GENETICS

Sheet no. 7

Writer:

Layan Daoud

Corrector:

Layan Daoud

Doctor:

Mohammad Al-shboul

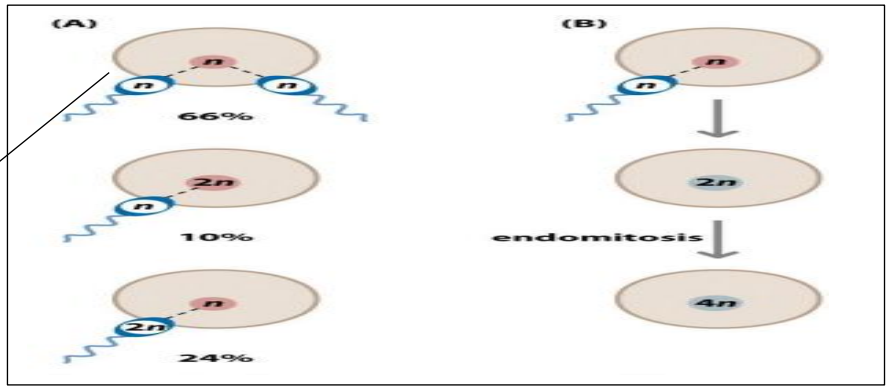
NOTE: The slide information was written in black, and the doctor's interpretation was written in blue.

(A) Origins of human triploidy. Dispermy is the principal cause, accounting for 66% of cases. Triploidy is also caused by diploid gametes that arise by occasional faults in meiosis; fertilization of a diploid ovum and fertilization by a diploid sperm account for 10% and 24% of cases, respectively.

- 69,XXX triploidy

- 69,XXY triploidy

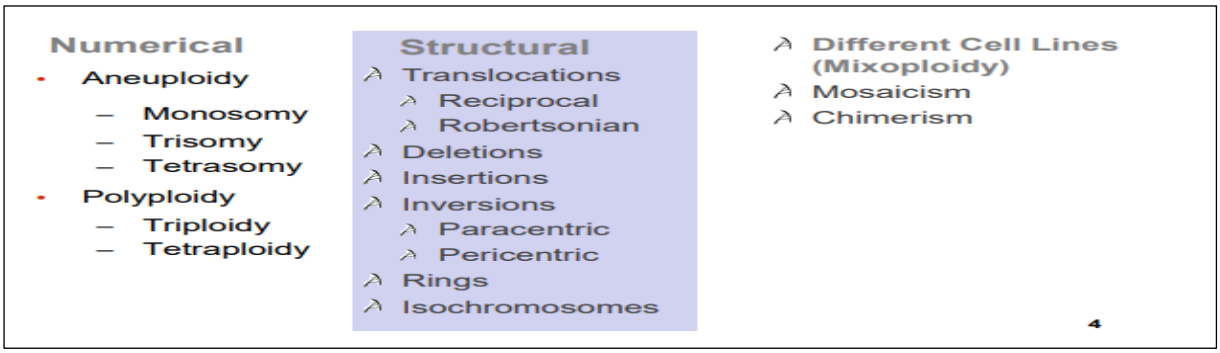
- 69,XYY triploidy



Two sperms each on is haploid fertilized one egg to produce triploidy (there are three copies of chromosomes)We have another scenario: Maybe diploid sperm fertilized a haploid egg

(B) Tetraploidy involves normal fertilization and fusion of gametes to give a normal zygote. Subsequently, however, tetraploidy arises by endomitosis when DNA replicates without subsequent cell division.

Structural Chromosomal Abnormalities



Chromosome Nomenclature

- **46,XY Normal male**
- **46,XX Normal female**

• 47,XXY Male with extra X chromosome (Klinefelter syndrome)

• 45,X Female with missing X chromosome (Turner syndrome)

• 46,XY,t(2p;8p) Male with translocation between short arms of chromosomes 2 & 8

• 46,XY, del(5p) Male with deletion in short arm of chromosome 5 (Cri Du Chat syndrome).

