MEDICINE
KING SAUD UNIVERSITY

436 TEAM
HUMAN GENETICS

Human genetics:
Chromosome Anomalies

For revision only

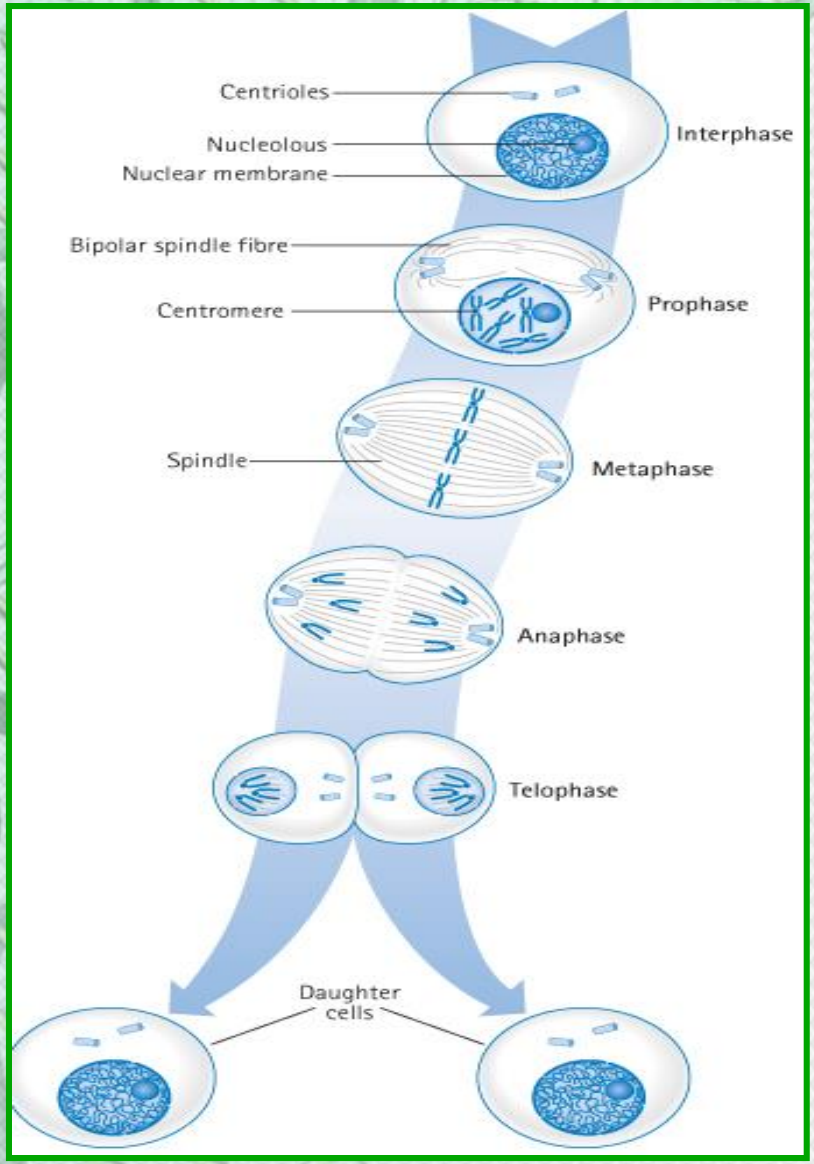
- **Important**
- **Notes**

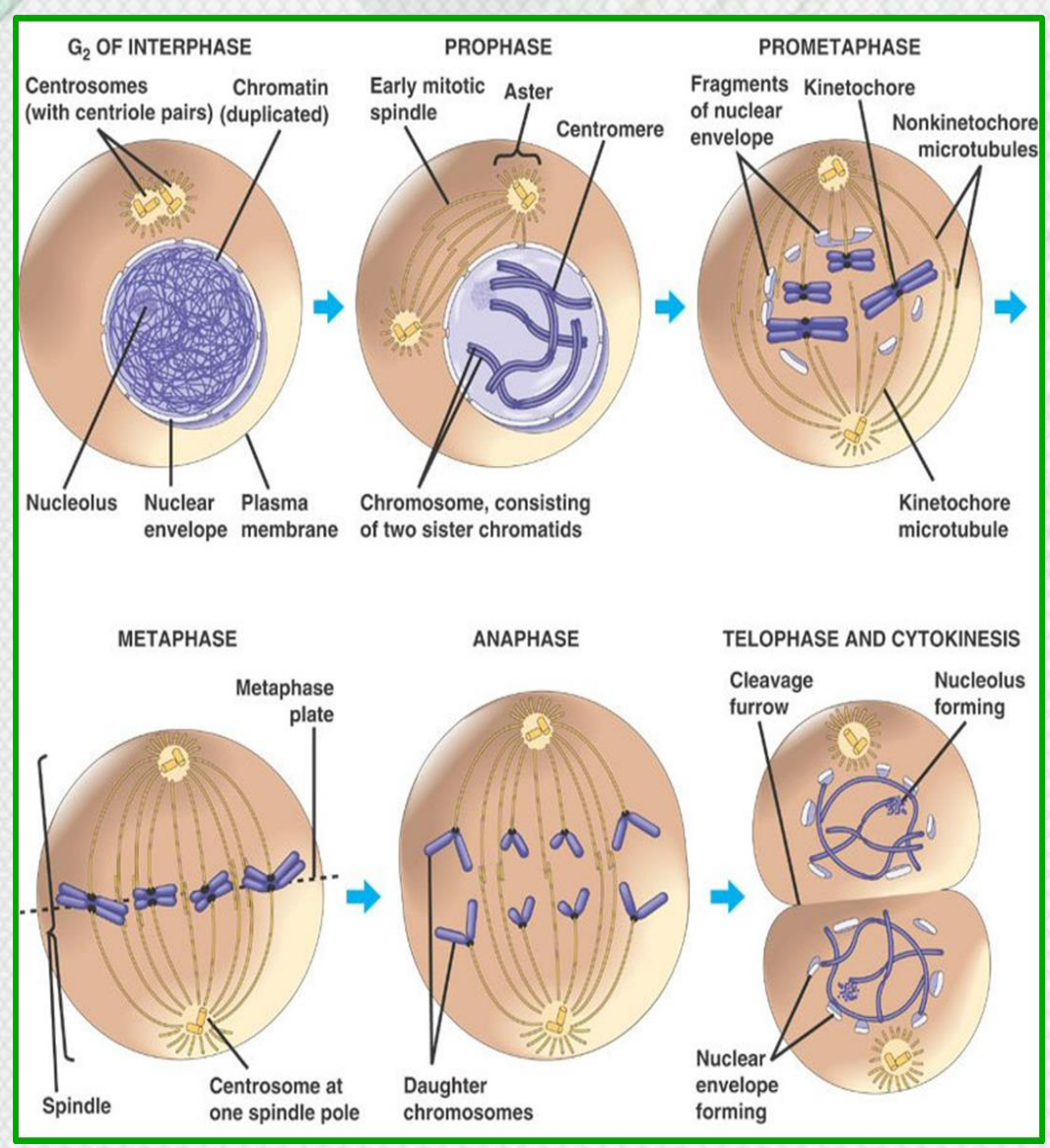
Objectives:

By the end of this lecture, the students should be able to:

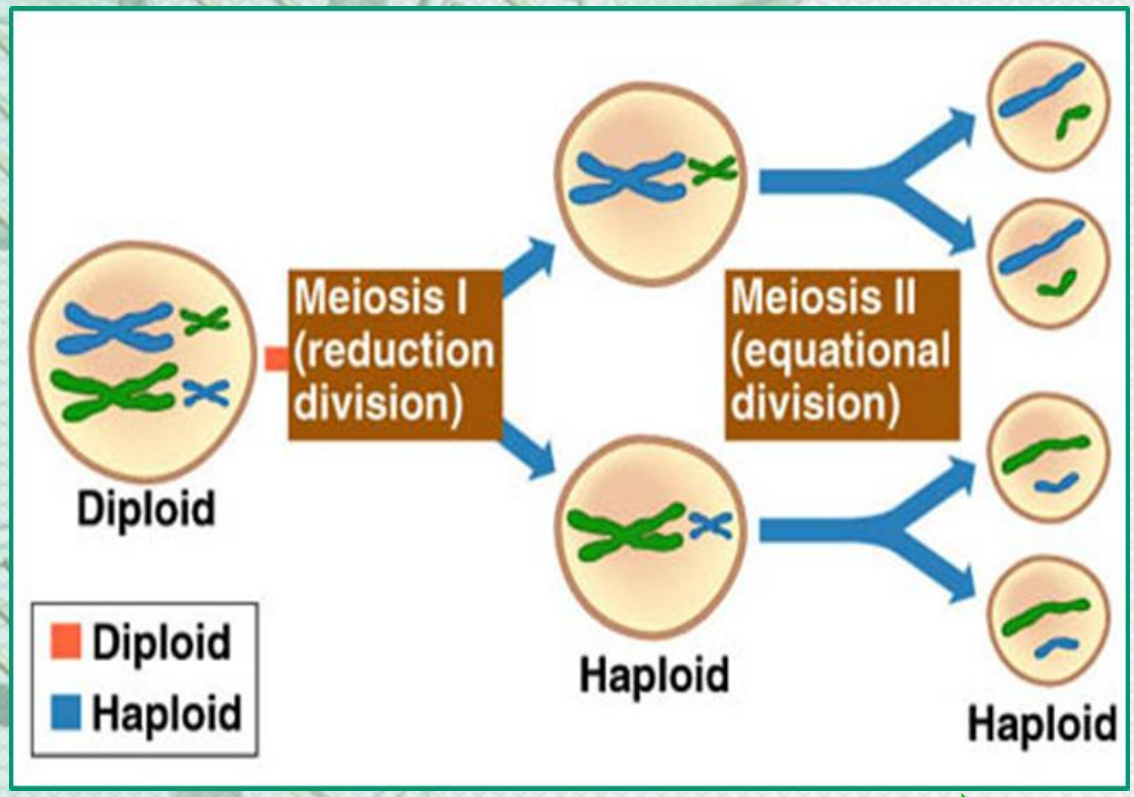
- Describe and explain the events in mitosis & meiosis.
- Define non-disjunction and describe its consequences for meiosis and mitosis.
- Classify and sub-classify chromosomal abnormalities
- Understand the common numerical autosomal disorders: trisomies 21, 13, 18.
- Understand the common numerical sex chromosome disorders: Turner`s & Klinefelter`s syndromes
- Recognize the main structural anomalies in chromosomes

