University of Zambia
School of Medicine

3rd/4th Year MBChB

Tembo

2023

Malaria

Phylum **APICOMPLEXA**

Class **SPOROZOEA**

Subclass **COCCIDA**

Order **EUCOCCIDIIDA**

Suborder **EIMERIINA**

e.g. **Crytosporidium, Pneumocystis, Sarcocystis, Toxoplasma, Isospora**

Suborder **HAEMOSPORINA**

e.g **Plasmodium**

Malaria Epidemiology

- Malaria has been haunting mankind for many years
- Has killed more people than all the wars
- Globally, about 3.2 billion people are at risk of malaria, and 1.2 billion are at high risk
- In 2015, malaria caused 214 million infections and 438000 deaths
- Nearly 90% of these deaths occurred in Africa, and 70% occurred in children <5 years

Causative Agents of Human Malaria

- *Plasmodium vivax*: Benign Tertian Malaria
- *Plasmodium falciparum*: Malignant Tertian Malaria
- *Plasmodium malariae*: Benign Quartan Malaria
- *Plasmodium ovale*: Benign Tertian Malaria

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- *Plasmodium knowlesi* (monkey-derived malaria)

Each disease has a distinct course

Tertian Malaria” (*P. falciparum, P. ovale and P. vivax*) fever occurs every third day.

“Quartan Malaria” (*P. malariae*) fever occurs every fourth day.

Distribution

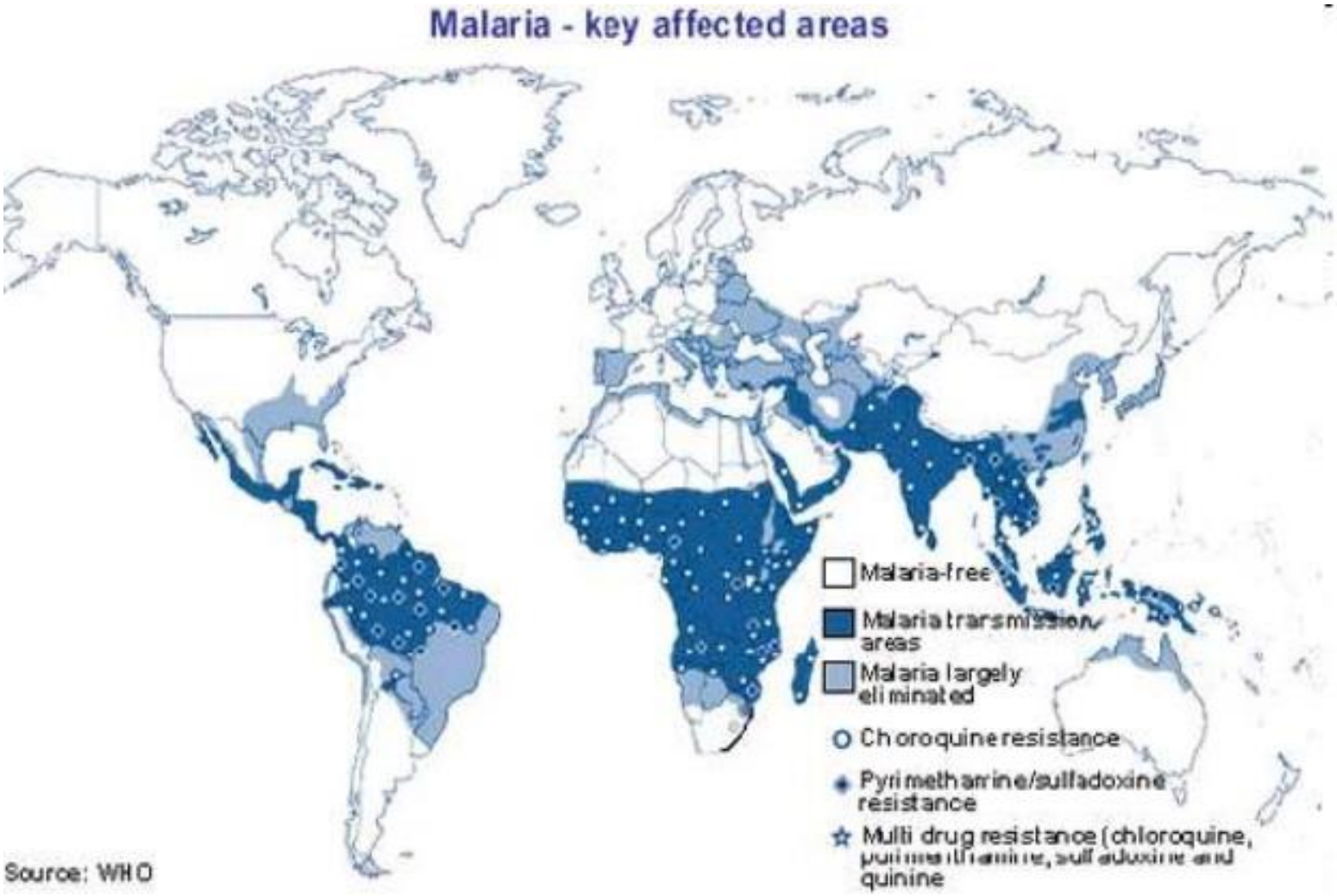
- *P*. *vivax* is the most widely distributed in Asia, North Africa, and Central and South America

- *P*. *falciparum*, the predominant species in Africa, Papua New Guinea, and Haiti, is rapidly spreading in South-east Asia and India

- *P*. *malariae* is present in most places but is rare, except in Africa

- *P*. *ovale* is virtually confined to West Africa where it ranks second after *P*. *falciparum*

Distribution of Malaria Infection



Transmission

- Transmitted by female Anopheles sp. mosquito; dusk until dawn

- Other forms of transmission
  - blood transfusion, congenitally acquired disease, organ transplantation, and sharing of contaminated needles

- “Airport malaria” → infected mosquitoes can enter a country via airplane thereby transmitting infection

Transmission Patterns

- Malaria may occur in endemic as well as epidemic patterns

  – It is described as **endemic,** when it occurs constantly in an area over a period of several successive years and

  – as **epidemic,** when periodic or occasional sharp rises occur in its incidence

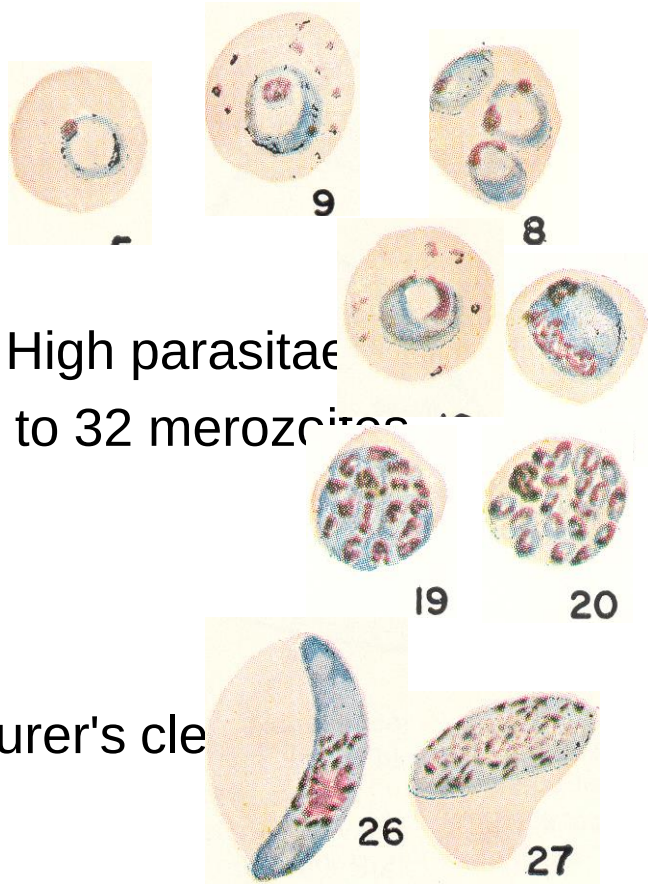
Transmission Patterns

- Hypoendemic (transmission is low)
- Mesoendemic (transmission is moderate)
- Hyperendemic (transmission is intense but seasonal)
- Holoendemic (transmission of high intensity)

