Human Genetics
434 team

MED 434 ICINE

Lecture 1:

Klinefelter, Turner & Down Syndrome

دعاء قبل المذاكرة
(اللهم إني أسألك فهم النبيين و حفظ المرسلين و الملائكة المقربين, اللهم اجعل ألسنتنا عامرة بذكرك و قلوبنا بخشيتك, إنك على كل شيء قدير و حسبنا الله و نعم الوكيل)

Lecture Objectives:

- Describe and explain the events in mitosis & meiosis.
- Define non-disjunction and describe its consequences for meiosis and mitosis.
- 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

Videos you may like:

Please make sure to check this link out it has additional material from the males' slides

Mind map

CHROMOSOMAL ANOMALIES

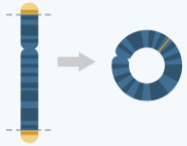
STRUCTURAL

- Inversions

- Deletions

- Translocations

- Isochromosome

- Ring chromosome


NUMERICAL

Sex chromosomes

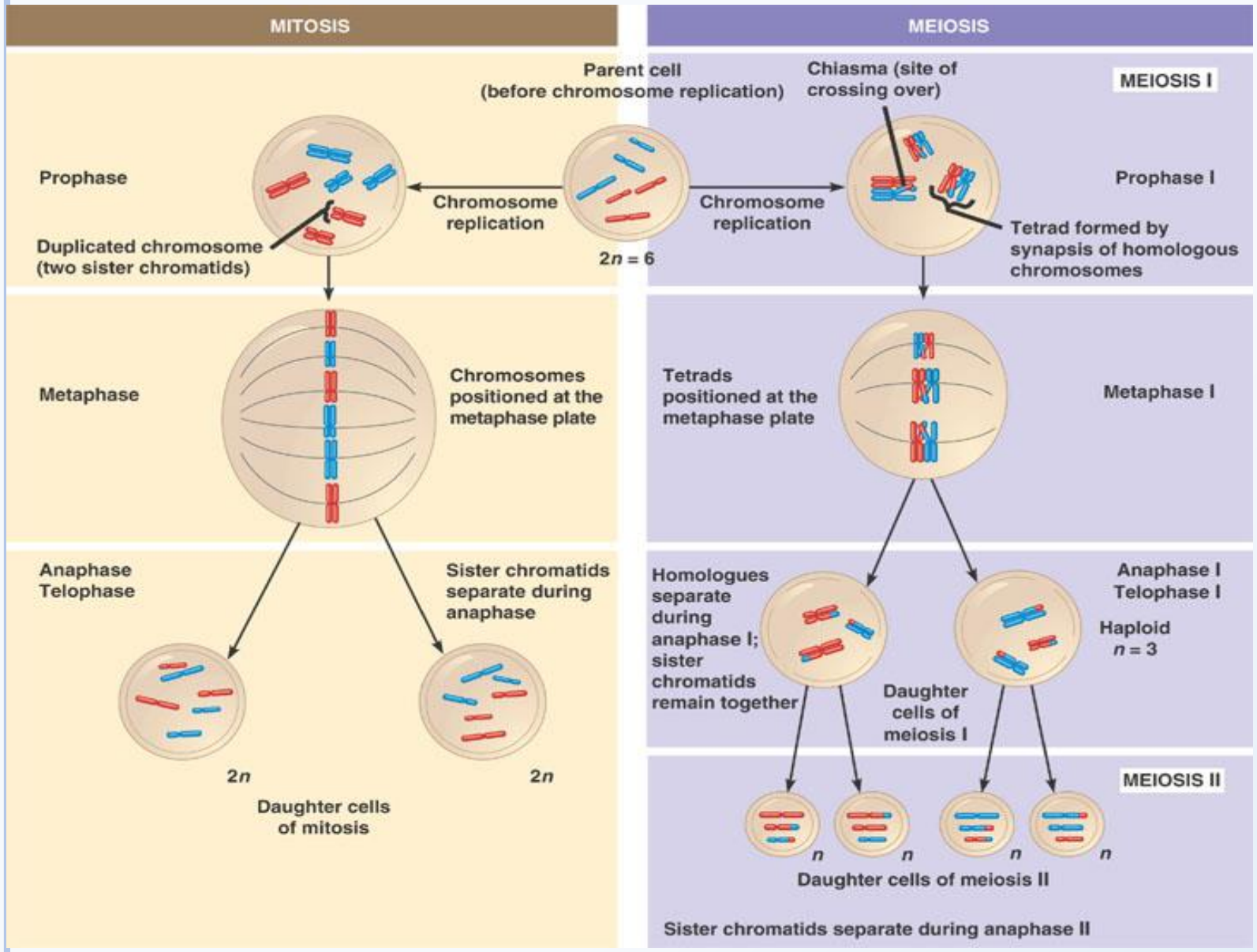
Turner's syndrome

Klinefelter syndrome

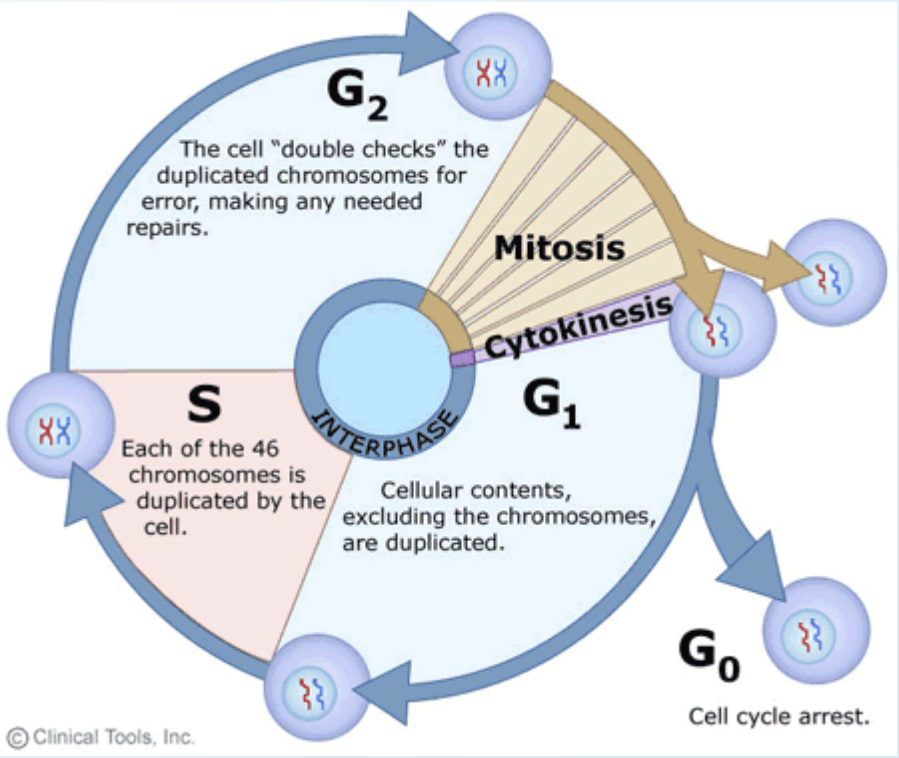
Autosomal chromosomes

- Down syndrome
- Edward's syndrome
- Patau syndrome

MITOSIS vs. MEIOSIS

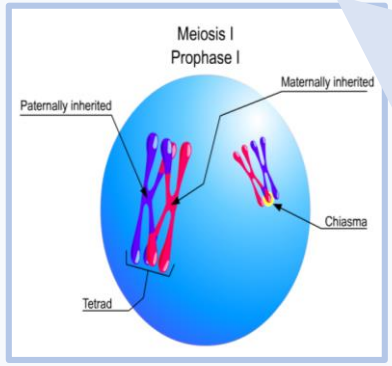


This slide is not new and you already know it !!
However, you can still refresh your memory by watching the first video in the previous slide and use the coming table to simplify the material ☺



