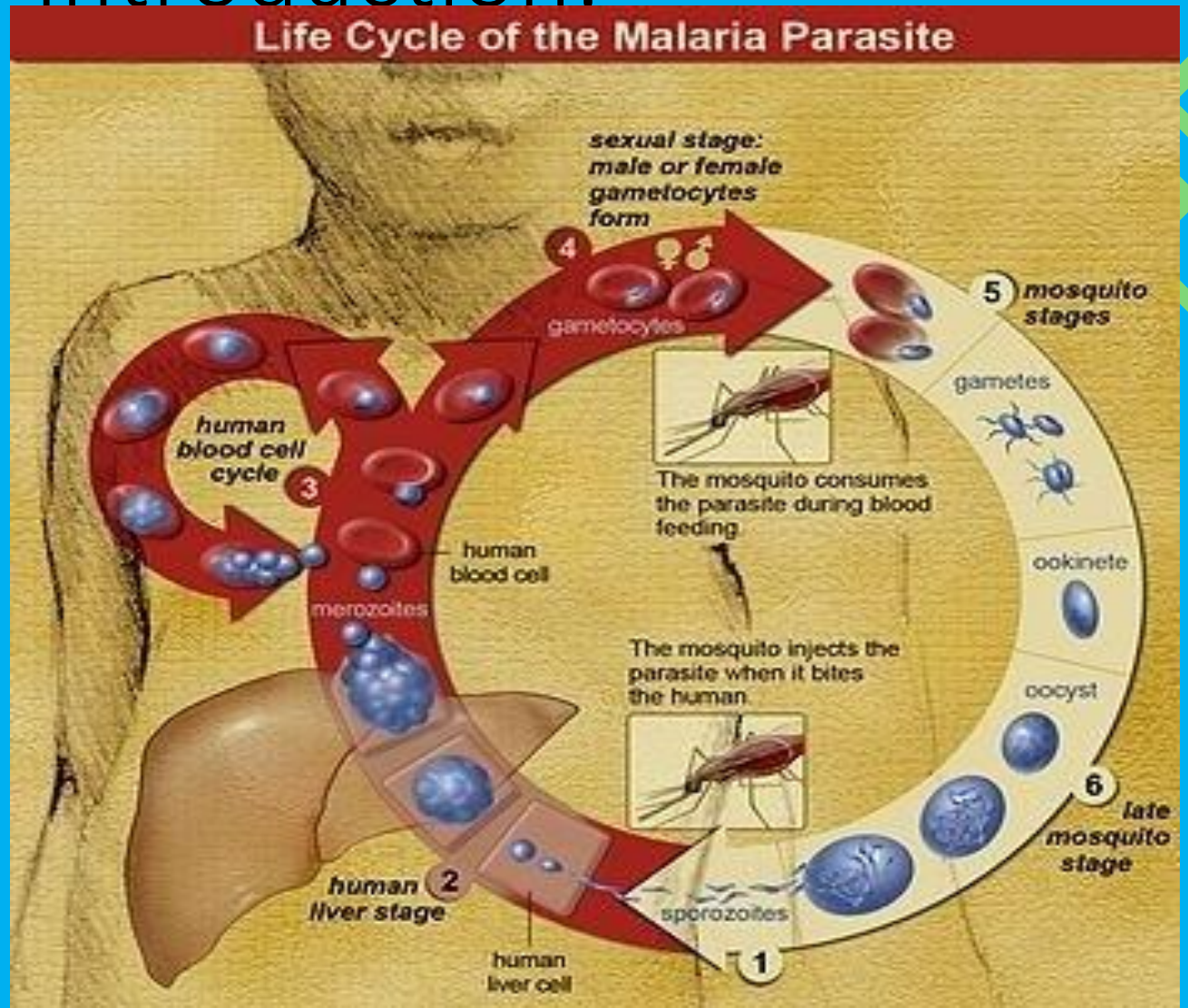
Infectious Diseases

PRESENTED BY

DR AFRAZ SHERAZI

Introduction:



- Malaria is a **mosquito-borne infectious** disease affecting **humans** and other animals caused by **parasitic protozoans** (a group of single-celled microorganisms) belonging to the **Plasmodium type.**

- The disease is most commonly transmitted by an **infected female Anopheles mosquito**. The mosquito **bite** introduces the parasites from the mosquito's **saliva** into a person's **blood.**
- The parasites **travel** to the **liver** where they **mature and reproduce**.

