HUMAN GENETICS

LECTURE 2: Chromosomal anomalies

Editing link:
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Color index:
- Important
- Slides
- Drs` notes
- Extra information

Objectives:

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

1. Describe and explain the events in mitosis & meiosis.
2. Define non-disjunction and describe its consequences on meiosis.
3. Classify chromosomal abnormalities: Numerical & structural

   - 3a Understand the common numerical autosomal disorders: trisomies 21, 13, 18.
   - 3b Understand the common numerical sex chromosome disorders: Turner`s & Klinefelter`s syndromes
   - 3c Recognize the main structural anomalies in chromosomes

Mitosis & Meiosis: Typical mitotic cell cycle

During G1	one diploid
S phase S= synthesis of DNA	duplication of each chromosome's DNA → Two sister chromatids
G2 Phase	chromosomes begin to condense and become visible
G1, S, and G2 phases = constitute **interphase** Interphase > "preparation for mitosis" **Cell cycle (G1 → S → G2 → M)**	

- Two daughter cells = equal genetic information

The result is two diploid daughter cells with identical genetic information

Events of Mitosis:

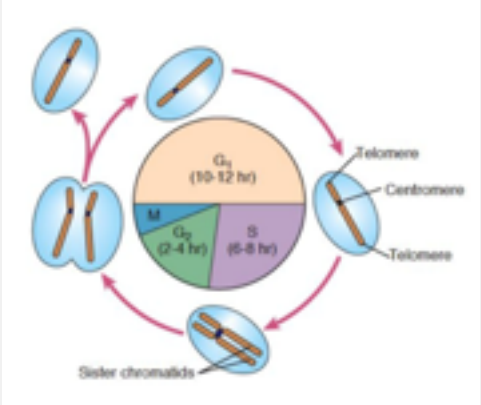
Prophase.
- formation of mitotic Spindle & pair of centrosomes

Prometaphase.
- Nuclear membrane dissolves
- Chromosomes to disperse & attach by kinetochores to mitotic spindle microtubules

Metaphase.
Chromosomes condensed & line up at the equatorial plane

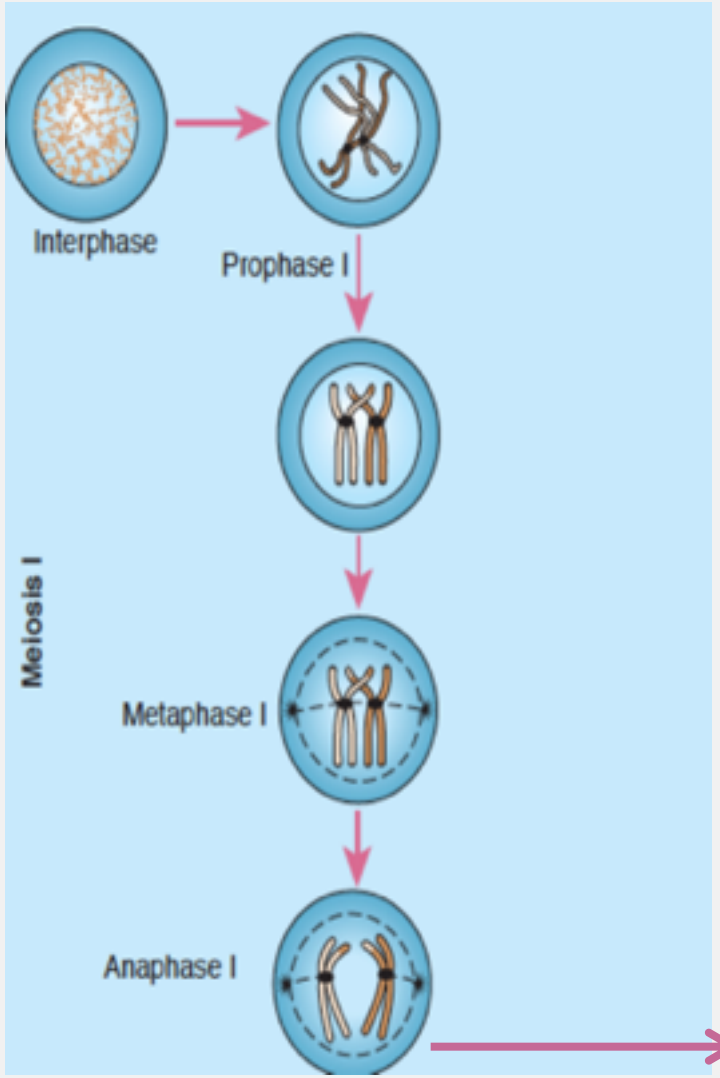
Anaphase.
- Chromosomes separate at centromere &
- Sister chromatids of each chromosome become independent daughter chromosomes

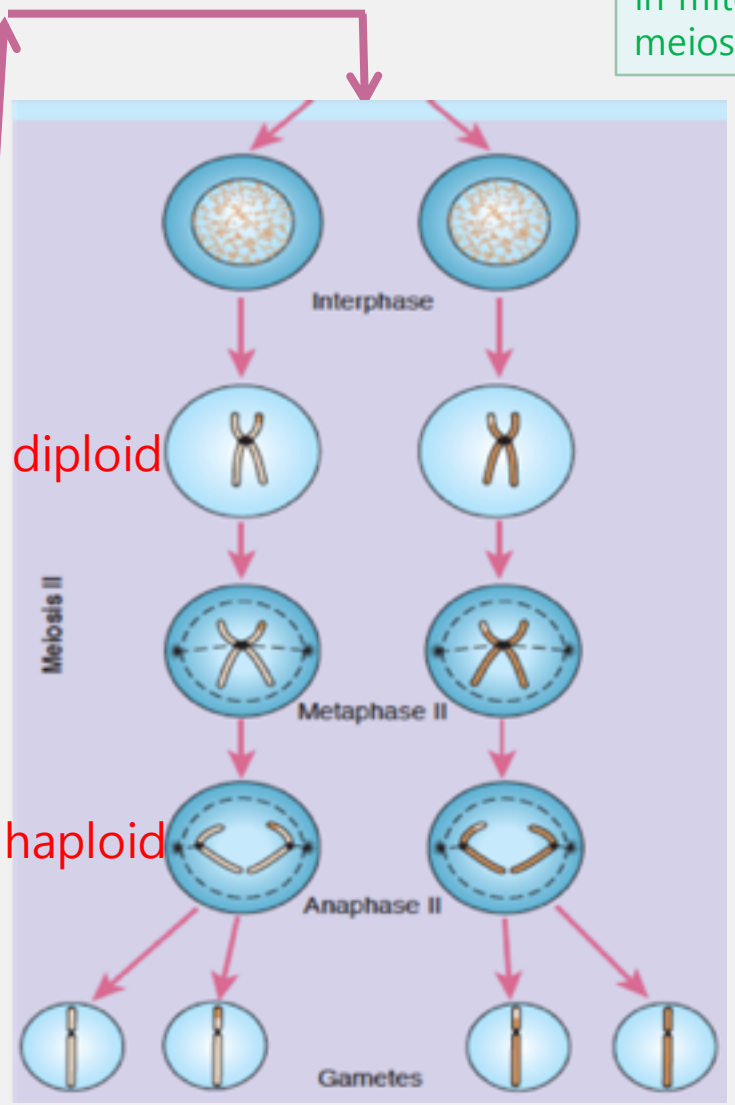
Telophase.
- Chromosomes de-condense from their highly contracted state,
- Nuclear membrane re-form around each of the two daughter nuclei.
- Division of the cytoplasm
- resume their interphase