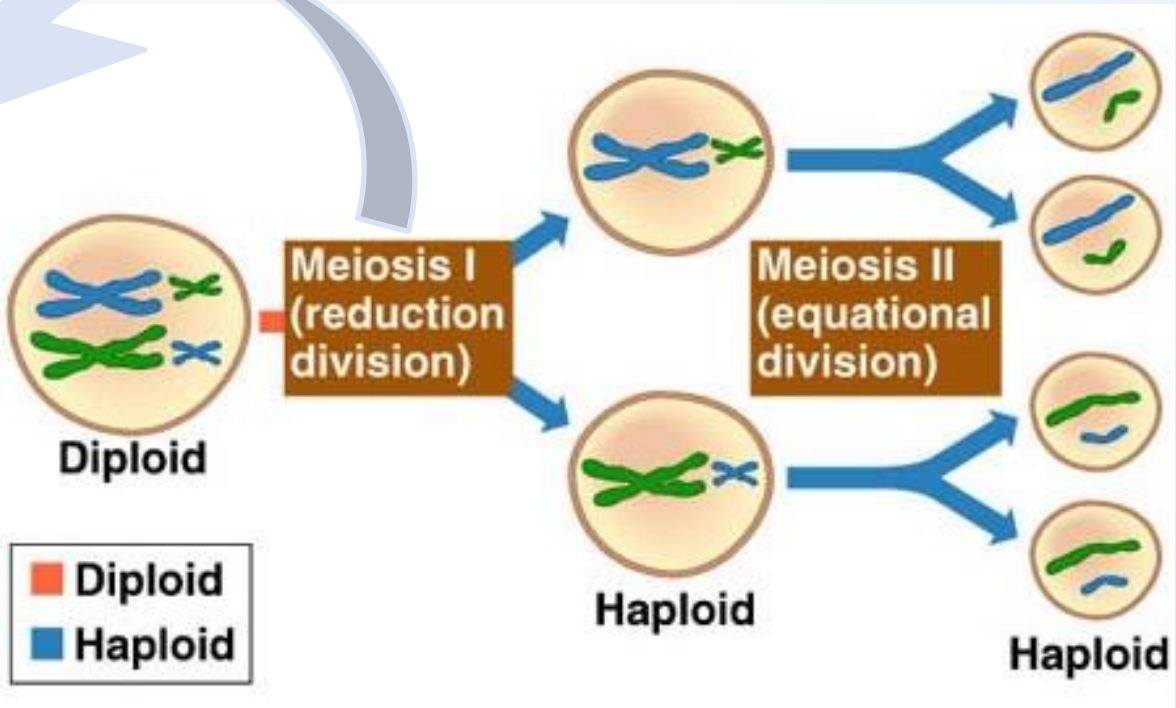
MITOSIS vs. MEIOSIS

Additional table

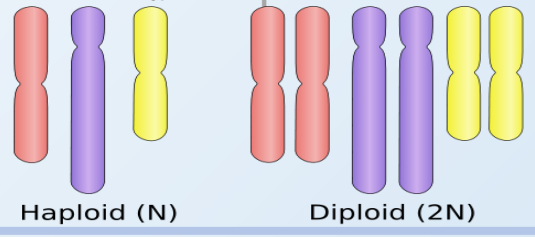


Event	Mitosis	Meiosis
DNA replication	Occurs during interphase before nuclear division begins	Occurs once, during the interphase before meiosis I begins
Number of divisions	One, including prophase, metaphase, anaphase, and telophase	Two, each including prophase, metaphase, anaphase, and telophase
Synapsis of homologous chromosomes	Does not occur	Synapsis is unique to meiosis: During prophase I, the homologous chromosomes join along their length, forming tetrads (groups of four chromatids); synapsis is associated with crossing over between nonsister chromatids
Number of daughter cells and genetic composition	Two, each diploid (2*n*) and genetically identical to the parent cell	Four, each haploid (*n*), containing half as many chromosomes as the parent cell; genetically nonidentical to the parent cell and to each other
Role in the animal body	Enables multicellular adult to arise from zygote; produces cells for growth and tissue repair	Produces gametes; reduces chromosome number by half and introduces genetic variability among the gametes

