Unit One
Reproduction and Genetics

Chapter One
Basic mechanisms of sexual reproduction

Document 1 : Male and female reproductive systems

Male reproductive system

The male reproductive system includes:

1- **Testes (Gonads):**

Role: Produce sperm (spermatozoa) and a male sex hormone called testosterone.

2- **Epididymis**

Structure : Highly coiled tube.

Location: Located on the top of each testis .

Role : Maturation and storage of sperm.

3- **Vas deferens (sperm duct)**

Role: Transportation and storage of the sperm and it is the site where the sperms acquire their motility.

4- **Accessory glands**

Kinds: Seminal vesicle, prostate and cowper's glands.

Role: They secrete seminal fluid which contains fructose and other nutrients that ensure the survival and the motility of the sperm.

5- **Semen :** Sperm + seminal fluid

6- **Penis :** Male copulatory organ.

Notes:

1) Number of sperm = 100 million / ml of semen or 300 million / ejaculation knowing that the volume of each ejaculation is 3 to 4 ml .
2) The activity of the male reproductive system is continuous and starts from puberty till death.

Female reproductive system

The female reproductive system includes:

1- **Ovaries (Gonads)**: There are two ovaries

Role : Produce oocytes and female sex hormones: Estrogen and progesterone.

2- **Oviducts (Fallopian tubes):**

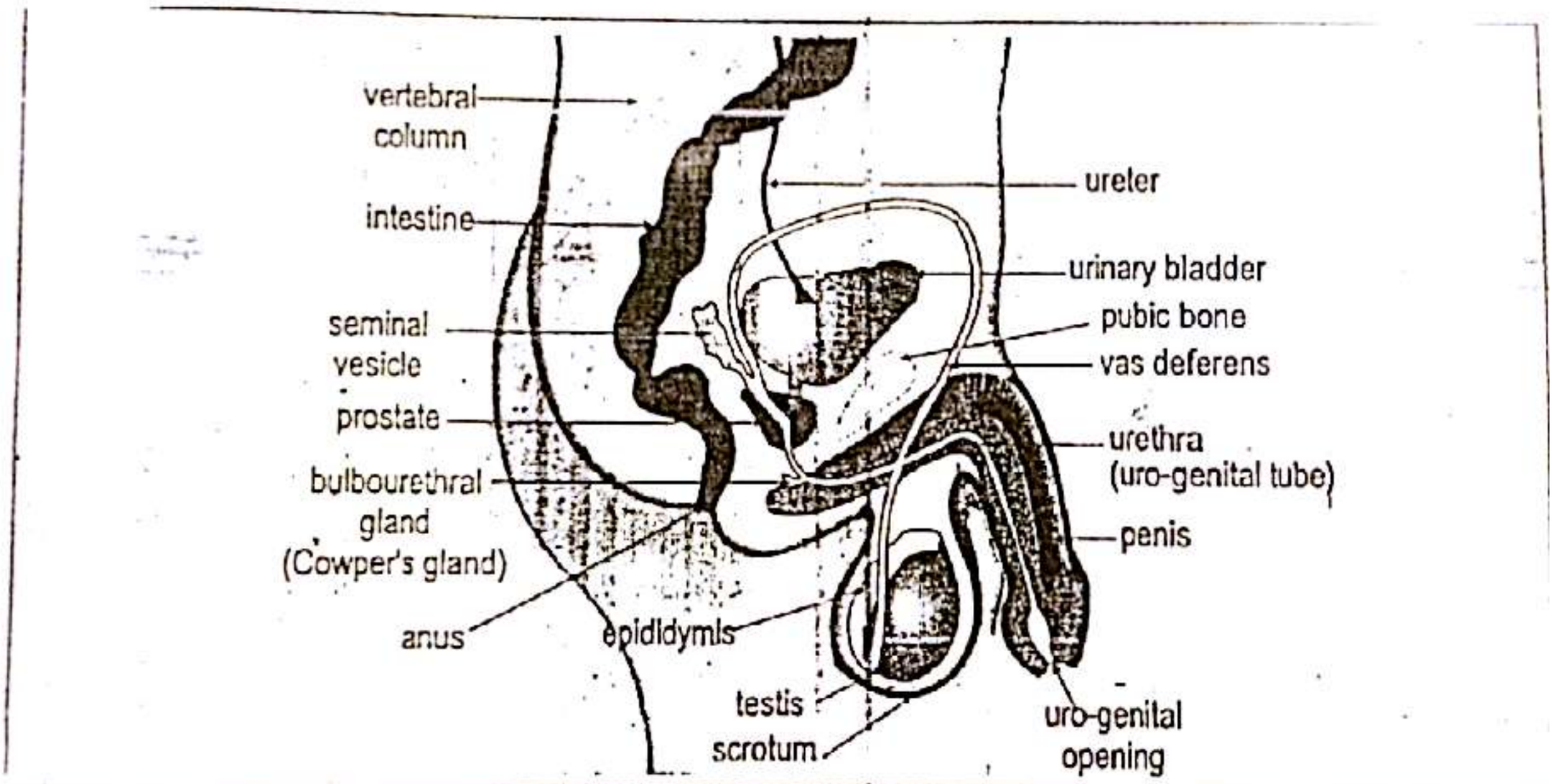
Role : Reception of released oocytes and site of fertilization. .

3- **Uterus (Womb)**

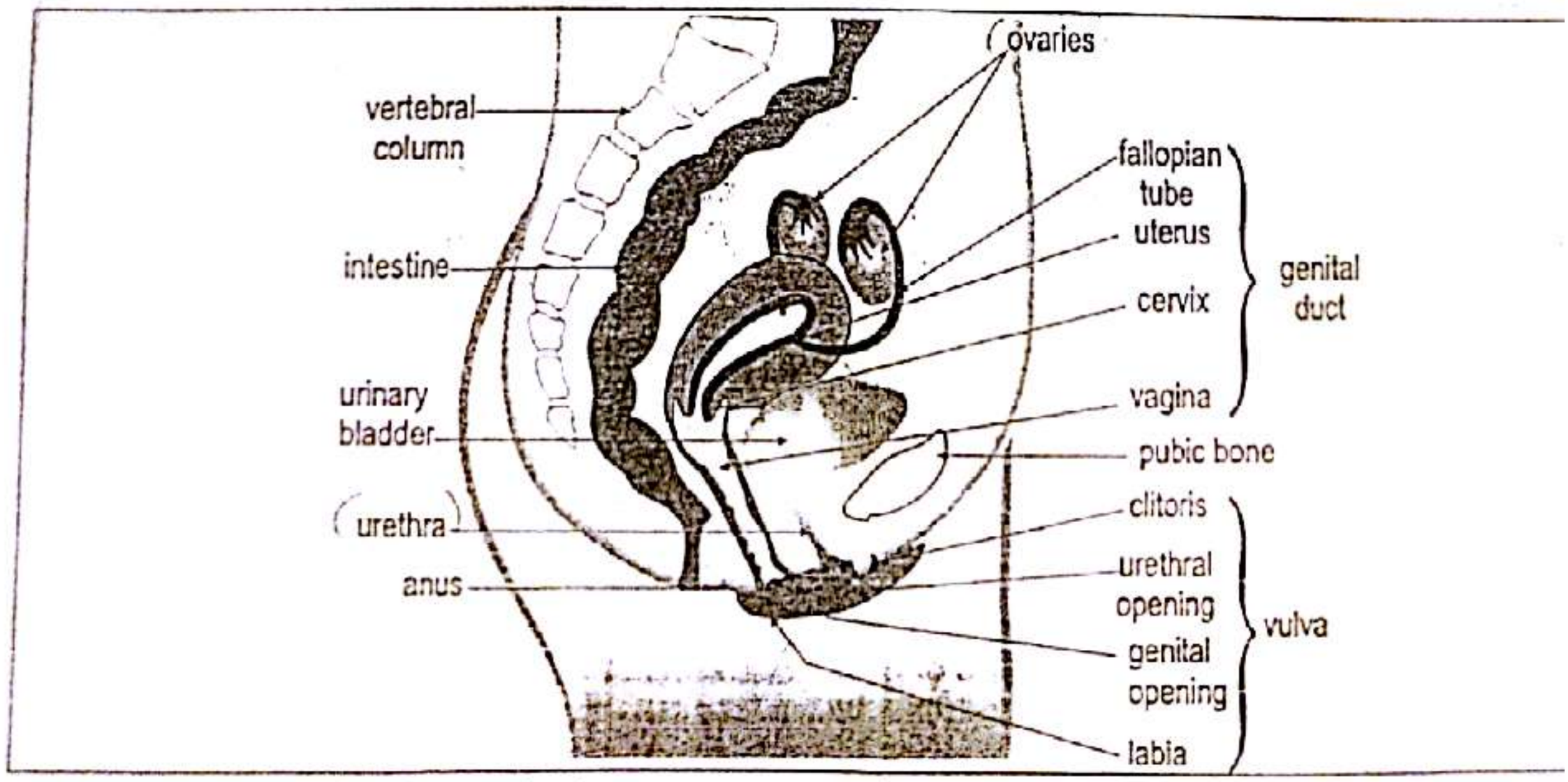
Role : Site of implantation and development of the embryo.

4- **Vagina** : Female copulatory organ .

Note: The activity of the female reproductive system is cyclic and the releasing of oocytes starts from puberty till menopause (around 45 years of age).



Anatomy of the male reproductive system.



Anatomy of the female reproductive system.

Document 2 : Diploid and haploid cells

1- Preparation of a karyotype:

Steps:

1- Take a sample of 5 ml of blood and pick out the lymphocytes (white blood cells).

2- Put the lymphocytes in a nutritive cultural medium for 3 days at 37^0C to activate the cell division.

3- Add colchicine to the cultural medium to stop the lymphocyte division at metaphase.

4- Spread the chromosomes by placing the cells in a hypotonic medium that leads to the swelling of the lymphocytes causing their lysis.

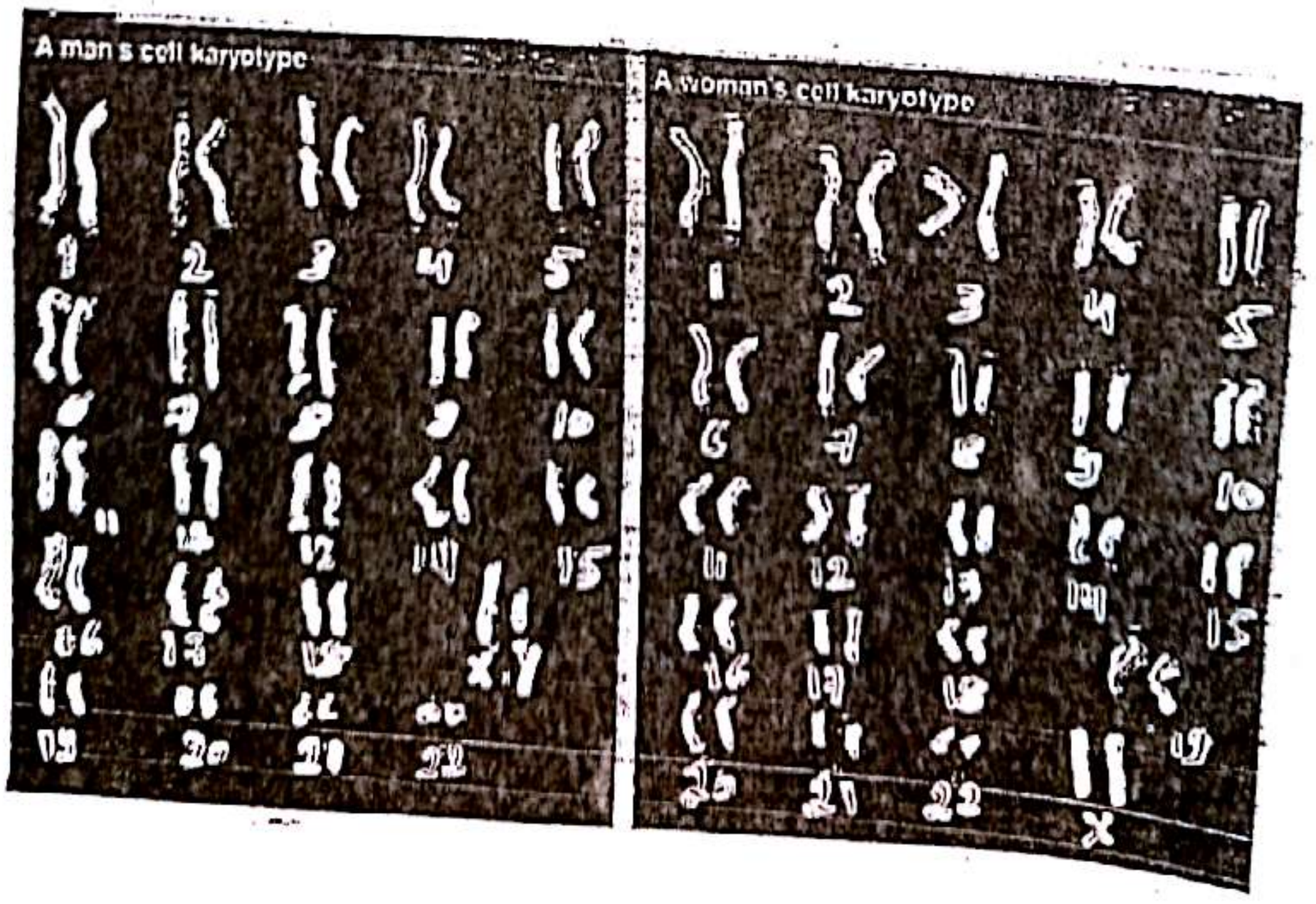
5- Add stains, photograph the chromosomes, cut them and arrange the chromosomes according to their length, position of centromere and banding pattern.

Diploid cells :

In diploid or somatic cells like skin, blood, bone ..... the number of chromosomes is represented by **2n** and the chromosomes are grouped in pairs, each chromosomal pair has 2 copies: one of maternal origin (mother) and the other of paternal origin (father).

In human somatic cells the number of chromosomes is **2n = 46** or **23** pairs. Chromosomic formula of a human male somatic cell is : **2n = 44** autosome + **XY** or **2n = 22** pairs autosome + **XY**.

Chromosomic formula of a human female somatic cell is **2n = 44** autosome + XX.



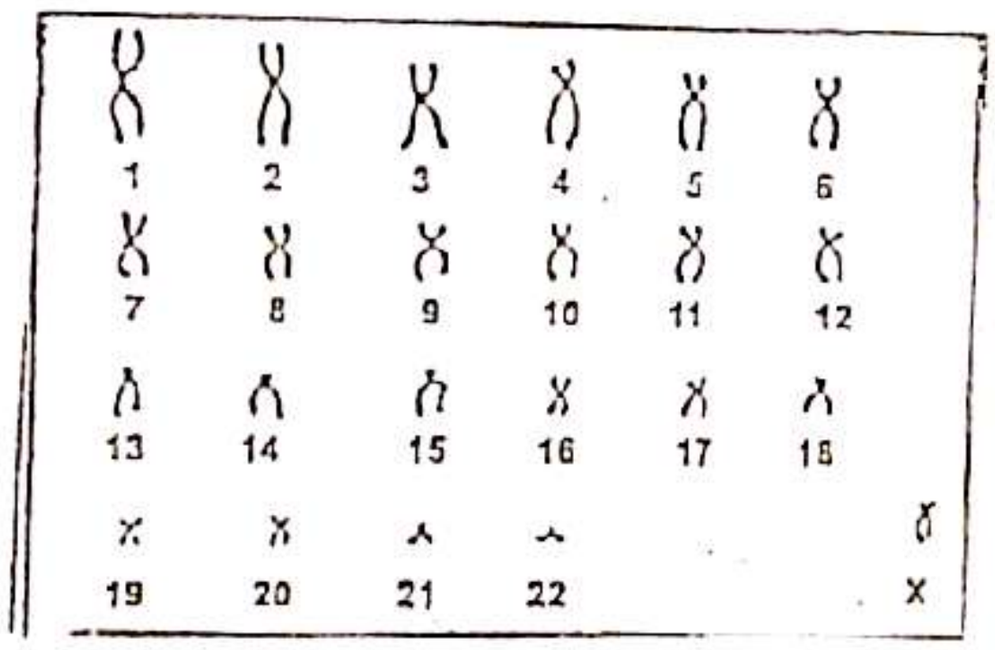
Haploid cells : Sperm and oocyte (Germ cells).

In haploid cells, the number of chromosome is represented by **n** where the chromosomes are not grouped in pairs and each chromosome has one copy only.

Chromosomic formula of a human oocyte is **n = 22** autosome + **X** .

Chromosomic formula of a human sperm is **n = 22** autosome + **X** or

n = 22 autosome + **Y**.



Document 3 : Mitosis and meiosis

Interphase: it is the rest state of the cell. it preceeds the cell division and includes 3 stages:

G1 = Gap one: Where the chromosome is made up of one chromatid.

S = Synthesis : Where the chromosome duplicates and becomes of 2 chromatids.

G2 = Gap two : Where the chromosome is still formed of 2 chromatids.

Mitosis : Mitosis takes place in diploid cells and it is important for repair of dead and injured cells and for growth of individuals.

Mitosis occurs in four phases:

Prophase:

1) Each chromosome, which is made up of two chromatids joined by a centromere, becomes shorter, thicker and more visible.
2) The centrosome divides into two asters, each one occupies a pole of the cell.
3) The nuclear membrane and the nucleolus will disappear.
4) Between the asters extend achromatic spindle fibers.

Metaphase

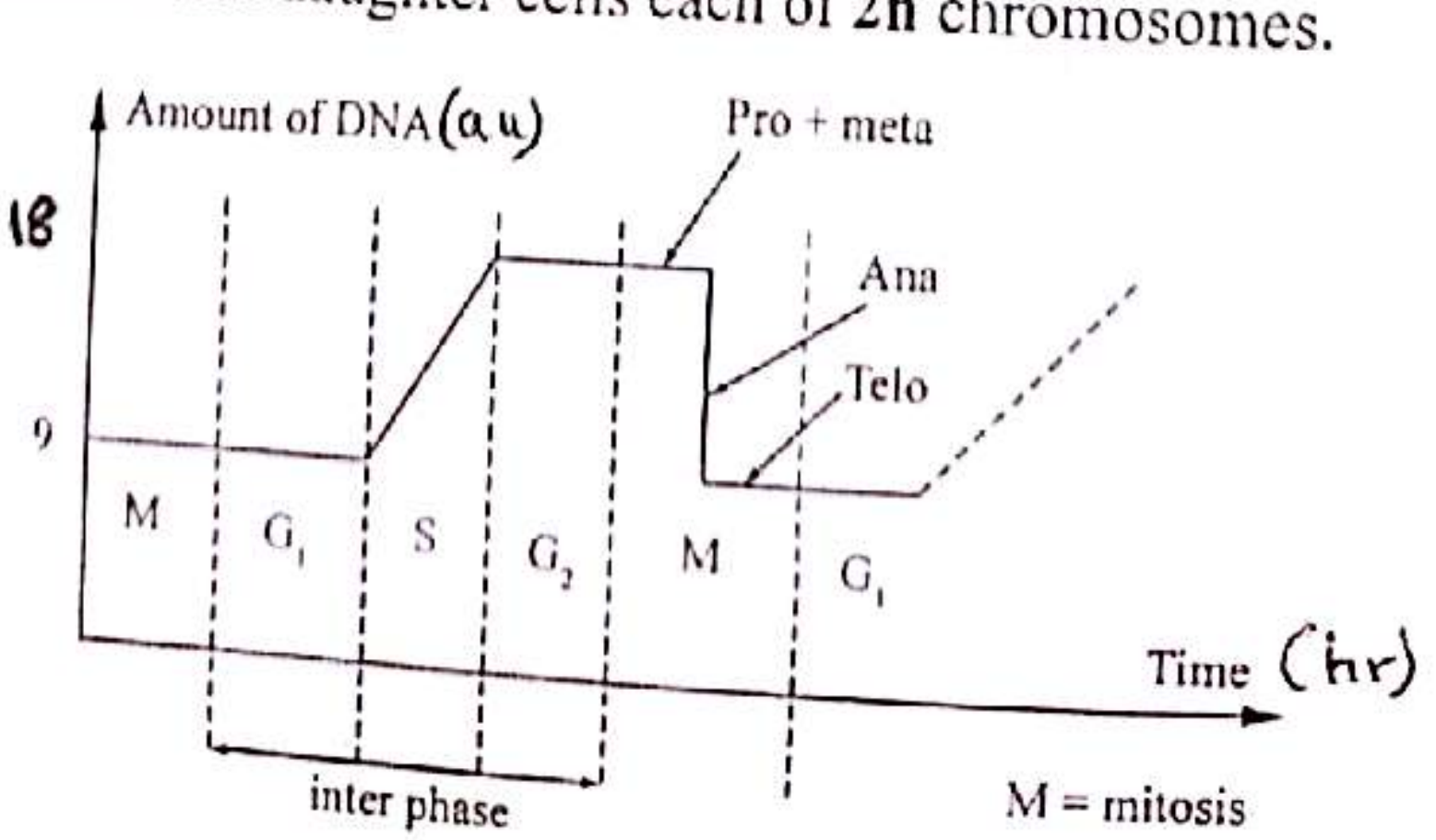
The split chromosomes are grouped at the equatorial plate. In this phase the chromosomes are distinct and can be counted.

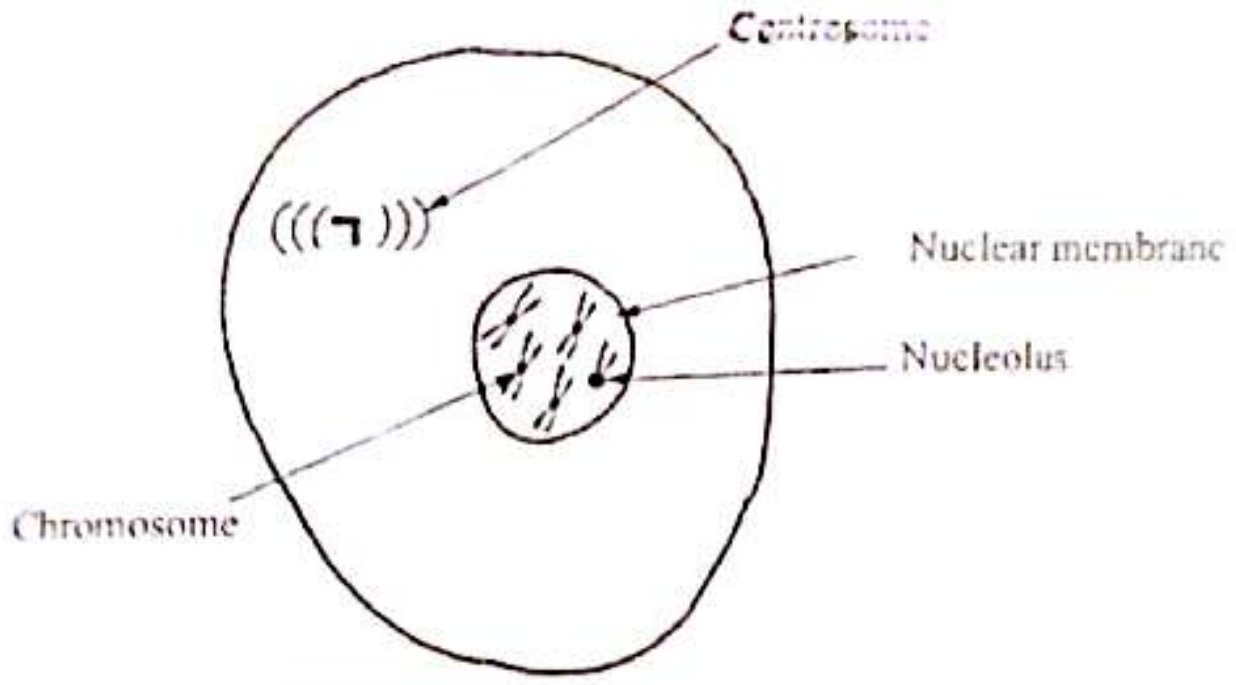
Anaphase

1) The centromere will divide and the free chromatids become chromosomes similar to the initial ones.
2) The chromosomes (sister chromatids), of the same origin , will slide and migrate to the opposite poles of the cell. (Pole formation or pole ascention).

