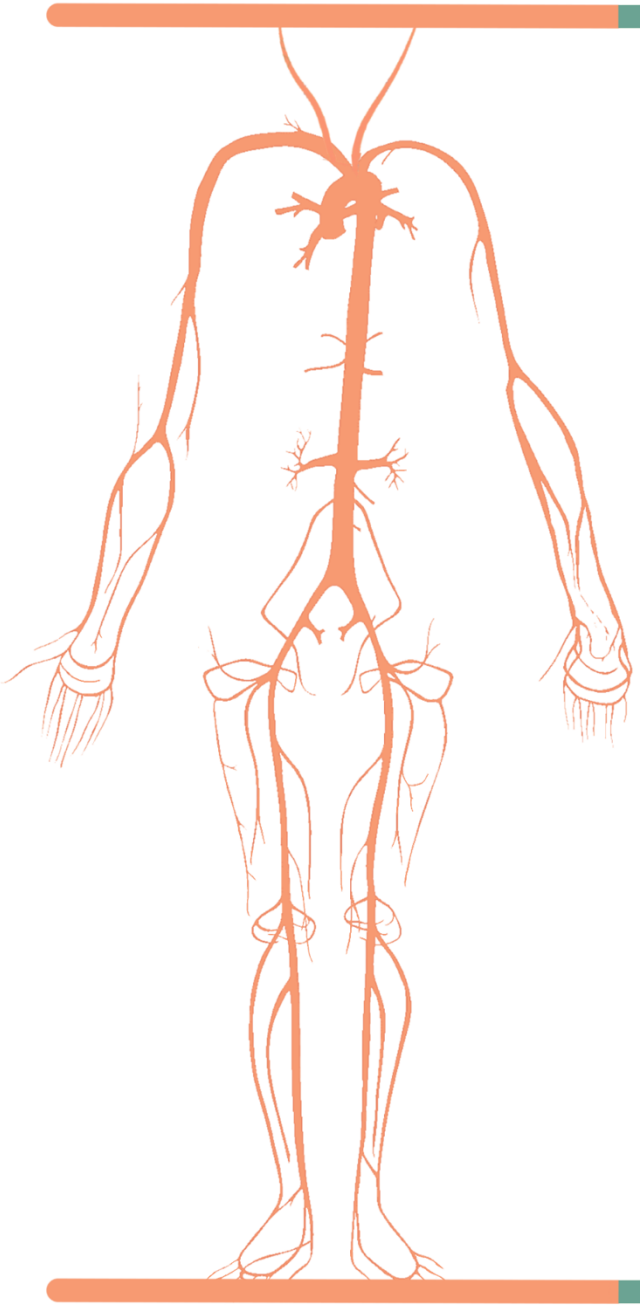
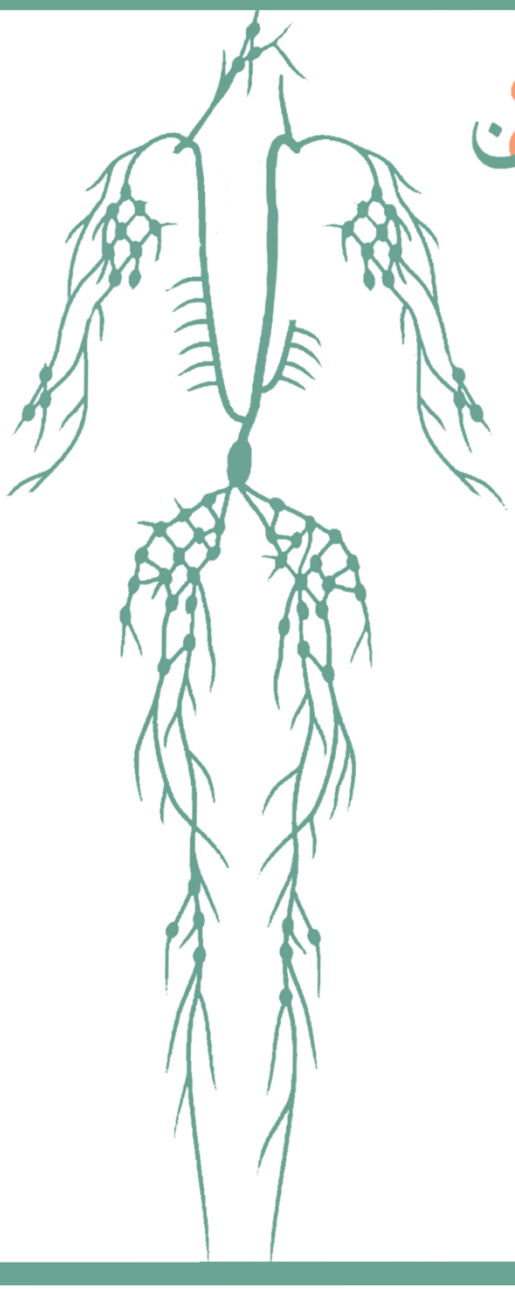
PBL

