الوراثة الطبية 1 / الكورس الاول

Genetic diseases

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المرحلـــــــــــــة الثالثة — Third Stage

الجانب النظري : الوراثة الطبية

Theoretical : Medical Genetics

محاضرة رقم 7

Lecture No. 7

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Learning Objectives

By the end of this lecture, you will be able to:

- Define the term genetic disease and explain how genetic abnormalities can lead to disease
- Differentiate between the major types of genetic disorders
- Identify examples of common genetic diseases
- Explain the genetic and environmental interaction in multifactorial disorders

Genetic disease

Genetic disease is any disease caused by an abnormality in the genetic material of an individual. This abnormality can be as small as a single-base mutation in one gene or as large as the addition or loss of an entire chromosome.

Some genetic diseases are inherited from parents, whereas others arise from new mutations that occur randomly or through environmental exposure.

Genetic mutations

- Genetic mutations may include:
- **Missense mutation:** change in one base causes a different amino acid.
- **Nonsense mutation:** premature stop codon leads to incomplete protein.
- **Frameshift mutation:** insertion or deletion shifts the reading frame.
- **Deletion/Insertion:** loss or gain of DNA segments.

Types of genetic disorders

There are different types of genetic disorders (inherited) and include:

1. Single gene disorder
2. Multifactorial disorder
3. Chromosome abnormalities
4. Mitochondrial disorder

1- Single gene disorder

Single-gene disorders have different patterns of inheritance, including:

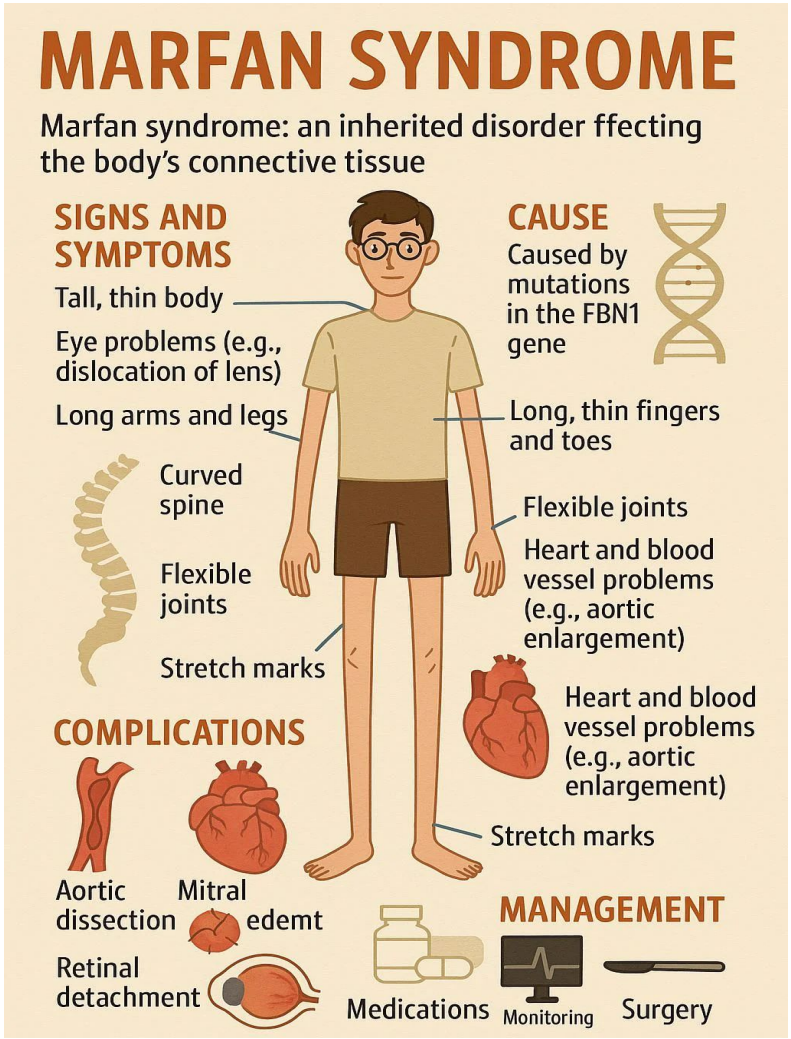
- **Autosomal dominant inheritance**, in which only one copy of a defective gene (from either parent) is necessary to cause the condition.
- **Autosomal recessive inheritance**, in which two copies of a defective gene (one from each parent) are necessary to cause the condition.
- **X-linked inheritance** is a pattern of inheritance in which the defective gene is located on the X chromosome. X-linked inheritance may be dominant or recessive.

Single gene inheritance disorders

- Cystic fibrosis
- Alpha- and beta-thalassemias
- Sickle cell anemia (sickle cell disease)
- Marfan syndrome
- Fragile X syndrome
- Huntington's disease
- Hemochromatosis

Marfan syndrome

- Marfan syndrome is inherited disease of connective tissues.
- The severity of Marfan syndrome differs from one individual to another and it progresses over time.
- A tall, thin body is characteristic of Marfan syndrome.
- Marfan syndrome affects the skeleton, eyes, heart and blood vessels, nervous system, skin, and respiratory system.
- Marfan syndrome can cause dislocation of the lens of the eye.

