Genetics

Modified no.

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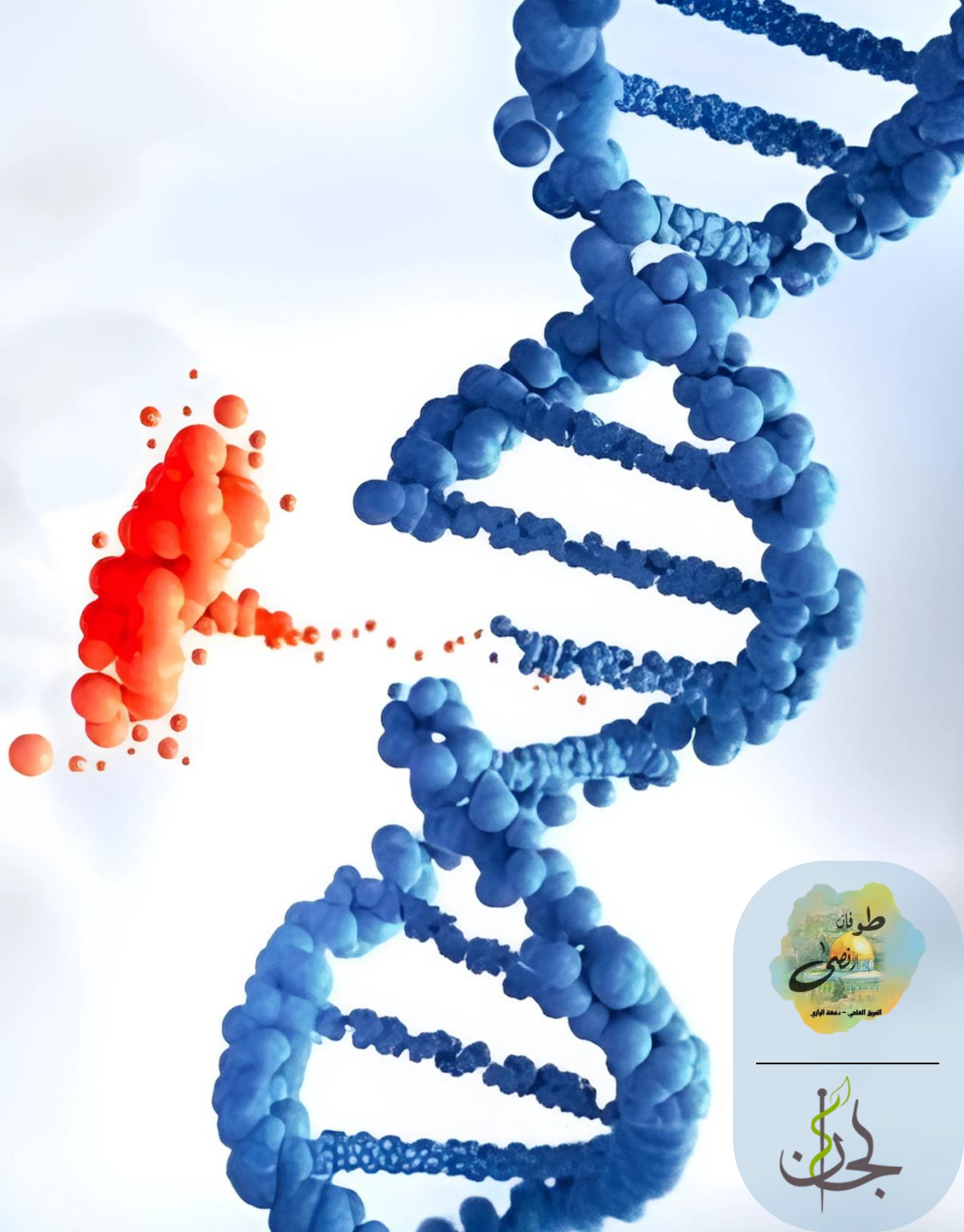


- Welcome to the 5th genetics lecture, this lecture is full of info that have been discussed in HLS, you will enjoy it 😊
- ‼ Every word in the slides was read by the doctor so kindly study them
- Say "بسم الله" and let's start

Color code

- Slides
- Doctor
- Additional info
- Important

Causes of Mutation

Induced mutations. attributed to a known environmental cause. **Spontaneous mutations**, arise naturally during the process of DNA replication.

Agents that cause induced mutations are known collectively as mutagens.

Animal studies have shown that radiation is an important class of mutagen.

Ionizing radiation, such as that produced by x-rays and nuclear fallout, can eject electrons from atoms, forming electrically charged ions, these charged ions promote chemical changes in the DNA that might change one or more bases of nucleotides leading to mutations.
This form of radiation can reach all cells of the body, including the germ line.

Nonionizing radiation does not form charged ions but can move electrons from inner to outer orbits in the atom. The atom becomes chemically unstable.

Ultraviolet (UV) radiation, which occurs naturally in sunlight, is an example of nonionizing radiation.

UV radiation causes the formation of covalent bonds between adjacent pyrimidine bases (i.e., cytosine or thymine]. These pyrimidine dimers are unable to pair ‘properly with purines during DNA replication; this results in a base pair substitution.

Because UV radiation is absorbed by the epidermis, **it does not reach the germ line but can cause skin cancer.**

Remember that ionising radiation reaches the germ line.

The UV light causes a covalent linking between adjacent pyrimidine bases and forms a kink appearance in DNA, then when DNA replication happens, the base pairing process will not be done correctly leading to a mutation.

