Case-Based Learning (CBL) for Dental Students

Genetic Disorders associated with Mutation

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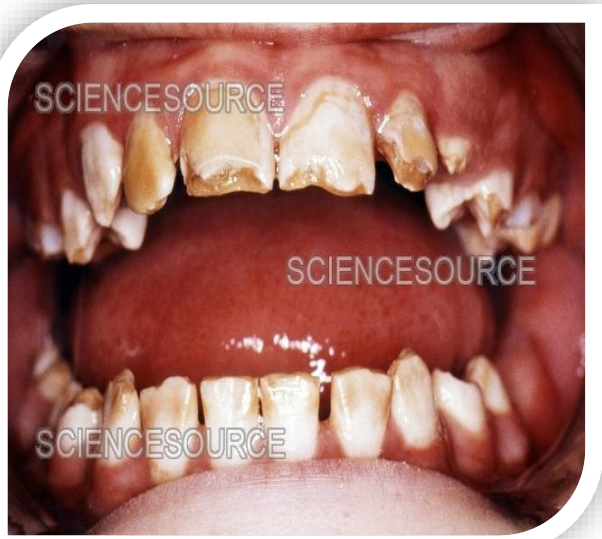
🦷CASE Scenario1
Amelogenesis Imperfecta (AI)

🎯Learning Objectives:

- Demonstrates how a **single gene mutation** can directly **affect tooth structure** and lead to **significant clinical dental problems.**

CASE Scenario1
Amelogenesis Imperfecta (AI)

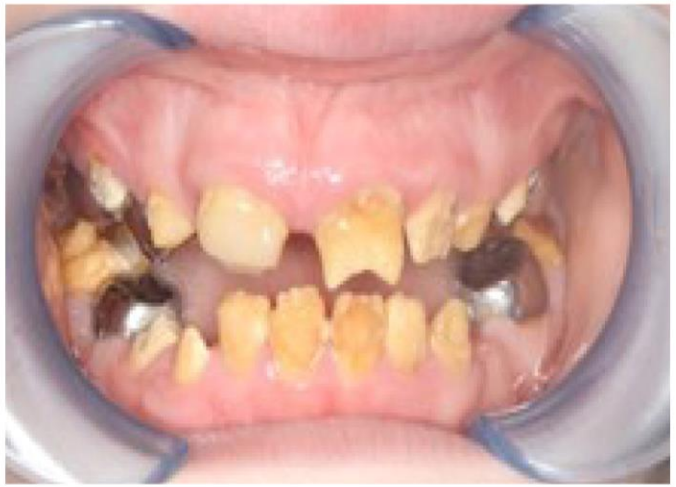
A 10-year-old child is brought to the dental clinic by his parents **complaining of**: **Yellowish-brown discoloration of teeth**, Increased **sensitivity to hot and cold** & Teeth appear **small and easily worn down**. **On examination**: Enamel is thin and poorly mineralized, Multiple teeth show **chipping and attrition**. **Family history** reveals that the **father** had similar dental problems.



CASE Scenario1
Amelogenesis Imperfecta (AI)

Discussion on case 1:

1. What is the most likely **diagnosis**?
2. What **part of the tooth** is affected?
3. Could this condition be **genetic?** If yes, how?
4. What is the **mode of inheritance**?
5. Can this condition be **prevented**?
6. How would you **manage** this case?



CASE Scenario1
Amelogenesis Imperfecta (AI)

Answer: Discussion on case 1:

- 1 What is the most likely diagnosis?
- → Amelogenesis Imperfecta

- 2 What part of the tooth is affected?
- → Enamel: It is: Thin, weak, poorly mineralized

- 3 Could this condition be genetic? If yes, how?
- → Yes, it is a genetic condition
- Explanation: It is caused by mutations in genes responsible for enamel formation, such as: AMELX & ENAM.. These mutations lead to Abnormal or defective protein production & failure of normal enamel development.

CASE Scenario1
Amelogenesis Imperfecta (AI)

Answer: Discussion on case 1:

- 4 What is the mode of inheritance?
- → It may be:
- **Autosomal dominant:** The most common form, often affecting multiple generations.
- **Autosomal recessive:** Often found in cases with high consanguinity. It occurs when two copies of the mutated gene are present.
- **X-linked:** Caused by mutations on the X chromosome, specifically the AMELX gene.
- The positive family history (father affected) supports a hereditary pattern

- 5 Can this condition be prevented?
- → The genetic mutation cannot be prevented…However, early diagnosis and proper management can significantly reduce complications..

🦷CASE Scenario1
Amelogenesis Imperfecta (AI)

Answer: Discussion on case 1:

- 5 How would you manage this case?

