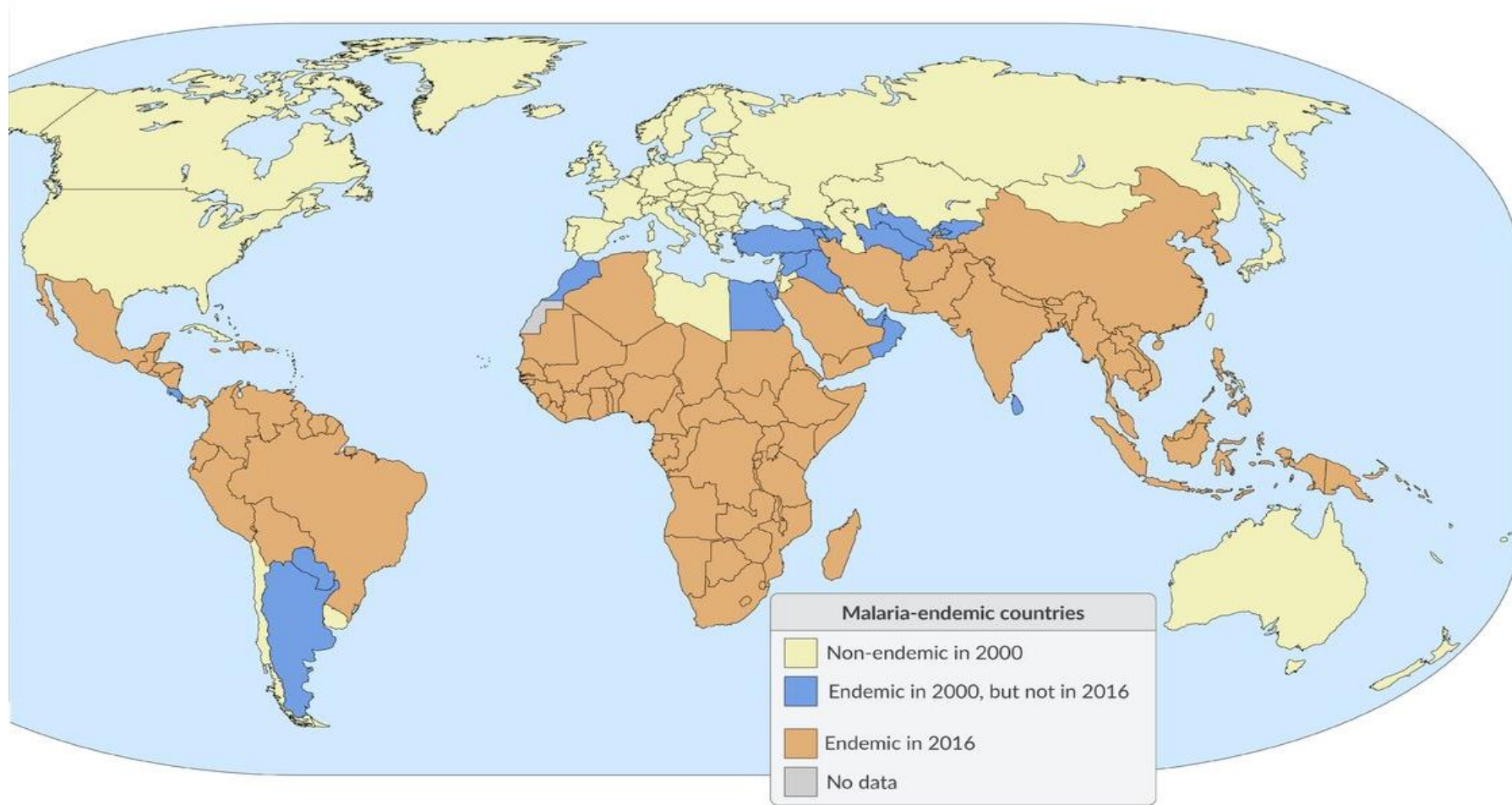
Malaria: Introduction

Epidemiology:

WHO's World malaria report (2024):

- Globally in 2024, there were an estimated **282 million** malaria cases and **610 000** malaria deaths in 80 countries.
- African Region was home to 95% of malaria cases (265 million) and 95% (579 000) of malaria deaths.
- **Children** under 5 accounted for **about 75%** of all malaria deaths in the Region.

Malaria: Epidemiology



Data taken from WHO World Malaria Report 2016.

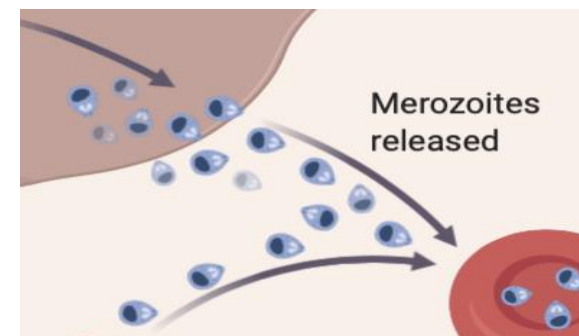
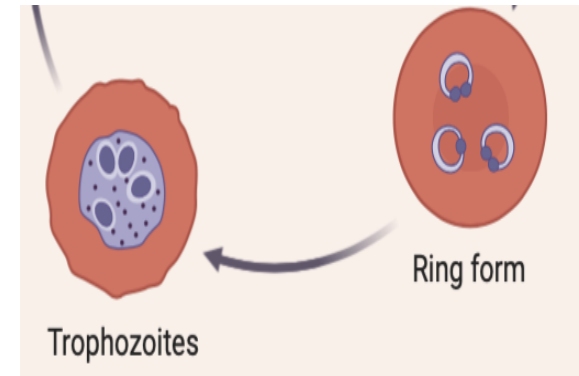
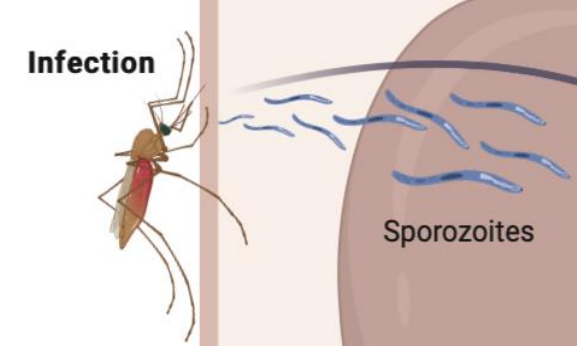
Malaria: Etiology



