

Biotechnology dep. Lec. 5 Medical Parasitology 2022 Dr: Alia Essam

Phylum: Protozoa Sub phylum: Apicomplexa Class: Aconoidasida

Order: Haemospororida Family: Plasmodiidae

Sporozoa or Apicomplexa are organisms that are characterized by being one-celled, non-motile, intracellular parasites, lack contractile vacuoles and spore-forming. Most of them have an alternation of sexual and asexual stages in their life cycle.

* The class includes main five species of parasites which produce malaria in man, and which belong to the genus *Plasmodium*.

* It also includes a group of parasites commonly called the coccidian; there are three genera of coccidian parasitic in man, namely *Isospora*, *Sarcocystis* and *Toxoplasma*.

1- Genus: *Plasmodium*

* Five species, all of this genus, may give rise to malaria disease in man, they are:

1- *P. vivax*, produce benign tertian malaria.

2- *P. malaria*, caused quatern malaria.

3- *P. ovale*, parasite produce benign tertian malaria.

4- *P. falciparum*, which causes malignant tertian malaria.

5- *P. knowlesi*, is a zoonotic malaria parasite, transmitted between non-human primate hosts by the *Anopheles* (An.) mosquitos.

Host:

* **The mosquitoes** play as essential hosts that have the sexual stages, man act as the intermediate host harbouring the asexual stages of parasites.

* **In the human body**, there are two cycles, one in the liver which is called the Exoerythrocytic cycle or Pre-erythrocytic cycle, the other takes place in the red blood cells, so-called the Erythrocytic cycle.

The life cycle:

The life cycle is rather similar in the four species, with slight differences. All have a sexual cycle in anopheline mosquito and an asexual cycle in man as follows:

1- The Asexual cycle (Schizogony)

* Human malaria infection begins when an anopheline mosquito injects into man the infective sporozoites, which circulate with the blood, within one hour, they reach the liver to lodge in the liver and disappear from the bloodstream to begin the exo-erythrocytic schizogony.

A- Exo-erythrocytic schizogony

* Sporozoite inside the liver cell enlarges to form trophozoite, and this liver cycle consists of two phases as follows:

1- Primary tissue phase

* Sporozoite gradually changes in liver cell to trophozoite form.

* This trophozoite becomes amoeboid in shape and consumes liver cells to grow and mature.

* After maturation, each trophozoite divides extremely and changes to a pre-erythrocytic schizont

* During that division, the nucleus of trophozoite divides into a large number of nuclei, followed by the division of the cytoplasm to form thousands of merozoites inside the liver cell.

* The time needed for the pre-erythrocytic schizont (incubation period) to form and the number of merozoites differs according to species of Plasmodium.

* The incubation period for *P. vivax* is eight days, *P. malaria* 12 days, *P. ovale* nine days and finally five days for *P. falciparum*.

2- Secondary tissue phase

* At the same time, some of the pre-erythrocytic merozoites invade the red blood cells thus initiating the erythrocytic schizogony.

* In *P. falciparum*, once pre-erythrocytic merozoites are liberated from the liver cells, they invade only the red blood cells and never reinvade the liver, so the relapses are absent in *P. falciparum*.

* The reinvasion of the liver cells in the three benign malaria species is responsible for relapses after apparent cure.

B- Erythrocytic Schizogony * Merozoites discharged from pre-erythrocytic schizont enter the red cells by invagination of its cell membrane.

* The merozoite is transformed into:

* Ring stage or young trophozoite

* Amoeboid stage or old trophozoite, which digests hemoglobin to form the malarial pigments namely Schuffner's dots in *P. vivax* and *P. ovale*, Ziemann's dots in *P. malariae* and Maurer's dots in *P. falciparum*.

