GENETIC DISEASE

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Classification of genetic diseases:

I. **Chromosomal** disorders (Cytogenetic).
II. **Single gene** disorders (unifactorial or Mendelian disorder).
III. **Multifactorial** disorders.

I- Chromosomal(cytogenetic)disorders:

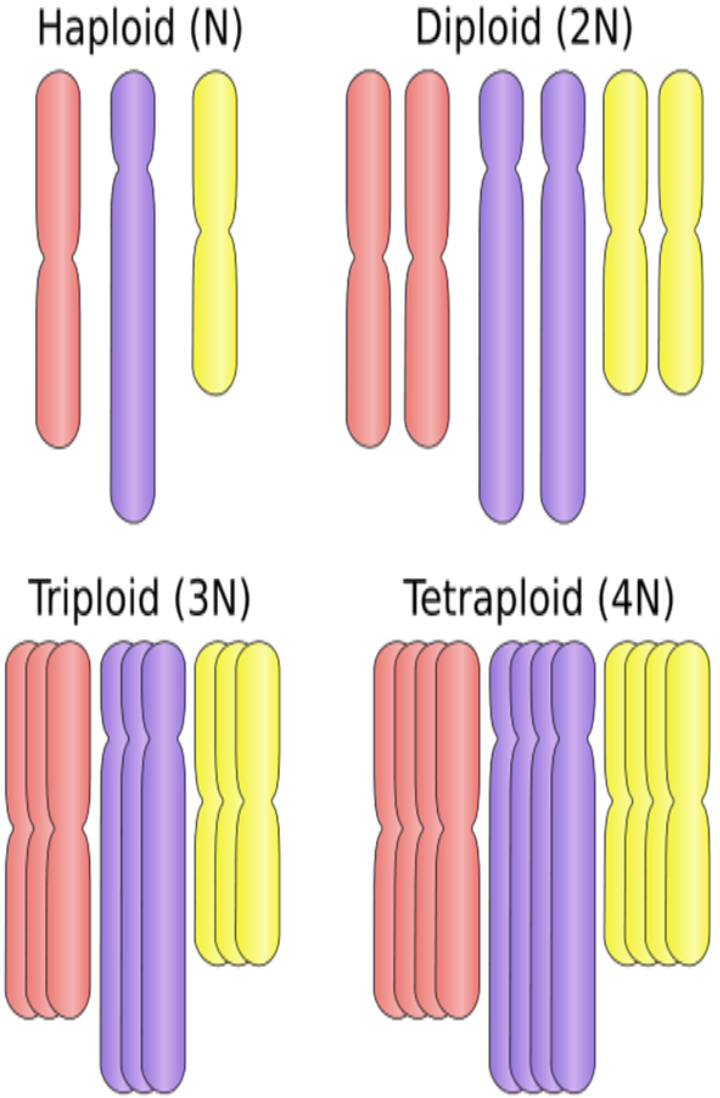
1- Numeric Abnormalities: (Disturbances in number).

2. Structural Abnormalities: (Disturbances in structure)

1- Numeric Abnormalities: (Disturbances in number)

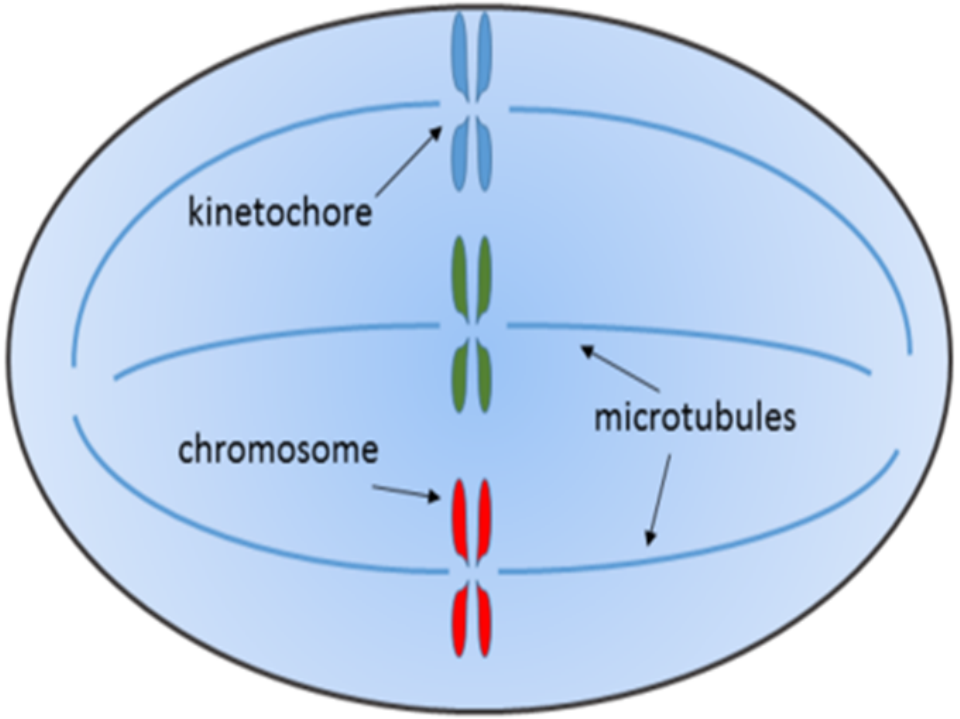
- *Euploid:* The normal number of chromosomes for a species.

- Polyploid: Chromosome numbers such as 3n and 4n which are generally results in a *spontaneous abortion*.
- Aneuploid: Any number that is not an exact multiple of n.(trisomy)

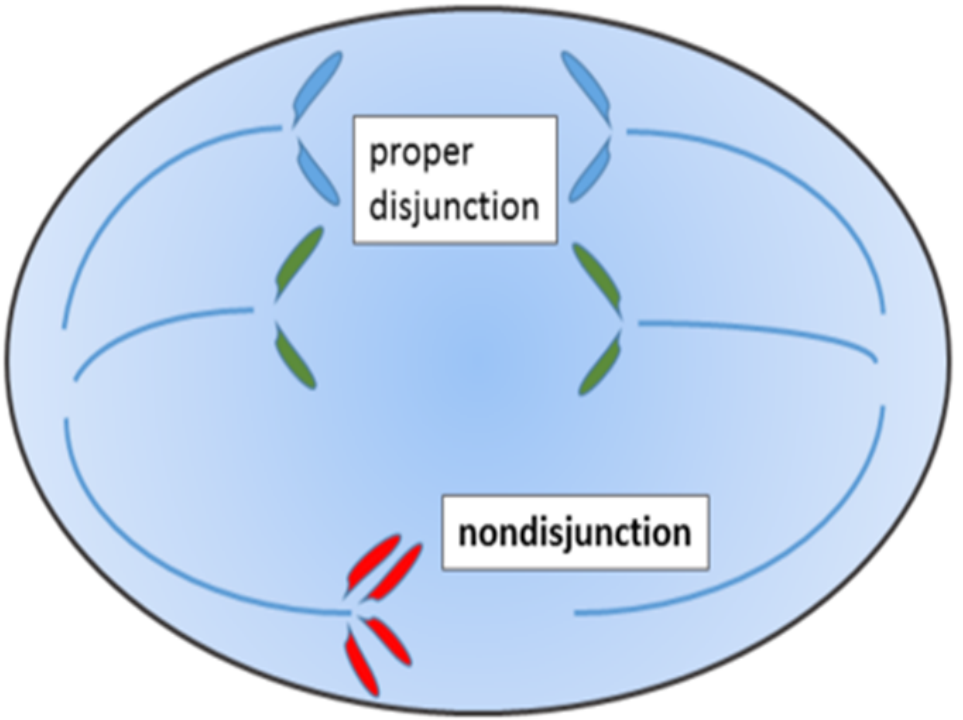


Causes of aneuploidy:

- Nondisjunction.
- anaphase lag

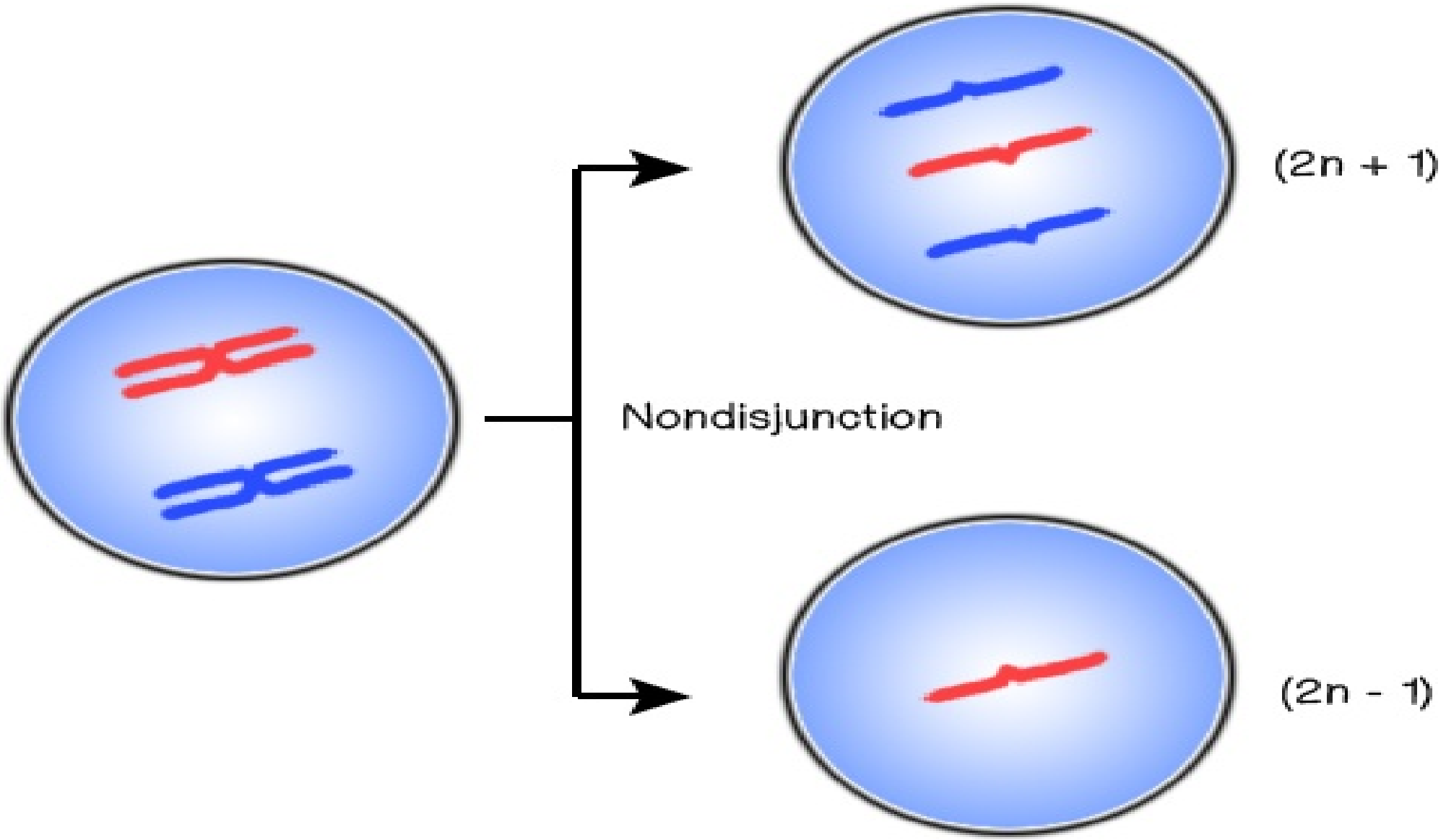


metaphase



anaphase

Nondisjunction in Mitosis

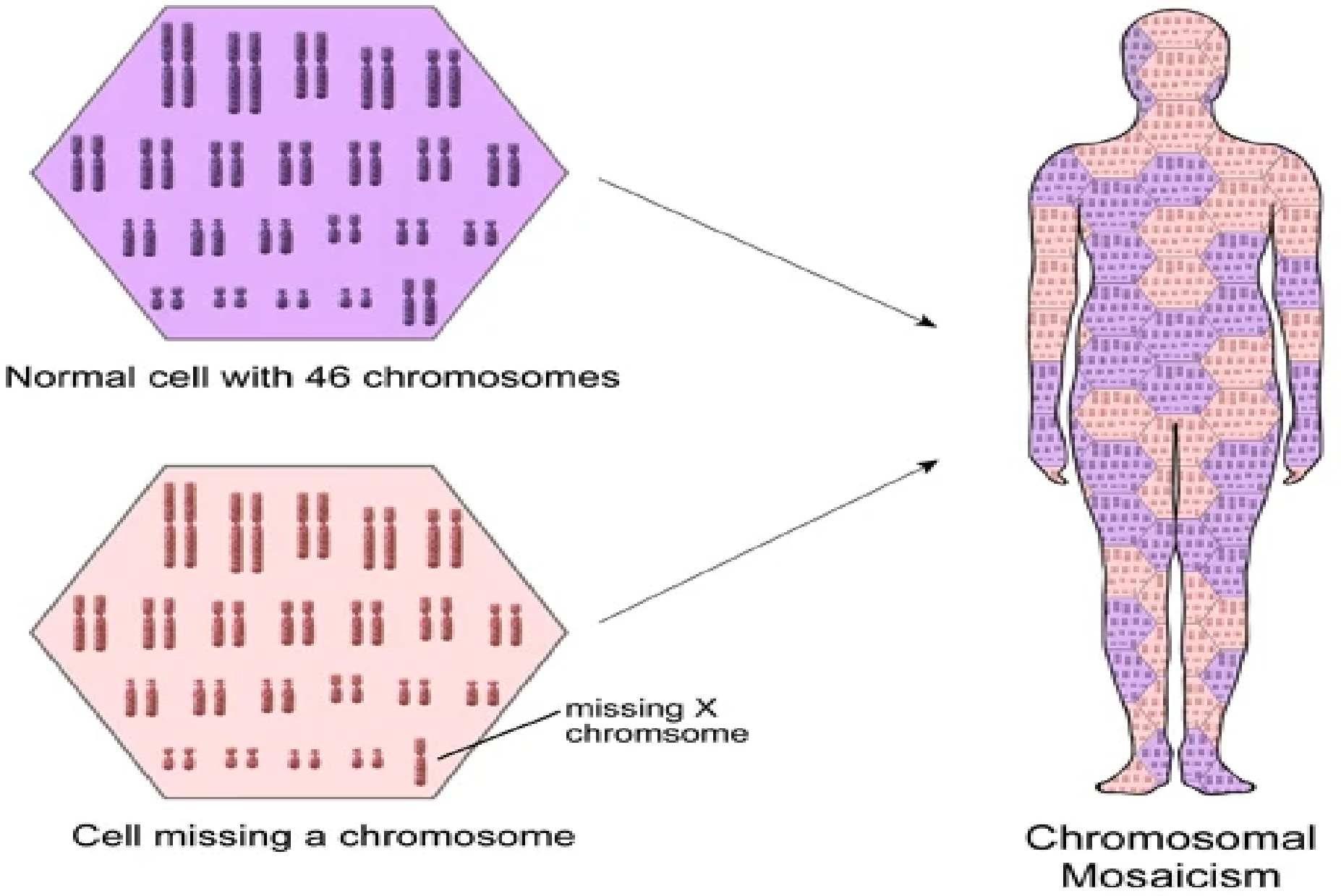


- **Fertilization** of such gametes by normal gametes would result in two types of zygotes:

I. Trisomic, with an extra chromosome (2n + 1).
II. Monosomic with one less chromosome (2n – 1).

Monosomy involving an autosome is incompatible with life and end by abortion.
As it generally causes loss of too much genetic information to permit live birth or even embryogenesis.

Trisomies of certain autosomes and monosomy involving sex chromosomes are compatible with life.



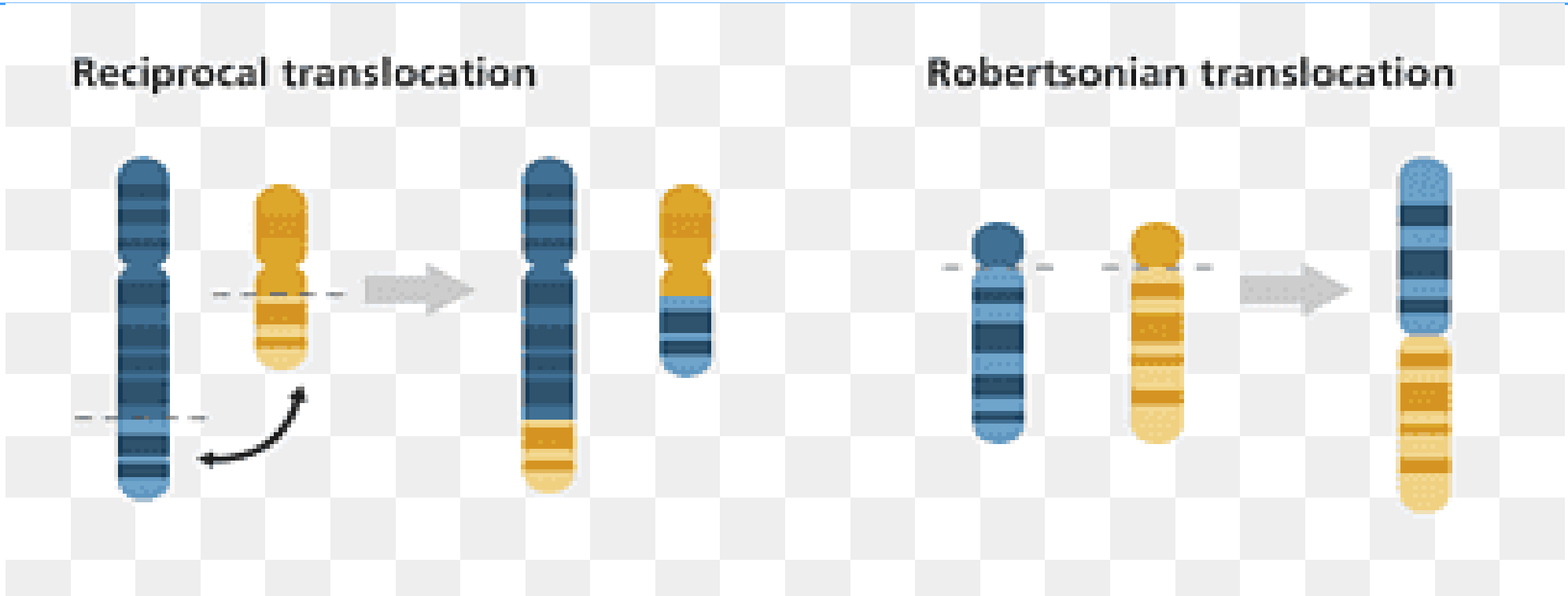
2.Structural Abnormalities: (Disturbances in sructure)

1-Translocation:

Transfer of a part of one chromosome to another chromosome.

