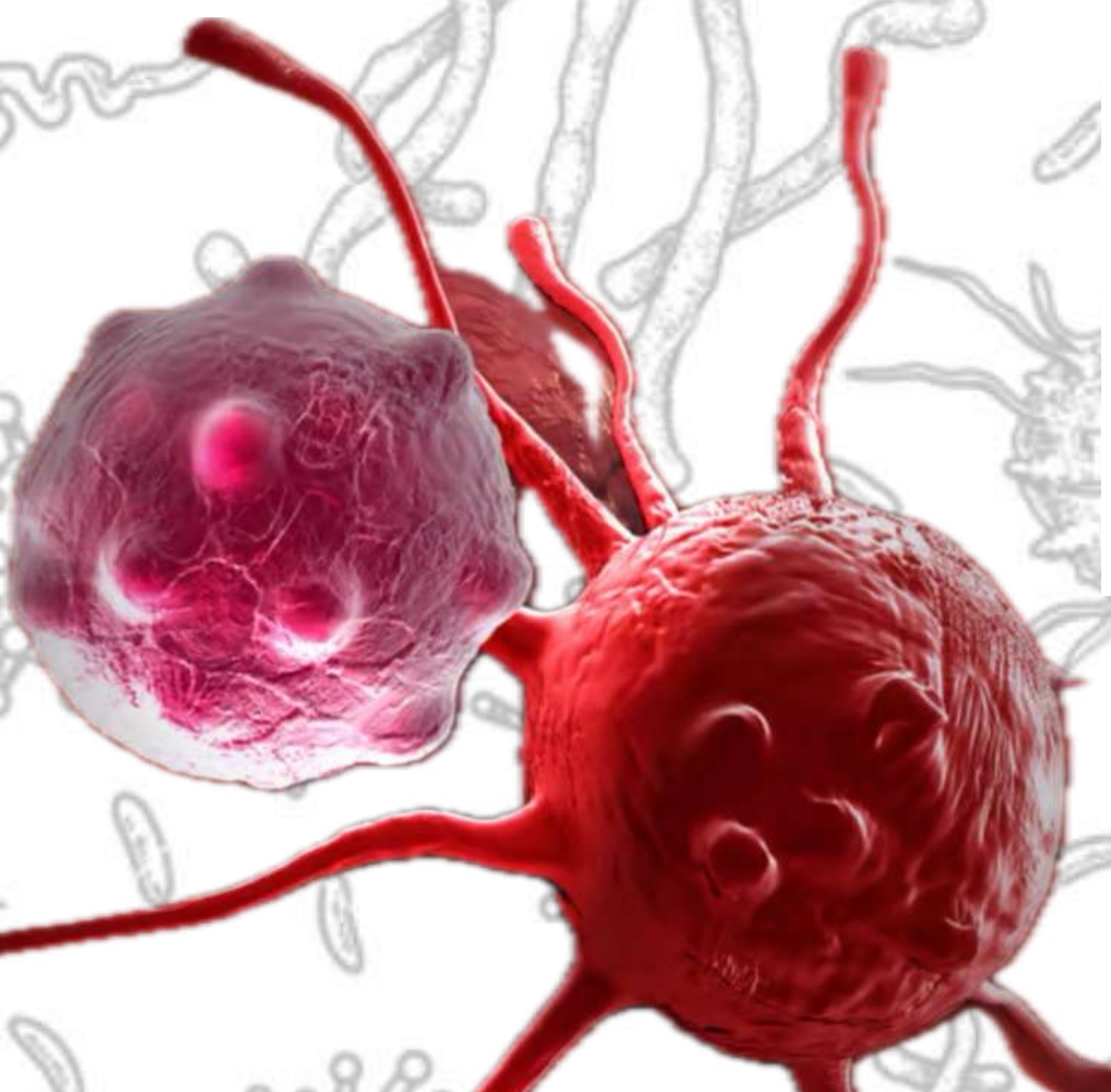
النادي الطبي

الفريق العلمي

HLS PATHOLOGY Summaries



DONE BY :

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Introduction

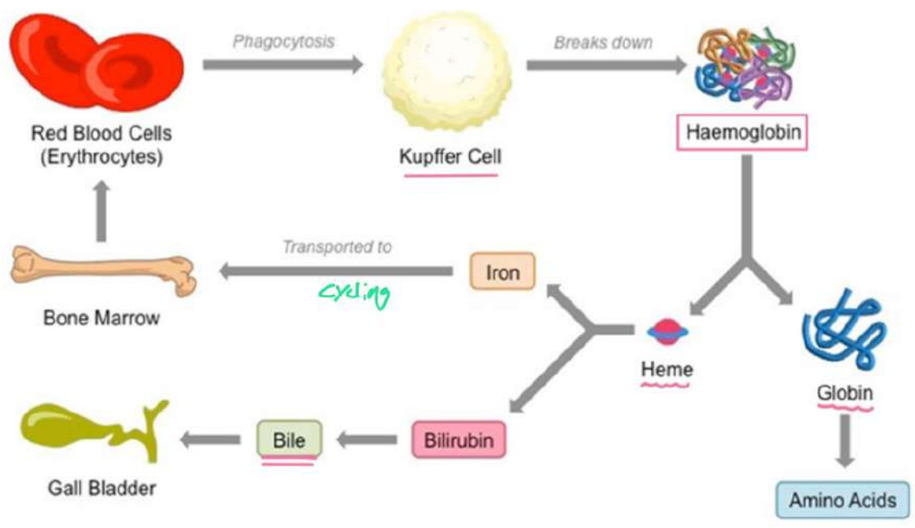
- Hematopoiesis in adults occurs mainly in the bone marrw can also occur outside the bone marrow (spleen & liver). This is termed extramedullary hematopoiesis

