Hematology

Medical Committee
The University of Jorda

- Histology
- Biochemistry
- Pathology
- Pharmacology
- Physiology
- Microbiology

Dr. name : **Hassan Abu Al-Ragheb**

lecture number : **3**

Done BY : **Doa'a S. Dahboor**

Handout | Sheet | Slide

By: Anwer Abu Shanab

MALARIA 2

** Malaria is associated with other genetically inherited diseases of RBCs . This association is shown in two points :

1- Malaria and these diseases have similar distribution globally .
2- These disease show a kind of protection against malaria .

These diseases are : sickle cell anemia , thalassemia (a disease related to hemoglobin) and G6PD deficiency .

Indeed , these diseases DON'T prevent you from being infected by malaria . A person with one of the previously mentioned diseases may get malaria but with less severity and fatality than normal i.e. these diseases have some kind of protection against malaria .

Now , what's the reason behind this protection ?

There are some theories and suggestions that explain this selective advantage for people with these diseases but before we start discussing them ...

Be careful !

There are two different scenarios . A case in which there'll be complete resistance to the infection by malarial parasites , and another case where the disease will show milder pattern and less fatality . The selective advantage for patients with sickle cell disease , thalassemia and G6PD deficiency is related to decreased severity of malaria but still patients may get infected by it (There's no full resistance to the parasite) .
So when does complete resistance against the parasite occur ?

Remember from the previous lecture that a special kind of receptors for the malarial parasites must be present on the RBC surface to enable the parasite to enter the cell .Example : Duffy blood group antigen for P.vivax . If you don't have the duffyantigen , you'll NEVER get infected by P.vivax (still you may get infected by any other malarial parasite if you have its special receptor on your RBCs).

Now let us discuss the theories we talked about ☺

Written by Doa'a S. Dahboor

1) In case of sickle cell anemia (the most associated with malaria) the following happens : Once an RBC is stressed (stress in this case is the infection of malaria i.e. entry of the parasite into RBCs) , it sickles . Note that the cells are already sickled since there's sickle cell disease . I think the doctor means further sickling will happen after the entry of malarial parasite into the cells which is a stress factor for them . Sickled cells will be phagocytosed in the spleen which means the parasite's life cycle has been interrupted and that will end the story !
2) Remember that in P.falciparuminfection , the parasite expresses certain molecules on the surface which leads to the adhesion of RBCs with each other and with endothelial cells . This leads to complications in the kidney as well as the brain cerebri , BUT in the presence of sickle cell trait , parasites won't be able to express the adhesive molecules ⟶ no adhesion of RBCs ⟶ less malignancy of falciparum .
   Please pay attention if you listen to the record or if you wrote notes during the lecture that the doctor mistakenly said at first that this happens in thalassemia , I checked it from the handout and it's written that this mechanism is related to sickle cell trait and not thalassemia .
3) Now we move to thalassemia . As you know , in thalassemia , MORE but SMALLER-than-normal RBCs are produced with low amount of hemoglobin . When the parasite comes to destroy RBCs and consume their hemoglobin , the effect will not be disastrous as in normal cases of malaria since the amount of hemoglobin in the cells is already low due to thalassemia mutation . Professor Hassan says that losing more RBCs with less amount of hemoglobin (as in thalassemia) is of milder consequences than losing less RBCs with concentrated hemoglobin inside .
4) In G6PD deficiency , lack of G6PD leads to production of free oxygen radicals inside RBCs which are harmful to all invasive pathogens including malarial parasites , so these parasites will be killed by the free radicals produced in RBCs .