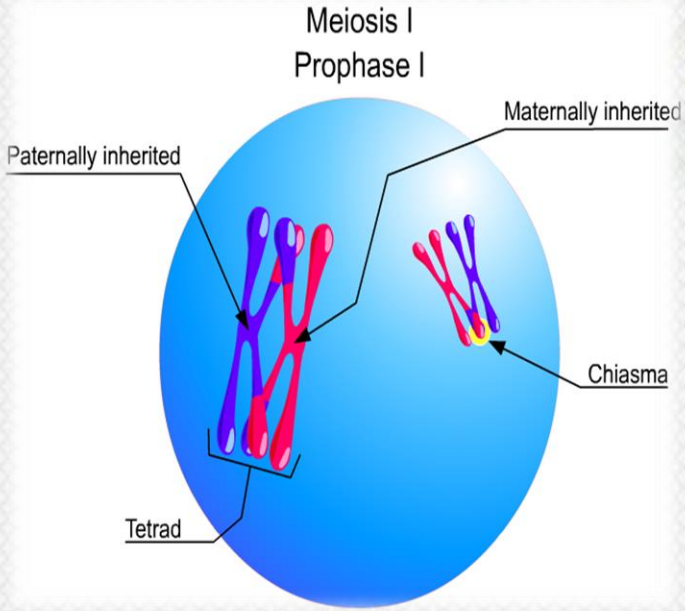
Events of Mitosis





Events of Meiosis

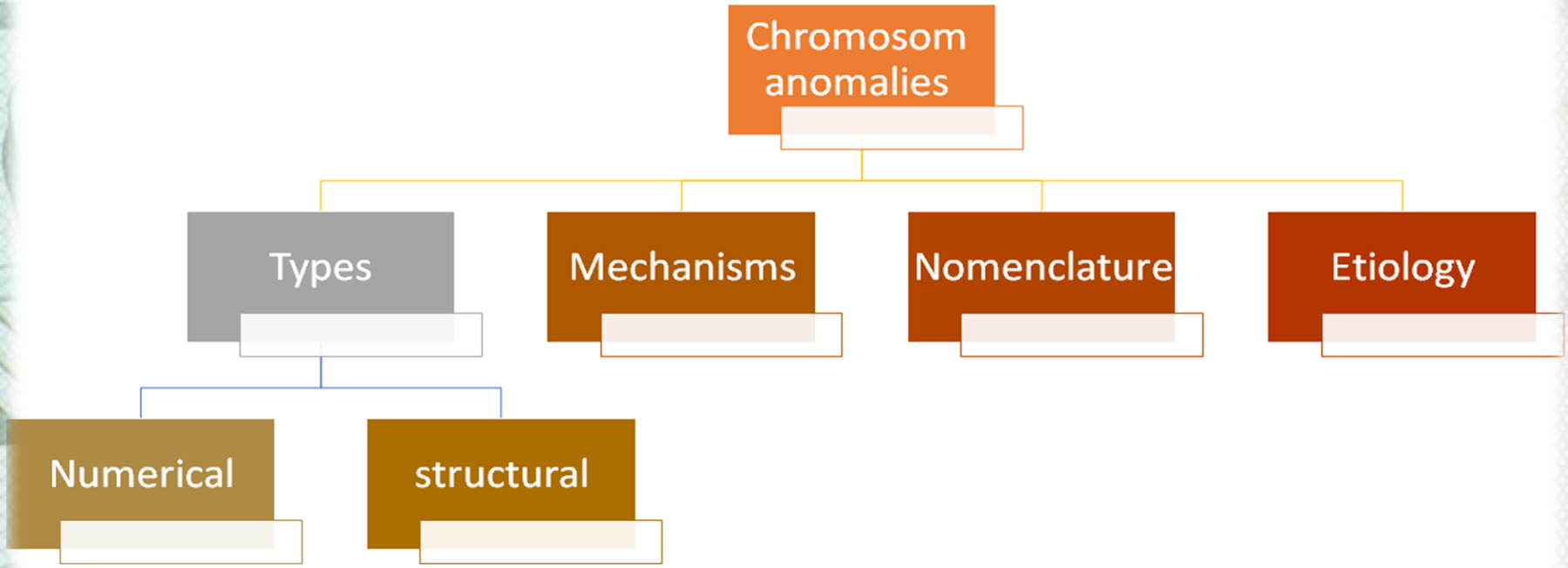




*CHIASMATA

*A CHIASMATA is a point where two homologous non-sister chromatids exchange genetic material during chromosomal crossover during meiosis

Chromosome Anomalies



Non-disjunction in Meiosis

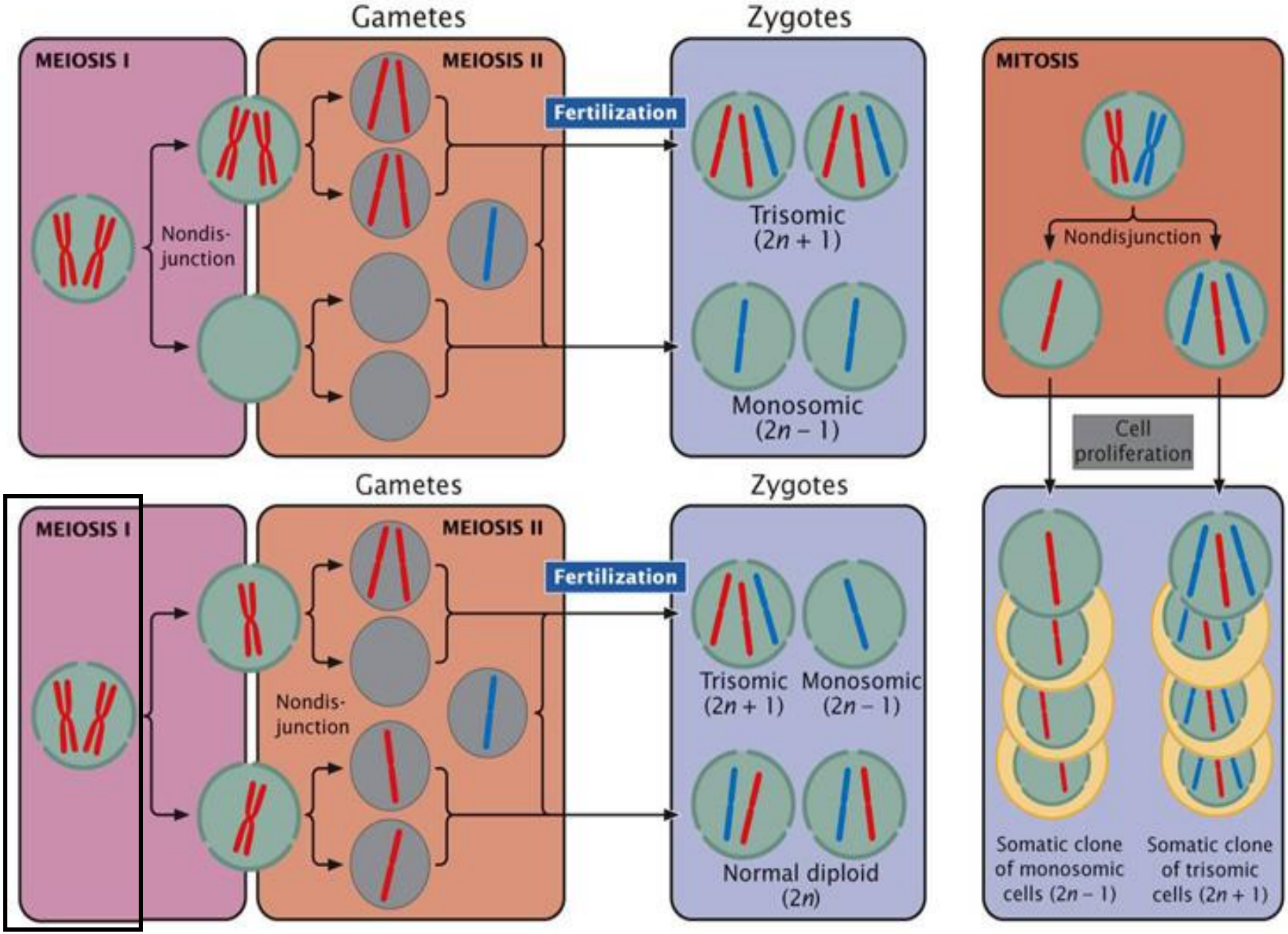
- Nondisjunction ("not coming apart"): is the failure of chromosome pairs to separate properly during meiosis stage 1 or stage 2.

another definition: any change in the normal structure or number of chromosomes; often results in physical or mental abnormalities.