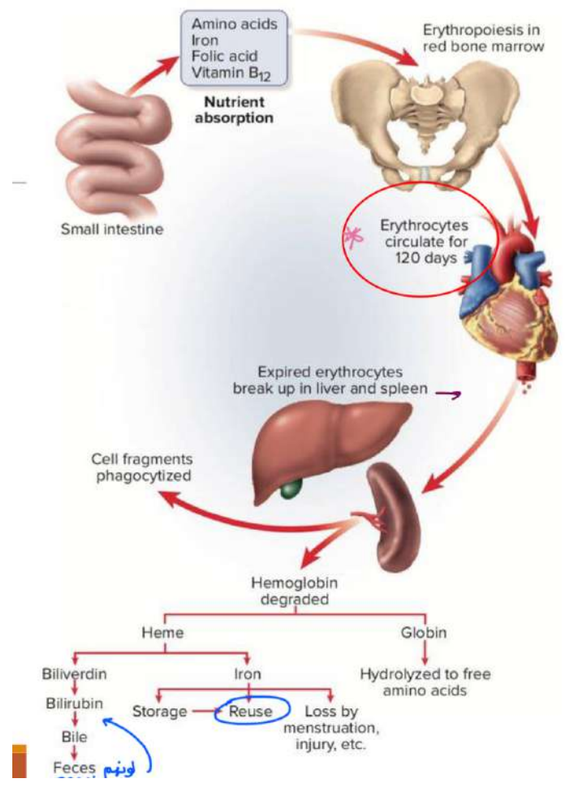
-Erythropoiesis is the process which produces red blood cells (erythrocytes) … stem cell to mature red blood cells

-DNA synthesis requires B12 and folate ; erythropoietin, thyroid , and androgens are crucial for RBC production; iron incorporation is essential too; deficiencies lead to anemia.

-Hb = Heme + globin (2a,2B)

- Life cycle of RBC :





Anemia

- Anemia : reduction in the oxygen transporting capacity of blood … RBCs ⬇️

- In males: Hb<13 g/dl , In females: Hb<12 g/dI … CBC عن طريق فحص ال

- Anemia Clinical cues : Jaundice, gallbladder stones, red urine…anemia due to hemolysis

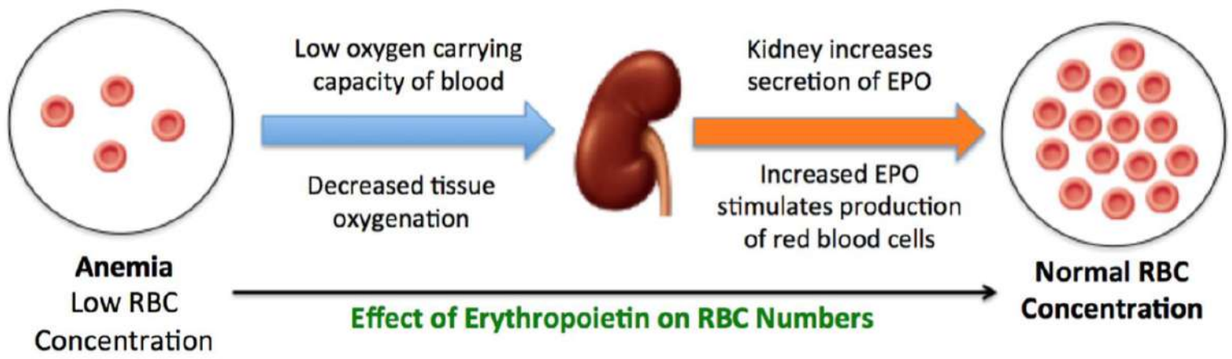
-Anemia workup : CBC ,blood smear

Complete Blood Count

- **RBC Count:** the number of RBCs per unit of volume
- **Hematocrit:** is a measure of the proportion of blood that is composed of red blood cells.
- **Mean Corpuscular Volume (MCV):** The average size of the red blood cells.
- **Mean Corpuscular Hemoglobin (MCH):** The average amount of hemoglobin per red blood cell
- **Mean Corpuscular Hemoglobin Concentration (MCHC):** The average amount of hemoglobin in a given volume of red blood cells.
- **Red Cell Distribution Width (RDW):** The variation in size of red blood cells in a sample

- MCH : Hyperchromic (Hb⬆️) , Normochromic , Hypochromic (Hb⬇️)
-MCV : Macrocytes , Normocytes , Microcytes
-The lower the hemoglobin level, the paler the RBCs appear, and vice versa.

- Body response to anemia :



- Reticulocytes : immature RBCs , remains in BM for 2 Day

- Reticulocytosis reflects marrow response to anemia

- Retic count ⬆️ ..... BM response to increase hymolysis or acute / chronic blood loss ... effictive erythropoiesis ✅

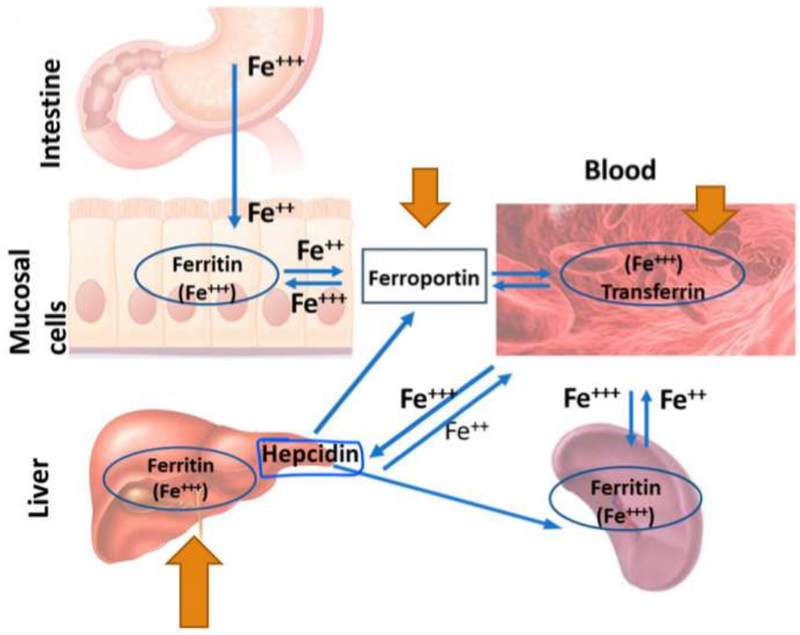
-Retic count ⬇️ ..... defective BM ..... ineffictive erythropoiesis ❌