Plasmodium falciparum

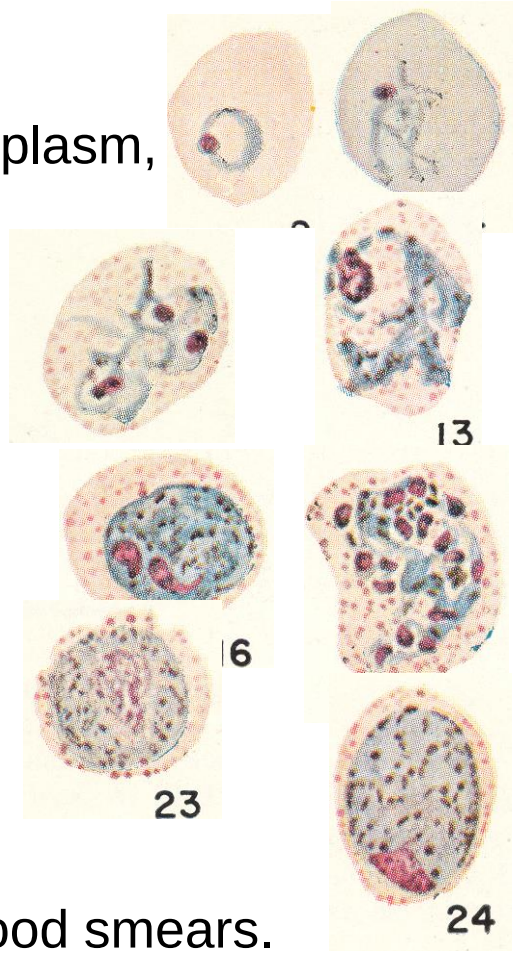
- World wide
- **Habitat**: rbcs of all ages
- **Morphology:**

1. Trophozoite, ring stage. multiple infections, High parasitae
2. Schizont infected cell ruptures to release up to 32 merozoites
3. Gametocytes: enclosed in rbc membrane
   Banana shaped, called crescents
4. Zygote, Ookinete, Oocyst, Sporozoites
5. Infected rbc show stippling on the surface (Maurer's cle



Plasmodium vivax

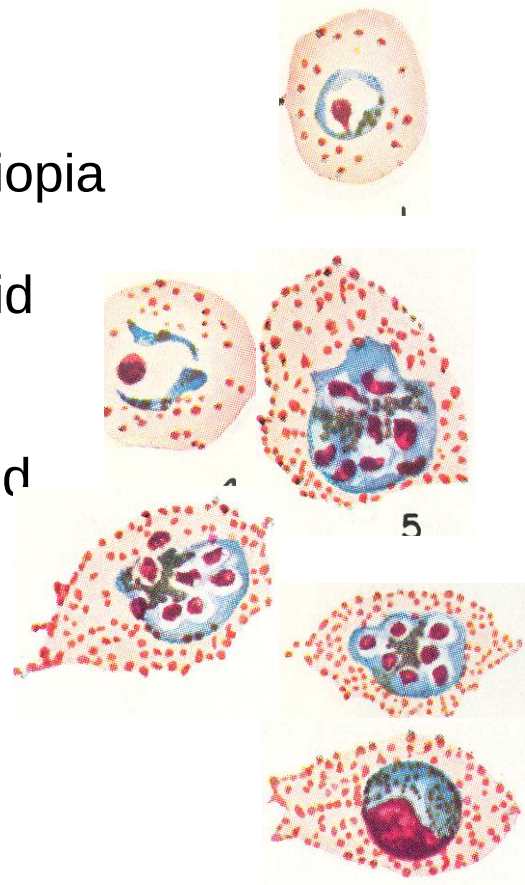
- Nearly Worldwide, 16 Degrees North -20 degrees South. **P. vivax rare in West Africa**
- **Habitat – Infects young RBCs**
- 1. Trophozoites- large, fragmented amoeboid cytoplasm,
- infected rbcs enlarged and pale,
- Schuffner's dots in infected rbc cytoplasm
- 2. Schizonts 8-24 merozoites,
- schizogony 48hourly
- 3. Gametocytes compact and round,
- fill rbc without sign of schizogony
- 4. **Hypnozoites**: Latency for several years
- = Dormant sporozoites in hepatocytes
- Uninucleate, Explains clinical malaria relapses.
- **Krotoski (1980). Brit. Med J. 1:153-154**
- 5. No Knobs,no sequestration, all stages seen in blood smears.



Plasmodium ovale

- Least common malaria, Vivax –like
- **Habitat- infects young RBCs**
- Tropics, esp W.Africa, Burma, China, S.E.Asia, Ethiopia
- **Morphology:**

1. Trophozoites: compact cytoplasm, not amoeboid , large prominent nuclei
2. Schuffner's dots, infected rbc slightly enlarged
3. 20-30% parasitised rbcs oval, show fimbria, ragged end, artifact
4. Low merozoite numbers 8-10, central darker pigment
5. Gametocytes: oval, rbcs fimbriated, show Schuffner's dots.
6. Hypnozoites present

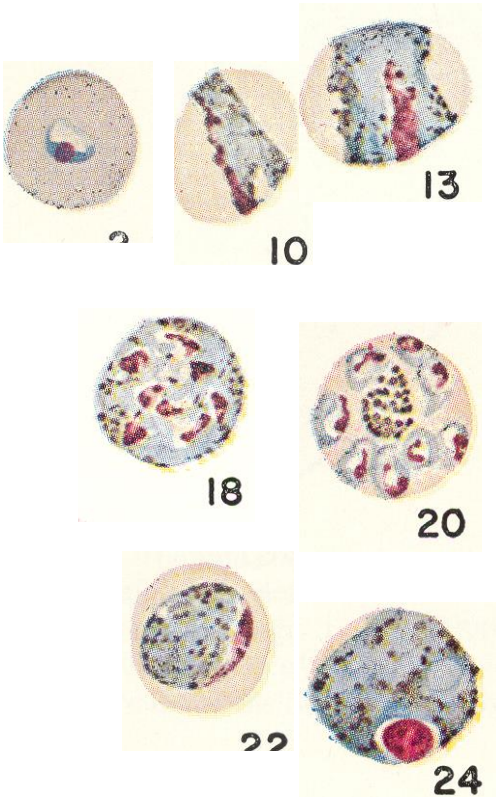


Plasmodium malariae

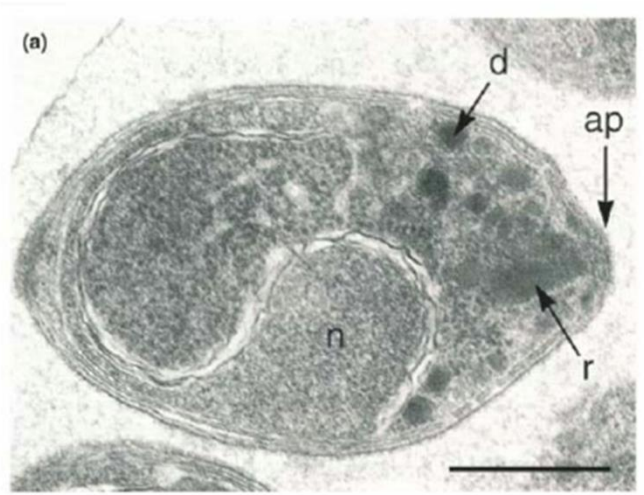
- Tropical Africa, Asia, India, used to
- in Europe and USA, uncommon in S.America
- **Habitat- Infects old RBCs**

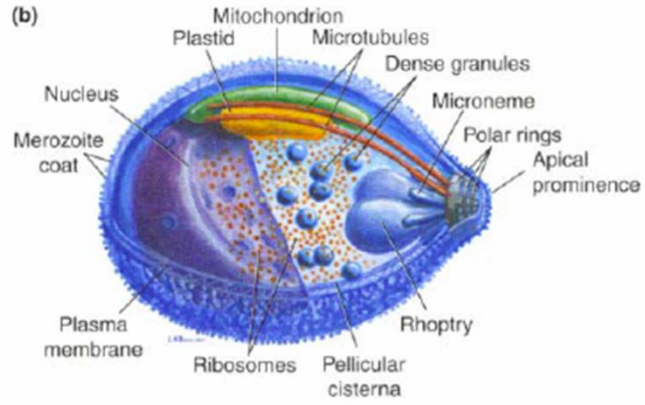
Morphology:

1. Trophozoites form bands around rbc , invades mature cells
2. Schizogony 72 hourly
3. No Schuffner's dots,Zieman's stippling
4. Schizonts: 6 - 12 merozoites, with malaria pigment at the center forming Daisy heads or marguerites
5. Gametocytes oval
6. No Hypnozoites: 40 year recrudescence