Events of meiosis I & II

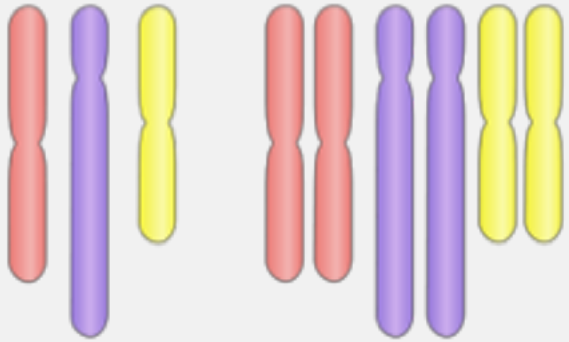
Events of meiosis
- Consists of tow successive nuclear division
- In the first nuclear division the homologous chromosomes are separated from each other (daughter chromosomes consists of two chromatids)
- The second nuclear division resembles a mitotic division but there is no DNA replication (already replicated before the first division)
- **The result is four haploid daughter cells**



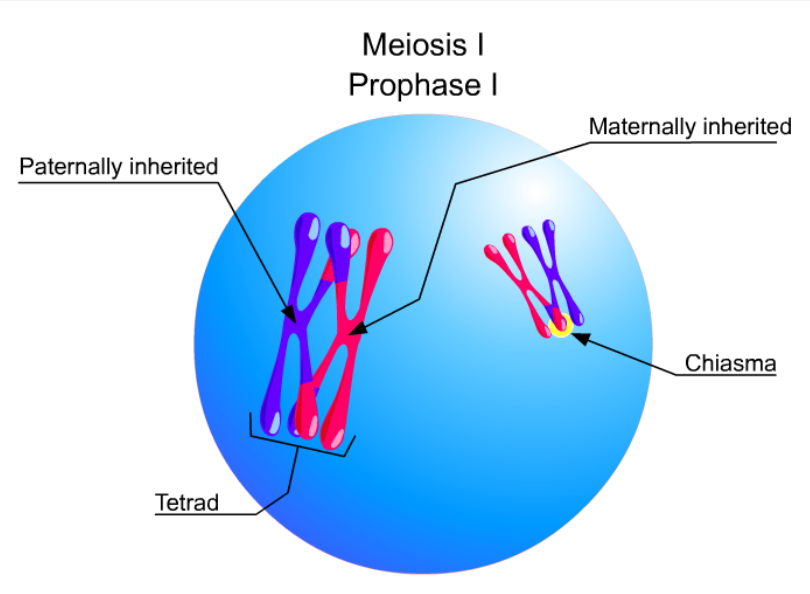


Note that the anaphase occurs once in mitosis and twice in meiosis

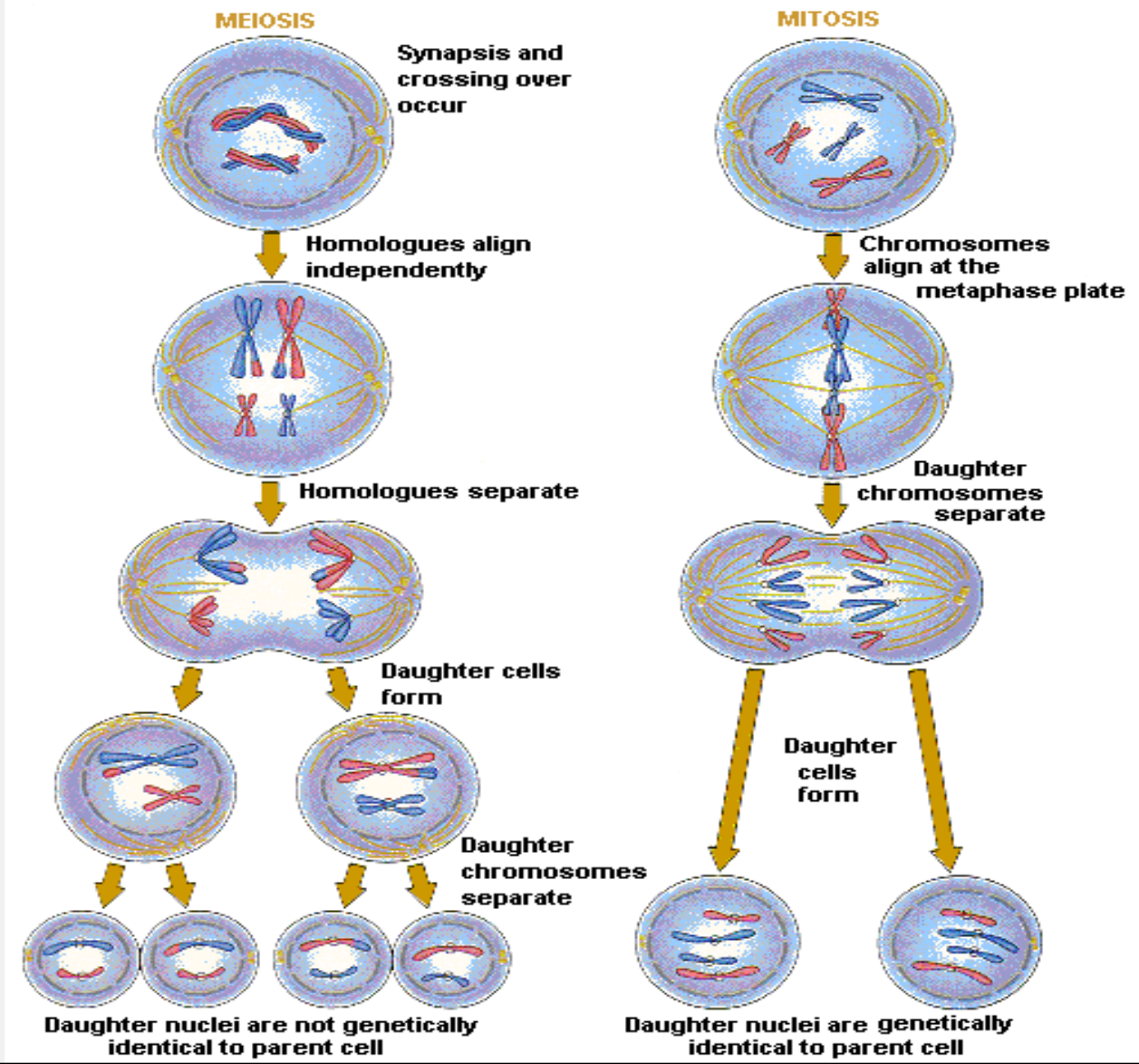
Meiosis



Normal Gametes → 4 Haploids



Meiosis Vs. Mitosis

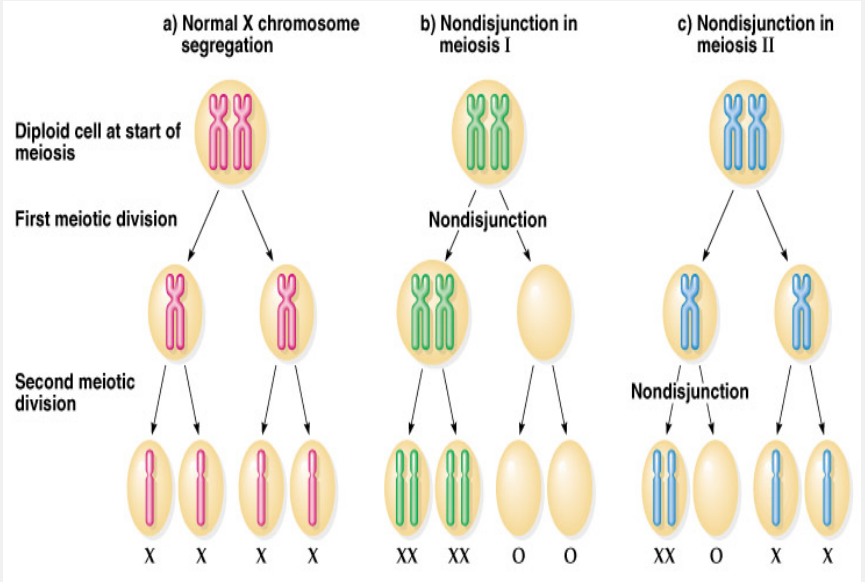


Non-disjunction in Meiosis

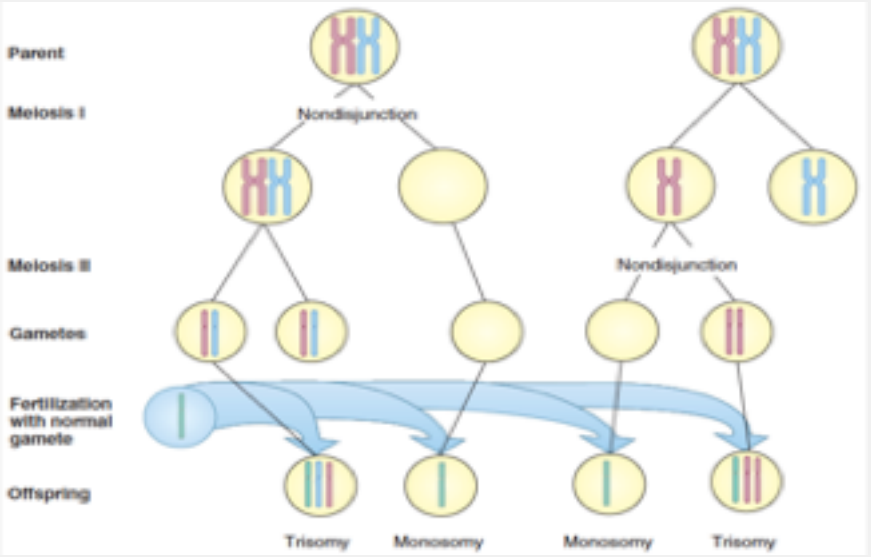
- The failure of chromosomes to disjoin normally **during meiosis phase 1 or phase 2**.
