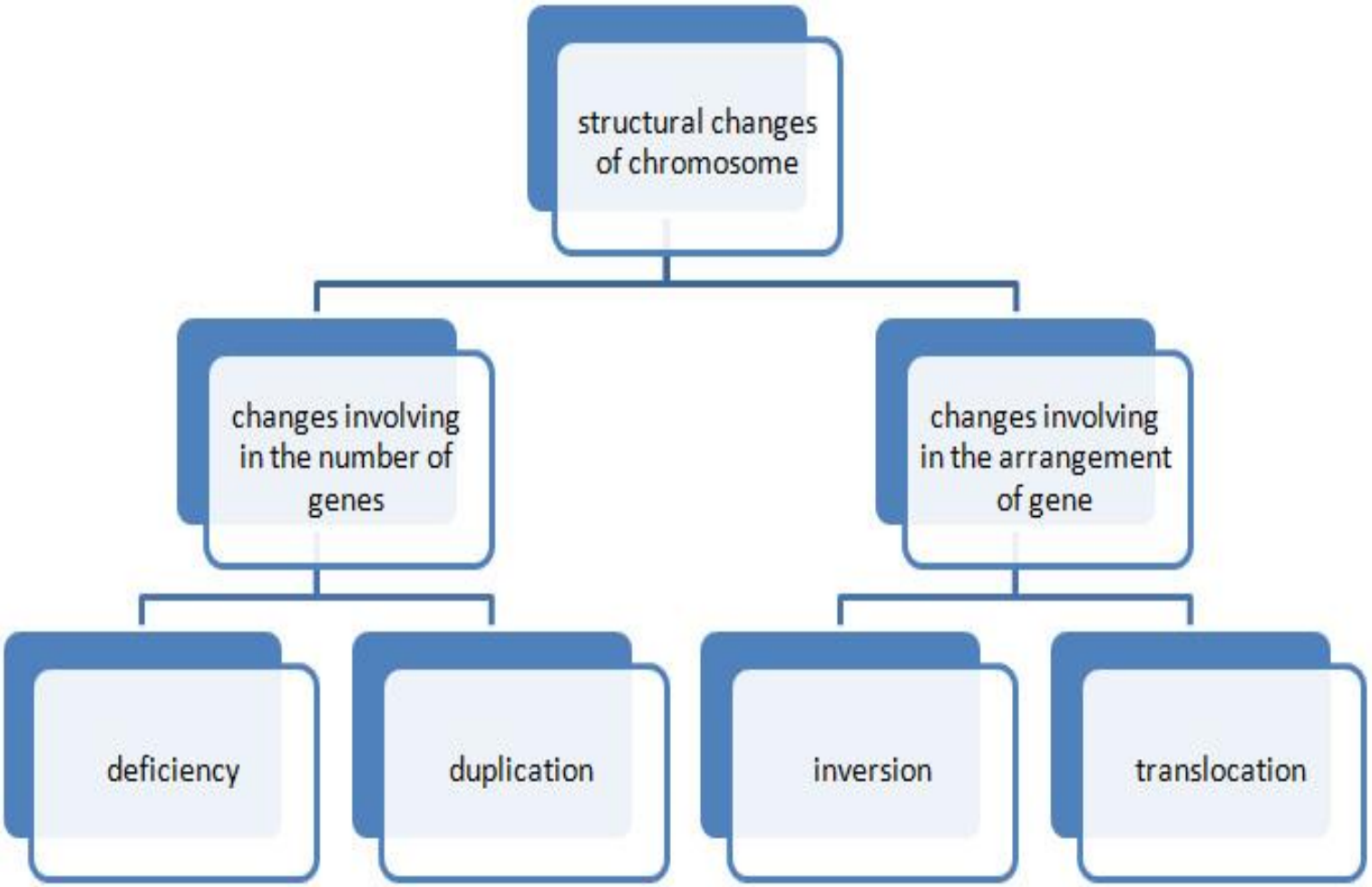
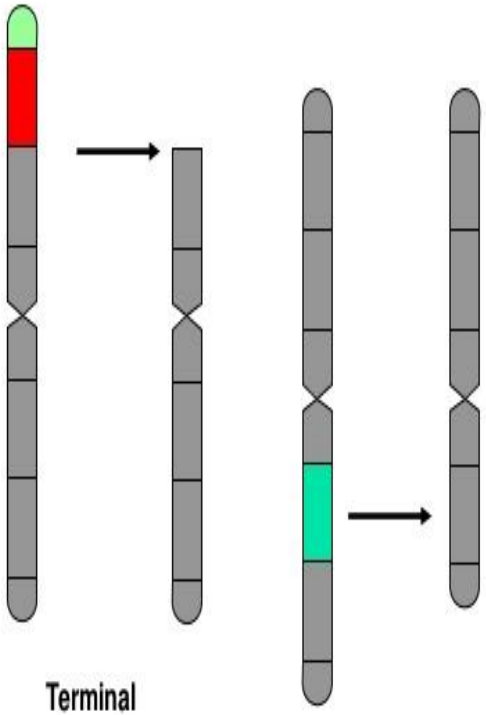
- الوراثة البشرية \ المرحلة الثالثة - العام الدراسي ٢٠٢٠-٢٠٢١
- المحاضرة السادسة \ التغييرات الصبغية - الكروموسومية التركيبية (Chromosomes Abnormalities Structural)
- المحاضر \ الأستاذ الدكتور اياد احمد الطويل
- كلية الأسراء الجامعة \ قسم تقنيات المختبرات الطبية
- وزارة التعليم العالي و البحث العلمي


