Current Perspectives on Malaria:

Challenges and Solutions

Presented by

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Learning Objectives

1. Introduction
2. Epidemiology
3. Clinical classification & Incubation period
4. Route of transmission & Life cycle of Malaria
5. Clinical presentation of Malaria & types of fever
6. Laboratory diagnosis & treatment of Malaria
7. Complication & prevention of Malaria

Introduction

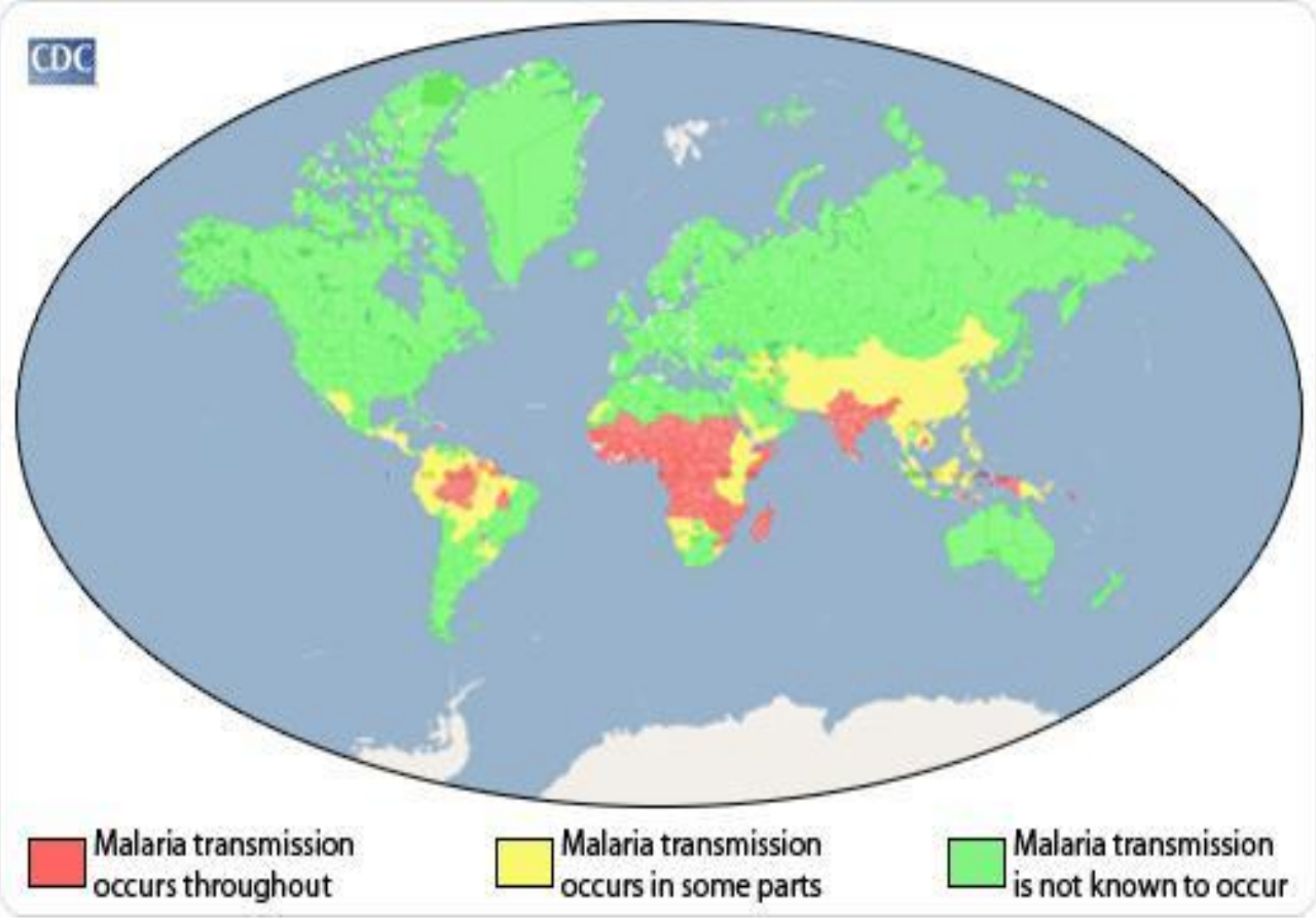
- Malaria is a Mosquito-Borne febrile disease caused by malarial parasites.
- Malaria (Mala means Bad and Aria means Air) is a protozoal infection.
- A disease caused by members of the protozoan genus ***Plasmodium***, a wide spread group of sporozoans that parasite affect the human liver and red blood cells.
- Human are infected with Plasmodium protozoa when bitten by an infective **female Anopheles mosquito vector.**

Epidemiology

- Malaria continuous to be **one of the most important** and devastating infectious diseases in developing areas of the world.
- As of the **World Health Organization's 2025** malaria update (data reflecting 2024), the global malaria situation is **characterized by a continued, alarming increases in cases despite significant efforts in vaccination and control.**

- As estimated **282 million** malaria cases occurred in 2024, a **3% increase** (approx. 9 million more) compared **to 2023.**
- Estimated malaria deaths in **2024 stood at 610,000, slightly higher than 598,000 reported in 2023**.

Epidemiology of Malaria



Species of Malaria

There are 4 species of malarial parasites:

1. *Plasmodium Falciparum*
2. *Plasmodium Vivax*
3. *Plasmodium Ovale*
4. *Plasmodium Malariae*

- **The most dangerous of the four is *P.falciparum* .**

Malarial Species Found in Bangladesh

- The following 2 species of plasmodium are more common in Bangladesh-

i. ***Plasmodium vivax***: common in plain land areas.

ii. ***Plasmodium Falciparum***: common in hilly areas.

Newer Species

- A fifth species, ***Plasmodium knowlesi*** malaria in macaques but can also infect humans.

- Discover in **2004.**

Clinical Classification of Malaria

Clinical types of malaria	**Plasmodium parasite**
Benign tertian malaria	*Plasmodium vivax* *Plasmodium ovale*
Malignant tertian malaria	*Plasmodium falciparum*
Quartan malaria	*Plasmodium malariae*

Incubation Period

Malaria Parasite Name	Incubation Period
P. falciparum	9 to 14 days
P. vivax	8-17 days
P. ovale	16-18 days
P. malariae	18-40 days

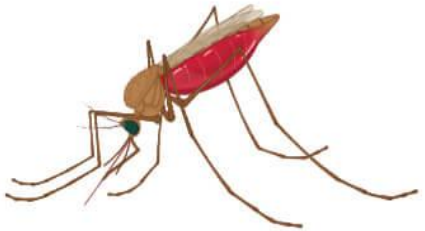
Routes of Transmission

- **Vector transmission:** Bite by an infective female anopheles mosquitoes.
- **Direct transmission.**
- **Blood transfusion**, the parasite can live for 14 days in blood bottles under - 4°C.
- **The use of contaminated needles.**
- **Mother to new born (via placenta).**

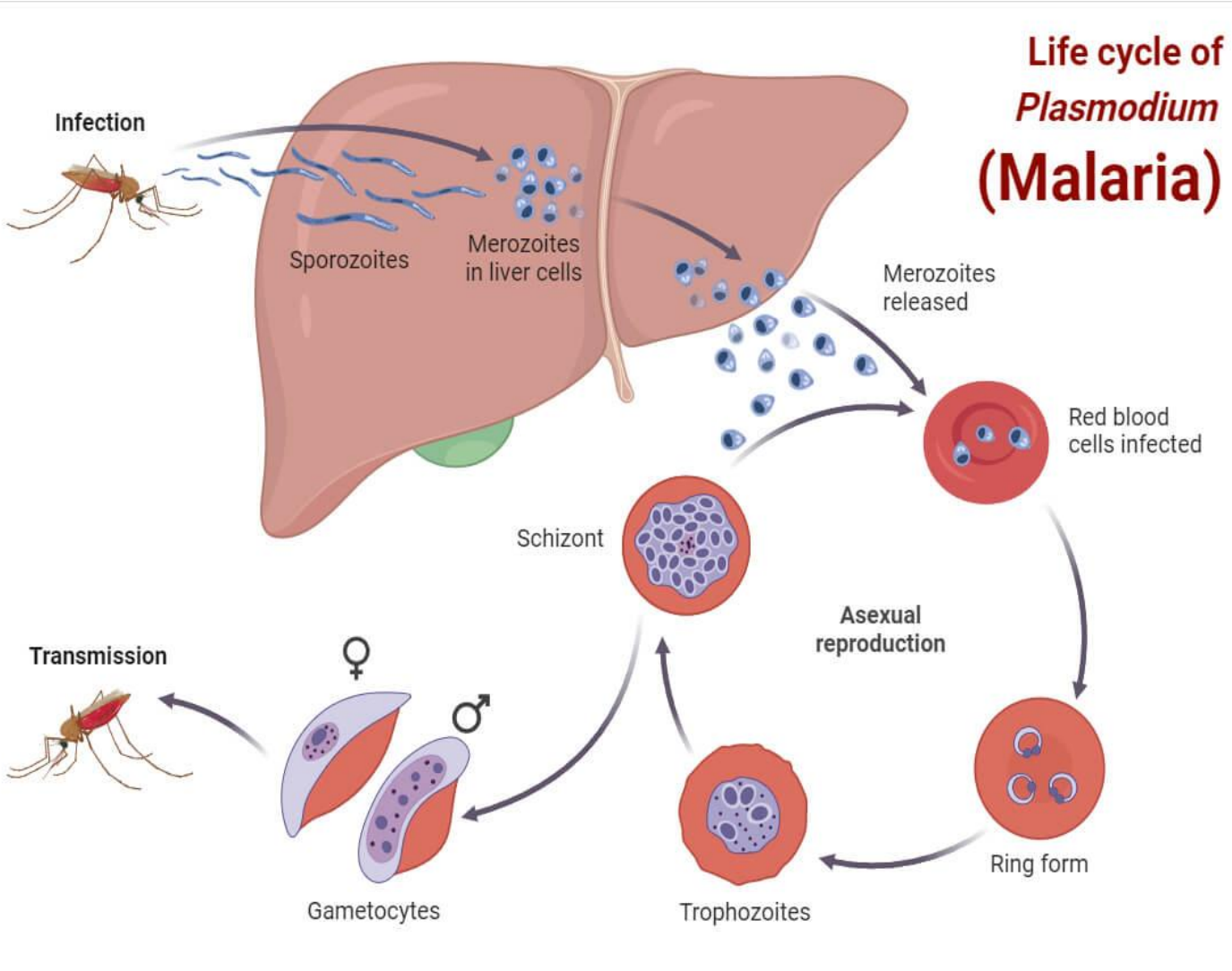
Life Cycle of Malaria (Human)

