جامعة الانبار

كلية : الصيدلة

قسم : الصيدلة

اسم المادة باللغة العربية: الطفيليات الطبية

اسم المدة باللغة الإنكليزية: **Medical Parasitology**

المرحلة: الثانية

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عنوان المحاضرة باللغة العربية: كوكسيديا (سبوروزوا)

عنوان المحاضرة باللغة الإنكليزية: **Coccidia (Sporozoa)**

محتوى المحاضرة:

COCCIDIA (SPOROZOA)

INTRODUCTION

Coccidia are members of the class sporozoa, Phylum Apicomplexa. Apical complex is present at some stage and consists of elements visible with electron microscope. The life cycle is characterized by an alternation of generations, i.e. sexual (gametogony) and asexual (schizogony) reproduction and most members of the group also share alternative hosts.

The locomotion of a mature organism is by body flexion, gliding, or undulation of longitudinal ridges. The genus Plasmodium that is the causes of malaria is the prototype of this class.

Malaria:

There are four species normally infecting humans, namely, *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, and Plasmodium malariae.*

Life cycle:

The life cycle of malaria is passed in two hosts (alternation of hosts) and has sexual and asexual stage (alternation of generations).

Vertebrate host - man (intermediate host), where the asexual cycle takes place. The parasite multiplies by **schizogony** and there is formation of male and female gametocytes (**gametogony**).

Invertebrate host - mosquito (definitive host) where the sexual cycle takes place. Union of male and female gametes ends in the formation of sporozoites (sporogony).

The life cycle passes in four stages:

Three in man:- Pre - erythrocytic schizogony

- Erythrocytic schizogony
- Exo- erythrocytic schizogony

One in mosquito - Sporogony

Introduction into humans - when an infective female Anopheles mosquito bites man, it inoculates saliva containing sporozoites (infective stage).

Pre- Erythrocytic schizogony - sporozoites reach the blood stream and within 30 minutes enter the parenchymal cells of the liver, initiating a cycle of schizogony. Multiplication occurs in tissue schizonts, to form thousands of tiny merozoites.

Merozoites are then liberated on rupture of schizonts about 7th – 9th day of the bites and enter into the blood stream. These merozoites either invade the RBC's or other parenchymal liver cells. In case of *P. falciparum*

and possibly *P. malariae*, all merozoites invade RBC's without re-invading liver cells.

However, for *P. vivax* and *P. ovale*, some merozoites invade RBC's and some re-invade liver cells initiating further *Exo-erythrocytic* schizogony, which is responsible for relapses. Some of the merozoites remain dormant (hypnozoites) becoming active later on.

Erythrocytic schizogony (blood phase) is completed in 48 hrs in P. vivax, P.ovale, and P. falciparum, and 72 hrs in P. malariae. The merozoites reinvade fresh RBC's repeating the schizogonic cycles.

Erythrocytic merozoites do not reinvade the liver cells. So malaria transmitted by blood transfusion reproduces only erythrocytic cycle.

