Chapter 1: Basic mechanisms of reproduction

organ	Function
Ovaries (female gonads)	- Production of oocytes - Secretion of the female sexual hormones : estrogen and progesterone in the BLOOD.
Oviduct or Fallopian tube	- Reception of the released oocytes - Site of fertilization
Uterus	- Site of implantation - Site of the development of the embryo
Cervix	Possesses cervical glands that secrete cervical mucus that prevents infection
Vagina	Organ of copulation

Table showing the different organs of the FEMALE reproductive system and the functions of each organ

organ	Function
Testes (male gonads)	- Production of sperm cells - Secretion of the male sexual hormone : testosterone in the BLOOD.
Epididymis	- Storage of the sperm cells - Where sperm cells acquire their motility and maturity
Vas deferens (spermiduct)	- Storage and conduction of sperm cells
Accessory glands	- Secrete the seminal fluid which provides the sperm cells with their nutritive needed substances The accessory glands are **Seminal vesicle, Prostate & Bulbo-urethral gland (or cowper's gland)**
Urethra (urogenital tube)	- Conduction of sperms - Conduction of urine
Penis	Organ of copulation
Urogenital opening	Opening where urine and semen are ejected at different times

Table showing the different organs of the MALE reproductive system and the functions of each organ

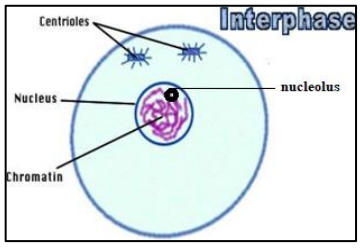
Cell cycle of a somatic cell

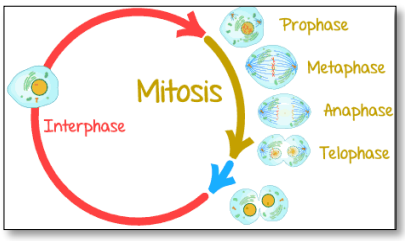
The cell cycle is made of 2 phases

- Interphase
- cell division (mitosis).

Interphase:

- is the period between two cell divisions or mitosis.
- It is the period of growth, where chromosomes are not visible, long, thin filamentous but can duplicate.
  - Long and thin chromosomes are called chromatin material





Mitosis

- is the cell division of somatic or body cells.
- Each division includes 4 phases (prophase, metaphase, anaphase, telophase)
- It produces two daughter cells genetically identical to the mother cell
- The daughter cells and the mother cell have the same number of chromosomes.

Importance of mitosis

- Development of embryos
- Development and growth of our bodies
- Tissue repair
- Cell renewal

Phases of mitosis:

Mitosis can be divided into four stages: Prophase- metaphase- anaphase- telophase (Mitosis means the division of nucleus)

a- Prophase:

- Chromatin condenses and becomes chromosomes (Each chromosome is made of 2 chromatids attached at the centromere).
- Centrosomes duplicate & transform into 2 asters.
- Nuclear membrane and the nucleolus disappear
- Spindle fibers (achromatic spindle) form between the 2 asters that start to move apart.

b- Metaphase:

- Chromosomes are aligned at the "equator"forming the "equatorial plate".
- Asters move to opposite poles.

c- Anaphase:

- The 2 sister chromatids of each chromosome separate after the division of the centromeres.
- "Polar Ascension": Chromatids migrate toward opposite poles of the cell.

d- Telophase:

- Chromosomes uncoil or decondense to chromatin.
- Nuclear membrane reappears.
- Spindle fibers disappear.
- Asters change back to centrosome.
- The cell divides into 2 daughter cells:There is constriction of the cell membrane and division of the cytoplasm. Each daughter cell contains "2n" chromosomes as in the mother cell, but each chromosome is made of 1 chromatid.

Then, the 2 daughter cells enter interphase to duplicate chromatin, and the cycle repeats.

- At the beginning of mitosis, the cell is made of 2n = 4 chromosomes. Each chromosome is made of 2 sister chromatids.
- By the end of Mitosis, each cell contains 2n=4 chromosomes same number of mother's cell chromosomes, but each chromosome is made of 1 sister chromatid.

➨ Karyotype: process of counting and arranging the chromosomes of a certain species depending on certain criteria. (photo of chromosomes during metaphase).

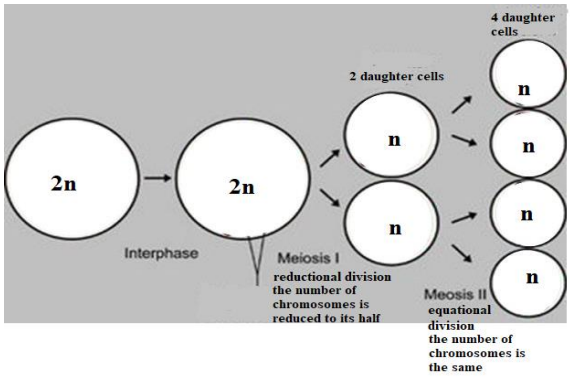
➨ Criteria to classify chromosomes:

Decreasing order size of chromosomes
Position of centromere
Distribution of dark and light bands

These chromosomes are arranged into pairs. Each pair represents homologous chromosomes.
Homologous chromosomes carry the same

Meiosis definition

- Cellular division during which a diploid germ cell gives rise to 4 haploid gametes
- Takes place in the ovaries and testes.
- Includes 2 successive divisions.



Before meiosis: Interphase occurs during which duplication of DNA occurs: each chromosome of 1 chromatid becomes of 2 chromatids.

No interphase between meiosis 1 and 2.

I- Meiosis I or reductional division

Prophase 1:

- Nuclear membrane disappears.
- Centrosome changes into asters that migrate to opposite poles.
- Spindle fibers appear between the 2 asters.
- Chromatin condenses into chromosomes.
- Homologous chromosomes pair up to form tetrads. Crossing over occurs.

2- Metaphase 1:

Homologous chromosomes pair & line up at the equator, forming the "equatorial plate".

3- Anaphase 1:

- "Polar Ascension": **Homologous chromosomes** separate & each chromosome migrates toward opposite pole.

4- Telophase 1:

- Two daughter cells are formed. Each cell contains (1n) chromosomes i.e. half the number of chromosomes of the mother cell.
- Each chromosome is still made up of 2 sister chromatids.

II. Meiosis II or equational division:

5- Prophase 2: Same events as in Meiosis I, but each cell contains (1n) chromosomes.

