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Hemolytic anemia

caused by:
1- accelerated destruction of RBCs
2- ↑ Hb catabolism (↑ hb breakdown → jaundice)
3- ↓ Hb
4- ↑ Efforts of BM to regenerate product
compensation رح يحاول يعمل ← BM hyperplasia ←

Acute and chronic disease

Immune vs. non-immune mediated
(Depending on mechanism)

→ Inherited or acquired
(Cause)

Intracorpuscular or extracorpuscular

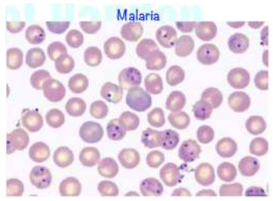
A. Acquired Defects:
– Membrane defect: PNH

B. Hereditary defects:
- Membranopathy (Spherocytosis)
- Hemoglobinopathies (Sickle cell)
- Enzymopathy (G6PD Deficiency)
- Deficient globin synthesis (Thalassemia syndromes)

→ Antibody-mediated.

→ Mechanical trauma to red cells.

→ Infection: Malaria.
لانه بصيرلها replication في RBC



Intravascular or extravascular (Site of hemolysis)

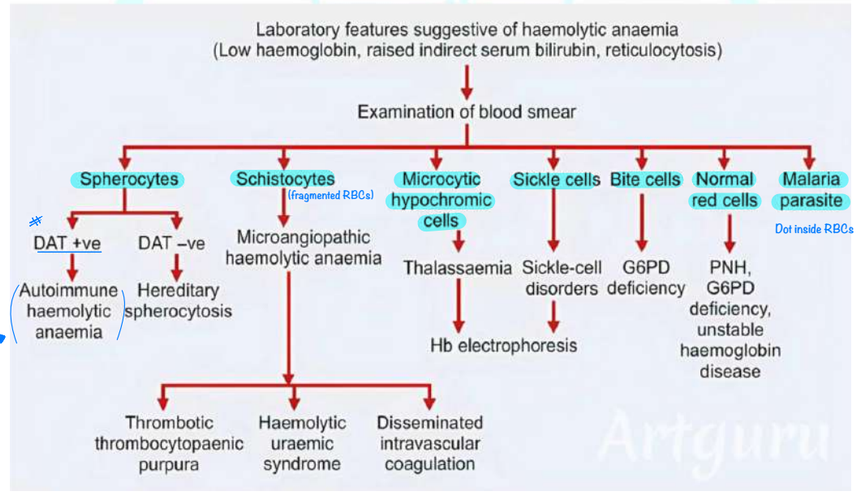
- Cell destruction inside the B.V
– Hemoglobinemia.
– Hemoglobinuria.
– Hemosiderinuria.
– Marked decrease in Haptoglobin
"almost absent"
لانه استهلكته حتى يمسك free Hb

للتوضيح:

- Destruction of red cells by phagocytes
–In reticuloendothelial system (spleen & liver)
–Splenomegaly
– Hyperbilirubinemia and jaundice.
Occur in both IV. H and EV. H
–Mild decrease in Haptoglobin
–No (Hburia, Hbemia, Hemosiderinuria)

A simplified approach to diagnosis of haemolytic anaemias

CBC → ↓ Hb
مريض Anemia وعنده H.A للـ sign
Next step ← ؟؟؟
اعمل peripheral blood smear



DAT يعمل ←
Detection of presence Ig على RBC
اذا RBC عليها Ig

Activation of complement in RBC membrane	Physical or Mechanical Trauma to the RBC	Toxic Microenvironment of the RBC
– Paroxysmal nocturnal hemoglobinuria – Paroxysmal cold hemoglobinuria – Some transfusion reactions – Some autoimmune hemolytic anemias	–Microangiopathic hemolytic anemia – Abnormalities of heart vessels ↑ risk ← تخبط بهاي المناطق RBC ← Turbulent B.F ← Narrowing of BV – DIC	– Bacterial infections – Plasmodium falciparum infection (Malaria) – Venoms – Thermal injury – Acute drug reaction in G6PD deficiency

➢ Features of Hemolytic Anemia :

↓ RBCs survival

↑
- erythropoietin (Due to tissue hypoxia) → increased erythropoiesis and early release of RBCs from marrow
- products of Hb. Catabolism
- indirect Bilirubin and LDH
- Rate of production RBC → ↑ circulation (Reticulocytosis)

Hereditary Spherocytosis

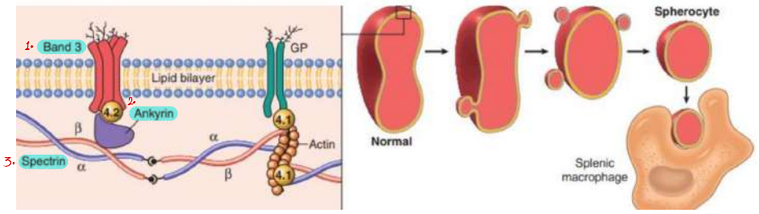
– Inherited (intrinsic) defects in the red cell membrane / Run in families , AD , fx of splenectomy

lead to ⟶ formation of spherocytes, nondeformable cells (Rigid RBC) that are highly vulnerable to sequestration and destruction in the spleen.