- **Five species** of Plasmodium can infect and be spread by humans.
- Most deaths are caused by *P. falciparum* because *P. vivax, P. ovale*, and *P. malariae* generally cause a milder form of malaria.
- The species *P. knowlesi* rarely causes disease in humans.

- Other modes of transmission:

❖From mother to unborn child

❖Through blood transfusions

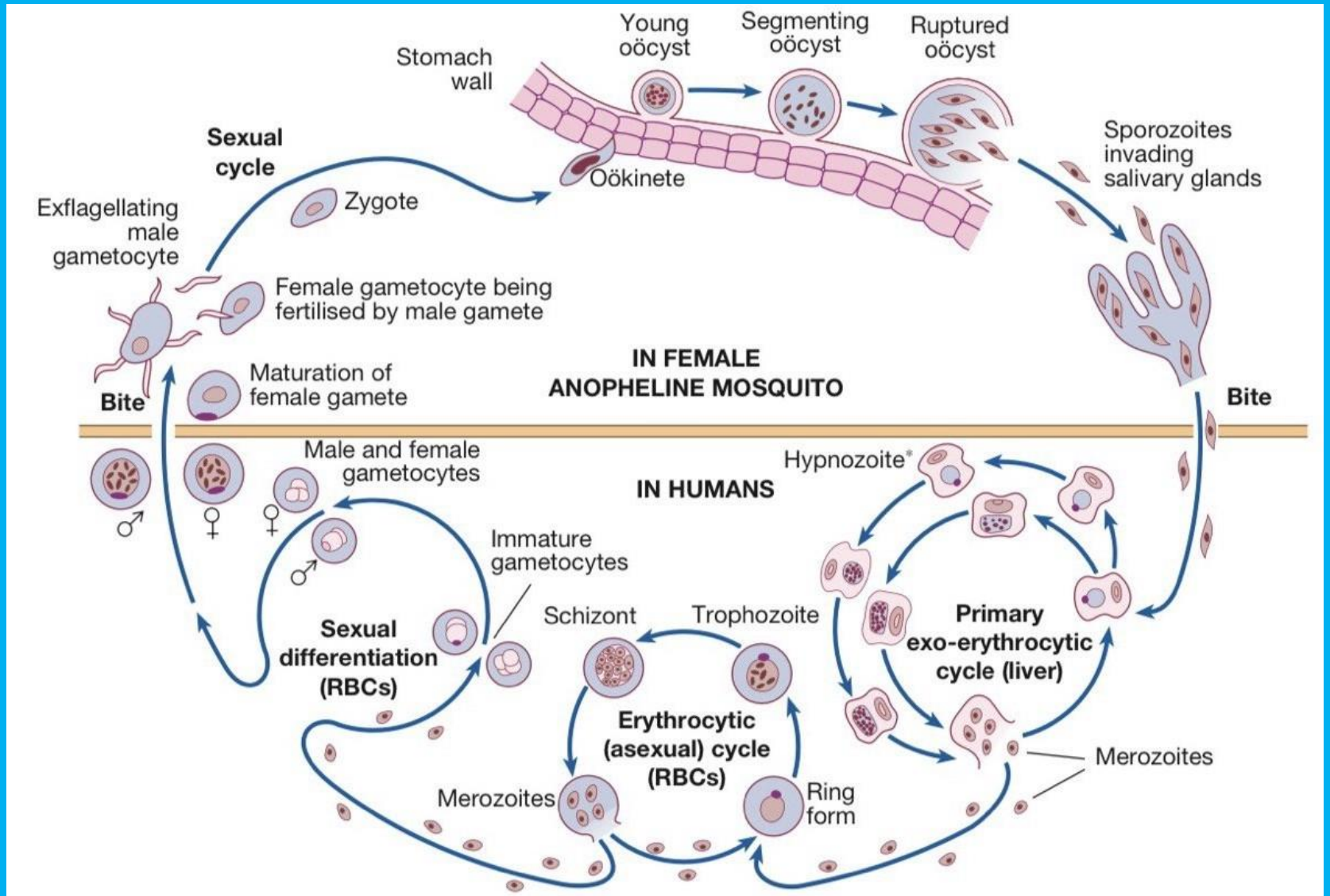


Fig. 13.32 Malarial parasites: life cycle. Hypnozoites(*) are present only in *P. vivax* and *P. ovale* infections. (RBC = red blood cell)