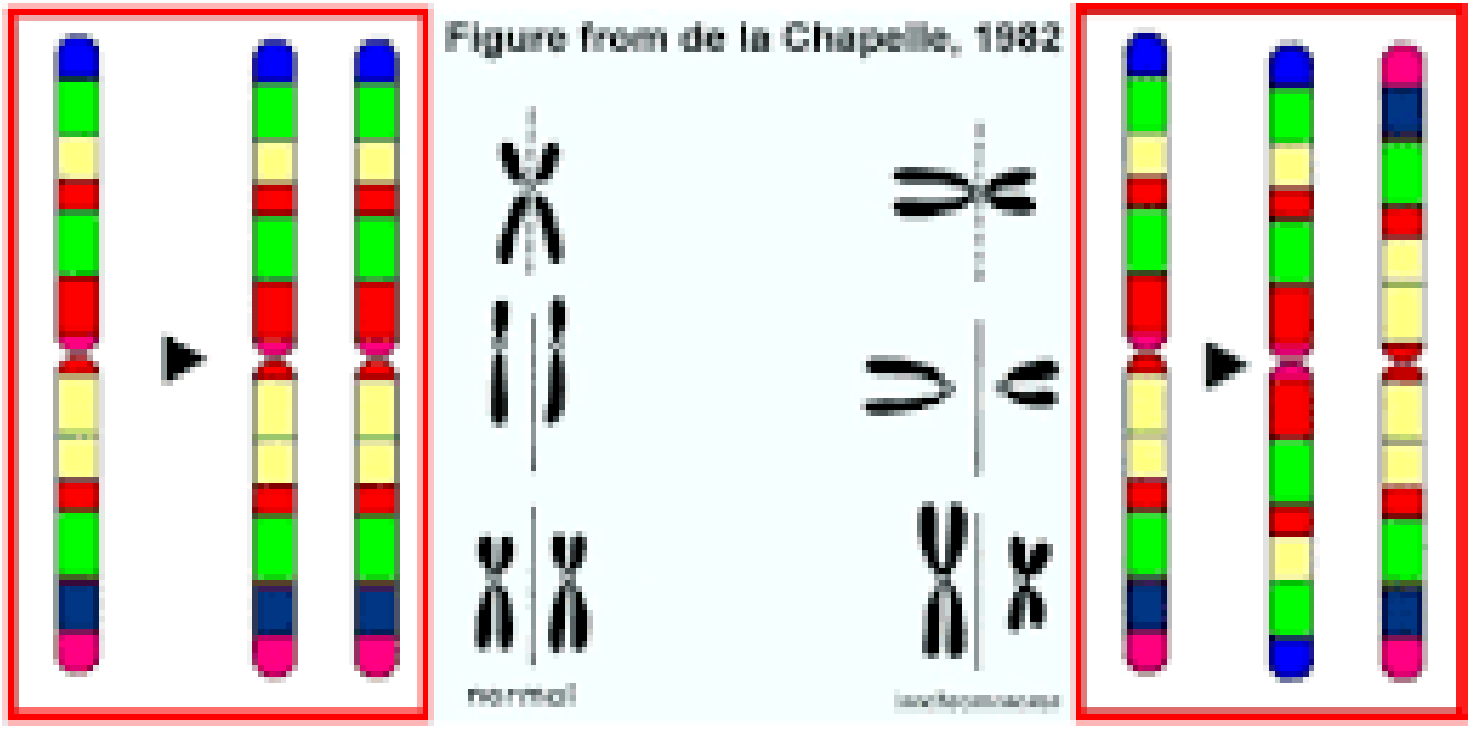
A-Balanced reciprocal translocation:

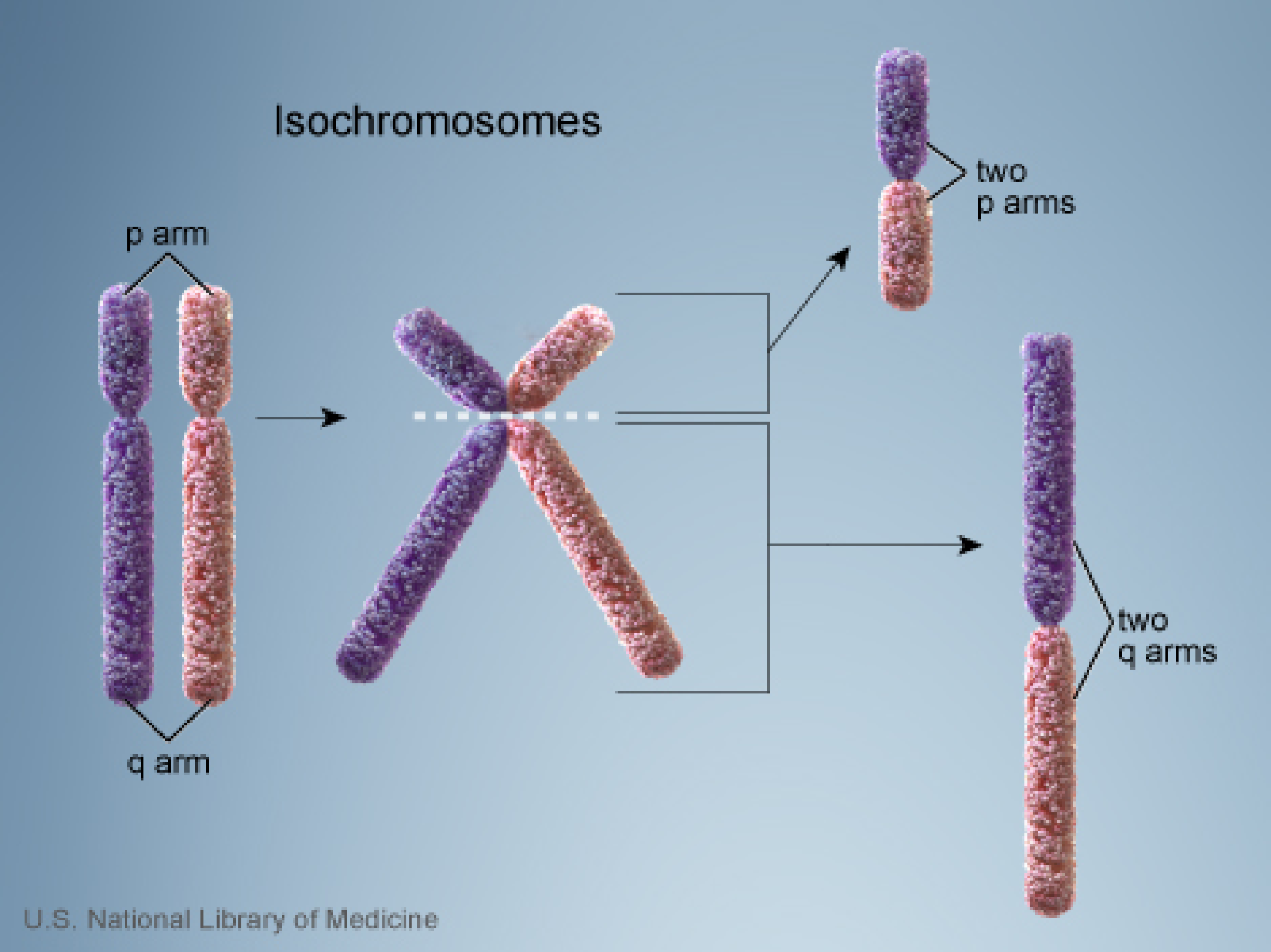
B- Centric fusion translocation (robert-sonian):



2-Isochromosomes

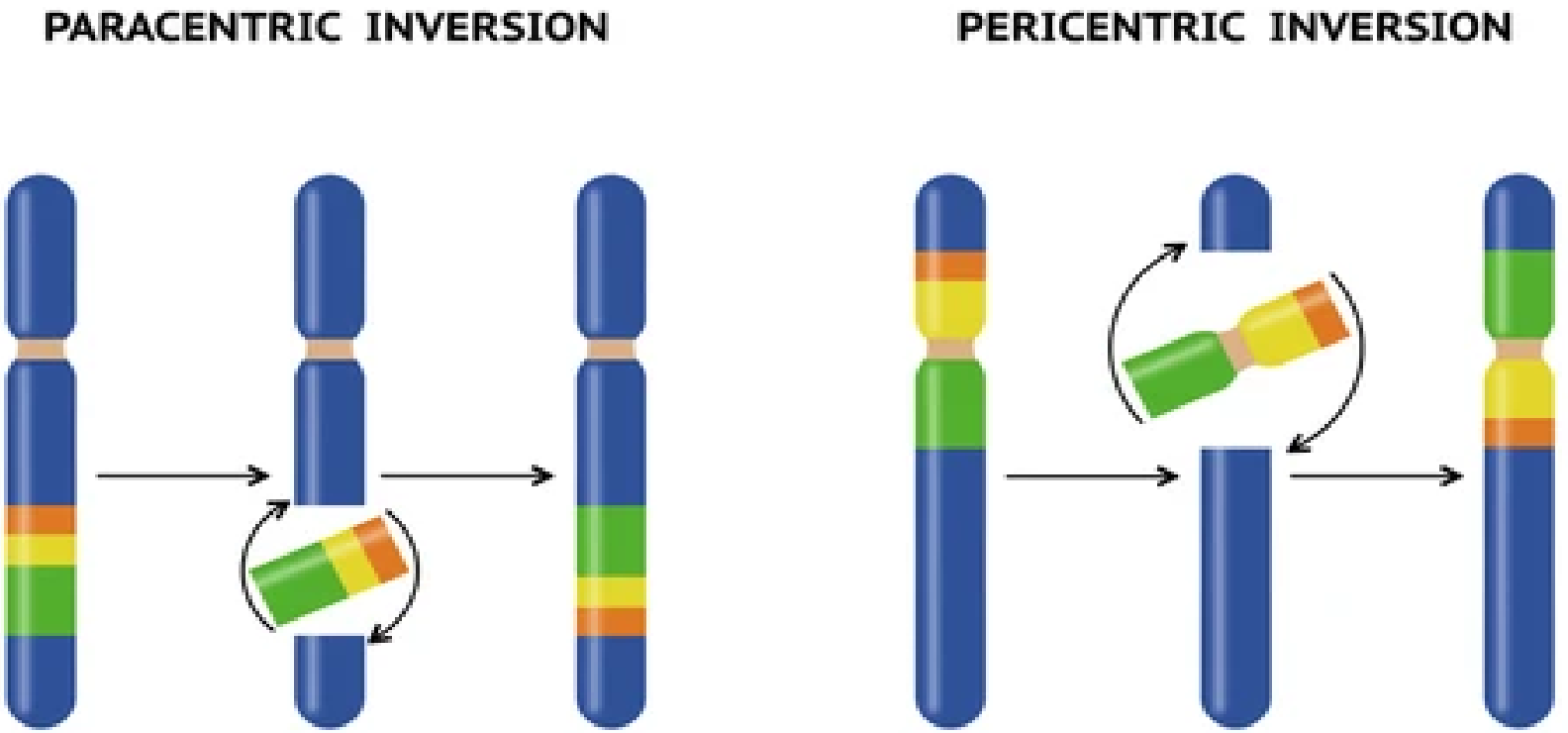
- It results when the *centromere divides horizontally* rather than vertically.
- One of the two arms of the chromosome is then lost, and the remaining arm is duplicated.
- Resulting in a chromosome with two short arms only or two long arms only.





