KING SAUD UNIVERSITY
COLLEGE OF MEDICINE
FOUNDATION BLOCK

LECTURE 2
CHROMOSOME ANOMALIES

HUMAN GENETICS 433

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.22
- Recognize the main structural anomalies in chromosomes.

Color index:

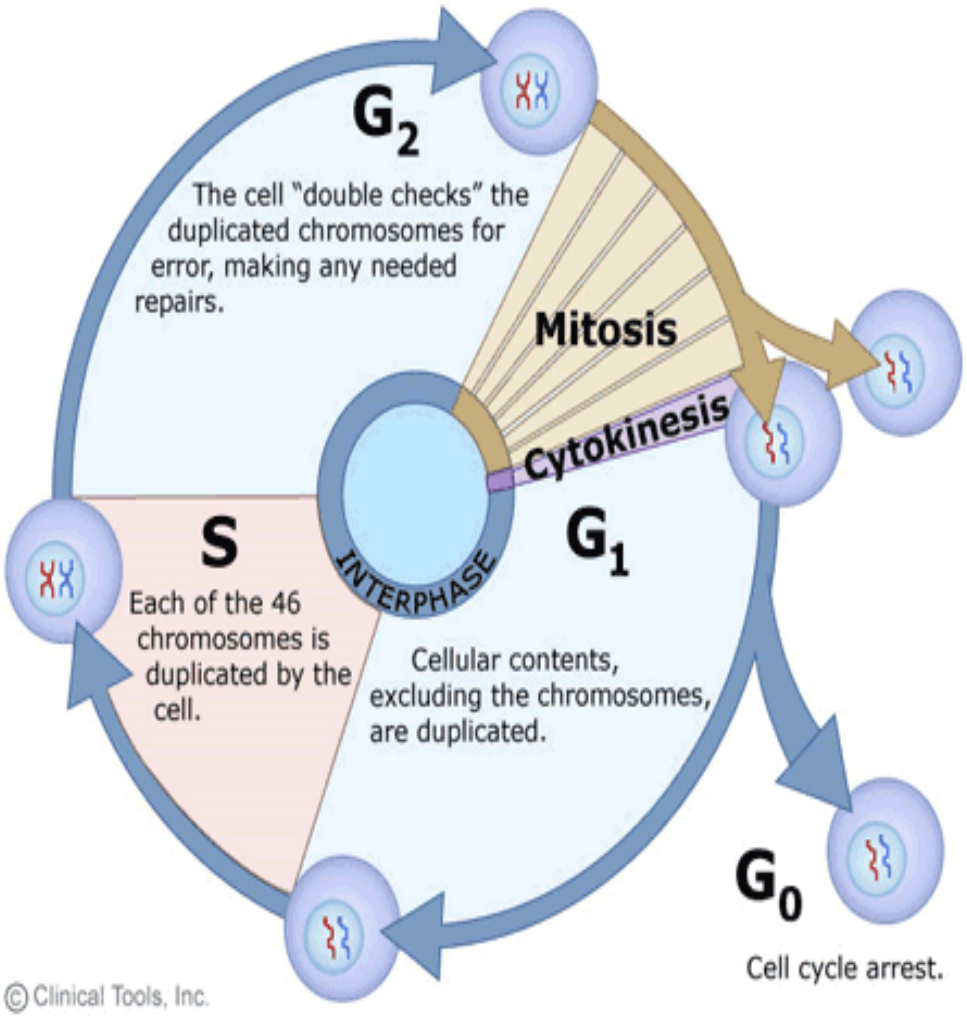
Red → Important

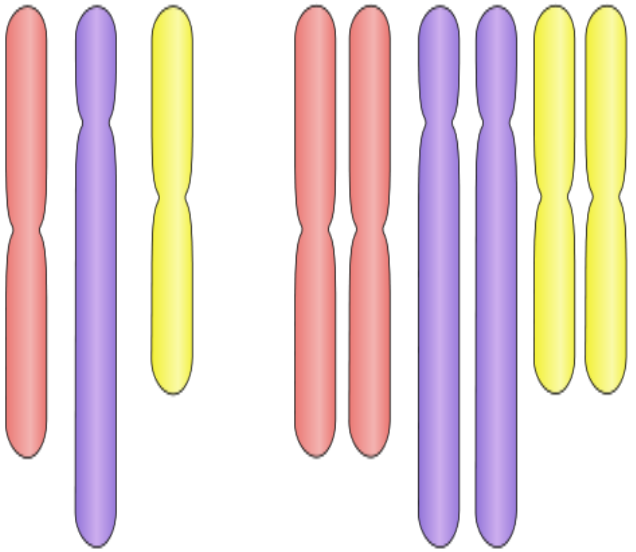
Yellow → Notes