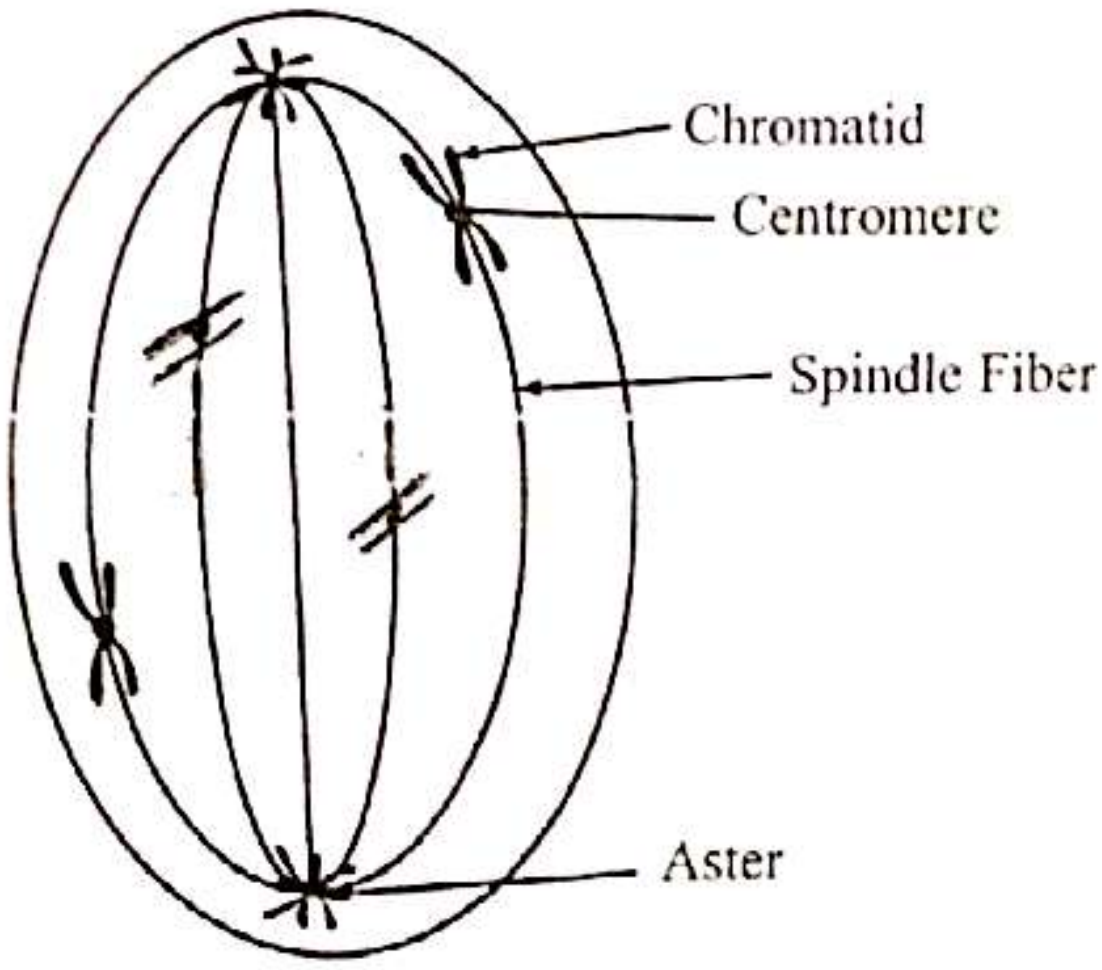
Telophase

1) The chromosomes become chromatin material.
2) The spindle fibers will disappear.
3) The nuclear membrane and the nucleolus reappear.
4) The aster becomes a centrosome.
5) A constriction will appear at the equatorial plate dividing the mother cell into two identical daughter cells each of **2n** chromosomes.

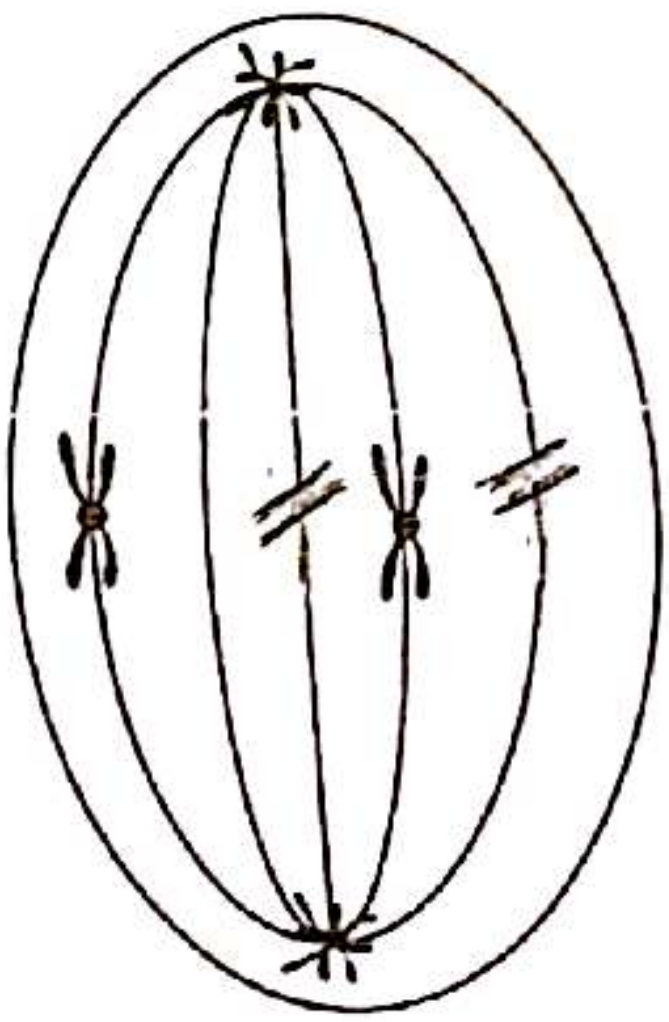




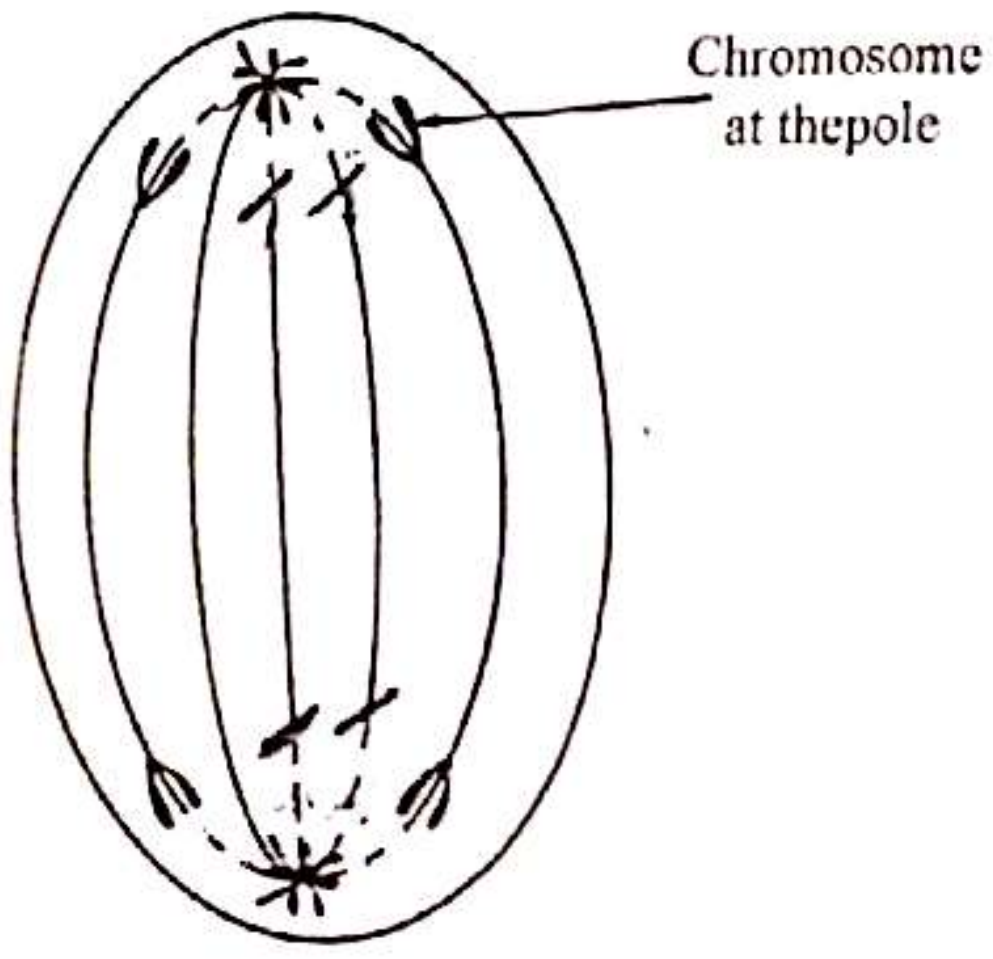
Mother cell ready for mitosis



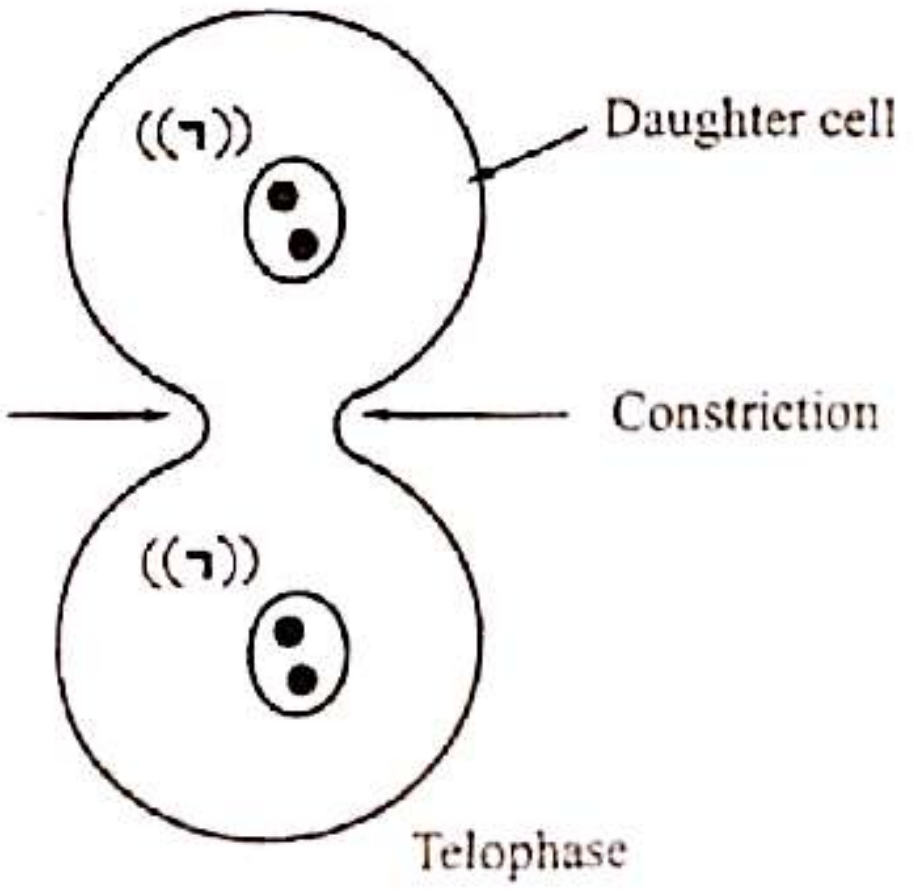
Prophase



Metaphase



Anaphase



Telophase

Meiosis

Meiosis takes place in germ or sex cells, it occurs in two divisions: Reductional and equational division.

First meiotic division : Reductional division it is like mitosis but with the following exceptions:

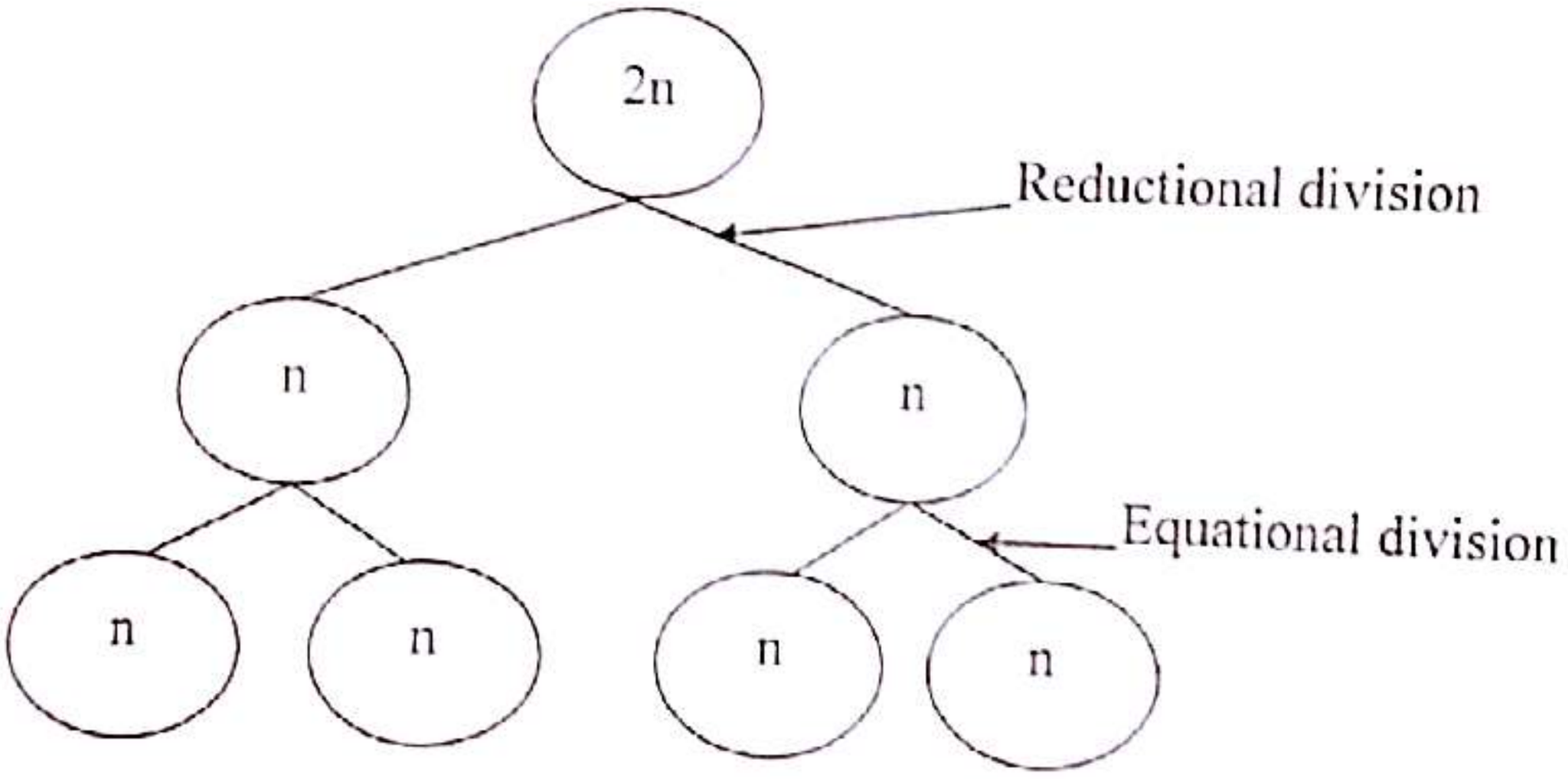
Prophase I : The homologous chromosomes synapse and form tetrad.

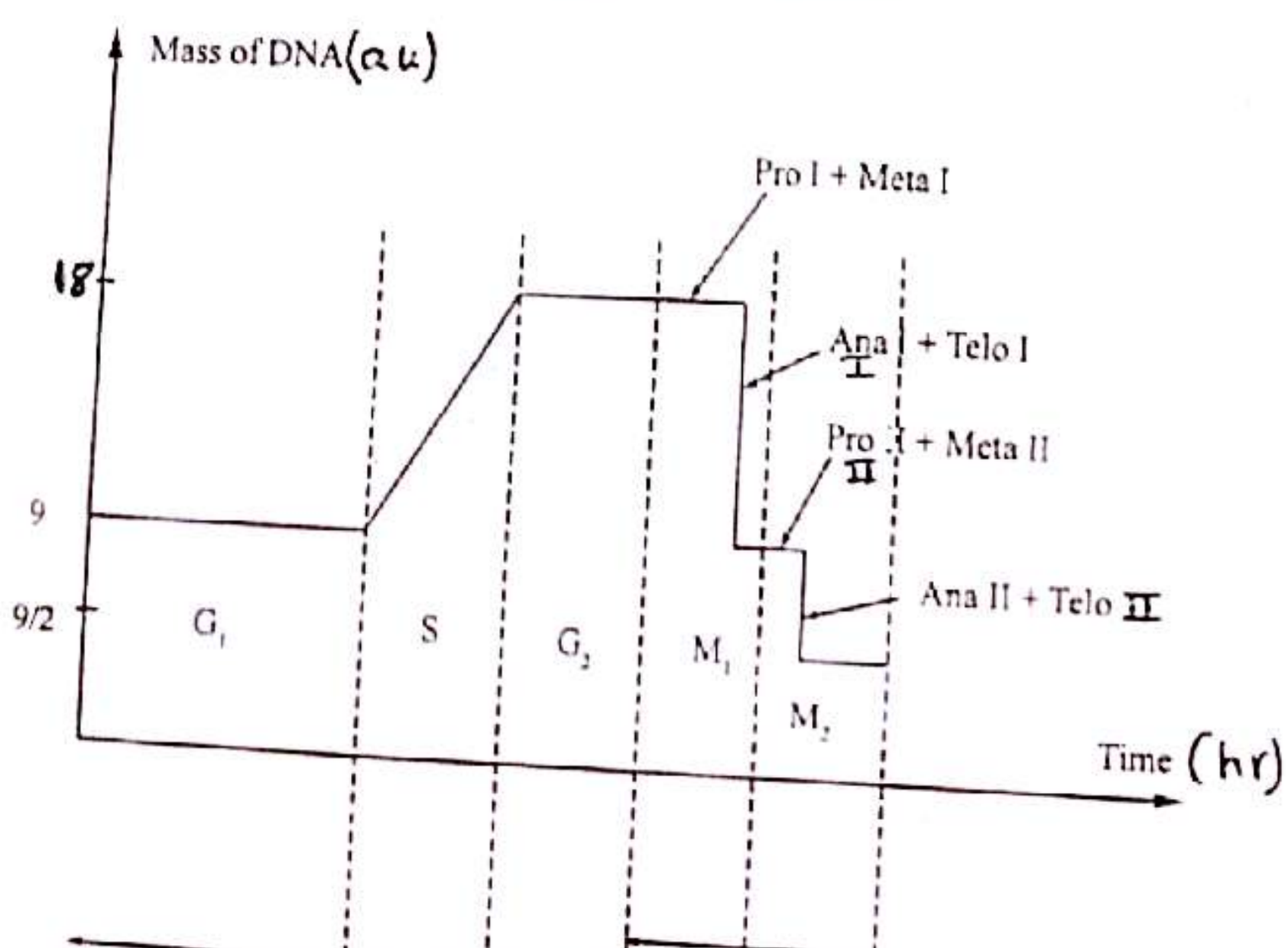
Metaphase I: The tetrads are grouped at the equatorial plate.

Anaphase I : The homologous chromosomes will separate and migrate to the opposite poles of the cell without the division of centromere. In this phase the number of chromosome is reduced from **2n** into **n** chromosome at each pole.

Telophase I: first cytokinesis (division) will occur dividing the mother cell into two daughter cells but the chromosomes are still formed of chromatids.

Second meiotic division : Equational division it is like mitosis but each obtained cell is of n chromosome.





Phase	Number of chromatid/ chromosomes	Number of chromosome / cell
G1	1	2n
S	2	2n
G2	2	2n
Pro I	2	2n
Meta I	2	2n
Ana I	2	2n or n/pole
Telo I	2	n
Pro II	2	n
Meta II	2	n
Ana II	1	2n or n /pole
Telo II	1	n

First meiotic division

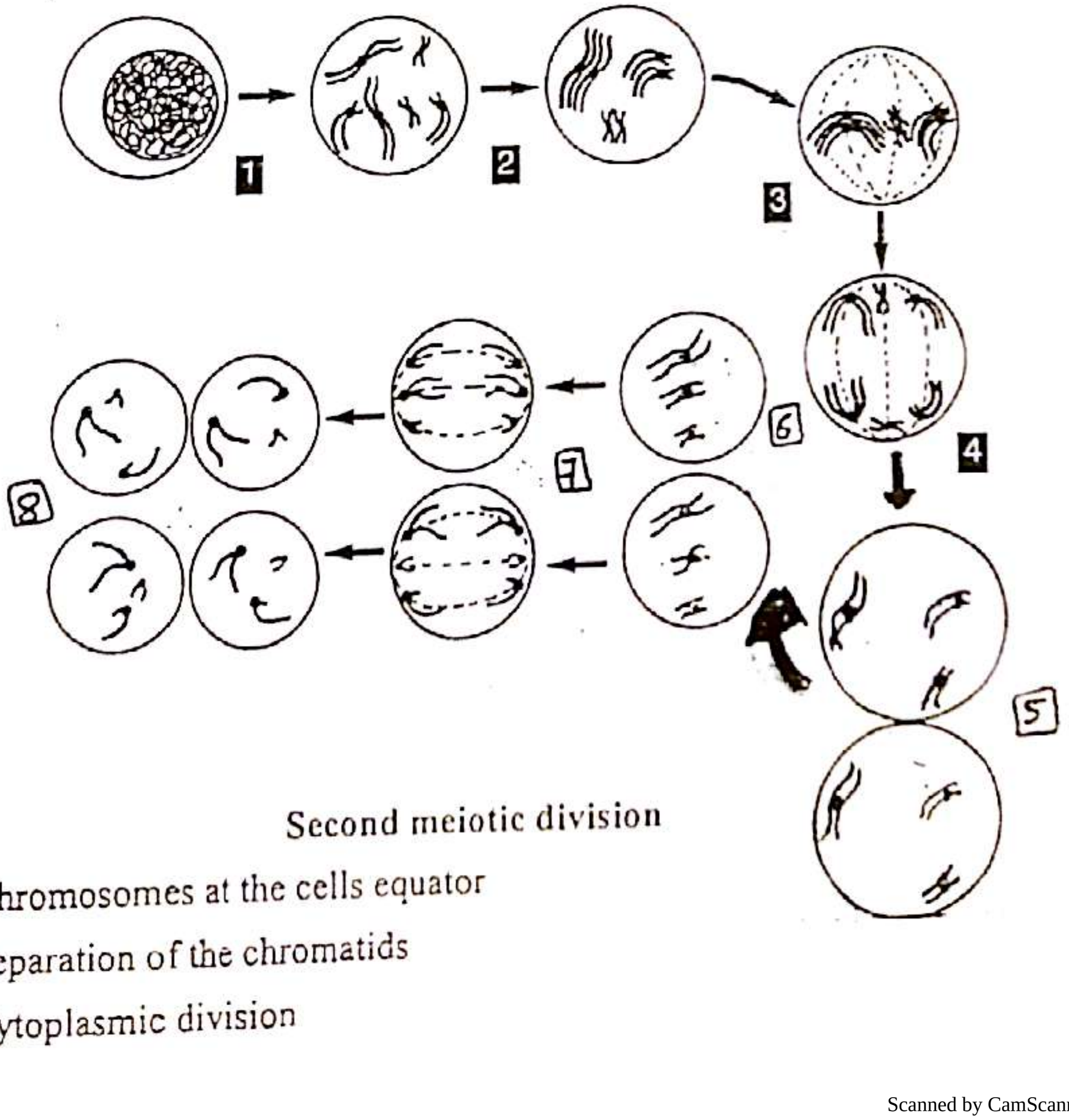
1- Individualized chromosomes

2- Production of the homologous pairs

3- Homologous pairs are arranged at the cell's equator.

