431 Teams
medical students

Haematology

431 Team

2/4

THALASSAEMIA

Team Leaders

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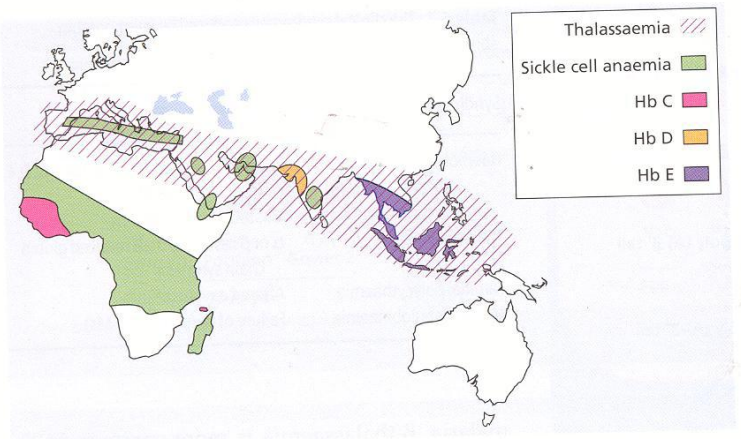
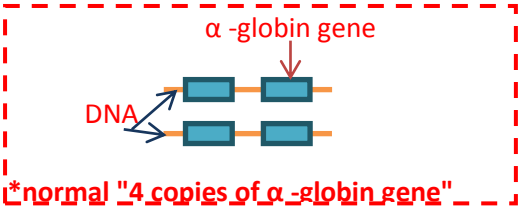
THALASSAEMIA

Thalassemia: Is an inherited (homozygous or heterozygous) blood disorder passed down when the body makes an abnormal form of hemoglobin. The disorder results in excessive destruction of red blood cells, which leads to anemia.
Thalassemia is very common disease in saudi arabia due to familly marriages.

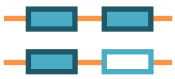
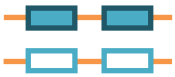
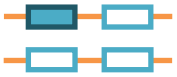
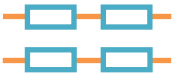


α-Thalassaemia

Are gene defects affecting the production of the α globin protein (α chain at chromosome 16).
As there are normally four copies of the α -globin gene, the clinical severity can be classified according to the number of genes that are missing or inactive into four groups :

