Doctor.021

no. 1+2

HLS P.B.L

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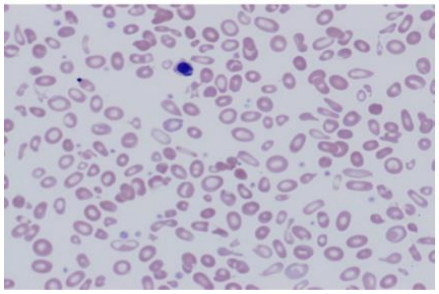
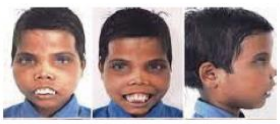
CASE 1

A 12-year-old male is requiring blood transfusion on regular basis since the age of 10 months. He received 1 unit every 3-4 weeks on regular basis. He has family history of similar conditions.





- **requiring blood transfusion→low Hb, has family history of similar conditions and since young age→inheritance**
- **DX:Thalassemia:**
- **Thalassemia syndromes are a group of hereditary disorders characterized by a genetic(mutation) leading to deficiency in the synthesis of globin chains.**
- **One of the hemoglobinopathies diseases leading to premature destruction of RBC, Autosomal recessive, with 2status: carrier, affected.**
- **Hemoglobin electrophoresis is used as a screening test to identify normal and abnormal hemoglobins and assess their quantity**
- **Hemoglobin, a tetramer protein that comprises 4 globin chains bound to the heme molecule. There are 4 major types of globins: alpha (a), beta (B), gamma (y), and delta (8). The dominant hemoglobin in adults (hemoglobin A) is composed of 2 alpha and 2 beta chains.**

❖ **Notes:**

- **premarital tests are important to prevent having a child with this disease rather than to deal with its complications and treatment.**

- **People who depend on regular blood transfusion are called (transfusion dependence) and it indicates significant anemia that cannot be corrected in any other method.Also, those patients suffer from repeated transfusions complications such as increasing iron overload in the body which leads to transfusional hemosiderosis.**

Abnormal face features (as a result of prematurely RBC destruction -the RBCs aren't surviving their normal life span- then the bone marrow tries to

produce more abnormal cells to compensate by increasing RBC production leading to bone marrow expansion which

- **is explaining the abnormality in face features (Maxillary prominence)-trying to increase quantity, but quality is affected-**

- **Looking at his blood film in the right image above You can see cells that are:**

- **microcystic**
- **hypochromic (the pale areas more than 1/3 of the RBCs, less Hb)**
- **aniopoikilocytosis (significant variations in the RBCs size and shape**
- **You can see elliptocytes as well and**

- **This disease doesn't affect WBCs or platelets, the abnormality in Hb.**

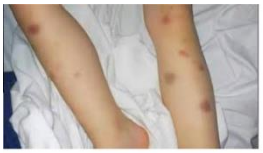
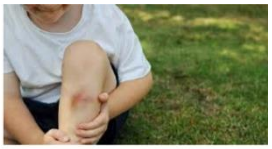
❖ **What are the causes of RBC premature destruction?**

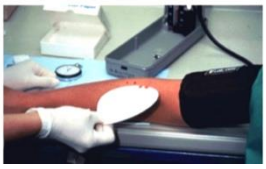
- **Extrinsic causes-not related directly to RBC-: immune response, infection, splenomegaly, portal hypertension.**
- **Intrinsic causes-related directly to RBC (hematological conditions):**

1- **Hb abnormalities in synthesis or production-as seen in this scenario.**
2- **RBCs enzyme deficits**
3- **RBC structural deficits**

CASE 2

• A 9-year-old girl presents with bleeding gums and bruises. The symptoms are recurrent. She also has episodes of nose bleeds. She has an older brother who has similar symptoms.



