Sheet No. 1

HLS MICROBIOLOGY

Written by: Alaa' Bany Amer & Salsabeel Aljawabrah

Corrected by: Alaa' Bany Amer & Salsabeel Aljawabrah

Doctor: Nader Alaridah

pay attention:

- The content of this lecture is a bridge between the basic and the clinical level - more clinically oriented.
- you will find all what is written in the slides included in this sheet, maybe I will reform some of them in an easier way.
- Click on the underlined blue word where ever you find it for additional clarification.

The index

The index

Note: you can skip the index, I wanted to highlight the main ideas so it is easy for you to summarize the lecture.

Section one: Overview of parasitology

1. Parasitology : Basic knowledge...

A. Definition of a “parasite”: An organism that lives (on or in) a host organism and gets its food from or at the expense of its host.

B. Classification of kingdoms in parasitology:

I. Arthropods (ectoparasites) such as fleas (نواقل الأمراض) - out of the scope.

II. Metazoa (helminths) which are macro-organisms.

III. Protozoa:

1. Unicellular eukaryotic microorganisms (microscopic).
2. Form an entire kingdom.
3. Are infectious to humans.
4. Classified according to the mode of production and locomotion to 4 classes:

*E. histolytica: the causative agent of amebiasis , a disease of GIT. (الزحار الأميبي)

*Balantidium coli: the causative agent of Balantidiasis, a disease of GIT.

	Oragan of locomotion	Production	Example
1.Sarcodina	Pseudopods الأرجل الوهمية	Asexual (binary fission)	Ameba (Entamoeba histolytica)
2.Mastigophora (flagellates)	Flagella السوط	Asexual (binary fission)	• Giardia lamblia (tissue flagellate/ intestinal flagellate) • Leishmania, Trypanosoma (blood flagellates)
3.Ciliophora (ciliates)	Cilia الشعيرات	Asexual (binary fission)	Balantidium coli*
4.Sporozoa	Their adult stage is not motile	Alternates between sexual and asexual reproduction	• Plasmodium • Cryptosporidium • Cyclospora • Isospora • Toxoplasma

2. Sporozoa: our interest ...

- Sporozoa : organisms whose adult stage is not motile.
- A complex life cycle with alternating sexual and asexual reproductive phases.
- **They are all intracellular parasites;** keep in mind, we will use this feature to differentiate between our two organisms today**.**
- Plasmodium,Cryptosporidium, Cyclospora, Isospora and Toxoplasma belong to a subclass of sporozoa called **Coccidia** .

PLASMODIUM BABESIA

Blood Protozoa

Today we will discuss the protozoal infections that target the RBCs

PLASMODIUM: CAUSATIVE AGENT OF MALRIA
BABESIA: CAUSAITIVE AGENT OF BABESIOSIS

Section two: Epidemiology of Malaria. General view

1. Important points about malaria epidemiology

- **Malaria** is one of the diseases that challenge the scientific and medical community and represent a threat for the human being, in addition to the **Tuberculosis** and **AIDS** (recently).

Historically said: “Famins, wars and fever are the leading causes of death”.

The most prominent causative agents for fever are: Malaria, Tuberculosis and HIV (recently).

These infections have a very high burden over the humans, it is very difficult to manage this burden.

Malaria is the parasitic killer number one, it is the most important parasitic disease .

The trend of malaria lately was decreasing, but it faces a resurgence recently because of human migrations, disasters, wars and the developing resistance of the vector against the insecticides. (Malaria is a vector mediated disease.

Also the disease Burden increasing due to: weakening public health, agricultural practices, global warming, lack of vaccine, drug resistance in parasite and vector, population growth in endemic areas.

- It’s one of the Leading **Infectious** killer of children.

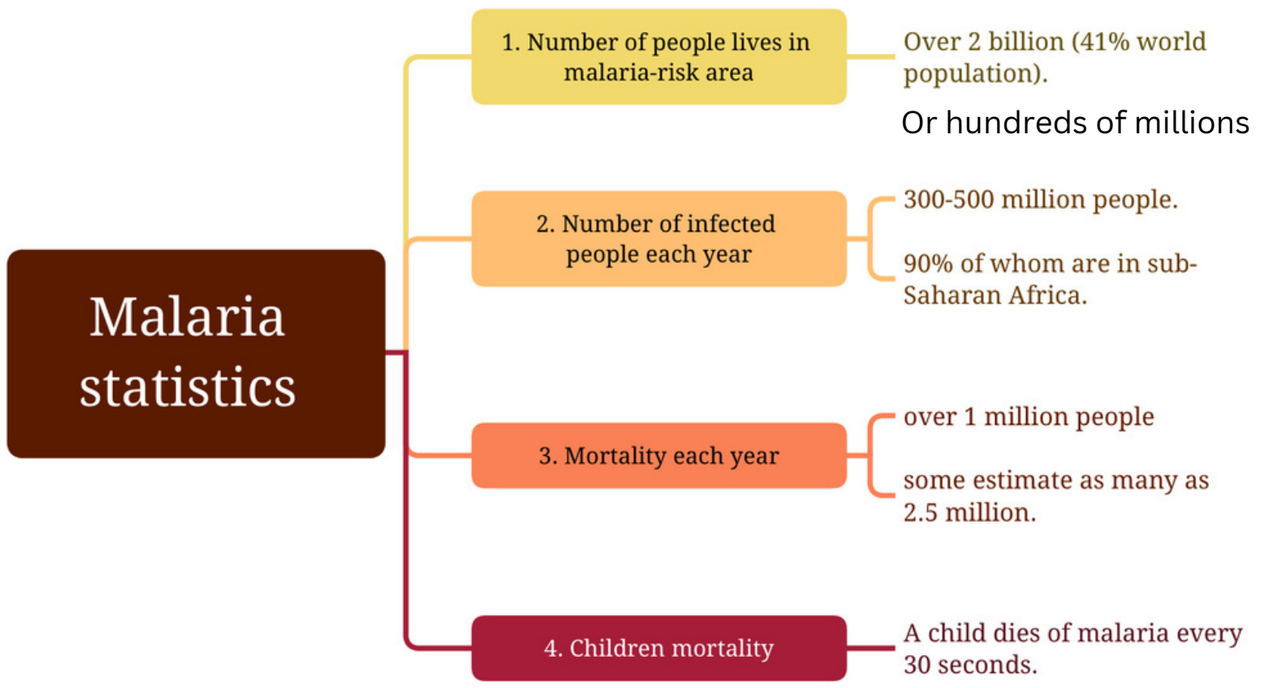
The children between 1-5 years of age, are the very high risk group of people, they suffer from malaria complication.