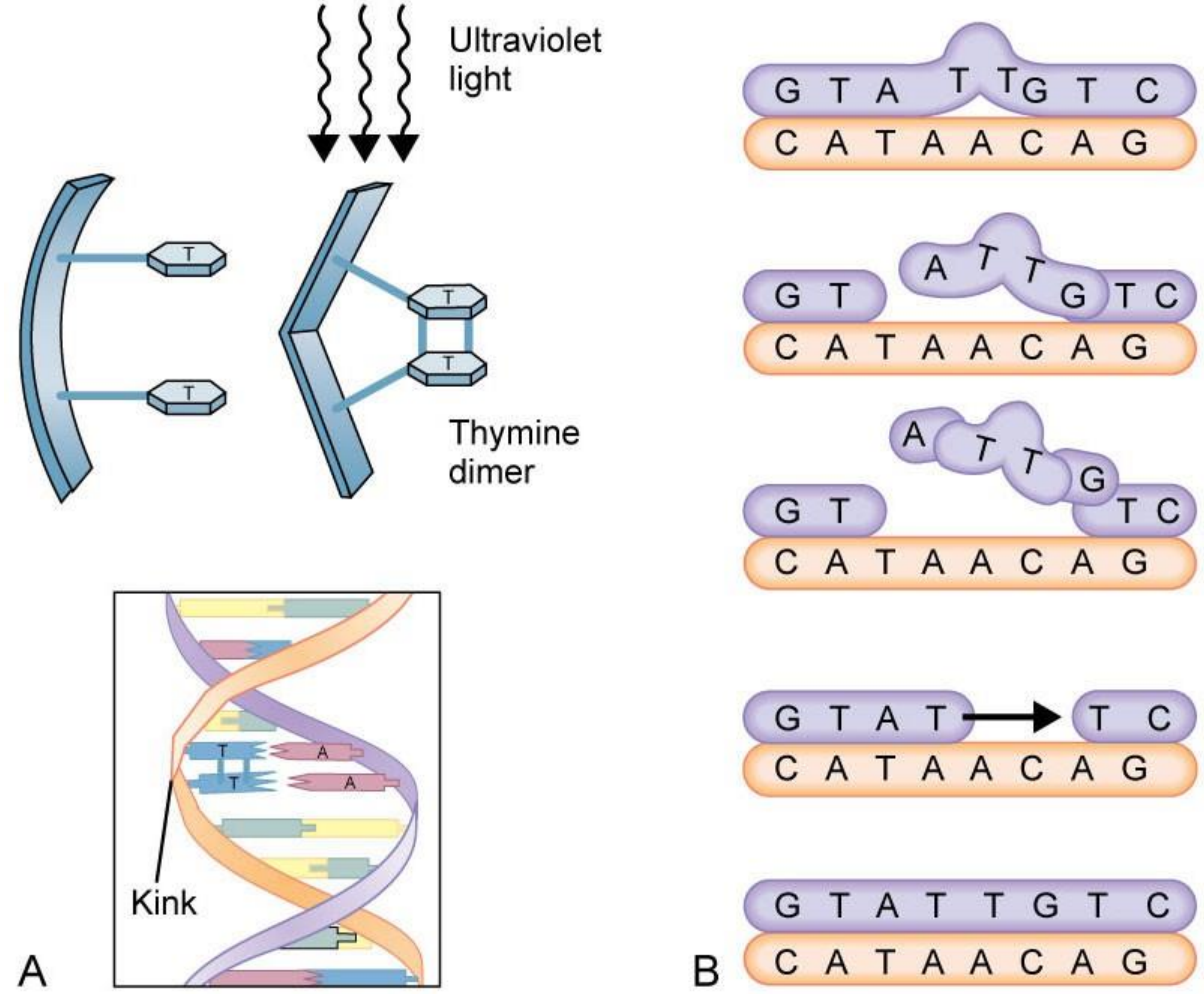


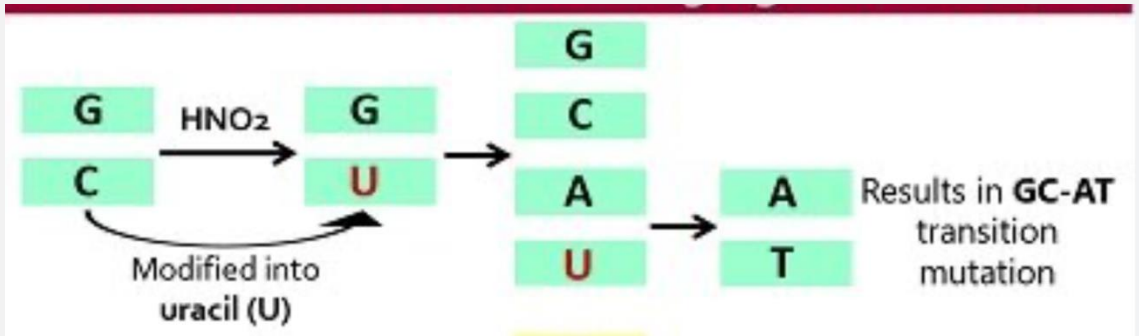
Fig. 3-11. **A,** Pyrimidine dimers originate when covalent bonds form between adjacent pyrimidine (cytosine or thymine) bases. This deforms the DNA, interfering with normal base pairing. **B,** The defect is repaired by removal and replacement of the dimer and bases on either side of it, with the complementary DNA strand used as a template.

Another example of induced mutations is chemicals that lead to the formation of **new bases** instead of the true bases of DNA during replication

Examples of them:

1. Base analogs (e.g., 5-bromouracil)
2. Nitrogen mustards
3. Vinyl chloride
4. Alkylating agents
5. Formaldehyde
6. Sodium nitrite
7. Saccharin
8. Acridine Dyes
9. Nitrous Acid (HNO_2)

Extra image about the effect of Nitrous acid



A variety of **chemicals** can also induce mutations, sometimes because of their chemical similarity to DNA bases. Because of this similarity, these **base analogs**, such as 5-bromouracil, can be substituted for a true DNA base during‘ replication.

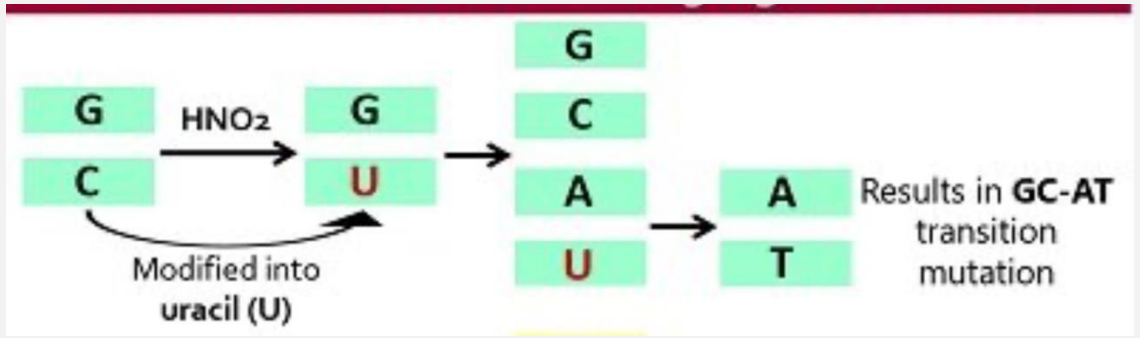
→ The analog (5-bromouracil) is not exactly the same as the base it replaces, so it can cause pairing errors during subsequent replications.

Other chemical mutagens, such as acridine dyes, can physically insert themselves between existing bases, distorting the DNA helix and causing frameshift mutations.

Other mutagens can directly alter DNA bases, causing replication errors, like nitrous acid, which removes an amino group from cytosine, converting it to uracil.

→ Although uracil is normally found in RNA, it mimics the pairing action of thymine in DNA. So, it pairs with adenine, instead of pairing with guanine, as the original cytosine would have done. The end result is a base pair substitution.

Extra image about the effect of Nitrous acid



DNA Repair

Considering that 3 billion DNA base pairs must be replicated in each cell division, and considering the large number of mutagens to which we are exposed, DNA replication is surprisingly accurate.

A primary reason for this is **DNA repair**, which takes place in all normal cells of higher organisms. Several dozen different enzymes (such as DNA polymerase) are involved in repairing damaged DNA.

They collectively recognize an altered base, excise it by cutting the DNA strand, replace it with the correct base (determined from the complementary strand), and reseal the DNA.

It is estimated that these repair mechanisms correct 99.9% of initial errors.

The DNA repair mechanism helps improve the accuracy of DNA replication by: (1) correcting replication errors, (2) repairing double-stranded DNA breaks, and (3) excising damaged nucleotides.

A defect in the repair mechanism can cause mutations, leading to many diseases.

Because DNA repair is essential for the accurate replication of DNA, defects in DNA repair systems can lead to many types of disease.

For example, inherited mutations in genes responsible for DNA mismatch repair result in the persistence of cells with replication errors (i.e., mismatches) and can lead to some types of cancers.

A compromised ability to repair double-stranded DNA breaks can lead to ovarian and breast cancer.

Nucleotide excision repair is necessary for the removal of larger changes in the DNA helix (e.g., pyrimidine dimers). Defects in excision repair lead to a number of diseases like xeroderma pigmentosum.

