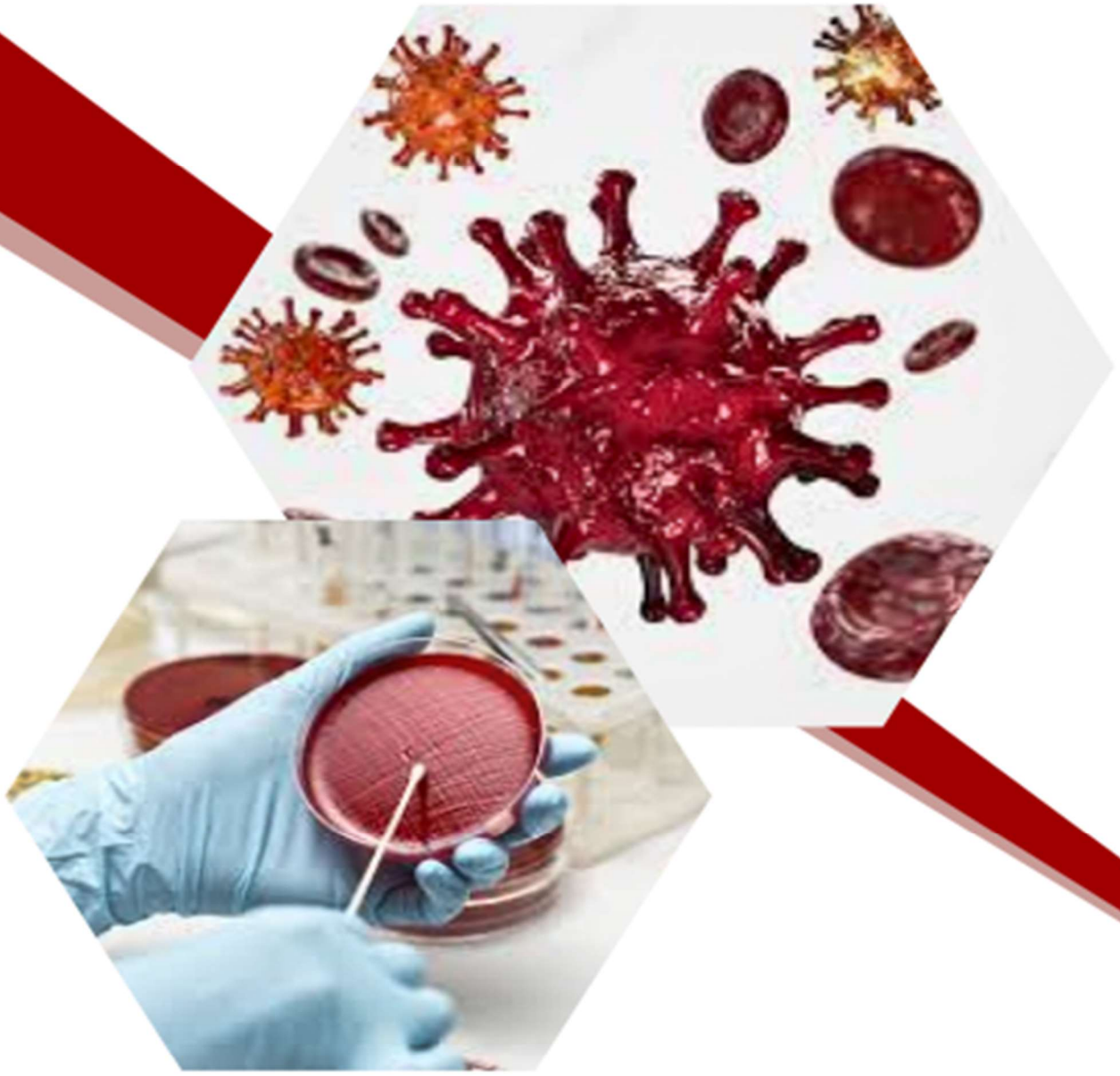
Doctor.021

no. 1

HLS MICROBIOLOGY



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Overview

❖A parasite is an organism that lives on or in a host organism and gets its food from or at the expense of its host.
❖Protozoa are unicellular eukaryotes that form an entire kingdom.

