جامعة الملك سعود
King Saud University

Revised By Hadeel Awartani Abdullah AlOmar

MED437
KING SAUD UNIVERSITY

Haemoglobinopathies

Objectives :

- To understand the normal structure and function of haemoglobin
- To understand how the globin components of haemoglobin change during development, and postnatally
- To understand the mechanisms by which the thalassaemias arise
- To appreciate the clinical presentations and complications of thalassaemia
- To appreciate the contribution of haemolysis and ineffective erythropoiesis to the pathophysiology of thalassaemia
- To understand the pathophysiology of sickle cell anaemia
- To be able to describe the clinical presentation and complications of sickle cell anaemia
- To understand the role of haemoglobin electrophoresis and high performance liquid chromatography in the investigation of globin disorders
- To appreciate the many other haemoglobin variants associated with disease

Team leaders :Abdulrahman Alageel, Ebtesam Almutairi.
Done by : khaled aldosari, Abdulaziz Aldrgam, Mohammed hakeem , Fahad alhumaid.

Impotent
Notes
Doctor’s slides

Normal Structure and function of Hemoglobin

- Hemoglobin is critical to the normal function of the red cell, the fundamental role of which is the transport of oxygen from the lungs to the tissues.

- The normal tetramer hemoglobin molecule comprises two 'alpha-like' globin polypeptide chains and two 'beta-like' globin chains; each globin molecule is associated with a hem group, which comprises a porphyrin ring with iron in its ferrous form at the center.

- **The α chains are encoded on chromosome 16.**

- The β-like globins are encoded on chromosome 11**.**

- Fetal haemoglobin HbF ($\alpha_2\gamma_2$)

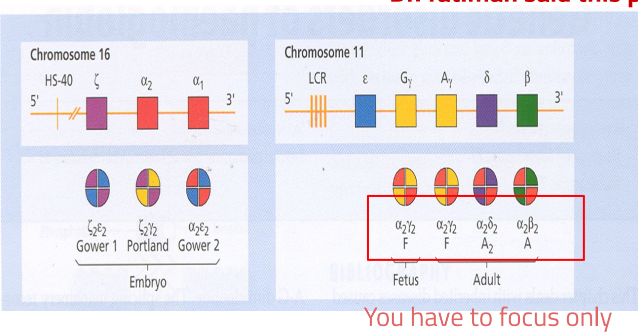
- The major adult haemoglobin is **HbA** ($\alpha_2\beta_2$) with a much smaller contribution from HbA2 ($\alpha_2\delta_2$ - usually 1.5-3.5% of adult haemoglobins).

- The **fetal haemoglobin HbF has a higher oxygen affinity than the adult haemoglobins, facilitating transfer of oxygen from the maternal to the fetal circulation.**[1]

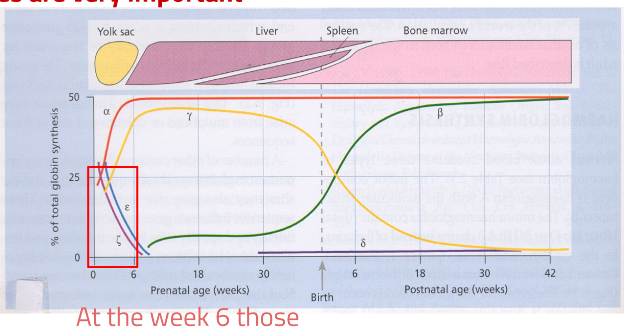
- Normally, the synthesis of α-like and β-like chains is balanced.

- An imbalance between the production of α and β chains is the pathophysiological basis of the thalassemias (a quantitative issue).

Dr. fatimah said this pictures are very important



You have to focus only on these types of Hb



At the week 6 those chains disappear

تلخيص لمعلومات الصورة

في كل فترة من حياتنا فيه نوع محدد من الهيموقلوبين , لذلك اذا طلع اي نوع في غير وقته يكون عندي شيء غير طبيعي_

-Chromosome 16 carries a1,a2 chains .. these chains form 3 types of Hb for the embryo, which are gower1,2 and portland ... these come from yolk sac.
-Chromosome 11 carries segma, Ggamma,Agamma, beta and delta chains.. these chains form 3 types of Hb for fetus and adult, which are:

1. F for fetus and comes from liver and spleen .
2. F, A and A2 for adult and come from the bone marrow.

[1] this property present in fetal life , if it is present in adult it will be another disease.