PHASES OF MEIOSIS



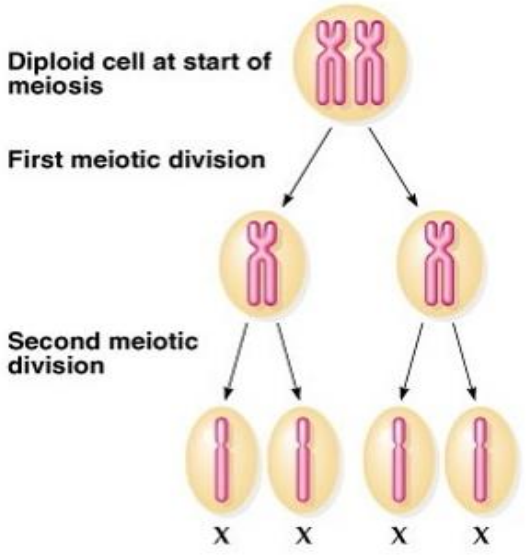
- Notice the cells resulting from the first phase (division are haploid "1n") , so Meiosis I starts with one diploid cell to give two haploid cells
- however., meiosis II starts and ends with the haploid number of the chromosomes. And that's make it similar to mitosis you can say meiosis II is a Mitosis of haploid cell !! ☺
- the deference is that mitosis produce two identical diploid cells.



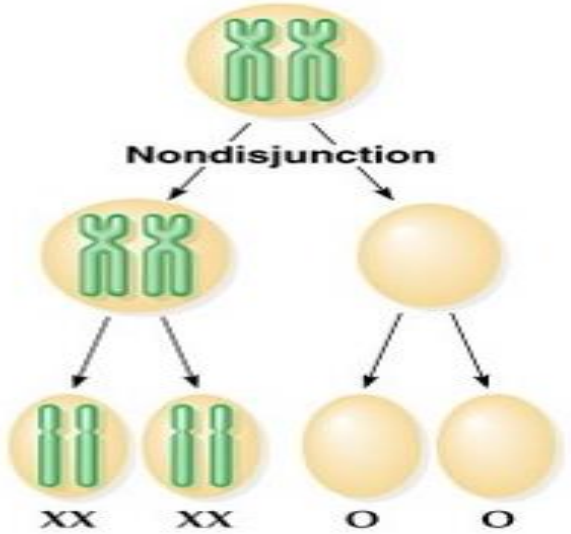
Non-disjunction in Meiosis

Normal: successful meiosis I&II

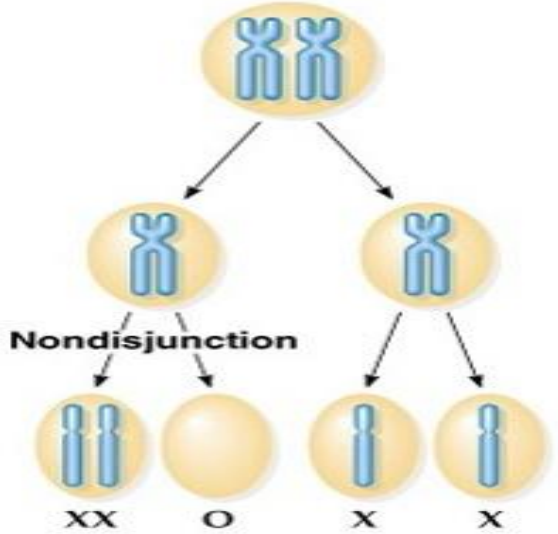
Nondisjunction ("not coming apart") is the failure of chromosome pairs to separate properly during meiosis stage 1 or stage 2. As a result, one daughter cell has two chromosomes or two chromatids, and the other has none. can affect each pair of chromosomes and **it is not a rare event**



In the first meiotic division



In the second meiotic division



Four, non-identical haploid gametes

produces 4 unbalanced gametes

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

produces 2 normal gametes & 2 unbalanced gametes.