structural changes of chromosome
changes involving in the number of genes
changes involving in the arrangement of gene
deficiency
duplication
inversion
translocation

Deficiencies

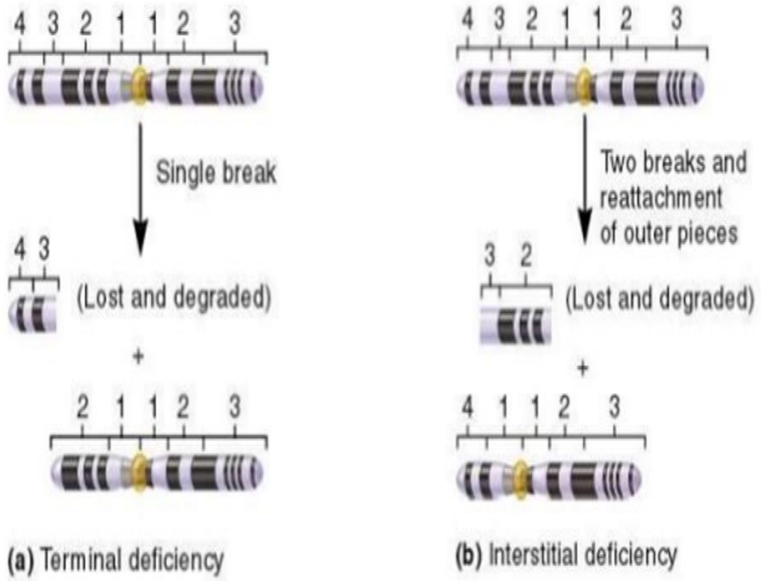
- Phenotypic consequences of deficiency depends on
  - Size of the deletion
  - Functions of the genes deleted
- Phenotypic effect of deletions usually detrimental



Two types of deletion

Deletion

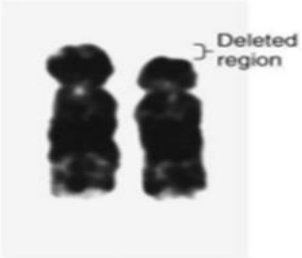
- Loss of a region of chromosome
- A chromosomal deficiency occurs when a chromosome breaks and a fragment is lost



- Known disorders in humans include
- Wolf-Hirschhorn syndrome, which is caused by partial deletion of the short arm of chromosome 4; and
- Jacobsen syndrome, also called the terminal 11q deletion disorder.

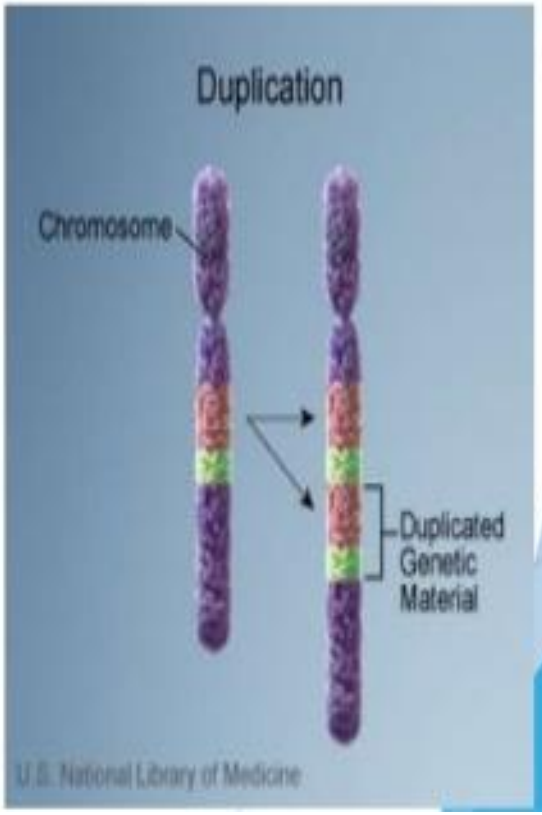
Cri-du-chat Syndrome

- High-pitched cry
- intellectual disability
- delayed development
- small head size
- low birth weight
- weak muscle tone in infant