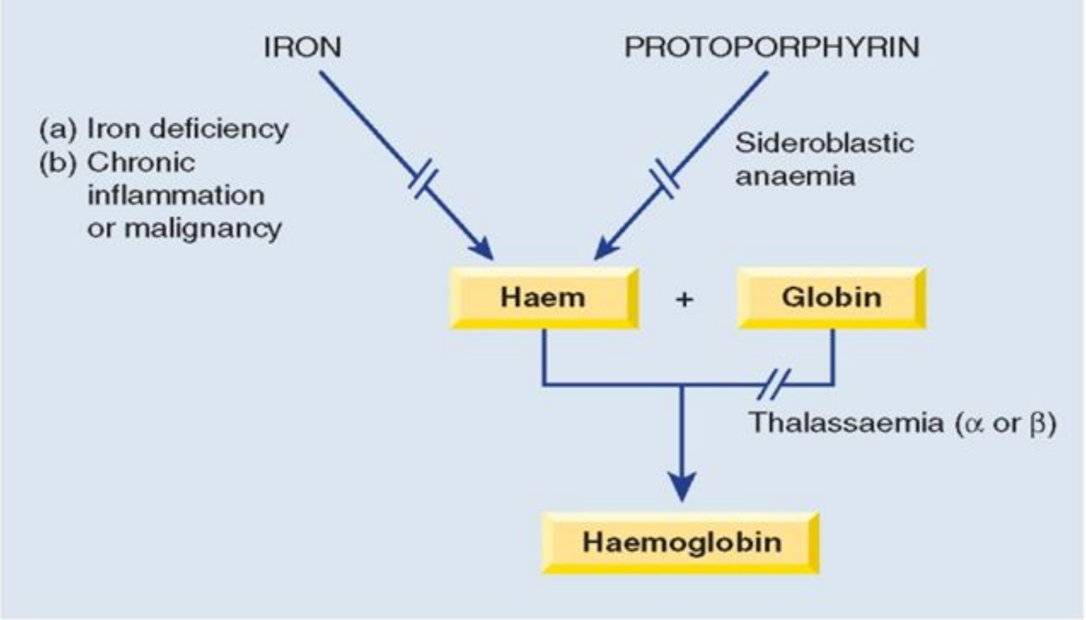


Figure 3.1 The causes of a hypochromic microcytic anaemia. These include lack of iron (iron deficiency) or of iron release from macrophages to serum (anaemia of chronic inflammation or malignancy), failure of protoporphyrin synthesis (sideroblastic anaemia) or of globin synthesis (α- or β-thalassaemia). Lead also inhibits haem and globin synthesis.

Hoffbrand's Essential Haematology, Seventh Edition. By A. Victor Hoffbrand and Paul A. H. Moss. Published 2016 by John Wiley & Sons Ltd.

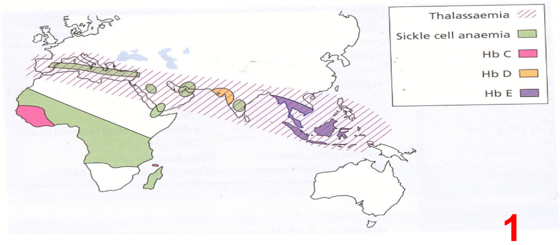
Most common cause of microcytic hypocromic anemia is iron deficiency , the second is thalasemia .
Thalasemia is intrinsic factor and inherited , and it is a disease of globin chain it self.

*in iron deficiency **low** RBC **high** RDW
*in thalasemia **high** RBC **normal** RDW

Both low MCV low MCH

Age	Hemoglobin	Chains		Percentage in Saudis %
Adult	Haemoglobin A	α2	β2	95.0%
	Haemoglobin F	α2	γ2	3.5%
	Haemoglobin A2	α2	δ2	1.5%
Fetal	Haemoglobin A	α2	β2	-
	Haemoglobin F	α2	γ2	
EMBRYONIC (Up to 8 Weeks gestation)	Haemoglobin Gower I	ζ2	Є2	
	Haemoglobin Gower II	α2	Є2	
	Haemoglobin portland	ζ2	γ2	
Diseased	Haemoglobin H	-	β4	
	Haemoglobin Bart's	-	γ4	
	Haemoglobin Lepore	α2	(δβ)2	

α and β THALASSAEMIA:



[1]

- The thalassaemias are divided into two main groups, the *α*-thalassaemias and the *β*-thalassaemias, depending on whether the defect lies in the synthesis.

- Its pathophysiology includes the chains which are present in excess will precipitate in the precursor red cells, leading to their premature death prior to release from the bone marrow (ineffective erythropoiesis) resulting to an increased erythroid drive and further expansion of the marrow into bones not typically used for hemopoiesis, and into the spleen. (extramedullary hematopoiesis)

- Thus, the long-term consequences of thalassemia therefore include splenomegaly, bony deformities and iron overload due to transfusion and infective erythropoiesis as well as chronic anemia.