4- Separation of the homologous chromosomes

5- Cytoplasmic division



Second meiotic division

6- Chromosomes at the cells equator

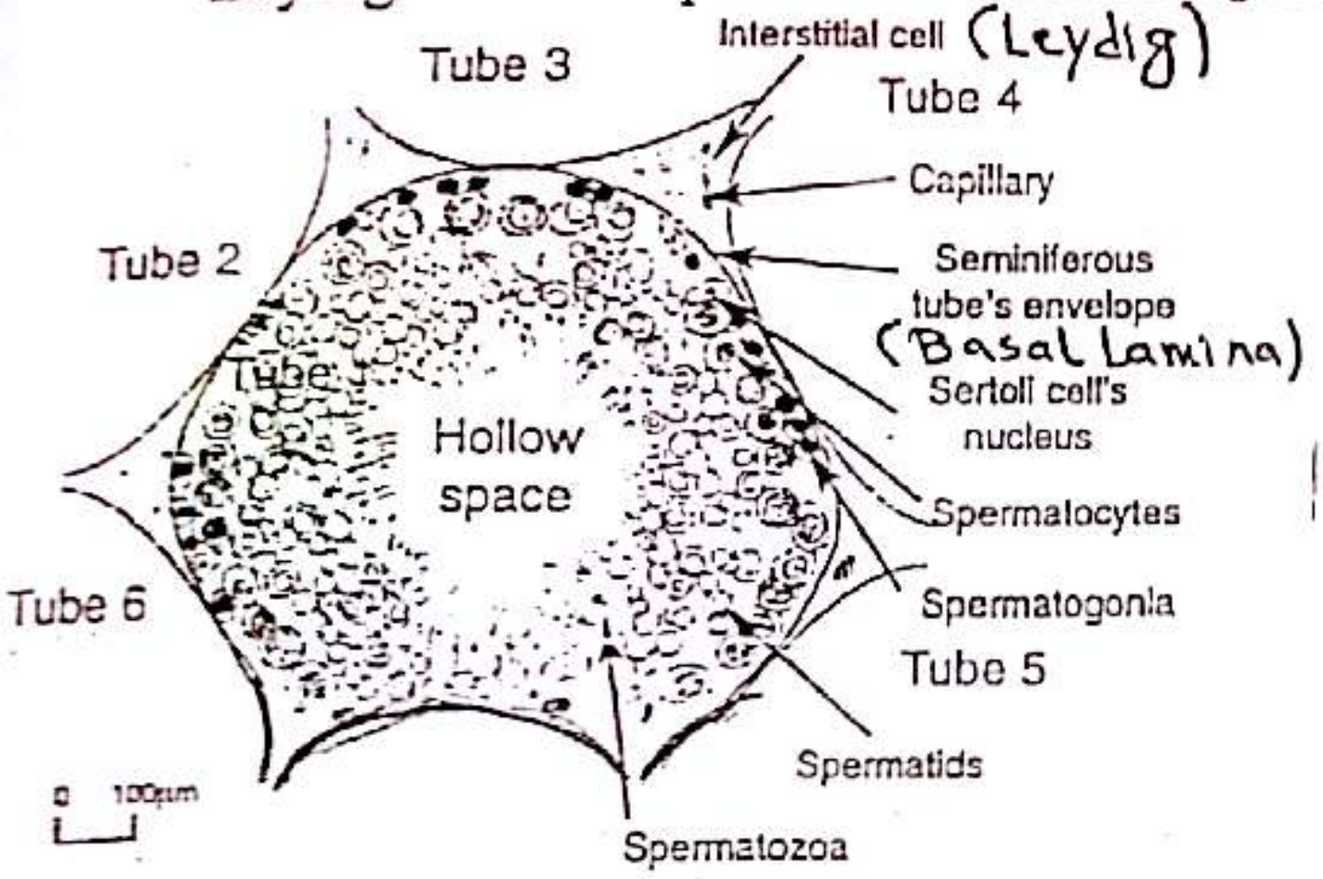
7- Separation of the chromatids

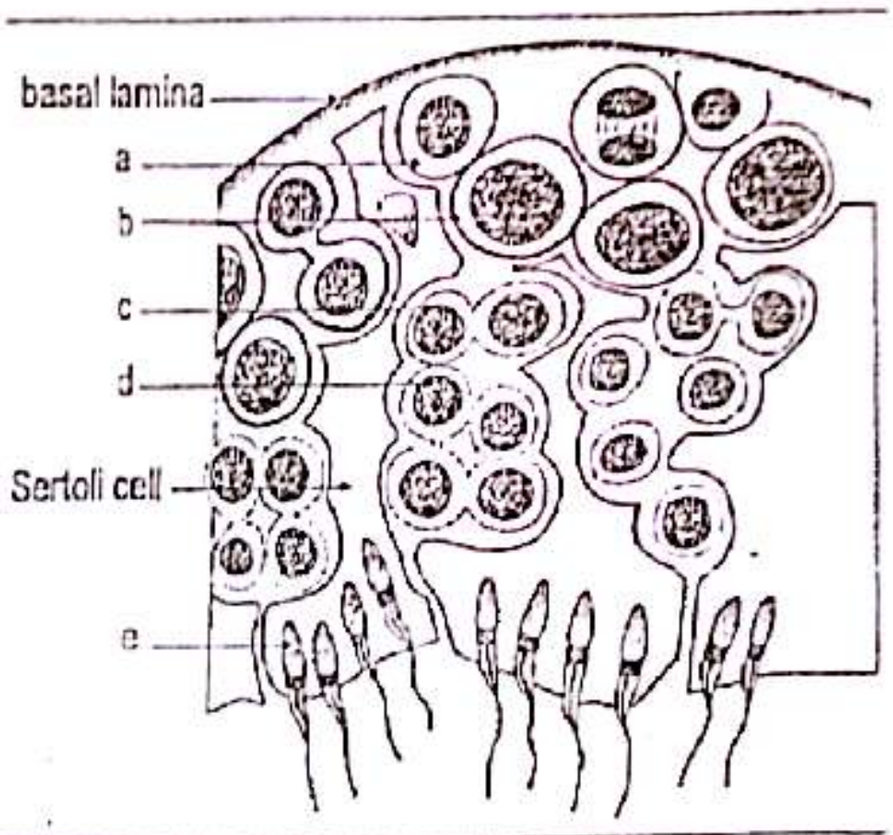
8- Cytoplasmic division

Document 4 : Spermatogenesis

Histology of testes

The microscopic observation for a longitudinal section of a testis shows that it is composed of seminiferous tubules which produce spermatozoa. In the seminiferous tubules there are reproductive cells of different developmental stages in addition to sertoli cells that produce nutritive substances for the development of reproductive cells. Between the seminiferous tubules there are Leydig cells that produce testosterone hormone.





Crosssection of a seminiferous tube

Spermatogenesis: Spermatogenesis takes place in the seminiferous tubules and it is the process by which haploid cells (sperm) are formed.

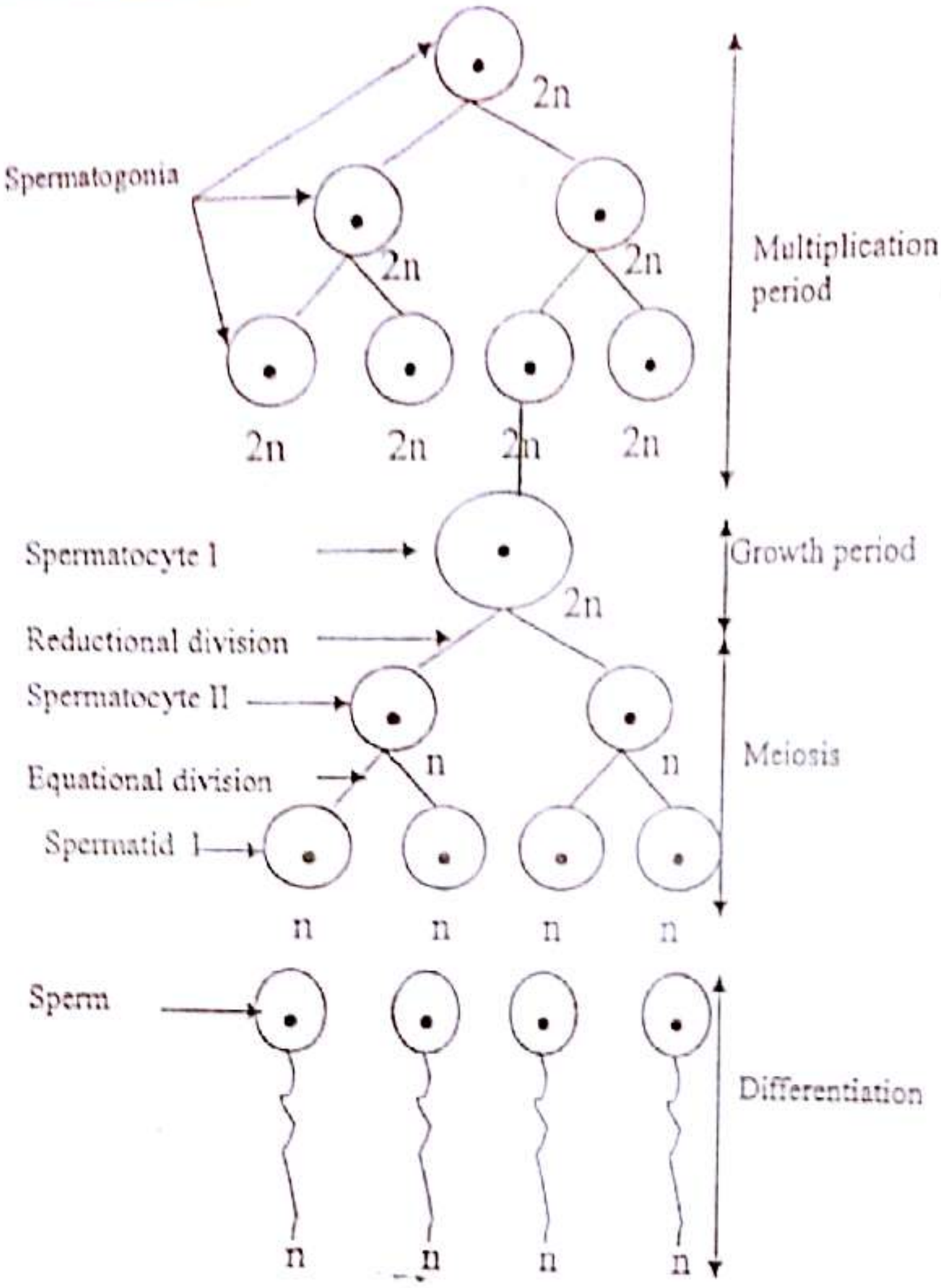
This process occurs in a centripetal direction that is from the basal Lamina to the Lumen. It lasts around 74 days and includes four stages or phases:

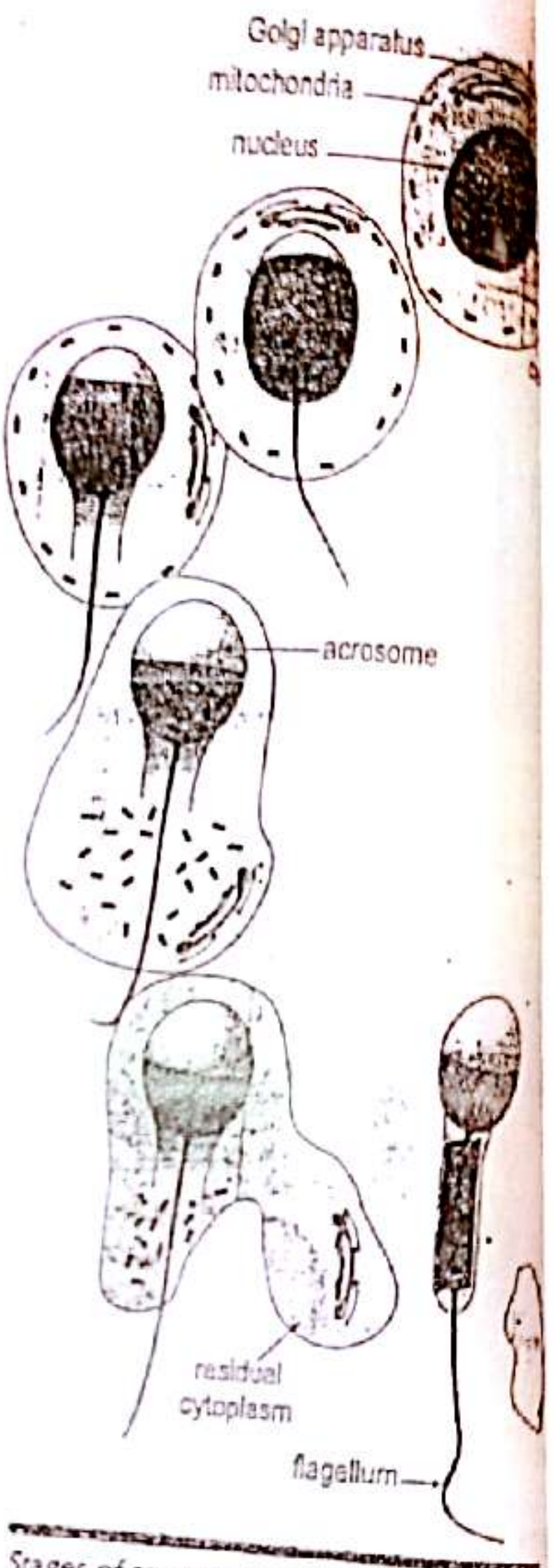
1) **Multiplication period:** The spermatogonia increase in number by successive mitotic divisions.
2) **Growth period:** each spermatogonium increases in size to give primary spermatocyte.
3) **Maturation period:** (Meiosis): Each primary spermatocyte is subjected to two divisions: Reductional and equational to give two secondary spermatocytes then four spermatids.
4) **Spermiogenesis (Differentiation):**

The spermatids are converted into spermatozoa with certain modification in the form and structure:

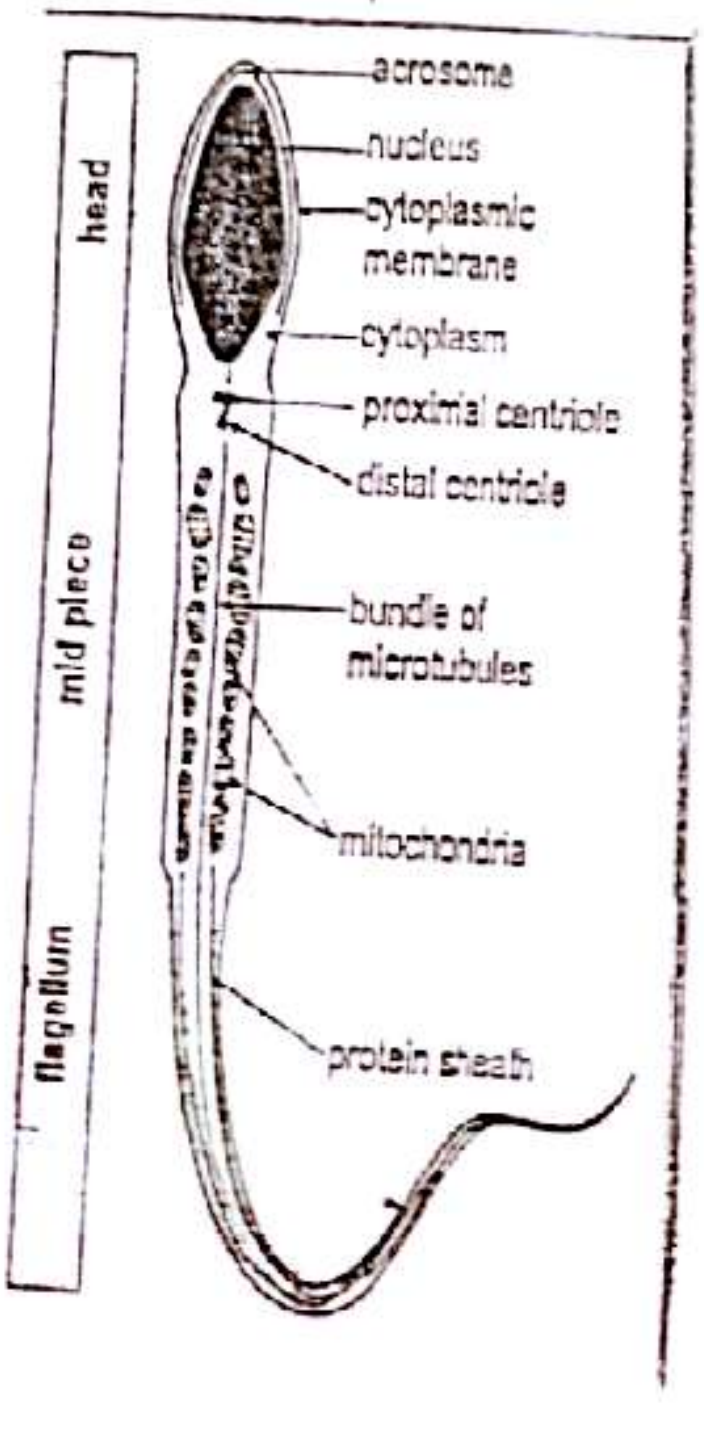
- Distal centriole of the spermatid will give rise to the flagellum of the sperm.
- Mitochondria are grouped together to form the midpiece of the sperm.
- Golgi body of the spermatid becomes the acrosome of the sperm.
- Most of the cytoplasm in the spermatid is restricted and eliminated.

Concept map of spermatogenesis:





Stages of spermiogenesis in humans.



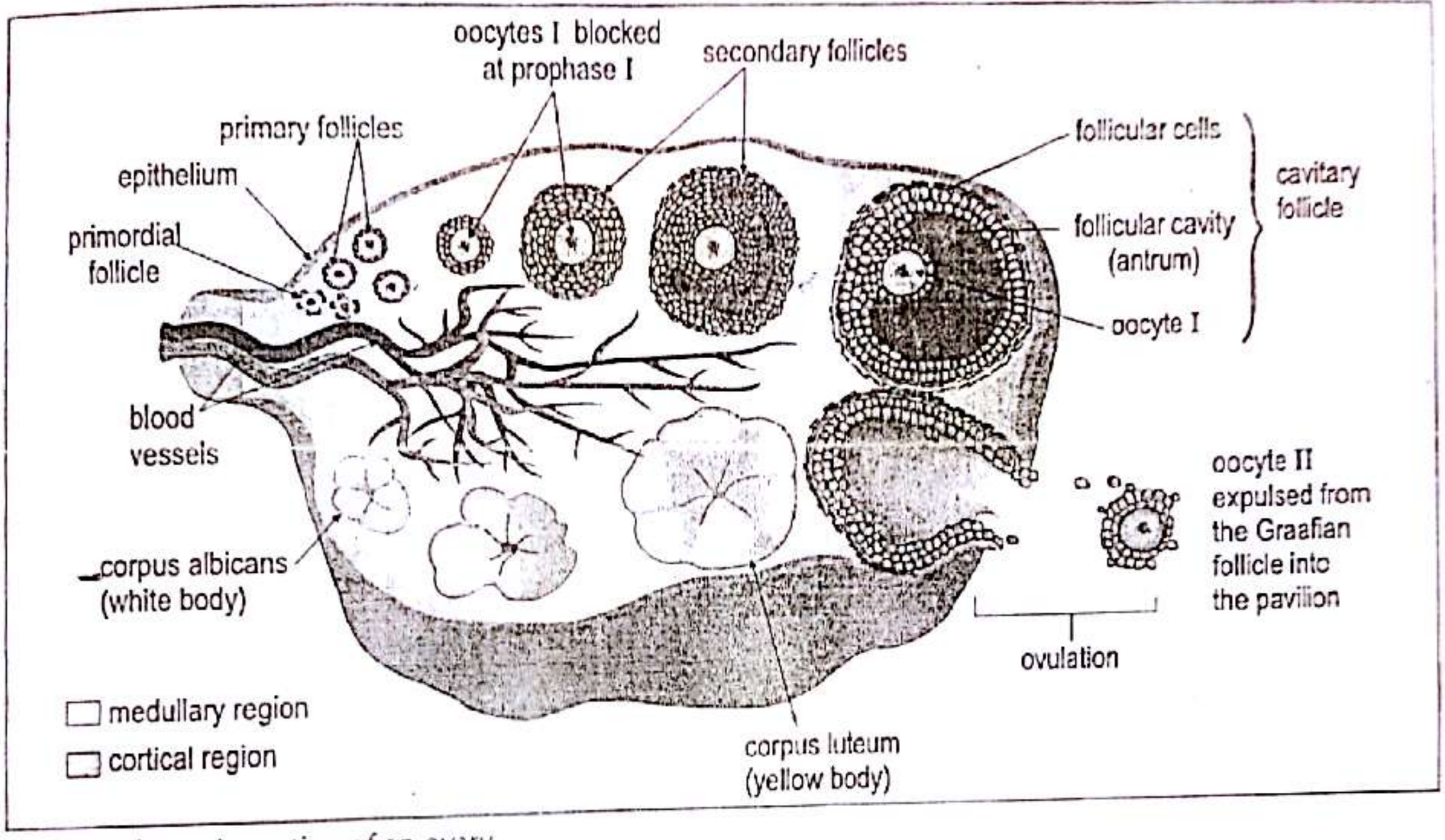
Structure of a sperm

Document 5 : Oogenesis

Histology of the ovary

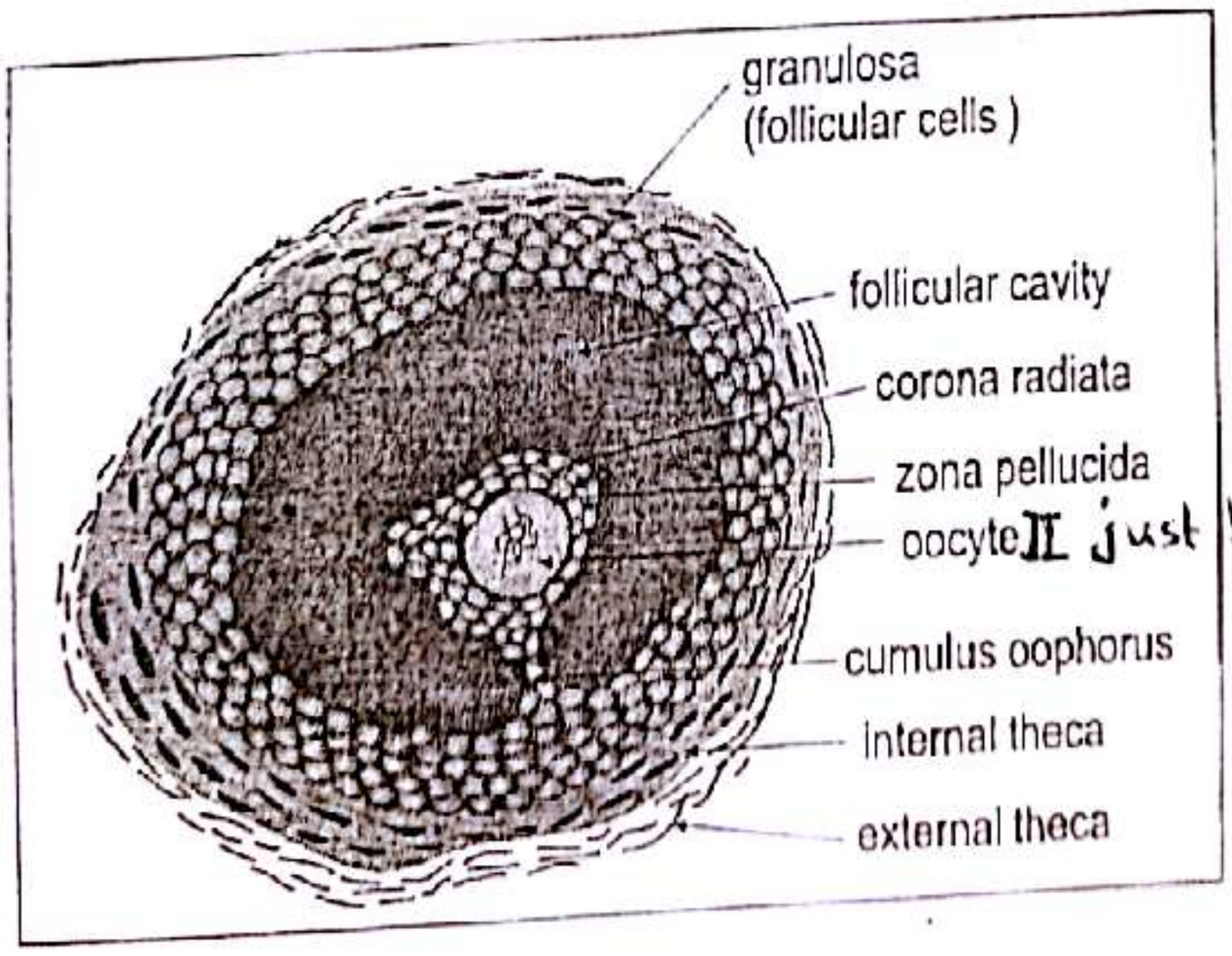
The microscopic observation for a section of a mammalian ovary shows the presence of many follicles at different developmental stages: These follicles start from :

Primordial → primary → secondary → tertiary → graafian → corpus luteum (yellow body) → corpus albicans (white body).



Doc.a Schematic section of an ovary.

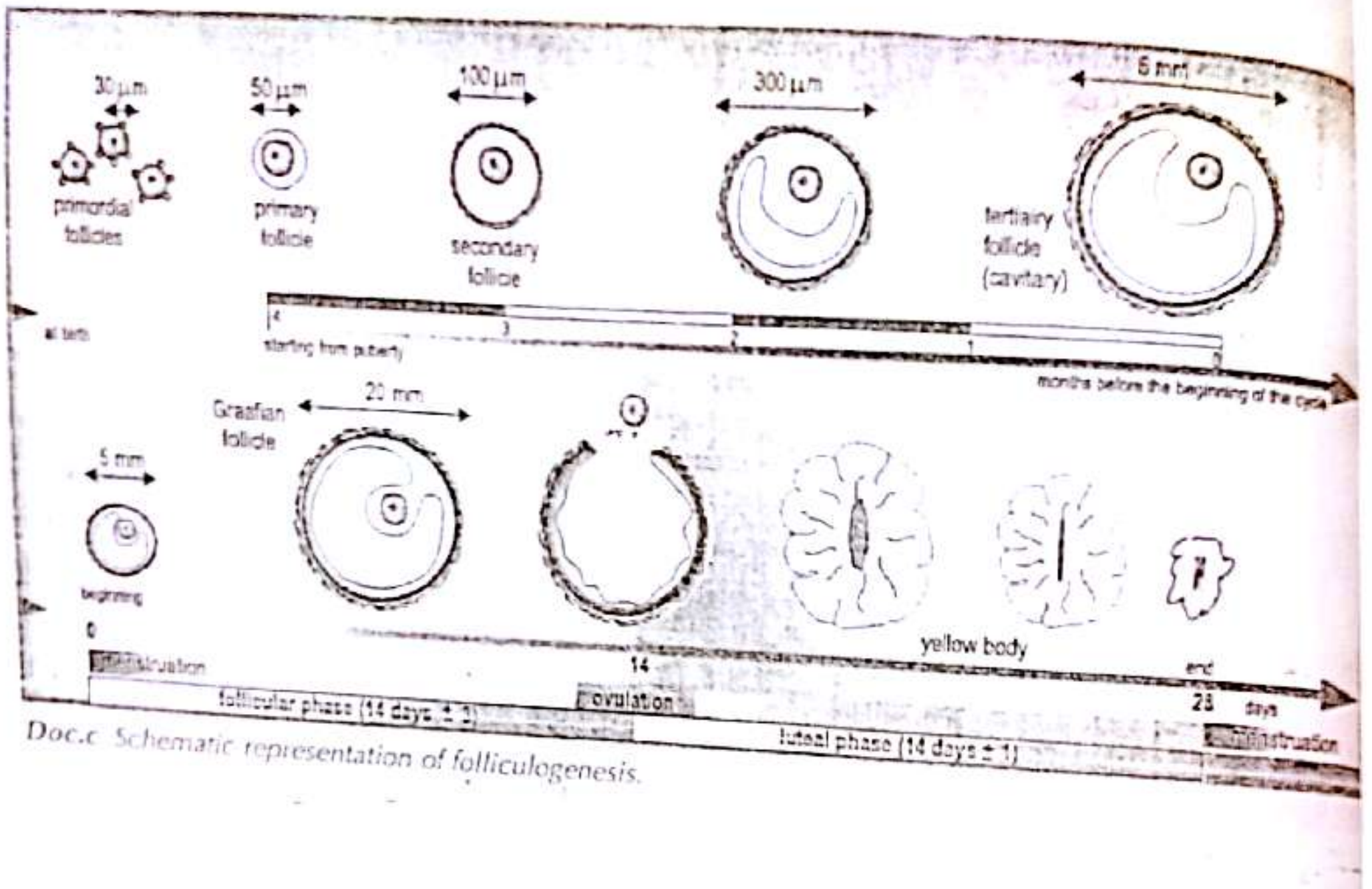
Graafian follicle structure



Folliculogenesis

Folliculogenesis is the developmental cycle of follicular cells which start during the fetal life and resumes its activity at puberty. Starting from puberty on wards, each group of 500 primordial follicles resumes their activity after their blockage

for about ten years and before each cycle by three to four months, only one o these follicles will reach its maturity and all the others will degenerate.