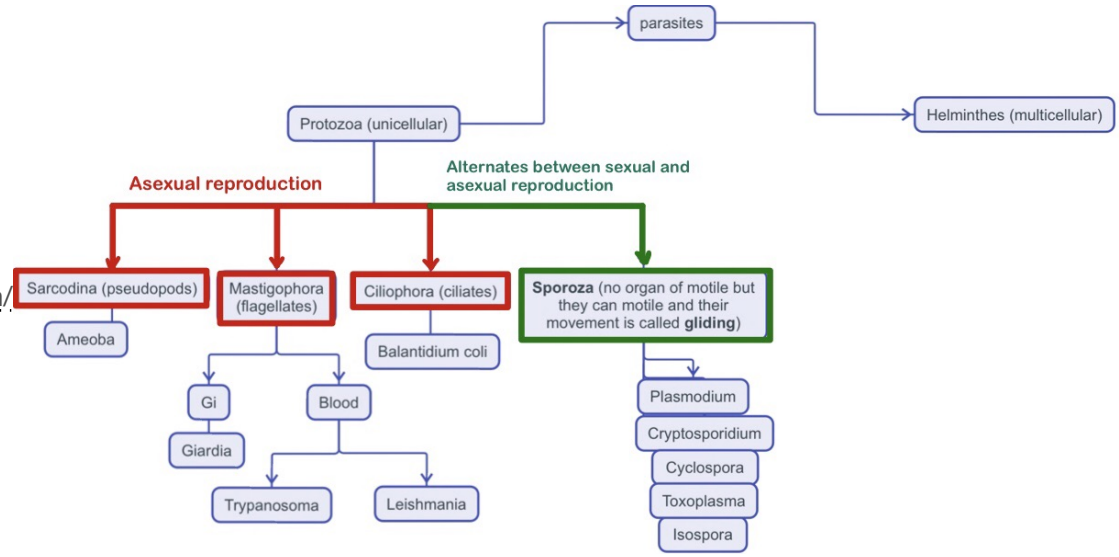
❖The protozoa that are infectious to humans can be classified into four groups
based on their mode of movement (possess an organ of locomotion and mode of reproduction): note that sacrodina ,mastigophora and ciliophora have asexual reproduction only.

1. Sarcodina – the ameba ameboid locomotion.

2.Mastigophora – the flagellates, Giardia (intestinal flagellates) , Leishmania and trypanosoma (blood flagellates).

3.Ciliophora – the ciliates, e.g., Balantidium coli (intestinal protozoa).

4.Sporozoa – organisms whose adult stage is not motile (don't possess an organ of locomotion but they are motile and their movement is called gliding movement) , (they are from phylum (apicomplexa) they possess an apicomplexe which is organ found in them and all of them intracellular protozoa at least in some point in their life cycle) e.g., Plasmodium, Cryptosporidium undergo a complex life cycle with alternating sexual and asexual reproductive phases (**what happen in vertebrates host included human is asexual reproductive phase -schizogony- but in invertebrates (vectors) is sexual reproductive phase -sporogony-**).
The human parasites Cryptosporidium, Cyclospora, and Toxoplasma and the malarial parasites (Plasmodium species) are all intracellular parasites.
Sporozoa has another subgroub other than the plasmodium called coccidia which includes: Cryptosporidium, Cyclospora and Isospora.



A helpful vid for malaria:
https://www.osmosis.org/learn/Plasmodium_species_(Malaria)?from=/md/foundational-sciences/microbiology/parasitology/protozoa/other-protozoal-infections

Epidemiology of malaria

- The most prominent causative agents for fever are malaria ,TB and HIV.
- Incidence rate = around 1 M each year new cases diagnosed with malaria

• Over 2 billion (41% world population) lives in malaria-risk area.
• Infects 300-500 million people per year, 90% of whom are in sub-Saharan Africa. Mainly in sub-saharan africa, but its occurance is world wide.
• Kills over 1 million people each year and some estimate as many as 2.5 million.
• Leading Infectious killer of children. Worldwide a child dies of malaria every 30 seconds.
• Disease Burden increasing due to: weakening public health, (wars ,tropical climate), agricultural practices, global warming, lack of vaccine, drug resistance in parasite and vector, population growth in endemic areas, increased travel.

Plasmodium

(Vector borne disease -female anopheline mosquito-)
Why not male? Because the female needs blood as a nutrition for her eggs maturation, but the male doesn't need it for his nutrition he lives on fruits.

- It is the number 1 killer of all parasritic infection is malaria which is caused by plasmodium species.

• Plasmodium is a genus of parasitic alveolates, many of which cause malaria in their hosts.
• The parasite always has two hosts in its life cycle: Dipteran ذات الجناحين insect host and a vertebrate host.

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• Species of plasmodium that cause human malaria:

1.P. falciparum (the most important)

- Plasmodium falciparum is the major species associated with deadly infections throughout the world.
- When you suspect malaria you should always keep it in your mind in the time of diagnosis, you should either role in or role out p.falciparum.
- Causes serious complications.
- Causes malignant tertain malaria.

1. Malignant comes from very high fever (hyperpyrexia) above 42c.
2. All complications that can happen in malaria happen in this type and it has highest mortality rate. Treatment is very different from other species.

2.P. malariae

- The oldest and classical form of malaria.
- Causes quartan malaria.

3.P. vivax

- The most common wide spread form.
- Causes benign tertian malaria.
- It is responsible in 70-80% cases of malaria in world.

P.vivax and ovale are very similar to each other, except in the degree of spread.

4.P. ovale

- Very rare.
- Causes benign tertian malaria.

5.Plasmodium knowlesi

- It was added in late 90s.
- Causes simian malaria, also known as the human 5th cause of malaria
- It was known to infect monkeys only, but now it also infect humans especially communities that live closely to monkeys in south east asia.

Mechanism of Infection of malaria

• The vector for malaria is the female anopheline mosquito.

• When the vector takes a blood meal, sporozoites contained in the salivary glands of the mosquito are discharged into the puncture wound.