Duplication

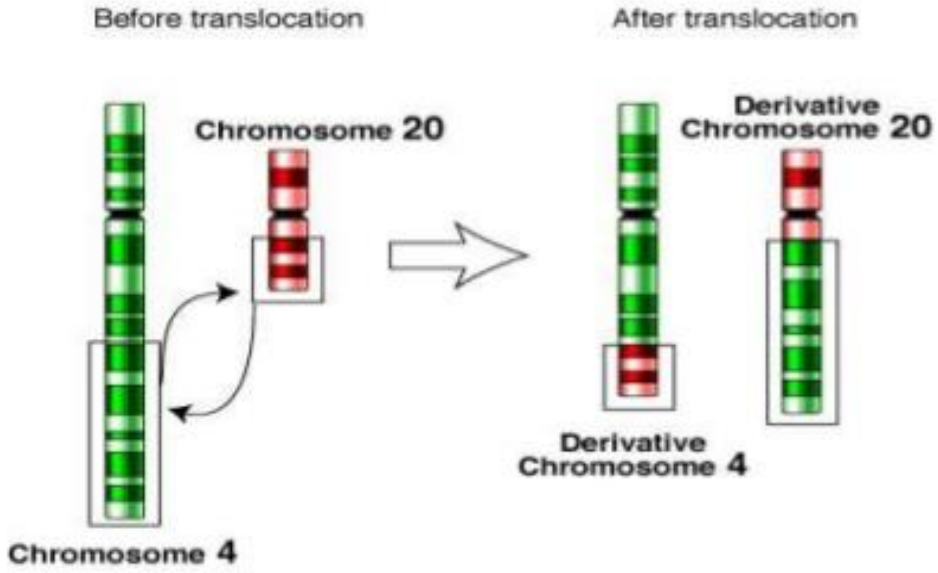
- *A duplication is a chromosomal mutation that results when a segment of DNA breaks off and attaches onto the homologous chromosome.*
- *There are different forms of chromosomal duplications or different tandem configuration* →
  1. *tandem*
  2. *reverse tandem*
  3. *terminal tandem*

