HAEMATOLOGY 436

MEDICINE
KING SAUD UNIVERSITY

تمت المراجعة
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Approach to Hemolysis

Objectives:

To know the function of platelets and the relationship between the platelet count in peripheral blood and the extent of abnormal bleeding.

- To know about the diseases associated with 1) a failure of platelet production 2) a shortened platelet lifespan, especially immune thrombocytopenic purpura (ITP).
- To know the principles of investigation of patient suspected of having a haemostatic defect.

To understand the role of platelets, blood vessel wall and coagulation factors in normal haemostasis.

- To know the classification of haemostatic defects.
- To know the platelet morphology and life span.
- To know the platelet function and diseases due to platelet function disorders.
- To know the causes of thrombocytopenic purpura and non-thrombocytopenic purpura.

References:

436 girls & boys' slides
435 teamwork slides

Notes Extra. Important.

Editing file

Do you have any suggestions? Please contact us!

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or simply use this form

❖Haemolysis:

It is a Premature destruction of RBCs.

Hemolysis is due to:

- Defect in the RBCs (intra-corpuscular) as in congenital hemolytic Anaemia.
- Defect in the surrounding environment (extracorpuscular) as in acquired Anaemia

❖Haemolytic Anaemias:

- Haemolysis is the shortening of the lifespan of a mature red blood cell.
- haemolysis will result in anaemia more readily
- increased red cell output from the bone marrow stimulated by erythropoietin
- This mechanism compensates the loss of RBCs, and this requires an adequately function bone marrow and effective erythropoiesis
- More marked reductions in red blood cell life span 5-10 days from the usual 120 days
- will result in ***haemolytic anaemia***
- a suboptimal marrow response is seen

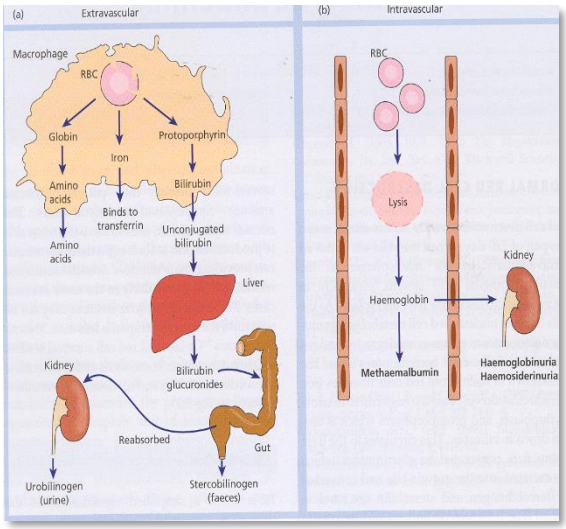
Clinical Features of Hemolysis:

- Pallor, lethargy
- Jaundice
- Splenomegaly
- Gall stones (Pigment – bilirubin)
- Dark urine (urobilinogen)
- Bone deformity (In some types of
- haemolytic anaemia) especially in congenital
- Leg ulcers (in some types of haemolytic
- anaemia). Especially in sickle cell

Intravascular haemolysis:	extravascular haemolysis:
It is the process of breakdown of red cells directly in the circulation.	It is the excessive removal of red cells by cells of RE system in the spleen and liver.
main laboratory features of intravascular haemolysis: • Haemoglobinaemia (free Hemoglobin in blood) and Haemoglobinuria. • Haemosiderinuria (Iron storage protein in the spun deposit of urine).	