• Within an hour, these infective sporozoites (the infective stage of plasmodium which is produced by the sexual reproduction that happened in the female of anopheline mosquito) are carried via the blood to the liver (they are non-motile), where they penetrate hepatocytes and begin to grow and start their asexual reproduction that happens in humans (schizogony), initiating the pre-erythrocytic or primary exoerythrocytic cycle (that occurs in hepatocytes where the daughter cells are now called merozoites).

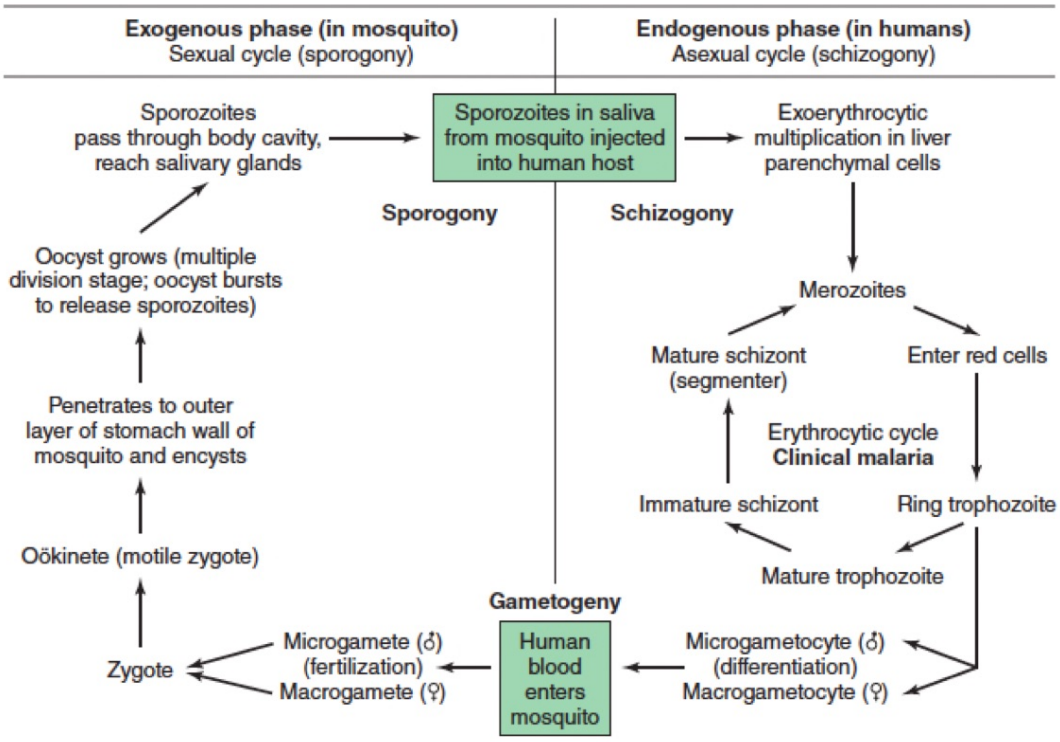
• The sporozoites become round or oval and begin dividing repeatedly.

• Schizogony results in large numbers of exoerythrocytic merozoites.

• Once these merozoites leave the liver, they invade the red blood cells (RBCs), initiating the erythrocytic cycle. (or some of them stay dormant inside the liver cells (in cases of P.ovale and P. vivax) and they are called hypnozoites).

In the erythrocytic cycle, the merozoites reproduce asexually, and multiply and duplicate filling the spaces in the RBCs, and it consumes Hb inside the RBCs, and when this schizont ruptures (schizont means asexual reproduction which can happen in the hepatocyte (exoerythrocytic cycle) or the RBCs (erythrocytic cycle)), once these merozoites are released in the peripheral blood, they either infect other RBCs or others form gametocytes (Macro (female) or micro (male) gametocytes), and when the female of anopheline mosquito sucks blood from the infected person, Sexual reproduction occurs between macrogametes (female mosquitos) and microgametes (male mosquitos) inside the mosquito producing zygote then they release sporozoites, sporozoites reach the salivary gland of the female .of anopheline mosquito and so on

Malaria life cycle



Summary of the malaria life cycle:
1.Sporogony: in the female anopheles mosquito (sexual reproduction), an uninfected mosquito bites an infected human and picks up the micro and macrogametes and they form the zygote then the ookinete then the oocyst then the sporozoites (the infective form).
2.Schizogony: in humans (asexual reproduction), happens in two cylces:
A.exoerythrocytic: sporozoites multiply in the liver paranchyma producing merozoites.
B.erythrocytic: merozoites infect RBCs in peripheral blood and produce macrogametes (females) and microgametes (males).

Mode of transmission from p-p (bloodborne):
* blood transfusion.
* organ transplantation.
* share contaminated syringes.
* vertical transmission from mom-fetus.
*In this case (transmission through blood) there will be no exoerythocytic cycle, because the peroson will be alredy infected with the erythrocytic cycle so it will continue from there.

A dormant schizogony may occur in P. vivax and P. ovale organisms, which remain quiescent (sleep) in the liver.