1)تخيل عندك 70 طالب يجي من العليا للجامعة هل تحتاج سيارات صغيرة تشيل طالبين فقط او باصيين هذا هو ineffective erythropoiesis انك تنتج سيارات صغيرة بكفاءة قليلة

α - Thalassaemia:

- α-Thalassemia is seen with the greatest frequency in south-east Asia (Thailand, the Malay Peninsula and Indonesia) and west Africa.but also in the Middle East

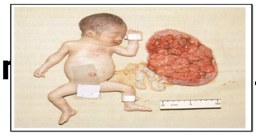
- Each chromosome 16 has an α-globin locus consisting of two α-globin (i.e; 4 genes) genes plus the regulatory sequences essential for their normal expression.

- In most patients with α-thalassemia, there is a deletion of one or more of the α-globin genes; there are occasional cases that are the consequence of non-deletional defects.

- Deletion of **one or two genes causes an asymptomatic condition with minor** hematological features; deletion of **three** of the four α-globin genes causes a more severe imbalance of α:β-globin chains and results in **hemoglobin H**, four beta globins, disease; and loss of **all four** α-globin genes causes **Hb Bart's**, four gamma globins, (hydrops fetalis syndrome). يولد الطفل ميت لعدم قدرة الهيموجلوبين على نقل الاوكسجين[1]

- 0.4% of deliveries are stillbirths due to Hb Bart's hydrops fetalis syndrome and HbH disease is found in about 1% of the population.

1- α⁺-Thalassaemia trait[2] (deletion of one or two α globin genes):



★ This is seen when an individual **inherits the α^+-thalasser** **one parent and a normal chromosome 16 from the** (i.e. heterozygotes for the α^+ determinant).

★ Affected individuals are asymptomatic, although they have minor hematological changes such as slight reductions in mean cell volume (MCV) and mean cell hemoglobin (MCH).

[1] Normally chromosome 16 has 4 copies of alpha gene ,, and in a-thalassemia there is a deletion of this gene
-Deletion of 1 or 2 copies —> asymptomatic condition (mild to moderate).
-Deletion of 3 copies—> hemoglobin H (moderate to severe).
-Deletion of 4 copies—> Hb Bart's (absente of all copies).

-Hemoglobin H and Bart't are the most common in pediatric.
[2] trait = very mild .

2- α^0-Thalassaemia trait (deletion of both α-globin genes on one chromosome 16):

The Hb is either normal or slightly reduced and the MCV and MCH are low. However, RBC count is elevated and RDW is not affected (**why?**).

3-Hb Bart's hydrops fetalis syndrome (deletion of all four α-globin genes):

No α-chains can be formed, and the fetal β-like chain γ-globin forms tetramers known as Hb Bart's.

This haemoglobin is **not useful for oxygen transport** and, despite the persistence of the embryonic haemoglobin Hb Portland ($\zeta_2\gamma_2$), there is intrauterine or neonatal[1] **death due to hydrops.**

4- Haemoglobin H disease (deletion of three α-globin genes): [2]

- This chronic haemolytic anaemia results from the **inheritance of both the α^+- and α^0-thalassaemia alleles**, leaving one functioning α-globin gene per cell. α-globin chains are produced at very low rates, leaving a considerable excess of β-chains, which combine to form tetramers (β_4). This tetramer is known as HbH.
- HbH is unstable and precipitates as the erythrocytes age, forming rigid membrane-bound inclusions that are removed during the passage of affected red cells through the spleen. The damage to the membrane brought about by this removal results in a shortened red cell lifespan.
- The damage to the membrane brought about by this removal results in a shortened red cell lifespan.
- Most patients are moderately affected, with anaemia of 7-11g/dl and markedly hypochromic, microcytic indices.
- **Supravital staining of the blood film demonstrates cells with many HbH inclusions**, giving a characteristic 'golf-ball' appearance.
- Most patients will be transfusion independent.
- Splenomegaly is seen in most patients.

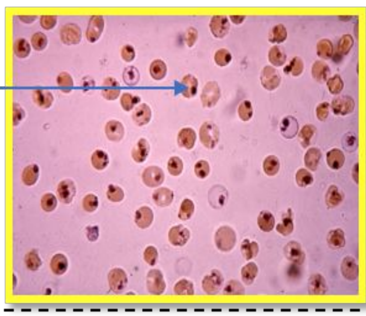
An example of the thalassemia intermedia is HB H

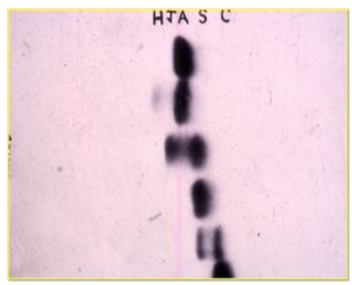
[1]they can't survive with absence of all copies of alpha .. death occur due to lose the ability to use the O2.
[2] both parents have thalassemia.

