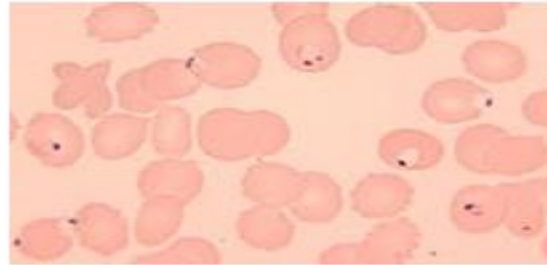


Hematozoa (Malarial parasites)

Malaria disease



Malarial sp. As a group that infect human :-

Malarial parasites are species of

Phylum :- Apicomplexa

Class :- Sporozoa

Suborder :- Haemosporina

The life cycle includes an asexual phase (schizogony) alternating with a sexual one (gametogony followed sporogony). However, the malarial parasites require two hosts

- 1- Vertebrate host in which the asexual phase develops and gametocytes are produced
- 2- A vector host in which the gametocytes become mature gametes

There are four *plasmodium* species that were considered responsible for malaria disease in humans:

- *P. vivax*,
- *P. falciparum*,
- *P. ovale*
- *P. malariae*.

P.vivax & P.falciparum are more common

Plasmodium is a wide distribution in many tropical or subtropical regions of the world

P. vivax= most extensive in distribution.

P. falciparum= tropical & subtropical.

P. malariae= Less common but wide distribution.

P. ovale= East & West Africa.

There are many factors influence the effectiveness of the parasite :-

- 1- Susceptibility of host to infection
- 2- Survival long enough for development and transmission of the sporozoites
- 3- Presence in sufficient numbers (infection dose)

Terms you should know when you talk about Plasmodium (malaria)

Sporozoite: the infectious, vegetative stage; carried by the mosquito

Merozoites: daughter cells resulting from sporozoites undergoing schizogony in liver cells. (humans)

Ring stage: The merozoites invade erythrocytes and become enlarged ring-shaped trophozoites (vegetative stage) in the RBC

Definitive host: mosquito; harbors the sexually reproducing stage

Intermediate host: human; host in which parasite undergoes asexual reproduction

Mode of transmission

- 1- The main mode of transmission of the disease is by bites from infected anopheles mosquitoes female .
- 2- Less common routes of transmission are via infected blood transfusion, organs transplantation, sharing infected needles, and from a mother to her fetus during pregnancy

Plasmodium life cycle

The life cycle (Figure 1) is almost the same for all the four species that infect humans and follows three stages:

- (I) infection of a human with sporozoites
- (II) asexual reproduction
- (III) sexual reproduction (**sporozoites** , **sporogony**).

The two first stages take place exclusively into the human body, while the third one starts in the human body and is completed into the mosquito organism.

