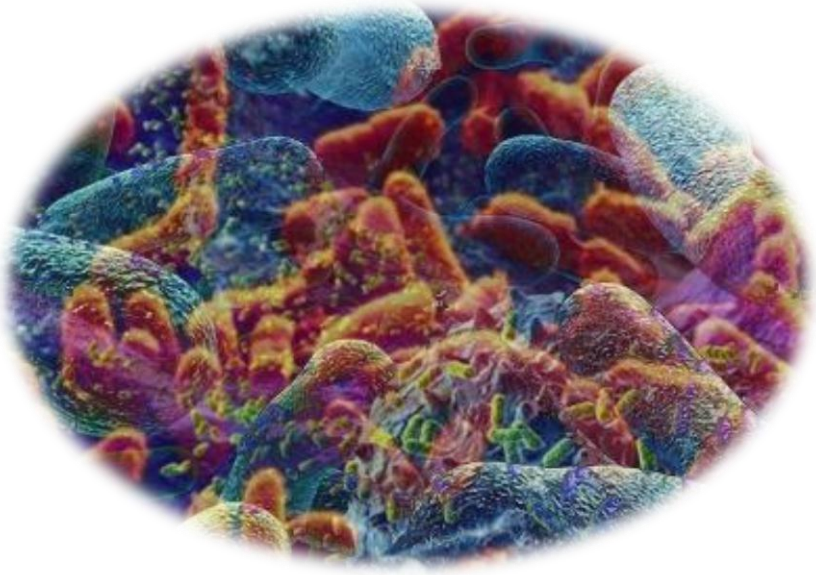
431 Microbiology Team

Malaria

GIT & HAEMATOLOGY BLOCK



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Species of malaria:

1. *Plasmodium falciparum:* malignant tertian malaria (most dangerous)
2. *Plasmodium vivax:* benign tertian malaria
3. *Plasmodium ovale:* benign tertian malaria
4. *Plasmodium malariae:* quartan malaria

- Mostly occur in warm areas

Tertian: occurs every 48 hours (every other day)

Quartan: occurs every 72 hours

Quatidian: Occurs everyday

Malaria life cycle:

- Exo-erythrocytic (hepatic) cycle: Mainly transmitted by mosquitos → Sporozoites are injected and travel to the liver → they divide and mature silently until they rupture as merozoites
- Erythrocytic cycle: Merozoites will invade RBCs and become immature trophozoites (ring stage) → mature trophozoites → Schizont → rupture and invade other RBCs
- Some of the ring stages will develop into Gametocytes (sexual stage)
- Pathogenicity occurs due to involvement of **red blood cells**
- The infective stage: Sporozoites
- The diagnostic stage: Gametocytes or during the ring stage

In P. vivax and P. ovale cases we might find Hypnozoites in the liver that are characterized by delayed primary development that even when they are treated from red blood cells they may cause relapses