HematoLymphatic





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Hello everybody!

It's nice to catch u up guys ✨; this document is a simplified conversion of the 2 PBL lectures, we saw that it would be more efficient to unite them..SoOo forgive us for the delay if u've been waiting 🤦 🏻; we will depend on lecture two time schedule to section this script. The hints added by the doctor during the case review will be highlighted by red.

The main purpose of these lectures is to manifest some clinical cases in order to create a link between the knowledge we've acquired during the system & the practical usage of them 📎.

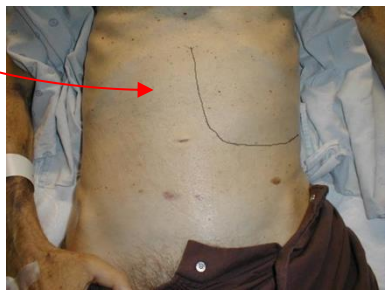
Now, with the name of Allah the most merciful the most compassionate let's start our journey.

Case 1 00:23

A 19-year-old male college student. Presents with history of yellowish discoloration of sclera (jaundice), exertional fatigue and shortness of breath. Additionally, there is left sided abdominal pain**. He has family members with similar symptoms**.

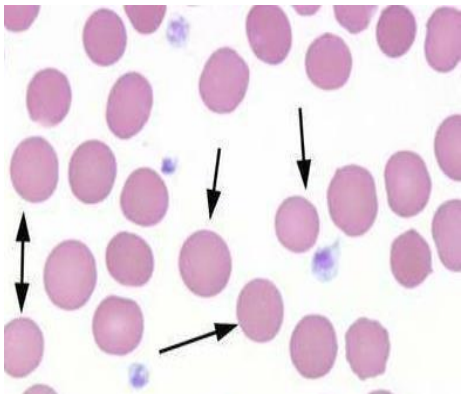
It could be **inherited**! Do u think symptoms are suggesting a sort of Anemia?

- Physical examination findings:
  - Pallor (this might confirm what we're thinking about Anemia).
  - Jaundice (yellowish discoloration) =of the sclera & the skin.
  - Splenomegaly (enlarged spleen) which explains the left upper abdominal pain.
  - Abnormal red cells on blood film.



- Laboratory findings:

Abnormal RBC's; spherical RBC's lacking the central pallor & the biconcave shape.



- Diagnosis:

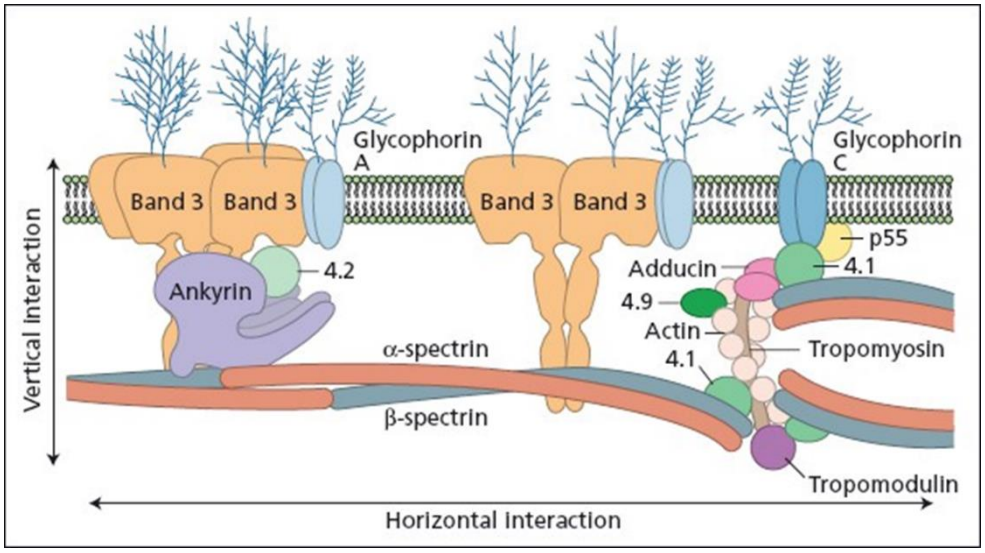
The Anemia related symptoms alongside the left upper abdominal pain (splenomegaly) suggests a congenital hemolytic type of anemia.