6- Metaphase 2: Same events as in Meiosis I, but each cell contains (1n) chromosomes.

7- Anaphase 2: Sister chromatids separate & migrate toward opposite poles.

8- Telophase 2: 4 daughter cells are formed: Each cell contains "n" chromosomes, and each chromosome is made of 1 chromatid

Role of meiosis

- Formation of haploid gametes.
- The gametes are genetically different and this increases diversity at the level of phenotypes in the species.
- Reduces the number of chromosomes to its half.

Spermatogenesis

Important notes:

Semen:

The semen is a white opalescent fluid.

Semen= seminal fluid + sperm cells

Composition of the seminal fluid

Fructose and other nutrients

Role of the seminal fluid

Ensure the survival and the motility of spermatozoa

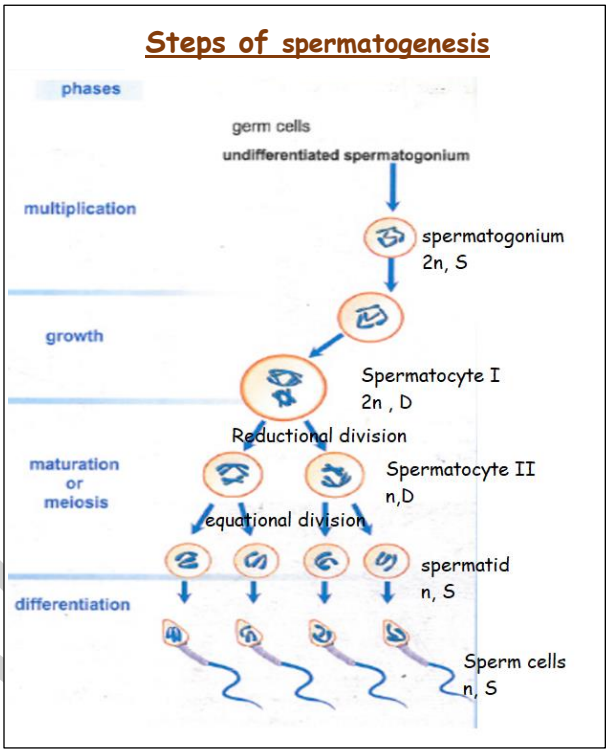
Don't forget: sperms are produced by the seminiferous tubules of the testes.

Leydig cells: are found between the seminiferous tubules.

They produce the male sexual hormone, the testosterone IN THE BLOOD

Sertoli cells are found IN THE SEMINIFEROUS TUBULES between the germ cells. They provide nutrition to the germ cells

Steps of spermatogenesis

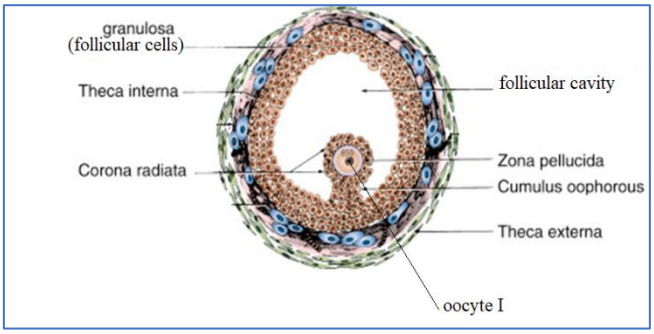


Oogenesis

Definition of oogenesis

Oogenesis is a process that leads to the formation of haploid female gametes from diploid germ cells. It is discontinuous; starts during embryonic life, stops at birth, then resumes at puberty and finally stops at menopause. This process does NOT end in the ovary.

Schematic representation of a graafian follicle



Folliculogenesis:

At birth, the female has primordial follicles in her ovaries.

4 months before the beginning of the cycle:

- The primary follicle transforms into secondary follicles then into tertiary (cavitary) follicles which has a diameter of 5 mm.

Phases of the female menstrual cycle:

Follicular phase (day1- 13): the tertiary follicle transforms into graafian (20mm).

Ovulation: (day 14): the follicle ruptures and the female gamete is released in the fallopian tube.

Luteal phase: (day 15- 28): the ruptured follicle transforms into yellow body (corpus luteum) and then degenerates at the end of the cycle to white body (corpus albicans).

Phases of Oogenesis

1- Multiplication:

- Takes place during embryonic life
- Oogonia undergoes mitosis.
- Oogonia (2n, s)

2- Growth

- Takes places during embryonic life
- Oogonium transforms into oocyte I (2n, d).

3- Maturation

- Starts in the embryonic life.
- The oocyte I (2n, d) starts meiosis, but stays blocked at prophase I.
- First stop of oogenesis occurs at birth.
- From birth till puberty, the oocyte I stays blocked at prophase I.
- At puberty, few hours before ovulation, oocyte I blocked at Prophase I resumes meiosis I (reductional division) and gives rise to oocyte II (n, d) and the first polar body (n, d).
- **This polar body** serves to eliminate one half of the diploid chromosome set produced by meiotic division in the oocyte I leaving behind a haploid cell (oocyte II).
- Oocyte II starts meiosis II (equational division) but stays blocked at metaphase II.
- Now the second arrest occurs, waiting for fertilization.
- Oocyte II is released to the fallopian tube.
- If fertilization does not occur, oocyte II stays 24 hours before it dies.
- If fertilization occurs, the oocyte II resumes meiosis II.
- As a result, ootid (n, s) is formed and a second polar body is released.

4- Differentiation: The fertilized ovum fertilized by the sperm cell gives rise to a zygote.

Oogenesis versus

During embryonic life:

- the female germ cells/ oogonia divide my mitosis to give a total number of 700 million oogonia. (multiplication phase)
- oogonia gives rise to the diploid primary oocyte (growth phase)
- each oocyte is surrounded by few follicular cells to form primordial follicle.
- During fetal life, a large number of primordial follicles degenerate. This is called follicular atresia.
- In the other primordial follicles, oocytes I undergo the first meiotic division but stay all blocked at prophase I until puberty.

From birth till puberty

- Follicular atresia continues during childhood.
- At puberty, the ovary will contain 400 000 primordial follicles.

At puberty

- Each month, 10 follicles will unblock. Usually one follicle will mature, while the others will degenerate.
- 4 months before the beginning of the cycle, the primary follicle develops into secondary and then tertiary follicle. During this time, oocyte I is still blocked at prophase I.