- The **clinical features** of malaria are **non-specific** and the diagnosis must be suspected in anyone returning from an **endemic area** who has features of infection.
- *P. falciparum* infection This is the most dangerous of the malarias and patients are either ‘killed or cured’.
- The **onset** is often **insidious**, with **malaise**, **headache** and **vomiting**.
- **Cough** and mild **diarrhoea** are also common.
- The **fever** has no particular pattern.
- **Jaundice** is common due to **haemolysis** and **hepatic dysfunction.**
- The **liver** and **spleen** enlarge and may become **tender**.
- **Anaemia** develops rapidly, as does **thrombocytopenia**.
- A patient with falciparum malaria, apparently not seriously ill, may rapidly develop **dangerous complications.**

- **Cerebral malaria** is manifested by **confusion**, **seizures** or **coma**, usually without **localising signs**.
- **Children die** rapidly without any special symptoms other than **fever**.
- **Immunity** is impaired in **pregnancy** and the parasite can preferentially bind to a placental protein known as **chondroitin sulphate A**.
- **Abortion** and intrauterine **growth retardation** from parasitisation of the maternal side of the placenta are frequent.
- Previous **splenectomy** increases the risk of **severe malaria.**

13.58 Relationships between life cycle of parasite and clinical features of malaria

Cycle/ feature	*P. vivax*, *P. ovale*	*P. malariae*	*P. falciparum*
Pre-patent period (minimum incubation)	8–25 days	15–30 days	8–25 days
Exo-erythrocytic cycle	Persistent as hypnozoites	Pre-erythrocytic only	Pre-erythrocytic only
Asexual cycle	48 hrs synchronous	72 hrs synchronous	< 48 hrs asynchronous
Fever periodicity	Alternate days	Every third day	None
Delayed onset	Common	Rare	Rare
Relapses	Common up to 2 yrs	Recrudescence many years later	Recrudescence up to 1 yr

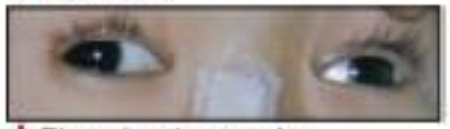
P. vivax and *P. ovale* infection:

- In many cases, the illness starts with several days of continued **fever** before the development of classical bouts of fever on alternate days.
- Fever starts with a **rigor**. The patient feels **cold** and the temperature **rises** to about 40°C. After **half an hour** to an hour, the **hot** or **flush** phase begins.
- It lasts **several hours** and gives way to profuse **perspiration** and a **gradual fall** in temperature. The cycle is repeated 48 hours later.
- Gradually, the **spleen** and **liver** enlarge and may become tender. **Anaemia** develops slowly.
- **Relapses** are frequent in the first **2 years** after leaving the malarious area and infection may be acquired from blood transfusion.

P. malariae infection:

- This is usually associated with **mild symptoms** and bouts of **fever** every third day.
- Parasitaemia may persist for **many years**, with the occasional recrudescence of **fever** or without producing any symptoms.
- Chronic *P. malariae* infection causes **glomerulonephritis** and long term **nephrotic syndrome** in children.

Neurological
Coma
Hypoglycaemia
Seizures
Cranial nerve palsies
Opisthotonus



Disconjugate gaze due to cranial nerve palsy

Optic fundi

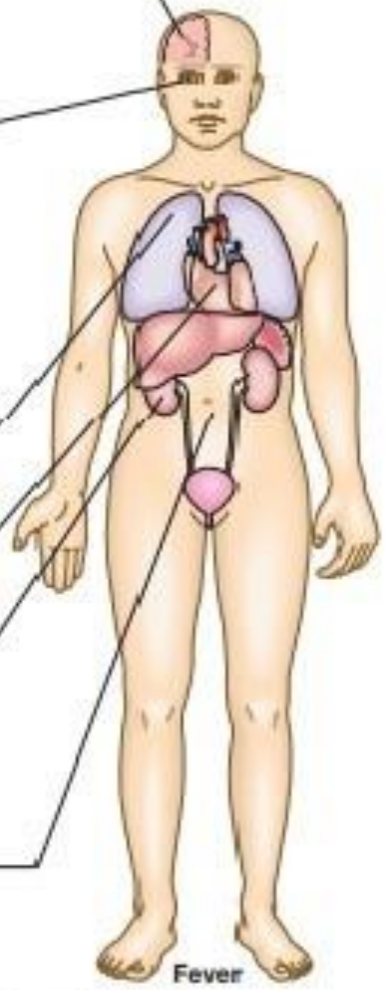
Malaria retinopathy with Dutton's spots

Respiratory
Pulmonary oedema
Secondary bacterial pneumonia

Cardiovascular
Shock
Cardiac failure ('algid malaria')
Dysrhythmias with quinine

Renal
Acute renal failure
Severe haemolysis resulting in haemoglobinuria ('blackwater fever')