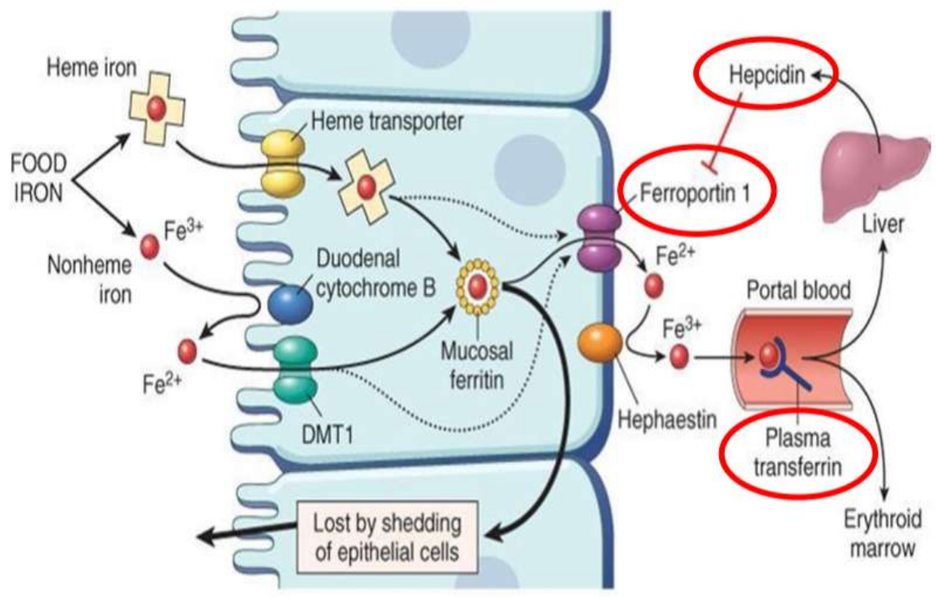
Microcytic anemia

-RBC is produced from subsequent division of erythroblasts, and during Hb deficiency, Hb⬇️ erythroblasts divides too much. As a result, RBCs become small and microcytic anemi occurs

1- IRON Deficiency anaemia

-Review of normal iron metabolism :





- 1 in every 3 transferrin in blood is bound to Fe.

-Hepcidin , it interacts with ferroportin, and inhibits iron absorption

-Causes of Iron deficiency anemia:
Malnutrition , Malabsorption, Increased demand, Chronic blood loss (menorrhagia) and GIT bleeding

-IDA is a chronic process :
Initially normal RBCs are produced (Normochromic Normocytic)
Later, decreased iron transport to bone marrow (microcytic hypochromic)

-Fe lab measurement:

- **Serum Fe** – measures Fe in blood (most of it is bound to transferrin) ⬇️
- **TIBC (total iron binding capacity)** – tells total transferrin in blood. Normally, 1 in every 3 transferrin in blood is bound to Fe. ⬆️

- **% saturation** – % saturation of transferrin by Fe ⬇️
- **Serum ferritin** – indication of how much Fe is in storage sites ⬇️

- **When ferritin↓, TIBC ↑ and vice versa**

-Blood smear:
Poikilocytosis (variable shapes), anisocytosis (variable size), cigarette-shaped RBC , pencil cell

-Clinical presentation:
with long-standing severe anemia spooning" of the fingernails sometimes appears. Also called Koilonychia (spoon shaped nails), Sometimes Pica ,Glossitis and angular stomatitis

- Treatment : iron supplementation

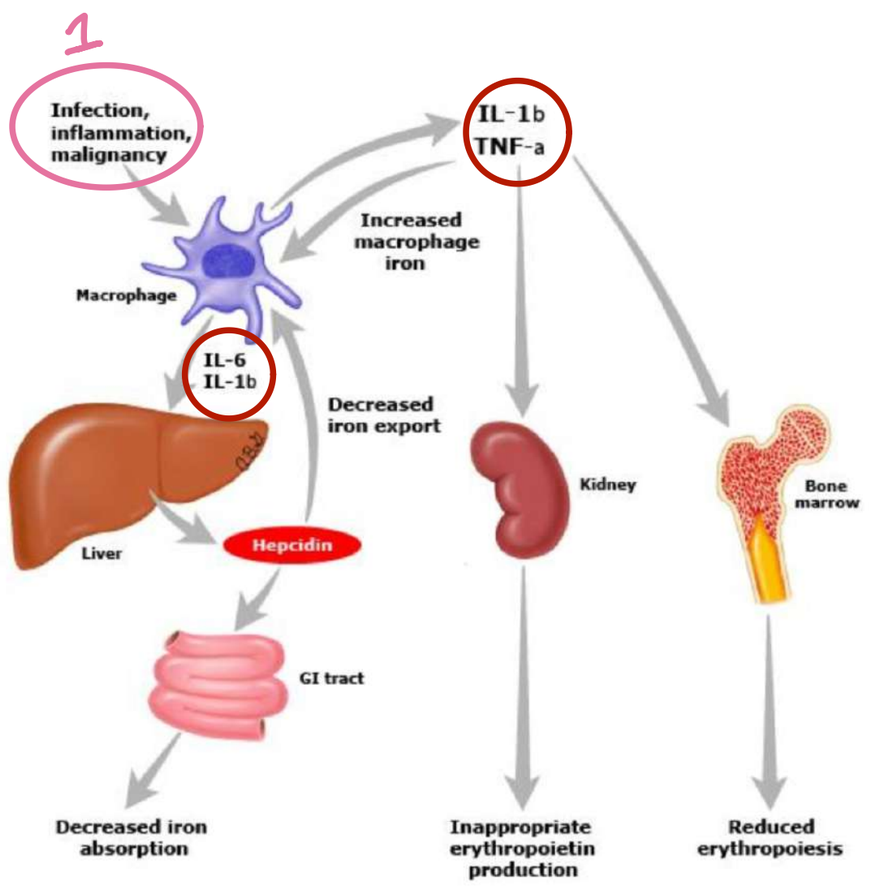
2-Anemia of chronic disease/anemia of inflammation:

-most common anemia in hospitalized patients

-during ACD acute phase proteins are produced an example is Hepcidin ,hepcidin reduces plasma iron levels

-advantage of Hepcidin is that bacteria need Fe to grow and flourish.

-Mechanism for ACD/AI:



-Lab findings in ACD:

	Iron Deficiency	AOCD
Serum iron	↓	↓
TIBC	↑	↓
% saturation	↓	↓
Serum ferritin	↓	↑

-Treatment of ACD:

Exogenous erythropoietin

3- Thalassemia:

-caused by mutations that decrease the rate of synthesis of α- or β globin chains.

-deficiency of hemoglobin, with additional secondary red cell abnormalities caused by the relative excess of the other unaffected globin chain.

1-α-thalassemia:

-gene deletion - chromosome 16 -4 α-gene loci (αα/αα) -autosomal recessive
-MCH⬇️ -MCV⬇️. -Hb⬇️

- 4 types:

1. Bart's hydrops fetalis syndrome:

-absence of all 4@. - Hb Barts (γ4) . -fetuses are still born , edema
-CBC: severe microcytic hypochromic + reticulocytosis

2.HbH disease:

-absence of 3@. -HbH (β4). -Chronic hemolytic anemia, mild jaundice
-CBC: reticulocytosis

3. α-thalassemia trait:

-absence of 2@ ,cis or trans. - Does not require treatment. -CBC: mild hypochromic microcytic

4. α-thalassemia silent carrier:

- absence of 1@ -No clinical abnormalities - Normal or mild MCH ,MCV

2-β-Thalassemia:

-autosomal recessive. -gene mutation (B0,B+). -2 beta alleles on chromosome 11
-3 types:

1-β Thalassemia Minor(B0,B/ B+,B):

-more common form of thalassemia -asymptomatic & anemia is mild - HbA2 ⬆️
- hypochromic microcytic anemia. - HbF normal or ⬆️

2-β-Thalassemia Major(B0,B0):

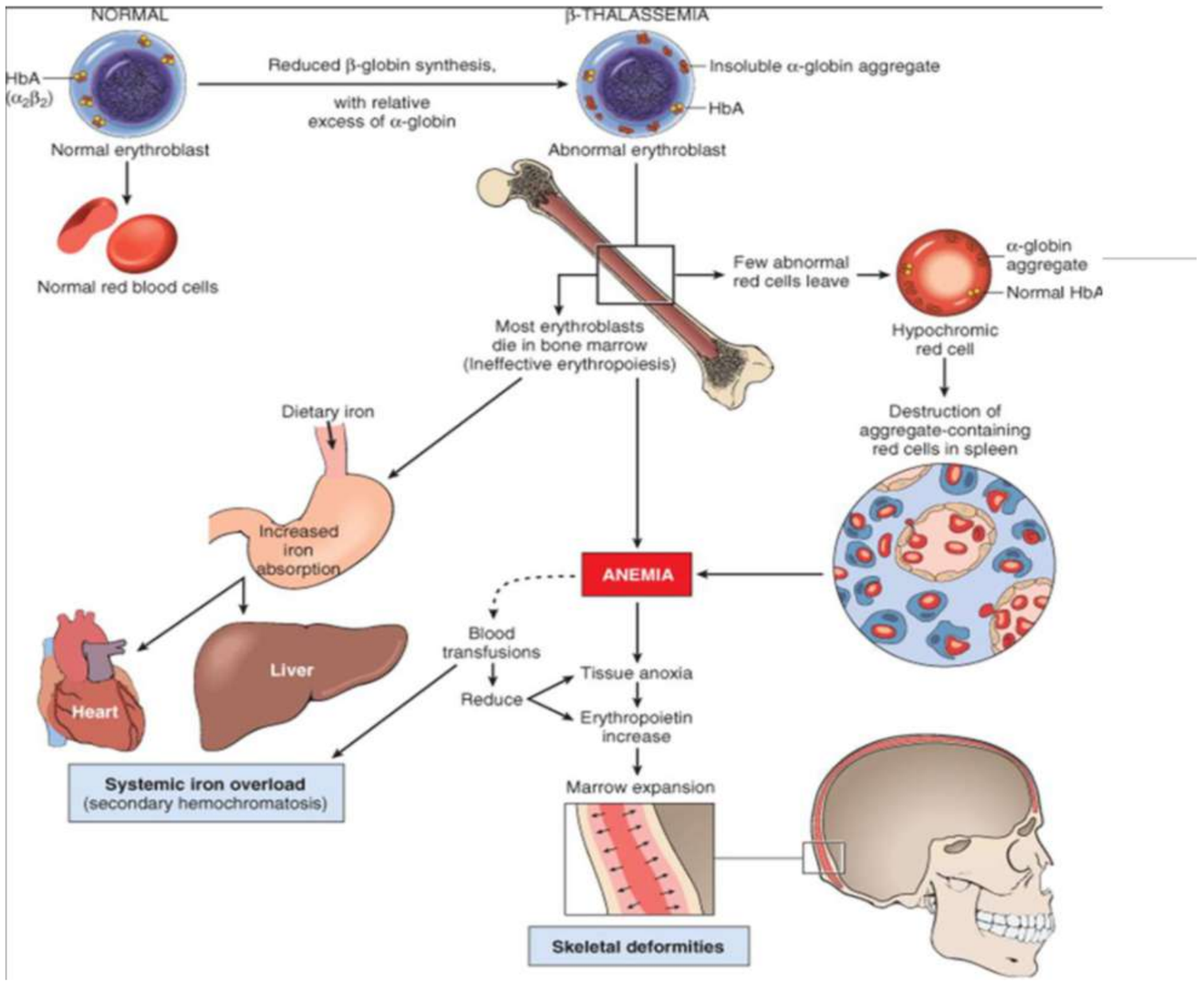
-Severe microcytic, hypochromic anemia. - severe bone deformities. - children fail to develop normally