LABORATORY DIAGNOSIS OF ALPHA THALASSEMIA SYNDROME: [1]

- High red cell count in the trait
- **Hypochromic microcytic red cells & target cells**
- Normal serum iron or low in children
- Normal total iron binding capacity or high in children
- Positive Hb H inclusion bodies in the blood film preparation & positive Heinz bodies with vital stains
- Hemoglobin electrophoresis show presence of hemoglobin H (Hb H disease)
- Hemoglobin electrophoresis show low Hb A2 level
- Genetic study to confirm the diagnosis

Heinz bodies

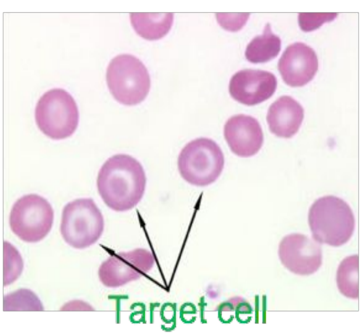


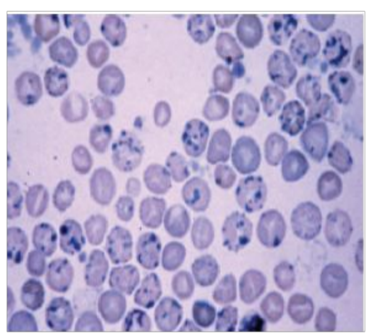


electrophoresis

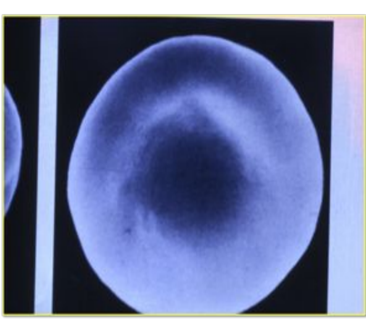
Heinz bodies we mix the violate stain (methyl violate) or supravitally stain with blood and then we have red pink inclusions bodies .

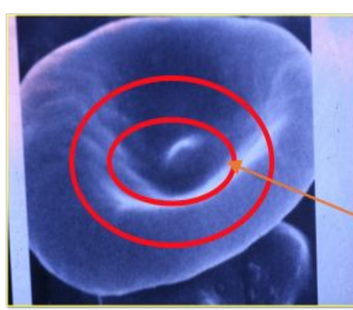
From 436 team



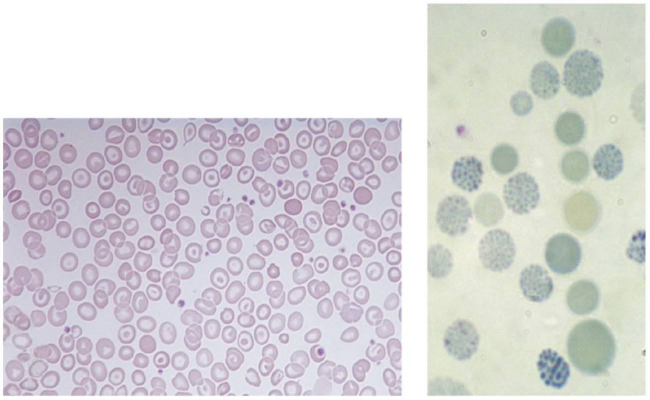


Sever Hb H
golf cell





Increase or folding of the membrane in the middle .
(نقطة في وسط الكرية الحمراء)



(a) (b)

Figure 7.7 **(a)** α-Thalassaemia: haemoglobin H disease (three α-globin gene deletion). The blood film shows marked hypochromic, microcytic cells with target cells and poikilocytosis. **(b)** α-Thalassaemia: haemoglobin H disease. Supravital staining with brilliant cresyl blue reveals multiple fine, deeply stained deposits ('golf ball' cells) caused by precipitation of aggregates of β-globin chains. Hb H can also be detected as a fast-moving band on haemoglobin electrophoresis (see Fig. 7.12).

Hoffbrand's Essential Haematology, Seventh Edition. By A. Victor Hoffbrand and Paul A. H. Moss. Published 2016 by John Wiley & Sons Ltd.

- Heterozygous a0 thalassaemia is more dangerous .
- a+ there is one alpha work but a0 the twe copies of alpha deleted.