As you know the hemolytic anemia could be either **acquired** or **inherited**, occurring due to **RBC's related factors** (plasma membrane abnormality, enzymopathies...), or due to **external-RBC's unrelated-factors.**

Some conditions may result in the presence of **spherocytes** in the blood film, but not in that percentage that we see in this case. So, our patient diagnosis is:

Hereditary spherocytosis

- ✓ A familial hemolytic disorder of red cell membrane. Generally inherited as an autosomal **dominant** disease; so we expect to see lots of family members with the same manifestations.
- ✓ There is a genetic heterogeneity of the disease; meaning that affected patients will experience different levels of severity, and this is reflected in the clinical presentation.
- ✓ The main site of red cell destruction is the spleen (extravascular form of hemolysis), so the spleen size reflects the intensity of the disease-with the consideration of other symptoms of course-.



This figure shows the normal arrangement of RBC membrane proteins; around 60% of the cases are caused by defects in the **SPECTRIN_ANKYRIN complex**. The rest of the cases involve a **BAND 3/PROTEIN 4.2** deficiencies. Either ways we will end up with rigid cells lacking elasticity with a higher susceptibility to lysis.

The disease diagnosis is confirmed by **Osmotic Fragility Test;** in which we incubate the RBC's in saline's with different tonicities; as u know in a low tonicity solution the water will start to get inside the RBC's causing them to swallow. Normal RBC's will bear the swelling for a long time increasing in size continuously before getting burst. In contrast to the anemic cells that will erupt on a **higher** salt concentration (less tolerance). When plotting the tonicity (on X axis) & the amount of lysed cells (on Y axis) you'll find the curve of spherocytosis shifted to the **right**.
or we can confirm it by identification of protein abnormalities or gene defects.

Case 2 07:10

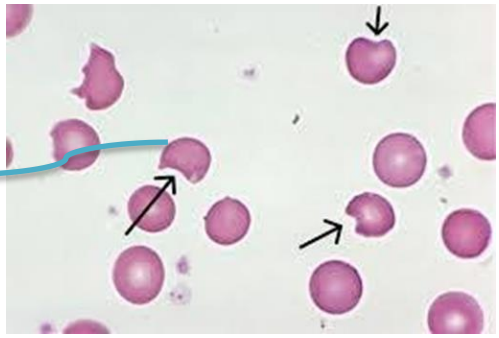
A 24-year-old male. Presents with new onset yellowish discoloration of sclera (jaundice) with exertional fatigue and shortness of breath (Anemia). Urine is very dark. Patient was normal before attack (sudden onset of a condition that was enriching or not causing issues before).**He had fava bean 1 day before onset of symptoms**.

When we have JUANDICE we should mainly think of hemolytic anemia; why? I think u know the answer.

- Physical manifestations:
  - Pallor.
  - Jaundice (yellowish discoloration).

- Laboratory findings:

Abnormal red cells on blood film (there's some defect in the RBC's membrane as they appear bitten; it's characterized by paroxysmal presentation of hemolytic attacks//the ingestions of fava beans will result of another form of abnormal RBC's.



- Diagnosis:

As the patient is getting back to his normal state after the shutting of the attack then symptoms must be caused by a trigger, in this case the fava beans ingestion.

The diagnosis is **Glucose-6-phosphate dehydrogenase (G6PD) deficiency**; one of the most common enzymopathies that leads to inherited hemolytic anemia; affecting 400 million people worldwide.