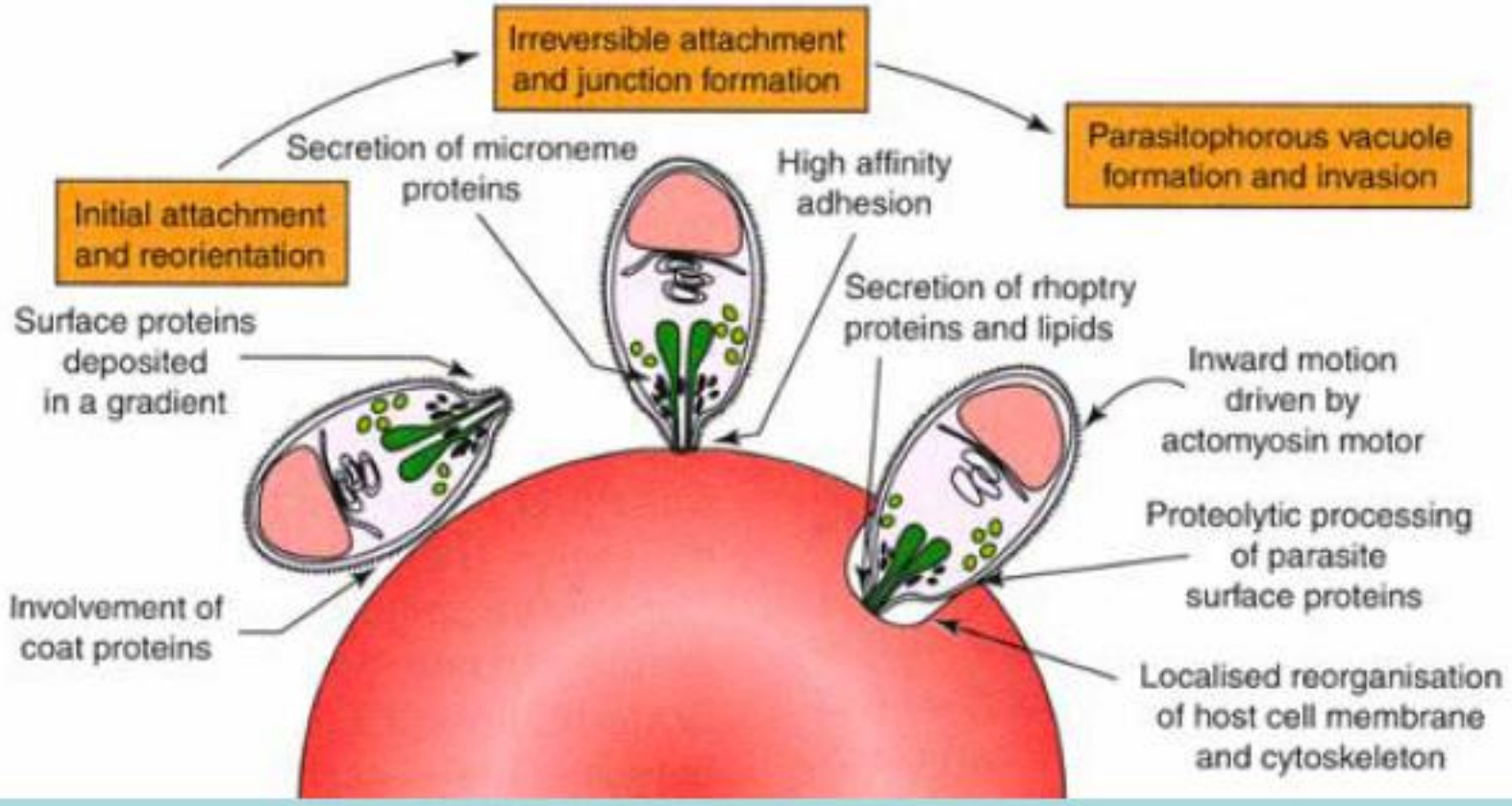
The Plasmodium parasite that invades





Plasmodium Anatomy

Mechanisms of Red Cell Invasion By Plasmodium



www.columbia.edu/itc/hs/medical/pathophys/parasitology/2006/PAR-05Color .pdf

Life Cycle

- Malaria parasite passes its life cycle in 2 hosts.
  - **Definitive host**: Female Anopheles mosquito
  - **Intermediate host**: Man

- an asexual phase occurring in humans, which act as the intermediate host and

- a sexual phase occurring in mosquito, which serves as a definitive host for the parasite

Life Cycle

Asexual phase:

- Malaria parasite **multiplies** by division or splitting a process designated to as **Schizogony** (from **schizo**: to **split**, and **gone = generation**)

- This asexual phase in man, is also called **vertebrate, intrinsic, or endogenous phase**

Life Cycle

- **In humans, schizogony occurs in 2 locations**
  - **I**n the red blood cell (**erythrocytic schizogony) and**
  - **In** the liver cells (**exoerythrocytic schizogony or the** tissue phase)
- Products of schizogony, whether erythrocytic or exoerythrocytic, are called **merozoites (meros: a part**, **zoon**: **animal**)

Life Cycle

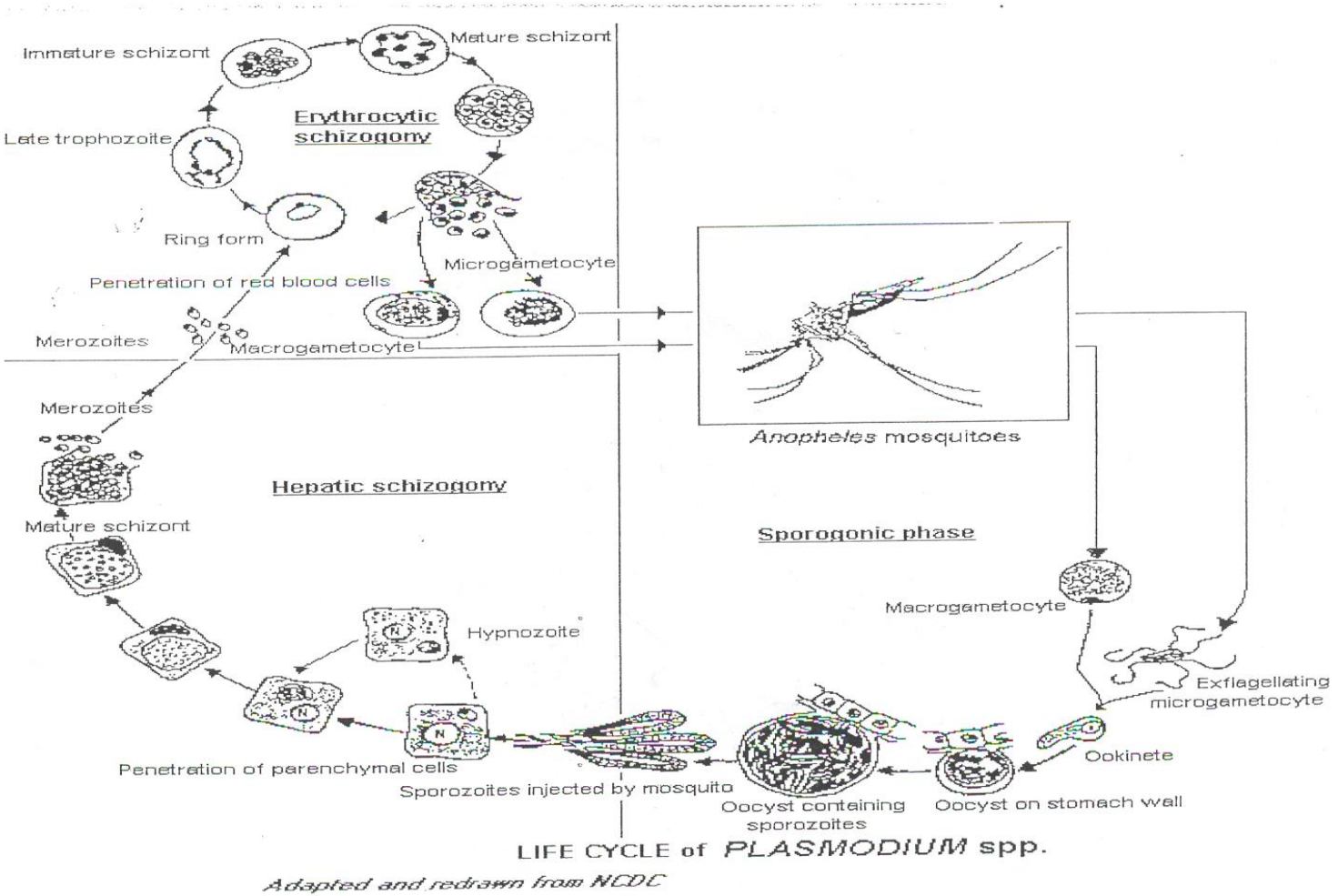
Sexual phase:

- Takes place in female Anopheles mosquitoes

- Maturation and fertilization give rise to a large number of sporozoites (from sporos: seed)

- Phase of sexual multiplication is called **sporogony or also called** the invertebrate, extrinsic, or exogenous phase

Life Cycle


Immature schizont
Mature schizont
Erythrocytic schizogony
Late trophozoite
Ring form
Microgametocyte
Penetration of red blood cells
Merozoites
Macrogametocyte
Merozoites
Hepatic schizogony
Mature schizont
Hypnozoite
Penetration of parenchymal cells
Sporozoites injected by mosquito
Oocyst containing sporozoites
Oocyst on stomach wall
Ookinete
Exflagellating microgametocyte
Macrogametocyte
Sporogonic phase
Anopheles mosquitoes
LIFE CYCLE of PLASMODIUM spp.
Adapted and redrawn from NCDC

Life Cycle-Human Cycle (Schizogony)

