جامعة الملك سعود
King Saud University

HUMAN GENETICS

Color index:
- Important
- Slides
- Drs' notes
- Explanation
- New terminology

LECTURE 2:
Chromosomal anomalies

EDITION FILE

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

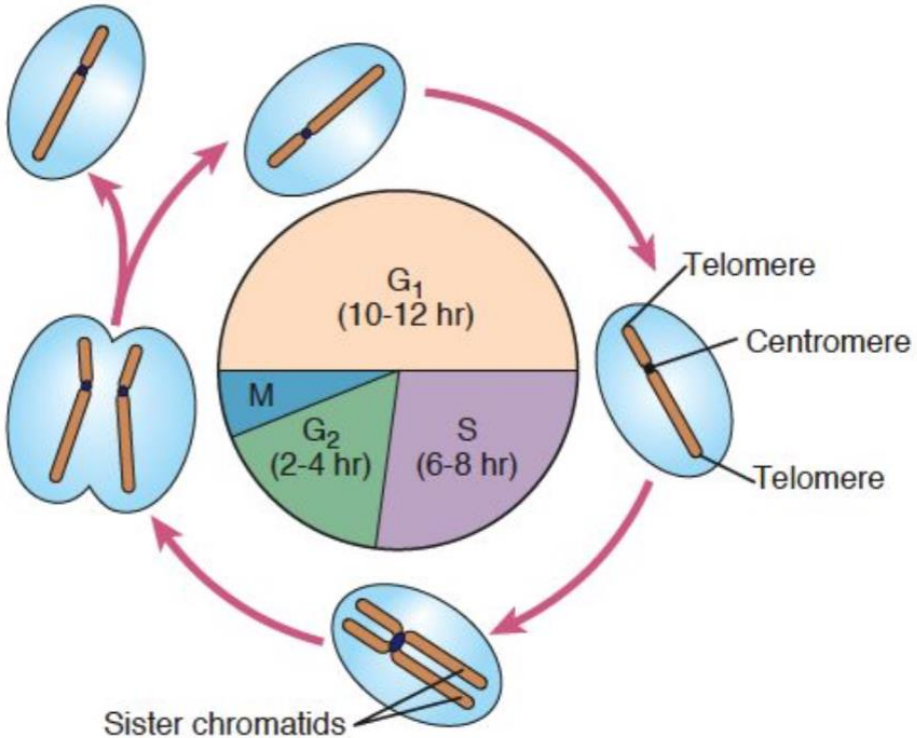
- 3a Understand the common numerical autosomal disorders: trisomies 21, 13, 18.

- 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.

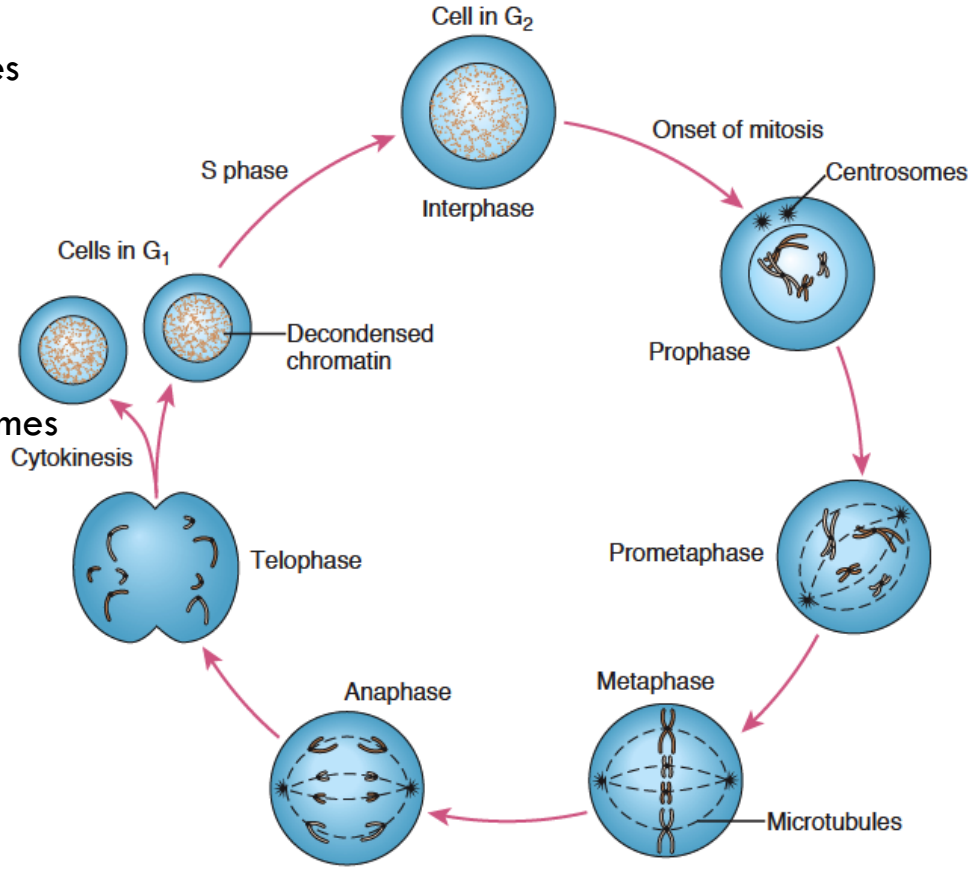
Chromosomes condensed & line up at the equatorial plane

Anaphase.

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

Telophase.

