Lec 7 Genetic Disease due to chromosomal abnormalities

A. Autosomal chromosome disorders

1-Trisomy 21 (Down syndrome) : is it is the most frequently occurring chromosomal abnormality, occurring approximately once in every 700- 800 live births , Caused by an extra chromosome 21. The extra chromosome results in abnormalities of the body and brain development. The physical development is slower and may also have delayed mental development.

The symptoms of Down syndrome vary from one person to another ranging from mild to severe and they may due to :

a. Non-disjunction, accounts for 95% of all cases of Trisomy 21.
b. Translocation accounts for 3-4 %
c. Mosaicism, accounts for the remaining 1%.

It is imperative to obtain a karyotype on all individuals with Trisomy 21 because about 1/3 of Down syndrome cases are caused by a translocation, which can indicate that a parent is a translocation carrier. This is important because the recurrence risk of having another child affected by Trisomy 21 is significantly higher for translocation carriers compared to those with Down syndrome caused by nondisjunction.

Figure (1) down syndrome

2-Trisomy 18 (Edwards syndrome) : caused by an extra chromosome 18. It is the second most common trisomy after Trisomy 21, occurring approximately once in every 6,000 to 8,000 births. Over 95% of infants with Trisomy 18 syndrome will have a full trisomy while the remainder will have a trisomy due to a translocation or mosaicism . Most cases lead to prenatal death; those who survive birth face high infant mortality rates, with over 50% dying within the first few months.

Figure (2) Edward syndrome

3-Trisomy 13 (Patau syndrome) : is a chromosomal disorder caused by an extra copy of chromosome 13. It is the third most common trisomy, following Trisomy 21 (Down syndrome) and Trisomy 18 (Edwards syndrome), with a frequency of about 1 in 10,000 births. The cause is usually nondisjunction (80%) or translocation (20%), where the extra chromosome material is sometimes attached to another chromosome. Most infants with Trisomy 13 die within the first month of life due to severe health complications. Forms of Trisomy 13 are

1. Complete Trisomy 13: An extra chromosome in all cells.

2. Mosaic Trisomy 13: Only some cells have the extra chromosome.

3. Partial Trisomy 13: Only part of chromosome 13 is duplicated.

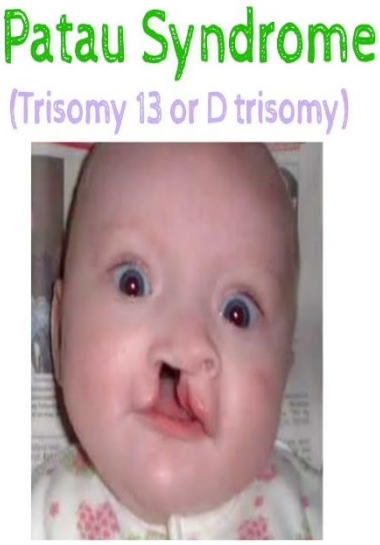

Figure (3) patau syndrome

B. Sex chromosome disorders

1-Turner Syndrome (45,X or XO Syndrome): is caused by the complete or partial absence of the second sex chromosome (X chromosome). Approximately 50% of cases involve a complete loss of the second X chromosome, while the other 50% include structural rearrangements or mosaicism (a mix of normal and abnormal cells). Occurs in about 1 in every 2,000–2,500 live female births. Estimated 99% of Turner syndrome conceptuses are lost prenatally, leading to high rates of spontaneous abortion.

Symptoms and Signs:

At Birth: Generally normal appearance, but may show puffy hands and feet due to impaired lymphatic flow.

In Childhood: Short stature, Soft nails that turn up at the tips, coarse facial features and low hairline at the back of the head

In Adolescence: Often, sexual development lags without the presence of a second X chromosome.