Abdomen
Jaundice
Tender liver edge with hepatitis
Pain in left upper quadrant with splenomegaly



Blood
Parasitaemia
Anaemia
Thrombocytopenia
Coagulopathy

Blood film showing parasitaemia

P. falciparum

Ring form in RBCs

P. vivax in RBCs

Ring form

Trophozoite

Schizont

Features of *P. falciparum* infection. (RBC = red blood cell)

Investigations:

- **Giemsa-stained** thick and thin blood films should be examined whenever malaria is suspected
- In the **thick film**, erythrocytes are **lysed**, releasing all blood stages of the parasite. This, as well as the fact that more blood is used in thick films, facilitates the diagnosis of low-level parasitaemia.
- A **thin film** is essential to confirm the diagnosis, to identify the species of parasite and, in *P. falciparum* infections, to quantify the parasite load (by counting the **percentage** of infected erythrocytes).
- *P. falciparum* parasites may be very scanty, especially in patients who have been partially treated.

With *P. falciparum*, only ring forms are normally seen in the **early stages**; with the other species, all stages of the erythrocytic cycle may be found.

Gametocytes appear after about **2 weeks**, persist after treatment and are **harmless**, except that they are the source by which more mosquitoes become infected.

Immunochromatographic tests for malaria antigens are extremely **sensitive** and specific for falciparum malaria but less so for other species.

The **QBC Malaria** Test is a **fluorescence microscopy-based** malaria diagnostic test which is also widely used.

DNA detection **(PCR)** is used mainly in research and is useful for determining whether a patient has a **recrudescence** of the same malaria parasite or a **re-infection** with a new parasite.

TREATMENT:

- The most effective treatment for *P. falciparum* infection is the use of **artemisinins** in combination with other antimalarials (known as artemisinin-combination therapy, or **ACT**)
- **amodiaquine**, **lumefantrine**, **mefloquine** or **sulfadoxine/pyrimethamine**.
- Another recommended combination is **dihydroartemisinin** and **piperaquine**.
- the WHO recommends the use of **quinine** plus **clindamycin** early in the pregnancy **(1st trimester)**
- **Mild** *P. falciparum* malaria Since *P. falciparum* is now resistant to **chloroquine** and **sulfadoxine-pyrimethamine** (Fansidar) almost worldwide, an **artemisinin**-based treatment is recommended.
- Alternatives are **quinine** by mouth (**600 mg** of quinine salt **3 times** daily for **5–7 days**), together with or followed by either **doxycycline** (200 mg once daily for 7 days) or **clindamycin** (450 mg 3 times daily for 7 days) or **atovaquone proguanil**.

Doxycycline should not be used in pregnancy and **artemether** should be avoided in early pregnancy.

Complicated *P.falciparum* malaria **Severe malaria** should be considered in any non-immune patient with a parasite count greater than 2% and is a medical emergency.

Management includes **early** and appropriate antimalarial therapy, active treatment of complications, correction of **fluid**, **electrolyte** and **acid–base balance**, and avoidance of harmful ancillary treatments.

The treatment of choice is intravenous **artesunate** given as 2.4 mg/kg IV at 0, 12 and 24 hours and then once daily for 7 days.

However, as soon as the patient has recovered sufficiently to swallow tablets, oral **artesunate** 2 mg/kg once daily is given instead of intravenous therapy, to complete a total cumulative dose of 17– 18 mg/kg.

Rectal administration of **artesunate** is also being developed to allow administration in remote rural areas.

Quinine salt can also be used and is started with a loading dose infusion of 20 mg/kg over 4 hours, up to a maximum of 1.4 g.

This is followed by maintenance doses of 10 mg/kg quinine salt given as 4-hour infusions 2–3 times daily, up to a maximum of 700 mg per dose until the patient can take drugs orally.

The loading dose should **not** be given if the patient has received quinine, quinidine or mefloquine during the previous 24 hours.