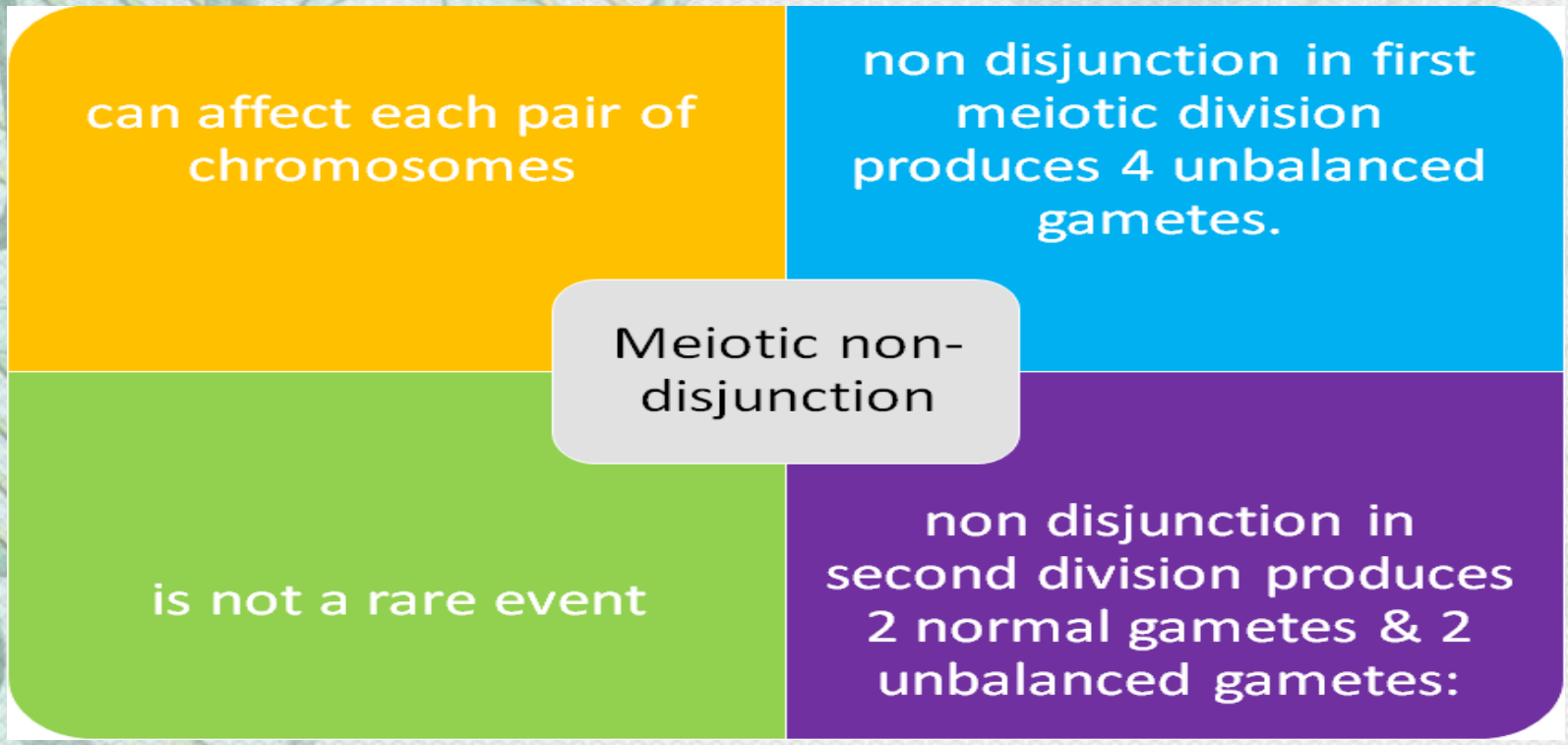
(*Nondisjunction*, the failure of chromosomes to sort properly during *meiosis*, it is not uncommon in humans. Its frequency increases with maternal age) .

- As a result, one daughter cell has two chromosomes, and the other has none.
- The result of this error is a cell with an imbalance of chromosomes (Aneuploidy)

Nondisjunction is the failure of homologous chromosomes or sister chromatids to separate properly during cell division. There are three forms of nondisjunction: failure of a pair of homologous chromosomes to separate in meiosis I, failure of sister chromatids to separate during meiosis II, and failure of sister chromatids to separate during mitosis


Gametes
Zygotes
MEIOSIS I
MEIOSIS II
Fertilization
Nondis-
junction
Trisomic
(2n + 1)
Monosomic
(2n – 1)
MITOSIS
Nondisjunction
Cell
proliferation
Gametes
Zygotes
MEIOSIS I
MEIOSIS II
Fertilization
Nondis-
junction
Trisomic
(2n + 1)
Monosomic
(2n – 1)
Normal diploid
(2n)
Somatic clone
of monosomic
cells (2n – 1)
Somatic clone
of trisomic
cells (2n + 1)

Meiotic non-disjunction

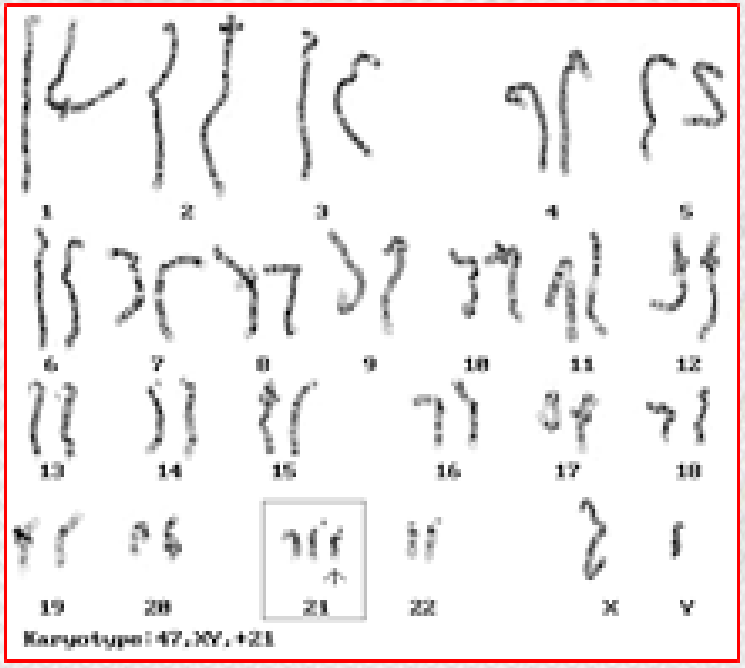


- Gamete with an extra autosome
- Nullosomic gamete
  (missing one chromosome)

