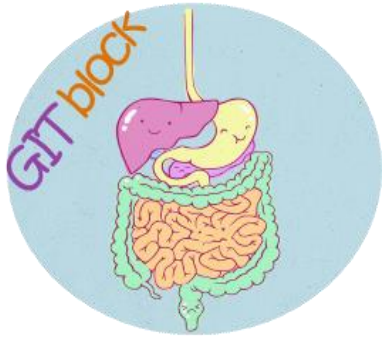


HAEMOGLOBINOPATHIES

NOTE : THIS TEAMWORK DON'T VIEW EVERYTHING IN THE SLIDES ONLY THE IMPORANT THINGS NOTED BY THE DOCTORS

Color coding

- important
- Extra info
- Notes from lecturer

دعاء قبل المذاكرة:

اللهم أني أسالك فهم النبين و حفظ الملرسلين و الملائكة المقربين اللهم اجعل السنتنا (أنك على كل شيئا قدير و حسبنا الله نعم الوكيل ,عامرة بذكرك و قلوبنا بخشيتك)

DON'T FORGET to check our editing file : haematology edit

Please don't hesitate to contact us on:Haematology434@gmail.com

Haematopoeisis

Stage	Site of blood formation
Up to 2 months before birth	Yolk Sac
2 – 3 months before birth	Liver & Spleen
After birth Begins 4 months before birth	Bone Marrow “ first formation starts in all bones including long bones, with aging formation only happen in Vertabrae & Sternum

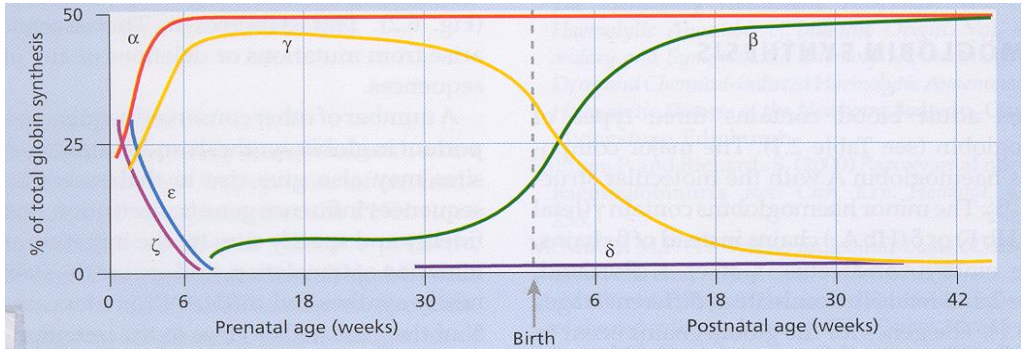
Globin Chains

Prenatal

(α - γ high amount)
(δ- ε – β low amount)

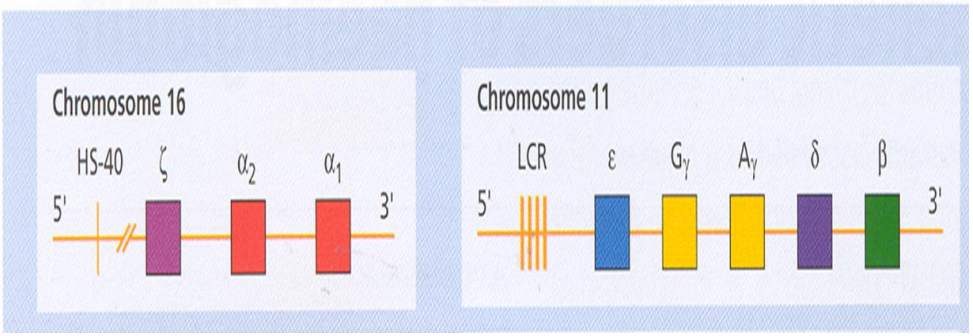
Postnatal

α (remain)
β (increase)
γ (decrease) & δ



Genes expressing Globin Chains

# of Chromosome	Globin Chains
Chromosome 16	α1, α2, ζ
Chromosome 11	(rest) β , ε , Aγ , Gγ ,δ



Normal Human Hemoglobin

Age Category	Type of Hemoglobin	Globin Chains	Percentage in Saudi
Embryonic Up to 8 weeks gestations	Hb Gower I	$\zeta_2 \epsilon_2$	
	Hb Gower II	$\alpha_2 \epsilon_2$	
	Hb Portland	$\zeta_2 \gamma_2$	
Fetal	HbF	$\alpha_2 \gamma_2$	
	HbA	$\alpha_2\beta_2$	
Adult "most important"	HbA	$\alpha_2 \beta_2$	95%
	HbA_2	$\alpha_2\delta_2$	2.5 - 3.5 %
	HbF	$\alpha_2 \gamma_2$	0.5 - 1.5 %

