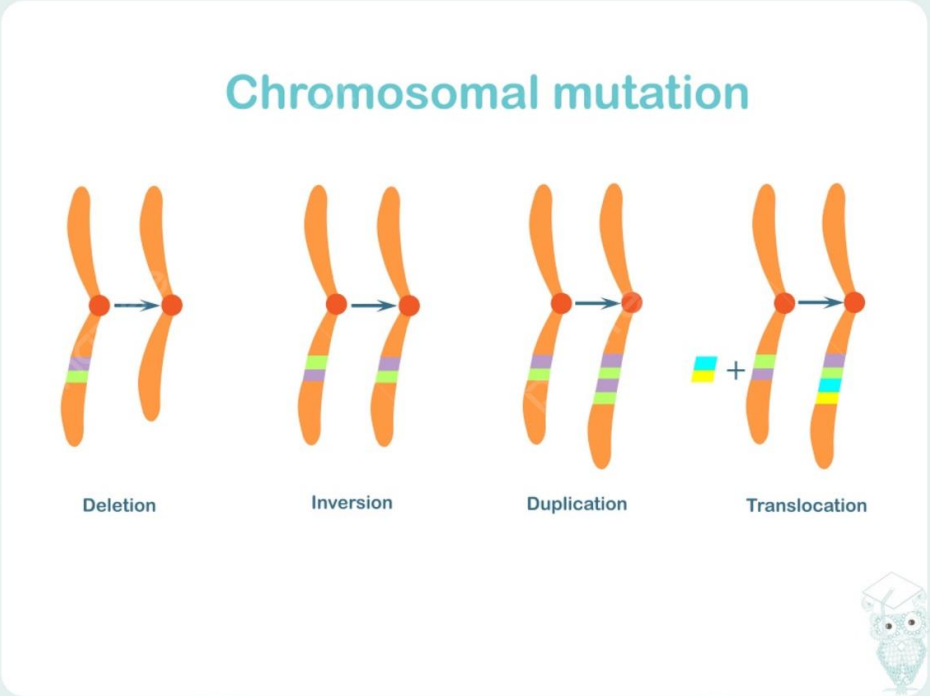
Chapter 5: Human Genetics

- Document 1: Inheritance of Genetic Traits
- Document 2: Autosomal Diseases
- Document 3: Sex-linked Diseases
- Document 4: Chromosomal Abnormalities
- Document 5: Prenatal Diagnosis

Document 4

Chromosomal Abnormalities



p.98

Chromosomal Abnormality

I- Numerical:

abnormal number **of chromosmes**(missing or extra chromosome)

Autosomal

-abnormality in number of autosomes

(extra or missing).

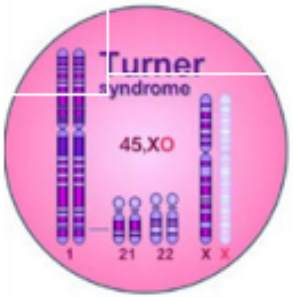
-ex: Trisomy 21(Down syndrome)

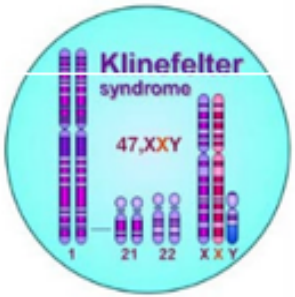
Gonosomal

- abnormality in number of gonosomes (extra or missing)

-ex: Turner syndrome 45,X

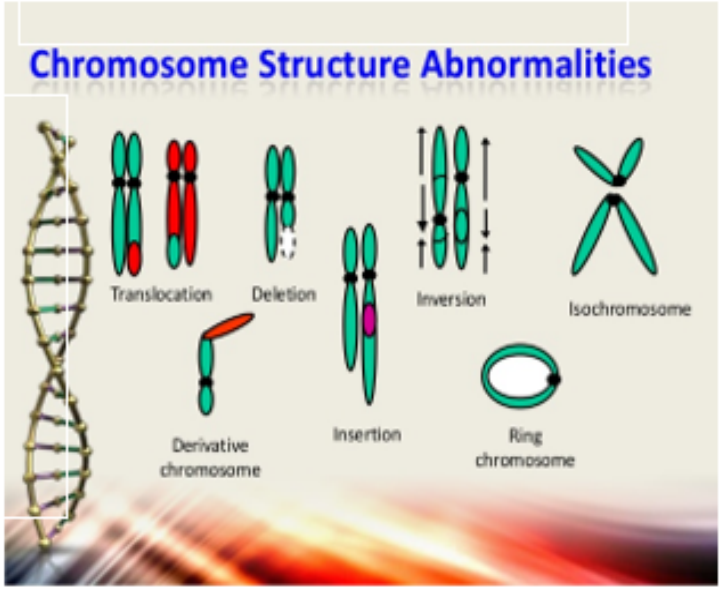
Klinefeltersyndrome:47,XXY





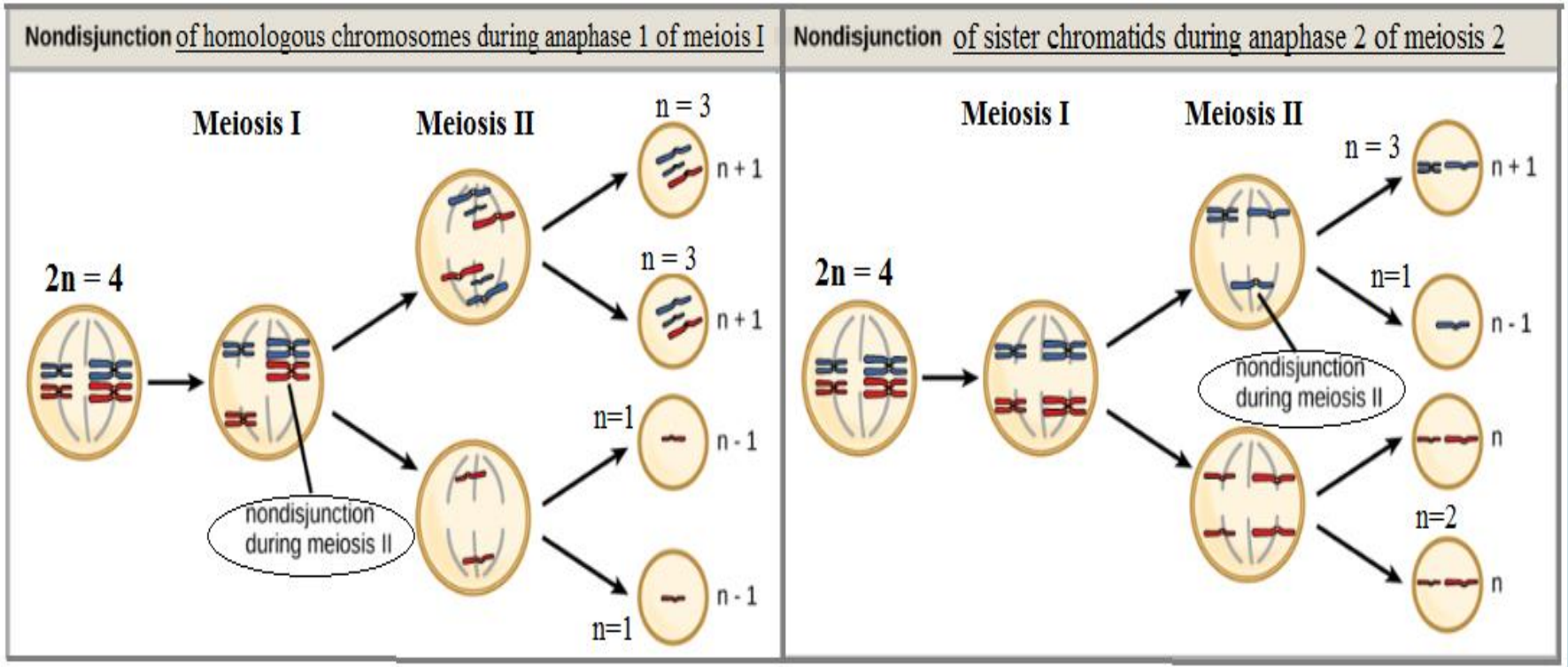
II- Structural:

Abnormal shape of chromosome



I. Chromosomal Numerical abnormalities:

- Cause: It is due to non-disjunction of homologous chromosomes during anaphase 1 of meiosis 1 or non-disjunction of sister chromatids during anaphase 2 of meiosis 2.
- There may be an extra (47) or missing chromosome (45).