The children <1 year of age are protected somehow by:

1. The HbF (mainly) and HbE (the doctor said that).
2. The antibodies that they get from the the breast feeding.

The children >5 years of age, are protected by phenomena exists in the parasites and certain bacteria in the endemic areas, called **premunition immunity**.

2. Statistics about malaria epidemiology



Section three: overview of species and their diseases.

Plasmodium is a **genus** of parasitic alveolates, many of which cause malaria in their hosts.

Human malaria is caused by 5 specie:
(in late ninetie, they were just 4 specie)

1. **P.vivax**:
- The most common wide spread form.
- Causes **benign** tertian malaria.
- Has a dormant stage (hypnozoites) in the liver.

2. **P.ovale**:
- Uncommon.
- Causes **benign** tertian malaria.
- Has a dormant stage (hypnozoites) in the liver.

very similar to each other except for the degree of wide spread

Hypnozoites (secondary or dormant schizogony): dormant quiescent resting plasmodium in the life cycle (P.vivax, P.ovale), they don’t show symptoms and signs, the patients with these hypnozoites are susceptible to relapse after 1-2 years

3. **P.malariae**:
- The oldest form of malaria.
- The most common recent ancestor of all plasmodium species.
- Causes quartan malaria.

1. **P.falciparum (highly important)**:

- Responsible for all deaths from malaria, the major species associated with deadly infections throughout the world.
- Causes serious post-infection complications; mainly, the cerebral malaria.
- Causes **malignant** tertain malaria.

2. **P.knowlesi**:

- It was added in late nineties.
- Causes simian malaria, fifth human malaria, non-human primate malaria in the human communities that live closely to monkeys (south-east Asia).
- It was known to infect monkeys, but in those communitie, it was found to infect humans as well.

Section four: the mechanism of infection in all species

Malaria disease is a **vector mediated disease**, the vector is **female anopheline mosquito (Dipteran insect, which is the order of anopheles genus)**; it is the female because it is the one that takes a blood meal, while the male feeds on fruit.

Some important definitions:

Intermediate host: the host of asexual reproduction.
Definitive host: the host of sexual reproduction.

Humans in the malaria, are the intermediate hosts.
The female anopheline mosquito is the definitive host.
There is another classification of hosts:
vertebrate host: humans.
unvertebrate host: the mosquito.

How does the infection take place?

1. The vector takes a blood meal.
2. The **infective stage**, **sporozoites** contained in the salivary glands of the mosquito are discharged into the puncture wound.
3. Within an hour, these infective sporozoites are carried via the blood to the **liver** (Moving with the flow of blood, remember: they are **non- motile** by themselves).
4. They penetrate hepatocytes (parenchyma of the liver).
5. They begin to grow in the liver, initiating the **pre-erythrocytic** or **primary exoerythrocytic** cycle (outside RBCs).

6. The sporozoites become round or oval and begin dividing repeatedly (this process is the **asexual reproduction** which is called **schizogony** or **merogony**), they keep reproduce until they occupy all available space in the hepatocyte.

7. After the rupture of hepatocytes, schizogony results in large numbers of exoerythrocytic **merozoites (**Daughter cells**).**

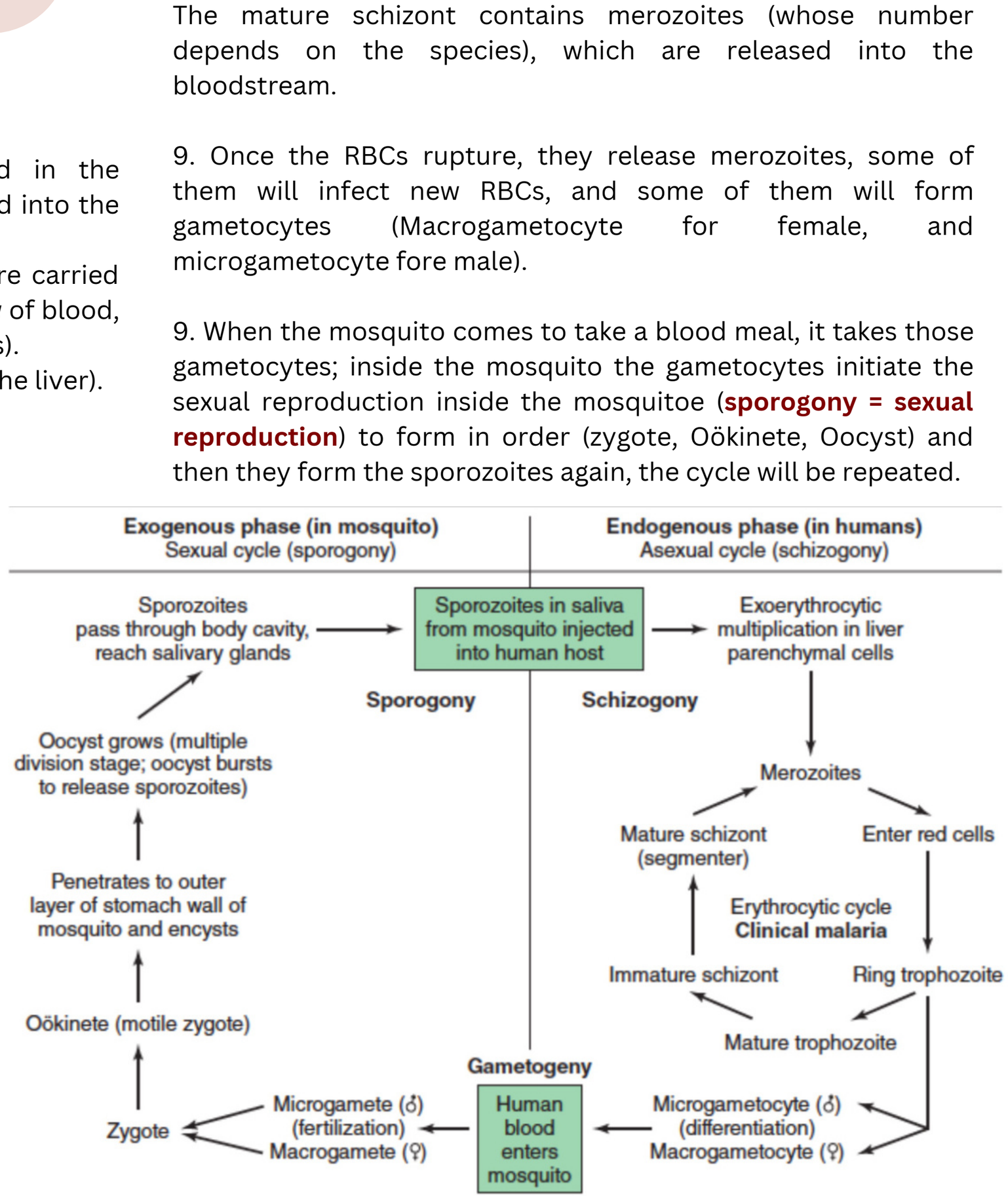
Regarding step 7; in **P.ovale** and **P.vivax**, the exoerythrocytic cycle produces merozoites **to infect RBCs**, and some of these merozoites form **hypnozoites** to be the dormant stage in liver.
Those patients with quiescent latent P.ovale or P.vivax hypnozoites, will relapse when their immune status goes down or somehow, the activation of the parasite.
The relapse happens in 1-5 years. (Mainly within the first two years)
The dormant stage need a further step of treatment to eradicate malaria, you don't need a drug to kill the active parasites only, also you need a drug to kill the hypnozoites.