Gametogony

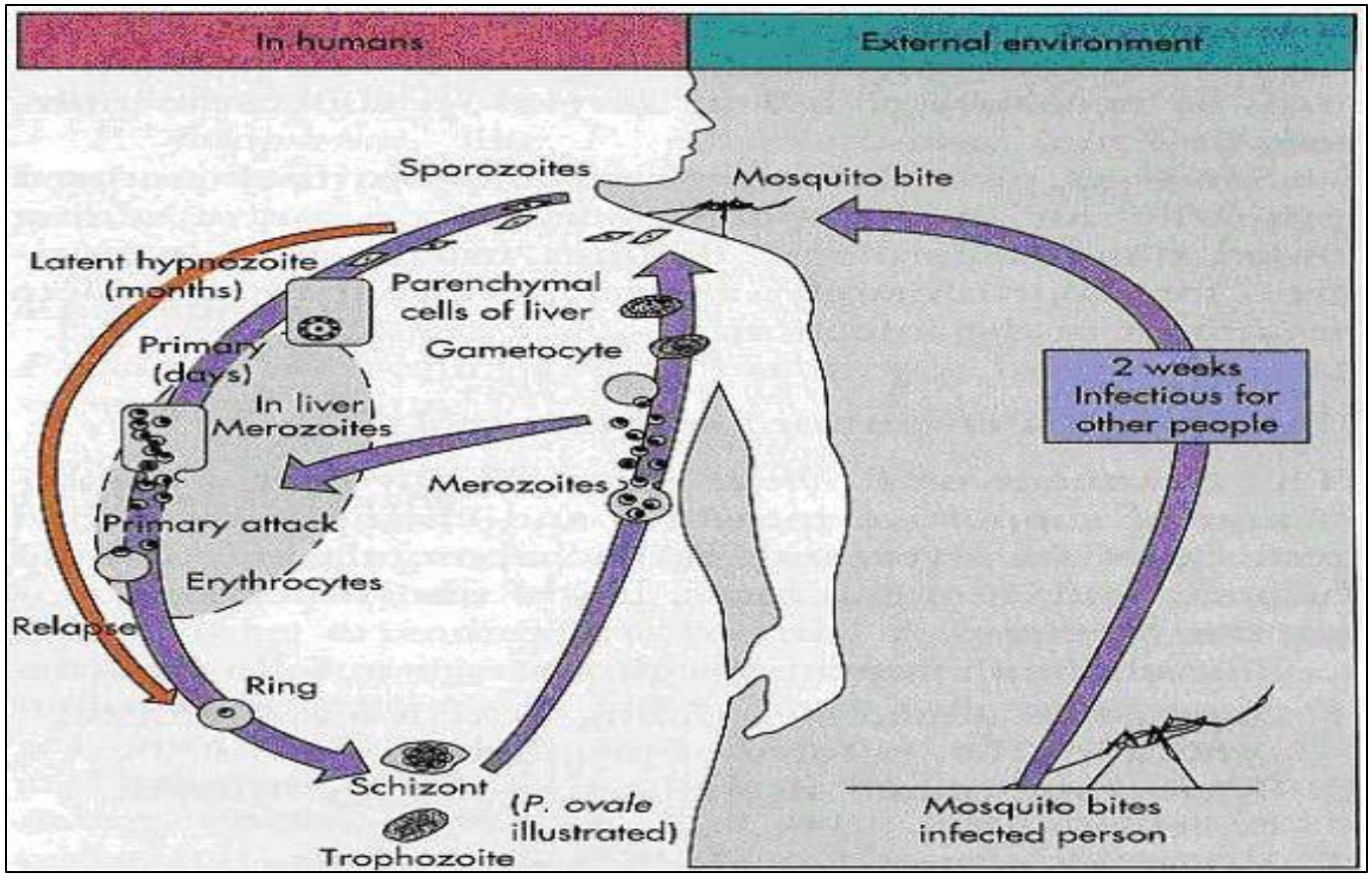
Some merozoites that invade RBC's develop into sexual stages (male and female gametocytes). These undergo no further development until taken by the mosquito.

Sporogony (extrinsic cycle in mosquito):

When a female Anopheles mosquito vector bites an infected person, it sucks blood containing the different stages of malaria parasite. All stages other than **gametocytes** are digested in the stomach.

The **microgametocyte** undergoes ex-flagellation. The nucleus divides by reduction division into 6-8 pieces, which migrate to the periphery. At the same, time 6-8 thin filaments of cytoplasm are thrust out, in each passes a piece of chromatin. These filaments, the microgametes, are actively motile and separate from the gametocyte.

The **macrogametocyte** by reduction division becomes a macrogamete. Fertilization occurs by entry of a micro gamete into the macro gamete forming a zygote. The zygote changes into a worm like form, the ookinete, which penetrates the wall of the stomach to develop into a spherical oocyst between the epithelium and basement membrane. The oocystes increase in size. Thousands of **sporozoites** develop inside the oocysts. **Oocysts** rupture and sporozoites are liberated in the body cavity and migrate everywhere particularly to the salivary glands. Now the mosquito is infective. The sporogonous cycle in the mosquito takes 8-12 days depending on temperature.