❖ Intravascular and extravascular haemolysis:

RBC Lysis (Extravascular Vs. intravascular)



Important diagram

Causes of intravascular haemolysis:

- Mismatched blood transfusion (usually ABO)
- G6PD deficiency with oxidant stress
- Red cell fragmentation syndromes
- Some autoimmune haemolytic anaemias
- Some drug-and infection-induced haemolytic anaemias
- Paroxysmal nocturnal haemoglobinuria
- March haemoglobinuria
- Unstable haemoglobin

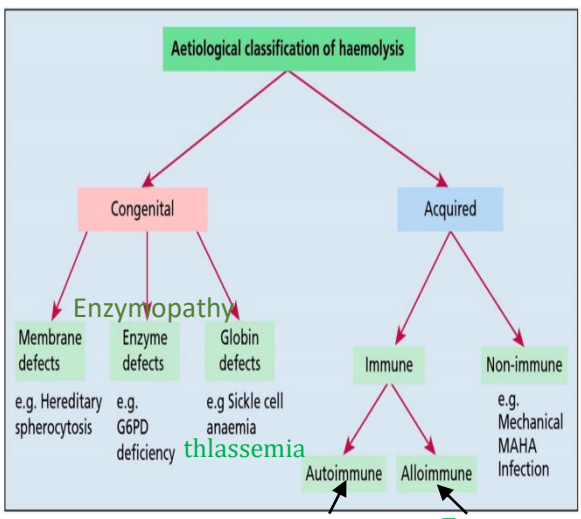
❖Laboratory Features of Hemolysis:

Features of increased red cell breakdown	Features of increased red cells production.	Damaged red cells.
• serum bilirubin is raised (unconjugated and bound to albumin). • urine urobilinogen. • Faecal • stercobilinogen. • lactate dehydrogenase (LDH). Absent serum haptoglobins. Haptoglobins= binds free hemoglobin fro erythrocyte with high affinity & therefore inhibits its oxidation activity.	• Reticulocytosis • Bone marrow erythroid hyperplasia.	• Morphology (e.g. microspherocytes, elliptocytes, red cells fragmentation). • Increased osmotic fragility, autohaemolysis..etc) • Shortened red cell survival (This can be shown by ^{51}Cr labeling with study of the sites of destruction.

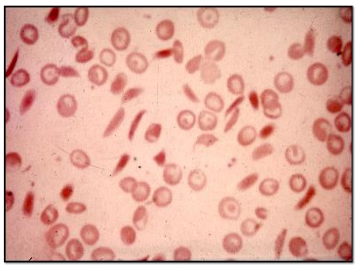
Haemolytic Anaemia

Congenital **Acquired**

- ☐ SICKLE CELL DISEASE & OTHER HAEMOGLOBIN DISORDERS
- ☐ THALASSAEMIAS
- ☐ ENZYMOPATHIES
- ☐ MEMBRANOPATHIES



Sickle Cell Anemia



Target cells + sickle shape

❖Abnormal Haemoglobins

❖(Haemoglobinopathies):

- Some Known Haemoglobin Mutants : (all in beta chain)

Name	Substitution
Hb. S	α2 β2 - 6 GLU → VAL
Hb. C	α2 β2 - 6 GLU → LYS

❖ DNA Coding for the Amino-Acid in the sixth position in the β-chain

- **Normal:-**

	5	6	7
Amino Acid	pro	glu	glu
DNA Base Composition	CCT	G A G	G A G

- **Sickle:-**

DNA Base Composition	CCT	G T G	G A G
Amino Acid	pro	val	glu
	5	6	7

In position 6 it is supposed to be the amino acid glutamic acid but it transformed into Valine

1910: 1st published report of sickle cell anaemia (Herrick)

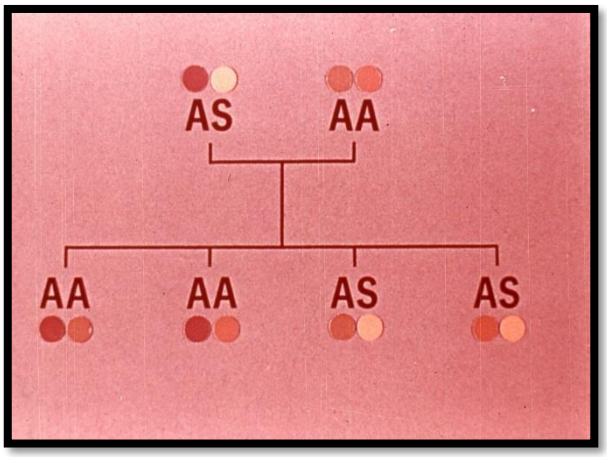
1949: Pauling et al : chemical difference between HbA and HbS

