Malaria

Plasmodium species

Phylum - Apicomplexa

Class- Sporozoa

Subclass – Coccidia

Order – Haemosporidia

Family – Plasmodidae

Genus- Plasmodium

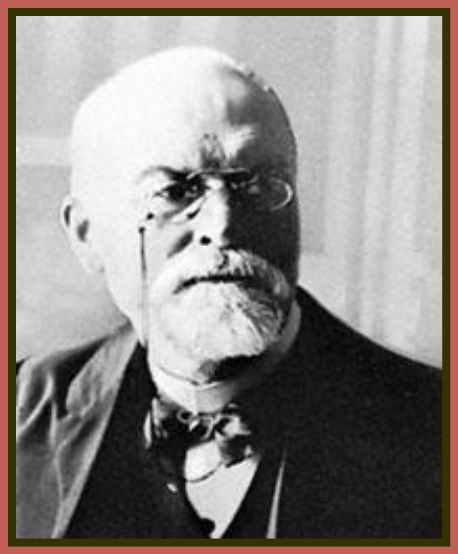
Why Apicomplexa ?

- They possess a structure called apical complex for the penetration and attachment to host cell
- Why sporozoa ?
  - Resistant stage in most parasites of this group called spore
- Why coccidia?
  - Do not possess any organ of locomotion

Species parasitic to human

- Plasmodium vivax
- Plasmodium falciparum
- Plasmodium malariae
- Plasmodium ovale

Malaria - History



Alphonse Laveran
1880

Sir Ronald Ross
1898

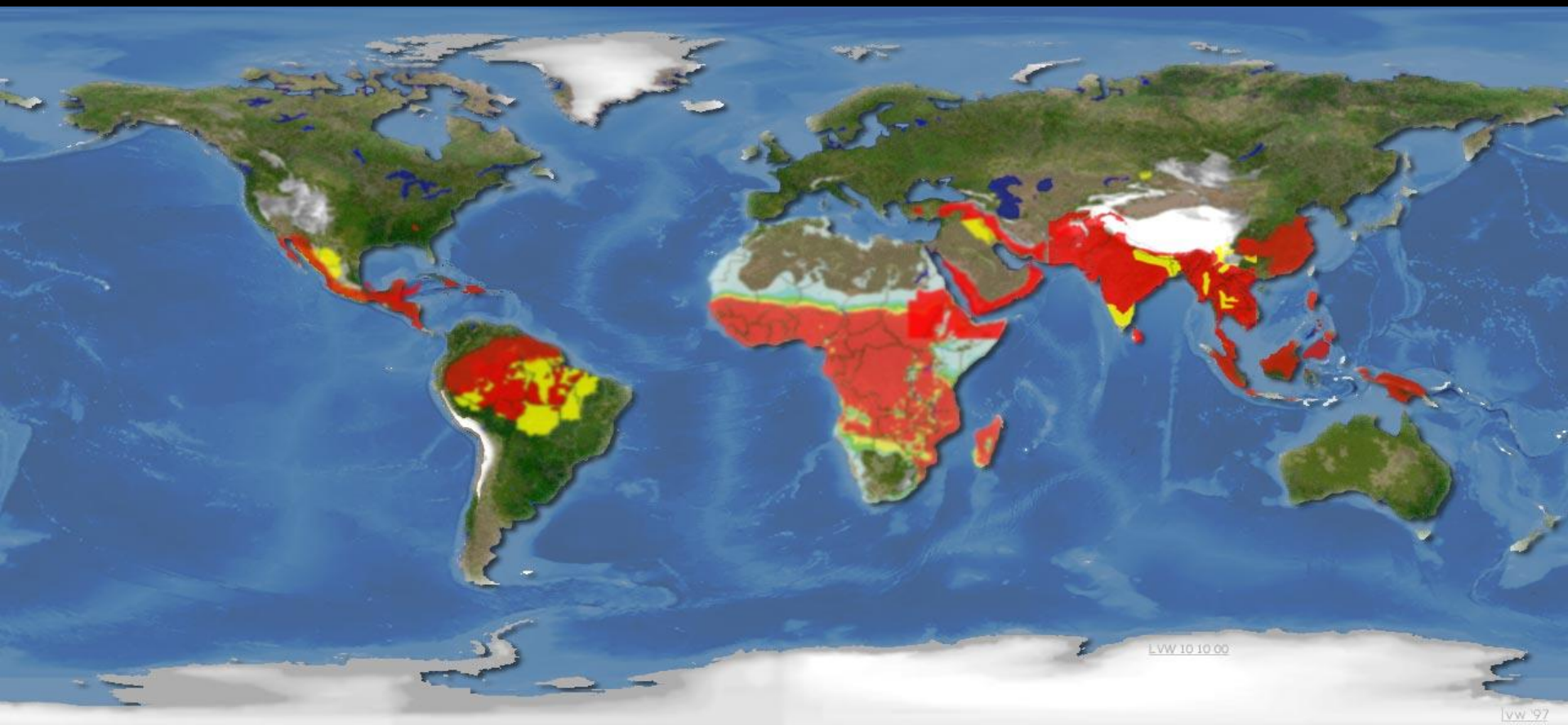
Patrick Manson
1900

Landmarks in development of malaria

- 1880 – Laveran discovered parasite
- 1891 – Romanowsky introduced staining technique
- 1898 – Ross worked out mosquito cycle
- 1900 – Manson proved role of mosquito in transmission

Geographical distribution

- Found in >100 countries
- Tropical zone is endemic area
- P.ovale – East & west Africa
- P.malariae – subtropical zone

