Malaria

Plasmodium falciparum exists in the tropics and sub-tropics, and is responsible for approximately 50% of all malaria cases. The incubation period of P. falciparum malaria is the shortest, between eight and 11 days and has a periodicity of 36–48 hours. It can be differentiated from the other species by the morphology of the different stages found in the peripheral blood. In infections with Plasmodium falciparum usually only young trophozoites and gametocytes are seen in peripheral blood smears, the schizonts are usually found in capillaries sinuses of internal organs and in the bone marrow. The disease it produces runs an acute course and often terminating fatally. It is a significant cause of abortions and stillborns and even death of non-immune pregnant women.

Morphological Differences:-

The blood-stage parasites of human Plasmodium species exhibit differences in their morphology and modify the host erythrocyte differently .These differences can be used to distinguish the four species.

1-P. falciparum :-

- No change in size and color of RBCs.
- Stained RBCs may contain Maurer's spots.
- Blood smears are characterized by the presence of young trophozoites (rings) in the absence of trophozoites and schizonts.
- The ring stages of P. falciparum tend to be slightly smaller than the other species and are generally more numerous.
- The crescent-shaped gametocytes of P. falciparum are very distinctive.

2-P. vivax :-

- The most distinctive features of P. vivax are the enlarged infected erythrocytes.
- Appearance of red granules, called 'Schüffner's dots', over the erythrocyte cytoplasm.
- The growing trophozoite of P. vivax often has an ameboid appearance

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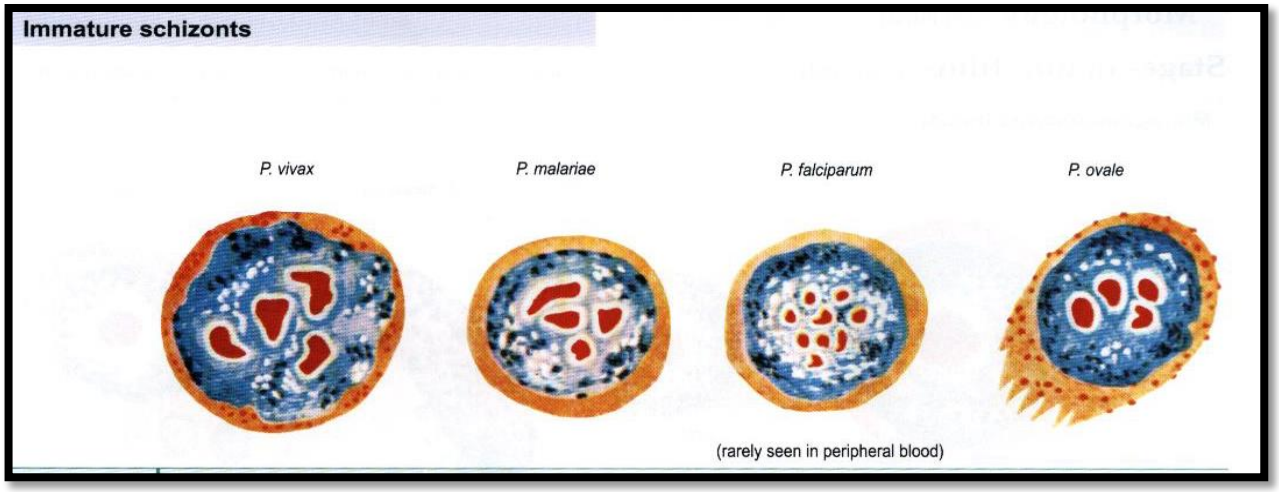
- The schizonts can have more than 20 merozoites.

