MALARIA

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Roll no:1

Introduction

- Malaria is a protozoan disease caused by Plasmodium.
- Human malaria is usually caused by one of four species of the genus Plasmodium namely

1. P. falciparum
2. P. vivax
3. P. ovale
4. P. malariae.

- P. falciparum causes the most severe form of malaria
- P. vivax is the most common cause of malaria in India.

Mode of transmission

- By the bite of female anopheline mosquitoes. Malaria can also be transmitted through contaminated blood transfusions.

Life cycle

Mosquito Stage (Sexual Phase)

- Female **Anopheles mosquito** feeds on human blood containing **gametocytes** (sexual forms).
- Development in mosquito lasts **7–20 days**, producing **sporozoites** in salivary glands.
- Sporozoites are injected into human bloodstream during the next bite.

Liver Stage (Exoerythrocytic / Pre-erythrocytic Phase)

- Sporozoites enter liver **within 30 minutes**, invade hepatocytes.
- Mature into **merozoites**, which are released into blood after several days.
- **P. vivax** and **P. ovale** form **hypnozoites** (dormant liver stage) → can cause **relapses months or years later**.

Red Blood Cell Stage (Erythrocytic Phase / Asexual Phase)

- Merozoites invade RBCs → develop into **trophozoites** → **schizonts** → RBC rupture releases more merozoites.
- RBC rupture causes **fever**, with periodicity dependent on species.
- **P. falciparum, P. malariae, and P. knowlesi** have no dormant liver stage, but **recrudescence** may occur from residual RBC parasites.