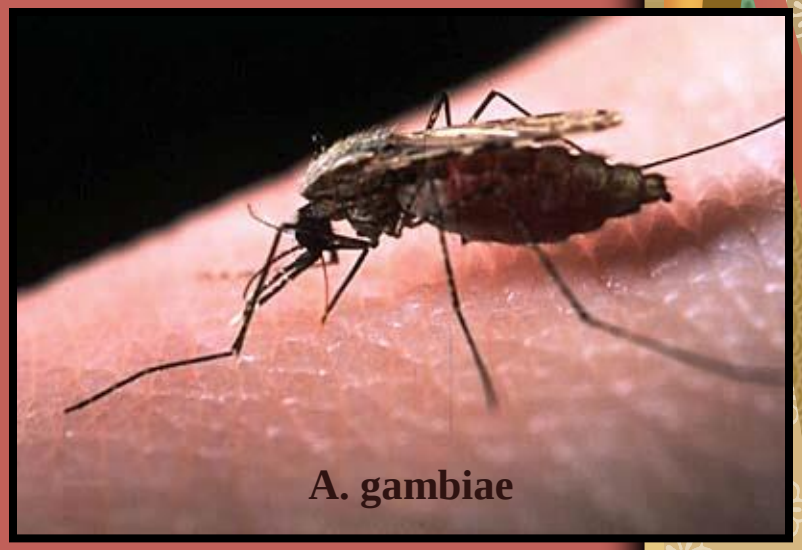


Life cycle :

- Life cycle has got 2 hosts
  - Human – intermediate
  - Mosquito – definitive
- Life cycle has got 2 types of development
  - Asexual cycle – Schizogony (Schizont)
  - Sexual cycle – Sporogony (Sporozoite)
- Possess a life cycle which shows an alteration of generation accompanied by an alteration of host

Malaria – Vectors (cont.)