Sporozoite

Merozoite

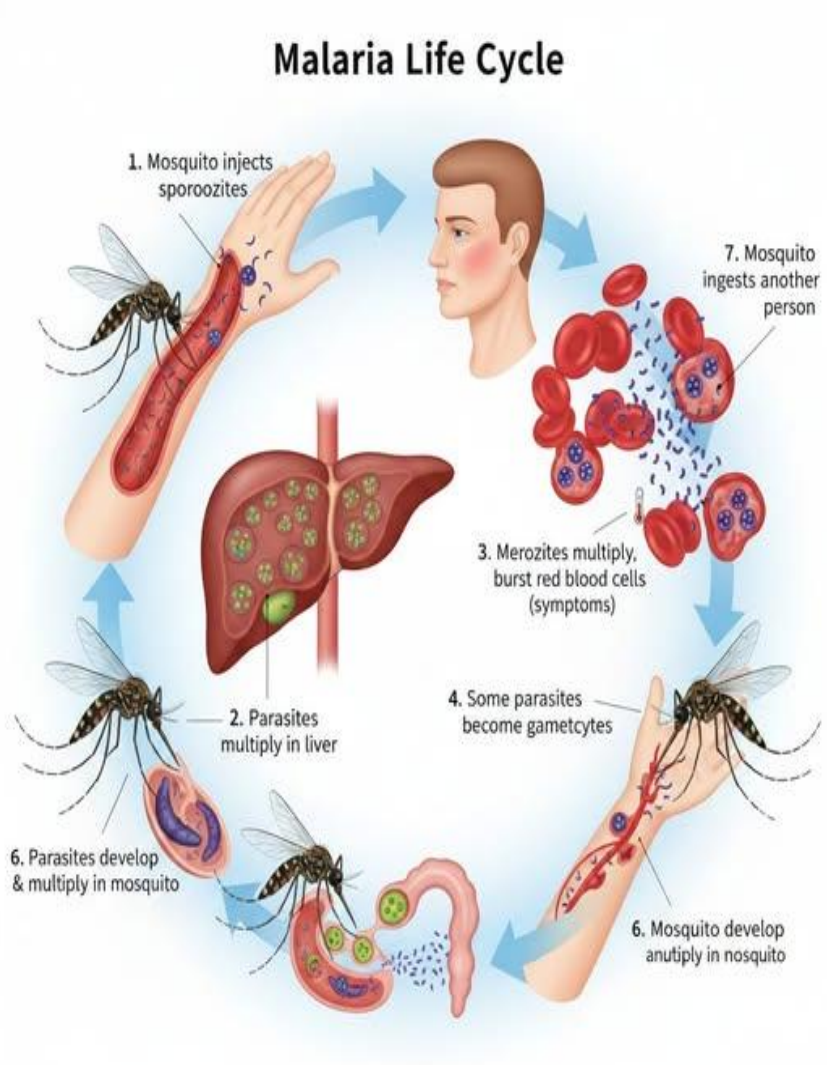


Female Anopheles Mosquito



Event Occurs in Human (after bite of mosquito)

- Man-Intermediate host.
- Mosquito-definitive host
- **Sporozoites are the infective form.**
- Present in the salivary gland of **female anopheles mosquito.**
- After bite of infected mosquito **sporozoites are introduced into blood circulation.**



Pre-erythrocytic schizogony

cont….

Mosquito bite

↓

Sporozoites injected to host

↓

Spreads to surrounding tissue

↓

Peripheral circulation

↓

Enter into liver parenchyma

↓

Sporozoites become schizonts

Continue…..

Rupture of schizonts

Liberation of merozoites

- Micro-merozoites ➡ Enter into circulation.
- Macro-merozoites ➡ Re-enter into liver cell.

Erythrocytic Schizogony

Micro-merozoites enters into RBC

Then merozoites, which mature into ring forms **(Trophozoites)**

Schizont

Rupture of schizonts

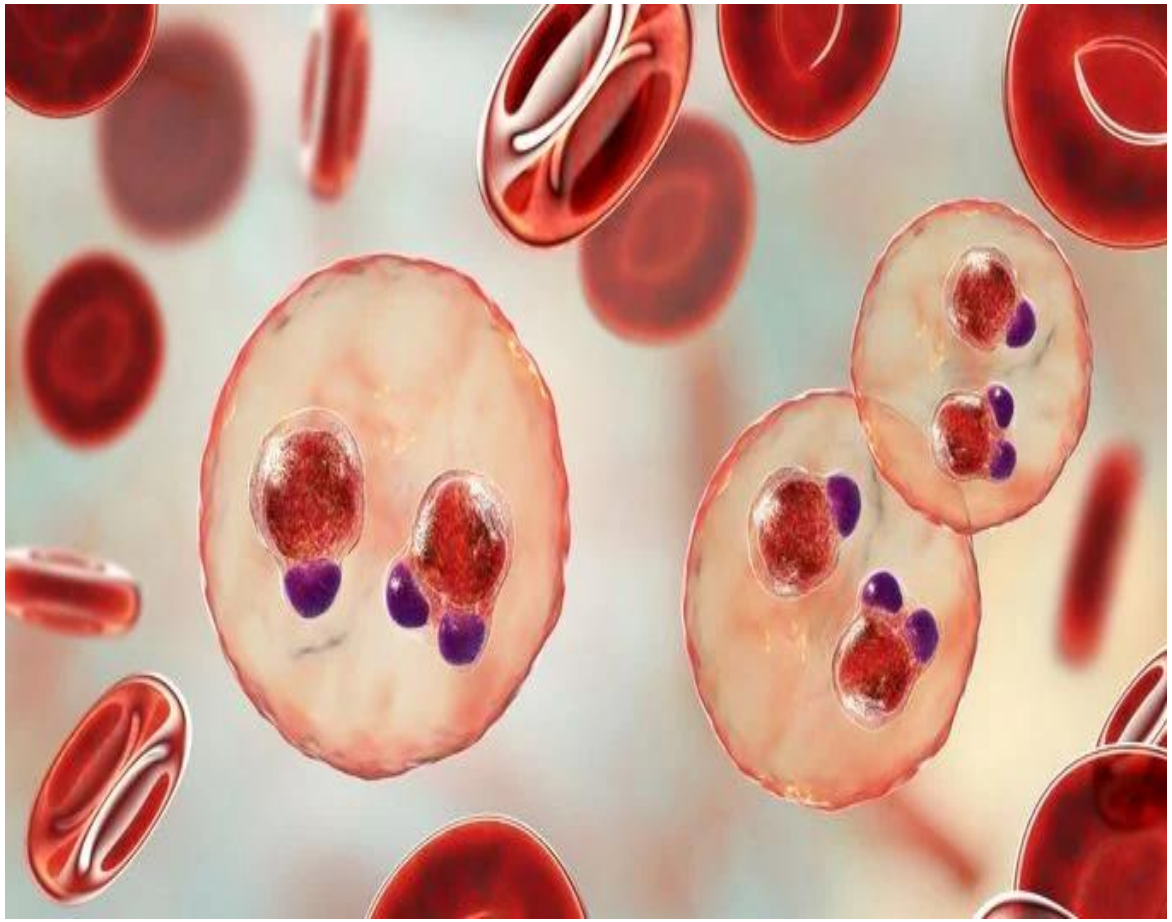
Liberation of merozoites

Attack healthy RBC

↓

Cycle is repeat.

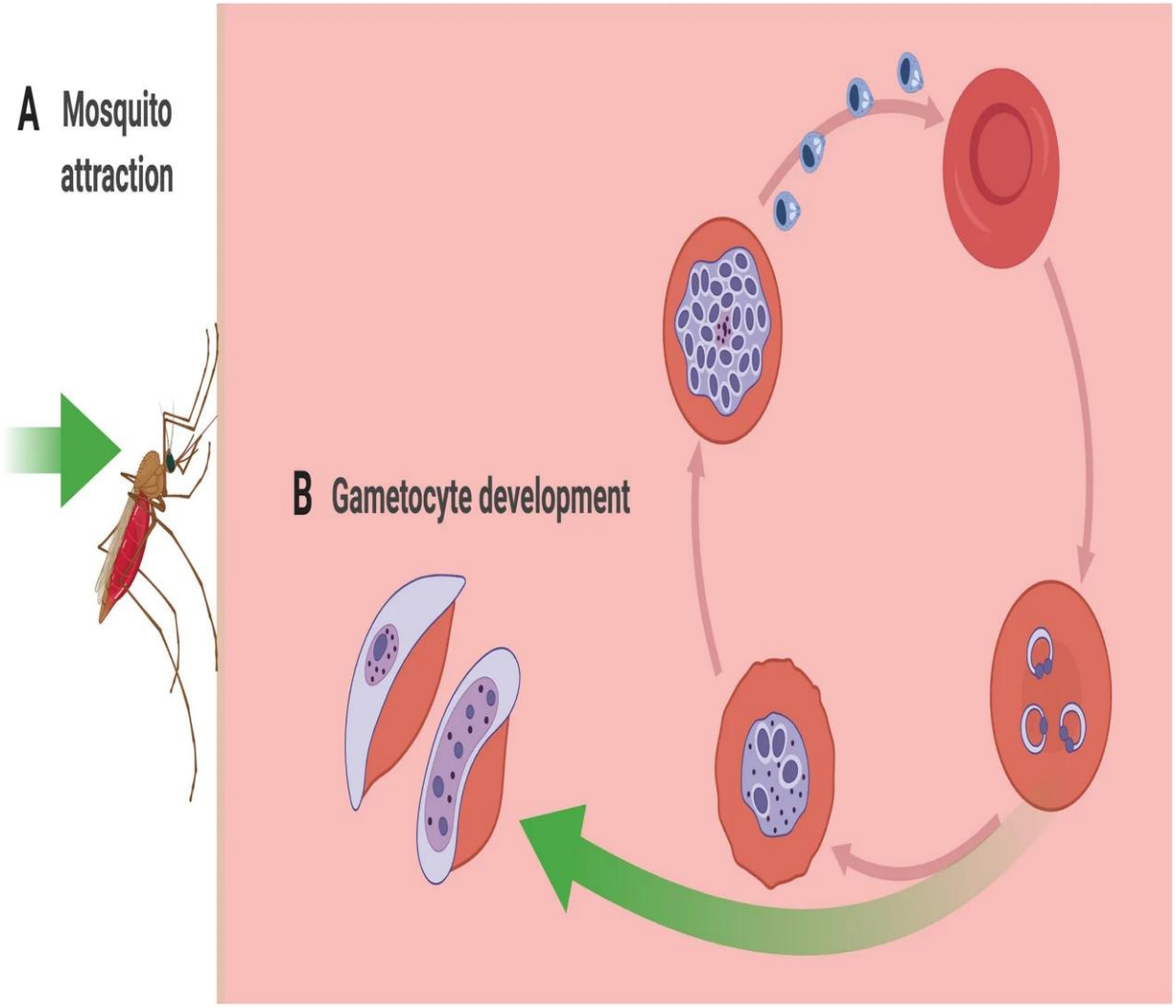
This phase is responsible for clinical attack of malaria.