- Human infection comes through the bite of the infective female Anopheles mosquito
- Sporozoites, which are infective forms of the parasite are present in the salivary gland of the mosquito
- Injected into blood capillaries when the mosquito feeds on blood after piercing the skin
- Usually, 10–15 sporozoites are injected at a time

Life Cycle-Human Cycle (Schizogony)

- Within an hour of being injected into the body by the mosquito, the sporozoites reach the liver and enter the hepatocytes

  – To initiate the stage of **pre-erythrocytic schizogony or merogony** (tissue) stage or exoerythrocytic stage

- The sporozoites undergo repeated nuclear division to become schizonts

Life Cycle-Human Cycle (Schizogony)

- Mature liver stage schizonts contain 2000–50,000 **merozoites**

- Mature schizonts rupture in 6–15 days and release thousands of merozoites into the blood stream

- The merozoites infect the erythrocytes

Life Cycle-Human Cycle (Schizogony)

Erythrocytic stage

- The merozoites released by pre-erythrocytic schizonts invade the red blood cells

- Transform to become young parasites ‘ the **ring forms or young trophozoites’**

- **Young trophozoites become late (mature) trophozoite and transform into schizonts or meronts**

- Then become mature schizont containing 8–32 merozoites and haemozoin

Life Cycle-Human Cycle (Schizogony)

- The mature schizont bursts releasing the merozoites into the circulation

- The merozoites invade fresh erythrocytes within which they go through the same process of development (young ringforms – mature trophozoites)

- This cycle of **erythrocytic Schizogony or merogony is** repeated sequentially
  - leading to progressive increase in the parasitaemia, till it is arrested by the development of host immune response

Life Cycle-Human Cycle (Schizogony)

- Rupture of mature schizont releases large quantities of pyrogens.
- This is responsible for the febrile paroxysms characterizing malaria
- In *P*. *falciparum*, erythrocytic schizogony always takes place inside the capillaries and vascular beds of internal organs

Life Cycle-Human Cycle (Schizogony)

- The parasite feeds on the haemoglobin of the erythrocyte

- It does not metabolize haemoglobin completely and
  - therefore, leaves behind a haematin-globin pigment called the **malaria pigment or haemozoin pigment as** residue

Life Cycle-Human Cycle (Schizogony)

Gametogony

- After a few erythrocytic cycles
  - some of the merozoites that infect RBC's do not proceed to become trophozoites or schizonts but instead develop into sexually differentiated forms of **gametocytes**

- Development of gametocytes takes place within the internal organs and only the mature forms appear in circulation

Life Cycle-Human Cycle (Schizogony)

- The mature gametocytes are round in shape, except in *P. falciparum*, in which they are **crescent-shaped**
- In all species, the female gametocyte is larger (**macrogametocyte)**
- In the smaller male gametocyte (**microgametocyte)**
- Female gametocytes are generally more numerous than the male gametocytes

Life Cycle-Human Cycle (Schizogony)

- Gametocyte appear in circulation
  - 4–5 days after the first appearance of asexual form in case of *P. vivax*
  - and 10–12 days in *P. falciparum*

- A person with gametocytes in blood is a carrier or reservoir

- The gametocytes do not cause any clinical illness in the host, but are essential for transmission of the infection

Life Cycle-The Mosquito Cycle (Sporogony)

- When a female Anopheles mosquito ingests parasitized erythrocytes along with its blood meal
  - the asexual forms of malaria parasite are digested
  - but the gametocytes are set free in the midgut (stomach) of mosquito and undergo further development

- The nuclear material and cytoplasm of the male gametocytes divides to produce 8 microgametes with long, actively motile, whip-like filaments **(exflagellating male gametocytes)**

Life Cycle-The Mosquito Cycle (Sporogony)

- The female gametocyte does not divide but
  - undergoes a process of maturation to become the female gamete or macrogamete
  - It is fertilized by one of the microgametes to produce the **zygote**

- The zygote, which is initially a motionless round body, gradually elongates and
  - within 18–24 hours, becomes a **vermicular motile form ca**lled the **ookinete** (**travelling vermicule)**

Life Cycle-The Mosquito Cycle (Sporogony)

- The **ookinete develops into oocyst**
  - **which is yet** another multiplicatory phase, within which numerous **sporozoites are formed**

- The mature oocyst ruptures releasing sporozoites which find their way to the salivary glands

Life Cycle-The Mosquito Cycle (Sporogony)

- The mosquito is now infective and when it feeds on humans
  - the sporozoites are injected into skin capillaries to initiate human infection

- The time taken for completion of sporogony in the mosquito is about **1–4 weeks (extrinsic incubation period)**
  - **depending on the environmental temperature** and the species

Incubation period

- The average incubation periods of different species of *Plasmodium* are as follows –
  - *P*. *vivax*—14 (8–31) days
  - *P*. *falciparum* —12 (8–14) days
  - *P*. *ovale* —14 (8–31) days
  - *P*. *malariae* —28 (18–40) days

Incubation and Pre-patent period

- The incubation period:
  - is the interval between the entry of sporozoites into the host and the earliest manifestation of clinical illness is the **incubation period**

- The pre-patent period:
  - is the interval between the entry of the parasites into the host and the time when they first become detectable in blood

Recrudescence

- In *P*. *falciparum* and *P. malariae* infections after the primary attack, sometimes there is a period of latency
  - during which there is no clinical illness

- But some parasites persist in some erythrocytes,
  - although the level of parasitemia is below the fever threshold or sometimes below the microscopic threshold

- Fresh malarial attacks then develop after a period of latency

Recrudescence

- Usually within 8 weeks after the primary attack and
  - resulting from persistence of the erythrocytic cycle of the parasites are called **recrudescences**

- Recrudescence may be due to
  - waning immunity of the host, or possibly due to antigenic variation, drug resistance or under dosage

- In *P. falciparum* infections, recrudescences are seen for 1–2 years

- In *P. malariae* infection, they may last for long periods, even upto 50 years

Relapse

- It is seen in *P. vivax* and *P*. *ovale* infections

- In both these species, 2 kinds of sporozoites are seen
  - some of which multiply inside hepatocytes promptly to form schizonts and others which remain dormant

- These latter forms are called **hypnozoites (from hypnos: sleep)**
  - **Hypnozoites** remain inside the hepatocytes as uninucleated forms for long periods

Relapse

- Such new attacks of malaria, caused by dormant exoerythrocytic forms

- Reactivated usually from 24 weeks to 5 years after the primary attack to cause **relapse**

Pathogenesis of Malaria

1. Erythrocytic infection
2. Cytoadherence, rosetting and sequestration - P. f
3. Host defense mechanism -immunopathology

Pathogenesis of Malaria

1. Erythrocytic infection

- Particularly in *P. falciparum infection* results in
    - progressive and dramatic structural changes, biochemical and mechanical modifications of the red cells
- Several pathophysiological factors occur:
    - the parasite biomass; ‘malaria toxin(s)’ and inflammatory response

Pathogenesis of Malaria

1. **Erythrocytic infection**

   Anaemia: Normocytic, hemolytic

   a. Erythrocytic infection, Parasite multiplication and survival - Hb digestion

   b. Destruction of parasitized rbcs at end of schizogony

   c. Auto-antibodies specific for unparasitized cells: - autoimmune, nonspecific sensitization, rbcs bind Ab/Ag complexes that fix complement

Pathogenesis of Malaria

2. Cytoadherence, sequestration and rosetting - Pf leads to

- altered deformability and fragility of parasitized erythrocytes;

- endothelial activation,

- The above have been found to be involved in the development of severe malaria due to Pf

Pathogenesis of Malaria

Cytoadherence

- Structural changes in the infected red cells and the resulting increase in their rigidity and adhesiveness are major contributors to the virulence for *P. falciparum* malaria

- Owing to the increased adhesiveness,
  - the red cells infected with late stages of *P. falciparum* adhere to the capillary and postcapillary venular endothelium in the deep microvasculature (**cytoadherence)**

Pathogenesis of Malaria

Sequestration

- Cytoadherence leads to **sequestration** of the parasites in various organs such as
  - the heart, lung, brain, liver, kidney, intestines, adipose tissue, subcutaneous tissues and placenta
- Sequestration of the growing *P. falciparum* parasites in these deeper tissues provides them the microaerophilic venous environment
  - that is better suited for their maturation and the adhesion to endothelium allows them to escape clearance by the spleen and to hide from the immune system

Pathogenesis of Malaria

- Certain **proteins** expressed on the surface of the infected red cells mediate the adhesion of parasitized RBCs to the endothelium walls of capillaries, organs and to uninfected red cells

  - E.g. *P. falciparum* erythrocyte membrane protein 1 (**PfEMP1**), Histidine rich protein II (**HRP II**) bind to ligands on endothelial cells
    - chondroitin sulfate A (**CSA**) protein (placenta)

Pathogenesis of Malaria

- **Ligands** include CD36, thrombospondin, vascular cell adhesion molecule 1 (VCAM I), intercellular adhesion molecule II (ICAM II) and E-selectin