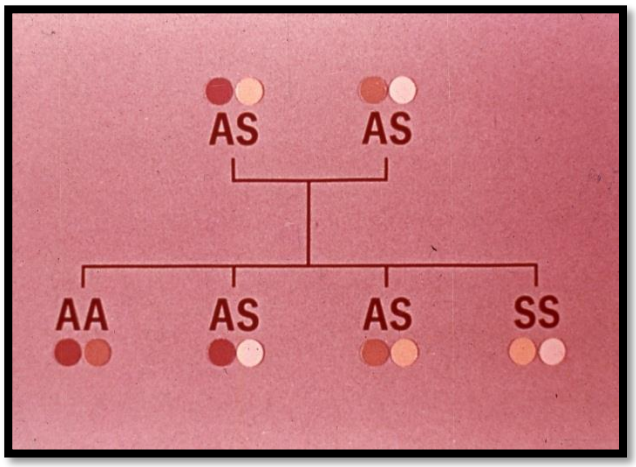
1956: Ingram: Fingerprinting

β glu ⟶ val

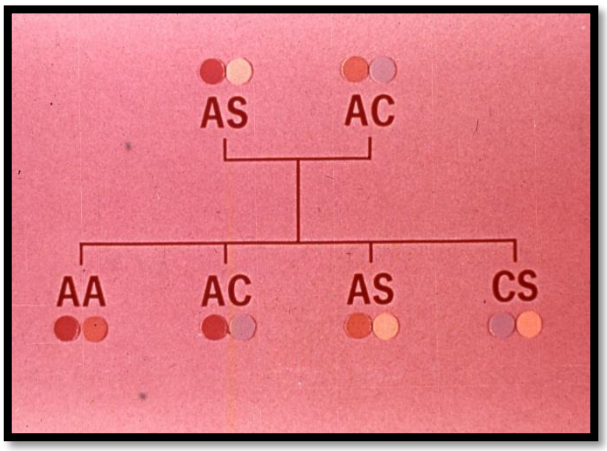
- It is important to Know that the HbS is Due to abnormal Beta-Chain in Amino Acid number 6 wich transforms from glutamate to valine due to mutation!

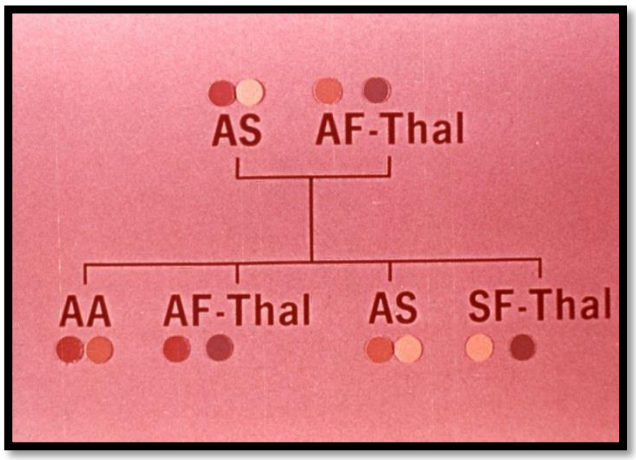
- Traits heredity: عشان كذا نسوي فحص الزواج