Gametogony

Gametocytes develop within RBC, primarily in the capillaries of internal organ (spleen, bone marrow).

Peripheral blood film.



Exo-erythrocytic Schizogony

- Except ***P. falciparum***, in other species of plasmodium, there is an exoerythrocytic schizogony. Because the tissue phase persists in the form of merozoites life cycle, parasite remains dormant of potentially infective to give rise to infection to time (relapse).

Clinical Presentation

❖ Cold Stage

- lasts approximately **15 min to 1 hour.**
- During which time the parasites invade the red blood cells and destroy them, resulting in fever, shivering, headache, cough, high blood pressure etc.

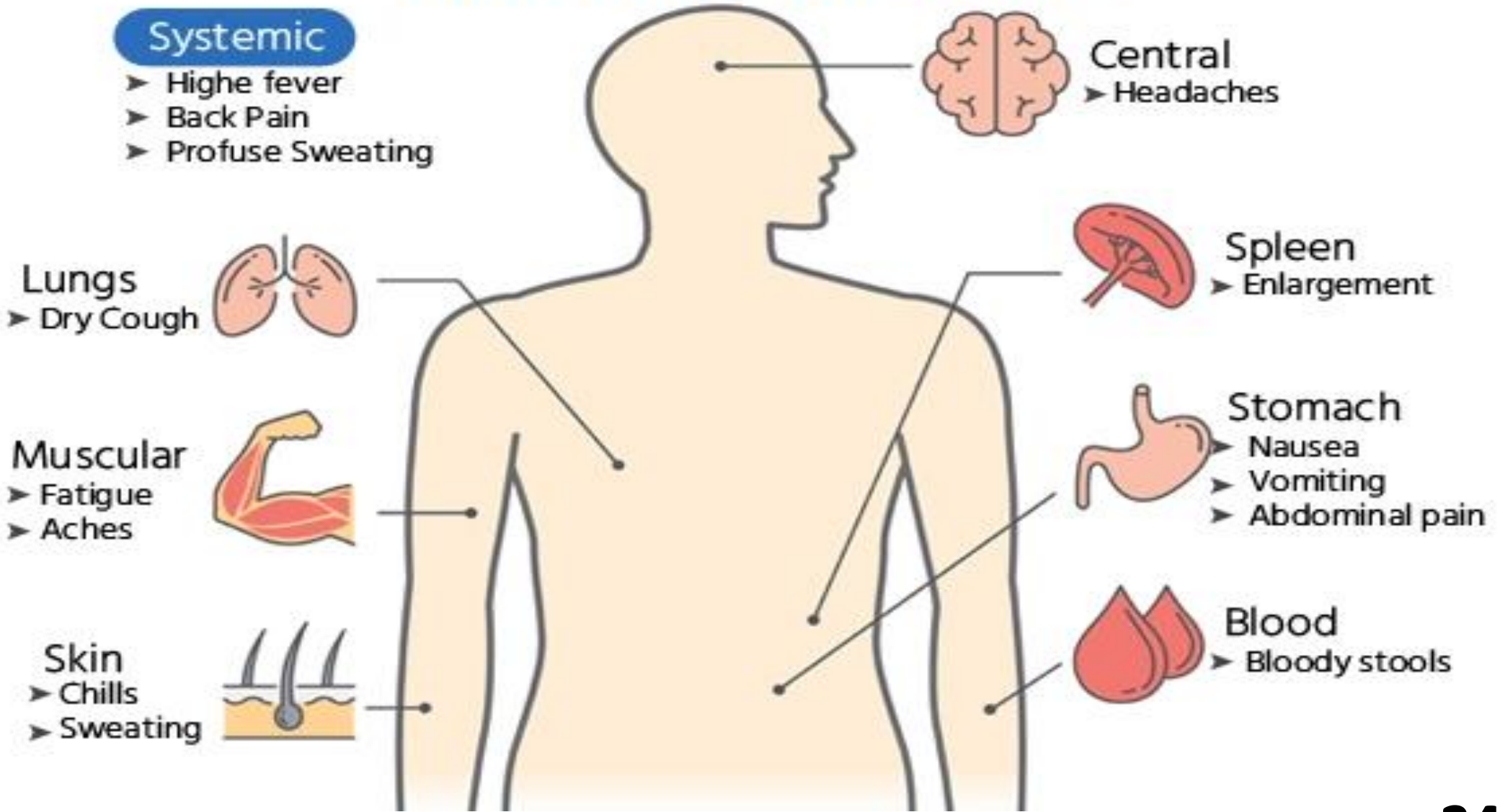
❖ Hot Stage

- **Approximately 2 hours after first stage and lasts for 2-4 hours.**
- High fever may reach upto **40°- 41°C.**
- **Severe headache, vomiting and hot, dry flushed skin.**

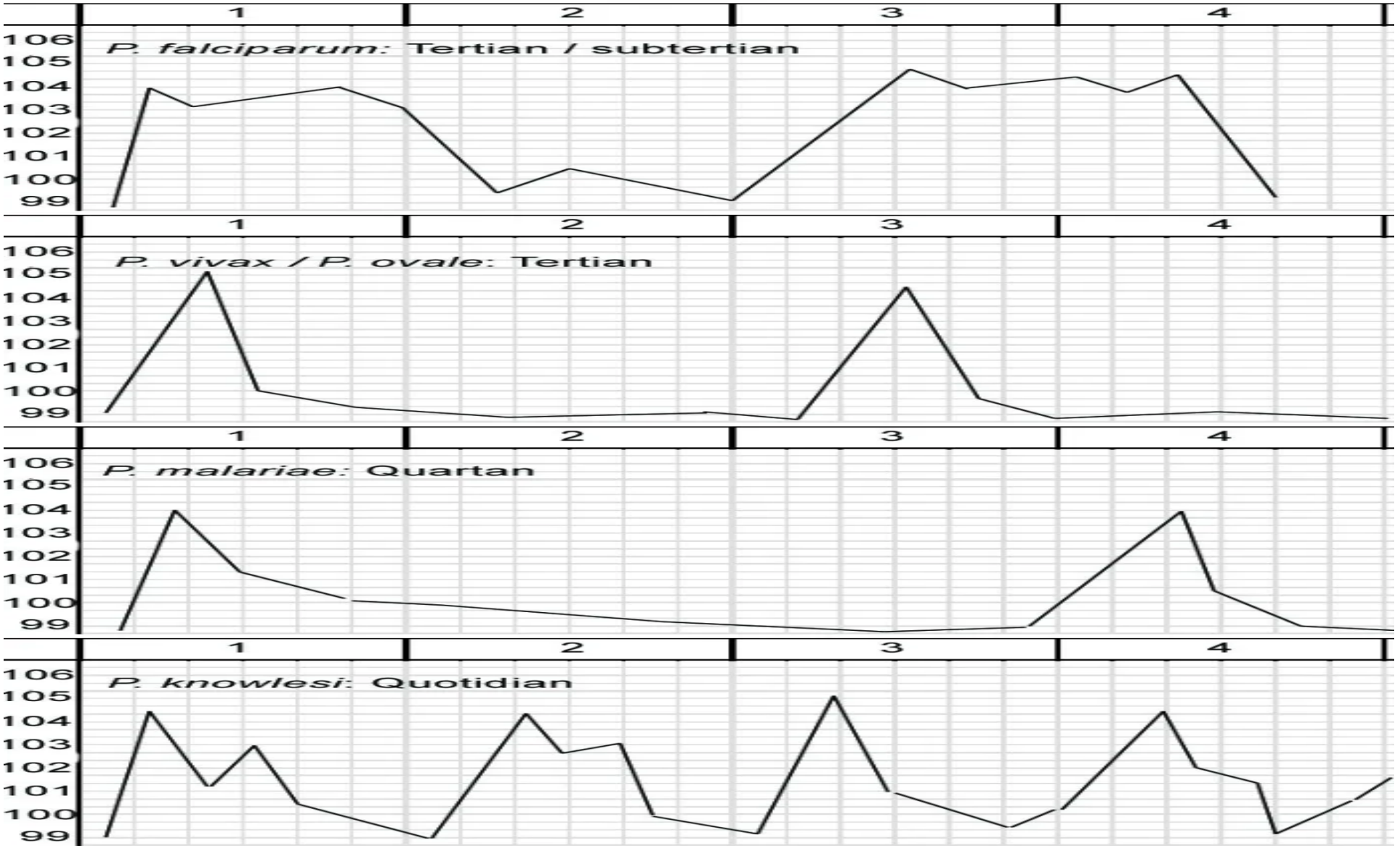
❖ Sweating Stage

- Patient starts with sweating, follows the hot stage and the temperature comes down to normal.
- The patient often feels exhausted and falls into a deep sleep.
- **Lasts for 2-4 hours.**

MALARIA SYMPTOMS



Types of Fever in Different Types of Malaria



P. Falciparum is More Dangerous

- They can infect **both mature & immature RBC (reticulocytes).** So there is **severe anemia**. **On the other hand, other malaria species only infect immature RBC.**
- Falciparum shows resistance to common antimalarial drugs.
- **Complications are higher and fatal**, e.g.-cerebral malaria, black water fever etc.
- **Early diagnosis is difficult,** so patient rapidly developed complications.