Caused by ⟶ inherited defects in the membrane skeleton, a network of proteins that stabilizes the lipid bilayer of the red cell.

(Loss of cell membrane in the form of blebs due to membrane instability
Decrease cell membrane to cytoplasmic ration > spherical RBCs that are non-deformable)

* mutations in (1+2+3)
↓
رح اخسر
lipid belayer stability & biconcave shape



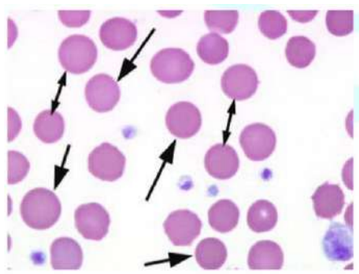
Clinical

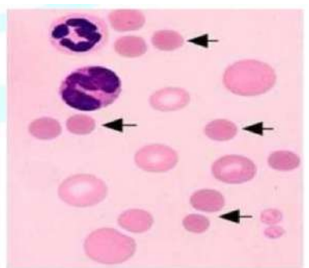
✓ Anemia, splenomegaly and jaundice.
✓ Gallbladder stones. → bilirubin مكونة من Bigmented stone نوع (chronic hemolysis) اذا المريض عنده

(Severity of anemia correlates with spectrin deficiency)

✓ Aplastic crisis: 2ry to Parvovirus B19.

BM suppression ↩
erythroid precursor inside B.M يعمل infection لل
Sheddown of RBCs production ⟵



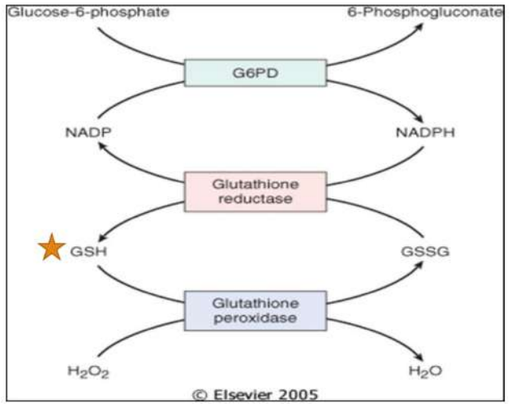


G6PD Deficiency

-More common in males
- on chromosome X
-Anti-oxidant (disposal of H2O2)
-↓ in GSH causes hemolysis in cells exposed to oxidant agent

Patients are asymptomatic until exposed to:
✓ Drugs: Antimalarial, sulfonamides.
✓ Favism.
✓ Products of FR in infections.

Pathogenesis:

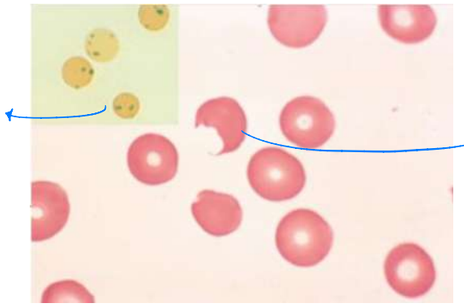


Loss of G6PD enzyme → Inability to form NADPH
→ Inability to maintain GSH in reduced form → ↑ susceptibility to FR

regeneration of GSH is impaired
"attack" red cell components(globin chains)

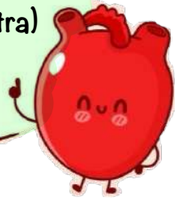
(intravascular hemolysis)	(extravascular hemolysis)
Oxidized hemoglobin denatures and precipitates, forming Heinz bodies, which can damage the red cell membrane	cells with lesser damage lose their deformability and suffer further injury when splenic phagocytes attempt to remove the Heinz bodies → creating bite cells

Heinz body



Bite cell

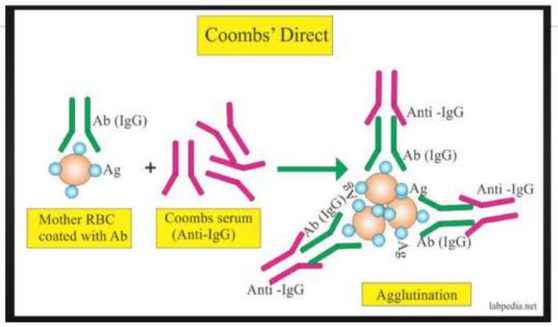
Type of hemolysis:
Both (intro & extra)