- Causing stickiness of iRBCs to endothelial cell lining of small blood vessels (sequestration) , slugging, stasis of blood = “blockage” cause lesions, local anoxia, ischaemia, Increased vascular permeability and unparasitized cells leak in perivascular space

Pathogenesis of Malaria

Rosetting

- The infected red cells also adhere to the uninfected red cells resulting in the formation of red cell rosettes (resetting)
- **Rosetting** is mediated by binding of
  - PfEMP1-DBLα on the surface of infected red cells to complement receptor 1
  - CD31, and heparin sulfate-like glycosaminoglycans of uninfected RBCs

Pathogenesis of Malaria

- Due to the sequestration
  - only the ring-stage trophozoites of *P. falciparum* are seen circulating in the peripheral blood

  - **Cytoadherence - rosetting-sequestration** of infected and uninfected rbcs in the vital organs can lead to
    - ultimately blocking blood flow, limits the local oxygen supply
    - This contributes to the development of severe disease

Pathogenesis of Malaria

3. Immunopathology of malaria:

- includes:

1. **Anaemia**= autolysis of unparasitized rbcs, increases splenic clearance, drug induced haemolysis, dyserythropoeisis in BM

2a. **Nephropathies** = Ab/Ag complexes cause lesions in

Kidney glomerular walls

- In *P. falciparum*: Acute nephropathy, reversible, oliguria, renal failure due to IgM,
- Malaria antigen and Complement
- Clears after treatment

Pathogenesis of Malaria

2b. Nephropathies = In *P. malariae*: Nephropathy is Chronic

- - progressive, severe
- - Deposits of IgG, IgM, complement
- and Pm antigen in glomerular walls
- - Auto immune response to damaged tissue
- - Quartan Malaria nephrosis with persistent heavy proteinuria, hypoalbinaemia, oedema,
- - Deterioration of renal functions
- - Hypertension.
- - Treatment - little effect

Pathogenesis of Malaria

3. Splenomegaly:

- Oedema of the pulp, RES hyperplasia, increased phagocytic fxn
- Tropical Splenomegaly Syndrome (TSS) in young and adults

4. Immunodepression:

. Bone marrow depression (iron sequestration-dyserythropoeisis; dysthrombopoeisis)

. Auto antibodies

. Pregnancy

. Burkitt's lymphoma; endemicity correlating with malaria endemicity

Clinical Features

Uncomplicated (Benign) Malaria

- The typical picture of malaria consists of
  - **Prodromal** phase (early signs & symptoms)
    - Severe headache, nausea, and vomiting are common & intermittent fever or paroxysms of chills
- **Paroxysms** of chills (intermittent fever)

  Sudden attack of fever 104- 105 F (40-40.6 C).

  Release of schizogony products
- **Paroxysm** comprises of 3 successive stages i.e. **cold stage, hot stage and sweating stage**

Clinical Features

Uncomplicated (Benign) Malaria

Cold stage: rigor

- lasts for 15–60 minutes, the patient experiences intense cold and uncontrollable shivering
- **Malarial** pyrogens stimulate secretion of endogenous pyrogens (monocytes/macrophages to release cytokines like TNF & IL-1 = chills & high-grade fever)

stimulate thermoregulatory centers in the hypothalamus to conserve heat.

- Shivering, chills, intense cold feeling
- Vasoconstriction = cyanotic lips and fingers
- Muscular pain, malaise, goose flesh

Clinical Features

Uncomplicated (Benign) Malaria

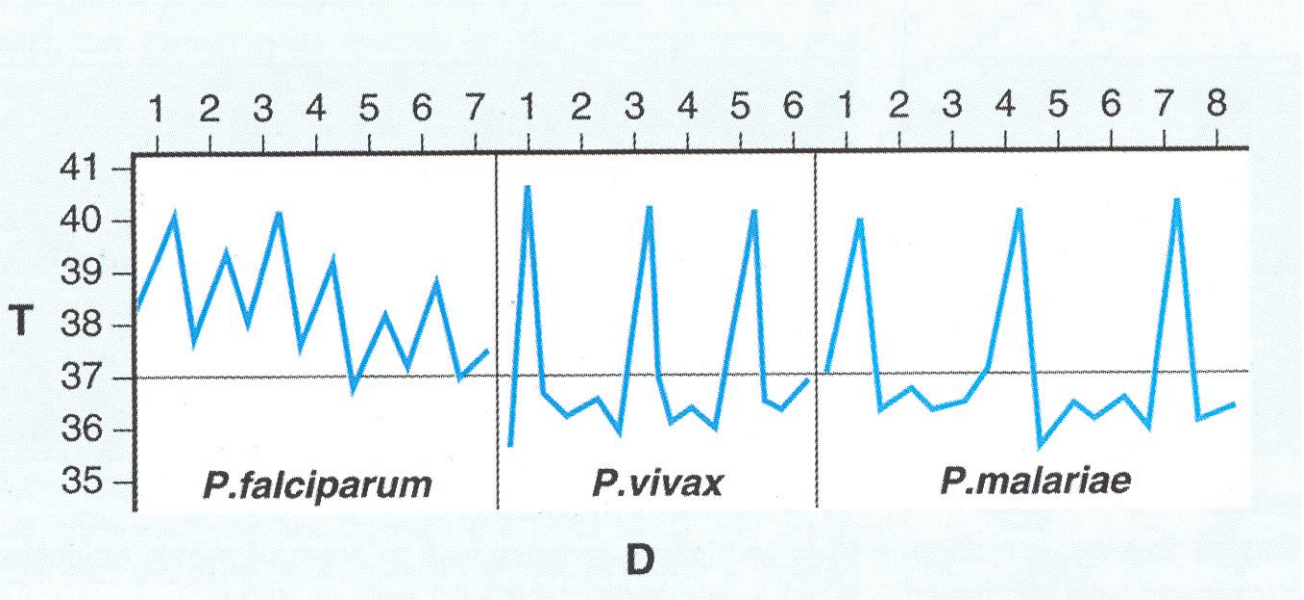
Hot Stage:

- Body temperature reaches “set Point” 41^0 C (106^0F)or higher, lasting for 2 – 6 hours
- The patient feels intensely hot
- Dry burning skin, full bounding pulse
- Nausea, vomiting. intense headache

Clinical Features

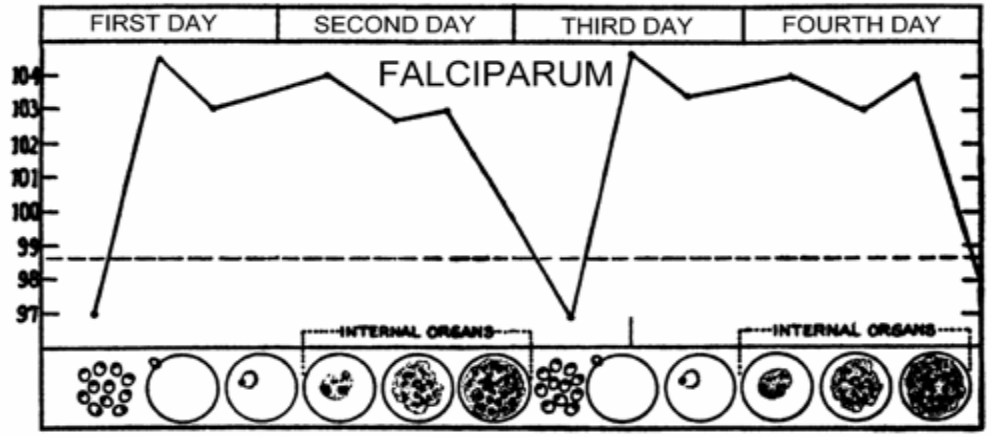
Uncomplicated (Benign) Malaria
Sweating Stage:

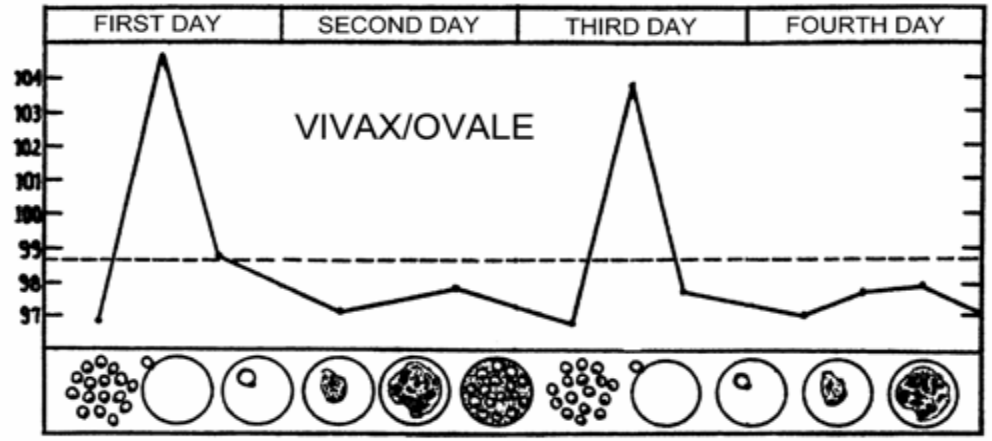
- Return to normal temperature “set point “ by profuse sweating
- Body temperature falls rapidly below normal
- On waking patient feels weak but normal, lasts for 2-4hours