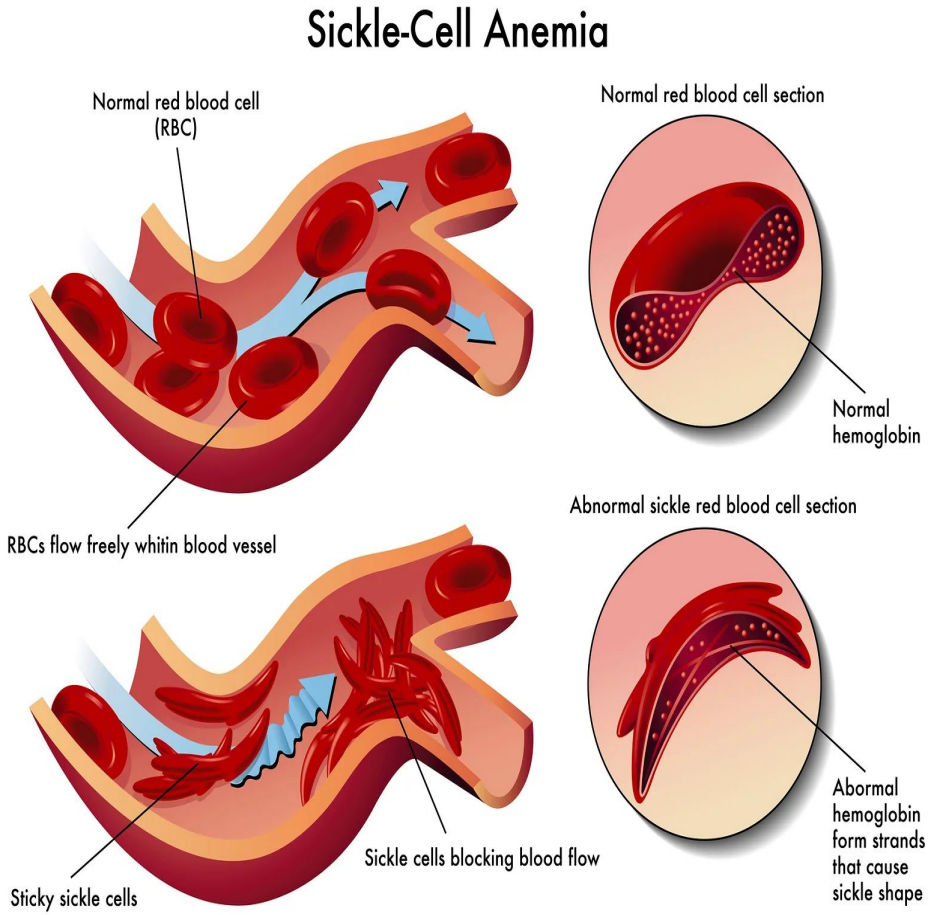


Hemochromatosis

- Hemochromatosis is an inherited disorder in which there is excessive accumulation of iron in the body (iron overload).
- It is a common genetic disorder among Caucasians in the United States, affecting approximately 1 million people in the United States.
- Individuals affected with hereditary hemochromatosis may have no symptoms or signs, or they can have severe symptoms and signs of iron overload that include heart failure, joint pains, cirrhosis of the liver, diabetes, and darkening of the skin.