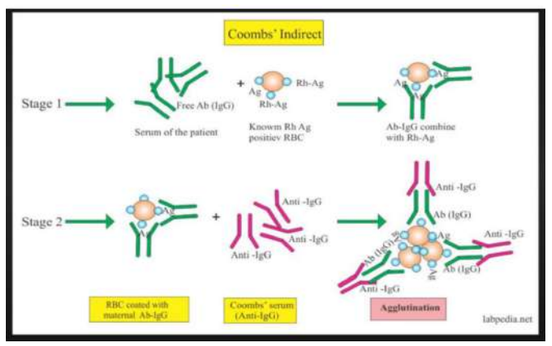
Immune Hemolytic Anemia

caused by → antibodies (spontaneously / 2ry to exogenous agents) that bind to determinants on red cell membranes

diagnosis → detection of antibodies and/or complement on red cells



You took Blood sample from the pt (RBCs coated by Ab)
You add coombs reagent (anti IgG abx)
If agglutination occur = autoimmune hemolytic anemia



You took serum sample from the pt (Abs)
Step 1 :You add synthetic RBCs
Step 2 :You add coombs reagent (anti IgG abx)
If agglutination occur = autoimmune hemolytic anemia

Hemolytic Anemia Due to Mechanical Trauma to RBC

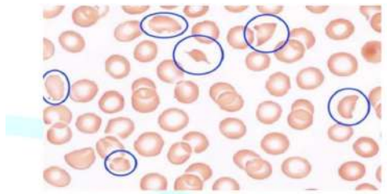
Etiology:

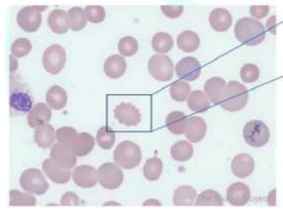
Macro-angiopathic Hemolytic anemia	Microangiopathic hemolytic anemia
Artificial valves. (Aortic stenosis)	o DIC. o Malignant hypertension. o TTP. o Hemolytic uremic syndrome.

Morphology:

(Variation in RBCs shape) poikilocytosis with & helmet cells/schistocytes, burr cells, and triangle cells

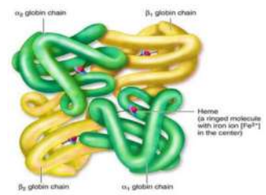
(Spike RBC)





Hemoglobinopathies

* are a group of hereditary disorders caused by inherited mutations that lead to structural abnormalities in Hb.



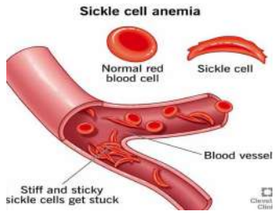
* Normal Human Hbs :

- Hb A (α2β2): 95% of adult Hb
- Hb A2 (α2δ2): 3% of adult Hb
- Hb F (α2ɣ2):
  - ✓ 75% at birth.
  - ✓ < 5% at 6 months.
  - ✓ < 1% in adults.

Sickle Cell Disease

* the prototypic hemoglobinopathy and the most common

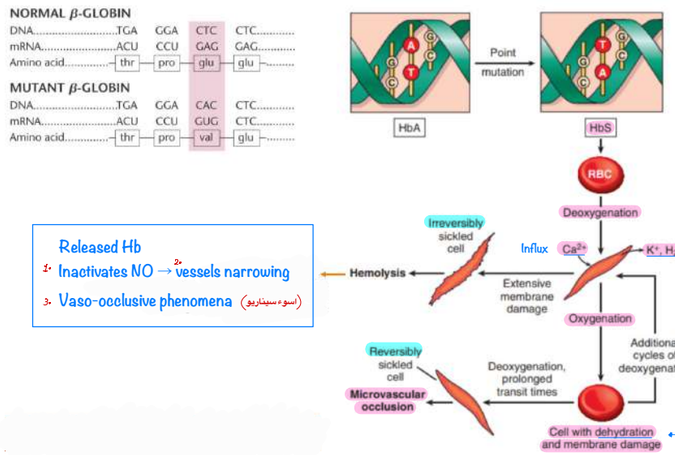
RBC life span ↓ from a normal 120 days to 10-12 days



mutation : in β-globin

Substitution mutation at position 6 in B globin gene
Lead to change in the 6th a.a from glutamic acid
(water soluble) to valine (water insoluble)