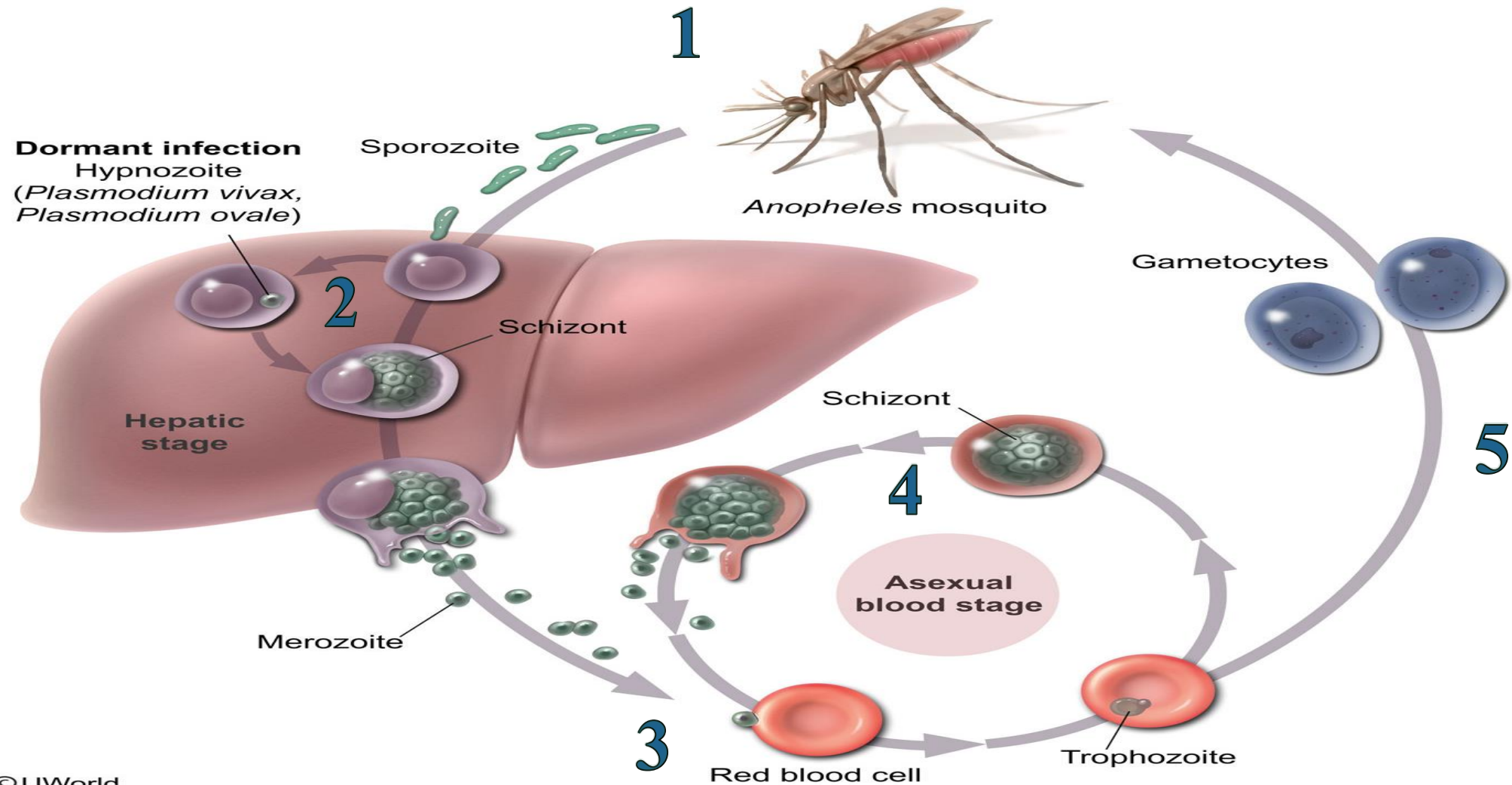
- Pathogen: ***Plasmodium* genus** →
 - Single-celled, eukaryotic parasites (**Protozoa**) belonging to the Sporozoa group.
 - Obligate parasites of **vertebrates** and **insects**.
- Carried by **Anopheles mosquitoes** and transmitted to humans through **bites**
- **Species that affect humans:**
 - *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- Plasmodium life stages