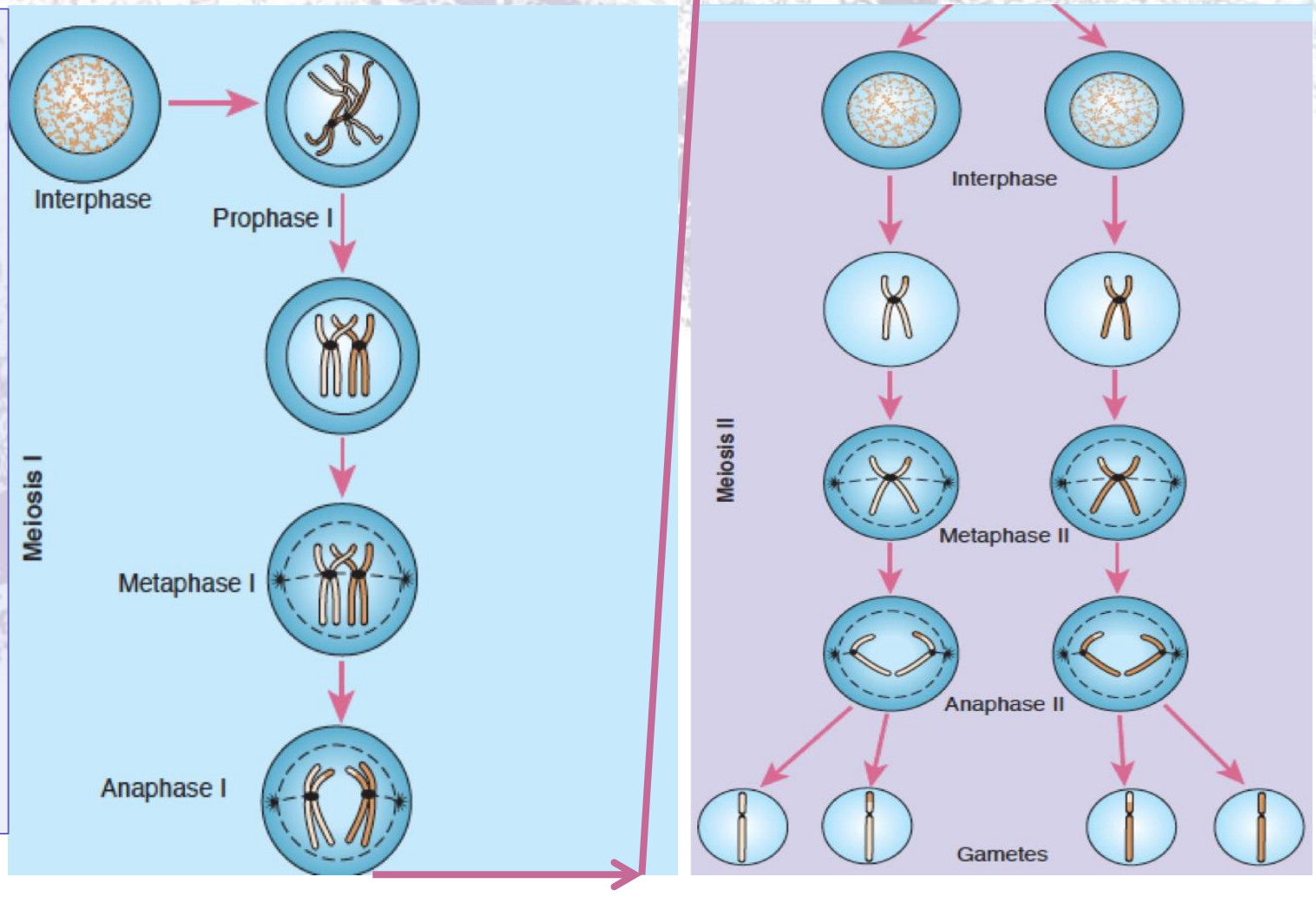
- Chromosomes de-condense from their highly contracted state,
- Nuclear membrane re-form around each of the two daughter nuclei.
- Division of the cytoplasm
- resume their interphase



EVENTS OF MEIOSIS I & II

Events of meiosis

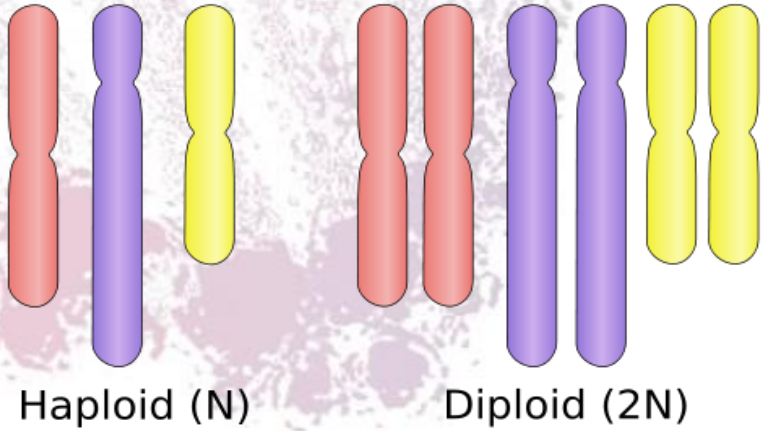
- Consists of tow successive nuclear division
- In the first nuclear division the homologous chromosomes are separated from each other (daughter chromosomes consists of two chromatids)
- The second nuclear division resembles a mitotic division but there is no DNA replication (already replicated before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



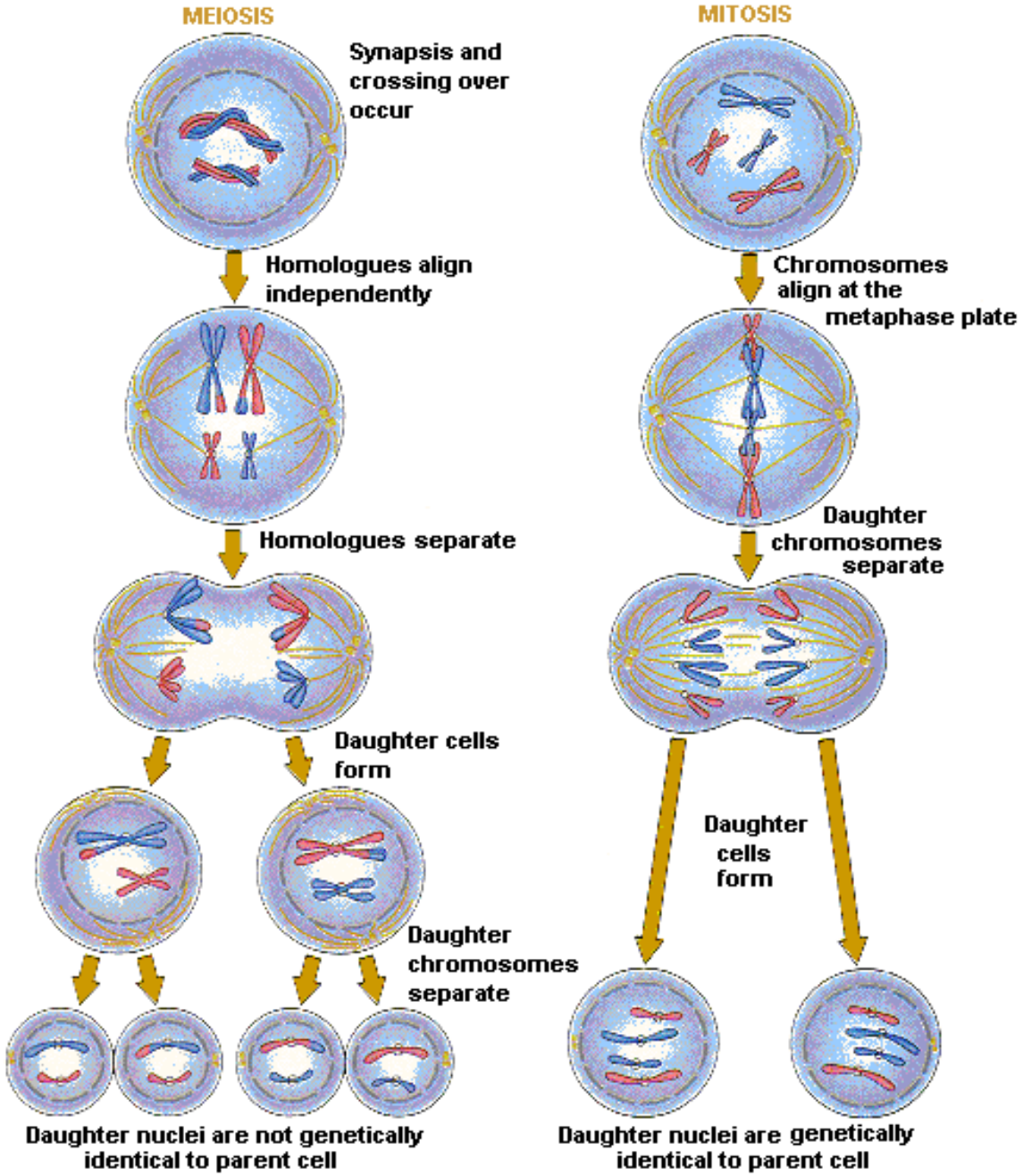
Note that the anaphase occurs once in mitosis and twice in meiosis