- Two chromosome homologs migrate to the same daughter cell instead of disjoining normally and migrating to different daughter cells.
- The result of this error is a cell with an imbalance of chromosomes (**Aneuploidy**)

A normal disjunction in first meiotic division produces 4 balanced gametes

Meiosis 1 produce: 2 diploid cells
Meiosis 2 produce: 4 haploid cells



- Can affect each pair of chromosomes
- is not a rare event
- Non disjunction in first meiotic division produces 4 unbalanced gametes.
- Non disjunction in second division produces 2 normal gametes & 2 unbalanced gametes:
- Gamete with an extra autosome
- Nullosomic gamete **(missing one chromosome)**

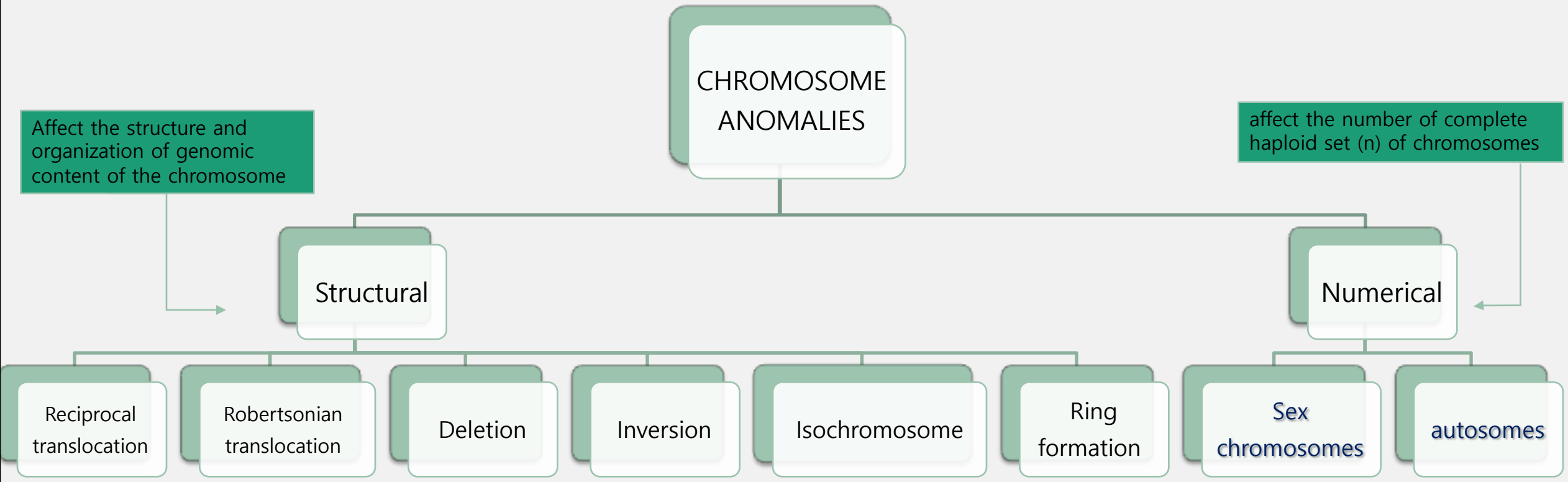


In meiotic nondisjunction
- This product of fertilization with normal gamete would be monosomic and trisomic offspring (**Aneuploidy**)