(Life cycle of Plasmodium species)

1- *Plasmodium falciparum:*

Plasmodium falciparum demonstrates no selectivity in host erythrocytes, i.e. it invades young and old RBCs cells. The infected red blood cells also do not enlarge and become distorted.

• Multiple sporozoites can infect a single erythrocyte, and show multiple infections of cells with small ring forms.

• The trophozoite is often seen in the host cells at the very edge or periphery of cell membrane at accole position.

• Occasionally, reddish granules known as Maurer's dots are observed

• Mature (large) trophozoite stages and schizonts are rarely seen in blood films, because their forms are sequestered in deep capillaries, liver and spleen.

• Peripheral blood smears characteristically contain only **young ring** forms and occasionally **crescent shaped gametocytes**.

Epidemiology:

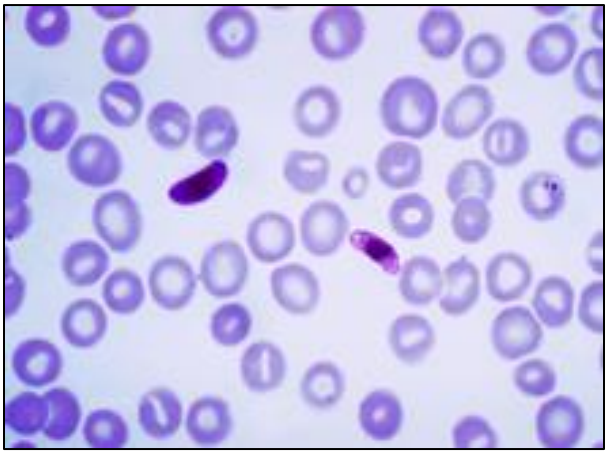
P.falciparum occurs almost exclusively in tropical and subtropical regions. Weather (rainfall, temperature & humidity) is the most obvious cause of seasonality in malaria transmission. To date, abnormal weather conditions are also important causes of significant and widespread epidemics. Moreover, drug-resistant infection of *P.falciparum* is the commonest challenge in many parts of the world. In Ethiopia, even though all the four species of plasmodium infecting man have been recorded, *P.falciparum* is the one that most causes the epidemic disease and followed by vivax and

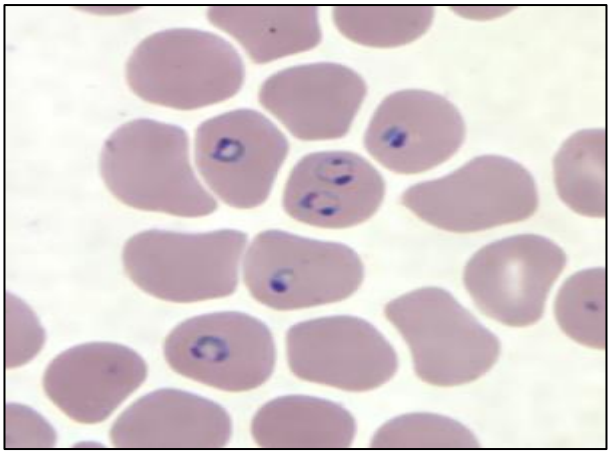
malariae. *P.ovale* is rare. Infection rates in Ethiopia are 60%, 40%, 1%, and <1% for *P. falciparum, P. vivax, P. malariae,* and *P. ovale*, respectively.

Clinical features:

Of all the four Plasmodia, *P. falciparum* has the shortest incubation period, which ranges from 7 to 10 days. After the early flu-like symptoms, *P.falciparum* rapidly produces daily (quotidian) chills and fever as well as severe nausea, vomiting and diarrhea. The periodicity of the attacks then becomes tertian (36 to 48 hours), and fulminating disease develops.

Involvement of the brain (cerebral malaria) is most often seen in *P.falciparum* infection. Capillary plugging from an adhesion of infected red blood cells with each other and endothelial linings of capillaries causes hypoxic injury to the brain that can result in coma and death. Kidney damage is also associated with *P.falciparum* malaria, resulting in an illness





called “black water” fever. Intravascular hemolysis with rapid destruction of red blood cells produces a marked hemoglobinuria and can result in acute renal failure, tubular necrosis, nephrotic syndrome, and death. Liver involvement is characterized by abdominal pain, vomiting of bile, hepatosplenomegally, severe diarrhea, and rapid dehydration.