1. Protect tooth structure: Full coverage crowns
2. Improve esthetics: Veneers (in mild cases),
3. Reduce sensitivity: Desensitizing agents,
4. Prevent complications: Regular follow-up and preventive care

🎯 **Teaching Wrap-up**

- **This case highlights how a gene mutation can directly affect tooth structure and result in significant clinical dental problems.**

CASE Scenario: 2
Aflatoxin & Chemical Mutation

🎯Learning Objectives:

1. Define **chemical mutagens** and give examples
2. Explain how **Aflatoxin acts as a mutagen**
3. Understand the role of **environmental exposure in cancer development**
4. Correlate: **Chemical exposure (environment) → DNA mutation → →disease (cancer).**
5. Enhancing **clinical thinking beyond oral cavity**

CASE Scenario: 2
Aflatoxin & Chemical Mutation

❑ A 50-year-old male **presents with:**

•General fatigue
•Loss of appetite
•Yellowish discoloration of eyes and skin

➢ **Medical history:**

•Lives in a rural area
•Consumes stored grains and peanuts regularly

➢ **Clinical findings:**

•Jaundice
•Enlarged liver (hepatomegaly)

Further investigation suggests **liver pathology**.

CASE Scenario: 2
Aflatoxin & Chemical Mutation

Discussion Questions:

1. What is the most likely diagnosis?
2. What is the causative agent in this case?
3. What type of mutagen is involved?
4. How does this agent cause DNA mutation?
5. Which gene is commonly affected?

CASE Scenario: 2
Aflatoxin & Chemical Mutation

Answer: Discussion on case 2:

1 What is the most likely diagnosis?

→ Hepatocellular carcinoma (liver cancer)

2 What is the causative agent?

→ Aflatoxin

Produced by fungi:

Aspergillus flavus

3 What type of mutagen is involved?

→ Chemical mutagen

CASE Scenario: 2
Aflatoxin & Chemical Mutation

Answer: Discussion on case 2:

4 How does it cause mutation? 🧬 Mechanism:Aflatoxin is metabolized in the liver → becomes active Binds to DNA → forms DNA adducts Leads to: replication errors & permanent mutations

5 Which gene is commonly affected?

→ p53 tumor suppressor gene → uncontrolled cancer cell division

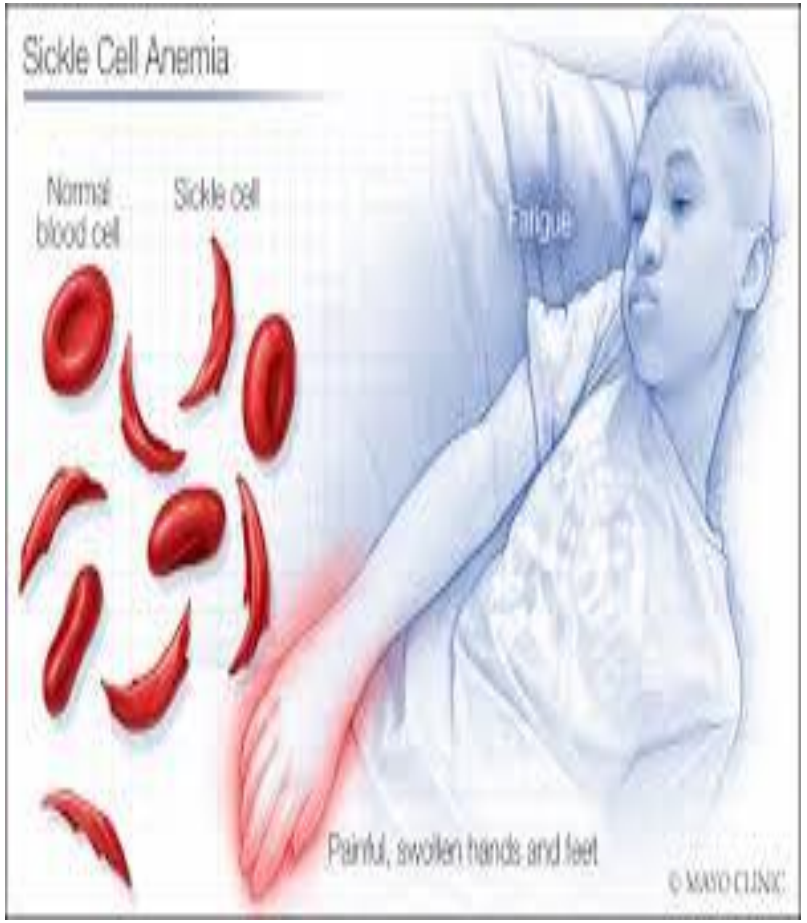
CASE Scenario: 3
Sickle Cell Disease

🎯Learning Objectives:

1. Define **hemoglobinopathies** and recognize **Sickle Cell Disease** as a classic example .
2. Describe the **genetic mutation** responsible for Sickle Cell Disease
3. Explain how this mutation leads to **abnormal hemoglobin (HbS)**
4. Correlate: **Gene mutation with clinical manifestation**

CASE Scenario: 3
Sickle Cell Disease

- A three-year-old male child presented with mild pallor, jaundice, and a history of on and off abdominal and joint pains. On examination, the child had fever, anemia mild splenomegaly. He had a history of two prior hospital admissions, and blood transfusions till now. CBC revealed anemia with leukocytosis. Red cell morphology showed microcytic hypochromic sickled red cells. Hb was 7.7 g/dl. HbS was detected.



CASE Scenario: 3
Sickle Cell Disease

Discussion Questions:

1- What is the possible diagnosis?

2- What is the biochemical basis of the disease?

3- Discuss the oral and dental manifestations?

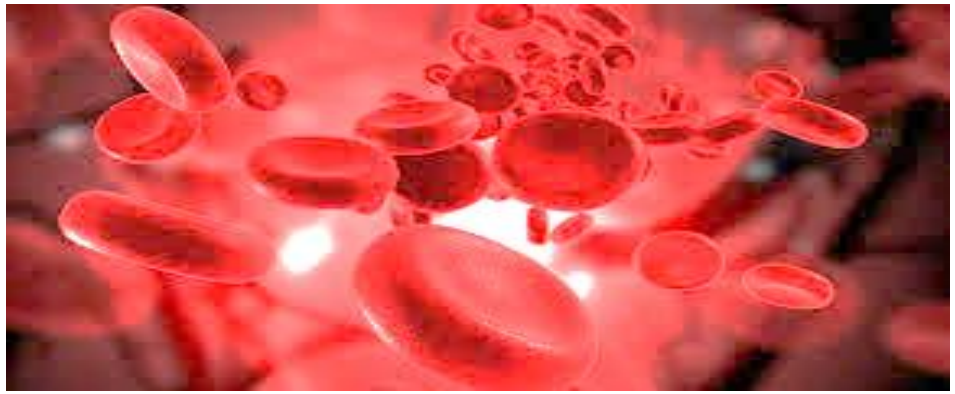
4- Explain the dental considerations in management.

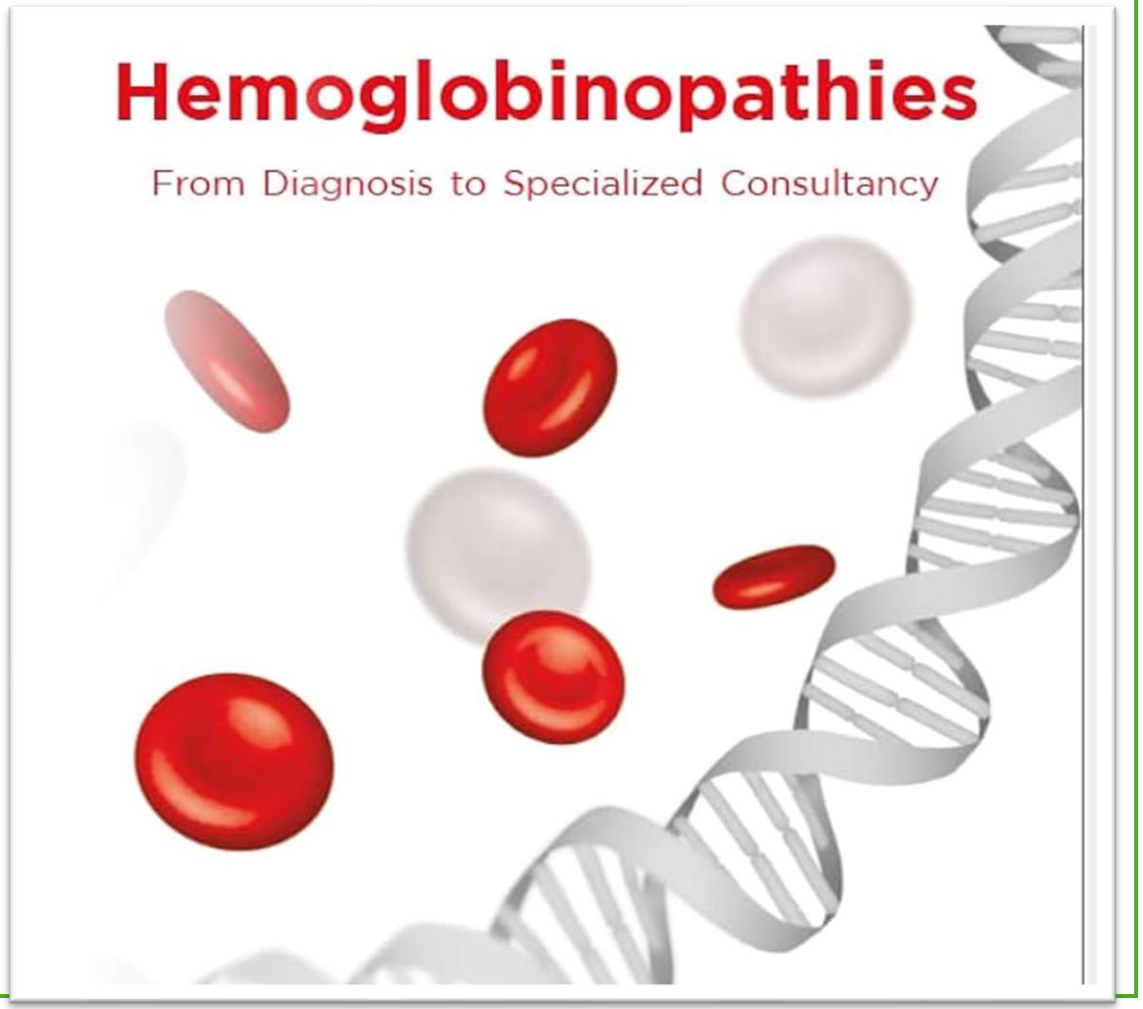
Common genetic diseases caused by DNA mutation