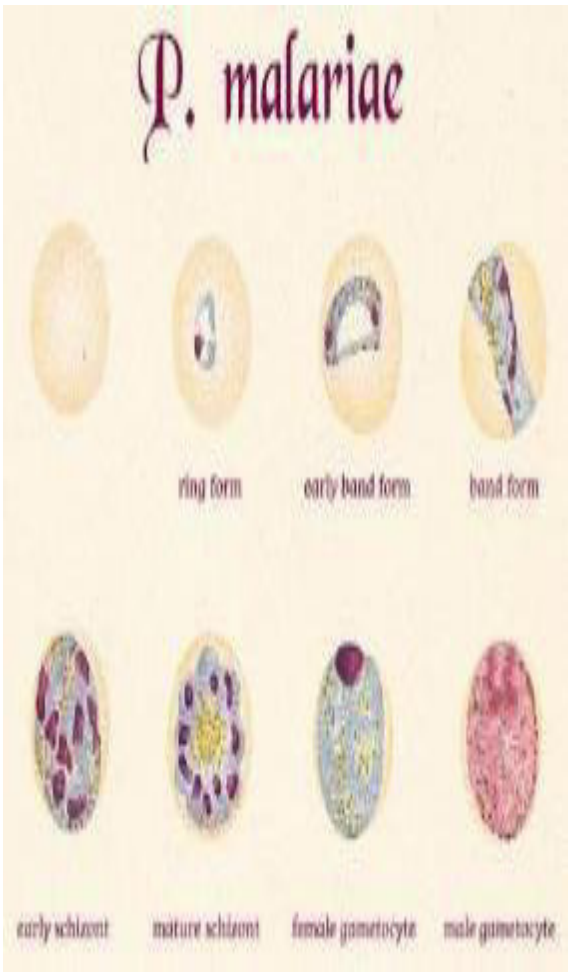
   Done with mechanisms of protection against malaria by some RBCs abnormalities ☺☺☺

* Diagnosis :

If malaria is suspected especially in endemic areas , we rely on the clinical picture for diagnosis . Diagnosis is mainly based on blood smear examination . Two blood smears are prepared **; thick and thin .** A thick smear is prepared by spreading a small amount of blood on a glass slide using a stick whereas the thin smear is prepared by spreading the blood on a glass slide by putting another glass slide above it . Thick smear reveals too many cells in terms of number ,so if you are interested in detecting the presence of the disease , then you should prepare a thick smear . Remember that generally in malarial infections , only 2-3% of RBCs contain the parasite inside , that's why too many cells are needed to detect the presence of the disease and this property is provided by thick smears.

Next step after detecting the presence of the disease is studying the morphology of the parasite . The morph will not be clear if cells are accumulated in a such crowded way i.e. thick smears are not useful for detecting the morph so we use thin smears for that purpose .

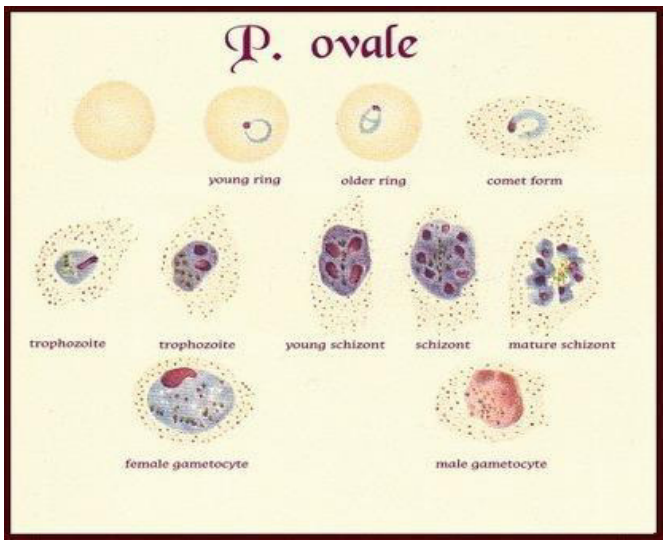
After that , we rely on certain criteria to determine the exact type of the infecting malarial parasite .



Features seen in P.malariae :

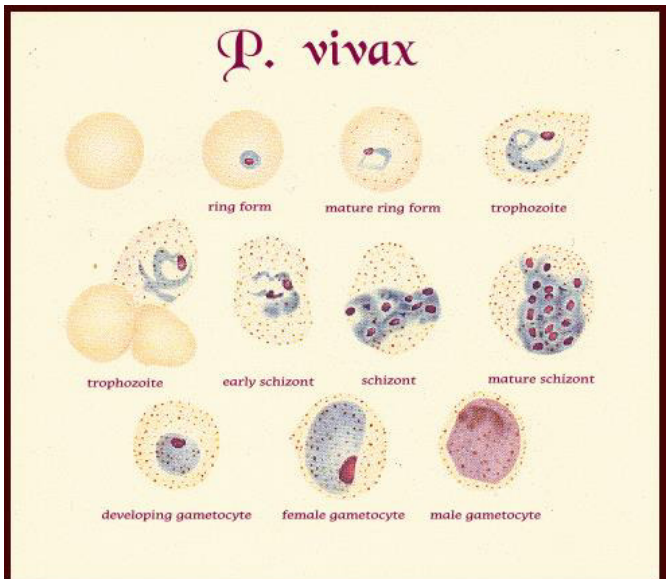
1- Since P.malariae infects old RBCs , the majority of infected cells in the smear appear **small .**
2- The **signet ring** appearance of the trophozoites can be noticed .
3- A **band form** is noticed . During schizogony , the trophozoites may assume a rectangular band appearance .
4- **Rosette** formation in schizonts stage . The schizont is divided into several nuclei that arrange around the periphery of the cell . Haemozoin pigment which is hemoglobin remnants is left in the center . The result of this arrangement is rosette shape (flower-like appearance) .