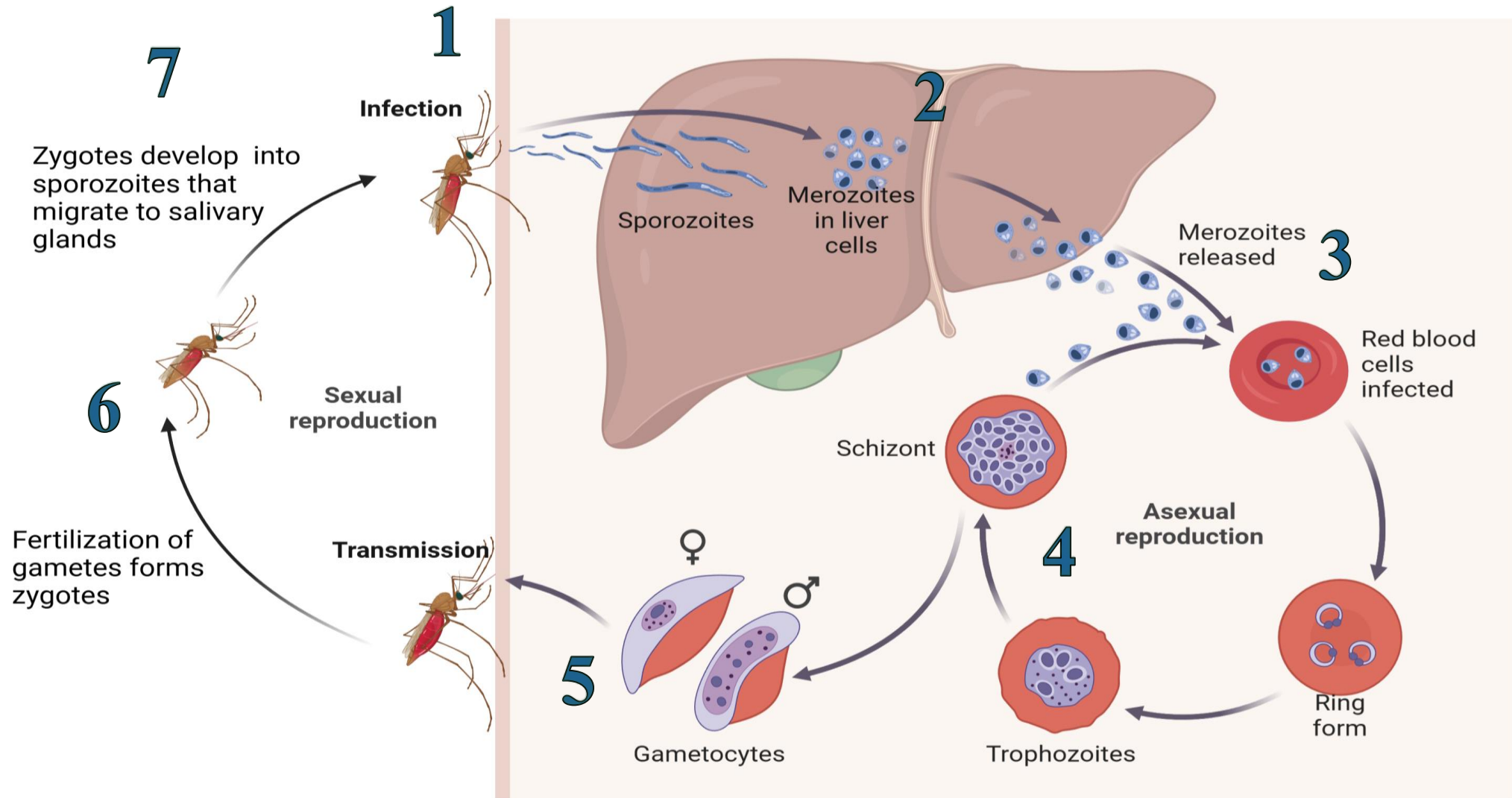
- **Sporozoite** (Sporozoa): **The infective form**. Sporozoites are slender, motile cells stored in the mosquito's salivary glands.
- **Trophozoite**: The feeding and growing form. Once inside a host cell (either a hepatocyte or a red blood cell), the parasite transforms into a trophozoite.
- **Schizont**: **The dividing form**. When the trophozoite finishes growing, it undergoes repeated asexual division (called schizogony)
- **Merozoite**: The released daughter cells- **the invasive blood-stage form**.
- **Gametocyte**: **The sexual form** — the stage meant for the mosquito.



Malaria: Etiology- Life cycle of Plasmodium



Malaria: Etiology- Life cycle of Plasmodium



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** mature 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)

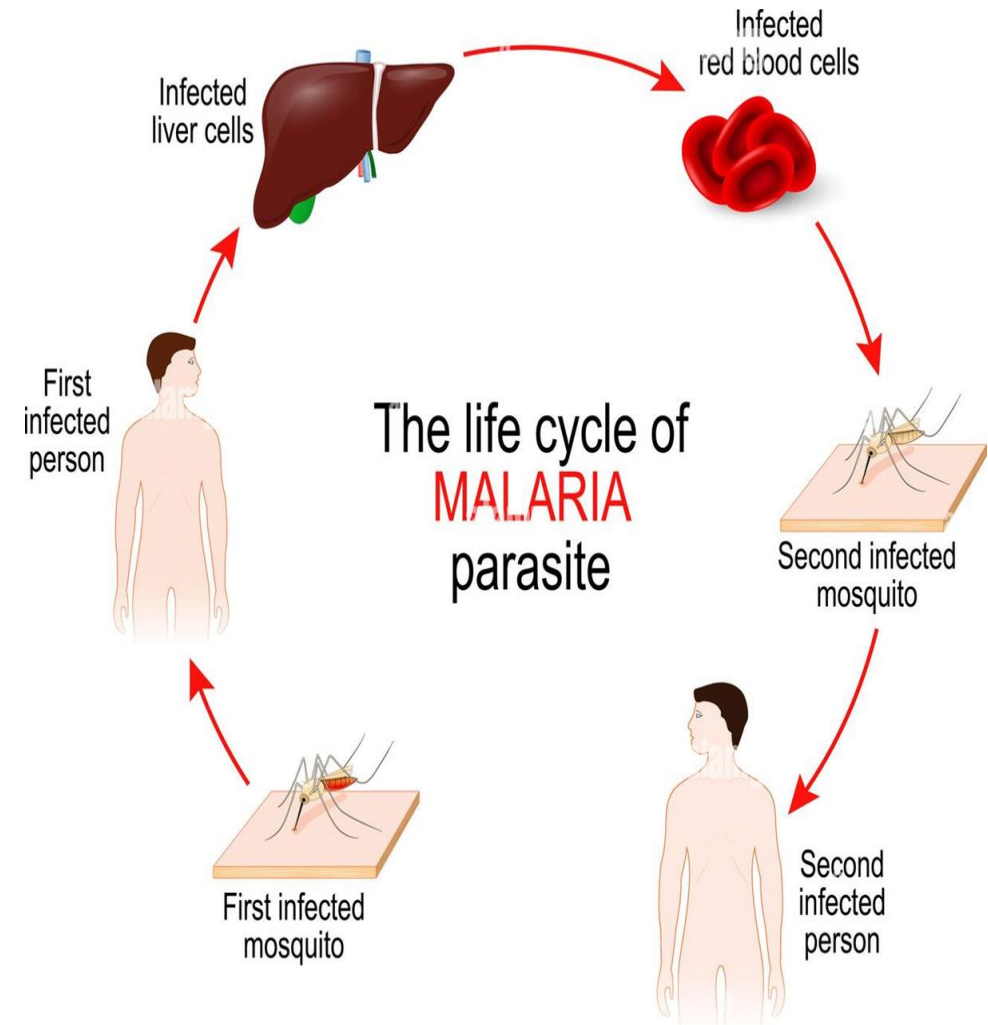
Malaria: Etiology- Life cycle of Plasmodium

