PBL

Hematolymphatic System

Sheet No. 1+2

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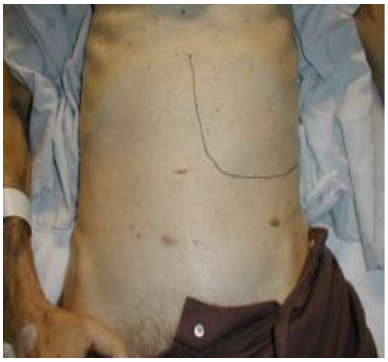
Problem based learning

Before you start ^_^:

*Doctor's notes are in *italic* *findings are physical examination findings and blood smears *We start always with history then physical examination then we start investigating to confirm diagnosis.

Case 1:

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



• **Findings**:

Pallor

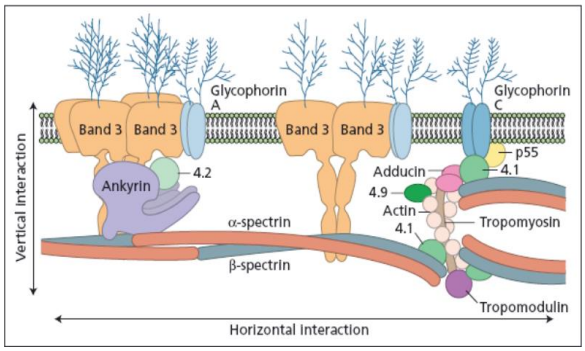
Jaundice (yellowish discoloration)

Splenomegaly (enlarged spleen)

Abnormal red cells on blood film

• **Hereditary spherocytosis**: A familial hemolytic disorder of red cell membrane. Generally inherited as an autosomal dominant disease The patient presents with mild anemia and jaundice, with a modestly enlarged spleen. There is a genetic heterogeneity of the disease and this is reflected in the clinical presentation.

✓ The main site of red cell destruction is the spleen so the spleen size reflects the severity of hemolysis.
✓ In addition to the clinical features described above, the blood film shows small spherocytic red cells lacking area of central pallor
✓ Arrangement of RBC membrane proteins. 60% of HS cases result from a defect in ankyrin-spectrin complex. The reminder involve a deficiency in band 3 or protein 4.2.
✓ *Severity of HS depends on the type of cytoskeleton protein mutated.*
✓ *Removing the spleen in some of these patients will help them to not have regular blood transfusion.*
✓ *Severity of symptoms depends on degree of anemia and physical activity.*



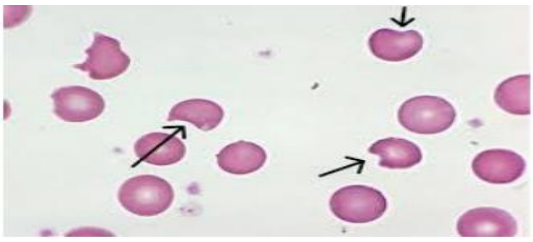
✓ *Other anemia symptoms that the patient would present with: chest pain, presyncopal feeling, flu like symptoms.*
✓ *The weaker the patient is(cardiac, pulmonary problems ,etc..) , the worse the symptoms.*
✓ *Jaundice + anemia= hemolytic anemia(extravascular). Remember: hemolysis is either intravascular or extravascular, and it is either acquired or congenital.*
✓ *Family history= think of hereditary and congenital diseases.*
✓ *Request reticulocytes count and blood film/smear.*

• Diagnosis is by Osmotic fragility test or by identification of protein abnormalities or gene defects.

Case 2:

• 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

• **Glucose-6-phosphate dehydrogenase (G6PD) deficiency:** Episodic acute hemolytic anemia following exposure to triggering factors. The most common enzymatic disorder of red blood cells, affecting 400 million people worldwide. 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.

