Malaria

This sheet is from both sections recording and includes all slides and diagrams.

Malaria is caused by protozoa family called *plasmodium* (Genus) mainly affect blood system specially RBCs and each year it is responsible for 1-3 million death in tropical and subtropical areas, Children are most susceptible due to their immature immune systems.

The name itself is derived from Mal-Air. Mal: Latin word means bad, so malaria means the bad air around swamps and dirty ponds, Malaria is caused by a *female anopheles mosquito* living around those ponds.

Jordan had eradicated malaria since 1940 in effort of swamp elimination and spraying, but the doctor says you must know that the disease is spread worldwide and any visitor or traveller might be affected by the disease.

Most protozoa have 2 reproductive cycles; sexual and asexual, depending on the host they are in, as in malaria human is the primary host where asexual multiplication takes place and is referred to as *schizogony* (the form of malaria is called *schizont*) while in mosquito which is the intermediate host sexual multiplication take place and is referred to as *sporogony* (there is some asexual reproduction take place in mosquito but mainly it is sexual)

There are many different species of plasmodium but only 4 are relevant and the others are very rare, here the doctor just mentioned the 4 majors which are

1. *Plasmodium Vivax*
2. *Plasmodium Falciparum*
3. *Plasmodium Malaria*
4. *Plasmodium Ovale*

*They are in order of frequency from most to least.

There is another specie which is very rare and affects both humans and monkeys known as *plasmodium knowlesi* which is found mainly in South East Asia (doctor hasn’t mentioned it later on)
Life Cycle

We will start by biting of *female anopheles mosquito* to human(Only female bite and suck blood as to get food to nourish its eggs while male don’t). Here the infective form of plasmodium is called *sporozoite*, and found specifically in mosquito saliva where it is with the anticoagulant agents that are injected to let it suck the blood easily. Once sporozoite enter blood stream it spreads to the whole body but it will only infect the liver because of special protein on the surface of sporozoite CSP (*circumsporozoite protein*) and receptor on hepatocytes, once sporozoite enter hepatocytes it will start reproduce asexually *intracellularly* by process known *schizogony* and its morphology change to be *schizonts*(derived from schizogony) . It will continue dividing for 2-6 weeks and at this time no symptoms appear hence it would be the incubation period.

When taking history from patient and suspect malaria you must ask where he travelled in the last 6 weeks especially for *plasmodium malaria* as the incubation period usually is longer.

The process of replication in liver is also known as *extraerythrocytic stage (EE stage)* or hepatic stage.

-Inside the hepatocytes schizonts divide by special way, first the nucleus divides into several nuclei inside the same schizont then the cytoplasm will divide around these nuclei and a number of organelles produce (12-20 schizonts produce each cycle).

After the incubation period the schizonts are released from liver and enter blood circulation to start its pathology by this time its morphology change to *merozoite*. 
In case of *P. Falciparum* and *P. Malaria* once it is released from liver and become **merozoites**, its liver role and pathology stops but in *P. Vivax* and *P. Ovale* some of them will continue as **hypozoites** where it is a sleeping plasmodium that will be reactivated later in life causing what is known as **relapse of disease**, (it is as same as the original disease but from the latent plasmodium). Here we prescribe different drug for killing hypozoites. *(Double treatment, one for merozoites and another for hypozoites).*

Once schizonts are released from hepatocytes they only infect RBCs, finding their way by specific protein receptors known as **sialoglycoprotein receptor**. As in *P. Vivax*, they have another special protein receptor the **Duffy receptor** for Duffy +ve blood group (A protein on RBC surface which presence is Duffy +ve).

*If person is Duffy negative he will be immune to *P. Vivax* but not to any other plasmodium species.*

*P. Vivax* and *P. Ovale* tend to infect young RBCs and reticulocytes, while *P. Malaria* tend to infect the old ones. But the *P. falciparum* is the worst as it could infect any RBC despite its age that’s why **PARASITAEMIA (number of infected cells)** is very large in *P. falciparum* reaching up to 40% while in the remaining species is only 2-3%.
Once merozoites enter RBC it will become **trophozoite**, its shape looks like a singlet ring and has one and rarely two dots which represent the chromatin. Now it will start growing and degrading the Haemoglobin of the RBC by the end of this the degraded haemoglobin will be known as **haemozoin** and appear as brownish pigment in cytoplasm.

Now it get complex, after the appearance of haemozoin, trophozoite would go in development and become schizont again in the RBC (the asexual multiplying plasmodium as found in liver) and start dividing asexually to increase in number, then it will become merozoites again, after that it will burse the RBC and spread the merozoite to blood to infect another fresh RBC. The process from entrance to exit of RBC is known as **intraerythrocytic stage**, and this replicate itself again and again.

The differences between the species are in Shape, number of merozoites and schizonts inside the RBC, which is used in diagnosis to decide which specie of plasmodium is present.
The period of intraerythrocytic stage differ from one specie to another as in *P.Ovale, P.Vivax* and *P.falciparum* it is around 48 hours while in malaria it is 72 hours.

During the **intraerythrocytic stage**, some proteins are transported from trophozoite to RBC surface by Actin which act as Actin Bridge. In case of *P.falciparum* one of the parasitic molecule (which is transported by Actin bridge) act as adhesion factor which let the RBCs cluster around each other as rose shape known as **rosette** which might close some tiny capillaries in the body leading to thrombus formation. While another protein act as adhesion factor for endothelial cells which let it adhere to vascular endothelial cells and is referred as **sequester**.

*As a result from sequestration and rosette, the measured PARASITAEMIA (number of infected cells) of *P.falciparum* from blood smear would be lower than expected (40%) but actual is higher as infected cells are adherent to endothelial cells.*

As merozoites infect RBCs some granules appear:

1- **SCHUFFNER GRANULES** : *P.Ovale* and *P.Vivax*

   ![SCHUFFNER GRANULES](image)

2- **MAURER SPOTS** : *P.falciparum* (red in colour and have coma shape)

*No granules in malaria.*
Some of the merozoites inside the RBCs don’t develop to schizont and keep growing till become unicellular, becoming *gametocytes* (male and female gametes). There is a variation in gametocytes number and size (*macrogametocytes; female* & *microgametocytes; male*) from species to another and they don’t cause any rupture to the RBC, just waiting the mosquito to come and suck them to continue the cycle. (Here the original merozoites; the gametes, no division happen just growing in size).

When infected person is bitten by *female anopheles mosquito*, the gametocytes are sucked and go to mosquito gut, they are released from RBCs and fusion between macrogametocytes and microgametocytes (sexual reproduction of plasmodium) happen, producing zygote then asexual reproductive cycles happen to the formed zygote to increase in number and then migrate to salivary glands as sporozoite to continue its cycle (the whole process from fusion to sporozoite is known as sporogony).
Prepared By: Fares Ghanem

Special Thanks to Lara Ajailat and Issa Smairat

Dedicated to Majed Ftaiha, Barjas, Batool, Ameer, Issa, Amjad, Farraj, Zetawi, Khalid, Mohammad Shekh, Atef Lami, Mohammad Qdah, Mohannad Qaiseyeh.