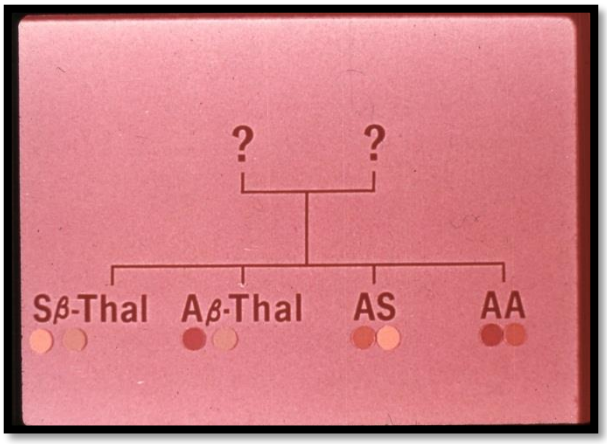


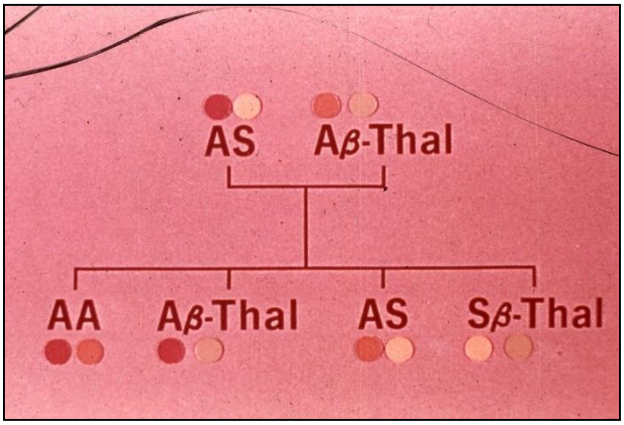
AA: Normal
AS: trait – carrier (could transmit the disease)
SS: Diseased





AC: Trait (carrier)
AS: Trait (carrier) for another disease.
CS: Diseased





AS: Sicle cell trait
AF-Thal: thalassemia trait
SF-Thal: diseased

Sickle cell disease:

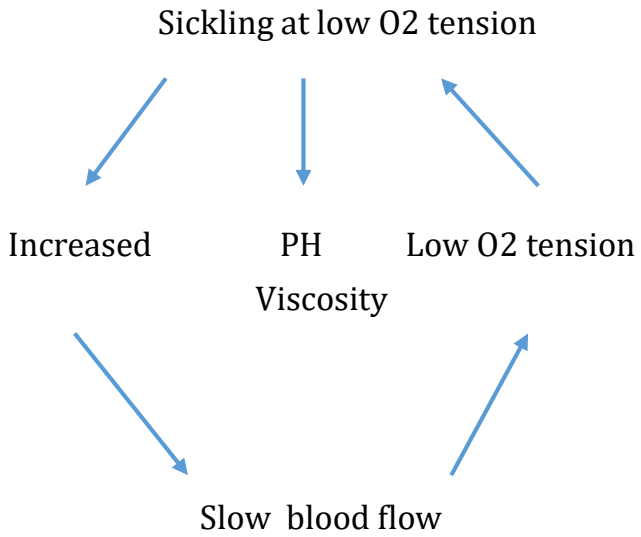
1. The sickle cell trait (AS)	-
2. Homozygous sickle cell disease (ss)	Sickle cell anemia
3. Doubly heterozygous sickle cell disease (2 diseases together)	sickle cell / hemoglobin C disease
	sickle cell / thalassemia

Properties of Hb S :

1. Solubility decrease
2. Conformational changes- "tactoid formation" when exposed to O2
3. → Sickled cells
4. → Irreversibly sickled cells
5. Increase mechanical fragility → hemolysis
6. Increase viscosity → organ infraction