α globin consists of 141 Amino acids e.g. (ζ) , while β has 146 Amino acids e.g. (β , ε , Aγ , Gγ ,δ)

Abnormal Human Hemoglobin Types

Name	Globin Chains
Hb H	4β
Hb Bart's found normally at birth but shouldn't exceed 0.5%	4γ
Hb Lepore	rare 2 (δβ) 2α (not important)

Hemoglobins present at birth in normal newborn

Hemoglobin	Percentage
HbA	15 – 40 %
HbA_2	< 0.3 %
HbF	**60 – 85 %**
Hb Bart's	< 0.5

Haemoglobinopathies

Thalassemia

•An **inherited autosomal recessive** disorder in which the protein part (Globin) of the hemoglobin is completely or partially missed, resulting in inability of the formed Hemoglobin to carry Oxygen and Carbon dioxide to and from the lung.

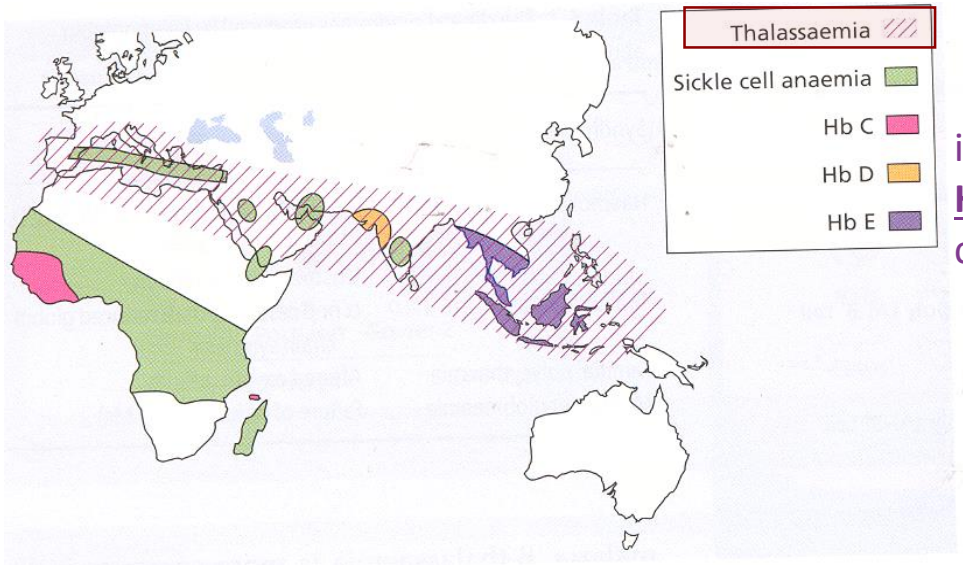
Example

Thalassemia

Abnormal Hemoglobins

- A condition characterized by abnormal hemoglobin structure, due to an error in the sequence of amino acids which form the globin.

Sickle Cell Anemia



Thalassemia

it can be **Heterozygous** "defect of 1 copy from parents" or **Homozygous** " Defect of 2 copy from parents = pair of chromosome

Epidemiology

It's common in Arab peninsula, Mediterranean countries, India and Pakistan, South east Asia and saudi arabia. May be due to familial marriages.