Presence of an abnormal number of chromosomes in a cell

Important information:
Nullosomic gamete : is missing one chromosome

CHROMOSOME ANOMALIES



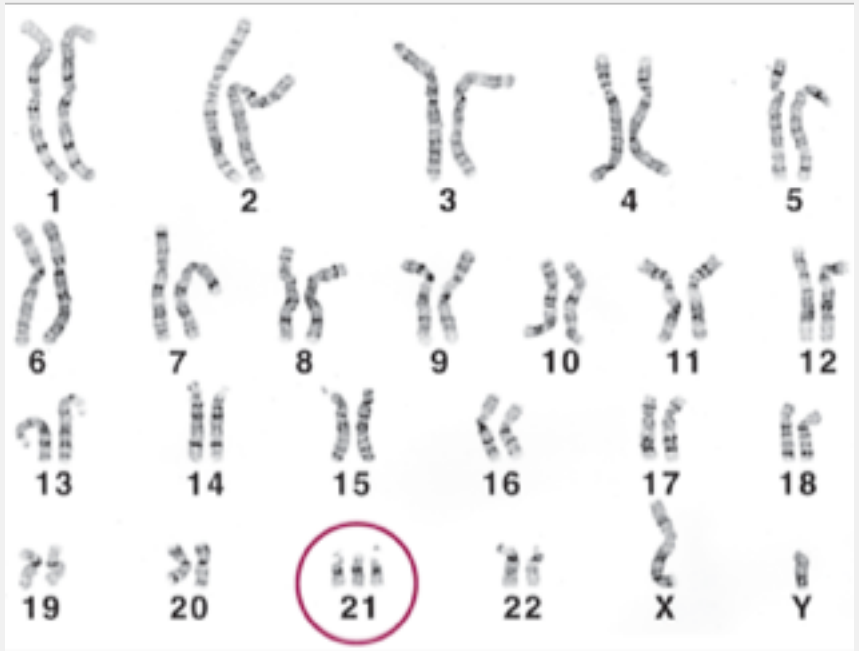
- In structural
The structure of the chromosome has been affected
- In numerical
Excess or loss of the chromosome

NUMERICAL CHROMOSOMAL ANOMALIES

Down syndrome, trisomy 21

Karyotype: 47, XY, +21

Numerical anomalies in autosomes



Autosomes:
chromosomes 1-22

NOTE: read it while you're drinking your coffee.

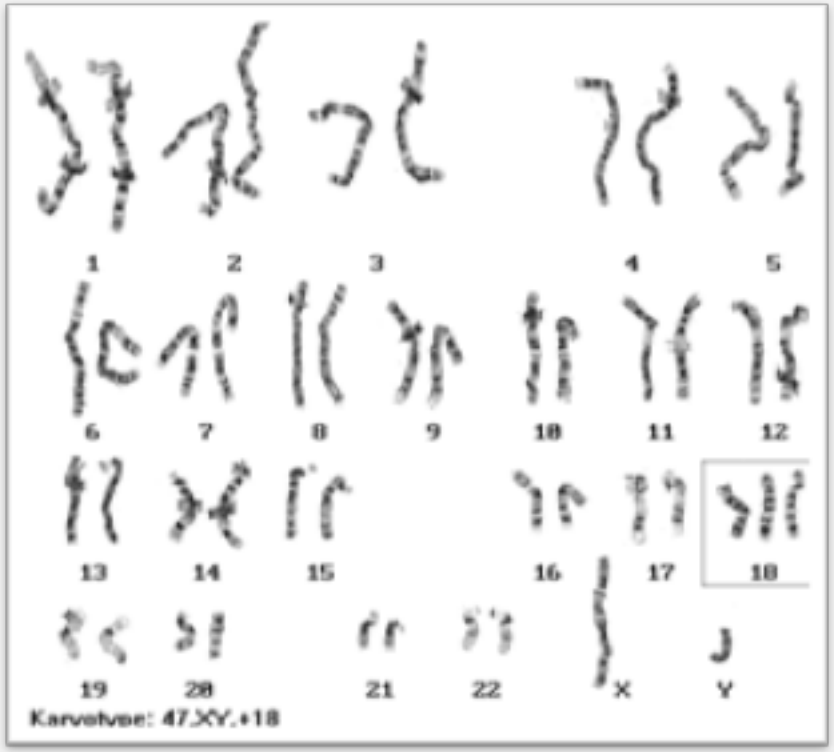
- Most cases arise from non disjunction in the first meiotic division
- The incidence of trisomy 21 rises sharply with increasing maternal age
- The father contributing the extra chromosome in 15% of cases
- The symptoms include characteristic facial dysmorphologies, and an IQ of less than 50.

Important information:
The doctor will give you the karyotype and he will ask you about the name of the syndrome Or the doctor will give you the name of the syndrome and he will ask you about the karyotype

Edward's syndrome, Trisomy 18

Karyotype: 47, XY, +18

Numerical anomalies in autosomes



NOTE: read it while you're drinking your coffee.

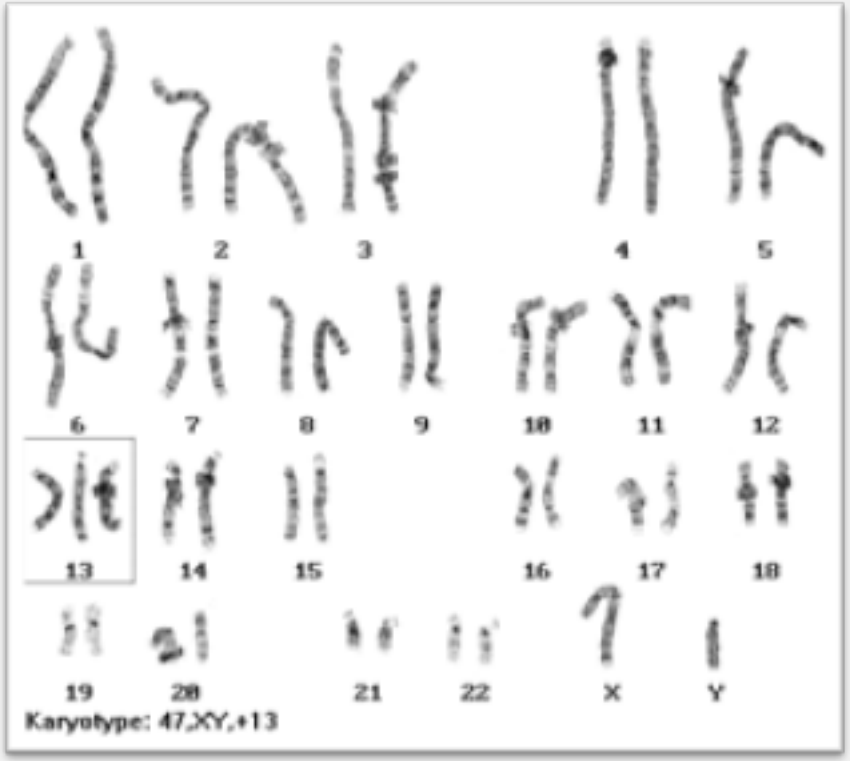
- the second most common autosomal trisomy, after Down syndrome.
- It occurs in around one in 6,000 live births.
- Most babies die in the first year and many within the first month & has a very low rate of survival.
- Common anomalies are heart abnormalities, kidney malformations, and other internal organ disorder.