Anopheles balabacensis


A. gambiae


A. freeborni

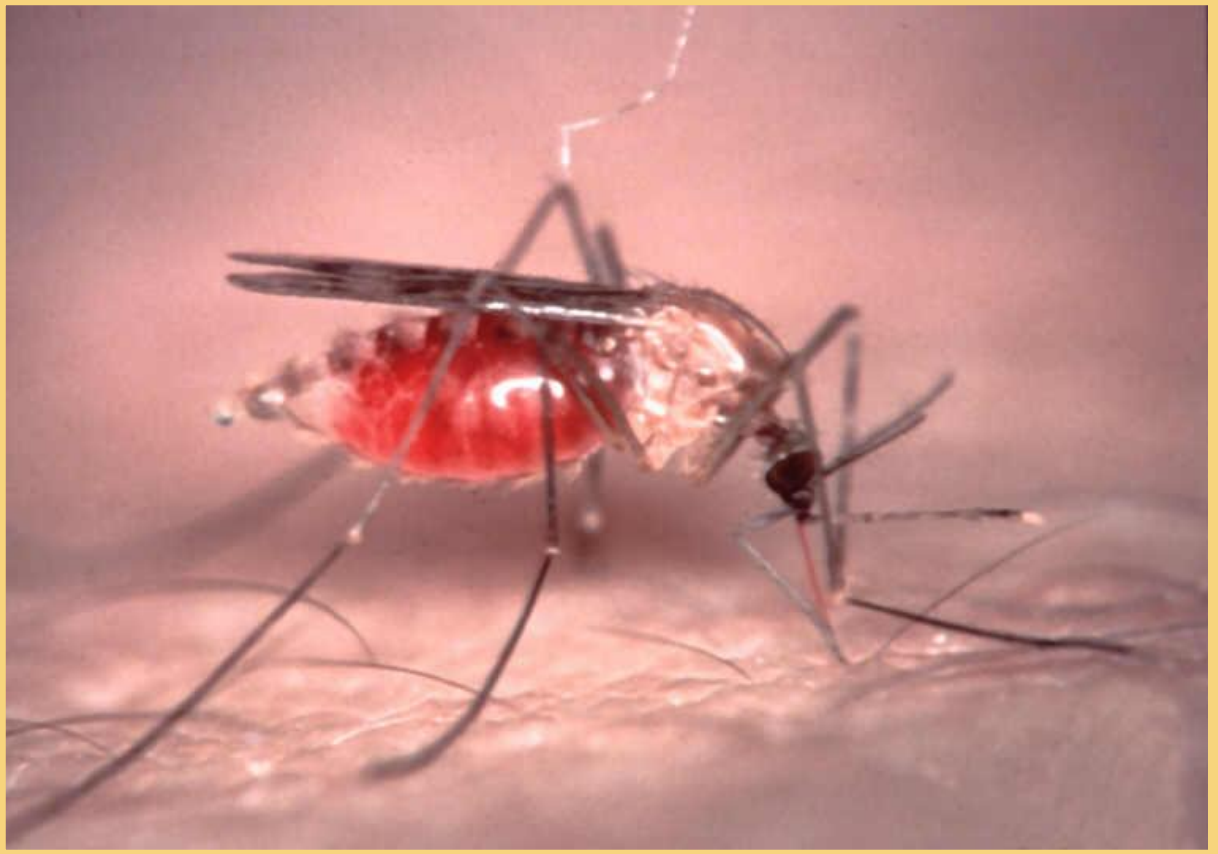

A. stephensi

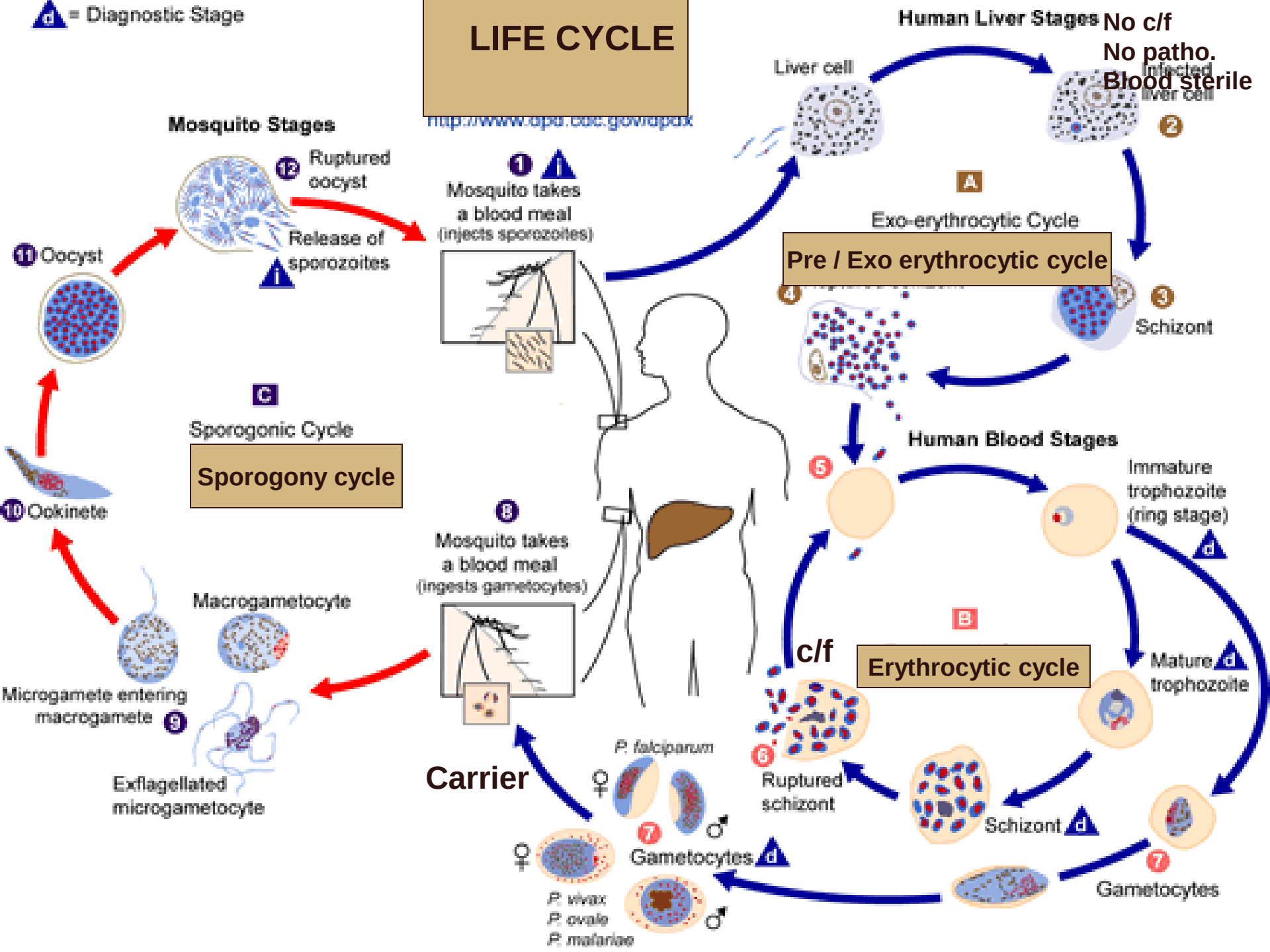
Transmission

- **Mosquito vector: *ANOPHELES***

- **Transmission also possible through:**

1. Blood transfusion
2. Contaminated needle
3. Organ transplant
4. Congenital




d = Diagnostic Stage
LIFE CYCLE
http://www.dpd.cdc.gov/dpdx
Human Liver Stages
No c/f
No patho.
Blood sterile
Liver cell
Infected liver cell
2
A
Exo-erythrocytic Cycle
Pre / Exo erythrocytic cycle
4
3
Schizont
Mosquito Stages
12 Ruptured oocyst
Release of sporozoites
1
Mosquito takes a blood meal (injects sporozoites)
11 Oocyst
C
Sporogonic Cycle
Sporogony cycle
10 Ookinete
8
Mosquito takes a blood meal (ingests gametocytes)
Human Blood Stages
5
Immature trophozoite (ring stage)
Macrogametocyte
B
c/f
Erythrocytic cycle
Mature trophozoite
Microgamete entering macrogamete 9
Exflagellated microgametocyte
Carrier
P. falciparum
6
Ruptured schizont
Schizont
7
Gametocytes
Gametocytes
P. vivax
P. ovale
P. malariae

LIFE CYCLE : STAGES

In Human

- Pre Erythrocytic Schizogony
- Erythrocytic Schizogony
- Gametogony
- Exo Erythrocytic Schizogony

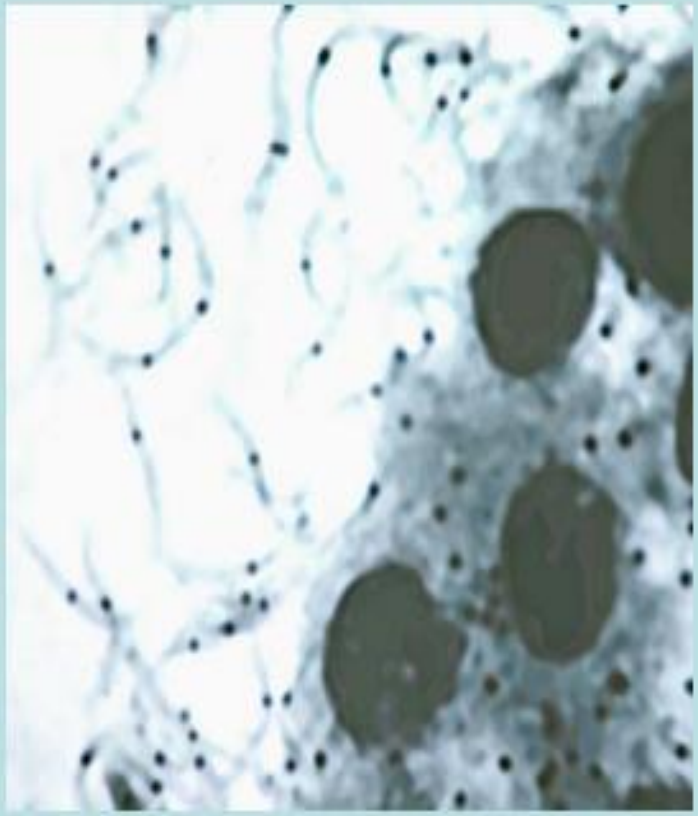
In Mosquitoes

- Exflagellation & fertilization
- Zygote
- Oocyst
- Sporozoite

Human cycle

- Introduction of sporozoite by mosquito
- Liver – Pre-erythrocytic schizogony
- RBC – Erythrocytic schizogony
- Gametogony
- Exoerythrocytic schizogony

