***“Anemia of increased blood loss part-1-“***

***First: anemia of blood loss (hemorrhage)***

1. Acute blood loss: the immediate threat is hypovolemic shock rather than anemia, but if the patient survived the shock he will suffer anemia that is normocytic & normochromic. Recovery from blood loss anemia is enhanced by a rise in erythropoietin which stimulates red cell production and reticulocytosis appears within 5 -7 days.
2. Chronic blood loss: with chronic loss of blood ----***🡪*** iron stores are depleted ----***🡪***chronic anemia of under production.

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***Second: hemolytic anemia (increased destruction)***

Normal red cells have a life span of 120 days but in hemolytic there is accelerated red cell destruction. Destruction can stem from an:

1. Intrinsic (intracorpuscular) red cell defects= defects in the red cell itself----***🡪*** inherited except paroxysmal nocturnal hemoglobinuria which is acquired
2. Extrinsic (extracorpuscular) = abnormalities outside the red cell which leads to its destruction------***🡪***usually acquired

***Hemolytic anemia characteristics:***

1. **Decreased red cell life span**
2. **Compensatory increase in red cell production (reticulocytosis) in an equivalent pace to hemolysis leading to erythroid hyperplasia in the marrow.**
3. **Retention of the products of the degraded cells (iron).because the recovered iron is efficiently recycled, red cell regeneration may almost keep pace with the hemolysis .consequently, hemolytic anemias are associated with erythroid hyperplasia in the marrow and increased numbers of reticulocytes in the peripheral blood.**
4. **Severe hemolytic anemias are associated with extramedullary hematopoiesis (spleen, liver, lymph nodes)**
5. **Destruction of the red cells can occur within:**
6. **The vascular compartment (intravascular hemolysis):**

**Causes: mechanical forces (e.g. Turbulence created by a defective heart valve) / biochemical or physical forces (e.g. Fixation of complement, exposure to clostridial toxins, or toxins)**

**Results in:**

* **Hemoglobinemia, hemoglobinuria, hemosiderinuria, the conversion of heme to bilirubin results in unconjugated hyperbilirubinemia and jaundice.**
* **Haptoglobin, a circulating protein that binds and clears free hemoglobin, is completely depleted from the plasma.**
* **Lactate dehydrogenase (LDH) is elevated in the plasma due to its release from hemolyzed red cells.**
1. **Within tissue macrophages (extravascular hemolysis) takes place within the spleen and liver:**

**Causes: diminished deformability of red cells is the cause of destruction because extreme alterations of shape are required for red cells to pass into the splenic sinusoids.**

**Results in:**

* **Jaundice, which if long standing leads to the formation of bilirubin rich gall stones (pigment stones)**
* **Haptoglobin is decreased as some hemoglobin escapes into the plasma**
* **LDH is elevated**
* **No hemoglobinemia, no hemoglobinuria.**
* **Reactive hyperplasia of macrophages (cells that destruct RBCs in the spleen) which results in splenomegaly.**

***First: Hemolytic anemia resulting from mechanical trauma to red cells:***

Abnormal mechanical forces result in red cell hemolysis

Created in several circumstances:

1. Traumatic hemolysis: occurs during any activity involving repeated physical blows (marathon racing / karate chopping/ bongo drumming), it is of little significance.
2. Defective cardiac valve prostheses (the blender effect): the turbulent blood flow shears red cells.
3. Microangiopathic hemolytic anemia : occurs when small vessels become partially obstructed or narrowed by lesions, it occurs in several conditions such as:
* Disseminated intravascular coagulation: in which vessels are narrowed by the intravascular deposition of fibrin.
* Malignant hypertension
* Systemic lupus erythematosus
* Thrombotic thrombocytopenic purpura
* Hemolytic uremic syndrome
* Disseminated cancer

Morphology: injured red cells (schistocytes) includes: burr cells /helmet cells / triangle cells.

***Second: Immunohemolytic anemia:***

The presence of antibodies that recognize antigens on red cell membrane and cause hemolytic anemia. These antibodies may arise spontaneously or induced by exogenous agents such as drugs or chemicals.

Diagnosis:

1. Detection of antibodies and/ or complement on red cells by direct Coombs test, in which the patients red cells are incubated with antibodies against human immunoglobulin or complement.

If the antibodies cause the patient red cell to agglutinate we proceed to the indirect Coombs test

1. Indirect Coombs test: red cells carrying specific antigens are mixed with the patient’s serum to identify the type of immunoglobulin responsible of the anemia.

Types:

1. **Warm antibody immunohemolytic anemias (IgG / rarely IgA)**
* Active at 37 C
* Causes: 60% idiopathic / B cell neoplasm (e.g. chronic lymphocytic leukemia) ,autoimmune disorder (e.g. systemic lupus erythematosus),drugs (e.g. alpha-methyldopa ,penicillin , quinidine)
* Mechanism: opsinization of red cells by the autoantibodies which leads to RBCs phagocytosis in the spleen .some erythrocytes are incompletely phagocytosed (nibbled) but parts of their membrane are removed and lost, with loss of cell membrane the cells become spherocytes which are rapidly destroyed in the spleen.
* Symptoms and manifestations: mild chronic anemia with moderate splenomegaly.
* Note: drugs induce this anemia in several ways :
1. Alpha-methyldopa: triggers antibodies against red cell constituent’s especially Rh antigens. The drug may alter the immunogenicity of native epitopes and thereby circumvents T cell tolerance.
2. Penicillin : acts as hapten (inducing an antibody response by binding to membrane proteins)
3. Sometimes antibodies recognizes drug in the circulation and form immune complexes that are deposited on red cell membrane. Here they may fix complement or act as opsonins.
4. **Cold antibody immunohemolytic anemia (IgM):**
* Below 30 C
* Occurs in distal parts in the body (ears / hands /toes)
* Causes:
1. Chronic: idiopathic / with certain B cell neoplasm.
2. Acute: Recovery from pneumonia caused by mycoplasma spp and infectious mononucleosis
* Mechanism: when temperature < 30 C ----🡪 IgM binds to red cell membrane---🡪 IgM fixes complement (C3b) well but the latter steps of the complement fixation cascade don’t occur efficiently at temperature below 37 C--🡪when these cells reach warmer areas in the body IgM is released but C3b remains ------🡪 RBCs are phagocytosed by macrophages in the liver and spleen (extra vascular hemolysis)

***Done by: Fekra….Good luck!!!***