• 46,X,r(X) Female with ring chromosomes X (Turner syndrome)

Term	Explanation	Example
p	Short arm	
q	Long arm	
cen	Centromere	
del	Deletion	46,XX,del(1)(q21)
dup	Duplication	46,XY, dup(13)(q14)
fra	Fragile site	
i	Isochromosome	46,X,i(Xq)
inv	Inversion	46XX,inv(9)(p12q12)
ish	In-situ hybridization	
r	Ring	46;XX,r(21)
t	Translocation	46,XY,t(2;4)(q21;q21)
ter	Terminal or end	Tip of arm; e.g., pter or qter
/	Mosaicism	46,XY/47,XXY
+ or –	Sometimes used after a chromosome arm in text to indicate gain or loss of part of that chromosome	46,XX,5p–

Chromosome Structural Aberrations

- Structural chromosome abnormalities are relatively frequent in human populations

- Chromosome breaks in the germline can lead to heritable structural abnormalities; those occurring in somatic cells may increase the risk of cancer.

- Chromosomes may break at almost any point, but there are sites of preferred breakage, called hotspots.

- The breaks may be repaired, but because any two broken ends that are sufficiently close together in the nucleus may rejoin, an extremely wide variety of structurally altered chromosomes occur.

- Balanced or unbalanced

Hot spot region means this region can get a mutation.

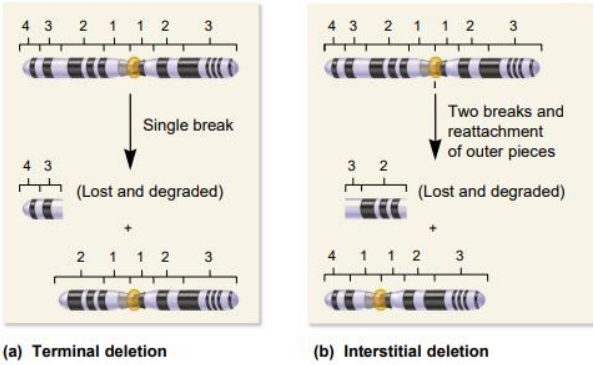
Balance may be transformed to unbalanced in the next-generation buzz the maternal and paternal genome has the silent mutation.

(Deletions)

• A chromosomal deficiency occurs when a chromosome breaks and a fragment is lost (Involve loss of chromosomal material).

On the chromosomal level, many regions could affected and each region consists of a lot of DNA fragments.

Terminal deletions are caused by a single break with loss of the segment distal to the break. Interstitial deletions result from two breaks in a chromosome, loss of the intervening segment, and reunion of the breakpoints. del(5)(p15.3) This describes a terminal deletion of the short arm of chromosome 5. All chromosomal material distal to band p15.3 is missing. del(20)(q11.2q13.3) This represents an interstitial deletion of the long arm of chromosome 20. The material between



Buzz we have two copies of gene may be person is not affected by mutation!

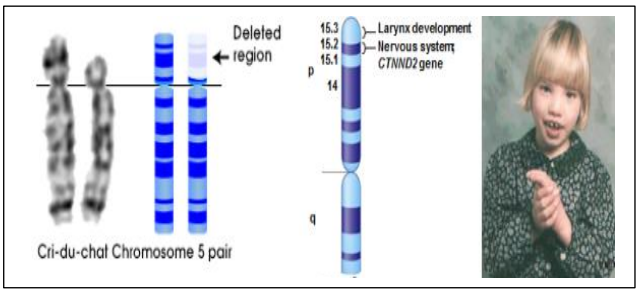
(الحمد لله)

- Associated with several genetic disorders

Deletion	Syndrome	Phenotype
5p–	Cri du chat syndrome	Infants have catlike cry, some facial anomalies, severe mental retardation
11q–	Wilms tumor	Kidney tumors, genital and urinary tract abnormalities
13q–	Retinoblastoma	Cancer of eye, increased risk of other cancers
15q–	Prader-Willi syndrome	Infants: weak, slow growth; children and adults: obesity, compulsive eating

Terminal Deletion

- When deletions have a phenotypic effect, they are usually detrimental – Example: cri-du-chat (cat's cry) syndrome in humans
- Associated with an array of malformations
- The most characteristic of which is an infant cry that resembles a meowing cat due to defects in the larynx.