Sporozoites of malaria in infected mosquito stomach preparation



Light micrograph

SEM

Human cycle – 1. Pre-erythrocytic

- Sporozoite enter liver tissue, undergo a series of development
- Pre-erythrocytic schizont
  - P.vivax – 8 days
  - P.falciparum – 6 days
  - P.ovale – 9 days
  - P.malariae – 15 days
- Ruptures – liberates merozoites-cryptozoites
  - Smaller – RBC
  - Larger – re-enter liver cell

Erythrocytic schizogony

- Liberated merozoite from liver tissue invade RBC
- Stages
  - TROPHOZOITE
  - SCHIZONT
  - MEROZOITE
- Duration of cycle :
  - P.falciparum – 48 hours
  - P.vivax & P.ovale – 48 to 72 hours
  - P.malariae – 72 hours
- Parasitic multiplication & rupture of RBC – clinical attack

2. Erythrocytic stage

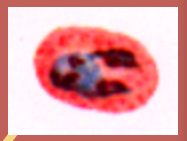
early trophozoite → **later trophozoite**

P.f/36-48hrs

P.v/48hrs

merozoite

immature schizont



Mature schizont

Gametogony

- Some of merozoite - convert into gametocyte – inside capillaries of internal organs
- Only mature forms are found in blood
- Capable of sexual function when leave human host
- Time : 4 days

Gametogony

- Merozoite
- ↓
- Gametocyte
- ↓
- Taken up by mosquito

Mosquito cycle

Mosquito bite a human carrier

↓

1 male (micro) gametocyte – 4-8 thread like microgametes
1 female (macro) gametocyte – 1 macrogamete

↓

Fusion – zygote formation

↓

Zygote –lengthens – ookinete

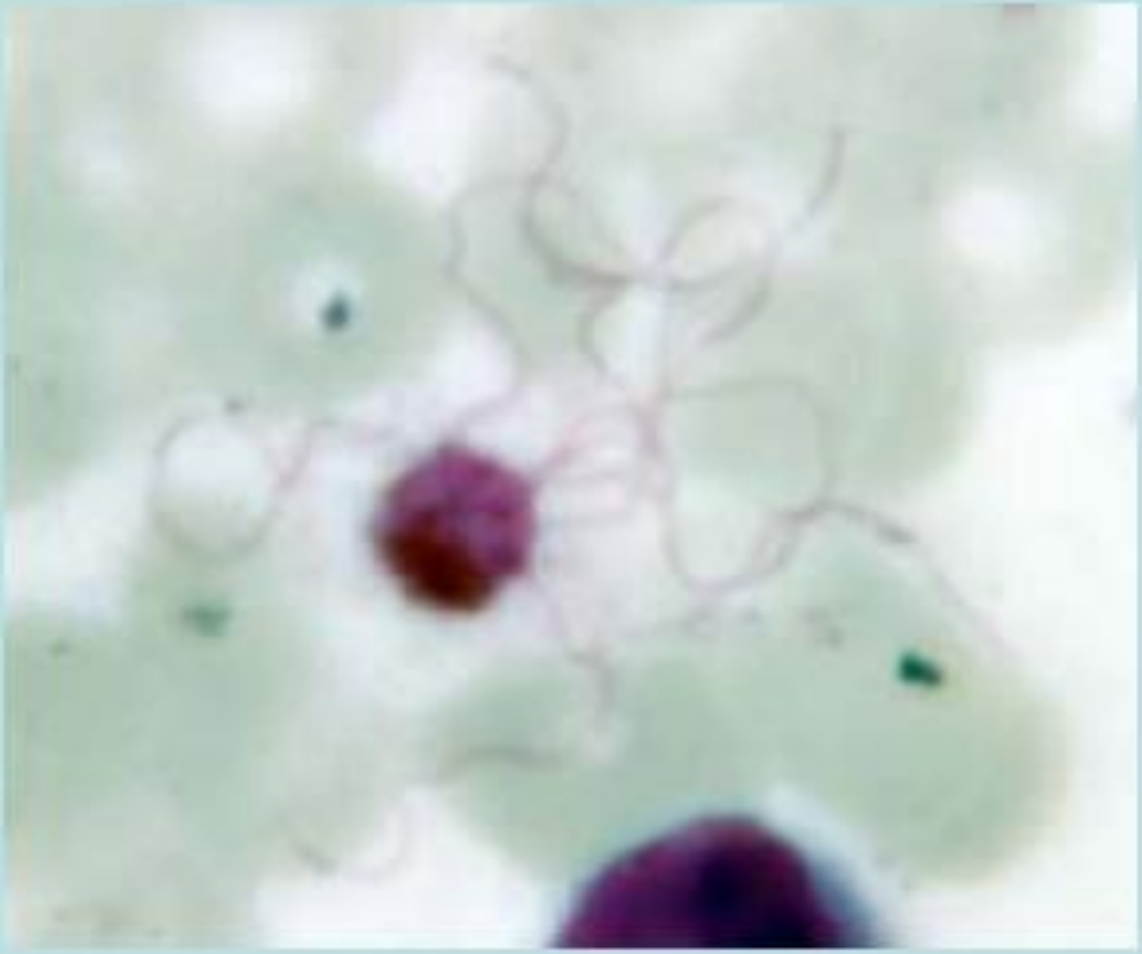
↓

Ookinete comes to lie at peritrophic membrane-penetrate mucosal cell

↓

Convert into oocyst – 6-12 µ -matures – 60 µ contains hundreds to thousands of sporozoites