Objective 1: Describe and explain the events in mitosis & meiosis.

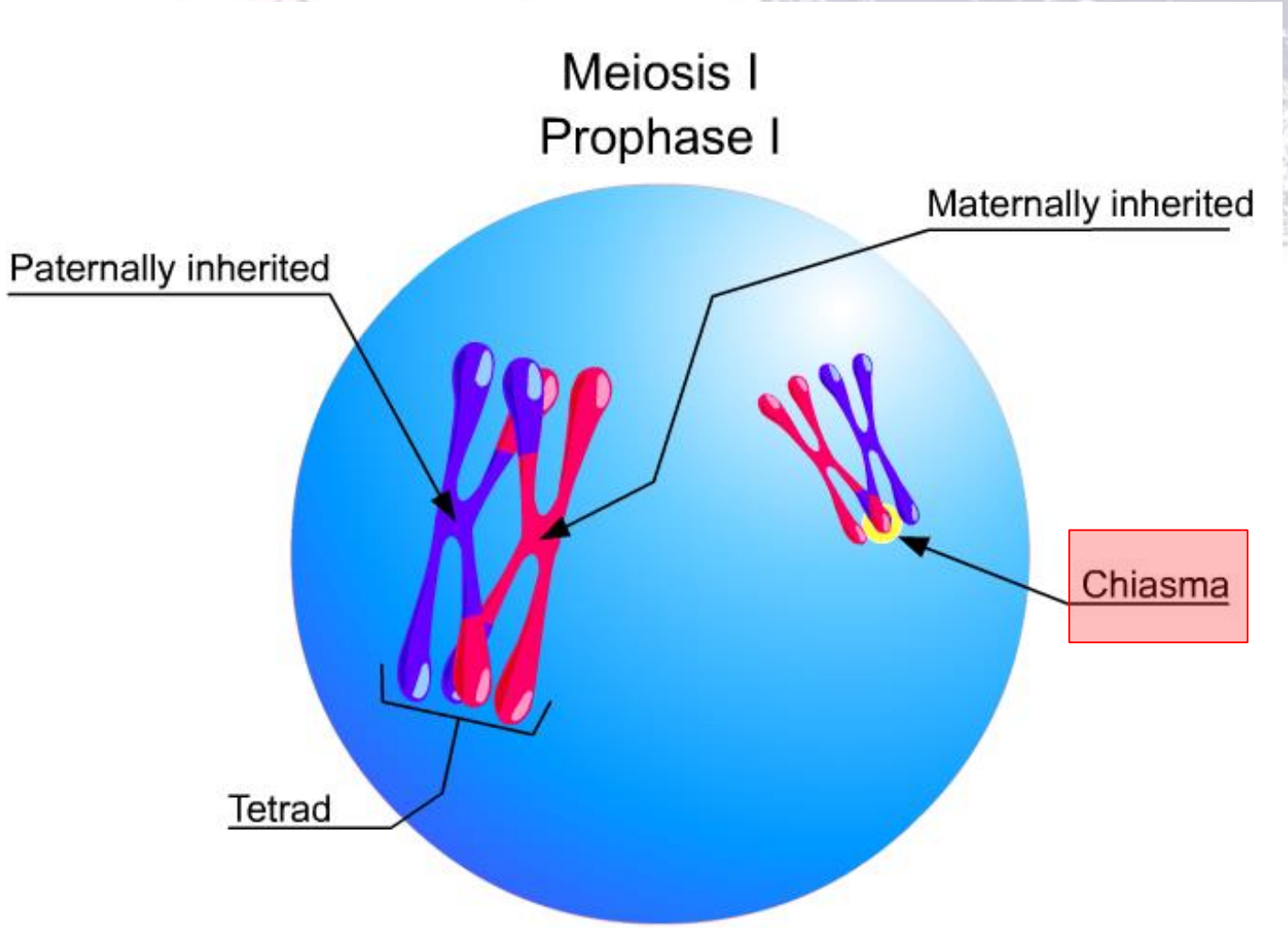
Meiosis Vs. Mitosis



Normal Gametes → 4 Haploids



Objective 1: Describe and explain the events in mitosis & meiosis.