The disorder is characterized by:

- Intellectual disability
- Delayed development
- Small head size (microcephaly),
- Low birth weight,
- Hypotonia in infancy.
- **Distinctive facial features:**
- Widely set eyes (hypertelorism),
- Low-set ears,
- Small jaw, and a rounded face.
- Some children are born with a heart defect

Translocations (t)

- A translocation is an abnormality resulting from an exchange of genetic material between nonhomologous chromosomes.
- Translocations may be reciprocal and Robertsonian (the latter resulting in derivative chromosomes and loss or gain or material)

Reciprocal Autosomal Translocations

• **Reciprocal translocations represent one of the most common structural rearrangements observed in humans.**

• **A reciprocal translocation forms when two different chromosomes exchange segments.**

• **The resulting chromosomes are called derivative chromosomes.**

• **Reciprocal translocations are frequently balanced because the entire genetic material is present.**

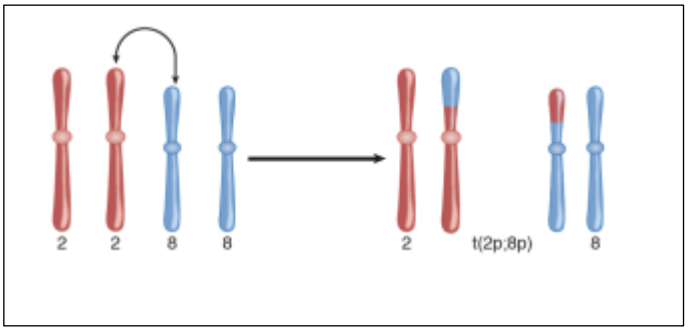
• **In the example shown in this figure, a balanced translocation involving chromosomes 2 and 8 has occurred.**

• **The distal short arm of chromosome 2 has replaced the distal short arm material on chromosome 8, and vice versa**

The karyotype would be: 46,XY,t(2p;8p) or 46,XX,t(2p;8p)

• **Although individuals who carry truly balanced reciprocal translocations are themselves clinically normal, they do have an increased risk for having children with unbalanced karyotypes secondary to meiotic malsegregation of their translocation.**

46,XY,t(5p13;10q25) A male with translocation between 5p13 (band 3 of region 1 of short arm of chromosome 5) and 10q25 (band 5 of region 2 of long arm of chromosome 10) 46,XY,t(5;10)(p13;q25



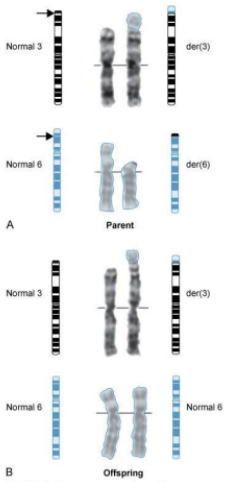


FIG 6-15 A, The parent has a reciprocal balanced translocation involving the short arms of chromosomes 6 and 3.
The distal short arm of the 6 has been translocated to the very distal tip of the 3. A small piece of chromosome 3 is attached to the derivative 6. This person had a child whose chromosomes are depicted in B

This karyotype is 46,XX,t(3p;6p).

The **offspring of this woman received the derivative chromosome3, termed der(3), and the normal 6; thus, the child had a partial trisomy** of the distal portion of chromosome 6 (i.e., 6p trisomy). This is a well-established but rather uncommon chromosomal syndrome.

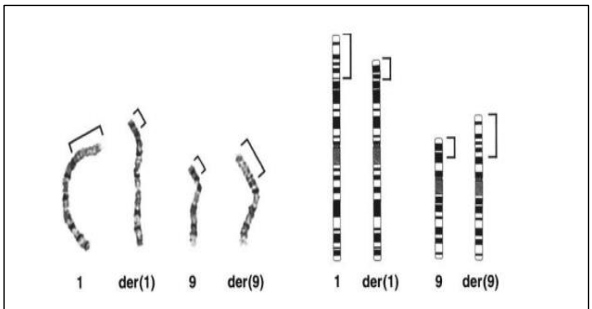


Fig. 9.16 A balanced reciprocal translocation involving the short arm of chromosomes 1 and 9 [t(1;9)(p32.3;p21)]. The translocated segments of each chromosome have been bracketed.
der Derivative or structurally rearranged chromosome: A chromosome that has been altered as a result of a translocation