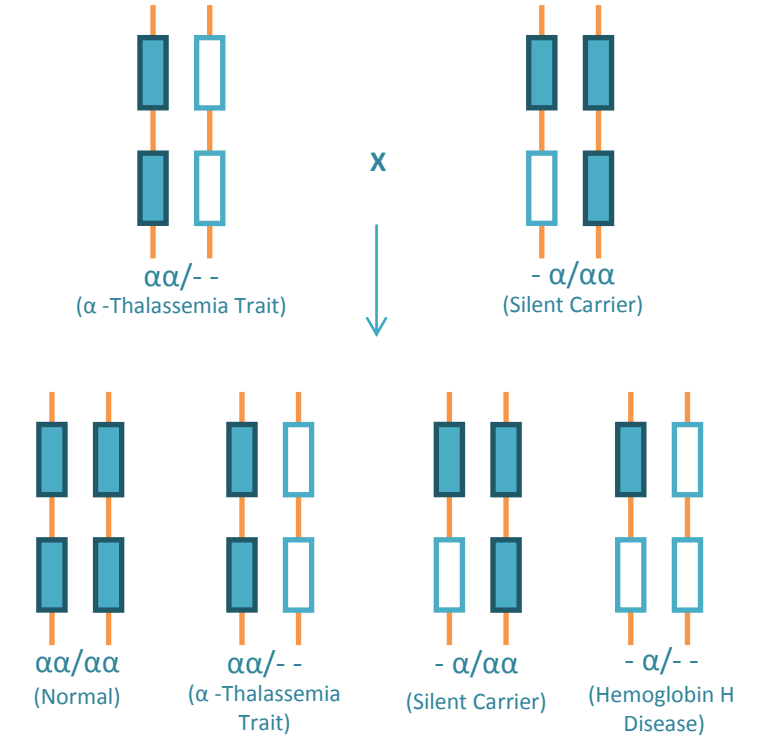


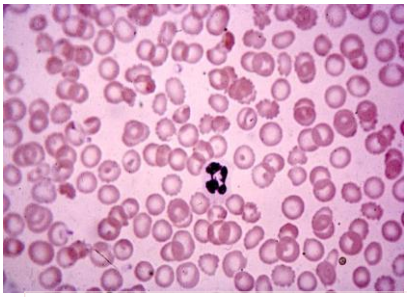
*normal "4 copies of α -globin gene"

	α-Thalassaemia			
	Silent Carrier	**α -Thalassemia Trait**	**Haemoglobin H Disease**	**Hydrops Fetalis**
Genotype of the α-thalassemia syndromes.	 Loss of **one** α-globin gene	 Loss of **two** α-globin gene	 Loss of **three** α-globin gene	 Loss of **all** α -globin gene
	No sign for illness	No anemia but there is minor increase in RBC count with microcytosis and hypochromia	A clinical disease that needs treatment and regular blood transfusion.	-Severe condition -if the fetus get the disease he will die before delivery
	The patient is normal but if he/she get married with a person who has same trait or has any genotype of the α–thalassemia syndromes their children may get HbH disease, hydrops fetalis or they will be silent carriers "see example below".		Common in Eastern area of Saudi Arabia "Sharqia"	

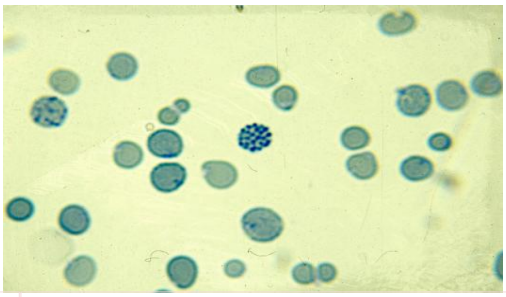
in α-Thalassaemia HB A_2 is low <1.5

Inheritance of HbH (- α/- -)disease

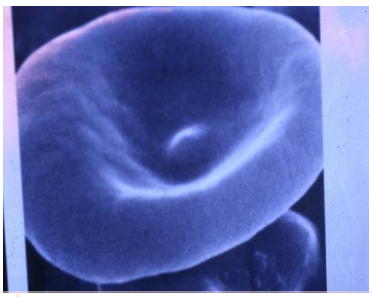




Blood Film Morphology:
-Hypochromic microcytic RBCs
- α-thalassemia



Blood film stained by supravital stain shows:
-target cell & Golf Ball cell Appearance
-Indicates HbH α-thalassemia disease

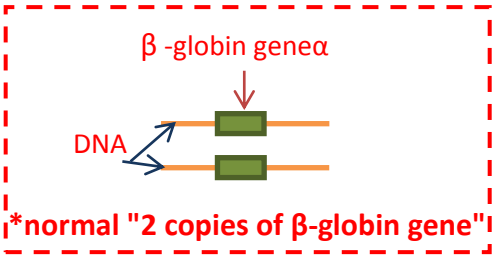


Electron Microscope:
- Target Cells
"Bull's-eye appearance of RBC"

** Golf Ball cell Appearance is a diagnostic feature for Hb H disease**

β-Thalassaemia

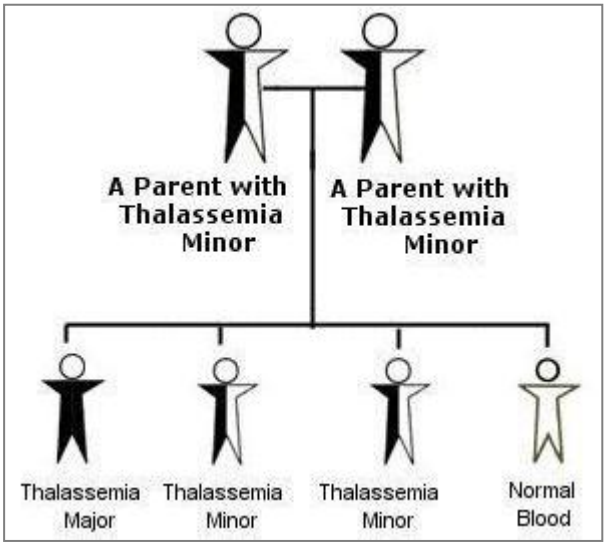
Are gene defects affecting the production of the β globin protein (β chain at chromosome11) ،As there are normally two copies of β -globin gene.