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

The result of the two errors is a cell with an imbalance of chromosomes (Aneuploidy)

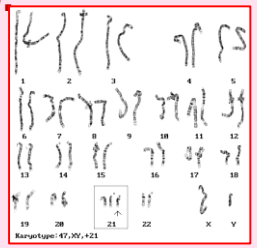
Numerical anomalies in autosomes

Down syndrome

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

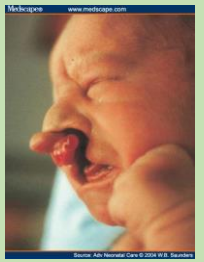
Karyotype: 47, XY, +18

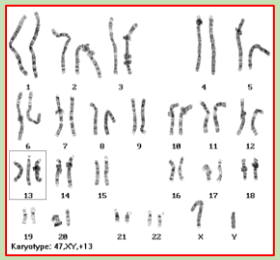
- It is the second most common autosomal trisomy, after Down syndrome, that carries to term
- It occurs in around one in 6,000 live births and around 80 percent of those affected are female
- Most babies die in the first year and many within the first month & has a very low rate of survival
- Common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

Patau Syndrome

Karyotype: 47, XY, +13

- Fifty % 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

Klinefelter Syndrome

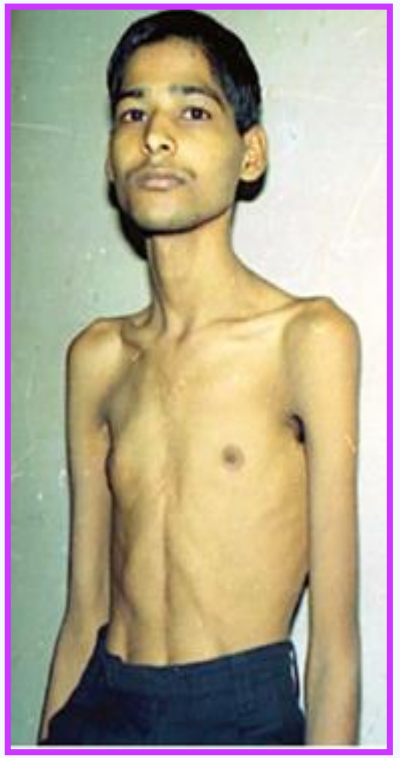
Karyotype: 47, XXY

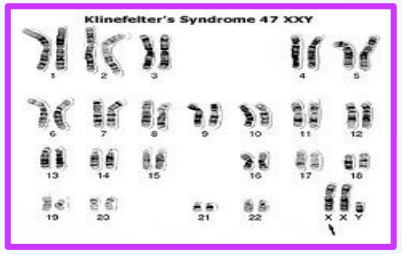
Male sex organs; unusually small testes which fail to produce normal levels of testosterone→ breast enlargement (gynaecomastia) and other feminine body characteristic

No spermatogenesis → sterile

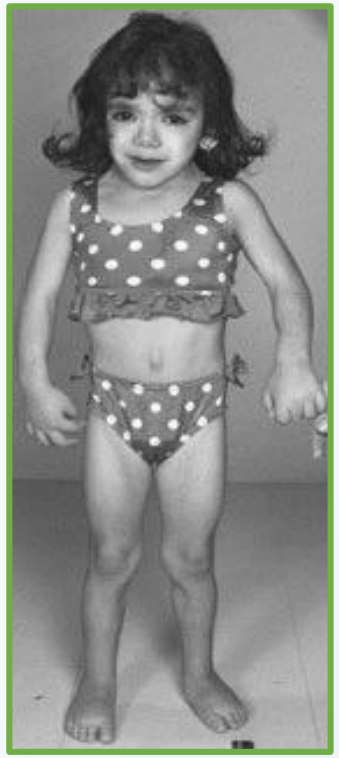
Patients are taller and thinner than average and may have a slight reduction in IQ but generally they have normal intelligence

