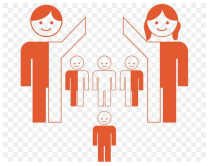
بسم الله الرحمن الرحيم

1

Blood and Immunity Module
Case Based Learning
1st Year MBBS
Thalassemia



H.O.D
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Presenter: Dr Sana Latif
(Senior Demonstrator)

Updated Date: 24-01-25

2

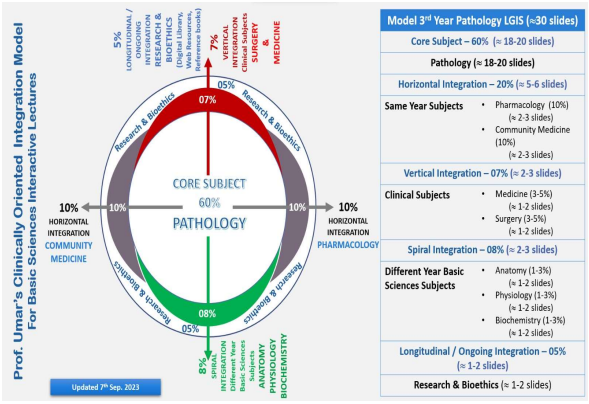
Motto, Vision, Dream

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

3

3

Professor Umar Model of Integrated Lecture



4

4

CBL- MCQ Assessment

1. Which protein in red blood cells carries oxygen?
A) Hemoglobin
B) Albumin
C) Myoglobin
D) Fibrinogen
E) Ferritin

2. Which metal ion is essential for hemoglobin function?
A) Zinc
B) Iron
C) Copper
D) Calcium
E) Magnesium

3. Which enzyme is required for heme biosynthesis?
A) Catalase
B) Hexokinase
C) Transaminase
D) Pyruvate kinase
E) ALA Synthase

4. Which type of hemoglobin is increased in β-thalassemia?
A) HbA2
B) HbA
C) HbF
D) HbS
E) HbC

5

CBL- MCQ Assessment

5. Which biochemical test is used for thalassemia diagnosis?
A) Electrophoresis
B) PCR
C) Western blot
D) ELISA
E) Spectrophotometry

6. Which globin chain is absent in α-thalassemia?
A) Alpha
B) Beta
C) Gamma
D) Delta
E) Epsilon

7. Which genetic mutation causes β-thalassemia?
A) Deletion
B) Frameshift
C) Point
D) Insertion
E) Duplication

8. Which organ is responsible for iron storage?
A) Brain
B) Kidney
C) Heart
D) Liver
E) Pancreas

6

CBL- MCQ Assessment

9. Which vitamin enhances iron absorption?
A) Vitamin B12
B) Vitamin D
C) Vitamin K
D) Vitamin A
E) Vitamin C

10. What is the most common inheritance pattern of thalassemia?
A) Autosomal recessive
B) Autosomal dominant
C) X-linked recessive
D) X-linked dominant
E) Mitochondrial

Answers

1. **A**
2. **B**
3. **E**
4. **C**
5. **A**
6. **A**
7. **C**
8. **D**
9. **E**
10. **A**

7

Learning Objectives

At the end of this session students will be able to:

1. Discuss the structure of haemoglobin
2. Explain the types of haemoglobin
3. Tell the normal range of haemoglobin in children and adults
4. Classify haemoglobinopathies.
5. Describe the biochemical basis of thalassemia
6. Explain the clinical manifestations of thalassemia
7. Discuss briefly about the treatment of thalassemia
8. Explain & correlate the clinical aspects of core concept
9. Correlate and build core knowledge on the basis of latest research

8

Interactive Session

An 8 years old boy was brought to hospital for blood transfusion. A diagnosed case of beta Thalassemia Major since he was one and a half year old, for which he had been undergoing blood transfusions since then.

On general examination he was malnourished with a short stature, had yellow tinged fingernails, frontal bossing and maxillary expansion.

His peripheral blood smear examination and hemoglobin electrophoresis reports showed beta thalassemia major.