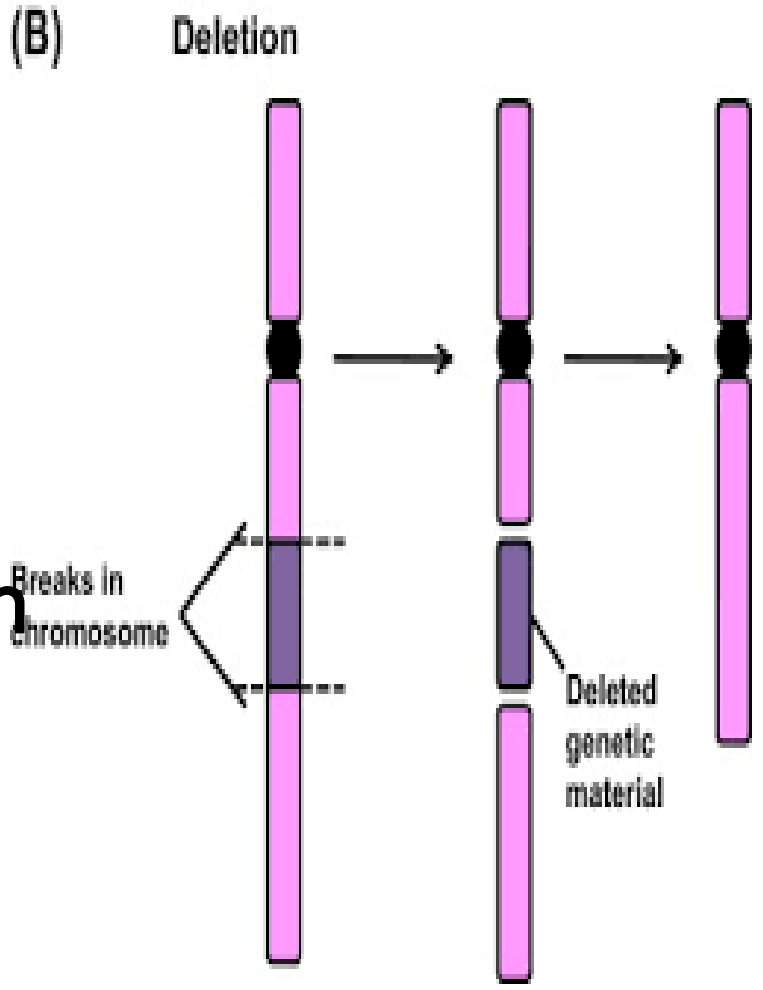
3-Inversions:

Occur when there are two interstitial breaks in a chromosome, and the segment reunites after a complete turnaround.



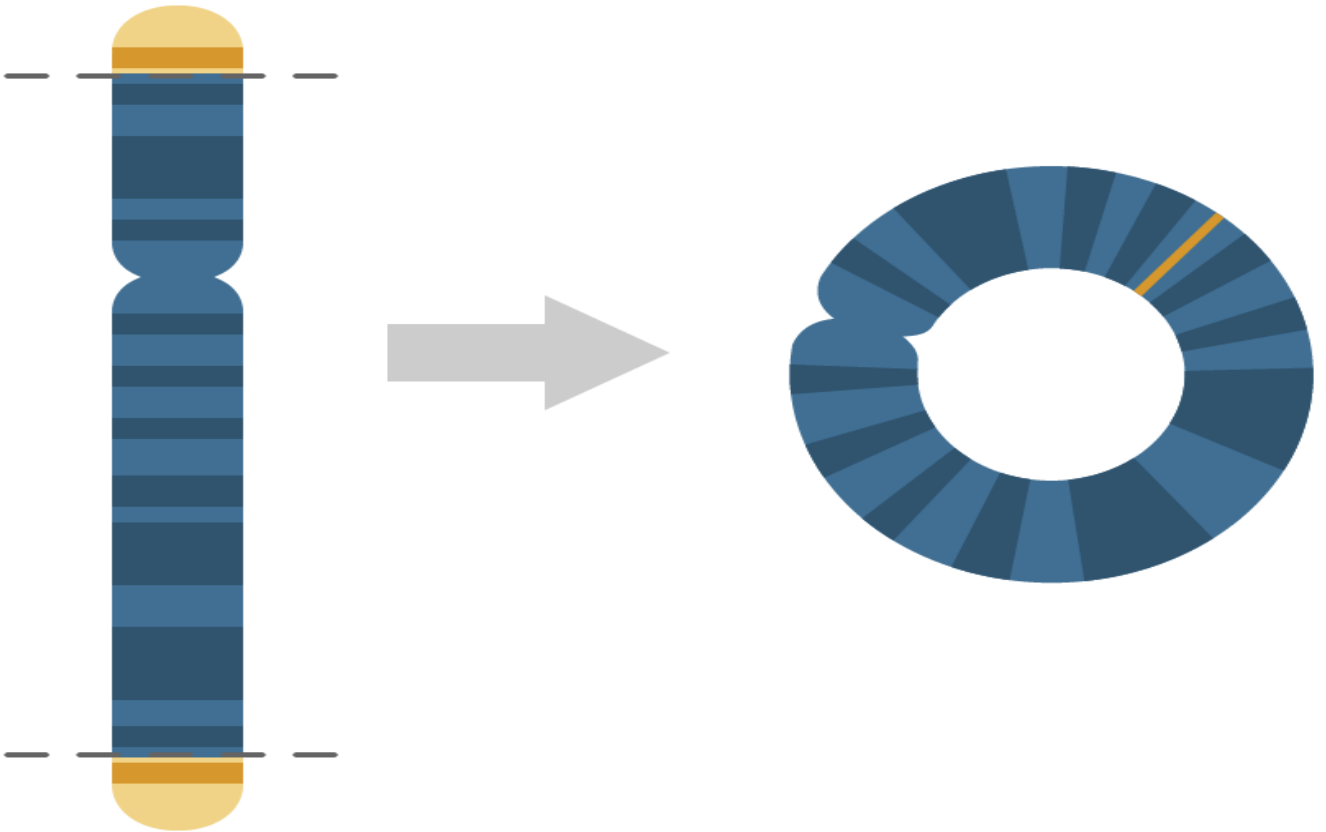
4-Deletion:

- loss of a portion of a chromosome.
- A single break may delete a terminal segment.
- Two interstitial breaks, with reunion of the proximal and distal segments, may result in loss of an intermediate segment.
- The isolated fragment, which lacks a centromere, almost never survives, and thus many genes are lost.



5- Ring chromosome:

It is a variant of a deletion. After loss of segments from each end of the chromosome, the arms unite to form a ring.



Chromosomal(cytogenetic) disorders:

A- autosomes:

- Down syndrome.

B- sex chromosome:

- Kleinfelter syndrome
- Turner syndrome.

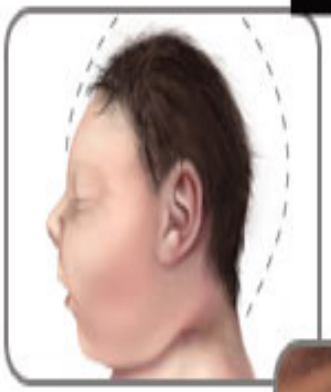
Down syndrome (DS), also known as trisomy 21, is caused by the presence of all or part of a third copy of chromosome 21.

The karyotype for Down syndrome
Trisomy 21 (47,XY,+21)

Symptoms:

Alzheimer's disease, heart defects, leukemia, hypertension and gastrointestinal problems