-With transfusions alone the survival into the second & third decades is possible, but gradually they develop iron overload , hemochromatosis & heart failure .

3-Thalassemia intermedia(Bo:B/B+,B):

-normal life. -may need occasional transfusions

-Pathogenesis of β thalassemia:



-Morpholog of β-Thalassemia Major:

-poikylocytosis,anisocytosis,target cell -Extramedullary hematopoiesis (spleen ,liver)

-Bone marrow is hypercellular with erythroid hyperplasia - skeletal deformities (hair on end)

-secondary hemochromatosis

-Diagnosis of β thalassemia :

-Minor : Hb electrophoresis. **-Major :**be made on clinical grounds.

-Treatment:

-chronic blood transfusion. -splenectomy -iron chelation

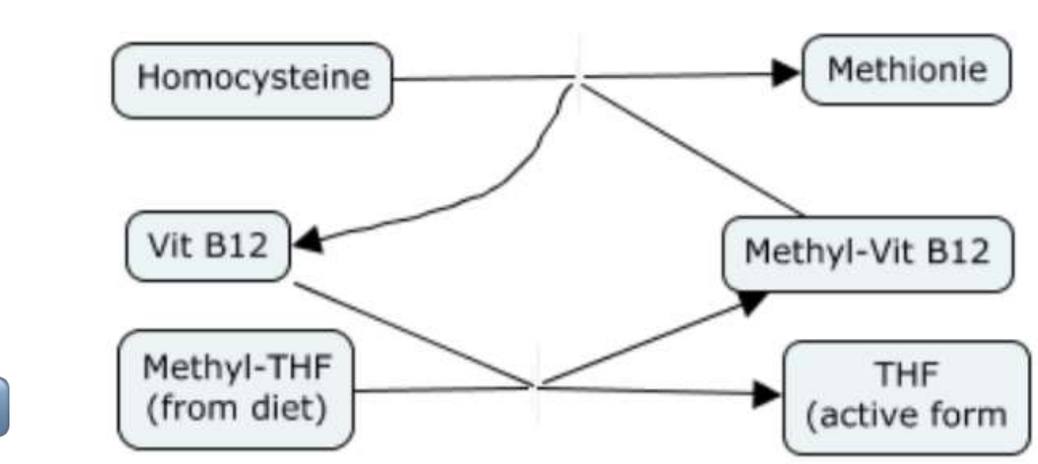
-Parvovirus B19 :

-affects erythrocyte precursors and shuts down RBC production.

-It was found that patients with thalassemia are protected against malaria infection by plasmodium falciparum.

Macrocytic anemia

Folate and V.B12 :



Megaloblastic anemia:

- impaired DNA synthesis → delayed nuclear maturation → normal RNA synthesis nuclear (immature) : cytoplasmic (mature) dyssynchrony

-Macrocyte: mature red blood cell with increased MCV (100 - 110 fL)

-Vitamin B12 deficiency takes years to develop due to large hepatic storage

-Folic acid deficiency develops in months as body stores are minimum

-autoimmune gastritis→auto-antibody against the parietal cells & intrinsic factor → pernicious anemia

Clinical features :

-Anemia (Macrocytic RBCs and hypersegmented neutrophils)

-Subacute combined degeneration of the spinal cord (only in Vit B12 deficiency) patients present with neurological manifestations

Morophology:

-morphologic hallmark → Megaloblasts

-giant metamyelocytes +hypersegmented neutrophils

Diagnosis :

-CBC: MCV ⬆️ +leukopenia, and thrombocytopenia (pancytopenia) + retic count ⬇️

-Peripheral smear : Macrocytes+Anisocytosis+poikilocytosis+hypersegmented neutrophils

Treatment: Supplementation of B12 and folate with dramatic increase of reticulocytes in blood 2-3 days after vit.B12 injection

Normocytic anemia

1- Aplastic Anemia:

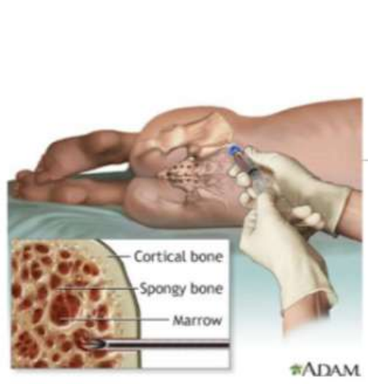
-**Cause**: Bone marrow disorder leading to ineffective hematopoiesis.