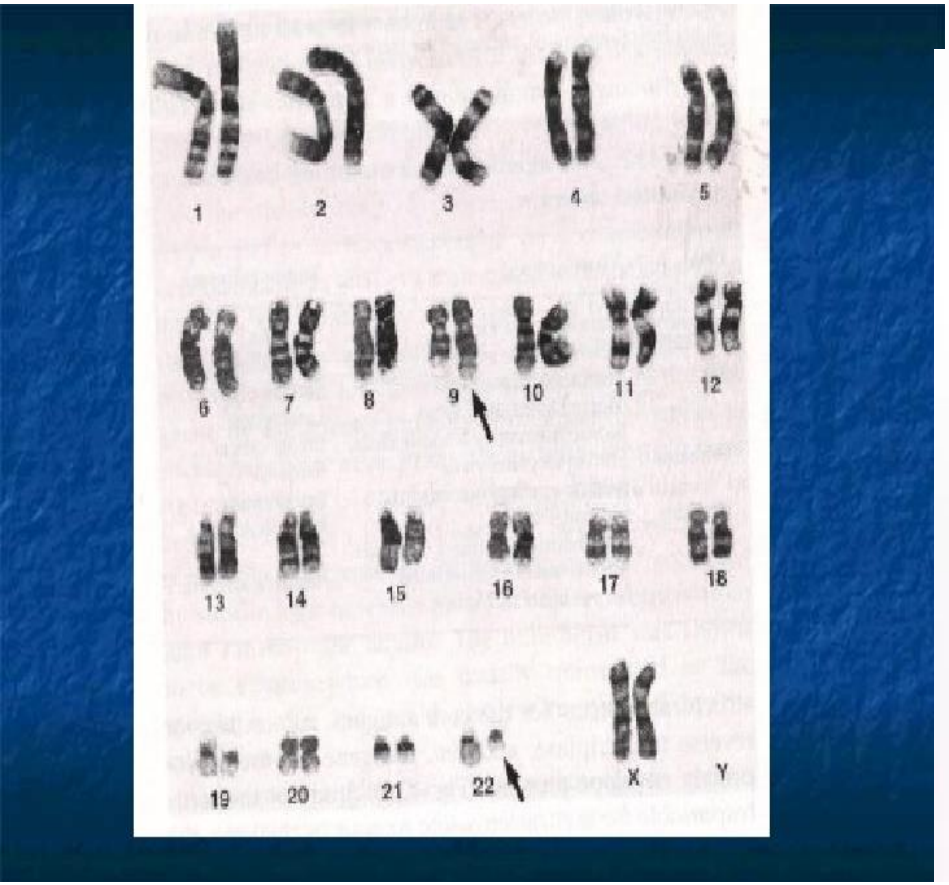


- Translocations: A portion of one chromosome is transferred to another chromosome. There are two main types of translocations:
- Reciprocal translocation: Segments from two different chromosomes have been exchanged.
- Robertsonian translocation: An entire chromosome has attached to another at the centromere - in humans these only occur with chromosomes 13, 14, 15, 21 and 22.