** Sometimes we use the term " Rosette " to describe appearance of cells in P.falciparum . **Be careful !** "Rosette" formation in P.falciparum is used to describe the accumulation of RBCs in a sticky way to form a flower-like structure , whereas " Rosette " in P.malariae means the arrangement of the nuclei of the parasite inside an RBC to give a flower-like appearance .



Features seen in P.ovale :

1) P.ovale infects young RBCs that's why the infected cells in the smear tend to be **large .**
2) The pathogen distorts the shape of the infected RBCs by arranging itself in an elongated pattern inside the cell which gives the cells **an oval appearance** and hence the name of the parasite .
3) Appearance of granules on the surface of RBCs **(Schuffner granules).**

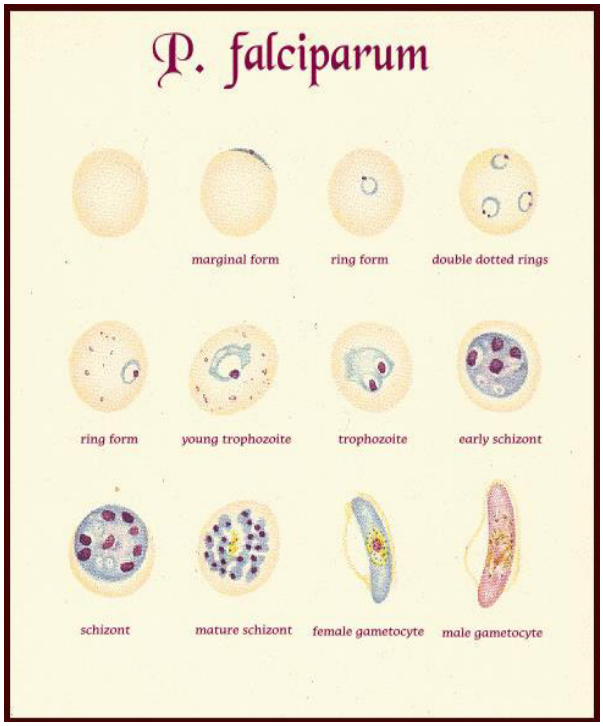


Features seen in P.vivax :

1) P.vivax infects the young immature RBCs mainly reticulocytes that's why the infected cells appear **large** in the smear .
2) Unlike P.ovale , there's no distortion in cells' shape due to a specific arrangement of the parasite . Instead , the parasite assumes a random arrangement inside the RBCs to give them a **random non-specified shape** .
3) Appearance of granules on the surface of RBCs **(Schuffner granules).**

Schuffner granules :

Nobody exactly knows what these granules are !Probably , they appear due to the changes in cell membrane structure . They appear as pink/red spots in the smear and they are a distinctive feature of **P.vivax and P.ovale infection .**



Features seen in P.falciparum :

1) The trophozoite has **2 dots of chromatin** which is more than normal (double the normal amount of chromatin in a single trophozoite) .
2) **Double infection** is common .It is the presence of 2 parasites or more in one RBC .
3) Although parasitemia is high (40%), **only (2-4%) infected RBCs can be seen** in the smear . This is due to the fact that infected RBCs adhere to the endothelium of the blood supply of the viscera to be sequestered there .
4) **Maurer (comma shaped) dots / granules** (different from Schuffner granules) .

So …

Maurer granules ⟶ P. falciparum .

Schuffner granules ⟶ P.ovale and P.vivax .

P.malariae has no distinctive granules .