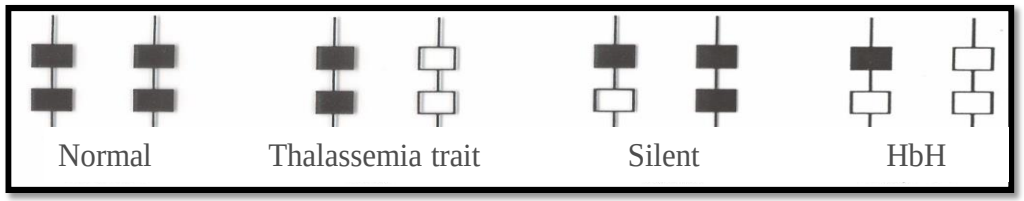
Clinical Manifestation of Thalassemia

Pallor → Jaundice → Apathy & Anorexia → Failure to Thrive → Hepato-splenimegaly → Skeletal Deformity → Iron overload manifestation

Types of Thalassemia
α-Thalassemia

Type	Description
Silent (carrier)	Missing one gene in one of the chromosome pairs (Heterozygous),usually no presenting symptoms.
Thalassemia trait “mild”	Missing two genes, either in the same chromosome (Asian type) - one on each chromosome (African type).
HbH (moderate)	genes are missed. Only one gene remains
Hydrops fetalis	All 4 genes are missed, the fetus cannot live without intervention.

- When a man whit silent alpha-Thalassemia get married with a trait Asian alpha- Thalassemia woman,
Their children’s probabilities can be show below:



alpha-Thalassemia

is a condition in which α globin is partially or completely absent due to missed genes, which are responsible to express it. Usually happens in relatives marriage

Lab Diagnoses of α-Thalassemia

- 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

- A decrease in HbA2, indicates a benign form of α-Thalassemia.
- While an increase in the percentage of HbA2 is an indicator of β-Thalassemia

Types of B-Thalassemia

Classification according Molecular Factors

- **1- Beta+:** the synthesis of Beta globin is partially decreased.
- **2- Beta0:** the synthesis of Beta globin is completely lost.

he gene expressing Beta in both types could be present (Ferrara) or partially decreased (Indian).

- **3- δβ-Thalassemia**
- **4- Hereditary Prominent Fetal Hb (HPFH):** HbF is the prominent type here (not HbA)

In the last 2 types, the gene is deleted and the synthesis is completely lost.

Classification according the Concentration of Hob

Type	Hb Count
Major "most severe"	Less than 7g/dl
Intermedia	7-10 g/dl
Minor	More than 10g/dl
Minima	Normal

Molecular Defects in the β-Thalassemia Syndrome

	β-Globin synthesis	β-mRNA	β-Globin Gene	δ-Globin Synthesis	γ-Globin Synthesis
1. β^+-Thalassemia	Decreased	Decreased	Present	Present	Present
2. β^0-Thalassemia	Absent	Absent	Present	Present	Present
Ferrara Variant	Absent	Inactive	Present	Present	Present
Indian Variant	Absent	Absent	Partially Deleted	Present	Present
3. δβ-Thalassemia	Absent	Absent	Deleted	Absent	Increased
4. HPFH	Absent	Absent	Deleted	Absent	increased

β-Thalassemia con..

Genotypes of β-Thalassemia:

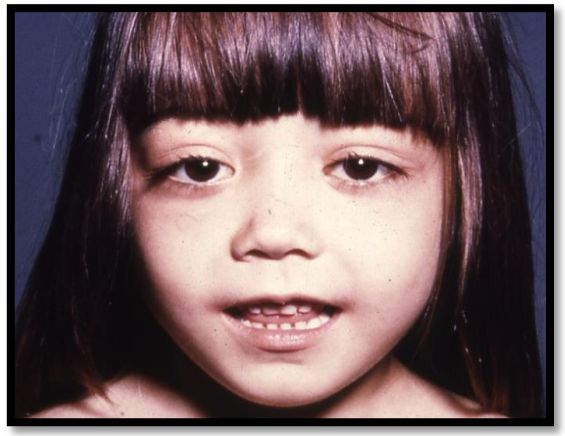
1. β-thalassemia major: (very severe)
2. β-thalassemia intermediate: inherited two β+ alleles (moderate to severe)
3. β-thalassemia minor: inherited one abnormal allele (trait, asymptomatic or mildly symptomatic)
4. β-thalassemia minima : (Silent like α thalassemia trait, not causing problem unless the carrier married to the same inherited abnormality)