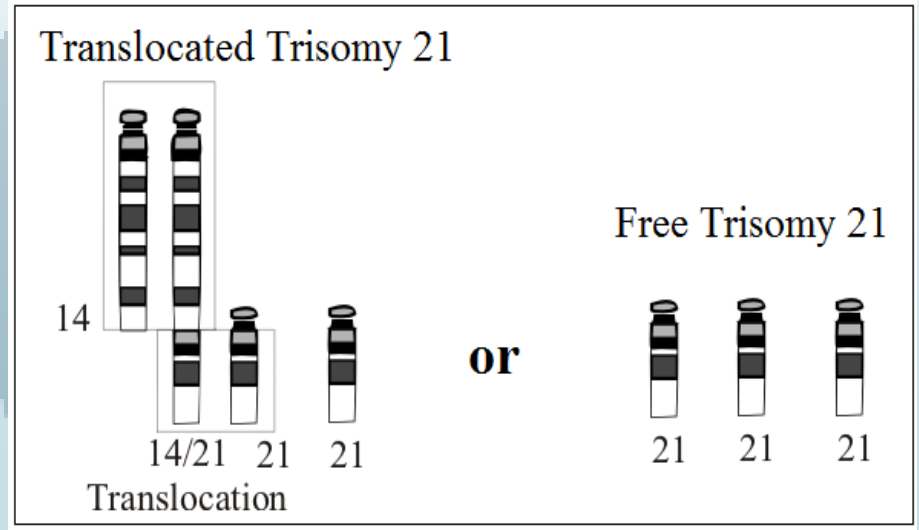


- If there is excess or missing genetic information (due to extra or missing chromosome), then this leads to an abnormal phenotype.

I. 1- Chromosomal Autosomal (Numerical) Abnormality:

- **example**: Trisomy 21 or Down Syndrome.

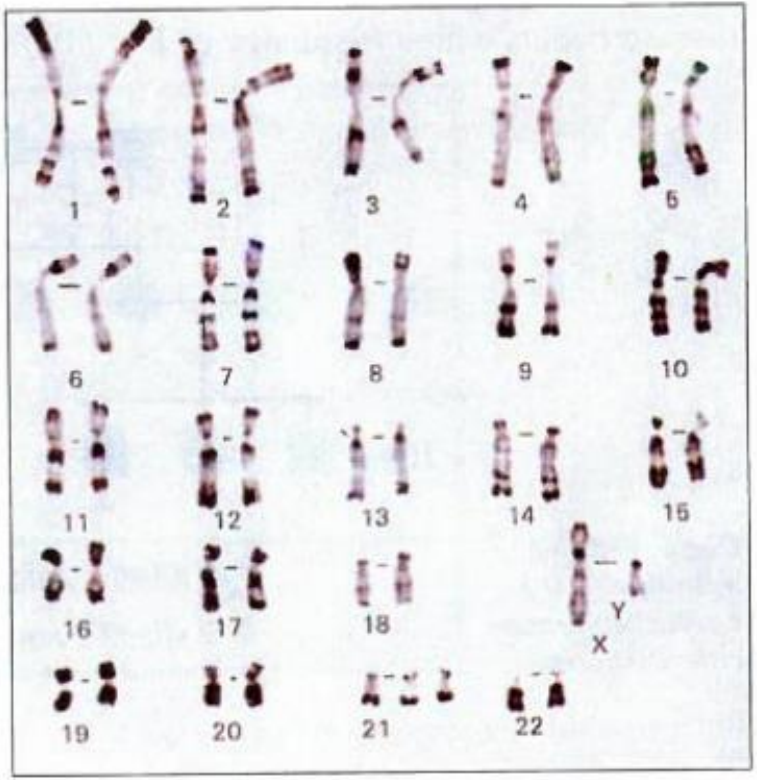
- Cause: It is due to numerical abnormality in autosome 21 where there is an extra copy of chromosome 21 (3 instead of 2).



- **Doc a shows familial or free trisomy 21, 3 chromosomes 21 instead of 2 at pair number 21**

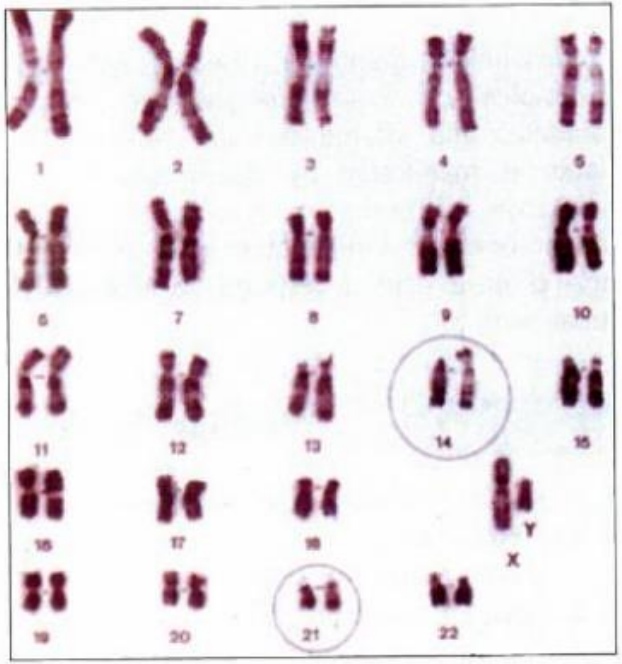
⇨abnormal karyotype and abnormal phenotype.

-Chromosomal formula: 47, XX or XY



Doc.a *Karyotype of a child with familial (free) trisomy 21.*

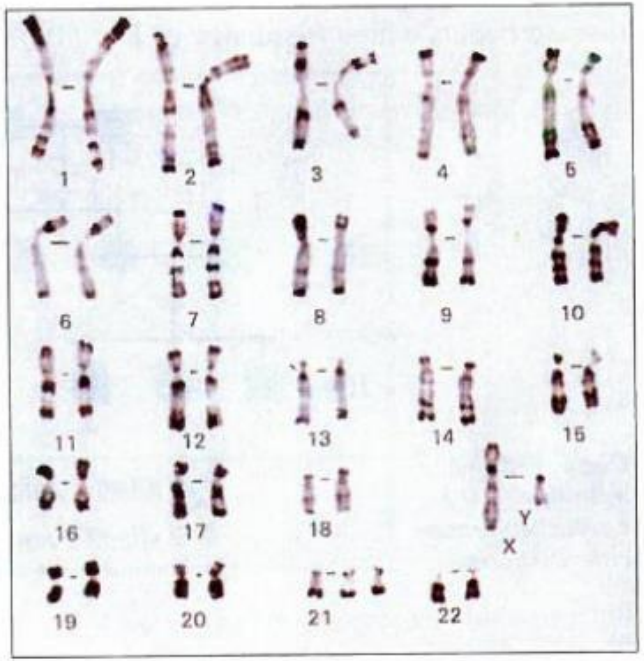
- **Doc c, p.98 shows linked or translocated trisomy 21, 2 chromosomes 21 at pair number 21 and the third copy of chromosome 21 is translocated to chromosome number 14.**
  ⇨ abnormal karyotype and abnormal phenotype.
  -Chromosomal formula: 46, XX or XY, t (21:14)



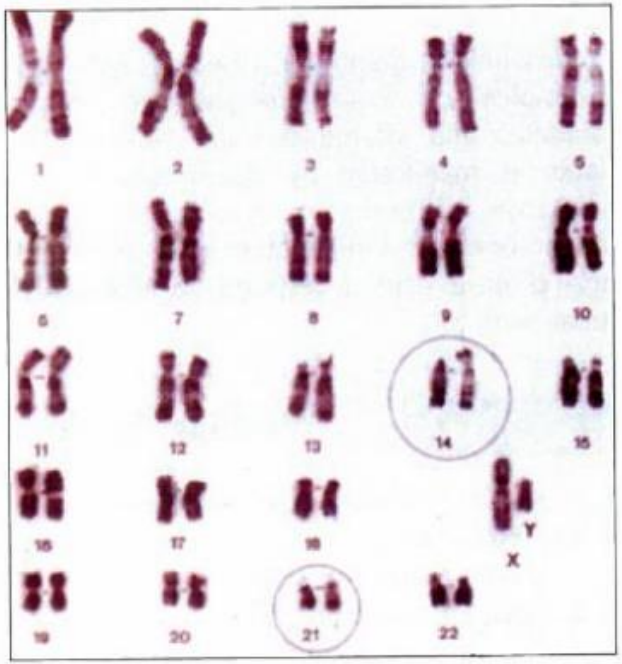
Doc.c *Karyotype of a child with linked (translocated) trisomy 21.*

- Application 1:

➢ Referring to Doc a and c p.98, answer the following questions:



Doc.a *Karyotype of a child with familial (free) trisomy 21.*



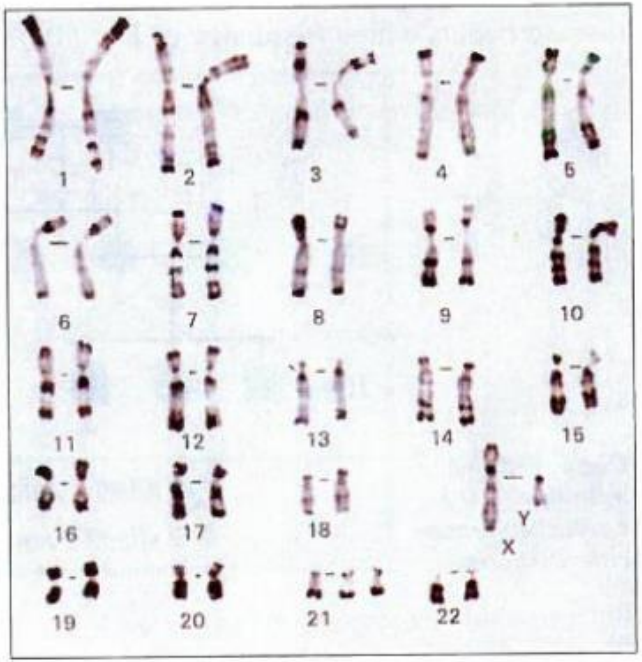
Doc.c *Karyotype of a child with linked (translocated) trisomy 21.*

1- Write the chromosomal formula in each of the two documents a and c.

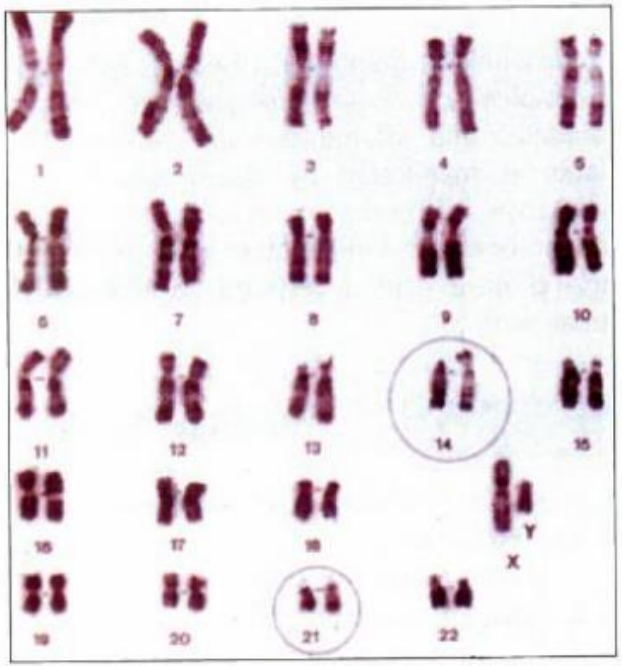
Document a: 47, XY, +21.

Document c: 46, XY, t (21:14) .

- Referring to Doc a and c p.98, answer the following questions:



Doc.a *Karyotype of a child with familial (free) trisomy 21.*

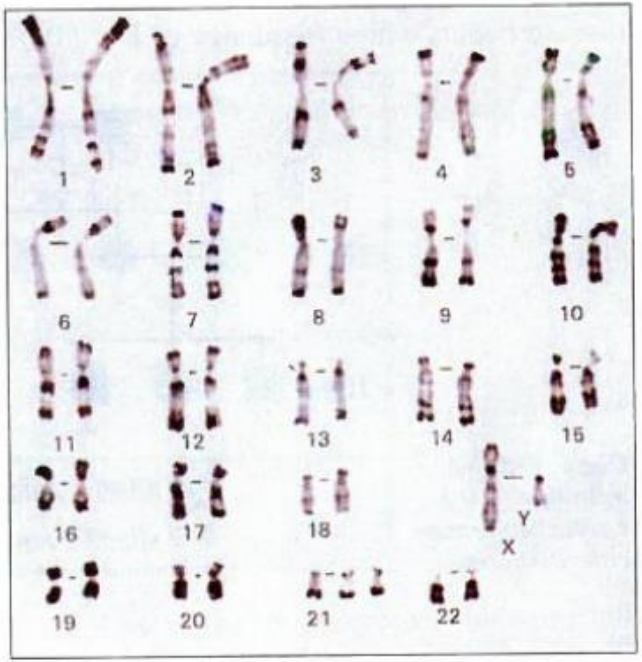


Doc.c *Karyotype of a child with linked (translocated) trisomy 21.*

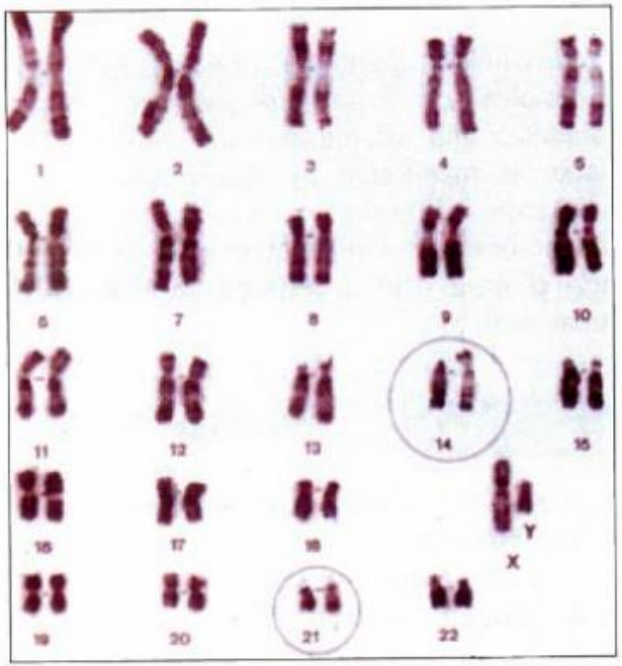
2- Name the disease represented in these documents.

Trisomy 21

- Referring to Doc a and c p.98, answer the following questions:



Doc.a *Karyotype of a child with familial (free) trisomy 21.*

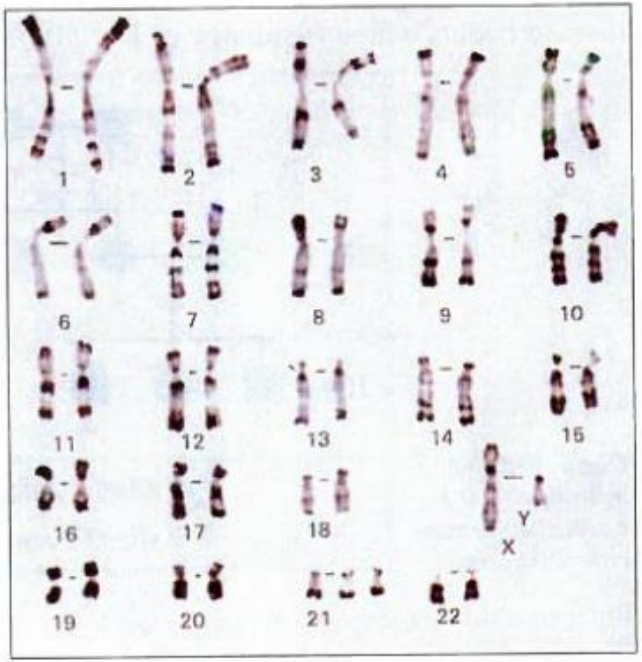


Doc.c *Karyotype of a child with linked (translocated) trisomy 21.*

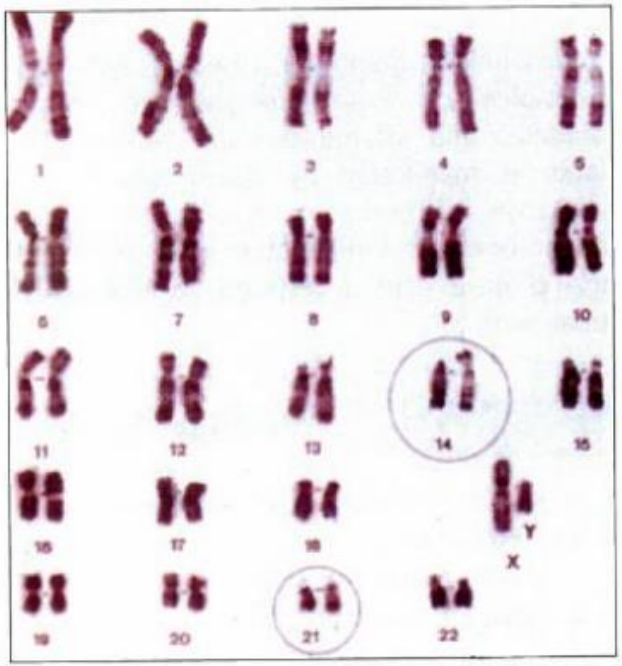
3- Specify the sex of the individual to which karyotype a belongs.