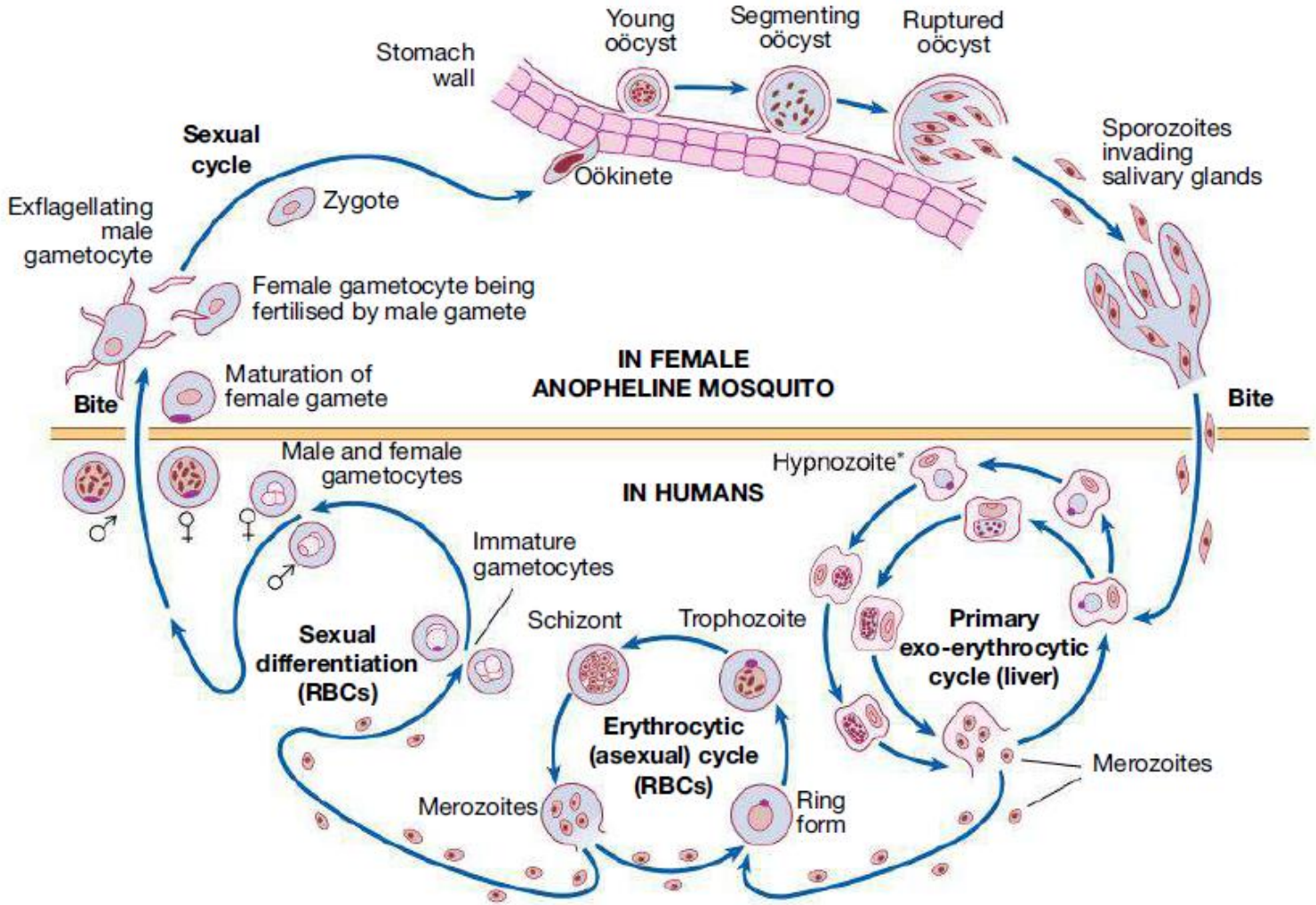


Fig. 13.36 **Malarial parasites: life cycle.** Hypnozoites (*) are present only in *Plasmodium vivax* and *P. ovale* infections. (RBC = red blood cell)

PATHOLOGY

- Infected red blood cells (RBCs) undergo **haemolysis** → anaemia.
- Most severe in **Plasmodium falciparum** (invades RBCs of all ages).
- **Plasmodium vivax** and Plasmodium ovale infect young RBCs;
  Plasmodium malariae infects older cells → lower parasitaemia.

Severe P. falciparum Pathology

- Infected RBCs adhere to vascular endothelium (via "knob" proteins).
- Formation of **rosettes and rouleaux**.
- Causes microvascular obstruction → brain, kidney, liver, lung damage.
- Schizont rupture releases toxic substances → worsens organ injury.

Genetic Protection (Evolutionary Influence)

- Protection against severe **P. falciparum**:
- Sickle-cell trait (HbAS)
- Thalassaemia
- G6PD deficiency
- HLA-B53
- HbF, HbC, HbS reduce parasite growth

Plasmodium vivax cannot infect Duffy-negative RBCs → protection in many West Africans

P. vivax & P. ovale malaria

Incubation Period:

P. vivax: 12–17 days , P. ovale: 15–18 days

Prodromal Symptoms

- Headache,Fatigue,Abdominal discomfort,Muscle aches

Fever Pattern

- Characteristic **paroxysms of fever**
  - Begins with rigor (chills)
  - Synchronizes with erythrocytic cycle
- **Tertian fever:** occurs every 3rd day (48-hour cycle between spikes)

P. vivax

- Anaemia
- Thrombocytopenia
- Mild jaundice
- Tender hepatosplenomegaly
- Splenic rupture more common

P. ovale

- Acute illness similar to P. vivax
- Anaemia usually milder
- Splenic rupture less common

P. malaria

- **Incubation Period:** 18–40 days

Prodromal Symptoms

- Headache,Fatigue,Abdominal discomfort,Muscle aches

Fever

- Paroxysms correspond to erythrocytic cycle
- **Quartan fever pattern**: fever every 4th day (72-hour cycle between spikes)

Clinical Features

- Gross splenomegaly common
- Splenic rupture uncommon
- Anaemia usually mild

Complications

- Chronic infection may cause:
  - Glomerulonephritis
  - Nephrotic syndrome

P. falciparum Malaria

- **Incubation Period:** 7–14 days (average ≈ 21 days)

1. Prodromal Symptoms

- Insidious onset
- Malaise, headache, Myalgia, Anorexia,Vomiting

2. Fever

- No typical periodicity
- High, irregular, unremitting fever
- May show daily (quotidian) spikes

3. Jaundice

- **Severe haemolysis** → ↑ unconjugated bilirubin
- **Malarial hepatopathy** (hepatic dysfunction without true inflammation)