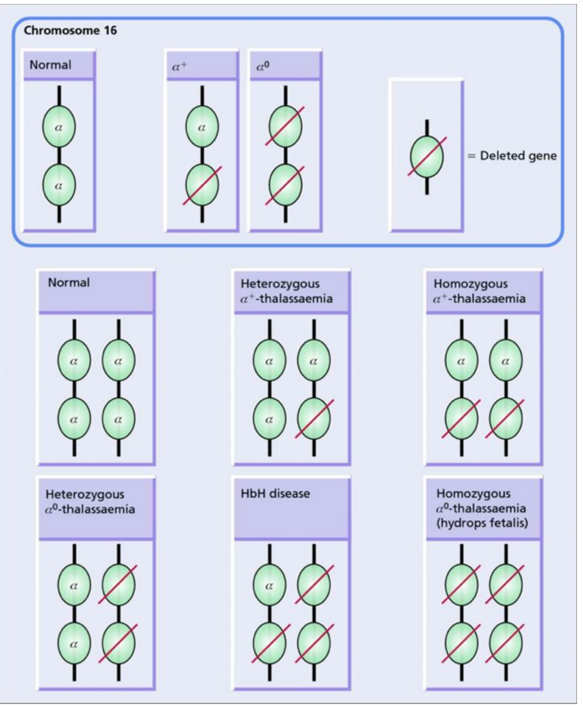


Figure 4.3 A diagram to show how the two forms of abnormal chromosome 16 (α^+ and α^0) are arranged to give the different forms of α-thalassaemia. Homozygotes for α^0-thalassaemia die from Hb Bart's hydrops fetalis syndrome.

B -Thalassaemia:

- According to WHO there are 1.5% of the world's population are carriers of β-thalassaemia.
- The prevalence of the β-thalassaemia trait is particularly high in southern Europe (10-30%) and south-east Asia (5%), common in Africa, the Middle East, India, Pakistan and southern China.

Difference between α & β-thalassaemias:

α –Thalassaemia : arises from gene **deletions**.

β-Thalassaemia: results from a **multiplicity** of different single nucleotide substitutions, insertions or small deletions affecting the β-gene itself or occasionally in promoting regions.(MUTATIONS). 1

- The difference between deletion and mutation is ...... deletion (whole gene is gone). And mutation(abnormality in some subsequences).
- main characteristics of heterozygous are thalassemia picture and target cells.

Heterozygous *β*-thalassaemia (Beta-thalassaemia trait). 2	Homozygous *β*-Thalassaemia
• Most affected subjects with beta thalassaemia trait are asymptomatic. • The **Hb concentration is either normal or slightly reduced, hypochromic and microcytic** red cell indices are seen. • Examination of peripheral blood film may show red cell abnormalities such as **target cells** and poikilocytes. • **HbA2 levels will be raised above the normal range** to 3.5-7.0%. • Slightly increased HbF levels, in the range of 1-5%.	• Defects of *β*-globin Genes on both copies of chromosome 11 • **Marked anaemia** • Transfusion dependent

Clinical classification of the thalassemias

Thalassemia minima	describes the presence of a thalassaemia mutation that is without clinical consequences[1].
Thalassemia minor	describes patients with microcytosis and hypochromic red cells secondary to thalassemia mutations, but with only mild anemia or a normal hemoglobin. **Patients who inherit a single affected allele are usually in this category.**[2]
Thalassemia intermedia	patients will also have a microcytic hypochromic anemia, increased erythroid drive to maintain their hemoglobin, packed bone marrow with a decreased myeloid to erythroid ratio, and extramedullary hematopoiesis, giving **splenomegaly**. Transfusion may be required to maintain the hemoglobin at times of additional physiological stress.
Thalassemia major[3]	have severe anemia and are transfusion dependent. Their increased erythroid drive leads to a packed erythroid marrow and splenomegaly, **development of bony abnormalities secondary to unchecked marrow expansionu** [4] Patients in this category are those with complete loss of β-globin expression from both copies of Ch11.

[1]this type occurs suddenly, and it is very mild.
[2] راح يجيبون اطفال واحتمالية اصابتهم تكون trait ويتزوج وحده برضو عندها trait الخطورة في هذا النوع لما شخص عنده sever
[3] sever typre.
[4] see in children manly in skull bone and face bone,, so that is why they call it thalassemic face.

The clinical course and complications of thalassemia major

Anemia - is the principal feature of thalassemia major, the massive expansion of erythroid activity results in several complications:

A. Splenomegaly.[1]
B. Bony deformities.
C. Growth retardation.
D. Iron absorption from the gut is increased.[2]
E. Marked iron overload.[3]

Iron deposition due to overload occurs in the myocardium, resulting in congestive cardiac failure and potentially fatal arrhythmias; in the liver, leading to cirrhosis; in the pancreas, causing diabetes mellitus; and in other endocrine organs, leading to delayed puberty.