Hemoglobin Fractions in the Genotypic Variants of the β-Thalassaemia Syndromes

Genotype	HbA%	HbA2%	HbF (%)	comment
Normal (β/β)	97	2.5 –3.5	<1.5	Normal
Thalassaemia major	0	High >3.5	High	-both genes are abnormal -severe and needs regular blood transfusion
Thalassaemia intermedia	present	High >3.5	High	moderate& sometimes need transfusion
Thalassaemia minor	>90	High 3.5 –10.0	1-2 "sometimes higher"	- one gene is abnormal - asymptomatic -mild anemia in some patients. **If both parents carry β-thalassemia trait (minor) there is a 25% risk of a thalassemia major child**
Thalassaemia minima	97	<3.2	<1	silent

* in β -Thalassaemia, HB A_2 is high >3.5
While in α- Thalassaemia HB A_2 is <1.5

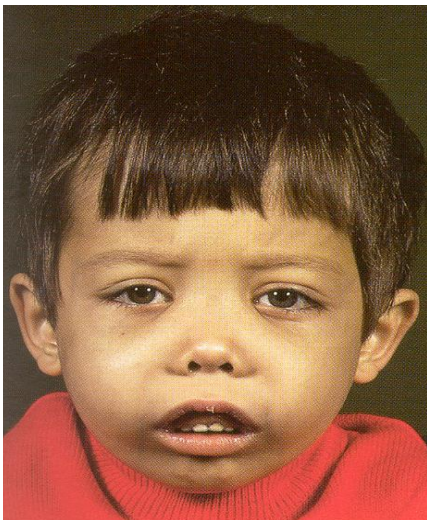


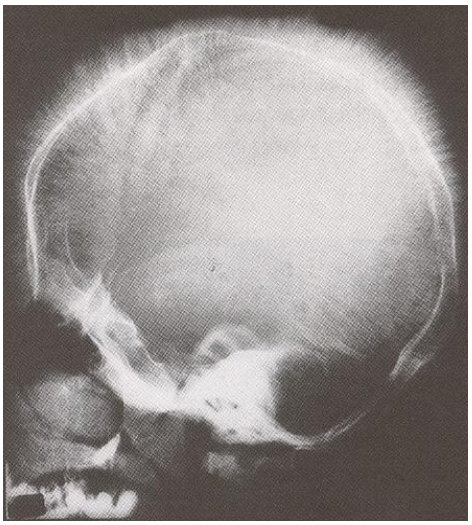
Clinical Manifestations

- Anemia
- Pallor
- Jaundice: Due to hemolysis.
- Apathy and Anorexia
- Failure to Thrive
- Hepato-splenomegaly: the bone marrow can't handle the over production of RBCs so it induces an abnormal RBCs production from liver and spleen and this will enlarge them.
- Iron Overload manifestations: due to regular blood transfusion.
- Skeletal Deformity & Bone Expansion:
  the intense marrow hyperplasia* leads to "β-thalassemia major faces": board maxillary bone, frontal boozing of the skull, wide+depressed Nasal bridge and hair on end appearance on X-Ray.

*Bone Hyperplasia: Occurs as a result of the increase demand on RBCs, so the whole bone morrow will become hyper-active.