Doc.c Schematic representation of folliculogenesis.

Oogenesis : Oogenesis is the process by which oogonia are transformed into female gametes. It is a discontinuous process which does not end in the ovary and includes four phases:

1- **Multiplication period:** During embryonic life, the oogonia will increase in number by mitosis.

2- **Growth period:** During embryonic life, each oogonium will increase in size to form oocyte I.

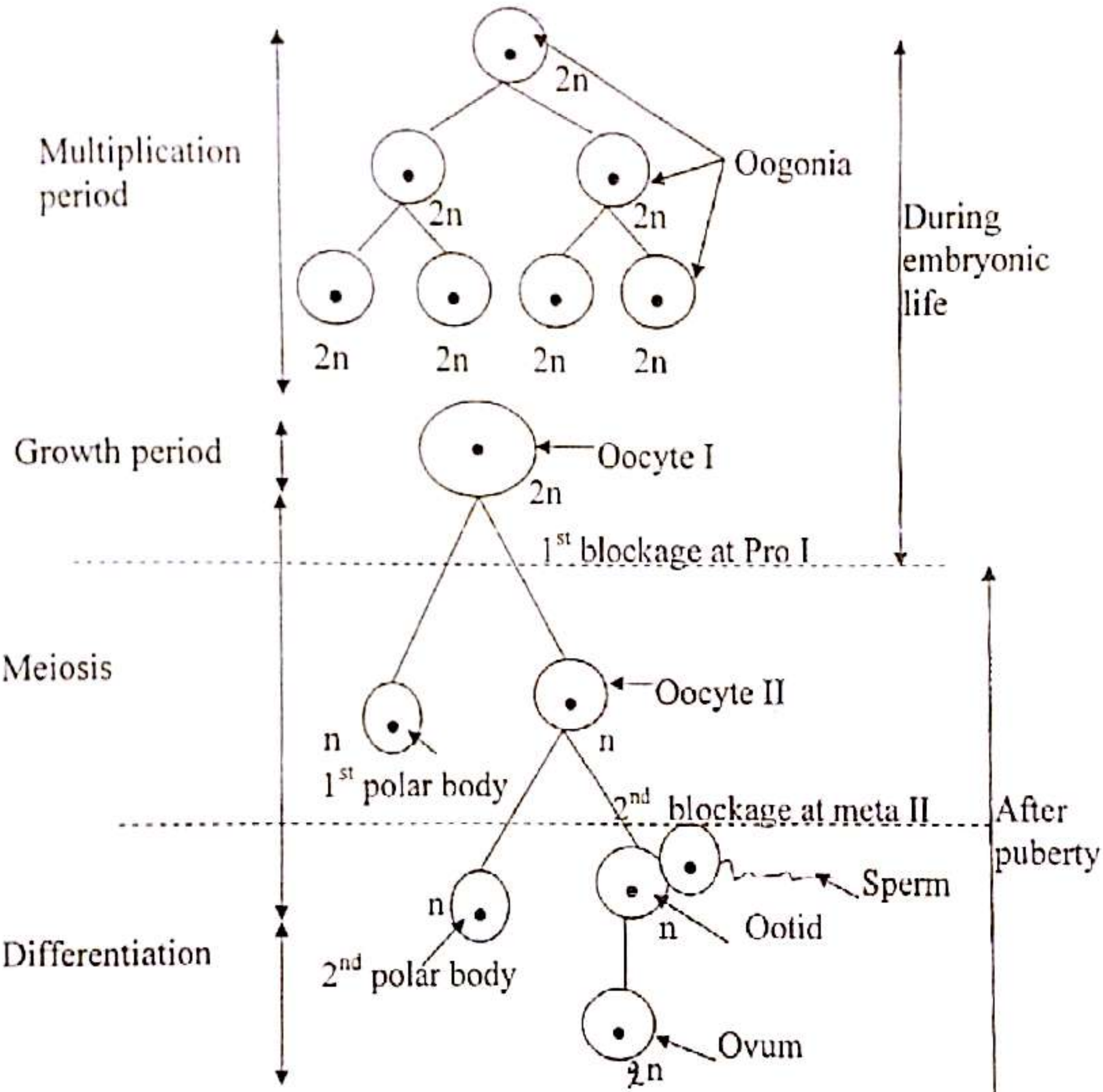
3- **Maturative period (Meiosis):** During embryonic life, the primary oocyte starts its first meiotic division and at prophase I it blocks its division. (Time of birth) till puberty then resumes its activity to divide into two unequal cells: first polar body and secondary oocyte.

The secondary oocyte starts its second meiotic division and at metaphase II it blocks its division to be released into the oviduct. This blocked oocyte can survive for 24 hours without fertilization but in the presence of the sperm (fertilization) it resumes its activity to give two unequal cells: A second polar body and an ootid.

4- **Differentiation period** :

The ootid will develop and becomes an ovum .

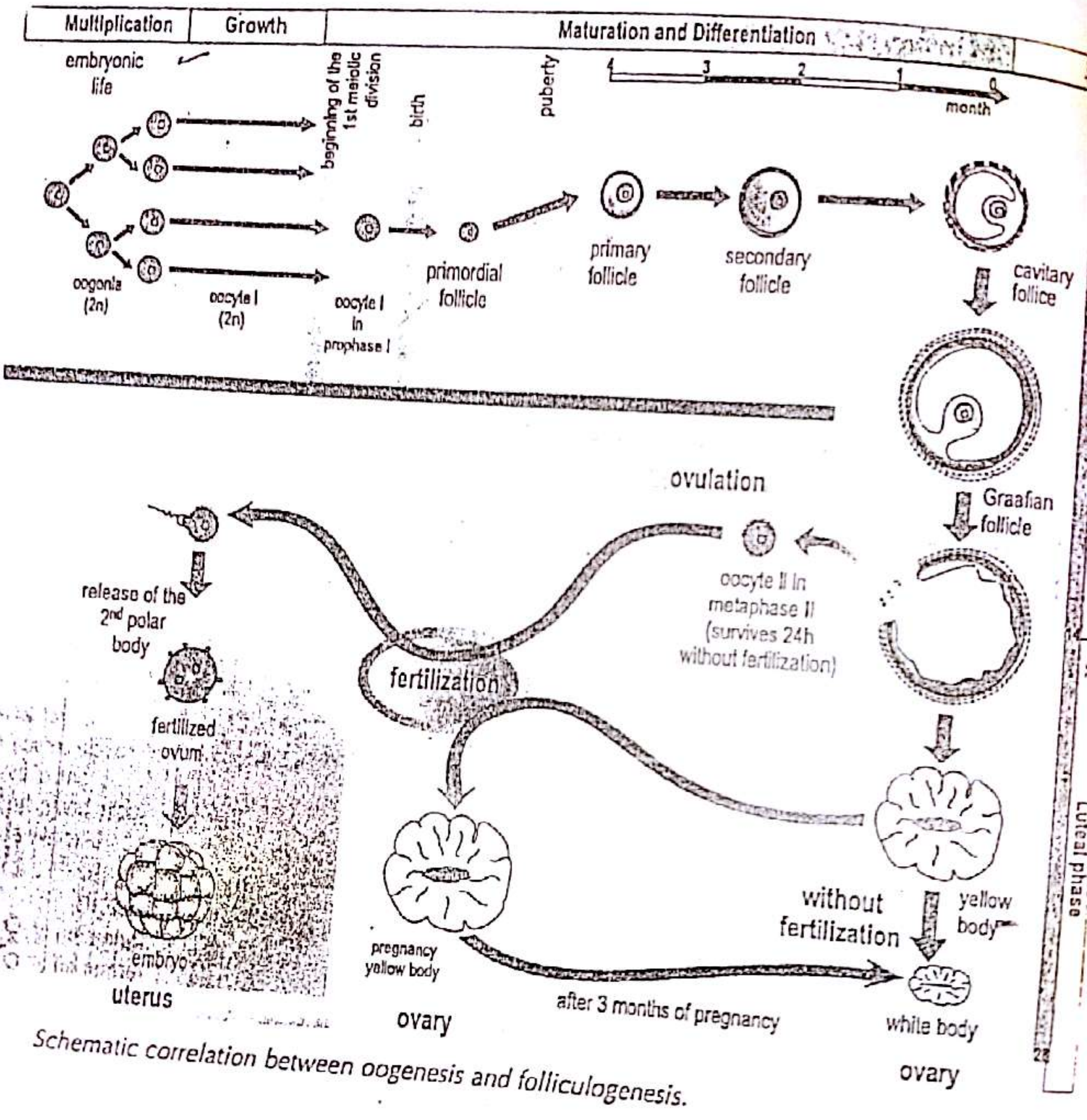
Concept map:



Oogenesis and folliculogenesis

A large number of oocytes are formed very early, by the 15th week of fetal life. The ovaries of a five months – old fetus contain more than six million oocytes. A large number of these degenerate during embryonic life. At puberty, each female has in her ovaries around 400.000 oocytes and releases, by ovulation, not more than 400.

The total depletion of these oocytes correspond to menopause.



Schematic correlation between oogenesis and folliculogenesis.

Document 6 : Fertilization

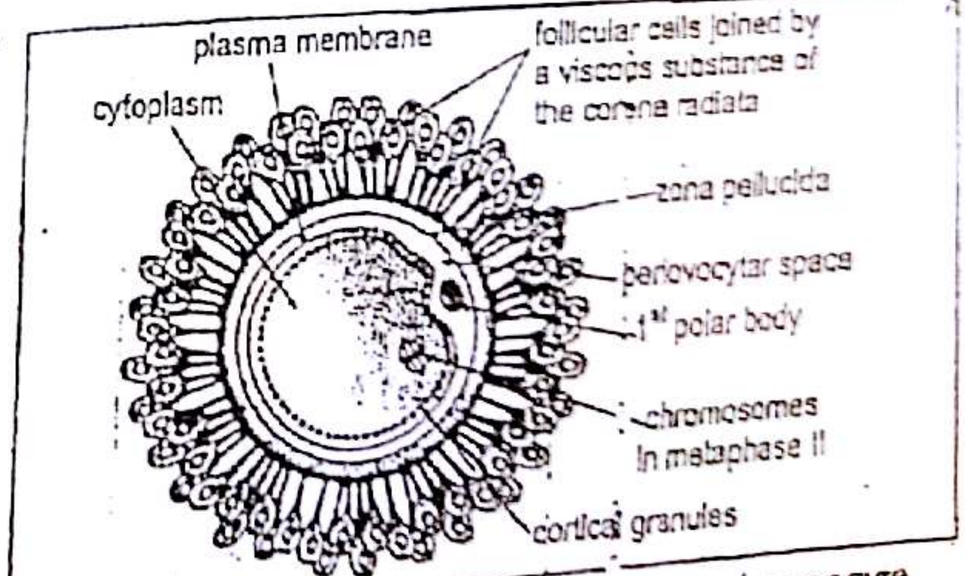
Definition : Fertilization is the union of two haploid gametes: a sperm cell and an oocyte giving rise to a diploid cell called zygote that is the first cell of a new individual.

The passage of male gametes in the female reproductive tract:

During sexual intercourse millions of sperm are deposited in the vagina, but less than 1% can reach the uterus and only a few hundreds can reach to oviduct.

Sperm capacitation: The sperm cells acquire their capacity for fertilization and retain it for 48 hours in the female tract. This capacitation is due to a biochemical change in the plasma membrane.

Structure of a secondary oocyte



Schematic representation of a secondary oocyte.

Test cross : It is a cross to show the real genotype of a dominant character.

but how?

We cross a dominant character like gray with a recessive character like black. If the result obtained is 100% gray then gray is a pure race but if the result is 50% gray and 50% black then the gray character is of hybrid race.

Note: The recessive character is always pure.

Co – dominance = Non-dominance

How to answer ?

How to interpret ?

Result → variable → Indicate that

Analyse — Significance

Interpret

- The phenotypes obtained and their proportion or % : 2(45%) + 2(5%) reflect the gamete variety of the parents, but the father is birecessive so the mother is responsible for the production of four different gametes with different % (two high % & two low %). This indicates that it is the case of partial linkage with crossing over
- Since the parental gametes consist of bidominant or birecessive alleles, then they are in cis position.
- Since the parental gametes consist of 1 dominant & 1 recessive allele, then they are in trans position

- How to explain?

Explain = result + reason

Deny two of three then the 3rd will be automatically verified

- If we obtain 4 phenotypes with equal % 25% each, then the genes are said to be independent.
- If we obtain 2 phenotypes with equal % 50% each, then the genes are said to be absolutely/completely linked
- If we obtain 2 phenotypes with high % and 2 phenotypes with low %, then the genes are partial linkage with crossing over in cis or trans position.

How to distinguish between autosomal alleles & gonosomal ones?

1. If the phenotypes of the offspring changed when we inverse the phenotypes of the parents
2. If the phenotype of the male offspr

is different from the female offspring.
Then the allele is located on a sex chromosom
mainly X, since this trait is presented in
both sexes

3. If no change in the results upon
inversing parent's phenotype

4. If the phenotypes of males & females
obtained are common

Then the allele is autosomal

Summary

	Self cross	Test cross
Independent Genes	$\frac{9}{16}, \frac{3}{16}, \frac{3}{16}, \frac{1}{16}$	$\frac{1}{4}, \frac{1}{4}, \frac{1}{4}, \frac{1}{4}$
Absolute/complete linkage	75%, 25%	50%, 50%
Partial Linkage With crossing over	High % [AB]	2 High % parental
	Mid % [ab]	2 low % recombine
	low % [Ab], [aB]	

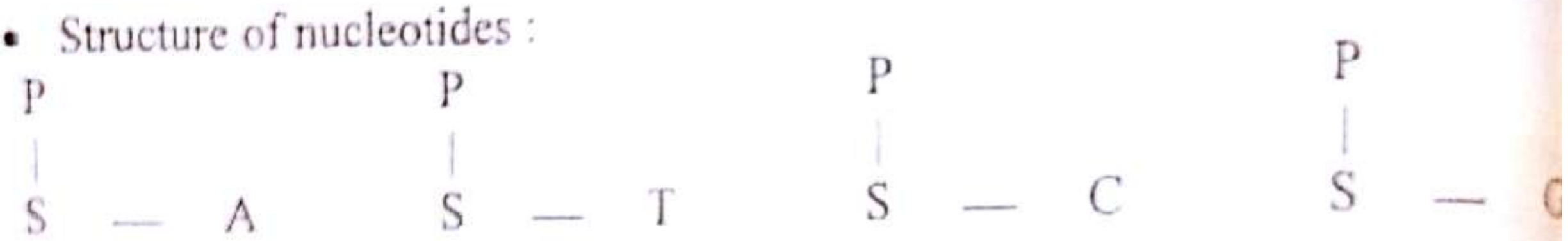
Chapter Three
Genetic variation and polymorphism

Revision notes on nucleic acids

Nucleic acids: DNA and RNA

DNA: Deoxy ribo nucleic acid:

- Nitrogenous bases: Adenine (A), Thyamine (T)
  Cytosine (C) and Guanine (G)
- Affinity : A to T and C to G
- Kinds of nucleotides: Adenine – Deoxyribose – Phosphorus
  Thyamine – Deoxyribose – Phosphorus
  Cytosine – Deoxyribose – Phosphorus
  Guanine – Deoxyribise - Phosphorus
- Structure of nucleotides :



- Structure of DNA :

RNA: Riobo nucleic acids .

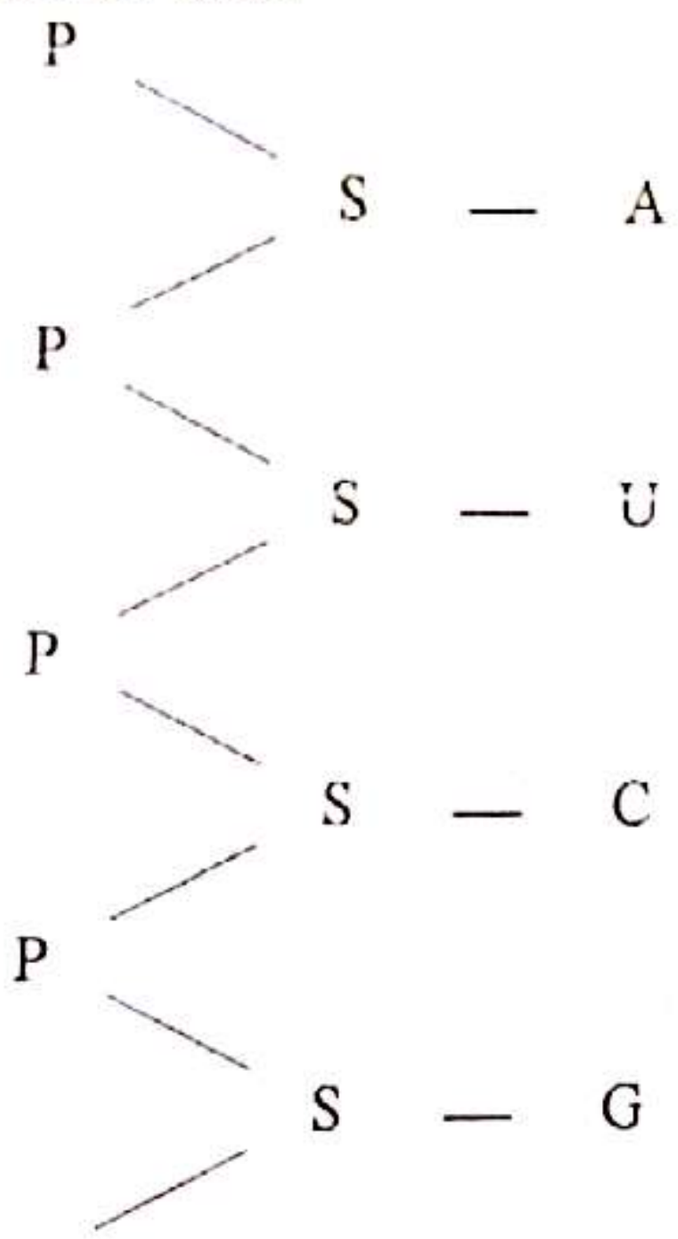
- Nitrogenous bases: Adenine (A) , Uracil (U), Cytosine (C) and Guanine (G)
- Affinity : A to U and C to G.

- Kinds of nucleotides : Adenine – Ribose – Phosphorus

  Uracil – Ribose – Phosphorus
  Cytosine – Ribose – Phosphorus
  Guanine – Ribose – Phosphorus

- Structure of nucleotides:

- Structure of RNA



What are the differences between DNA and RNA?

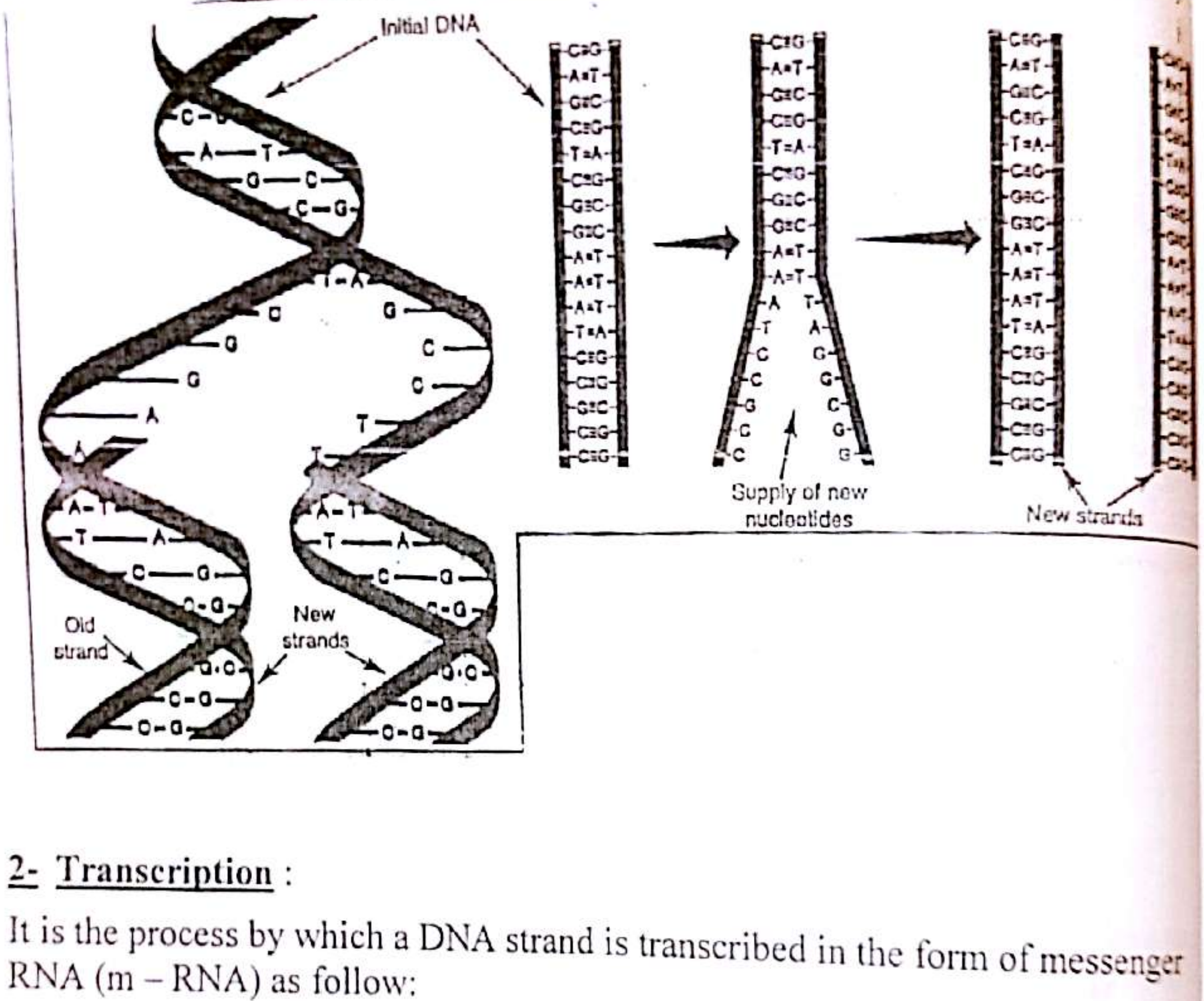
DNA	RNA
1) Big molecule	1) Small molecule
2) Stable molecule due to the presence of strong hydrogen bond between the bases	2) Unstable molecule
3) Double chained molecule	3) Single chained molecule
4) The bases are: A, T, C and G	4) The bases are : A, U, C and G.
5) DNA are located in the chromatin material.	5) RNA are located in the nucleolus, ribosome and cytoplasm.
6) DNA plays a role in the support of genetic information.	6) RNA plays a role in protein synthesis.
7) The sugar is deoxyribose	7) The sugar is ribose.

DNA and protein synthesis

Synthesis of protein starts from DNA to RNA to ribosome in the cytoplasm. It occurs in three steps:

1- **Replication:** During the S – stage of the interphase the cell doubles its DNA molecules. This duplication or replication can take place only in the presence of the DNA – polymerase enzyme.

Replication of DNA



2- **Transcription** :

It is the process by which a DNA strand is transcribed in the form of messenger RNA (m – RNA) as follow:

ATCGAC ..... Transcribed DNA.

