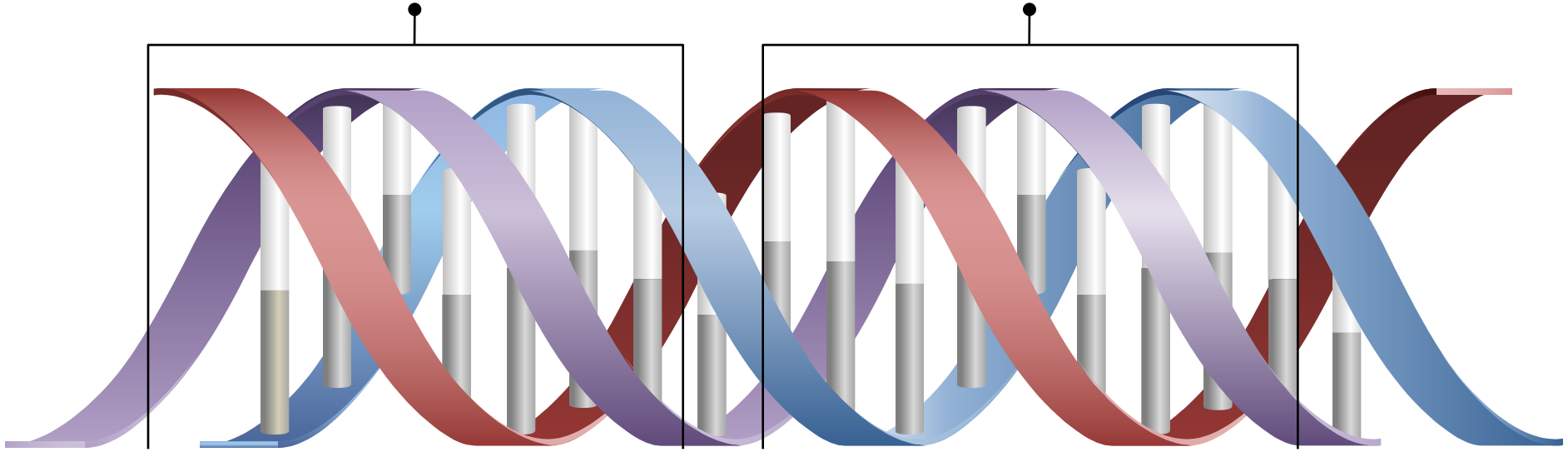
جامعة الملك سعود
King Saud University

Human Genetics 439

Lecture 2

CHROMOSOME ANOMALIES



Index color:

- Important
- Slides
- Notes
- Extra information

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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

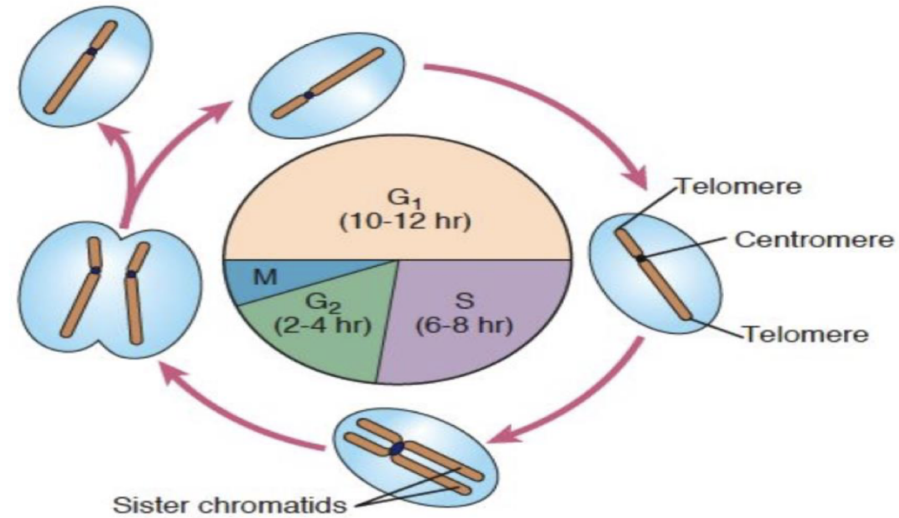
MITOSIS & MEIOSIS: TYPICAL MITOTIC CELL CYCLE

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

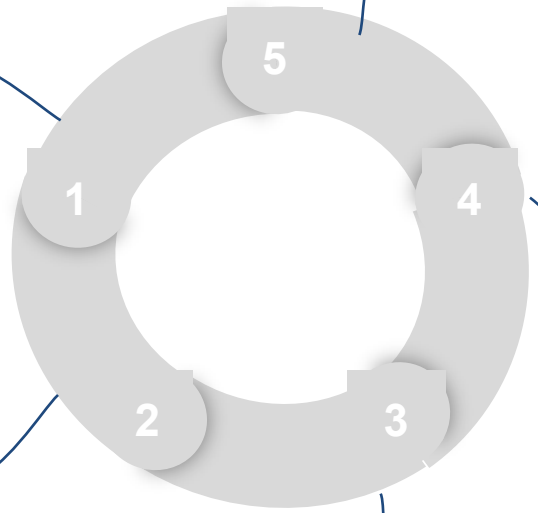
Prophase:

formation of mitotic Spindle & pair of centrosomes.

Prometaphase:

-Nuclear membrane dissolves.

- Chromosomes to disperse & attach by kinetochores to mitotic spindle microtubules.



Telophase:

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

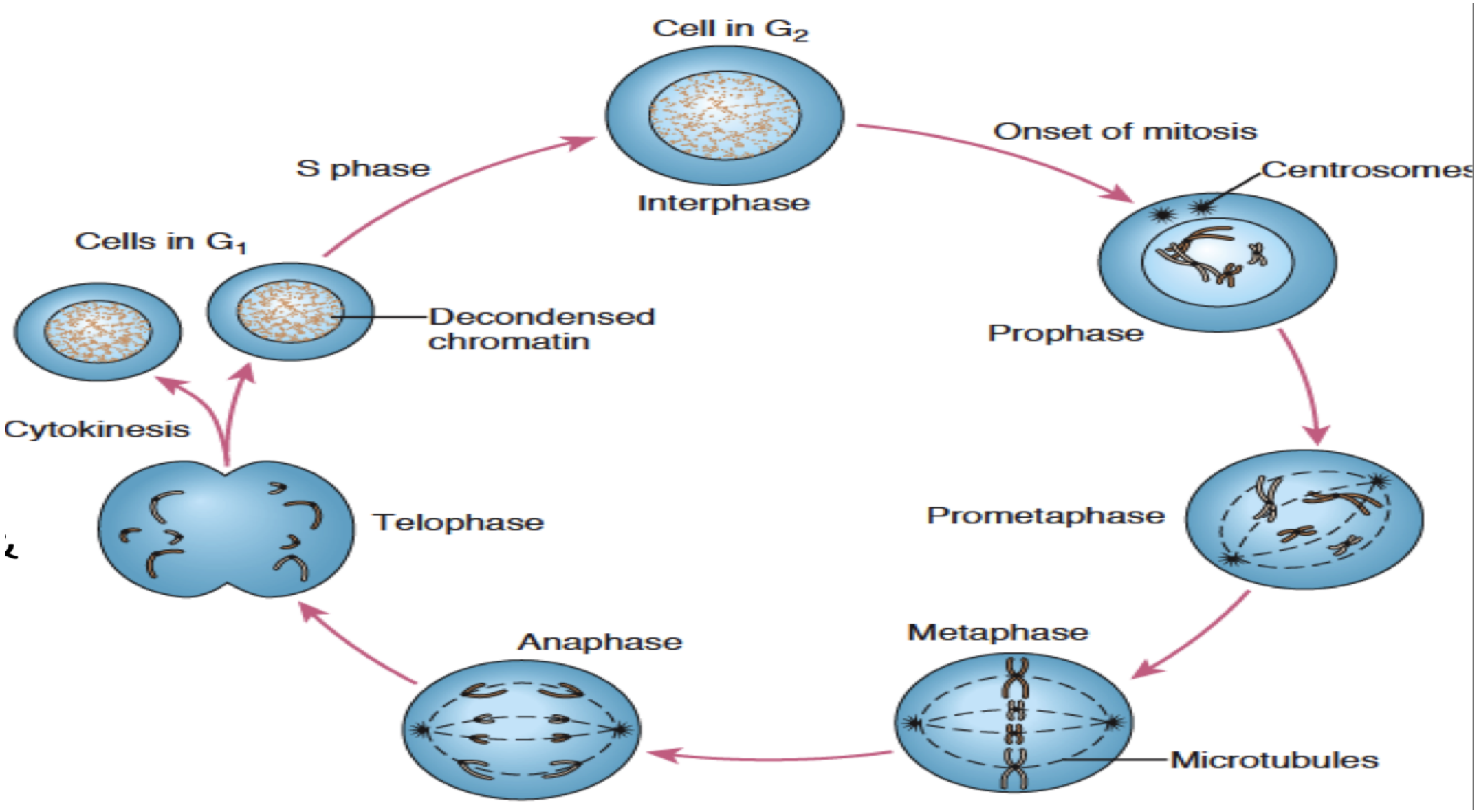
Anaphase:

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

Metaphase:

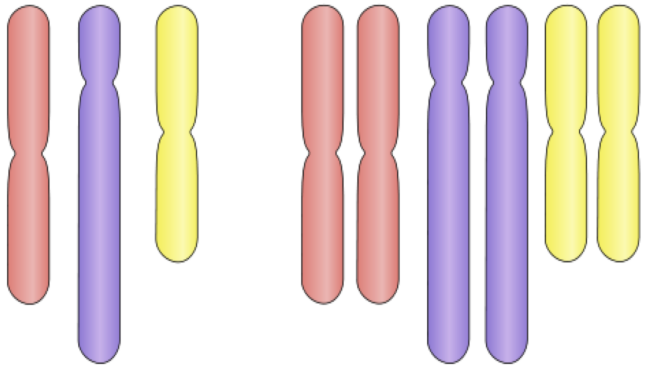
Chromosomes condensed & line up at the equatorial plane.