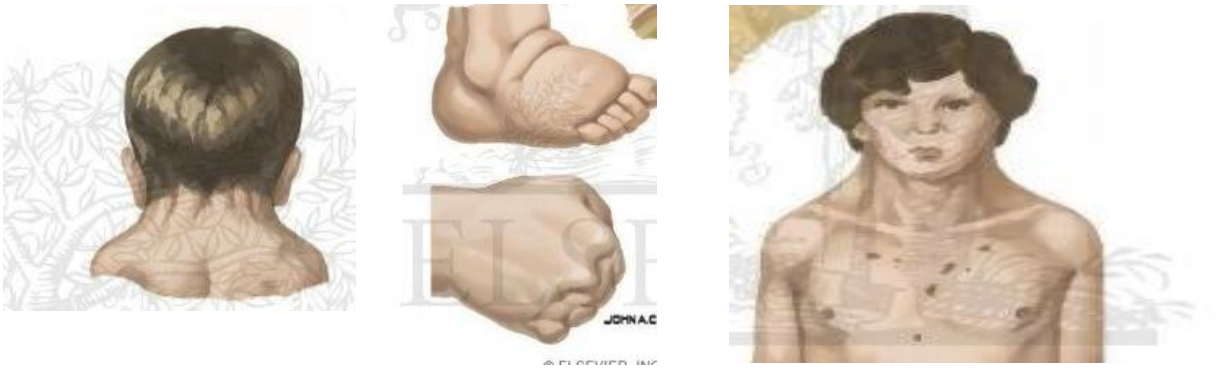

Figure (4)Turner syndrome

2-Klinefelter syndrome (47, XXY) is caused by the presence of two X chromosomes and one Y chromosome (47,XXY). It occurs in approximately 1 in every 500 live male births. Male development typically occurs due to the presence of the Y chromosome, but the extra X chromosome in Klinefelter syndrome affects sexual and physical development.

Symptoms and Signs:

1. Males with XXY syndrome are often underdeveloped sexually.

2. They typically have long arms and legs and may develop breast tissue (gynecomastia).

3. Infertility: XXY syndrome is the most common genetic or chromosomal cause of male infertility.

- Detection and Diagnosis:

Many cases are not diagnosed until adolescence or adulthood, though increased prenatal testing has led to earlier detection in some cases.

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1. What is the most common cause of Trisomy 21 (Down syndrome)?

a) Translocation
b) Non-disjunction
c) Mosaicism
d) Mutation

2. What percentage of Down syndrome cases are caused by translocation?

a) 1%
b) 95%
c) 3-4%
d) 10%

3. Why is it important to obtain a karyotype for individuals with Trisomy 21?

a) To confirm the presence of nondisjunction
b) To determine the severity of symptoms
c) To check if the parents are translocation carriers
d) To identify mosaicism

4. Which of the following is true about Trisomy 18 (Edwards syndrome)?

a) It is the most common trisomy.
b) It is caused by an extra chromosome 13.
c) Most infants survive beyond the first year of life.
d) Over 95% of cases involve full trisomy.

5. What is the most common cause of Trisomy 13 (Patau syndrome)?

a) Mosaicism
b) Translocation
c) Non-disjunction
d) Mutation

6. Which chromosomal disorder is characterized by the presence of 45 chromosomes (45, X)?

a) Turner syndrome
b) Down syndrome
c) Klinefelter syndrome
d) Edwards syndrome

7. What is the most common feature of Turner syndrome in adolescence?

a) Puffy hands and feet
b) Coarse facial features
c) Delayed sexual development
d) Gynecomastia

8. What chromosomal abnormality causes Klinefelter syndrome?

a) 47, XXY
b) 45, X
c) 46, XX
d) 47, XYY

9. What is a common symptom of Klinefelter syndrome?

a) Coarse facial features
b) Gynecomastia
c) Short stature
d) Delayed mental development

10. Which trisomy is associated with the highest mortality rate in infancy?

a) Trisomy 21
b) Trisomy 18
c) Trisomy 13
d) Klinefelter syndrome