Malaria Kills More People Than AIDS

- Malaria kills in **one year** what AIDS kills in **15 years**. For every death due to HIV/AIDS there are about **50 deaths** due to malaria. To add to the problem is the increasing drug resistance to the established drug.

Diagnosis of Malaria

Laboratory Diagnosis of Malaria

1. Microscopic diagnosis:

- **Light microscopy**
- **Fluorescent Microscopy**

2.Antigen detection:

- **Immunochromatographic Dipstick: RDT**
- **Parasite -F Test**
- **Dual Antigen Test**

3. Culture of malarial parasite:

- RPMI 1640

4. Serology:

- IFA
- ELISA

4.Molecular diagnosis:

- PCR

Procedure of Preparing of Blood Film

- **Three basic steps to make blood film:**

1. Preparation of blood film
2. Fixation of blood film.
3. Staining of blood film.

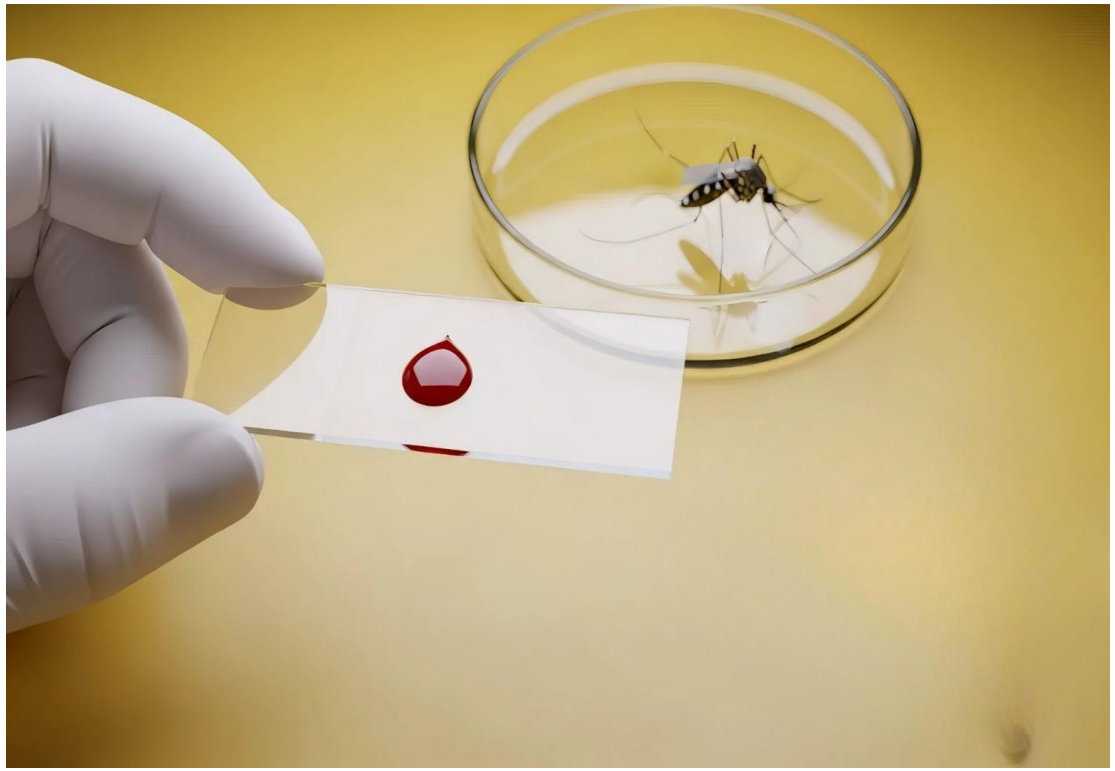
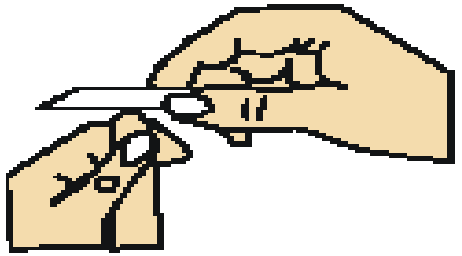
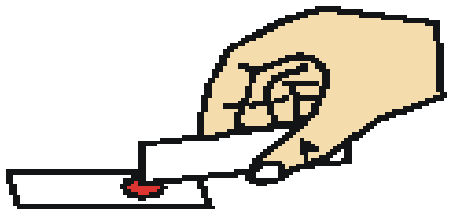


Figure A-2. Preparation of a thin and a thick blood film on the same slide.



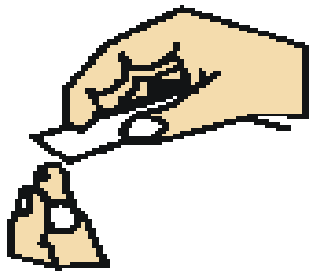
1

Touch the blood drop with a clean slide.



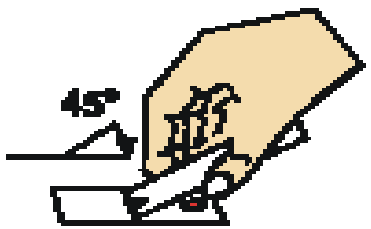
2

Using the corner of another slide, spread the blood drop into the shape of a circle or square of ~1cm^2.



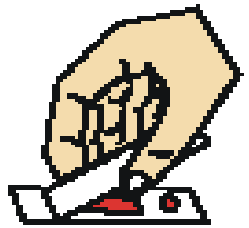
3

Gently squeeze the patient's finger again, and touch the edge of a clean slide to the newly formed blood drop.



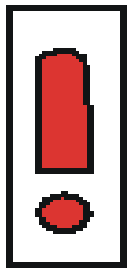
4

Take this slide and hold the edge that has the blood drop at an ~45° angle against the surface of the first slide. Wait until the blood completely spreads along the edge of the second slide.



5

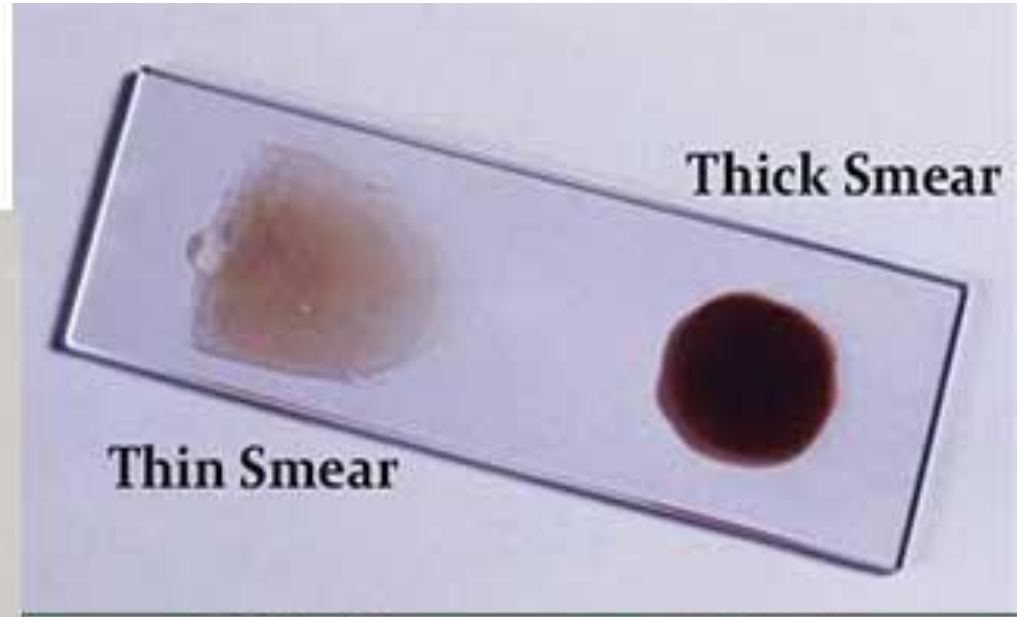
While holding the second slide at the same angle, rapidly and smoothly push the slide forward.