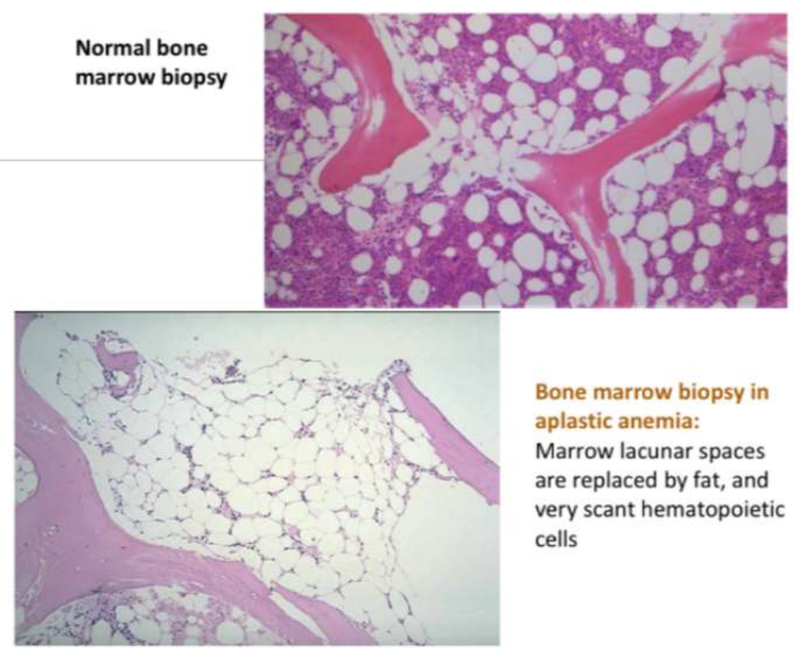
-**Etiology**: Acquired (infections, toxins, drugs, autoimmune diseases, idiopathic) or constitutional (e.g., Fanconi anemia).

-**Morphology**: Markedly hypocellular bone marrow with lacunar spaces replaced by fatty cells

-**Treatment**: Bone marrow transplant, treating underlying cause, immunosuppression, transfusion support.

-**Clinical Features**: Pancytopenia, fatigue, shortness of breath, bleeding/bruising, frequent infections.





2-Hymolytic anemia :

	Extravascular hemolysis	Intravascular hemolysis
Site of hemolysis	Endothelial system: mainly in spleen, liver, lymph nodes By macrophage	In blood vessele
Life span of RBCs	Short	Short
Erythropoietin & Reticulocytes & LDH	High	High
Unconjugated bilirubin & gall stones	High (Jundice)	Normal
Hemoglobinemia; serum hemoglobin Hemoglobinuria;hemoglobin in urine Hemosiderinuria; iron in urine	Absent	High
Serum haptoglobin	Normal	High

Normocytic Anemia
Hemolytic Anemia
↳↑ Reticulocytes

extra: Sickle cell disease

Autosomal Recessive

What is the cause of formation hbss

↳ Point mutation in B globin gene; A to T substitution ; converting glutamic acid into valine...leads to formation Hbs (2 alpha,2Bs), abnormal beta :(} ⟶ Homozygous mutation;in two genes

What is the problem ؟

When these RBCs that contain Hbs are exposed to hypoxia,dehydration and acidosis, the Hbs are polymerised inside RBCs. These RBCs become rigid sickle cells

Causes ischemia

When they enter the blood vessel, they aggregate and prevent blood supply to tissue

Vaso occlusive

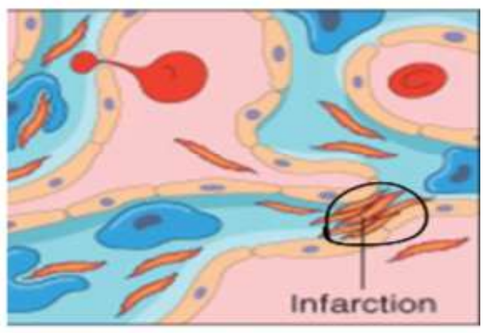
Hemolysis ocuurs

When?

Sickling occurs in hypoxia, once the RBC is oxygenated , it returns to normal (disc shape)..... Reversible sickling

Sickling & desickling damages membrane, the cell becomes irreversibly sickled leading to hemolysis; abnormal cells.

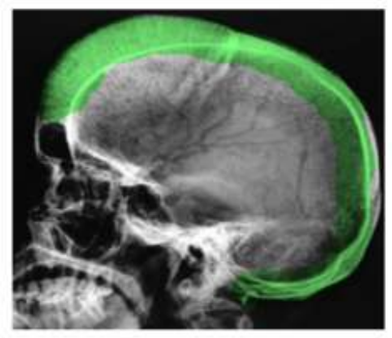
*th'e spleen begins hemolysis but these sickled cells block the blood vessels in spleen leading to to formation micro infarctions everywhere!😭
After a period,the patient loses his spleen (autosplenectomy)



Clinical manifestations

-Reticulocytosis(no problem in BM)

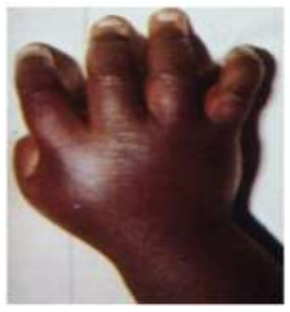
-Expansion in BM due to ⬆️ erythropoiesis, leading to prominent cheek bones & changes in skull ; hair on end appearance