Important information:
The doctor will give you the karyotype and he will ask you about the name of the syndrome Or the doctor will give you the name of the syndrome and he will ask you about the karyotype

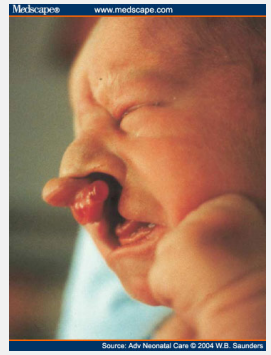
Patau Syndrome, Trisomy 13

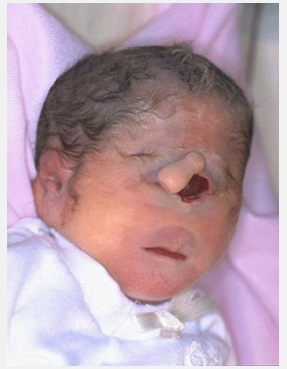
Karyotype: 47, XY, +13

Numerical anomalies in autosomes



In **Edward's syndrome** and **Patau Syndrome** there is a very low survival rate , because: the affected chromosome has an important function contributing with some vital organs





NOTE: read it while you're drinking your coffee.

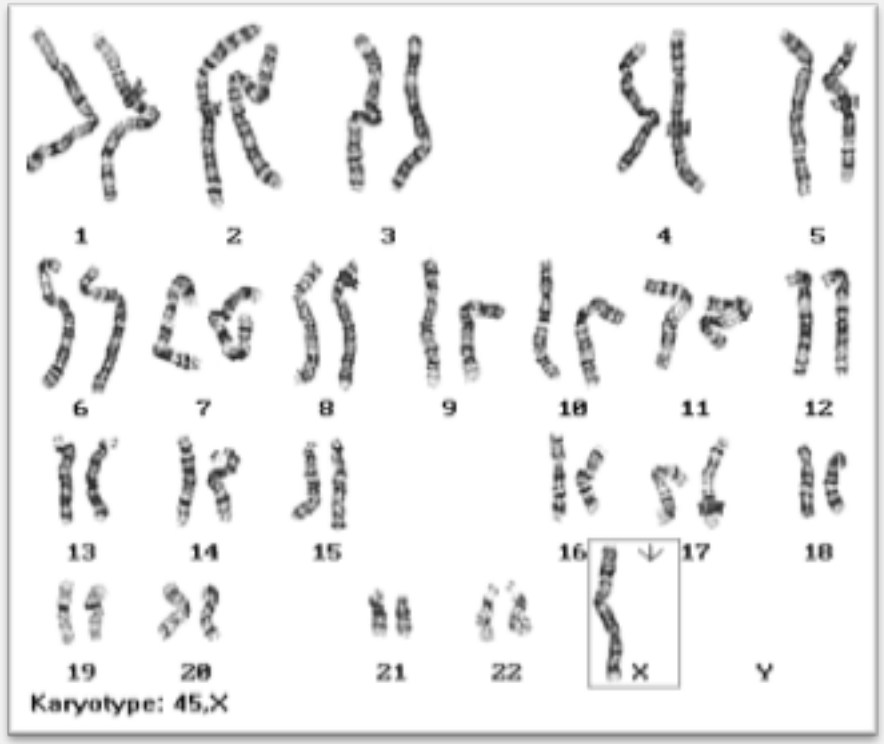
- 50 % of these babies die within the first month and very few survive beyond the first year.
- There are multiple dysmorphic features.

Most cases, as in Patau syndrome, involve maternal non-disjunction.

Important information:
The doctor will give you the karyotype and he will ask you about the name of the syndrome Or the doctor will give you the name of the syndrome and he will ask you about the karyotype

Monosomy X (Turner's syndrome, 45,XO)

Numerical anomalies in sex chromosomes



Sex chromosomes: chromosome 23

NOTE: read it while you're drinking your coffee.

- Occurring in 1 in 4000 phenotypic females
- As a result of paternal meiotic nondisjunction
- The only viable monosomy in humans
- Characteristics:

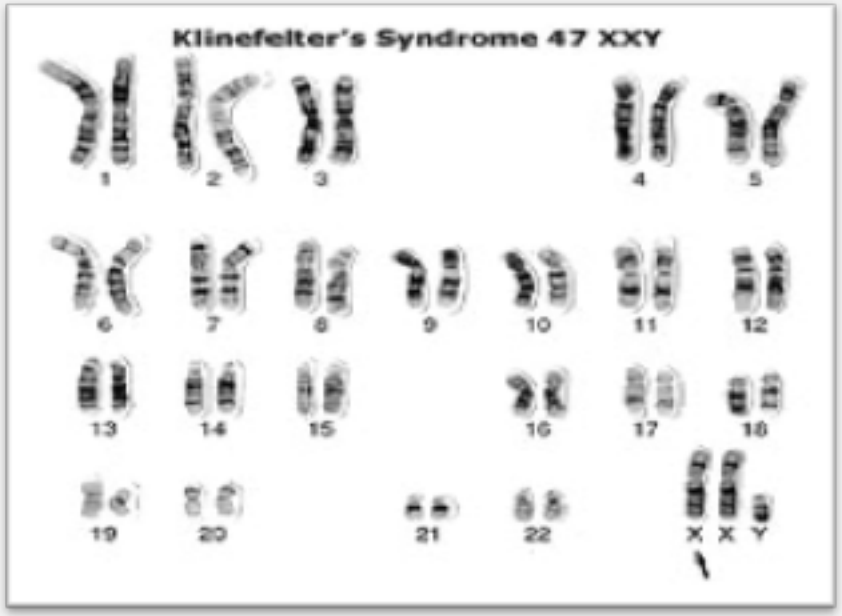
Webbed neck, Individuals are genetically female, not mature sexually, Sterile, Short stature, Broad chest, Low hairline, Streak ovaries, Normal intelligence, Normal life span

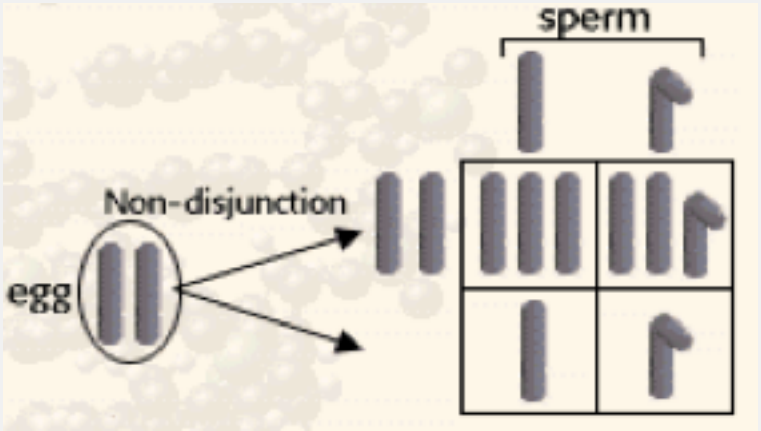
Streak = non developed

Important information:
NUMERICAL CHROMOSOMAL ANOMALIES of sex chromosomes has no affect on intelligence level