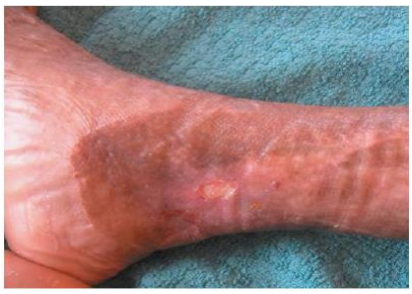
G6PD catalyzes the first step of the pentose phosphate pathway which is the major generator of reducing power within red cells. Oxidative stress that exceeds red cell ability leads to acute hemolysis and anemia in affected patients.

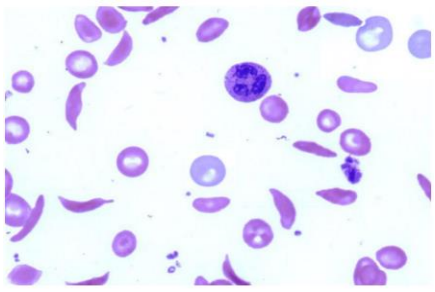
- ✓ Denatured hemoglobin forms Heinz bodies in red cells. Such cells get recognized by macrophages in the spleen where the precipitate and a small piece of the membrane gets removed, leading to characteristic bite cells on standard blood film.
- ✓ *G6PD deficiency is characterized by intermittent episodes of hemolysis.*
- ✓ *Hemolysis is triggered by certain medications, dyes, fava beans.*
- ✓ *Heinz bodies are stained with supravital stain.*
- ✓ *Treat acute hemolysis as acute bleeding.*

CASE 3:

• 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

• **Sickle cell disease**: An inherited chronic hemolytic anemia 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.

- ✓ *It is an autosomal recessive disease. RBC's polymerize due to hypoxia (sickling) which is responsible for many crises. Sickle cell disease patients and carriers are protect from p.falciparum malaria.*
- ✓ *The crisis in this case is simple pain crisis(bone pain secondary to vaso-occlusive crisis, leads to ischemia and necrosis to bone cortex) which is very common.*
- ✓ *SC disease causes acute chest syndrome –medical emergency-, nephropathy, retinopathy, stroke, increase susceptibility to encapsulated microorganisms.*
- ✓ *Screening is very important → by electrophoresis, to measure the physical properties of a patient's hemoglobin.*
- ✓ *Thalassemia also needs electrophoresis (recall thalassemia types). Premarital test is very important. Thalassemia major patients need blood transfusion which lead to accumulation of iron in them (hemochromatosis/hemosiderosis secondary to transfusion). This affect organs and expose them to blood borne infections.*
- ✓ *Spleen function is impaired in sickle cell disease which leads to autosplenectomy.*
- ✓ *Any patient with chronic hemolysis is at increased risk to develop folate deficiency.*

• **Clinical Features**: Anemia, acute painful episodes, abnormal growth and development, infections, neurological manifestations, pulmonary complications, sickle cell retinopathy and nephropathy, leg ulcers.

Hematinics: are nutritional components that are required for hemoglobin synthesis. (Iron, folic acid, B12).

CASE 4:

• 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**:

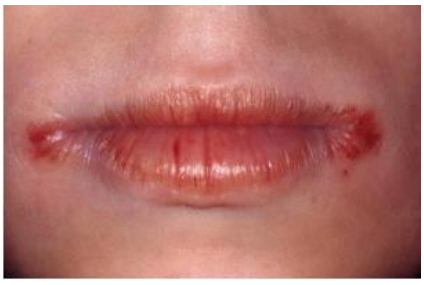
-Pallor

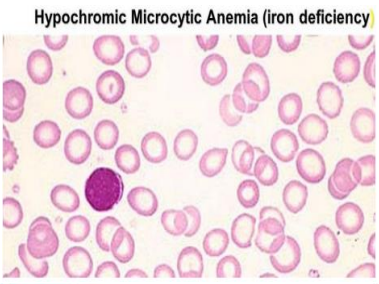
-Angular stomatitis

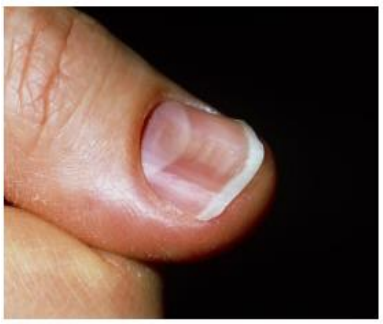
- Hair loss

-Koilonychia (spooning of fingernails)