-Hyperbilirubinemia &gallstones due to extravascular hemolysis

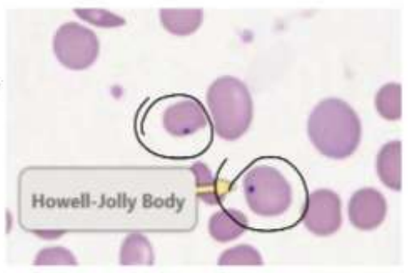
-ischemia in different organs , ex:

1-Dactylitis; infarctions in the bones of the fingers hands and feet



2-spleen autoinfraction(autosplenectomy), no spleen:(

Increase risk of different infections and howel jolly bodies appear



3-renal papillary necrosis; vaso occlusion in blood vesseles of kidney

4-acute chest syndrome; vaso occlusion in pulmonary microcirculation

Treatment:

*prophylactic penicillin to prevent infections(ما في spleen يقضي على الكائنات المسببة للانفكشن)

*hydration

*transfusion ; ⬇️ Hbs

*hydroxyurea therapy; ⬆️ Hbf

extra: G6PD deficiency

(X-linked Recessive)

What is happening exactly?

NADPH; due to G6PD deficiency ➡ reduced glutathione ➡ There is no glutathione to git rid of oxidative stress (Like drugs, favism, infections) ➡ RBC hemolysis

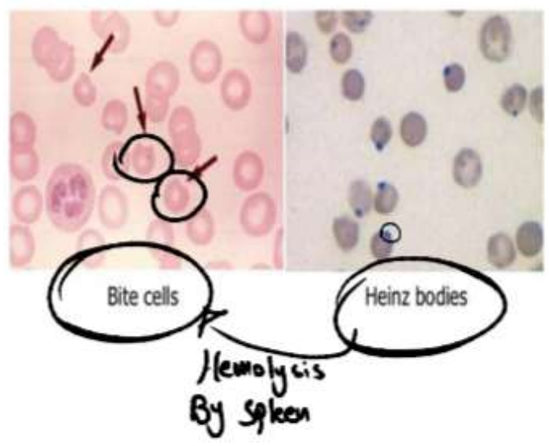
What results from this oxidation?

denaturation of globin chains, and precipitation at membranes forming Heinz bodies.

Hemolysis in spleen(extravascular)

Result in bite cells

Hemolysis in vessels (intravascular)



extra: Hereditary spherocytosis

(Autosomal Dominant)

What is happening exactly?

Abnormal spectrin & ankyrin proteins ➡ Defects in RBC membrane

↓

Blebs in membrane ➡ these blebs are lost over time by spleen ➡ RBCs become spherical& small ➡ hemolysis in spleen (extravascular;jundice ,splenomegaly

Spherocytosis if RBCs:

As the cell becomes smaller, the concentration of hemoglobin increases ; High MCHC.

The RBC loses it's shape disc;loss of central pallor.

Due to splenectomy; howel jolly bodies appear

Extra. Immune Hemolytic Anemia

-**Categories**: Alloimmune, autoimmune, drug-induced.

- **Pathophysiology**: Antibody-mediated destruction of RBCs (warm or cold antibodies). -

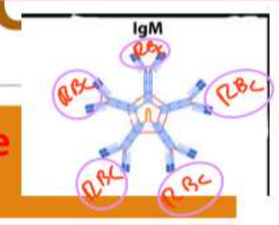
-**Clinical Features**: Anemia, jaundice, splenomegaly.

- **Diagnosis**: Antibody testing, direct antiglobulin test.

- **Treatment**: Address underlying cause, corticosteroids, immunosuppressive therapy.

Causes of autoimmune-IHA
IgG or IgM mediated destruction of RBC

Agglutination =RBCs+ IgM



Warm Antibody: IgG/IgA type	Cold Antibody: IgM type
Activated at body temp. (37 c) warm عشان هيك اسمها	Active at 0-4°C IgM binds to RBC in cold temp (extremities)
IgG-coated RBC lysis in spleen (predominantly extravascular) بيروح IgG بيرتبط بـ antigen على سطح RBC بيروح بودياهم الـ spleen حتى تتكسر	Clumping and complement fixation causes lysis in blood vessels and liver (intra- and extravascular)
Morphology: spherocytes (splenic macrophage phagocytose tagged RBC leading to formation of spherocytes) هيك بس بيروح RBC على الـ spleen بيلتهمها من جهة IgG -antigen الـ spleen بيلتهمها من جهة حتى يصير شكلها كروي فلك شوي	IgM agglutination (hemolysis occurs in the hands & feet in cold weather)
80% of immune hemolytic anemias: Primary (50-70%) We don't know the causes	• Infectious mononucleosis (EBV) • Mycoplasma infection • Lymphoproliferative disorders
Secondary: - Lymphoproliferative disorders We know the cause - Autoimmune diseases (SLE) - Drugs (penicillin and cephalosporins) بتعمل coat بعدين بيجي igG بيرتبط	