Green → Explanation

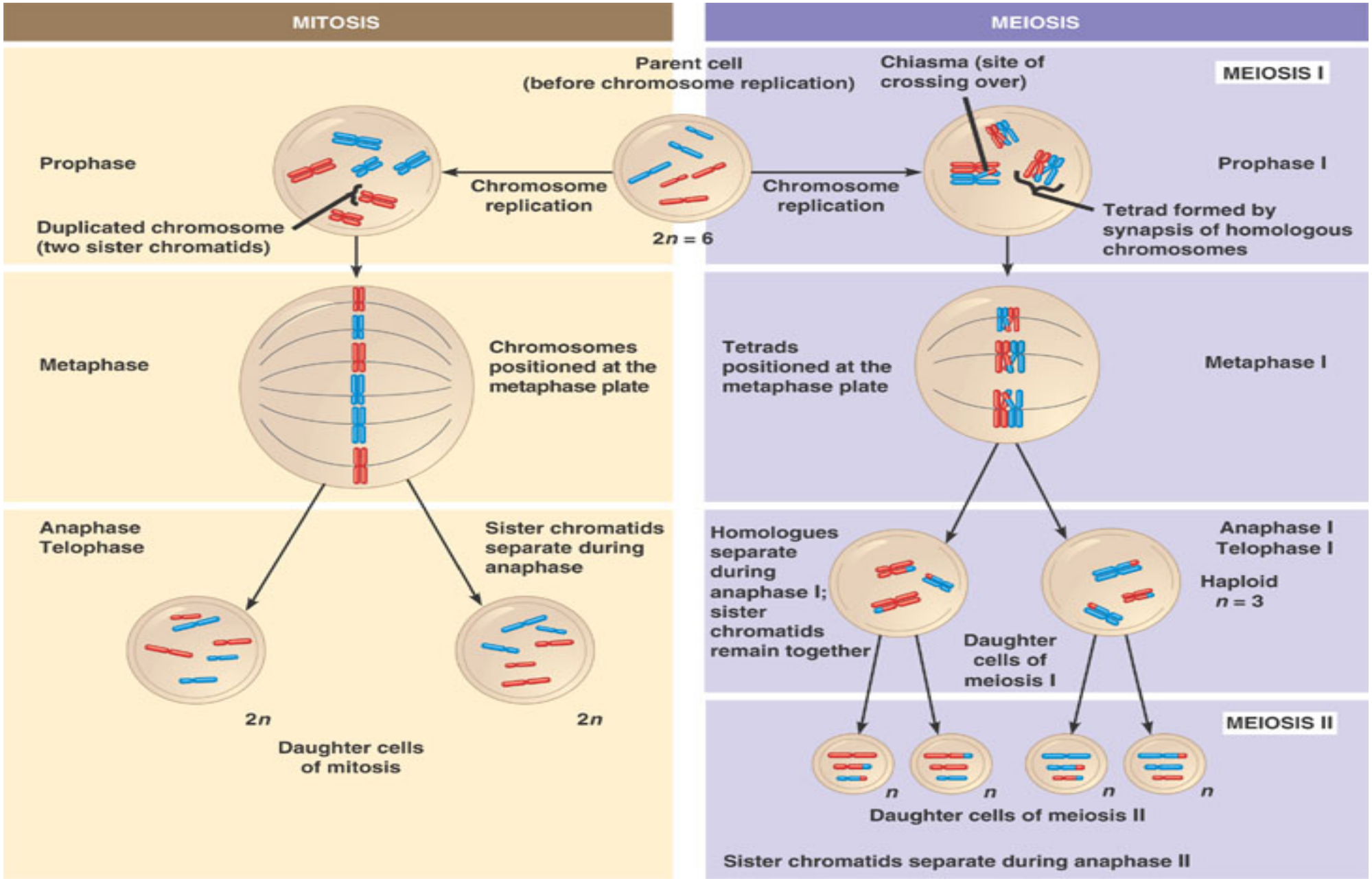
If you have any questions please contact us :
Genetics433@gmail.com

Remember



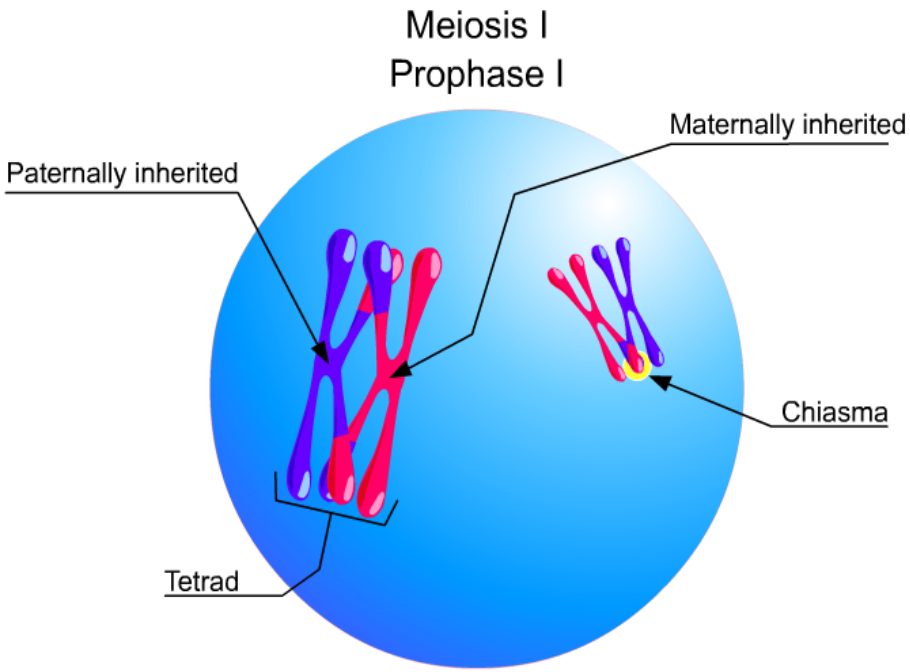


*Haploid number of chromosomes ((23))
*Diploid number of chromosomes ((46))



* Mitosis outcome : two daughter cells having diploid number of chromosomes (same as the mother cell).