Reciprocal Translocation

- Involves two chromosomes
- One break in each chromosome
- The two chromosomes exchange broken segments

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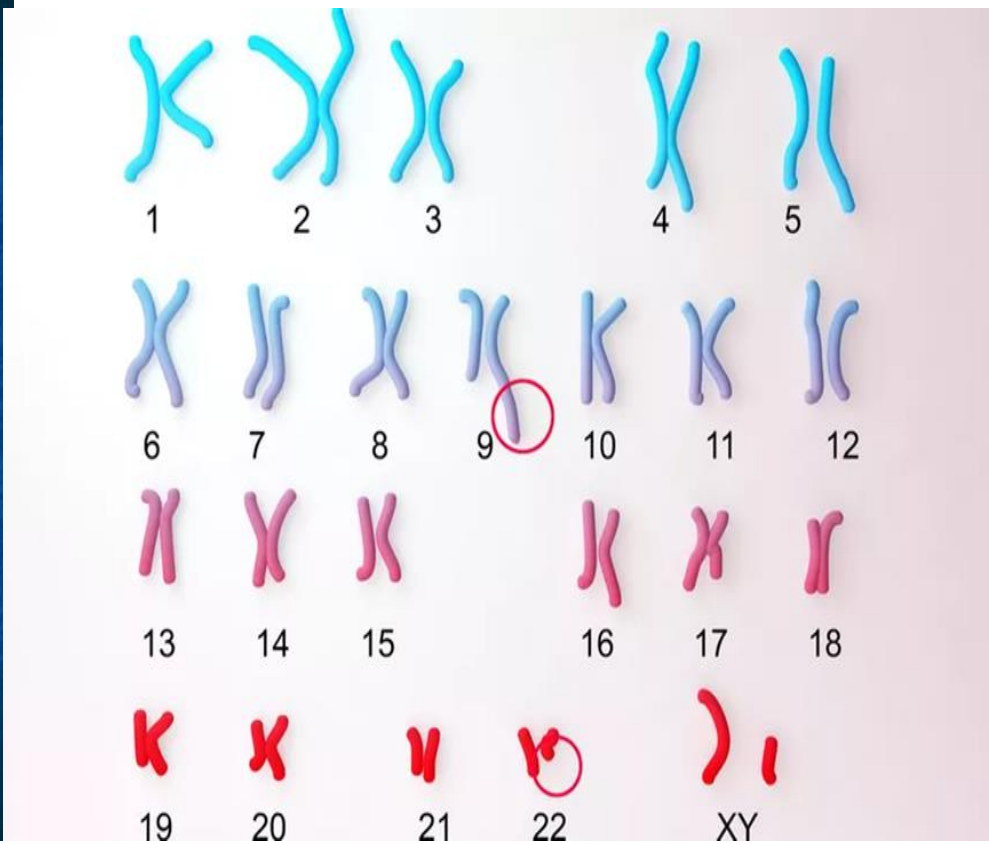
X
Y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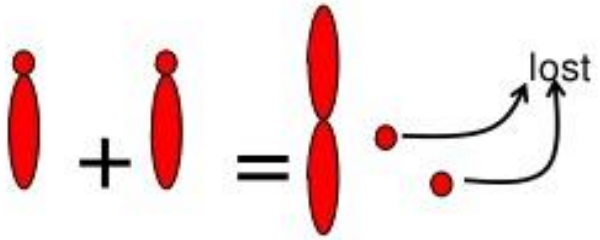
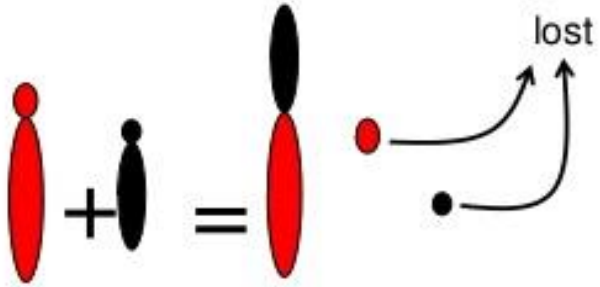
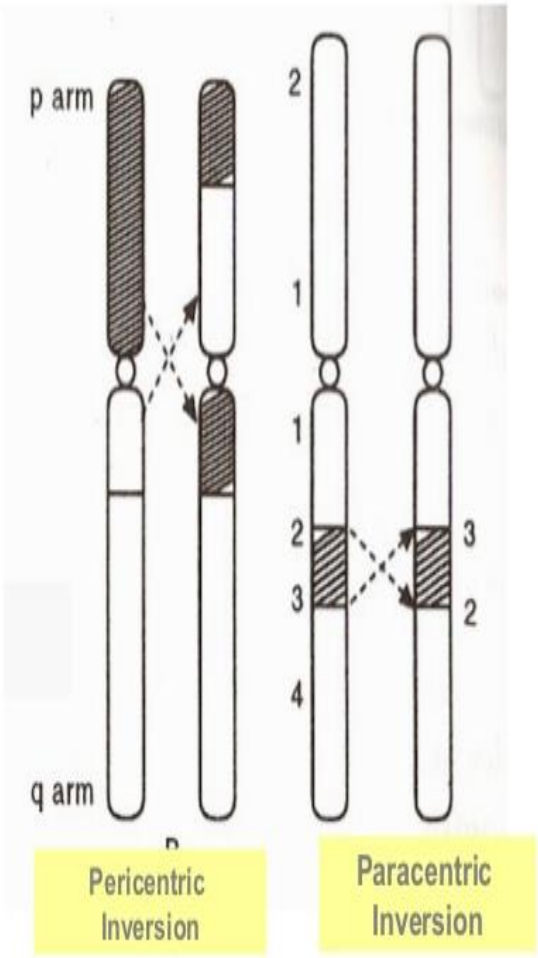
22
XY