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

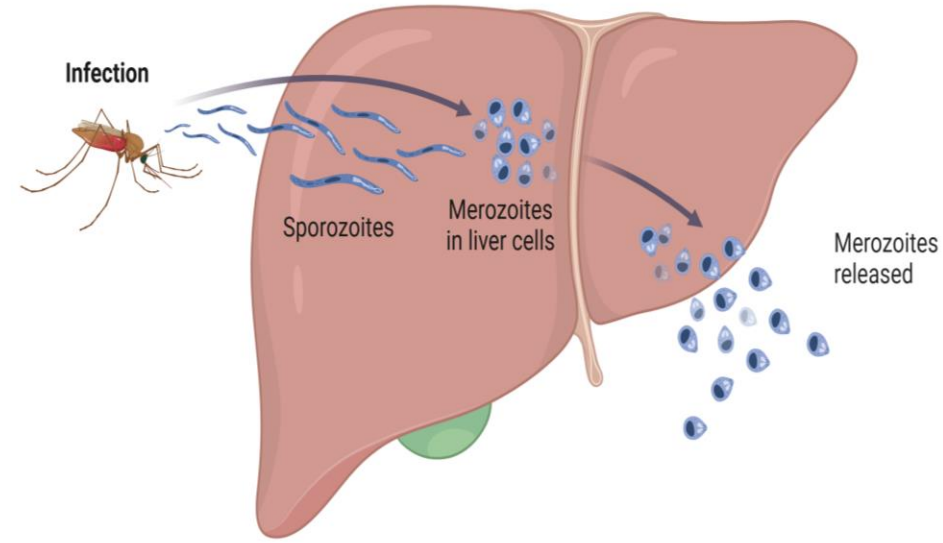
Malaria: Mode of Transmission

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



Malaria: Clinical Features- Exoerythrocytic or Liver stage

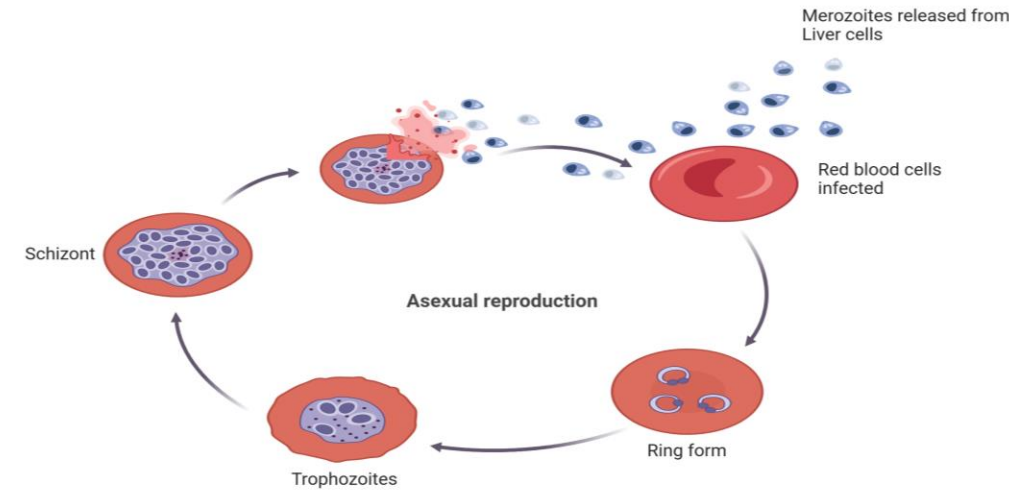
- Incubation period: 7-30 days.
- Exoerythrocytic stage: generally asymptomatic
 - For *P. malariae*, *P. knowlesi*, and *P. falciparum*, the duration of this stage is typically **1-2 weeks**, during which sporozoites undergo asexual multiplication in hepatocytes, resulting in the production of merozoites.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



Malaria: Clinical Features- Erythrocytic stage

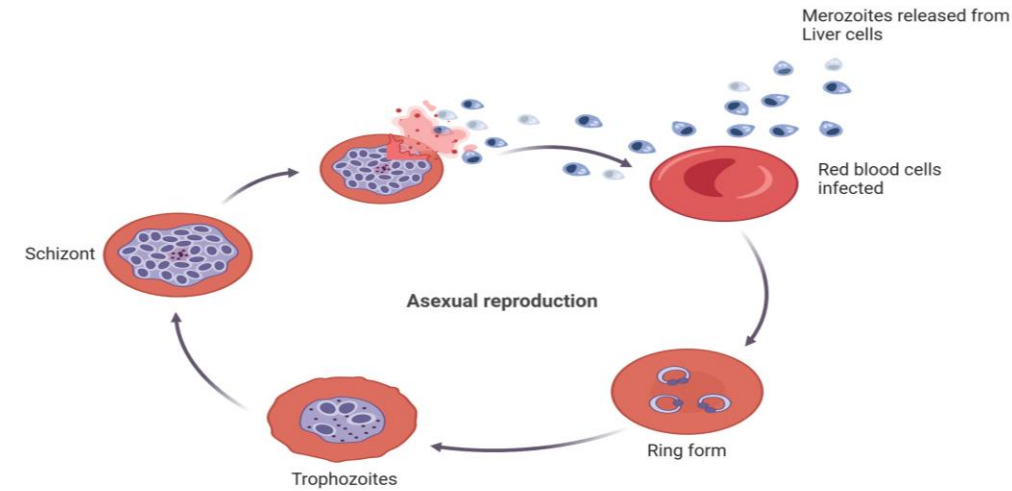
1. Paroxysm of fever (Fever spikes):