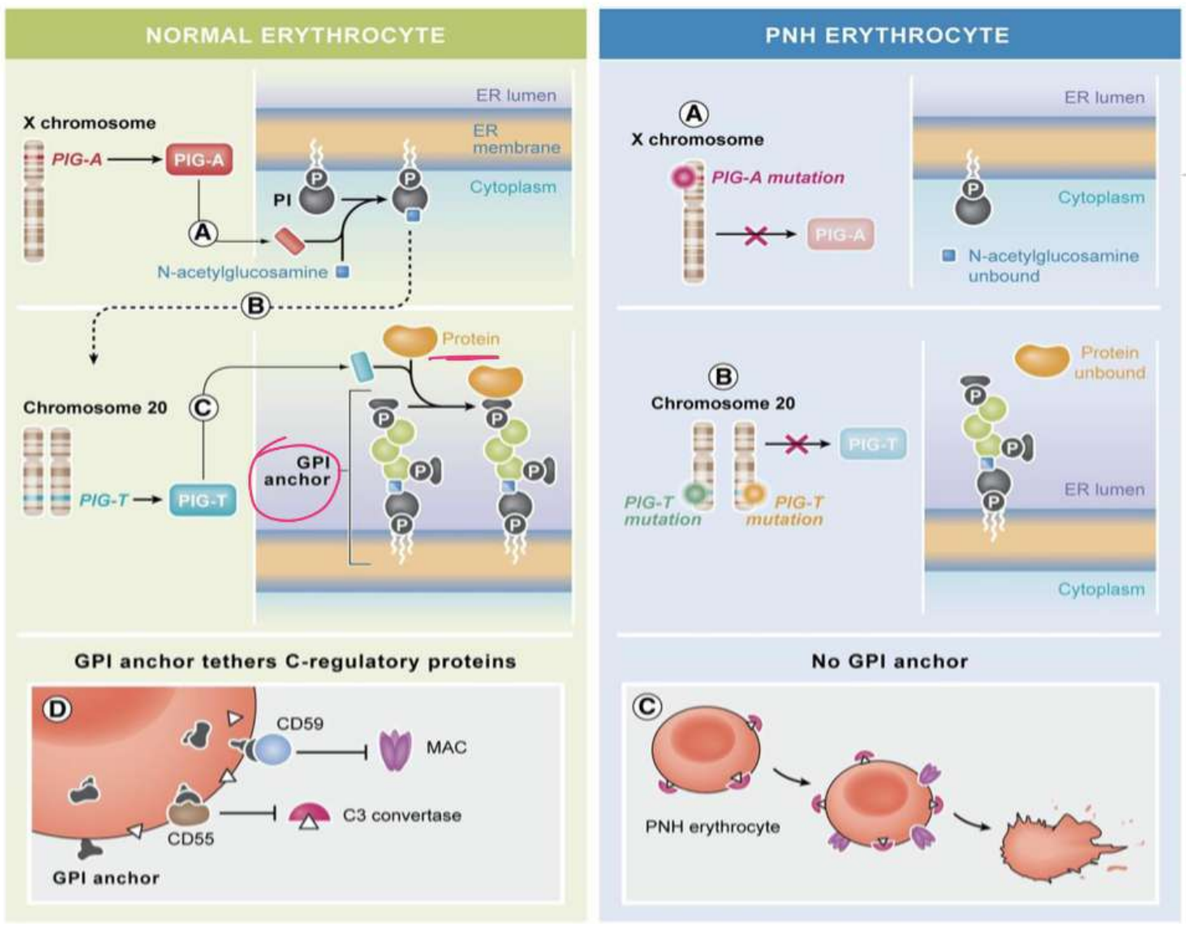
Intra.Paroxysmal Nocturnal Hemoglobinuria

-**Cause**: Acquired mutation in PIGA gene, leading to deficiency of GPI-anchored proteins

-**Clinical Features**: Hemoglobinuria, reticulocytosis, venous thrombosis.

- **Diagnosis**: Flow cytometry for absence of GPI-anchored proteins.

- **Treatment**: Eculizumab (complement inhibitor), supportive care.



ما الواحد يتنفس باليل النفس تبعه بكون very shallow
و لما يكون shallow معناته بتراكم عندي Co2
لما يتراكم الblood ph بقل
و بصير عندي acidosis
هسا الcomplements اللي قرفتكم فيهم بصير النهار activation
في حالة الacidosis

Hemolysis occurs mostly at night when there is fixation of complement which is enhanced by decrease of blood PH during sleep

- ✓ Chronic intravascular hemolysis with hemoglobinemia, hemosiderinuria -/+ hemoglobinuria
- ✓ Reticulocytosis ما في صله بالعضي
- ✓ Venous thrombosis (hypercoagulability due to free Hb in blood)

كُلّ عظيمٍ يحتاج إلى إعداد..

وكُلّ تغييرٍ لا بُدّ له مِن ثَمَن، تأكّد من ذلك؛ لن يرتفع بناؤك دون أساس، ولن تلتقط ثمرةً دون بذرة،
ولن يَبتَلَّ ريقُكَ دون طول ظمأ! فإن رُمتَ قِمَّةً لا بُدّ أن تَعبُرَ الصّخور
وإن أرَدتَ نَصرًا فارفَع رايةَ الصّدق والعمل! حتّى لا تخذلك أنفاسك يا فتىٰ،
ولا تهترئ بالطَّريق خطاك

لا تنسوا اهلنا في غزة والسودان من صالح دعائكم -

فيديوهات قصيرة بتساعدكم على مراجعة المادة وتثبيتها ✅
من خانه الباثولوجي .... ال guidance

MEDICAL CLUB

medicosis + osmosis

الفيديوهات المطلوبة 3	الفيديوهات المطلوبة2	الفيديوهات المطلوبة 1	الموضوع
-	causes and mechanism of anemia	introduction	Anemia
Iron Deficiency Anemia: All you need to know!	Review of normal iron metabolism : vidio 1 video2	introduction	Microcytic anemia
Beta thalassemia	Alpha thalassemia	anemia of chronic disease,inf	Microcytic anemia
-	Megaloblasti Folic acid Deficiency	Megaloblastic V.B12 Deficiency	Macrocytic anemia
Extravascular hymolysis	Intravascular hymolysis	Aplastic anemia	Normocytic anemia
Hereditary spherocytosis	G6PD deficiency	sickle cell disease	Extra. hymolysis
-	-	immune hymolytic anemia	Extra. hymolysis
	Bernard Soulier syndrome+ mann's throm asthenia	Hemophilia	COAGULATION DISORDERS