EVENTS OF MITOSIS

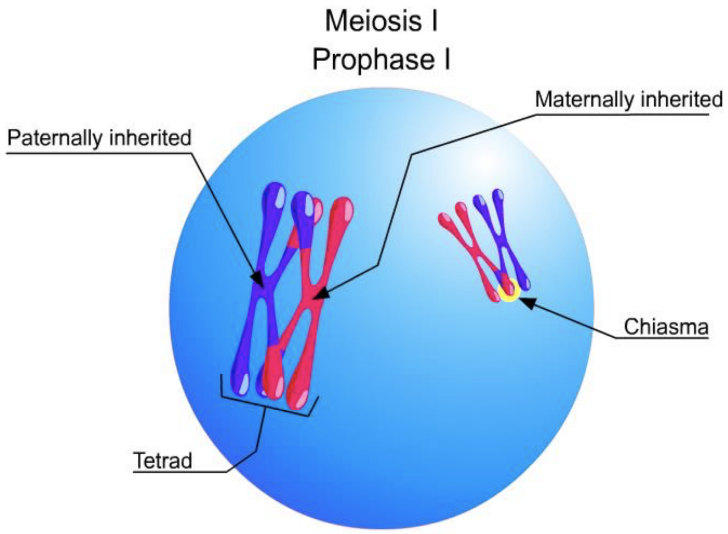


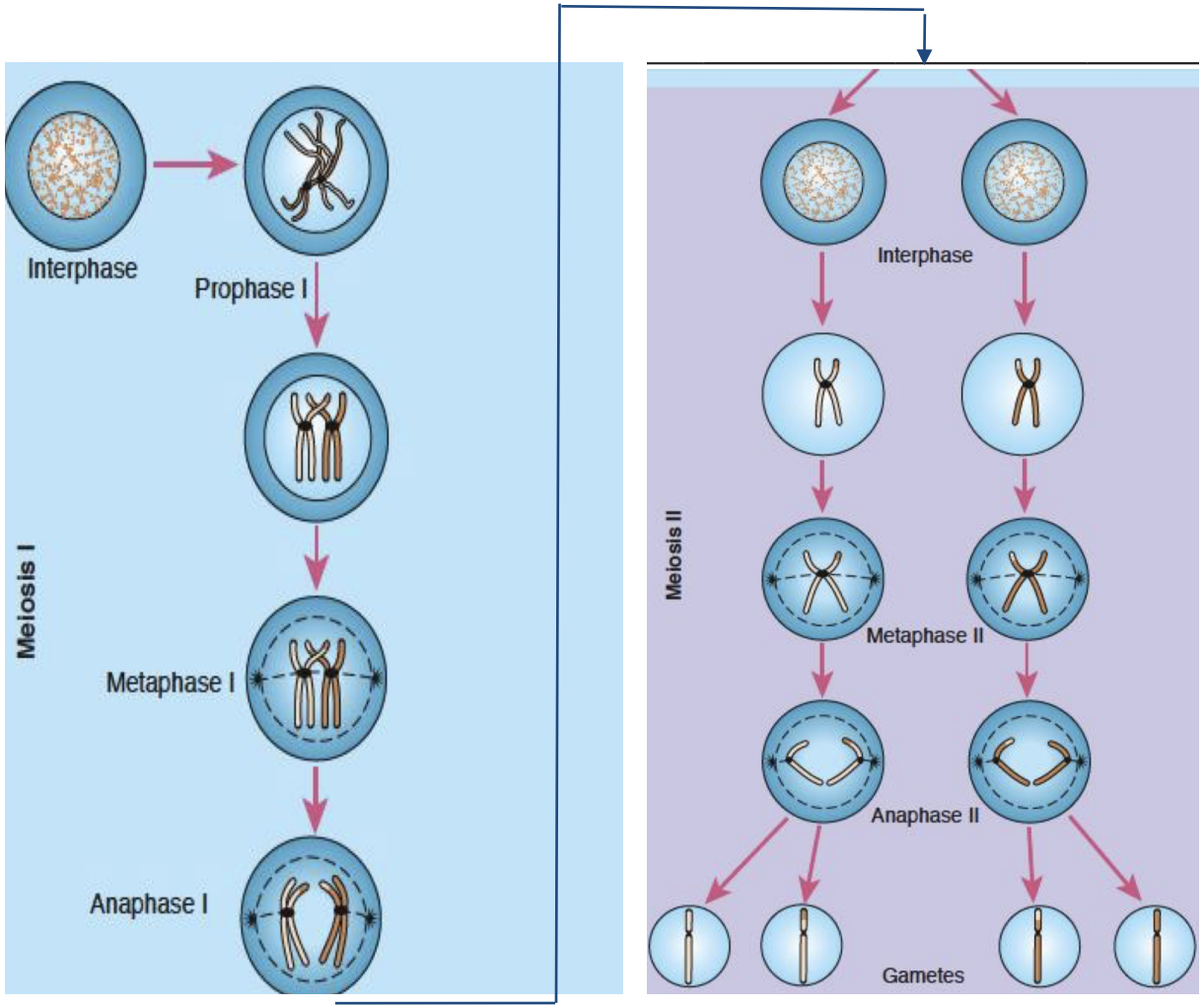
EVENTS OF MEIOSIS I & II

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



Normal Gametes → 4 Haploids





Events of meiosis
- Consists of two successive nuclear divisions .

- 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**

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NON-DISJUNCTION AND ITS IMPACT ON MEIOSIS

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)

Meiotic non-disjunction

Can affect each pair of chromosomes.

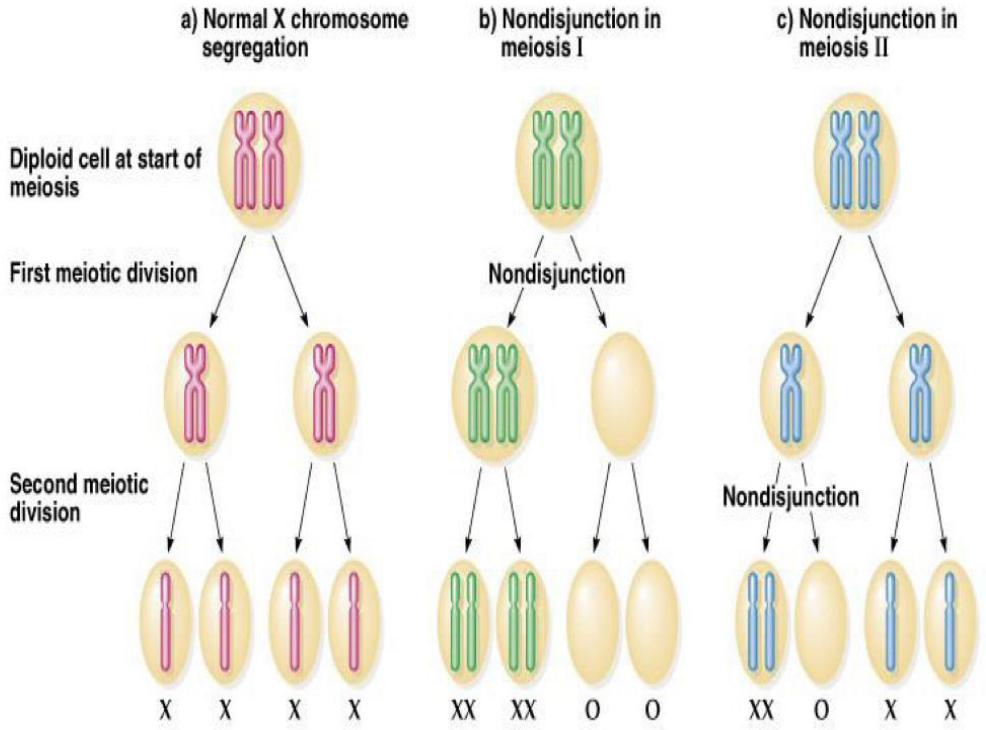
is not a rare event.

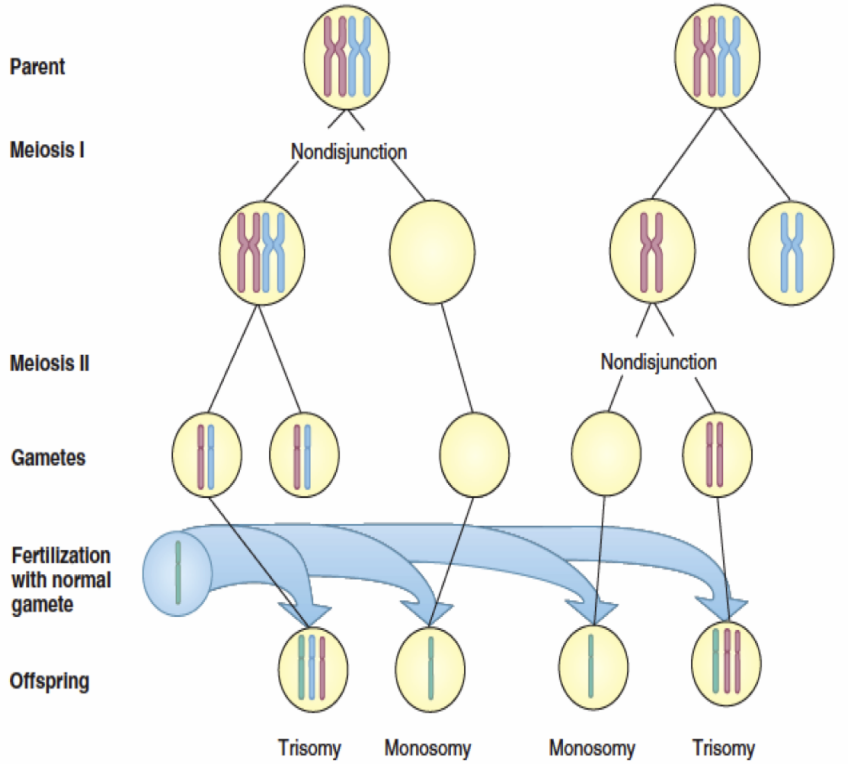
Non disjunction in first meiotic division produces 4 unbalanced gametes.