Hemoglobinopathies

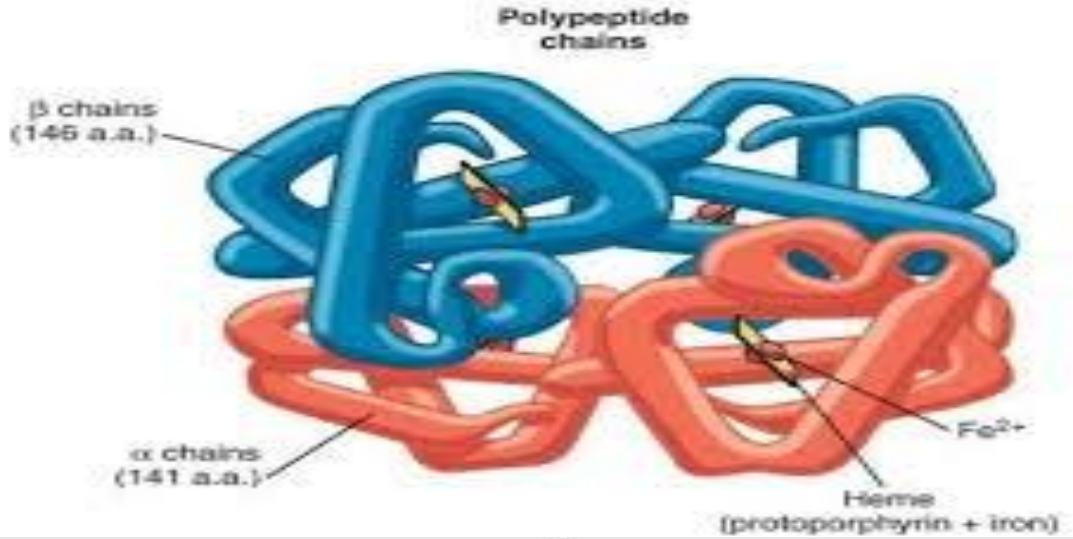
Answer: Discussion on case 3:

- ❑ **Hemoglobinopathies:**
  - Sickle cell anemia
  - Alpha thalassemia.
  - Beta thalassemia