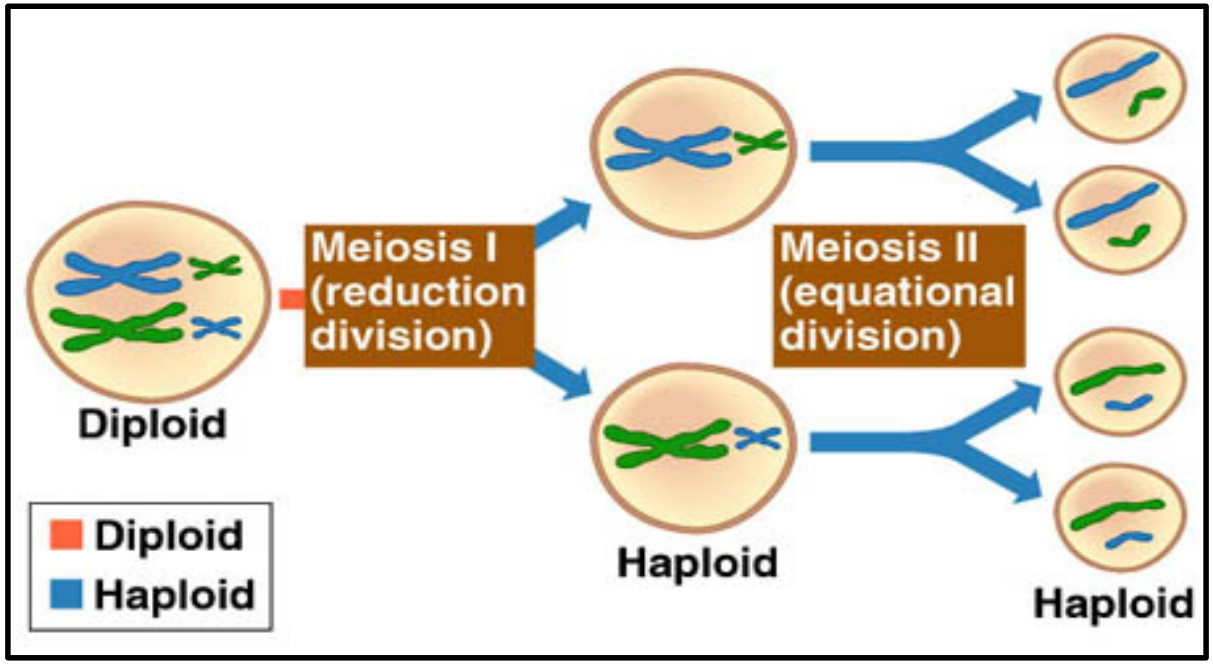
* Meiosis outcome : 4 daughter cells having haploid number of chromosomes (different from the mother cell).



*Crossing over happen in the "chiasma".

*Tetrad: 4 chromatids of homologous chromosomes are lined together.

The phases of meiosis I & II



Non-disjunction

What is it?

(not coming apart equally in anaphase stage) : 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. The result of this error is a cell with an imbalance of chromosomes (Aneuploidy) .

How does it happen?

The spindle fibers from one pole of the cell pulls the whole pair of chromosomes without them splitting up (pulling them in an unequal way) so the other spindle fibers get nothing.

Normally

During (anaphase stage) chromosomes separate into two equal halves.

while

in abnormal division they don't which leads to:

*Aneuploidy means gain or loss of chromosomes

Meiotic non-disjunction

Can affect each pair of chromosomes

Is not a rare event

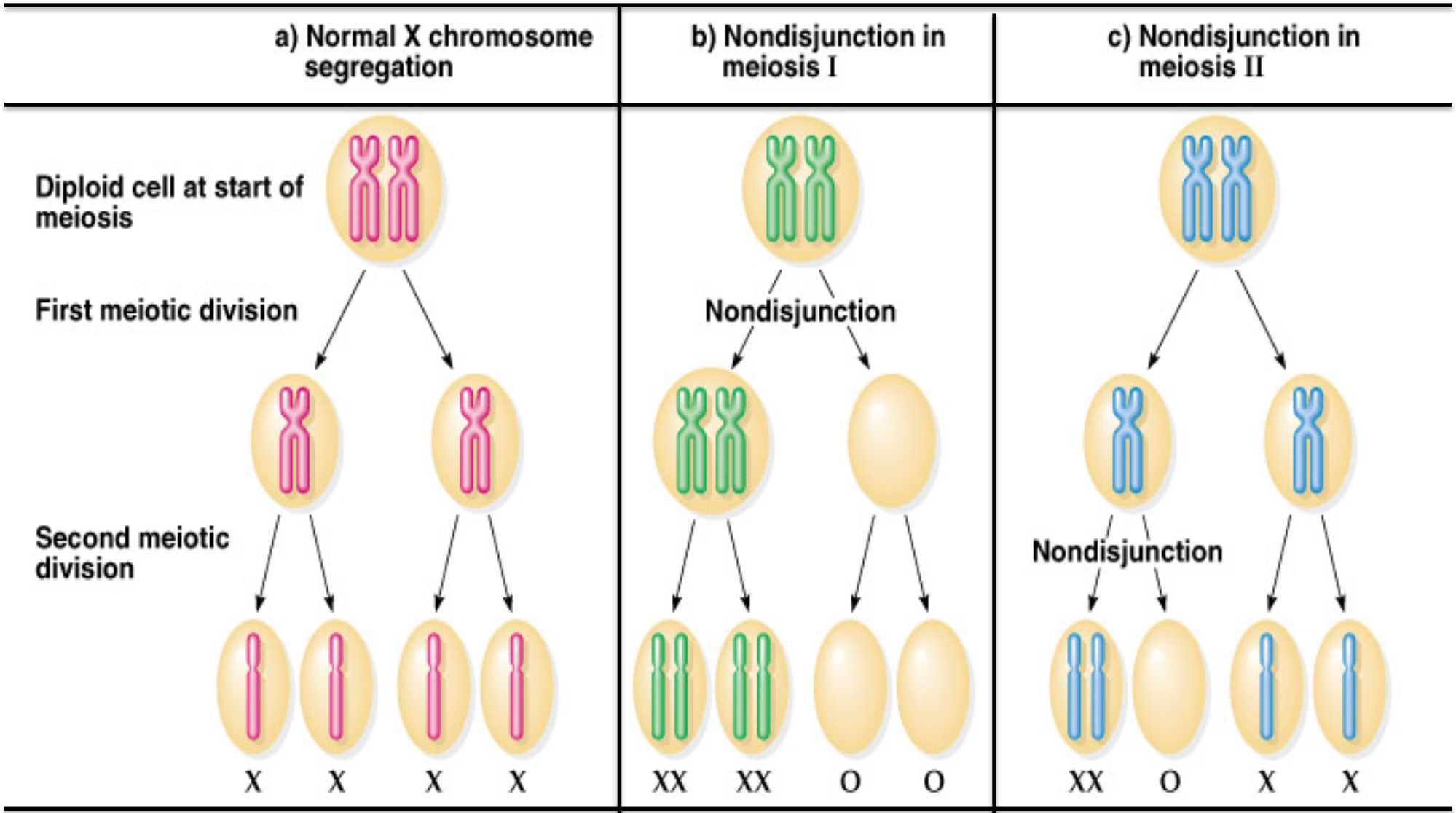
Non disjunction in first meiotic division