Numerical anomalies in AUTOSOMES

Down syndrome, trisomy 21 Karyotype: 47, XY, +21

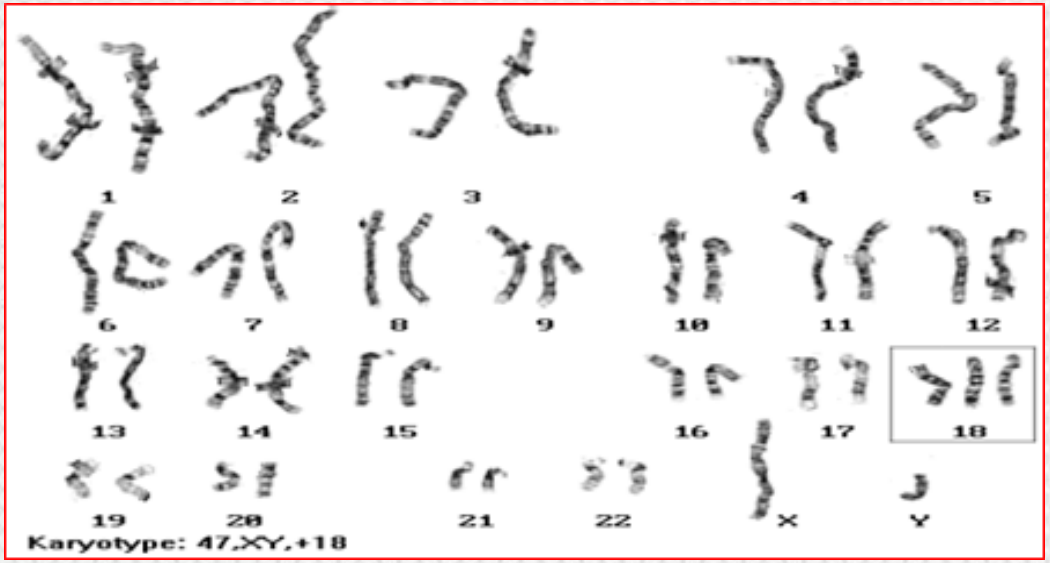
- The incidence of trisomy 21 rises sharply with increasing maternal age
- Most cases arise from non disjunction in the first meiotic division
- The father contributing the extra chromosome in 15% of cases
  (i.e. Down syndrome can also be the result of nondisjunction of the father's chromosome 21)
- A small proportion of cases are mosaic and these probably arise from a non disjunction event in an early zygotic division.
- The symptoms include characteristic facial dysmorphologies, and an IQ of less than 50.



Edward's syndrome, Trisomy 18

Karyotype: 47, XY, +18

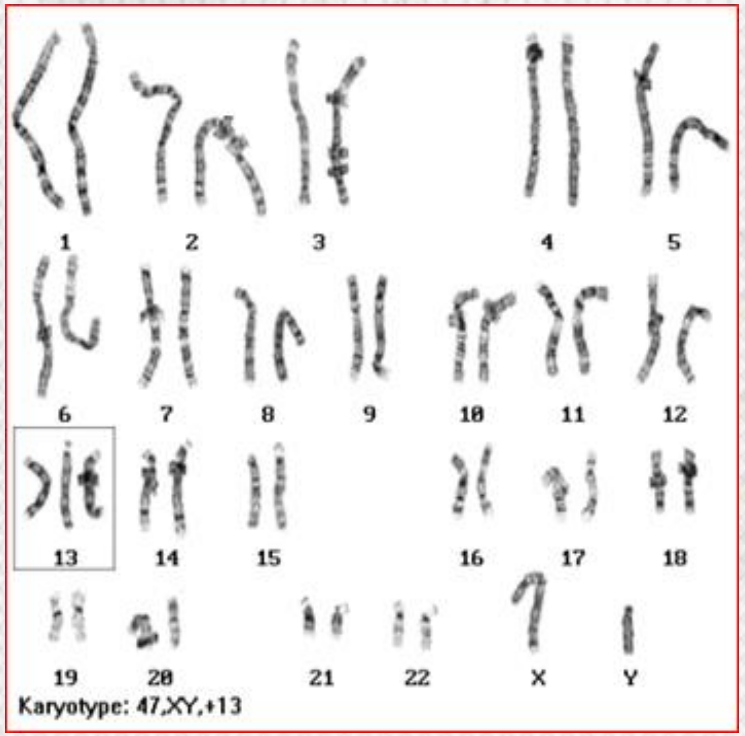
- It is the second most common autosomal trisomy, after Down syndrome, that carries to term
- It occurs in around one in 6,000 live births and around 80 percent of those affected are female
- Most babies die in the first year and many within the first month & has a very low rate of survival
- Common anomalies are heart abnormalities, kidney malformations, and other internal organ disorders



Patau Syndrome, Trisomy 13

Karyotype: 47, XY, +13

- 50% of these babies die within the first month and very few survive beyond the first year.
- There are multiple dysmorphic features.
- Most cases, as in Down's syndrome, involve maternal non-disjunction.