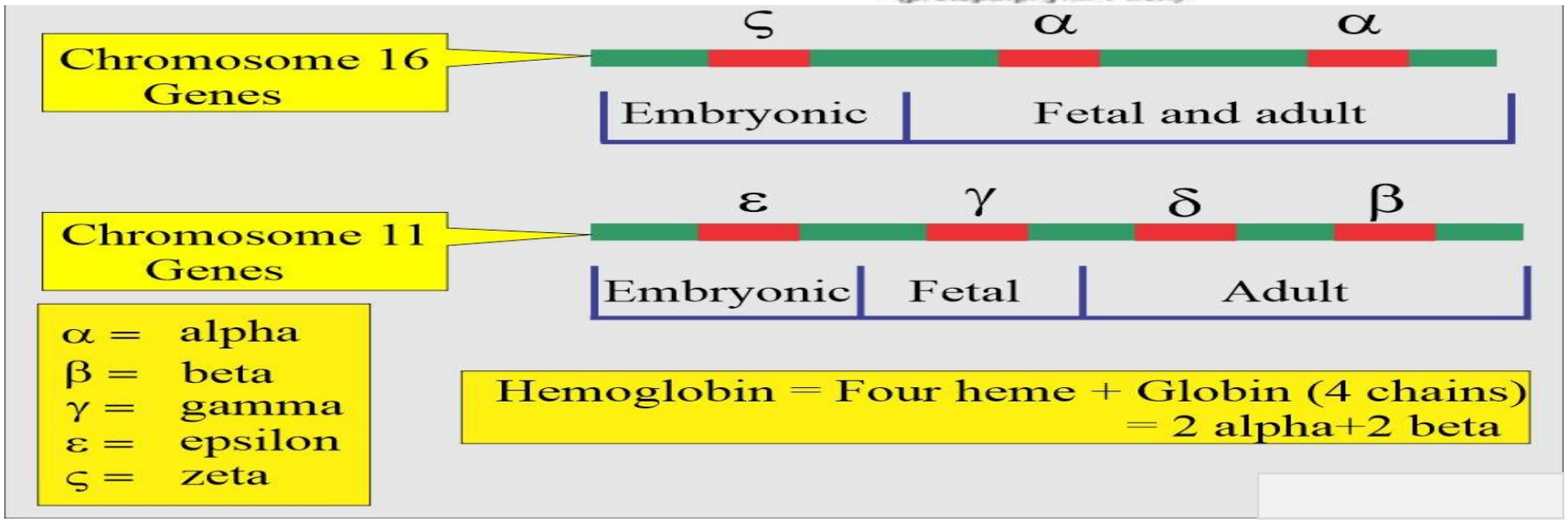




Haemoglobin structure:

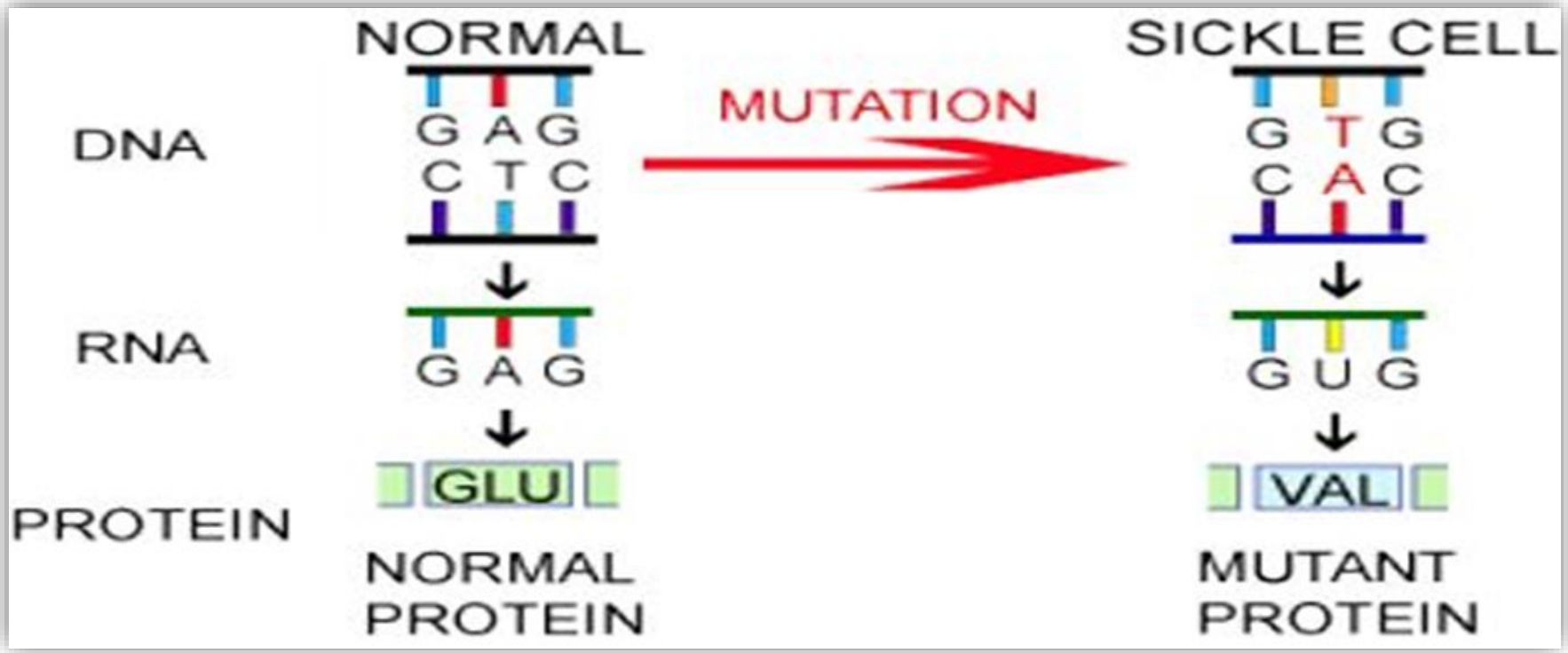


HB A

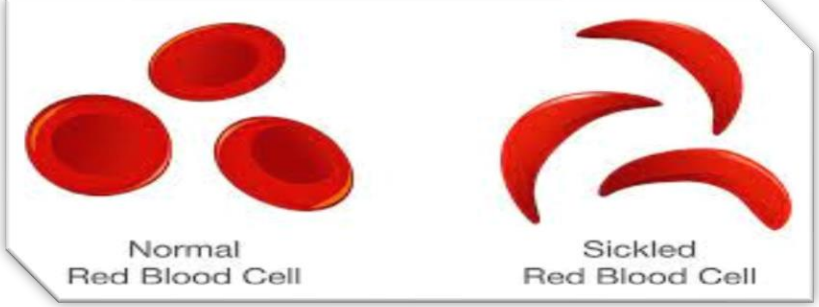


1- Sickle cell disease:

- Presence of a missense point mutation in the codon 6 of beta globin gene (GAG→GTG)
- Changing the 6th amino acid of the beta chains from glutamic acid to valine.



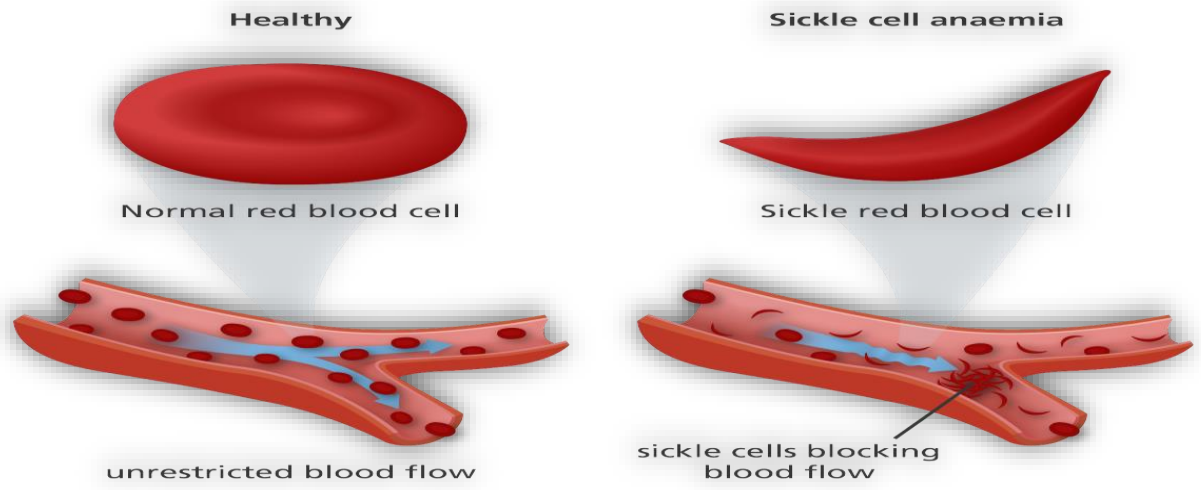
1- Sickle cell disease:



- Formation of abnormal hemoglobin S (Hb S)
- Glutamic is polar a.a., while valine is non-polar

→ Hydrophobic interaction between hydrophobic residues of HB-S

- This leads to polymerization of hemoglobin and distortion of the red blood cells into a sickle shape cell.