4. Haemolytic Anaemia

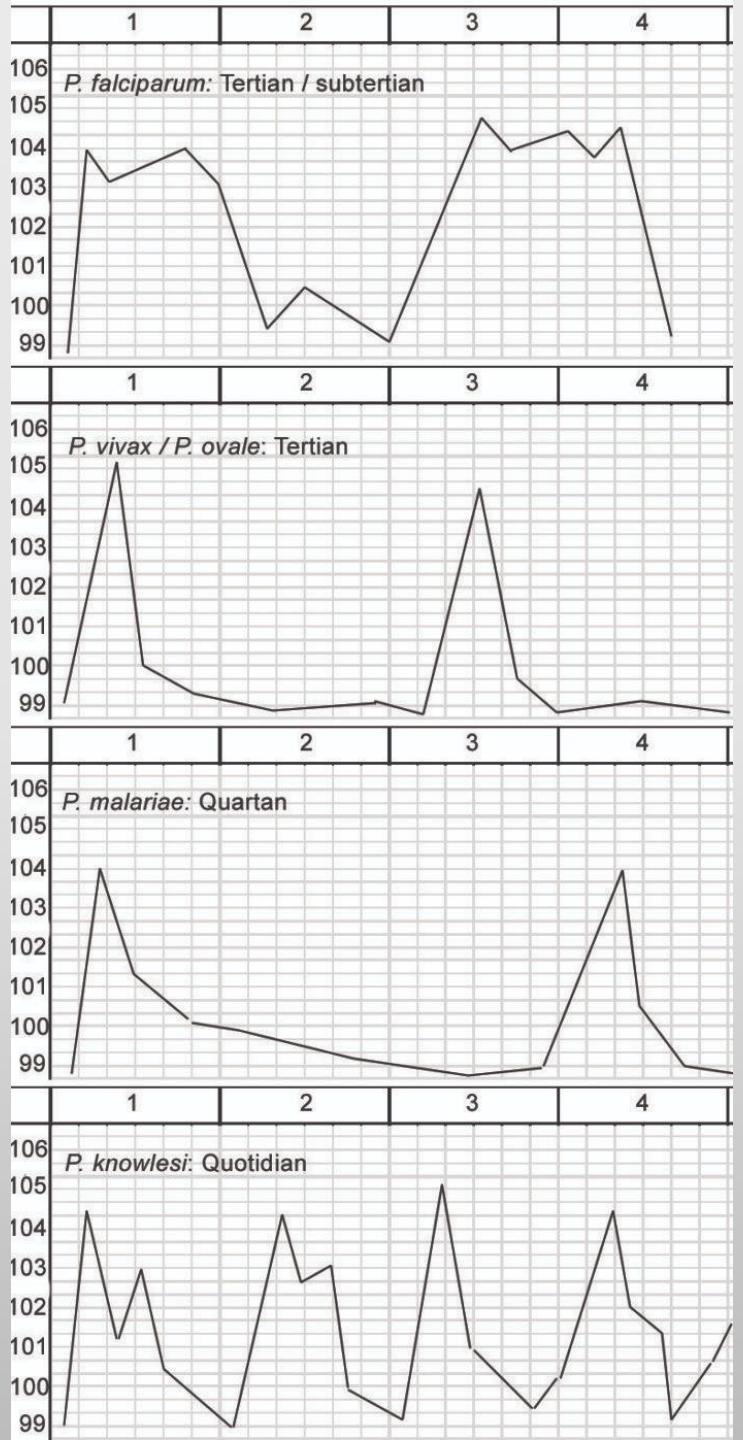
- Massive RBC destruction (parasite infects RBCs of all ages)
- Splenic sequestration
- Thrombocytopenia common

5. Physical Findings

- Anaemia
- Jaundice
- Moderate, tender hepatosplenomegaly

Neurological Complications (Cerebral Malaria)

- Severe headache
- Irritability, agitation
- Seizures
- Psychosis
- Impaired consciousness / coma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P. falciparum: Tertian / subtertian
P. vivax / P. ovale: Tertian
P. malariae: Quartan
P. knowlesi: Quotidian

13.56 Severe manifestations/complications of *falciparum* malaria and their immediate management

Coma (cerebral malaria)

- Maintain airway
- Nurse on side
- Exclude other treatable causes of coma (e.g. hypoglycaemia, bacterial meningitis)
- Avoid harmful ancillary treatments such as glucocorticoids, heparin and adrenaline (epinephrine)
- Intubate if necessary

Hyperpyrexia

- Tepid sponging, fanning, cooling blanket
- Antipyretic drug (paracetamol)

Convulsions

- Maintain airway
- Treat promptly with diazepam or paraldehyde injection

Hypoglycaemia

- Measure blood glucose
- Give 50% dextrose injection followed by 10% dextrose infusion (glucagon may be ineffective)

Severe anaemia (packed cell volume <15%)