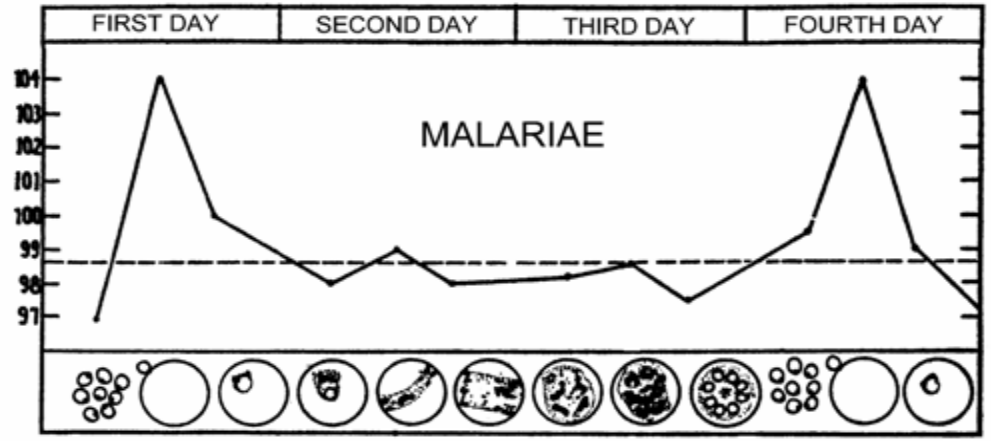


Tertian and quartan fever patterns The asexual blood stages of Plasmodium falciparum, P. vivax and P. ovale require 48 hours to complete their schizogony. Fever is produced when the schizonts mature, i.e. at 48-hour intervals. This gives the classic tertian periodicity, which is, however, uncommon in a primary attack of P. falciparum malaria. P. malariae requires 72 hours and is associated with quartan fever, i.e. 72 hours between paroxysms.

Malaria Paroxysm







Tertian malaria

quartan malaria

Complications

Severe (Malignant) Malaria

- The most serious and fatal type of malaria is malignant tertian malaria caused by *P. falciparum*
- When not treated promptly and adequately, dangerous complications develop.
  - Which may present in various forms, the most important of which are the cerebral, algid, and septicemic varieties

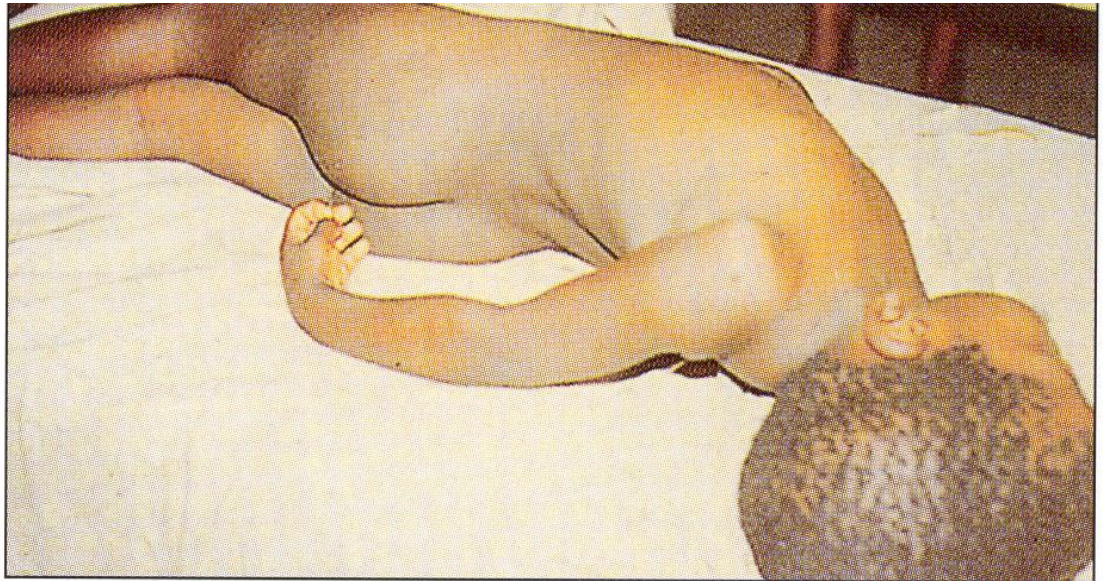
Complications

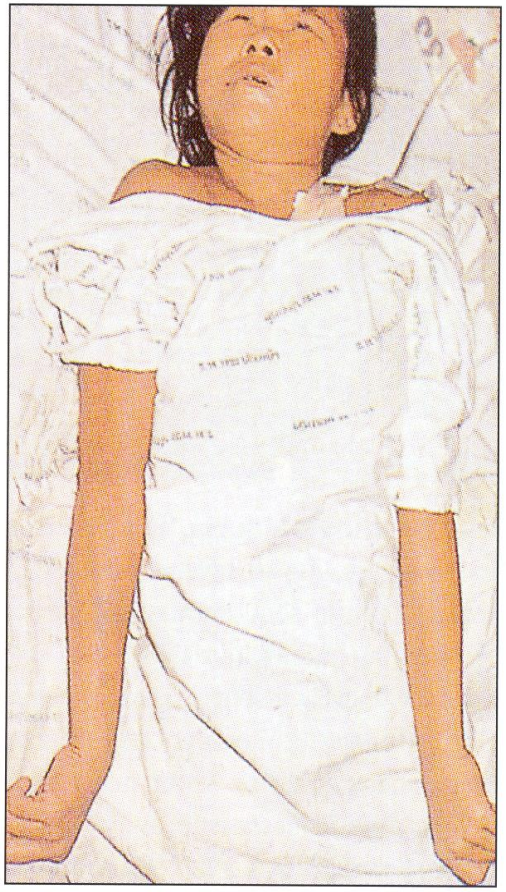
Severe (Malignant) Malaria

- **Cerebral Malaria/comatose:** most common cause of death in malignant malaria
- Even with treatment, death occurs in 15% of patients
- Restless, delirious, epileptic, violent, manic.
- Comatose,
- Behavioural changes
- Hyperpyrexia, 40.5oC, 5 % rbcs infected.
- Misdiagnosed as insanity, encephalitis, or meningitis.

Complications

Cerebral malaria in a comatose Malawian child with opisthotonus In holoendemic areas of Africa, cerebral malaria commonly occurs in children between six months and three years of age--- The opening pressures of cerebrospinal fluid are often raised in children when measured at lumbar puncture.





Classic decerebrate rigidity associated with Hypoglycaemia . This Thai woman with cerebral malaria displays classic decerebrate rigidity. which was almost certainly due to a profound quinine-induced hypoglycaemia. The latter is more common during pregnancy. when the warning signs are fits. abnormal behaviour and a change in the level of consciousness.

Complications

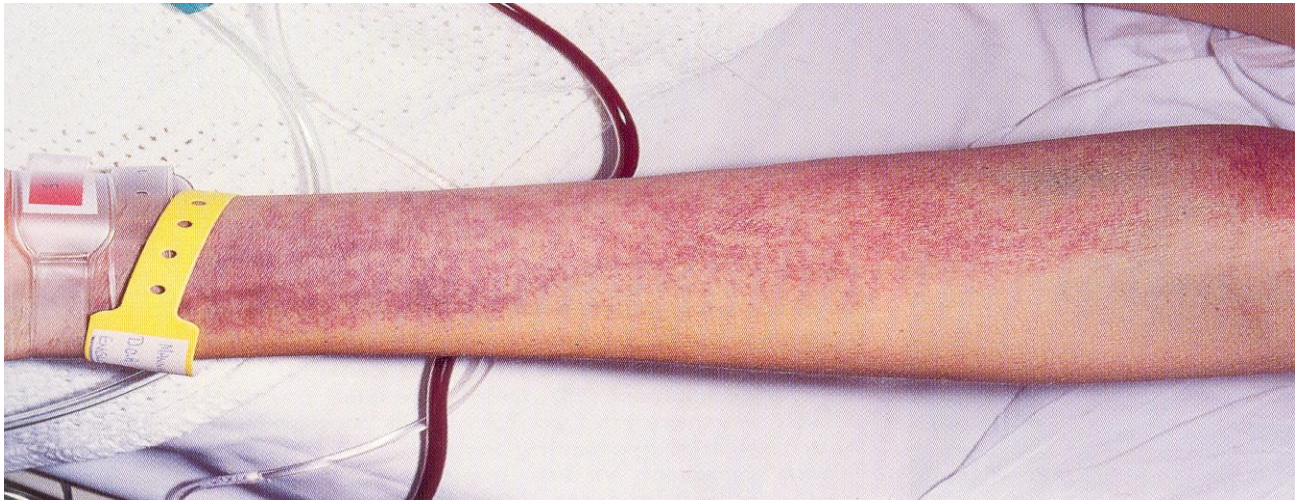
Severe (Malignant) Malaria

B. Algid: cold, pulseless, unconscious, peripheral vascular circulatory collapse, low BP. coma, overwhelming infection – death within hours

Complications

Severe (Malignant) Malaria

C. Haemorrhagic: Bleeding from skin or mucus membrane



Disseminated intravascular coagulation (DIC) in falciparum malaria. Bleeding into the skin with no signs of cerebral malaria.