-Abnormal red cells on blood film







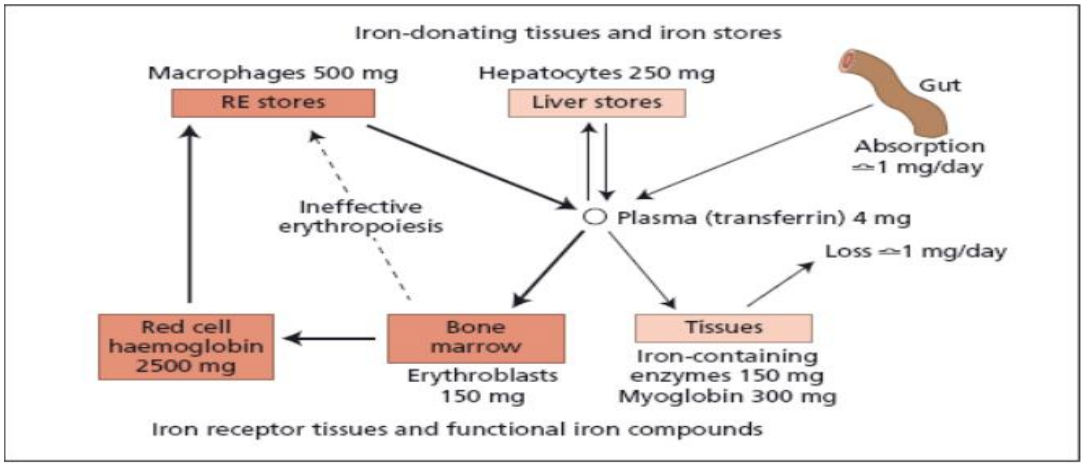


Figure 3.1 The major compartments of iron in a 70-kg man. Iron supply for erythropoiesis and release of iron from senescent red cells dominate internal iron exchange. RE, reticuloendothelial.

Figure from Postgraduate Haematology, 6th ed 2011

DX: Iron deficiency anemia

• Causes of iron deficiency anemia:

Blood loss | **Increased requirements** | **Diet** | **malabsorption**

- *Diet caused IDA is common in developing countries.*
- *40-50% of women in child-bearing age are iron deficient.*
- *Heme iron comes from meat products, not affected by acidity, easily absorbed.*
- *Non heme iron is not easily absorbed it needs to be converted.*
- *Daily requirement is 1 -3 mg so we need to ingest at least 15 mg of iron from diet, because it's not all absorbed.*
- *Vegetarians and vegans need to take supplements.*
- *(Using antacids a lot + surgeries+ H.Pylori+ celiac disease+ gastric cancers) leads to malabsorption → IDA*
- *Diverticulitis, menorrhagia and bleeding tendency patients lead to blood loss.*
- *Increased demand → multiple pregnancies within short time, growing.*
- *IDA should always be referred to a cause.*

CASE 5:

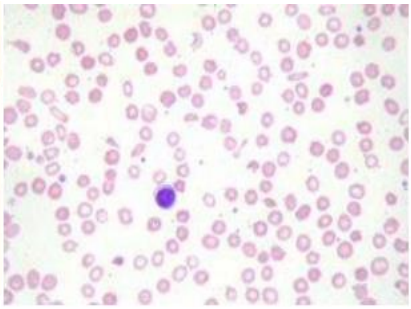
• A 62-year-old retired engineer. He has new symptoms of exertional fatigue and shortness of breath. This started around 2 months ago. He also noticed a change in his bowel habits recently and thinks he is losing weight.