Klinefelter Syndrome: 47,XXY males

Numerical anomalies in sex chromosomes

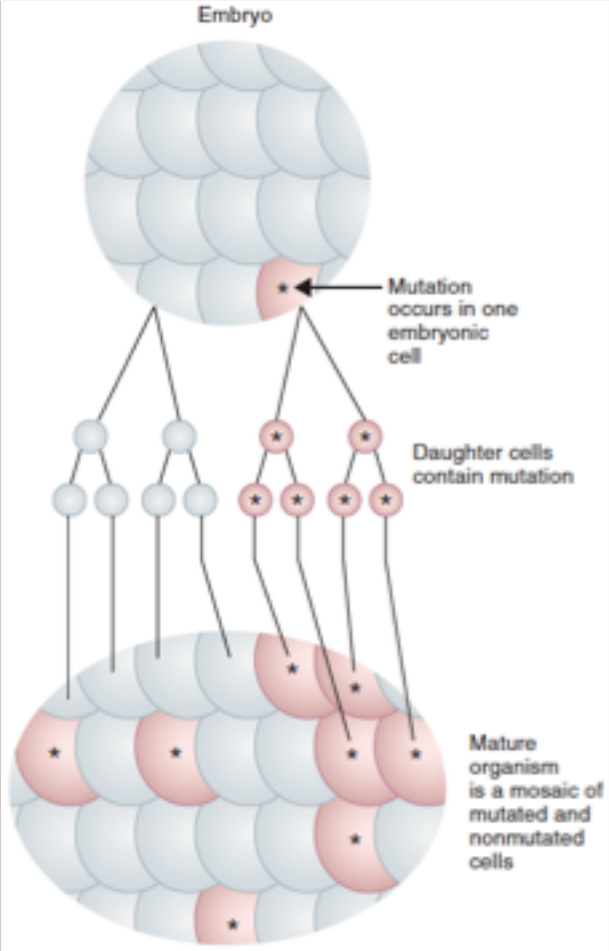




NOTE: read it while you're drinking your coffee.

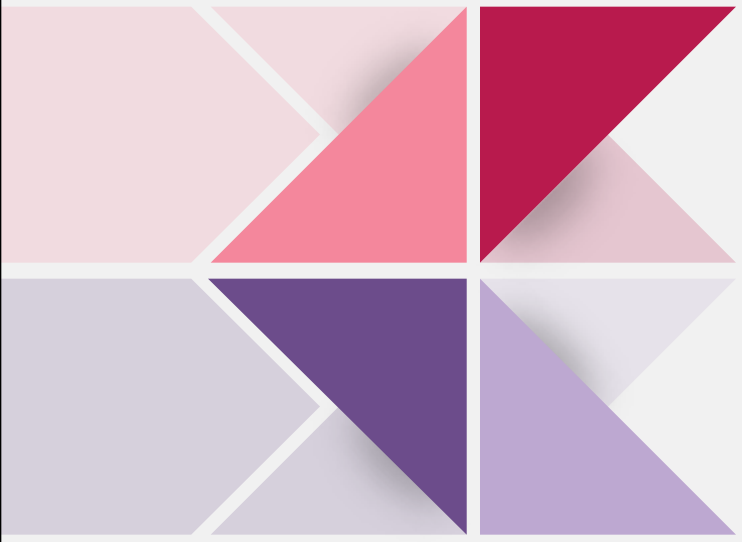
- 1/600 males
- Due to nondisjunction of X chromosomes during meiosis I in females
- Male sex organs; unusually small testes which fail to produce normal levels of testosterone→ breast enlargement (gynaecomastia) and other feminine body characteristic
- Patients are taller and thinner than average and may have a slight reduction in IQ but generally they have normal intelligence
- No spermatogenesis → sterile

MOSAICISM



Is The presence of more than one genetically distinct cell line in the body.

- 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 is the presence in an individual of two or more genetically distinct ce ll lines derive from more than one zygote (e.g. 2 sperms fertilize 2 ova → 2 zyg otes that fuse to form 1 embryo



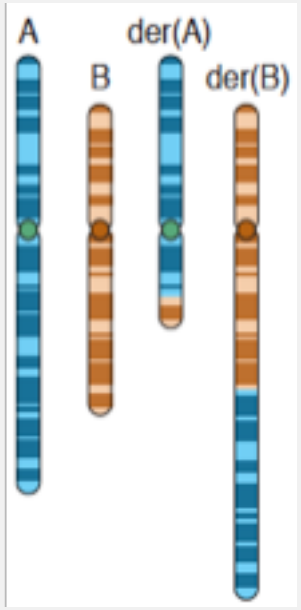
STRUCTURAL CHROMOSOMAL ANOMALIES

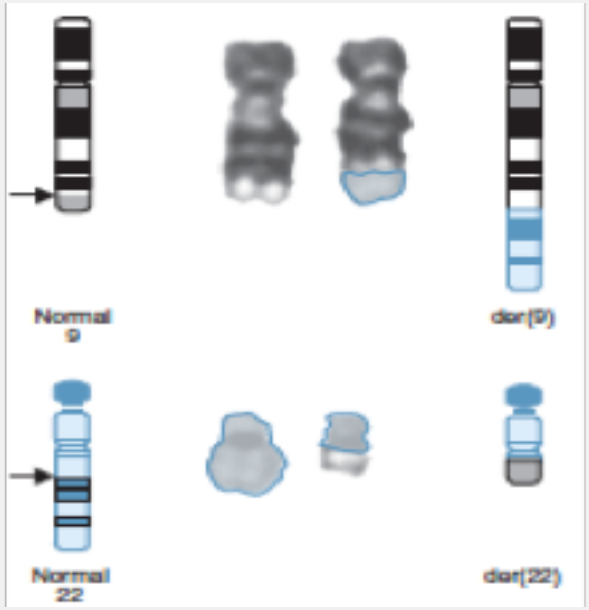
Reciprocal translocation

- Reciprocal translocation between chromosome 22 and the long arm of chromosome 9 (the Philadelphia chromosome).