Treatment of *β*-thalassemia major

1. Transfusion[4] are planned to maintain the pre-transfusion Hb concentration at 9-10g/dL or above.
2. Splenectomy can be performed[5]
3. Iron chelator[6], required subcutaneous infusion treatment over several hours on five days of the week.
4. Hematopoietic stem cell transplantation (HSCT) is curative.
5. gene therapy (see the NEJM quick tack),click here

Genetic counselling and antenatal diagnosis of *β*-thalassemia major

- **Antenatal diagnosis can be made early during pregnancy from an analysis of chorionic villous DNA (at 9-12 weeks) or amniocyte DNA (at 13-16 weeks), or later using DNA from blood obtained from an 18-20-week-old fetus.**
- Newer techniques focus on the non-invasive analysis of fetal DNA in the maternal circulation.
- **A pre-marital screening, national program, is one of the major intervention leading to reduced incidence of beta thal major.**[7]

---

[1]لانها مقبرة ال RBCs.
طيب وشو الهيبسيدين؟. هو إللي يوازن الحديد بالجسم

[2] Because of decrease of hepcidin.
[3]Because of 1-decrease of hepcidin. 2-transfusion dependent.
[4]The best treatment because they have severe anemia .
[5]In some cases.
[6]We **should** give it to beta thalassemia patients.
[7] This test do it **before** the pregnancy.. if they don’t do it and the pregnancy happened , the best method to diagnosis is Antenatal.

Table 4.1 Different clinical and haematological abnormalities associated with some structural haemoglobin variants.

Variant	Clinical and haematological abnormalities
HbS	Recurrent painful crises (in adults) and chronic haemolytic anaemia, both related to sickling or red cells on deoxygenation
HbC	Chronic haemolytic anaemia due to reduced red cell deformability on deoxygenation; deoxygenated HbC is less soluble than deoxygenated HbA
Hb Köln, Hb Hammersmith	Spontaneous or drug-induced haemolytic anaemia due to instability of the Hb and consequent intracellular precipitation
HbM Boston, HbM Saskatoon	Cyanosis due to congenital methaemoglobinaemia as a consequence of a substitution near or in the haem pocket
Hb Chesapeake, Hb Radcliffe	Hereditary polycythaemia due to increased O_2 affinity
Hb Kansas	Anaemia and cyanosis due to decreased O_2 affinity
Hb Constant Spring, Hb Lepore, HbE	Thalassaemia-like syndrome due to decreased rate of synthesis of abnormal globin chain
Hb Indianapolis	Thalassaemia-like syndrome due to marked instability of Hb

You should know just these two types.

Structural Hemoglobin Variants[1]

- Over 1000 abnormal hemoglobin variants have been reported. The majority of **structural Hb variants are the consequence of a single-point mutation with a single amino acid substitution in the affected globin chain (e.g. HbS, HbE, HbC and HbD).**
- When the amino acid substitution results in an overall change in the charge of the hemoglobin molecule, its migration in a voltage gradient is altered and this can be demonstrated by standard electrophoretic techniques. The speed of migration is characteristic for each abnormal hemoglobin.
- **Abnormal hemoglobin variants are now usually detected by high-performance liquid chromatography (HPLC). The most common structural Hb variant is hemoglobin S (HbS).**

Hemoglobin S:

- ➔ A mutation in the β-globin gene results inthe charged glutamic acid residue in position 6 of the normal β-chain being replaced by an uncharged valine molecule.
- ➔ The interaction of sickle β-globin chains with normal α-globin chains forms HbS.
- ➔ When deoxygenated, HbS is much less soluble than deoxygenated HbA, and HbS molecules polymerize, eventually forming long fibers. **These result in the deformation of the cell into the well-recognized sickle shape.**

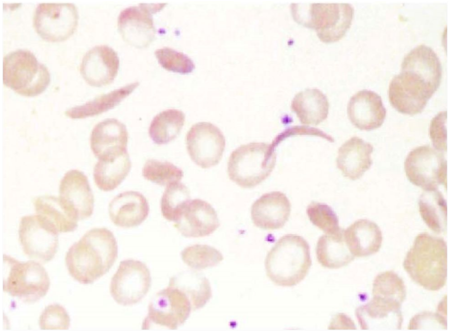


Figure 4.7 Two sickle-shaped red cells with pointed ends[2] and some partially sickled red cells from the blood film of a patient with sickle cell anaemia (homozygote for HbS).