• She was assessed by her primary care doctor who is referring her to haematology department. -indicating severity-

symptoms are recurrent: → (so there is a problem because the case symptoms aren't self-limiting and aren't temporarily produced by having infection or transient effect of something), several types of bleeding: (bleeding gums, bruises, nose bleeding) → they don't happen due to local effect such as infection in the gum or trauma to the nose , family history →inheritance, also you can observe the pattern of inheritance -both she and her brother are affected so it is not x-linked disorder-

DX: Von Willebrand Disease

- **It's the most common, inherited, genetically and clinically heterogeneous hemorrhagic disorder characterized by defective (VWF) caused by a deficiency or dysfunction of the protein.**
- **VWF, a large, multimeric glycoprotein that is released from storage granules in platelets and endothelial cells. It performs two major roles in homeostasis. First, it mediates the adhesion of platelets to sites of vascular injury-important in the primary homeostasis-**
- **Second it binds and stabilizes the procoagulant protein factor vIII-preventing it from being lost in urine-**
- **Normal platelets count**
- **It has 3 types, differs in etiology (qualitative or quantitative) and in the pattern of inheritance.**
  A. **Type 1: quantitative, autosomal dominant**
  B. **Type 2: qualitative**
  C. **Type 3: quantitative (very sever deficiency of the factor), autosomal recessive-very rare-**

❖ **notes:**

- **Normally, Bruises are more likely to be seen at the areas that exposed to traumas or minor injury such as upper and lower limbs.**
- **easy bruisability defined as (having more than 5 bruises each at the size of 1cm or more), this is the definition, but you don't have to have this situation to suspect a bleeding disorder, bruises at areas other than extremities for example: the trunk or other protected areas applies more significance.**
- **The patients usually bleed from skin, nose, ladies complain of heavy menstrual cycle leading to secondary anemia.**
- **The test to go for to diagnose this disease →bleeding time test:**
- **Very reliable test to assess platelet's function.**
- **they make a small cut with standard size and depth on the lower arm, they put sphygmomanometer of the arm then they inflate it to certain degree then they observed the time, because There is a time after which they would say this is abnormal, its subjective to different interfering things because it depends on Operation, patient situation...**

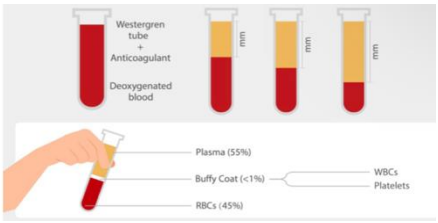
The phenotype of bleeding here → (<u>mucocutanieous</u> form of bleeding which is related to platelet disorders)

CASE 3

- **A 68-year-old male is presented with back pain for the last 3 months. The pain is located in the lower part and is worsening over the last few weeks. He has hypertension which is controlled on 2 medications. You find him pale by examination, but he has no motor or sensory weakness in his legs. Blood tests show anemia with high ESR.**

➢ **the last 3 months→ acquired, worsening over the last few weeks→ progressing, pale→ anemia, high ESR**

❖ **notes**

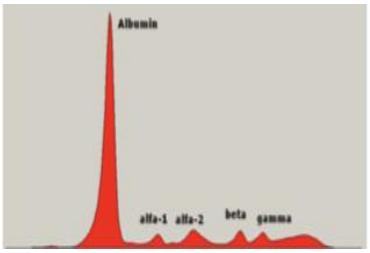


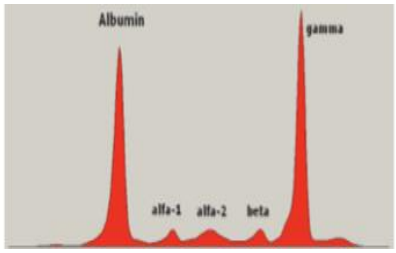
➢ **<u>ESR (erythrocyte sedimentation rate):</u>**

- **It's a nonspecific test where a tube containing blood+anticoagulant is put vertically and left to set, so the RBC will sediment in the bottom with time, to finally report the rate of sedimentation rate after 1 hour**
- **It's measured by ml/hour.**
- **Usually, its related to age and gender**
- **The upper limit of normal value for ESR:**
  - **Age/2 →males**
  - **(Age+10)/2 →females**
  - **Very high ESR >100 or 120 mm , associated with certain medical conditions.**
- **High ESR that indicates the presence of abnormal proteins in the blood secondary to infection, acute or chronic inflammation, Connective tissue disease, RA, IBD, malignancies interferes with the sedimentation of RBC .**
- **Anemic with↑ESR, and back-pain should let you think of disease associated with abnormal proteins in his blood interfering with sedimentation**

The second test is protein electrophoresis

- The serum is put between Negative and positive charges, observing how the proteins travel from one side to another, the proteins would travel depending on its physical features(protein net charge) depending on the sum of A.A making the protein and notice that Every protein has a unique charge