Meiosis

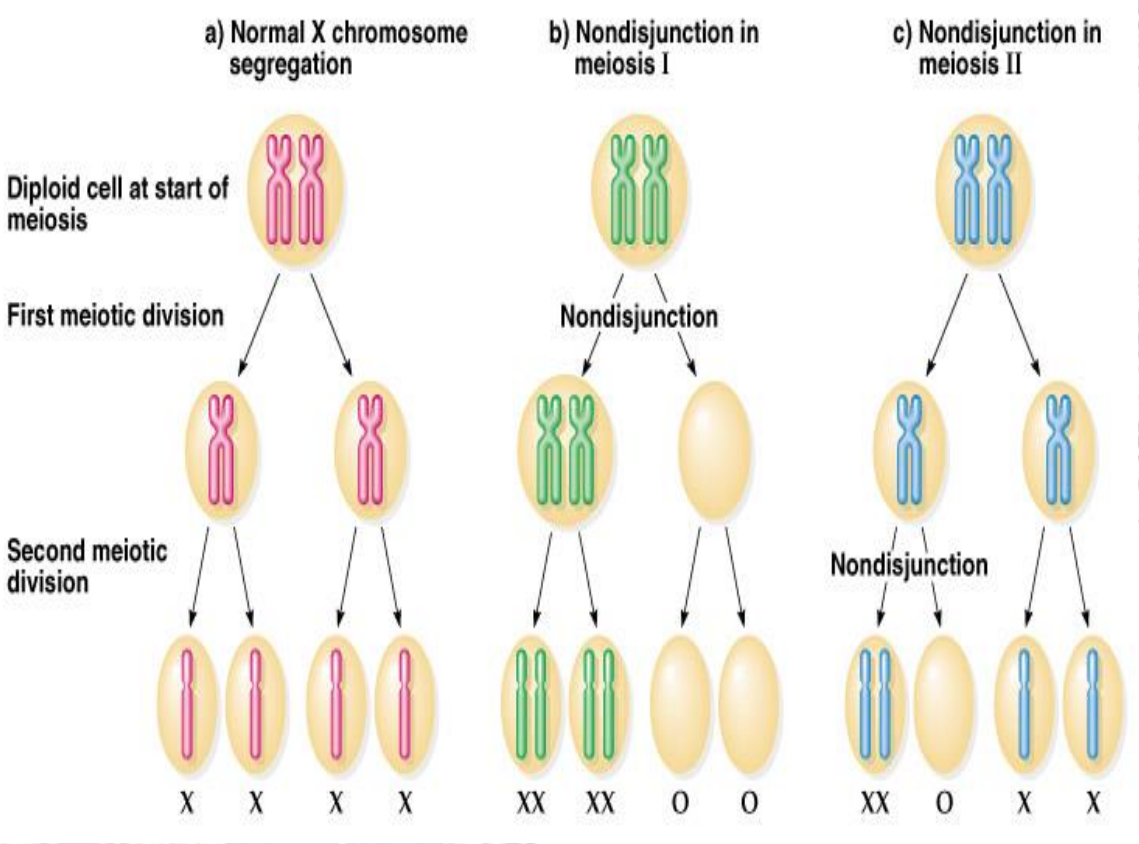
NON-DISJUNCTION IN MEIOSIS

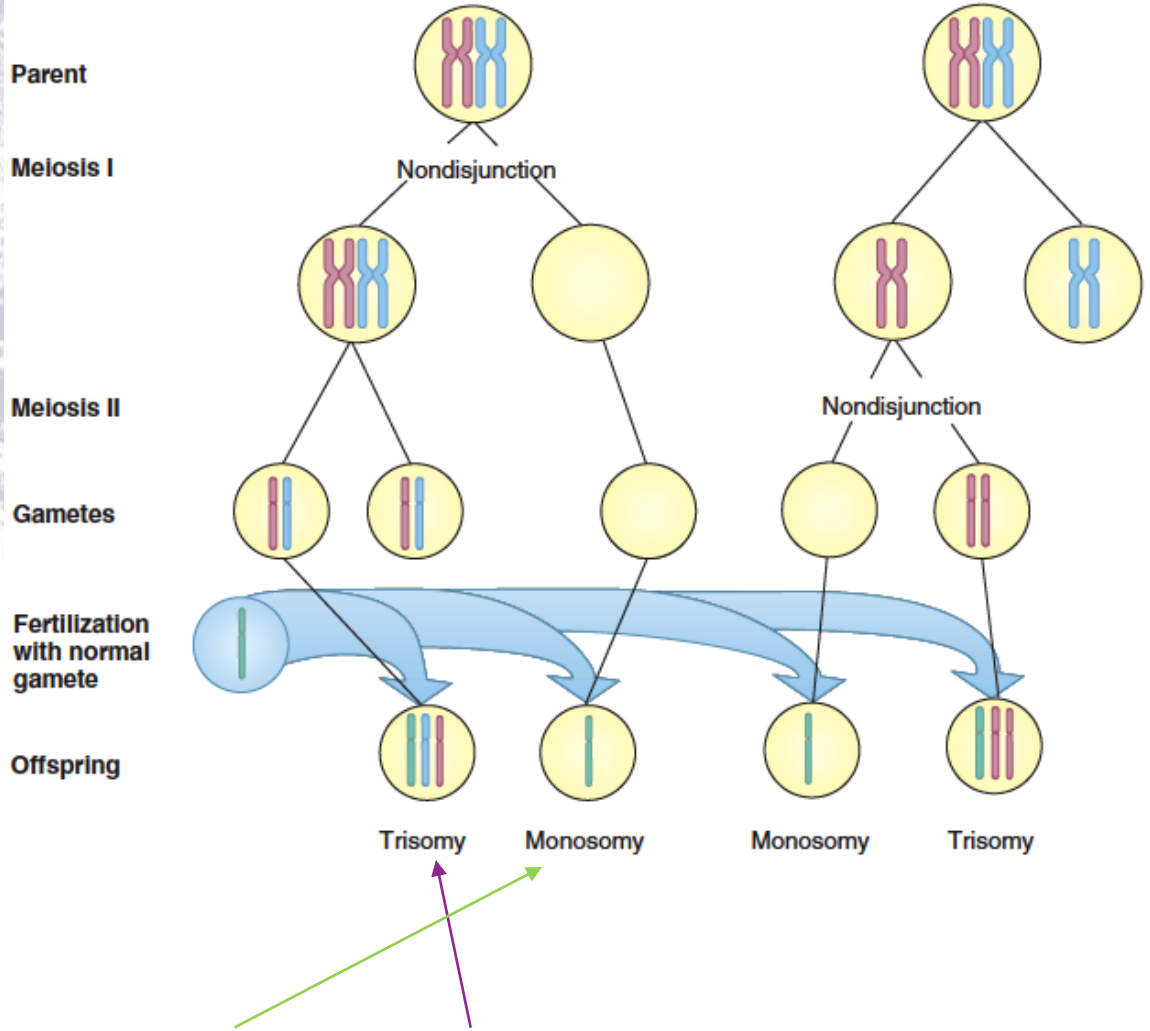
- The failure of chromosomes to disjoin normally **during meiosis phase 1 or phase 2.**
- Two chromosome homologs migrate to the same daughter cell instead of disjoining normally and migrating to different daughter cells.
- The result of this error is a cell with an imbalance of chromosomes (**Aneuploidy**)

A normal disjunction in first meiotic division produces 4 balanced gametes

- 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)**

Objective 2: Non-disjunction and its impact on meiosis.