• These resting stages have been termed hypnozoites and lead to a true relapse, often within 1 year or up to more than 5 years later.

Very important to know drug of choice is **Quinine**, but it can't kill hypnozoites in liver in case p.vivax and p.ovale so we use **Primaquine.**

Once the RBCs and reticulocytes have been invaded, the parasites grow and feed on hemoglobin, by the end of schizogony, they would have consumed 2/3 of hemoglobin content in RBCs and auto-immune hemolysis will happen, which lead to anemia, and then fever happens.

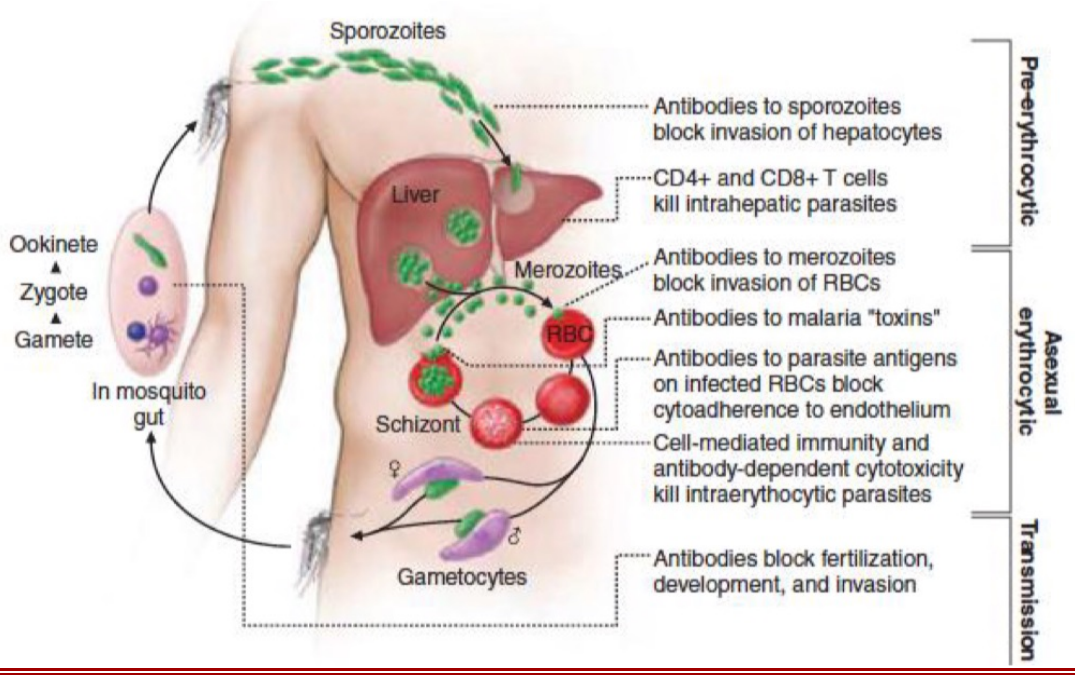
• Within the RBC, the merozoite (or young trophozoite) is vacuolated, ring shaped, more or less ameboid, and uninucleate.

• The excess protein and hematin present from the metabolism of hemoglobin combine to form malarial pigment **(hemozoin pigment) golden yellow pigment . (This pigment is important to distinguish it from (babesiosis; mild asymptomatic diseases, can have similar presentation as malaria).**

• 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.

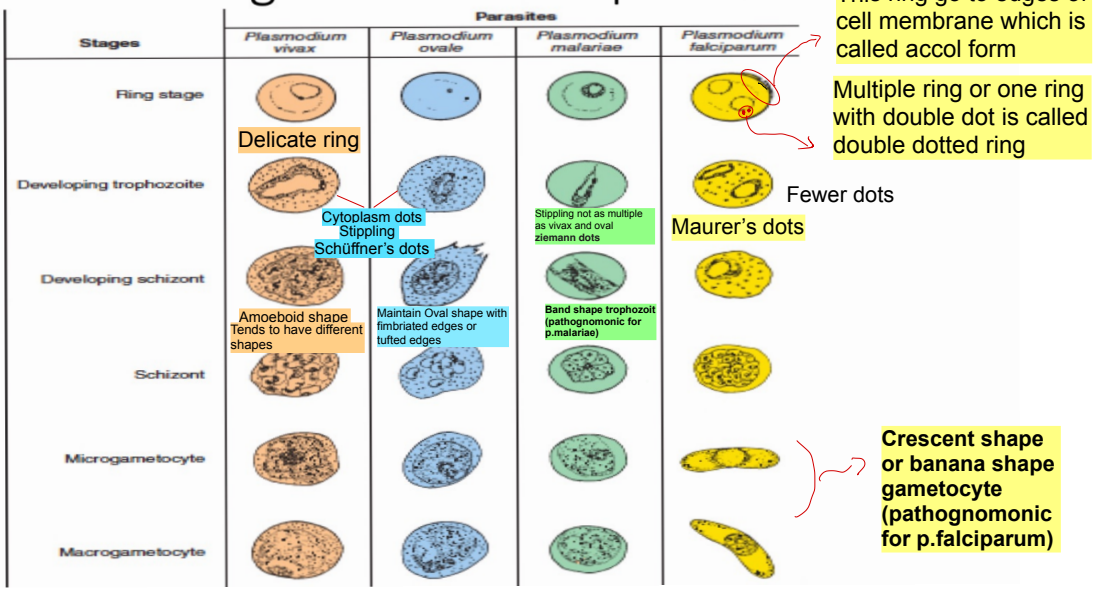
Malaria transmission cycle



Developmental stages of malarial parasites

All of these are diagnostic stages.
Invective stage in the sporozoit.