Ex-flagellation of the microgametocyte of a malaria parasite in mosquito stomach



Morphological features of P. vivax & P. falciparum

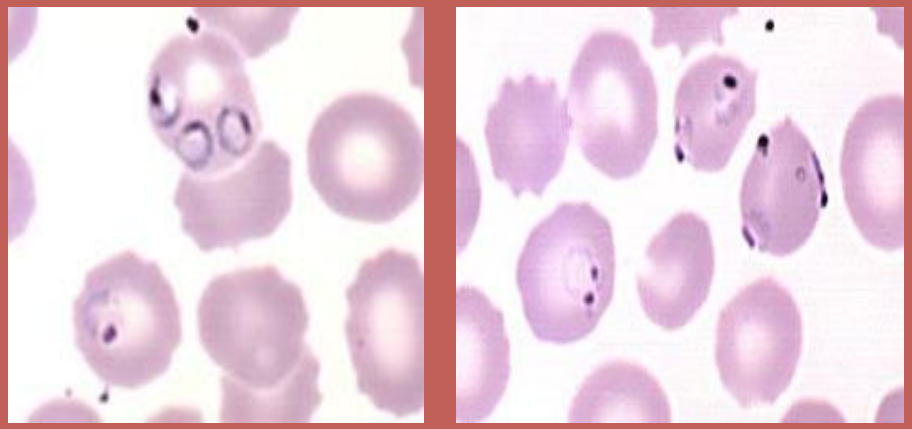
Pre-Erythrocytic schizont of vivax

- 42 µ diameter
- Parenchymal cells of liver
- No. of merozoites = 12,000

Pre-Erythrocytic schizont of falciparum

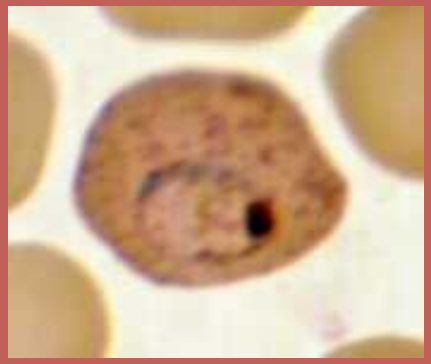
- 60 µ x 30 µ in diameter
- No of merozoites = 40,000

Trophozoite : Ring form



P. falciparum

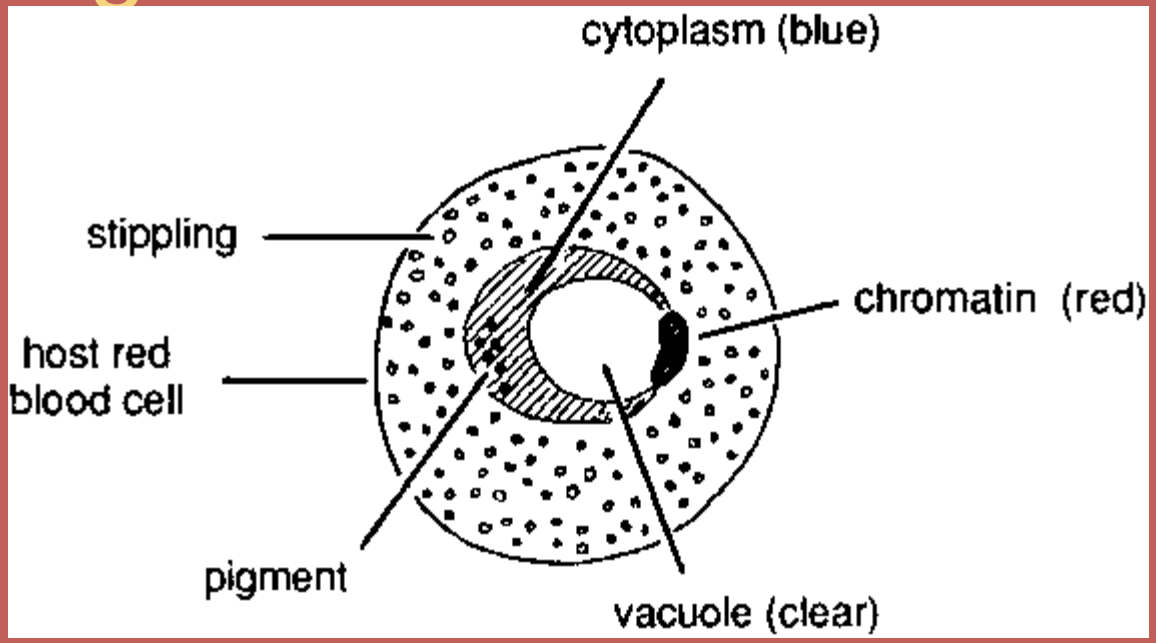
- Rings: double chromatin dots; **accole** forms; **1.25-1.5 µm**
- multiple infections in same red cell
- No enlargement of RBC



P. vivax

- **2.5-3 µm**
- Occupying 1/3 rd of cytoplasm
- RBC gradually enlarges

Changes in RBC – P.vivax



One side of ring thicker, nucleus situated at thinner

Vacuole present

Yellowish brown pigment appear in cytoplasm

Changes in RBC

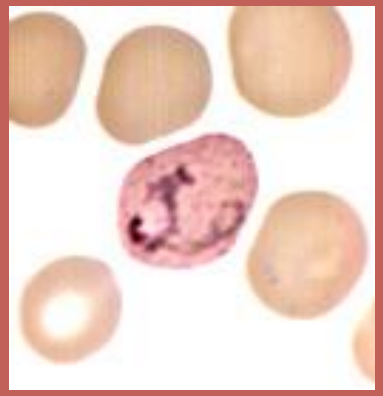
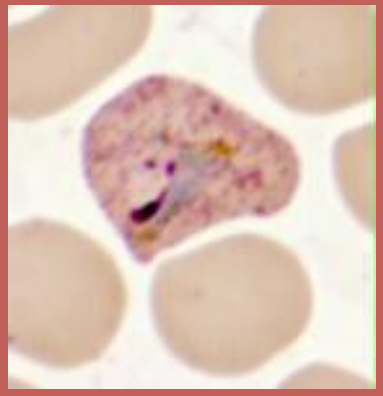
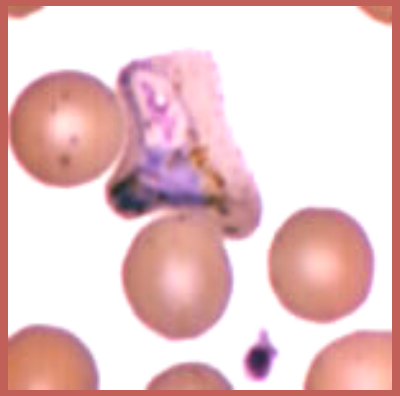
Size : Double

