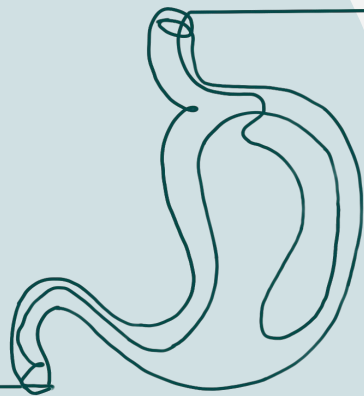


Malaria

Microbiology



Editing File
Summary

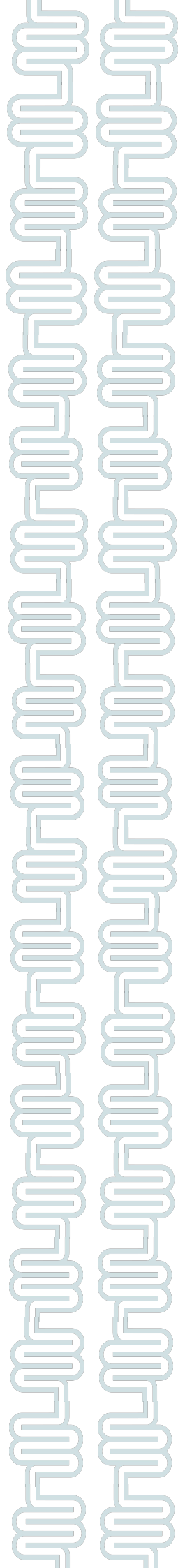
Color index

- | | |
|-----------------|----------------|
| ● Girls' slides | ● Boys' slides |
| ● Main content | ● Extra |
| ● Important | ● Drs' notes |



Objectives:

- Know the 5 species of malaria that infect humans
- Describe the life cycle of malaria, morphology and clinical picture
- Compare pathogenesis of different malaria species
- Know endemic countries of malaria species
- Know malaria Paroxysm
- Know complications of malaria
- Describe methods for laboratory diagnosis of malaria
- Know action of antimalarial drugs in different life stages of malaria parasite





Malaria is a life threatening disease. It's typically **transmitted through the bite of an infected Anopheles mosquito.**

Malaria is the most important of all tropical parasitic disease ,causes death and debility and is endemic throughout the tropics and subtropics.



Anopheles Mosquito

Epidemiology of Malaria:

- The world health organization (WHO) reported 229 million malarial cases in 2019, down from 239 million cases in 2010. It is endemic in several parts of the world .
- The African Region contributes most malaria cases (93%)followed by south east Asia(3.4%),and the Eastern Mediterranean region 2%.



Endemic countries

Human to human transmission can occur by:

- Blood transfusion
- Vertical transmission across the placenta

Signs & Symptoms^[1]



Periodic fever



Anorexia



Anemia



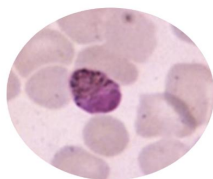
Headache

Species

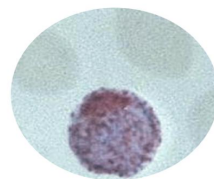
- | | |
|----------------------------------------------------------------------------------|----------------------------------------|
| ○ Plasmodium ovale (relapse,tertian) ^[2] | ○ Plasmodium malariae (quartan) |
| ○ Plasmodium vivax (relapse,tertian) ^[2] | ○ Plasmodium knowlesi |
| ○ Plasmodium Falciparum (Malignant tertian) ^[3] most important | |



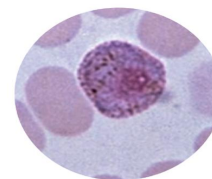
P. falciparum



P. malariae



P. ovale



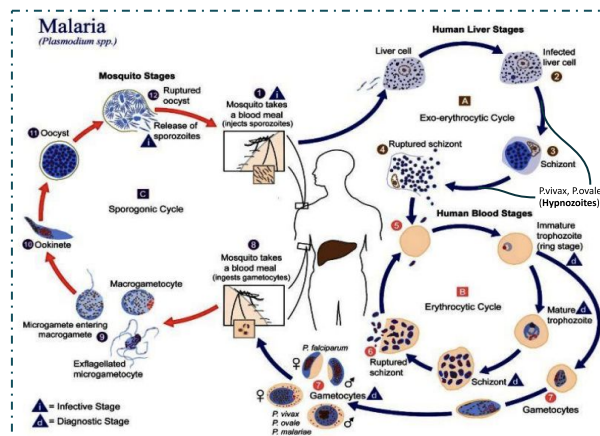
P. vivax

^[1] Fever/chills/symptoms in malaria is due to **rupture of RBCs' schizonts** (★NOT due to rupture liver schizonts★)

^[2] P. vivax and P. ovale have a special feature which is **relapse** (some sporozoites hide and lie dormant in hepatocytes (transform into **Hypnozoites**). Later on, these dormant (inactive) sporozoites can become active and trigger another attack of malaria symptoms months or years after exposure causing what is called relapse).