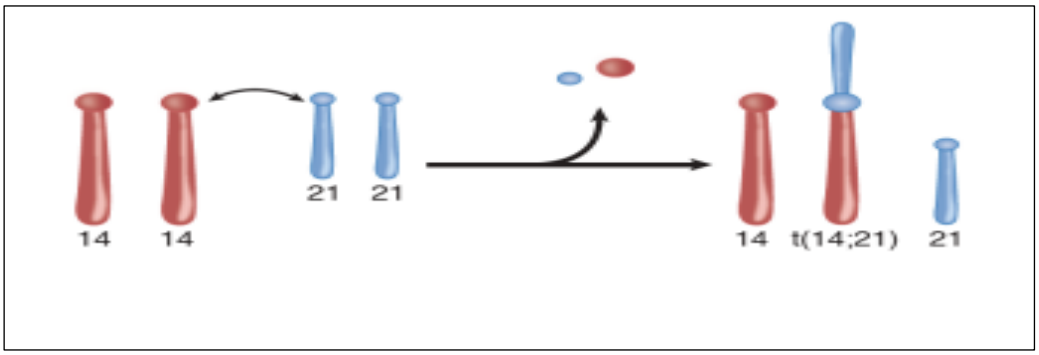
46,XY,t(5;17)(p13.3;p13) denotes a translocation between the short arms of chromosomes 5 and 17 and region 13, band 3, and region 13, respectively.

Robertsonian translocations

- **Much more common than reciprocal translocations**
- **They occur only in the acrocentric chromosomes (13, 14, 15, 21 and 22).**
- **They are also called whole-arm translocations or centric fusion translocations.**
- **Involved two homologous (paired) or non-homologous chromosomes**
- **Involve the loss of the short arms of two of the chromosomes and subsequent fusion of the long arms (the participating chromosomes break at their centromeres and the long arms fuse to form a single, large chromosome with a single centromere)**

A common Robertsonian translocation involves fusion of the long arms of chromosomes 14 and 21. The karyotype of a male carrier of this translocation would be: 45,XY ,der(14;21)(q10;q10). This individual lacks one normal 14 and one normal 21 and instead has a chromosome derived from a translocation of the entire long arms of chromosomes 14 and 21.

Approximately 5% of Down syndrome cases are the result of a Robertsonian translocation affecting chromosome 14 and chromosome 21.



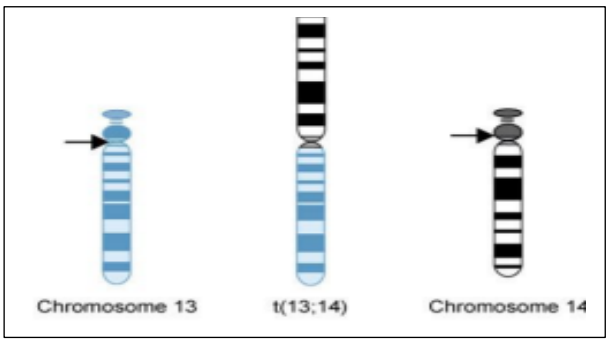
- The carrier of a Robertsonian translocation can produce conceptions with monosomy or trisomy of the long arms of acrocentric chromosomes.

- Carriers of Robertsonian translocations have an increased risk for infertility, spontaneous abortions and chromosomally unbalanced offspring, but are otherwise healthy.

- Balanced carriers of Robertsonian translocations therefore typically have 45 chromosomes rather than the usual 46.

- The only notable genetic material within the short arm region of each of these chromosomes is a nucleolar organizer region composed of multiple copies of the ribosomal RNA genes.