8. Once these merozoites leave the liver, they invade the **red blood cells (RBCs)**, initiating the **erythrocytic** cycle (reproduce asexually), they keep multiplying until occupying all available space in RBCs and they consume the hemoglobin (the end result is destruction of RBCs) this cycle is the one that is responsible for the symptoms and signs of human malaria.
Within the RBC, the merozoite (or young trophozoite) is vacuolated, ring shaped, more or less ameboid, and uninucleate; Once the nucleus begins to divide, the trophozoite is called a developing schizont.
The mature schizont contains merozoites (whose number depends on the species), which are released into the bloodstream.

9. Once the RBCs rupture, they release merozoites, some of them will infect new RBCs, and some of them will form gametocytes (Macrogametocyte for female, and microgametocyte fore male).

9. When the mosquito comes to take a blood meal, it takes those gametocytes; inside the mosquito the gametocytes initiate the sexual reproduction inside the mosquitoe (**sporogony = sexual reproduction**) to form in order (zygote, Oökinete, Oocyst) and then they form the sporozoites again, the cycle will be repeated.

Classical route to transmit malaria



Plasmodium leaves traces (stain) inside the RBCs, called (haemozoin (malarial pigment) because it consumes the hemoglobin and can't metabolite it completely (The excess protein and hematin present from the metabolism of hemoglobin combine to form malarial pigment) so it leaves those traces, we use those pigments to differentiate between Plasmodium and Babesia.

The destruction of RBCs leads to hemolytic anemia, the symptoms and signs of anemia depend on the level of anemia (the amount of destructed RBCs).

Remember: there are 2 schizogony, one inside the hepatocytes and the other one inside the RBCs.

other routes of transmissions:

1. Blood transfusion (you transmitted the merozoite which will continue the erythrocytic cycle).
2. Congenital transmission (from the mother to fetus).
3. Organ transplantation.
4. Syringes sharing (druge abuse).

The high risk group in Jordan to be infected with Plasmodium is the (doctors of Royal Medical Services in peace-keeping forces), so if they want to donate blood, you should screen for malaria.
In Jordan we don't have anopheles mosquitoe.

There is no certified vaccine for malaria, rather there is an experimental candidate vaccine لقاح تجريبي (RTS vaccine, recombinant protein-based malaria vaccine).

Remember: **Ovale and Vivax**, there are hypnozoites in liver that induce the relapse.
Falciparum and Malariae, the recrudescence may take place.

Relapse: the hypnozoites are dormant latent plasmodium in the **liver**.
Recurdescence: the plasmodium is in the **peripheral blood** but its level is under the threshol, so it can't initiate symptoms and signs, they initiate disease when the No. of merozoites increase or when the immune status decreases.

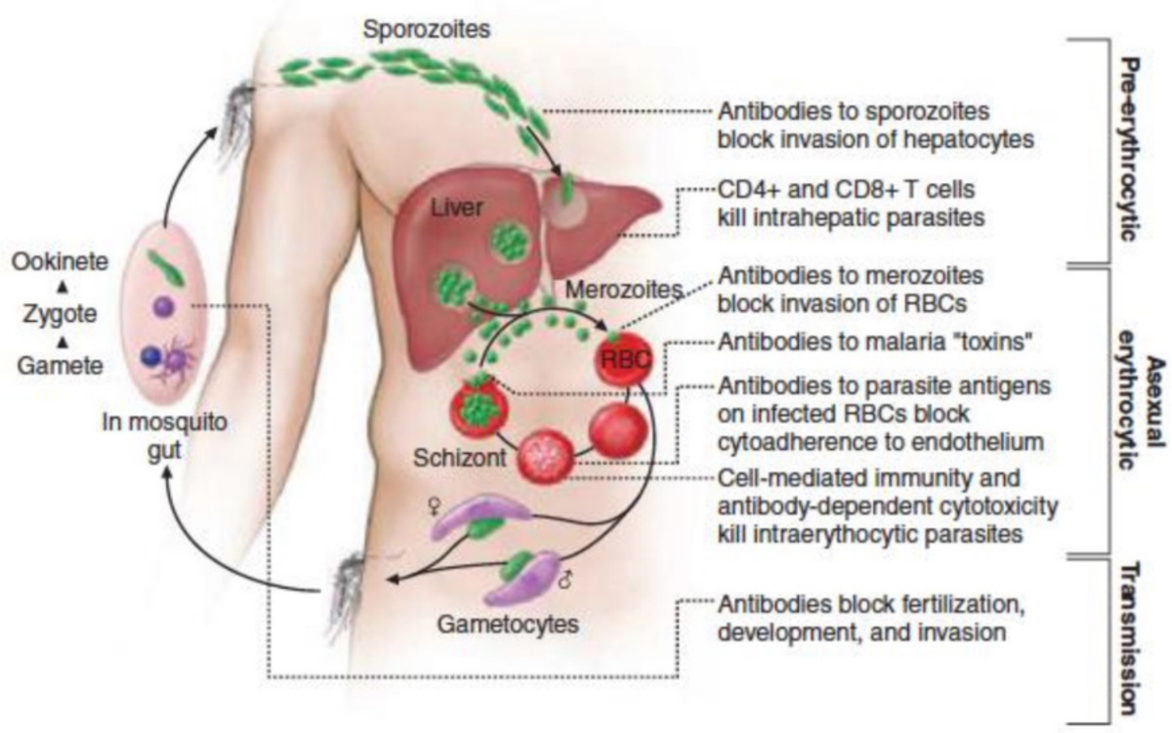
Section five: The human immune response

The immunity against malaria is not a life-long immunity, rather it prevent the super-infection not the reinfection.
The condition of immunity against malaria is called **premunition** .