Symptoms of Down Syndrome



Small head at birth

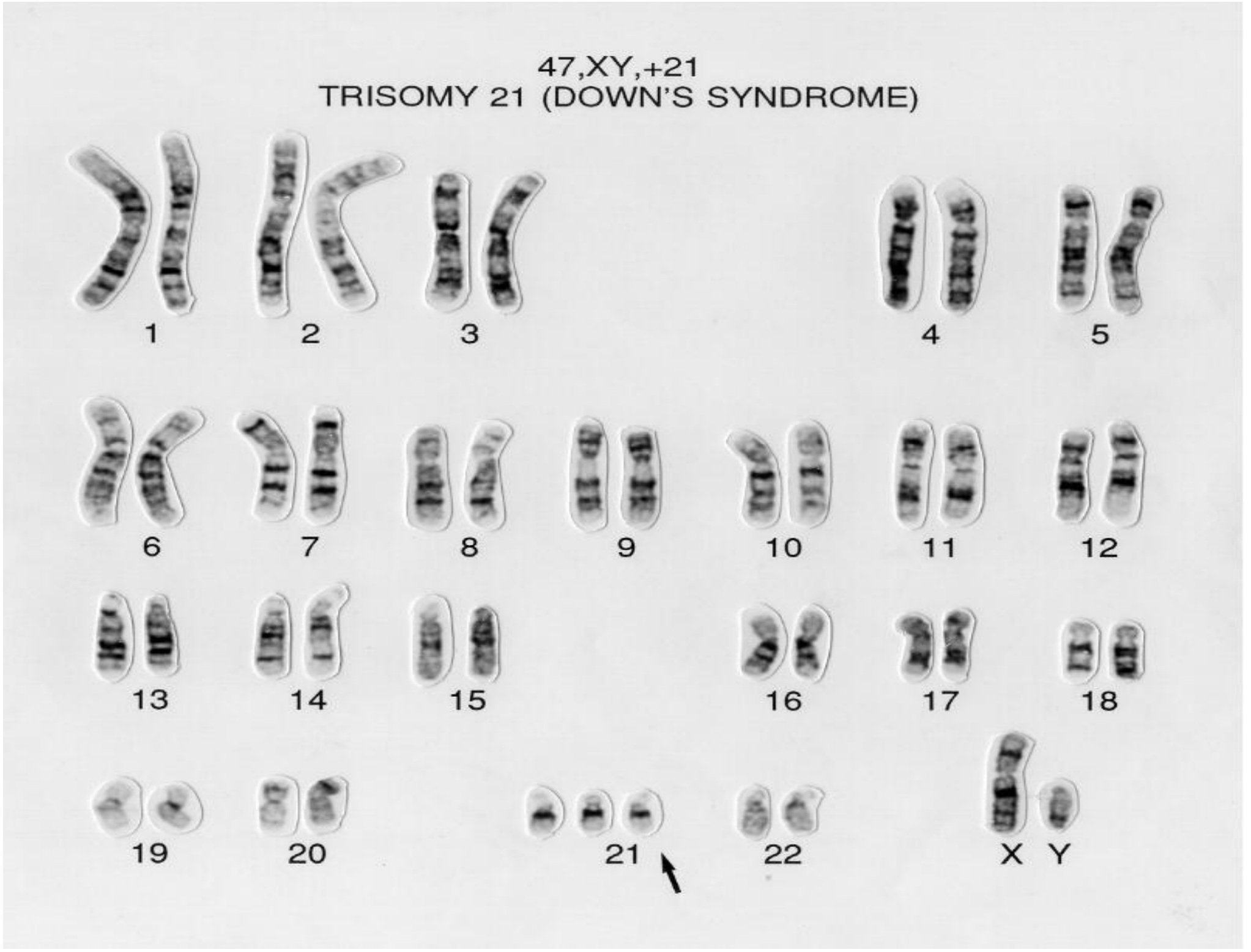
Dental problems

White spots on the colored part of the eye

Short ears

Congenital heart defects

Short /thick hand


47,XY,+21
TRISOMY 21 (DOWN'S SYNDROME)
1
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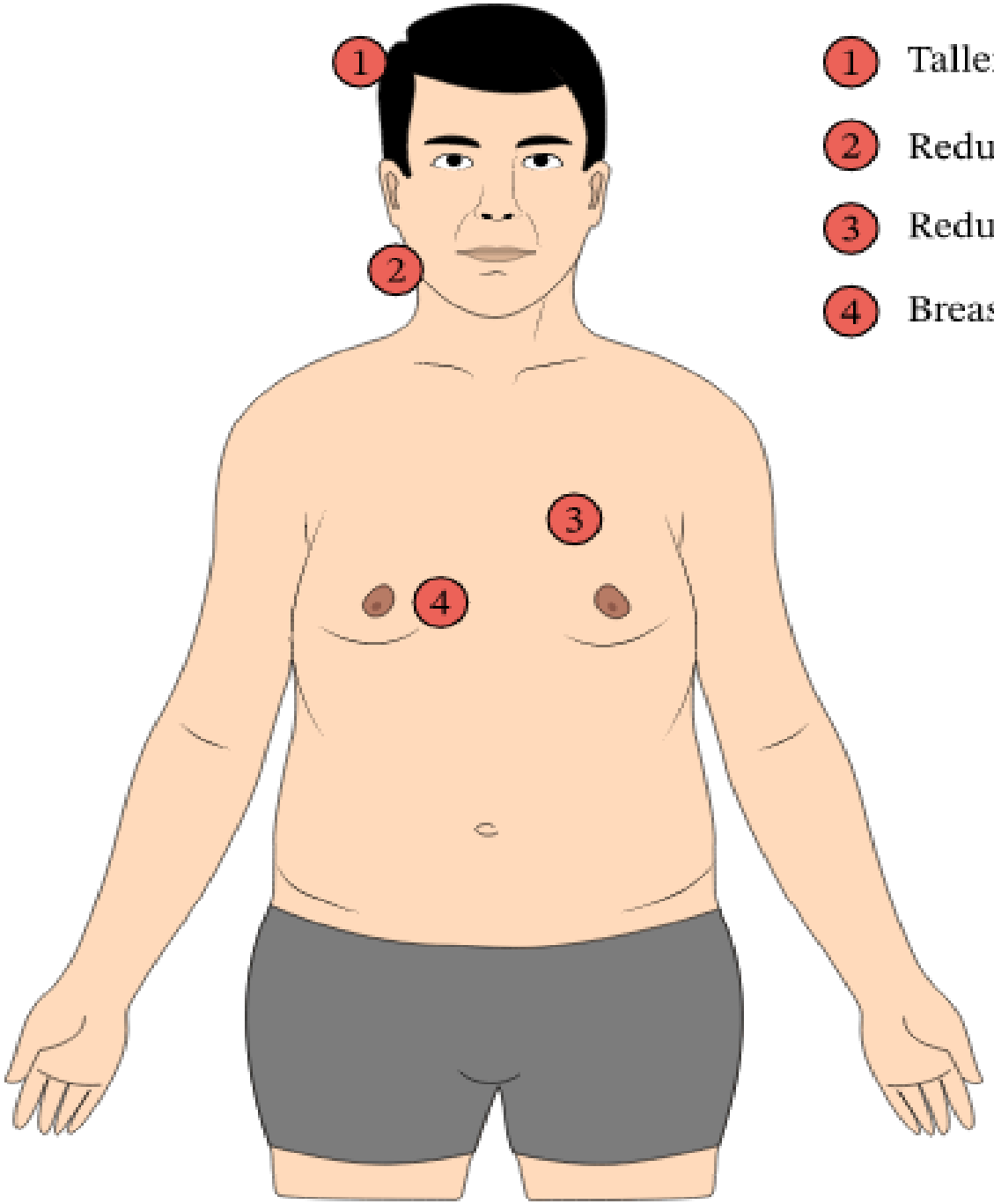
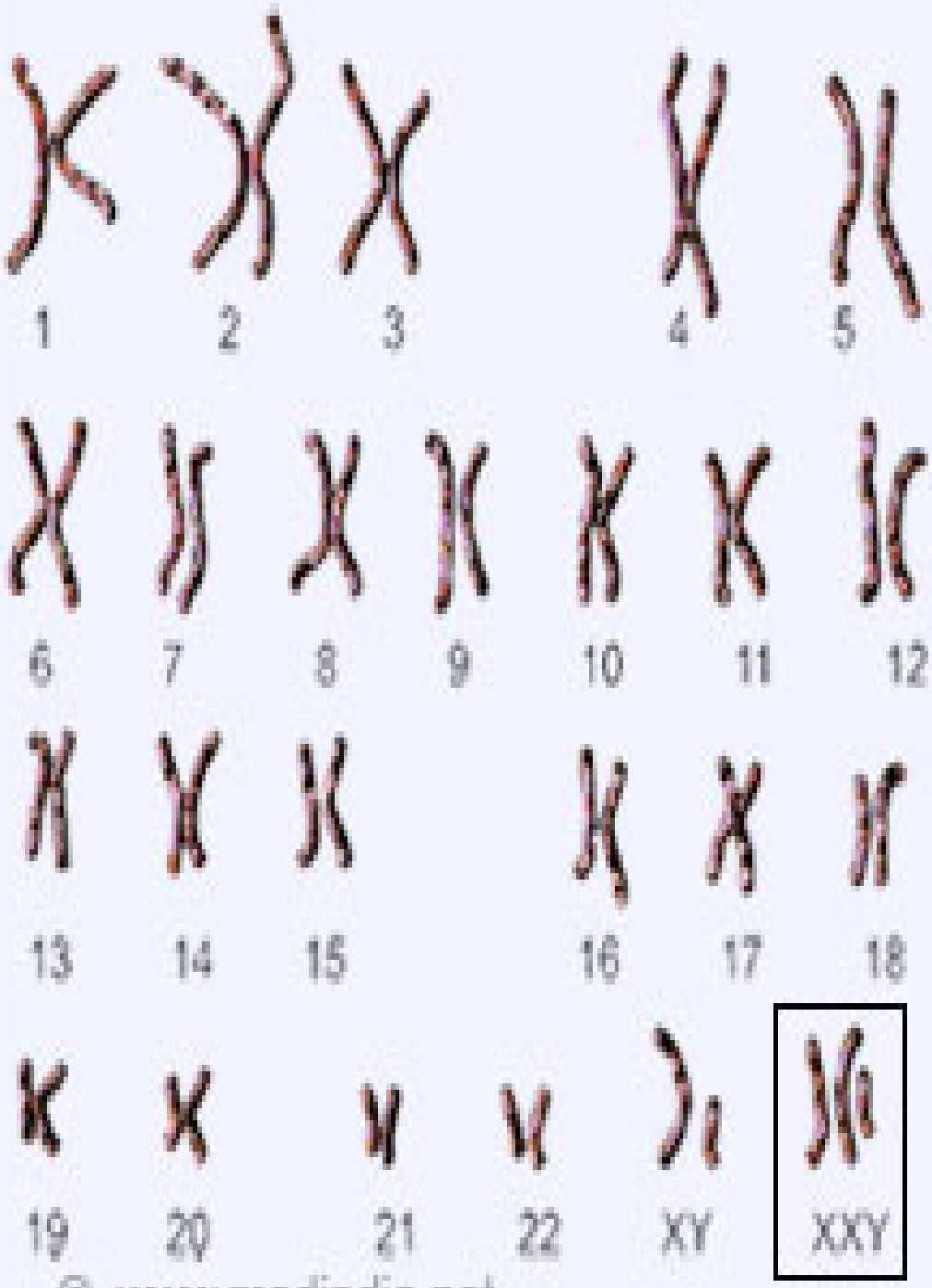
22
X
Y

KLINEFELTES SYNDROM

- It is *male hypogonadism* that develops when there are at least two X chromosomes and one or more Y chromosomes.
- Most patients are 47, XXY that results from nondisjunction of sex chromosomes during meiosis.