Non disjunction in second division produces 2 normal gametes & 2 unbalanced gametes:

- Gamete with an extra autosome.

- Nullosomic gamete (missing one chromosome)





In meiotic non-disjunction

- This product of fertilization with normal gamete would be monosomic and trisomic offspring (Aneuploidy).

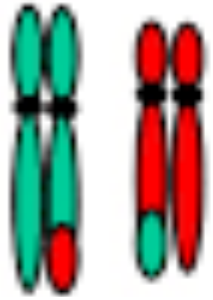
Types of chromosome anomalies

Numerical

affect the number of complete haploid set (n) of chromosomes.

Structural

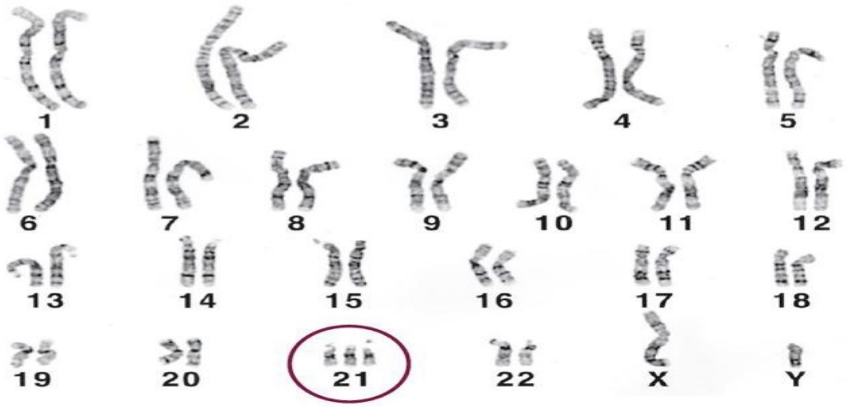
Affect the structure and organization of genomic content of the chromosome



NUMERICAL CHROMOSOMAL ANOMALIES
Numerical anomalies in autosome

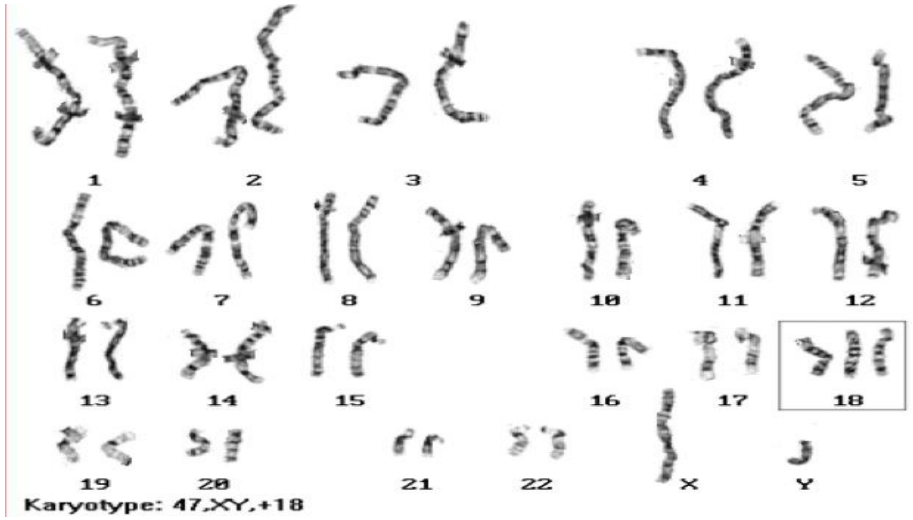
Down syndrome, trisomy 21
Karyotype: 47, XY, +21

- Most cases arise from nondisjunction 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.



Edward's syndrome, Trisomy 18
Karyotype: 47, XY, +18

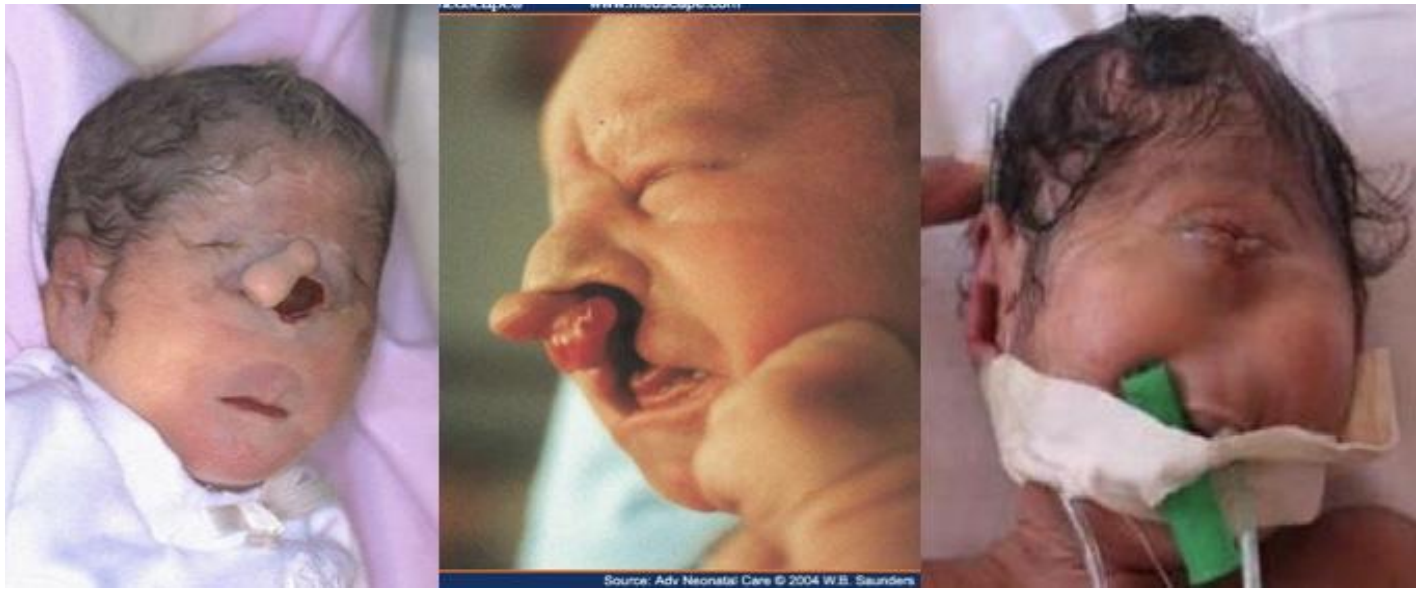
- the second most common autosomal trisomy, after Down syndrome - It occurs in around one in 6,000 live births - Most babies die in the first year and many within the first month & has a very low rate of survival
- Common anomalies are heart abnormalities, kidney malformations, and other internal organ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