Examples of Diseases That Are Caused by a Defect in DNA Repair

TABLE 3-2 Examples of Diseases That Are Caused by a Defect in DNA Repair

DISEASE	FEATURES	TYPE OF REPAIR DEFECT
Xeroderma pigmentosum	Skin tumors, photosensitivity, cataracts, neurological abnormalities	Nucleotide excision repair defects, including mutations in helicase and endonuclease genes
Cockayne syndrome	Reduced stature, skeletal abnormalities, optic atrophy, deafness, photosensitivity, mental retardation	Defective repair of UV-induced damage in transcriptionally active DNA; considerable etiological and symptomatic overlap with xeroderma pigmentosum and trichothiodystrophy
Fanconi anemia	Anemia; leukemia susceptibility; limb, kidney, and heart malformations; chromosome instability	As many as eight different genes may be involved, but their exact role in DNA repair is not yet known
Bloom syndrome	Growth deficiency, immunodeficiency, chromosome instability, increased cancer incidence	Mutations in the reqQ helicase family
Werner syndrome	Cataracts, osteoporosis, atherosclerosis, loss of skin elasticity, short stature, diabetes, increased cancer incidence; sometimes described as "premature aging"	Mutations in the reqQ helicase family
Ataxia-telangiectasia	Cerebellar ataxia, telangiectases,* immune deficiency, increased cancer incidence, chromosome instability	Normal gene product is likely to be involved in halting the cell cycle after DNA damage occurs
Hereditary nonpolyposis colorectal cancer	Proximal bowel tumors, increased susceptibility to several other types of cancer	Mutations in any of six DNA mismatch-repair genes

*Telangiectases are vascular lesions caused by the dilatation of small blood vessels. This typically produces discoloration of the skin.

Mutation Rates

↑ nucleotide level
↑ mutation rate

At the nucleotide level, the mutation rate is usually estimated to be about 10^{-9} per base pair (0.000000001) per cell division.

At the level of the gene, the mutation rate is quite variable, ranging from 10^{-4} to 10^{-7} per locus per cell division. There are at least two reasons for this large range of variation.

Example of a large protein: Hemophilia A gene

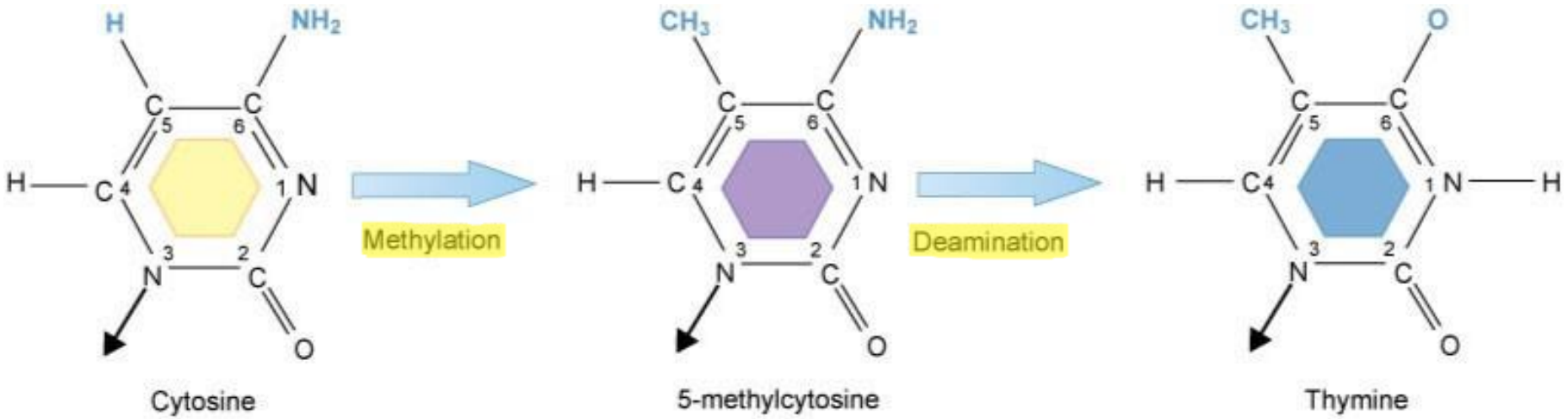
1. Genes vary tremendously in size. The somatostatin gene, for example, is quite small, containing 1,480 bp. In contrast, the gene responsible for Duchenne muscular dystrophy (DMD) spans more than 2 million bp. So the possibility of mutations increases as the size of the gene increases, and this explains the huge difference in mutations possibilities (10-4 to 10-7 per locus).
2. It is well established that certain nucleotide sequences are especially more susceptible to mutation. These are termed mutation hot spots.

The best-known example of hot spot mutation is the two-base (dinucleotide) sequence **CG**. In mammals, about 80% of CG dinucleotides are methylated: a methyl group is attached to the cytosine base.

Note: methylation causes inhibition of gene expression.

The methylated cytosine, 5-‘methylcytosine, easily loses an amino group, converting it to thymine. The end result is a mutation from cytosine to thymine.

Surveys of mutations in human genetic diseases have shown that the mutation rate at CG dinucleotides is about 12 times higher than at other dinucleotIde sequences.



Cytosine 5-methylcytosine Thymine

Fig. 3-12. Cytosine methylation. The addition of a methyl group (CH_3) to a cytosine base forms 5-methylcytosine. The subsequent loss of an amino group (deamination) forms thymine. The result is a cytosine → thymine substitution.

Osteogenesis imperfecta is an example of a **hot spot mutation**

Mutation rates also vary considerably with the age of the parent, Some chromosome abnormalities increase dramatically with elevated maternal age. In addition, single-gene mutations can increase with elevated paternal age.

This increase is seen in several **single-gene disorders**, including **Marfan syndrome and achondroplasia.**

The risk of producing a child with Marfan syndrome is approximately five times higher for a male over age 40 than for a male in his 20's.

This paternal age effect is usually attributed to the fact that the stem cells giving rise to sperm cells continue to divide throughout the life of males, allowing a progressive buildup of DNA replication errors.

We talked about 2 factors that can affect the mutation level:

1) Neoclutide level
2) Age of the parent

Extra

شرح الفقرة:

1. تأثير عمر الوالدين على معدل الطفرات (Mutation Rate and Parental Age)

معدل الطفرات الجينية **يتغير بشكل ملحوظ حسب عمر الوالدين**، حيث يمكن أن تزداد احتمالية حدوث **تغيرات جينية أو صبغية** مع تقدم العمر.

2. تأثير عمر الأم (Maternal Age Effect) على الطفرات الصبغية (Chromosomal Abnormalities):

- مع تقدم **عمر الأم**، يزداد خطر **الاضطرابات الصبغية**، مثل **متلازمة داون (Down syndrome)**، بسبب **أخطاء في الانقسام الاختزالي (Meiotic errors)** أثناء تكوين البويضات.

3. تأثير عمر الأب (Paternal Age Effect) على الطفرات الجينية (Single-Gene Mutations):

- مع تقدم **عمر الأب**، **يزداد خطر الطفرات الجينية الجديدة (De novo mutations)**، خاصة في الأمراض التي تسببها طفرات في **جين واحد (Single-gene disorders)**، مثل:
  - **Marfan syndrome** (متلازمة مارفان).
  - **Achondroplasia** (الودانة، وهي أحد أسباب التقزم).
- وفقًا للأبحاث، **الآباء الذين تزيد أعمارهم عن 40 عامًا لديهم احتمال أعلى بخمس مرات** لإنجاب طفل مصاب بمتلازمة مارفان مقارنة بالآباء في العشرينيات من العمر.