UAGCUG ..... m – RNA

T ACGACT ..... non – transcribed DNA

UACGACU ..... m – RNA

3- **Translation** :

It is the process by which the nitrogenous bases carried by m – RNA are translated into amino acids in a way that each triplet (codon = 3 bases) forms an amino acid under the action of transfer RNA (t – RNA) .

e.g UAU , CCG , GAC

Tyr , Pro , Asp

1st letter ↓ / 2nd letter →	U		C		A		G		3rd letter ↓
U	UUU	phenylalanine (Phe)	UCU	serine (Ser)	UAU	tyrosine (Tyr)	UGU	cysteine (Cys)	U
	UUC		UCC		UAC		UGC		C
	UUA	leucine (Leu)	UCA		UAA	stop	UGA	stop	A
	UUG		UCG		UAG		UGG	tryptophane (Trp)	G
C	CUU	leucine (Leu)	CCU	proline (Pro)	CAU	histidine (His)	CGU	arginine (Arg)	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	glutamine (Gln)	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	isoleucine (Ile)	ACU	threonine (Thr)	AAU	asparagine (Asn)	AGU	serine (Ser)	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	lysine (Lys)	AGA	arginine (Arg)	A
	AUG	methionine (Met)	ACG		AAG		AGG		G
G	GUU	valine (Val)	GCU	alaphine (Ala)	GAU	aspartique acide (Asp)	GGU	glycine (Gly)	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	glutamique acide (Glu)	GGA		A
	GUG		GCG		GAG		GGG		G

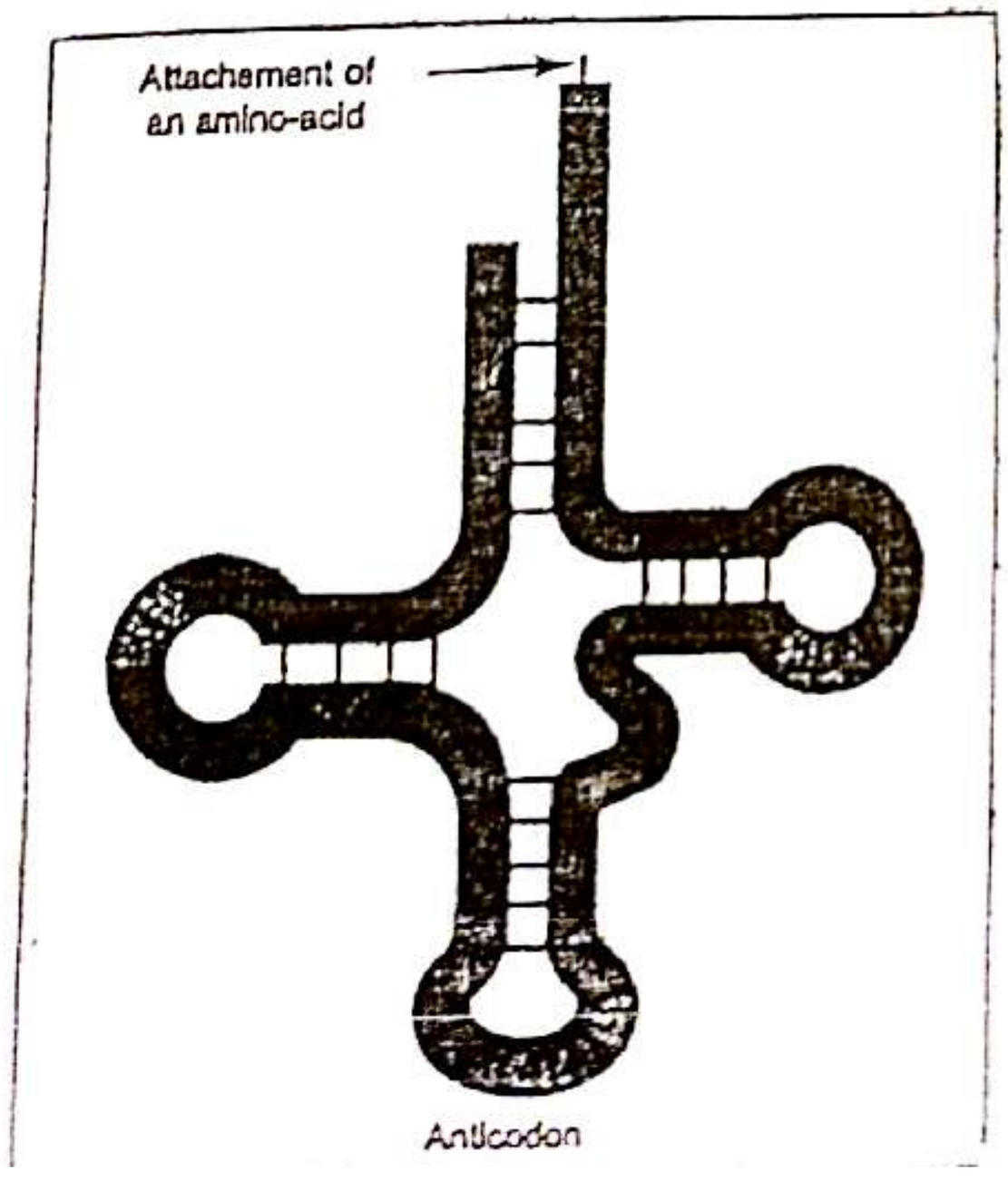
Genetic code

Process of protein synthesis

After copying the message from the DNA the m – RNA leave the nucleus through the pores of the nuclear membrane. The process of protein synthesis takes place in three steps:

1- Initiation:

The first amino acid translated by t – RNA in the ribosome is methionine (AUG). So, the first three bases of the t – RNA are UAC (anti codon) facing AUG on m – RNA.



2- Elongation :

A second t – RNA carring an amino acid is fixed on the ribosome near the first t – RNA facing the second triplet of the m – RNA to translate a new amino acid. Between the two amino acids a peptide bond is formed and this process is repeated till several amino acids are translated.

3- Termination :

Punctuation codons (stop codons): UAA, UAG and UGA are found on m – RNA to terminate the process of protein synthesis when any one of these codons face t – RNA.

Document One: Mutations and the environment

Definition of mutation: A mutation is a change in the nucleotide sequence of DNA.

Mutations and genetic variation

The genome of humans include coding sequence that we know their function and constitutes only 10% of the genome and non coding sequence that we don't know their function till yet and constitutes 90% of the genome.

1) *** Active and inactive mutation :**

Active mutation that leads to a change in the gene expression and includes favourable mutation that can reproduce and exist and unfavourable mutation that can't live much.

Example: Gray moth can escape from their predators by blending with gray trunk covered by fungi and lichens, but due to mutation these moths start produce dark gray moths that can be seen by their predators (contrast in color with the trunk).

This is unfavourable mutation.

With pollution, the trunks were blackened and the dark moths now are blended and increase in number while the light gray moths start to decrease (contrast in color). This is favourable mutation.

*** Inactive mutation** : This mutation does not lead to a change in the gene expression (silent) or affect the non coding genes.

2) **Transmission of mutations:**

Transmitted mutation : mutation that affects sex cells like sperms and oocytes is transmitted from one generation to another.

e.g. – Thalassemia , color of moth .....

Untransmitted mutation : Mutation that affect somatic cells can't be transmitted from one generation to another.

e.g. - lung cancer due to smoking

- skin cancer to U.V rays.

Can mutation be repaired (corrected)?

Yes, normally there are enzymes that can repair the DNA damage. These enzymes are coded by a repair gene in the cell but depends on the degree of mutagenic factor :

- Mutations occured however the repair gene is not destroyed. In this case the damage can be repaired, thus mutation go unnoticed and not expressed phenotypically.
- High exposure to U.V: more damage in the DNA strand. The repair gene still not affected, the repair gene repairs some of these damages while others will not be repaired thus mutation are expressed. e.g. black or brown spots, wart ..... etc.
- Higher degree of exposure to U.V.: The repair gene is damaged, thus mutation and damaged areas can't be repaired e.g. skin cancer .....etc.

Document 2 : Mutations and multiple alleles

Types of mutation : There are three types.

1) **Substitution mutation :** A process where by a base pair on DNA is replaced by another.

   e.g. ATCGTA → AGCGTA

2) **Deletion mutation :** A process whereby there is a loss of a segment of base pairs from DNA.

   e.g. ATCGTA → ATCG

3) **insertion mutation :** A process identified by the presence of an additional stretch of base pairs in DNA.

   e.g. ATGGCT → ATGGCTACT

Effects of mutations :

1) **Missence mutation** : A type of base-substitution that causes one amino acid to be substituted for another in the resulting protein product.

e.g. Pro – Glu – Thr → Pro – Val – Thr

2) **Non sense mutation** : A type of base – substitution that results in an amino acid – specifying codon being changed to a stop codon. The resulting protein is non functional.

3) **Frame shift mutation** : there is a total change in the sequence of amino acids after the site of mutation.

4) **Silent mutations** : Are mutations that don't change the product of a gene.

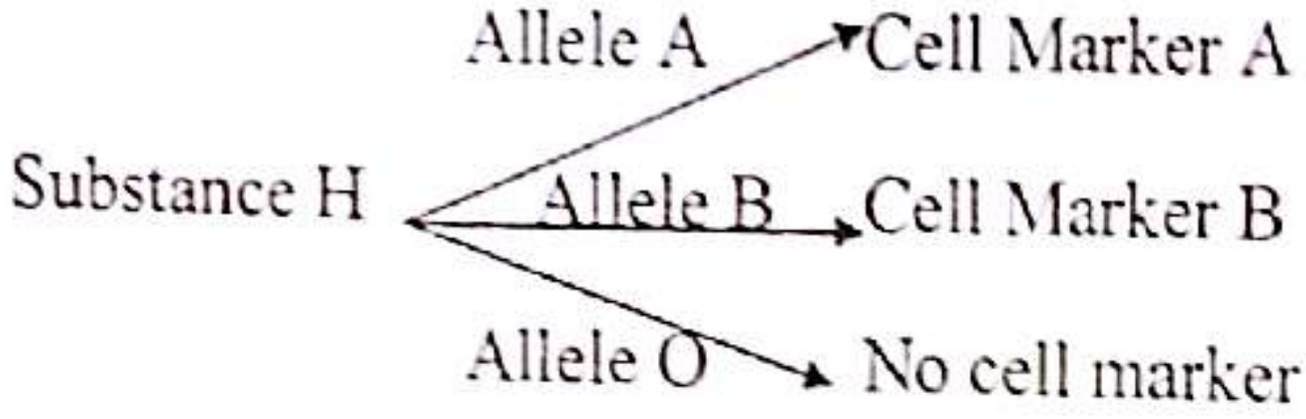
Note: point mutation leads to a change in one codon only.

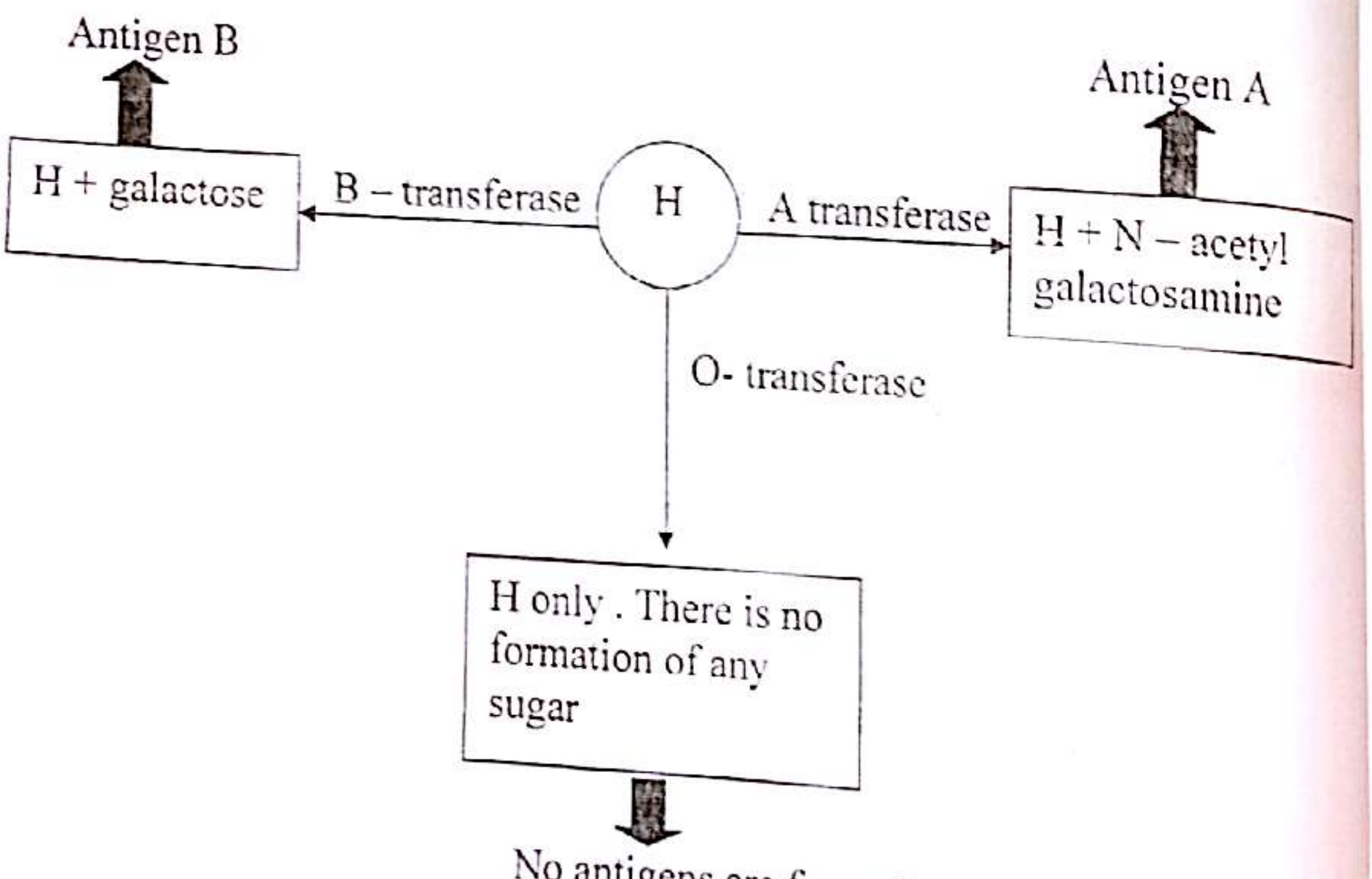
type of mutation	non-transcribed DNA strand of a normal gene and corresponding amino acids	non-transcribed DNA strand of the mutant gene and corresponding amino acids	effect of the mutation
substitution	...CCA-GAG-ACT... Pro - Glu - Thr	...CCA-GTG-ACT... Pro - Val - Thr	missense altered polypeptide
	...CCA-GAG-ACT... Pro - Glu - Thr	...CCA-GAA-ACT... Pro - Glu - Thr	silent no detectable change
	...CCA-GAG-ACT... Pro - Glu - Thr	...CCA-TAG-ACT... Pro - Stop -	nonsense incomplete polypeptide
deletion	...TAC-ACC-ACG - A... Tyr - Thr - Thr	...TAC-CCA-CGA... Tyr - Pro - Arg	frame-shift altered polypeptide
Insertion	...TAC-ACC-ACG - A... Tyr - Thr - Thr	...TAC-GAC-CAC - GA... Tyr - Asp - His	frame-shift altered polypeptide

Genes and multiple alleles

In an individual every gene has a maximum of 2 alleles while in a population we can consider multiple alleles.

e.g. Blood group of humans. This system is defined by the expression of any two of the three alleles A, B and O on the surface of red blood cells that have the same basic structure called H.





Role of mutation in this process.

The transferase enzyme is subjected to many mutation and for each mutation there is a change in the function of this enzyme.

Between A and B there is a modification of four amino acids done by substitution. While allele O is obtained by a small deletion leading to a truncated inactive enzyme.

Document 3 : Polymorphic genes in a population

Genetic polymorphism is a source of genetic variation in a population .

How do mutation alleles lead to genetic polymorphism?

1- Major Histocompatibility Complex (MHC) [HLA in humans]

MHC of the genes in a given population exists in multiple alleles and are said to be polymorphic.

HLA genes codes for two classes of glycoprotein:

- HLA class I (HLAI): are coded by loci A, C and B and expressed by all nucleated body cells. They are involved in graft acceptance or rejection.
- HLA class II (HLAII) : are coded by loci DP, DQ and DR and expressed by some cells of the immune system like macrophage.

Each locus of the two classes has a large number of alleles. So, it is impossible for two individuals, except in real twins, to have identical distribution if the alleles in the six loci.

2- β globin

Hemoglobin is a protein molecules made up of globin (protein) and 4 molecules of heme (iron). β globin is responsible for binding the iron to globin. The mutation of β globin leads to β - thalassemia that has several degrees of severity:

- If only one allele is mutated, it is not dangerous.
- If the two alleles are mutated then thalassemia is dangerous.

What is a wild type allele? The wild type allele is the allele that codes for the most common phenotype in a population.

Note: An allele is considered polymorphic if present at a frequency > 1% in a population.

Document 4 : Detection of genetic polymorphism

Restriction enzymes

Definition: Restriction enzymes are biological scissors produced by bacteria in order to defend themselves against viruses.

Restriction enzymes are needed to isolate the gene from the chromosome by fragmenting the linear DNA molecule into defined small pieces to do genetic analysis.

How do the restriction enzymes work?

Restriction enzyme recognize its restriction site which is of 4 to 6 base pair sequence.

e,g, consider this DNA molecule:

5'... ATCCATGAATTCGTAC ..... 3' non – transcribed

3' ...TAGGTACTTAAGCATG ..... 5' transcribed

this molecule is subjected to an enzyme which has a restriction site:

5' GAATTC 3'

3' CTTAAG 5'

Indicate the number of sites that cut the above DNA molecule then indicate the number and the sequences of fragments formed by this enzyme for the two sequences knowing that the enzyme reads DNA from 5' to 3' and the cut is done between G and A.

Restriction map : Application

e.g1) A DNA molecule is subjected to enzyme A, B then enzyme A and B at the same time, the following fragments are obtained:

$$A\begin{cases}1000\text{b.p}\\600\\400\end{cases} \qquad B\begin{cases}1200\text{b.p}\\800\end{cases} \qquad A+B\begin{cases}800\text{b.p}\\400\\600\\200\end{cases}$$

Draw the restriction map.

e.g 2) $$A\begin{cases}1400\text{b.p}\\400\\200\end{cases} \qquad B\begin{cases}1500\\500\end{cases} \qquad A+B\begin{cases}1100\\400\\300\\200\end{cases}$$

Draw up the restriction map.

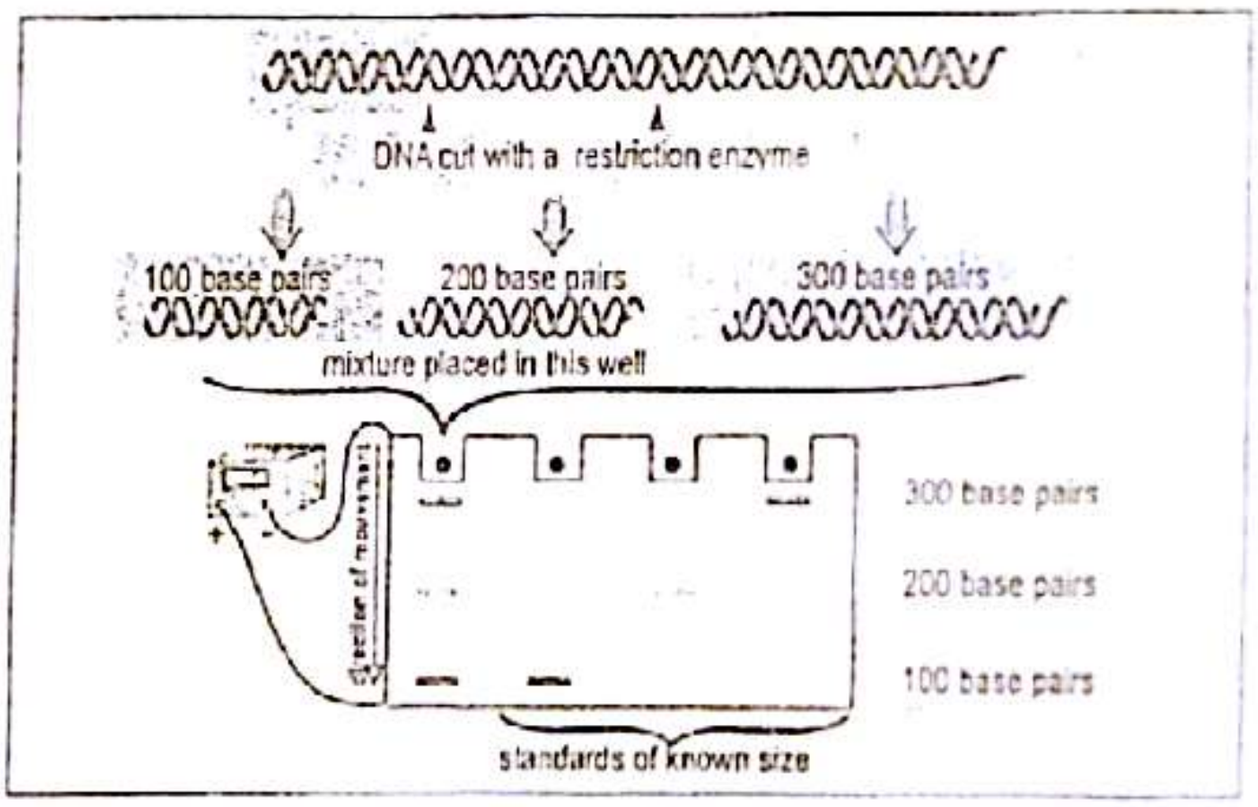
DNA Gel electrophoresis

The size or length of the DNA fragments can be determined by a method called DNA Gel electrophoresis.

Steps :

1) Use restriction enzymes to cut the DNA into many fragments.
2) Put this mixture of DNA fragments in a well made at one side.
3) Apply an electric current by putting the negative electrode at the side of the wells and the positive electrode at the opposite side since DNA has negative charge due to its phosphate group.
4) The bands are visualized by staining them with ethidium bromide and fluoresces under U.V light.

Result: The fragments of DNA will migrate toward the positive side in a way that the smallest in size is fastest and closest to the positive electrode.



Gel electrophoresis of DNA fragments.

How can we know if the gene has 2 similar or 2 different alleles?

e.g) The alleles of the gene are subjected to the same restriction enzyme.

$$\text{Allele I + enzyme A} \Rightarrow \begin{cases} 20\text{b.p} \\ 30 \\ 40 \end{cases}$$

$$\text{Allele II + enzyme A} \Rightarrow \begin{cases} 20\text{b.p} \\ 30 \\ 40 \end{cases}$$

∴ No mutation between the alleles .

e.g) Allele I + enzyme A $\Rightarrow$ $\begin{cases} 40 \text{b.p} \\ 60 \end{cases}$

Allele II + enzyme A $\Rightarrow$ $\begin{cases} 20 \text{b.p} \\ 50 \\ 30 \end{cases}$

$\therefore$ Mutation took place and the alleles of the gene are not identical.

Document 5: Genetic identify of individuals.

1- **FISH technique (Fluorescence In Situ Hybridization)**

Purpose of FISH: To determine the location of specific DNA sequence (location of a gene).

Steps :

1- Denature the double stranded DNA into single strands.

2- Add labeled, radioactive and specific probe to the single strands in order to hybridize with them.

3- Observe under a fluorescent microscope

Observation : As a result, the chromosome shows a fluorescent dot and hence the gene or the DNA sequence is located.

2- **Genetic maps:**

Genetic map is the distribution of genes on a chromosome.

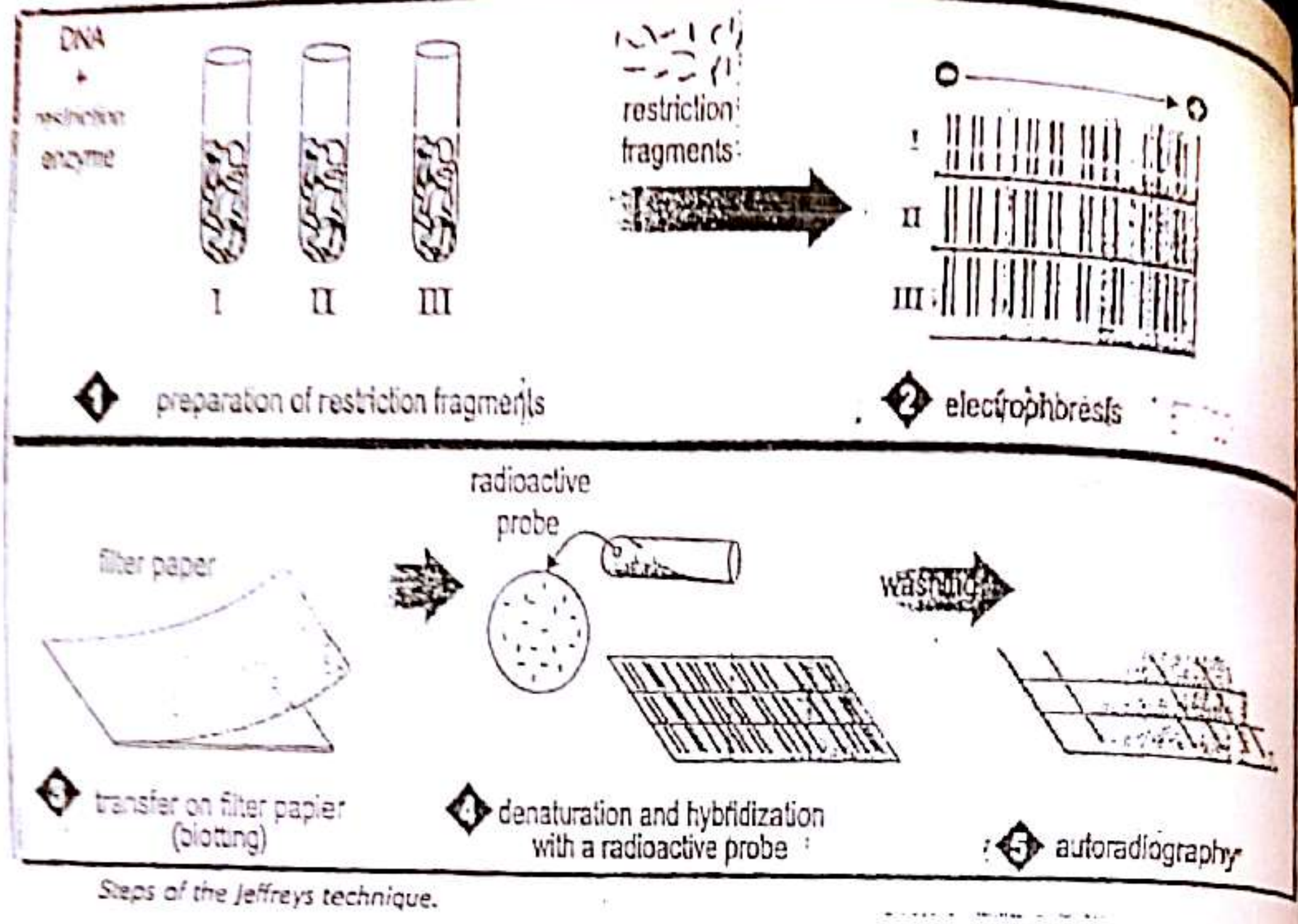
3- **DNA finger print** (Jeffreys technique)

Purpose: To show the uniqueness of the genotype.