Pale

Shape distorted

Schuffner's dots

Late trophozoite : Growing form

P. vivax

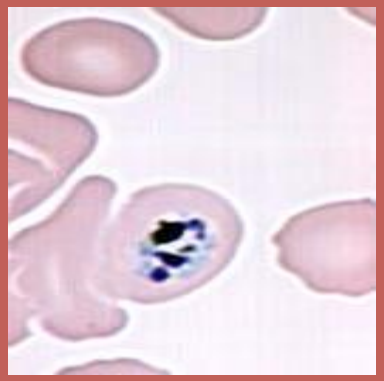
Irregular without vacuole

Actively amoeboid

deforms the RBC

Yellowish brown pigment

Schuffner’s dots



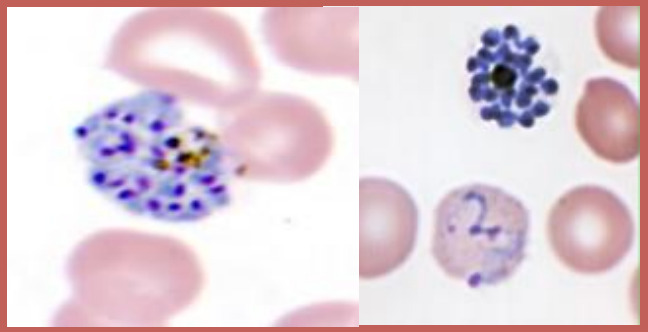
P. falciparum

Compact (rarely seen in peripheral blood)

Dark brown or black pigment

Maurer’s dots/ clefts -6-12 no

Schizonts



P. vivax

Rounded, lost all amoeboid movement

9-10 µm, regular. Vacoule disaapear

Completely fills an enlarged RBC

Merozoites 12-24, arranged in rosette

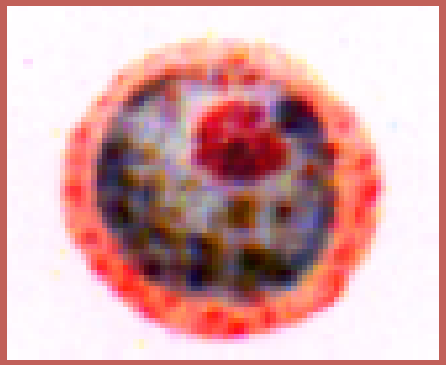
P. falciparum

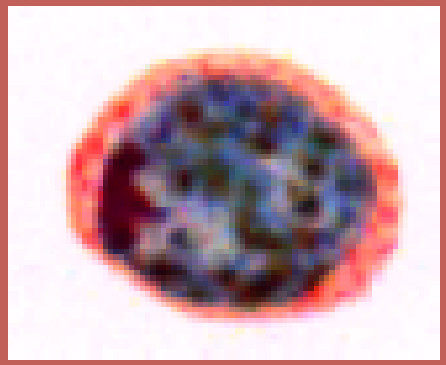
4.5-5 µm, fills 2/3 rd of RBC

8-32, merozoites, an irregular grape like structure

Rarely seen in peripheral blood

Gametocyte

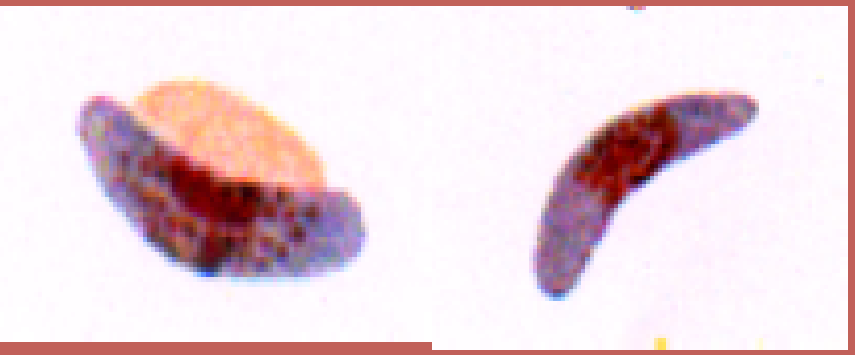




P. vivax

Spherical or globular
Much larger than RBC

	Male	Female
Size	9-10 µ	10-12 µ
Cytoplasm	Light blue	Deep blue
Nucleus	Laterally	Peripherally



P. falciparum

Crescentic, larger than RBC

	Male	Female
Size	8-10 x 2-3 µ	10-12 x 2-3 µ
Cytoplasm	Light blue	Deep blue
Nucleus	Scattered in fine granules	Compact mass in center
Shape	Short, Broad, blunt	Long, narrow & pointed

Comparison of the P.vivax & P.falciparum

	P. vivax	P. falciparum
Pre erythrocytic schizogony	- One cycle (8 days) - Schizont (42µm) -12,000 merozoites	- One cycle (6 days) - Schizont (60x30 µm) - 40,000 merozoites
Erythrocytic schizogony	- 48 hours - clinical attack of malaria	- 36-48 hours - clinical attack of malaria
Exo Erythrocytic schizogony	- Present (not > 3 years) - Relapse can occur	- Absent - Relapses do not occur - Recrudescence occurs
A single infection	- Lasts up to 3 years	- Lasts up to 1 month but maximum of 1 year