Robertsonian Translocation

- Named after W. R. B. Robertson who first identified them in grasshoppers in 1916
- Most common structural chromosome abnormality in humans
  - Frequency = 1/1000 livebirths
- Involves two acrocentric chromosomes
- Two types
  - Homologous acrocentrics involved
  - Non-Homologous acrocentrics involved







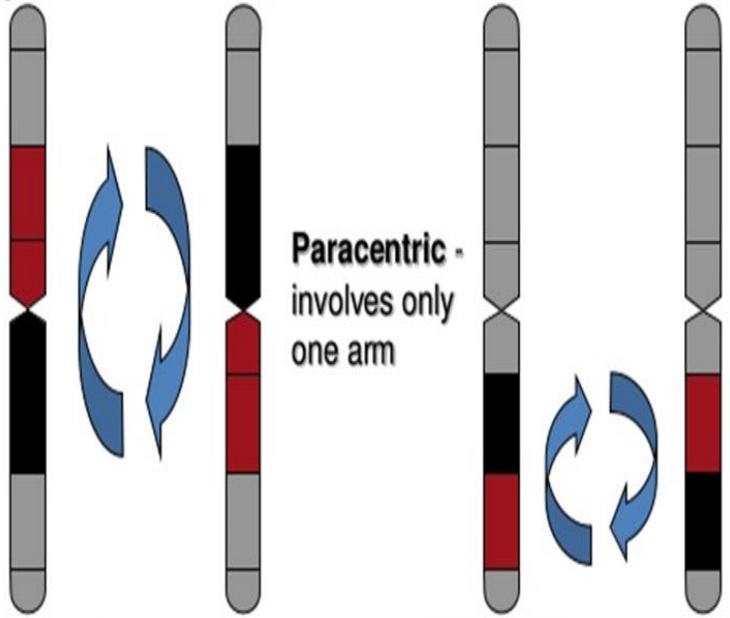
INVERSION

Inversion

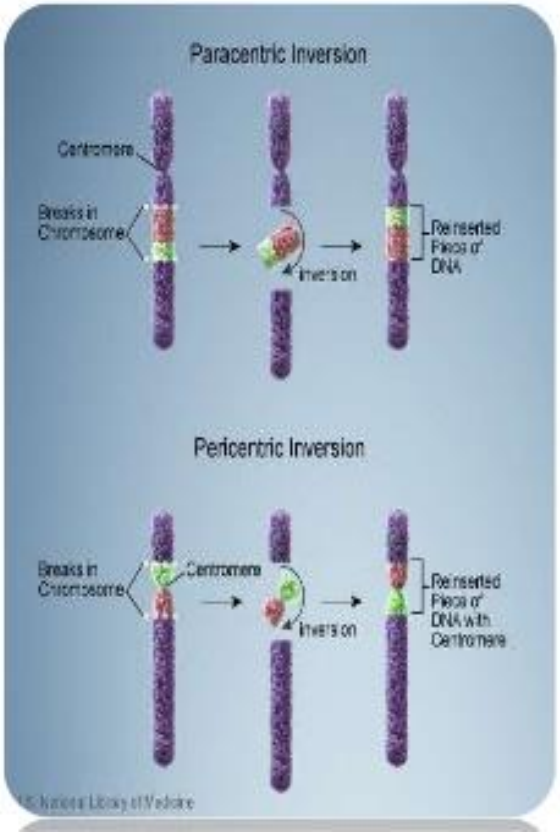
- A segment of chromosome that is flipped relative to that in the homologue
- Two breaks in one chromosome
- The fragment generated rotates 180° and reinserts into the chromosome

Pericentric - involves p and q arm

Paracentric - involves only one arm

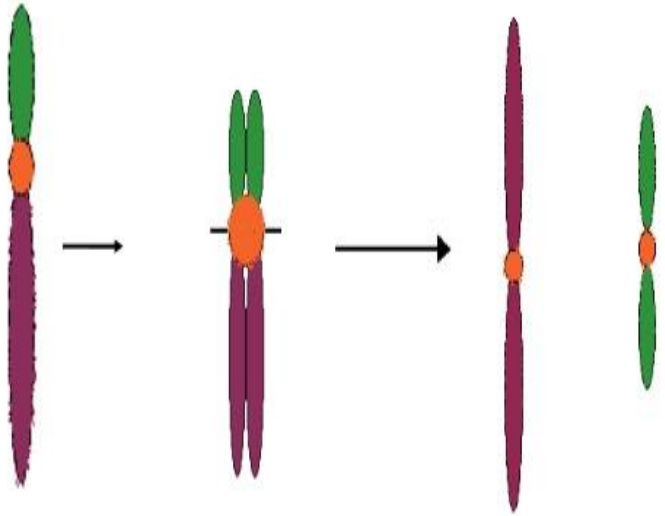


If the centromere is not part of the rearranged chromosome segment, it is a paracentric inversion.



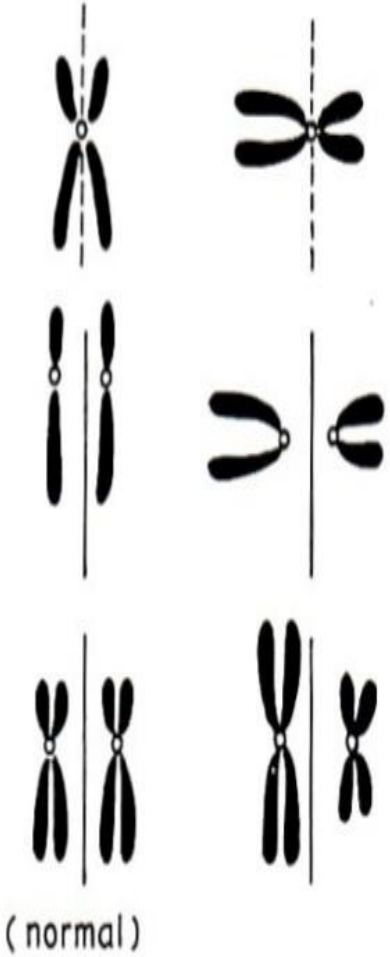
If the centromere is part of the inverted segment, it is described as a pericentric inversion.