- **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)

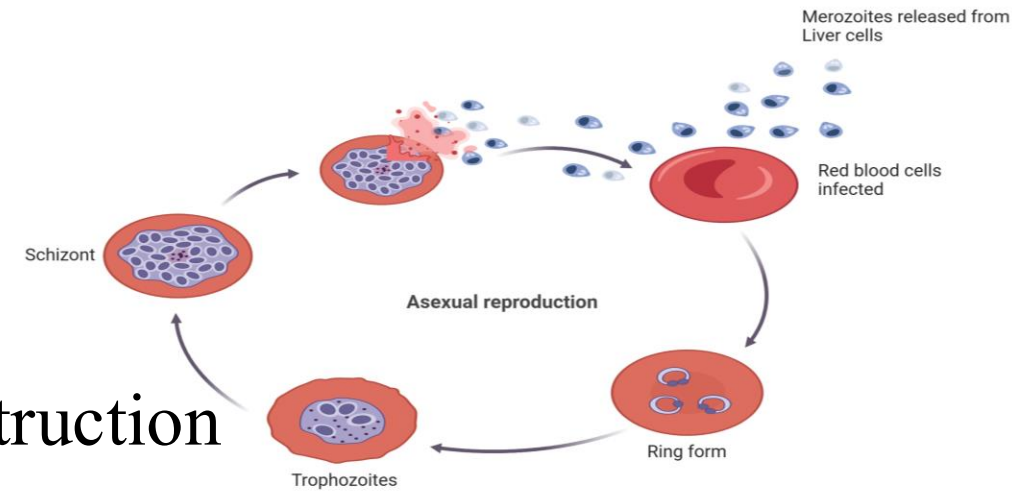
Fever patterns of different plasmodium species:



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

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

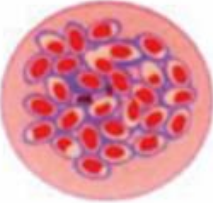



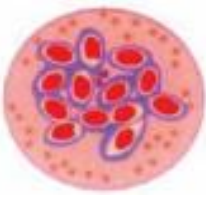



P. falciparum is **the most virulent** among other plasmodium species due to several factors:

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	
<i>P. falciparum</i>		All ages	
<i>P. ovale</i>		Young RBCs	
<i>p. vivax</i>		Young RBCs	
<i>p. malariae</i>		Old RBCs	

High Parasitemia

Levels:

- Rapid Multiplication
- Invade RBCs of all ages

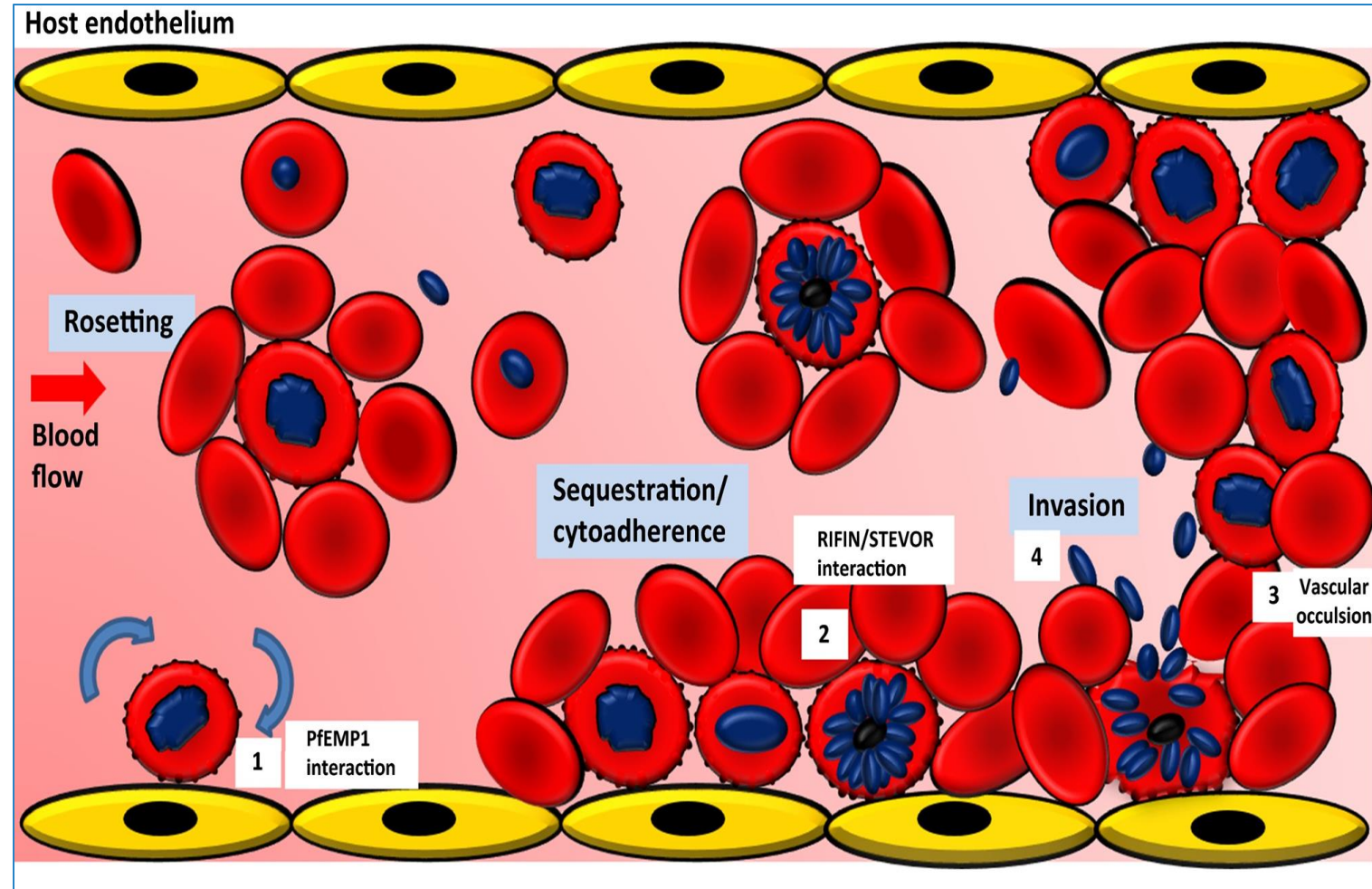
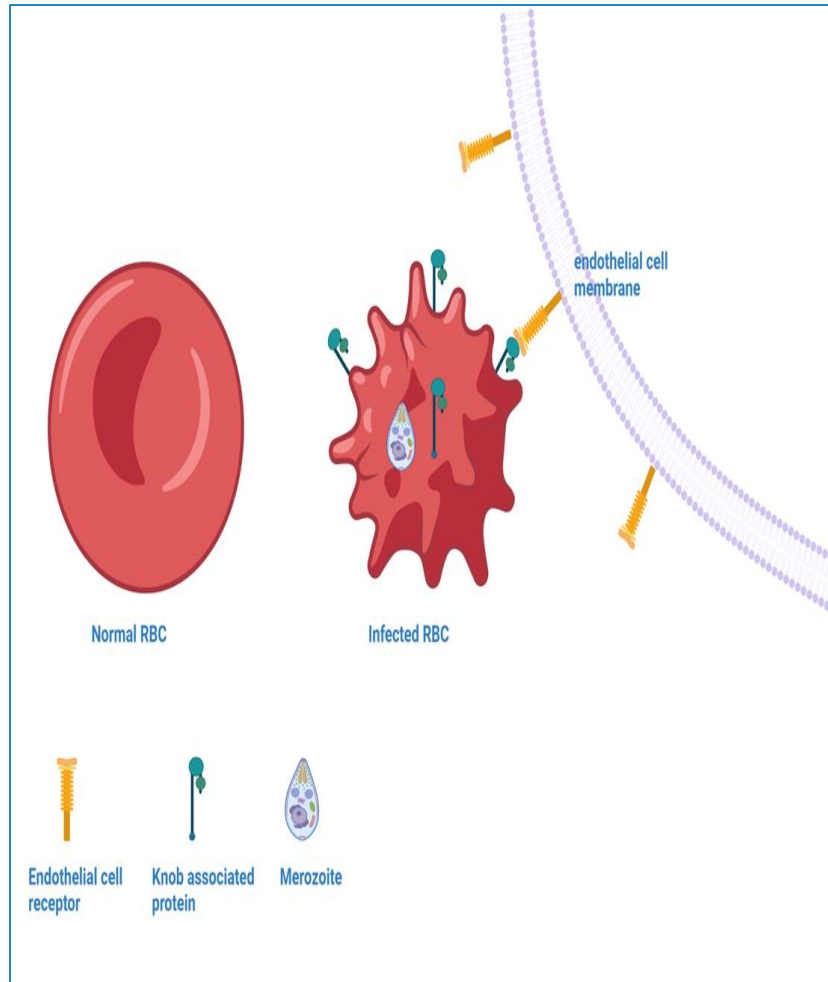
Malaria: Clinical Features-