Female cycle:

- During the follicular phase, the tertiary follicle develops into graafian follicle.
- In the graafian follicle, a few hours before ovulation, the oocyte I will complete the first meiotic division and gives oocyte II and the first polar body.
- Oocyte II begins the second meiotic division but remains blocked at metaphase II.
- This division will be completed only if fertilization occurs.

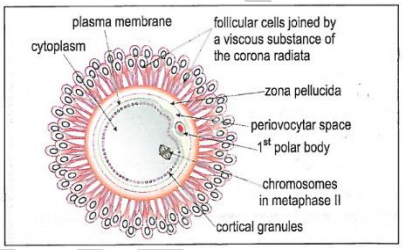
if no fertilization occurs

- The oocyte II stays alive for 24 hours then dies.
- The ruptured follicle transforms into corpus luteum which degenerates at the end of the cycle.

If fertilization occurs

- Oocyte II resumes meiosis II and gives ootid and the second polar body.
- A zygote is produced.
- The corpus luteum stays 3 months.

Document 6: Fertilization



1- Schematic representation of the oocyte II

2- Capacitation definition

Biochemical changes in the sperm that make them able to fertilize the oocyte.

Pay attention: oocyte lives only for 24 hours.

3- After fertilization

- A zygote is formed
- This zygote undergoes mitosis.

4- Role of fertilization

- Fertilization restores diploidy.

5- Life cycle in humans (doc.d)

In the human life cycle, there are two alternating phases

- Diploid phase which starts with fertilization
- Haploid phase which follows meiosis.

Chapter 15: Regulation of female sexual cycle

During the follicular phase (1-13 days):

FSH produced by the pituitary gland stimulates the development of the follicles. The follicles mature and release moderate amount of estrogen which stimulates the proliferation of the superficial layer of the endometrium and exerts a negative feedback on the hypothalamo-pituitary axis resulting in a decrease in FSH and LH.

At day 12, the amount of estrogen reaches a peak exerting a positive feedback on the hypothalamopituitary axis resulting in an increase in FSH and LH.

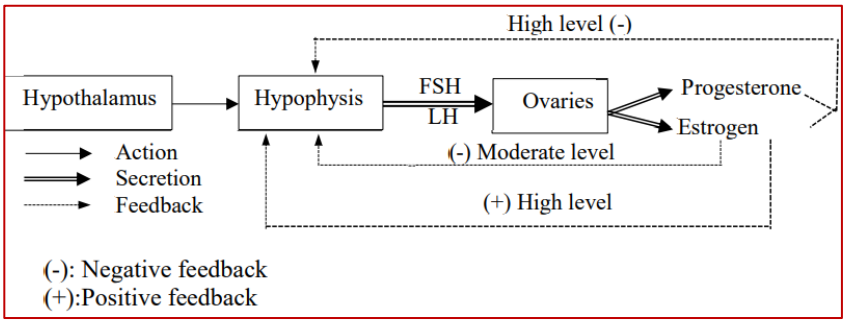
At day 13, a peak of LH triggers ovulation on day 14.

During the luteal phase (14-26 days):

Under the action of LH, the ruptured follicle transforms into corpus luteum, which secretes estrogen and progesterone. These hormones stimulates a further development and thickening of the endometrium and formation of the uterine lace and exert a negative feedback on the hypothalamopituitary axis resulting in a decrease in FSH and LH.

End of luteal phase (26-28 days):

if fertilization doesn't take place, corpus luteum transforms into a non-functional structure called corpus albicans. Now the level of estrogen and progesterone decreases. This leads to the sloughing off of the superficial layer of the endometrium called menstruation.



Chapter 2

a. Gene: fragment of DNA that carries a hereditary trait on chromosome. Ex. Blood group.
b. Alleles: different versions of a gene. Ex. A, B, and O for the blood group gene.
c. Genotype: set of genes: AA or A//A AO or A//O
d. Homozygote (pure race): organism having two identical alleles for the same gene AA, BB, OO.
e. Heterozygote (hybrid): organism having different alleles of the same gene: AB, AO, BO
f. Dominant allele: allele that is expressed in homozygote and heterozygote. It is represented by a capital letter. Ex. Allele A or allele B.
g. Recessive allele: allele that is only expressed in homozygote. It is represented by a small letter. Ex. Allele r/ allele O
h. Codominant alleles: alleles that are both expressed in the phenotype ex. AB
i. Incompletely dominant alleles: both alleles are not expressed in the phenotype (of the hybrid offspring). A new or intermediate phenotype appears in the offspring. Ex. Pure red flower crossed with pure white flower= pink (genotype: RW)
j. Phenotype: expression of the genotype on the individual. It is represented by [A] or word ex. White.
k. True breeding line: a group of genetically identical homozygous individuals that, when intercrossed, produce only offspring that are identical to their parents.
l. Hybridization: crossing two pure breeding organisms that differ in one or more traits to obtain a **hybrid.**

Table summarizing the phenotypic results of F1, F2, test cross and lethality in a monohybrid cross.

Monohybrid cross case	F1 result	F2 results	Test cross results
Dominance A>a	1 [A]	$\frac{3}{4}$ [A], $\frac{1}{4}$ [a]	1 [A] if the parent with dominant phenotype is homozygote $\frac{1}{2}$ [A] and $\frac{1}{2}$ [a] if the parent with dominant phenotype is heterozygote.
Codominance or incomplete dominance A=B	1 [AB]	$\frac{1}{4}$ [A], $\frac{1}{2}$ [AB] and $\frac{1}{4}$ [B]	No test cross in these cases

CHAPTER 3: GENETIC VARIATION AND POLYMORPHISM

1- Definition of mutation: Sudden and unpredictable changes that can affect the DNA molecule.

the types of point mutations: Deletion, insertion, substitution

Effect/consequence of mutation:

- Missense: if one amino acid is changed in the protein
- Silent: if nothing changed in the protein
- Nonsense: if the protein is incomplete (due to stop codon)
- Frameshift (in case of deletion and insertion mutations)

1- What is the difference between the recognition site and the cleavage site?

The recognition site is a double sequence of nucleotides having definite length (base pairs) and recognized by the restriction enzyme. However the cleavage site is a specific position of cutting in the recognition site.