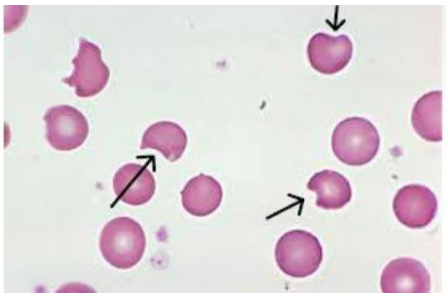


- Normally albumin is the main protein in our blood, it would show as peak sharp because it travels in a unique way .
- normal situation (left side)
- On the right side -abnormal one- you can see another sharp peak and this indicates another protein having unique features.
- Note that When there's inflammation you tend to see proteins of different types-multiple proteins- making a dome like peak, not a sharp peak (due to reactive reasons)
- but in this case it's a sharp peak(positive screening test) indicating a monoclonal protein, coming from monoclonal cell (due to malignant reasons)
- **DX:multiple myelomas:**
- **a malignant disease of the bone marrow in which there is a monoclonal proliferation of plasma cells.**
- **The plasma cells produce large amount of protein(immunoglobulin) detected by electrophoresis. (>3-5%)**
- How do we confirm the disease? By demonstrating that the bone marrow has this excess of plasma cells, also you can study the immunoglobulin chains then asset your patient for other symptoms of this disease such as (anemia, hypercalcemia, impaired renal function, lytic bone lesions leading to fracture)

CASE 4

• A 24 year old male. Presents with new onset yellowish discoloration of sclera with exertional fatigue and shortness of breath. Urine is very dark. Patient was normal before attack. He had fava bean 1 day before onset of symptoms.

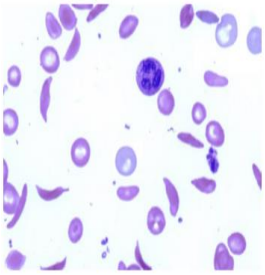
• Findings: Pallor, Jaundice (yellowish discoloration), Abnormal red cells on blood film

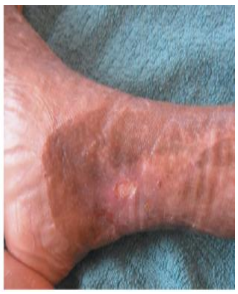


- **exertional symptoms(Dizziness, brain fogginess, inability to concentrate, fatigue, weakness , headache palpitations): all are symptoms caused by anemia due to hypoxia, and if they are sever they can faint, in order to compensation the body starts increase the cardiac output so they will develop a tachycardia, also to increase oxygen delivery they start to increase their respiratory rate leading to shortness in breath.**
- **This is Hemolytic anemia related to fava beans ingestion, Hemolysis due to intrinsic causes**
- **DX: Glucose-6-phosphate dehydrogenase (G6PD) deficiency:**
- **Episodic acute hemolytic anemia following exposure to triggering factors.(infection, keto acidosis, certain drugs, fava beans -in this case-**
- **The most common ezymatic disorder of red blood cells, affecting 400 million people worldwide-African, mediterranean, Asian ethnicity are more susceptible -**
- **Inherited as X-linked recessive disease. The gene for G6PD is located on the X-chromosome with more than 150 variants identified associated with variable degree of hemolytic severity**
- **The disease makes RBC more susceptible to hemolysis secondary to oxidative stress**
- **In the blood film: Denatured hemoglobin forms inclusions called: Heinz bodies in red cells. Such cells get recognized by macrophages in the spleen where the precipitate and a small piece of the membrane gets removed, leading to characteristic bite cells, these cells usually presents during acute hemolytic attacks caused by a trigger**

- Heinz bodies are stained with supravital stain (like methylene blue)

CASE 5





•A 20 year old female college student presents with acute pain in the back, shoulder and extremities. She reports this is not the first time; attacks are more frequent in cold and stressful conditions.

• On a previous occasion, she was admitted with respiratory symptoms and had her blood exchanged.