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



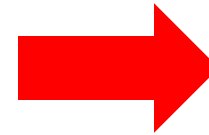
Malaria: Clinical Features-

Erythrocytic stage- *P. falciparum* Specific Features

**Haemolytic
Anaemia**

+

**Ischemic
Damage**



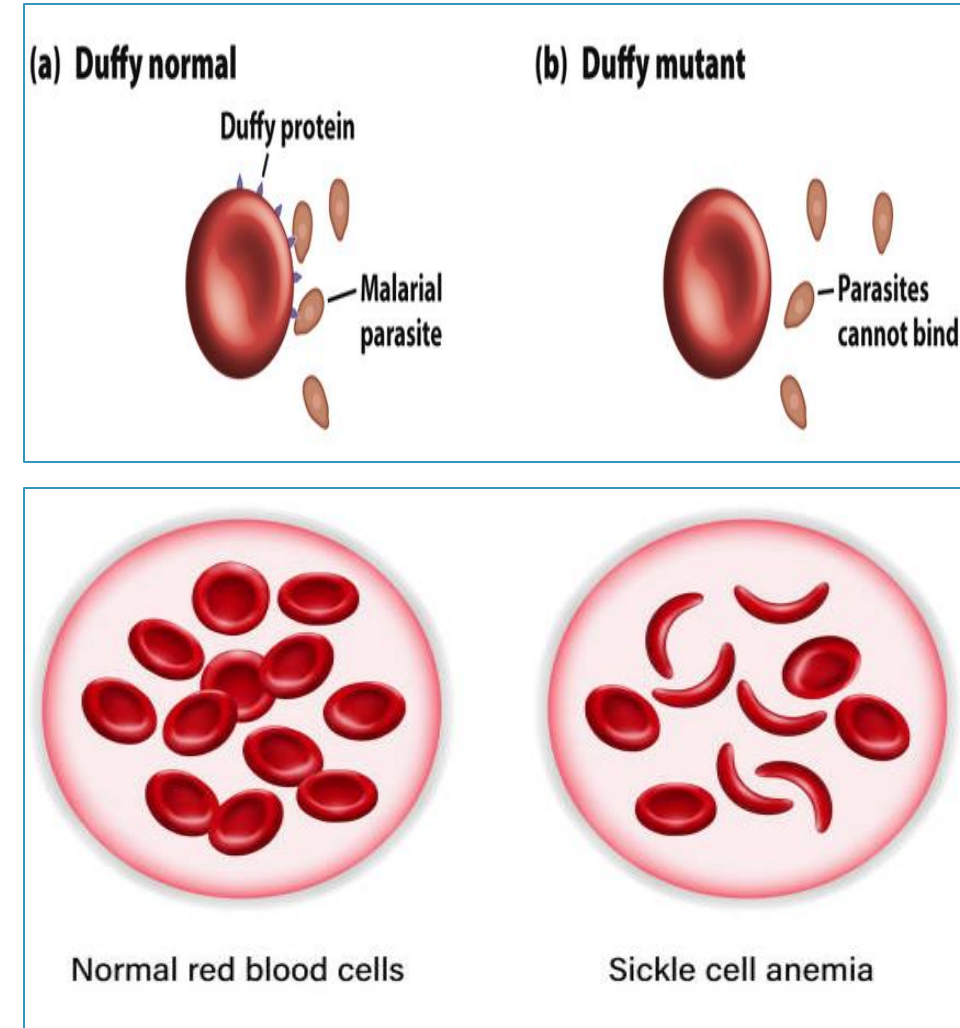
**Organ
Failure**

Disease	Causes
Acute Renal Failure	Renal microvascular obstruction + haemoglobinuria (blackwater fever)
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.