Male, due to the presence of Y gonosome.

- Referring to Doc a and c p.98, answer the following questions:



Doc.a *Karyotype of a child with familial (free) trisomy 21.*



Doc.c *Karyotype of a child with linked (translocated) trisomy 21.*

4- Compare karyotypes a and c.

- Title: A table showing chromosomal formulas and characteristics for a normal and abnormal karyotypes.

Chromosomal formula	*Characteristics*
46,XY	A normal male having 46 chromosomes per cell. Gonosomes are one X and one Y
46,XX	A normal female having 46 chromosomes per cell. Gonosomes are two X.
47, XX, +8	An abnormal female with trisomy 8 having 47 chromosomes per cell including extra copy of chromosome 8. Gonosomes are two X.
45, XY, -13	An abnormal male with monosomy 13 having 45 chromosomes per cell including a missing chromosome 13. Gonosomes are one X and one Y.
47, XXY	An abnormal male with Klinefelter syndrome having 47 chromosomes per cell with extra X gonosome. He is sterile having two X gonosomes and 1 Y gonosome.
45, XO or 45,X	An abnormal female with Turner syndrome having 45 chromosomes per cell with a missing X chromosome. She is sterile having 1 X gonosome only.

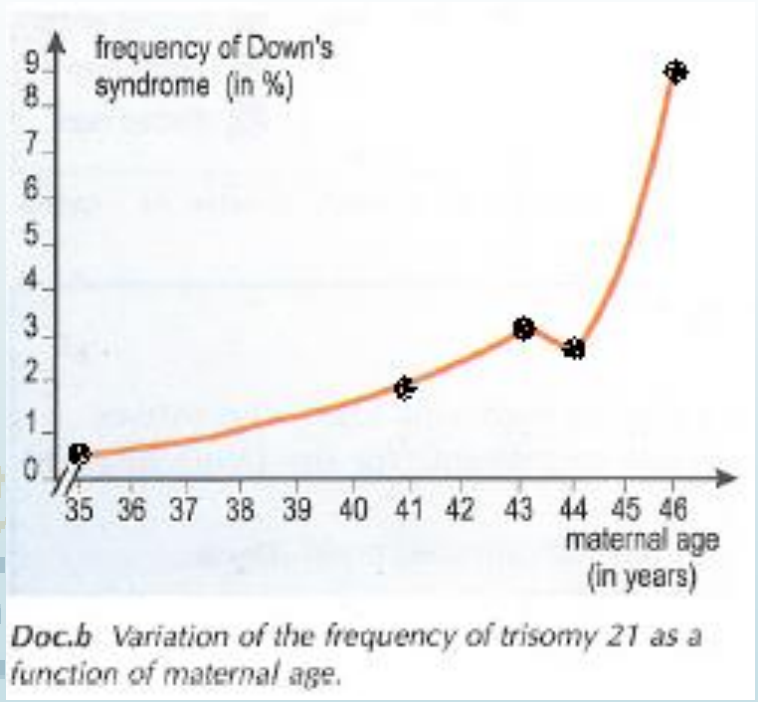
- Application 2:

Document b shows the frequency of trisomy 21 as a function of maternal age.

1- Convert document b into a table.

Title: A table showing the variation of frequency of Down's syndrome (%) as a function of maternal age (years)

Maternal age (years)	35	41	43	46
Frequency of Down's syndrome (%)	0.5	2	3	9

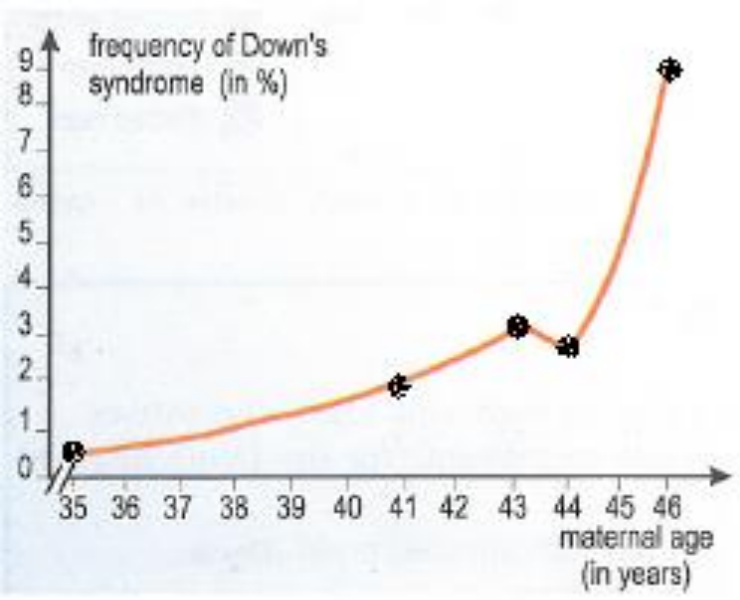


Doc.b Variation of the frequency of trisomy 21 as a function of maternal age.

2- Analyze document b. What do you conclude?

As maternal age increases from 35 to 46 years, the frequency of down syndrome increases from 0.5 to 9 %.

Therefore, maternal age is a risk factor for down syndrome.



Doc.b Variation of the frequency of trisomy 21 as a function of maternal age.

I. 2- Chromosomal Gonosomal (Numerical) Abnormality:

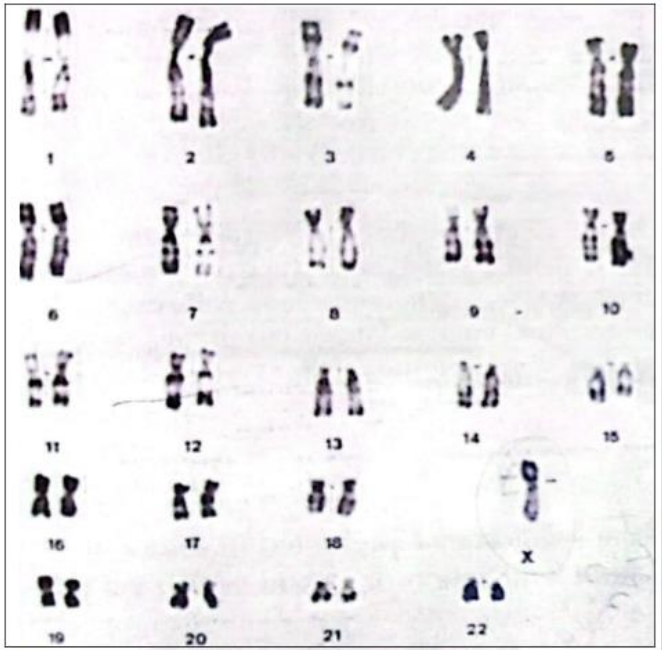
- Application 3:

Doc.e, p.99 shows the karyotype of an individual suffering from chromosomal abnormality:

1.Referring to doc e, indicate the chromosomal number and chromosomal formula.

chromosomal number: 2n-1= 45.

chromosomal formula: 45, X



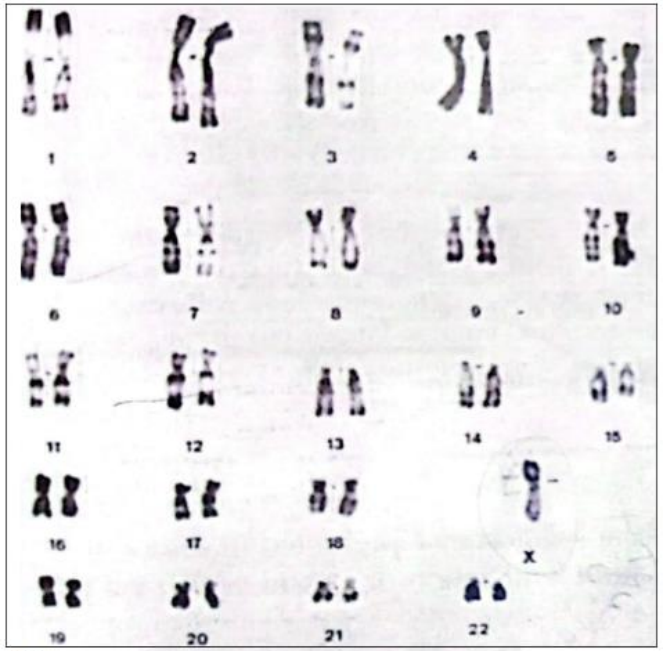
Doc. e

2. Name the disease represented in doc e.

Turner syndrome.