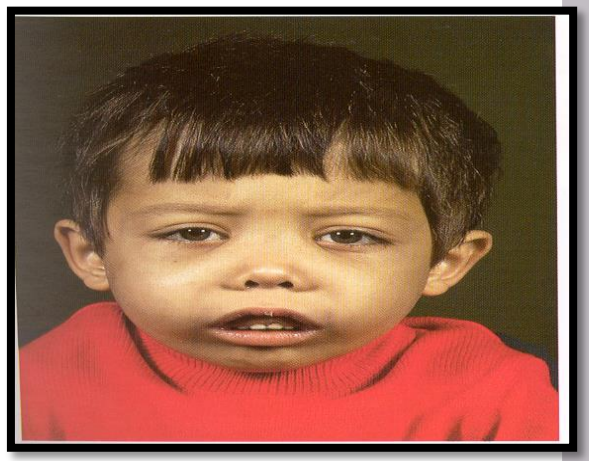
Hemoglobin Fractions in the Genotypic Variants of the β-Thalassemia Syndromes:

Genotype	HbA	HbA_2	HbF (%)	Other Hemoglobins
Normal β/β	97	2.5 – 3.2	<1	None
Thalassemia major β^0/β^0 β^0/β^+	0	1.0 – 5.9	>94	Free α-chains
Thalassemia intermedia β+/β^+, black	Present	5.4 – 10.0	30 – 73	None
Thalassaemia minor β^+/β - β^0/β - $(\delta\beta)^0/\beta$ $(\delta\beta)$ Lepore/ β - $(\gamma\delta\beta)^0/\beta$	>90	2.5 – 8.0	1 – 2	None
Thalassemia minima β^{silent}/β	97	<3.2	<1	None

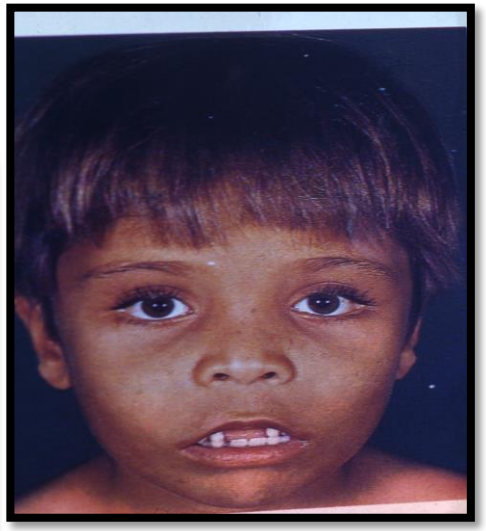
Clinical Manifestations in Thalassaemias

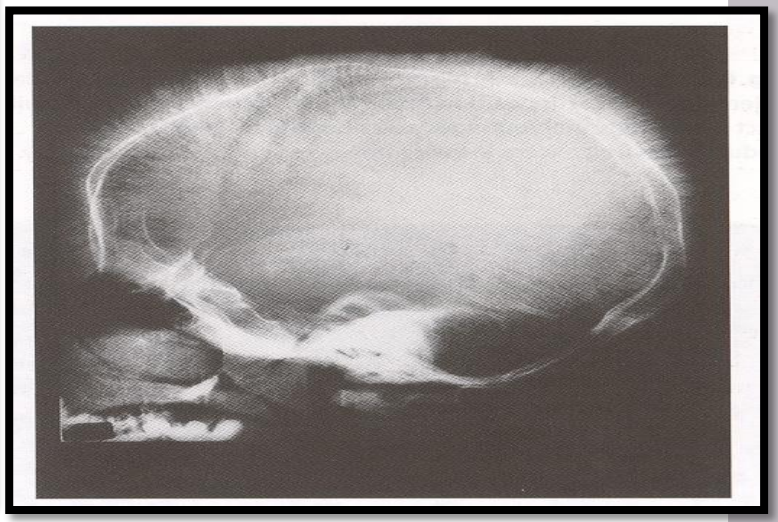
- Pallor
- Jaundice
- Apathy and Anorexia
- Failure to Thrive (*failure in growth*)
- Hepato-splenomegaly
- Skeletal Deformity
- Iron Overload mainfestations