Thalassemia patient





Hair on end appearance

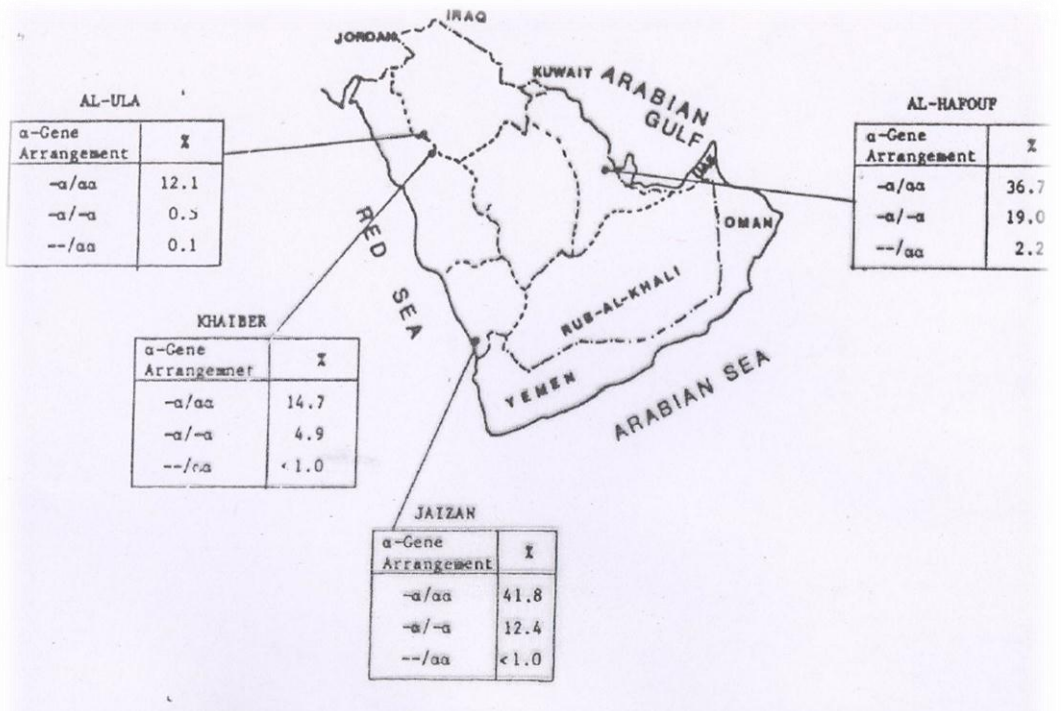
	Clinical and Hematologic Features of the β-Thalassemia Syndrome			
	Major	**Intermedia**	**Minor**	**Minima**
Severity of mainfestations	++++	++	+, ±	±, 0
Genetics *	Homozygotes, double heterozygotes	Homozygotes, double heterozygotes, rarely heterozygotes	Heterozygotes	Heterozygotes
Splenomegaly	++++	++,+++	+,0	0
Jaundice	+++	++,+	0	0
Skeletal changes	++++,++	+,0	+,0	0
Anemia(Hb, g/dl)	<7 sever	7 –10	>10	Normal
Hypochromia	++++	+++	++	+
Microcytosis	+++	++	+	0
Target cells	10 –35%	++	+	±
Basophilic stippling	++	+	+	0, +
Reticulocytes(%)**	5 –15	3 –10	2 –5	1 –2
Nucleated red cells	+++	+, 0	0	0