Pathogenicity

- Febrile Paroxysm (Periodic fever)

mechanism

-liberation of merozoites,malarial pigment; RBC debris into the blood stream.

symptoms (in a typical case)

- tertian fever – 48 hrs
- quartan fever – 72 hrs
- quotidian fever -24 hrs

Plasmodium Species

- ***P. Falciparum***
  - Most severe and prevalent
  - Malignant tertian malaria
  - 40-60% of cases
  - Widespread CHLOROQUINE resistance
  - Infects RBCs of all ages—Heavy parasitaemia

Plasmodium Species

- ***P. vivax***
  - 30-40% of cases
  - Benign tertian malaria
  - INFECTS YOUNG RBCs: LESS SEVERE THAN FALCIPARUM
- ***P. ovale***
  - Benign tertian malaria
  - INFECTS YOUNG RBCs
- ***P. malariae***
  - Benign qurtan malaria
  - Can persist SUBCLINICALLY for extended periods of time
  - INFECTS OLD RBCs

Incubation Period

P. Falciparum	12 days
P. Vivax	14 days*
P. Ovale	14 days*
P. Malariae	30 days

* May be 8 - 10 months or longer for some strains

Acute Symptoms

- Classical cyclic paroxysm:
  - Cold stage: chills and shaking – 30 min -1 hr
  - Hot stage: 1 – 4 hrs
  - Sweating stage: 2-3 hrs
  - Feel well for period of time, then cycle repeats itself

Clinical signs

- Anemia (Microcytic/hypochromic normocytic)
- Splenomegaly

- **Splenomegaly and anemia**

Cause : Rupture of the infected RBCs, autoimmunity and decrease Erythropoesis

Type : Hemolytic, normochromic and normocytic

Splenomegaly : in order to remove parasitized RBC & parasites

•Recurrence

a repeat attack/s that it is up to months or even years after the primary attack

Reasons :

1. Persistence of sporozoites/hypnozoites in the liver in dormant stage which can start erythrocytic stage again ---- Relapse only occurs in ***P.v. & P.ovale***

2. Persistence of blood infection at low level which can start erthryocytic stage ***-*** Recrudescence – seen in P.falciparum

Pernicious (malignant) malaria

Caused by P. falciparum (Fatal condition)

>5% RBCs are infected

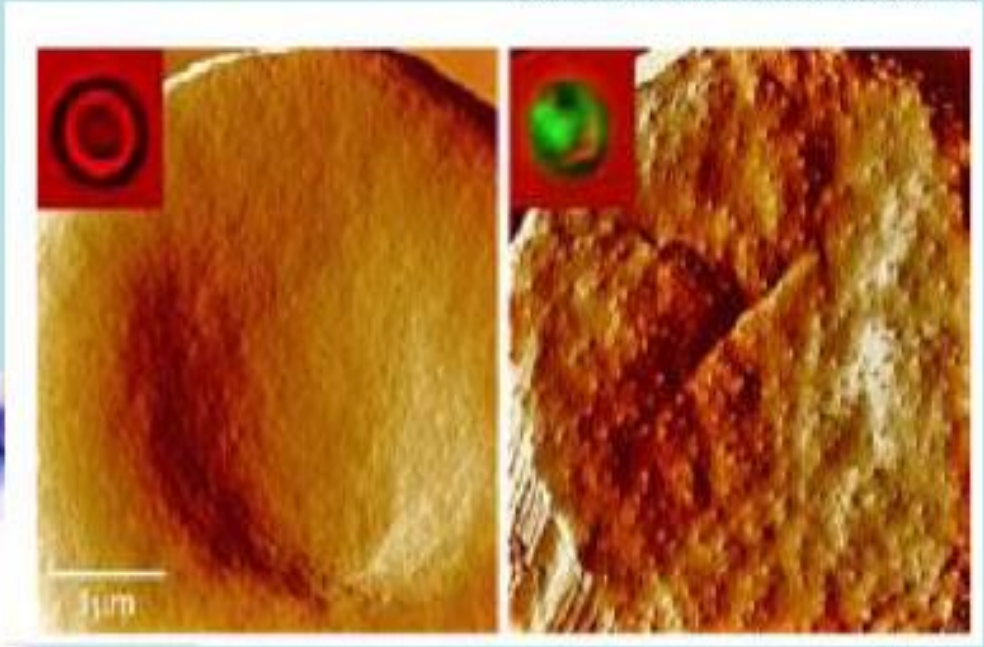
- Cerebral malaria
- Algid malaria
- Septicaemic malaria

Special feature of P.falciparum

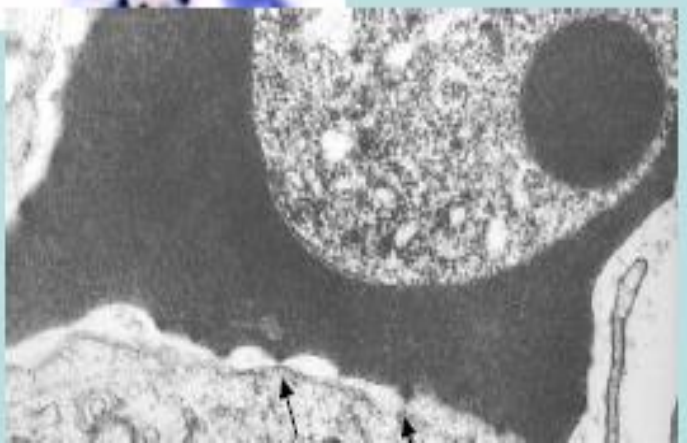
- RBC infected with P.falciparum has got knobs
- Adhesive proteins present over it
- Increase stickiness of RBC to capillary endothelial cells as well as with normal RBC
- Obstruction to blood supply to vital organs – brain & heart