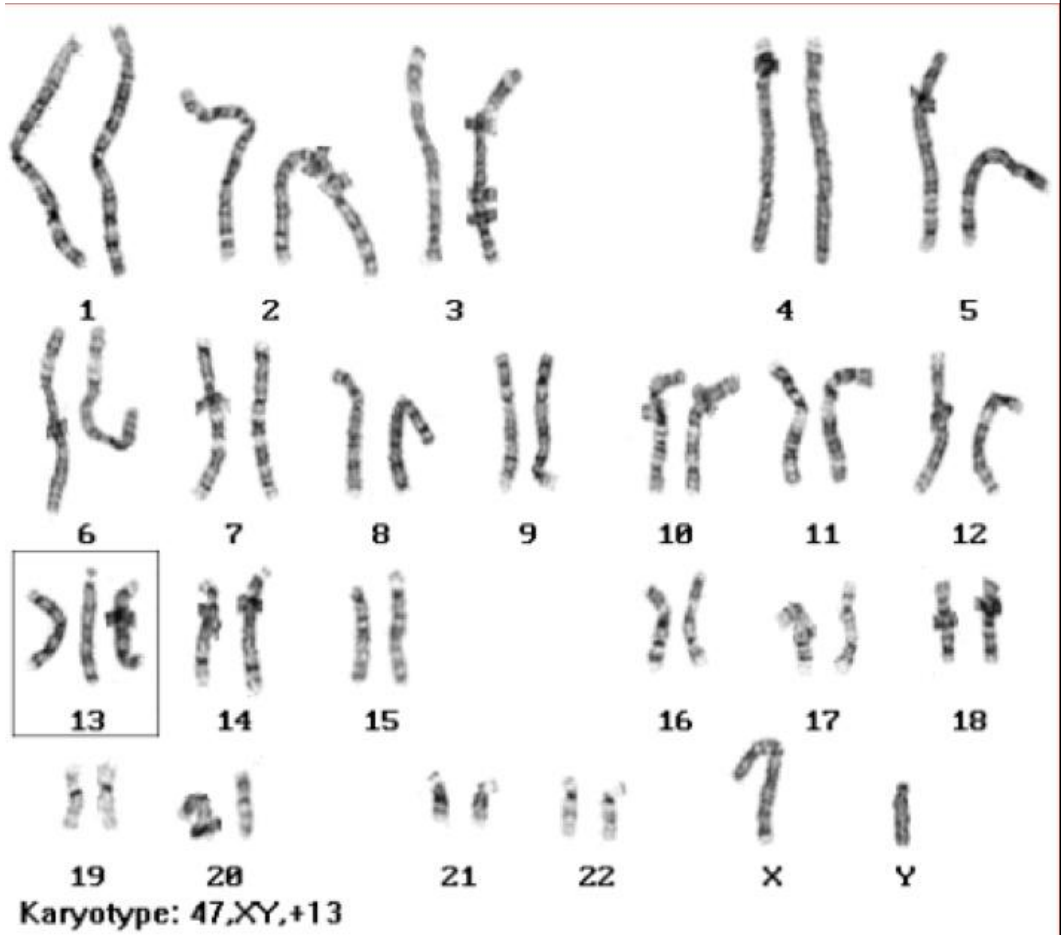


NUMERICAL CHROMOSOMAL ANOMALIES
Numerical anomalies in autosome

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 Patau syndrome, involve maternal non-disjunction.



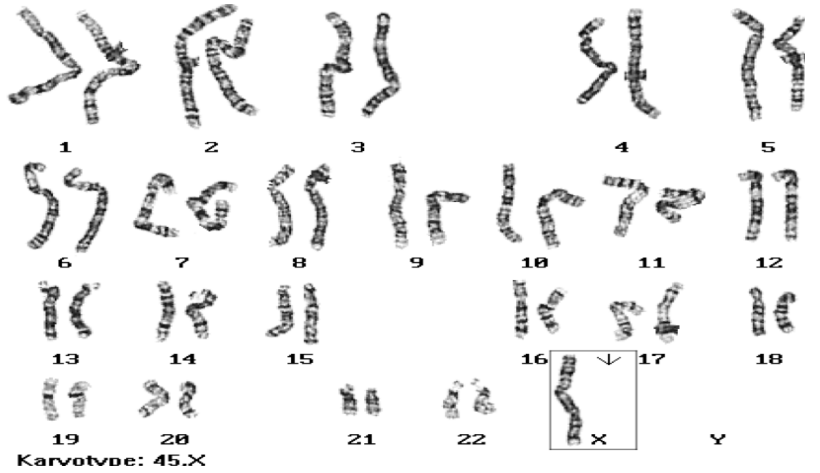


Numerical anomalies in sex chromosomes:

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

Occurring in 1 in 4000 phenotypic females

As a result of paternal meiotic nondisjunction



Note: NUMERICAL CHROMOSOMAL ANOMALIES of sex chromosomes has no effect on intelligence level