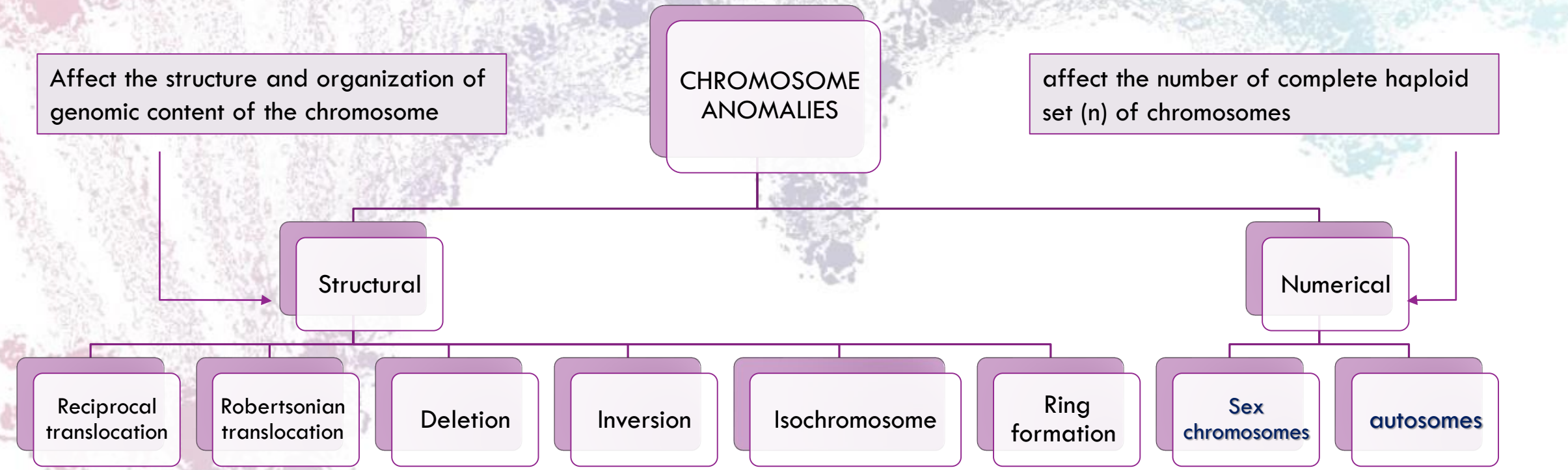
In meiotic nondisjunction

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

Presence of an abnormal number of chromosomes in a cell

الخريطة غير موجودة بالمحاضرة ولكن للتوضيح وتسهيل الفهم والربط

CHROMOSOME ANOMALIES



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

- Turner's syndrome
- Klinefelter Syndrome

- Down syndrome
- Edward's syndrome
- Patau Syndrome

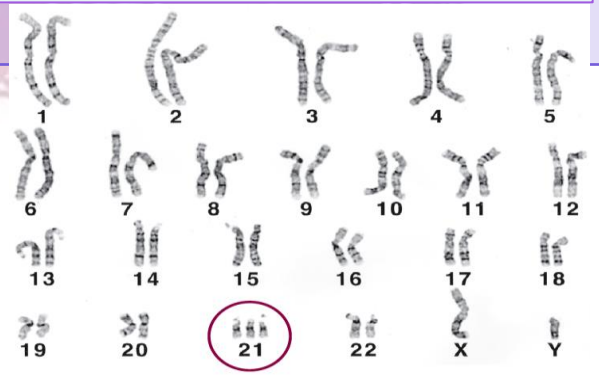
NUMERICAL CHROMOSOMAL ANOMALIES

"NUMERICAL ANOMALIES IN AUTOSOMES"

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

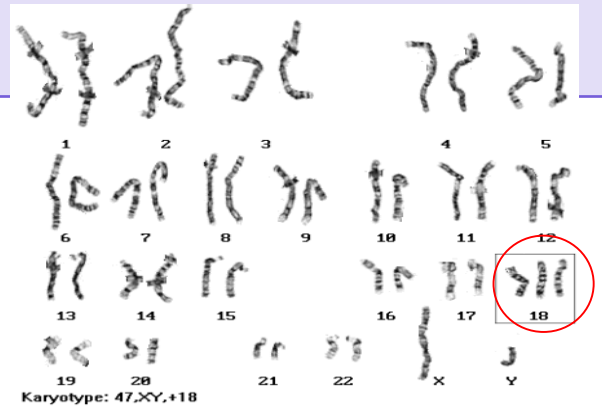
- Most cases arise from non-disjunction in the first meiotic division.
- The incidence of **trisomy 21** rises sharply with increasing **maternal age**.
- The father contributing the extra chromosome in 15% of cases.
- The symptoms include characteristic facial dysmorphologies, and an IQ of less than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

The maternal age of the ovum is the determinant of this abnormality.



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

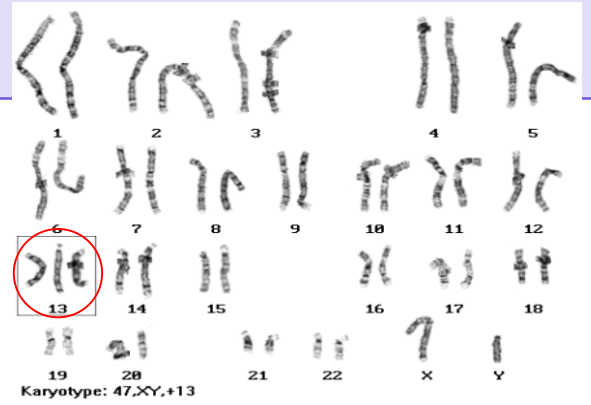
- the second most common autosomal trisomy, after Down syndrome.
- It occurs in around one in 6,000 live births.
- Most babies die in the first year and many within the first month & has a very low rate of survival.
- Common anomalies are heart abnormalities, kidney malformations, and other internal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



Patau syndrome, Trisomy 13
Karyotype: 47, XY, +13

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

The genomic content on chromosome 13 is very critic, so this syndrome is less popular than trisomy +21.