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.

*Nondisjunction in meiosis II: only one of the two resulted cells from meiosis I separates improperly and gives rise to two cells, one has the whole pair and the other one has none.



*the resulting gametes(daughter cells)are normal, **4** daughter cells with **haploid** number of chromosomes.

*the resulting gametes (daughter cells) are **abnormal**, **2** cells with **missing** chromosomes & **2** cells with **diploid** number of chromosomes.

*the resulting cells, **2 normal** cells with haploid number of chromosomes ,**1 abnormal** cell with **diploid** number of chromosomes & **1 abnormal** cell **without** chromosomes.
*half of the resulted gametes are normal.

CHROMOSOME ANOMALIES

- TYPES
- MECHANISMS
- NOMENCLATURE
- Etiology

Numerical → Abnormal number of chromosomes (decrease or increase)e.g. Down syndrome (47,XY,+21)

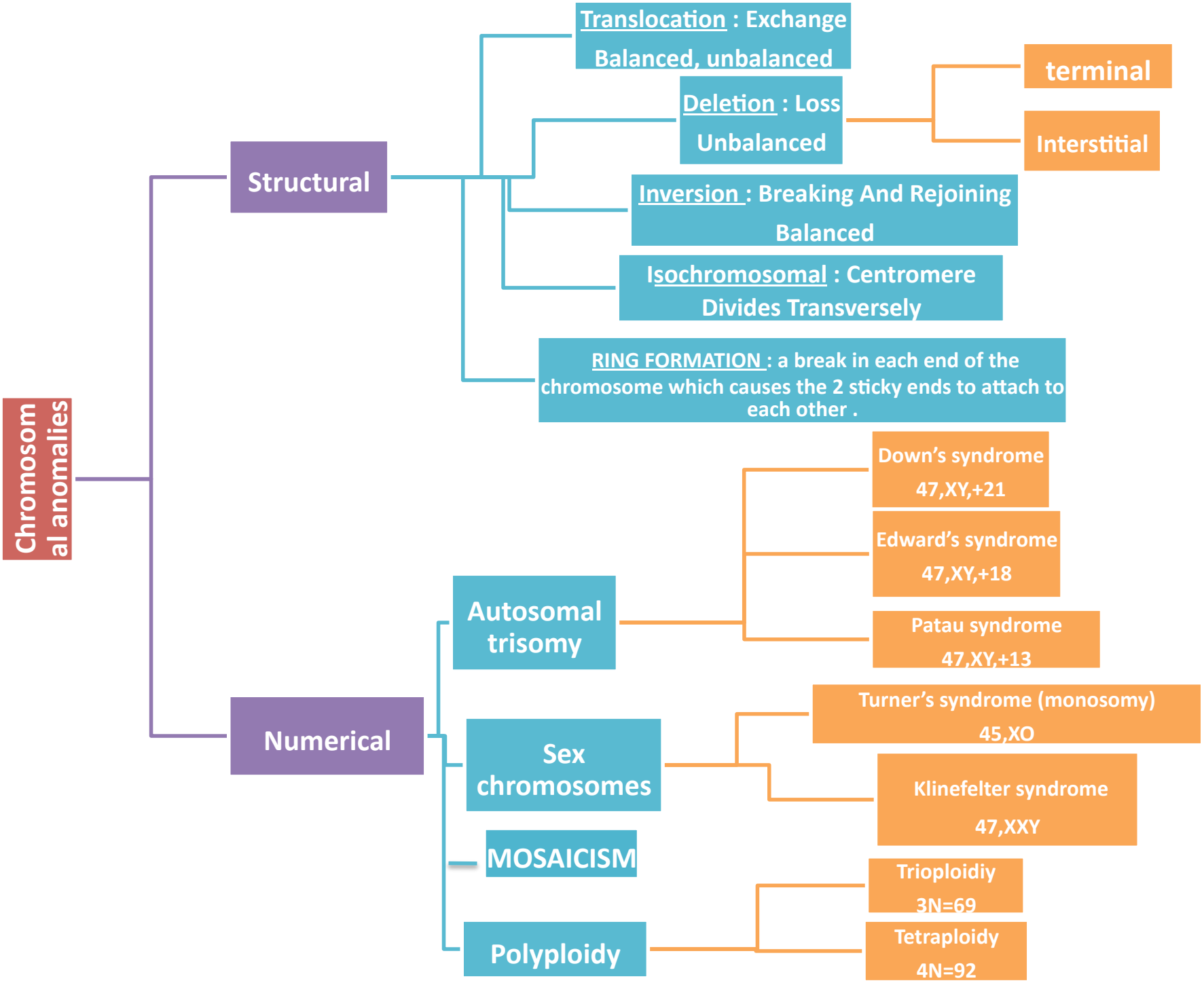
Structural → Abnormal change in the structure and shape of the chromosomes , could be caused by deleting or insertion e.g. insertion