The only **viable** monosomy in humans

Characteristics

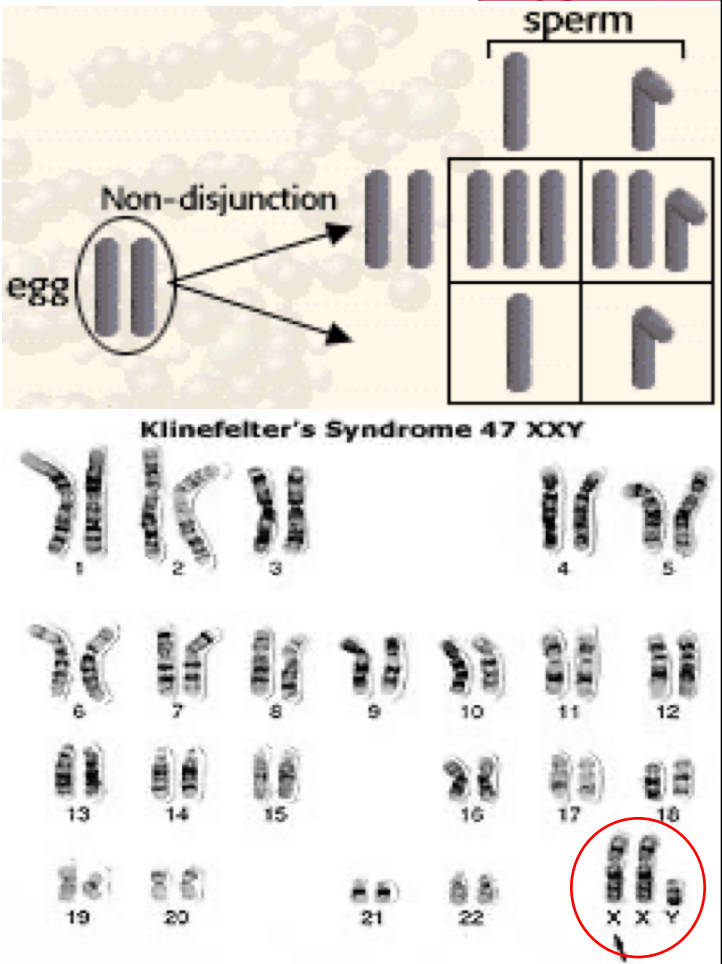
Webbed neck, Individuals are genetically female, not mature sexually, Sterile, Short stature, Broad chest, Low hairline, Streak ovaries, Normal intelligence, Normal life span

Numerical anomalies in sex chromosomes:
Klinefelter Syndrome: 47,XXY males

- 1/600 males

-Due to nondisjunction of X chromosomes during meiosis I in females

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



Male sex organs;

unusually small testes which fail to produce normal levels of testosterone -> **breast enlargement (gynaecomastia)** and other feminine body characteristic

No spermatogenesis

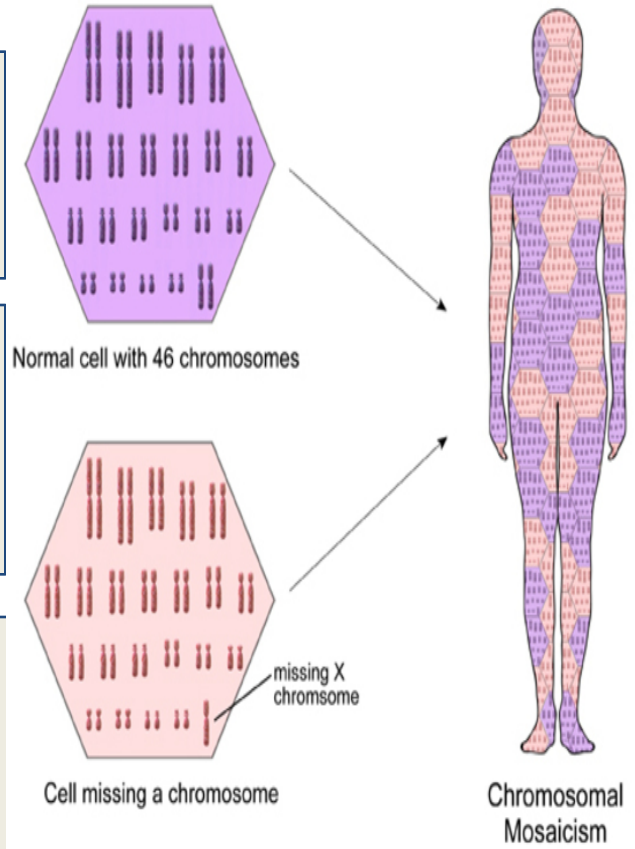
-> Sterile

MOSAIC

It is the presence of more than one genetically distinct line in the body.

A mosaic individual is made of 2 (or more) cell population coming only from **1 zygote**. .

It 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.

must not be confused with a chimera.

chimerism is the presence in an individual of two or more genetically distinct cell lines derived **from more than one zygote**.(e.g. 2 sperms fertilize 2 ova then the 2 zygotes fuse to form 1 embryo).

STRUCTURAL CHROMOSOMAL ANOMALIES

Reciprocal translocation:

An example is between chromosome 22 and the long arm of chromosome 9 (the Philadelphia chromosome).

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

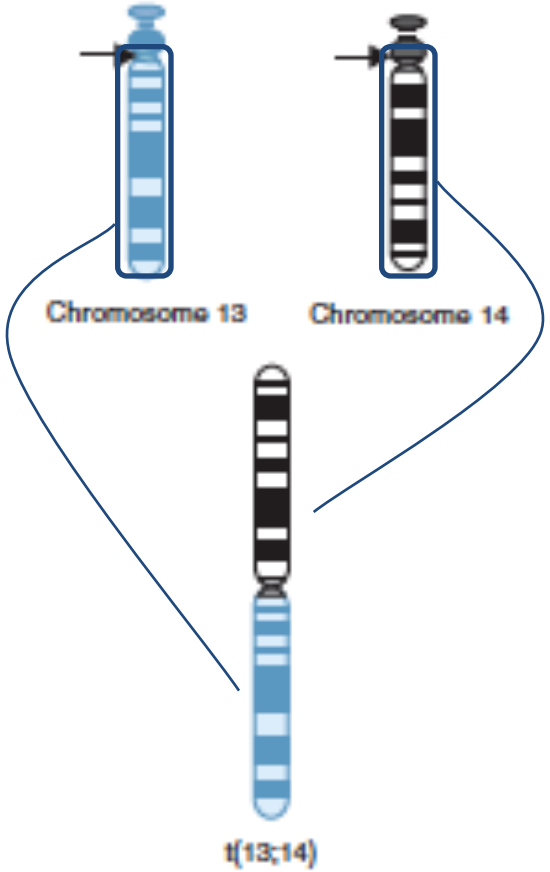
(green boxes translocate together, yellow boxes translocate together)

Robertsonian translocation:

the short arms of two non-homologous chromosomes are lost and the long arms fuse and the long arms fuse at the centromere to form a single chromosome.

It is 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

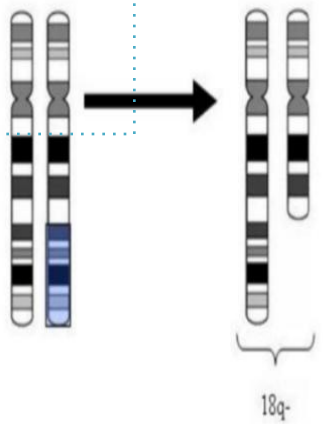
Loss of a segment from a chromosome, either terminal or interstitial.