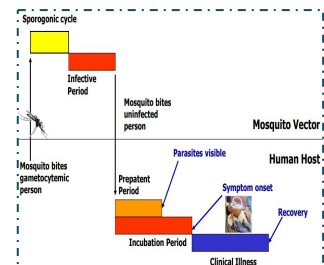
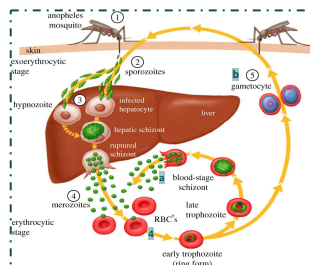
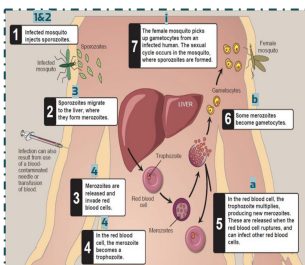
^[3] Plasmodium Falciparum (Malignant/tertian malaria) is the strongest malaria because it infects a very large number of RBCs, and because it tends to attach on blood vessels potentially leading to stroke, ischemia, and other complications.

Pictures' Explanation



- 1 Malaria is mainly carried by **female anopheles mosquito**.^[1]
- 2 The infected mosquito will **bite and inject sporozoites** from its salivary gland into the bloodstream of human.
- 3 Which then will travel through blood until it reaches the liver and enter the hepatocytes, where it will multiply asexually to form **merozoites inside the schizont (Exoerythrocytic schizont)**.
- 4 When the **hepatic schizont rupture** the merozoites will be released into blood, then it will enter the erythrocytes forming **immature trophozoites (ring stage)** which will have 2 pathways:
 - a **First pathway:** It goes through the **erythrocytic cycle** starting from ring stage then into Mature trophozoites, then the merozoites will multiply inside the RBCs forming **schizont (Erythrocytic schizont)**, which will rupture (hemolysis) and release the merozoites into the bloodstream (**Clinical attack of malaria is due to this stage**) and the cycle will repeat over and over again.
 - b **Second pathway:** Some immature trophozoites will become **gametocytes (male and female)** those gametocytes will be ingested by another mosquito; in the mosquito:
 - i There are Micro(Male) and Macro(Female) gametocytes, the microgametocytes will enter into the macrogametocytes in which they will form Ookinete then it will develop into Oocyst which will rupture **releasing sporozoites** in mosquito, then the cycle will go over and over again.

- Extra pictures for better understanding



[1] Definitive host is the female anopheles mosquito because it is where sexual stage takes place.

Life cycle and Pathogenesis

Life cycle

Asexual Stage

In human

Sporozoites (infective stage for human) are injected by an infected **Anopheles Mosquito** into the blood of human and enter liver cells and will become schizonts then become Merozoites which release in the circulation and penetrate the **Red Blood Cell** and cause **the main pathology^[1] of the disease hemolysis and anemia**. Some parasites develop into male and female **Gametocyte (the infective stage to mosquito)**.

Sexual Stage

In female Anopheles mosquito

Male and female **Gametocyte (the infective stage to anopheles mosquito) ★★** are taken up from the blood of an infected human. Further sexual development takes place in the mosquito gut to produce **SPOROZOITES**.

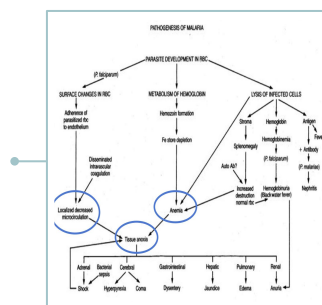
Pathogenesis

★★★ **Dr mona:** What is the infective stage to anopheles mosquito?
Gametocyte

- After a mosquito takes a blood meal, and introduce the sporozoites into the bloodstream
- The sporozoites will enter the hepatocytes (liver phase) within minutes and then emerge in the bloodstream again after a few weeks as merozoites.
- Merozoites rapidly enter the erythrocytes (red blood cells) they develop into trophozoites and then into schizonts (contains large number of merozoites) (erythrocytic phase).
- Rupture of infected RBCs (contains schizonts) leads to release a huge number of merozoites in the circulation with fever
- Merozoites enter another RBCs and the process repeated leading to severe hemolysis and anemia.