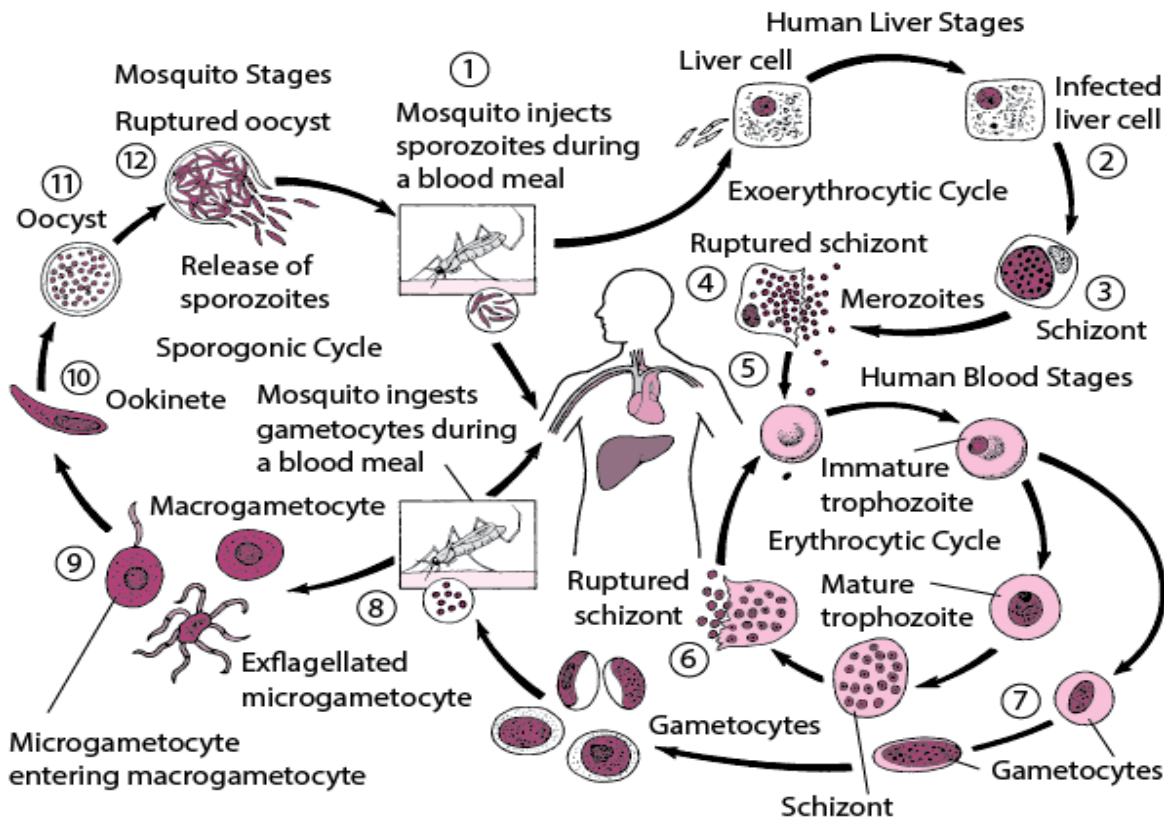
* The old trophozoite undergoes schizogony to form schizont stage containing merozoites. The liberated merozoites invade new red blood cells, repeating the cycle. Rupture of erythrocytic schizonts releases haematin pigments and parasite toxins, which are responsible for fever and sweating.

Human Malaria					
Stages Species	Ring	Trophozoite	Schizont	Gametocyte	
<i>P. falciparum</i>					<ul style="list-style-type: none"> Parasitised red cells (pRBCs) not enlarged. RBCs containing mature trophozoites sequestered in deep vessels. Total parasite biomass = circulating parasites + sequestered parasites.
<i>P. vivax</i>					<ul style="list-style-type: none"> Parasites prefer young red cells pRBCs enlarged. Trophozoites are amoeboid in shape. All stages present in peripheral blood.
<i>P. malariae</i>					<ul style="list-style-type: none"> Parasites prefer old red cells. pRBCs not enlarged. Trophozoites tend to have a band shape. All stages present in peripheral blood
<i>P. ovale</i>					<ul style="list-style-type: none"> pRBCs slightly enlarged and have an oval shape, with tufted ends. All stages present in peripheral blood.
<i>P. knowlesi</i>					<ul style="list-style-type: none"> pRBCs not enlarged. Trophozoites, pigment spreads inside cytoplasm, like <i>P. malariae</i>, band form may be seen Multiple invasion & high parasitaemia can be seen like <i>P. falciparum</i> All stages present in peripheral blood.

* When the schizonts rupture, fever and other symptoms take place, and this reoccurs every third day, and thus the fever is called tertian fever, and the disease is called benign tertian malaria.

* In *P. falciparum*, the fever is irregular, it may be tertian, quatrain or even continuous.

- * After completing a few schizogony cycles, some merozoites develop into male microgametocytes and female macrogametocytes.
- * All erythrocytic stages of Plasmodium are found in peripheral blood, except trophozoites and schizonts of *P. falciparum*, which are trapped in blood vessels of the internal organs.