مهم التفريق بينهم لانه ممكن يجيب سؤال عن الشكل ويسآل عن العلاج بدك تكون عارف



Microscopy is a gold standard for diagnoses

Thick blood film (very sensitive) It gives you an answer to the question of whether there is a plasmodium or not

Thin blood film (specific If you want to know which specie)

PLASMODIUM VIVAX (vivax means no regular shape in latin-amoeboid shape) (BENIGN TERTIAN MALARIA)

benign: compared with the falciparuim; complication is less and fever is considered benign <41.7c

Tertian: cycle of fever (Fever occurs every third day):

Day 1: fever
Day 2: free
Day 3: Fever

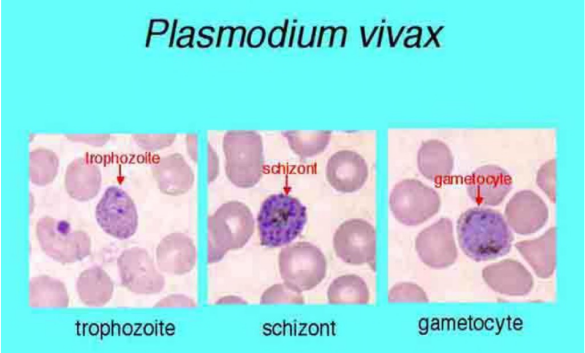
after 48 hr fever come back.

Erythrocytic cycle; merozoites enter inside erythrocyte and start to replicate asexual (schizogony) then cell is filled , rupture and release merozoites to peripheral blood, this induce fever; this cycle take 48 hr.

- **P. vivax infects only the reticulocytes (young RBCs)so the level of parasitemia is low,** since the percentage of reticulocytes is lower than RBCs'.
- Splenomegaly occurs during the first few weeks of infection, and the spleen will progress from being soft and palpable to hard, with continued enlargement during a chronic infection. And Infected cells are enlarged
- If the infection is treated during the early phases, the spleen will return to its normal size.
- A secondary or dormant schizogony occurs in P. vivax and P. ovale, which remain quiescent in the liver. Treatment with Primaquine
- These resting stages have been termed hypnozoites.

The hallmark of malaria Regardless cusative agent is **periodicity of fever and paroxysm (regularity)**, fever has specific regular pattern, which doesn't happen in babesia.

* All of malaria at beginning have irregular pattern (but at the first stages it won't be regular, important in diagnosis) as the disease progresses the pattern becomes clearer.



- After a few days of irregular periodicity, a regular 48-hour cycle is established.

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

In RBCs

Pathogenesis and Spectrum of Disease: flu like illness (nonspecific symptoms)

- In patients who have never been exposed to malaria:

Symptoms such as headache, photophobia, muscle aches, anorexia, nausea, and sometimes vomiting may occur before organisms can be detected in the bloodstream.

- In other patients with prior exposure to the malaria:

The parasites can be found in the bloodstream several days before symptoms appear.

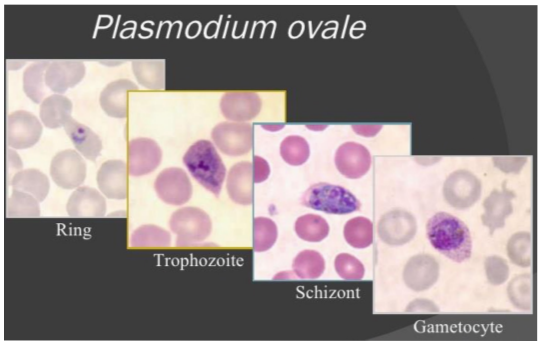
PLASMODIUM OVALE (lower incidence and milder than p.vivax)

- Although P. ovale and P. vivax infections are clinically similar, P. ovale malaria is usually less severe, tends to relapse less frequently, and usually ends with spontaneous recovery.
- **P. vivax, P. ovale infects only the reticulocytes.**

In p.ovale infected cells Will be enlarged.

- After a few days of irregular periodicity, a regular 48-hour cycle is established. Over time, the paroxysms become less severe and more irregular in frequency and then stop altogether.
- Maintains its oval shape

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 In RBCs



Pathogenesis and Spectrum of Disease:

- The incubation period is similar to that for P. vivax malaria, but the frequency and severity of the symptoms are much less, with a lower fever and a lack of typical rigors.