→ change in Hb structure from globular to sickled shape once deoxygenated or got dehydrated
→ change in RBC shape to sickle shape



-Sickling can be reversible initially , then be irreversible

• sickled RBC tend to aggregate inside Small BV lead to :

1-vaso-occlusive crisis

2- Intra-vascular Hemolysis

• permanently sickled RBCs will be sequestered and remove inside spleen : Extravascular hemolysis

Clinical presentation :

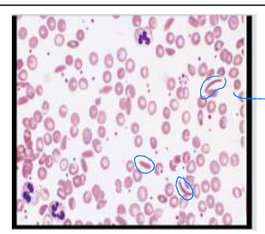
Due to presence of HbF

- Asymptomatic till 6 months of age.
- Moderate to severe anemia (6-8 g/dl).
- Unremitting course complicated by sudden crises.

1- hemolytic crisis (hemolysis) due to excessive sickling
Drop in Hb from baseline + high Retic count
2- aplastic crisis (parvo b19 infection)
Drop in Hb from baseline+ lwo retic count
3- vaso-occlusive crisis : pain

Laboratory investigation:

* CBC and blood smear(Sickled RBCs)
* Hemoglobin electrophoresis. (↑ Hbs)



Sickled RBC

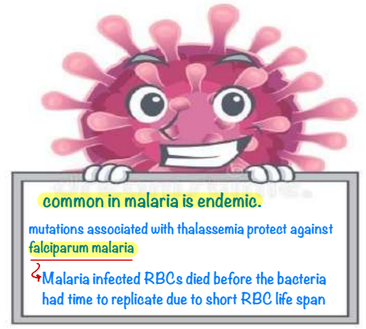
Treatment:

- Adequate hydration.
- Pain relief.
- Antibiotic therapy.
- Exchange transfusion to ↓ theHbS.

Thalassemia (Quantitive disorder)

* mutations in globin genes that decrease the synthesis of α- or β-globin ⟶ deficiency of Hb and red cell damage

Features :



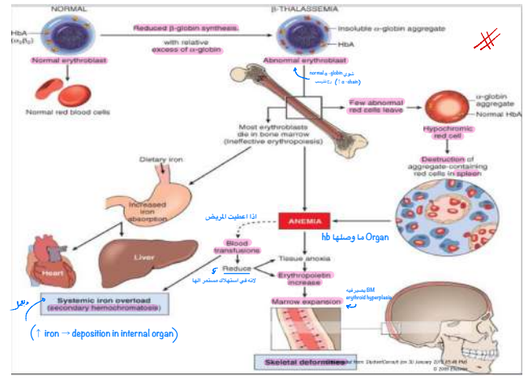
* hypochromic microcytic anemia
* Imbalance of globin chains → Reduced Hb synthesis and anemia
* Precipitation of abnormal Hb → hemolysis and ineffective erythropoiesis.

Presentation depend on the severity of the mutation
• if globin is present but in decreased amount : IDA like presentation : hypo-chromic microcytic anemia
• If certain globin is completely absent > the other globin will compensate > forming tetramers > tetramers precipitate inside RBCs lead to hemolysis (sever anemia)

1- severely defected RBCs (with tetramers) fail to leave BM : ineffective erythropoesis and got hemolyzied there

2- moderately defected RBCs :leave the BM but got hemolyzed at spleen due to hb defect

3- mildly defected RBCs : decrease Hb synthesis > decrease amount of hb inside each RBC : microcytic hypochromicanemia



β –Thalassemia

Defect in β-globin (Mutation) ⟶ leading to aberrant RNA splicing (M.C cause)

1. β0: No β-globin chains are produced.
2. β+: Reduced (but detectable) β-globin synthesis.

β–Thalassemia Major	β –Thalassemia Minor
* β0/β0, β+/β+, β0/β+.	* Heterozygous for β0 or β+ gene.
* Hb. Level: 3-6 gm/dl (if un-transfused).	* ↑ HbA2 (> 3.5%) and/or HbF (1- 5%).
* ↑ HbF / ↑ or normal (HbA2) / absent or ↓ (HbA) (Age :6-9 months)	* Mild microcytic anemia (Hb 9-11 g/dL).
* Treatment →transfusion dependent.	* Differential Dx: IDA

α-Thalassemia

Defect in α -globin (deletion)

• Severity of the disease is proportional to the number of a-globin genes that are missing →

-α/αα: silent carrier state: asymptomatic.
--/αα, -α/-α: α thalassemia minor: asymptomatic.
--/-α : Excess beta: Beta 4: HbH disease.
--/--: Excess Gamma: Hb Barts, Death in utero (Hydrops fetalis).