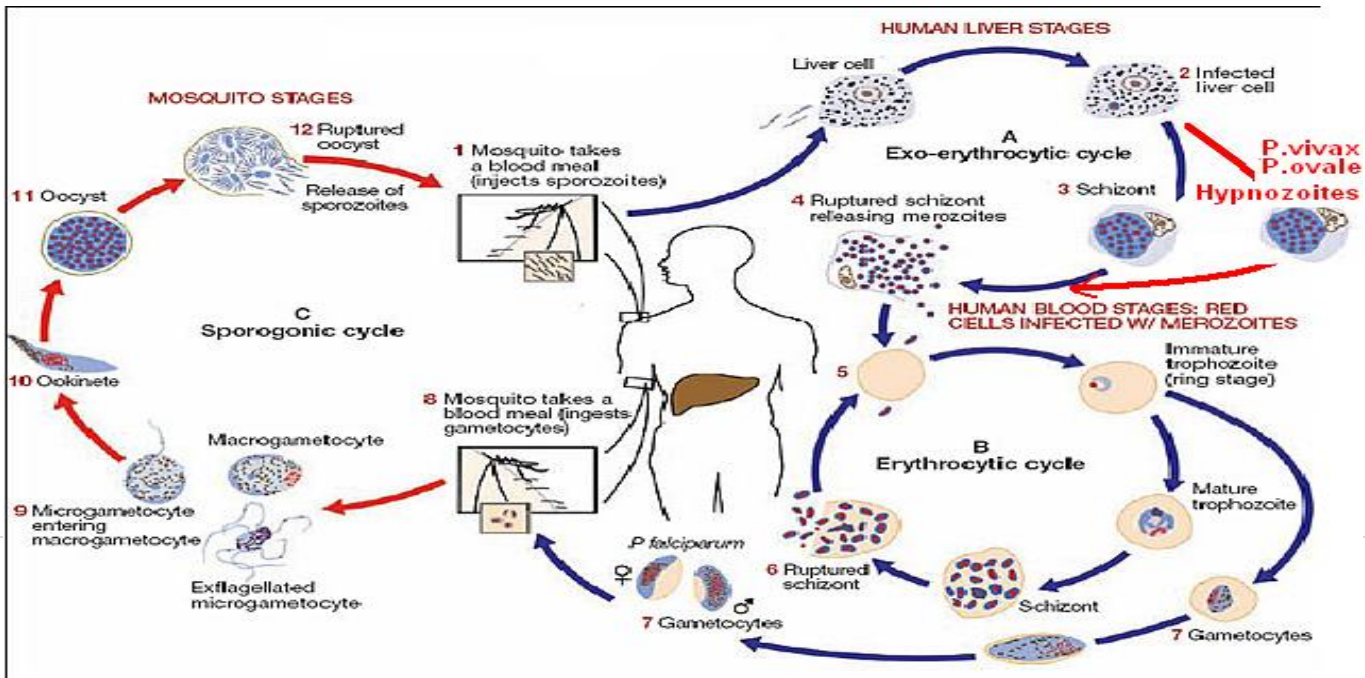


Figure 1—Malaria parasite life cycle. A malaria-infected female Anopheles mosquito inoculates sporozoites into the human host. Sporozoites infect liver cells and mature into schizonts, which rupture and release merozoites that infect red blood cells. Ring-stage trophozoites mature into schizonts, which rupture, releasing merozoites. Some parasites differentiate into sexual erythrocytic stages (gametocytes). Parasites in the blood are responsible for the clinical manifestations of the disease. Adapted from the CDC.

CLINICAL SIGNS & SYMPTOMS

Malarial Paroxysm

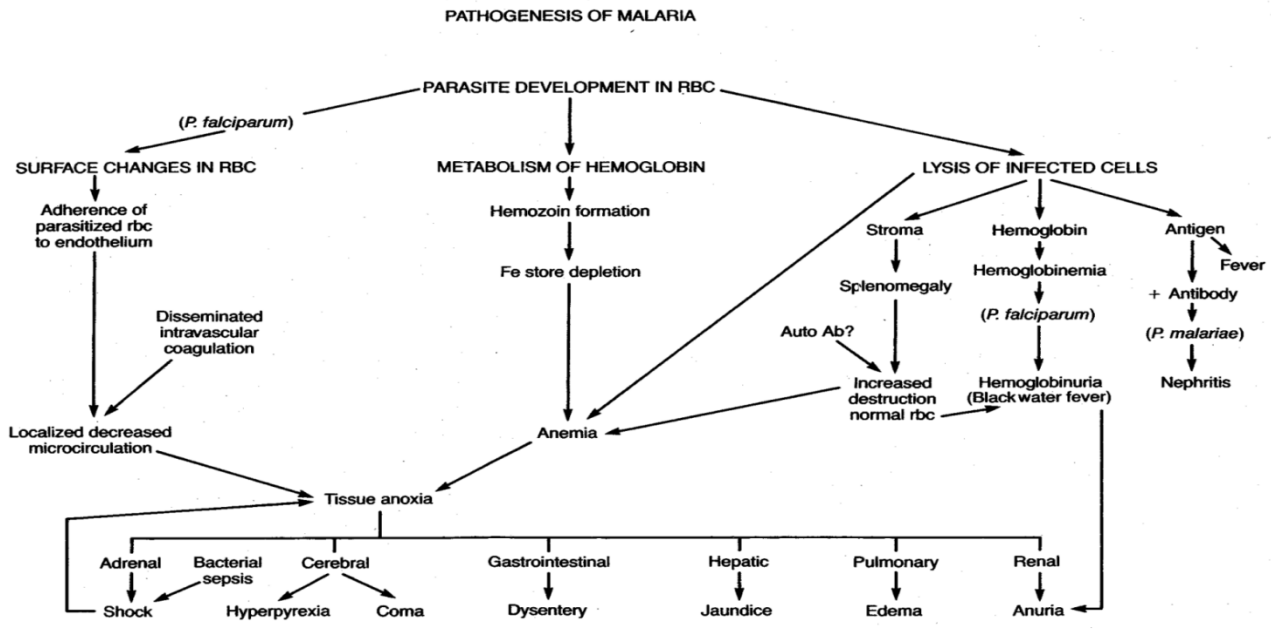
A cycle of cold stage followed by hot stage and then sweating stage