1. Taller-than-average height
2. Reduced facial hair
3. Reduced body hair
4. Breast development (gynecomastia)

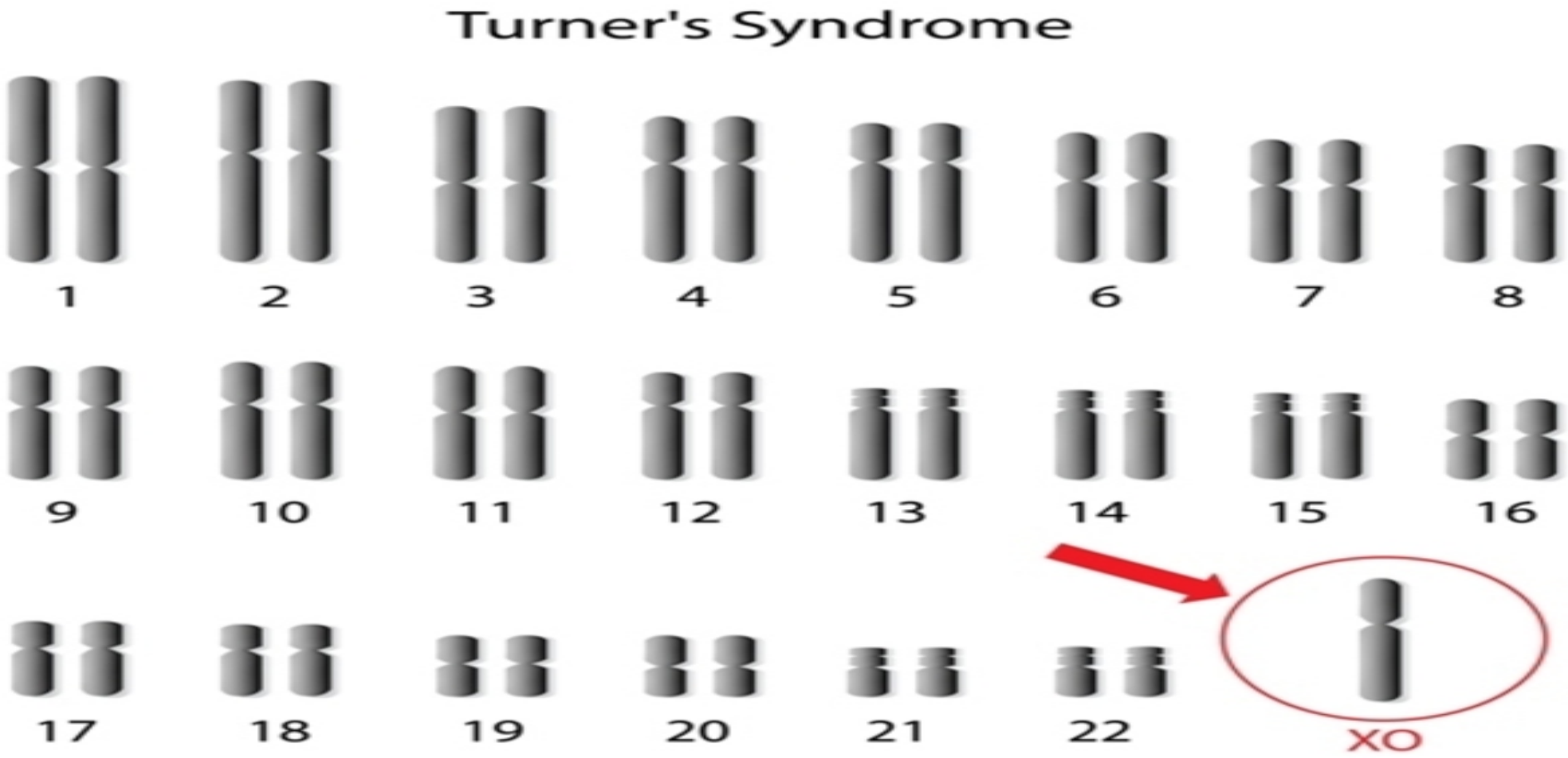


Klinefelter's Syndrome

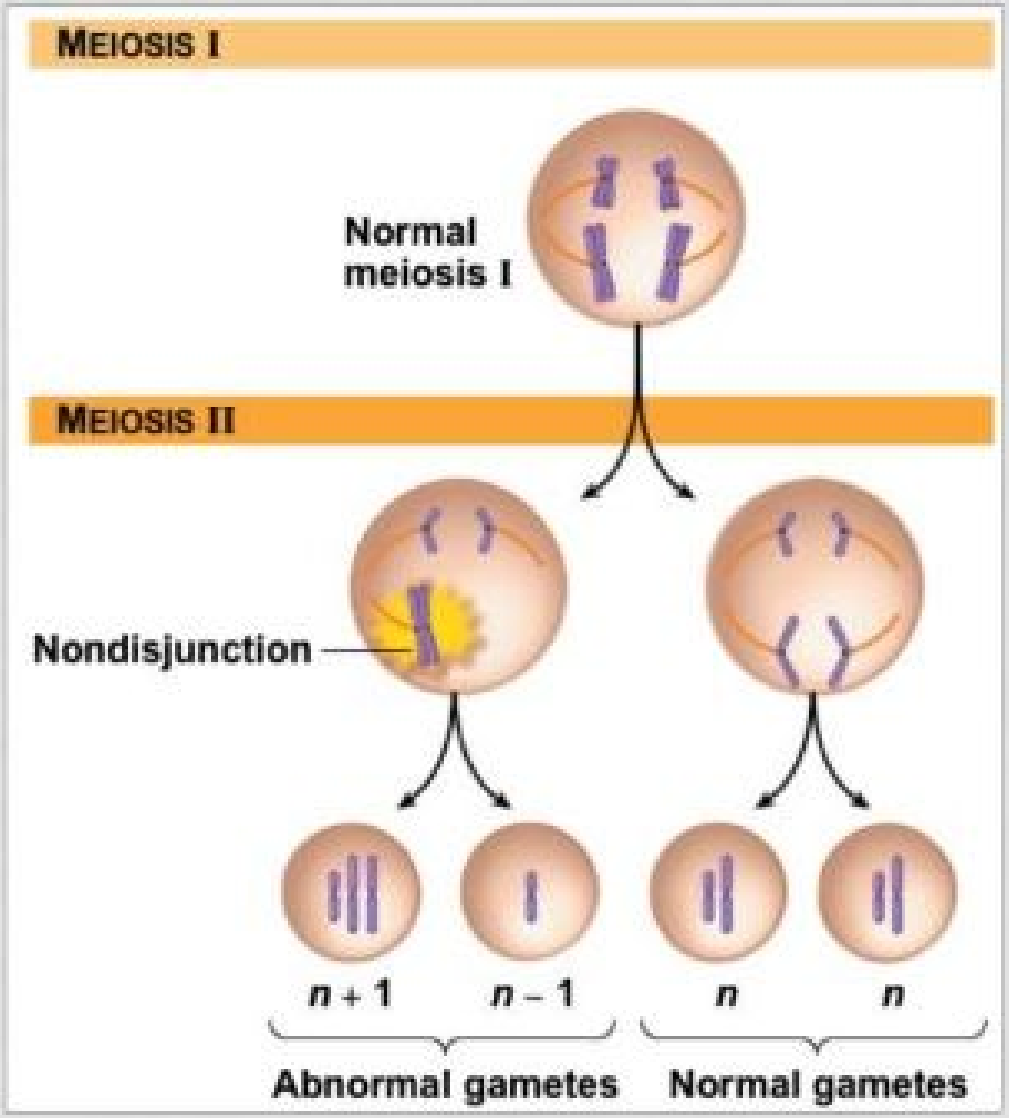
- ✓ It is the most frequent sex chromosomal genetic disorder
- ✓ Patients with Klinefelter's Syndrome have an extra X- chromosomes or 47 chromosomes

Turner Syndrome:

Characterized by primary hypogonadism in phenotypic females, results from monosomy of the X chromosome resulting in a 45, X karyotype.



HOW DOES IT OCCUR?