Steps :

1. The DNA of two individuals is cut with the same restriction enzyme.
2. DNA fragments are separated by electropherosis.
3. Fragments are then transferred (blotted) and fixed onto a solid membrane (filler paper). This technique is called "Southern blotting".
4. Put the blotting paper in a mixture containing radioactive 32P-DNA ~~which is a fragment of DNA complementary to a sequence that~~ occurs frequently through out the genome. (repetitive sequence).
5. Observe the fragments by auto radiography (x-ray film).

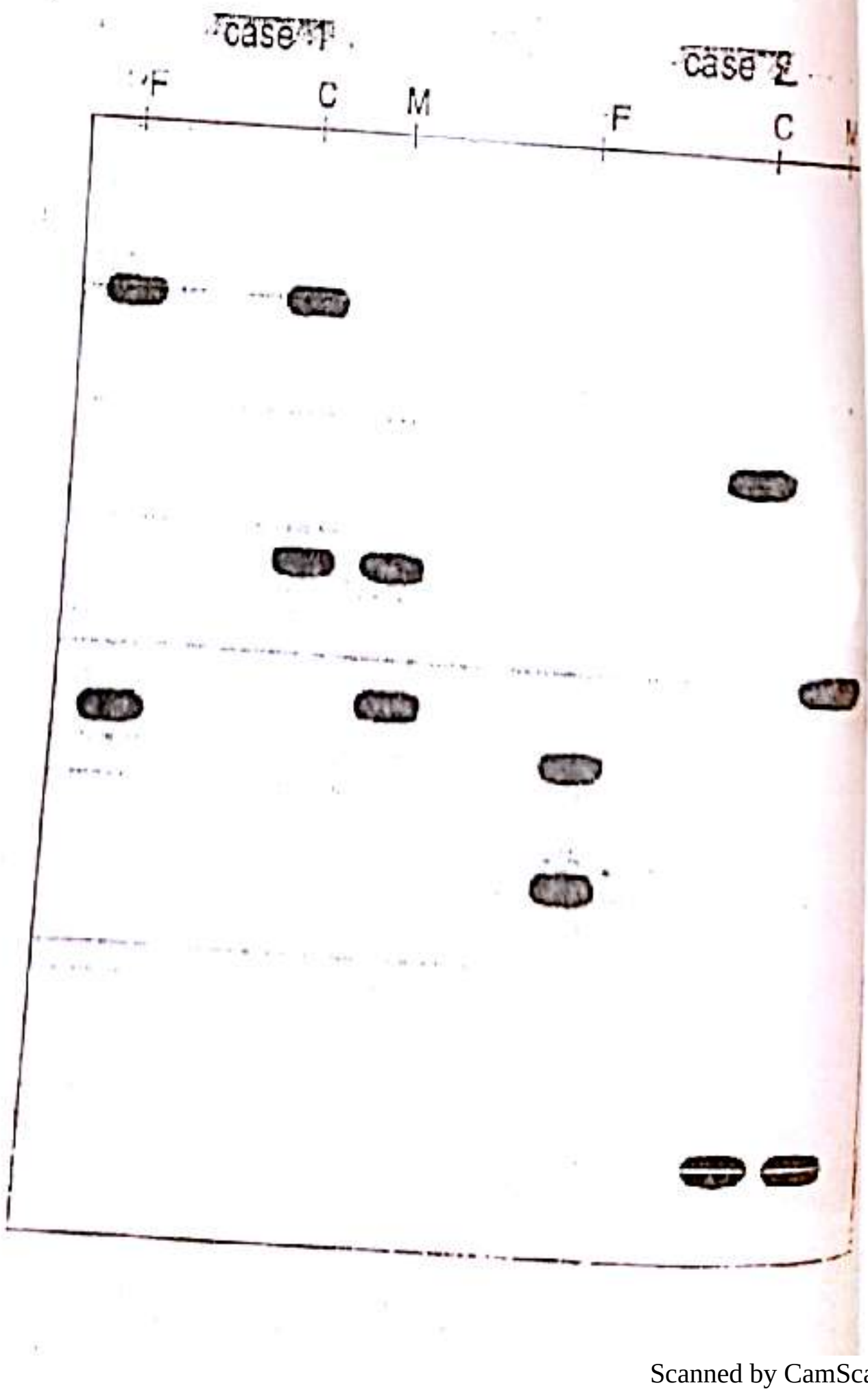
Observation : The resulting pattern of bands for each individual is referred to as a DNA finger print and is uniquely characteristic for that individual.



Steps of the Jeffreys technique.

4- DNA Finger print in paternity testing

The uniqueness of our DNA finger print can be used to determine parent hood. Each band of a child's DNA finger print should be shared with either the father's or the mother's DNA finger print.



pF = father

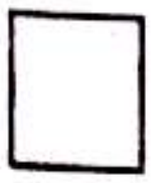
C = child

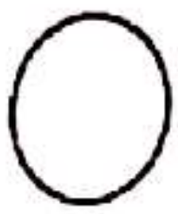
M = mother

In each case which father is the real one? Justify.

Chapter Four
Human Genetics

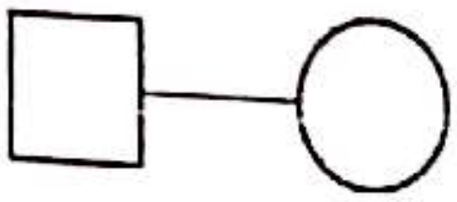
Document 1 : Constructing a pedigree: symbols used


= Normal boy

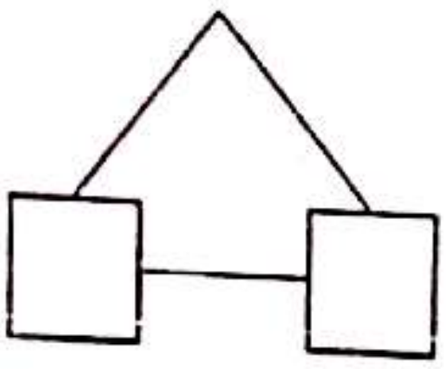

= Normal girl

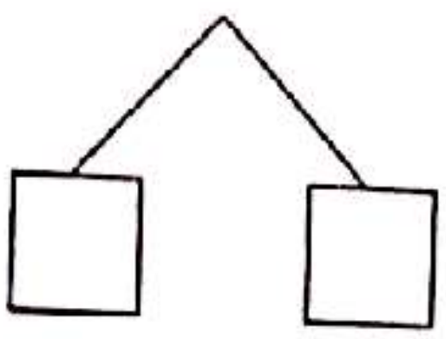

= Diseased boy

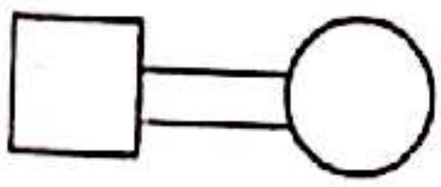

= Diseased girl


= Mating


= Fetus


= Identical twins

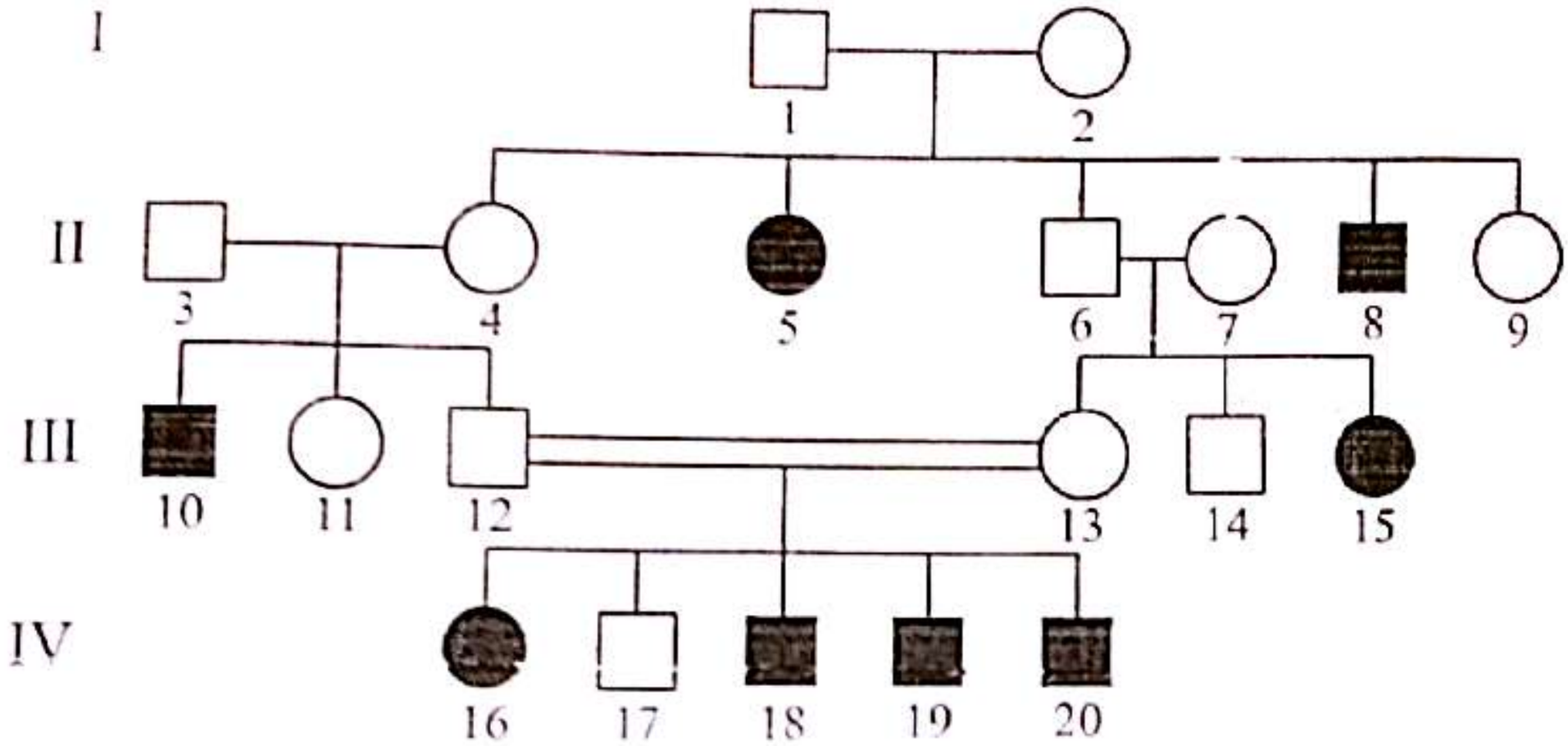

= Fraternal twins


= Consanguineous Mating

Document 2 : Autosomal diseases

Cystic fibrosis : a recessive disease

Cystic fibrosis is a severe disease leading to respiratory and digestive problems. The gene for cystic fibrosis is found on the pair of autosomal chromosomes seven.



DOC - a

Write the genotype of the family members represented in the pedigree of doc a.

Prediction of a genetic risk

The frequency of cystic fibrosis is relatively high due to the large number of heterozygous.

For example, in France, heterozygotes form 5% of the population.

In a randomly chosen couple without a family history for this disease, the probability of a female being heterozygous is $1/20$.

The risk for the couple to be both heterozygous is then $\frac{1}{20} \times \frac{1}{20} = \frac{1}{400}$ and the risk to get a diseased child is $\frac{1}{4}$.

Risk = Risk of the father to be hybrid × Risk of the mother to be hybrid × Risk for the couple to have a diseased child.

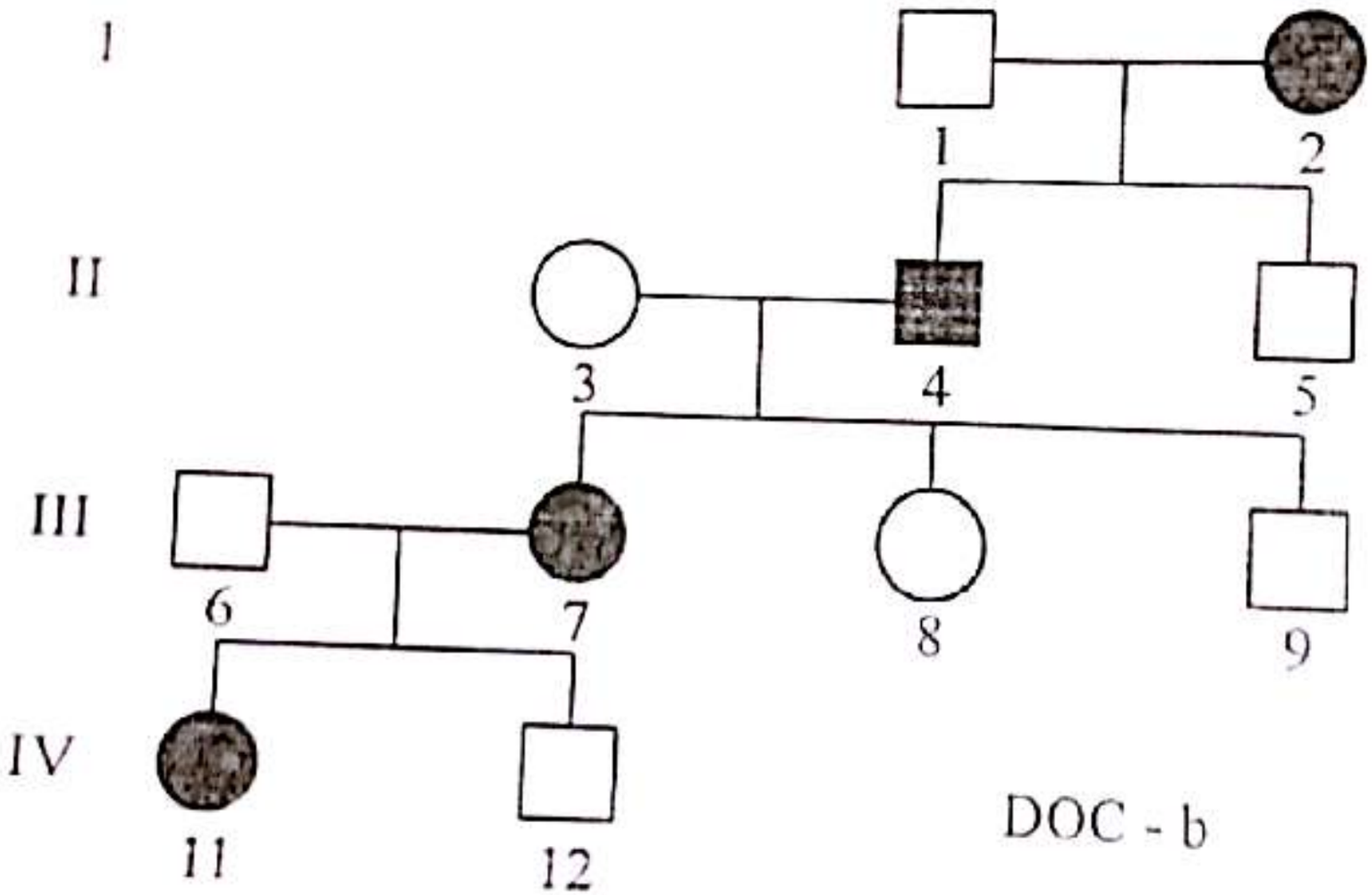
$$\text{Risk} = \frac{1}{400} \times \frac{1}{4} = \frac{1}{1600}$$

Example : Calculate the risk for a couple to have an affected child (Doca)

a) If they already have an affected child.
b) If each one has an affected sister.
c) If neither of them has a family history.

Huntington's chorea: a dominant disease

This disease appears only in adults between 30 and 50 years old. It is due to a lesion of certain neurons of the central nervous system. It is dominant and autosomal disease, its gene carried on the chromosome four.



DOC - b

Write the genotypes of the family members represented in the pedigree . (doc b.)

Document 3 : Sex – Linked diseases

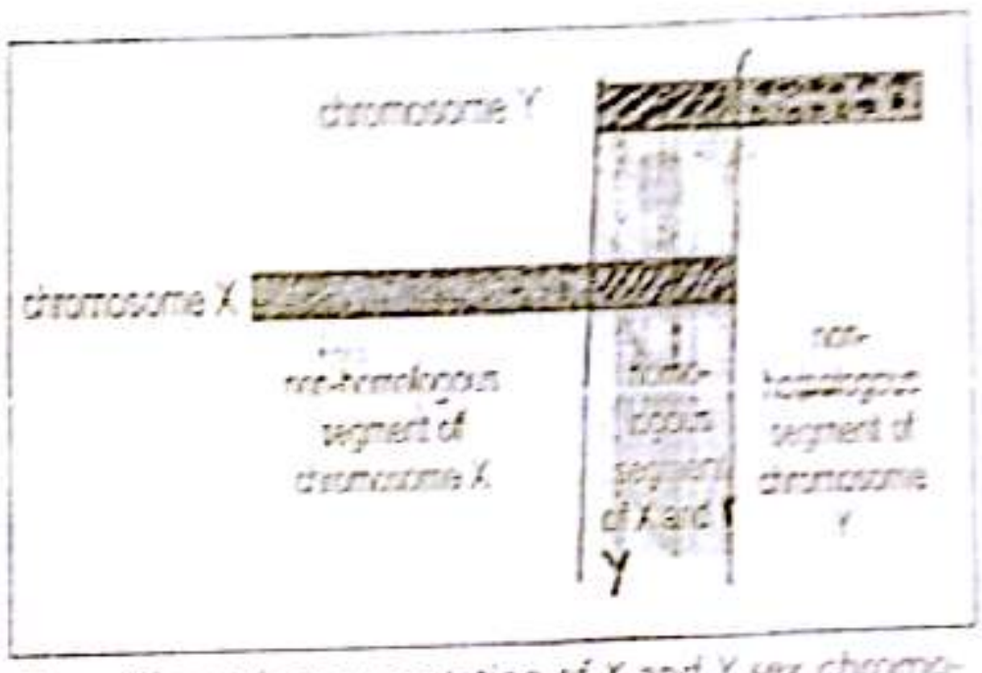
Sex chromosomes

Sex chromosomes X and Y or gonosomes have a common homologous segment and a non-homologous one.

Genes located on the homologous segment have two alleles both in males and females and thus behave as autosomal genes.

Genes found on the non-homologous segment are expressed differently in males and females and thus said to be sex-linked:

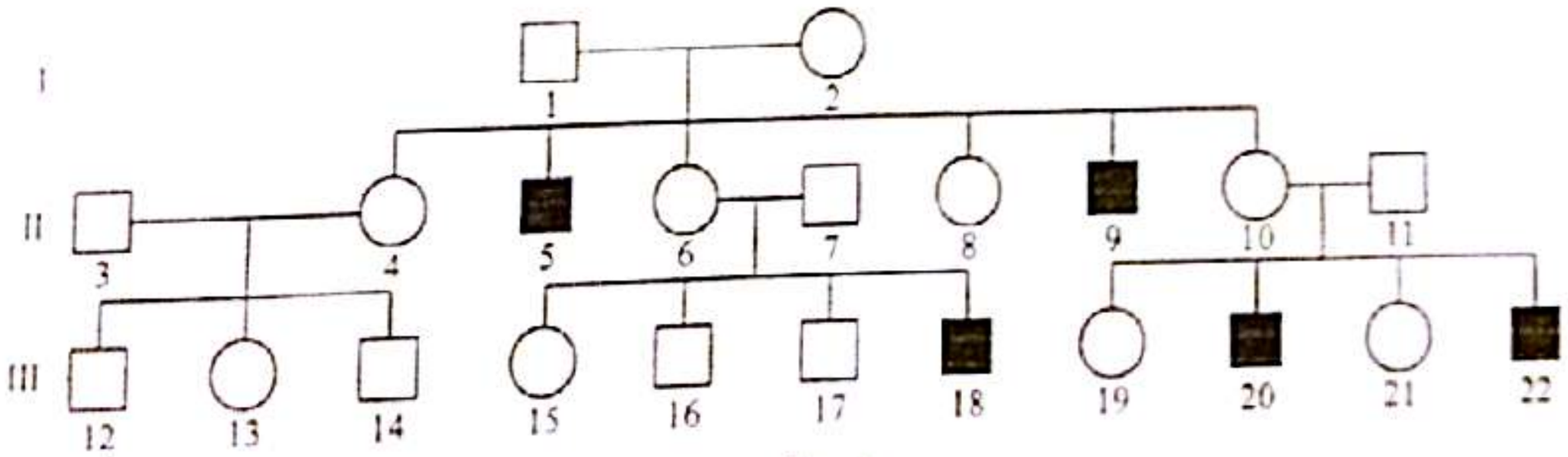
- Genes of the X chromosome exist in one copy in males and two in females. Males will thus express the single allele they have, whether it is dominant or recessive. Females express the dominant allele in the homozygous and heterozygous states while the recessive allele is expressed only in homozygotes.
- Genes located on the non-homologous segment of the Y chromosome are found in a single copy in males, who express the only allele they have, and are absent in females who never express the gene.



Doc.a Shematic representation of X and Y sex chromosomes.

Duchenne muscular dystrophy = a recessive disease

Myopathy or Duchenne muscular dystrophy is a gonosomal disease carried on X chromosomie and the affected girls only are not viable.

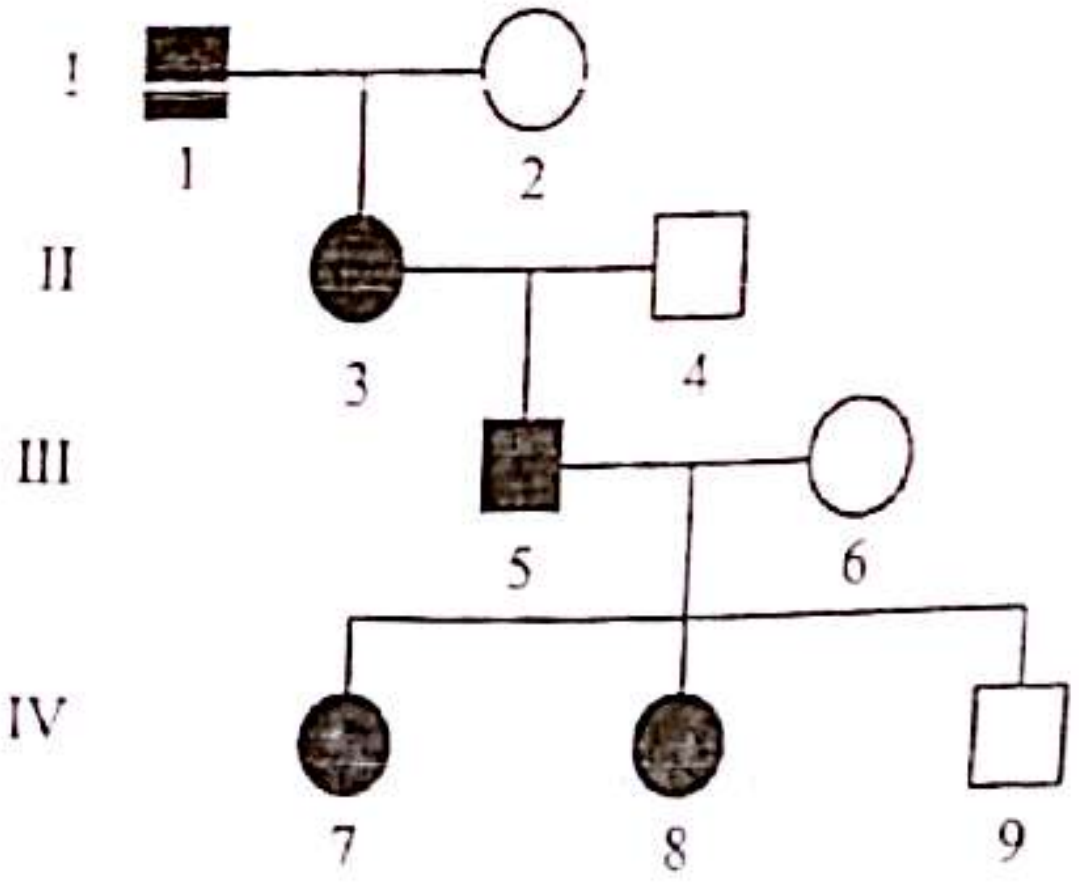


Doc b

Write the genotypes of the family members represented in the pedigree Doc.b.