- Transfuse fresh whole blood or packed cells if pathogen screening of donor blood is available

Acute pulmonary oedema

- Nurse at 45°, give oxygen, venesect 250 mL of blood, give diuretic, stop intravenous fluids
- Intubate and add PEEP/CPAP in life-threatening hypoxaemia
- Haemofilter

Acute kidney injury

- Exclude pre-renal causes
- Fluid resuscitation if appropriate
- Peritoneal dialysis (haemofiltration or haemodialysis if available)

Spontaneous bleeding and coagulopathy

- Transfuse screened fresh whole blood (cryoprecipitate/fresh frozen plasma and platelets if available)
- Vitamin K injection

Metabolic acidosis

- Exclude or treat hypoglycaemia, hypovolaemia and Gram-negative sepsis
- Fluid resuscitation
- Give oxygen

Shock ('algid malaria')

- Suspect Gram-negative sepsis
- Take blood cultures
- Give parenteral antimicrobials
- Correct haemodynamic disturbances

Aspiration pneumonia

- Give parenteral antimicrobial drugs
- Change position
- Physiotherapy
- Give oxygen

Hyperparasitaemia

- Consider exchange transfusion (e.g. >10% of circulating erythrocytes parasitised in non-immune patient with severe disease)

Specific therapy

- Intravenous artesunate
- Mefloquine should be avoided due to increased risk of post-malaria neurological syndrome