Complications

Severe (Malignant) Malaria

D. **Gastrointestinal**: vomiting, coughing, diarrhoea, or acute dysentery

E**. Pulmonary oedema:**

- Malaria Shock syndrome
- Fluid overload during treatment
- Disseminated intra-vascular coagulation – DIC Induce diuresis and haemodialysis

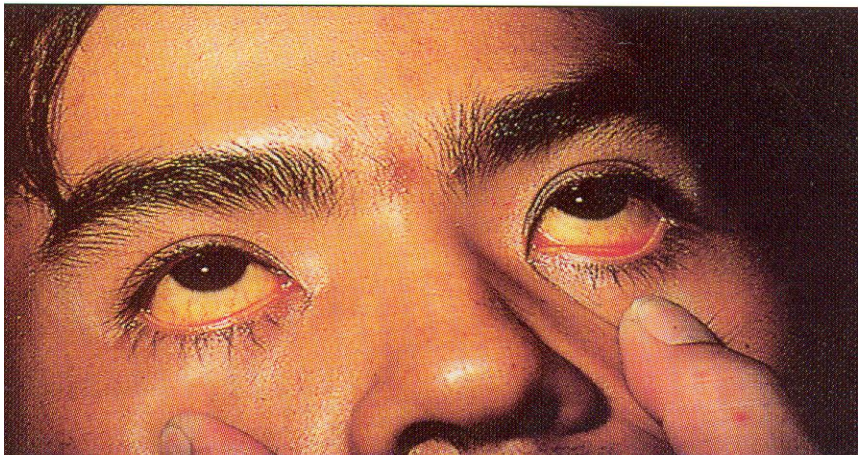
. Often fatal

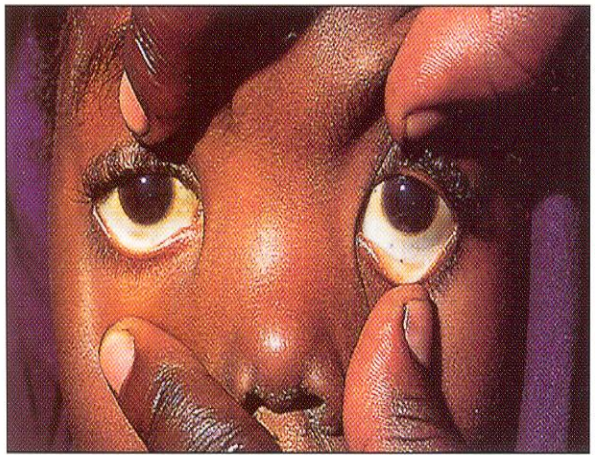
F. Respiratory distress (metabolic acidosis bicarbonate less than 15 meq/l

G. **Hepatorenal syndrome/**Haemolytic jaundice = jaundice and renal failure

Complications

Severe malarial jaundice Deep jaundice, which is clearly seen in this Vietnamese man who had severe falciparum malaria, is much more common in adults than in children. Liver failure, however, occurs only in individuals in whom a concurrent viral hepatitis is present.

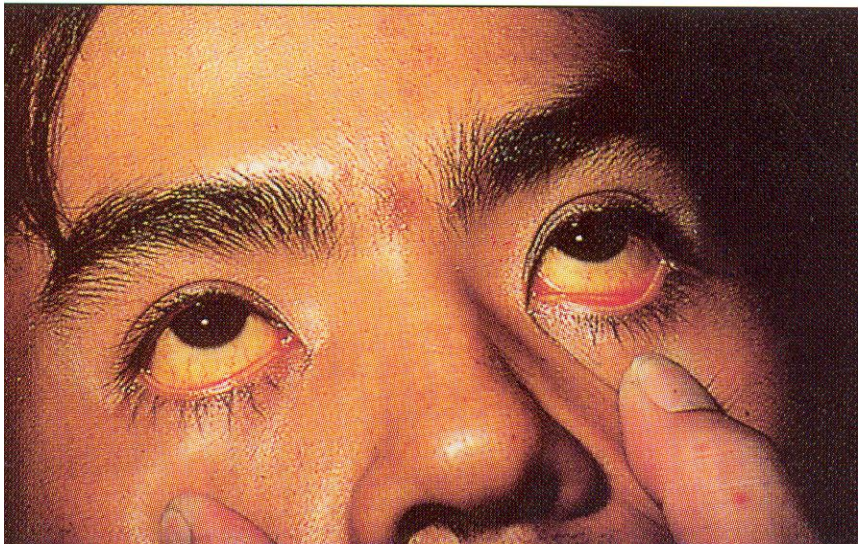




Malarial anaemia: is multifactorial, involving destruction of parasitised cells, haemolysis of uninfectedcells, dyserythropoiesis and iron sequestration, malarial anaemia is an important cause of death in children under two years of age.

Complications

H. Jaundice and kidney failure



Severe malarial jaundice

Complications

Severe (Malignant) Malaria

I. **Blackwater fever**:

in repeated infections with Pf with inadequate quinine treatment

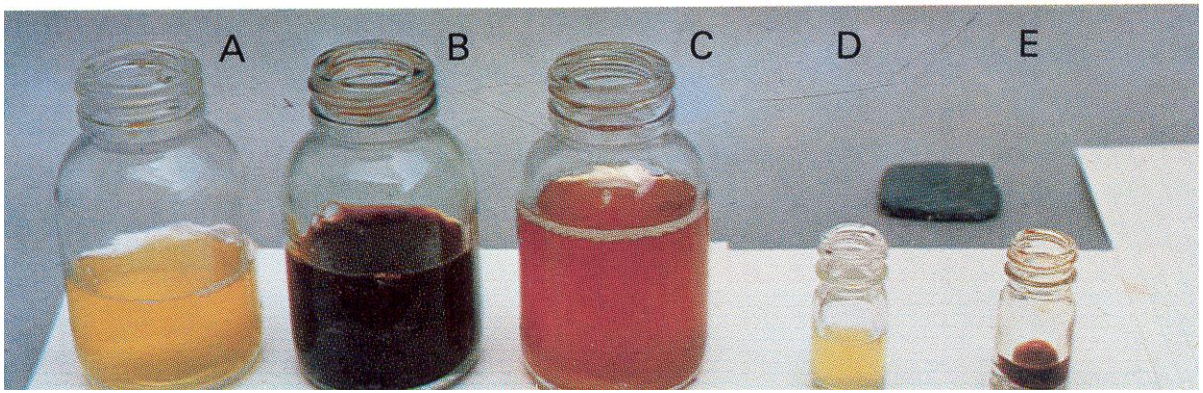
Haemolysins formed against quininized and unparasitised cells – autoimmine

Haemoglobinuria, bilirubinaemia, haemoglobinaemia

Fever, jaundice, nausea, vomiting, anuria, oliguria,

Complications

Black water fever: Quinine auto antibodies
derived from previous infection lyses rbcs
coated with new auto antigens.



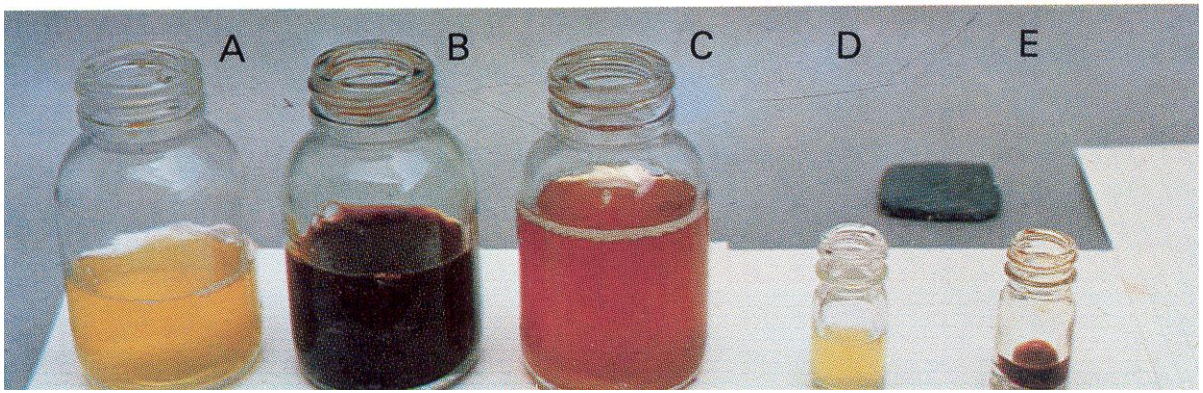
Blackwater urine and serum taken during course of illness An acute haemolytic crisis resulting in malarial haemoglobinuria occasionally occurs in severe attacks (Blackwater fever). Haemoglobinuria can also be drug induced in patients deficient in the enzyme glucose 6-phosphate dehydrogenase (G-6-PD). A = normal urine; B = patient's urine; C = patient's urine, diluted; D = normal serum; E = patient's serum.