Numerical anomalies in SEX chromosomes

Monosomy X (Turner syndrome):

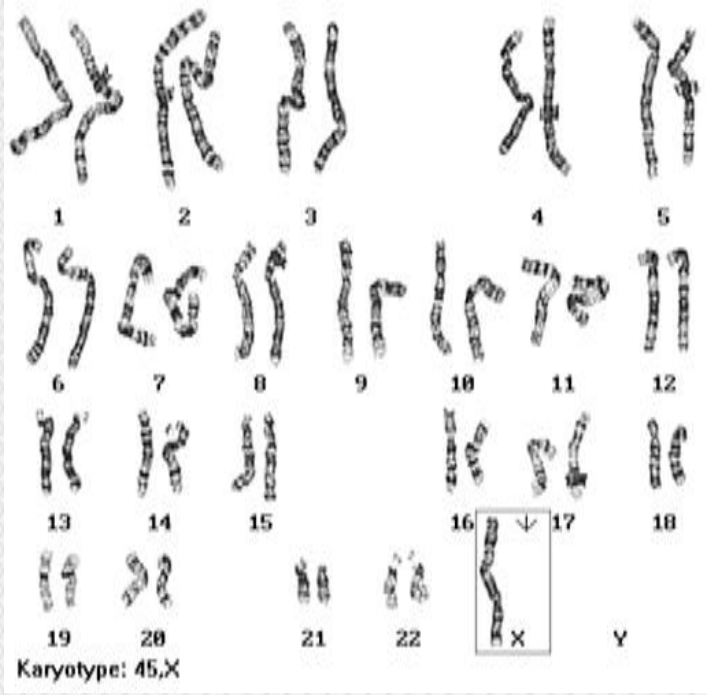
45, XO Females

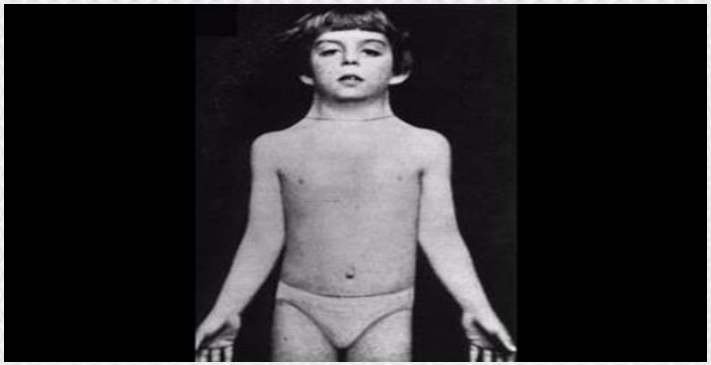
- ~ Turner syndrome is a genetic disorder that affects about 1 in every 5,000 baby girls and only affects females.

- ~ A girl with Turner syndrome only has one normal X sex chromosome, rather than the usual two (XX).

- ~ Main characteristics of Turner's syndrome:

1- are shorter than average.
2- have underdeveloped ovaries.
3- The only viable monosomy in humans.
4- Webbed neck, Broad chest, Low hairline.
5- Normal intelligence, normal span life, sterile.



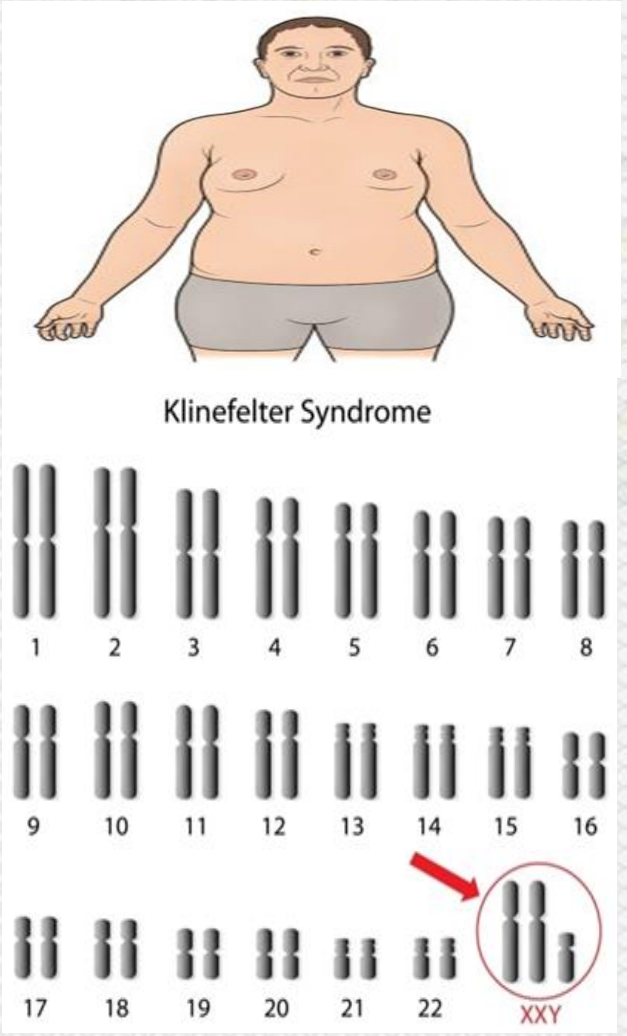


Klinefelter Syndrome:

47,XXY males

- ~Klinefelter syndrome is a genetic condition that results when a boy is born with an extra copy of the X chromosome, also known as the (XXY) condition.
- ~Affects male physical and cognitive development
- ~About one of every 500 males has an extra X chromosome.
- ~Affected individuals typically have small testes that do not produce as much testosterone as usual.
- ~Very rarely more extreme forms of Klinefelter syndrome occur where the patient has 48, (XXXY) or even 49, (XXXXY) karyotype. These individuals are generally severely retarded.
- ~Main characteristics of Klinefelter syndrome:

1-Fail to produce normal levels of testosterone.
2-Breast enlargement, normal intelligence, sterile.
3-Patients are taller and thinner than average.



Sex chromosome unbalance of much less deleterious effect

In males (47, XYY)

May be without any symptoms. Males are tall but normally proportioned. 10 - 15 points reduction in IQ compared to sibs .

In females (XXX)

It seems to do little harm, individuals are fertile and do not transmit the extra chromosome. They do have a reduction in IQ comparable to that of Kleinfelter's males .