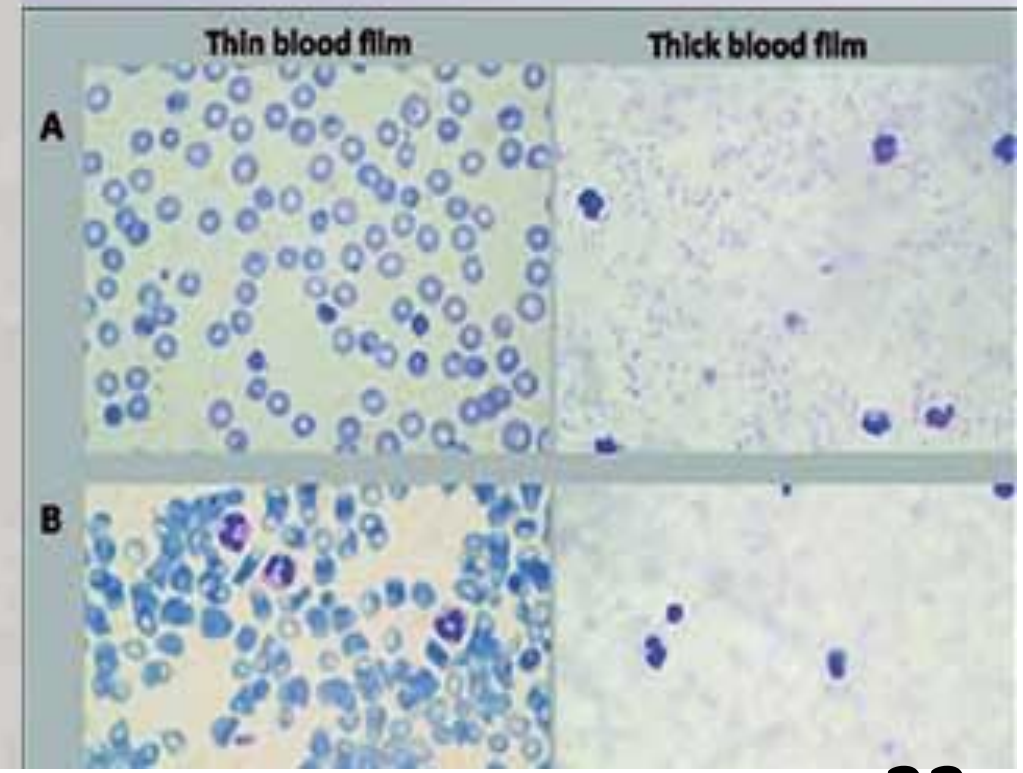


6

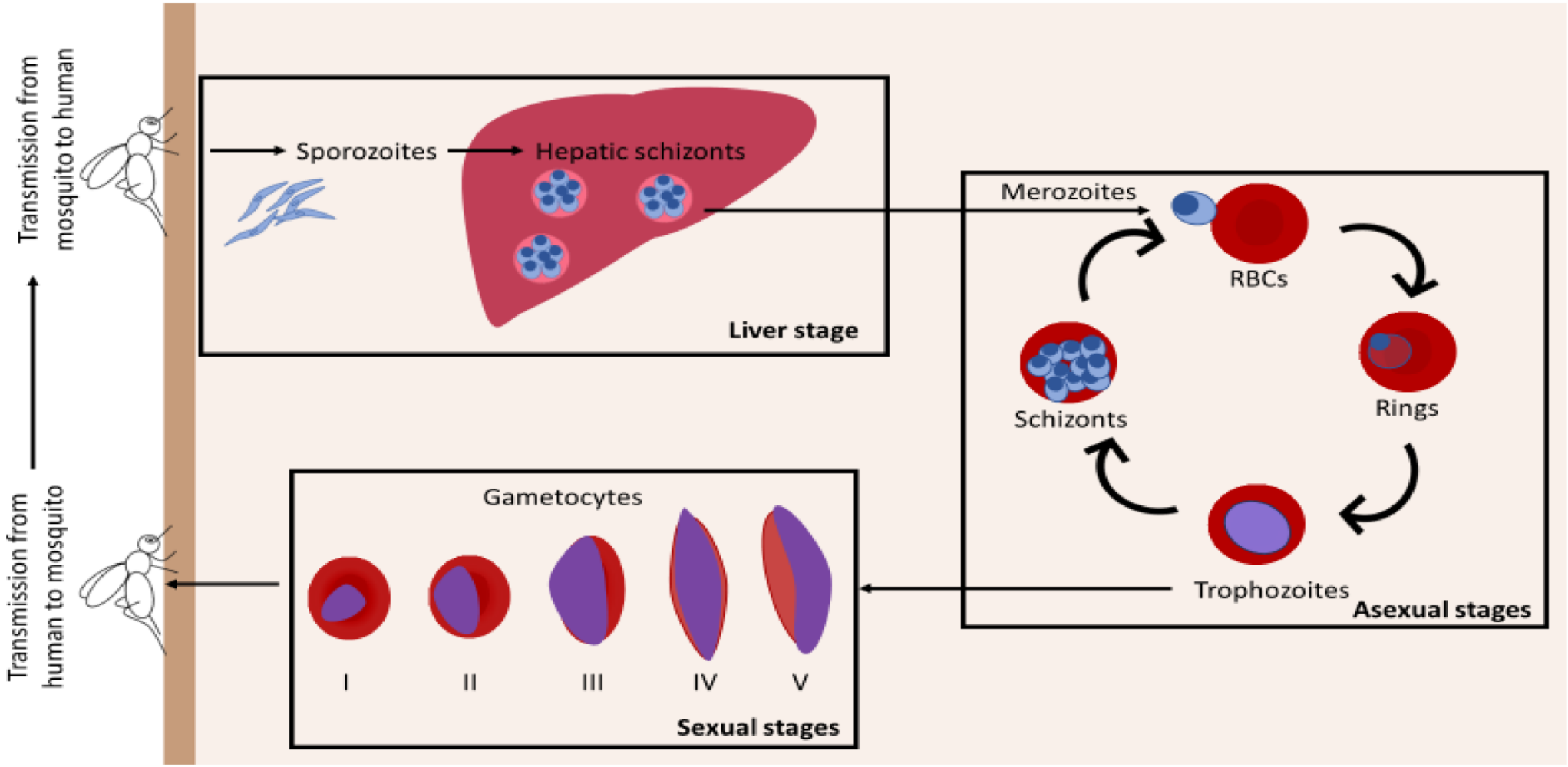
Write the identification number on the slide. Wait until the thick film is completely dry before staining it.