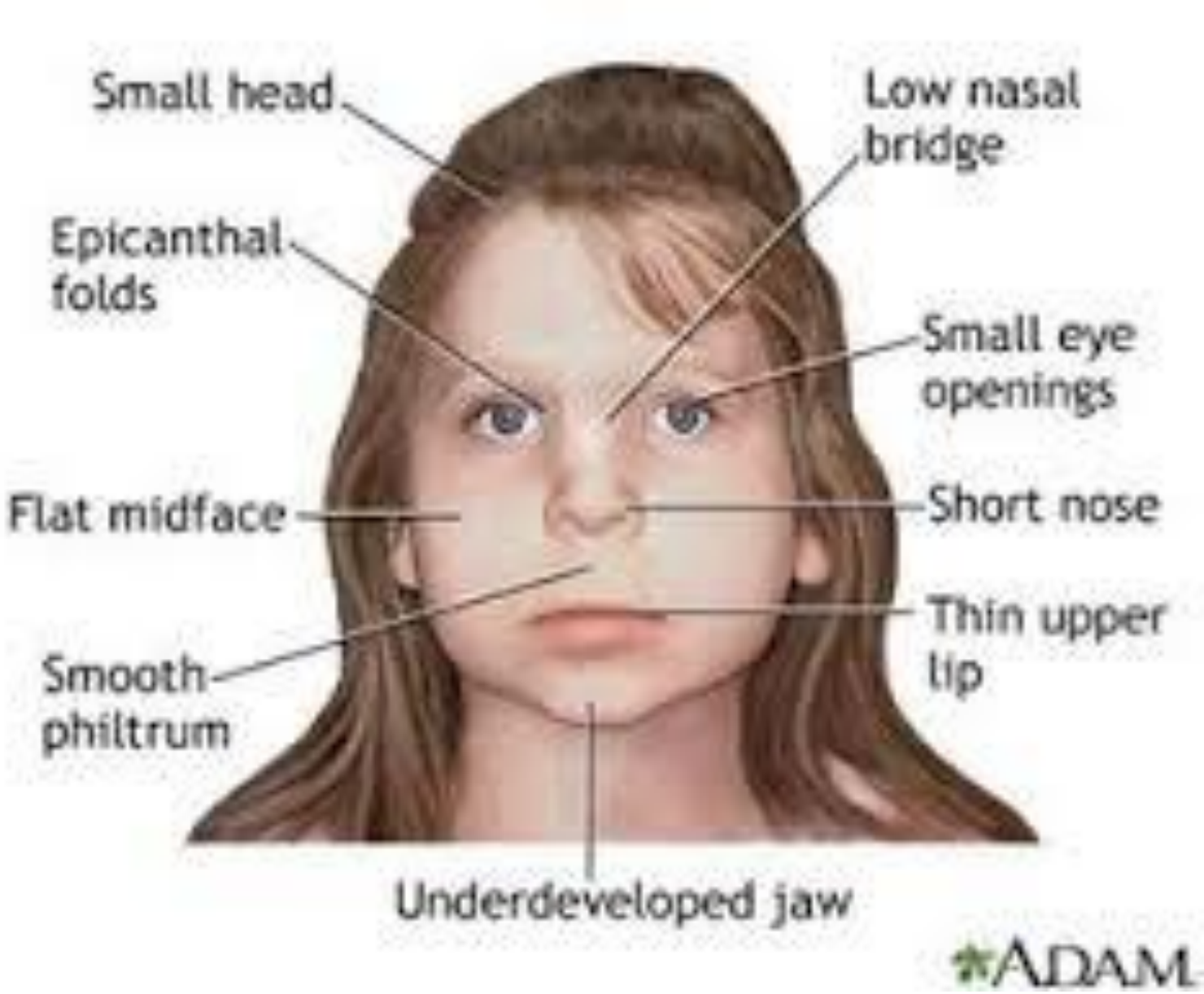
Thalassemic face in β-thalassemia major
They have the same facial characteristics:
1- **Forehead bossing** (protrusion)
2- **Prominent maxilla**
3- **Widen space between eyes**
Because of increasing the demand on bone marrow, facial
bones become expanded