Isochromosome
(Transverse centromeric division)



Example:

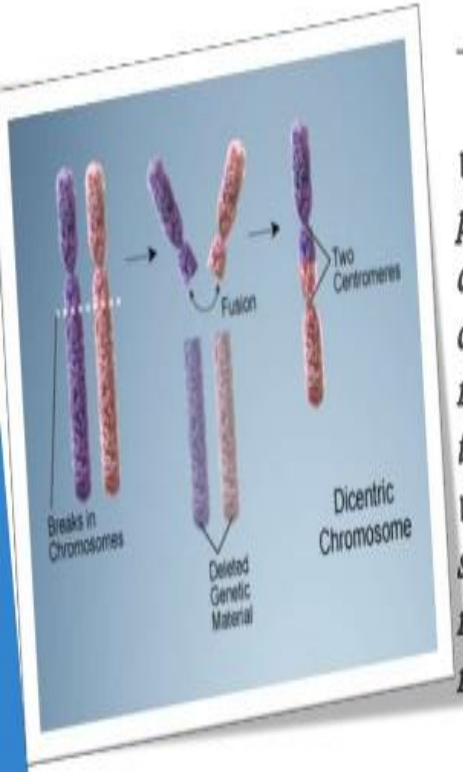
- Long arm of X- chromosome remains, short arms lost
- Cytogenetic variant of Turner's syndrome



(normal)

Isochromosome
(Transverse centromeric division)

Cont.....



Dicentric chromosomes:

Unlike normal chromosomes, which have a single constriction point (centromere), a dicentric chromosome contains two centromeres. Dicentric chromosomes result from the abnormal fusion of two chromosome pieces, each of which includes a centromere. These structures are unstable and often involve a loss of some genetic material.

Cont.....

Ring chromosomes:

Ring chromosomes usually occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure. The ring may or may not include the chromosome's constriction point (centromere). In many cases, genetic material near the ends of the chromosome is lost.

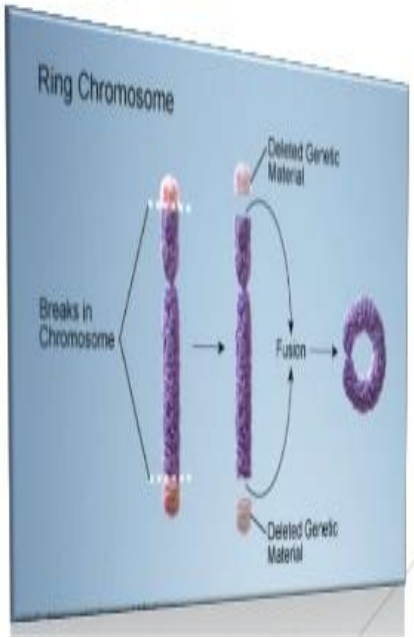
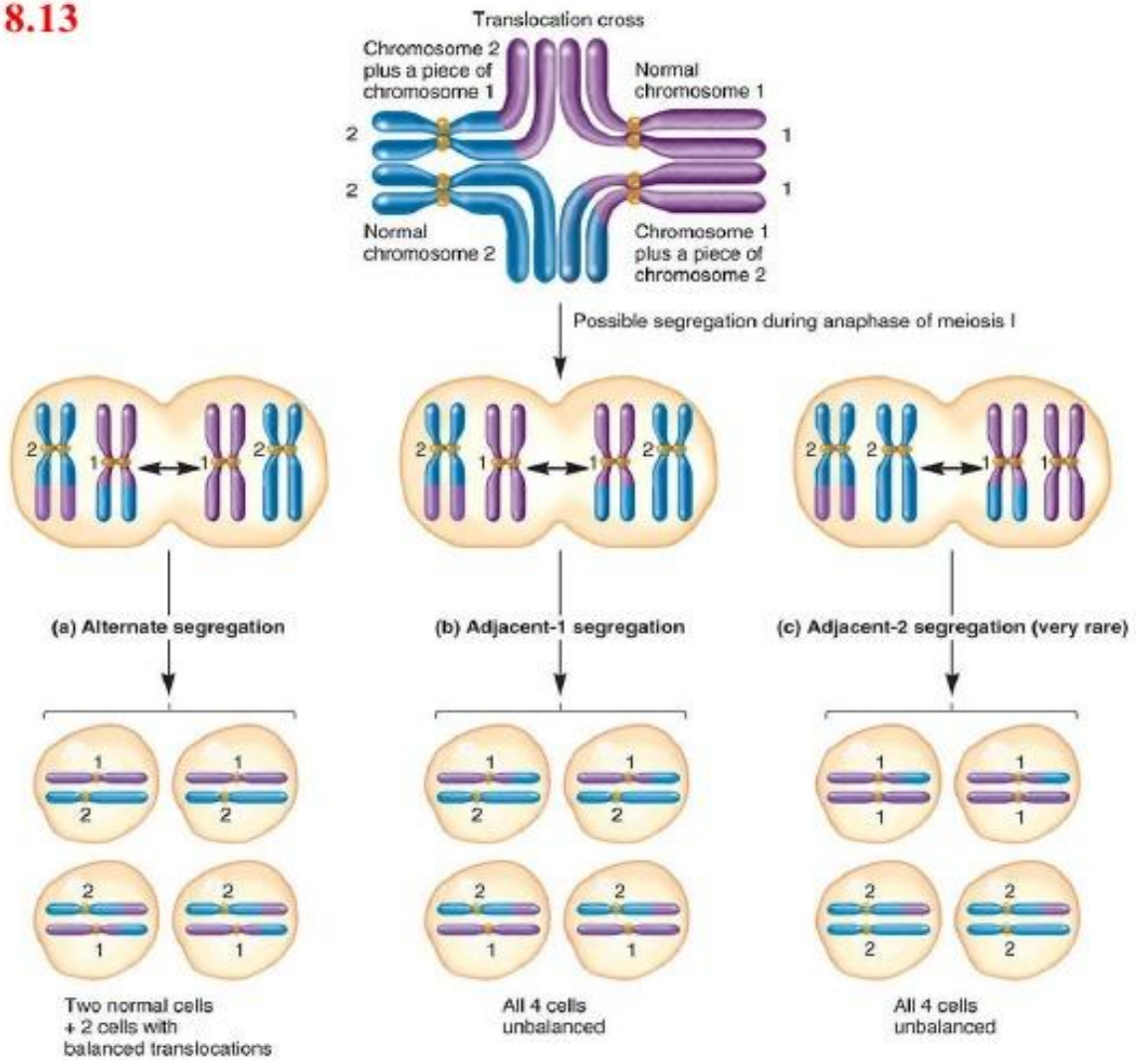