Thick Blood Smear and Thin Blood Smear

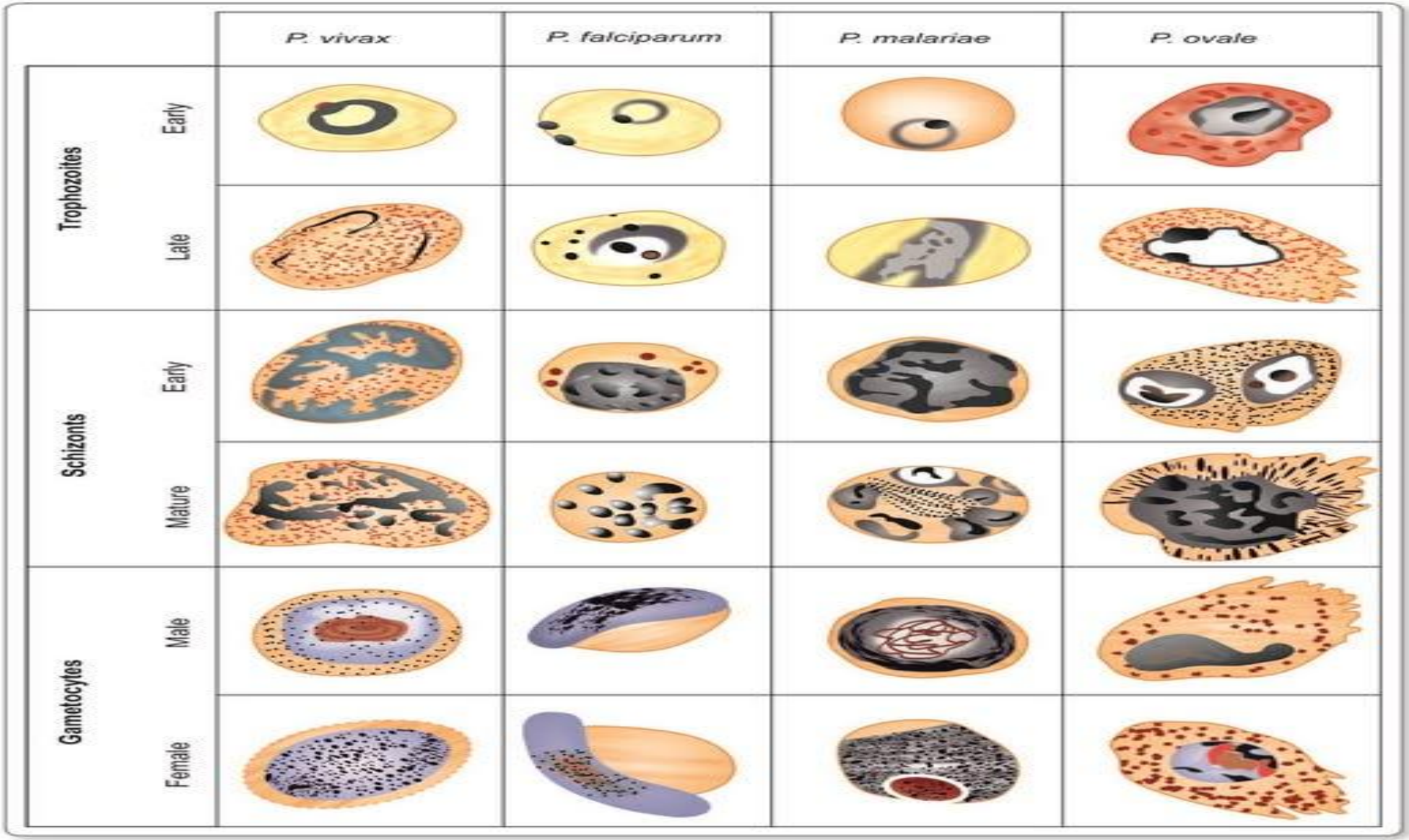




Malaria Parasite Erythrocytic Stage



Species Differentiation on Thin Film



Malaria Antigen Detection

❑Parasite -F Test

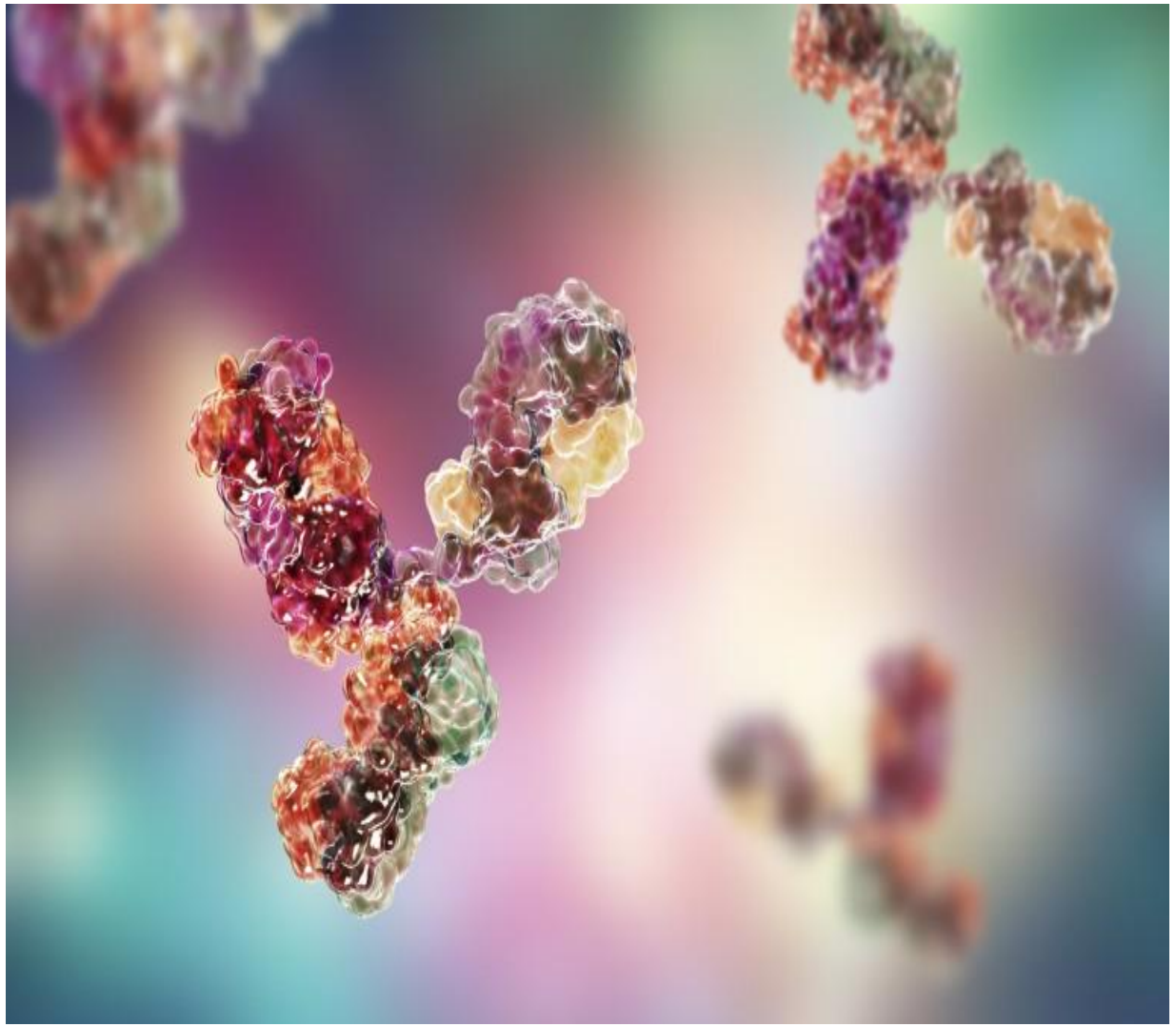
- This test is based on detection of **histidine rich protein-2** (HPR-2) antigen produced by asexual stages of ***P. falciparum*** expressed on the surface of red cells.
- Monoclonal antibody produced against HPR-2 antigen is employed in the test strip.

❑ Dual Antigen Test

- The test detects parasite **lactate dehydrogenase** produced by trophozoites and gametocytes of all plasmodium species and PfHPR-2 antigen produced by P. falciparum simultaneously.

Malaria Serology-Antibody Detection

- Immunologic assays to detect host response.
- Antibodies to asexual parasites appear some days after invasion of RBCs and may persist for month.
- Positive test indicates past infections.
- Not useful for treatment decision.



Treatment of Malaria

Treatment schedule

I) Vivax or ovale malaria (*P. vivax* or *P. ovale* infection):

I) Chloroquine + Primaquine

A. Chloroquine Phosphate: 250 mg tablet (150 mg base)

- Day−1: 10 mg/kg (4 tablets for an adult)
- Day−2: 10 mg/kg (4 tablets for an adult)
- Day−3: 5 mg/kg (2 tablets for an adult)

B. **Primaquine:** 15 mg tablet

Dose: 0.25 mg/kg daily for 14 days.

II)Uncomplicated falciparum malaria (UM):

A. Co-artemether: Artemether (20 mg) + Lumefantrine (120 mg):

- If body weight is >35 Kg: total 6 doses (each contains 4 tablets)

➢ Day−1: at 0 hour (stat) and 8 hours.

➢ Day−2: at 24 hours and 36 hours.

➢ Day−3: at 48 hours and 60 hours.

- Primaquine: 15 mg tablet

➢ Dose: 0.25 mg/kg single dose.

B. Alternative regimens:

- Artesunate + Amodiaquine: once daily for 3 days.
- Artesunate + Mefloquine: once daily for 3 days.
- Dihydroartemisinin + Piperaquine: once daily for 3 days.
- Quinine salt + Clindamycin/Doxycycline/Tetracycline:7 days+7 days.
- Atovaquone + Proguanil (Malarone): 4 tablets once daily for 3 days.

III) Complicated (severe) falciparum malaria(e.g; cerebral malaria):

A. I/V Artesunate followed by oral ACT full dose or alternative (with primaquine single dose).

- 2.4 mg/Kg at 0 (stat), 12, and 24 hours; and then every 24 hours.
  - Day−1: at 0 hour (stat) and 12 hours.
  - Day−2: at 24 hours.
  - Day−3 (maximum up to Day−5): at 24 hours.

B. Alternative regimens:

- I/M Artemether: 3.2 mg/Kg stat followed by 1.6 mg/Kg daily.
- I/V Quinine salt: 20 mg/Kg loading dose over 3−5 hours, followed by every 8 hours, 10 mg/Kg maintenance dose (over 4 hours).
- I/M Quinine salt (1:1 diluted): 10mg/Kg followed by 10 mg/Kg.

IV) Anti-malarial drugs in pregnancy:

Vivax malaria: chloroquine.

Uncomplicated malaria: coartemether, quinine + clindamycin, etc.

Complicated malaria: artesunate, artemether, quinine, etc.

PROPHYLAXIS OF MALATIA

Malaria Prophylaxis

- **In chloroquine sensitive areas:**

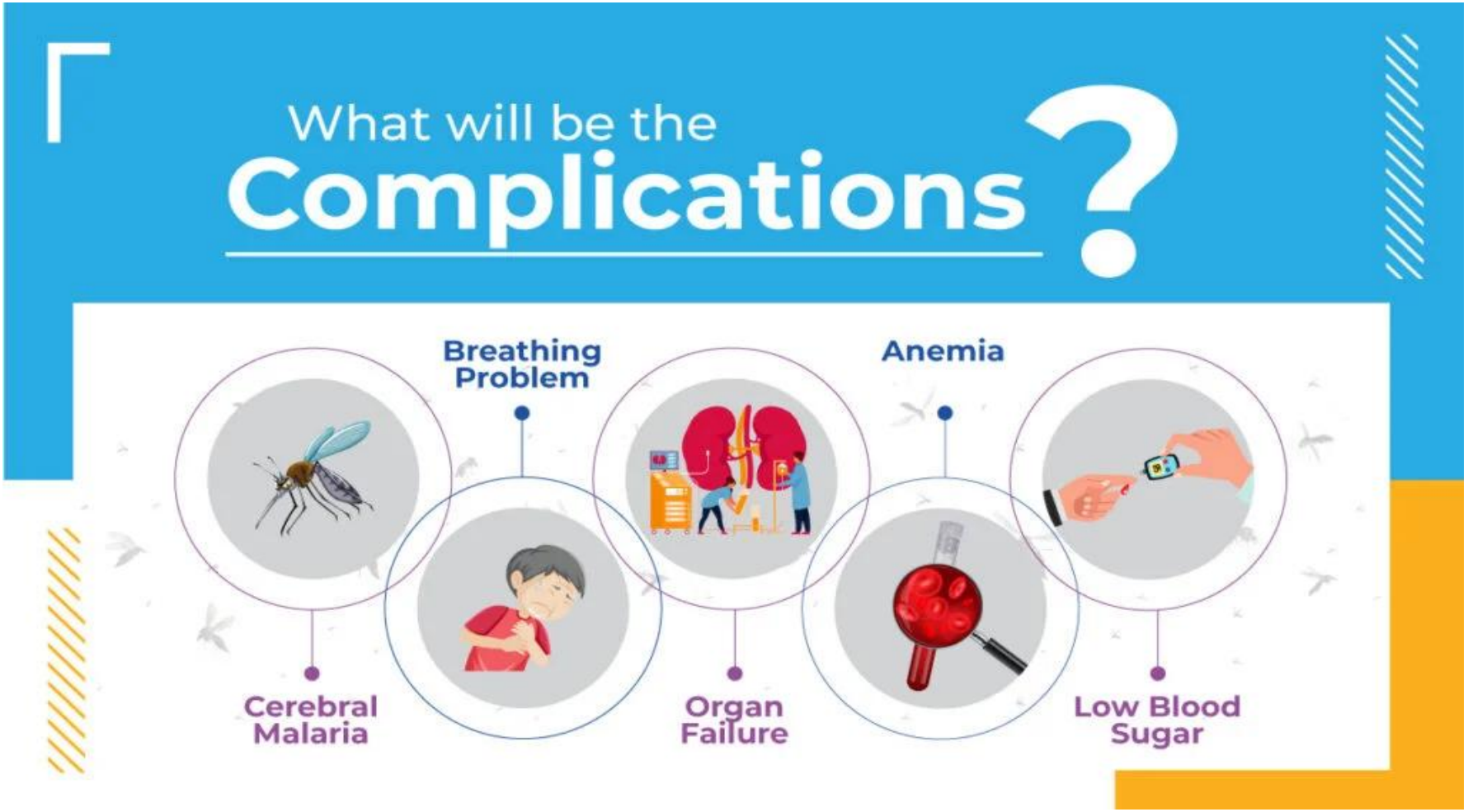
Drug	Note
Chloroquine (300mg base/week)+Proguanil (100-200 mg/day):	Start 1 week before the travel and continue up to 4 weeks after return.

Malaria Prophylaxis

- **In chloroquine resistant areas:**

Drug	Notes
Doxycycline(100mgonce daily):	Start 1 week before the travel and continue up to 4 weeks after return.
Mefloquine(250mg/weekly):	Start 2-3 weeks before the travel and continue up to 4 weeks after return.
Atovaquine + Proguanil (once daily):	Start 1-2 days before the travel and continue up to 1 week after return.