Symptoms are due to :

Hemolysis of Red Blood Cells : with release of metabolites and pigments from Malaria parasite and severe hemolysis and anemia is the main pathology of malaria.^[1]



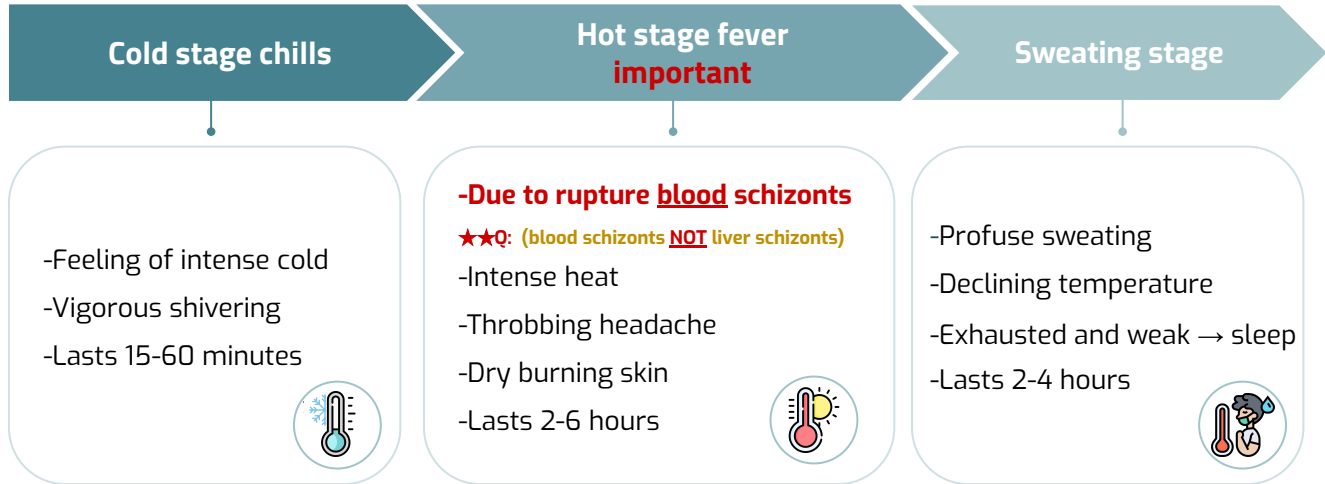
Symptoms are due to :

Plugging of capillaries by parasitized erythrocytes^[2]: In cerebral malaria there is sequestration of parasites in central nervous system capillaries **caused by Plasmodium Falciparum**