NUMERICAL CHROMOSOMAL ANOMALIES

"NUMERICAL ANOMALIES **IN AUTOSOMES**"

Down syndrome, Trisomy 21

Edward's syndrome, Trisomy 18

Patau syndrome, Trisomy 13

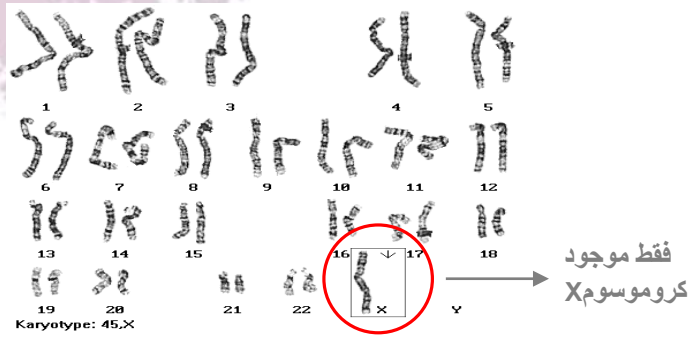
NUMERICAL CHROMOSOMAL ANOMALIES

"NUMERICAL ANOMALIES IN SEX CHROMOSOMES "

Turner's syndrome (Monosomy X أحادي الصبغة)
Karyotype: 45,XO, females

- Occurring in 1 in 4000 phenotypic females.
- As a result of paternal meiotic nondisjunction.
- The only viable"قابل للحياة" monosomy in humans.
- Characteristics: Webbed"قصيرة وعريضة" neck, Individuals are genetically female, not mature sexually, Sterile"عقيم", Short stature"قصير القامة", Broad chest, Low hairline, Streak ovaries, Normal intelligence, Normal life span.

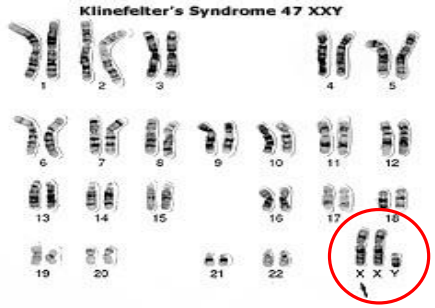
The dominant of this abnormality is the paternal genetic material(most of the time), so it may be maternal sometimes.

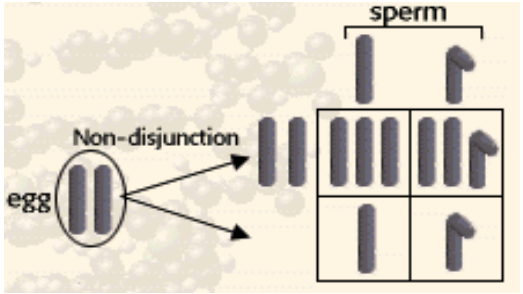


Klinefelter Syndrome
Karyotype: 47,XXY males

- 1/600 males, due to nondisjunction of X chromosomes during meiosis I in females. (maternal)
- Male sex organs; unusually small testes which fail to produce normal levels of testosterone→ breast enlargement (gynaecomastia "تثدي الرجل") 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

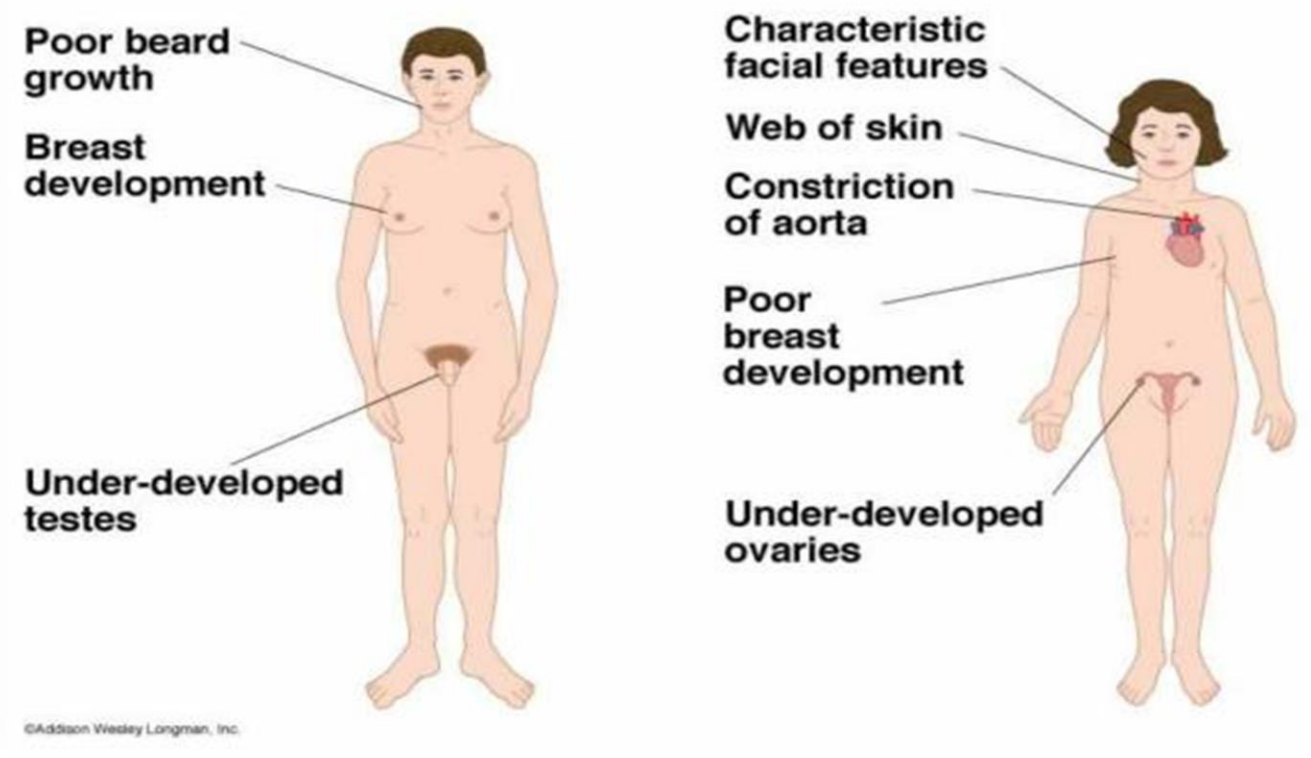
This one is caused by the mother.