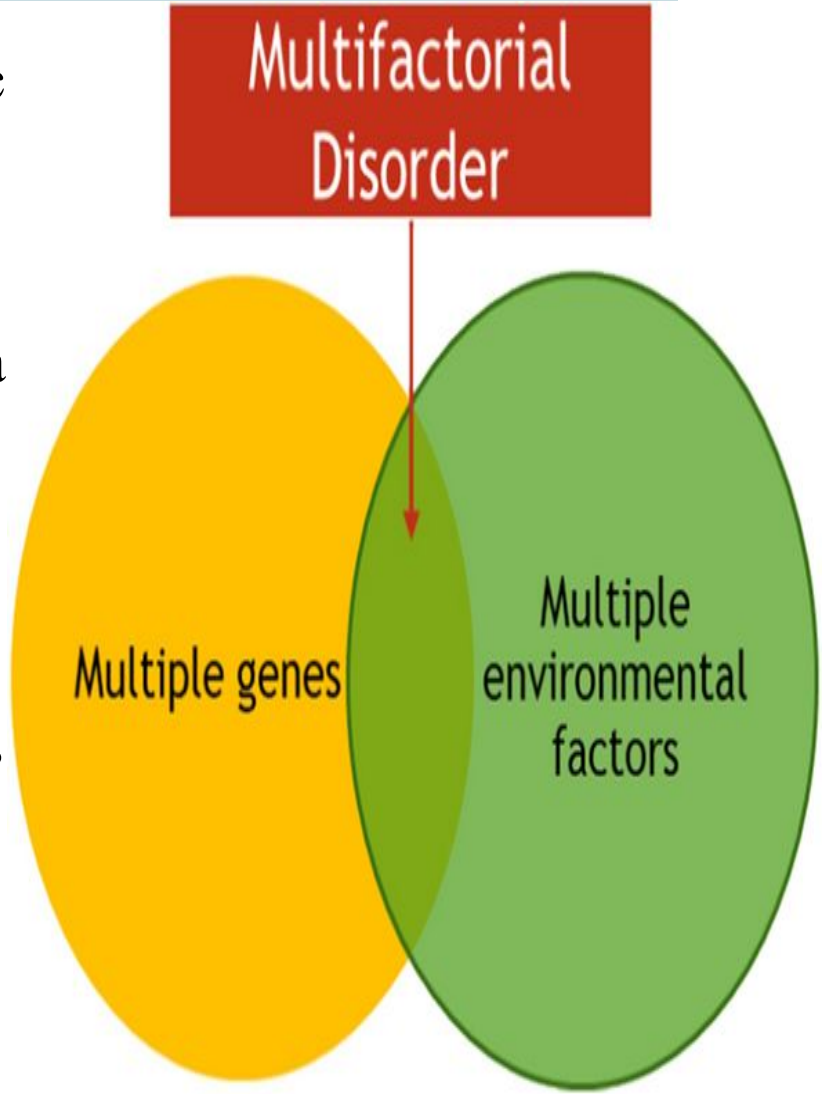
Sickle cell anemia

- ✔ Sickle cell anemia (SCD) is an inherited disorder of the hemoglobin in the blood.
- ✔ Sickle cell anemia occurs when an individual inherits two copies of the sickle cell gene, one from each parent.
- ✔ Sickle cell trait, which is the inheritance of one sickle gene, rarely causes problems.
- ✔ All of the major symptoms of sickle cell anemia are the direct result of the abnormally shaped sickled red blood cells blocking the flow of blood.



2- Multifactorial inheritance

- Multifactorial inheritance is also called complex or polygenic inheritance.
- Multifactorial inheritance disorders are caused by a combination of environmental factors and mutations in multiple genes. For example, different genes that influence breast cancer susceptibility have been found on chromosomes 6, 11, 13, 14, 15, 17, and 22.
- Some common chronic diseases are multifactorial disorders.



Multifactorial genetic disorders

- Heart disease
- High blood pressure
- Alzheimer's disease
- Arthritis
- Diabetes
- Cancer
- Obesity

Alzheimer's disease

- ✔ Alzheimer's disease (AD) is a slowly progressive disease of the brain that is characterized by impairment of memory and eventually by disturbances in reasoning, planning, language, and perception.
- ✔ Many scientists believe that Alzheimer's disease results from an increase in the production or accumulation of a specific protein in the brain that leads to nerve cell death.
- ✔ The likelihood of having Alzheimer's disease increases substantially after the age of 70 and may affect 38% of persons over the age of 85.
- ✔ Alzheimer's disease is not a normal part of aging and is not something that inevitably happens in later life. For example, many people live to over 100 years of age and never develop Alzheimer's disease.

3- Chromosomal abnormalities

Chromosomes, distinct structures made up of DNA and protein, are located in the nucleus of each cell. Because chromosomes are the carriers of the genetic material, abnormalities in chromosome number or structure can result in disease. Chromosomal abnormalities typically occur due to a problem with cell division.

Chromosomal abnormalities

Disorder	Description
Down's syndrome (Trisomy 21)	Extra chromosome 21
Edward's syndrome (Trisomy 18)	Extra chromosome 18
Patau's syndrome (Trisomy 13)	Extra chromosome 13
Turner's syndrome (Monosomy X)	Single X chromosome in females
Klinefelter's syndrome	Two X chromosomes in males (XXY)
Triple X syndrome (super females)	Three X chromosomes in females
XYY syndrome	Two Y chromosomes in males

4- Mitochondrial inheritance

- **Mitochondrial genetic disorders:**
- **Cause:** Mutations in **mitochondrial DNA (mtDNA)** or nuclear genes affecting mitochondrial function → impaired cellular energy production.
- **Inheritance:** Usually **inherited from the mother**, because the egg provides mitochondria to the embryo, while the father does not contribute.
- **Common symptoms:**
  - Muscle weakness and chronic fatigue
  - Heart or nervous system problems
  - Growth difficulties
  - Liver, eye, or kidney disorders
- These disorders are rare but often severe because they affect **energy production all the body**.

Mitochondrial genetic disorders

1. Leber's hereditary optic atrophy (LHON), an eye disease
2. Myoclonic epilepsy with ragged red fibers (MERRF)
3. Mitochondrial encephalopathy

Any questions?