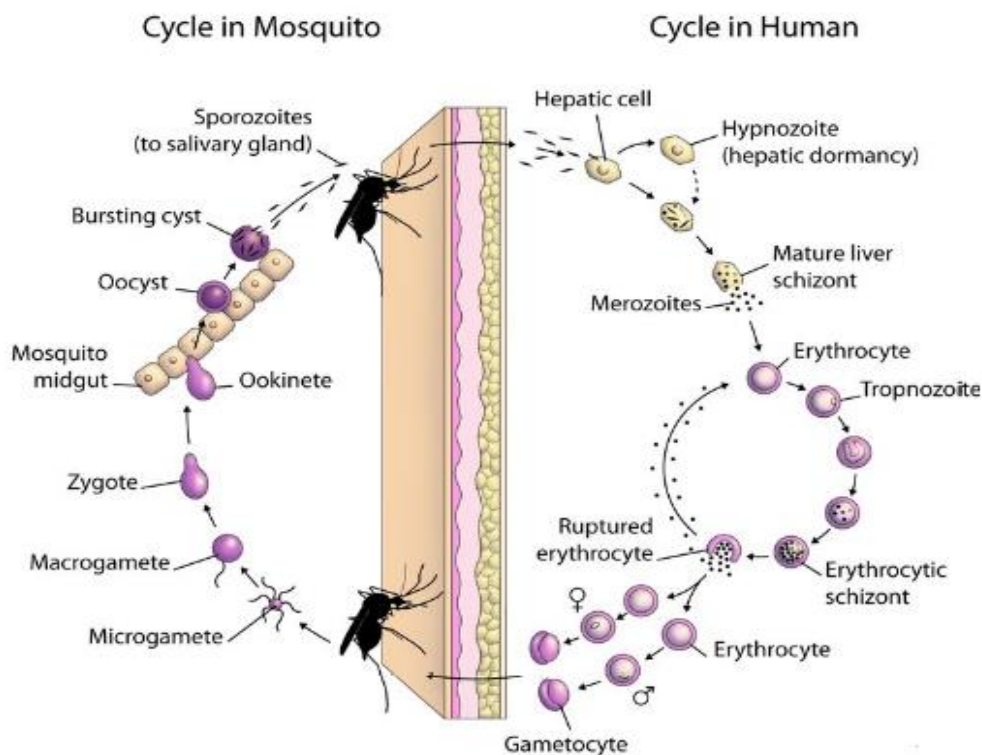


Figure 1. *Plasmodium* life cycle
(Source: Open Course Ware)

1-

The human gets infection when an infected female anopheles mosquito bites a person and injects **sporozoites** with saliva into the **blood circulation**. That is the first life stage of plasmodium (**stage of infection**).

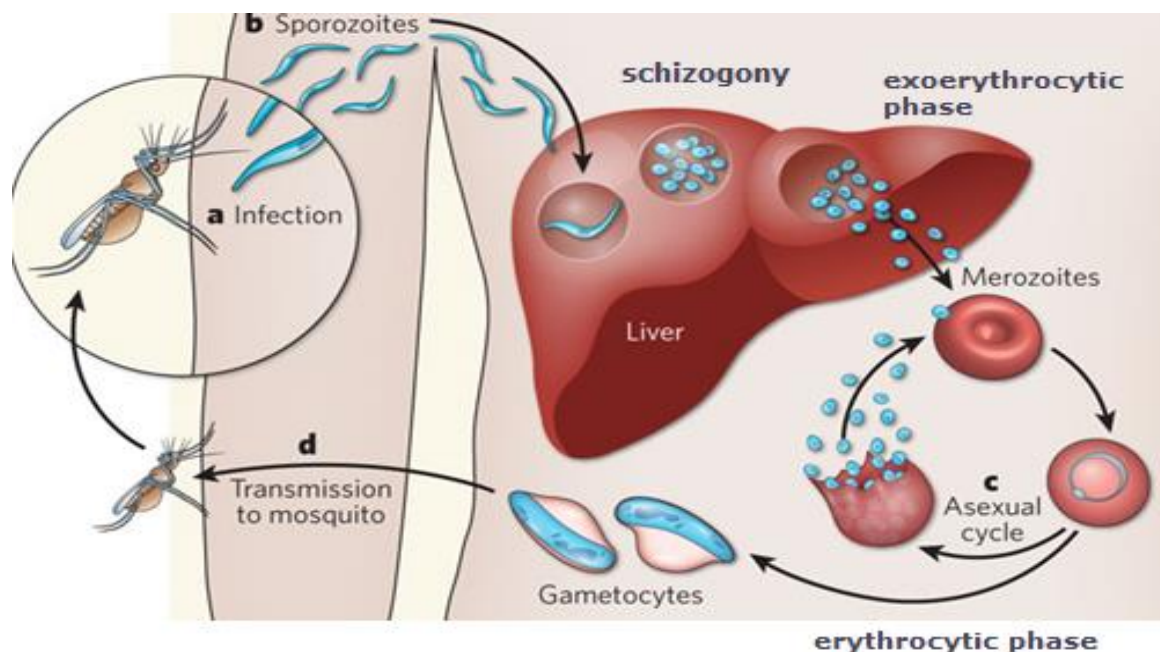
2- The next stage in malarial life cycle is asexual reproduction that will be divided into different phases:

- ❑ The pre- erythrocytic (or **exoerythrocytic**)
- ❑ The **erythrocytic phase**.