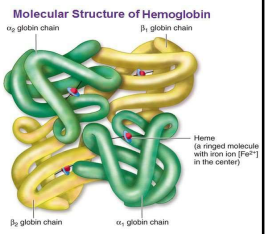
9

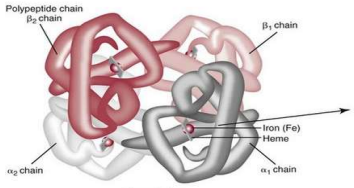
Core Knowledge

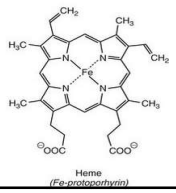
Haemoglobin

Structure of hemoglobin

- Hb is a spherical molecule consisting of 4 peptide subunits (**globins**) = **quartenary structure**
- Hb of adults (Hb A) is a tetramer consisting of **2** α- and **2** β-**globins** → **each globin contains 1 heme group with a central Fe^{2+} ion** (ferrous ion)







10

Core Knowledge

Types Of Haemoglobin

Type of Hb	Levels	Indication
Hemoglobin A1	12.1-16.3 g/dL, 90% of total hemoglobin	Low levels indicate anemia or blood loss.
Hemoglobin A2	1.5%-3.5% of total hemoglobin	High levels may indicate thalassemia.
Hemoglobin F	50-90% in neonates, 0%-1% of total hemoglobin in adults	Normally high in neonates, long term elevations may indicate a thalassemia.
Hemoglobin S	Presence is abnormal	Indicative of sickle cell disease.
Plasma	5mg/dL	High levels may indicate a hemolytic anemia.

11

Core Knowledge

Haemoglobinopathies

- A group of inherited disorders characterized by structural variations of the Hb molecule.
- They are **Disorders of Globin synthesis** rather than heme synthesis.

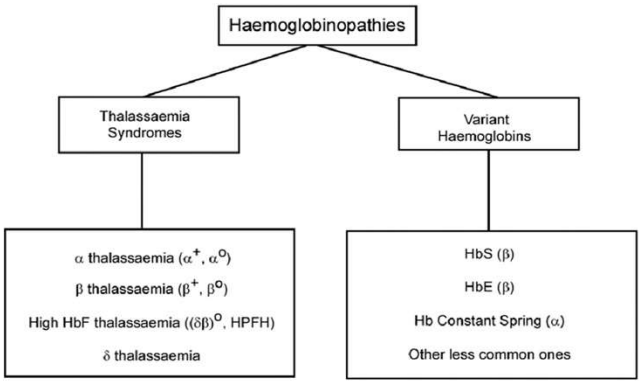
These may result from :

- Synthesis of **Abnormal Hb**
- **Reduced rate of synthesis** of NORMAL α or β globin chains
- Patients only have these **disorders** if they inherit two unusual hemoglobin genes – one each from both the parents.
- People who inherit just one unusual gene are known as **'carriers'** i.e have a **'trait'.**
- **Carriers are healthy and do not have the disorders.**