3. Indicate the type of abnormality represented in doc e.

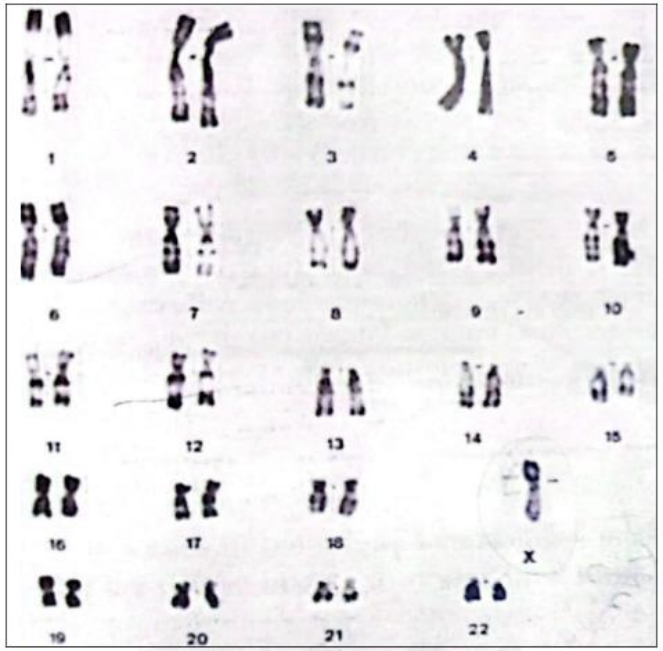
Numerical gonosomal abnormality.



Doc. e

4. Determine the sex of the individual to which the karyotype in doc e belongs.

Since there is absence of Y gonosome, then this karyotype belongs to a female.



Doc. e

→ ***Turner syndrome is a gonosomal numerical abnormality which affects females where there is a missing X gonosome. Females with Turner syndrome are sterile.***

- Application 4:

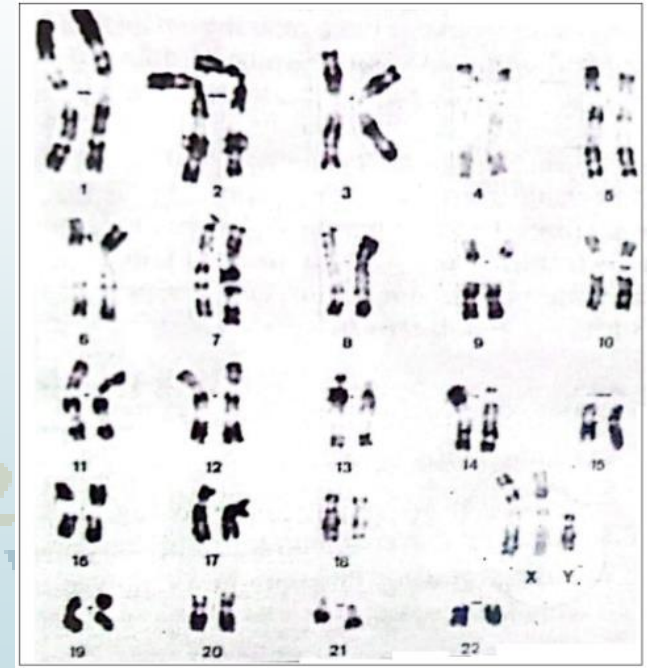
Doc.f, p.99 shows the karyotype of an individual suffering from chromosomal abnormality:

- Referring to Doc.f:

1- Indicate the chromosomal number and chromosomal formula.

chromosomal number: 2n+1= 47

chromosomal formula: 47, XXY



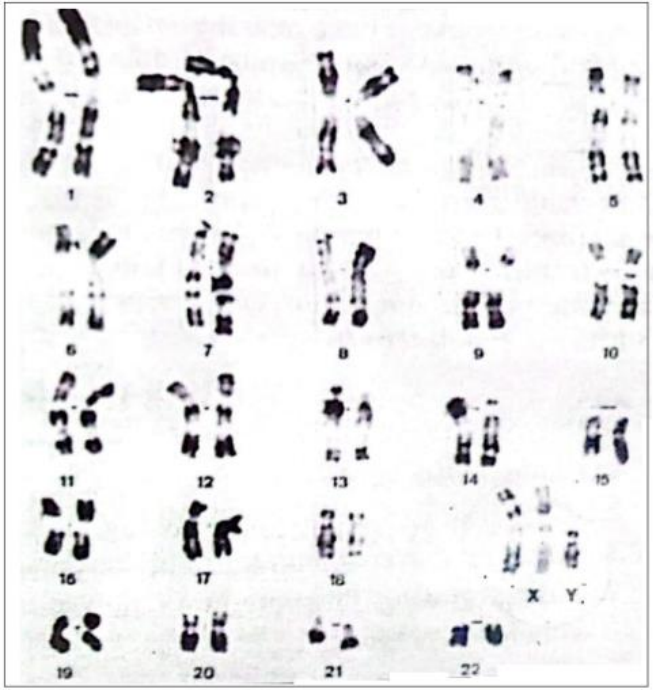
Doc.f

2. Name the disease represented in doc f.

Klinefelter syndrome.

3. Indicate the type of abnormality represented in doc f.

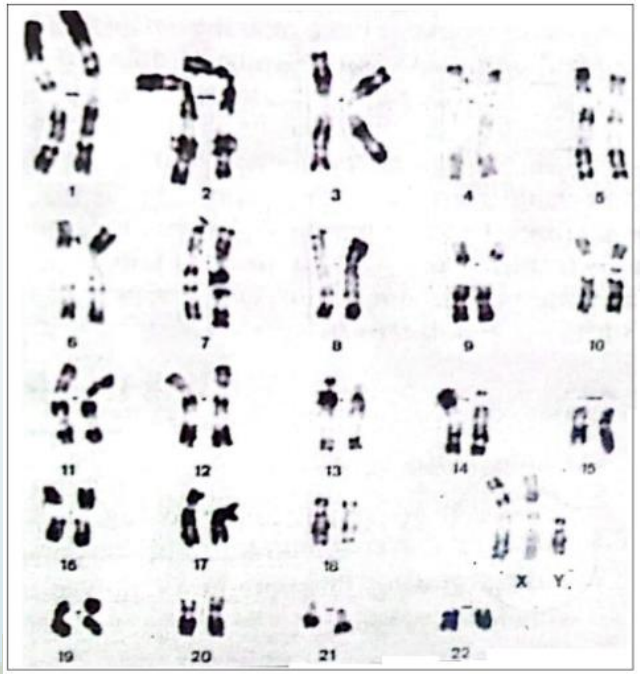
Numerical gonosomal abnormality.



Doc.f

4. Specify the sex of the individual to which the karyotype in doc f belongs.

Male, due to the presence of Y gonosome.