- Turner syndrome is typically caused by nondisjunction
- A pair of sex chromosomes fails to separate during the formation of an egg (or sperm)

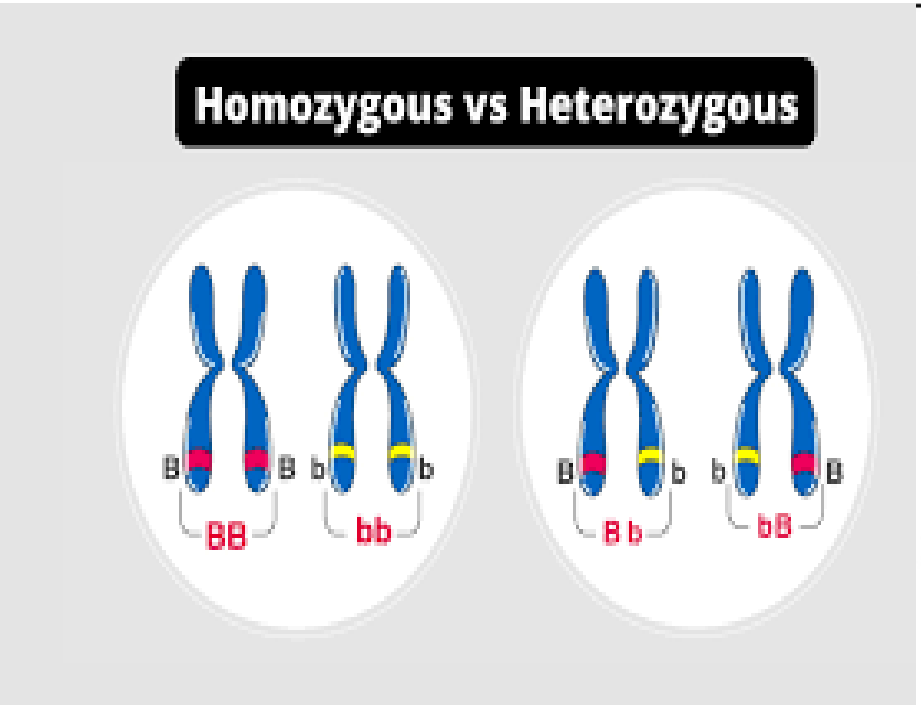
II.SINGLE GENE DISORDERS (UNIFACTORIAL): (MENDELIAN DISORDER)

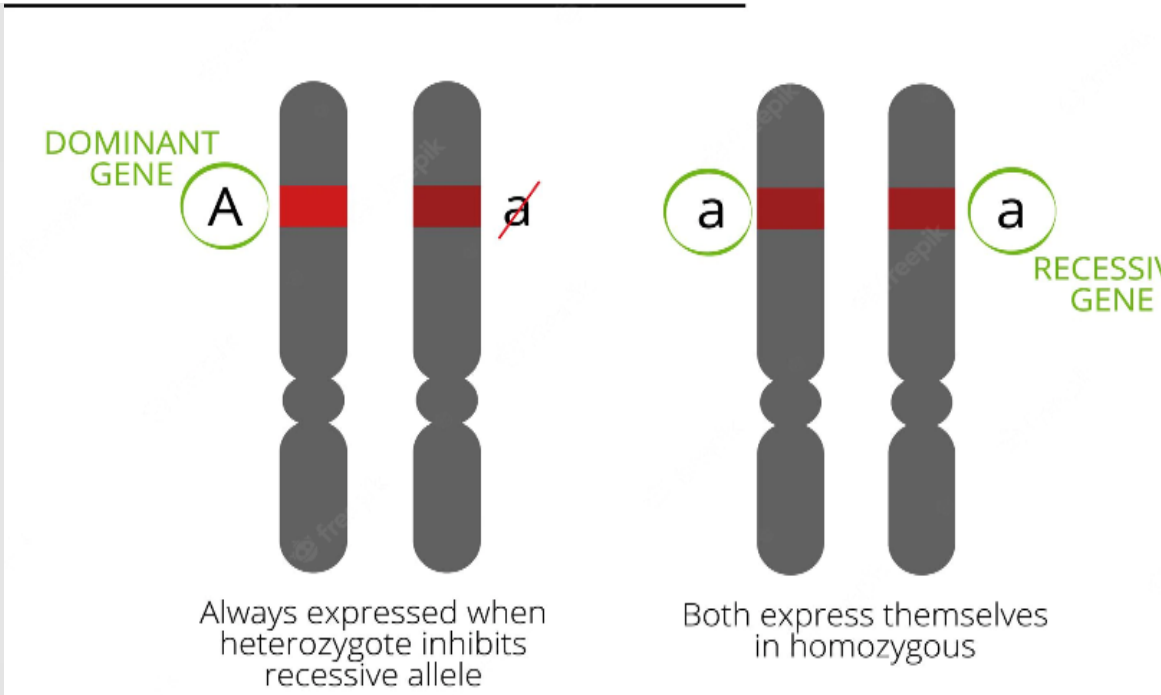
The two members of a gene pair, one inherited from the mother and the other from the father, are called alleles.

If the members of a gene pair are identical (*i.e.*, code the exact same gene product), the person is homozygous.
If the two members are different, the person is heterozygous.

- If the trait is expressed in the heterozygote (one member of the gene pair codes for the trait), it is *dominant;*

- if it is expressed only in the homozygote (both members of the gene pair code for the trait), it is *recessive*





Transmission Patterns of Single-Gene Disorders:

Mutations involving single genes follow one of three patterns of inheritance:

1. Autosomal dominant.
2. Autosomal recessive.
3. X-linked.

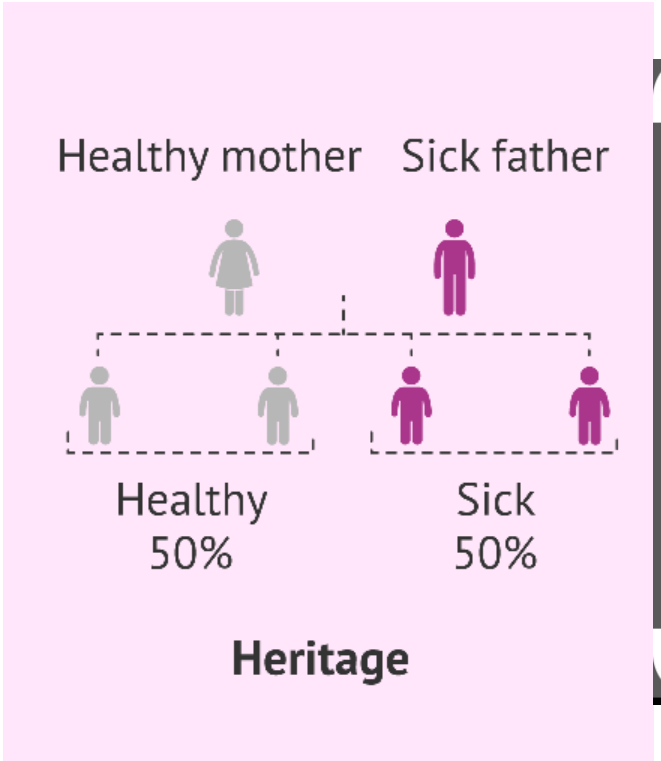
Example of autosomal dominant diseases:-

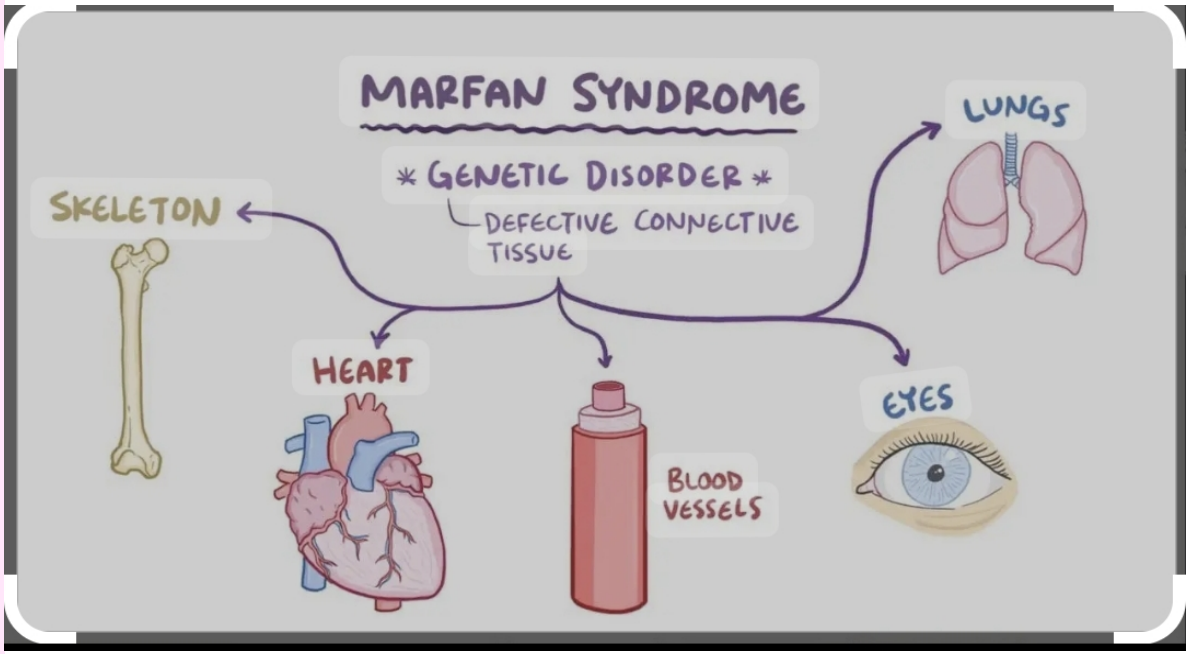
- **Marfan Syndrome**
- **Ehlers-Danlos Syndromes**