Gene mutation → abnormal Hb → sickling of RBCs → clinical manifestation

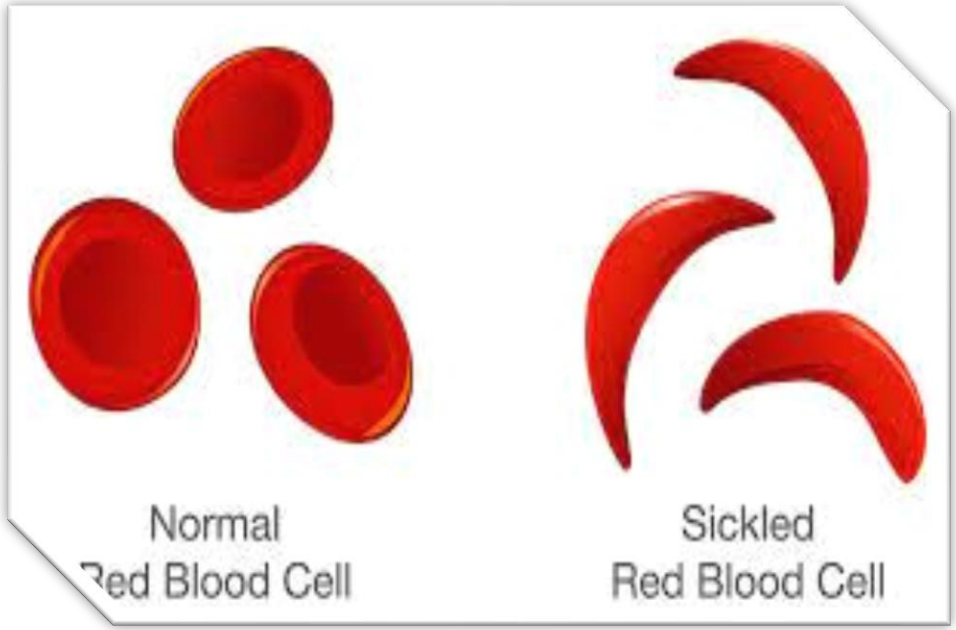
➢ This can lead to:

- RBCs rupture, anemia (hemolytic anemia).
- Vaso-occlusion, pain, and organ damage in liver, lung, bone, brain……

1- Sickle cell disease

❑Oral and dental manifestations:

1. Delayed tooth eruption
2. Mucosal pallor
3. Increased risk of infection



❑Dental considerations in management:

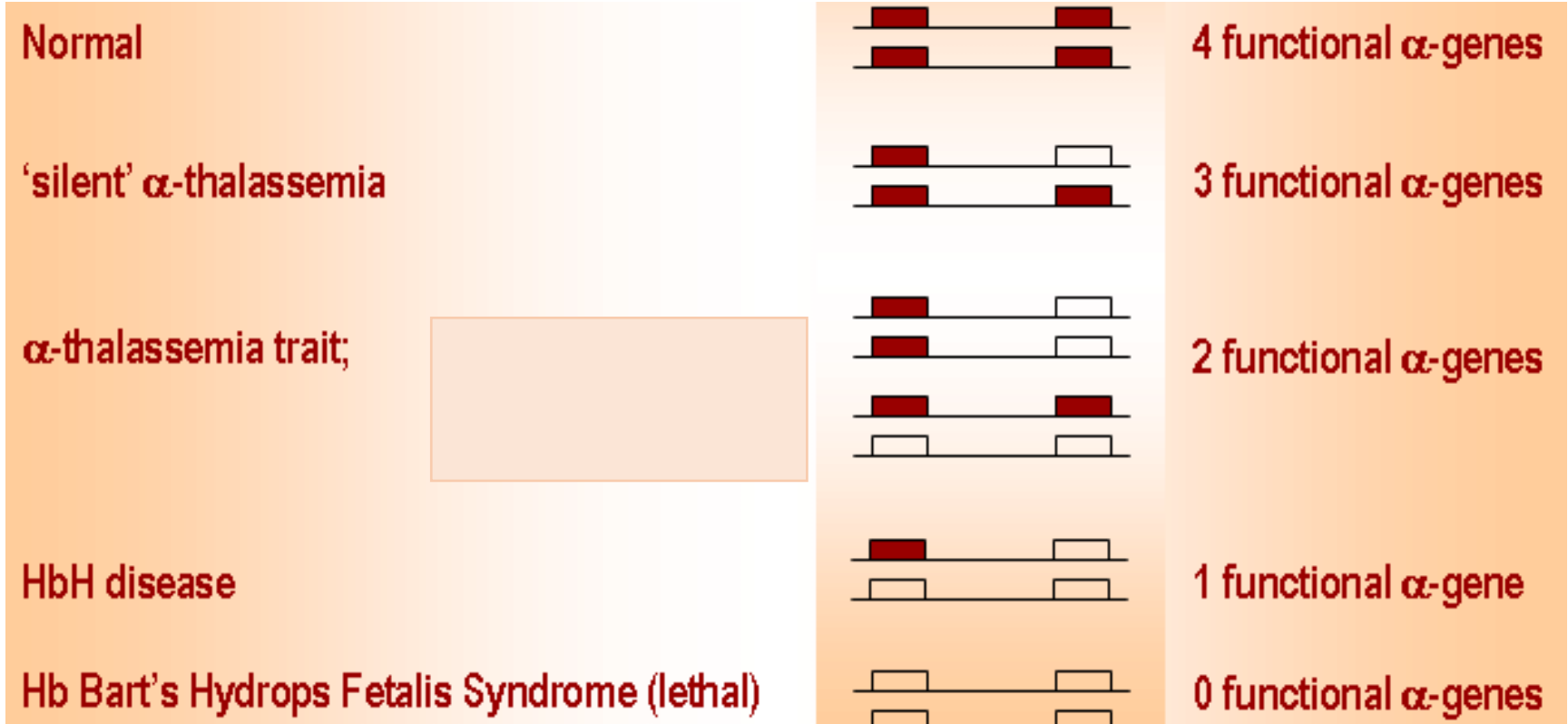
- Avoid hypoxia and stress
- Careful use of anesthesia (oral infections & periodontal disease)