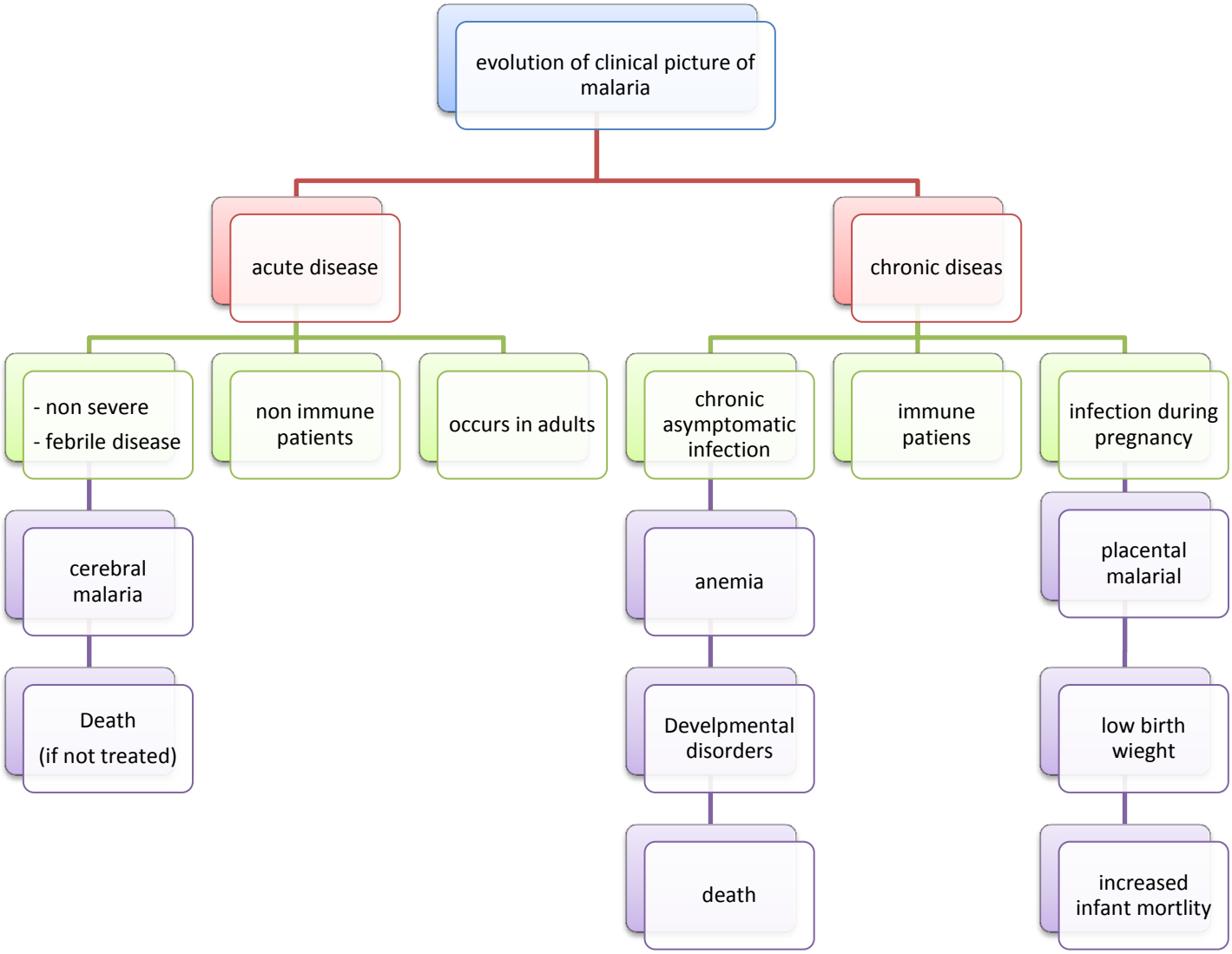
Clinical stages	*Plasmodium falciparum*	*Plasmodium vivax* ---------- *Plasmodium ovale*	*Plasmodium malariae*
Periodicity	Quotidian, tertian, irregular	48 hours, tertian	72 hours, quartan
Cold stage	• Feeling of intense cold • Vigorous shivering • Lasts 15-60 minutes		
Hot stage	• Intense heat • Dry burning skin • Throbbing headache • Lasts 2-6 hours		
Sweating stage	• Profuse sweating • Declining temperature • Exhausted and weak ⟶ sleep • Lasts 2-4 hours		