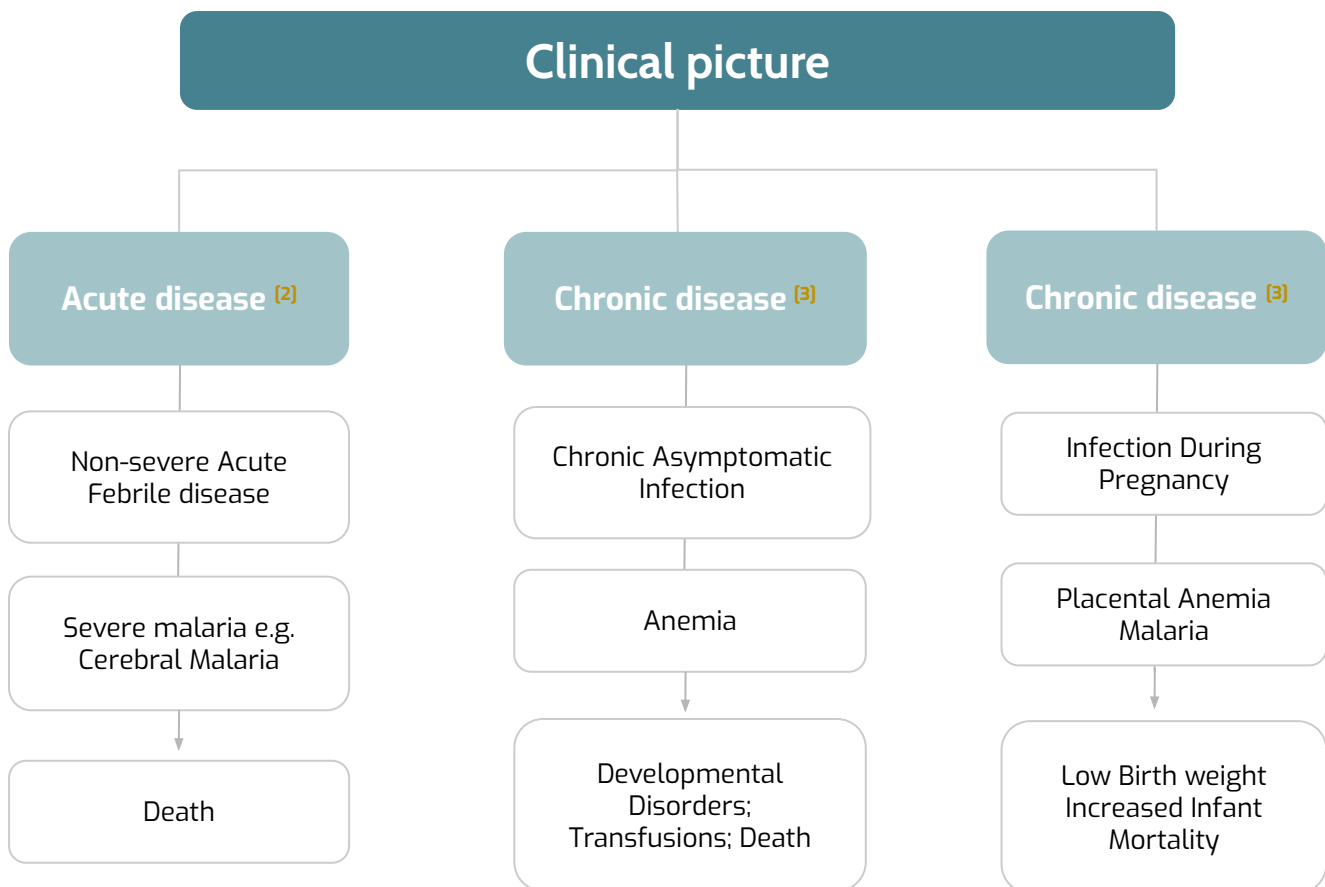
^[1] Main pathology of malaria is rupture of RBCs (**hemolysis**) and severe anemia ★

^[2] Erythrocytes become sticky which causes complications

Malarial paroxysm^[1]



Clinical picture



^[1] First, malaria starts with cold stage. Hours later, hot stage starts. Finally, the sweating stage starts. (Cycle keeps going every 3-4 days).

^[2] Acute disease (immediately after exposure) is usually associated with *P. falciparum* (malignant malaria), and it can lead cerebral malaria and death.

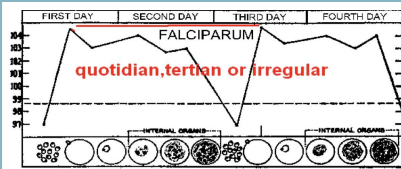
^[3] Chronic disease of malaria (more common than acute) is usually associated with *P. ovale* and *P. vivax*. It is mostly asymptomatic (mild infection & anemia goes on and off). However, when a woman gets the infection during pregnancy, it can be transmitted to placenta & baby and lead to infant mortality.

Complications

The pattern of fever in different species of malaria^[1]

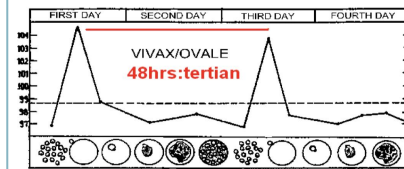
Plasmodium Falciparum (Malignant complicated malaria)

Fever tertian^[2], irregular



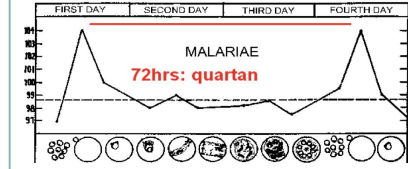
Plasmodium vivax Plasmodium ovale

Tertian **only**=
Fever every 48 hours
Relapse



Plasmodium malariae

Quartan=Fever every 72 hours






Complications of Severe Malaria^[3]

= *P. falciparum* (malignant tertian malaria) ★★★

Definition

symptomatic malaria in a patient with **P. falciparum (Malignant malaria)** with one or more of the following complications:

Complications

1- Cerebral malaria (unrousable coma not attributable to other causes).		2-Generalized convulsions (> 2 episodes within 24 hours).
3-Severe normocytic anaemia (Ht<15% or Hb < 5 g/dl).		4-Hypoglycemia (blood glucose < 2.2 mmol/l or 40 mg/dl) and pulmonary edema in pregnancy can lead to abortion and stillbirth, seen in Tropical Africa .
5-Metabolic acidosis with respiratory distress (arterial pH < 7.35 or bicarbonate < 15 mmol/l)		6-Fluid and electrolyte disturbances
7-Acute renal failure (urine <400 ml/24 h in adults; 12 ml/kg/24 h in children) (blackwater fever)		8-Acute pulmonary edema and adult respiratory distress syndrome
9-Abnormal bleeding		10-Jaundice 
11- Hemoglobinuria associated with malaria (blackwater fever): Uncommon and usually presents in adults as severe disease with anemia and renal failure.		12-Circulatory collapse, shock, septicaemia (algid malaria)
13-Hyperparasitaemia (>10% in non-immune; >20% in semi-immune)		14-Tropical splenomegaly

Uncomplicated malaria

Symptomatic infection with malaria patients without signs of severity and/or evidence of vital organ dysfunction.

^[1] Pattern of fever is very important for each species like *P. ovale* is every 48 hrs tertian

^[2] In some species, this cycle repeats every three days, hence called tertian (quartan if it repeats every 4 days)

^[3] The strain responsible for severe complications of malaria is *P. falciparum*. The RBCs infected with *P. falciparum* aggregate and attach to blood vessels which can potentially lead to occlusion, ischemia in the brain, black water fever, coma and other complications. When a patient is infected with a type other than *P. falciparum*, patient usually presents with severe anemia only (but NO other complications)

Diagnosis and Treatment

Diagnosis

Extremely important



★★★ Light microscopy^[1] (The GOLD standard)

- Thin film & thick film
- can be used to look for parasite density, species diagnosis and monitoring response to treatment^[2]

Three developmental stages seen in blood:

-Trophozoite -Schizont -Gametocyte



★ Rapid diagnostic tests (RDTs)^[3]: detect malaria antigens

The product comes in a number of formats:

- 1-Plastic Cassette
- 2-Card
- 3-Dipstick
- 4-Hybrid Cassette-dipsticks



Treatment

Sporontocides

Primaquine
Pyrimethamine
Proguanil

Tissue Schizonticides

primaquine
Pyrimetham
Proguanil
Tetracycline

Blood Schizonticides

Chloroquine
Quinine
Artemisinin
Sulfadoxine

Gametocytide

Primaquine

Anti-relapse (P.vivax)

Primaquine

Dr Mona: **Not important** (just know that some are used as prophylaxis whereas others are used to treat infected patients).

^[1] The common diagnostic method and **gold standard for diagnosing malaria is ★ light microscopy ★**.
We have 2 films;

- (1) Thick film: detects and confirm malaria but does not show the specific stage.
- (2) Thin film: shows the specific stage of malaria. → we see ring stage (trophozoite/merozoite) or gametocytes.

^[2] Some patients have 2-3 types of malaria in the same time (light microscopy is indicated to identify species and monitor treatment).

^[3] In areas endemic for malaria (where we need a fast detection/screening method), **rapid diagnostic test** (serological) test is used to detect **malarial antigens ★**