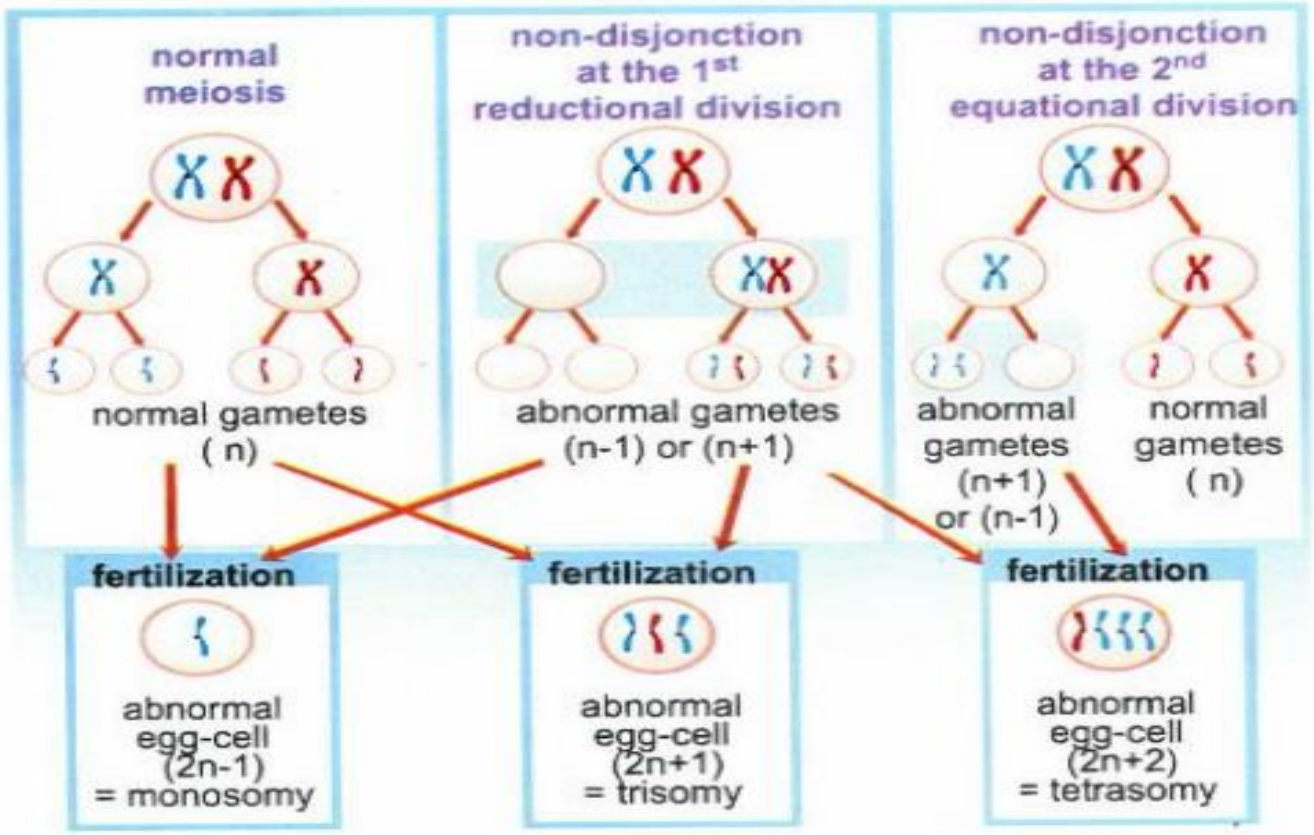


Doc.f

→ ***Klinefelter syndrome is a gonosomal numerical abnormality which affects males only where they are sterile.***

- Document g, shows mechanisms of occurrence of chromosomal numerical abnormalities.

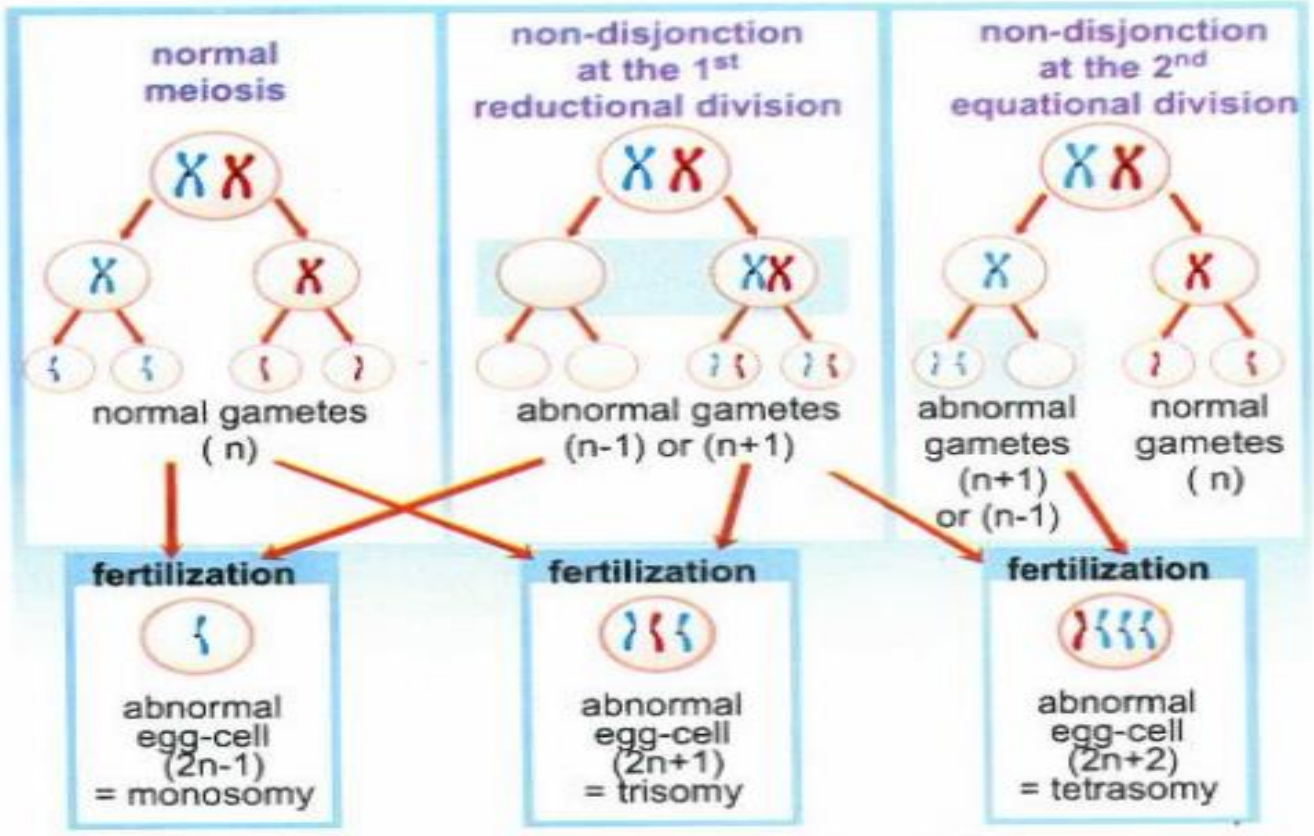
*Read and study doc g.



Doc.g *Mechanisms of occurrence of chromosomal numerical abnormalities.*

-This error may occur during oogenesis (females) or spermatogenesis (males).

-Individuals with the gonosomal abnormality (having extra or missing sex chromosome) are sterile = can't reproduce.



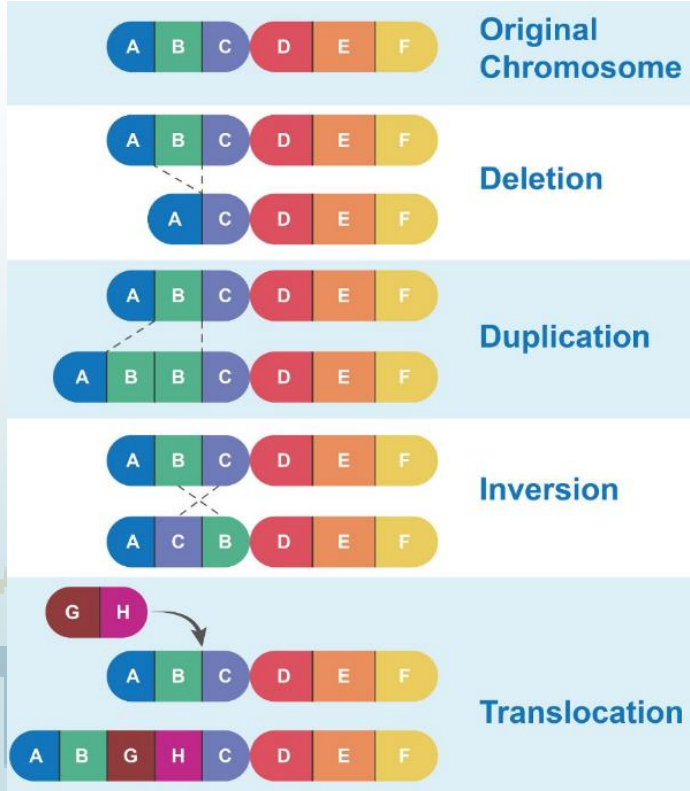
Doc.g *Mechanisms of occurrence of chromosomal numerical abnormalities.*

II- Chromosomal Structural abnormalities (mutation):

- They result from mistakes during cell division.

➢ **Types of chromosomal mutations:**

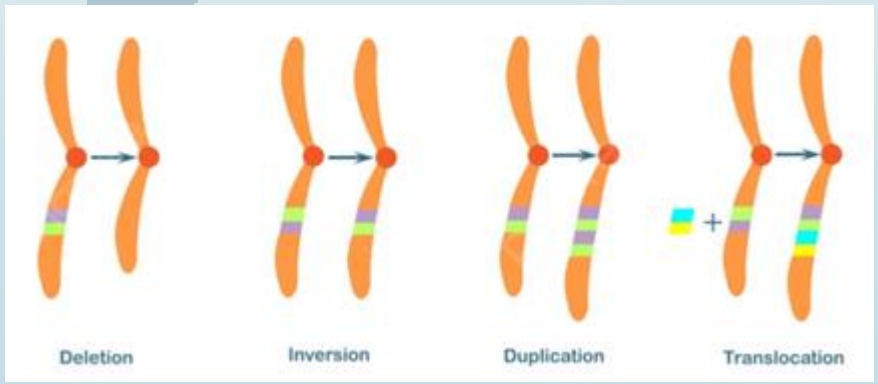
- Deletion: loss of part of chromosome.
- Duplication: extra copy made of part of chromosome.
- Inversion: reverses direction of part of chromosome.
- Translocation: part of one chromosome is translocated and attached to another chromosome.