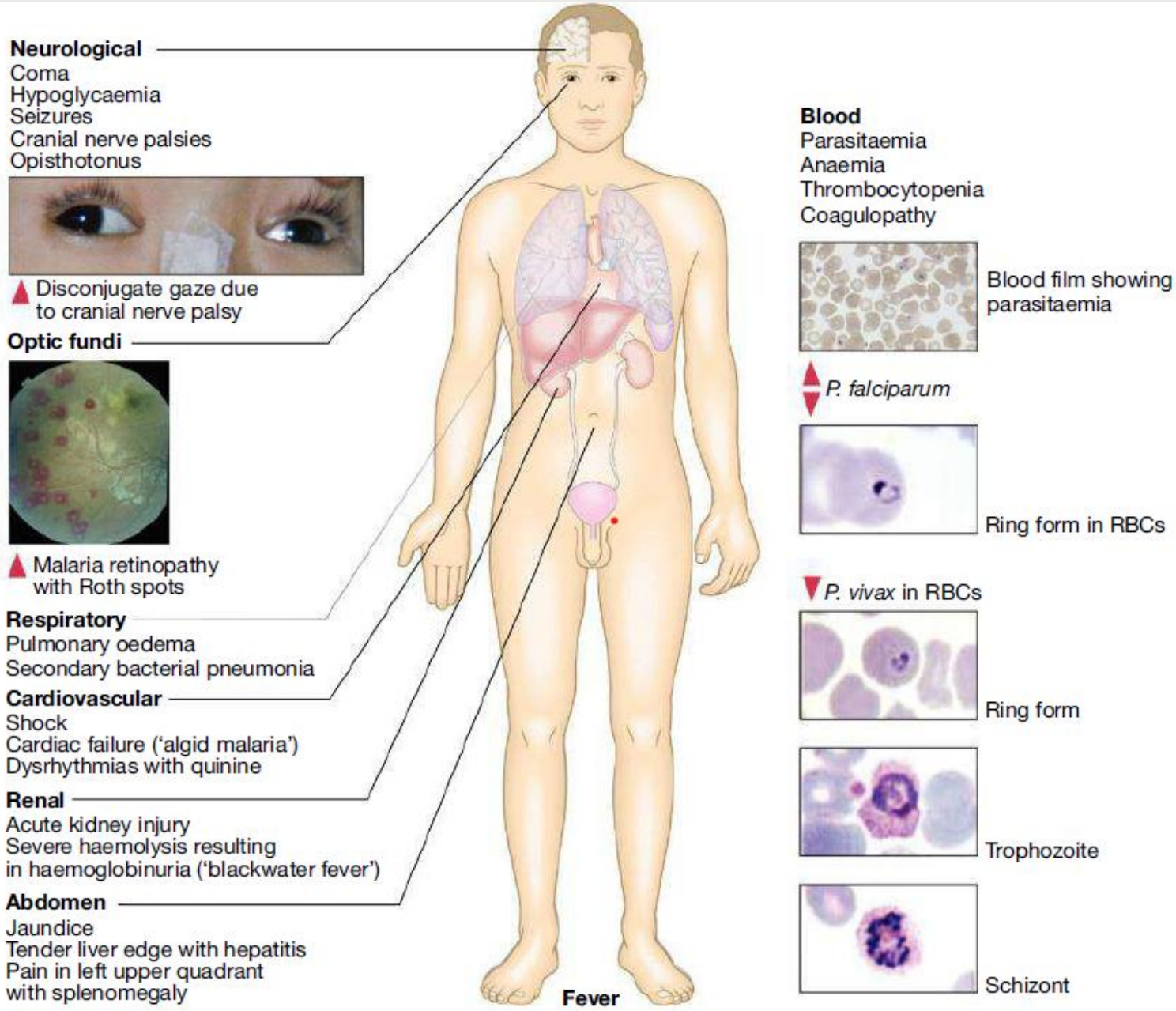


Fig. 13.37 **Features of *Plasmodium falciparum* infection.** (RBC = red blood cell). *Insets (malaria retinopathy) Courtesy of Dr Nicholas Beare, Royal Liverpool University Hospital; (blood films of P. vivax and P. falciparum) Courtesy of Dr Kamolrat Silamut, Mahidol Oxford Research Unit, Bangkok, Thailand.*

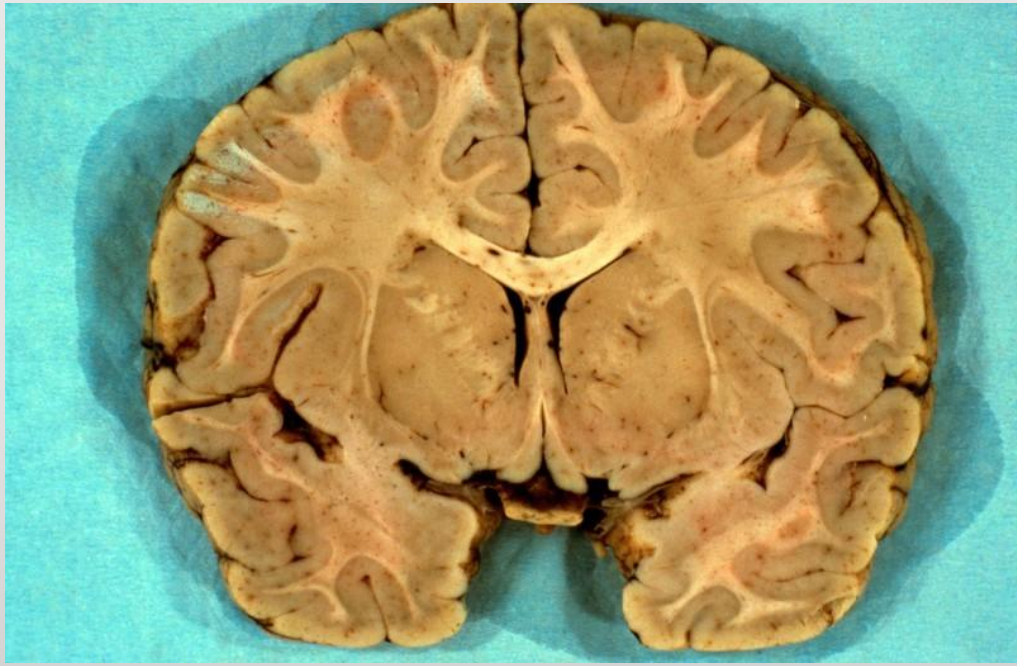
Cerebral malaria

- Malignant malaria can affect the brain and rest of CNS.
- Characterised by changes in the level of consciousness, convulsions and paralysis
- Present with hyperpyrexia
- Brain appears congested
- **Pathogenesis:**