12

Core Knowledge

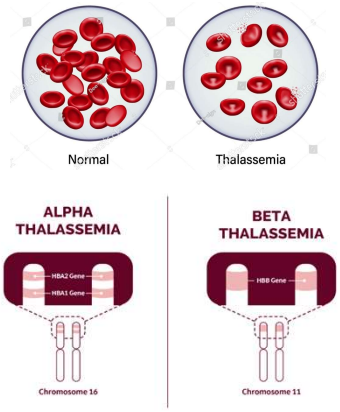
Types Of Haemoglobinopathies



13

Core Knowledge

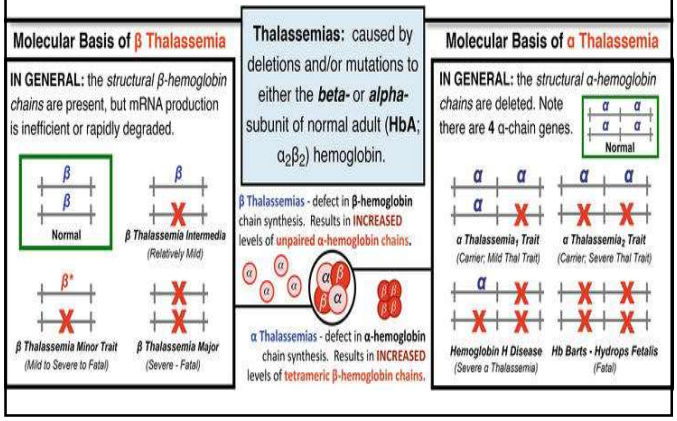
Thalassemia



14

Core Knowledge

Biochemical Basis Of Thalassemia



15

Core Knowledge

Alpha Thalassemia

1. A group of **genetic** disorders with **defective α-chain synthesis**.
2. **Chromosome 16** carries 2 α genes, the total number of α-genes is 4.

3.Severity depends upon the patient's affected number of genes.

4. **Decrease** in the **synthesis of HbA, HbF**, and **HbA2**.

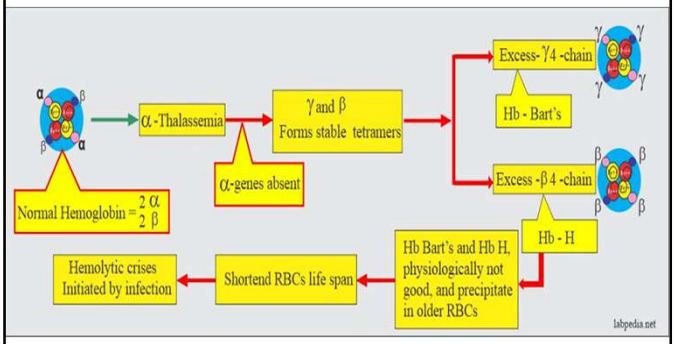
5. The net result is an **excess of β-chains and γ-chains** which may polymerize into tetrameric forms **γ4 called Hb Bart's** and **β4 called HbH**.
   These abnormal **Hb Bart's** and **HbH** are the **characteristics of α-thalassemia**.

Usually manifested **immediately after birth** or even **in utero** because the **α**-gene is activated early in fetal life.

16

Core Knowledge

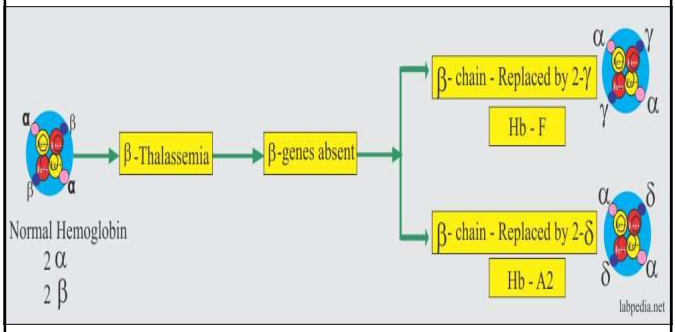
Alpha Thalassemia



17

Core Knowledge

Beta Thalassemia



18

Core Knowledge

Beta-thalassemia Major

Also known as Cooley's Anaemia:

1. The **homozygous** state of β-thalassemia **($\beta^0\beta^0$).**
2. A globin gene mutation causes partial β-gene or total β-gene chain loss.
3. **Increase** in the production of **γ-chains and δ-chains**
4. The β chain when replaced by the 2-γ chain forms **Hb F**; when replaced by δ-chains, will form **Hb A2**.
5. Only HbF (>90%) and HbA2 (3% to 8%) on Electrophoresis.
6. Marked **microcytosis** and **hypochromia**.
7. MCV is <70 fl, and Hb is 2 to 3 g/dL
8. Hepatosplenomegaly, bony deformities, and failure to thrive as an infant.
9. **patients are dependent upon blood transfusion.**

19

Core Knowledge

Beta Thalassemia

Beta – Thalassemia Intermedia:

1. partial deletion of **β^0** of **both beta genes.**
2. These are homozygous **($\beta^+\beta+$)** genes.
3. A wide spectrum of the disease with moderate to severe anemia, and Hb between 6 to 10 g/dL.
4. There are growth retardation and bony abnormalities.
5. This usually occurs later than the major thalassemia type.
6. Electrophoresis shows Hb F 20% to 40% and increased Hb A2, 3% to 8%.