Patients should be monitored by **ECG**, with special attention to **QRS** duration and **QT** interval.

Mefloquine should N**ot** be used for severe malaria since N**o parenteral form** is available.

5.20 Severe manifestations of *P. falciparum* malaria and their management

Cerebral malaria	
Coma	Maintain airway, exclude other causes, ventilate if necessary
Convulsions	Diazepam or paraldehyde
Hyperpyrexia	Tepid sponging, fan, paracetamol
Hypoglycaemia	Monitor blood glucose, IV dextrose infusion
Severe anaemia (PCV <15%)	Transfusion
Acute pulmonary oedema	Nurse at 45°, venesect, limit IV fluids, diuretics, CPAP, haemofilter
Acute renal failure	Exclude other causes, dialysis (peritoneal or haemodialysis)
Bleeding/coagulopathy	Transfuse screened fresh blood, or FFP, cryoprecipitate
Metabolic acidosis	Fluids, oxygen, treat sepsis and hypoglycaemia
Shock ('algid malaria')	Suspect Gram –ve septicaemia, IV antimicrobials, fluid resuscitation
Aspiration pneumonia	IV antimicrobials, oxygen, physiotherapy
Hyperparasitaemia	Partial or full exchange transfusion, haemapheresis

From WHO. Severe falciparum malaria. In: Severe and complicated malaria. 3rd edn. Trans R Soc Trop Med Hyg 2000; 94 (suppl. 1): S1-41.

Management of Non-falciparum malaria:

P. vivax, *P. ovale* and *P. malariae* infections should be treated with oral **chloroquine**: 600 mg chloroquine base, followed by 300 mg base in 6 hours, then 150 mg base twice daily for 2 more days.

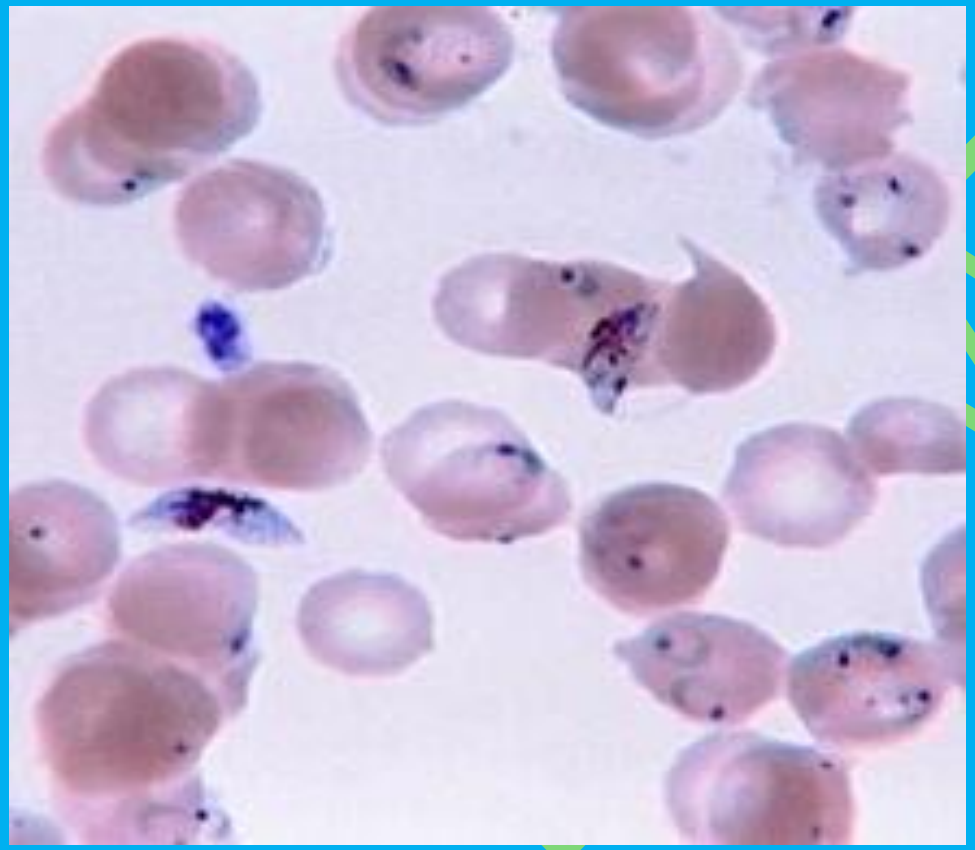
Some **chloroquine** resistance has been reported from Indonesia.