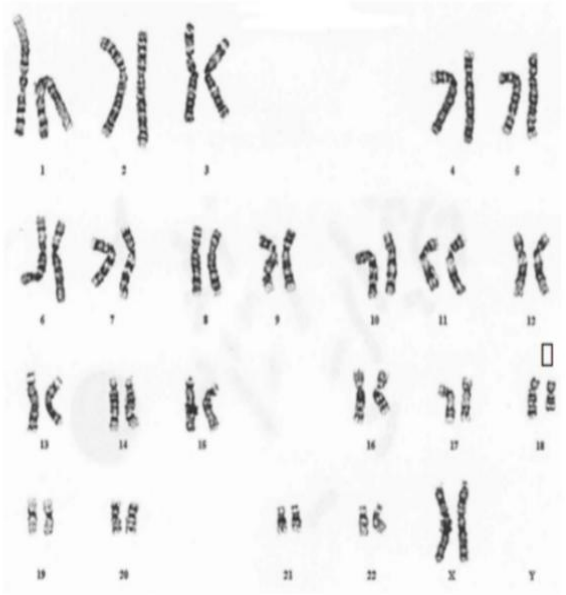
Invariably, but not always, results in the loss of important genetic material.

Deletion is therefore an unbalanced rearrangement.

Indicated in nomenclature del

Terminal deletion





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

karyotype description is as follows:

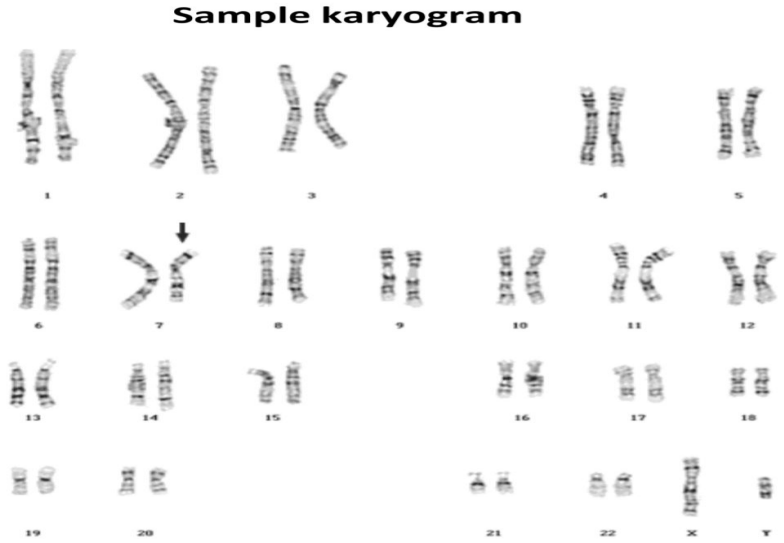
1- 46: the total number of chromosomes.

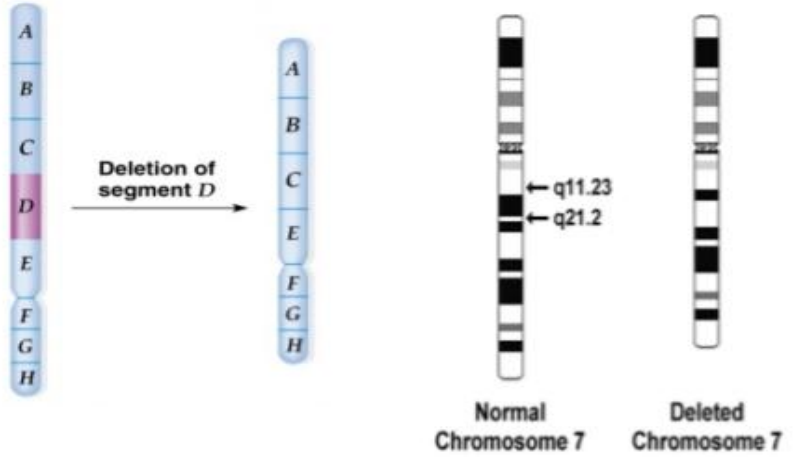
2- XY: the sex chromosomes (male).

3- del(7): deletion in chromosome 7.

4- (q11.23q21.2): breakpoints of the deleted segment.

interstitial deletion





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

Inversion

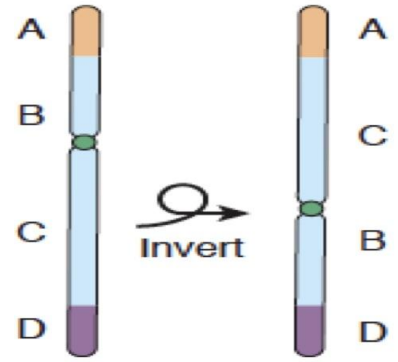
Occurs when a segment (piece) of chromosomebreaks and rejoining with the chromosome effectively

Written in nomenclature as inv.

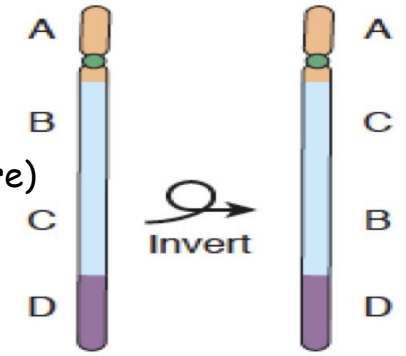
Only large inversions are normally detected.

(they are balance rearrangements that rarely cause problems in carriers)

Pericentric
(includes centromere)



Paracentric
(doesn't include centromere)



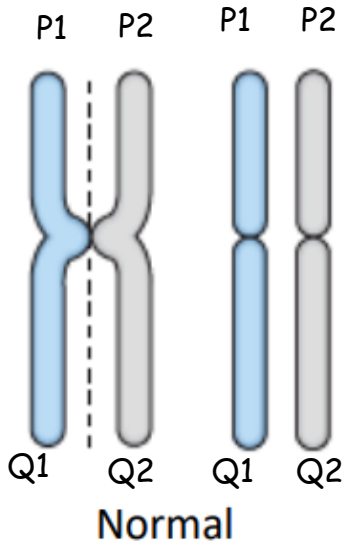
Note: the difference between peri/para is that
Peri: includes centromere in inverted part.
Para: doesn't include the centromere.