2- Gel electrophoresis

1- the alleles are cleaved by the restriction enzymes.
2- The normal allele yields 2 fragments a and b while the mutant allele yields 1 fragment only c.
3- The obtained fragments are separated on an electric agarose gel.
4- The DNA fragments migration in the gel depends on:
    - Charge: the fragments of DNA migrate from the negative pole to the positive pole as they are charged negatively.
    - Molecular weight: large fragments migrate slower than smaller ones.
5- Add a dye to stain the colorless DNA bands. This dye fluoresces under UV light.
   The obtained bands pattern is referred to a restriction map.

7- Restriction fragment Length Polymorphism (RFLP):

- Our DNA is made of both coding and non-coding regions.
- Any mutation at the level of the coding regions usually affect the phenotype.
- The non-coding regions are repetitive and abundant sequences in the DNA and have no function in gene expression neither in phenotype. Any mutation at the level in the non-coding regions do not affect the phenotype.
- Cuttings in the whole DNA will produce for each individual unique banding patterns on the gel which is called restriction map.
- The difference in restriction maps between two individuals is called a restriction fragment length polymorphism or RFLP.
- So the aim of RFLP is to ensure the fact that individuals are different at the level of their DNA in both coding and non-coding regions.

1- FISH or Fluorescence In Situ Hybridization:
   Aim: used to determine the loci of a specific allele on a chromosome.

2- List the utilization of DNA fingerprint.

- Ensuring the uniqueness of the genome of each organism.
- Paternity testing.
- Criminal investigations.
- Dead bodies' identification.

Chapter 5: Human genetics: Documents 2 and 3

Determine the localization of a gene:

1- Autosomal (males and females are affected)
   a- Elimination of non-homologous segment of Y: Father- son
   b- Elimination of non-homologous segment of x: Father- daughter
   c- Elimination of homologous segment of X & Y: Father- son & daughter
   c- the non-homologous segment of X.
   d- Therefore, autosomal
2- Gonosomal (only males are affected)
   Start by saying, since only males are affected, therefore the disease is sex linked
   a- Elimination of non-homologous segment of Y: Father- son
   b- Therefore, it is localized on

Notes:

1- Choose the son/daughter having recessive phenotypes (=> affected if the disease is recessive and normal if the disease is dominant)

2- When they ask to write the genotype, check first if the disease is autosomal (NN, Nm or mm…) or gonosomal (X^NX^m,X^NY…)

Document 4: Chromosomal mutations

1- Types of chromosomal mutations:

- Numerical abnormalities: abnormalities that affect the whole number of chromosomes. (extra or missing chromosome) (doc.a)
- Structural abnormalities: abnormalities that affect the shape of 1 or more chromosome (translocation, missing part or extra part of segment of chromosome) (doc.c)

2- Main syndromes:

- Down syndrome: trisomy 21
- Klinefelter syndrome: trisomy XXY
- Turner syndrome: monosomy X
- Cat cry syndrome: deletion of part of chromosome 5

Document 5: prenatal diagnosis

Definition of methods of prenatal diagnosis: is a genetic technique allowing predicting and detecting the presence of genetic diseases in the fetus before birth.

Method	**Chorionic villus biopsy**	**Amniocentesis**	**Sampling of fetal blood cells**
Procedure	Extract fetal cells from the chorion membrane of the placenta	Extract fetal cells sloughed off from the fetus skin from the amniotic fluid	Withdraw blood from the umbilical cord
Pregnancy time	Starting from the 8th week of pregnancy	Starting from the 16th week of pregnancy	Starting from the 20th week of pregnancy

Immunology

1- Table showing the HLA classes characteristics:

HLA class type	**HLA class I**	**HLA class II**	**Components of complement class III**
Expressed by	All nucleated cells including immune cells	Immune cells	In the blood (plasma)
Coded by loci	Loci A, B and C	Loci DP, DQ and DR	Locus on chromosome 6

Grafts:

- Autograft: is the tissue graft between two different sites in the same body individual
- Isograft: is the tissue graft between two animals of the same lineage. (Isograft in humans: is the tissue graft between 2 identical twins)
- Allograft: is the tissue graft between two individuals of different lineage of the same species
- xenograft: is the tissue graft between two different species.

- Graft is more likely to be accepted if both individuals, the donor and the recipient, have a higher no of compatibility at the level of HLA molecules as in the autograft and isograft.

Chemical nature of blood markers: Glycoprotein (oligosaccharides attached to protein). These glycoproteins are found on RBCs and determine the blood group of the individual and constitute the antigenic determinants of the ABO system.

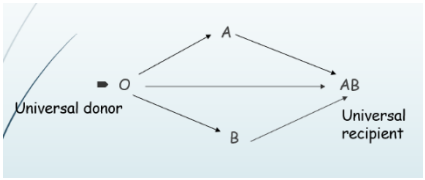
Table showing the different blood groups' phenotypes and genotypes, their agglutinogens and agglutinins

Blood group	Agglutinogen on RBC	Agglutinin (antibodies) in the plasma
AB	A and B	No agglutinins
B	B	Anti-A antibodies
A	A	Anti-B antibodies
O	NO agglutinogens	Anti-A and anti-B antibodies

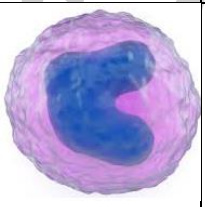
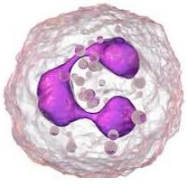
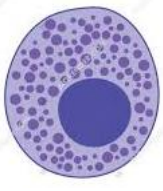
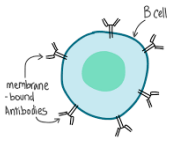
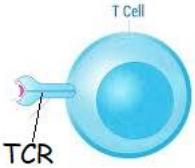
Table showing the difference between positive and negative group.

Phenotype	Allele	Genotype	Antigen on RBC	Antibodies (acquired)
Positive	Allele Rh	Rh^+Rh^+ or Rh^+Rh^-	Rh antigen	No
Negative	Inactive allele	Rh^-Rh^-	no	Anti-Rh

Blood transfusion



1- State the differences between ABO system and the rhesus system
   - ABO system: agglutinogens and agglutinins are found since birth.
   - Rhesus system: presence of Rh antigen since birth
   - Anti-Rh is produced in Rh- persons after the first contact with the antigen Rh.
   - The recipient Rh- considers antigen Rh as a foreign body and the immune system mounts an immune response producing antibodies anti-Rh.