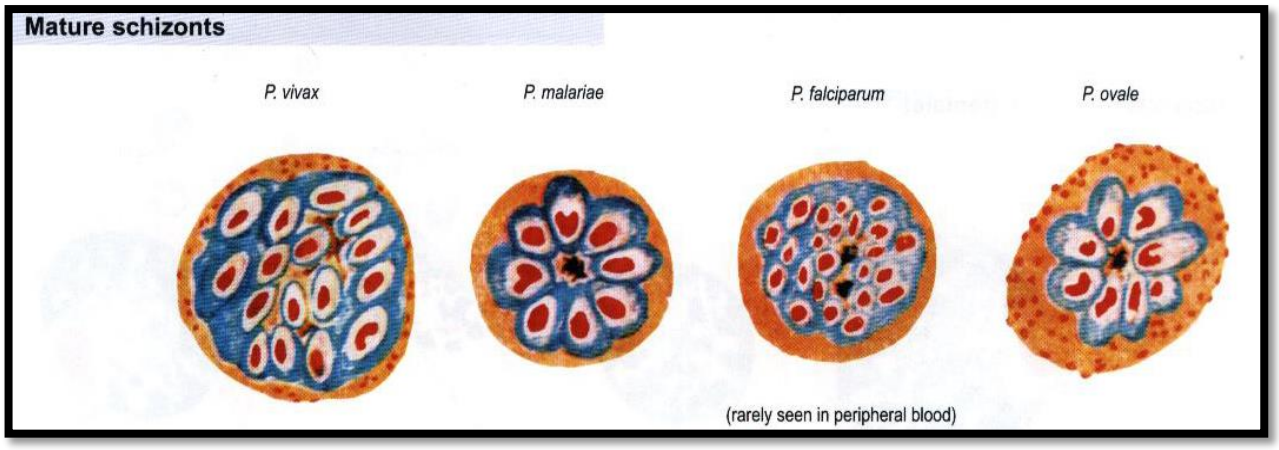
3-P. ovale :-

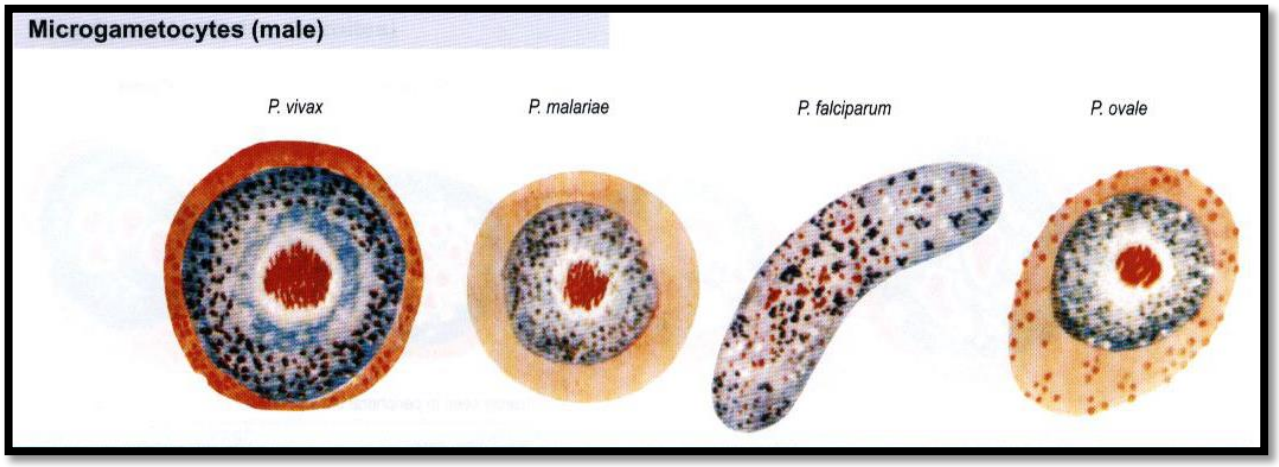
- Also exhibits Schüffner's dots.
- Enlarged erythrocyte, with irregular edges .
- In general P. vale is more compact parasite than P.vivax.
- Fewer merozoites (8-14)are found per schizont.
- P. ovale also has more of a tendency to form elongated host erythrocytes.