There are people how are innately resistant for malaria;

- The plasmodium enters the RBCs by a receptor called Duffy antigen receptor, so Duffy antigen receptors negative people are innately resistant to malaria.
- The people with high HbE and HbF levels (so children <1 are protected from malaria, after 1 year they become a high risk group), and they get antibodies from their mothers and start to develop their own adaptive immunity until one year of age.
- Sickle cell traits are also resistant.

Pregnant Women and patients with splenectomy have serious complications and suffer from sever attacks of malaria. (There is an essential role for spleen in immunity).



Section six: Developmental stages of the species .

The prognosis, treatment and pathogenesis is highly dependent on the species itself, so as a doctor you have to distinguish between the different morphological appearance of malarial species:

1. The first species to be detected in the blood is called the ring stage (early Trophozoite stage, you know that the parasites inside the tissues are called Trophozoite).
- Delicate ring in vivax.
- Double dotted rings in ovale.
- Double rings in falciparum.

2. In **falciparum**, if we have a blood film we will find a **banana-shaped crescent gametocytes**.

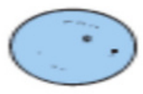
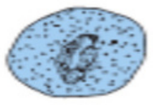
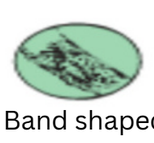
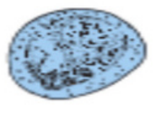
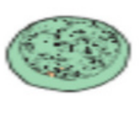
3. In malariae, we usually find the band-shaped Trophozoite) developing schizogony in the table below.

4. In **vivax and ovale** we have stippling in the cytoplas, called **Schüffner's dots,** those dots are **multiple.**

5. **Falciparum**, we have **Maurer's clefts** which are single, large and bluish.

6. Malariae doesn't have stipplings.

7. Schizont and developing schizont are not seen in falciparum in the peripheral blood because they are present in the internal organs (spleen, liver, bone marrow), but if they are detected in blood in case of falciparum, that reflects a very bad prognosis (grave prognosis).

Stage	Vivax	Ovale	Malariae	Falciparum
Ring stage				
Developing Trophozoite				
Developing schizont			 Band shaped	
Schizont				
Microgametocyte				
Macrogametocyte				

	P.vivax	P.ovale	P.malariae	P.falciparum	P.knowlesi
Notes	The most common worldwide	• Very similar to vivax but less common and less in severity and tendency for relapse, with a lower fever and a lack of typical rigors. • Usually ends with spontaneous recovery. • Same incubation period of vivax	The longest incubation period among plasmodium species	The most sever fatal form	• Newly added, infects the monkeys • The early blood stages of P. knowlesi resemble those of P. falciparum. • Whereas the mature blood stages and gametocytes resemble those of P. malariae. • Unfortunately, these infections are often misdiagnosed as the relatively benign P. malariae; however, infections with P. knowlesi can be fatal.
The causative agent of *	Benign tertian malaria	Benign tertian malaria	Quartan malaria	Malignant tertian malaria	Simian malaria, the fifth human malaria
Target cells	Reticulocytes (low parasitemia) so the RBCs would be enlarged	Reticulocytes (low parasitemia) so the RBCs would be enlarged with fimbriated edges (oval)	**Old cells** (low paracytemia) the RBCs would be in the normal size	All Ages all sizes (high parasitemia)	All Ages all sizes, the RBCs size tends to be normal
Relapse/ recrudescence	Hypnozoites (relapse)	Hypnozoites (relapse)	Recrudescence	Recrudescence	-
Stippling	Schüffner's dots	Schüffner's dots	-	Maurer's clefts	-
No. of merozoites released from the mature schizont (erythrocyteic cycle)	**12-24**	**8**	**6-12**	-	**16**

	P.vivax	P.ovale	P.malariae	P.falciparum	P.knowlesi
Most prominent morphological features	• **The delicate ring (the early stage).** • It changes its shape (it's called vivax (in Latin, which means many shapes).	Double doted ring	Trophozoites form bands Thick ring and large nucleus	Banana shaped (crescent) gametocytes and the delicate double ringed structure	
Complications	1. **Splenomegaly** occurs during the first few weeks of infection, and the spleen will progress from being soft and palpable to hard due to autoimmune hemolysis, with continued enlargement during a chronic infection; If the infection is treated during the early phases, the spleen will return to its normal size.		The most common complication in P.malariae is the **nephrotic syndrome** because with a chronic infection, kidney problems result from deposition within the glomeruli of circulating antigen antibody complexes.... • **Proteinuria** is common in P. malariae infections and may be associated with clinical signs of nephrotic syndrome. • A **membrane proliferative type of glomerulonephritis** is the most common lesion seen in quartan malaria.	All complications can happen in either species, but the following ones are most probably to happen with falciparum: 1. cerebral malaria due to cytoadherance that results in plugging the blood capillaries of brain. 2. Black water due to intravascular hemolysis, so the urine will be dark in color (close to the dark red or even black). 3. Algid malaria	

Benign tertiary malaria:

Benign because the complications less probably happen in comparison to falciparum and the fever is lighter 38-39.

Tretian because the erythrocyteic cycle takes 48 hours to be completed and the merozoites will be released in the blood in the third day so the fever (symptoms and signs) happens in the third day (2 days window period + 1 day of fever) and this shows the periodicity and paroxysmal nature.

Malignant tertian malaria:

Malignant because it has so many serious complications on top of them is the cerebral malaria and extreme fevers, 41.7° C (107° F) or higher, may occur in an uncomplicated malaria attack or in cases of cerebral malaria. Without vigorous therapy, the patient usually dies.

Tretian for the previously explained paroxysm.

Quartan malaria:

Quartan because the erythrocyteic cycle needs 72 hours to be completed and to release the merozoites in the fourth day, so the fever appears in the fourth day.

All complications can happen in any species of plasmodium, but some complications are more probably happen with a specific one, such as cerebral malaria and the nephrotic syndrome.

The paroxysm of P.knowlesi needs **24 hours** to be completed, so the fever happens in the second day, (one day window period and one day fever).