Vitamin-ressitant rickets, a dominant disease

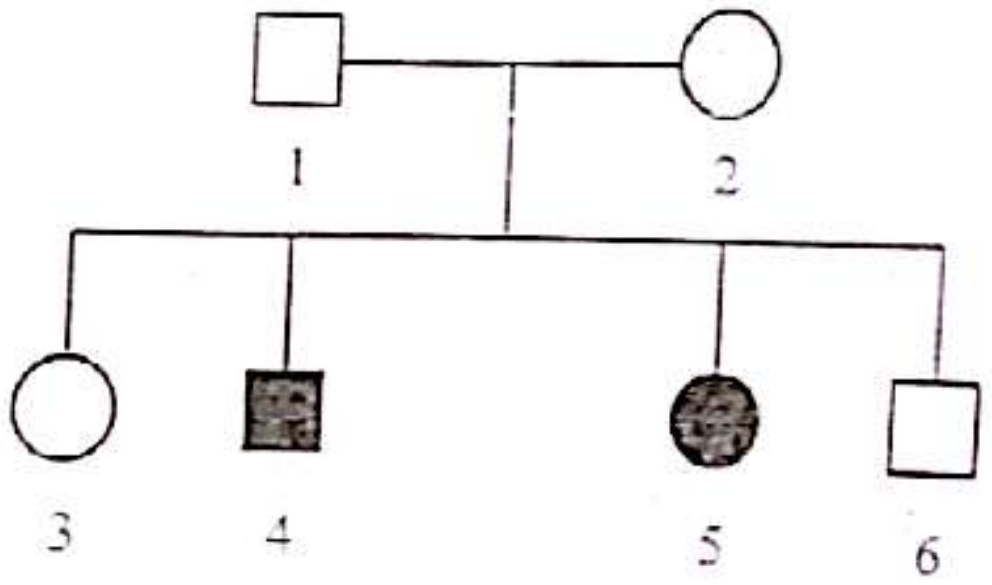
It is a gonosomal dominant disease carried on sex chromosome X



Doc - c

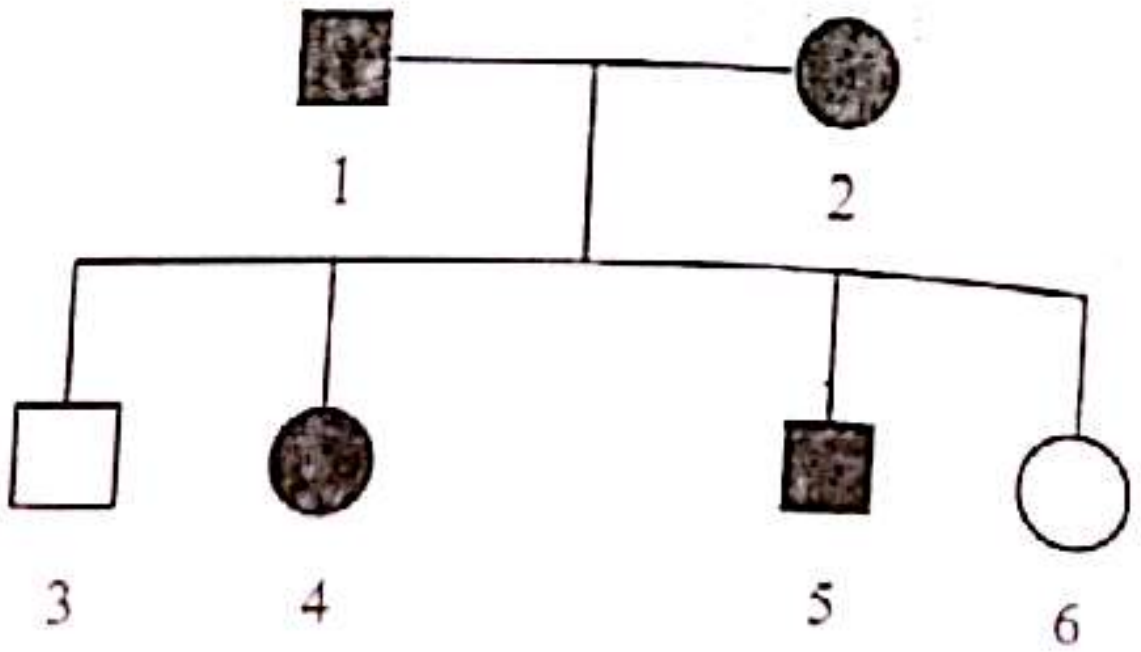
Write the genotype for each member of Doc. c.

Example 1 : Consider this pedigree



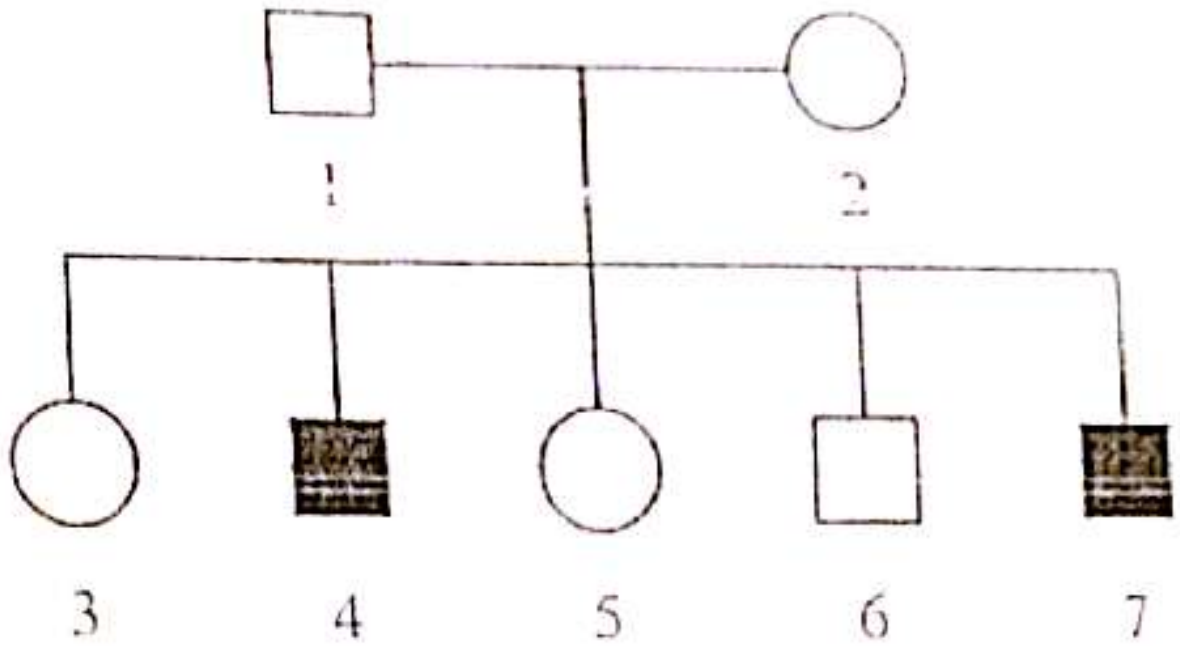
1) Is the allele of the disease dominant or recessive? Justify.
2) Discuss logically the chromosomal localization.
3) Write the genotype for 1, 2, 4 and 6. Justify.

Example 2 :



1) Is the allele of the disease dominant or recessive? Justify.
2) Discuss logically the chromosomal localization.
3) Write the genotype for 1, 2, 5 and 6 . Justify.

Example 3



1) Is the allele of the disease dominant or recessive? Justify.
2) Discuss logically the chromosomal localization.
3) Write the genotype for 1, 2, 4 and 5 . Justify.

Document 4 : Chromosomal mutations

Abnormalities in chromosome number

Autosomal abnormalities :

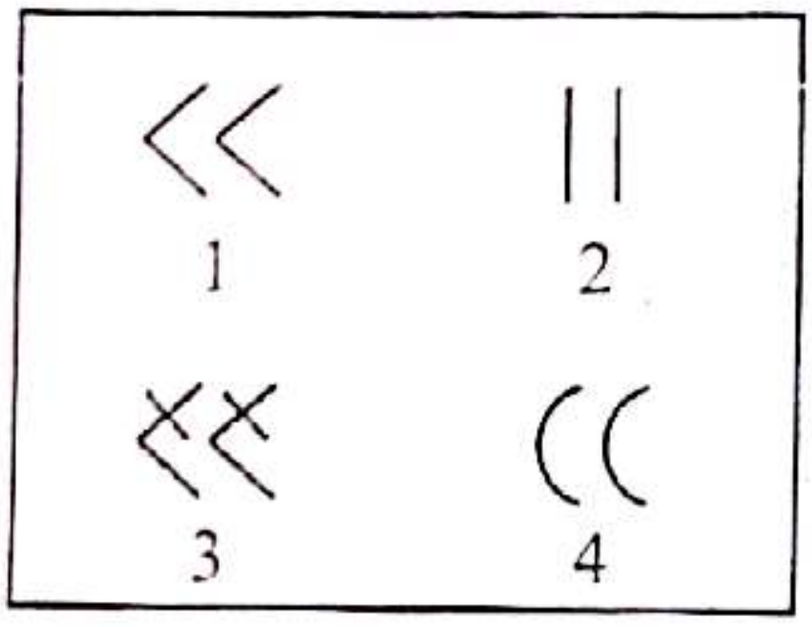
Trisomy 21: Down syndrome

Such individuals are characterized by the presence of 3 copies of chromosome 21 instead of two.

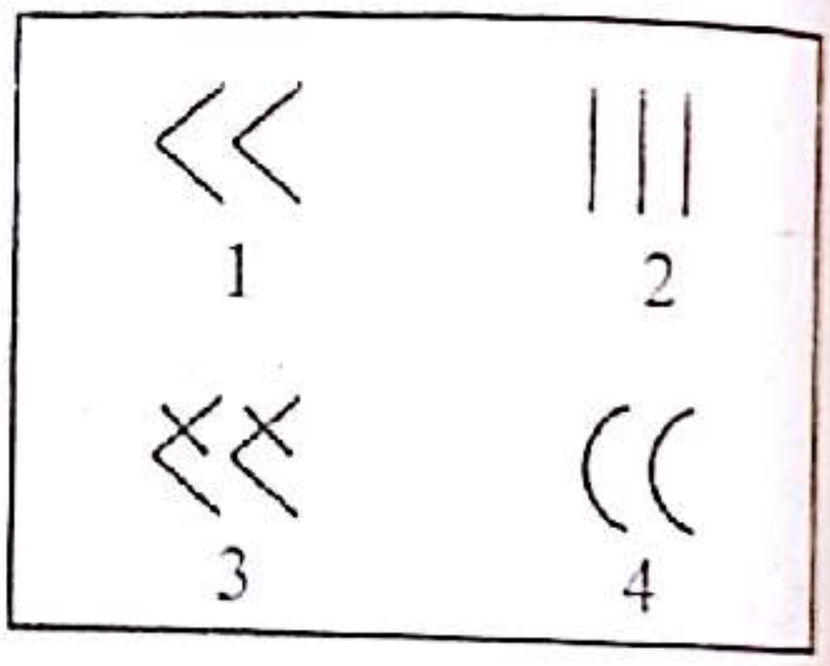
Symptoms: Oblique eyes, short hands, one palmar crease, cardiac deformities and mental retardation. Sexual maturity is usually attained.

Trisomy 21 with transcolation: One of the three copies of chromosome 21 is translocated and attached to another chromosome.

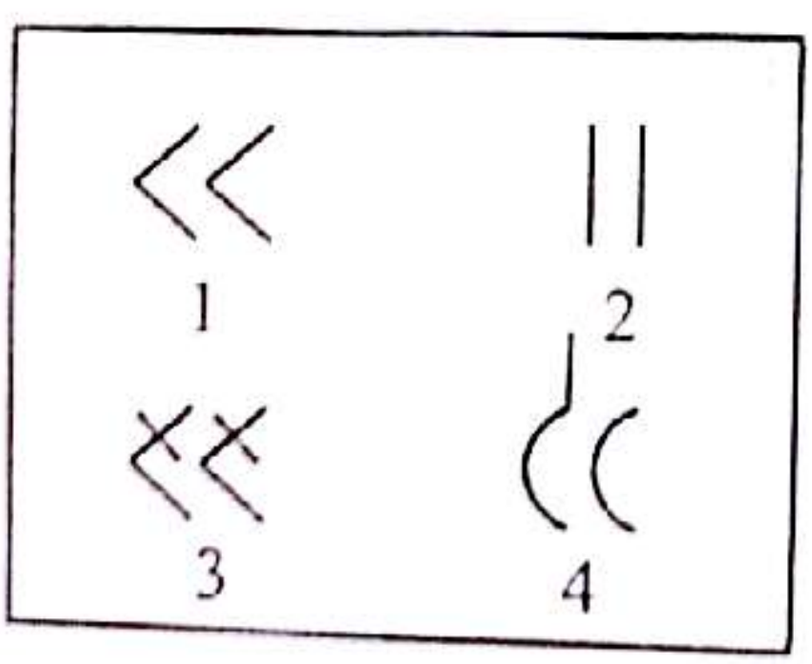
e.g. Consider these karyotypes



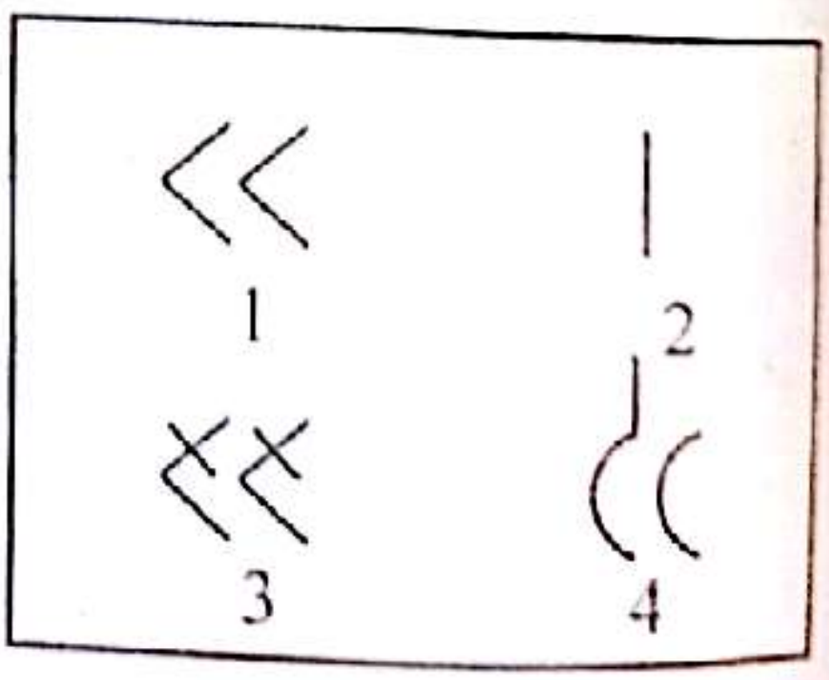
Normal Karyotype



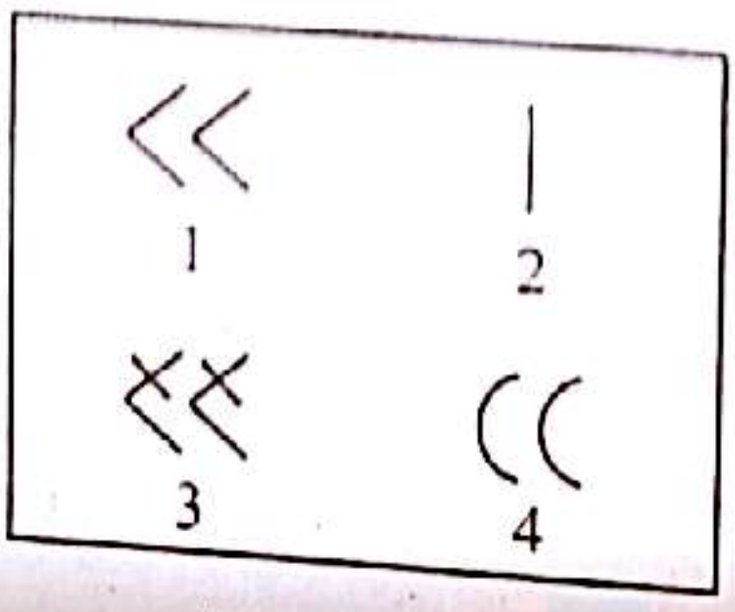
Trisomy 2



Trisomy 2 with translocation

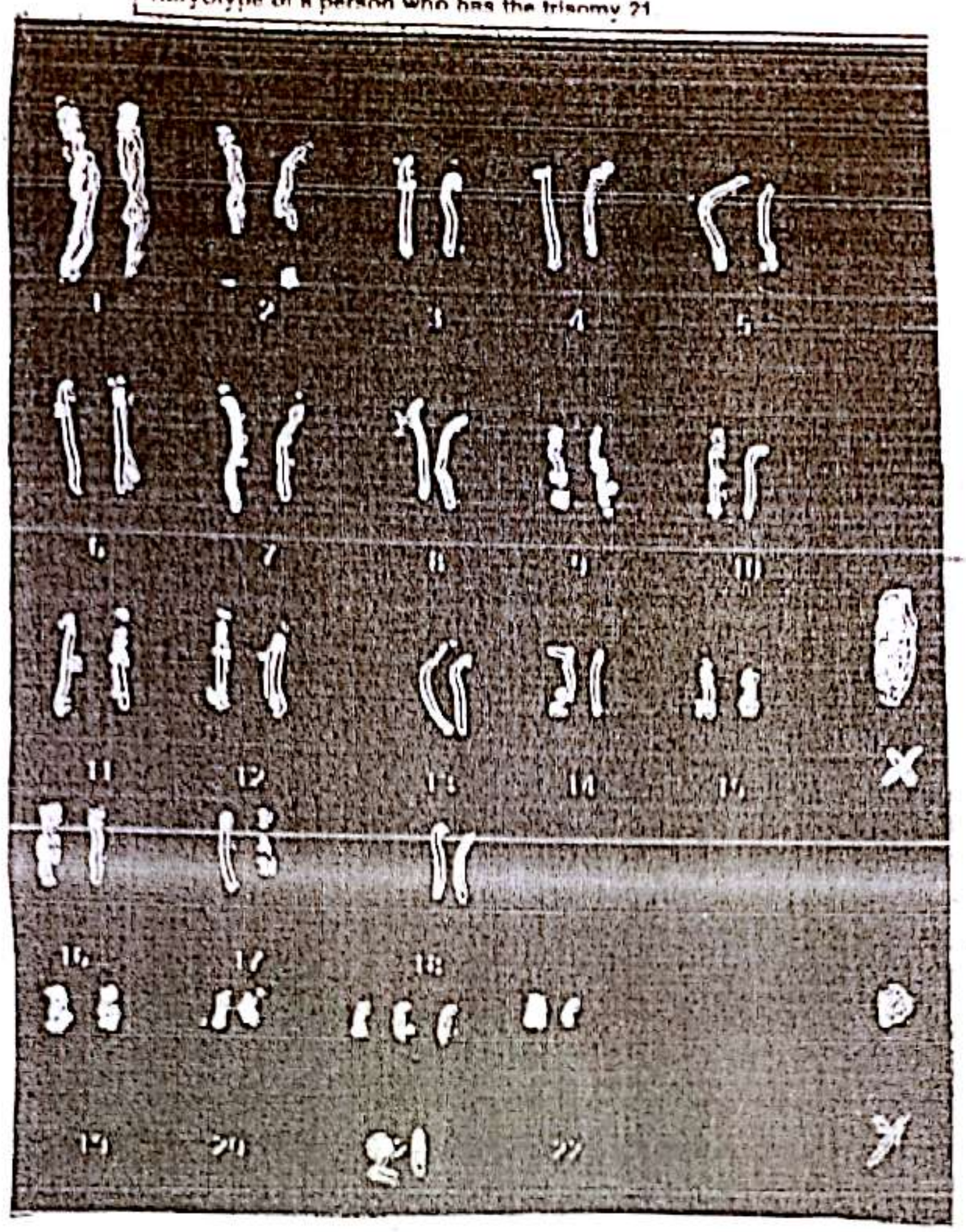


Normal Phenotype but abnormal Karyotype



Monosomy 2

Karyotype of a person who has the trisomy 21



- Sex chromosome gonosome abnormalities:

- Turner syndrome (XO)

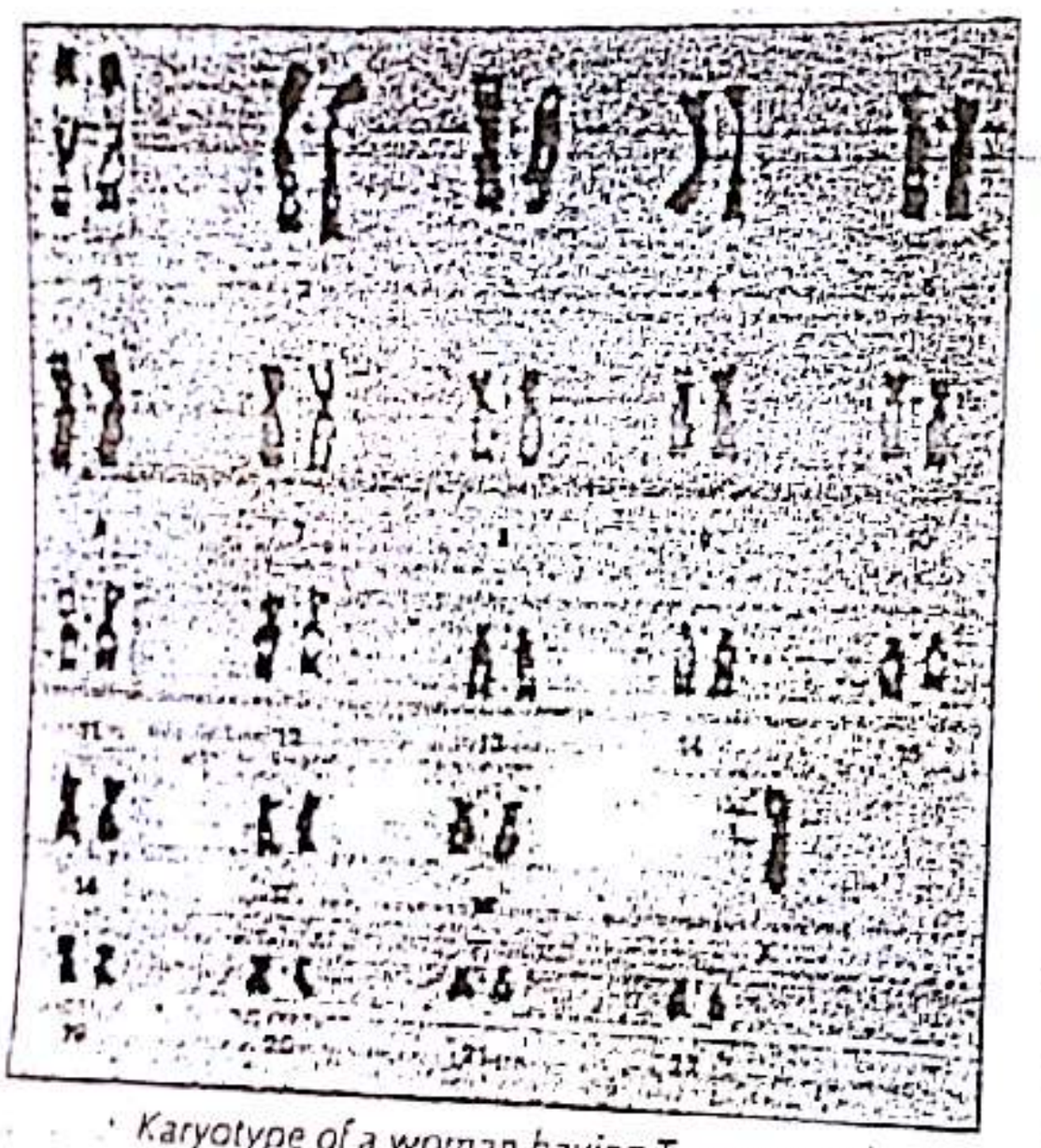
Such disease s characterized by the absence of a copy of X chromosome.
It affects only women and has the following symptoms:

- Patients are sterile due to the atrophy of the ovaries.
- They have a short stature.
- Secondary sexual characteristics don't develop.

- **Kline Felter syndrome (XXY)**

  Such disease is characterized by the presence of an extra copy of chromosome X. It affects only male and has the following symptoms:

- Patients are sterile due to the atrophy of the testes.
- They exhibit both male and female secondary sexual characteristics (abnormal development of breast).
- They are mentally retarded.

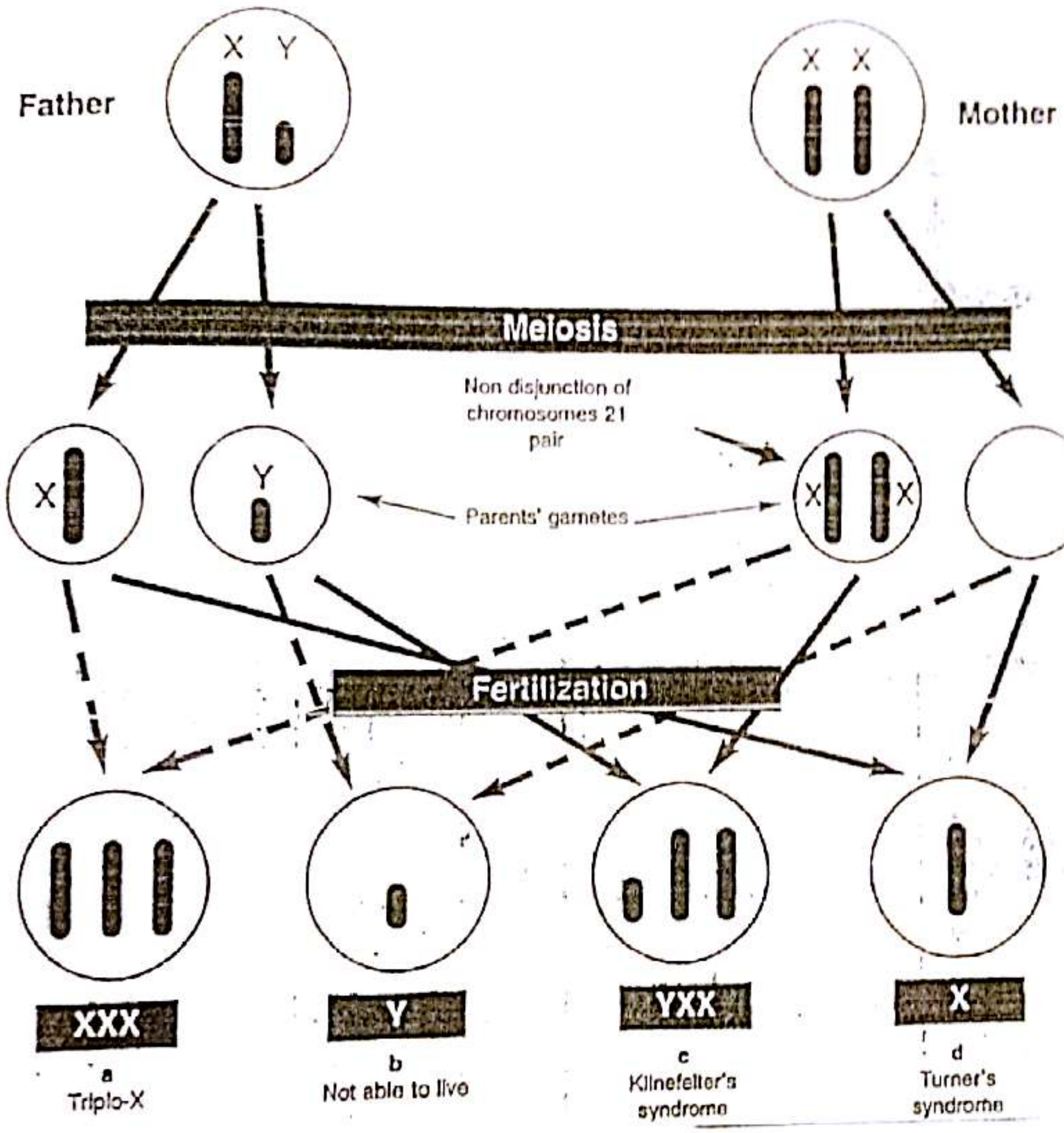


Karyotype of a woman having Turner syndrome.