Numerical anomalies affecting the number of Complete Haploid Set (n) of chromosomes

Polyploidy

- Cells are polyploid if they contain more than two haploid (n) sets of chromosomes

- **Triploidies are the most frequent,**

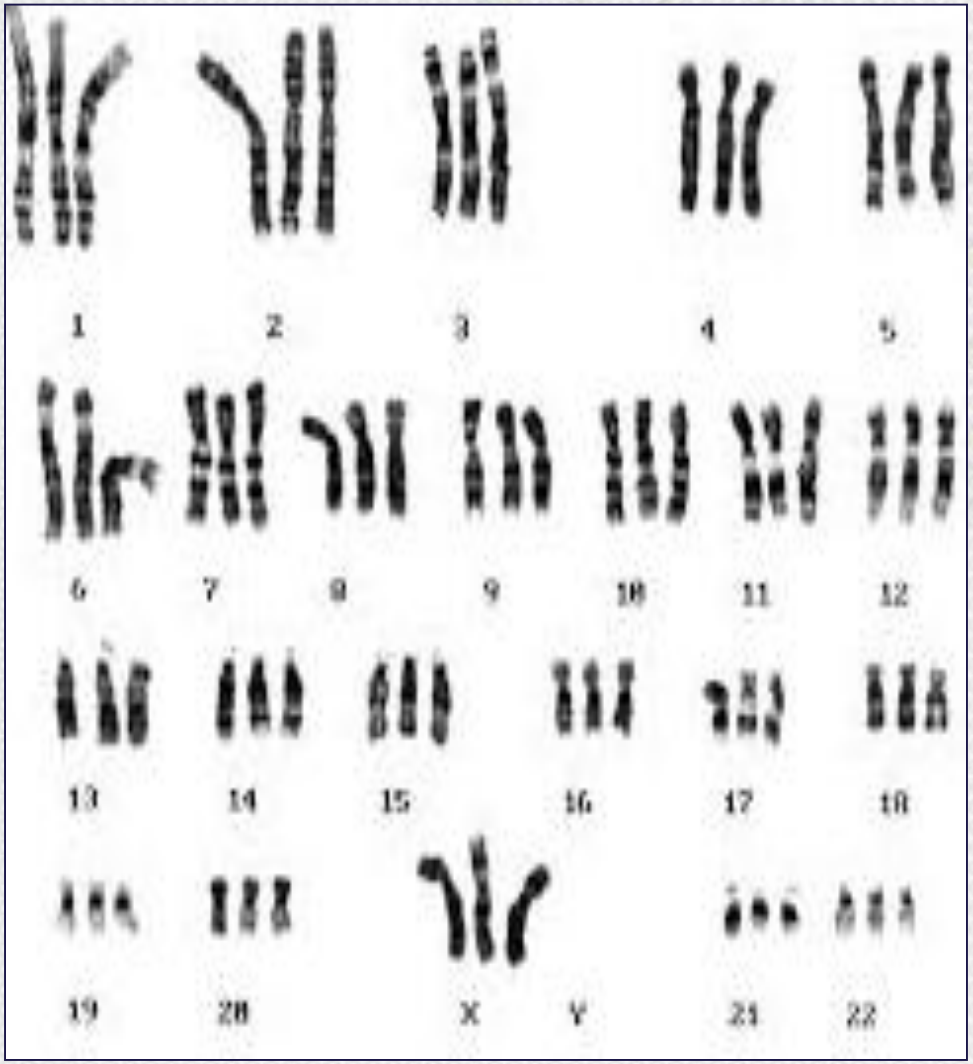
-3N=69 chromosomes: e.g 69XXX or 69XYY or 69XXY

-Found in 20% of spontaneous miscarriages

- **Tetraploidy :**

4N=92 chromosomes

* An individual can have normal chromosomal number with numerical chromosomal anomalies .(combination)

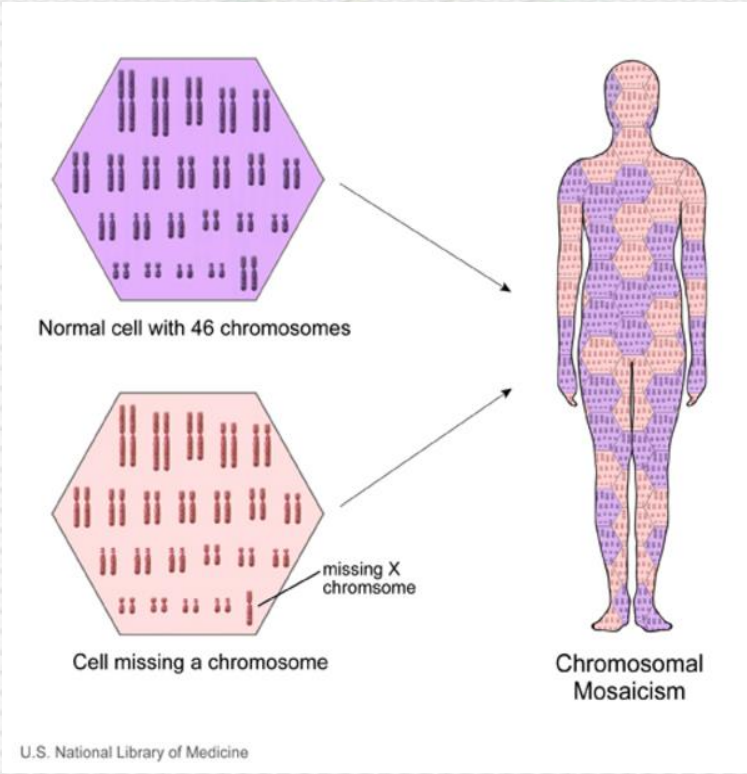


Mosaicism

Mosaicism : describe a situation in which different cells in the same individual have different numbers or arrangements of chromosomes .

- It is called “mosaicism” because the cells of the body are similar to the tiles of a mosaic.
- A mosaic individual is made of 2 or more cells populations coming from one zygote .
- Is denoted by a slash between the various clones observed, e.g. 46,XY / 47,XY,21+) .
- Usually due to a mitotic non-disjunction .
- Can affect any type of cells, including :

  * Blood cells .
  * Egg & Sperm cells (gametes) .
- A mosaic must not be confused with a chimeras
- Chimerism is the presence in an individual of two or more genetically distinct cell lines derive from more than one zygote (e.g. 2 sperms fertilize 2 ova → 2 zygotes that fuse to form 1 embryo