2- The Sexual cycle (Sporogony)

- * This occurs inside the insect which is an anopheline mosquito.
- * When it sucks a blood meal of a patient containing all stages and the gametocytes, all stages of malaria are digested in the insect mid-gut except the gametocytes.
- * The male microgametocyte nucleus divides into 4-8 fragments, to form finally the microgametes.
- * The female macrogametocyte throws two polar bodies to reduce its chromatin before the fertilization occurs.
- * After fertilization by fusion of the macro and micro gametes, the zygote is formed.
- * The zygote throws out pseudopodia to form a motile stage called Ookinete.
- * Ookinete penetrates the mucous membrane of gut, to settle beneath it, which is called oocyst.
- * Its nucleus divides many times to produce fine spindle-shaped called sporozoites.

* The oocyst ruptures and sporozoites are free to migrate to the salivary glands, they pass with saliva into the human body while the mosquito is taking a blood meal.

[Pathogenesis]

After a mosquito takes a blood meal, the malarial sporozoites enter hepatocytes (liver phase) within minutes and then emerge in the bloodstream after a few weeks. These merozoites rapidly enter erythrocytes, where they develop into trophozoites and then into schizonts over a period of days (during the erythrocytic phase of the life cycle). Rupture of infected erythrocytes containing the schizont results in fever and merozoite release. The merozoites enter new red cells, and the process is repeated, resulting in a logarithmic increase in parasite burden.

Three organs show gross pathological lesions namely the liver, the spleen and bone marrow. Liver shows necrosis and enlargement, spleen may enlarge and tender, bone marrow becomes vascular, chocolate brown due to deposition of pigment.

* In *P. falciparum*, the disease is characterized by its common malignant features, due to:

1- Agglomeration of parasitized and non-parasitized red blood cells inside capillaries of the internal organs, this causes plugging of the human capillaries, and causes thrombosis and sometimes hemorrhages

2- In chronic malignant malaria, rapid intravascular haemolysis occurs, leads to passage of dark urine due to presence of haemosiderin, which called "black water fever".

[Diagnosis]

* Clinical symptoms and signs such as fever, sweating, enlarged and tender spleen and liver, and Jaundice may occur.

* Direct methods such as thin and thick blood film.

* Serological test.

[Prevention and control]

* Treatment of patients.

* control the *Anopheles* mosquitoes, adults and larvae.

2- *Toxoplasma gondii*

Phylum: Protozoa Sub phylum: Apicomplexa Class: Conoidasida

Order: Eucoccidiorida Family: Sarcocystidae

Hosts: Cats are the main definitive host where sexual and asexual cycles take place inside the cytoplasm of columnar epithelial cells of their small intestine.

[Accidental host] The asexual cycle occurs in any nucleated cell with a special preference for reticulo endothelial cells, brain and retinal cells.

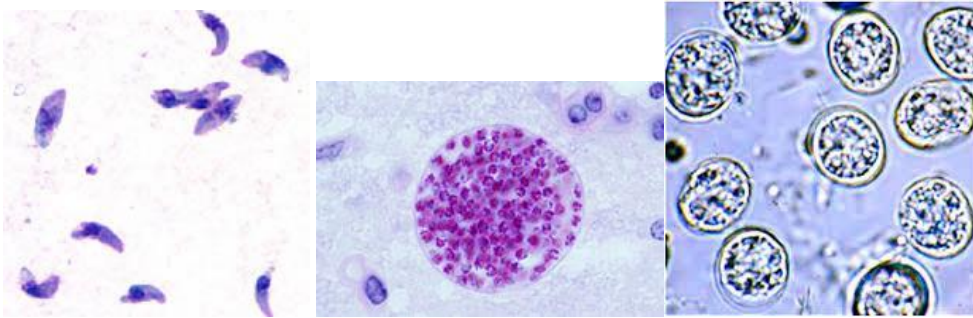
[Morphology] All the morphological forms are considered as the infective stage, these are:

* Trophozoite: has a crescent shape with a central nucleus, its size from 4-6 micron.

* Pseudocyst: macrophage containing a number of rapidly multiplying trophozoites (Tachyzoites) within a vacuole occurs in acute infection.

True cyst: round with well-defined wall, contains numerous slow multiplying trophozoites (bradyzoites), and occurs in chronic infection, cysts are found in brain, liver, heart and muscles.

Oocyst: contains two sporocysts, each sporocyst contains four sporozoites.