Autosomal trisomy

Patau Syndrome

Down syndrome

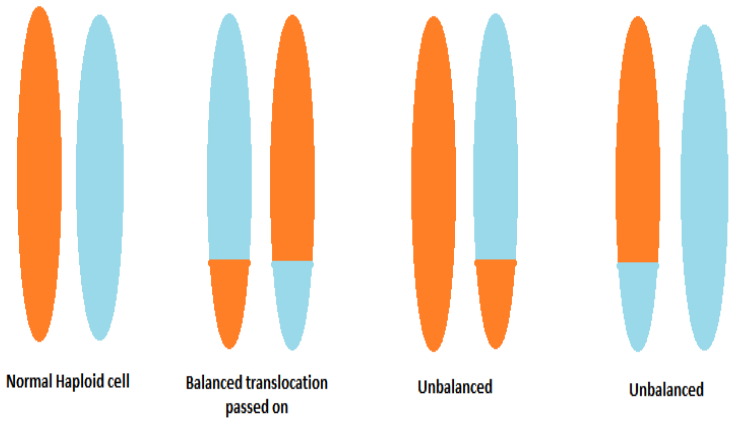
Edward's syndrome


Chromosomal anomalies
Structural
Translocation : Exchange
Balanced, unbalanced
Deletion : Loss
Unbalanced
terminal
Interstitial
Inversion : Breaking And Rejoining
Balanced
Isochromosomal : Centromere
Divides Transversely
RING FORMATION : a break in each end of the chromosome which causes the 2 sticky ends to attach to each other .
Numerical
Autosomal trisomy
Down's syndrome
47,XY,+21
Edward's syndrome
47,XY,+18
Patau syndrome
47,XY,+13
Sex chromosomes
Turner's syndrome (monosomy)
45,XO
Klinefelter syndrome
47,XXY
MOSAICISM
Polyploidy
Trioploidiy
3N=69
Tetraploidy
4N=92

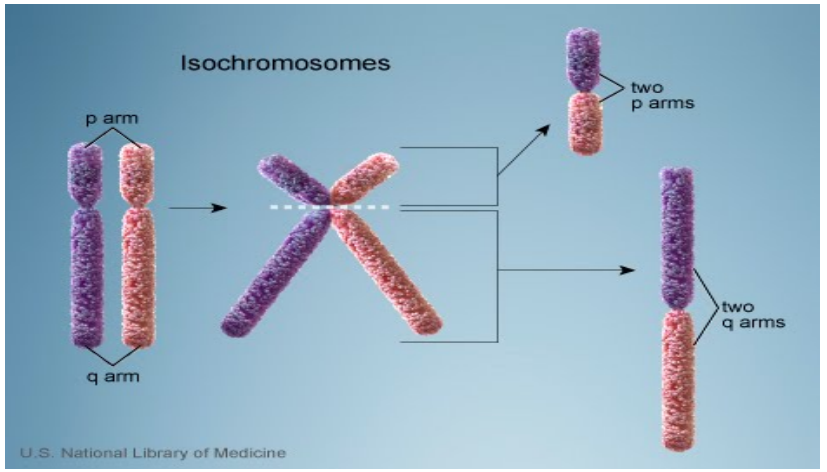
STRUCTURAL CHROMOSOMAL ANOMALIES

Reciprocal translocation	Deletion	Inversion	Isochromosome	Ring formation (Ring chromosome)
- 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.	- 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. -Has to types: 1- Interstitial deletion: is deletion at the middle of the chromosome. 2- Terminal deletion	- Inversion occurs when a segment of chromosome breaks, and rejoin 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.	-The most probable explanation for isochromosome is that the centromere has divided transversely rather than longitudinally.	- 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.