Note: chromosomal mutations are different from gene mutations.

- Individuals with chromosome structural abnormality may have normal or abnormal phenotype, depending on the genetic information altered:

→If there is no change in the quantity of genetic information i.e. genetic information is conserved ⇨ abnormal karyotype but normal phenotype, ex: inversion or translocation



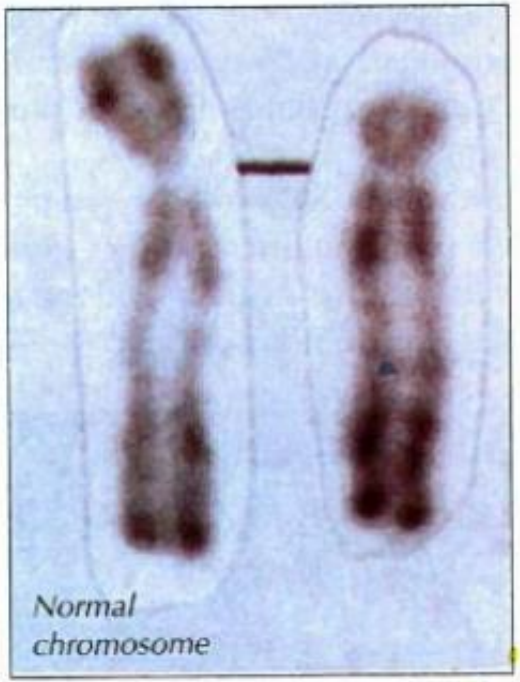
→ if there is excess or missing genetic information

⇨abnormal karyotype and abnormal phenotype ex :

Deletion, insertion, extra or missing chromosome.

- Document h, shows deletion in the short arm of one of pair chromosome number 5, which causes a disease known as cri-du-chat.

The "cri-du-chat" disease (cat cry syndrome) causes severe mental retardation and larynx malformations so that a baby emits sounds like a cat's mewing. The karyotype of affected individuals shows an abnormality of one of the copies of human chromosomes 5.



Doc.h *A pair of chromosomes 5 of a child affected with the "cri- du-chat" (cat cry) syndrome.*

☐ *Exercise VI*

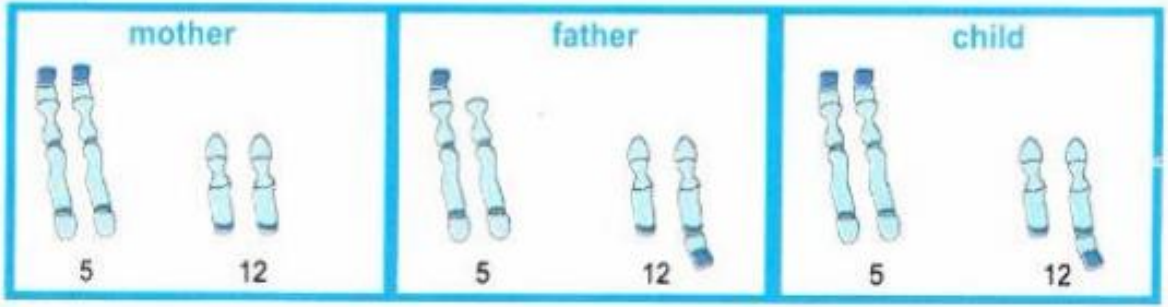
A couple having a normal phenotype gave birth to an abnormal child.

Examination of the karyotypes of this family revealed a disorder found only in the father and the child in the chromosome pair 5 and 12 (the document below). The remaining pairs were all normal.

a- Compare the chromosome pairs 5 and 12 of the father and the child to those of the mother.

b- Basing on your acquired knowledge, explain the presence of the abnormal phenotype in the child and the absence of this phenotype in the father.

Lebanese Bac; Mock exam, 2001



Exercise VI Solution:

a- By comparing the pairs of chromosomes 5 and 12 of the child with those of the mother: for pair number 5 the two chromosomes of pair 5 have the same length in the child same as that in the mother. For pair number 12, the child has one chromosome having the same length as that of pair 12 of the mother and one taller chromosome.

By comparing the karyotype of the father with that of the mother, we notice that for pair number 5: the father has one chromosome having the same length as that of pair 5 of the mother but 1 shorter chromosome. For pair number 12 :the father has one chromosome having the same length as that of pair 12 of the mother and one taller chromosome.

Exercise VI Solution:

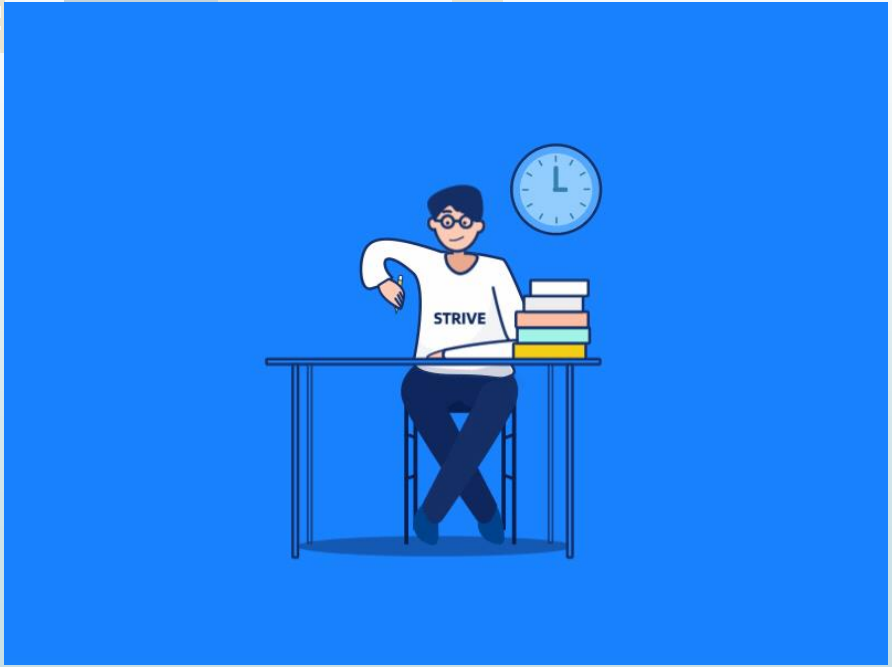
b- The mother had given the child both normal chromosomes 5 and 12.

The father had given the child normal chromosome 5 and abnormally long chromosome 12. The child has excess genetic material located in chromosome 12. Since chromosomes carry the genetic information, any excess in this information leads to a genetic disorder which explains the abnormal phenotype in the child.

As for the father, a fragment of chromosome 5 (upper part) had been detached and translocated to the lower part of chromosome 12 (translocation of 5 – 12). The genetic material of the father had not changed, there is neither loss nor gain of the genetic material and that's why he doesn't have an abnormal phenotype.

Selected Exercises of Official Exams

Official exam 2007 (2)



Exercise 2 (5pts)

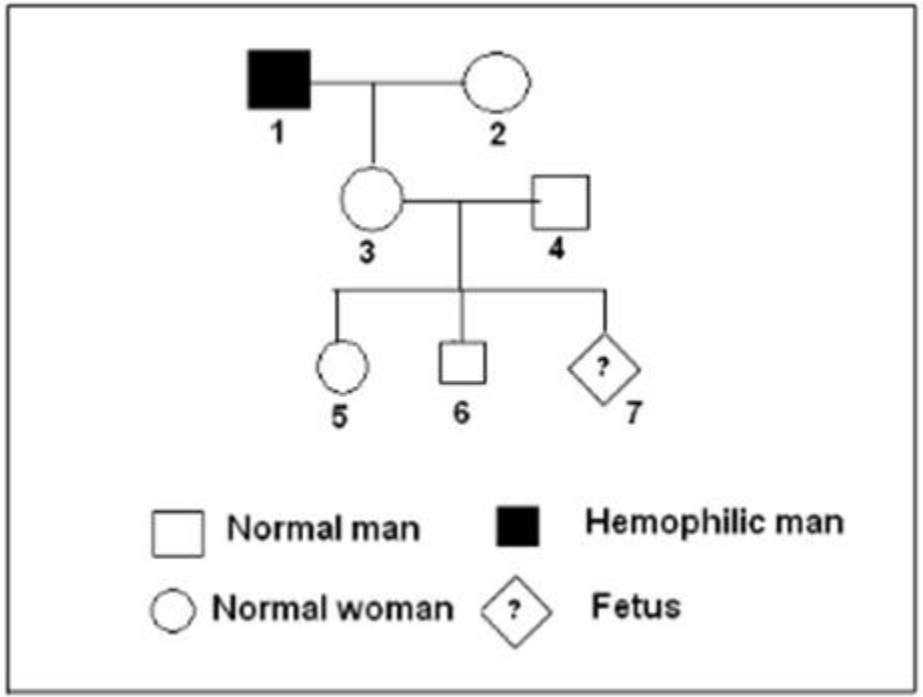
Hemophilia B is characterized by the absence of blood clotting, which may lead to significant hemorrhage. It is linked to the absence of a clotting factor, factor IX, whose synthesis is controlled by a gene located on the non-homologous segment of the X chromosome. This abnormality affects boys and not girls.