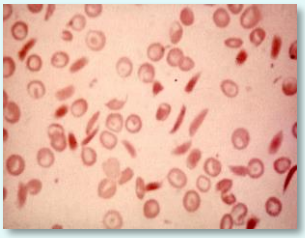
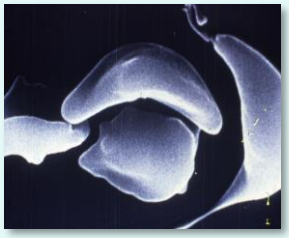
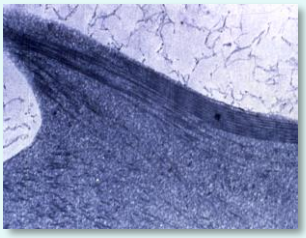
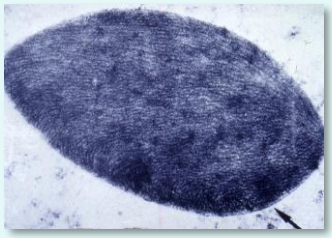
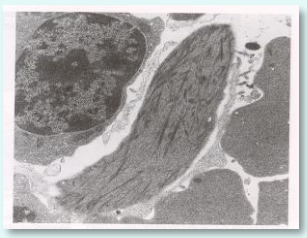
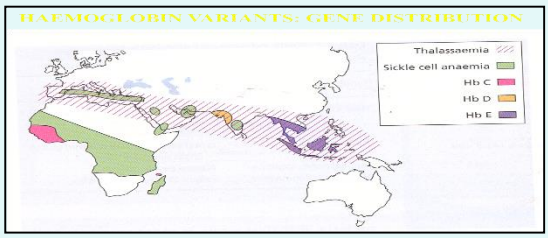
Factors affecting sickling

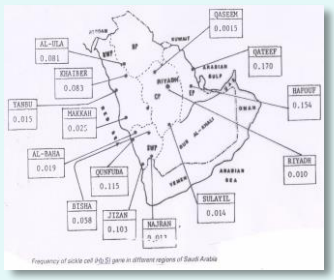
1. Oxygen tension:
   - 50-60 mm Hg for SS
   - 20-30 mm Hg for AS
2. pH :
   - inhibited at alkaline pH (Alkalosis blood decrease sickling attacks)
   - Exacerbated by acidification
3. Concentration of Hb S
4. Presence of other hemoglobins
   - Polymerisation: S > D > C > J=A > F



Factors Precipitating Crises In Sickle Cell Disease :

- Infections (Especially Malaria)
- Pyrexia fever
- Exposure To Cold
- Dehydration (the most important factor with pregnancy)
- Pregnancy



Crises in sickle cell disease:

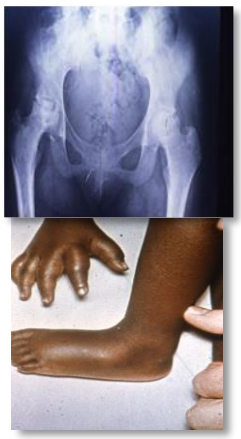
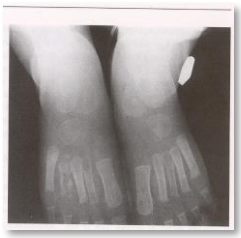
- Hyperhaemolytic.
- Aregenerative or aplastic.
- Small vessel occlusion.

Clinical manifestations of sickle cell disease:

- Haemolytic anemia
- Tissue infraction

Clinical Manifestations in Sickle Anaemia

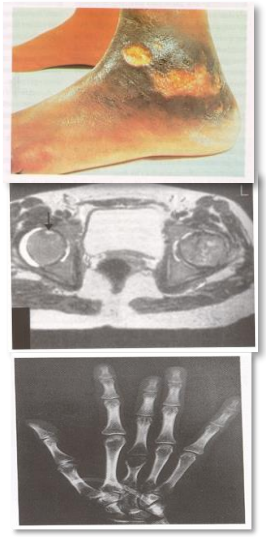
- Pallor (Anaemia)
- Jaundice & Dark Urine
- Apathy & Anorexia
- Hand-Foot Syndrome (Young Children) (one of earliest signs of sickle cells anemia)
- Splenic sequestration (Young children) Hepatic Sequestration
- Bones and Joints Pain very sever (the patient may scream from pain).
- Abdominal Pain