NUMERICAL CHROMOSOMAL ANOMALIES

"NUMERICAL ANOMALIES IN SEX CHROMOSOMES "



Klinefelter Syndrome

Turner Syndrome

*ممكن يعطونك الكاريو تايب و يسألونك عن أي أبنورمال أو العكس، يعني يعطونك السيندروم و يقولون لك اختر الكاريوتايب تبع هذا السيندروم.

او ما الطرف المسبب للأبنورمالِتي الفلاني ؟ (الام او الاب)

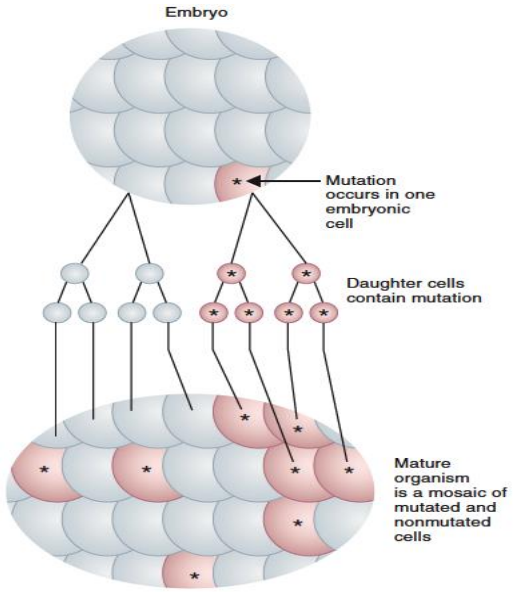
MOSAICISM

- 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 "كيف يكتب الكاريوتايب" 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.**

What's the difference between mosaicism and the 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.)

This abnormality (mosaicism) well develop after fertilization as a non-disjunction abnormality in the zygote. While in chimerism there's two normal zygotes are fused together.

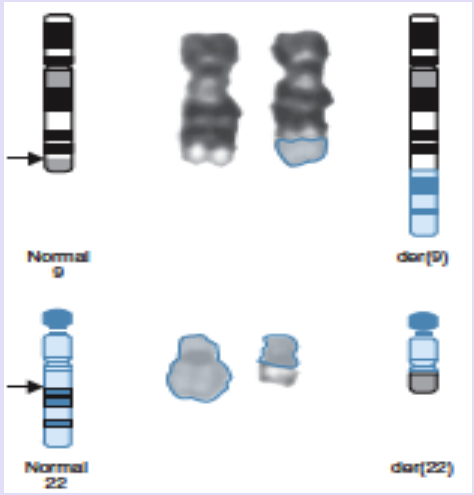


Chimerism isn't important for us (in exam) but it's mentioned to let us know the deference between them .

STRUCTURAL CHROMOSOMAL ANOMALIES
"Translocation"

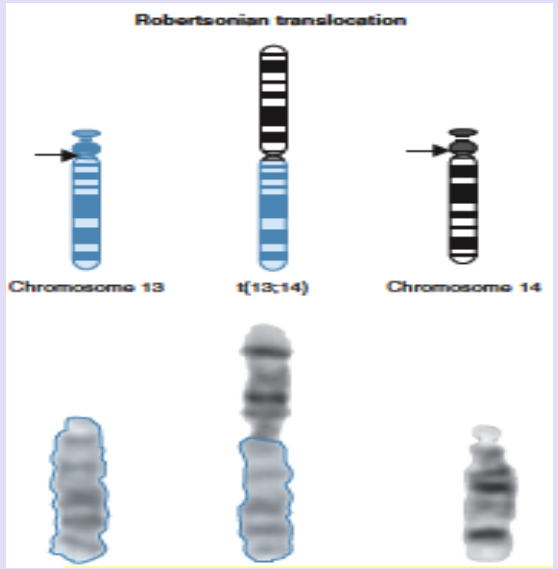
• Reciprocal translocation

- Reciprocal translocation 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)**



• 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

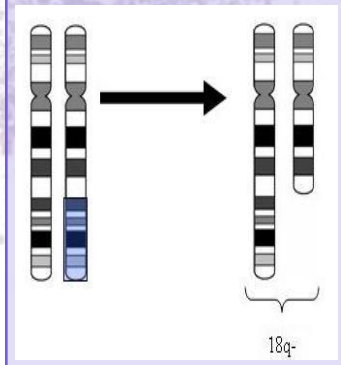


STRUCTURAL CHROMOSOMAL ANOMALIES
"Deletion"

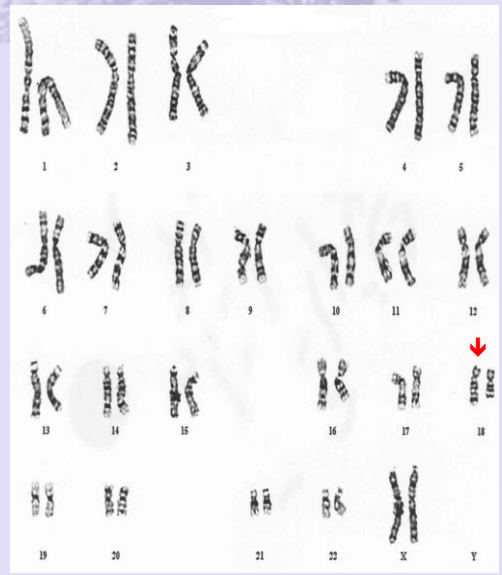
Deletion

- 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

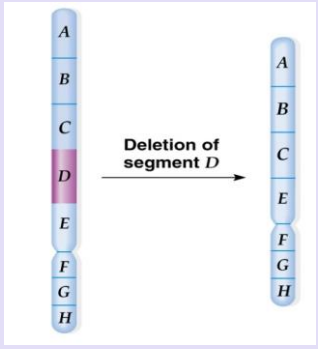


Sample karyogram of *Terminal deletion*

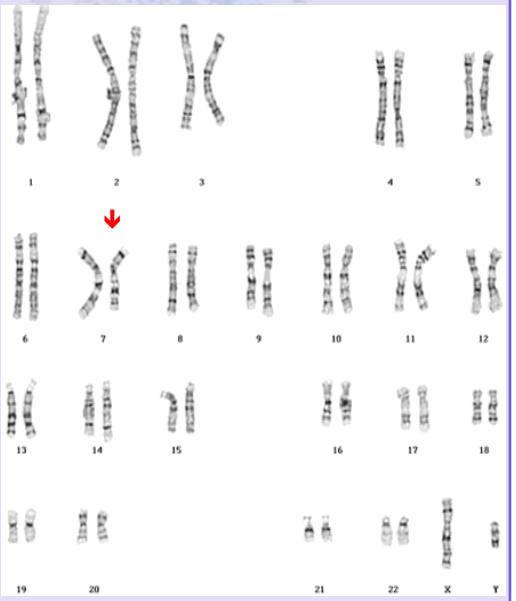


46,XX,del(18)(q21.3)

Interstitial deletion



Sample karyogram of *Interstitial deletion*



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

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.