Complications of Malaria



Complications

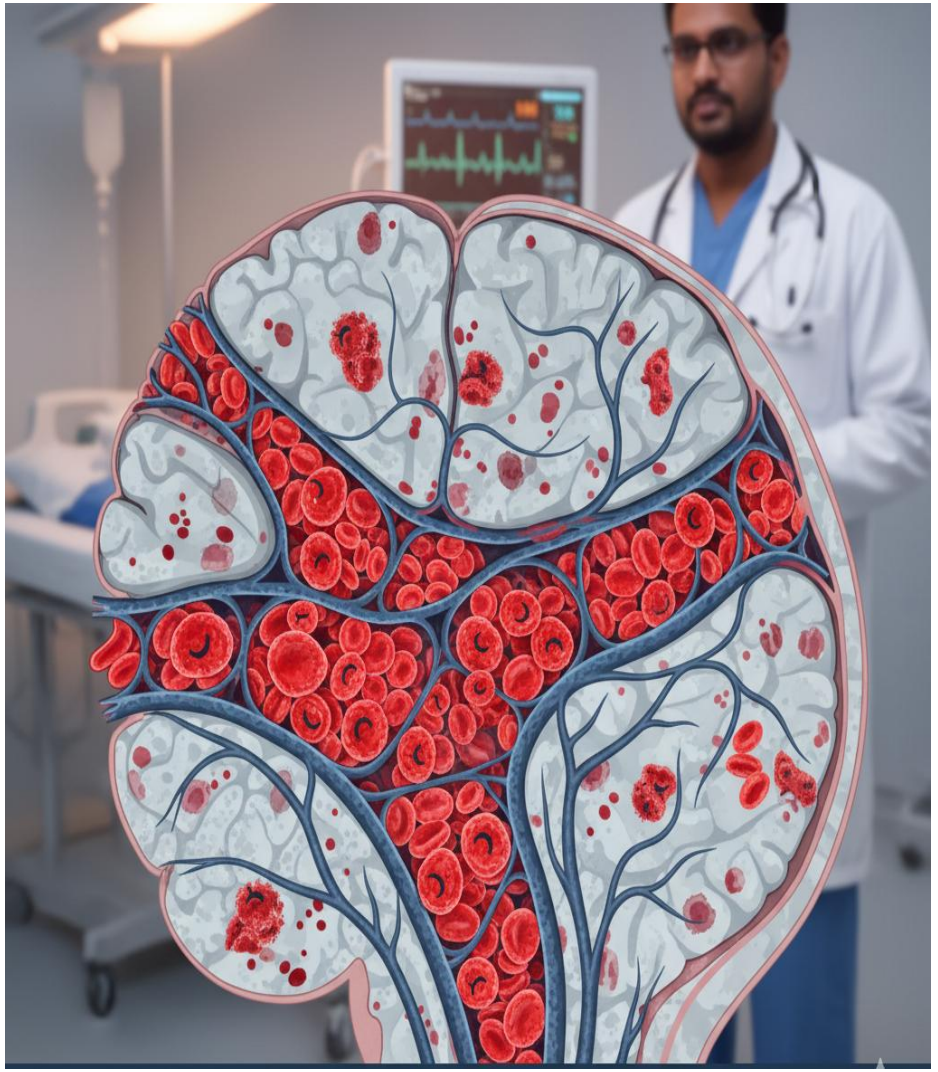
- Cerebral malaria
- Algid malaria
- Black water fever
- Hypoglycemia
- Pulmonary edema
- Acute renal failure
- Severe anemia
- Metabolic acidosis
- Bleeding disturbance
- Hyperparasitemia

Cerebral Malaria

- It is a serious complication of ***Plasmodium falciparum*** infection.
- Manifest as diffuse symmetric encephalopathy.
- **Common in children and young adults.**
- Despite treatment fatality rate is **~20%.**
- Long term sequelae is rare with appropriate treatment.

Pathogenesis

- Usually develops after several days after patient has become ill, but may develop suddenly.
- Occurs with parasitaemia >5%



Pathogenesis

Late schizonts secrete protein on the surface of RBCs

⬇

Protein cause aggregation of non infected RBCs capillary endothelium in brain

⬇

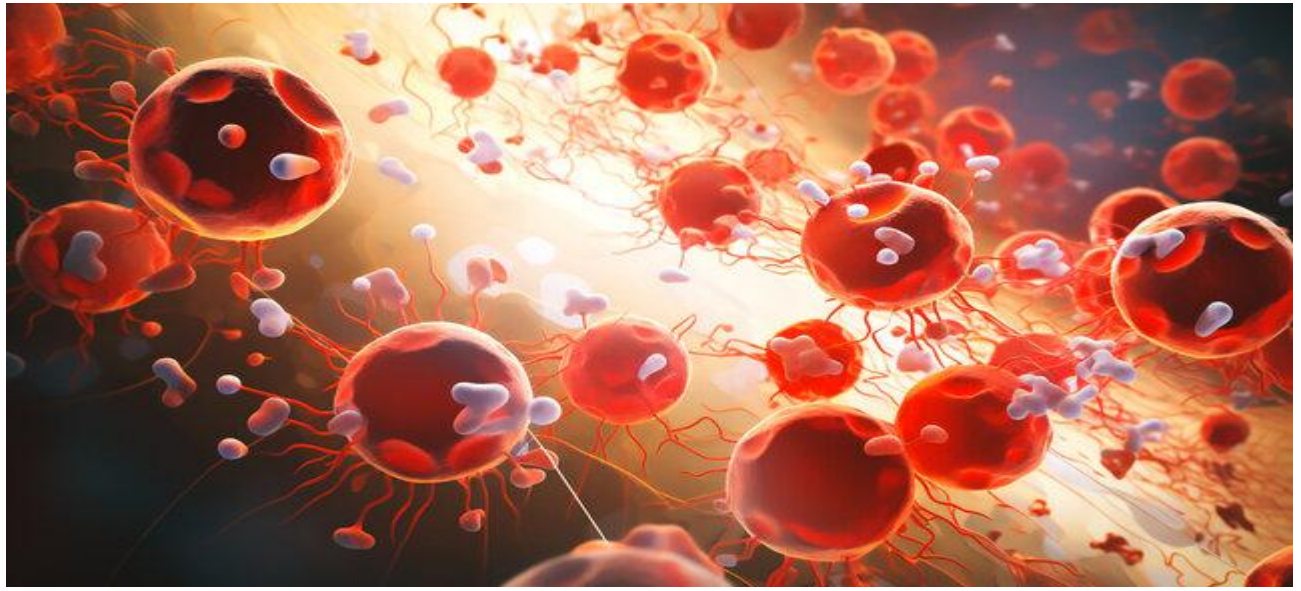
Capillary plugging

⬇

Anoxia, ischemia and hemorrhage.

Algid Malaria

- Characterized by cold and clammy skin with vascular collapse leading to peripheral circulatory failure and profound hypotension.
- There may be **severe abdominal pain, vomiting, diarrhea and profound shock.**
- Overwhelming infection of ***Plasmodium falciparum.***

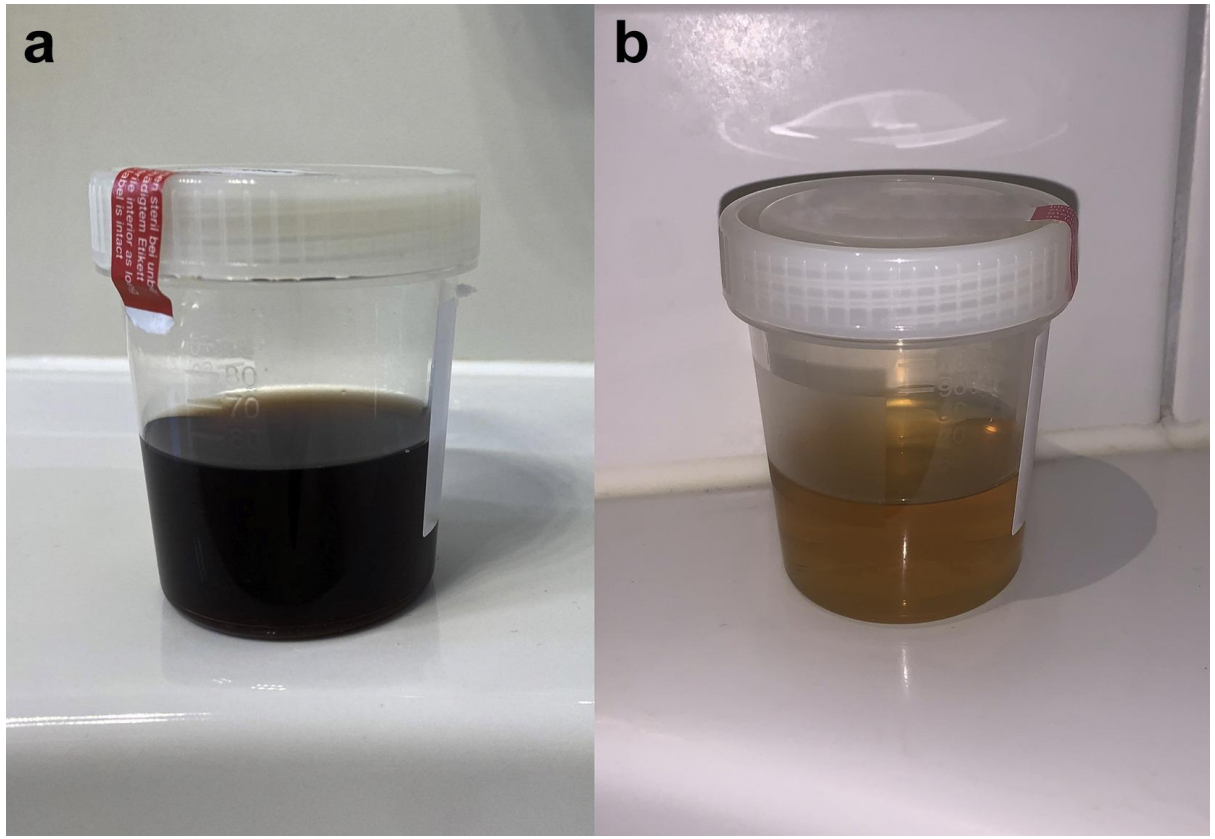


Black Water Fever

- Also called malarial hemoglobinuria, one of the less common yet **most dangerous complications of malaria.**
- It occurs almost exclusively with infection of the parasite ***plasmodium falciparum.***
- Black water fever has a **high mortality.**

Sign and Symptoms

- High fever
- Hemoglobinuria
- Icterus
- Bilious vomiting
- Circulatory collapse
- Acute renal failure.