1- Explain the absence of this abnormality in girls?

Document 1 shows the pedigree of a family, one member of whom has the abnormality.

2- Show that this disease is recessive.

3- Determine the genetic risk that the fetus will be hemophilic.



Document 1

Exercise 2 (5pts)

Answer Key

1- The allele of hemophilia is lethal in the homozygous state. The girl has two X chromosomes. If she is X^hX^h, she dies before birth. **(0.5pt)**

2- The disease is carried by the X chromosome. The sick individual 1 has only one X, which carries the allele responsible for hemophilia, which he will certainly transmit it to his daughter 3. Girl 3 is normal. She carries an X chromosome having the allele without expressing it. Hence the disease is recessive. **(0.5pts)**

3- Fetus 7 has a heterozygous mother. If it is a boy, there is a risk of ½ to have the X chromosome carrying the allele of hemophilia. If it is a girl, the risk is null because her healthy non-hemophilic father cannot give her except one normal X. **(0.5pt)**

Ultrasound scan was done to determine the sex of the fetus. It revealed that it is a boy. The doctor

then prescribed analysis of DNA by the method of Southern blotting. The used probe permits to distinguish the mutated and normal forms of the implicated gene. The obtained results appear in document 2.

4- Specify the band that corresponds to the defective allele. Justify the answer.

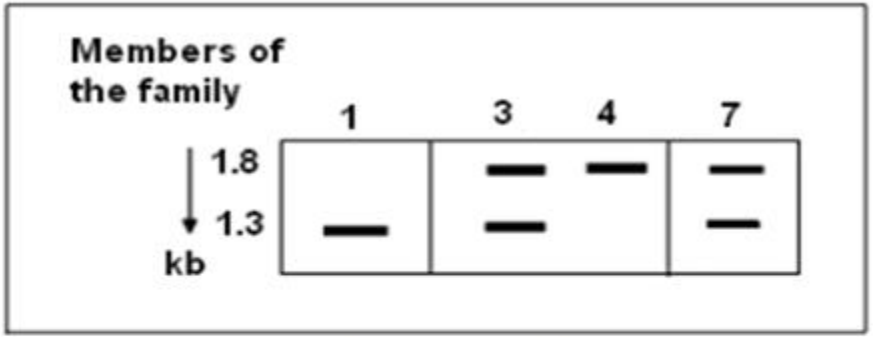
5- Identify, from the DNA analysis, the problem of the child that will be born.

The doctor completed the diagnosis by establishing the karyotype of the fetus, document 3.

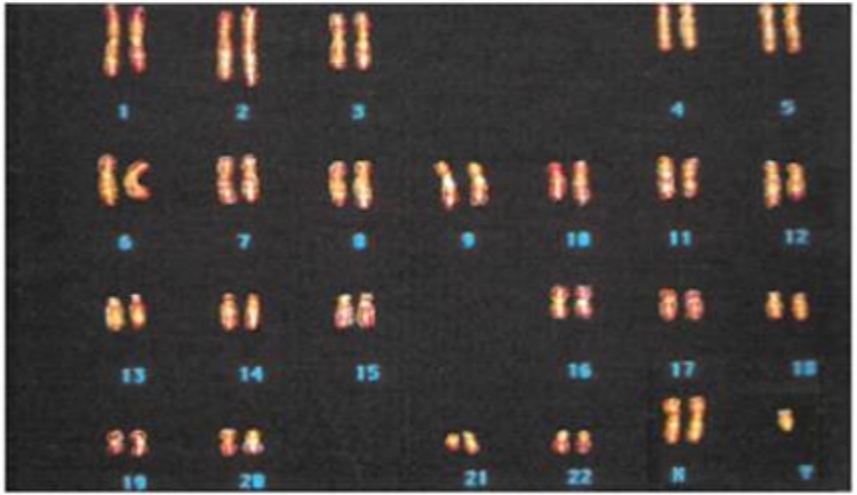
6- Establish, based on documents 2 and 3, the diagnosis of the fetus.

7- Specify the stage of meiosis at which the abnormality took place. Justify the answer.

8- Schematize the behavior of chromosomes at the origin of this abnormality.



Document 2



Document 3

4- The 1.3 kb-band, because document 2 reveals that individual 1, who is a sick man and has only one X, has only one band of 1.3 kb. **(0.5pt)**

5- The fetus is a boy, hence he has only one X chromosome, then he must have only one band of DNA, but according to document 2 he presents two bands. Therefore, it is a boy with 2 X. **(0.5pt)**

6- Fetus 7 is a nonhemophilic boy (doc 2), but he has XXY (doc 3). Thus he will have Kleinfelter syndrome. **(0.5pt**

Ultrasound scan was done to determine the sex of the fetus. It revealed that it is a boy. The doctor

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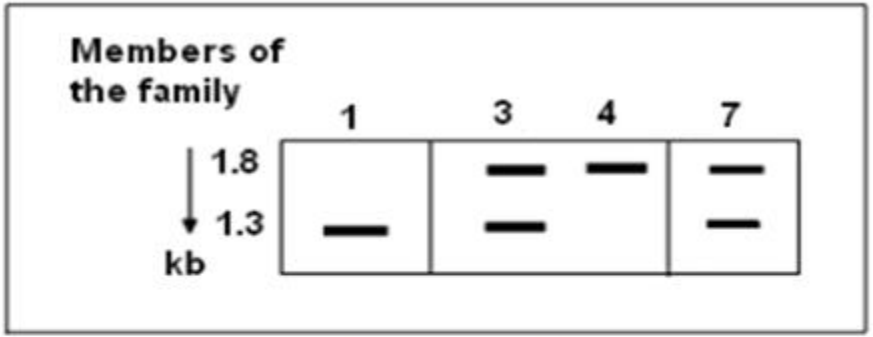
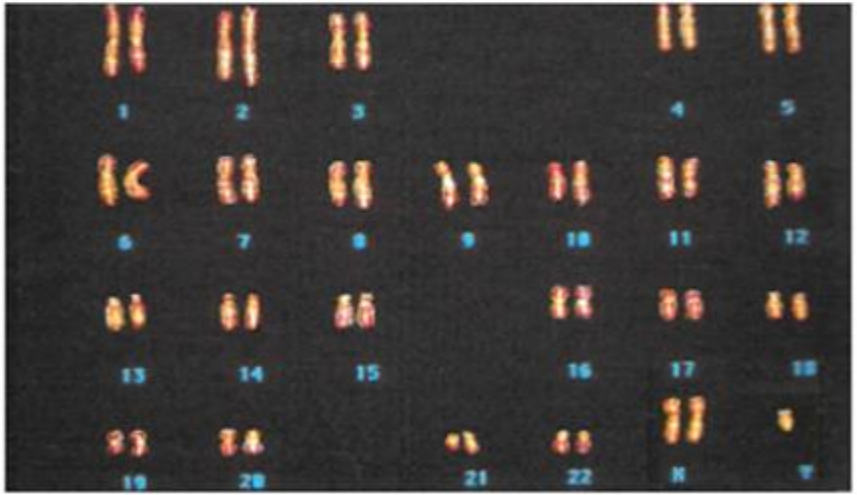


Document 2



Document 3

7- The abnormality of meiosis had taken place during the anaphase of the reductional division by nondisjunction of chromosomes XX or XY, because upon the analysis of DNA there are two different bands that correspond to two X and not to two chromatids of the same X chromosome. In this case the father or the mother could be at the origin of this abnormality. **(1pt)**

8- (1pt)