You may found a malarial patient who feces fever every day, then it is most probably to be infected withP.knowlesi or mixed infection (two or more species together).

All species begin with unspecific flu-like symptoms and signs depending on the incubation period (headache, photophobia, malaise, fatigu, muscle aches, anorexia, nausea, and sometimes vomiting may occur before organisms can be detected in the bloodstream) and irregular fever, then they will tend to show a periodicity and regular fever as a paroxysm (a hall mark to differentiate between Babesia and plasmodium), the patients will suffer from anemia depending on the level of hemolysis and in case of falciparum the patient mighsuffer from neurological symptom.

In ovale: Over time, the paroxysms become less severe and more irregular in frequency and then stop altogether.

The parasites can be found in the bloodstream several days before symptoms appear, you should distinguish 2 definitions:

1. Incubation period: the time between the exposure of pathogen to the appearance of symptoms and signs.
2. Prepatent period: the period between infection with a parasite and the demonstration of the parasite (merozoites) in the blood.

If the merozoites are present in the blood, that doesn't necessarily mean there are symptoms and signs, because the parasite must reach a certain level of parasitemia to start show symptoms and signs.

Falciparum tends to be aggressive because of the high parasitemia.

Cytoadherance in falciparum:

Cytoadherance means that cells are sticking to each other; A decrease in the ability of the RBCs to change shape when passing through capillaries or the splenic filter, so that they will lead to plugging and obstruction of vessels in the capillaries of internal organs, but the most serious one is in the brain where the patient starts to show neurological symptoms.

The mechanism of cytoadherance is by formation of projecting knobs on the surface of RBCs, and by secreting adhesins from the surface of RBCs, that will induce the adherence, so the RBC membrane becomes sticky and the cells adhere to the endothelial lining of the capillaries of the internal organs.

Ischemia caused by the obstruction of vessels within these organs by parasitized RBCs will produce various symptoms, depending on the organ involved.

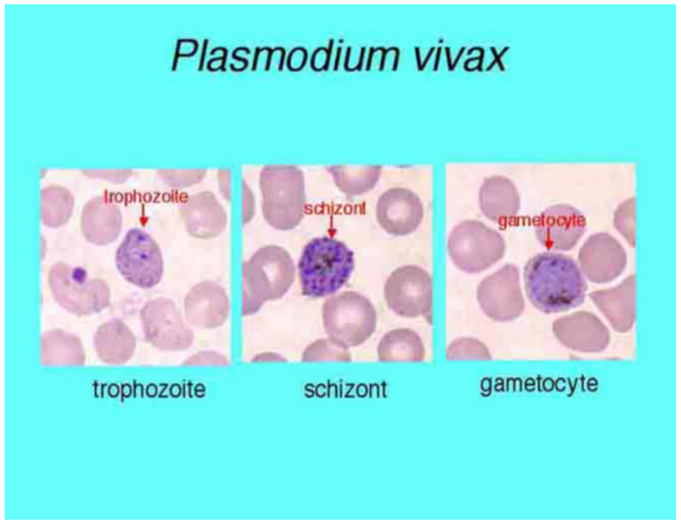
Blackwater fever:

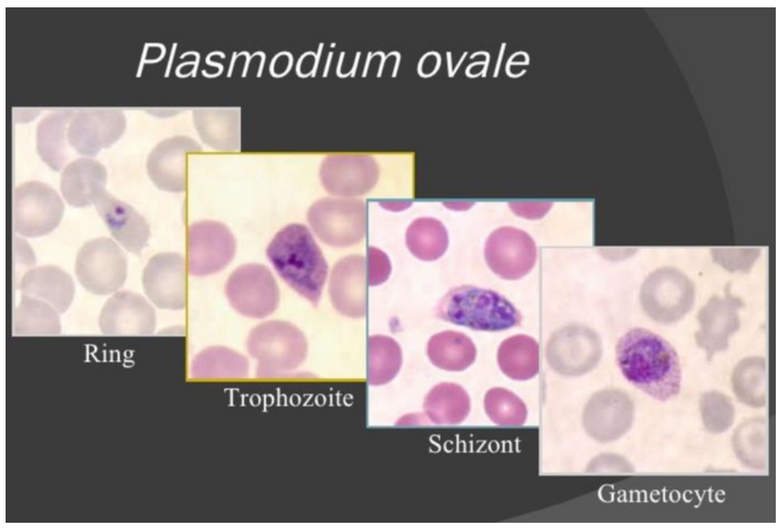
Is a complication of malaria that is a result of red blood cell lysis, releasing hemoglobin into the bloodstream and urine, causing discoloration.

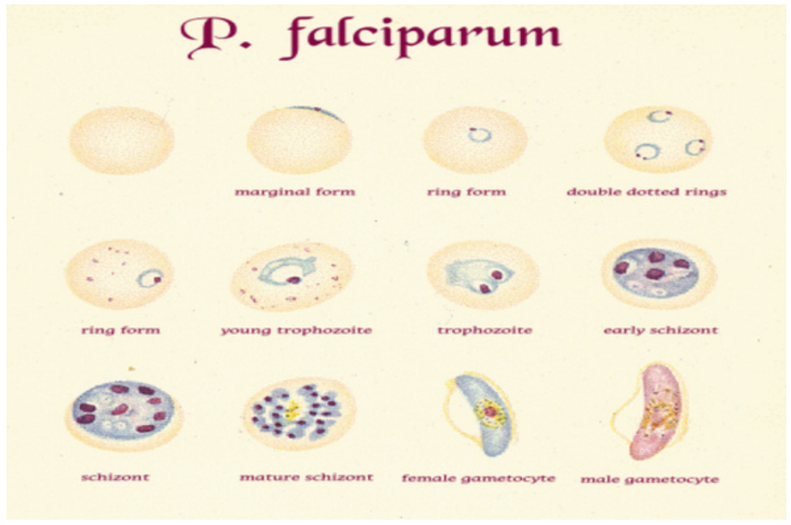
Algid malaria:

Hypovolemic shock or circulatory shock which is fatal and involves multiple systems such as adrenal gland and GIT.