[1] باختصار يكون المشكله في الهيموقلوبين هي استبدال الامينواسيد بنوع اخر فينتج عندي هيموقلوبين غير طبيعي
[2] It should be sickle shape with **pointed end.**

Sickle Cell Trait[1]:

- Heterozygotes (one gene for normal β-globin and one for β^S) are described as having sickle cell trait. **Their red cells contain between 20% and 45% HbS**[2]**,** the rest being mainly HbA**.**
- Individuals with sickle cell trait are usually asymptomatic. However, spontaneous hematuria may occur occasionally due to microvascular infarctions in the renal medulla. Renal papillary necrosis may rarely occur. **The red cells do not sickle until the O_2 saturation falls below 40%.**

Sickle Cell Anemia[3]:

- It is a descriptive name when patient have at least a copy of beta globin being S and another beta harbor any mutations (beta that/S, S/S, S/D, ect).
- Homozygotes for sickle β-globin are described as having sickle-cell anemia. Their red cells contain almost exclusively HbS and **NO HbA;** there is a small but variable percentage of fetal hemoglobin**.**
- Sickled red cells then occlude the microvasculature, with poor downstream perfusion and oxygenation. They may be lysed directly in the circulation, where the resulting free hemoglobin scavenges nitric oxide.
- HbS are less deformable than normal red cells and this results in a chronic, extravascular, hemolytic anaemia. The Hb usually varies between 6 and 9 g/dL.

Diagnosis:

- Sickled cells are invariably present on the blood films of patients with HbSS. HbSS is made by finding;

1) a positive result with a screening test for HbS (Sickle solubility test); and
2) a peak at an appropriate position on an HPLC trace, confirmed by isoelectric focusing or hemoglobin electrophoresis.

- In young children, a classic acute painful presentation is with **dactylitis**[4], or the '**hand-foot syndrome**', in which there is occlusion of the nutrient arteries to the metacarpals and metatarsals (Figure 4.8) and painful swelling of the hands and feet.
- In the central nervous system, cerebral infarction occurs in approximately 10% of patients under the age of 20, and is a cause of significant morbidity in sickle cell patients. It has been found that children with an increased velocity of blood flow in the major cerebral vessels are at particular risk of stroke.

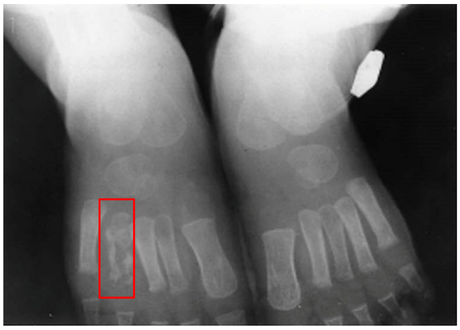


Figure 4.8 An X-ray of the feet of a child with sickle cell anaemia two weeks after the onset of hand-foot syndrome, showing necrosis of the right fourth metatarsal.

Figure 4.9 A chronic leg ulcer with increased pigmentation of the surrounding skin in a woman with sickle cell anaemia.

[1] trait = one parent is normal and the other is carrier.
[2] they do Hb electrophoresis , in sickle trait the HbS will be from 20%-45% , if it is above 45% will be sickle anemia.
[3] in diseased type they have one HbS and the other one form any type of abnormal Hb ,, you can see patient with HbS and thalassemia.
[4] dactylitis is inflammation of an entire finger
-The most common complications of sickle cell anemia are leg ulcer and necrotic bone (hand foot syndrome).

Treatment:

The principles of the management of sickle cell anemia include:

1. Management of the increased infection risk by immunization.
2. Administration of folic acid daily to prevent secondary folate deficiency.
3. Avoidance of factors precipitating painful crises such as dehydration, hypoxia, circulatory stasis.
4. Treatment of painful crises with oral or intravenous fluids and analgesics, including opiates when necessary.
5. Early detection of the acute chest syndrome (blood gas measurements and chest X-ray). Exchange transfusions are often needed to lower the patient's HbS levels and limit ongoing sickling.
6. Blood transfusion when necessary.
7. SCT and gene therapy.

Table 4.2 Clinical manifestations of sickle-cell anaemia.
Chronic haemolytic anaemia and consequent cholelithiasis
Splenic sequestration syndrome; rarely, hepatic Sequestration
Acute chest syndrome
Cerebral infarction, TIA, intracranial haemorrhage
Widespread painful vaso-occlusive crises
Bone infarction (osteonecrosis)
Osteomyelitis (*Salmonella, Staphylococcus*)
Chronic leg ulcers
Priapism
Chronic pulmonary disease and pulmonary hypertension
Haematuria, proteinuria, chronic renal failure
Pregnancy: increased peripartum fetal loss, preterm births, babies small for gestational age
Aplastic crises due to parvovirus infection
Proliferative sickle retinopathy (more common in HbSC disease)

Hemoglobin E and C:

Among the commonest are HbE and HbC, both of which result from single amino acid substitutions in the β-chains.