- Because this is redundant information, loss of this material from the two chromosomes involved in the translocation is therefore not clinically significant



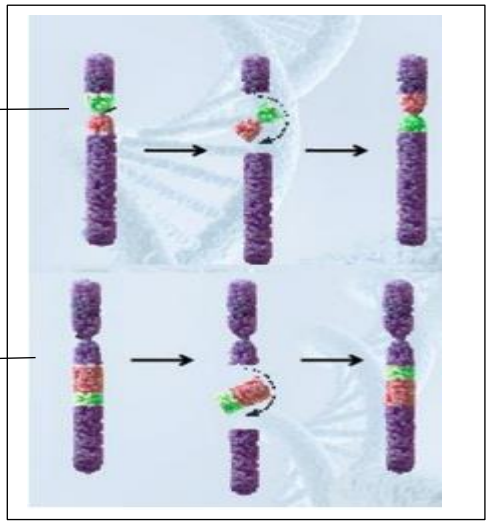
Inversions (inv)

- **In an inversion, a chromosomal segment breaks, reorients 180°, and reinserts itself.**
- **If an inversion involves the centromere, with one break in each chromosome arm, it is said to be pericentric (pericentric which involves both arms of a chromosome).**
- **A paracentric inversion is isolated to one chromosome arm and does not involve the centromere. (involve only one arm of a chromosome)**

ABCDEFG might become ABEDCFG after an inversion

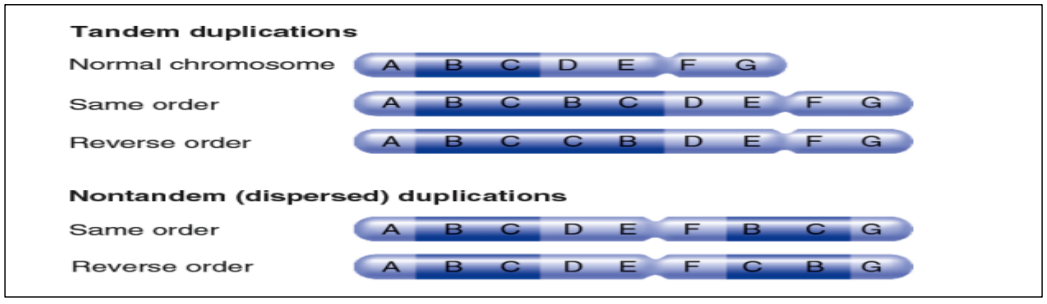
Centromeres are included so it called pericentric

Centromeres are not included so it called paracentric.



- **46,XX,inv(16)(p13.1q22)**
- **This is a pericentric (both arms) inversion of chromosome 16. A break has occurred in the short arm at band 16p13.1 and the long arm at band 16q22.**
- **The chromosome segment between these bands is present but inverted.**
- **This aberration is commonly observed in acute myelomonocytic leukemia with eosinophilia**
- **Parents with inversions are usually normal in phenotype but can produce offspring with deletions or duplications**

Types of duplications (Dp)



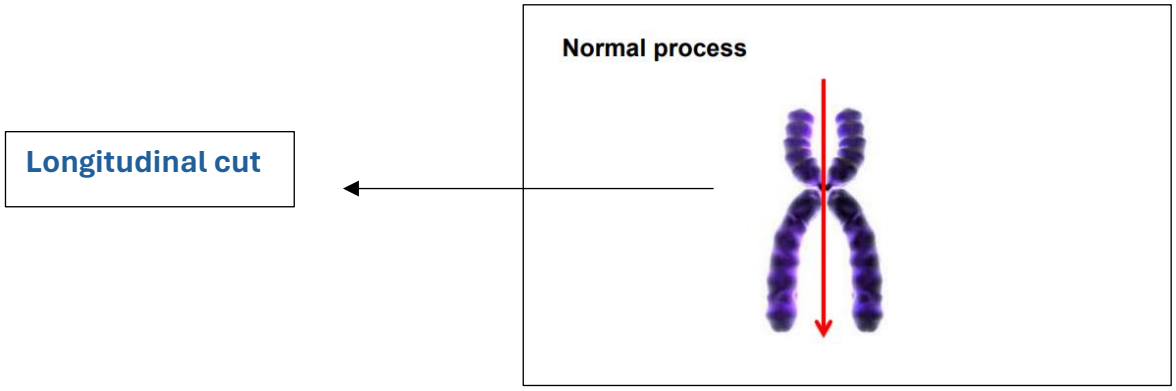
• The orientation of duplications is either direct or inverted and is indicated by the order of the bands with respect to the centromere in the karyotype designation.