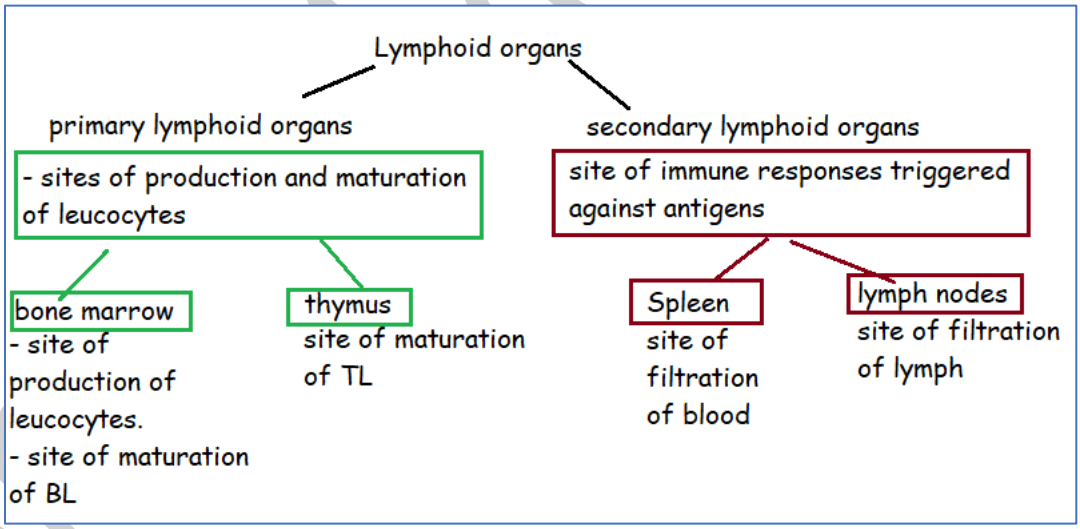
Type of leucocyte	Monocytes	Granulocytes - neutrophils - eosinophils - basophils	Mast cells	B lymphocytes	T lymphocytes	
					T4 or TH cells	T8 or Tc cells
schema						
Shape of nucleus	Horse shoe shape	Multilobed nucleus (granulated cytoplasm)	Round nucleus (cytoplasm rich in histamine vesicles)	Large round nucleus occupying most of the cytoplasm		

Antigenic receptors	No antigenic receptors			Antibodies	T.C.R called CD4	T.C.R called CD8
Function	In the tissues, monocytes transform into macrophages performing phagocytosis of bacteria	Phagocytosis	Role in allergic reactions and phagocytosis of microbes at the level of mucus in the mucosa tissue.	After their activation, they differentiate into plasmocytes that secrete antibodies neutralizing the foreign body.	"Manager" They activate B and Tc cells.	Kill the infected or modified self-cells (cancerous, allograft, virus infected cells.)
Type of immune response	Non-specific immune response			Humoral specific immune response	Activates humoral and cell-mediated immune response	Cell-mediated immune response

Different types of leucocytes/WBC

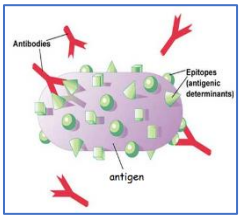
Note: B cells and plasmocytes: The B lymphocyte transforms into plasma cell or plasmocytes which has a more developed endoplasmic granulated reticulum and a larger cytoplasm. These features help the plasmocytes to secrete antibodies.

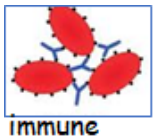
Lymphoid organs



The difference between antigen and antigenic determinant (epitope):

An antigen is the substance recognized by the immune system as being as non-self. While, antigenic determinants or epitopes are molecules (parts) of the antigen. The antigen may carry many antigenic determinants which bind to the antigen binding sites.

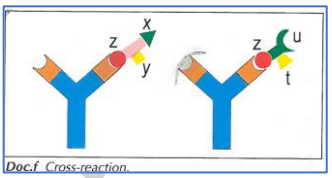




immune complex

Immune complex: is a large molecular aggregate consisting of several antibodies and antigen molecules related to each other.

Cross reaction: is the process of binding of an antibody to 2 different Antigens sharing a common epitope.



Doc.f Cross-reaction.

Differences between antibody and TCR.

	Antibody	TCR
Cell localization	On BL or free in the plasma	TL
Structure	Y shaped with 4 polypeptide chains	Rod shape with 2 polypeptide chains
Antigen recognition	Direct combination (between epitope and antigen binding site)	Double recognition between self HLA-non-self-peptide and TCR.
Number of antigen binding sites	2 binding sites	1 binding site

Double recognition by TCR (T Lymphocytes)

1- Normal cell: self-proteins are fragmented, attached to HLA class I and transported to the cell surface. This self is presented to Tc. However there is no mature Tc specific for self-peptides.
2- Cell infected by a virus: viral peptides are attached to HLA class I and transported to the surface of the cell where they are presented to Tc. These Tc recognize these viral proteins and are activated.
3- Macrophage phagocyte bacteria: The antigenic bacterial peptides are attached to HLA class II molecules. they are transported to the cell surface and are presented to T_H. These TH recognize these non-self-peptides and are activated.

Note: modified self: HLA (class I or II) attached to non-self-peptide

Non specific immune response

1- **Inflammation:** are the physiological events leading to inflammatory signs such as redness, hotness, pain
2- **phagocytosis:** is the process by which the macrophage kills/ destroys/ digests the microbe.
The macrophage does not recognize the antigen, any macrophage can bind to several types of microbes to phagocyte them. This justifies that phagocytosis is a non-specific immune response.

Induction of Specific immune response

induction of the SIR by macrophages

Macrophages phagocyte an intruder at the site of infection. The resulting peptides are attached to HLA class II and presented on the surface of the macrophage. This macrophage migrates to the closest lymph node and becomes an APC (antigen presenting cell). T_H cells circulate continuously between lymph nodes, where they inspect the HLA-peptide complexes of APCs.
Only T_H cells that are specific for the peptides presented by the APC remain attached to it. They are then activated (clonal selection) and they proliferate. The others leave the lymph node and recirculate.

Specific immune response (SIR)

- Is the body second line of defense.
- Induced in the secondary lymphoid organs closest to the infected site.
- Involves: APC, B and T lymphocytes
- It occurs in 3 phases.

1- The induction phase (antigen presentation to TH by APC)

- Macrophages digest non-self-proteins.
- Non-self-peptides are associated to HLA II and transported to the cell surface.
- The macrophage migrates to the nearest lymph node to the inflammation site.
- The macrophage becomes an APC that activates specific TH.