🎯 **Teaching Wrap-up**

- **Sickle Cell Disease affects oxygen delivery → this impacts oral tissues, healing, and infection risk, and must be considered during dental treatment.**

2- Alpha thalassemia:

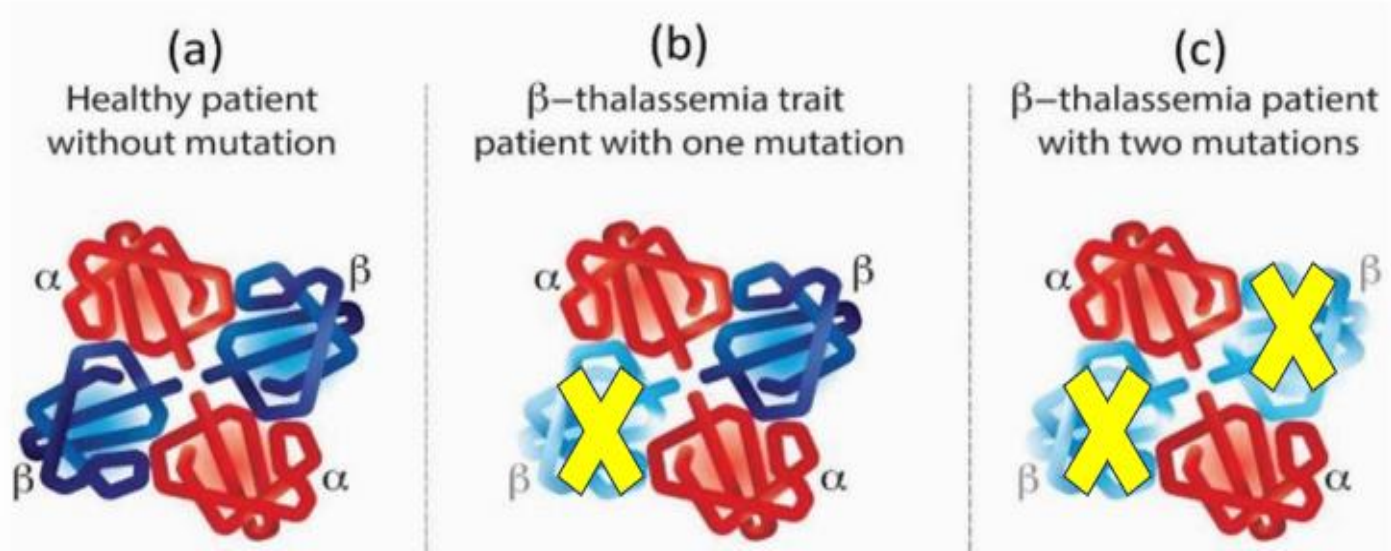
- Large scale deletion mutation in α-globin gene on chromosome 16.
- Decreased alpha-globin production resulting in an excess of β chains in adults.



3- Beta thalassemia (Mediterranean Anemia):

- It can be caused by mutation in beta globin gene on chromosome 11
- It is characterized by reduced synthesis of the hemoglobin beta chain that results in:

- Reduced amounts of hemoglobin A (HbA)……. microcytic hypochromic anemia
- Increase amount of HB A2 and HB F



Common Hemoglobinopathies:

Sickle cell anemia	Alpha thalassemia	Beta thalassemia
Point mutation (Substitution)	Large scale mutation	Different gene mutations (point mutation, frameshift, or even large deletion).
Affected gene on chromosome 11	Affected gene on chromosome 16	Affected gene on chromosome 11
Missense point mutation in the codon 6 of beta globin gene (GAG→GTG) Changing the 6th amino acid of the beta chains from glutamic acid to valine. Formation of abnormal hemoglobin S (Hb S)	Mutation in α-globin gene on chromosome 16. Decreased alpha-globin production resulting in an excess of β chains in adults.	Mutations in beta globin gene on chromosome 11. It is characterized by reduced synthesis of the hemoglobin beta chain that results in: reduced amounts of hemoglobin A and increased amount of HB A2 and HB F


BELIEVE IN
YOURSELF.