- HbE is very common in south-east Asia (being found in about 50% of the population in some parts of Thailand).
- HbC is the consequence of a glutamine to lysine[1] substitution in the β-globin chain. HbC is also seen in homozygosity; here the hemoglobin does not polymerize as with HbSS, but can **crystallize**, with a resulting reduction in the flexibility of the red cell and a reduction in its survival.
- Homozygotes have a mild anemia, low MCV, splenomegaly and many target cells in their blood film. HbC is found in patients of West African origin.
- When one allele being S and other being C or E, it is an example of a sickle cell disease (the most benign form is S/E).

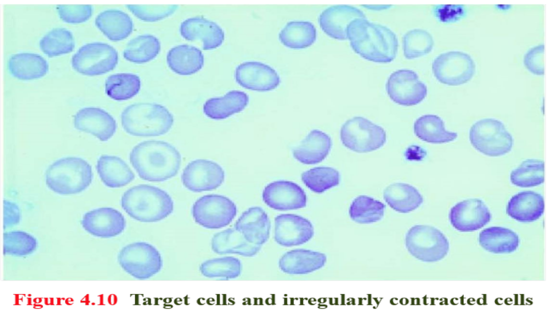


Figure 4.10 Target cells and irregularly contracted cells in the blood film of a homozygote for HbC.

[1] In same position of Hbs , which is in 6 of beta chain

Review question \ doctor questions

Q1) **Which ONE of the following statements is TRUE about sickle cell anemia?**

A) The oxygen dissociation curve is shifted to the left.
B) It may cause ankle ulcers.
C) It is NOT associated with stroke.
D) It is NOT associated with atrophy of the spleen

Q2) **Which ONE of the following statements is TRUE about β-thalassemia trait?**

A) It is associated with a raised hemoglobin A2 level with normal CBC indices.
B) It is associated with iron overload.
C) It is associated with a normal reticulocyte index.
D) It is associated with splenomegaly.

Q3) I **Which ONE of the following statements is TRUE about beta-thalassemia?**

A) It may cause hemoglobin H disease.
B) It causes a microcytic hypochromic blood picture.
C) It is frequently cause a hydrops fetalis.
D) It is very common in the Far East.

Q4) **Which ONE of these statements is TRUE aboutβ-thalassemia major?**

A) It presents at birth.
B) It is usually caused by deletion of β globin genes.
C) It is associated with an increased risk of bone infarction.
D) It is associated with stunted growth.

Q5)I **Which ONE of the following is a feature of thalassemia intermedia?**

A) It may be due to homozygous βo thalassemia without coinheritance alpha thalassemia.
B) It does NOT associated with extramedullary hematopoiesis.
C) It is usually associated with splenomegaly.
D) It can NOT cause iron overload.

Q6)**Which ONE of these statements is TRUE concerning sickle cell trait?**

A) It is a cause of anemia
B) It protects against malaria.
C) It is usually associated with splenomegaly.
D) It is a cause of frequent sickle cells in the peripheral blood

Answers and explanations

Q1) Explanation:

A) oxygen dissociation curve is shifted to the left which happens in HbF while in sickle cell there's a shift to the right.
B) Sickle cell anemia may cause ankle ulcers
C) Sickle cell anemia is associated with stroke
D) Sickle cell anemia may result in splenomegaly

Correct answer: **B**

Q2)Explanation:

A) It is associated with a raised hemoglobin A2 level with **abnormal** CBC indices.
B) It is **not** associated with iron overload.
C) t is associated with a normal reticulocyte index because there`s no hemolysis.
D) Not associated with splenomegaly

Correct answer: **C**

Q3)Explanation:

A) Beta thalassemia does not cause HbH disease
B) t causes a microcytic hypochromic blood picture.
C) Very rare only caused by alpha
D) Its common in a lot of places

Correct answer: **B**

Q4) Explanation:

A) **No, it's not** present at birth.
B) It's usually caused by **mutation** of beta globin genes.
C) It's **not** associated with bone infarction instead with bone deformity
D) Non-functioning epiphyseal plates

Correct answer: **D**

Q5) Explanation:

A) _ _ _ _
B) It may associate with extramedullary hematopoiesis
C) Associated with splenomegaly
D) It can cause iron overload by blood transfusions rarely

Correct answer: **C**

Q6)Explanation:

A) It does not cause anemia
B) Protects against malaria
C) Not associated b\c no hemolysis
D) Very rare to find sickle cells considered normal

Correct answer: **B**