Complications

. **Blackwater fever**:

Coca –Cola urine

complications of quinine treatment



Complications

J. Severe anaemia (haemoglobin less than 5g/dl or haematocrit less than 15%)

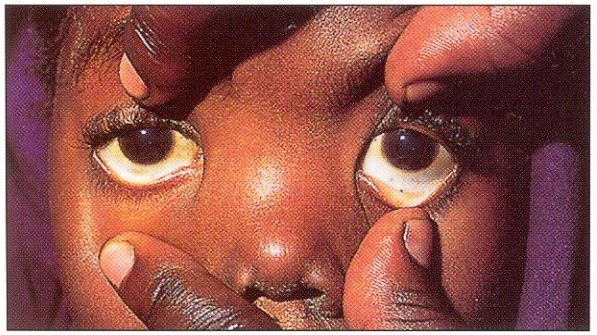
K. Renal failure-presenting as oliguria or anuria

L. Confusion or drowsiness with extreme weakness

Complications

Malaria in children

1. Pf common
2. Symptoms atypical
3. Drowsiness, vomiting, diarrhoea, unproductive cough, fever without periodicity.
4. Cerebral manifestations- convulsions and coma twitching
5. High body temperature
6. Spleen enlargement, jaundice
7. Severe anaemia fatal in babies



Malarial anaemia: malarial anaemia is an important cause of death in children under 5 years

Complications

Malaria in children

5. Hyperpyrexia
6. medical shock, renal involvement
7. splenic enlargement, jaundice
8. severe normocytic anemia
9. Pv and Po - milder in children.
10. Pm - Nephrotic syndrome, glomerulonephritis leads to gross edema, proteinuria and hypoprotinemia

Complications

Malaria in pregnancy

1. high prevalence: highly susceptible
2. haemolytic anemia- jaundice, ,splenomegaly, death
3. acute renal insufficiency
4. abortions, stillbirths, awaken latent malaria
5. low birth weight
6. Treatment must not be withheld, Intermittent Preventive Treatment (IPTp) or chemophylaxis for at least 3 months

Immunity

- **Influenced by**
  - Genetics
  - Age
  - Health condition
  - Pregnancy status
  - Intensity of transmission in region
  - Length of exposure
  - Maintenance of exposure

Immunity

Innate

- Red cell polymorphism associated with some protection
  - Haemoglobin S sickle cell trait or disease
  - Haemoglobin C and haemoglobin E
  - Thalassaemia a and b
  - Glucose – 6 – phosphate dehydrogenase deficiency (G6PD)
- Rbc membrane changes
  - Absence of certain Duffy coat antigens improves resistance to *P. vivax* (lack fya and fyb-)

Immunity

Acquired

1. Transferred from mother to child
   - 3-6 months protection
   - Then children have increased susceptibility
2. Increased susceptibility during childhood
   - Hyper and holoendemic areas
     - By age 5 attacks usually less frequently and severe
     - Can have more parasite densities with fewer symptoms

Immunity

Acquired

3. Meso or hypoendemic areas
    - Less transmission and repeated attacks
    - May acquire partial immunity and be at higher risk for symptomatic disease as adults

Immunity

Acquired

- No complete immunity
  - Can be parasitaemic without clinical disease
- Need long period of exposure for induction
- May need continued exposure for maintenance

Immunity

Acquired

- Immunity can be unstable
  - Can wane as one spend time outside endemic areas
  - Can change with movement to area with different endemicity
  - Decreases during pregnancy, risk improves with increasing gravidity

DIAGNOSIS

1. Clinical diagnosis – based on S/S being presented by a patient

2. LAB diagnosis of malaria is confirmed by blood tests i.e. *microscopic* and *non-microscopic* tests

DIAGNOSIS

Microscopic methods

Demonstration of malarial parasites in thick and thin blood smear ***Light Microscopy***

- Giemsa-staining of thick and/or thin blood smears → conventional method of diagnosing malaria
  - combination is gold standard
- smears allow species identification
- can calculate the parasite density (prognosis)

DIAGNOSIS

Non – microscopic methods

- Immunoflourescence staining and QBC smear

<u>Fluorescent Microscopy</u>

- Is not as specific and sensitive as light microscopy

- cannot differentiate species and special microscope is required

DIAGNOSIS

Non – microscopic methods

- Rapid immunochromatographic test (ICT/RDTs) for detection of malaria antigen (PfHRP2 and PLDH)
- A rapid simple dipstick test → results in 10-15 minutes
- useful in situations where diagnostic expertise or microscopic facilities are limited
- Limitations:
  - cannot determine degree of parasitemia
  - false positives
  - not fully reliable for accurate species diagnosis

- 3 assays currently used for testing: HRP-2, aldolase and pLDH

DIAGNOSIS

Non – microscopic methods

- Molecular diagnosis: DNA probe and PCR

<u>Polymerase Chain Reaction (PCR)</u>

- Has the ability to detect parasitemia at very low levels
- Is helpful in species identification when microscopy is equivocal

- Disadvantages are high cost, labor intensive

Principles of Treatment

- Treatment of malaria depends on the following factors:
- Type of infection
- Severity of infection
- Status of the host
- Associated conditions/ diseases

Treatment

- Supportive treatment, anti-malarial drugs
- *P*. *vivax*, *P*. *ovale*, and *P*. *malariae* are mostly treated on an outpatient basis
- *P. falciparum* pts are generally admitted for observation of any complications
  - hospitalized until they are improving clinically and parasite count is declining
  - most can be treated with oral therapy→ severe malaria requires IV therapy/ICU

NEW DRUG POLICY - 2020

For simple or uncomplicated malaria in adults

First Line Drug:

- Coartem^{R} **(Artemisinine Based Combination Therapy = ABCT, ACT) e.g.** Artemether 20mg + Lumefantrine 120mg (AL)

Second Line Drugs:

- Oral Quinine 300mg tablet
- Quinine 10mg/kg – IM diluted in saline or water for injection

For severe or complicated malaria

- Injectable artesunate 2.4mg/kg body weight IV/IM
- If unavailable artemether (IM) or Quinine 20mg/kg (IV/IM) diluted in 5% or 10% dextrose

Malaria in Pregnancy

Uncomplicated malaria

First line

- Oral Quinine in 1st. Trimester (can be used in all trimesters)
  Injectable artesunate 2.4mg/kg BW in 2nd and 3rd trimesters
- In absence of Quinine, Artemether 20mg+Lumefantrine 120mg can be used in 1st trimester

Severe malaria

Quinine is 1st. Line in this case

Injectable artesunate 2.4mg/kg BW in 2nd and 3rd trimesters

Intermittent preventive treatment(IPT) – Sulphadoxine + Pyrimethamine given 16 weeks following last monthly period (LMP)

- 2 consecutive doses given at least 16 weeks apart during the 2nd and 3rd trimester
- A total of 3 doses should be given during the entire duration of pregnancy

Malaria in Children

For simple or uncomplicated malaria

First Line Drug:

Coartem® **(Artemisinine Based Combination Therapy = ABCT, ACT)** for children above 5kg

- Artemether 20mg +Lumefantrine 120mg (AL)
- Sulphadoxine 500mg + Pyrimethamine 25mg – single treatment of half a tablet

Second Line Drugs:

- Quinine 10mg/kg BW diluted in saline (IM)

For severe or complicated malaria

- Injectable artesunate 2.4mg/kg BW IV or IM
- Quinine 20mg/kg BW diluted in dextrose (IV)

Prognosis

- Mortality of untreated falciparum is almost 100% and 10-40% for treated

- Poor prognostic factors:
  - Age<3
  - Seizures
  - Acidosis
  - Respiratory distress

Control of Malaria

- Control would therefore involve three living beings:
    - **Man** *(The host)*,
    - **Plasmodia** *(The agent)*, and
    - **Anopheles mosquito** *(The vector)*
- Control of malaria is possible only by concerted community efforts

Control of Malaria

- Early diagnosis and treatment – treat early to reduce parasite load, hence spread; prevent deaths
- Treat completely to prevent spread and relapse
- Ensure compliance with complete treatment
- Personal Protection- prevent malaria by using Insecticide Treated Bednets (ITNs),
- insecticide sprays etc.,
- **Intermittent preventive treatment(IPTp):**
  3 doses SP in 2^{nd}. & 3^{rd}. trimesters
- and by chemoprophylaxis (for travellers)

Assignment

- Mode of action and drug resistance of the antimalarials

Thank you