STRUCTURAL CHROMOSOMAL ANOMALIES

"Inversion, isochromosome, and ring chromosome "

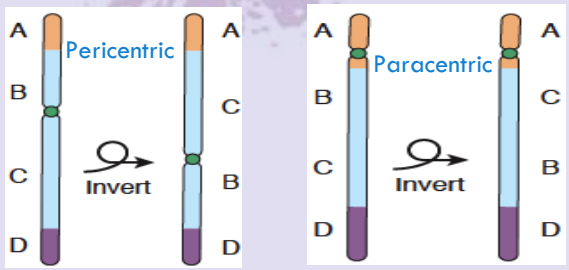
• Inversion

- Occurs when a segment of chromosome breaks, and rejoining within the chromosome effectively.

- Written in nomenclature as ***inv.***

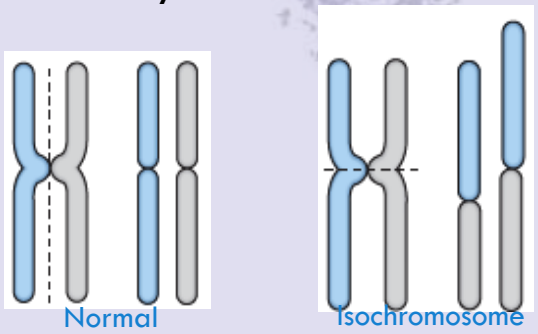
- Only large inversions are normally detected.

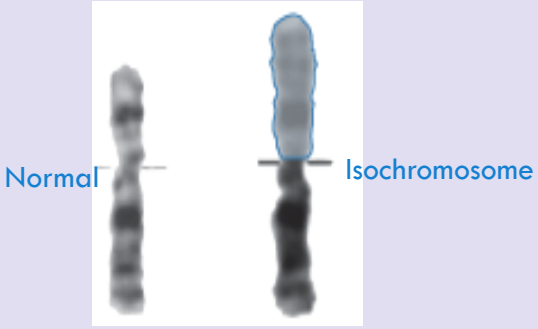
They are balance rearrangements that rarely cause problems in carriers



• Isochromosome

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

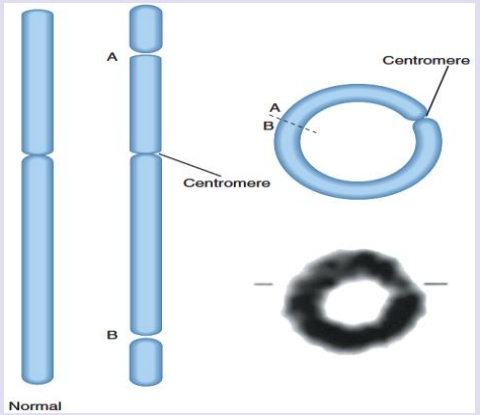




• Ring formation(Ring chromosome)

- A break on each arm of a chromosome
- Two sticky ends
- Reunion of the ends as a ring loss of the 2 distal chromosomal fragments

- Ring chromosomes are often unstable in mitosis



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 arise from one zygote while Chimera from the fusion of two fertilized eggs
- Structural abnormalities include translocations (balanced or unbalanced), inversions, deletions, isochromosome & rings.

MCQ

1- During which phase of the cell cycle DNA is replicated?
A- G1
B- S
C- G2
D- none of the above

2- Nuclear membrane dissolves at…
A- Prophase
B- Telophase
C- Metaphase
D- Prometaphase

3- Non disjunction in second division produces…
A- 2 unbalanced gametes
B- 2 normal gametes
C- 2 unbalanced gametes and 2 normal gametes
D- 4 unbalanced gametes

4- Which syndrome is known as Trisomy 18?
A- Down Syndrome
B- Patau Syndrome
C- Edward Syndrome
D- Klinefelter Syndrome

5- Fail to produce normal levels of testosterone is a characteristic of
A- Turnur's Syndrome
B- Klinefelter Syndrome
C- Edward Syndrome
D- Patau Syndrome

6- Which of the following chromosome abnormalities is known as Turner Syndrome?
A- 47, XXY
B- 44, XO
C- Trisomy 18
D- Trisomy 21

MCQ

7- Occurs when a segment of chromosome breaks, and rejoining within the chromosome effectively:
A- Inversion
B- Isochromosome
C- Ring Formation
D- Deletion

8- Loss of a segment from a chromosome, either terminal or interstitial
A- Inversion
B- Isochromosome
C- Ring Formation
D- Deletion

9 - Presence of an abnormal number of chromosomes in a cell known as
A- Aneuploidy
B- Mosaicism
C- Chimerism
D- None of the above

10- ..... is a result of maternal non-disjunction.
A- Turner's Syndrome
B- Klinefelter Syndrome
C- Edward Syndrome
D- none of the above

11- Meiosis result in
A- 2 haploid daughter cells
B- 2 diploid daughter cells
C- 4 haploid daughter cells
D- 4 diploid daughter cells

1 B
2 D
3 C
4 C
5 B
6 B
7 A
8 D
9 A
10 B
11 C

تمّ بحمدِ الله

نسعدُ باستقبالِ اقتراحاتكم و ملاحظاتكم على البريد الإلكتروني:
GeneticsTeam437@gmail.com

TEAM LEADERS:

Abdulmajeed Alwardi

Haifa Alessa

GIRLS TEAM:

Ghaida Alsanad

Munira Alhadlg

Batoul Alruhaimi

Dimah Alaraifi

Arjuwana Alaqeel

Marwah Alkhalil

BOYS TEAM:

Abdullah Alzahrani

Abdulaziz Aljohani

Adel Alzahrani

Hamdan Aldossri