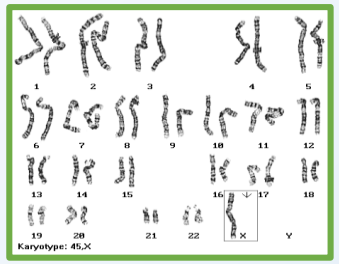
Very rarely more extreme forms of Klinefelter syndrome occur where the patient has 48, XXXY or even 49, XXXXY karyotype. These individuals are generally severely retarded





Extra X chromosome





Missing X chromosome

Turner's syndrome

Karyotype: 45, XO

Occurring in 1 in 5000 phenotypic females

The only viable monosomy in humans

Characteristics: Webbed neck, Individuals are genetically female, not mature sexually, Sterile, Short stature, Broad chest, Low hairline, Streak ovaries, Normal intelligence, Normal life span

Sex chromosome unbalance Of <u>much less deleterious effect</u>

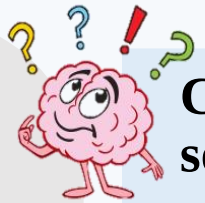
47, XYY

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

XXX females

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

Polyploidy



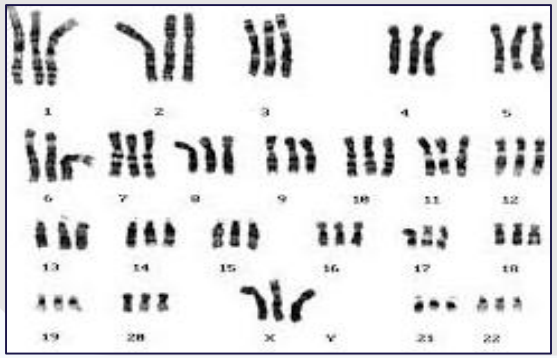
Is the Numerical Anomalies affecting the number of complete haploid set (n) of chromosomes

- **Triploidies: are the most frequent**

It means having 3N = 69 chromosomes in the body cells. e.g. 69, XXX, or 69, XXY, or 69, XYY.

Are found in 20 % of spontaneous miscarriages

- **Tetraploidy: 4N = 92 chromosomes**



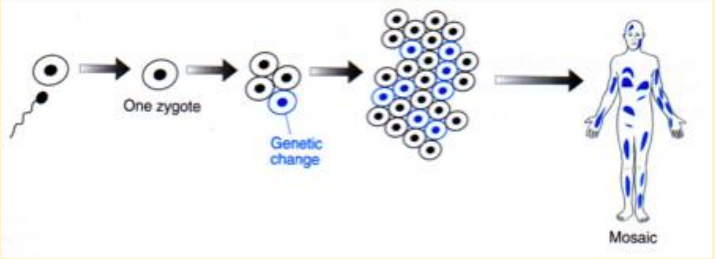
Triploidies:3n

In mosaicism and chimerism the whole body cells has 2 types. In some cases cancer for example the abnormal cells are located therefor you should use biopsy to conform it by molecular studies unlike mosaicism and chimerism which are detectable by blood.

Can an individual have A combination of cells: some cells with normal chromosomal numbers, & some cells with numerical chromosomal anomalies?