The sporozoite circulate in the blood stream but within only 30- 60 minutes after inoculation , the sporozoites find their way through blood circulation to their first target (parenchymal cells of the **liver**).

3- In **exoerythrocytic** phase (**schizogony**) the sporozoites enter the liver cells and start dividing leading to **schizonts** creation in 6- 7 days. Each schizont gives birth to thousands of **merozoites** that are then released into the blood stream marking the end of this phase of asexual reproductive stage.

4- The exoerythrocytic phase is not pathogenic and does not produce symptoms or signs of the disease. Its duration is not the same for all parasite species as it P.V 8 d., P.F 6 d., P.O. 9 d. & P. M. 9 d. P.F 6 d., P.O. 9 d. & P. M. 9 d.



5- **Merozoites** released into the blood stream, are directed towards their second target, the **red blood cells (RBCs)**. As they invade into the cells, they mark the beginning of the erythrocytic phase.

6- The first stage after invasion is a ring stage that develops into a **trophozoite** (uninuclear cell). The trophozoites are not able to digest the haem so they convert it in haemozoin and digest the globin that is used as a source of aminoacids for their reproduction.

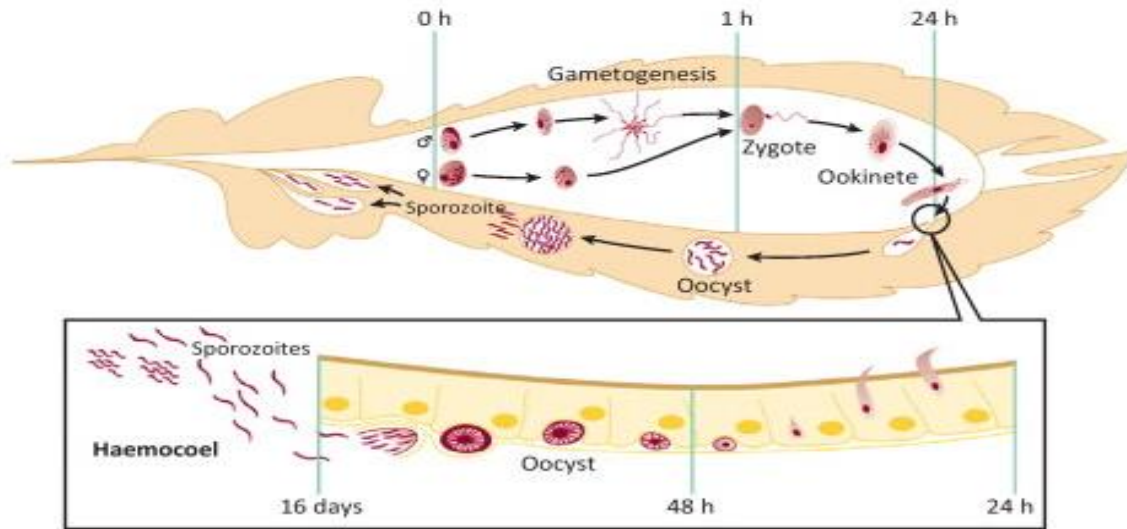
7- The next cellular stage is the **erythrocytic schizont** (initially immature and then mature schizont). Each mature schizont gives birth to **new generation merozoites** (**erythrocytic schizogony**) that, after RBCs rupture, are released in the blood stream in order to invade other RBCs. This is when parasitaemia occurs and clinical manifestations appear. The incubation period between sporozoites & the first appearance of clinical signs of which fever is the most common is 12 d. P.F. , 13-17 d. P.V. & P.O. , and 28-30 d. for P.M.

The liver phase occurs **only once** while the erythrocytic phase undergoes **multiple cycles**; the merozoites release after each cycle creates the febrile waves.

8- Plasmodium enter to sexual reproduction cycle when some of merozoites in the RBCs will differentiate into male and female **gametocytes** that is a non pathogenic form of parasite.

9- When a female anopheles mosquito bites an infected person, it takes up these gametocytes with the blood meal (mosquitoes can be infected only if they have a meal during the period that gametocytes circulate in the human's blood).