ISOCHROMOSOME

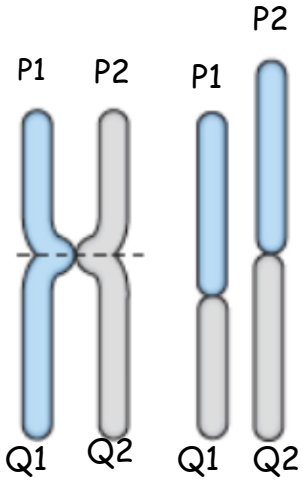
The most probable explanation for isochromosome is that the centromere has divided transversely rather than longitudinally

one chromosome will have 2 "p arms" while the other have 2 "q arms"(team438"edited")

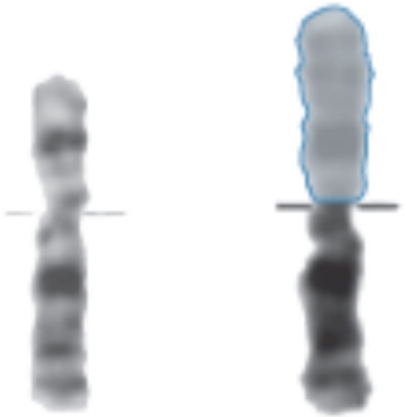
P1: P arm of chromosome 1.
P2: P arm of chromosome 2.
Q1: Q arm of chromosome 1.
Q2: Q arm of chromosome 2.



Normal



Isochromosome


Normal Isochromosome

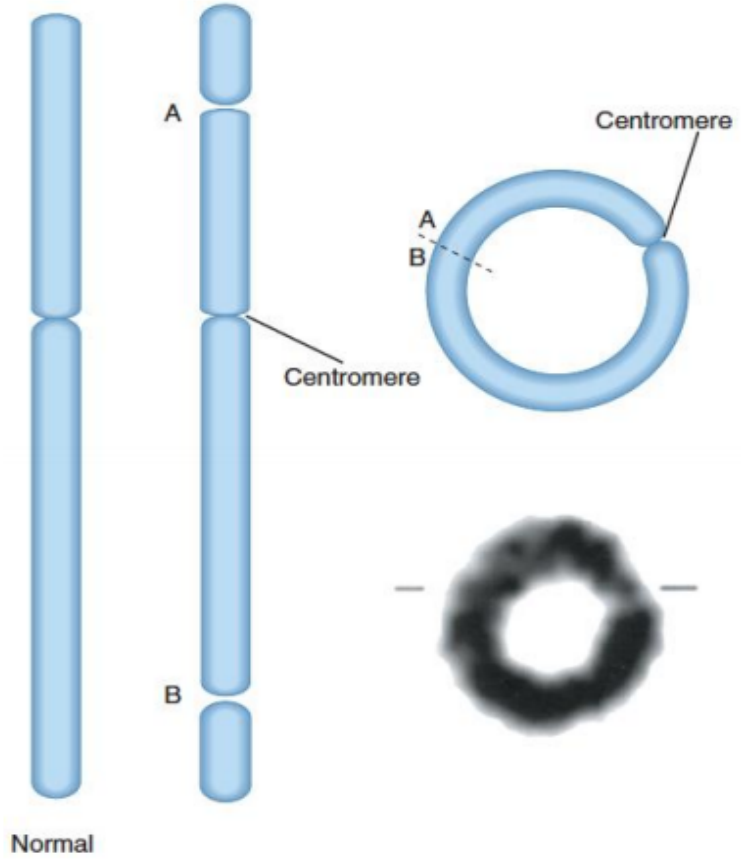
RING FORMATION (RING CHROMOSOME)

A break on each arm of a chromosome.

Two Sticky ends.

Reunion of the ends as a ring loss of the 2 distal chromosomal fragments.

Ring chromosomes are often unstable in mitosis.



Chromosome anomalies	Numerical	Autosome	Down's, Edward's & patau's syndromes
		Sex chromosome	Turner's & Klinefelter's syndromes
		Mosaicism	_____
		Chimerism	_____
	Structural	Translocation	_____
		Isochromosome	_____
		Ring	_____
		Deletion	Terminal
			Interstitial
		Inversion	Pericenteric
			Paracenteric

TAKE HOME MESSAGES

- Chromosome abnormalities can be numerical or structural.
- Normal meiotic division result in four haploid gametes
- In trisomy, a single extra chromosome is present, usually as a result of non-disjunction in the 1st or 2nd meiotic division.
- Mosaicism arize from one zygote while Chimera from the fusion of two fertilized eggs
- Structural abnormalities include translocations (balanced or unbalanced), inversions, deletions, isochromosome & rings.

MCQs

Q1)What are the common numerical sex chromosome disorders?			
A)Turner's	B)22+X	C)22+Y	D)Meiosis
Q2)After fertilization the only type of division for cells is?			
A)Meiosis 1	B)Meiosis 2	C)interphase	D)mitosis
Q3)What are the results of meiosis?			
A)23+X or Y	B)46	C)22+ X or Y	D)22+XXorYY
Q4)What are the results of mitosis?			
A)23+XorY	B)23	C)44+XX or XY	D)45

MCQs answers

1)A
2)D
3)C
4)C

Q5)Where does the mitotic error occur?			
A)Whole cell	B)mitosis	C)meosis	D)Part of the cell population
Q6)Where does the meiotic error occur?			
A)All the cell population	B)Part of the cell population	C)Meiosis 2	D)Mitosis
Q7)State the type gametes in fertilization (What sperm and what egg) for non viable cell condition?			
A)Sperm Y	B)Egg null X and sperm X	C)Egg null X and sperm Y	D)Egg X
Q8) Types of acrocentric chromosomes (Robertsonian translocation) are :			
A)10-11-12-20-21	B)13-14-15-21-22	C)1-2-3-4-5	D)6-7-8-9-21

MCQs

MCQs answers

5)D
6)A
7)C
8)B

Boys team:

- Ahmed AlKhawashki
- Nawaf Alghamdi
- Bassam Alasmari
- Rayan Alzahrani
- Khalid Alosaimi
- Abdulrahman Alsawwat
- Faisal AlFadel
- Hadi Alhemsi
- Hisham Alsaqabi
- Yazeed Alomar
- Mohammed Hajji
- Badr Alshahrani
- Homod Alqadeb

Girls team:

- Ghaida Alasiri
- Arwa Alqahtani
- Albandri Ahmad
- Aljohara Albnyan
- Aljohara alshathry
- Alanoud Alshahrani
- Raghad Alasiri
- Renad Alhmidi
- Sara Alharbi
- Taif Almutari
- Abeer Awad
- Ghada Alabdi
- Noura Almassad
- Hind Almotywea

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#Editing file

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