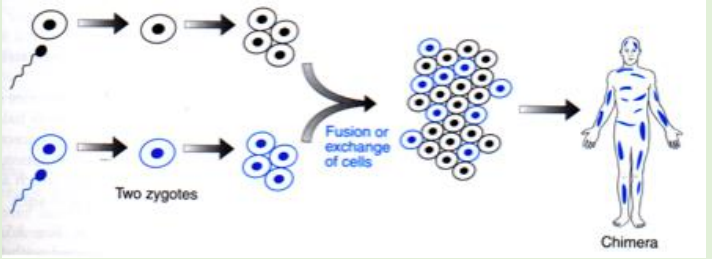
MOSAICISM

- A mosaic individual is made of 2 (or more) cell populations, coming from only 1 zygote
- Is denoted by a slash between the various clones observed e.g.46, XY / 47, XY, +21).
- Numerical mosaic anomaly is usually due to a mitotic non-disjunction
- A mosaic must not be confused with a chimeras



CHIMERISM

- 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

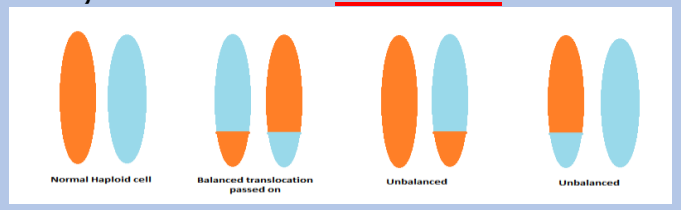


STRUCTURAL CHROMOSOMAL ANOMALIES

Reciprocal translocation

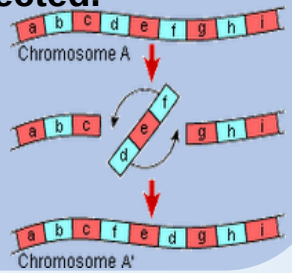
A mutual exchange between terminal segments from the arms of 2 chromosomes.

Provided that there is no loss or alteration at the points of exchange, the new rearrangement is genetically balanced, and called a **Balanced rearrangement**.



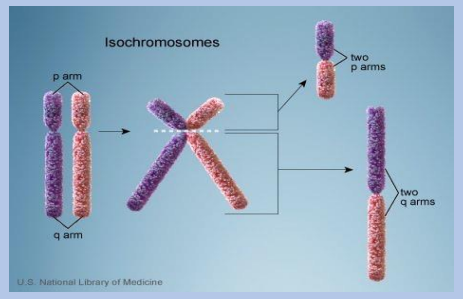
Inversion

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



Isochromosome

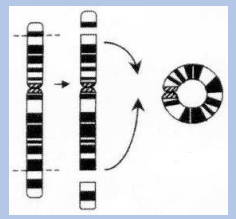
The most probable explanation for isochromosome is that the **centromere** has divided transversely rather than longitudinally



Ring formation (Ring chromosome)

A break on each arm of a chromosome → two sticky ends on the central portion → Reunion of the ends as a ring → loss of the 2 distal chromosomal fragments

Ring chromosomes are often unstable in mitosis



Deletion

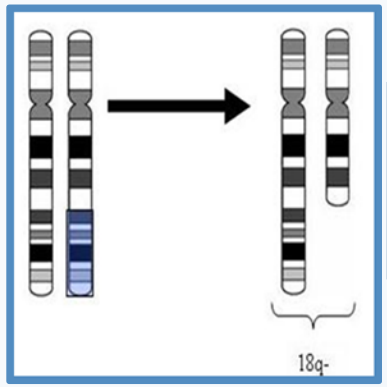
Loss of a segment from a chromosome, either terminal or interstitial

Recorded as del

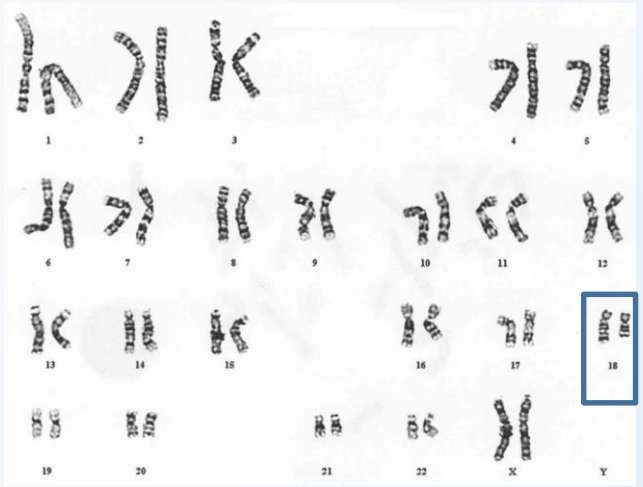
Invariably, but not always, results in the loss of important genetic material