Type of Malaria	Characteristics
***Plasmodium vivax* (benign tertian malaria)**	1. 48-hour cycle 2. Tends to infect young cells 3. Enlarged RBCs 4. Schüffner's dots (true stippling) after 8-10 hours 5. Delicate ring 6. Very ameboid trophozoite 7. Mature schizont contains 12-24 merozoites
Plasmodium ovale	1. 48-hour cycle 2. Tends to infect young cells 3. Enlarged RBCs with fimbriated edges (oval) 4. Schüffner's dots appear in the beginning (in RBCs with very young ring forms, in contrast to *P. vivax)* 5. Smaller ring than *P. vivax* 6. Trophozoite less ameboid than that of *P. vivax* 7. Mature schizont contains an average of 8 merozoites
***Plasmodium malariae* (quartan malaria)**	1. 72-hour cycle (long incubation period) 2. Tends to infect old cells 3. Normal size RBCs 4. No stippling 5. Thick ring, large nucleus 6. Trophozoite tends to form "bands" across th cell 7. Mature schizont contains 6-12 merozoites
***Plasmodium falciparum* (malignant tertian malaria)**	1. 36-48-hour cycle 2. Tends to infect any cell regardless of age, thus very heavy infection may result 3. All sizes of RBCs 4. No Schüffner's dots (Maurer's dots: may be larger, single dots, bluish) 5. Multiple rings/cell (only young rings, gametocytes, and occasional mature schizonts are seen in peripheral blood) 6. Delicate rings, may have two dots of chromatin/ring, appliqué or accolé forms 7. Crescent-shaped gametocytes
Plasmodium knowlesi (simian malaria)*	1. 24-hour cycle 2. Tends to infect any cell regardless of age, thus very heavy infection may result 3. All sizes of RBCs, but most tend to be normal size 4. No Schüffner's dots (faint, clumpy dots later in cycle) 5. Multiple rings/cell (may have 2-3) 6. Delicate rings, may have two or three dots of chromatin/ring, appliqué forms 7. Band form trophozoites commonly seen 8. Mature schizont contains 16 merozoites, no rosettes 9. Gametocytes round, tend to fill the cell Early stages mimic *P. falciparum*; later stages mimic *P. malariae*







Remember: itis difficult to find the middle stages of falciparum in the blood because they are present in bone marrow, liver and spleen, if you see them in the blood this means a bad prognosis.

Characteristic	Finding for Indicated Species[a]			
	P. falciparum	*P. vivax*	*P. ovale*	*P. malariae*
Duration of intrahepatic phase (days)	5.5	8	9	15
Number of merozoites released per infected hepatocyte	30,000	10,000	15,000	15,000
Duration of erythrocytic cycle (hours)	48	48	50	72
Red cell preference	Younger cells (but can invade cells of all ages)	Reticulocytes and cells up to 2 weeks old	Reticulocytes	Older cells
Morphology	Usually only ring forms[b]; banana-shaped gametocytes	Irregularly shaped large rings and trophozoites; enlarged erythrocytes; Schüffner's dots	Infected erythrocytes, enlarged and oval with tufted ends; Schüffner's dots	Band or rectangular forms of trophozoites common
Pigment color	Black	Yellow-brown	Dark brown	Brown-black
Ability to cause relapses	No	Yes	Yes	No

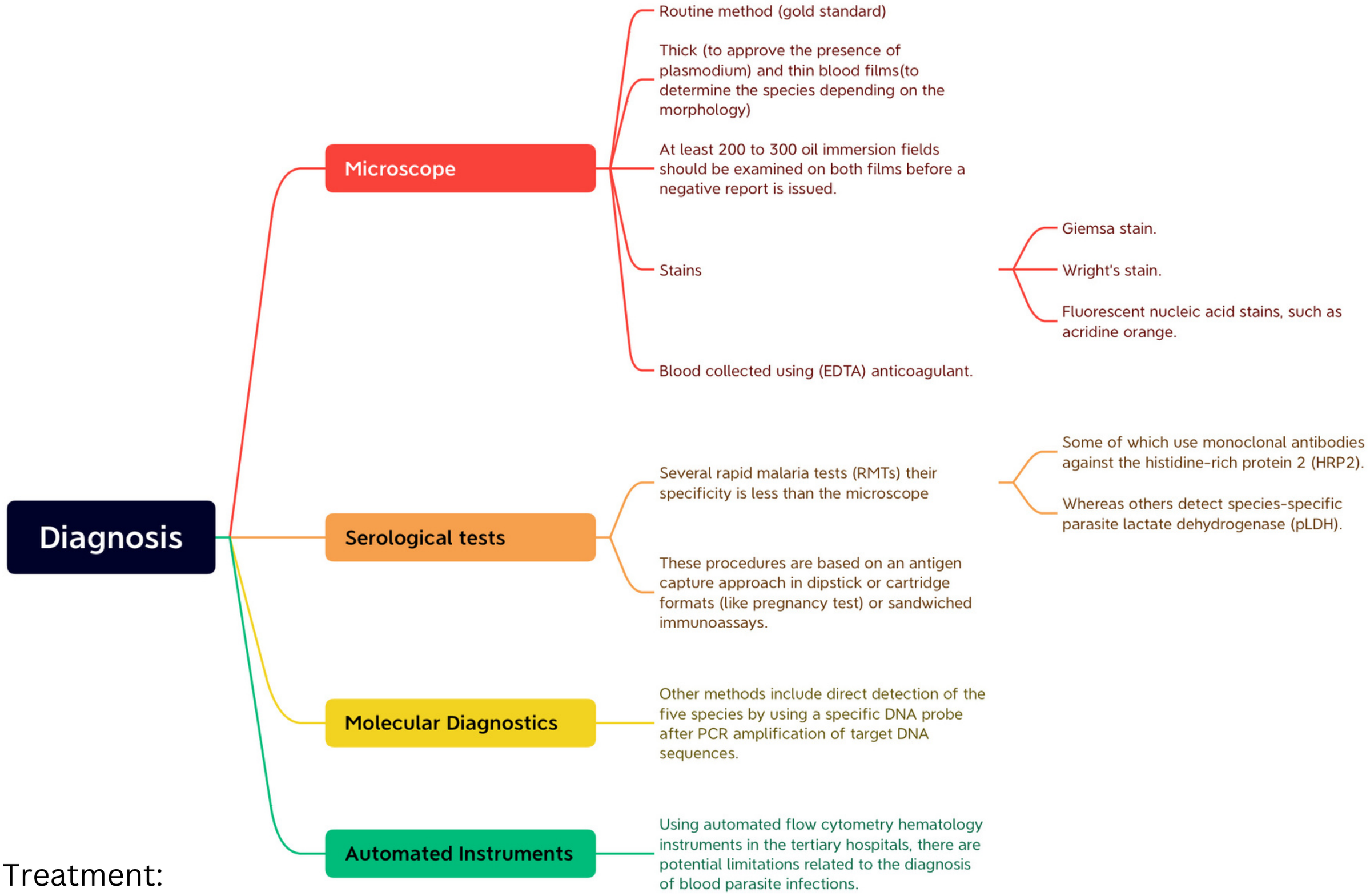
CLINICAL FEATURES

- Malaria is a very common cause of fever in tropical countries. The first symptoms of malaria are nonspecific; the lack of a sense of wellbeing, headache, fatigue, abdominal discomfort, and muscle aches followed by fever are all similar to the symptoms of a minor viral illness.