2- Activation phase (proliferation and differentiation of activated lymphocytes)

- An activated TH proliferates to give a clone.
- Some cells of the clone remain undifferentiated and become memory cells.
- Others differentiate into interleukin secreting cells. (interleukin is a type of cytokines)
- If TH secretes IL-2, Tc is activated (cell-mediated SIR)
- f TH secretes IL-4, BL is activated (Humoral SIR)

3- Effector phase (humoral or cell-mediated)

A- Specific humoral immune response (agents: antibodies/B lymphocytes)

- Only B cells that recognize the specific epitopes of the antigen are activated and proliferate in the presence of IL-4, giving a clone.
- Some cells of the clone remain undifferentiated and become memory cells.
- Others differentiate into plasma cells (plasmocytes) that secrete circulating antibodies.
- These antibodies neutralize soluble toxins or antigens on surface of cells by neutralizing interacting with its active site.
- Opsonization or complement cascade.

B- Specific cell-mediated immune response (agents: Tc lymphocytes)

- Only T cells that recognize the complex HLA I – antigenic peptides are activated and proliferate in the presence of IL-2, giving a clone.
- Some cells of the clone remain undifferentiated and become memory cells.
- Others differentiate into effector cytotoxic cells.
- Cell-mediated is essential in fighting intra-cellular pathogens.
- When a Tc cell adheres to the target cell, it first releases perforin that form channels in the target cell membrane. Then granzymes enter the infected cell through this channel and causes DNA degradation. (apoptosis)

Secondary immune response

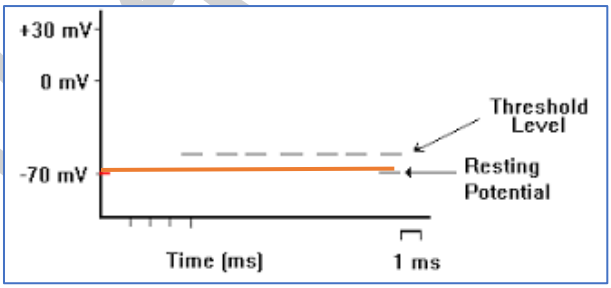
The secondary immune response is amplified, durable (long lasting) and rapid.

Immune response	NSIR	SIR	
		HUMORAL SIR	CELL-MEDIATED SIR
Effector	Gran, macro and Mast cells	BL	Tc
Membrane receptor	None	BCR, antibody	TCR
Targeted pathogen	Bacteria virus	- Soluble antigen - Cellular antigen	- Cancer cell - Allograft - Intra-cellular microbes
Mechanism	Phagocytosis	neutralization	cyto-toxicity
Passive transfer	No	serum	blood cells
Latency or delay	Few hours	15 days	15 days
Memory	No	yes	yes
Efficiency	Average	excellent	excellent

Differences between vaccination and serotherapy

Therapy	Vaccination	Serotherapy
Substance injected	Attenuated toxin or microbes	Prepared antibodies
Origin of antibodies produced	Endogenous, produced by the body	Exogenous, prepared outside the body
Type of immunity	Active	Passive
Latency or delay	1-2 weeks	Few hours
Duration of protection	Several years	2 weeks
Objective	Preventive	Curative
Immunological memory	Yes	No

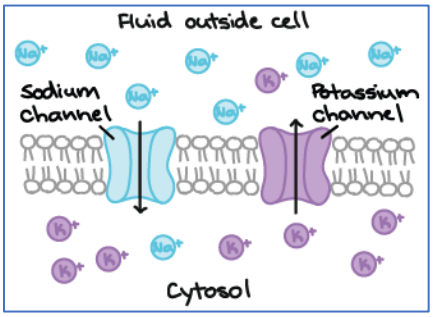
Chapter 9: Document 1: Resting potential



1- Definition of the resting potential (membrane potential): is the difference in the potential (difference in charges) between in the internal and external medium of a neuron **at rest**.

2- Origin of the resting potential:

- Unequal distribution of ions in the two sides of the plasma membrane of the neuron: Na+ and Cl- dominates in the external medium. However, K+ dominate in the internal medium.
- The cell membrane is selectively permeable to ions: it is more permeable to K+ than Na+ and Cl-. Therefore, more K+ ions move outside, down their concentration gradient (from high concentration to low concentration), through the potassium leak channels. Na+ ions diffuse inside the neuron, down their concentration gradient, but in lower amount through the sodium leak channels.
  As a result, inside the cell becomes electronegative with respect to outside. This potential difference (pd) is called resting potential and is = -70 mV.



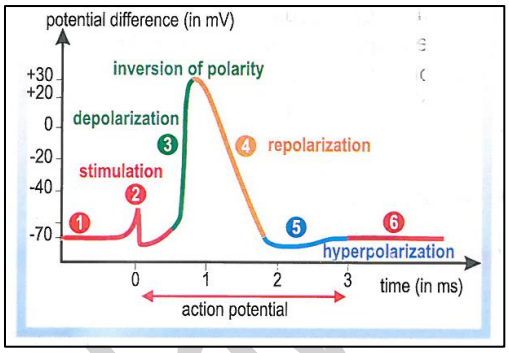
Notes: the passage of ions through the escape ion channels (or leak channels) doesn't require energy, it occurs down the concentration gradient and therefore called passive diffusion.

3- Maintenance of the resting potential (RP):

- To maintain the RP= -70 mV, Na+/K+ ATPase (also called Na+/K+ pump/ a protein) pumps K+ inside the neuron and Na+ outside the neuron, against their concentration gradient (from low to high).
- This mechanism needs energy (from ATP) and called active transport.
- In other words, when K+ leaves to the external medium passively, down the concentration gradient, the Na+ K+ pump takes it back to the internal medium. And when Na+ ions enter the neuron, the Na+ K+ pump takes it back to the outside.
- For every exit of 3Na+, there is an entry of 2K+.

Document 2: Action potential

1- Definition of action potential: A short-term change in the electrical **potential** on the surface of a nerve cell in response to an effective stimulation, and then leads to the transmission of an electrical impulse (nerve impulse) that travels across the cell membrane. (amplitude = 100 mV: from -70 to +30mV)



2- How an action potential is created?

An effective stimulation causes a modification in the membrane potential of the cell that corresponds to an inversion in its charges: the internal medium becomes + and the external becomes -. This inversion in charges is called depolarization. When the membrane potential reaches -55mV, an action potential appears of amplitude 100 mV. (-70 mV to + 30 mV)

3- Phases of action potential

3: Depolarization: the internal medium of the neuron becomes + due to the massive inflow of Na+ through the Na+ voltage dependent channels.