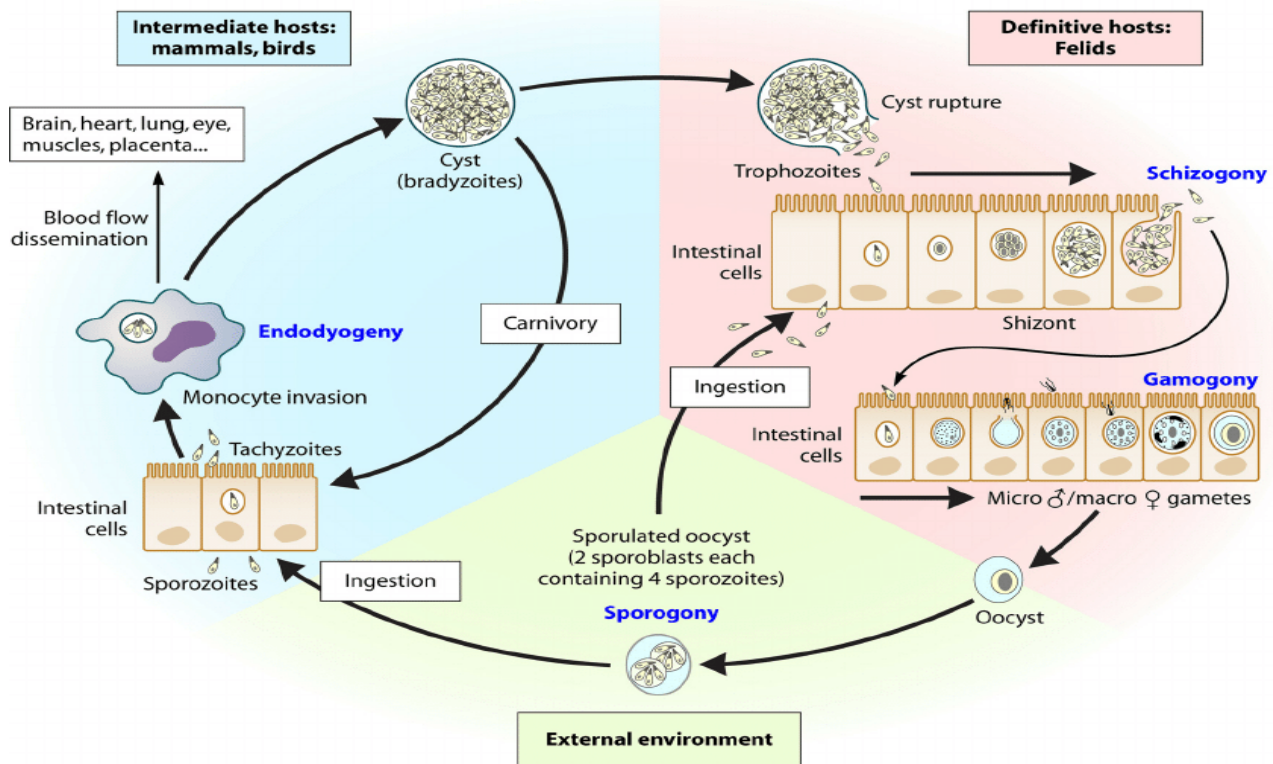
[Life cycle]

Inside the definitive host, the sporozoites or trophozoites penetrate epithelial cells of intestine, where they round up and grow.

Asexual division occurs first leading to the formation of merozoites, which invade new intestinal cells.