Done with diagnosis ☺☺☺

** Treatment :

Will be discussed in details in pharmacology . The only thing you need to know that in case of P.vivax and P.ovale , a dormant form of the parasite (the hypnozoite) stays in the liver . It can be activated after the infection has gone leading to relapse . To avoid relapses , two sets of drugs must be given to the patient ; a set that's specific for the parasite in the RBCs and another one that's specific for the dormant parasitein the liver i.e. both stages of development ; the erythrocytic and the extra-erythrocytic (the hepatic) must be put into consideration .

Done with treatment ☺☺☺

Written by Doa'a S. Dahboor

** Prevention :

1) Prophylactic treatment especially for those who are willing to travel to an endemic area . These people must be given a prophylactic treatment one week before they travel , continue taking the drug while they are in the endemic area and when they come back , they must be also given a prophylactic treatment for 4 weeks to eradicate any multiplying parasite in their bodies .
2) In endemic areas , you should protect yourself from mosquito bites . You should avoid being in open-air areas especially at night , use anti-mosquito sprays and use a mosquito-net (a curtain that covers the bed) when you sleep . Some mosquito-nets are designed to have a mosquito repellent .

Done with prevention ☺☺☺

** Babesiosis :

Babesia :Another parasite of the apicomplexan family (the family of malaria) . It is similar to malaria and related to it . It infects animals mainly. Occasionally , some Babesia species may infect human beings ; one of these is Babesia microti . Babesia is the pathogen and Babesiosis is the disease .

The problem is that the clinical picture of Babesiosis is very similar to that of malaria (in terms of symptoms like fever , hemolytic anemia , ... etc.) which leads to a diagnostic confusion even after blood examination if the examiner was not a skilled specialist .

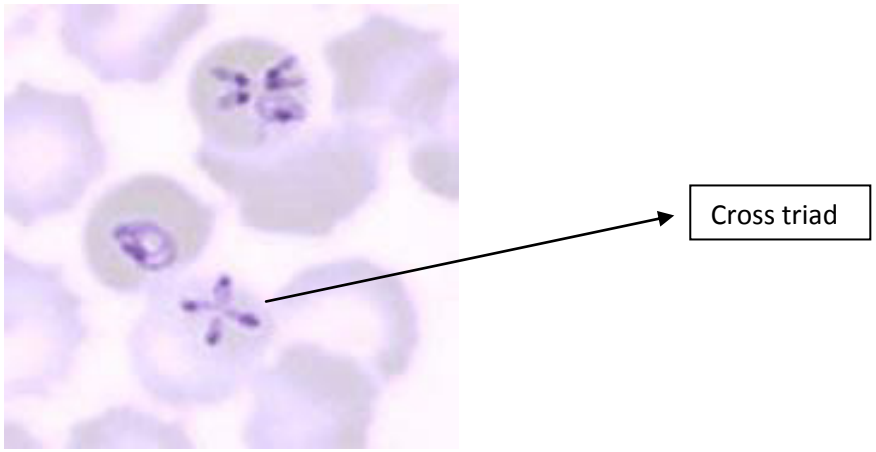
The intermediate host of Babesiosis is different than that of malaria . It is the tick – القراد.The tick usually bites an animal and transmits the parasite to it (that's why the tick is the intermediate host) and if a human being was occasionally bitten by the tick , the disease is transferred to him .

Life cycle :The tick bites the primary host (animal / human) . It injects sporozoites into the blood stream (same as malaria) . These sporozoites invade the RBCs immediately(No liver stage) . They divide in the RBCs by binary fission(They DON'T undergo schizogony thus there are no schizonts ; unlike malaria) . The binary fission gives rise to merozoites

.Merozoites get out of the RBCs they are in to infect other RBCs and this goes on and on and on !

Some of the sporozoites do not divide after entry to RBCs .Instead , they form what's known as pre-gametocytes (not proper gametocytes as in malaria that's why we added the prefix pre-) . When another tick comes and bites the primary host , it takes up the blood cells that contain the pre-gametocytes . In the gut of the tick , the pre-gametocytes produce gametocytes that will fuse to form sporozoites (sexual reproductive cycle in the gut of the intermediate host) . The sporozoites will be injected into a new primary host and the whole cycle is repeated again .

Diagnosis :It is based on a blood smear (same as malaria) . Schizonts are not noticed since there is no schizogony . Merozoites are seen . They form **tetramers (cross triads)** in some RBCs . These tetramers are a distinctive feature of Babesiosis .



Done with Babesiosis ☺☺☺

AND

Done with the sheet ☺☺☺

Best of luck everyone ☺☺☺

Written by :Doa'aDahboor .