10- The gametocytes, then, mature and become **microgametes** (male) and **macrogametes** (female) during a process known as gametogenesis (that process take place in the midgut of mosquito). The time needed for the gametocytes to mature differs for each plasmodium species: 3- 4 d. for *P. vivax* and *P. ovale*, 6- 8 d. for *P. malariae* and 8- 10 days for *P. falciparum*.



11- In the mosquito gut, the microgamete nucleus divides three times producing eight nuclei; each nucleus fertilizes a macrogamete forming a **zygote**. The zygote, after the fusion of nuclei and the fertilization becomes the so- called **ookinete**. The ookinete, then, penetrates the midgut wall of the mosquito, where it encysts into a formation called oocyst. Inside the oocyst, the nucleus divides to produce thousands of **sporozoites (sporogony)**. That is the end of the third stage (stage of sexual reproduction/ sporogony). Sporogony lasts 8- 15 days.

12- The oocyst ruptures and the sporozoites are released inside the mosquito cavity and find their way to its salivary glands but only few hundreds of sporozoites manage to enter. Thus, when the above mentioned infected mosquito takes a blood meal, it injects its infected saliva into the next victim marking the beginning of a new cycle.

The duration of each above described phase is different for each of the plasmodia as it about 11 d. for P.V. &P.O. ,10-11 d. for P.F. & 18-21 d. for P.M.

Malaria stages are

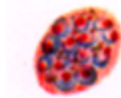
1- Ring form (immature trophozoite) :- 1 red nucleus on the ring-like light blue cytoplasm. single infection in a cell. *infected RBC like normal RBCs.*



2- Mature 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 (fine red granules)*



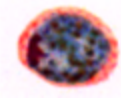
3- Schizont with merozoite:- nucleus divided into 12-24 ;and cytoplasm also divided , each nucleus surrounded by a portion of cytoplasm to form merozoites, malarial pigment clumped.



4- Male gametocyte :- oval in shape; 1 loose nucleus nearly in center of it ; malarial pigments diffuse .



5- Female gametocyte :- oval in shape ; 1 compact nucleus not in center of it .



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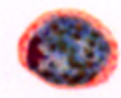
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Pathogenicity :-

Incubation period about 12-17 days

((Paroxysm (attack of malaria)))

periodic Paroxysms (malarial attack): the characteristic symptom of malaria occur because of the sudden liberation of merozoites, malarial pigment and RBC debris into the blood stream. It's characterize by three stages:

1- The cold stage (chill)- caused due to the parasites rupture their host red cells and escape into the blood, lasting for 30min-1hr (Nausea, vomiting, and headache are common at this time).

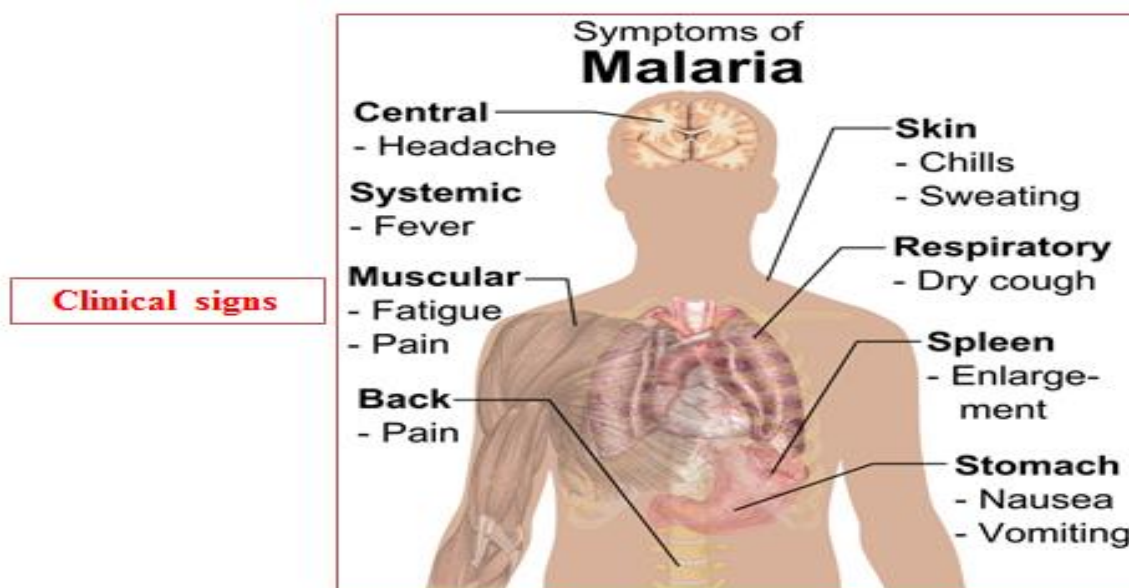
2- The hot stage(fever reach to 40⁰C) lasting for 1-4hr (once every two days)- perhaps due to the time require for the parasites invade new red cells.