- ✓ The disease is Inherited as **X-linked recessive** disease (thus males are affected & females are asymptomatic carriers usually). The gene for G6PD is located on the X-chromosome with more than 150 variants identified (ex. Mediterian variant) associated with variable degree of hemolytic severity as each mutation have a different effect on the enzyme activity.
- ✓ G6PD catalysis the first step of the pentose phosphate pathway which is the major generator of reducing power within red cells. Oxidative stress that exceeds red cell ability leads to **acute hemolysis and anemia** in affected patients as the oxidative reactants build up in the cells causing the Hb to become denatured & the enzyme activity to get reduced.
- ✓ The denatured hemoglobin forms **Heinz bodies** in red cells (remember we use a **supra-vital stain** to see them). Such cells get recognized by macrophages in the

spleen where the precipitate and a small piece of the membrane gets removed (partial engulfment), leading to characteristic **bite cells** on standard blood film.

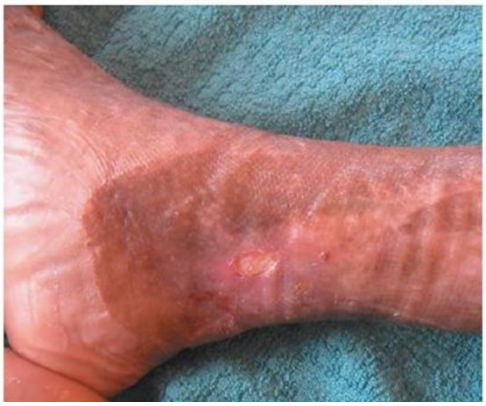
The patients constantly need to be admitted to the hospital for monitoring & for supportive measures such as blood transfusion during the attacks.

Case 3 12:18

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 (like cold weather) and stressful conditions (there is some presetting factors for such attaches). On a previous occasion, she was admitted with respiratory symptoms and had her blood exchanged.

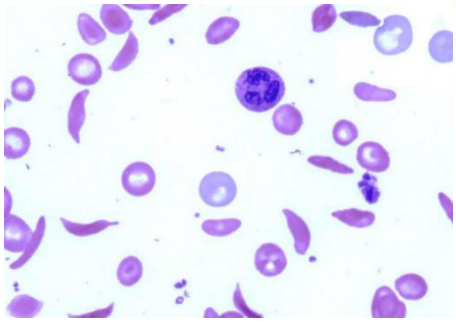
So: she had some severe forms of this attack which required her to be admitted into the hospital & needed blood transfusion leading to some skeletal abnormalities with repeated attacks of pain in the back & shoulders.

- Physical manifestations:
  - Pallor Jaundice.
  - Underweight.
  - Skeletal abnormalities (medullary and epiphyseal infarction (total BM infraction), dactylitis, marrow hyperplasia).
  - Leg ulcers.
  - Abnormal red cells on blood film.



- Laboratory findings:

We see abnormal sickled (bout/crescent) cells appearance alongside the **polychromasia** that indicate **reticulocytosis**.



Diagnosis:

The patient is showing a classic history of **Sickle Cell Anemia** which is one of the congenital hemoglobinopathies **(autosomal recessive)** that leads to chronic hemolytic anemia.

- ✓ The disease is mainly with different clinical manifestations arising from the tendency of hemoglobin to deform red blood cells into the characteristic sickle shape. This property is due to a **single nucleotide change** in B-globin gene leading to substitution of **valine** for **glutamic acid** at position 6 of the B-globin chain.
- ✓ The clinical features of the affected people are widely variable, they suffer from Anemia, Acute painful episodes due to the repeated sickling that triggers the hypoxia, Abnormal growth and development, Infections, Neurological manifestations **[as the microvasculature of the brain & CNS will be affected by the repeated vaso-occlusive crisis's]**, repeated Pulmonary implosions (complications) **[which lead to pulmonary hypertension that can result in heart cor pulmonale failure]**, Sickle cell retinopathy and nephropathy **[because of the sickling effect on the knee]**, Leg ulcers because of the **venous insufficiency.**

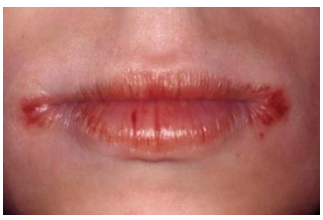
The attacks experienced by the patient can be due to infection, dehydration, extraneous exercise or even smoking as they induce a hypoxia state.

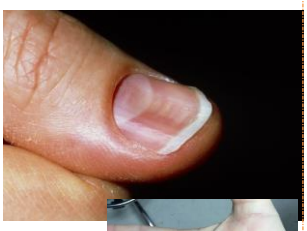
Case 4 16:44

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** (no signs of BM failure-no leukopenia, no cytopenia). Her diet sounds balanced and she has no nausea, vomiting or altered bowel habits.