Hand foot syndrome: swelling-pain-inflamed small bones

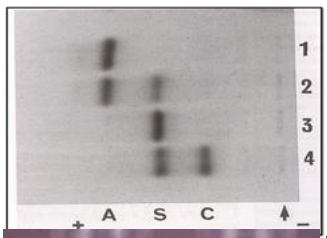
Clinical Manifestations in Sickle Anaemia

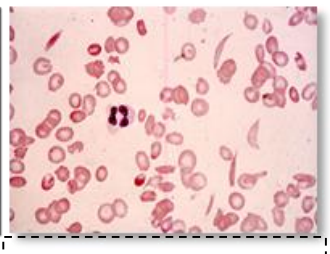
- Recurrent Infections & Chest Symptoms (Acute Chest Syndrome)
- Hepato-Splenomegaly but more significant with thalassemia
- → (Early Childhood)
- → (Association with Thalassaemias)
- CNS Presentations
- Leg Ulceration characteristic for sickle cell patients
- Skeletal Deformity

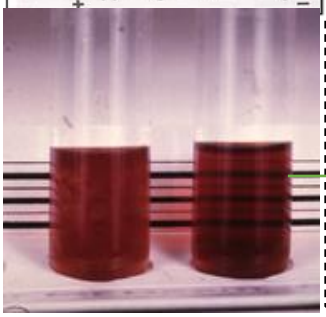


Laboratory Diagnosis of Sickle Cell Disease:

- CBC
- Blood Film
- Sickle Solubility Test
- Hb Electrophoresis (Most accurate)
- Genetic Study







We put the blood in a media
Right: normal (translucent).
Left: abnormal (turbid due to RBCs breakdown).

Indications for Blood Transfusion in Sickle Cell Anaemia: Not important

- Splenic sequestration (Stuck RBCs-spleen enlargment-dysphanction)
- Hepatic sequestration
- Aplastic crisis
- Overwhelming infections
- Elective or emergency surgical operation
- Severe painful crisis associated with severe
- haemolysis
- Pregnancy

Indications for exchange transfusion: Not important

- Strokes
- Pulmonary infarcts with infection
- Pregnancy (Severe persistent painful crisis)
- Priapism prolonged erection of the penis
- Preparation for major surgery

Summary:

Hemolysis

Causes

- Congenital: membrane defects, enzyme defects, globin defects.
- Acquired: Immune , Non-immune.

Clinical features

- Pallor, lethargy
- Jaundice
- Splenomegaly
- Gall stones
- Dark urine
- Bone deformity
- Leg ulcers

Labratory findigs

- Features of increased RBCs breakdown
- Features of increased RBCs production
- Damaged RBCs

Mechanisms

- Intravascular haemolysis: inside the circulation
- Extravascular haemolysis: in the spleen and liver (RES organs)

Sickle cell disease

Substitution of amino acid number 6 in beta-chain → (6 GLU > VAL) → Haemoglobin mutation

MCQs:

1-A patient came to the ER complaining of dark urine. On examination, they found jaundice in his sclera, splenomegaly and haemoglobinuria. What is the most common cause of these manifestations?
A-Extravascular haemolysis.
B-Intravascular haemolysis.
C-Both A&B.

2-What is the substitution mutation in Hb.S?
A-α2 β2 - 6 GLU > VAL
B-α2 β2 - 6 GLU > LYS
C-α2 β2 - 26 GLU > VAL

3-Haemolytic anemia is associated congenitally with which of the following:
A-Sickle cell disease.
B-Thalassemia.
C-Both A&B.

4-In Which of the following we will find sickle cell disease & Alpha-Thalassemia in the patient at the same time?
A-The sickle cell trait (AS)
B-Homozygous sickle cell disease (ss)
C-Doubly heterozygous sickle cell disease .

ANSWERS:
1-B
2-A
3-C
4-C

Good Luck!

Team members
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