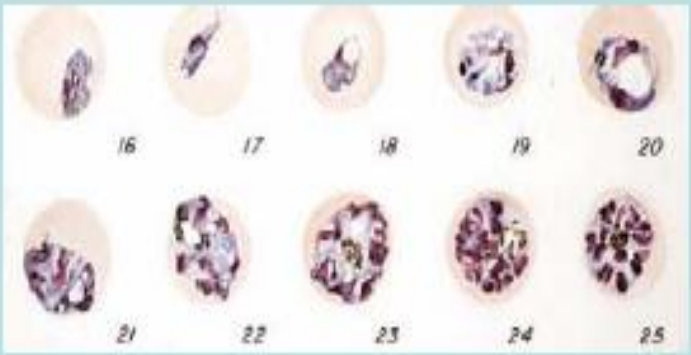
Normal RBC

Atomic force microscopy of knobs



In situ RBCs
with *P. falciparum*





Stages of *P. falciparum* with knobs

Cerebral malaria

- Commonest cause of death in malignant malaria
- Hyperpyrexia, convulsion & coma
- High TNF level – vascular endothelial adhesiveness
  - direct CNS effect
- Increased endothelial permeability

Algid malaria

- Cold, clammy skin with circulatory collapse
- Sever abdominal pain, vomiting, diarrhoea
- Mucosal & sub mucosal capillaries packed with parasitized RBCs

Septicaemic malaria

- High degree of parasitaemia leading to high degree of continuous fever
- Acute lung injury
- Alveolar capillaries & coronary blood vessels are congested & filled with parasitized RBCs

Blackwater fever

- Malarial haemoglobinuria is some time associated with falciparum malaria, particularly in patients who have experienced repeated infections & inadequate quinine therapy
- Auto antibodies against RBCs

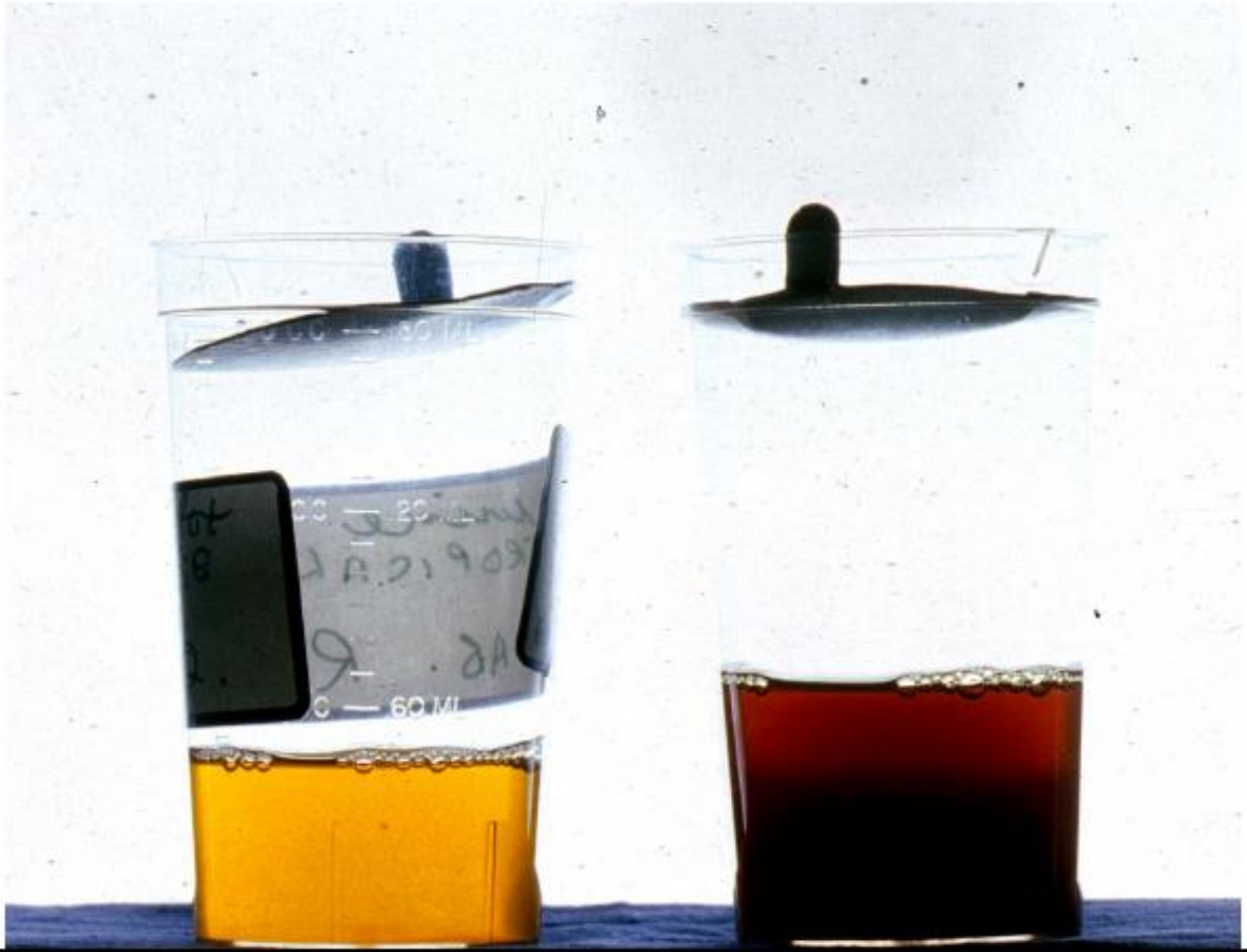
↓

I/V haemolysis

- Parasites are not detected in blood during & just after the attack but may reappear after an week of acute attack

- Fever with rigor, aching pain in loins, bilious vomiting, icterus, haemoglobinuria, circulatory collapse, ARF.
- Urine – red to dark red (port-wine / cola)

  - acidic



Genetically determined conditions conferring protection against death from malaria

- Sickle-cell trait
- Ovalocytosis
- Absence of Duffy blood group antigen
- G6PD deficiency