- In some instances, a prominence of headache, chest pain, abdominal pain, cough, arthralgia, myalgia, or diarrhea may suggest another diagnosis. Although headache may be severe in malaria, the neck stiffness and photophobia seen in meningitis do not occur. While myalgia may be prominent, it is not usually as severe as in dengue fever, and the muscles are not tender as in leptospirosis or typhus. Nausea, vomiting, and orthostatic hypotension are common.

- The classic malarial paroxysms, in which fever spikes, chills, and rigors occur at regular intervals, are relatively unusual and suggest infection with P. vivax or P. ovale.

- The fever is usually irregular at first (that of falciparum malaria may never become regular); the temperature of nonimmune individuals and children often rises above 40C in conjunction with tachycardia and sometimes delirium. Although childhood febrile convulsions may occur with any of the malarias, generalized seizures are specifically associated with falciparum malaria and may herald the development of encephalopathy (cerebral malaria).



Treatment:

Antimalarial drugs are classified according to the stage of malaria against which they are targeted.
-Tissue schizonticides (which kill tissue schizonts).
-Blood schizonticides (which kill blood schizonts).
-Gametocytocides (which kill gametocytes).
-Sporonticides (which prevent formation of sporozoites within the mosquito).

In the past all species were treated by QUINOLINES, but now all circulating falciparum are resistant to quinolines.

In vivax and ovale you must administrate primaquine to eradicate the hypnozoites.

For falciparum we use Artemisinins (ACTs) artimisinins based combinations (like Atovaquone).

Tetracycline, doxycycline, and clindamycin are used increasingly in combination
with other antimalarials to improve their efficacy.

Type of control	Measures
Personal protection	Insecticide treated mosquito nets; Mosquito proofing of dwellings; Repellents; Site selection
Environmental management	Drainage & water management; Land reclamation by filling and drainage
Chemical (Insecticides) control	Residual house spraying; larviciding; space spraying
Other measures	Biological control, Genetic control, Zooprophylaxis

Prophylactically, for those who travel to endemic areas, they are advised to get tetracyclines or macrolides before a week from traveling and continue after 4 weeks of back to home.

Babesiosis

Epidemiology

- tick-borne (victor-mediated) infectious disease caused by protozoan parasites of the genus **Babesia** that invade and target RBCs (causing RBCs lysis).
- Most cases are due to Babesia microti: a parasite of small rodents. i.e.: B.macroti is the primary causative agent for human babesiosis worldwide and in USA while B.divergens in Europe. However, Babesia venatorum and B. microti also have been reported.
- The infection typically is mild in young and otherwise healthy individuals but can be severe and sometimes fatal in persons >50 years of age and in immunocompromised patients. Sporadic cases have been reported in Europe and the rest of the world.

Mode of transmission*

Babesiosis is primarily transmitted by **nymphal stage of the deer tick (vector)**

B.macroti Is transmitted by **Ixodes scapularis** the same tick that transmits the causative agents of **Lyme disease**

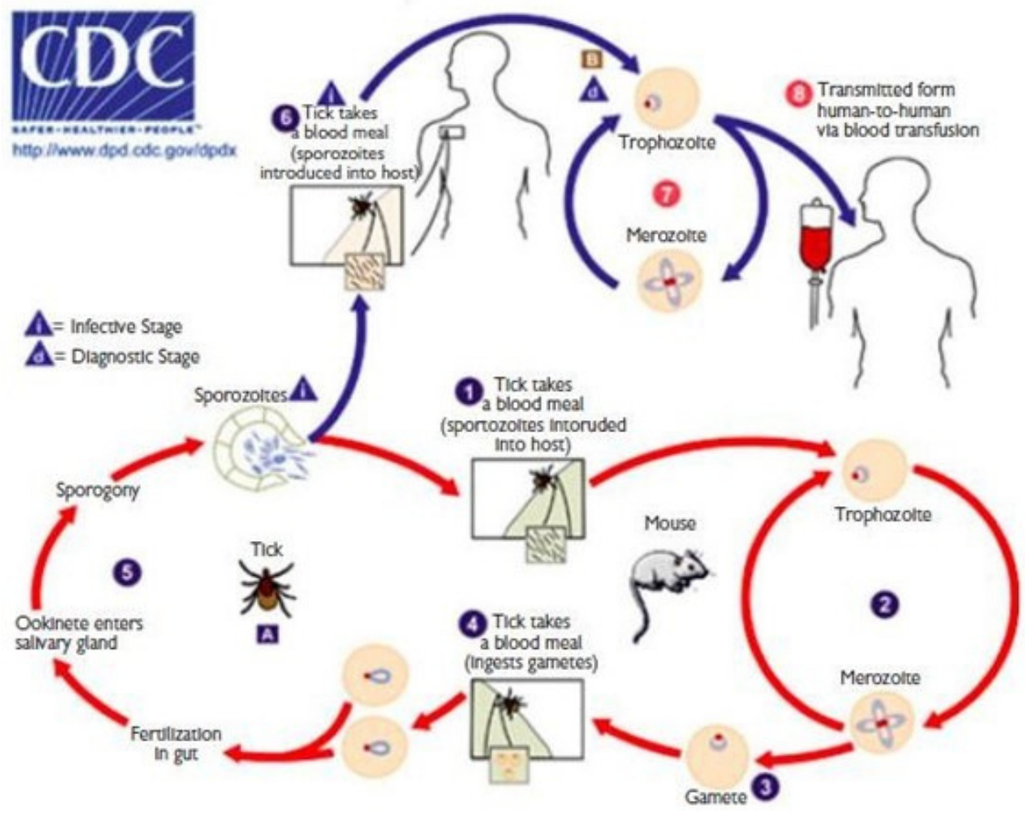
B. duncani Is transmitted via **Ixodes pacificus**

B. divergens is transmitted via **Ixodes dentatus**

it can be transmitted by the same routes as malaria transmitted such as: **blood transfusion**, **organ transplantation**, **congenital transmission** as well as **sharing syringes between drug abusers.**

Babesia life cycle*

- infective stage: **trophozoites**.
- dead-end host: **human**; thus, no sexual or asexual reproduction occur in human (no exoerythrocytic cycle occur).
- definitive host: **laxodes tick** (the sexual reproduction occurs inside vectors).
- intermediate host: **white footed mouse**.