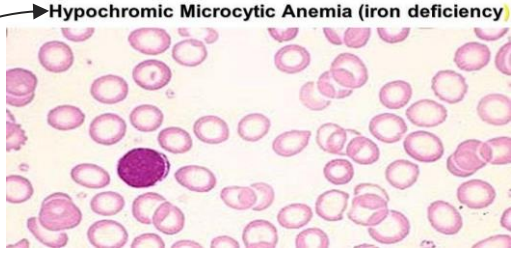
Physical findings:

- Pallor Hair loss.
- Koilonychia in the nails.
- Angular stomatitis.
- Abnormal red cells on blood film.





Laboratory findings:



Diagnosis:

Iron deficiency anemia secondary to the increased blood loss in the heavy menstruation & increased consumption of iron stores during pregnancies.

- ✓ Our normal total amount of iron is around **3000-4000mg**, **2500mg** are used in the RBC'S Hb, **500-600mg** in the reticuloendothelial stores, & we lose about 1-2mg that should be compensated from the diet.
- ✓ Each pregnancy consumes around **500mg** of iron, so if there weren't enough time between pregnancies to maintain iron amounts anemia would presume.

Causes of iron deficiency anemia:

- ✓ **Blood loss** from the Genitourinary System or the upper/lower GIS, & rarely from congenital bleeding disorder that come in the form of recurrent episodes of anaphylaxis/gum bleeding.
- ✓ **Increased requirements** [pregnancy, adolescence].
- ✓ **Diet** [the usual balanced diet should be sufficient].
- ✓ Malabsorption; any problem in the first 2 parts of the duodenum/distal stomach affects the iron absorption leading to IDA.

Case 5 23:18

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 (which may indicate blood lost from the GI tract) recently and thinks he is losing weight.

He is not vegetarian, and his diet sounds balanced.

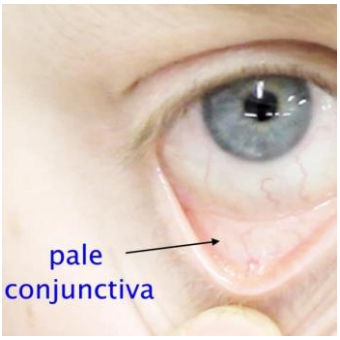
➢ Physical manifestations:

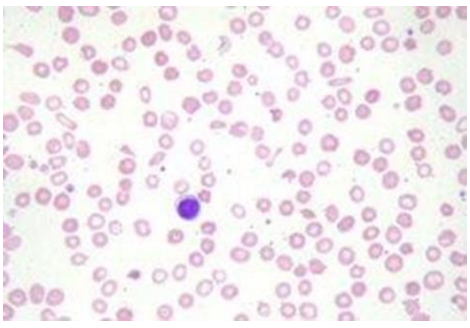
- Pallor. Hypochromia, microcytosis & anisocytosis.

laboratory manifestations:

Diagnosis:

We're suspecting **IDA**; the altered bowel habits suggest **bleeding** of the GI tract so we should do a colonoscopy & endoscopy for the upper & lower GI.





Case 6 26:09

A 42-year-old female with history of surgery done 10 years ago for morbid obesity (bariatric surgery; resection of the stomach), (gastric bypass) 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 (neurological symptoms in addition to anemia onset). She is not attending her scheduled clinic visits and not taking her prescribed medications (she's not compliant with her treatment so she's at increased risk of having anemia).

- Physical manifestations:
  - Pallor.
  - Mild jaundice.
  - Symmetric paresthesia/numbness Shuffling gait (neurological symptoms).
- Laboratory findings:

We're seeing a hyper-segmented neutrophil that have more than 5 lobules, in addition to asynchrony between the cytoplasm & the maturation of the nucleus indicating the hallmark of megaloblastic anemia.

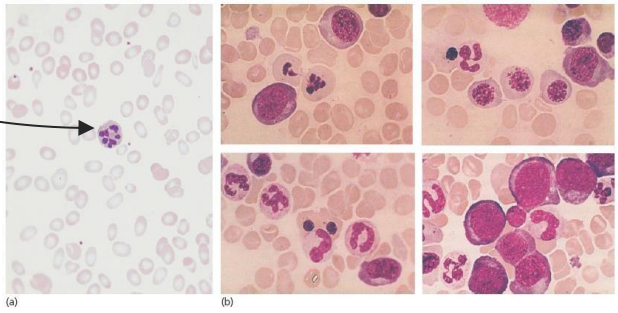


Figure 5.4 Severe megaloblastic anaemia: (a) peripheral blood; (b) bone marrow.