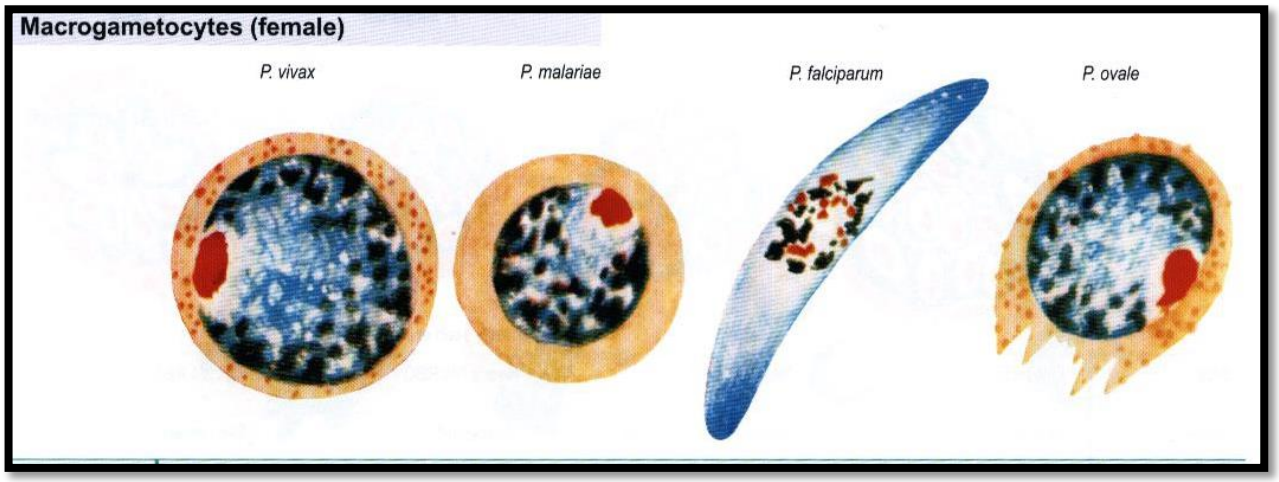
4-P. malariae :-

- Is characterized by a compact parasite (all stages).
- Not alter the host erythrocyte or cause enlargement.
- Elongated trophozoites stretching across the erythrocyte, called band forms, are sometimes observed.
- Schizonts will typically have 8-10 merozoites that are often arranged in a rosette pattern with a clump of pigment in the center.
- See small granules called ziemann,s dots.









Duration of erythrocytic phase :-

The duration of this phase varies according to the species. All mature schizonts in body burst at the same releasing merozoites and pyrogens in circulation cause febrile paroxysm it suggested that schizogonic periodicity is related to human

circadian rhythm. Tertian and quartan refer to the differences in the periodicity of paroxysms.

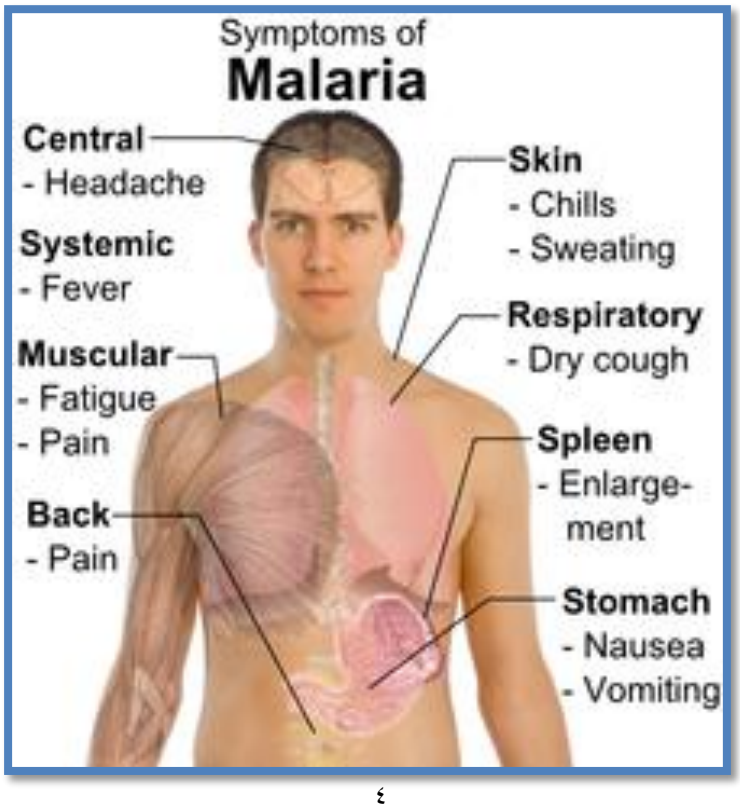
P. vivax------cause benign tertian malaria fever recurs after interval of 48 hours or every third day.