• He is not vegetarian and his diet sounds balanced.

• **Findings**: Pallor

What is the next thing to do?

Dx: Also **iron deficiency anemia**.



CASE 6:

• A 42-year-old female with history of surgery done 10 years ago for morbid obesity (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. She is not attending her scheduled clinic visits and not taking her prescribed medications.

• Findings:

Pallor

Mild jaundice

Symmetric paresthesia/numbness

Shuffling gait

What is the next thing to do?

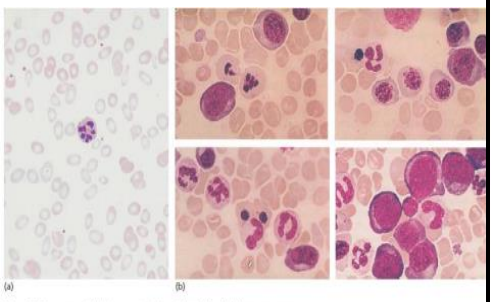


Figure 5.4 Severe megaloblastic anaemia: (a) peripheral blood; (b) bone marrow.

• **Vitamin B12 deficiency**: Main causes are dietary and malabsorption. *And some medications like metformin and colchicine.*

- ✓ *B12 needs to be disassociated from animal protein by saliva first.*
- ✓ *There's no condition that increases demand for B12.*
- ✓ *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.*

In addition to anemia, neurological symptoms can occur and should be corrected as soon as possible once the disease is suspected. Such symptoms can occur regardless of presence of anemia.

In severe cases, ineffective erythropoiesis and hemolysis occur.

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

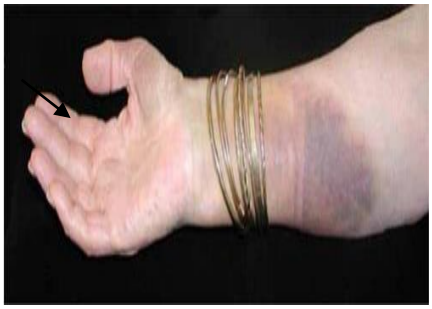
- ✓ *Folate deficiency could be caused by malabsorption, lack of dietary intake and some drugs like phenytoin and methotrexate.*

The next 2 cases are related to bone marrow failure which is divided to either infiltrating cells, hematological or non-hematological cells, or hypo productive bone marrow

And we can have clinical bone marrow failure like signs but it is caused by peripheral destruction of cells

These are causes of pancytopenia.

CASE 7:• 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**:

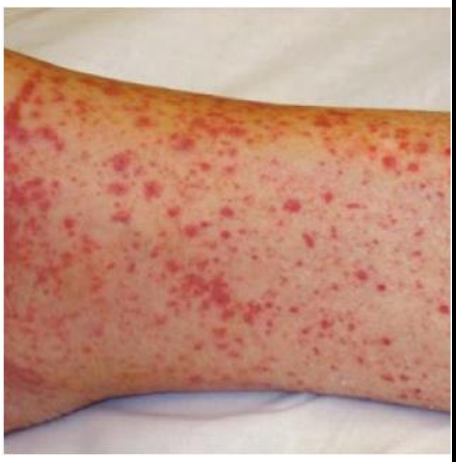
- Pale

- Documented fever

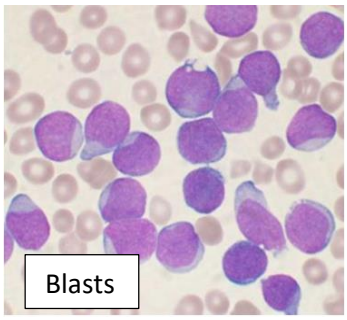
- Skin bleeding (Ecchymosis, petechial rash)

- Abnormal blood film and bone marrow

- Bone marrow is hyper cellular and replaced by abnormal cells



The triad of anemia, infection and bleeding suggests **pancytopenia.**



- ✓ Reduced hematopoiesis
- ✓ Low platelets, low RBCs but high WBCs.

