Malaria parasite (plasmodium)

- Pathogen of malaria
- P.vivax ; P.falciparum ;P.malariae ; P.ovale
- P.vivax ; P.falciparum are more common
- Plasmodium is a wide distribution in many tropical or subtropical regions of the world

Definition

- Malaria is a mosquito-borne infectious disease of humans and other animals caused by the genus Plasmodium, transmitted by the bite of female anopheles mosquito.

Malaria is the most important parasitic disease being widespread in tropical and subtropical regions in a broad band around the equator, including much of Sub-Saharan Africa, Asia, and the Americas.

- The disease results from the multiplication of malaria parasites within red blood cells, causing symptoms that typically include fever and headache, in severe cases progressing to coma, and death. Name is derived from Italian Mal’ aria or bad air

Why it is important in Medicine

- Malaria remains the world's most devastating human parasitic infection.

Malaria affects over 40% of the world's population. WHO, estimates that there are 350 - 500 million cases of malaria worldwide, of which 270 - 400 million are Falciparum malaria, the most severe form of the disease.
Etiology

Causative organism: Plasmodia

- P. Vivax: tertian malaria
- P. Malariae: quartan malaria
- P. Falciparum: malignant malaria
- P. Ovale: tertian malaria

Pathogenicity: merozoite, malarial pigment & products of metabolism

Mode of transmission

- Malaria is transmitted by the bite of an infective female Anopheles mosquito. Rarely, transmission can be congenital (via the placenta) or can occur through blood transfusions or the use of contaminated needles.

Wright’s stain—reddish nuclei; bluish cytoplasm and yellowish brown malarial pigment

1. Morphological features of P. vivax

   - Early trophozoite (ring form)

     1 red nucleus on the ring-like light blue cytoplasm; single infection in a cell.
infected RBC like normal RBCs.

- **Late trophozoite**

  It is irregular shape like ameboid form with pseudopodia; within cytoplasm, brown pigment granules (malarial pigment---haemozoin) appear.

  *infected RBCs* are pale in color, and have *Schuffner’s dots* in it.

  ![Image of infected RBCs]

  *fine red granules*.

- **Immature schizont**

  Oval in shape, nucleus divided into 2-4 or more, malarial pigment begins to concentrate in a mass.

- **Mature schizont**

  ![Image of mature schizont]
nucleus divided into 12-24; and cytoplasm also divided, each nucleus surrounded by a portion of cytoplasm to form merozoites, malarial pigment clumped.

- **Male gametocyte**
  oval in shape; 1 loose nucleus in centre of it; malarial pigments diffuse.

- **Female gametocyte**
  oval in shape; 1 compact nucleus not in centre of it.

2. **Morphological features of P. falciparum**
- **Early trophozoite (ring form)**

  1 or 2 red nuclei on the ring-like light blue cytoplasm; multiple infection in a cell.

  *infected RBC like normal RBCs.*

  *P. falciparum:* only can the early trophozoites and gametocytes be seen in the peripheral blood.

- **Male gametocyte**

  Sausage in shape; 1 loose nucleus in centre of it; malarial pigment diffuse.

- **Female gametocyte**

  Crescentic in shape; 1 compact nucleus in centre of it.
Life cycle of *Plasmodium spp.*

The life cycle of the plasmodium is spent in two hosts’ man and anophele mosquito. The mosquito is the definitive host as the sexual development and multiplication of the parasite occurs in it. Man is the intermediate host. Sporozoite is the infective form of malarial parasite which is passed on to man through the bite of infected vector, the female anopheles mosquito. The various stages of the parasite in man are:

(a) Pre-erythrocytic schizogony

(b) Erythrocytic schizogony

(c) Gametogony

(d) Exoerthrocytic schizogony

(a) **Pre-erythrocytic schizogony:** This phase lasts for 8 days. Sporozoites are elongated and spindle shaped. The sporozoites enter the liver parenchymal cells and become rounded. They undergo multiple divisions and develop into schizonts. One schizont contains 20,000 – 30,000 merozoites. The liver cells ruptures and releases the merozoites into blood.

(b) **Erythrocytic schizogony:** This has a duration of 48 hours. The merozoites
penetrate the red blood cells. The merozoites enlarge in size and develop into trophozoites. The trophozoites develop into schizont which further develops into merozoites. There may be 6-24 merozoites in red blood cells. In the case of Plasmodium falciparum the schizonts aggregate in the capillaries of the brain and other internal organs. So that only ring forms are formed in the peripheral blood.

(c) Gametogony: Some merozoites enlarge and get transformed to microgametocyte and macrogamete.

The malarial parasite now becomes infective as the presence of gametocytes is a must for sexual development in the mosquito. The mosquito gets these gametocytes after taking a blood meal from a patient of malaria.

(d) Exo-erythrocytic schizogony: This phase resembles the pre-erythrocytic schizogony. Some sporozoites after entering the liver cells do not undergo multiplication but go into resting phase. The resting stage of the parasite is known as hypnozoite. These can reactivate up to after 2 years and become schizonts and release merozoites. This phase is responsible for relapse of malaria

**Development in the mosquito**

The female anopheles mosquito takes a blood meal from a malaria patient and the plasmodium gametocytes (Both microgametes and macrogametes) reach the gut of the mosquito. Only the mature gametocytes undergo further development. (In the midgut of the mosquito one microgamete develops into 4-8 filamentous structures called microgamete).

Microgametes penetrate the macrogametes and fertilize it leading to the formation of zygote. The zygote matures into an ookinete. The ookinete further develops into oocyst.