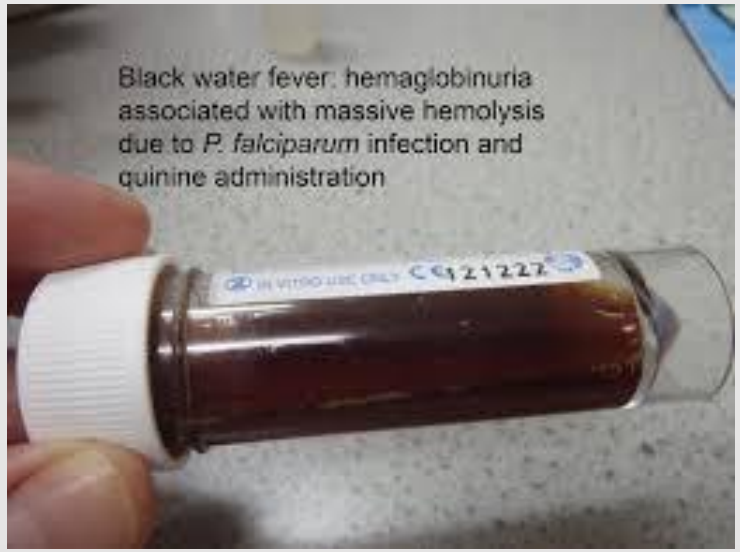
Sequestration: Infected RBCs adhere to brain endothelium via knob proteins → **capillary blockage**.

Rosettes & Rouleaux: Infected RBCs stick to uninfected cells → worsen microvascular obstruction.

Inflammation: Cytokines (TNF-α, IFN-γ) activate endothelium → **blood-brain barrier disruption- cerebral edema**



Black water fever



- **Definition:** Acute intravascular hemolysis with dark (“black”) urine.
- **Risk Factors**
  - Non-immune patients
  - Chronic falciparum malaria
  - Irregular use of antimalarials (quinine, primaquine)
  - **G6PD deficiency** or other RBC enzyme deficiencies
- **Clinical Features**
- Rapid hemolysis → sudden drop in hemoglobin
- Dark red/black urine
- Fever (up to 39.4°C) with rigors
- Headache, nausea, vomiting
- Severe loin pain, prostration

Algid malaria

Definition: Sudden **peripheral circulatory failure** in severe malaria.

Clinical Features

- Hypotension:
  - Adults: systolic < 80 mmHg
  - Children: systolic < 50 mmHg
- Cold, clammy, cyanotic skin
- Constricted peripheral veins
- Rapid, weak pulse

May also occur with:

- Pulmonary edema
- Metabolic acidosis
- Massive GI hemorrhage
- Dehydration / hypovolemia

Renal failure

Common in adults with severe **Plasmodium falciparum** infection.

- **Clinical Course:**
  - Progressive **oliguria → anuria**
  - Rising **serum creatinine and urea**
  - Usually **reversible** with proper management

Pathogenesis

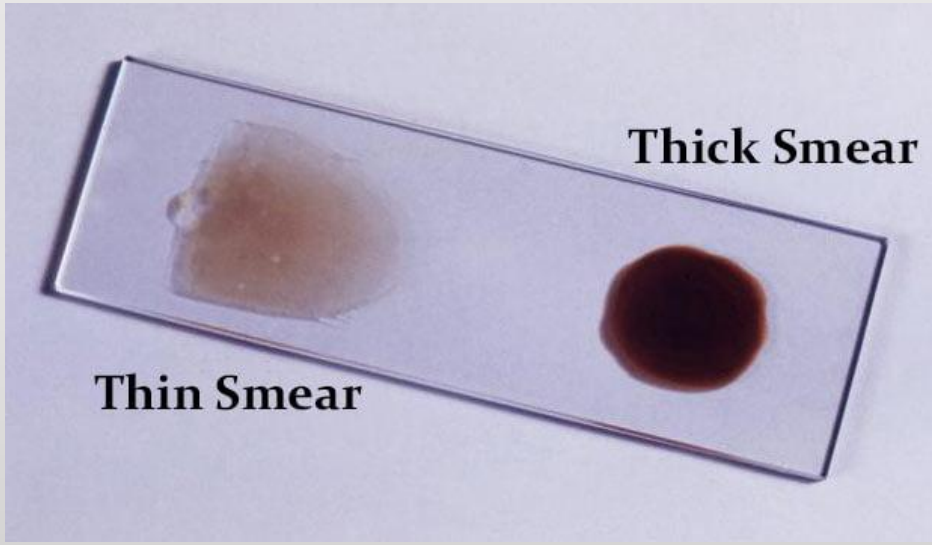
1. **Renal cortical vasoconstriction → hypoperfusion**
2. **Microvascular obstruction** from sequestered parasitized RBCs → **acute tubular necrosis**
3. **Massive intravascular hemolysis** (e.g., in blackwater fever)
4. **Dehydration / hypovolemia** → reversible renal hypoperfusion