Treatment:

Because chloroquine – resistant stains of *P.falciparum* are present in many parts of the world, infection of *P.falciparum* may be treated with other agents including mefloquine, quinine, guanidine, pyrimethamine – sulfadoxine, and doxycycline. If the laboratory reports a mixed infection involving *P.falciparum* and *P.vivax*, the treatment must eradicate not only *P.falciparum* from the erythrocytes but also the liver stages of *P.vivax* to avoid relapses provided that the person no longer lives in a malaria endemic area.

2- Plasmodium vivax:

P.vivax is selective in that it invades only young immature erythrocytes.

Infections of *P. vivax* have the following characteristics:

• Infected red blood cells are usually enlarged and contain numerous pink granules or schuffner's dots.

• The trophozoite is ring-shaped but amoeboid in appearance.

• More mature trophozoites and erythrocytic schizonts containing up to 24 merozoites are present.

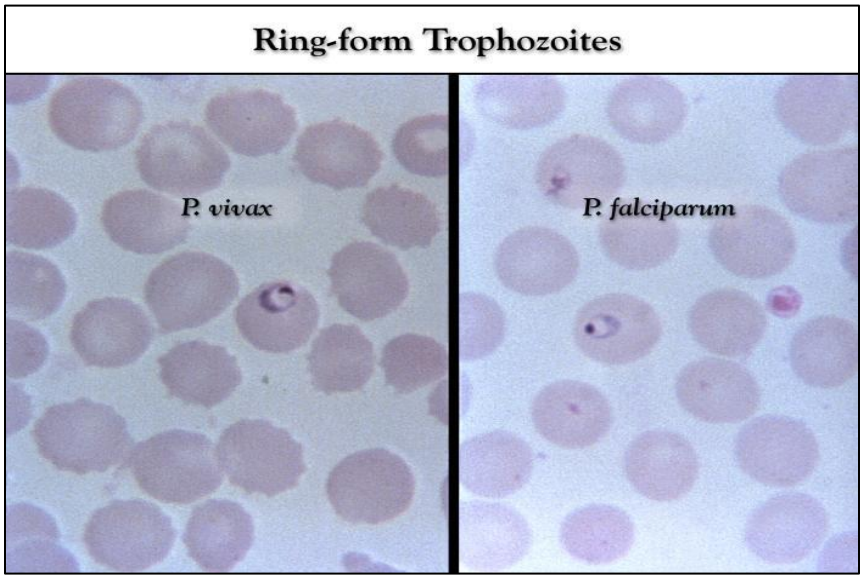
• The gametocytes are round

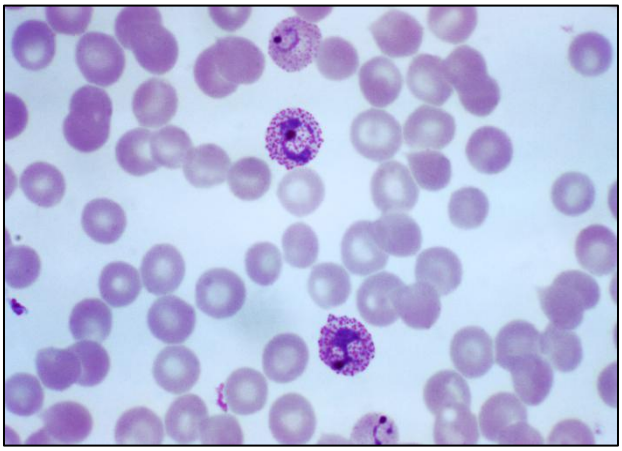
Epidemiology:

P. Vivax is the most prevalent of the human plasmodia with the widest geographic distribution, including the tropics, subtropics, and temperate regions. However, it is the second most prevalent in Ethiopia following *P. falciparum.*

Clinical features:

After an incubation period (usually 10 to 17 days), the patient experiences vague flu-like symptoms, such as headache, muscle pains, photophobia, anorexia, nausea and vomiting. As the infection progresses, increased numbers of rupturing erythrocytes liberate merozoites as well as toxic cellular debris and hemoglobin in to circulation. In combination, these substances produce the typical pattern chills, fever and malarial rigors. These paroxysms usually reappear periodically (generally every 48 hours) as the cycle of infection, replication, and cell lyses progresses. The paroxysms may remain relatively mild or may progress to severe attacks, with hours of sweating, chills, shaking persistently, high temperatures
(103^0F to 106^0F) and exhaustion. Since *P.vivax* infects only the reticulocytes, the parasitemia is usually limited to around 2 to 5% of the available RBCs.





Plasmodium vivax **ring** form and **trophozoites**

Treatment*:*

Chloroquine is the drug of choice for the suppression and therapeutic treatment of P.vivax, followed by premaquine for radical cure and elimination of gamatocytes.

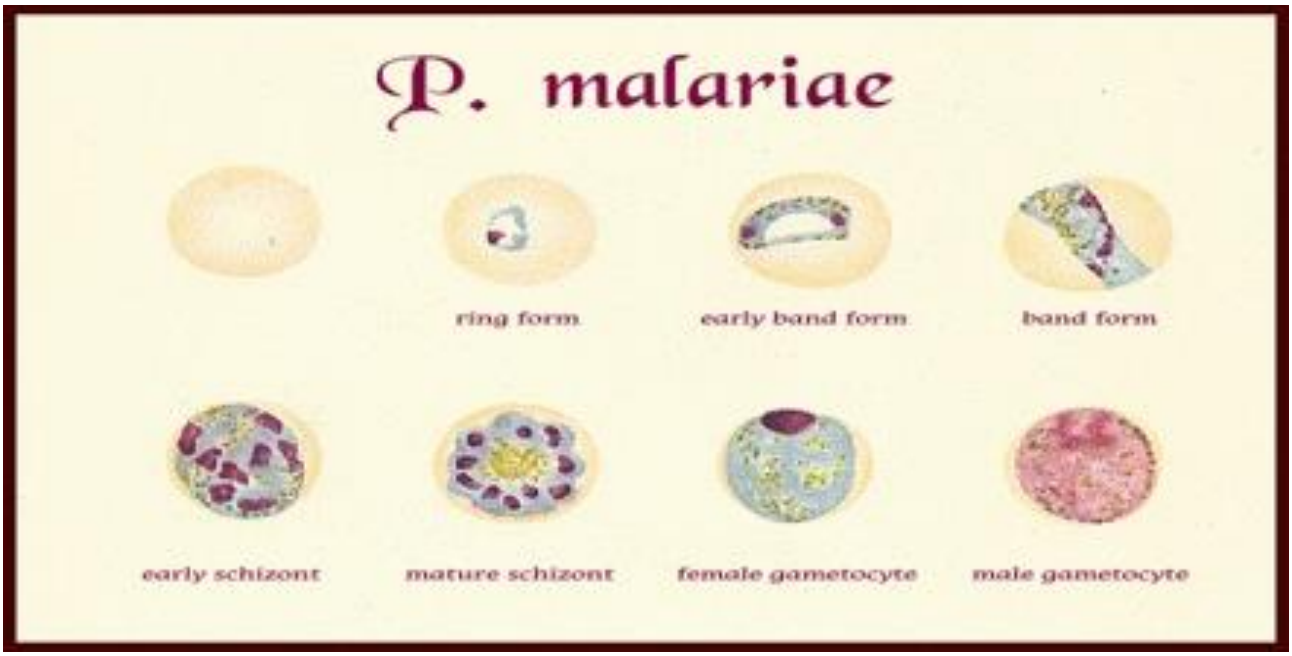
3- *Plasmodium malariae*:

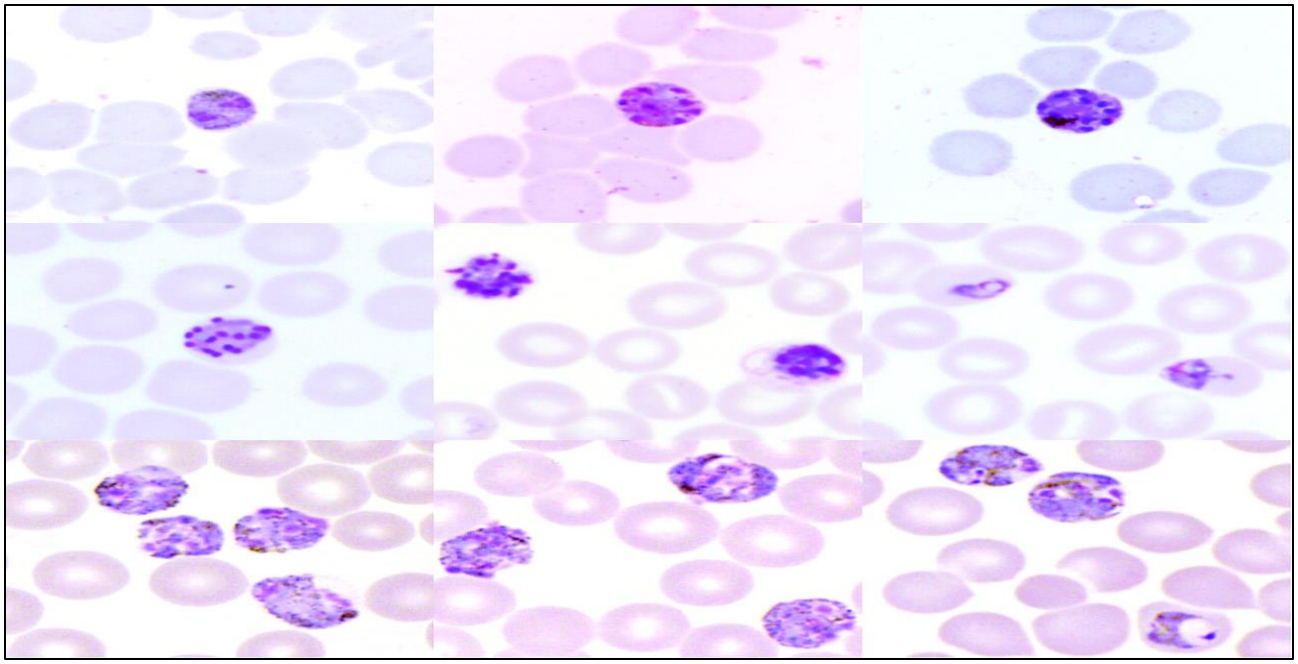
In contrast with *P.vivax* and *P.ovale*, *P.malariae* can infect only mature erythrocytes with relatively rigid cell membranes. As a result, the parasite's growth must conform to the size and shape of red blood cell.

This requirement produces no red cell enlargement or distortion, but it results in distinctive shapes of the parasite seen in the host cell, "band and bar forms" as well as very compact dark staining forms. The schizont of *P.malariae* is usually composed of eight merozoites appearing in a rosette.

Epidemiology:

P. malariae infection occurs primarily in the same sub-tropical and temperate regions as infections with the other plasmodia but is less prevalent.





***(Plasmodium malariae*)**

Clinical features:

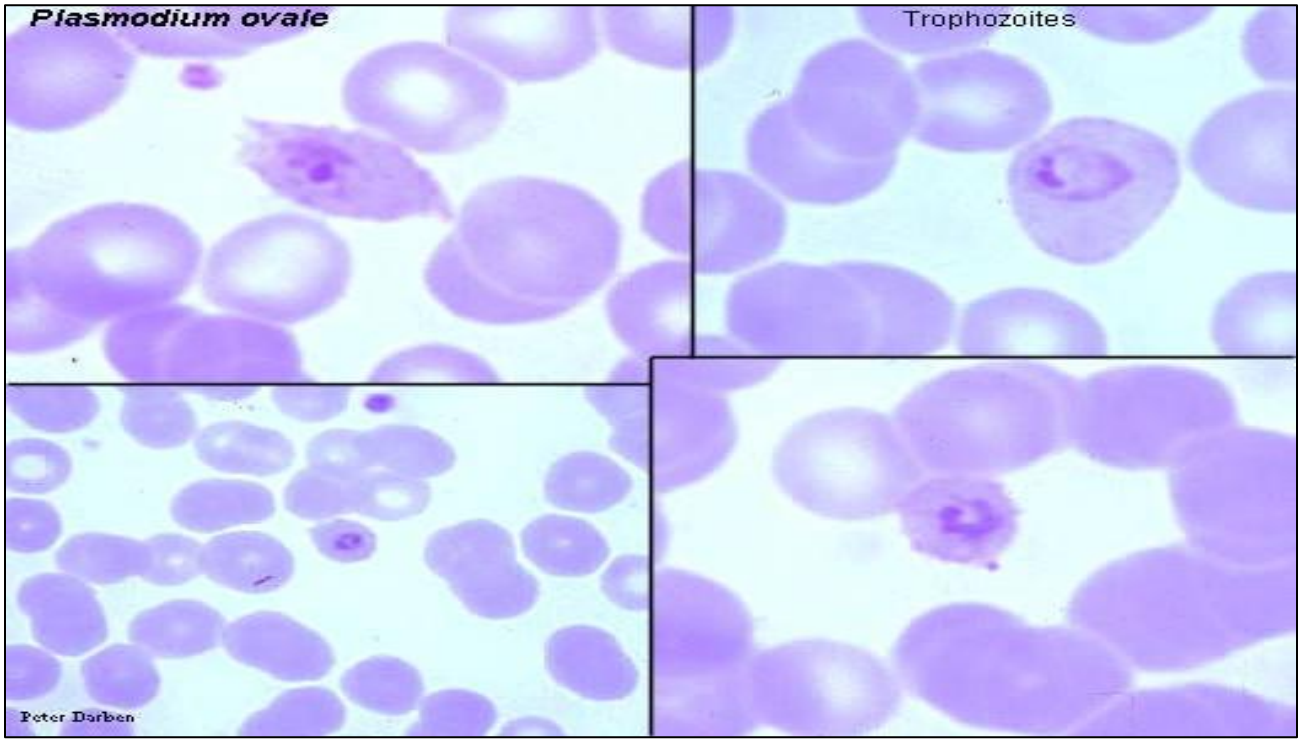
The incubation period for *P. malariae* is the longest of the plasmodia, usually 18 to 40 days, but possibly several months to years. The early symptoms are flu-like with fever patterns of 72 hours (quartan or malarial) in periodicity.

Treatment
Treatment is similar to that for *P.vivax* and *P.ovale.*

4- *Plasmodium ovale:*

P. ovale is similar to *P. vivax* in many respects, including its selectivity for young, pliable erythrocytes. As a consequence the classical characteristics include:

• The host cell becomes enlarged and distorted, usually in an oval form.
• Schiffner's dots appear as pale pink granules.
• The infected cell border is commonly fimbriated or ragged
• Mature schizonts contain about 10 merozoites.



Epidemiology
P.ovale is distributed primarily in tropical Africa. It is also found in Asia and South America.

Clinical features
The incubation period for *P.ovale* is 16-18 days but can be longer. Clinically, ovale malaria resembles vivax malaria with attacks recurring every 48-50 hours. There are however, fewer relapses with *P.ovale*. Less than 2% of RBCs usually become infected.

Treatment
The treatment regimen, including the use of primaquine to prevent relapse from latent liver stages is similar to that used for *P.vivax* infection.