4: Repolarization: gradual closure of Na+ voltage dependent channels and massive opening of K+ voltage dependent channels. This leads to the massive outflow of K+.

5: hyperpolarization: the internal medium of the nerve fiber becomes highly negative due to excessive leakage of K+ ions to the external medium (due to the delay in the closure of K+ voltage dependent channels).

Notes:

- Stimulation: physical or chemical change in the external environment of a cell.
- Excitation: is the maximal response of the cell to the stimulation. This response is an action potential
- Threshold intensity: is the minimum intensity that creates the first response (first action potential)..

Document 3: Nerve impulse and action potential

A- Characteristics of nerve impulse in a NERVE FIBER.

3- The AP doesn't appear unless the threshold intensity is reached.
4- The AP propagates
5- Starting from the threshold the AP have the same amplitude.
6- The AP keeps the same amplitude no matter how much is the covered distance (without any decrease).

Notes:

1-The law applied by the nerve fiber is called **the law of all or none.**

Definition of **law of all or none:** for an intensity below threshold, the nerve fiber does not respond; but starting from the threshold intensity, the nerve fiber responds by APs having the same maximum and constant amplitude.

2- type of modulation/coding in a nerve fiber?

the type of coding modulation in a nerve fiber is the frequency.

B- Characteristics of the nerve impulse in a nerve.

the nerve is a bundle of nerve fibers. In one nerve, the nerve fibers can differ by their diameter, and myelination.

1- No recordings are obtained if the stimulations are not effective.
2- the amplitude of the Global potential increases when the stimulations are effective (above threshold) because more nerve fibers are being excited producing many action potentials that are summed up together to produce a high global potential
3- the amplitude remains constant even if we increase the intensity because all the nerve fibers are already excited at I5.
4- The law applied by the nerve is called **law of summation**
5- **type of coding /modulation in a nerve:** the type of coding modulation in the nerve is the **amplitude** since the amplitude of global potential increases with the increase of stimulation.

Very important:

After stimulation of a NERVE:

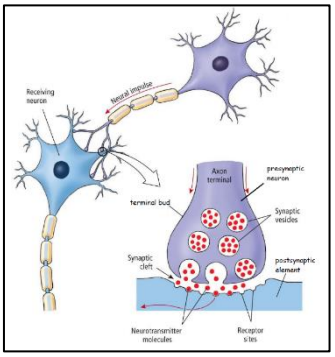
7- Every trace or peak corresponds to a type of fiber.
8- The amplitude of every trace reflects the number of fibers of the same type.
9- The formation of two traces in this case is due to the speed of the message that varies from a type of fiber to another (diameter and myelin).

C- Table showing the differences between the response of a nerve fiber and a nerve to an effective stimulations.

Criteria	nerve fiber	NERVE
Name of the response	Action potential	Global potential
Threshold intensity and maximal intensity	Ith = I max	Ith ≠Imax
Response for I<Ith	For I < I th, there is no response	For I < I th, there is no response
Response for I≥Ith	For I ≥ Ith, the response is maximum and constant	For I ≥ Ith, the amplitude of the global potential increases with the increase of intensity until reaching max intensity at which the amplitude of the GP becomes constant.
Applied law	Law of all or none	Law of summation
Type of coding modulation	Frequency	Amplitude

Document 4: Sensory receptor and nerve impulse

when the receptor potential exceeds -55mV at the level of the cell body (Threshold of depolarization), an AP is generated at the level of the nerve fiber (axon).



Document 5: Synapses: structure and function

Definition of synapse: is the junction between a terminal bud of an axon of a neuron and another structure. This structure could b e a neuron or an effector cell (muscle or gland cell).

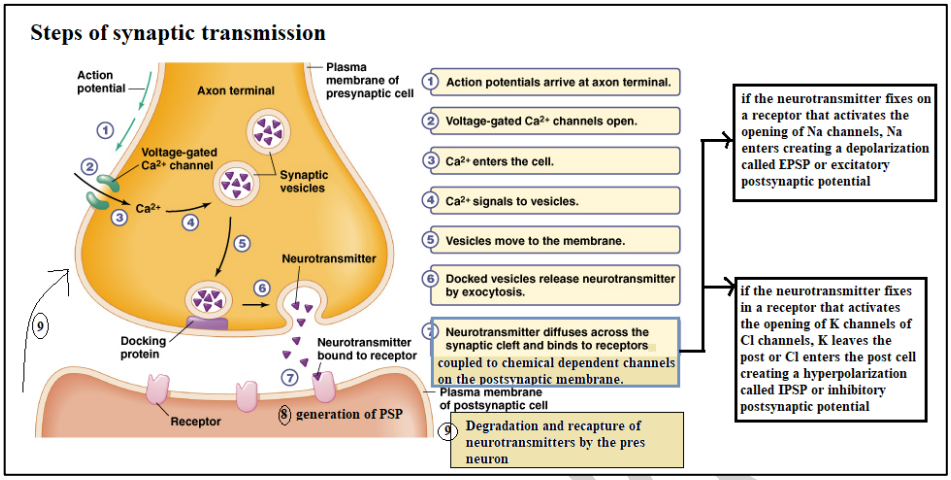


Table showing the difference between voltage dependent channels and chemical dependent channels.

Type of channel	Voltage dependent channel	Chemical dependent channel
Definition	Open under the action of membrane potential	Open under the action of chemical substances
Example	Ca^{++} voltage dependent channels	Na^{+}, K^{+} and Cl^{-} chemical dependent channels found on the postsynaptic membrane

the transmission of the nervous message at the level of a synapse is unidirectional taking place in the presence of Ca++ by means of neurotransmitters and the nervous message in the synapse in coded by the concentration of neurotransmitter.

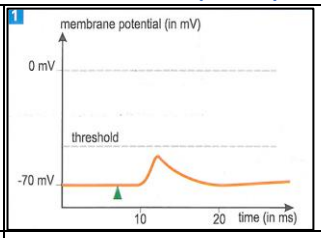
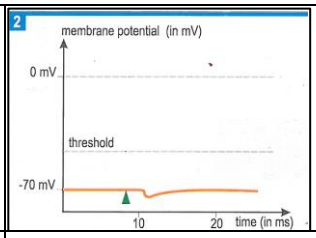
1- **Very important:** as the intensity of stimulation increases, the frequency of AP reaching the terminal bud increases. Then, more neurotransmitters are released in the synaptic cleft and fixed on their specific receptors leading to a more important PSP. We say that the nervous message at the level of the synapse is coded by the concentration of neurotransmitter.