4. لماذا يزداد تأثير عمر الأب على الطفرات الجينية؟

- السبب الرئيسي هو أن **الخلايا الجذعية المكونة للحيوانات المنوية تستمر في الانقسام طوال حياة الذكر**، بينما تكون البويضات عند النساء موجودة منذ الولادة.
- مع **كل انقسام خلوي جديد**، يمكن أن تحدث **أخطاء في تضاعف الحمض النووي (DNA replication errors)**، مما يؤدي إلى تراكم الطفرات في الحيوانات المنوية بمرور الوقت.

الخلاصة:

- **تقدم عمر الأم** يزيد من خطر **الطفرات الصبغية (مثل متلازمة داون)**.
- **تقدم عمر الأب** يزيد من خطر **الطفرات الجينية في جين واحد (مثل متلازمة مارفان والودانة)** بسبب **تكرار انقسام الخلايا المنتجة للحيوانات المنوية** وتراكم الأخطاء الوراثية.

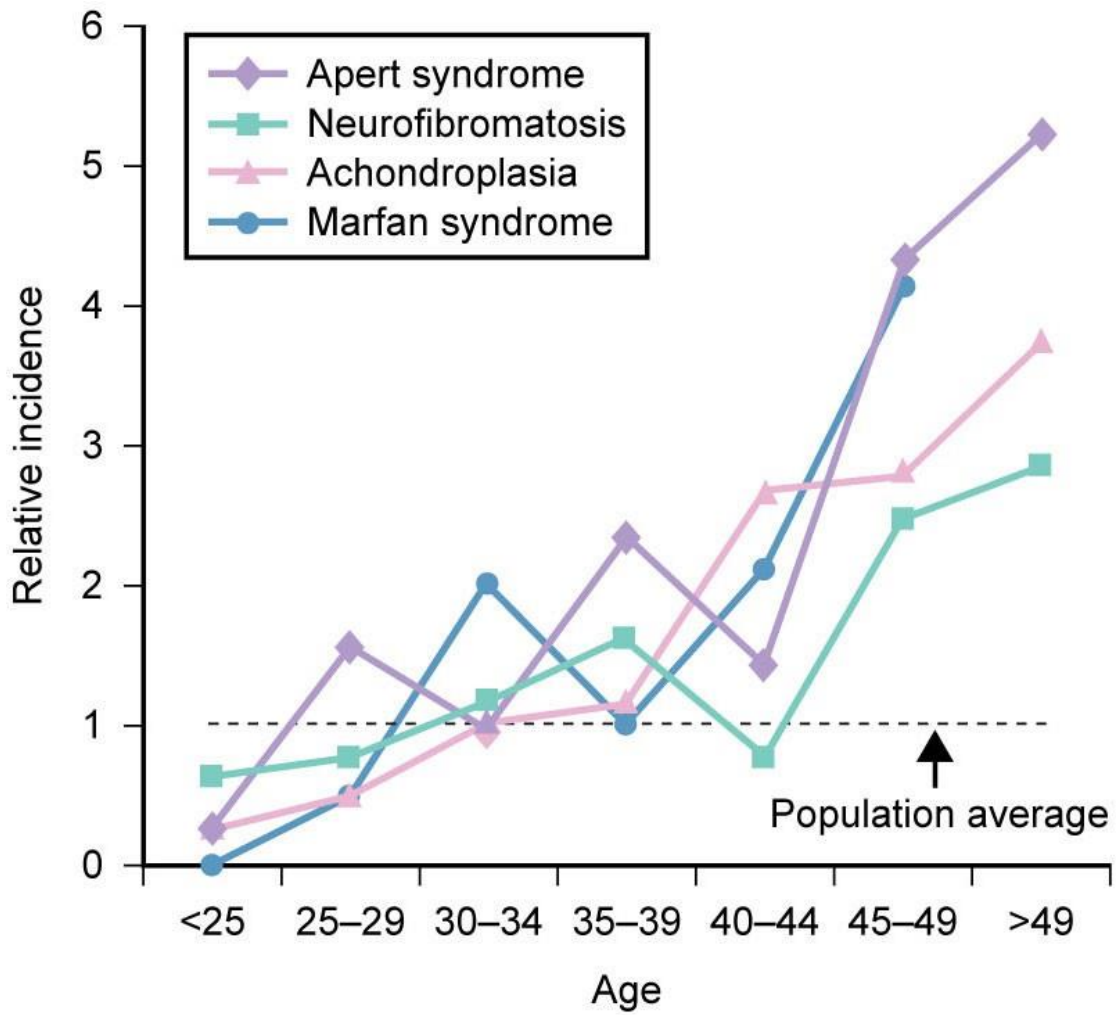


Fig. 3-13. Paternal age effect. For some single-gene disorders, the risk of producing a child with the condition (*y-axis*) increases with the father's age (*x-axis*).

Clinical Consequences of Mutation: The Hemoglobin Disorders

Remember that hemoglobin molecule is composed of 4 polypeptide chains (2 alpha and 2 beta), each polypeptide chain has a heme group that can bind to one oxygen molecule (O2). So the major function of hemoglobin is to carry oxygen through the blood.

Genetic disorders of human hemoglobin are the most common group of single-gene disorders

An estimated 5% of the world's population carries one or more mutations of the genes involved in hemoglobin synthesis.

The hemoglobin molecule is a tetrarmer composed of four polypeptide chains, two of which are labeled α and two of which are labeled β.

The β chains are encoded by a gene on chromosome 11, and the α chains are encoded by two genes on chromosome 16 that are very similar to one another.

A normal individual would thus have two normal β genes and four normal α genes.

This is a beta globin cluster on chromosome 11 ,we can see one **epsilon gene** , **2 gamma genes**, **psuedogene**, **delta gene** and **beta gene** (respectively as in the image). And alpha globin cluster on chromosome 16.

let's start discussing beta cluster

- We know that adult Hb is composed of 2 alpha polypeptide chains & 2 beta polypeptide chains
- Epsilon gene from beta cluster will be expressed instead of beta chain in early embryonic life (first 4 weeks)
- While gamma is in the fetal Hb (starts at 1month of pregnancy & continues till birth) & it is the highest expressed [Hb] at birth (HbF= 2 alpha, 2 gamma chains)
- HbA2 (Low concentration) = 2 delta chains (poorly expressed) + 2 alpha chains
- Beta gene expression almost starts at the 6th month after birth (so we will have a complete switch from gamma to beta by age of 6months-2yrs) & HbF becomes HbA gradually , and that's why in beta thalassemia major, clinical symptoms start to appear after 6months -2yrs of birth

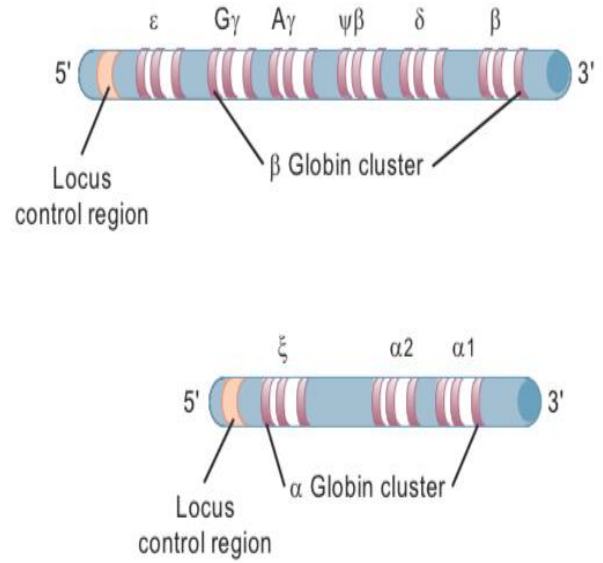
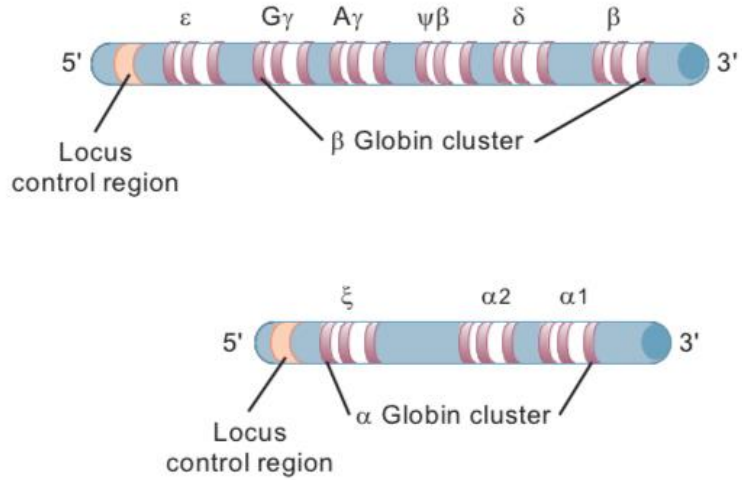