Late relapses can be prevented by prescribing antimalarial drugs in suppressive doses.

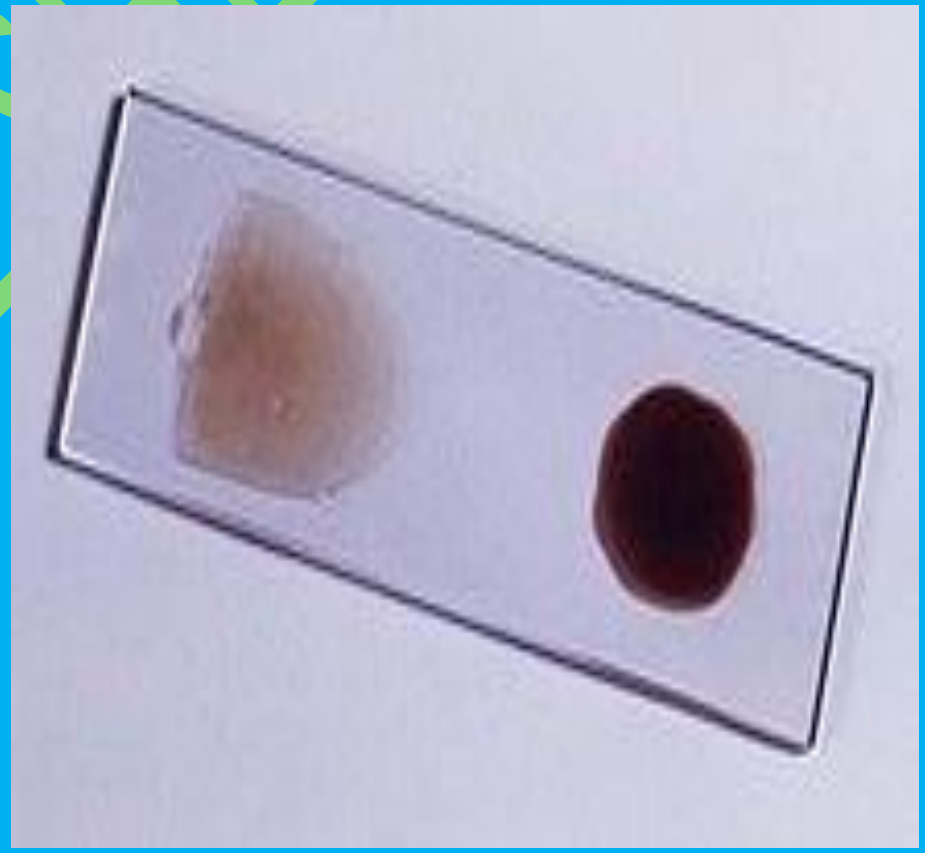
However, **'radical cure'** is now achieved in most patients with *P. vivax* or *P. ovale* malaria using a course of **primaquine** (15 mg daily for 14 days), which destroys the hypnozoite phase in the liver.

Haemolysis may develop in those who are D-deficient. **Cyanosis** due to the formation of methaemoglobin in the red cells is more common but not dangerous.

Ring-forms and gametocytes of Plasmodium falciparum in human blood



blood film is the gold standard for malaria diagnosis.



Immunity can wane:

- Residents of a malaria region may be exposed to the disease so frequently that they acquire a **partial immunity**, which can lessen the severity of malaria symptoms.
- However, this partial immunity can disappear if you move to a country where you're no longer frequently exposed to the parasite.

Prevention:

- Clinical attacks of malaria may be preventable with chemoprophylaxis using **chloroquine**, **atovaquone** plus **proguanil** (Malarone), **doxycycline** or **mefloquine**.
- **Fansidar** should Not be used for chemoprophylaxis, as **deaths** have occurred from **agranulocytosis** or **Stevens– Johnson syndrome** . **Mefloquine** is useful in areas of multiple drug resistance, such as East and Central Africa and Papua New Guinea.

- **Chloroquine** should Not be taken continuously as a prophylactic for more than **5 years** without regular ophthalmic examination, as it may cause irreversible **retinopathy**.
- **Pregnant** and **lactating** women may take **proguanil** or **chloroquine** safely.
- Prevention also involves advice about the use of high-percentage **diethyltoluamide** (DEET), covering up extremities when out after dark, and sleeping under permethrin-impregnated mosquito nets.

Thank you