Plasmodium malariae (quartan malaria)

***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 the cell 7. Mature schizont contains 6-12 merozoites

Pathognomonic

Quartan cycle of fever (Fever occurs every fourth day):
Fever Day 1: Fever
Day 2: free
Day 3: free
Day 4: Fever
72 hours = Duration of pathogen's cycle in the blood.

Pathogenesis and Spectrum of Disease:
• **Proteinuria** is common in P. malariae infections and may be associated with clinical signs of nephrotic syndrome.
• With a chronic infection, kidney problems result from deposition within the glomeruli of circulating antigen antibody complexes deposition on renal glomeruli.
• A membrane proliferative type of glomerulonephritis (antigen-antibody caomplex mediated, deposited in kidneys) is the most common lesion seen in quartan malaria, can lead to acute kidney failure.
Complications can happen with any species, but the possibility to happen is less than p.falciparium.

PLASMODIUM FALCIPARUM (MALIGNANT TERTIAN MALARIA)

Malignant for two reasons1- hyperpyrexia 2- complications are more prominent.
• Plasmodium falciparum invades **all ages of RBCs** (which explains the severity of the disease and the high level of parasitemia).
• Schizogony (in all species this can happen in the peripheral blood, except in p.falciparum, it prefers to happen in the primary and secondary lymphoid organs, but still it can happen also in peripheral blood) occurs in the spleen, liver, and bone marrow rather than in the circulating blood.
• Ischemia caused by the obstruction of vessels within these organs by parasitized RBCs will produce various symptoms, depending on the organ involved.

• A decrease in the ability of the RBCs to change shape when passing through capillaries or the splenic filter may lead to plugging of the vessels Also, only P. falciparum causes cytoadherence, a feature that is associated with severe malaria.

• In P. falciparum infections, as the parasite grows, (in the late stages of the disease), the RBC membrane becomes sticky (produce ECAM protein which forms projecting knobs on the surface of RBCs, releasing adhesins) and the cells adhere to the endothelial lining of the capillaries of the internal organs (called cytoadherance) can lead to organ failure, and the most organ affected is the brain, so they call it cerebral malaria which causes febrile seizures\convulsion.

• Thus, only the ring forms and the gametocytes (occasionally mature schizonts) normally appear in the peripheral blood.

***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

Pathogenesis and Spectrum of Disease

• Symptoms such as aches, pains, headache, fatigue, anorexia, or nausea. This stage is followed by fever, a more severe headache, and nausea and vomiting.

• Severe or fatal complications can occur at any time and are related to the obstruction of vessels in the internal organs (liver, intestinal tract, adrenal glands, intravascular hemolysis/black water fever, and kidneys).

• **Blackwater fever** is a complication of malaria that is a result of red blood cell lysis (hemolytic anemia happens with all species but more severe in p.falciparum) , releasing hemoglobin into the bloodstream and urine, causing discoloration and extremely dark red urin . Can cause acute renal failure. Blackwater fever if it was extremely excessive may leads to circulatory shock is called **algid malaria.**

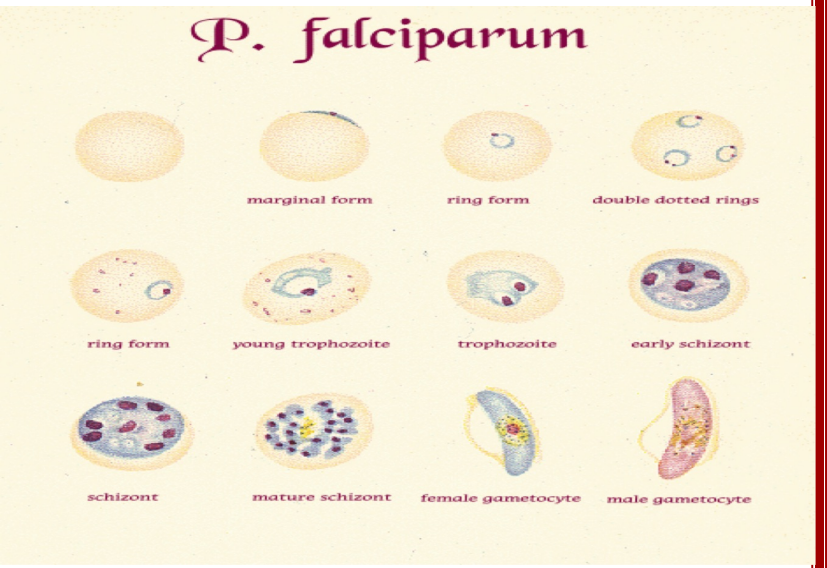
The fever is presented in 3 stages:1.clod (rigors and chills, eveb though the temp is high) 2.hot (flushing, headache, nausea with fever) 3.sweatnig stage (profound sweating).

• 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, which causes seizures and fibrile convulsions as the patient's chief complaint

• **Cerebral malaria** is considered to be the most serious complication and the major cause of death with P. falciparum.

TSS another complication of p.falciparum (tropical splenomegaly syndrome) abnormal function of spleen.

P.falciparum and p.malariae patients to a less degree, can have recrudescence phenomenona, merozoits that are found in blood are in small amount that doesn't reach the threshold level to induce fever.