• Findings: Pallor, Jaundice, Underweight, Skeletal abnormalities (medullary and epiphyseal infarction, dactylitis, marrow hyperplasia), Leg ulcers, Abnormal red cells on blood film

❖ Notes:

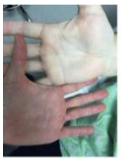
- There are 2 types of blood transfusion : (top-up transfusions, Exchange transfusion-in this case-)

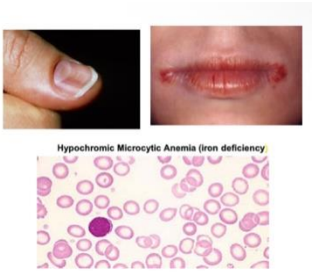
Most blood transfusions involve adding blood or blood products without removing any component of patient's blood, these are also known as top-up transfusions. Exchange transfusion is used in the treatment of a number of diseases, including sickle-cell disease by extracting patient's RBCs and keeping the plasma only, (separating blood components by centrifugation), replacing patients RBCs with healthy donor RBCs.

- There is also plasma exchange which is more common with other different diseases.
- DX:Sickle cell disease: (common in Africa, another hemoglobinopathies disease along with thalassemia)
- An inherited -autosomal recessive-chronic hemolytic anemia with different clinical manifestations arising from the tendency of hemoglobin to deform red blood cells into the characteristic sickle shape. -There are Sickle cell disease patients and asymptomatic carriers-
- This property is due to a single nucleotide change in B-globin gene leading to substitution of valine for glutaminc acid at position 6 of the B-globin chain.
- Clinical Features:

- **Anemia, Acute painful episodes, Abnormal growth and development, Infections, Neurological manifestations, Pulmonary complications, Sickle cell retinopathy and nephropahty, Leg ulcers**
- **The most common crisis in this case is simple pain crisis(bone pain secondary to Vaso-occlusive crisis, leads to ischemia and necrosis to bone cortex)**
- **The patients experience recurrent episodes of acute sickeling leading to different manifestations depending on the organ being mainly involved**
- **It usually occurs secondary to hypoxia-due to infection, excessive exercise, anesthesia-**
- **The image above shows the sickle cell shape (crescent).**

CASE 6





• A 29 year old housewife presents with exertional fatigue, shortness of breath and palpitations. This started few months ago but is progressive. She had 3 complete pregnancies in the last 5 years. Her menstrual blood loss is heavy. She has no bleeding or infective symptoms. Her diet sounds balanced, and she has no nausea, vomiting or altered bowel habits.

• Findings: Pallor, Hair loss, Koilonychia, Angular stomatitis, Abnormal red cells on blood film, these symptoms are related to IDA not anemia in general.

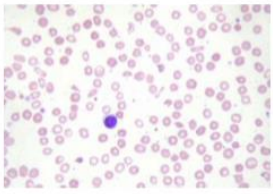
- **Pregnancy: increased iron demand, Heavy menstruation: increased iron loss**
- **Microcystic hypochromic cells as seen in the blood film.**
- **General note for you to remember: the patient tells you the symptoms, you observe and see the signs**
- **DX: Iron deficiency anemia.**
  - **Causes of iron deficiency anemia: 1-excess Blood loss(chronic long-term bleeding like: menorrhea , vWf disease ,hemorrhoids, diverticulosis, ulcers or malignancies of GI tract), 2-increased demand, 3-dietary reasons (the heme iron -from animal sources- is absorbed more easily than the non-heme iron),4-decreased absorption(like: decreased stomach acidity, H-pylori gastritis ,excess use of anti-acids, celiac disease due to duodenal villous**

atrophy , the removal of duodenum and stomach in bariatric surgeries.

- IDA should always be referred to a cause-in this case its increased demand and blood loss

CASE 7

• A 62 year old retired engineer. He has new symptoms of exertional fatigue and shortness of breath. This started around 2 months ago. He also noticed a change in his bowel habits recently and thinks he is losing weight.



• He is not vegetarian and his diet sounds balanced.

- Findings: Pallor

DX: Iron deficiency anemia

- IDA should always be referred to a cause-in this case its decreased absorption-not dietary reasons-.
- What is the next thing to do?

➢ We should perform Endoscopy(camera test) it is likely to be bleeding secondary to GI tract malignancies, and iron supplements should be given, the underlying cause should be treated.

CASE 8

• A 42 year old female with history of surgery done 10 years ago for morbid obesity (gastric by pass) presents with exertional fatigue and shortness of breath. She reports some mental sluggishness and inability to walk normally. Her family think she is becoming depressed and more forgetful. She is not attending her scheduled clinic visits and not taking her prescribed medications.