Investigations

- Blood film examination (Microscopy)
- QBC system
- Rapid Diagnostic Tests (RDTs)
- PCR

Microscopy

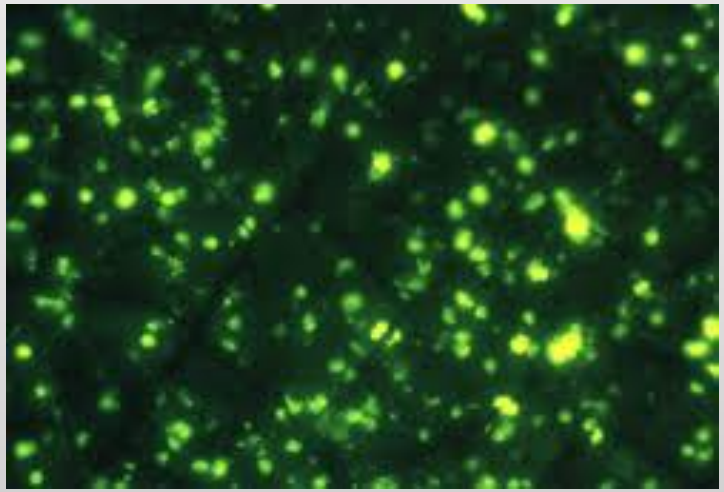
- Malaria parasites can be identified by examining under the microscope a drop of the patient's blood, spread out as a "blood smear" on a microscope slide. Prior to examination, the specimen is stained (most often with the Giemsa stain) to give to the parasites a distinctive appearance.
- Gold standard for laboratory confirmation of malaria.



QBC system

The QBC Malaria method is the simplest and most sensitive method for diagnosing the following diseases.

- Malaria
- Babesiosis
- Trypanosomiasis (Chagas disease, Sleeping Sickness)
- Filariasis (Elephantiasis, Loa-Loa)
- Relapsing Fever (Borreliosis)

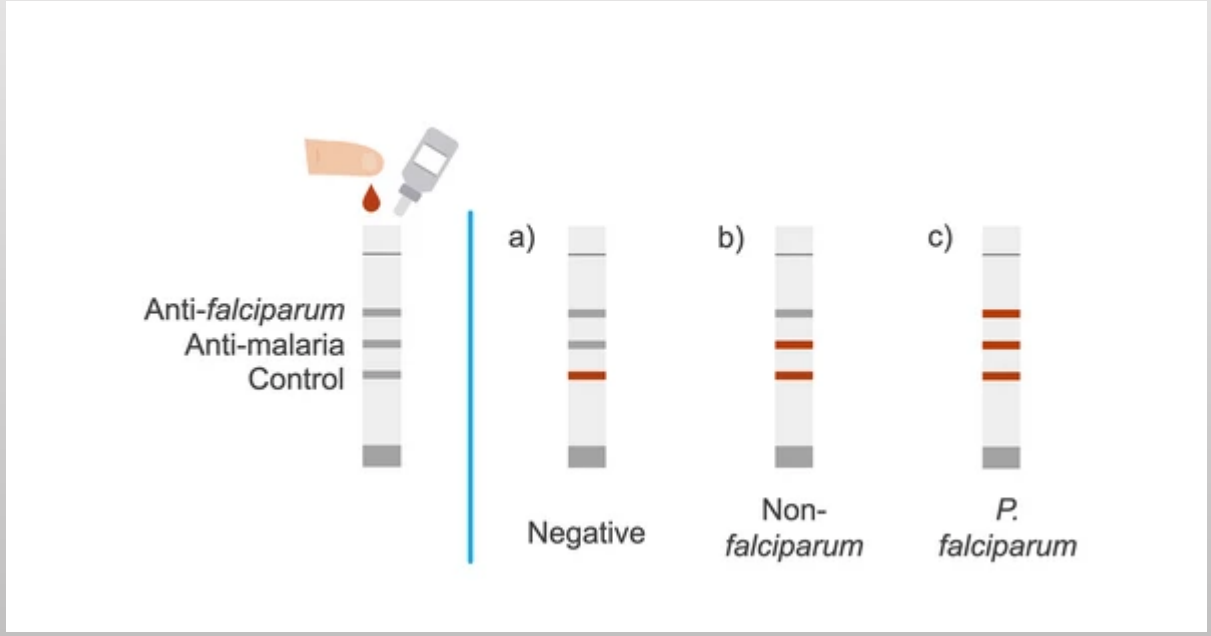


Rapid Diagnostic Tests

- Antigen Detection
- Various test kits are available to detect antigens derived from malaria parasites and provide results in2-15 minutes. These "Rapid Diagnostic Tests" (RDTs).
- RDTs are immunochromatographic tests based on detection of specific parasite antigens.
- Tests which detect histidine-rich protein 2 (HRP2) are specific for P.falciparum while those that detect parasite lactate dehydrogenase (pLDH)-OptiMAL* or aldolase have the ability to differentiate between P.falciparum and non-P.falciparum malaria