PLASMODIUM KNOWLESI

(SIMIAN MALARIA,THE FIFTH HUMAN MALARIA) In its early stages it resembles p.falciparum and in its final stages it looks like p.malariae.

- P. knowlesi invades all ages of RBCs.
- 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.

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*

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 بالالوف	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 OF P.KNOWLESI

• 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.

• RBCs are being destructed so patient also has anemia, but symptoms start showing depending on level of anemia.

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.

All species leave a stain in the infected RBC called malarial pigment or hemozoin

• 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).

LABORATORY DIAGNOSIS (ALL SPECIES)

1.Routine Methods:

- Thick and thin blood films.
- At least 200 to 300 oil immersion fields should be examined on both films before a negative report is issued.
- Stains:

1. Giemsa stain.
2. Wright's stain.
3. Fluorescent nucleic acid stains, such as acridine orange.

- Blood collected using (EDTA) anticoagulant.

2.Serologic Methods: Fast, used worldwide but lower sensitivity and specific

- Several rapid malaria tests (RMTs): Look for 2 proteins on surface of plasmodium (Antigens). This method is highly sensitive

1.Some of which use monoclonal antibodies against the **histidine-rich protein 2 (HRP2).**

2. Whereas others detect species-specific parasite **lactate dehydrogenase (pLDH).**

- These procedures are based on an antigen capture approach in dipstick or cartridge formats.

Immune-assays are also used (changes color like pregnancy tests).

3. Molecular Diagnostics:

• Other methods include direct detection of the five species by using a specific DNA probe after PCR amplification of target DNA sequences.

4. Automated Instruments:

• Using automated flow cytometry hematology instruments, there are potential limitations related to the diagnosis of blood parasite infections.

THERAPY

• Antimalarial drugs are classified according to the stage of malaria against which they are targeted.

• QUINOLINES , ARTEMISININS

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

• These drugs are referred to as :

1.Tissue schizonticides (which kill tissue schizonts).

2.Blood schizonticides (which kill blood schizonts).

3.Gametocytocides (which kill gametocytes).

4.Sporonticides (which prevent formation of sporozoites within the mosquito).

First line of management for non-falciparum malaria: quinolines

In vivax and ovale, you have to kill hypnozoites: Primaquine

First line of management for falciparum: ACT (Artemisinin-based combination therapies), (combination to prevent resistance).

resistance

- People living in endemic areas have **premunition**. These patients have antibodies and cell-mediated immunity that protects them from super-infection, but not from reinfection by plasmodium species. Thus, the acquired immunity from malaria is called premunition and is it not long lasting.
- Plasmodium species need to bind to a specific receptor (**Duffy Antigen**) on RBCs to enter them. Duffy negative individuals have inherited resistance to plasmodium species.
- People with HbS trait and G6PD, as well as neonates (HbF) all have inherited resistance to malaria.

CONTROL

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

Babesiosis (common in USA and Europe)

• Babesiosis is an emerging tick-borne infectious disease caused by protozoan parasites of the genus Babesia that invade and eventually lyse red blood cells (RBCs).

• Most cases are due to Babesia microti. **B. microti**, a parasite of small rodents, is the most common etiologic agent of human babesiosis

• The primary causative agent of human babesiosis in Europe is **B.divergens**, but 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.

Very similar to malaria so it is important to differentiate it from malaria (blood-borne disease) , Target: RBC , Vector-mediated as well , **NO PERIODICITY**.

Modes of Transmission

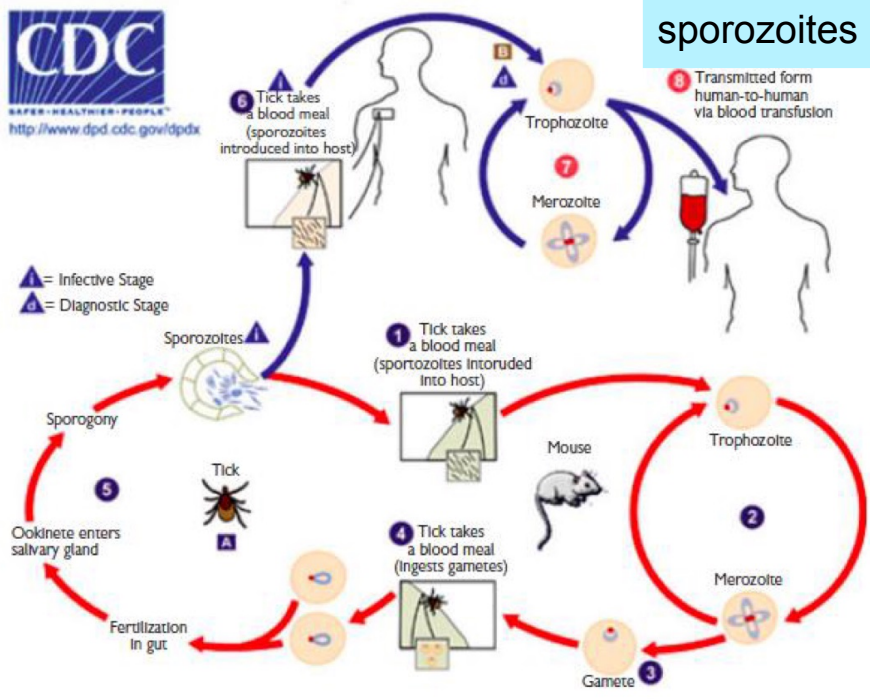
• B. microti is transmitted to humans primarily by the nymphal stage of the deer tick (**Ixodes scapularis**), the same tick that transmits the causative agents of Lyme disease . **No exo-erythrocytic cycle**, directly to RBCs and their mainstay of pathogenesis is hemolysis.