Diagnosis:

We must suspect **vitamin B12 deficiency anemia** as we are seeing **neurologic symptoms** alongside the anemia indications accompanied with a risk factor of vitamin B12 insufficiency.

- ✓ The main causes are dietary and malabsorption problems. In addition to anemia, neurological symptoms can occur and should be corrected as soon as possible once the disease is suspected; we do the tests & start the treatment before getting the results.
- ✓ Such symptoms can occur regardless of the presence of anemia with the company of a risk factor such as **dietary insufficiency**, **risky medications** (that causes vit. B12 malabsorption), or it's happening in **elderly people** who have low ability to absorb the vitamin from animal products [specially meat], or even **gastric resection** like in our patient case.
- ✓ In severe cases, ineffective erythropoiesis and hemolysis occur [intramedullary hemolysis] & we should see jaundice.

Gastric surgeries are highly risky as the patients lose the **intrinsic factor** assessing in the vitamin absorption.

Notes//

- ✓ Any problem in the ilium is going to affect the vitamin as it's the main site of its absorption.
- ✓ Pernicious anemia is an autoimmune disease that targets the parietal cells/the intrinsic factor.

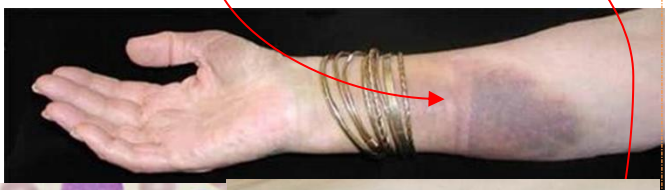
Table 5.5 Causes of cobalamin deficiency causing megaloblastic anaemia.

Nutritional
Vegans
Malabsorption
Pernicious anaemia
Gastric causes
Congenital intrinsic factor deficiency or functional abnormality
Total or partial gastrectomy
Intestinal causes
Intestinal stagnant loop syndrome: jejunal diverticulosis, ileocolic fistula, anatomical blind loop, intestinal stricture, etc.
Ileal resection and Crohn's disease
Selective malabsorption with proteinuria
Tropical sprue
Transcobalamin deficiency
Fish tapeworm

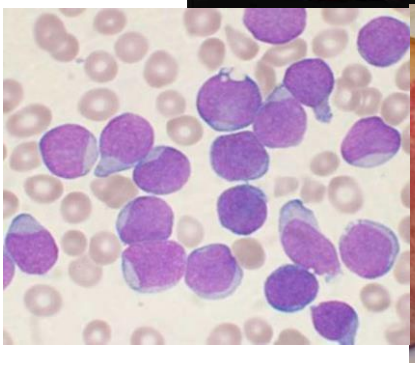
Case 7 31:46

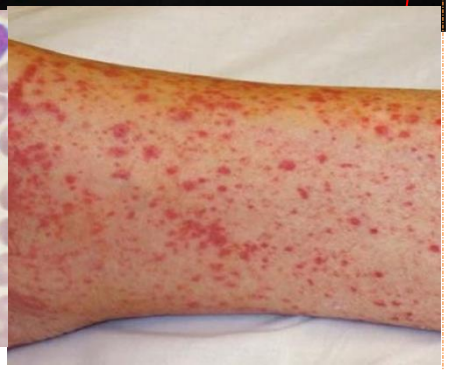
A 64-year-old lady presents with acute onset of symptoms that started one week ago. Fatigue, Palpitations, Shortness of breath, Fever, Cough with sputum, Gum bleeding & Skin bruising (these symptoms create a suspension of having an anemia with abnormal white functioning white blood cells with low platelets count). She didn't have any previous episodes and no family history of similar conditions.

- ➢ Physical manifestations:
  - Pale.
  - Documented fever.
  - Skin bleeding (Ecchymosis bruises, petechial rash)[when u see these bleeding bruises u think of platelets dysfunctioning or a low platelets quantitative disorder which indicates a PRIMARY HEMOSTATIC DEFECT] .
  - Abnormal blood film and bone marrow.
  - Bone marrow is **hypercellular** and replaced by abnormal cells.
- ➢ Laboratory findings:



We're seeing high nuclear-cytoplasm ratio, premature nuclei, open (non-condensed) chromatin & large cells.