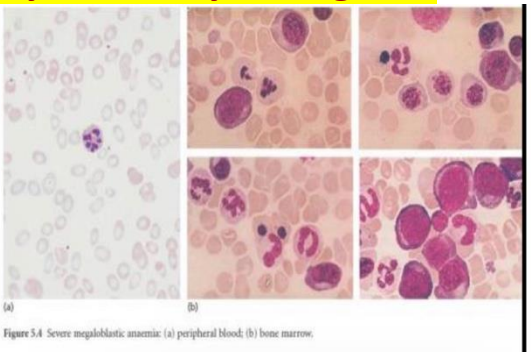


Figure 5.4 Severe megaloblastic anaemia: (a) peripheral blood; (b) bone marrow.

Findings: Pallor, Mild jaundice, Symmetric paresthesia/numbness Shuffling gait

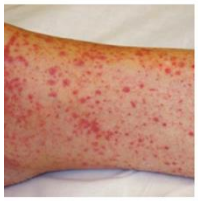
What is the next thing to do?

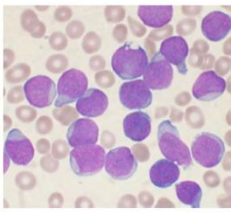
➢ surgery done 10 years ago for morbid obesity→ a risk factor

- **prescribed medications→ all gastrectomy or bypass patients will be put in a certain medications because they should receive the vitamins in regular basis.**
- **DX: megaloblastic anemia caused by Vitamin B12 deficiency:**
- **The main causes of B12 deficiency are:**
  1- **dietary (like in vegetarians or vegan)**
  2- **malabsorption (like pernicious anemia which is autoimmune disease attack the parietal cells of the stomach, and selective malabsorption with proteinuria)**
  3- **Gastric causes: congenital intrinsic factor deficiency or functional abnormality and total or partial gastrectomy.**
  4- **Intestinal causes: intestinal stagnant loop syndrome (jejunal diverticulosis ,ileocolic fistula, anatomical blind loop, intestinal stricture) ,ileal resection and Crohn's disease.**
  5- **Tropical sprue ,transcobalamin deficiency ,fish tapeworm**

- **B12 is important in DNA synthesis and the health of neurons(the neurological conditions usually start with symmetrical and bilateral paresthesia that can involve lower limbs then progress to loss of function for the vibratory sensation and loss of proprioception for the lower limbs :so that B12 deficiency leads to anemia and neuropathy.**
- **Notice the blood smear above:**
  macrocytic cells (asynchronous maturation between the nucleus and cytoplasm), also hypersigmented neutrophils(its nucleus has more than 5 segments it is another term that is seen in all stressed erythropoiesis in general).
  -Due to anemia they will have low hemoglobin, in sever B12 deficiency, they may have hemolysis leading to ineffective erythropoiesis and hematopoiesis leading to intramedullary destruction ,so you need to treat them as soon as you suspect the condition because the neurological damage can be irreversible.

CASE 9





- A 64 year old lady presents with acute onset of symptoms that started one week ago:

- Fatigue, Palpitations, Shortness of breath, Fever, Cough with sputum, Gum bleeding, Skin bruising

No previous episodes and no family history of similar conditions

Findings: - Pale, Documented fever(it is measured) Skin bleeding (Ecchymosis, petechial rash), Abnormal blood film and bone marrow, Bone marrow is hypercellular and replaced by abnormal cells

- Cough with sputum→WBC problem, Gum bleeding and Skin bruising→ platelets problem
- When you find the combination of anemia, bleeding and infection symptoms, you must think about bone marrow problems (the bone marrow fails to produce the end products of hematopoiesis).
- Causes of Bone marrow failure:
- 1-infiltration by abnormal cells (in this case)
- 2-Reduced production
- You can see thrombocytopenic rash(pinpoints reddish spots usually present in the extremities like in the anterior aspects of the legs ,but unusual in the side and trunk) and bruising due to problems in their platelets either quantitative or qualitative problems.
- Look at her blood film: there are Immature large cells abnormal and non-condensed nuclei (high nuclear cytoplasmic ratio),the bone marrow is infiltrated with blasts .
- DX: acute leukemia