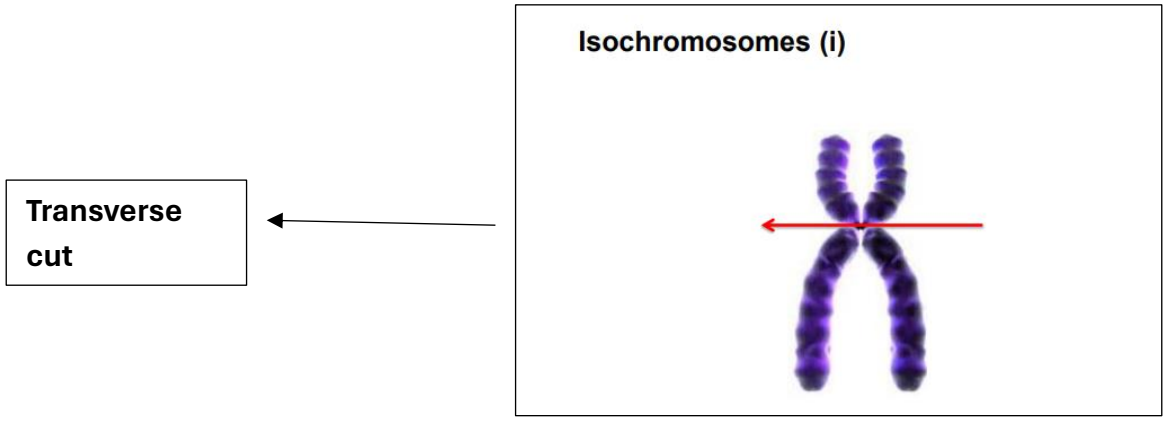
• 46,XY,dup(1)(q21q42)

• This is a direct duplication of the segment between bands 1q21 and 1q42 in the long arm of chromosome 1.

• 46,XX,dup(13)(q34q21)

• This is an inverted duplication of the segment between bands 13q21 and 13q21 in the long arm of chromosome 13





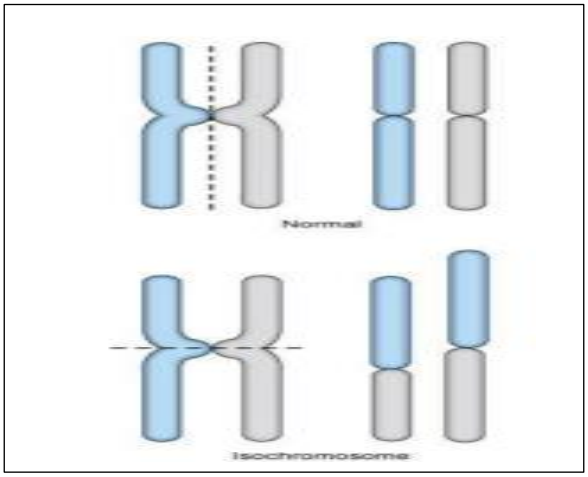
Isochromosomes (i)

Autosomal isochromosome is lethal

• Is an abnormal chromosome with two identical arms due to duplication of one arm and loss of the other arm

• An isochromosome consists of two copies of the same chromosome arm joined through a single centromere in such a way that the arms form mirror images of one another.

• 46,XY,i(6)(p10): An isochromosome for the short arm of chromosome 6 has replaced one copy of chromosome 6.



• Individuals with 46 chromosomes, one of which is an isochromosome, are monosomic for the genes within the lost arm and trisomic for all genes present on the isochromosome.

• The neoplasia created from i(17q) is caused by a decrease and increase in gene dosage from the monosomy of the p arm and trisomy of the q arm, respectively.

• In general, the smaller the isochromosome, the smaller the imbalance and the more likely the survival of the fetus or child that carries the isochromosome.

• It is therefore not surprising that, with few exceptions, the most frequently reported autosomal isochromosomes tend to involve chromosomes with small arms.

• Some of the more common chromosome arms involved in isochromosome formation include 5p, 8p, 9p, 12p, 18p, and 18q. it could be existed in all chromosome ,but these chromosome are the most affected

• isochromosomes of most autosomes are lethal

هاي الوردة إلك عشان خلصت الشيت يا شاطر