3- Sweating stage :-1-2hr (The fever subsides, and the patient falls asleep and awake, relatively feel well after that)

Attack occurs P.v. every (48 hours); P.f./36 hrs to 48 hrs ;P.m. & P.o /72 hrs

Pre -patent period :- Time from introduction of sporozoite till appearance of parasite in blood (pre-or exoerythrocytic cycle) in liver.

Incubation period :- The time between inoculation (introduction) of sporozoite and the first appearance of clinical signs of which the fever is most common .



Splenomegaly and anemia

Causes of anemia

- 1-Direct RBCs lysis as a result of the life cycle of the parasite .
- 2-Splenic removal of both infected and uninfected RBCs (both coated with immune complexes) .
- 3-Auto-immune lysis of coated infected and uninfected RBCs.
- 4-Increased fragility of RBCs.
- 5-Decreased RBC production due to bone marrow suppression.

Finally, these evidence will be lead to enlargement of the spleen.

P. vivax and *P. ovale* infect only reticulocytes(young RBC) so they cause low grade anemia.

P. malariae infect older RBCs and cause mild anemia.

P. falciparum infect all types of RBCs so it cause severe anemia.

Relapse

Renewal of clinical manifestations and new series of malarial paroxysms following termination of primary attack . There is one to several more attack , months or years after termination of primary attack (either naturally or following treatment)

The parasite completely disappear from the blood after primary attack but there is hypnozoite which is a dormant sporozoite (exo-erythrocytic form) in liver which is responsible for these relapse . Hypnozoite present only in *P.vivax* and *P.ovale* .

The hypnozoites 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.

Malignant malaria

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

The serious complication of P.f. involves:-

- 1- Short incubation period
- 2- Crebral malaria (involving the brain).
- 3- Massive haemoglobinuria (black water fever) in which the urine becomes dark in color, because of acute hemolysis of RBC.
- 4- Acute respiratory distress syndrome.
- 5- Severe gastrointestinal symptoms; shock and renal failure which may cause death.

Diagnosis

➤ Signs & symptoms

➤ Laboratory diagnosis of malaria is confirmed by

1- Demonstration of malarial parasites in **the blood film** under microscopic examination.

- Thin film
- Thick film

2- Serology by ELISA:-is not capable of diagnosing current infection, but can tell a lot about infection history.

3-PCR polymerase chain reaction

Vaccines

- Repeated infection has afforded some individuals immunity, but this is short lived unless the person is frequently exposed to *P. infection*.
- As yet there is no vaccine for malaria and there are many researches in this area

Treatment

- Chloroquine most common and effective drug used to treat malaria.
- Not much funding is available for the development of new treatments for malaria.
- The locations where malaria is endemic are some of the poorest countries in the world and development of new medicines is not seen for over 10 years.

Prevention and control:

Three common methods used to prevent malaria include

1. Treatment of **patients with antimalarial drugs.**
2. Mosquito elimination (by using insecticide, insect eradication program)
3. Prevention of bites (by using nets during sleeping outdoor and insecticide indoor).

Chemoprophylaxis

-----**Chloroquine / pyrimethamine**

used for prophylaxis of malaria ; 1 week before entry into the endemic area ; for 4 weeks after returning from the endemic area.