  Reciprocal = Balance

- The occurrence of this translocation in hematopoietic cells can produce chronic myelogenous leukemia (CML)

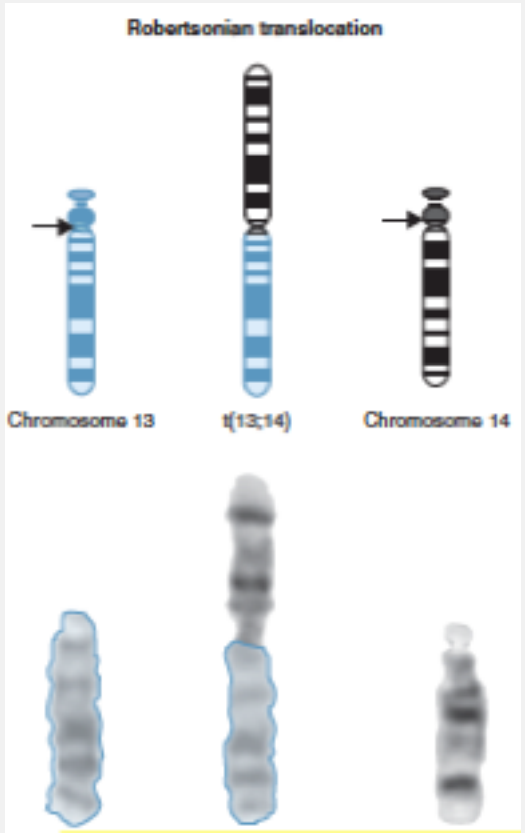




Important information:
Reciprocal translocation is exchanging parts between chromosomes (that why we call it balanced) : occur between chromosome 9 and 22

Robertsonian translocation

- Short arms of two non homologous chromosomes are lost and the long arms fuse at the centromere to form a single chromosome.
- Confined to the acrocentric chromosomes(13, 14, 15, 21, and 22).
- Although carriers have only 45 chromosomes in each cell, they are phenotypically unaffected

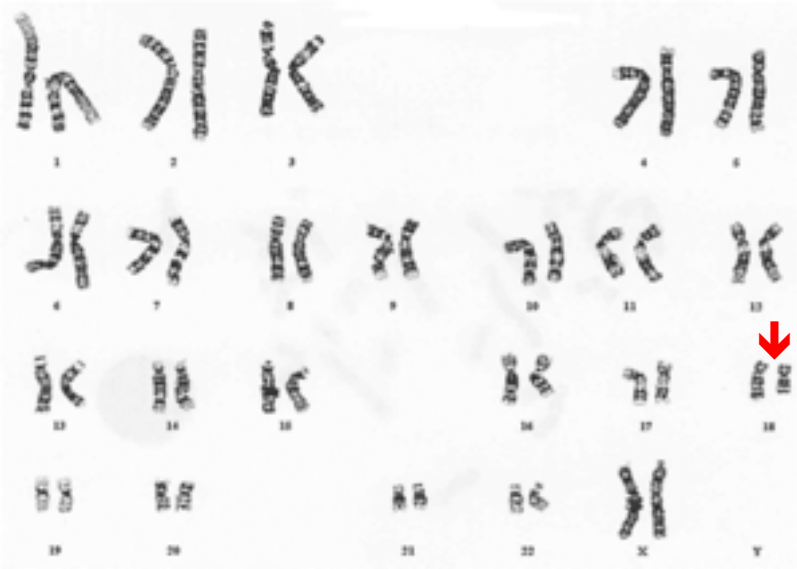


Deletion

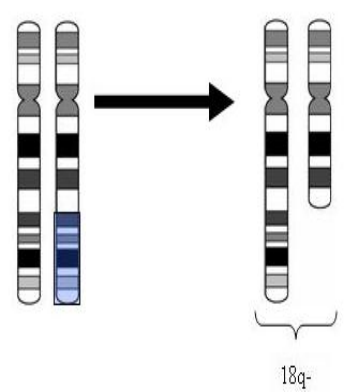
- Terminal deletion.
- Interstitial deletion.

- 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 therefore an unbalanced rearrangement.
- Indicated in nomenclature deletion.

Terminal deletion



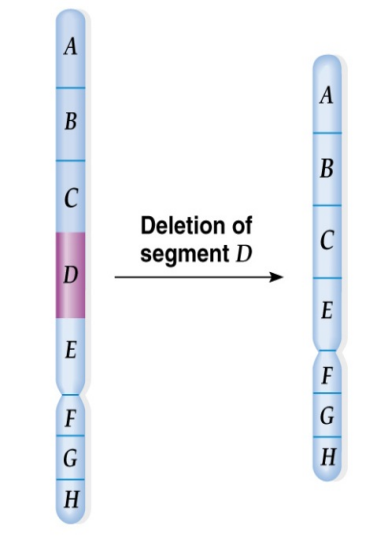
46,XX,del(18)(q21.3)

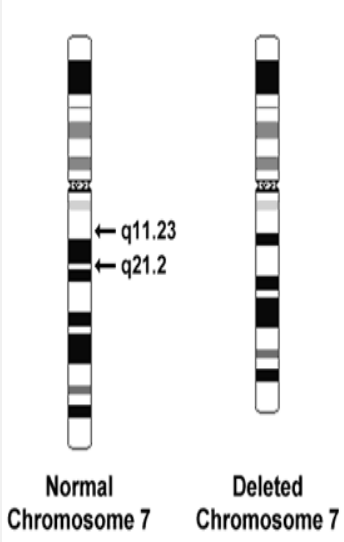


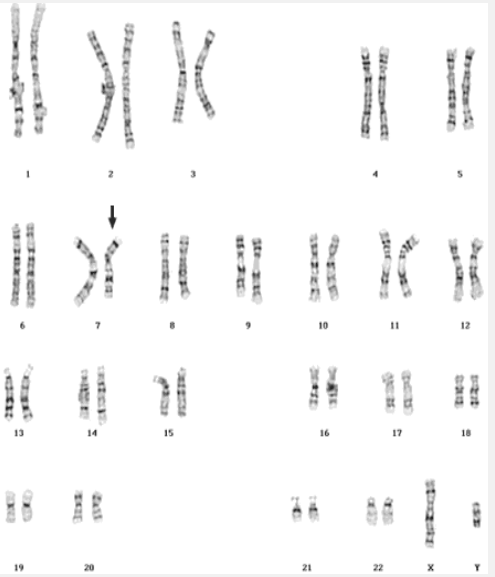
Interstitial deletion

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): breakpoints of the deleted segment.







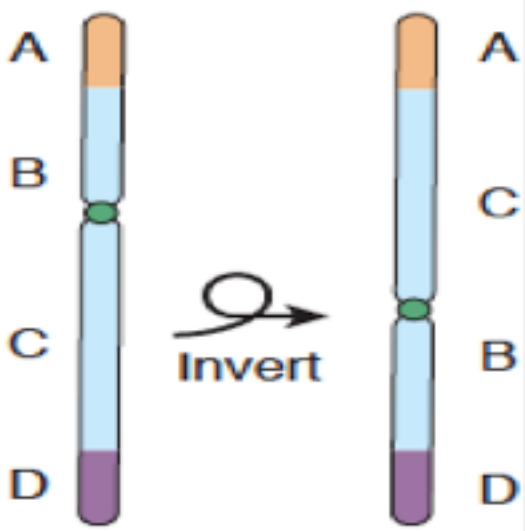
46,XY,del(7)(q11.23q21.2)

Inversion

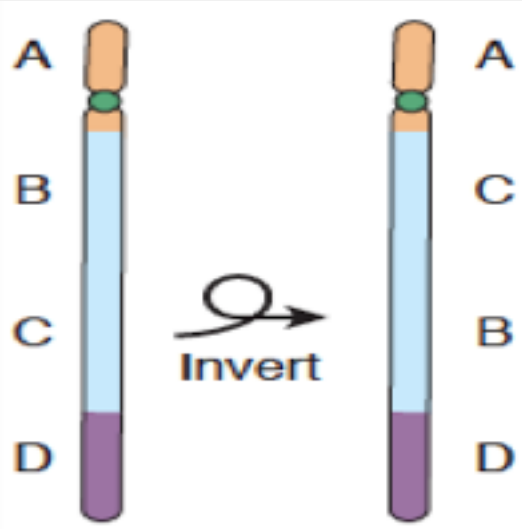
- Occurs when a segment of chromosome breaks, and rejoining within the chromosome effectively.
- Written in nomenclature as inv.
- Only large inversions are normally detected.