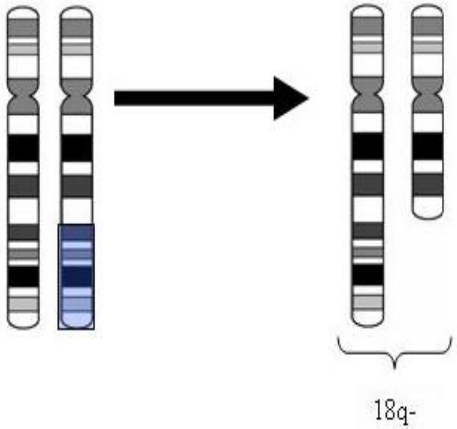
Reciprocal translocation



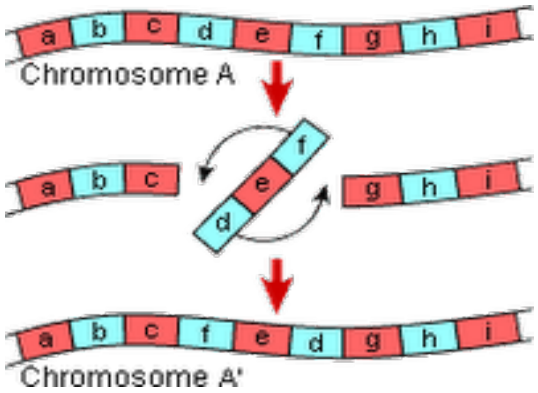
Isochromosome



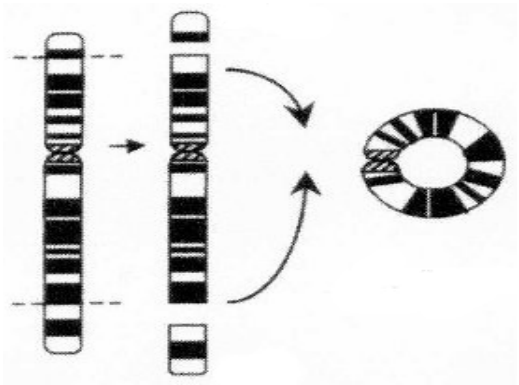
Terminal Deletion



Inversion



Ring Formation



	Down' s syndrome Trisomy 21	Edward's syndrome Trisomy 18	Patau syndrome Trisomy 13
Karyotype	47 XX/XY +21	47 XX/XY +18	47 XX/XY +13
Abnormality type	Nondisjunction in the first meiotic division	Nondisjunction	nondisjunction
Height	Men: 154 cm. Women: 144 cm. *height below normal*	_____	_____
Prevalance	1 in 800-1000 Most common	1 in 6000 Second most common	1 in 10,000 to 1 in 21,700
Characteristics Complications	-facial dysmorphologies -Microgenia -Oblique eye fissures -Muscle hypotonia -Flat nasal bridge -Protruding tongue -microglossia	-Heart abnormalities -Kidney malformation -Organs disorders -lung abnormalities -brain abnormalities -abnormal hand structure	-Multiple dysmorphic features.
Risk Factors	-Increased maternal age. -15% of the cases from paternal contribution(i.e. Down syndrome can also be the result of nondisjunction of the father's chromosome 21).	80% of affected are females.	_____
Intelligince	IQ less than 50	Retarded	Retarded
Life Expectancy	Increased from 12 to 60 years, due to health care	Most die in the first year,and many within the first month*it has a very low rate of survival*	50% of these babies die within the first month and very few survive beyond the first year
Special cases	Mosaic case which arises from a non disjunction event in the mitosis division after the zygote forms.This results in a body that has both normal and abnormal (trisomic) cells (mosaic) which causes a mild down syndrome	_____	_____

*Down syndrome is affected by the age of the mother because as the cells grows older it becomes weaker therefore the spindle fibers pulling the chromosomes becomes weaker resulting in trisomy. So as the mother gets older the incidence of down syndrome increases.

Numerical anomalies in Sex chromosomes

Turner's syndrome

45, XO - Monosomy

- 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.

*Normal intelligence indicates that the X chromosome doesn't have a gene related to mental intelligence .

Klinefelter Syndrome

47,XXY - Trisomy

- 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.
- 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.

*IQ reduction is mainly in writing and mathematics and critical thinking.

MOSAICISM

What is it?

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

denoted

by a slash between the various clones observed e.g.46, XY / 47, XY, +21).

cause

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 cell lines derive from more than one zygote (e.g. 2 sperms fertilize 2 ova → 2 zygotes that fuse to form 1 embryo)

Sex chromosome unbalance is much less deleterious

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

- Happens in all sets (pairs) of chromosomes.
- Common in animals and not common in humans.

Triploidies

- The most frequent
- 3N = 69 chromosomes: e.g. 69, XXX, or 69, XXY, or 69, XYY.
- Are found in 20 % of spontaneous miscarriages.

Tetraploidy

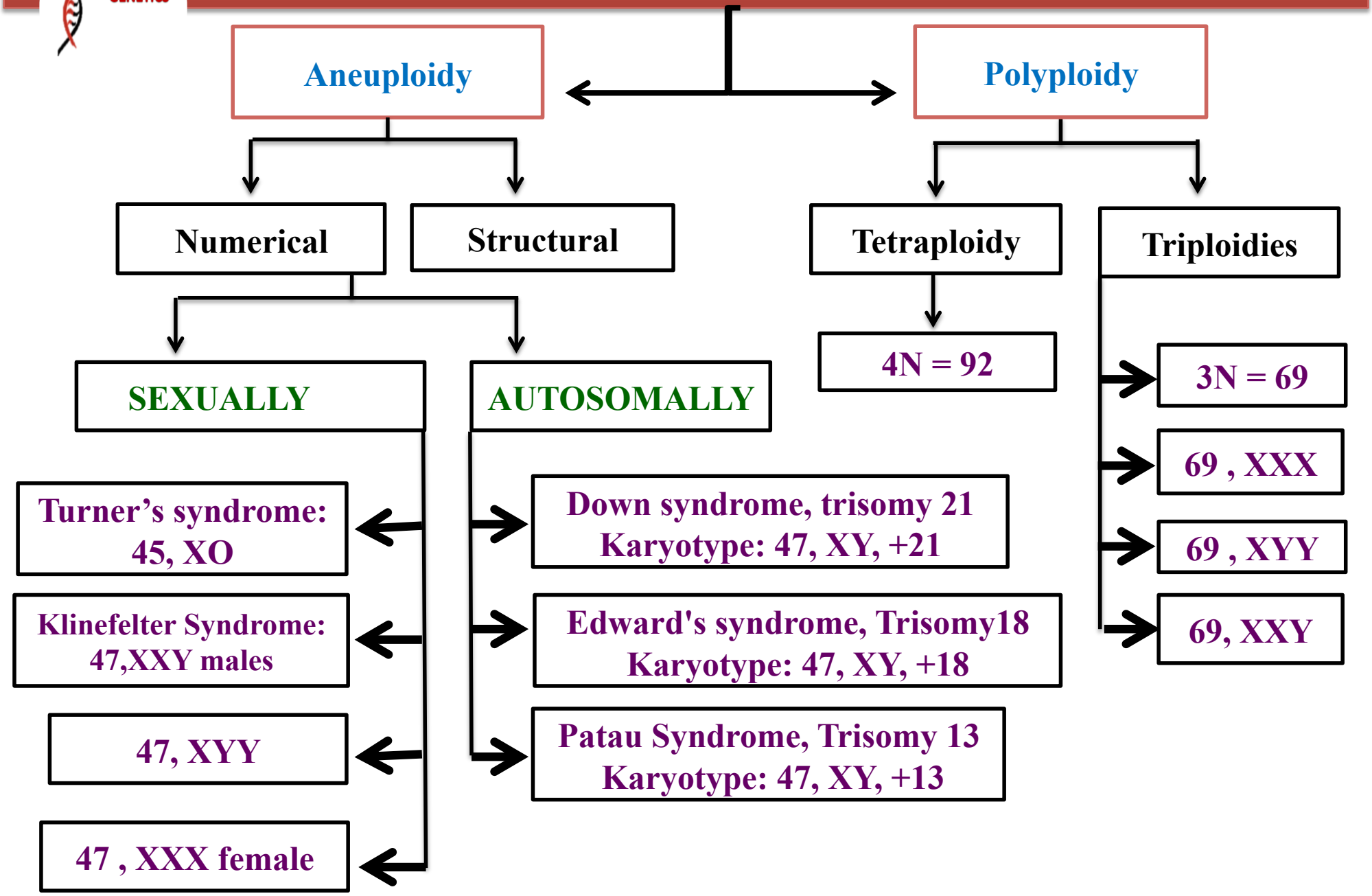
- 4N = 92 chromosomes.
- two extra chromosomes in each pair.