The oocyst further matures and increases in size. A large number of sporozoites (100-1000) develop inside the oocyst. The oocyst ruptures and releases the sporozoites in the body cavity of the mosquito. The sporozoites go to all the organs but prefer to go to the salivary glands. The mosquito is now infective to man.
There are two forms of sporozoites:

----tachysporozoite and bradysporozoite

They are genetically distinct at the time of maturation when they enter the hepatic cells at the same time. tachysporozoite grow in the hepatic cell and multiply to form exoerythrocytic schizonts and then invade RBCs to clinic malaria. Bradysporozoite is the cause of relapse of malaria. Bradysporozoite stay in the hepatic cells and will multiply later.

2. Erythrocytic stage

early trophozoite    later trophozoite
P.f/36-48hrs
P.v/48hrs
merozoite immature schizont
Mature schizont

*the process from trophozoite to merozoite is called schizogony.*

3. Gametogenesis

----After completing a few schizogonic cycles, some merozoites develop into sexual cells, the male and female gametocytes. They continue their development in the mosquito.

**Characteristic of life cycle**

- Intermediate host: human
- Final host: mosquito
- Infective stage: sporozoite
- Infective way: mosquito bite skin of human
- Parasitic position: liver and red blood cells
- Transmitted stage: gametocytes
- Schizogonic cycle in red cells: 48 hrs/P.v
- Sporozoite: tachysporozite and bradysporozite

**Pathogenicity**

- Paroxysm (attack of malaria)

**mechanism**

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

**symptoms (in a typical case)**
---p.v. attack occurs once every other day (48 hours); P.f./36 to 48 hrs; P.m./72 hrs

**How Malaria present Clinically**

- Stage 1
  - Chills for 15 min. to 1 hour
  - Caused due to rupture from the host red cells escape into Blood
  - Preset with nausea, vomiting, headache

- Stage 2
  - Fever may reach up to 40°C may last for several hours (4 hr.) starts invading newer red cells.

- Stage 3
  Patent starts sweating, concludes the episode Cycles are frequently Asynchronous Paroxysms occur every 48 – 72 hours

In P.malariae pyrexia may lost for 8 hours or more and temperature my exceed 41°C

More commonly, the patient presents with a combination of the following symptoms

- Fever
- Chills
- Sweats
- Headaches
- Nausea and vomiting
- Body aches (back and joint pain)
- General malaise.
• Gastrointestinal symptoms

**What are the characteristics of a malaria attack**

• Fever and shivering. The attack begins with fever, with the temperature rising as high as 40ºC and falling again over a period of several hours.

• A poor general condition, feeling unwell and having headaches like influenza.

• Diarrhea, nausea and vomiting often occur as well. ----Rupture of the infected RBCs and destruction of normal RBCs enhance phagocytosis stimulate phagocytes to grow in number and enhance in function. Finally, lead to anemia and enlargement of the spleen.

Question: Which reasons are there in the anemia of malaria?

----a specific attack that it is up to months or even years after the primary attacks.

----The bradysporozoites in the liver spend a rest and sleeping times of months or even years, then they start develop in exoerythrocytic stage and erythrocytic stage. at this time, the patient occurs paroxysm, showing as periodic fever like the primary attacks, it is called relapse.

----Relapse only occurs in *P.v*.

Malaria caused by *P.f.* is more severe than that caused by other plasmodia.

----The serious complication of *P.f.* involves cerebral malaria (involving the brain); massive haemoglobinuria (blackwater fever) in which the urine becomes dark incolor, because of acute hemolysis of RBC; acute respiratory distress syndrome; severe gastrointestinal symptoms; shock and renal failure which may cause death.

Black Water Fever
• In malignant malaria a large number of the red blood corpuscles are destroyed. Haemoglobin from the blood corpuscles is excreted in the urine, which therefore is dark and almost the colour of cola

**How long Malaria infection can lost in Man**

• Without treatment P.falciparum will terminate in less than 1 year.

• But in P.vivax and P.ovale persist as hypnozoites after the parasites have disappeared from blood.

• Can produce periodic relapses up to 5 years

• In P.malariae may last for 40 years

( Called as **recrudescence X relapse** )

**Why Falciparum Infections are Dangerous**

(Pernicious Malaria)

• Can produce fatal complications,

1. Cerebral malaria

2. Malarial hyperpyrexia

3. Gastrointestinal disorders.

4. Black water fever can lead to death

**Other Complications In Malaria**

• Acute kidney failure

• Hyperparasitemia, where more than 5% of the red blood cells are infected by malaria parasites

• Metabolic acidosis (excessive acidity in the blood and tissue fluids), often in association with hypoglycemia

**Laboratory diagnosis**
laboratory diagnosis of malaria is confirmed by the demonstration of malarial parasites in the blood film under microscopic examination.

- Thin film
- Thick film

Question: Which stages are there in the blood film of P.v. or P.f.?

**treatment**

- **Chlorquine and quinine** — anti-erythrocytic stage drugs. (question: Which stage of plasmodium can these drugs kill?)

- **Primaquine and pyrimethamine** — anti-exoerythrocytic stage drugs.

**Prevention**

- **Chemoprophylaxis**

--- Chloroquine / pyrimethamine

  used for

  prophylaxis of malaria

  --- Chemotherapy: 1 week before entry into the endemic area; for 4 weeks after returning from the endemic area.

- **Mosquito control**

  (1). Reconstruction of environment: eradicate the breeding places of mosquitoes.

  (2). Spry insecticides: DDVP and so on.

  (3). Use mosquito nets, screen, or mosquito repellents to protect the person from mosquito bites.