Acute Respiratory Distress	Pulmonary sequestration → hypoxia and respiratory failure

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 anaemia
 - Thalassemia (reduced parasite multiplication)



Malaria: **Diagnosis**

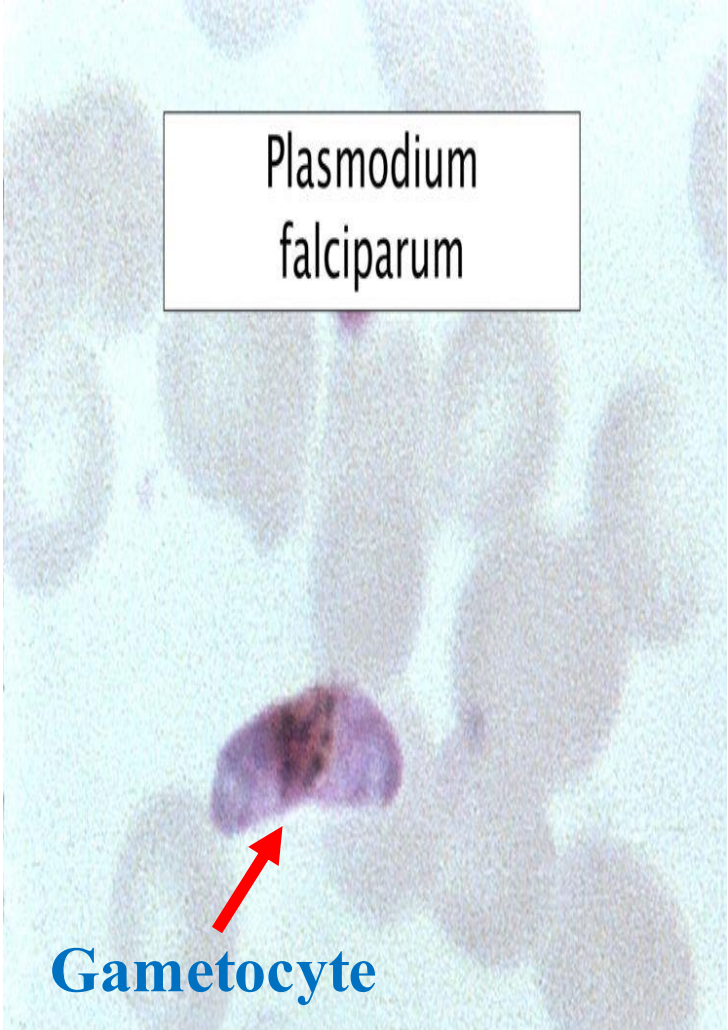
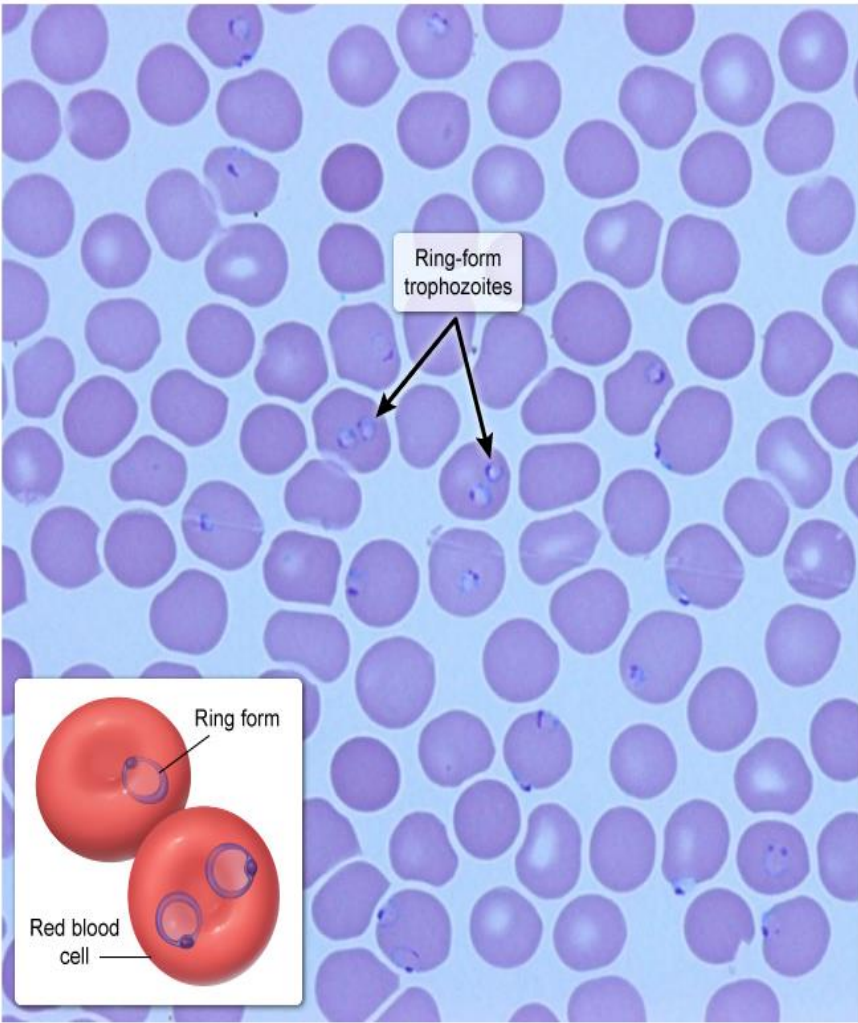
1. History and physical exam
 - Residence or travel to an endemic region
 - Evaluate for signs of severe malaria.
2. Routine laboratory studies: anaemia (decreased haemoglobin and haematocrit), increased reticulocyte counts