Pathogenesis of Malaria:

Due to two mechanisms:

- Anemia (due to lysis of RBC and metabolism of hB)
- Impairment of microcirculation (affect all organs):
  Due to abnormal surface of RBC it adheres to the endothelial surface of the blood capillaries which results in impairment of microcirculation and tissue anoxia





Uncomplicated Malaria:

Symptomatic infection with malaria parasitemia **without** signs of severity or evidence of vital organ dysfunction

* Mostly fever attacks

Complicated (Severe) Malaria:

Symptomatic malaria in patients with ***P. falciparum* asexual parasitaemia** with one or more of the following complications:

- **Cerebral malaria** Most series
- **Generalized convulsions** (more than 2 episodes within 24 hours)
- Severe normocytic anemia
- **Hypoglycemia** Very common
- Metabolic acidosis with respiratory distress
- Fluid and electrolyte disturbances
- **Acute renal failure** *(urine <400 ml/24 h in adults; 12 ml/kg/24 h in children)*
- **Acute pulmonary edema** and adult respiratory distress syndrome
- Abnormal bleeding
- Jaundice
- Malarial Hemoglobinuria
- Circulatory collapse, shock, septicemia (algid malaria)
- **Hyperparasitaemia** *≥10% in non-immune; ≥20% in semi-immune (Semi-immune is a patient that lives in an area where P. falciparum is widely spread)*

Cerebral Malaria: unrousable coma, not caused by other issues, CSF cell count is normal

Malarial Hemoglobinuria: Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency may develop intravascular haemolysis and haemoglobinuria precipitated by primaquine and other oxidant drugs, even in the absence of malaria. Haemoglobinuria associated with malaria ("blackwater fever") is uncommon and malarial haemoglobinuria usually presents in adults as severe disease with anaemia and renal failure

Common methods for parasitological diagnosis of malaria

The two methods common in use:

1. **Light microscopy: The gold standard**
   - ❖ Parasite density
   - ❖ Species diagnosis
   - ❖ Monitoring response to treatment
   - ❖ Features of Plasmodium : Vacuole | Neucleus (with chromatin dot) | Cytoplasm | stippling
2. **Rapid diagnostic tests (RDTs):** for the detection of malarial antigens

The products come in a number of formats:

- ❖ Plastic cassette
- ❖ Card
- ❖ Dipstick
- ❖ Hybrid cassette-dipstick

Plasmodium falciparum (trophozoite stage)

Diagnostic Points:

- ❖ Small, regular, fine to fleshy cytoplasm
- ❖ Infected RBCs not enlarged
- ❖ Numerous, multiple infection is common
- ❖ Ring, comma, marginal or accole forms are seen; often have double chromatin dots
- ❖ Maurer's dots not clearly visible

ACTION OF ANTIMALARIAL DRUG IN THE DIFFERENT LIFE STAGES OF THE MALARIA PARASITE

Anti-relapse *(P.vivax)*
- primaquine

Gametocyide
- Primaquine

Blood Schizontocides
- Chloroquine
- Sulfadoxine/Pyrimethamine
- Quinine
- Quinidine
- Artemisinins

Sporontocides
- Primaquine
- Pyrimethamine
- Proguanil

The dr. mentioned that the drugs should be studied from the pharmacology lecture

Summary

- Pathogenicity occurs due to involvement of RBCs

- P. Falciparum is the most infectious because it affects RBCs of all ages and causes severe malaria.

Species:

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Pathogenisis:

- Anemia
- Impairment of microcirculation

Complicated (severe) malarial symptoms:

- Cerebral malaria most serious
- Hypoglycemia very common
- Acute pulmonary edema

Common methods for diagnosis:

- The gold standard: light microscopy
- Rapid diagnostic test for detection of malarial Ags

Questions

A. Most pathogenic parasite is:

A. Plasmodium falciparum
B. Plasmodium vivax
C. Plasmodium ovale
D. Plasmodium malariae

B. A patient comes to the hospital with a fever recurring every 72 hours (3 days). Which of the following is the most likely pathogen?:

A. Plasmodium ovale
B. Plasmodium malariae
C. Plasmodium falciparum
D. Plasmodium vivax

C. At which stage will the red blood cells get invaded

A. Sporozoite stage
B. Merozoite stage
C. Gametocyte stage

D. If a patient got the parasite from a blood transfusion, which stage of malaria life cycle will he miss?

A. Exo-erythrocytic Cycle.
B. Erythrocytic Cycle.
C. Sporogonic cycle.

Answers: -

1- (A)
2- (B)
3- (B)
4- (A)