P. falciparum ----cause malignant tertian malaria also called sub-tertian because the cycles are often poorly synchronized and febrile paroxysm recur after intervals of less than the expected 48 hours also called pernicious malaria.

P. malariae -------cause quartan malaria refers to a 72 hour periodicity (occurring every forth day) .

P. ovale ----------cause ovale tertian because of its tertian periodicity and the irregular oval shape of infected RBCs.

Pathogenecity of malaria:-



Clinical manifestation in a typical case are series of febrile paroxysm followed by anemia and splenomegaly.

Febrile paroxysm:-

start generally in early afternoon but actually it may start at any time, each paroxysm shows succession of three stages :-

1-cold stage (lasting 20-60 min).

2- hot stage (lasting 1-4 hours).

3-sweating stage (lasting 2-3 hours).

The total duration of febrile cycle is from (6-10 hours) according to species , the febrile paroxysm synchronizes with erythrocyticschizogony of parasite.

A- with 48 hrs cycle the fever recur every third day tertian fever.

B-with 72 hrs cycle the fever recur every forth day quartan fever.

C-sometimes , especially in early infection with P. vivax there may be two independent broads of parasites with overlapping cycles so the fever recurring at intervals of 24 hrs , this called (quotidian periodicity) .

D- in P.vivax and P.malariae this due to the maturation of two generations of terian parasite on two successive days (tertian duplex).

E-in P.falciparum may not show three successive cold, hot ,sweating stages fever in this case continuous instead of intermittent or is (remittent). This explain that several generation of parasites multiplying at different intervals.

Anemia:-

After febrile cycle or fever paroxysm ,anemia of mycrocytic or normocytic , hypochromic develops as resulting of breaking down of red blood cells during the phase of segmentation of the parasite.

Splenomegaly:-

Enlargement of spleen is the important physical signs of malaria.

- liver cell necrosis producing hypoglycaemia via impaired gluconoegenesis
- renal ischaemia and cortical haemorrhage causing renal impairment and failure.
- dysfunction of cells of the small intestine contributing hypoglycaemia and causing diarrhoea.
- placental dysfunction and degeneration causing low fetal birth weight and stillbirth in the pregnant women.

Pernicious malaria:-

The term refers to a series of phenomena occurring during the cause of infection with plasmodium falciparum , which is effectively treated threatening of life for patient within 1-3 days.

The pathogenesis of pernicious malaria has been attributed to certain pecular biological features of plasmodium falciparum which cause agglutination of parasitized RBCs leading to blockage of the capillaries vessels of internal organs , these features are:-

1- Erythrocytic schizogony of plasmodium falciparum occurring inside the capillary vessels of the internal organs.

2- Segmenting forms of parasites being unable to alter their shapes during their passages onside the capillaries vessels act as emboli.

3- The growing trophozoites and sexual forms (ovoids) become adhesion to each other as well as the vessels wall, resulting in agglutination and blocking of the vessels.

Parasitaemia , schizonts as well as ring forms are commonly present in large number in peripheral blood.

Black water fever:-

It is manifestation of plasmodium falciparum occurring in previously infected subject and characterized by sudden intravascular hemolysis followed by fever and passage of hemoglobin in the urine.

It is associated with infection by plasmodium falciparum most commonly observed amongest the non-immune population who have resided in malarious countries for 6 months to 1 years and have inadequate doses of quinine for both suppressive prophylaxis and treatment of repeated clinical attacks.

Intravascular hemolysis , the exact mechanism hemolysis in black water fever is not yet clearly known . There appears to be some hemolytic agent involved where by RBCs undergo lysis and liberate a large quantities of oxy-hemoglobin in to the blood stream ,in the plasmodium falciparum the intravascular occurs periodically at the time of schizogony.