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**



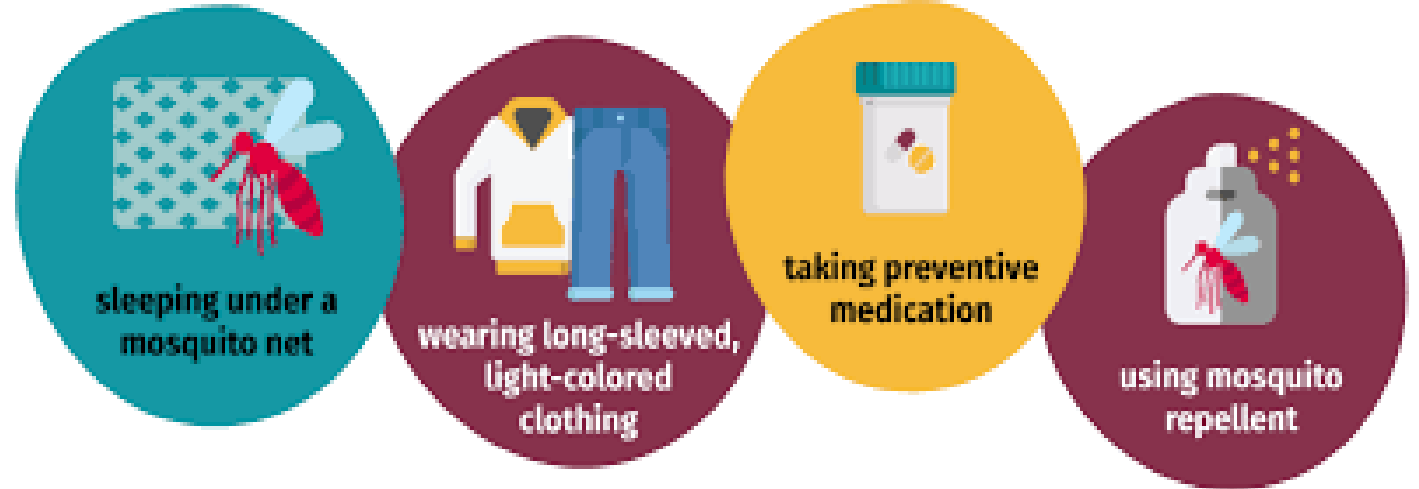
Malaria: Treatment

- All confirmed cases of malaria must be reported.
- Most cases of uncomplicated malaria resolve with treatment
- Treat with antimalarial drugs:
 - 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: 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: **Mnemonic**



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...

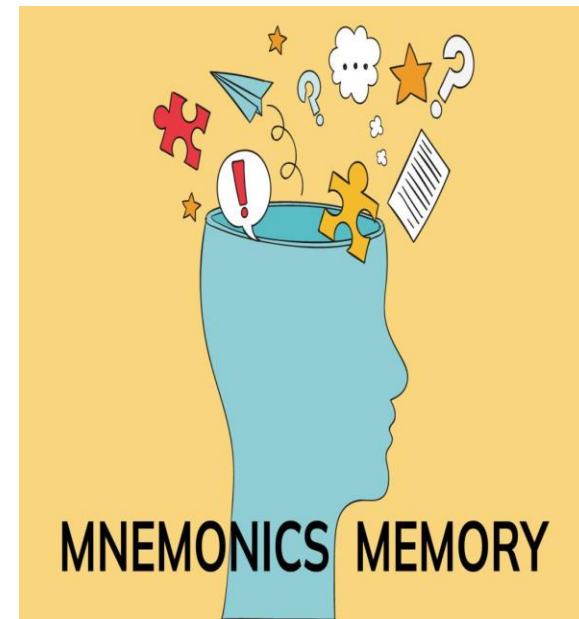
Hiding in the liver, they won't go away!

Get Primaquine, clear them today...

No more relapses, keep them away!



Tip: Music is a powerful memory booster!



USMLE Question

- 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?
- A. Kill trophozoites
 - B. Prevent haemolysis
 - C. Prevent disease relapse



USMLE Question

- 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



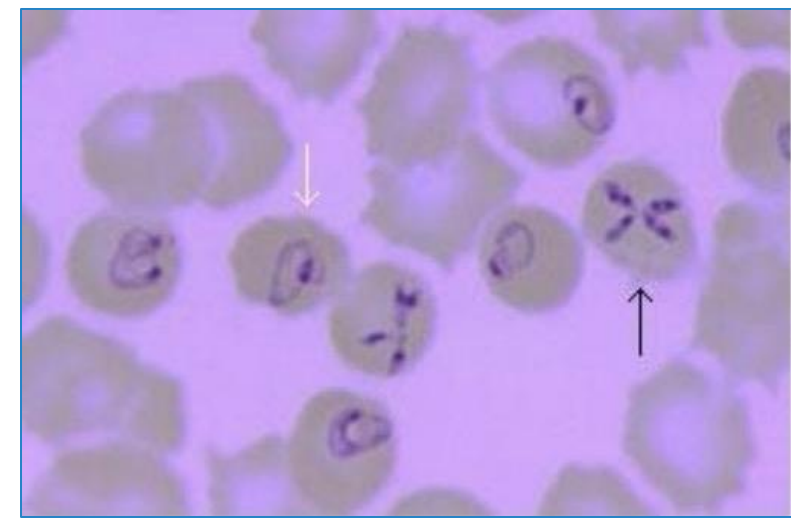
Babesiosis: Clinical features

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: **Diagnos**tics



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 parasitaemia $> 10\%$ and/or severe disease