- Definitive host is the female anopheles mosquito because it is where sexual stage takes place.
- Life Cycle:
 - 1- A clean/non infected mosquito bites someone infected with malaria
 - 2- The mosquito will ingest male & female **gametocytes** from malaria-infected person
 - 3- **Inside the mosquito**, male & female gametocytes produce sporozoites in mosquito's gut (**Sexual stage**)
 - 4- The infected mosquito will bite someone else and release the sporozoites into his bloodstream.
 - 5- Sporozoite enters blood circulation and goes to liver cells (within 30 minutes) → called liver stage
 - 6- Multiply inside hepatocytes and form **liver schizont** with merozoites inside
 - 7- The **liver schizont ruptures** and merozoites are released into **blood**
 - 8- Upon release in the blood, merozoites will enter RBCs (called ring stage). There are two scenarios for merozoites in RBCs:
 - Some merozoites will invade RBCs and multiply causing **RBC schizonts** (erythrocytic phase) that will rupture (hemolysis)
 - Others will become **gametocytes** (male/female) to be ingested by a mosquito to infect others (repeat steps 1,2,3,4)
- ★ **Important:**
 - **Main pathology** of malaria is rupture of RBCs (**hemolysis**) and severe anemia ★
 - Fever/chills/symptoms in malaria is due to **rupture of RBCs' schizonts** (★NOT due to rupture liver schizonts★)
- ★ Stages:
 - **Infective stage of anopheles mosquito:** gametocytes ★★★
 - **Infective stage of human:** sporozoites
- ★ *P. vivax* and *P. ovale* have a special feature which is **relapse** (some sporozoites hide and lie dormant in hepatocytes. Later on, these dormant sporozoites can become active and trigger another attack of malaria symptoms months or years after exposure causing what is called relapse).
- Plasmodium Falciparum (Malignant/tertiary malaria) is the strongest malaria because it infects a very large number of RBCs, and because it tends to attach on blood vessels potentially leading to stroke, ischemia, and other complications.
- Acute disease (immediately after exposure) is usually associated with *P. falciparum* (malignant malaria), and it can lead cerebral malaria and death.
- Chronic disease of malaria (more common than acute) is usually associated with *P. ovale* and *P. vivax*. It is mostly asymptomatic (mild infection & anemia goes on and off). However, when a woman gets the infection during pregnancy, it can be transmitted to placenta & baby and lead to infant mortality.
- ★ The type responsible for severe complications of malaria is the malignant tertiary malaria (***P. falciparum***★★). The RBCs infected with *P. falciparum* aggregate & attach to blood vessels which can potentially lead to occlusions, ischemia in the brain, black water fever, coma, and other complications.
- When a patient is infected with a type other than *P. falciparum*, patient usually presents with severe anemia only (but NO other complications)
- ★ The common diagnostic method and **gold standard for diagnosing malaria** is ★ **light microscopy** ★. We have 2 films;
 - (1) Thick film: detects and confirm malaria but does not show the specific stage.
 - (2) Thin film: shows the specific stage of malaria. → we see ring stage (trophozoite/merozoite) or gametocytes.
- ★ In areas endemic for malaria (where we need a fast detection/screening method), **rapid diagnostic test** (serological) test is used to detect **malarial antigens** ★

- Symptoms of malaria result from RBCs bursting / ruptures.
- First, malaria starts with cold stage. Hours later, hot stage starts. Finally, the sweating stage starts. (Cycle keeps going every 3-4 days).
- In some species, this cycle repeats every three days, hence called tertian (quartan if it repeats every 4 days)
- Some patients have 2-3 types of malaria in the same time (light microscopy is indicated to identify species and monitor treatment).

Quiz

MCQ

Q1: All of the following can contribute to tertian fever except?

- A- P.falciparum
- B- P.malariae
- C- P.ovale
- D- P.vivax

Q2: Where does the sexual development take place to produce sporozoites?

- A- Liver
- B- RBC
- C- Mosquito
- D- schizonts

Q3: Which of the following species can cause erythrocytes to become sticky and plug blood vessels?

- A- P.falciparum
- B- P.malariae
- C- P.ovale
- D- P.vivax

Q4: What is the gold standard method to diagnose malaria ?

- A- RDTs
- B- Light microscope
- C- PCR
- D- Serology

Q5: Which of the following , cause malaria infection to human and mosquito respectively?

- A- Sporozoites, Merozoites
- B- Sporozoites, Gametocyte
- C- Gametocyte, Sporozoites
- D- Merozoites, Sporozoites

Q1: Which two of the following malaria species have the ability to relapse?

- A- P.falciparum
- B- P.malariae
- C- P.ovale
- D- P.vivax

Answers: Q1:B | Q2:C | Q3:A | Q4:B | Q5:B| Q6:C,D

SAQ

Case: A 34 years old male came to the ER complaining from headache and high-grade fever with occasional chills and sweats. Physical examination reveals a palpable spleen and decrease level of consciousness and the patient was somnolent, the ER physician ordered some lab tests for the patient and the lab results indicated that the patient is anemic and hemoglobin was traceable in urine, after taking the patient history, appeared that the patient traveled to Africa recently for a volunteer work.

Q1: What is the most likely diagnosis?

A:Malaria.

Q2: What is the most likely causative agent?

A: Plasmodium falciparum.
Because of the decrease of consciousness level(since P.falciparum is the only strain that commonly has cerebral involvement) and the hemoglobinuria.

Q3: What are the best diagnostic methods for this case?

A: Light microscopy, Rapid diagnostic tests.

Q4: Mention 4 complications for this disease.

A:Occlusions, ischemia in the brain, black water fever, coma, and [other complications](#).

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