Cerebral Malaria

Cerebral malaria is an acute disease of the brain, which is accompanied by fever, convulsions and paralysis or coma. It is due to the sequestration of brain capillaries and venues with parasitised red blood cells and nonparasitised red blood cells.

Laboratory diagnosis:-

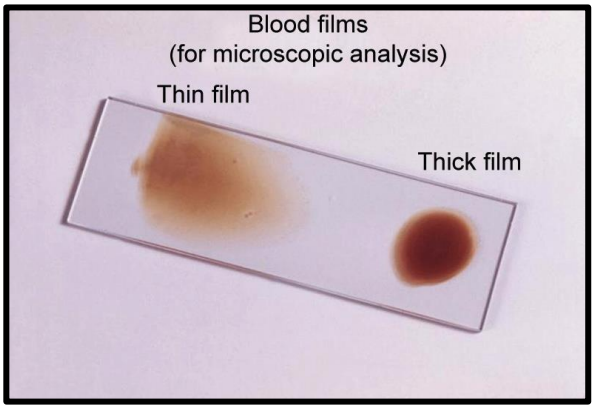
Microscopically examination of blood film is considered as most important diagnostic procedure in malaria.

Specimen

Peripheral blood is collected from ear lobe or by finger prick in older children & adults and from the great toe in infants. Blood films should be prepared directly from the capillary blood. In case of ethylene diamine tetra acetic acid (EDTA) anticoagulated blood, smears should be made within an hour of collection of blood. In pregnant women, cord blood and placental impression smears are used. In postmortem cases, smears from cerebral grey matter can be used

Time for taking blood: Blood should be collected few hours after the height of the paroxysm of fever and before taking antimalarial drugs. Parasite density is maximum during this period

Frequency: Smears should be examined at least twice daily until parasites are detected. Blood film , Thick blood film for quick identification of malarial infection, Thin film for identification of species.



Other methods for diagnosis:-

1-culture examination , for differentiation between trophozoite (ring stage) of different species.

RPMI 1640 medium(Roswell Park Memorial Institute and 1640 denotes the number of passages) in a continuous flow system mixed with a thin layer of RBC and an overlay medium consists of human serum maintained with 7% CO2 and 1–5% O2.

2- Quantitative Buffy Coat Examination :- The quantitative buff y coat (QBC) malaria test is an advanced microscopic technique for malaria diagnosis. It consists of three basic steps—

(1) concentration of blood by centrifugation,

(2) staining with acridine orange stain and

(3) examination under ultravoilet (UV) light source

3- blood count, little importance.

4-serological diagnosis:-

a-specific complement fixation test and priciptin test.

b-non-specific test, Henry's melano-flocculation.

5-molecular diagnosis by polymerase chain reaction.

Treatment :-

Natural alkaloid (quinine).

Synthetic antimalarial drugs, includes :- 4-aminoquinoline, chloroquinecamoquine, pyrimidines (dorapram, pyrimethmine).