• In this case, pancytopenia is due to replacement of normal bone marrow by abnormal immature cells (blasts) indicating presence of **acute leukemia.**

• Acute leukemia is either myelocytic or lymphocytic. Differentiating both conditions clinically can be difficult and certain additional tests are needed to do so.

• This patient needs treatment of her infection, support by blood and platelets and needs to start treatment with chemotherapeutic agents appropriate for her disease.

CASE 8:

A 40-year-old gentleman presents with acute onset of symptoms that started one week ago:

- Fatigue - Palpitations - Shortness of breath - Fever - Gum bleeding - Skin bruising No previous episodes and no family history of similar conditions

• **Findings**:

- Pale

- Documented fever

- Skin bleeding (Ecchymosis, petechial rash)

- Blood film showing reduced cell numbers but no abnormal cells.

- Bone marrow is markedly hypocellular

• Another collection of clinical symptoms suggesting pancytopenia with different findings in the bone marrow.

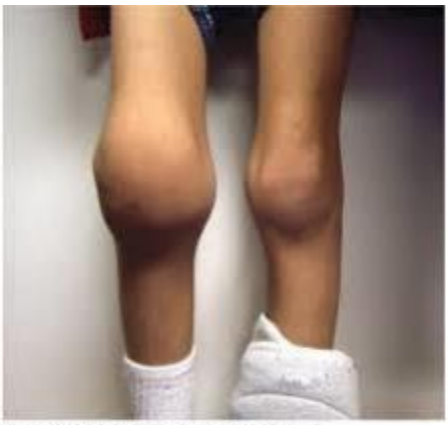
• The bone marrow is hypo cellular or aplastic. This is seen in **aplastic anemia** which can be inherited or acquired.

• The severity of aplastic anemia depends on the residual cellularity in the examined bone marrow and the degree of pancytopenia present.

• If severe disease present, this patient treatment options includes immunosuppression or hematopoietic stem cell transplant. Chemotherapy or steroids are not effective.

CASE 9:

• 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 and hot skin. • His mother reports he bled abnormally after circumcision. He has not had any surgical procedures done. His mother thinks that some of her family members had similar symptoms.



• Findings: - Swollen knee (with effusion) with hotness and reduced movement.

• **Hemophilia X- linked recessive disease** leading to low coagulation factors (FVIII low in hemophilia A and FIX low in hemophilia B) The disease is usually inherited but sporadic cases (without family history, presumed due to a new mutation) is also common. *History is very important to determine the pattern of bleeding and what to expect.*

• Symptomatic patient are usually those with severe disease (Factor level <1%).

- *Most common bleeding disorder is Von Willebrand disease. Form of bleeding here is mucocutaneous.*
- *Acquired bleeding disorders(caused by drugs like anti-platelets) are more common than congenital.*
- *Platelet count , platelet receptors, von willebrand factor are all very important.*
- *We have qualitative and quantitate platelet disorders*

• Increased bleeding episodes mainly affecting load- or strain-bearing joints (ankles, knees, and elbows). Recurrent bleed into particular joints lead to joint deformities and disabilities. Other forms of bleeding include large muscular bleed 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. • This can vary according to patient life style and level of physical activity • Additional doses may be needed to treat breakthrough bleeding or before and after surgical procedures

019 final exam questions:

Q1. 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 and hot skin. Choose the wrong statement:

Answer: Bone marrow examination

Q2. Wrong complication of Iron deficiency anemia?

Answer: Leg ulcer

Q3. Not seen in Vitamin B12 deficiency: Answer: Menorrhagia

Good luck