- ❖ The mucocutaneous bleeding suggests a primary hemostatic defect; the platelet quality disorder.

Diagnosis:

we're viewing cells that don't usually exist in the BM; which is a condition resulting from the BM being replaced by abnormal cells that dominate on the resources & potential of the BM preventing it from producing healthy cells; these new cells could be hematological/ non-hematological cells that infiltrate to enter the BM.

- ✓ The triad of anemia, infection and bleeding suggests pancytopenia (BM failure). In this case, pancytopenia is due to replacement of normal bone marrow by abnormal immature cells (blasts) indicating presence of acute myeloid leukemia.

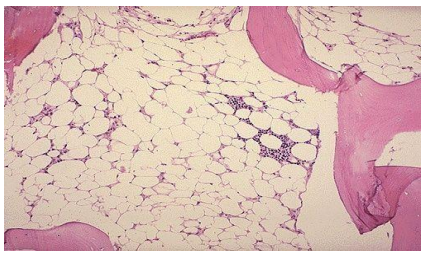
-Acute leukemias are either **myelocytic** or **lymphocytic**. Differentiating both conditions clinically can be challenging & sometimes non possible, so certain additional tests are needed to do so.

- ❖ This patient needs treatment of her infection after determining her type of leukemia, support by blood and platelets and needs to start treatment with chemotherapeutic agents appropriate for her disease.

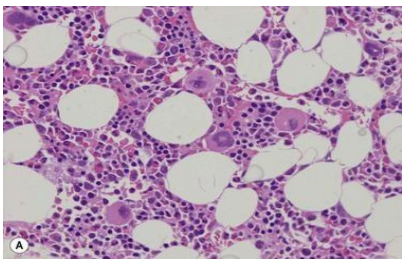
Case 8 35:41

A 40-year-old gentleman presents with acute onset of symptoms that started one week ago: Fatigue, Palpitations, Shortness of breath, Fever (Anemia symptoms), Gum bleeding & Skin bruising (which show a BM WBC's, Platelets production failure). No previous episodes and no family history of similar conditions.

- ➢ Physiological manifestations: (acute symptoms)
  - Pale.
  - Documented fever.
  - Skin bleeding (Ecchymosis, petechial rash).
  - Blood film showing reduced cell numbers but **no abnormal cells** (not showing the blasts).
  - Bone marrow is markedly **hypocellular** (meaning that there aren't enough precursor cells in the BM thus inability to produce adequate no. of cells suggesting pancytopenia).
- ➢ Laboratory findings:



Abnormal BM with only 5-10% cellulated regions.



Normal BM with 80% hematopoietic areas.

BM failure + anemia symptoms + infection= leukopenia.

These situations may also proceed in the case of sever leukemia as u'll have functional neutropenia/leukopenia as the produced WBC's will be **immature** =unfunctional.

Diagnosis:

We're viewing another collection of clinical symptoms suggesting **pancytopenia** with different findings in the bone marrow & blood film. The bone marrow is hypocellular or aplastic. This is seen in **aplastic anemia** which can be inherited or acquired.

- ✓ The severity of aplastic anemia depends on **the residual cellularity in the examined bone marrow** and **the degree of the peripheral pancytopenia present.**
- ✓ If severe disease present, this patient treatment options includes immunosuppression or hematopoietic stem cell transplant. Chemotherapy **isn't** indicated as compared to acute leukemia. Steroids **should** also be **avoided** as they increase the risk of infections (especially fungal ones) in these patients who already have neutropenia.

Case 9 40:45

A 7-year-old boy presents with swollen knee of few days' duration. This **is not the first time** it happens. Both knees and ankles are affected but **his right knee is affected most**. Symptoms start by feeling of **hotness in the joint** followed by swelling, pain, reduced ability to move the joint (impairing its flexion & extension) and hot skin.

His mother reports he bled abnormally after circumcision (notice she had a form of bleeding other than the one happening inside the joint-**HEMARTHROSIS**-). He has not had any surgical procedures done (we don't have any clue if he would bleed after a surgery). His mother thinks that some of her family members had similar symptoms (the patient might have some maternal relatives with the same condition).