Hair-on-ends appearance in x-ray

Thalassemia Face

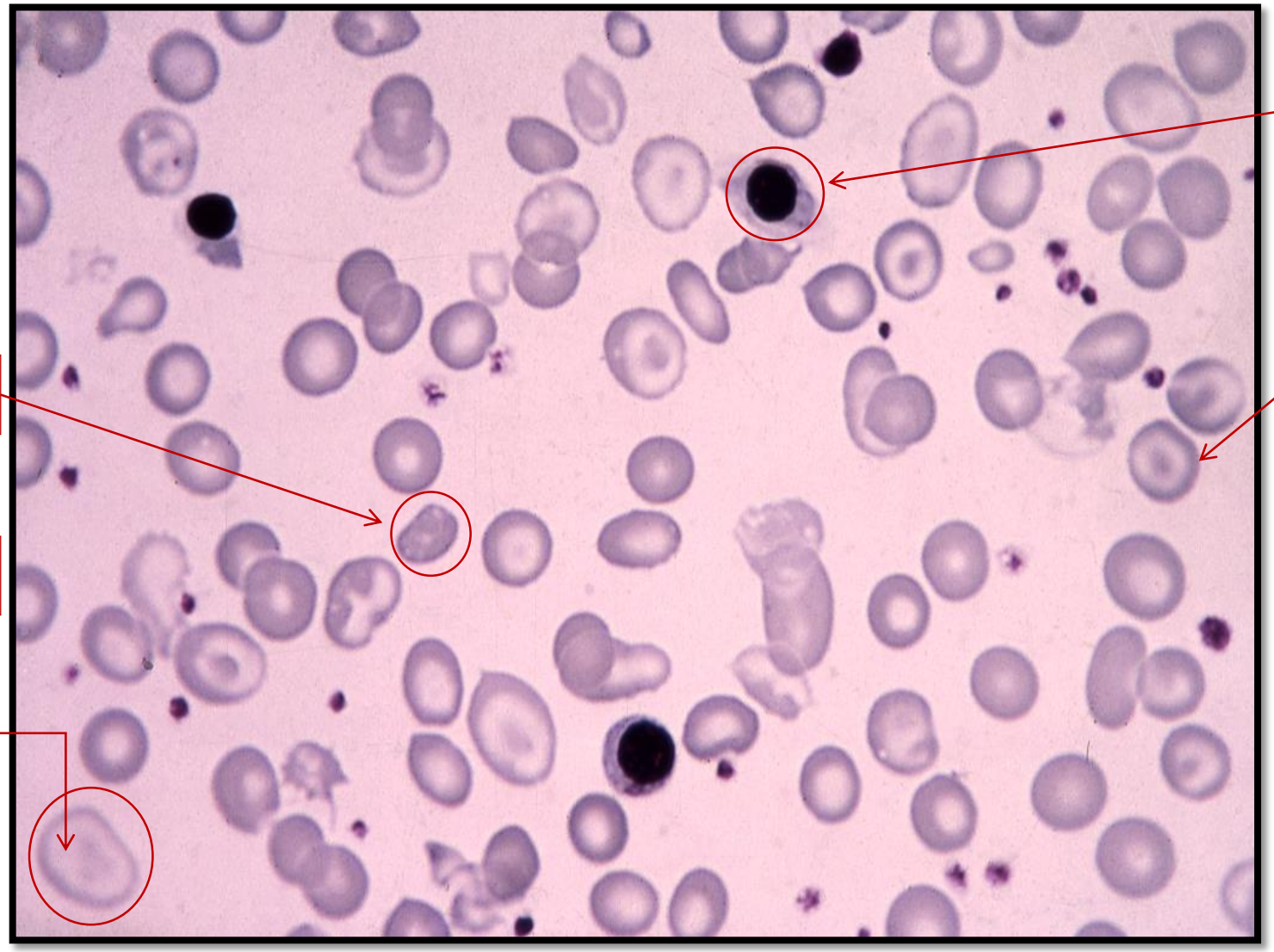


Clinical and Hematological Features of the β-Thalassemia Syndrome

	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	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

This table is not important to memorized just things noted


Nucleated red cells
Microcytosis
Target cells
Hypochromia
Target cells are the ones with a darker centre

Prenatal diagnosis of the haemoglobinopathies (Including thalassaemia)

Not that important just read it

DNA Analysis:

A-Chorionic villus sampling Transcervical approach (9 – 11 weeks of pregnancy)

Transabdominal approach (up to 15 weeks of pregnancy)