Figure 8.13



- **Chromosomal translocations play a large role in blood cancers. It's estimated that translocation are presented in up to 90% of LYMPHOMAS and over 50% of LEUKEMIAS.**

Following some examples :

t (8;22) : Acute myeloblastic leukemyia

t (9;22) : Philadelphia Chromosome

t (15;17) : Acute promyelotic leukemyia

t (12;15), t(1;12) Acute myelogenous leukemyia

t (2;5) Anaplastic large cell lymphoma

t (8;14) Burkitt's lymphoma

t (11;14) Mantle cell lymphoma

t (14;18) Follicular lymphoma

SOME Diseases resulted from chromosomal deletion

Cri-du-chat (cat cry) Syndrame	46,XX/XY,5p15.2 / 46,XX/XY,5p15.3
Retinoblastoma	46,XX/XY,13q14
Wilms Tumor	46,XX/XY, 11P13
Wolf-Hirschhorn Syndrome	46, XX/XY, 4 short arm
Williams Syndrome	46,XX/XY, 4 long arm
Prader- Willi Syndrome	46,XX/XY,15 long arm (q11-q13) – Paternal
Angelman Syndeome	46,XX/XY, 15 long arm(q11-q13) -- Maternal

SOME types of chromosomal duplication

Duplication of chromosome 4, short arm 46,XX/XY

Duplication of chromosome 4, long arm 46, XX/XY

Duplication of chromosome 7, long arm 46, XX/XY

Duplication of chromosome 9, short arm 46, XX/XY

Some types of chromosomal inversion/ below are 3 types of inversion in human chromosome

Chromosomal inversion in human is known as inv(9)(p12q13) (Paracentric inversion }

Chromosomal inversion in human is known as inv(3)(q24q27) { Pricentric inversion }

Chromosomal Inversion in human as inv(2)(p11.2q13) { Paracentric inversion }

IMPORTANT NOTE

- في الملزمة الصفحتين ٤٢ و ٤٣ توجد ثلاثة جداول تتضمن عدد من التغييرات الصبغية \ الكروموسومية العددية و التركيبية و تأثيراتها في الانسان ، مثلا الجدول في صفحة ٤٢ يوضح التغييرات الصبغية \ الكروموسومية التركيبية خصوصا النوعين الفقدان و التضاعف و ماهي الاعراض التي تحدث عنها في الانسان.
- اما الجدولين في الصفحة ٤٣ فيوضحان (الجدول الاول يبين المختصرات و ماذا تعني و الجدول الثاني يبين نوع التغيير و مفهومه)

Thanks for your listening

Dr. Ayad