FIG 3-7 The α-globin gene cluster on chromosome 16 and the β-globin gene cluster on chromosome 11. The β-globin cluster includes the ε-globin gene, which encodes embryonic globin, and the γ-globin genes, which encode fetal globin. The ψβ gene is not expressed. The α-globin cluster includes the ζ-globin gene, which encodes embryonic α-globin.

- alpha globin cluster on chromosome 16.

let's start discussing alpha cluster

- We know that adult Hb is composed of 2alpha polypeptide chains & 2 beta polypeptide chains
- **zeta gene** from alpha cluster will be expressed instead of alpha chain in early embryonic life (first 4 weeks)
- While **alpha gene** is expressed in fetal Hb (starts at 1month of pregnancy & continues throughout life)
- There're 2 alpha genes (similar in structure & produce the same alpha polypeptide chain)
- When expression happens, notice that we have two alpha-globin genes and one beta-globin gene. So, the products of both alpha-globin genes equal the product of one beta-globin gene, ensuring equal quantities of beta and alpha globin.



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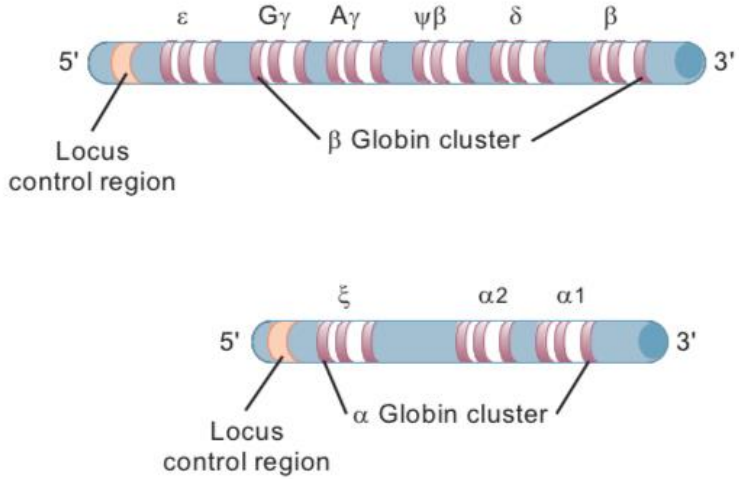
- Recall **alternative splicing.**

- Starting with the beta-globin cluster, **epsilon (ε)** is expressed first, while the other genes are silenced (excised) early in embryonic life. Then, **gamma (γ)** becomes the predominant expressed gene , replacing epsilon (and others will be excised). Finally, **beta (β)** becomes the main expressed globin in adulthood.

- A similar process occurs in the alpha-globin cluster. Initially, **zeta (ζ)** is expressed, but it is later silenced. Then, **alpha (α)** becomes the dominant expressed gene throughout fetal development and adulthood.



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Each of these globin chains is associated with a heme group (which gives the blood its red colour), which contains an iron atom and binds with oxygen. So 1 hemoglobin molecule can bind 4 oxygen molecules

This property allows hemoglobin to perform the vital function of transporting oxygen in erythrocytes.

The hemoglobin disorders can be classified into two broad categories:

1-structural abnormalities, in which the hemoglobin molecule is altered,(hemoglobinopathies)

2- thalassemias, a group of conditions in which the hemoglobin is structurally normal but reduced in quantity or not present at all.

Summary of the major hemoglobin disorders

- Doctor read all highlighted parts.
- **Sickle cell disease:** mutation makes a structural defect & it is at the 6th position of the polypeptide chain.
- **HbH disease:** 3 out of the 4 alpha globin genes are deleted.
- **Hydrops fetalis:** (the baby is born dead) the 4 alpha genes are deleted.
- **Beta null thalassemia:** Beta globin is not produced at all
- **Beta+ thalassemia:** missense mutation leads to production of only a small amount of Beta globin.

TABLE 3-1 **Summary of the Major Hemoglobin Disorders**

	DISEASE	MUTATION TYPE	MAJOR DISEASE FEATURES
structural Defect ←	Sickle cell disease	β-globin missense mutation	Anemia, tissue infarctions, infections
3/4 α-globin are deleted ←	HbH disease	Deletion or abnormality of three of the four α-globin genes	Moderately severe anemia, splenomegaly
4/4 α-globin are deleted ←	Hydrops fetalis (Hb Barts)	Deletion or abnormality of all four α-globin genes	Severe anemia or hypoxemia, congestive heart failure; stillbirth or neonatal death
No β-globin ←	β^0-Thalassemia	Usually nonsense, frameshift, or splice-site donor or acceptor mutations; no β-globin produced	Severe anemia, splenomegaly, skeletal abnormalities, infections; often fatal during first decade if untreated
Small amount of β-globin ←	β^+-Thalassemia	Usually missense, regulatory, or splice-site consensus sequence or cryptic splice-site mutations; small amount of β-globin produced	Features similar to those of β^0-thalassemia but often somewhat milder

Sickle Cell Disease

The most important of the structural hemoglobin abnormalities is sickle cell disease, a disorder that affects approximately 1/400 to 1/600 African-American births. (So beta chain is produced in normal amounts but with an abnormal folding –structural defect.)

It is even more common in parts of Africa, where it can affect up to one in 50 births (very high frequency), and it is also seen occasionally in Mediterranean and Mideastern populations. (But its frequency is lower)

Sickle cell disease is caused by a single missense mutation that effects a substitution of valine for glutamic acid at position six of the B-globin polypeptide chain.

In homozygous form (both alleles have sickle cell mutation), this amino acid substitution alters the characteristics of the hemoglobin molecule such that the erythrocytes assume a characteristic ”sickle" shape under conditions of low oxygen tension. so instead of being a biconcave disc (which helps it to squeeze in small capillaries), it becomes sickled (leads to trapping of erythrocytes in narrow blood vessels & resulting in tissue infarction)

- In laboratory, we call it HbS.
- It can be detected in laboratory settings by **electrophoresis**.
- But genetically, for this mutation detection, we can use **PCR** & screen for it.