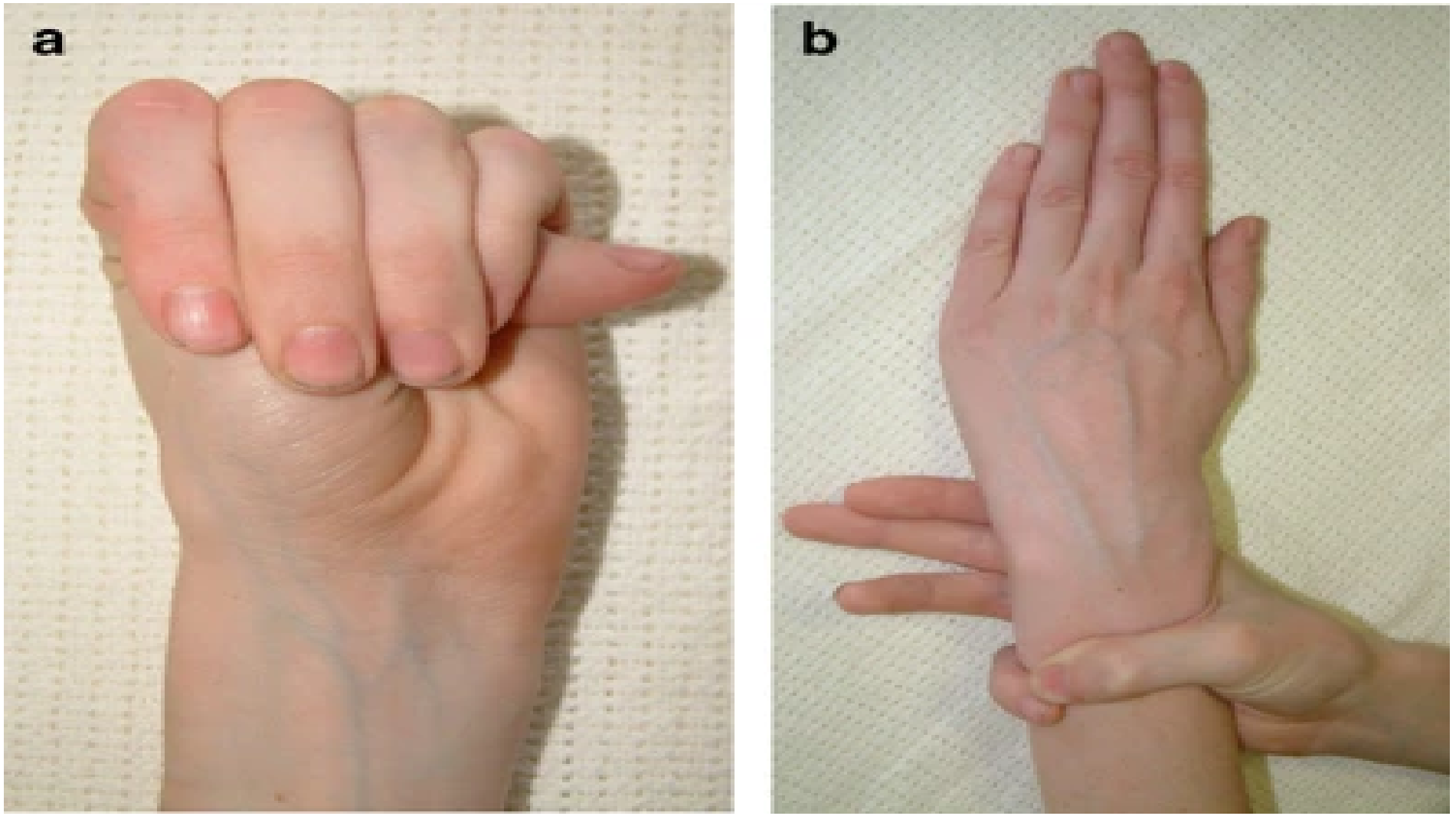
Marfan Syndrome:

Caused by a mutation in the gene encoding *fibrillin*,(fibrilline-1 FBN1on chromosome15) which is required for structural integrity of connective tissues.

The major tissues affected are the skeleton, eyes, and cardiovascular system







MARFAN SYNDROM

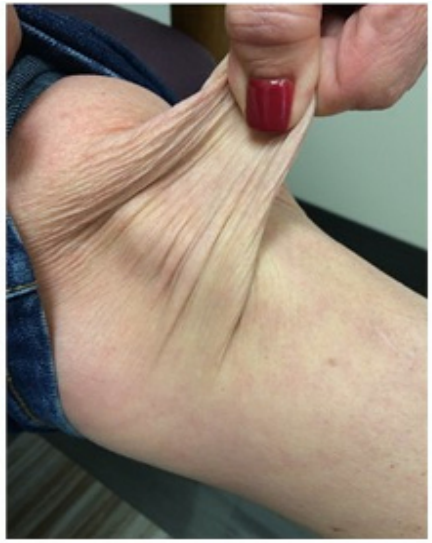
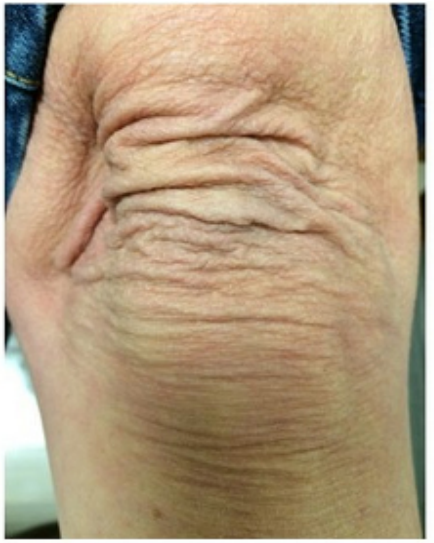
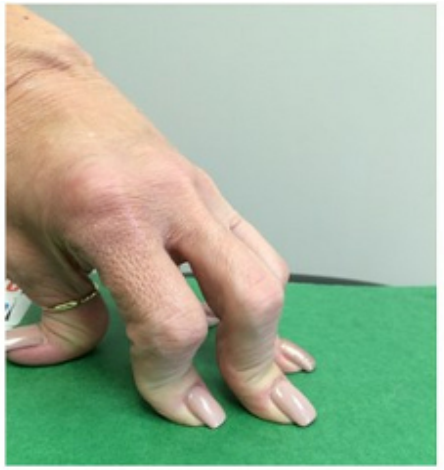
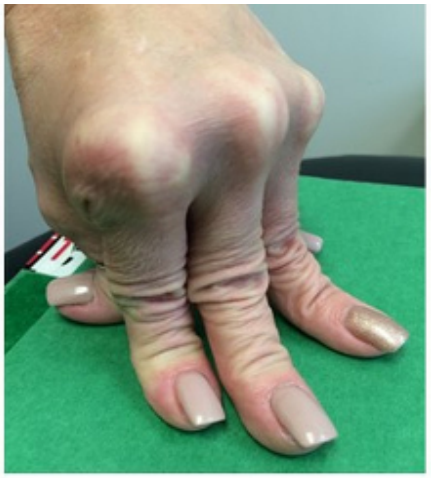
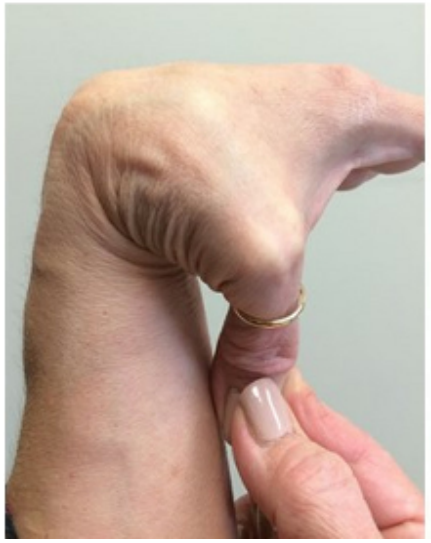
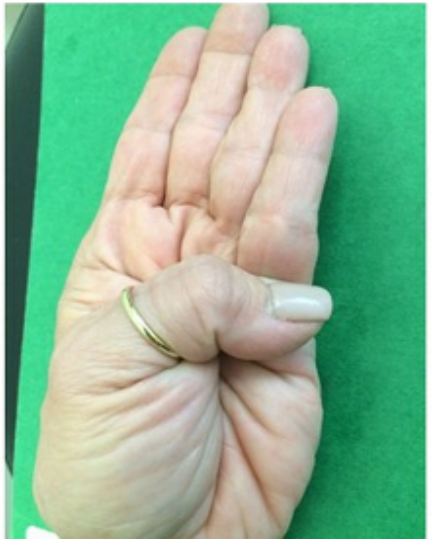
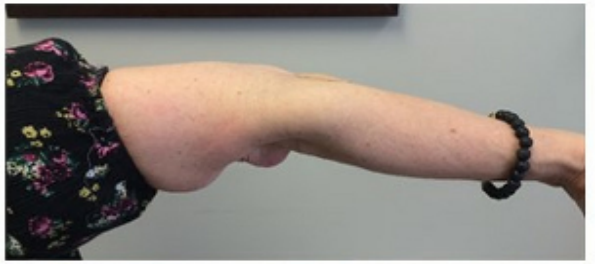
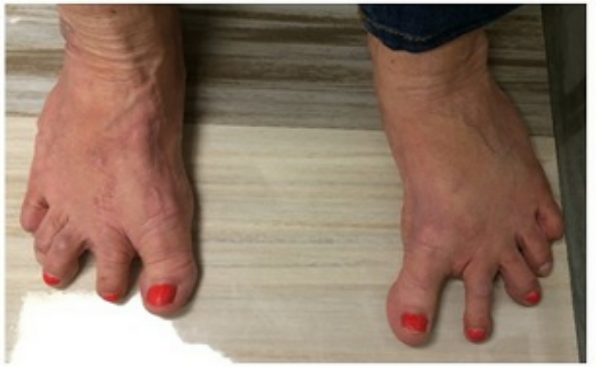
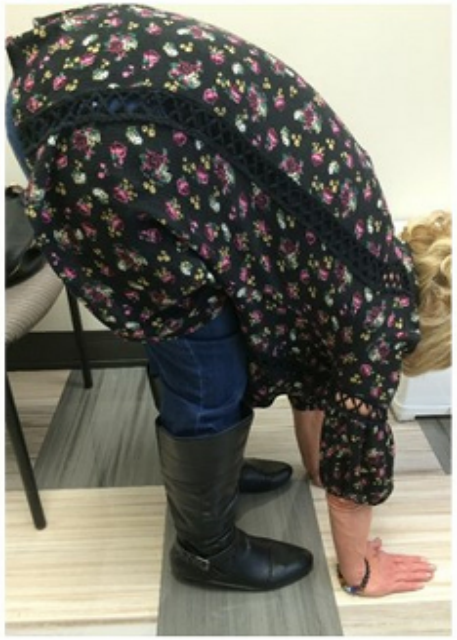
(a) positive thumb sign: entire thumbnail protrudes beyond ulnar border of hand.

(b) Positive wrist sign: thumb and fifth finger overlap when encircling the wrist.

Ehlers-Danlos Syndromes(EDS)

Caused by mutation in the gene encoding *collagen* result in defects in *collagen synthesis*

Hyperextensible skin

EDS

Skin hyperextensibility and Generalized Joint Hypermobility


THANK YOU