Karyotype of a male having Klinefelter syndrome

Abnormalities affecting the structure of chromosome

The cri-du-chat disease (cat cry syndrome) causes severe mental retardation and larynx malformation so that the baby emits sounds like a cat's mewing. It is due to an abnormality in one of the copies of human chromosome five.

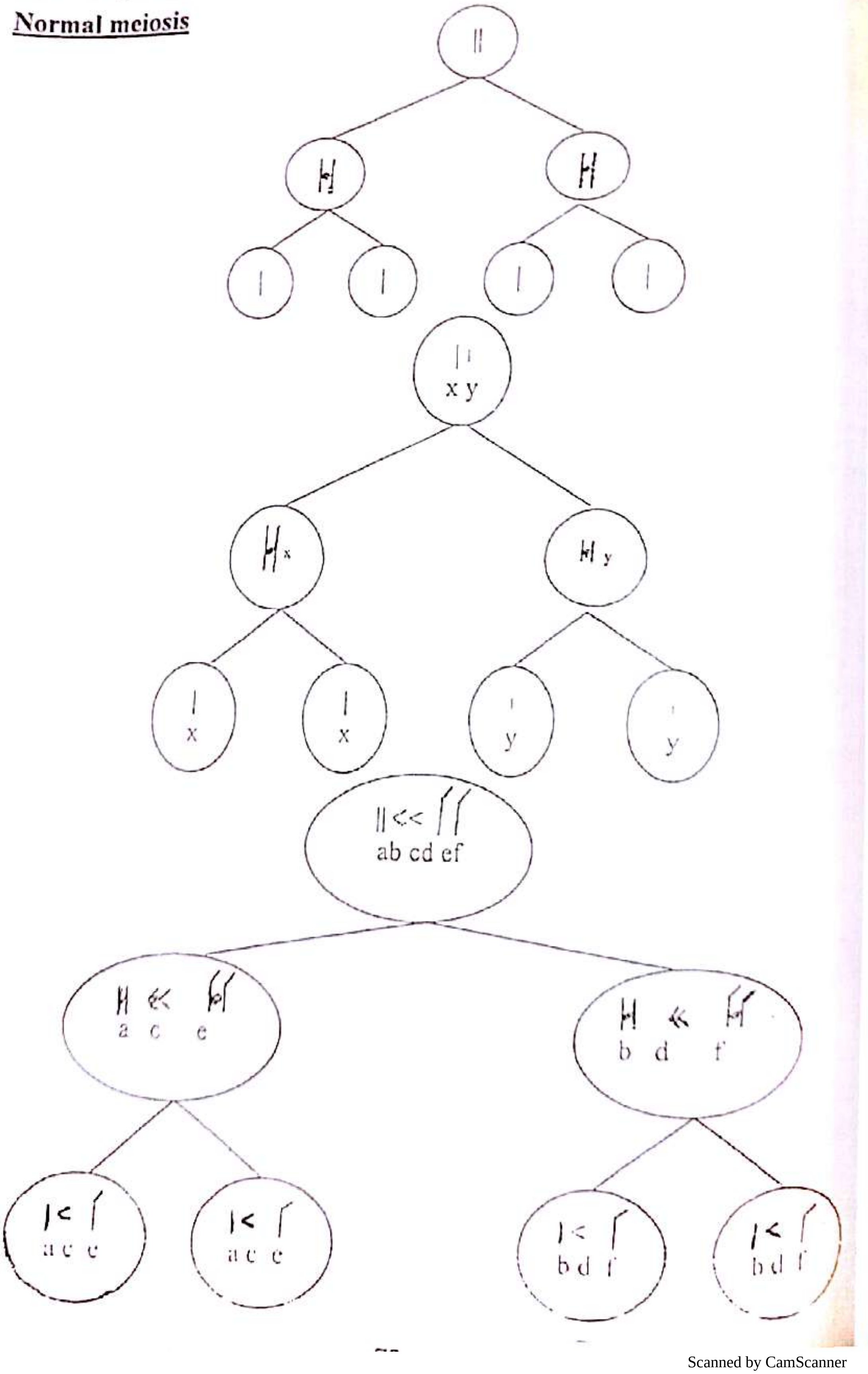


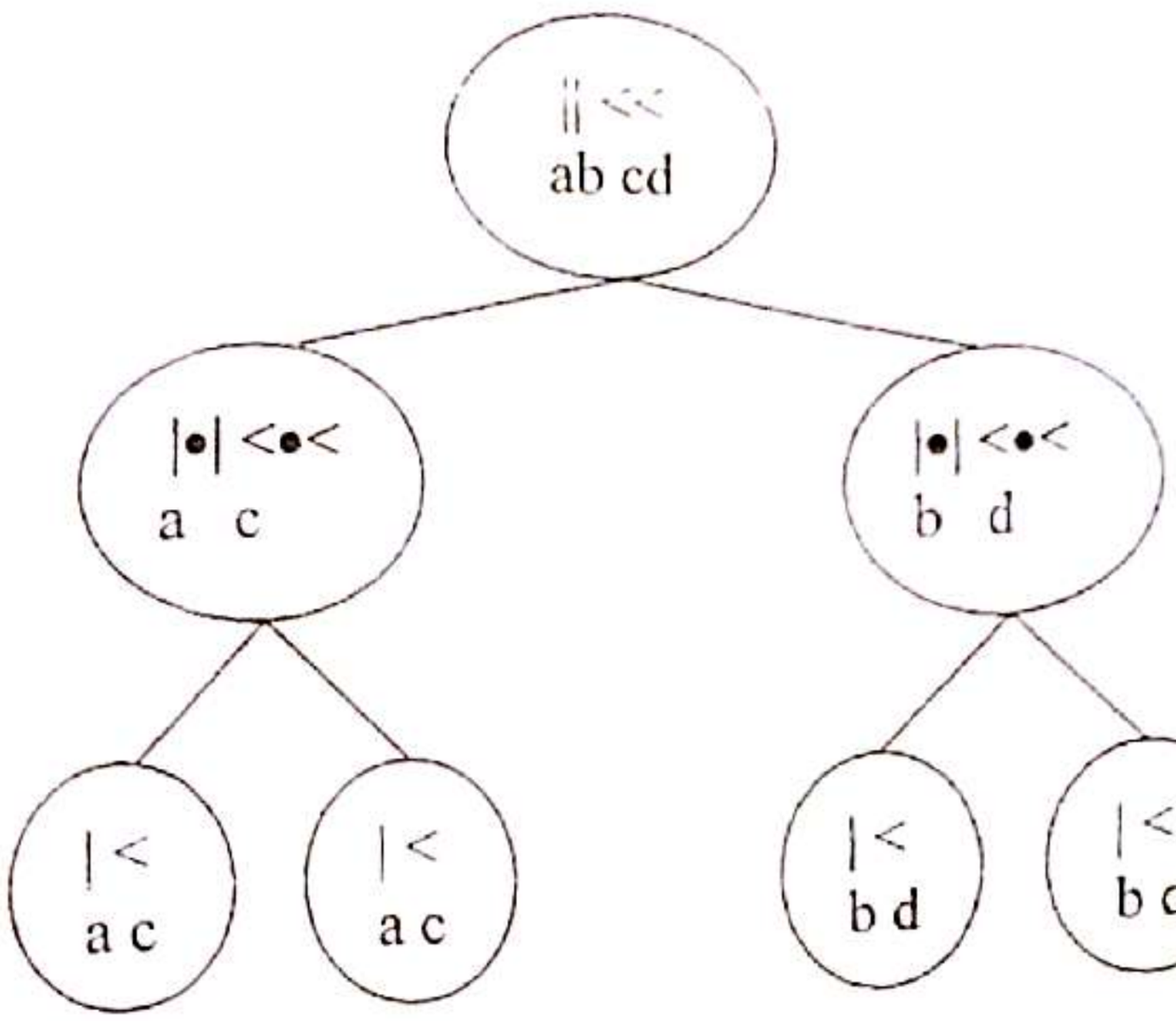
Causes of abnormalities in chromosome number

Abnormalities in chromosome number are usually due to errors in meiosis during gametogenesis.

A non-disjunction of the homologous chromosomes leads to abnormal gametes.

Normal meiosis





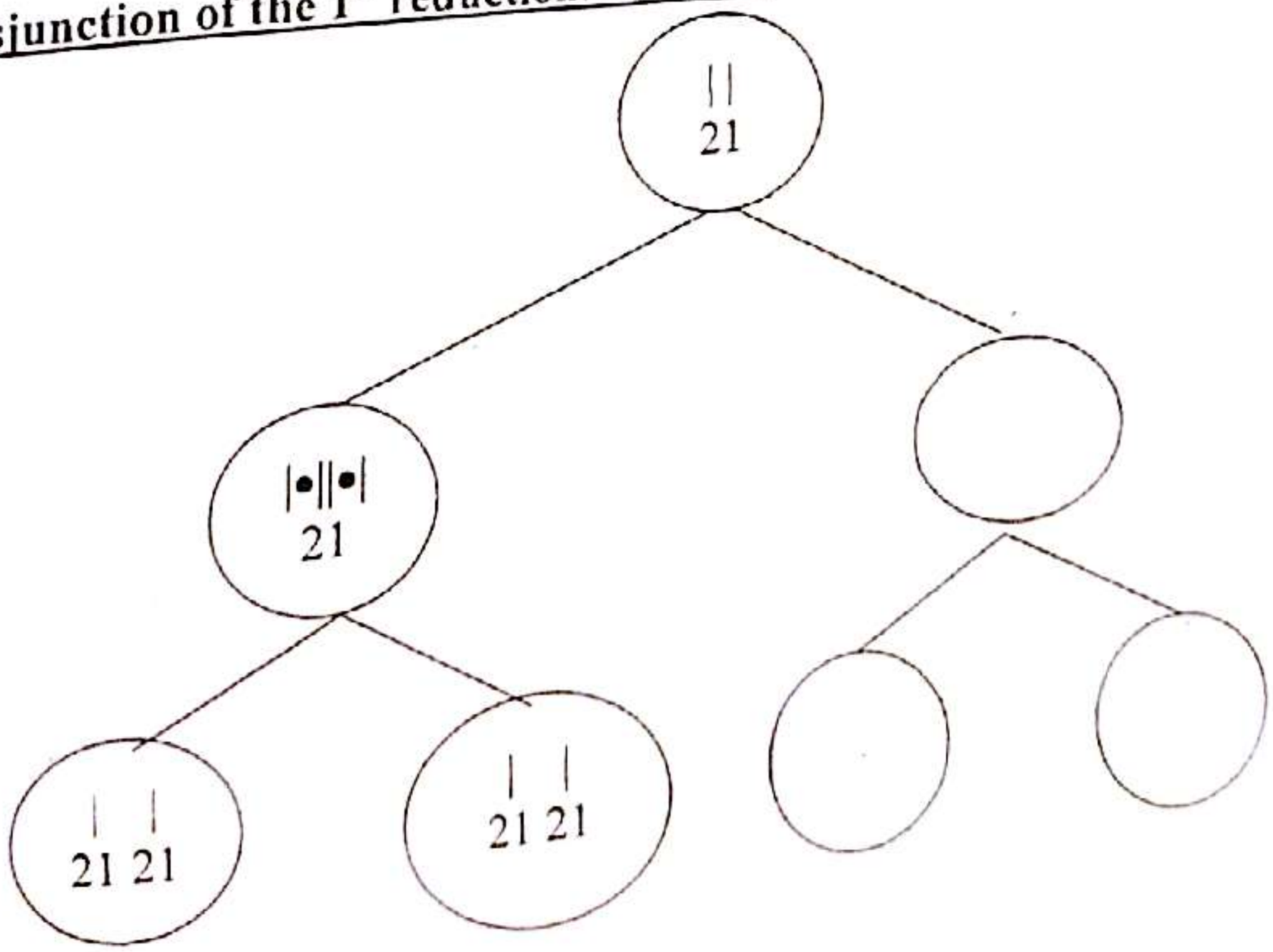
There are 8 possibilities of chromosomic formula according to the formula 2^n :

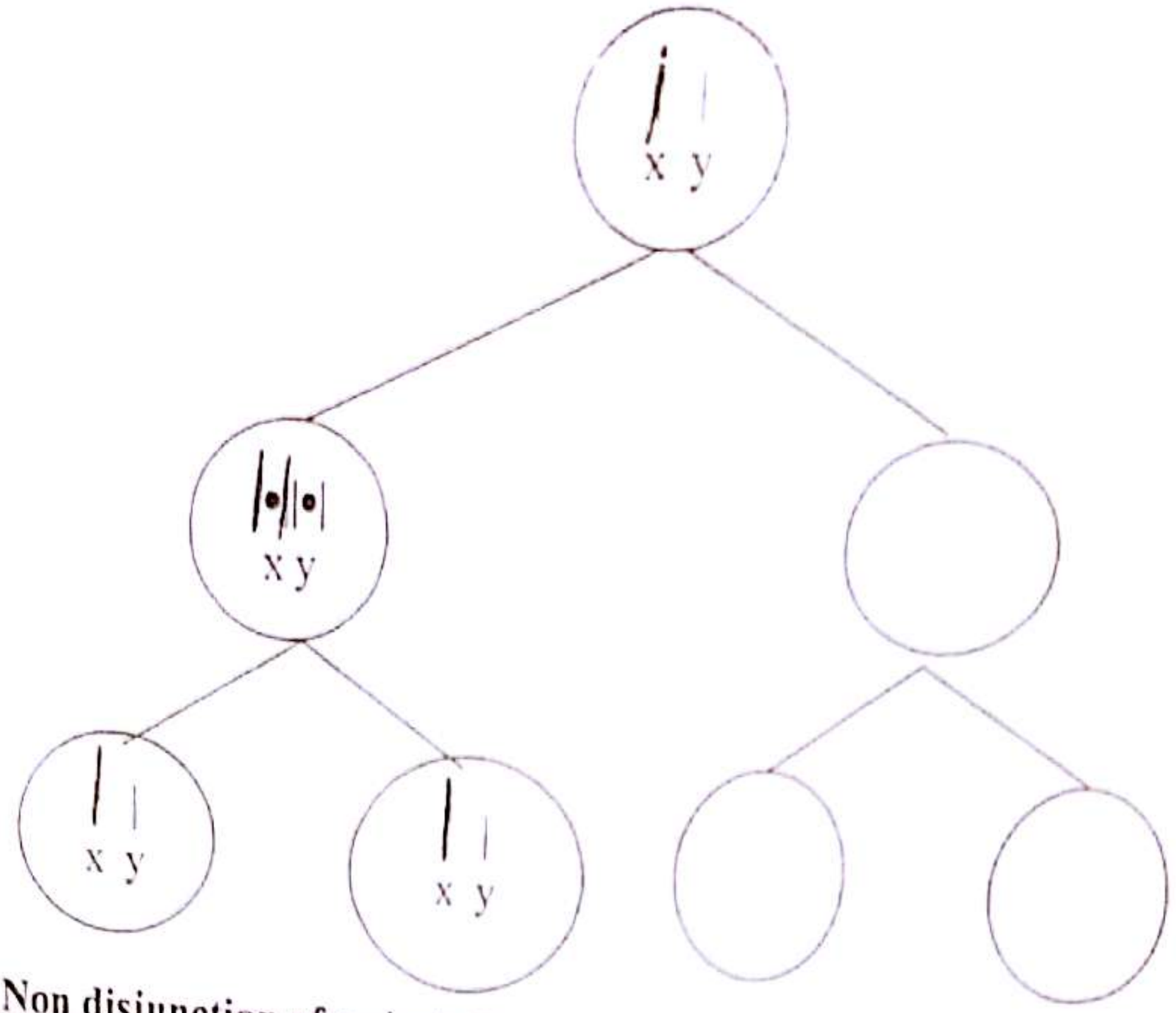
$2n = 6 \Rightarrow n = 3$

(a, c, c) , (a, c, f) , (a, d, e) , (a, d , f)

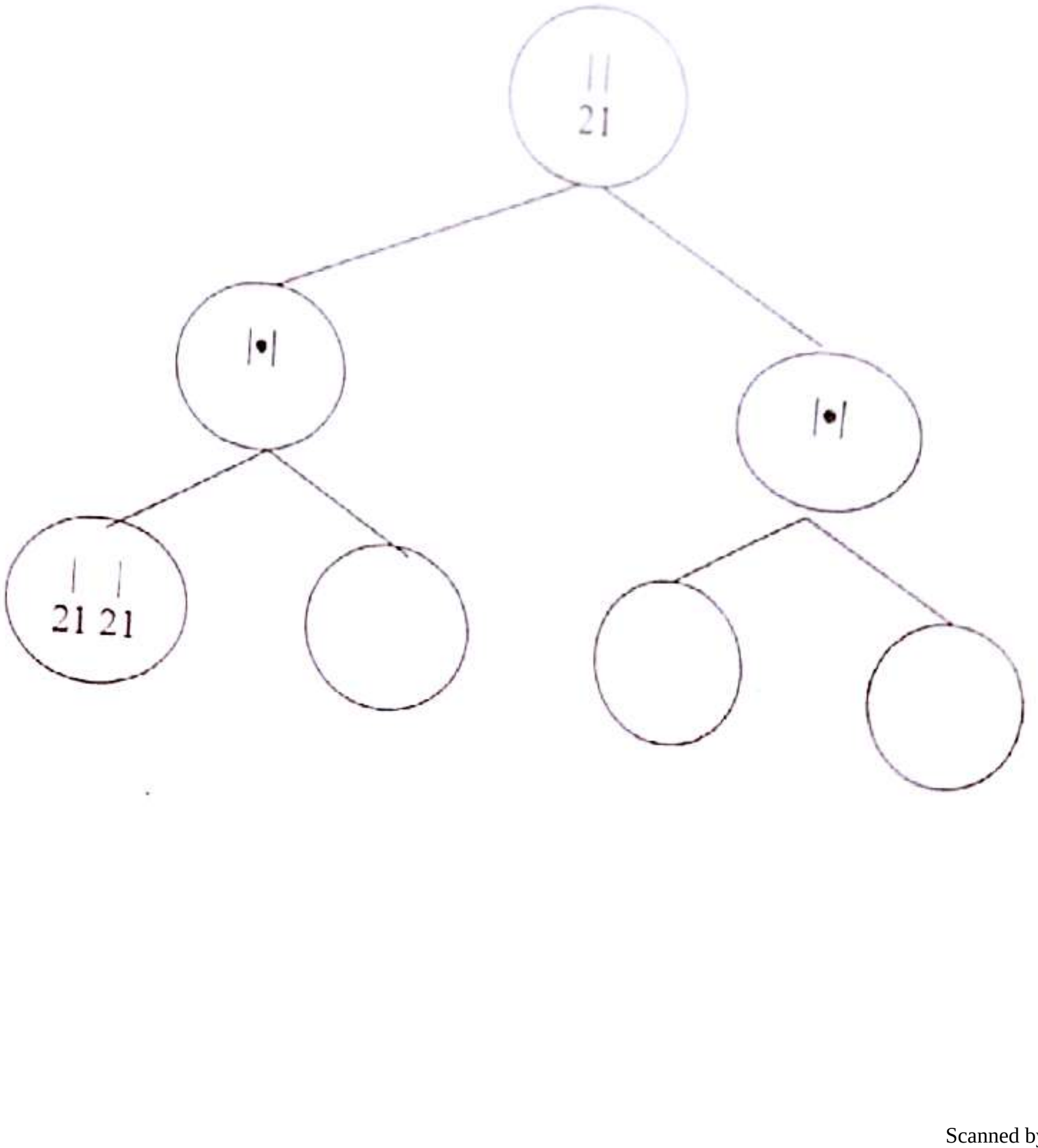
(b, c, e) , (b, c, f) , (b, d, e) , (b, d, f)

Non-disjunction of the 1st reductional division





Non disjunction of meiosis II



Document 5 : Prenatal diagnosis

Methods used in prenatal diagnosis

There are three methods:

1st method: amniocentesis: This is done by taking a sample from amniotic fluid that contain fetal cells. This method is done starting from 16th week of pregnancy.

2nd method : Chorionic villus biopsy: This is done by taking a sample of the chorionic cells that is from fetal membrane. This method is done starting from the 8th week of pregnancy.

3rd method: Fetal blood: This is done by taking a sample of blood from the umbilical cord of the fetus. This method is done starting from the 20th week of pregnancy.

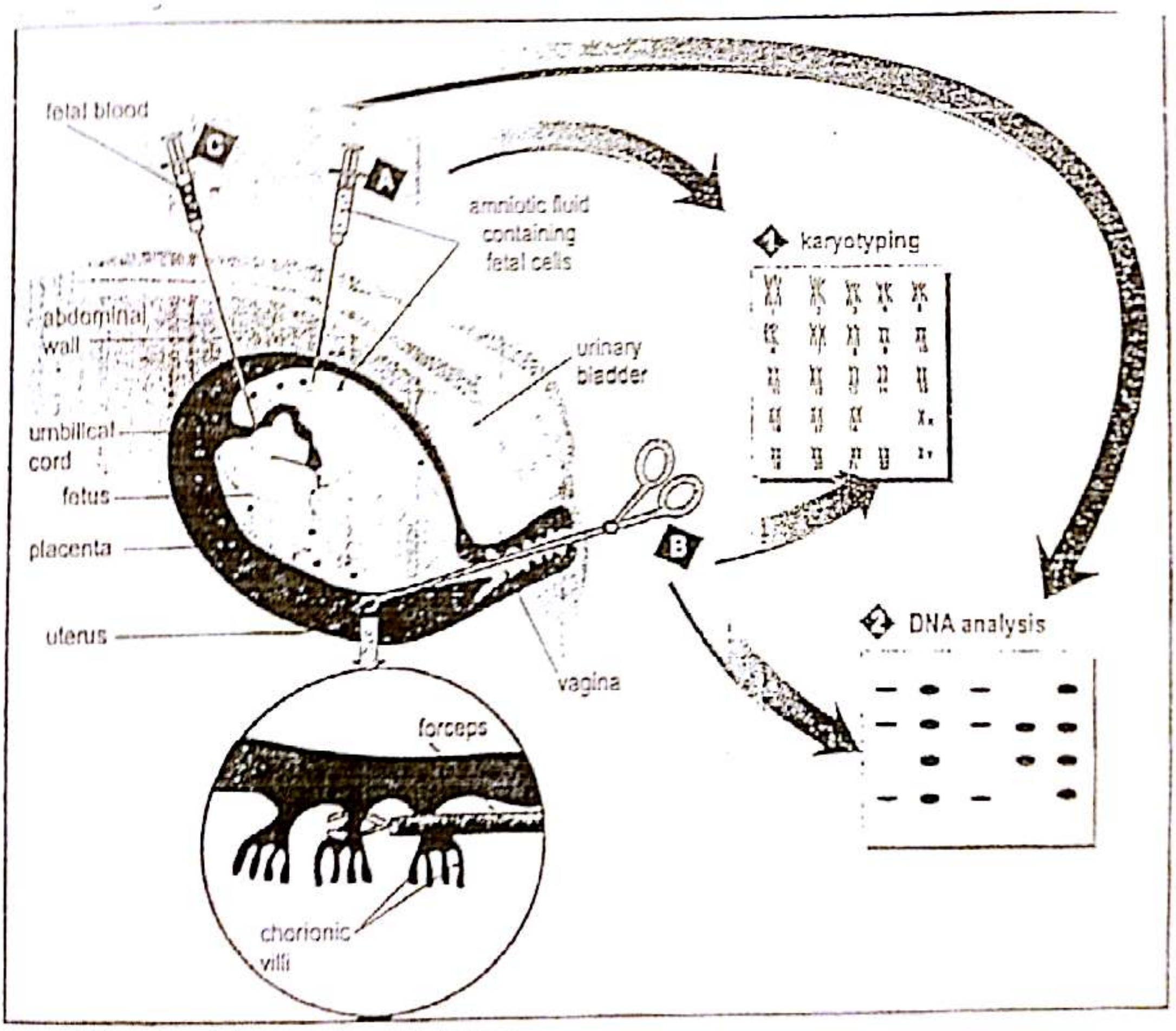


Illustration of the steps of prenatal diagnosis

A = amniocentesis

B = chorionic villus biopsy

C = Fetal blood