Beta – Thalassemia Minor:

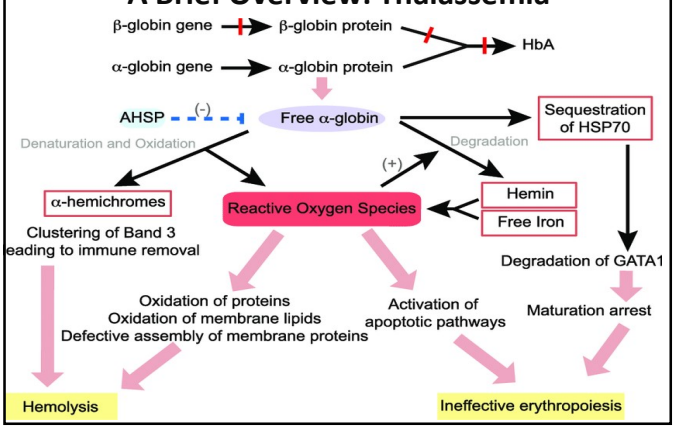
where a **single β-gene** is affected **(β^0/β).**

1. There is mild anemia Hb 9 to 11 g/dL or no anemia.
2. Normal to increased RBC count.
3. RBCs are microcytes, MCV 60 to 70 fl.
4. Electrophoresis shows a mild increase in Hb F and Hb A2 (3% to 8%).

20

Core Knowledge

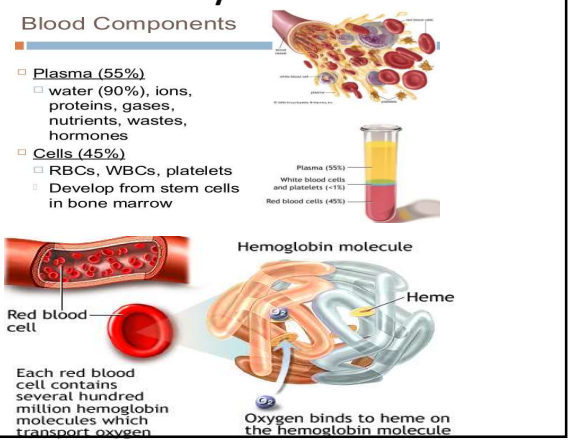
A Brief Overview: Thalassemia



21

Horizontal Integration

Anatomy Of The Blood

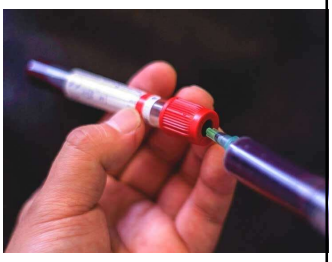


22

Horizontal Integration

Normal Range of Hb

Males	
Age 12 - 18 years	13.0 to 16.0 (mean 14.5)
Age > 18 years	13.6 to 17.7 (mean 15.5)
Females	
Age 12 - 18 years	12.0 to 16.0 (mean 14.0)
Age > 18 years	12.1 to 15.1 (mean 14.0)
Children	
Birth	13.5 to 24.0 (mean 16.5)
Age < 1 month	10.0 to 20.0 (mean 13.9)
1 - 2 months	10.0 to 18.0 (mean 11.2)
2 - 6 months	9.5 to 14.0 (mean 12.6)
6 months - 2 years	10.5 to 13.5 (mean 12.0)
2 - 6 years	11.5 to 13.5 (mean 12.5)
6 - 12 years	11.5 to 15.5 (mean 13.5l)



23

Horizontal Integration

Physiology Of the Blood

- Each red blood cell (RBC) comprises approximately 280 million molecules of Haemoglobin.
- There are more than 350 types of abnormal hemoglobin
- An average adult is said to have close to 1.74 pounds or 790 grams of Hb.
- Our red blood cells are red due to the heme groups in haemoglobin. Heme contains iron imparting a red colour to the molecule.
- Haemoglobin forms an unstable and reversible bond with oxygen. It is referred to as oxyhaemoglobin in the oxygenated state and is bright red in colour and is purplish blue in shade in the reduced state.