• The vectors for transmission of **B. duncani and B. divergens**– like organisms are thought to be **Ixodes pacificus and Ixodes dentatus**, respectively.

Vector in malaria is female anopheles. In Babesia, it's called Ixodes tick.

babesia life cycle

Definitive host: Ixodes tick (sexual reproduction)
- Accidental host: rats
- Infective stage: sporozoites



CLINICAL MANIFESTATIONS

• 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.
• 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 and is accompanied by one or more of the following: chills, sweats, headache, myalgia, arthralgia, nausea, anorexia, and dry cough.
• 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.

Most cases are asymptomatic, self-limited or mild. Significant disease in Babesiosis: >50 years old and immunocompromised.

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.
• 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.

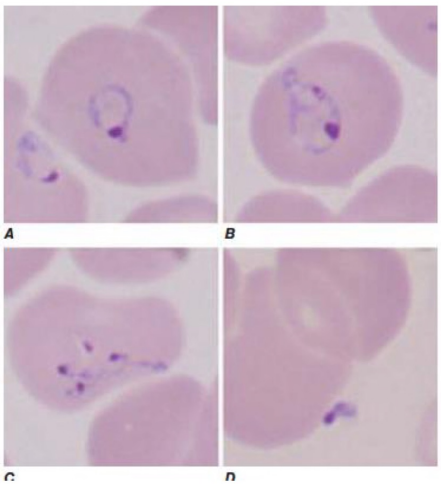
DIAGNOSIS

• Microscopic examination of Giemsa-stained thin blood smears.
• Polymerase chain reaction (PCR).
• Serology can suggest or confirm the diagnosis of babesiosis. An indirect immunofluorescent antibody test for B. microti is most commonly used.

Pathognomonic for babesia:

1. Trophozoites tend to form **tetrads**. Sometimes we find 4 rings like in image C connected by a line (drawn in red) called maltese cross appearance.

2. The presence of **extracellular trophozoites** like in image D.



TREATMENT

• **Atovaquone 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.

Preventive measures against Ixodes ticks.

https://mega.nz/folder/VuUFFQrZ#zKktM105APnElLedXIA3Lg/file/538kwaxA

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*

	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: Sporozoite 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 stage
treatment	Atovaquone (ARTEMISININS derivative) for falciparum. Quinilines for non falciparum infection + primaquine for ovale and vivax	Atovaquone plus azithromycin for moderate cases Clindamycin plus quinones for severe cases

Past papers

1.The highest rate of relapsing in plasmodium species:
a. P. ovale
b. P. vivax
c. P. falciparumm
d. P. knowlesi

2. Wrong statement about malignant tertian fever :
a. shows 2 chromatin dots with crescent gametocytes
b. Affects RBCs of all ages and shows all sizes
c. irregular fever with usually episodes every (36-48) hours
d. shows Schuffner's dots

3. Babesia Microti is transmitted by which of the following vectors:
a. Ixodes scapularis
b. Ixodes pacificus
c. Ixodes dentatus
d. Tsetse fly

4. Which is not true about P. malariae :
a. chronicity
b. glomeriolonephritis
c. hepnozoites
d. benign
e. band form

5. Which is wrong about malraia :
a. sporogony in the liver
b. it has two cycles
c. falciparum is the most severe one

6. The asexual cycle of Plasmodia occurs in :
a. vector
b. RBCs

7. The infectious phase of Plasmodia is :
a. Sporozoites
b. schizont
c. trophozoite

8. Wrong about P. falciparum :
a. it invades all ages of RBCs
b. only has schizogony in the erythrocytes
c. no schuffner's dots

9. Wrong about P. malariae:
a. relapse
b. tends to infect old cells
c. band form

10. Cerebral malaria is seen in:
a. P. falciparum
b. P. ovale
c. P. knowlesi
d. P. malariae
e. Plasmodium vivax

11. Newly produced RBCS are usually the only target for:
a. None of the mentioned
b. P. knowlesi
c. Plasmodium vivax
d. P. falciparum
e. P. malariae

12. wrong about p. malariae:
a. Relapse
b. no Schüffner's dots
c. glomerulonephritis

1.B	7.A
2.D	8.B
3.A	9.A
4.C	10.A
5.A	11.C
6.B	12.A

V2: the drugs and the infective stage for babesia in page 17.

V3: In page 8, p.ovale infected cells WILL be inlaged, not won't.