***“Hemolytic anemia –part 2”***

This part will discuss hemolytic anemia caused by: malaria & hereditary spherocytosis

**First: malaria**

1. **Malaria:**  is an infectious disease caused by one of the four types of protozoa; of these the most important is plasmodium falciparum, which causes tertian malaria or falciparum malaria. The other three species of plasmodium that infect humans (plasmodium malariae / plasmodium vivax / plasmodium ovale) cause relatively benign disease.
2. **Transmission**: Allforms are transmitted by the bite of female anopheles mosquitoes, and humans are the only natural reservoir.
3. **Life cycle of plasmodia:**

Mosquitoes feed on human blood---🡪sporozoites are introduced from the mosquito’s saliva---🡪within minutes they infect the liver--🡪in the liver the parasites multiply rapidly ----🡪forms schizont containing thousands of merozoites --🡪after several days or weeks the infected hepatocytes release the merozoites ----🡪which quickly infect red cells---🡪here, the intraerythrocytic parasites:

1. Either, continue asexual reproduction by developing into trophozoites which will ultimately produce more merozoites which escape by lysing the red cells.
2. Or, give rise to gametocytes capable of infecting the next hungry mosquito.
3. **Malaria features:**
4. The parasites destroy large numbers of infected red cells, thereby causing a hemolytic anemia.
5. Showers of new merozoites are released from the red cells at intervals of 48 hours in (p.ovale /p.vivax /p.falciparum) and 72 hours for p. malariae .this release is accompanied by the episodes of shaking, chills, and fever.
6. **Symptoms and manifestation of falciparum malaria:**
7. It is usually a chronic disease with 48 hours episodes of chills, shaking, and fever. It may be disrupted by black water fever.
8. Massive intravascular hemolysis resulting in: Hemoglobinemia, jaundice, and hemoglobinuria.
9. Cerebral malaria: a fatal complication occurs when falciparum malaria involves the brain.

Cause: normally red cells bear negatively charged surfaces that interact poorly with endothelial cells. Infection of red cells with falciparum malaria induces the appearance of positively charged surface knobs (projections) containing parasitic proteins, which bind to adhesion molecules (intracellular adhesion molecule 1\_ICAM 1) expressed on activated endothelium. This interaction leads to the trapping of red cells in post capillary venules .this process involves cerebral vessels in a minority of patients (especially children) which becomes occluded and ultimately leads to cerebral malaria.

Symptoms and manifestation: convulsions, coma, and death within days to weeks.

1. **Diagnosis:**
2. A characteristic brown malarial pigment derived from hemoglobin called hematin is released from the ruptured cells and produces discoloration of the spleen, liver, lymph nodes, and bone marrow.
3. Trophozoites have a distinctive appearance which differs among different species, thus the species of malaria that is responsible for an infection can be identified by examining stained thick smears of peripheral blood.

**Important**

1. Activation of defense mechanisms in the host leads to a marked hyperplasia of mononuclear phagocytes producing massive splenomegaly and sometimes hepatomegaly.
2. **Treatment:**

Chemotherapy is good, but treatment of falciparum malaria is becoming more difficult with the emergence of drug resistant strains.

But!!!

The best solution is effective vaccination.

***Second: hereditary spherocytosis***

1. **Cause:**

Inherited (intrinsic) defects in the red cell membrane skeleton that lead to the formation of spherocytes (non deformable cells that are highly vulnerable to sequestration and destruction in the spleen)

How do membrane defects result in spherocytosis??

Mutations in membrane skeleton proteins (spectrin / band 3 /ankyrin). These pathogenic mutations weaken the vertical interaction between the membrane skeleton and the intrinsic membrane proteins (i.e. proteins embedded in the phospholipid bilayer).

So these mutations destabilize the lipid bilayer of the red cells, which shed membrane vesicles into the circulation as they age. Little cytoplasm is lost in the process and as a result the surface area to volume ratio decreases until the cells become spherical.

How does spherocytosis lead to anemia??

Spherocytes have limited deformability and are sequestered in the splenic cords, where they are destroyed by the resident macrophages.

1. **Mode of inheritance :**

Autosomal dominant ,but a more severe autosomal recessive form affects a small minority.

1. **Symptoms and manifestations:**
2. General features of anemia (fatigue, pallor, etc…) which is highly variable ranging from subclinical to severe and most commonly moderate.
3. General features of extravascular hemolytic anemia (jaundice, bilirubin rich gallstones, cholelithiasis, etc….)
4. Splenomegaly is more common and prominent in hereditary spherocytosis than in any other hemolytic anemia.

Spleen enlargements results from marked congestion of splenic cords and increased numbers of tissue macrophages.

1. Systemic hemosiderosis
2. The clinical course is stable but may be disrupted by aplastic crises which are triggered by parvovirus B19 (B19 infects and destroys erythroblasts in the bone marrow.

How does aplastic crises worsen the situation?

 red cells with hereditary spherocytosis already have a short life span and, so a lack of red cell production for a few days results in a rapid worsening of the anemia. Such episodes of aplastic crises are self limited but some patients need supportive blood transfusion.

1. **Diagnosis:**
2. Because of their spherical shape, red cells in hereditary spherocytosis have Increased osmotic fragility when placed in hypotonic salt solutions.
3. Spherocytes are dark red and lack central pallor.
4. Excessive red cell destruction leads: to hyperplasia of red cell progenitors in the bone marrow / reticulocytosis.
5. **Treatment:**

Splenoctomy provides relief by removing the major site of red cell destruction although the red cell defect and spherocytosis persist.

The benefit of Splenoctomy must be weighed against the risk of increased susceptibility to infections and that’s why partial Splenoctomy is gaining favor.

**Done by: Fekra….good luck!!!**