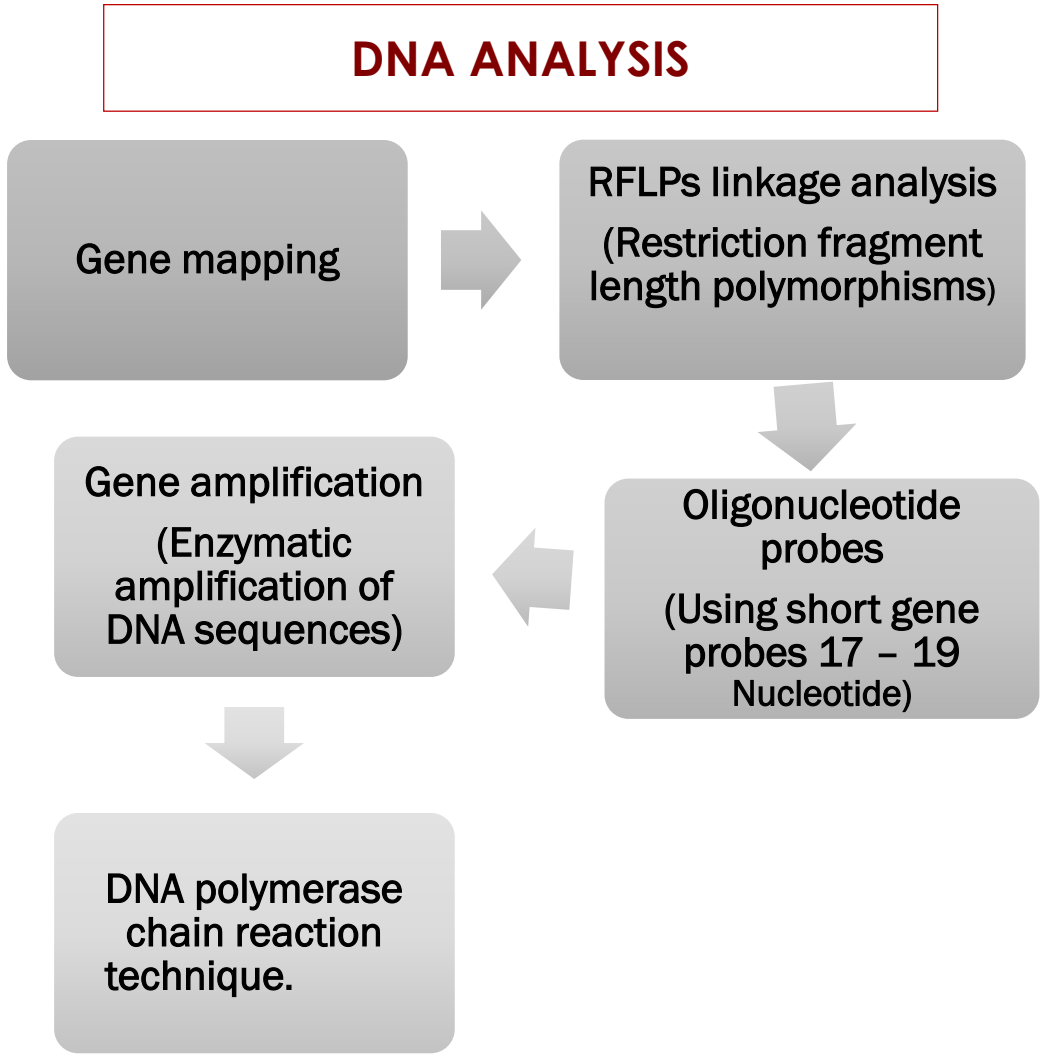
B-Amniotic fluid cell analysis (16 – 20 weeks gestation)