Aneuploidy

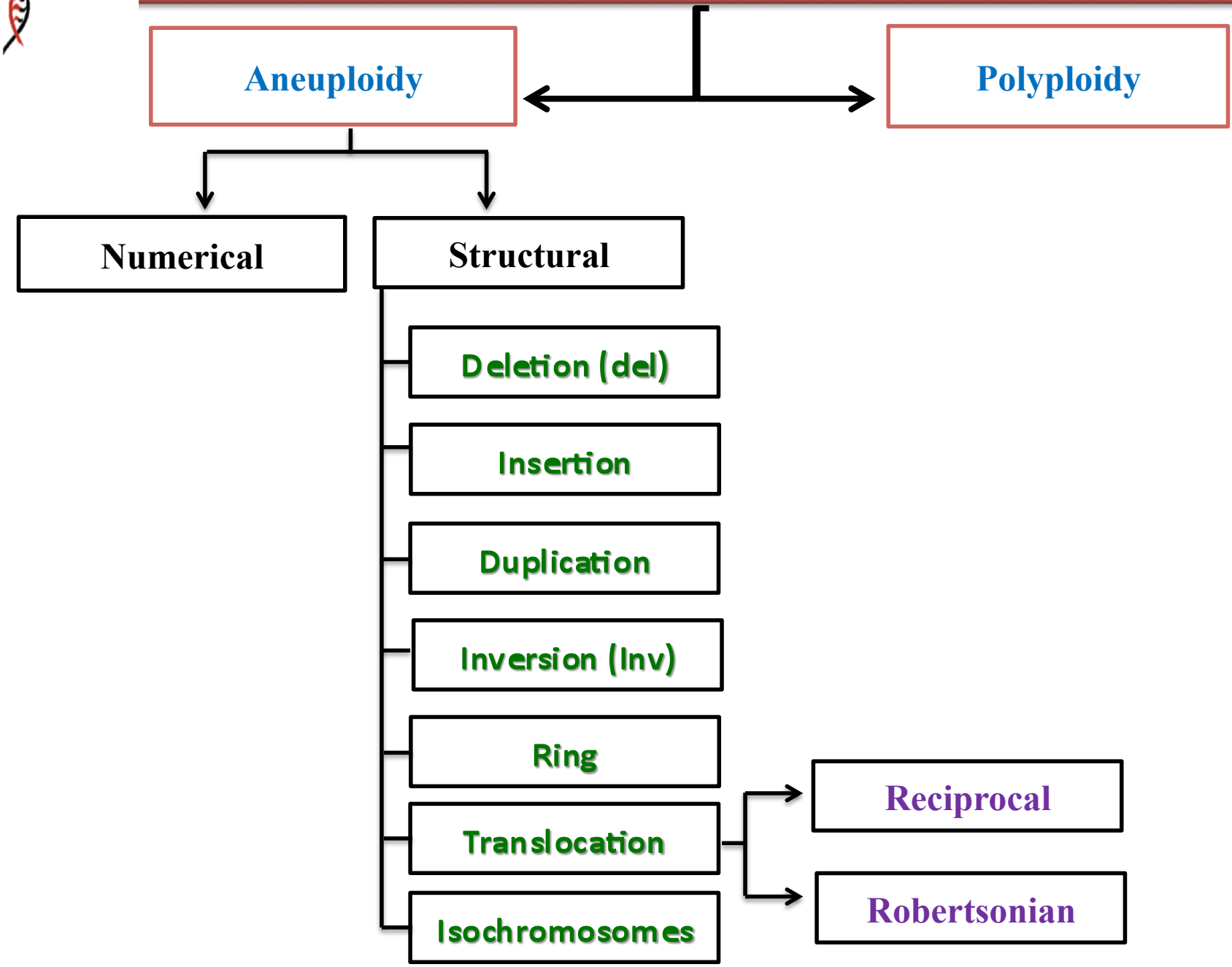
Happens to a specific set (pair) of chromosomes.

e.g. down syndrome: trisomy in chromosome 21 only, turner's syndrome: monosomy in the sex chromosome (X only).