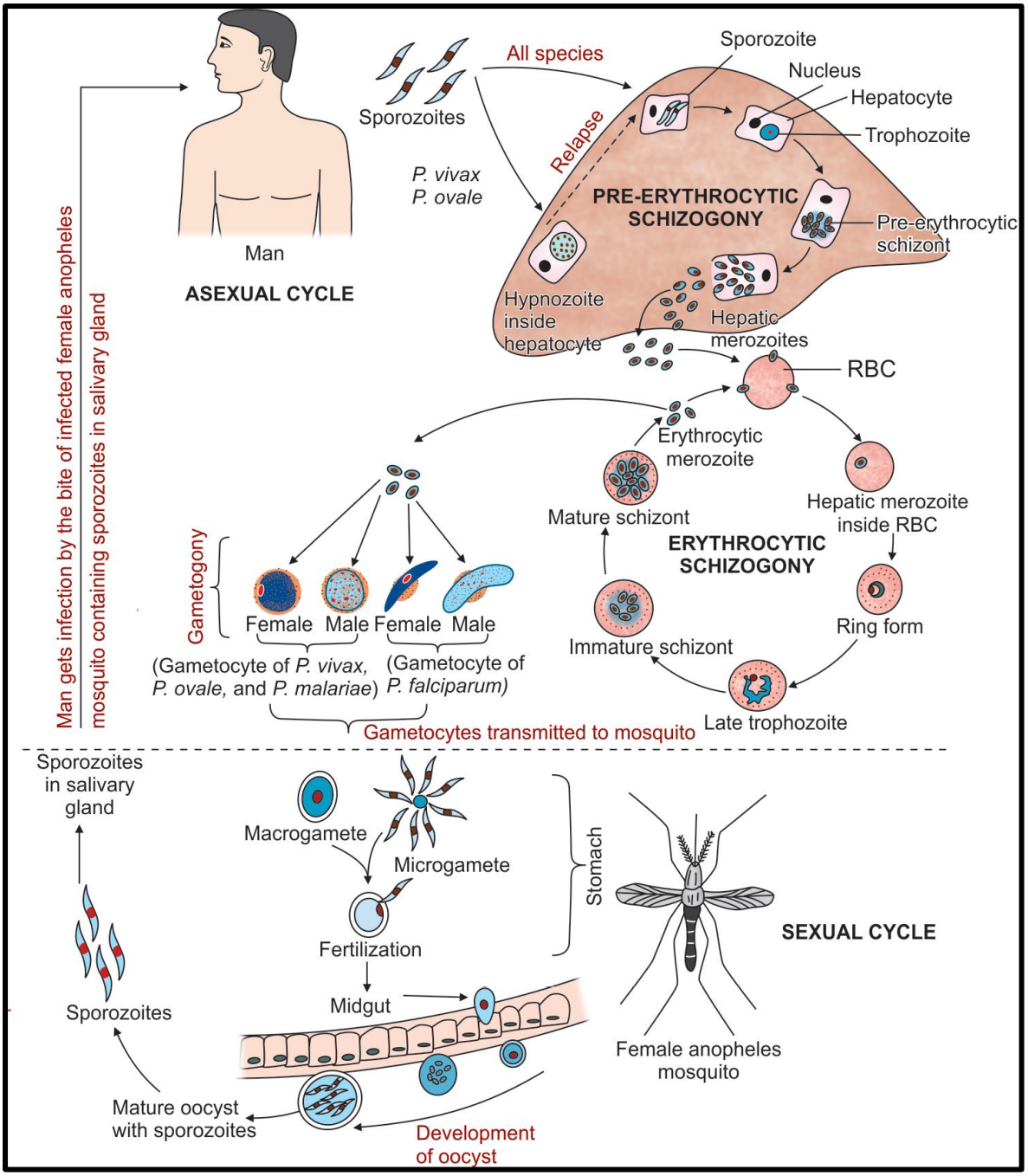
Prophylaxis:-

Protection against mosquito bites.

Systemic use of antimalarial drugs.

Prevention of carriers by 8-aminoquinoline.

Anti-mosquito measures as destruction of adults by DDT and antilarval measures.


Man
ASEXUAL CYCLE
Sporozoites
All species
P. vivax
P. ovale
Relapse
Sporozoite
Nucleus
Hepatocyte
Trophozoite
PRE-ERYTHROCYTIC SCHIZOGONY
Pre-erythrocytic schizont
Hypnozoite inside hepatocyte
Hepatic merozoites
RBC
Erythrocytic merozoite
Mature schizont
Hepatic merozoite inside RBC
ERYTHROCYTIC SCHIZOGONY
Ring form
Immature schizont
Late trophozoite
Gametogony
Female Male Female Male
(Gametocyte of P. vivax, P. ovale, and P. malariae)
(Gametocyte of P. falciparum)
Gametocytes transmitted to mosquito
Man gets infection by the bite of infected female anopheles mosquito containing sporozoites in salivary gland
Sporozoites in salivary gland
Macrogamete
Microgamete
Fertilization
Stomach
SEXUAL CYCLE
Sporozoites
Midgut
Female anopheles mosquito
Mature oocyst with sporozoites
Development of oocyst