Deletion is therefore an unbalanced rearrangement

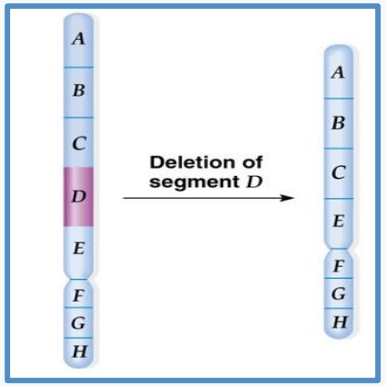
Terminal Deletion



e.g.

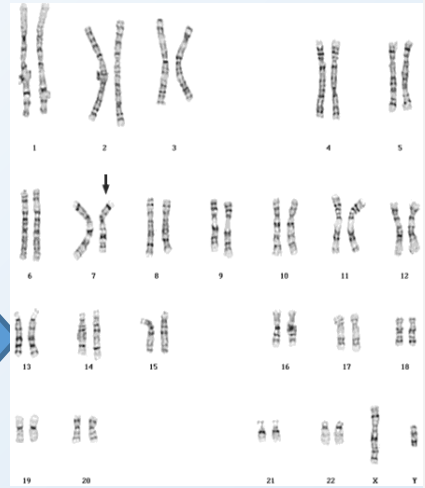


46,XX,del(18)(q21.3).



Interstitial deletion

e.g.



The key to the karyotype description is as follows:

- **46**: the total number of chromosomes.
- **XY**: the sex chromosomes (male).
- **del(7)**: deletion in chromosome 7.
- **(q11.23q21.2)**: **breakpoint** of the deleted segment.

46,XY,del(7)(q11.23q21.2)

MCQs

1- which of the following is resulted from Non-disjunction of the first meiotic division:

a. One gamete with an extra chromosome and one Nullosomic gamete.
b. Four unbalanced gametes
c. Two gametes with an extra chromosome
d. 4 non-identical haploid gametes

2- choose the answer you think it does not belong to the rest :

a. Down stndrome
b. Patau syndrome
c. Turner's syndrome
d. Edward's syndrome

3- a 19 year old male with relatively high stature has a normal IQ and has no facial hair neither secondary sexual characteristics. he also has gynaecomastia. his family was told that he has a congenital syndrome causing all his feathers. what do you expect his karyotype is :

a. 47,XYY
b. 45,XO
c. 47,XY,+21
d. 47,XXY

4- Which of the following structural chromosomal anomalies gives unbalanced rearrangement:

a. Translocation
b. Inversion
c. Deletion
d. Ring formation

5- which of the following is true regarding mosaicism:

a. Having 2 or more cell populations resulted from the union of two zygotes to form one embryo.
b. It is a form numerical chromosomal anomaly affecting the whole haploid set.
c. Having 2 (or more) cell populations, coming from only 1 zygote
d. both A &C

6- which of the following is the karyotype of turner's syndrome:

a. 47,XXX
b. 45,XO
c. 47,XX,+18
d. 47XX,21

Key answers: 1- B , 2-C , 3- D ,4-C , 5-C, 6- B

Thank you for checking our work

- **Done by:**

Sarah M. Aljasser

- **Revised by:**

Nouf Alharbi

دعاء بعد المذاكرة
(اللهم إني استودعتك ما قرأت وما حفظت وما تعلمت فرده لي عند حاجتي إليه إنك على كل شيء قدير وحسبنا الله و نعم الوكيل)

For any questions or suggestions please email us:

embryology434@gmail.com