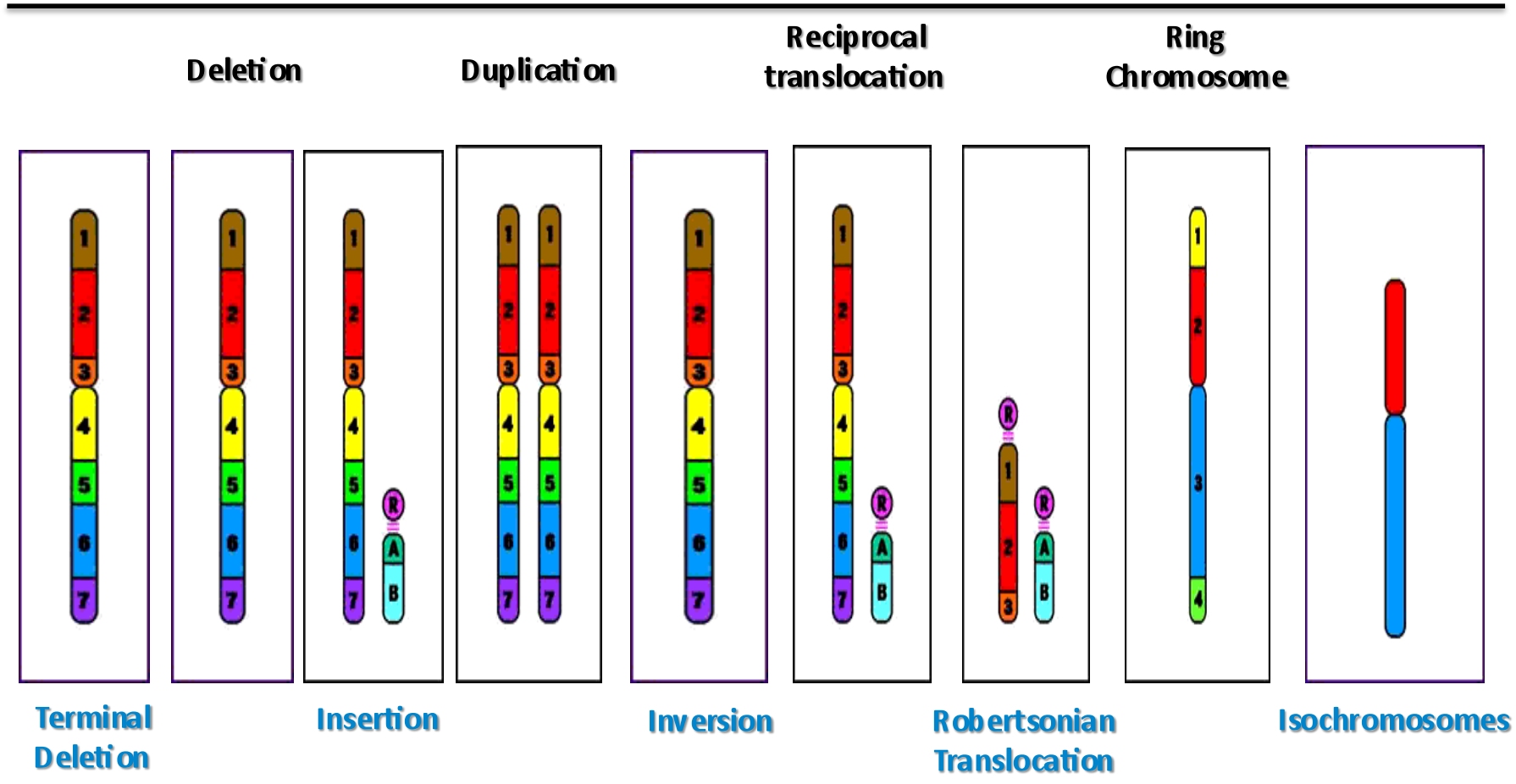
CHROMOSOME ANOMALIES



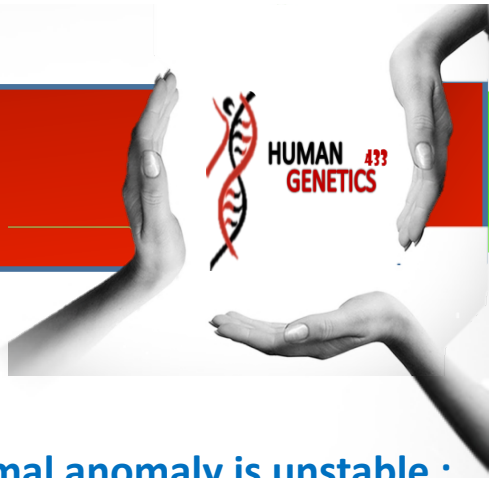
CHROMOSOME ANOMALIES



STRUCTURAL CHROMOSOMAL ANOMALIES



MCQs



1) A result of non-disjunction in meiosis :

A. Aneuploidy
B. Myelogenous Leukemia
C. Cri Du Chat
D. Fragile X

2) (47, XY, +18) is the Karyotype of :

A. Down Syndrome
B. Patau Syndrome
C. Klinefelter Syndrome
D. Edward's Syndrome

3) Diseases that only\mostly affect females :

A. Turner's and Klinefelter Syndrome.
B. Turner's and Edward's Syndrome.
C. Klinefelter and Down Syndrome.
D. Turner's and Patau Syndrome.

4) If the Centromere is divided transversally rather than longitudinally, the chromosome anomaly is :

A. Translocation
B. Inversion
C. Isochrome
D. Insertion

5) This kind of chromosomal anomaly is unstable :

A. Ring form
B. Translocation
C. Inversion
D. Isochromosome

6) Tetraploidy is the kind of polyploidy that has ……. Chromosomes :

A. 69
B. 46
C. 92
D. 23

7) This happens in the G1 in the interphase of the cell cycle :

A. Cytokinesis.
B. Chromosome duplication.
C. Cellular contents, excluding the chromosomes, are duplicated.
D. Segregation of chromosomes.

Human Genetics Team

Team leaders :

Layan Al Tawil

Hussain Al Salman

Team members :

Noura Ahmed
Sara khaled Alkarashi
Nada Al Dammas
Maha Al Rajhi
Shahad Al Muhaideb
Maha Alzahrani
Sara Aldokhayel
Razan Aldhahri

Fahad Alotaibi
Salman Al-rwiba'ah
Hassan Almalaq
Yazeed Al-Ghamdi
Mohammed Almana
Khalid Al-Anazi

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