Clinical manifestation

- Asymptomatic B. microti Infection: At least 20% of adults and 40% of children do not experience symptoms following B. microti infection. There is no evidence of long-term complications following asymptomatic infection; however, people who are asymptomatically infected may transmit the infection when they donate blood.

ركزوا على الأشياء الي عليها خط بس هاي الاشياء الي ركز عليها الدكتور و حكاها بالمحاضرة و الباقي كلام سلايدات ما جاب سيرته
و اذا في جمب الموضوع * ادرسوه كله + الجدول الي تحت هي الاشياء الي بتهم الدكتور انكم تعرفوها بخصوص ال
babesia

- Mild to Moderate B. microti Illness Symptoms typically develop following an incubation period of 1–4 weeks after tick bite and 1–9 weeks (but as long as 6 months) after transfusion of blood products. Patients experience a gradual onset of malaise, fatigue, and weakness. Fever can reach 40.9C (some patients can develop high fever) and is accompanied by one or more of the following: chills, sweats, headache, myalgia, arthralgia, nausea, anorexia, and dry cough (nonspecific symptoms).
- Severe B. microti Illness Severe babesiosis requires hospital admission and typically occurs in patients with one or more of the following: age of >50 years, neonatal prematurity, male gender, asplenia, HIV/AIDS, malignancy, hemoglobinopathy, and immunosuppressive therapy.

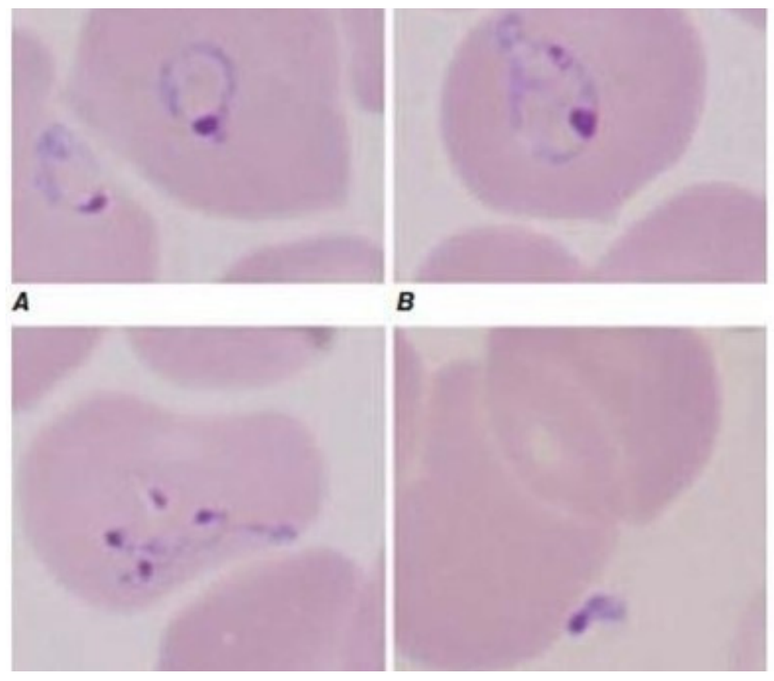
Pathogenesis

- Anemia is a key feature of the pathogenesis of babesiosis. Hemolytic anemia caused by rupture of infected RBCs generates cell debris that may accumulate in the kidney and cause renal failure or heart failure.
- Anemia also results from the clearance of intact RBCs as they pass through the splenic red pulp and encounter resident macrophages.
- Babesia antigens expressed at the RBC membrane promote opsonization and facilitate uptake by splenic macrophages. In addition, RBCs are poorly deformable as a result of oxidation generated by the parasite and the host immune response and are filtered out as they attempt to squeeze across the venous vasculature. Bone marrow suppression due to cytokine production may also contribute to anemia.

Diagnosis*

- **Microscopic examination** of Giemsa-stained **thin blood smears (gold standard method to diagnose babesiosis)**
  morphology (pathognomonic): **Maltese cross** as well as **extracellular development stage**.

Maltese cross: 4 dots (babesia) crossed by lines these lines are called Maltese lines, (Babesia tends to present in pairs).
-extracellular development stage: babesia can grow extracellularly unlike p.malaria which shows only intracellular development stages; recall that schizogony in P.malaria occur in erythrocytes and after a certain level these erythrocytes goanna burst, فممكن تشوف البارasيت برا الخلية اذا راقبت خلال هاي اللحظة بالفيمتو ثانية بالذات و احتمال انك تشوفه برا ضعيفة فعشان هيك هي pathognomonic for babesiosis.



- **PCR**: if probes are available by encoding genes from babesia antigens (mostly used in USA and Europe).
- **Serology** can suggest or confirm the diagnosis of babesiosis. An indirect immunofluorescent antibody test for B. microti is most commonly used.

Treatment

- **Atovaquone (ARTEMISININS derivative)** plus azithromycin is the recommended antibiotic treatment combination for mild to moderate babesiosis.
- **Clindamycin plus quinones is the choice for severe infections.**

Prevention

- Wear clothing that covers the lower part of the body, apply tick repellents (such as DEET) to clothing, and limit outdoor activities where ticks may abound from May through October + vector control methods such as insecticides for ticks and mouses.

	P.Malaria	Babesia
target cell	both target RBCs causing their lysis	
vector that mediates the disease	female anopheline mosquito	B.macroti Is transmitted via Ixodes scapularis and B. divergens is transmitted via Ixodes dentatus
life cycle	infective stage: sporozoites intermediate host: human	infective stage: trophozoites dead-end host: human
symptoms	it shows sign and symptoms with different fever periodicity according to malaria type	asymptomatic to mild symptoms without fever periodicity
fever	it comes in 3 stages: cold stage, hot stage and sweat stage	Is not Regular, you might suffer from it day by day or once a week or once each three days, etc...
diagnosis (microscopic) pathognomonic	differ according to malaria type	Maltese cross as well as extracellular development stag
treatment	Atovaquone (ARTEMISININS derivative) for falciparum. Quinilines for non falciparum infection + primaquine for ovale and vivax	QUINOLINES, ARTEMISININS