±, little or no abnormality; +, mild abnormality; ++++, prominent abnormality

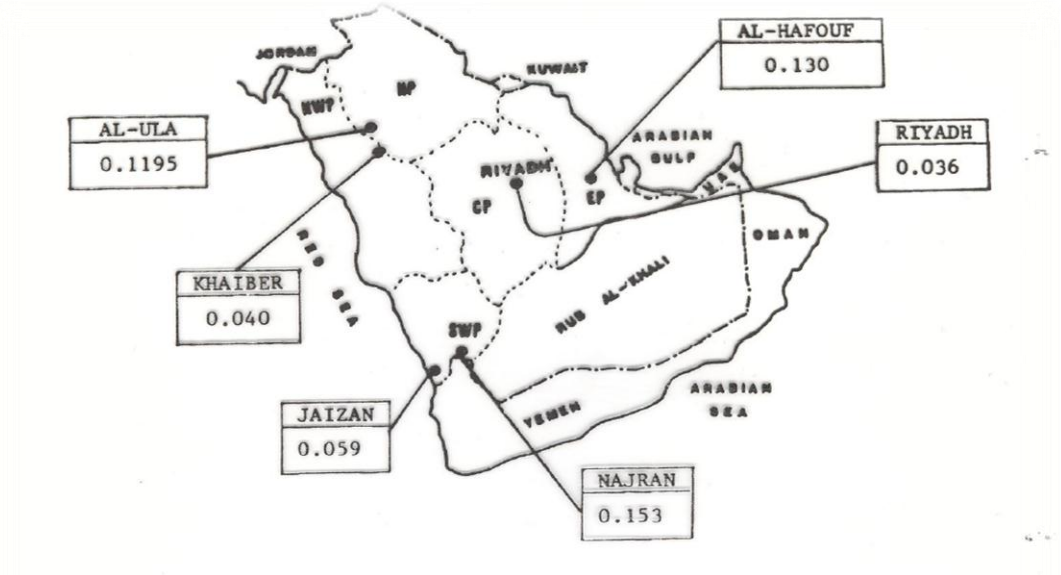
***Homozygote: made up of two of the same alleles(genes).Heterozygote: is made up of two different alleles(genes).**

****Reticulocytes: immature RBCs that appear because of stress on the bone marrow.**

Epidemiology of Thalassaemia



Frequency of α-thalassaemia due to α-gene deletion in different regions of Saudi Arabia (diagnosed using restriction endonuclease Bam HI).



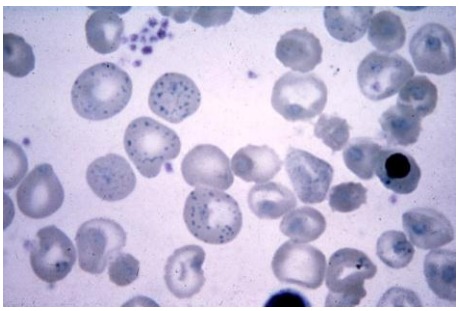
Frequency of β-thalassaemia in different regions of Saudi Arabia. (From Ref. No. 20.) (No. investigated: Al-Hafouf 300; Riyadh 250; Al-Ula 427; Khaiber 500; Jizan 1271; Najran 301.) f = 8.8353; df = 10; p < 0.01

Diagnosis

A)These laboratory findings are mostly found in β-Thalassemia major.

1) Blood Film :

- Erythroid precursor (immature RBCs)
-Hypochromic cells
-microcytic cells.
-Target cells



2) Haemoglobin Electrophoresis

- used to indicate the levels of different types of Hb

B)Prenatal Diagnosis of the Haemoglobinopathies (Including Thalassemia)

- Important when both partners show an abnormality and there is a risk of a serious defect in their offspring.
- Several techniques are available, the choice depends on the stage of pregnancy and the potential nature of the defect :
  - Fetal blood sampling DNA Analysis
    - Include DNA analysis, Haematological parameters, and Biochemical & globin chain analysis.
    - Samples to be analyzed are obtained by different ways depending on the pregnancy stage.

MANAGEMENT OF THE THALASSEMIAS

- Blood Transfusion.
- Iron chelation therapy: Desferrioxamine S.C.
- Splenectomy.
- Hormone replacement.
- Bone marrow transplantation.
- Gene therapy.

Questions

1-Parents of a patient with HbH:

A- Both are silent
B- Both are trait
C- One of the parents is silent and the other is alpha thalssemia triat
D- One alpha thal major and one beta thal major

2- Which one of the following is a laboratory feature of beta thalassemia major?

A- Low reticulocyte count
B- Normochromic normocytic anemia
C- Low hemoglobin F level
D- Presence of many nucleated Rbc

3- alpha thalassaemia silent, found mostly in which region of kingdom:

A- Jaizan
B- Alhafuf
C- Al-ula
D- Khaiber

4-Which one is correct regarding beta thalassaemia major:

A- Mild anemia
B- Both genes are affected
C- One gene is affected
D- Silent

Answers : 1- C 2-D 3- A 4-B