They are balance rearrangements that rarely cause problems in carriers.

Pericentric



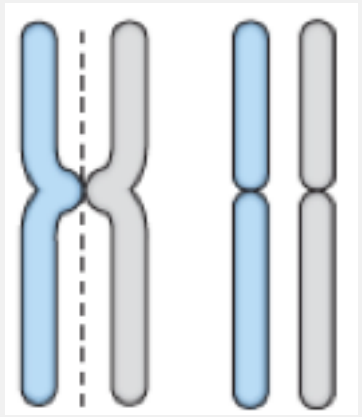
Paracentric



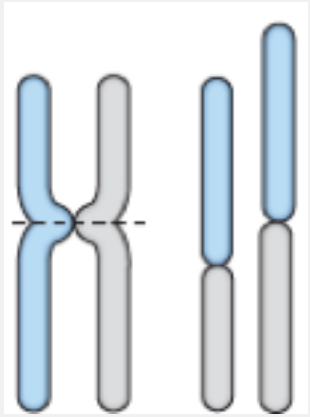
Isochromosome

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

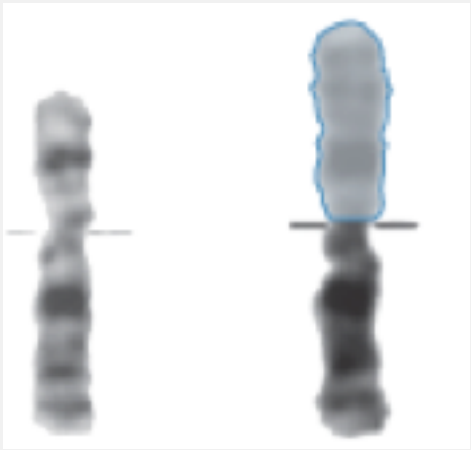
The chromosome will have 2 p arms or 2 q arms



Normal



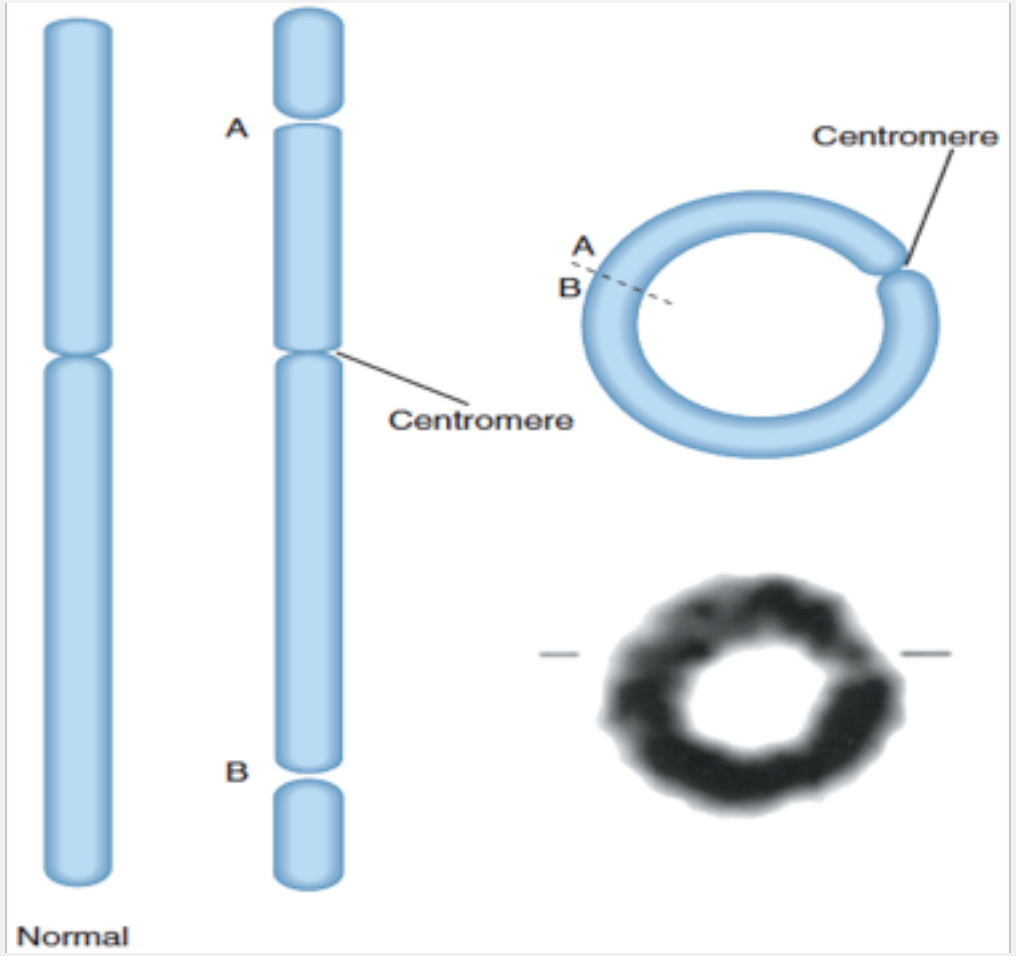
Isochromosome



Normal Isochromosome

Ring formation (Ring chromosome)

- A break on each arm of a chromosome
- Two sticky ends
- Reunion of the ends as a ring loss of the 2 distal c hromosomal fragments.
- Ring chromosomes are often unstable in mitosis



Important information

Important information:
Nullosomic gamete : is missing one chromosome

Important information:
NUMERICAL CHROMOSOMAL ANOMALIES of sex chromosomes has no affect on intelligence level

Important information:
The doctor will give you the karyotype and he will ask you about the name of the syndrome Or the doctor will give you the name of the syndrome and he will ask you about the karyotype

Important information:
Reciprocal translocation is exchanging parts between chromosomes (that why we call it balanced) : occur between chromosome 9 and 22

Quiz

1-Chromosomes condensed & line up at the _____ phase.			
A)metaphase	B)anaphase	C)prophase	D)telophase
2-**Edward's syndrome is characterized by**			
A)18 trisomy	B) 21 trisomy	C)13 trisomy	D)15 trisomy
3-The syndrome in which individual somatic cell contains only one x is			
A)turner	B)Edward	C)Klinefelter	D)Patau
4-Nuclear membrane dissolves at _____			
A)prophase	B)Metaphase	C)anaphase	D)telophase
5-chromosomes begin to condense at _____			
A)G1	B)G2	C)S	D) A and C

Answers: 1-B | 2-A | 3-A | 4-A |5-B

Thank You

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Special thanks to Team 437