➢ Physical manifestations:

- Swollen knee (with effusion-most likely secondary to the blood presence inside the joint-) accompanied with hotness and reduced movement (range of motion of the joint).

Diagnosis:

The muscles atrophy around the knee indicate **lack of exercising the joint; inability to move the joint.**

Our diagnosis is Hemophilia; a **congenital** bleeding **X- linked recessive** disease, affecting males more than females. It leads to low coagulation factors (FVIII(factor 8) in hemophilia A and FIX(factor 9) in hemophilia B). Type A hemophilia is much more common; for each **5** cases of A hemophilia we have **1** B hemophilia case.

- ✓ The disease is usually inherited; but sporadic cases (without family history, presumed due to a new mutation) is also common [about 1/3 of the cases].

- ✓ Symptomatic patients are usually those with severe disease (have a factor level <1%); they'll have a non-triggered (without a challenge) bleeding which suggest a bleeding possibility after surgeries & procedures.
- ✓ Increased bleeding episodes mainly affecting **load- or strain-bearing joints** (ankles, knees, and slightly elbows). Recurrent bleeding in particular joints leads to joint deformities and disabilities because it's happening in the dependent limbs; this will end up by having target joints affected more than the others. Other forms of bleeding include large muscular bleeding and less commonly urinary or CNS bleeding.

  - ❖ Patient with severe disease should be treated with **replacement therapy**. Factor VIII or IX should be given as prophylaxis in order to keep level between **5-30%** as this would prevent most bleeding episodes. Additional doses may be needed to treat breakthrough bleeding or before and after surgical procedures.

This can vary according to the patient's lifestyle and the level of physical activity.

<<وينبَغِي لِمَن كَان صادِقَ الرَّغبَةِ، قَوِيَّ الفَهمِ، ثاقِبَ النَّظَرِ، عزِيزَ النَّفسِ، شَهمَ الطَّبعِ، عالِيَ الهِمَّةِ، سَامِيَ الغَرِيزَةِ: أن لا يَرضَى لِنفسِهِ بِالدُّونِ، ولا يَقنَع بِما دُونَ الغَايةِ، ولا يَقعُد عَنِ الجِدِّ والاجتِهَادِ المُبَلِّغَينِ لهُ إلى أعلَى مَا يُرادُ وأرفعُ ما يُستفَاد؛
فَإنَّ النُّفُوسَ الأبِيَّةَ والهِمَمَ العَلِيَّةَ لا تَرضَى بِدُونِ الغَايَةِ في المَطَالِبِ الدُّنيَوِيَّةِ مِن جَاهٍ أو مَالٍ أو رِئَاسَةٍ أو صِنَاعَةٍ أو حِرفَةٍ؛ حتَّى قالَ قائِلُهُم:

إذَا غَامَرتَ في شَرَفٍ مَرُومٍ
فَلا تَقنَع بِمَا دُونَ النُّجومِ

فَطَعمُ المَوتِ في أمرٍ حَقِيرٍ
كَطَعمِ المَوتِ في أمرٍ عَظِيمِ

وإذا كان هَذا شَأنُهُم في الأمُورِ الدُّنيَوِيَّةِ الَّتِي هِيَ سَرِيعَةُ الزَّوَالِ قَرِيبَةُ الاضمِحلَالِ؛ فكيفَ لا يَكُونُ ذلِكَ مِن مطَالِبِ المُتوجِّهِينَ إلى مَا هُوَ أشرَفُ مطلَبًا، وأعلى مكسَبًا، وأرفَعُ مُرَادًا، وأجلُّ خطرًا، وأعظَمُ قدرًا، وأعوَدُ نفعًا، وأتمُّ فائِدَةً وهِيَ المَطالِبُ الدِّينِيَّة؟
فَأكرِم بِنفسٍ تطلُبُ غَايَةَ المَطَالِبِ في أشرَفِ المكَاسِب، وأحبِب بِرَجُلٍ أرَادَ مِنَ الفضَائِلِ مَا لا تُدانِيهِ فضِيلَةٌ، ولا تُسَامِيهِ مَنقَبَةٌ ولا تُقَارِبُهُ مكرُمَةً>>.
-الشَّوكَانِيُّ -رَحِمهُ اللهُ-.
[أدَبُ الطَّلبِ ومُنتَهَى الأربِ || ٨٨]