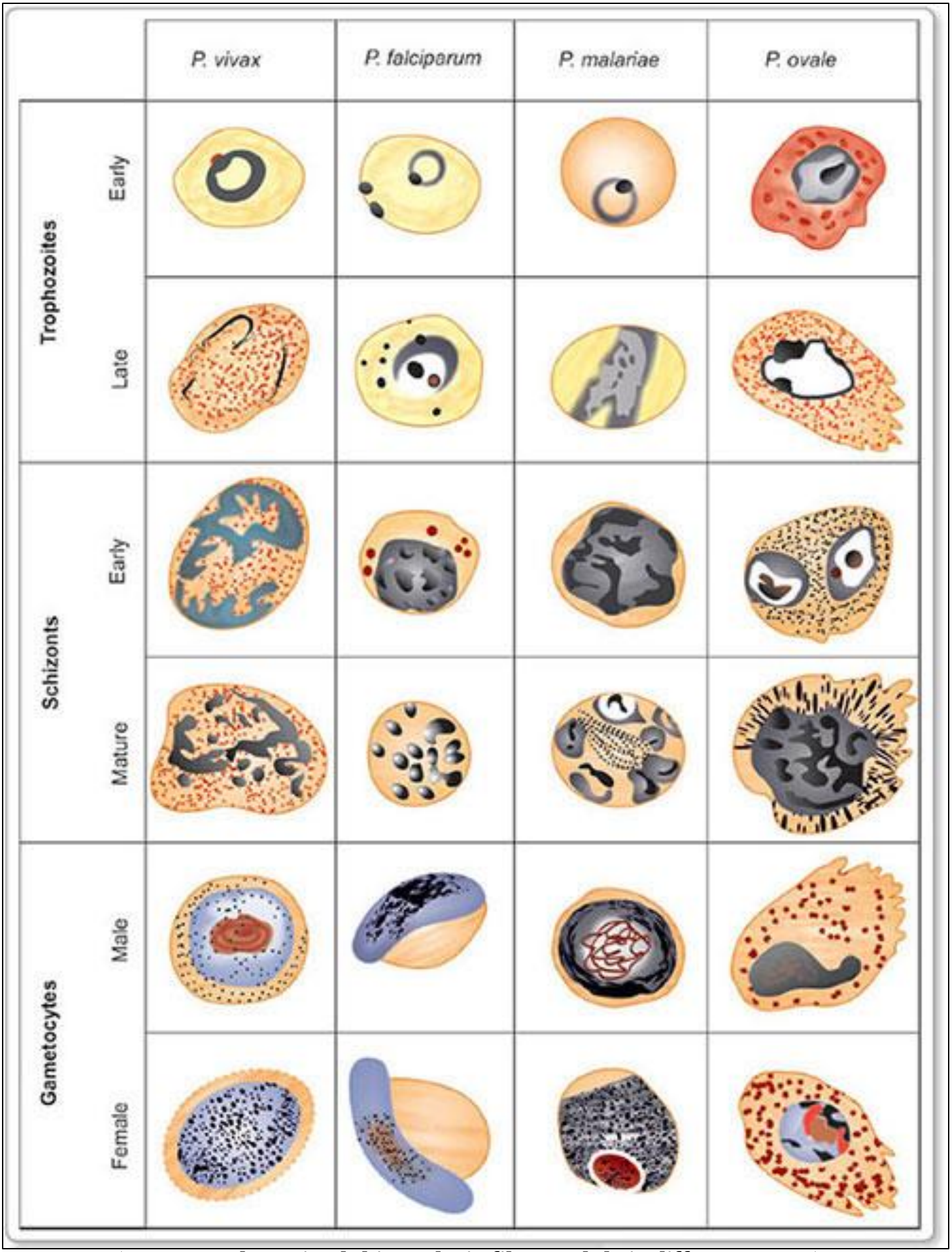
Laboratory diagnosis
Microscopic examination of thick and thin films of blood is the method of choice for confirming the clinical diagnosis of malaria and identifying the specific species responsible for disease. Malaria parasites in thick and thin blood films are best stained at pH 7.1 – 7.2 using a Romanowsky stain (contains azure dyes and eosin).

The thick film is a concentration method that may be used to detect the presence of organisms. The thin film is most useful for establishing species identification. Serologic procedures are available but they are used primarily for epidemiological surveys or for screening blood donors.

Immunity
There is evidence that antibodies can confer hormonal immunity against malaria infection.

Prevention

- Chemoprophylaxis and prompt diagnosis and treatment.
- Control of mosquito breeding
- Protection of insect bite by screening, netting and protective clothing
- Use of insect repellents.



(Romanowsky stained thin malaria films and their different stages)