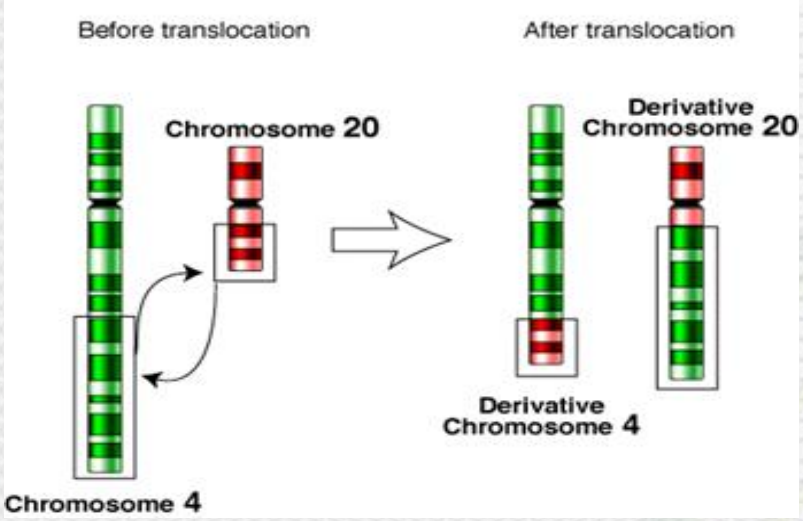


Structural Chromosomal Anomalies:

Reciporcal & Deletion

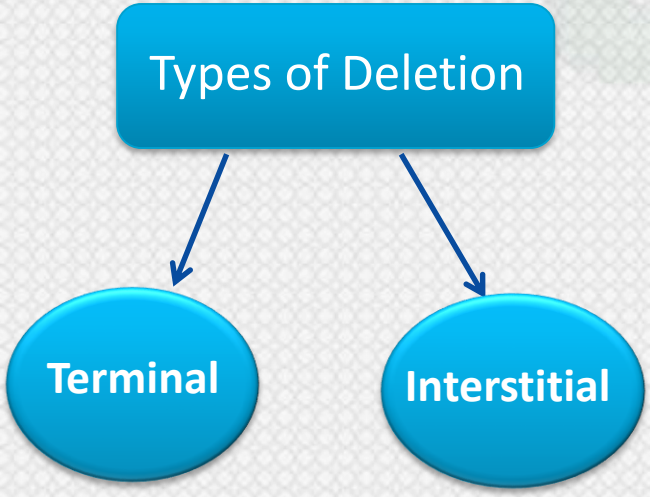
Reciprocal translocation :

- A mutual exchange between terminal segments from the arms of 2 chromosomes.
- There is no loss or alteration at the points of exchange, the new rearrangement is genetically balanced, and called a Balanced rearrangement .



Deletion :

- Loss of a segment from a chromosome, either terminal or interstitial
- Invariably but NOT always, Results in the loss of important genetic material
- Deletion is an unbalanced rearrangement .
- Recorded as del .



* Terminal deletion means loss a part of chromosome number 18 .

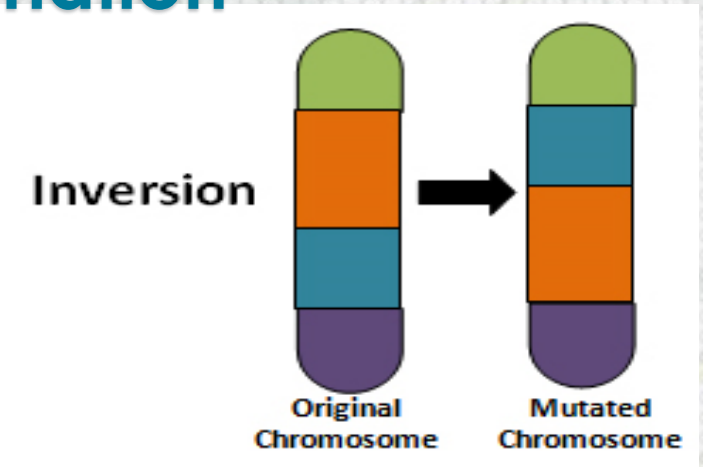
* Interstitial deletion means loss a part of chromosome number 7 .

Structural Chromosomal Anomalies:(cont.)

Inversion, Isochromosome and Ring formation

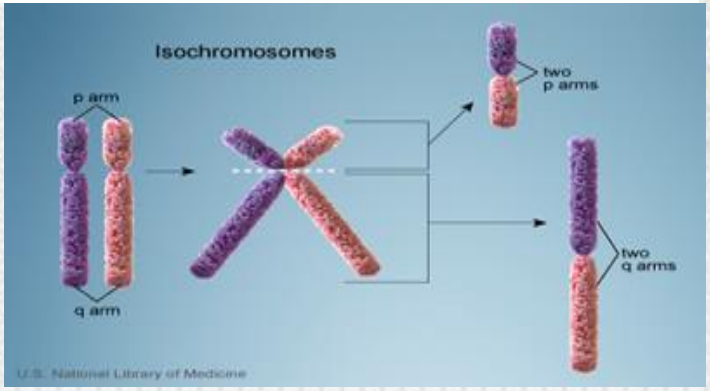
Inversion :

- Inversion occurs when a segment of chromosome breaks, and rejoining within the chromosome effectively inverts it.
- Recorded as inv.
- Normally only large inversions are detected.
- They are balance rearrangements that rarely cause problems in carriers .



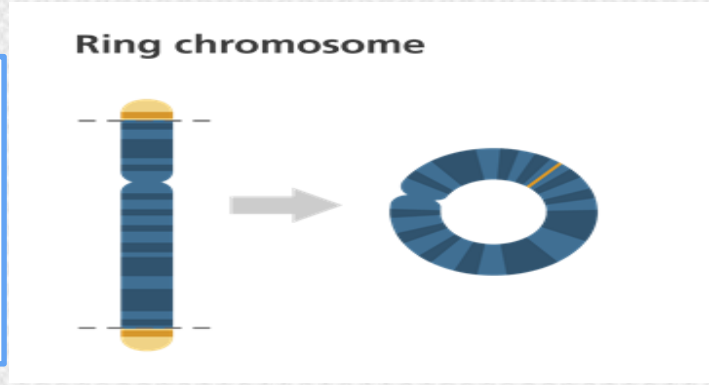
Isochromosome :

- Unbalanced structural abnormality in which the arms of the chromosome are mirror image of each other .
- Isochromosome is that the centromere has divided transversely rather than longitudinally .



Ring Formation :

- A break on each arm of a chromosome a two sticky ends on the central portion a Reunion of the ends as a ring a loss of the 2 distal chromosomal fragments .
- Ring chromosomes are often unstable in mitosis .



Online Quiz

Click Here

For more Knowledge

* Difference between Meiosis & Mitosis Here
* Understanding Chromosomal Translocation Here

Thank You !

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- Nada Alsomali
- Leen Altamimi
- Nora Almohideb

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