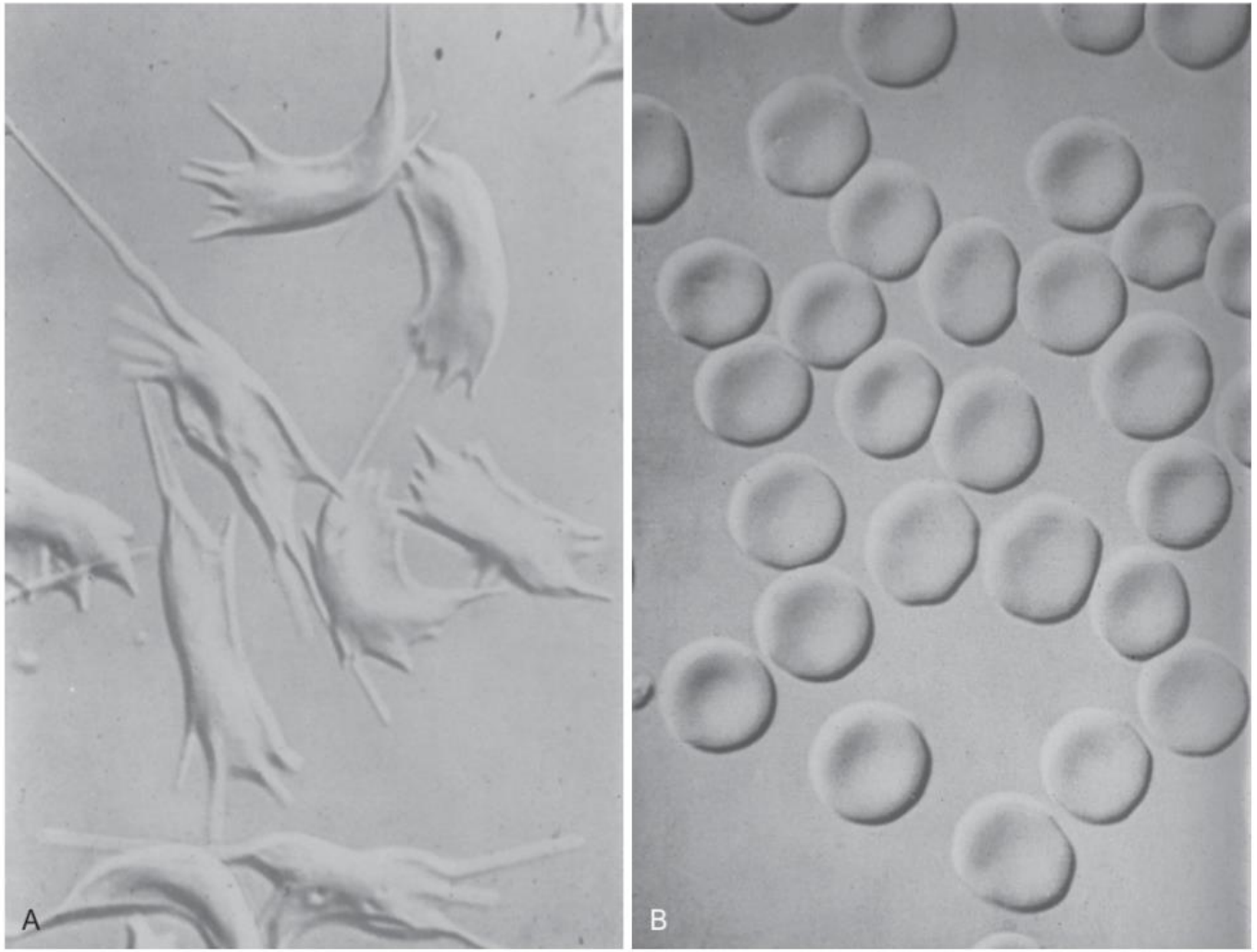

FIG 3-8 **A,** Erythrocytes from patients with sickle cell disease assume a characteristic shape under conditions of low oxygen tension. **B,** Compare with normal erythrocytes.

Normal erythrocytes can squeeze through capillaries,but sickled erythrocytes are less flexible and are unable to do so.

The resultant vascular obstruction produces localized hypoxemia, painful sickling ”crises," and infarctions of various tissues, including bone, spleen, kidneys, and lungs.
Premature destruction of the sickled erythrocytes decreases the number of circulating erythrocytes and the hemoglobin level, producing anemia.

The spleen becomes enlarged (splenomegaly), but infarctions eventually destroy this organ, producing some loss of immune function. (abnormal sickle cells will be engulfed by macrophages in spleen & their accumulation there will lead to “**splenomegaly**)

This contributes to the recurrent bacterial“ infections (especially pneumonia) that are commonly seen in individuals with sickle cell disease and that frequently cause death. In North America, it is estimated that about 15% of children with sickle cell disease die before the age of 5 years. So, Management includes blood transfusion, and sometimes splenectomy.

Thalassemia

The term ”thalassemia” is derived from the Greek word for ”sea," thalassa. & “emia” for conditions in the blood

→ thalassemia was first described in populations living near the Mediterranean Sea. It is also common in portions of Africa, south of Europe, the Mideast, India, and Southeast Asia.

Divided into two major groups, α-thalassemia (if alpha gene is absent / reduced) and β-thalassemia (if beta gene is absent / reduced), depending on the globin chain that is reduced in quantity.

When one type of chain is decreased in number, the other chain type, unable to participate in normal tetramer formation, tends to form molecules consisting of four chains of the excess type only [these are termed homotetramers, in contrast to the heterotetramers normally formed by α and β chains).

يعني اذا بيتا مفقودة الألفا حيتجمعوا و يعملوا homotetramers

In α-thalassemia, the α-globin chains are deficient, so the β chains after birth ≈ by 6 months (or γ chains in the fetus) are found in excess. They form homotetramers that have a greatly reduced oxygen-binding capacity, producing hypoxemia leading generally to anemia

In β-thalassemia, β-chains are reduced or absent, so the excess α-chains form homotetramers that precipitate and damage the cell membranes of red cell precursors. This leads to premature erythrocyte destruction in the spleen and anemia due to destruction of bone marrow's synthesized RBCs by the spleen.

Most cases of α-thalassemia are caused by deletions of the α-globin genes. (Remember that we have 4 alpha genes normally) A loss of one or two of these genes has no clinical effect. The loss or abnormality of three of the α genes produces moderately severe anemia and splenomegaly (Hb H disease).

Loss of all four α genes, a condition seen primarily among Southeast Asians, produces hypoxemia in the fetus and hydrops fetalis ""تجمع السوائل حول الجنين"". Severe hypoxemia invariably causes Stillbirth or neonatal death. After the third month of fetal development, the fetus relies entirely on HbF to extract oxygen from the mother's blood. However, if alpha chains are absent, HbF cannot form since it requires alpha chains to pair with gamma chains. This absence prevents proper oxygen transport, leading to severe fetal complications.

Individuals with a β-globin mutation in one copy of chromosome 11 (heterozygotes) are said to have B-thalassemia minor, a condition that involves little or no anemia and does not ordinarily require clinical management. So they don't need blood transfusion, and their blood volume is on its minimal limit. They are carriers with one defected allele.

Those in whom both copies of the chromosome carry a β-globin mutation develop B-thalassemia major (also called Cooley's anemia) or the less serious condition, β-thalassemia intermedia . Intermedia or major is determined based on the type of the developed mutation

β-globin may be completely absent (β°-thalassemia) (mutations: nonsense codon frameshift splice site)
or reduced to about 10% to 30% of the normal amount (β^{+}-thalassemia). (Mutation in regulatory sequences ↓ expression of beta chain)

Because β-globin is not produced until after birth, the effects of β- thalassemia major are not seen clinically until the age of 2 to 6 months.

These patients develop severe anemia. If the condition is left untreated, substantial growth retardation can occur. Nowadays, scanning for such diseases is available to start management earlier on → blood transfusion (done twice a week for life).