24

Vertical Integration

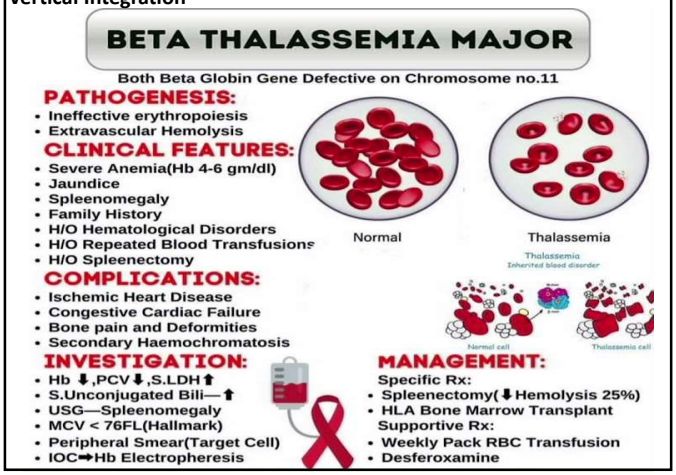
Clinical Manifestations Of Thalassemia

Thalassemia signs and symptoms can include:

- Fatigue
- Weakness
- Pale or yellowish skin
- Facial bone deformities
- Slow growth
- Abdominal swelling
- Dark urine

25

Vertical Integration



26

Spiral Integration **Family Medicine**

Management of Thalassemia

Family Medicine plays important role in following manner:

- Diagnosis
- Education
- Dietary Guidance
- Monitoring
- Refer to Specialists

27

27

Spiral Integration **Artificial Intelligence**

Role of Artificial Intelligence in Managing

Artificial Intelligence plays role in following aspects:

- Personalized Nutrition
- Diagnostic Tools
- Food Recommendations
- Drug Development

28

28

Spiral Integration Bioethics

Ethical Consideration

- Informed Consent
- Resource Allocation
- Ethical Consideration
- Access to Healthcare

29

29

Spiral Integration Research Article

Unveiling Extramedullary Hematopoiesis: A Case Report Highlighting the Causes, Symptoms, and Management Strategies

Link:
https://www.mdpi.com/2039-4365/14/2/4

Journal Name:
***Thalass. Rep.*, Volume 14, Issue 2 (June 2024)**

Author Name:
Konstantinos Manganas, Aikaterini Xydaki ,Angeliki Kotsiafti ,Olympia Papakonstantinou and Sophia Delicou

Abstract

- Extramedullary hematopoiesis (EMH) serves as a compensatory mechanism in chronic hemolytic anemias, such as thalassemia, and can result in spinal cord compression. This case report highlights a 36-year-old woman with transfusion-dependent β-thalassemia (TDT) who presented with lower extremity motor deficiency, pelvic paresthesia, and bladder dysfunction. The patient had a history of lower back pain, bilateral lower limb weakness, and demonstrated poor compliance with iron chelation therapy. MRI findings indicated spinal cord compression attributable to extramedullary hematopoiesis. Due to the infeasibility of surgical intervention, the patient underwent hypertransfusion and iron chelation therapy. While neurological symptoms improved, urinary retention persisted. The patient continues to receive iron chelation treatment and undergo transfusions. Managing extramedullary hematopoiesis in thalassemia necessitates an individualized treatment approach.

30

CBL- Assessment

1. Which globin chain is defective in β-thalassemia?

2. What mutation causes α-thalassemia?

3. Which hemoglobin type increases in β-thalassemia?

4. What biochemical test diagnoses thalassemia?

5. How does thalassemia affect RBC lifespan?

31

How to use HEC Digital Library

Steps to Access HEC Digital Library

1. Go to the website of HEC National Digital Library
   http://www.digitallibrary.edu.pk
2. On Home Page, click on the INSTITUTES.
3. A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library (HNDL).
4. Select your desired Institute.
5. A page will appear showing the resources of the institution
6. Journals and Researches will appear
7. You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal.

32

Learning Resources

- Lippincott Illustrated Reviews - BIOCHEMISTRY, Eighth Edition, Chapter 3, Page # 36 - 43.
- Google images
- Google scholar

33

34