Causes of Anemia in Malaria

- Destruction of large number of RBCs by **complement mediated and autoimmune hemolysis.**
- **Suppression of erythropoiesis in the bone marrow.**
- Increased clearance of both **parasitized and non parasitized RBC by the spleen.**
- Antimalarial therapy **in G6PD deficient patients**.

Malaria in Pregnancy

Malaria in Pregnancy

- Malaria is more common in pregnancy compared to the general population.
- Malaria in pregnancy tends to be more atypical in presentation. This could be to the **hormonal, immunological and hematological changes of pregnancy.**
- The parasitemia tends to be **10 times higher.**
- ***P. falciparum* malaria in pregnancy being more severe,** the mortality is also double (13%) compared to the non-pregnant population (6.5%).

Complications of Malaria in Pregnancy

Pregnant women	Fetus	Newborn
Parasitemia	Abortions	Low birth weight
Anaemia	Stillbirths	Prematurity
Cerebral Malaria	Congenital infection	IUGR
Hypoglycemia	-------	-------
Miscarriage	--------	--------
Hemorrhage	--------	--------
Puerperal sepsis	--------	--------

Airport Malaria

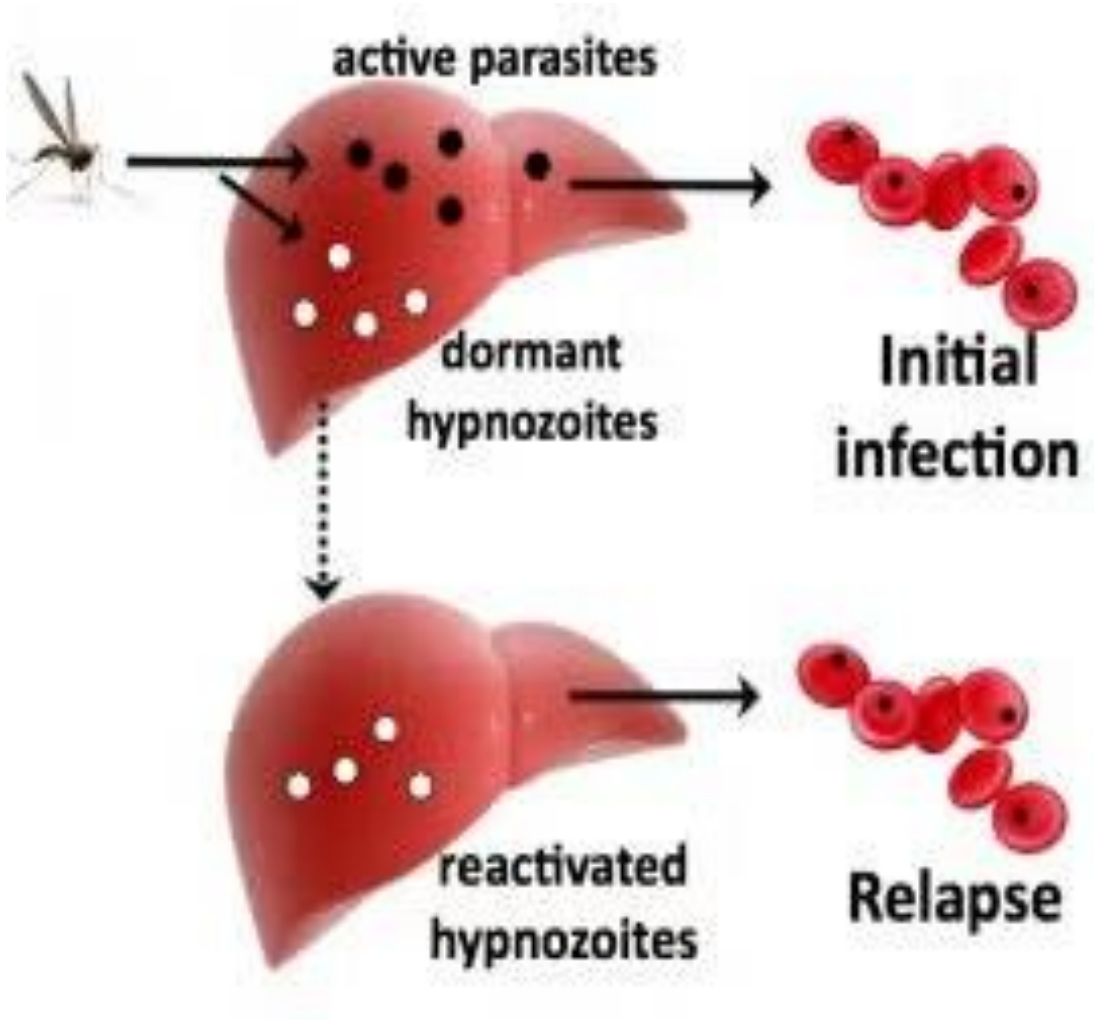
Airport malaria is a rare form of locally acquired malaria where infected **Anopheles mosquitoes** travel on aircraft from endemic regions to non-endemic regions, malaria free countries. The mosquitos typically bite people at or near international airports, often causing severe, delayed-diagnosis case of ***P. falciparum.***

Transfusion Induced Malaria

- Blood transfusion can accidentally transmit malaria, if the donor is infected with malaria.
- **The parasites may remain viable in blood bank for 1-2 weeks.**
- As this condition is induced by direct infection by red cells by the merozoites, **pre-erythrocytic schizogony and hypnozoites are absent.**
- Relapse doesn't occur and incubation period is short.

Relapse

- Seen in ***P.vivax and P.ovale.***
- Due to reactivation of hypnozoites present in liver cells.
- Occurs usually 24 weeks to 5 years after the primary attack.
- Can be prevented by giving primaquine to eradicate hypnozoites.



Recrudescence

- Seen *in* ***P.falciparum and P. malariae.***
- Due to persistence of the erythrocytic cycle at a subclinical level in circulation.
- Occurs within a few weeks or months of a previous attack.
- Can be prevented by adequate drug therapy or use of newer antimalarial drugs in case of drug resistance.

Prevention of Malaria

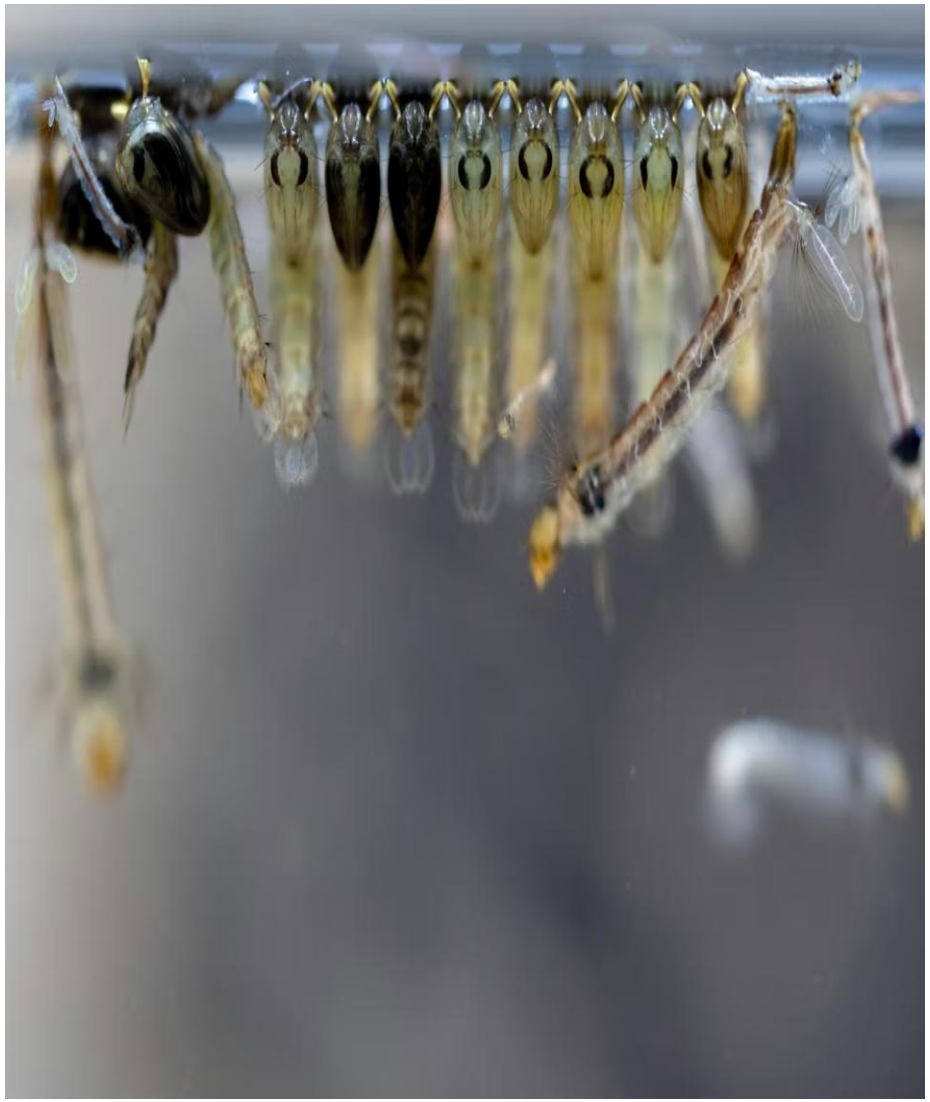
Personal Protection

- ✓Preventing the mosquitoes from entering the house-close door/ windows, specially toilets.
- ✓Well-constructed houses with window screens.
- ✓Preventing the mosquitoes from hiding- Avoid dark corners/hanging clothes in room.
- ✓Mosquito control-avoid stagnant water, insecticide spraying etc.

Protection from Mosquito Bites

- Protective clothing.
- Mosquito repellants(containing DEET)
- Insect vaporizers(coils containing pyrethroids).
- Insecticide treated bed nets(most effective).
- Airconditioning .

Anti-larval Measure



- Using the anti-larval measure such as oiling the collection of standing water or dusting them with paris green effectively controlled malaria.
- Some **modern larvicides such as temephos** which confer long effect with low toxicity are more widely used.

Vector Control Strategy

✓Residual spray:

Spraying indoor surface of house with **DDT/malathion.**


WORLD
MALARIA
APRIL 25 DAY


THANK YOU