In the past, those patients had suffered from complications:
The anemia causes bone marrow expansion (Recall that bone marrow is 50% white and 50% red, and in anemia, the white becomes red marrow. If anemia is very severe, bone cells themselves become red marrow), which in turn produces skeletal changes, including a protuberant upper jaw and cheekbones and thinning of the long bones (making them susceptible to fracture). → if not treated

Splenomegaly and infections are common, and untreated β-thalassemia major patients often die during the first decade of life.

B-thalassemia can vary considerably in severity, depending on the precise nature of the responsible mutation.

- This is splenomegaly

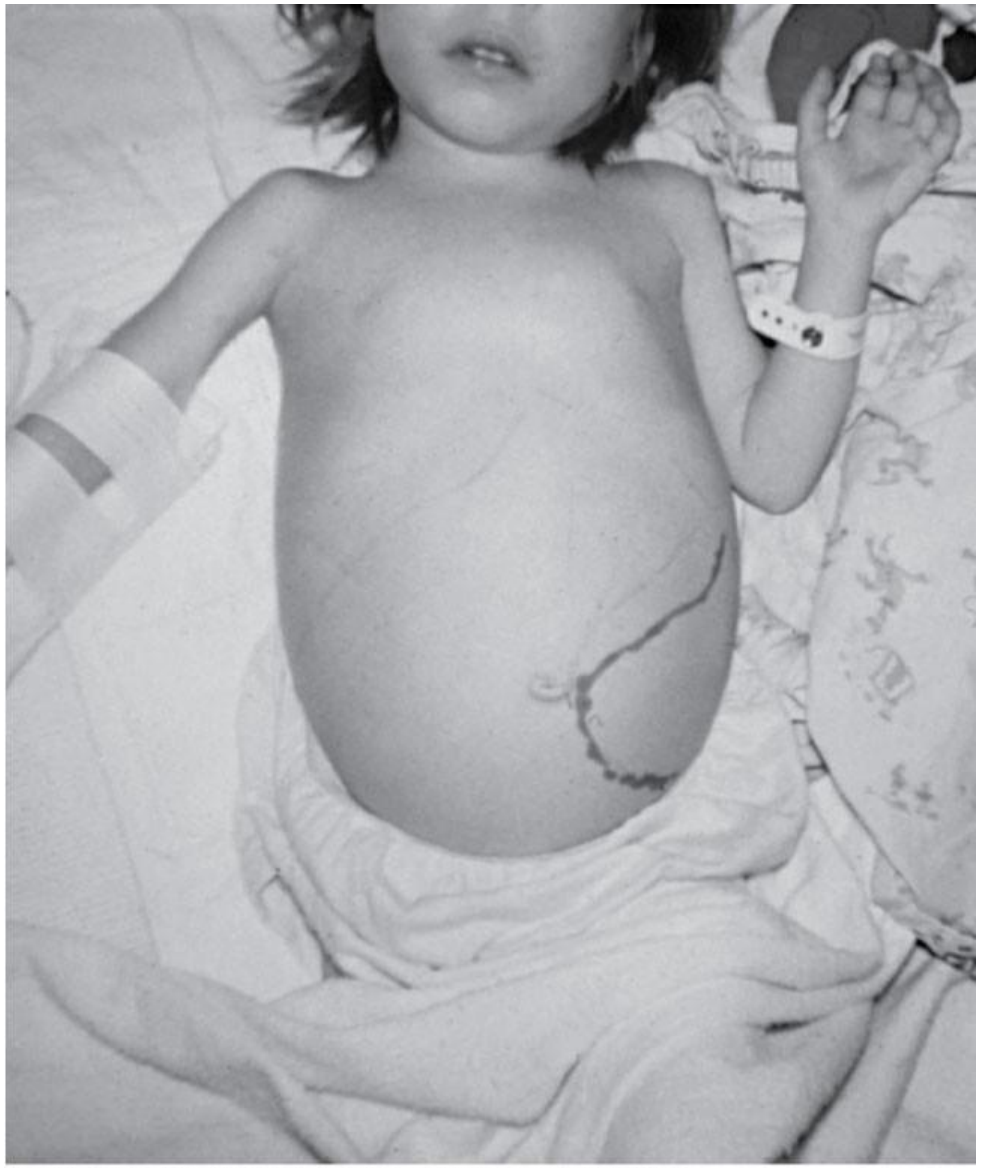

Fig. 3-9. A child with β-thalassemia major who has severe splenomegaly.

In contrast to α-thalassemia, gene deletions are relatively rare in β-thalassemia. Instead, most cases are caused by single-base mutations.

Nonsense mutations, which result in premature termination of translation of the β-globin chain (so no protein product), usually produce β°-thalassemia (beta null thalassemia). Frameshift mutations also typically produce the β° form.

In addition to mutations in the β-globin gene itself, alterations in regulatory sequences are often seen.

β-globin transcription is regulated by a promoter, two enhancers, and an upstream region known as the locus control region (LCR) which lies before (upstream) all these sequences .

so any mutation in these regulatory sequences, which are located before the beta globin cluster, leads to reduced expression of the gene

Resulting in beta+ thalassemia

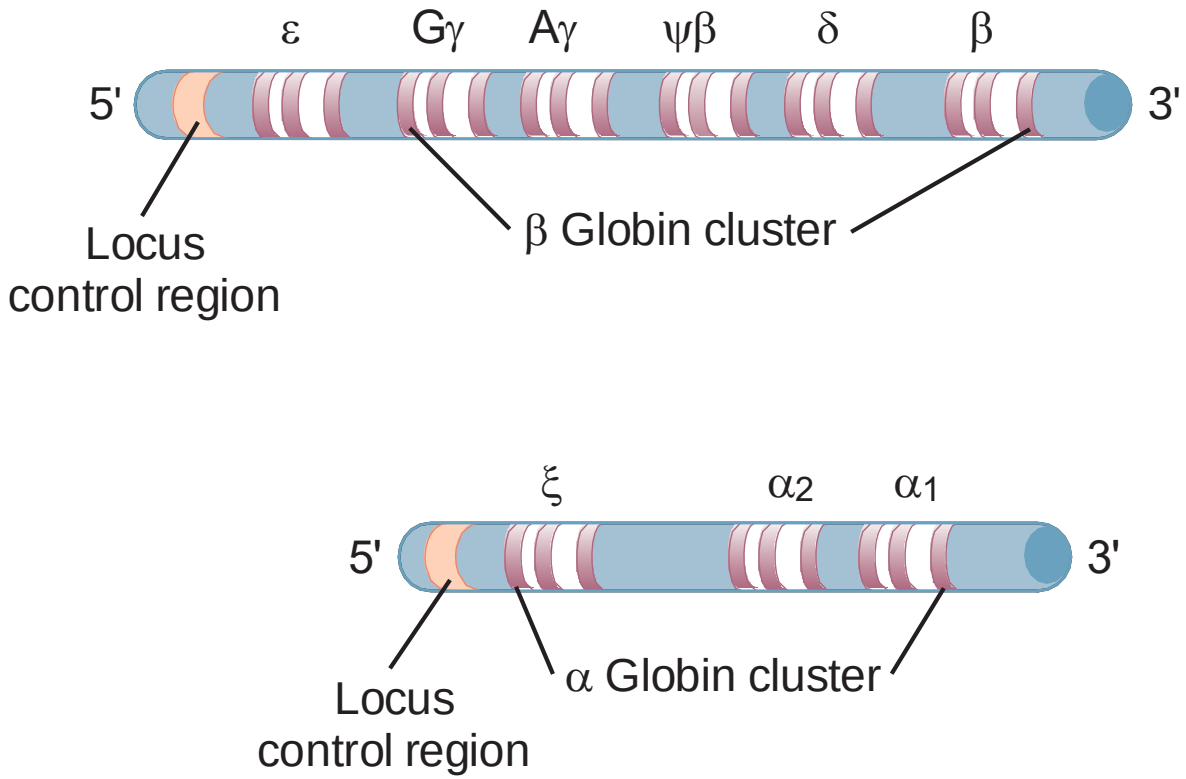

FIG 3-7 The α-globin gene cluster on chromosome 16 and the β-globin gene cluster on chromosome 11. The β-globin cluster includes the ε-globin gene, which encodes embryonic globin, and the γ-globin genes, which encode fetal globin. The ψβ gene is not expressed. The α-globin cluster includes the ζ-globin gene, which encodes embryonic α-globin.