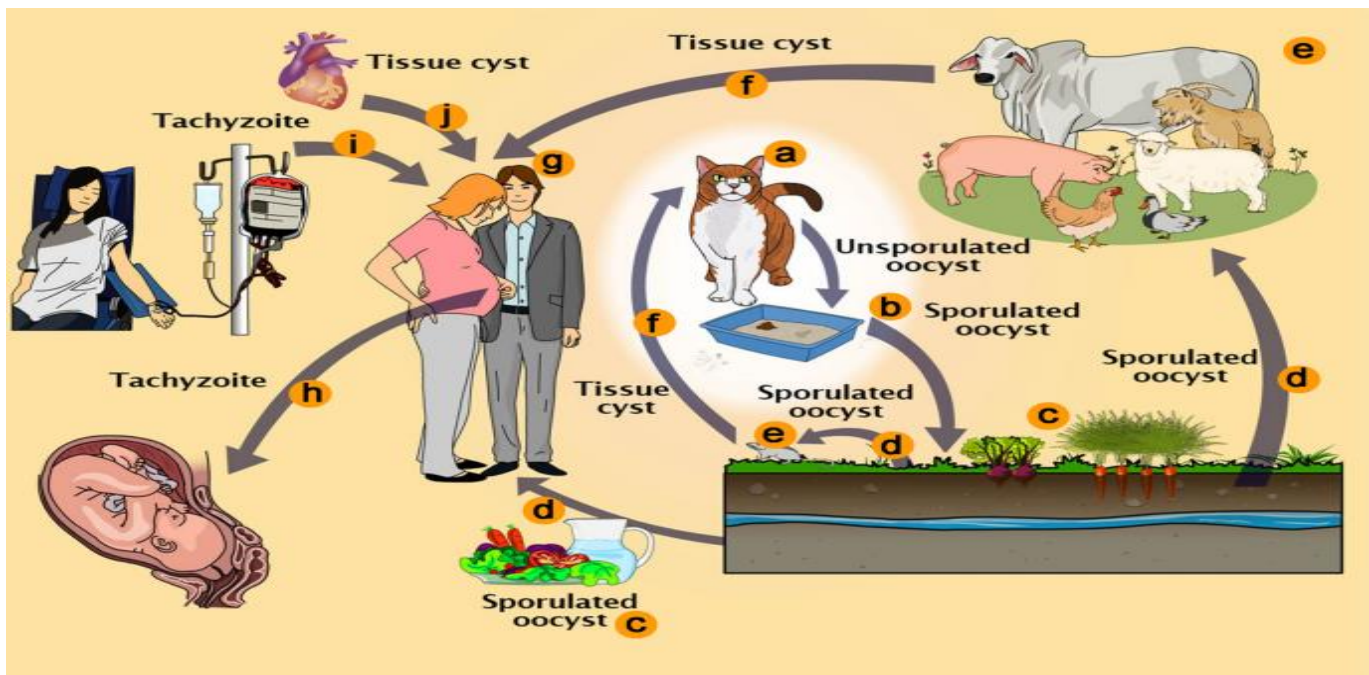
After few cycles, some merozoites change to sexual stages initiating gametogony. A macrogamete is fertilized by a motile microgamete forming a zygote, which changes to oocyst. Oocysts pass out with faeces after breakdown of intestinal epithelium. In accidental hosts, the sporozoites and trophozoites penetrate cells lining small intestine, and spread via blood or lymph all over the body, where they multiply in any nucleated cell, forming true cysts or pseudocysts according to rate of multiplication and host's immunity.

Toxoplasma in men has a blind-end life cycle since the cat does not eat human tissues.



* *Toxoplasma* life cycle in pregnant infected women is an open cycle, which the trophozoites pass through the placenta, if eating this placenta by cat completes the life cycle.

[Transmission]



Toxoplasma gondii pathways of transmission. **a** Feline definitive host (cat). **b** Unsporulated oocysts in cat feces. **c** Food contaminated with sporulated oocysts. **d** Oocysts may be ingested by intermediate hosts *via* water or raw vegetables. **e** Intermediate hosts (e.g. cattle, sheep, poultry and swine). **f** Ingestion of

tissue cysts in uncooked meat. **g** Intermediate hosts (humans). **h** Tachyzoites transmitted through the placenta to the foetus. **i** Transmission by blood transfusion and organ transplant (**j**)

A- In accidental or non specific hosts and man the transmission occurs by:

- * Ingestion of oocysts with food or water contaminated with infected cats faeces.
- * Ingestion of undercooked meat containing pseudocysts or true cysts.
- * Congenitally from infected mother to her fetus through placenta.
- * Rarely by blood transfusion or organ transplantation.

B- Infection to definitive host occurs by:

- *Ingestion of true or pseudocysts in muscles of rats or other animals.
- * Ingestion of infected placenta containing trophozoites after labour of infected women
- * Ingestion of oocysts in soil.

[Pathogenesis]

- *Acute toxoplasmosis caused maculopapular rash and lymphadenopathy.
- *Latent toxoplasmosis, usually due to congenital infection, may result in retinochoroiditis and lymphadenopathy.

If patient is immunocompromized, activated latent infection may cause myocarditis, meningoencephalitis and pneumonitis. In congenital toxoplasmosis, infection in first trimester results in abortion, Infection in second trimester results in still birth, and hydrocephalus intracerebral calcification and retinochoroiditis results from infection in third trimester.

[Diagnosis]

- * Direct diagnosis by: 1- staining of suspected tissues or body fluids, biopsy from lymph node, bone marrow, blood or smear from placenta to see trophozoites.
- 2- Mouse inoculation with the suspected material to detect the strain virulence.
- 3- Detection of *Toxoplasma* antigen.
- * Indirect serodiagnosis test

[Prevention and control]

- * Washing of fruit and vegetables.
- * Cooking of meat well.
- * Pregnant females should avoid cats, and pet cats are fed cooked food with proper disposal of their stools.