C-Fetal blood sampling (> 20 weeks gestation) DNA analysis

Haematological parameters

Biochemical analysis Globin chain synthesis

α/β Ratio , α/ɣ Ratio, α/δ Ratio



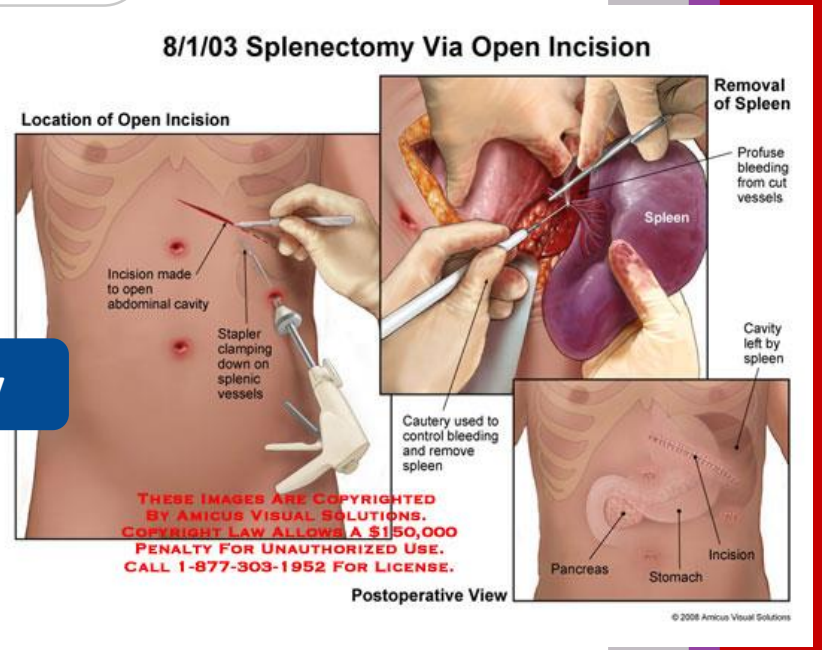
MANAGEMENT OF THE THALASSEMIAS

Blood Transfusion

is a drug therapy for iron overload uses drugs called iron chelators to remove extra iron from your body e.g Deferoxamine or Deferiprone(or potent)

Iron chelation therapy

Splenectomy



Hormone replacement

For Failure to Thrive

Bone marrow transplantation

Gene therapy

Watch me when you have time

From the name inserting a gene into a patient's cells . STILL EXPERIMENTAL

Assessment of Iron Stores

- Serum ferritin
- Serum iron and percentage saturation of transferrin (**iron-binding capacity***)
- Liver CT scan or MRI
- Bone marrow biopsy (Perl's stain) for reticuloendothelial stores

Diagnosis of Haemoglobinopathies including Thalassaemias

- Personal & Family History
- Physical Examination
- Laboratory Investigation

Haematological Tests – CBC

Quantitation of HbA2 and HbF

Sickle cell test

*Note that in thalassemia it'll be low while in IDA it'll be high

Assessment of tissue damage caused by iron overload

Cardiac	X-ray - ECG
Liver	Liver function tests -liver biopsy -CT scan
Endocrine	Clinical examination (growth and sexual development) - glucose tolerance test – thyroid and parathyroid

1- The hematopoiesis in the embryo start at the:

A. A. Liver B. Spleen

C. Yolk sac D. bone marrow

2- Most of the hematopoiesis in ADULTs is in:

A. Vertebrae

B. Tibia

C. Ribs

D. Sternum

3- -In Embryo we see what type of HB:

A. Hb A

B. Hb F

C. Hb A2

D. Hb Portland

4- -In Adults the prominent type of Hb is:

A. Hb F

B. Hb Portland

C. Hb A_2

D. Hb A

5- How many amino acids found in Alpha chine?

A. 141

B. 146

C. 148

D. 114

6- Normal percentage of Hb F in Adults is:

A. A. 91-97%

B. B. 0.5-1.5%

C. C. 11-15%

D. D. 20-30%

7- In Alpha Thalassemia how many deleted copies are in Hb H?

A. one copy

B. two copies

C. Three copies

D. four copies

8- We preformed a HbA_2 Test for Thalassemia patient and it was elevated, what type of thalassemia he is probable having?

A. Alpha

B. Beta

1- C

2- A

3- D

4- D

5- A

6- B

7- C

8- B

Q1 How can we manage thalassemia ?

Blood Transfusion - iron chelation therapy – Splenectomy

Hormone replacement - Bone marrow transplantation - Gene therapy

Q2 Under microscope what do we see in thalamic patient?

Microcytic – Hypochromic cells -Nucleated red cells - Target cells

Q3 What Hb types are found in adult ?

Hb A (95-97%) – Hb A_2 (2.5-3.5%) – Hb F (0.5-1.5%)

Thank you for checking our work

Now you can check a lecture out :D

DONE BY:

Nouf Alharbi

Amal Afrah

Ghaida Almasaad

Reviewed by:

Hadeel B.Alsulami

Abdullah M. Albasha

دعاء بعد المذاكرة:

(اللهم اني أستودعتك ما قرأت وما حفظت وما تعلمت, فرده لي عند حاجتي
وحسبنا الله ونعم الوكيل, اليه أنك على كل شيء قدير)