Mutations in the regulatory regions usually result in reduced synthesis of mRNA and a reduction, but not complete absence, of β-globin (β^+- thalassemia).

Several types of splice site mutations have also been observed. When a point mutation occurs at the donor or acceptor sites, normal splicing is destroyed completely, producing B°-thalassemia.due to the production of a completely different protein

Mutations in the surrounding consensus sequences usually produce B^+- thalassemia.

Mutations also occur in the cryptic splice sites found in introns or exons of the B-globin gene, causing these sites to be available to the splicing mechanism.

Cryptic splice sites: hidden splicing sites that become active when introns are not properly recognized due to mutations. These mutations make the cryptic sites available for splicing, leading to incorrect splicing, which results in the production of a faulty protein

These additional splice sites then compete with the normal splice sites, producing some normal and some abnormal β-globin chains. The result is usually β^+-thalassemia.

More than 300 different β-globin mutations have been reported.

Consequently, most β-thalassemia patients are not ”homozygotes" in the strict sense: they usually have a different β-globin mutation on each copy of chromosome 11 and are termed compound heterozygotes.

Even though the mutations differ, each of the two β-globin genes is altered, producing a disease state. It is quite common to apply the term ”Homozygote” loosely to compound heterozygotes.

- True homozygous → when the 2 alleles have the same mutations.
- Compound heterozygous → when the 2 alleles have different mutations within the beta locus.

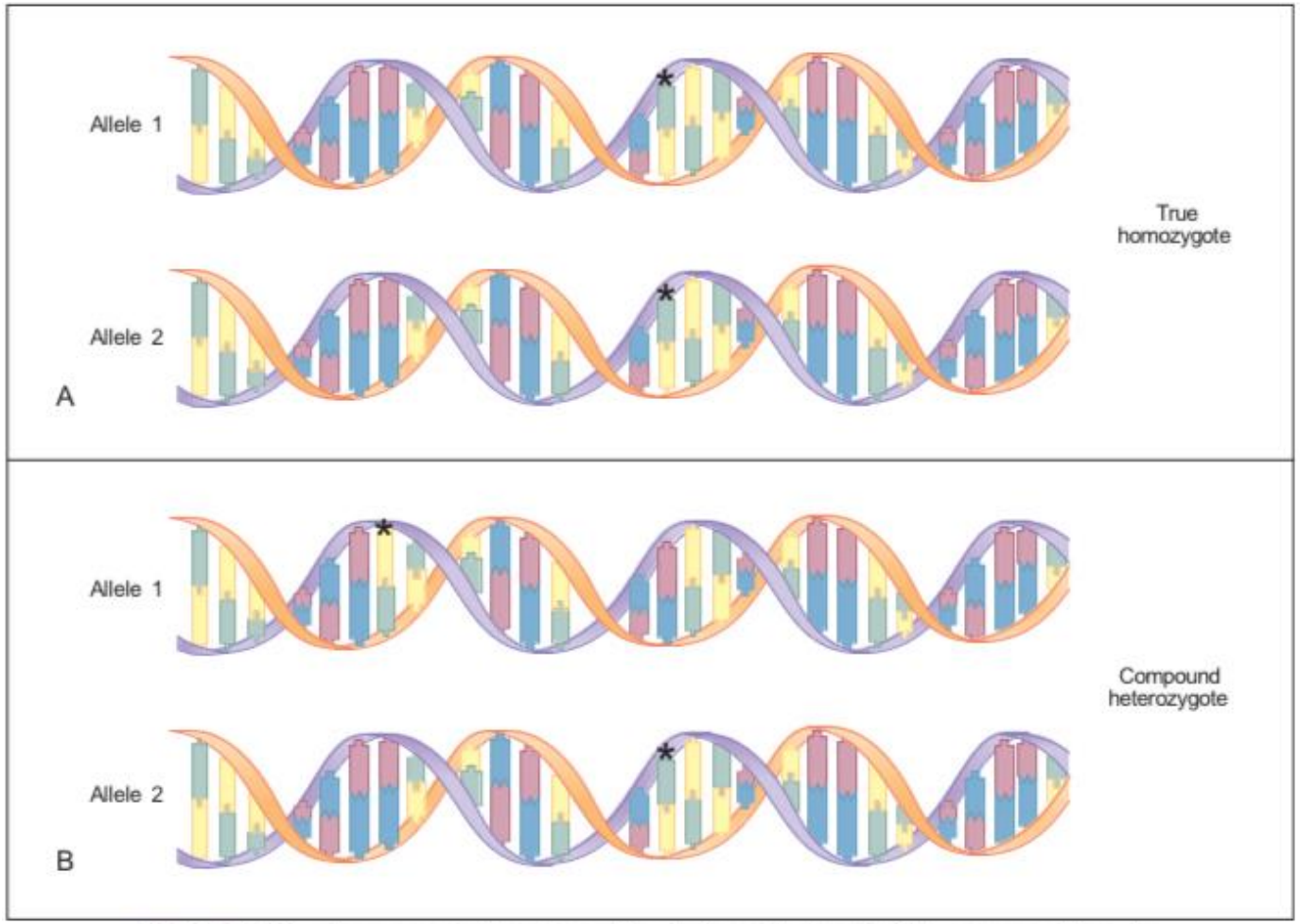

FIG 3-10 **A,** True homozygotes have two alleles that are identical in DNA sequence. Here, the homozygote has two copies of a single-base mutation, shown by the *asterisk* in the same position in the DNA sequence. Both mutations (alleles 1 and 2) have a loss-of-function effect, giving rise to a recessive disease. **B,** The same effect is seen in a compound heterozygote, which has two different mutations *(asterisks)* in two different locations in the gene's DNA sequence. Each allele has a loss-of-function effect, again causing a recessive disease.

Sickle cell and B-thalassemia major patients are sometimes treated with blood transfusions and with chelating agents that remove excess iron introduced by the transfusions. This excess iron leads to organ damage if not removed.

Prophylactic administration of and antipneumococcal vaccination are used to diminish bacterial infections in sickle cell disease patients, and analgesics are administered for pain relief during sickling crises.

Bone marrow transplants, which provide donor stem cells that produce genetically normal erythrocytes, have been performed on patients with severe B-thalassemia and sickle cell disease.
(here we kill all dividing cells in the patient's bone marrow, then we transplant stem cells from the donor to produce a complete healthy bone morrow)

It is often impossible to find a suitably matched donor, and the mortality rate from these transplants is still fairly high (approximately 5% to 30%, depending on the severity of disease and the age of the patient).

The hemoglobin disorders are a possible candidate for gene therapy (still there is no success).

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!