Molecular diagnosis

- Parasite nucleic acids are detected using polymerase chain reaction (PCR).
- More accurate than microscopy.
- However, it is expensive, and requires a specialized laboratory



Treatment of Uncomplicated Malaria

a) For acute attack of malaria due to P, vivax, P. ovale, P. malariae Oral chloroquine is the drug of choice

- Chloroquine 600 mg base (10 mg/kg) stat, followed by 600 mg base (10 mg/kg) -2nd day + 300 mg base (5 mg/kg) – 3rd day
- Primaquine 15 mg base orally, from day 1 OD for 14 days (for P vivax, P ovale malarla)
- Chloroquine & primaquine produces radical cure

(b) For acute attack of malaria due to P. falciparum

ACT regimen + Primaquine single dose . ACT acts on erythrocytic stage, primaquine is gametocidal.

- Artesunate (4 mg/kg) 100 mg BD x 3 days

  + Sulfadoxine and Pyrimethamine (S/P) 1500 mg/75 mg as a single dose - day 1 (except north eastern states)

  + Primaquine (on Day 2), single dose 0.75 mg/kg body weight
- Artemether + Lumefantrine (AL) FDC - 20 mg + 120 mg, 4 FDCs BD x 3 days

  + Primaquine (on Day 2), single dose 0.75 mg/kg body weight (recommended in north-eastern states)
- Artesunate 100 mg BD x 3 days

  + Mefloquine 750 mg (15 mg/kg) - 2nd day and 500 mg (10 mg/kg) - 3rd day

  + Primaquine (on day 2), single dose 0.75 mg/kg body weight
- Artesunate 4 mg/kg/day + Amodiaquine 10 mg/kg/day OD x 3 days

  + Primaquine (on day 2), single dose 0.75 mg/kg body weight

For severe or complicated P. falciparum malaria (cerebral malaria)

- Parenteral antimalarials should be administered for at least 24 hours once started. Then complete the treatment with full course of oral ACT once the patient is able to take orally.
- Artesunate: Dose: 2.4 mg/kg at 0 hour (i.v./i.m.); repeat at 12 and 24 hours. Then, once a day till patient is able to take oral medication.
- ACT containing mefloquine should be avoided in cerebral malaria because of risk of neuropsychiatric complications.
- Supportive measures: Tepid sponging for fever, Sodium bicarbonate to correct acidosis, Intravenous diazepam to control convulsions, 10% dextrose to combat hypoglycemia, Blood transfusion to correct anemia

13.58 Chemoprophylaxis of malaria[1]

Antimalarial tablets	Adult prophylactic dose	Regimen
Chloroquine resistance high		
Mefloquine[2]	250 mg weekly	Started 2–3 weeks before travel and continued until 4 weeks after
or Doxycycline[3,4]	100 mg daily	Started 1 week before and continued until 4 weeks after travel
or Atovaquone plus proguanil (Malarone)[4]	1 tablet daily	From 1–2 days before travel until 1 week after return
Chloroquine resistance absent		
Chloroquine[5] *and* proguanil	300 mg base weekly 100–200 mg daily	Started 1 week before and continued until 4 weeks after travel

Monitoring and follow up

- Blood smear should be repeated daily (twice daily in severe infection). Within 48-72 hr after start of treatment, patients usually become afebrile and improve clinically except in complicated cases.
- All patients should be investigated with repeated blood film of malarial parasite one month upon recovery of malarial infection, to ensure no recrudescence

Prevention

- ❑Avoid mosquito bites:
- Wearing long sleeves, trousers.
- Insecticide Treated Bednets
- Repellent creams or sprays.

References

- **Davidson's Principles and Practice of Medicine** 24th edition
- Exam Preparatory Manual for Undergraduates Medicine-Archith Boloor

THANK YOU