Document 6: Integrating properties of nerve centers

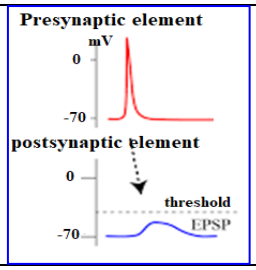
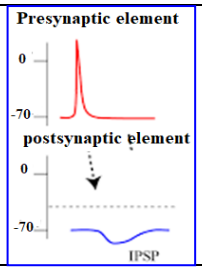
1- What is the meaning of "integrating role of the nervous center"

The motor neurons in the nerve centers (brain and spinal cord) receive several afferent messages and elaborate one efferent message.

2- Identify the type of synapse represented in doc. b by completing this table

Schema (recording at the level of the postsynaptic membrane)		
Type of synapse according to its function	Excitatory	Inhibitory
Justify the answer	The effective stimulation of the presynaptic neuron has led to a hypopolarization in the postsynaptic element	The effective stimulation of the presynaptic neuron has led to a hyperpolarization

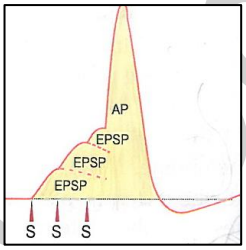
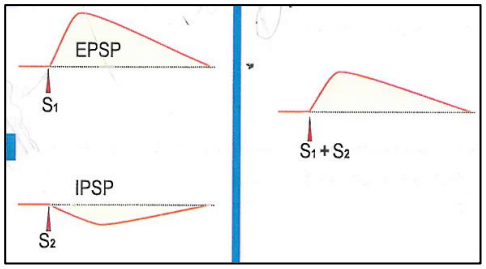
3- Differences between EPSP and IPSP

Criteria	EPSP	IPSP
Recording		
Chemical variation/ ionic variation in the post	The binding of nt on the post receptor lead to the opening of Na+ chemical dependent channel. This increases the permeability of the membrane to Na+ ions leading to the entry of Na+	The binding of nt on the post receptor lead to the opening of K+ and Cl- chemical dependent channels. This increases the permeability of the membrane to K+ that goes outside the post element and Cl- ions that enters the post element.
Electric variation/ charge behavior in the post	The internal side of the post membrane becomes less electronegative (more positive)	The internal side of the post membrane becomes more electronegative (less positive)

4- Explain how Acetylcholine **nt is excitatory in the skeletal muscle and inhibitory in the cardiac muscle**

The excitatory or inhibitory characteristic of a synapse depends mainly on the nature of the receptor that is found in the postsynaptic membrane.

5- Spatial summation and temporal summation

	Temporal summation	Spatial summation
Conditions	Stimulate the presynaptic neuron many times successively	Stimulate simultaneously many presynaptic neurons one time
Recordings		
Explanation	Temporal summation is the sum up of successive PSP (EPSP or IPSP) that takes place from the activation of the same presynaptic neuron. It triggers an AP in the postsynaptic element when the sum of successive EPSP ≥ threshold.	Spatial summation is the sum of EPSP and IPSP that take place simultaneously at a certain moment from different presynaptic neurons to the postsynaptic membrane. It triggers an AP in the postsynaptic element if the algebric sum of the EPSPs and IPSPs ≥ threshold.

Chapter 12: Neurotransmitters and medical applications

Document 1: Neurotransmitters and membrane channels

1- the neurotransmitters are chemical molecules synthesized by the neurons. Once liberated in the synaptic cleft, they bind to specific receptors on the postsynaptic membrane producing many effects.

Function (that depends on the receptor where this nt fixes)	**Excitatory:** since the nt fixes on receptors coupled to Na+ channels (once fixed, the channels open and Na+ rushes inside the postsynaptic neuron triggering a depo.)
	Inhibitory (since the nt fixes on receptors coupled to K+ or Cl- channels (once fixed, the channels open, and K+ rushes ouside while Cl- rushes inside the postsynaptic neuron triggering a hyperpo.**)**

Document 4: action of drugs on synapse

1- Important definitions:

- Drug: is a substance that affects the normal reactions of the nervous system and more precisely at the level of synapses. They interact or compete with the nt.
- Physical dependence (biological adaptation): the user cannot interrupt the drug consumption because it leads to a great uncomfortable state (withdrawal syndrome)
- Psychic dependence: is the repetitive use of the drug in order to obtain the sensation of pleasure.
- Tolerance: is the desire to increase the dose of the drug in order to obtain the desired effect.

2- Mode of action of curare:

Curare has approximately the same spatial configuration as ACH. Curare occupies the receptors of ACH, leading to muscle relaxation (paralysis).

3- Mode of action of cocaine

in normal cases, dopamine is released for a few seconds giving a sensation of pleasure for a short time then recaptured very quickly.

Cocaine prevents the recapture of dopamine which stays for a longer time fixed on the receptors prolonging its pleasure effect.

4- Mode of action of amphetamines

In normal cases, dopamine is released in few amounts leading to a pleasure and motricity feeling for a limited time . Amphetamines facilitate the exocytosis of dopamine causing an increase in the dopamine causing an increase of pleasure and motricity and activity for longer duration.

5- Mode of action of benzodiazepine (barbiturates)

Benzodiazepine enhances the fixation of GABA on their own receptors on Cl- channels, leading to a longer opening of these channels which increases the hyperpolarization or IPSP in the postsynaptic neuron, provoking relaxation or calming state.

Very important comparative tables

Substance	Agonistic substances	Antagonistic substances
Definition	Substance that has the same function as the nt	Substance that has an opposite function to that of nt
Example	Morphine and enkephalin (both are analgesic)	Curare and Acetylcholine (curare inhibits the contraction of the muscle by ACH)

Substance	Endogenous	Exogenous
Definition	Produced naturally in the body	Substance produced artificially outside the body
Example	neurotransmitter	Drug

Transport across the cell membrane

The cell membrane provides structure for the cell, protects cytosolic contents from the environment, and allows cells to act as specialized units. This phospholipid bilayer determines what molecules can move into or out of the cell. Cell membranes are semipermeable, meaning they have control over what molecules can or cannot pass through.

Movement Across a Membrane and Energy

- Passive mechanisms like diffusion use no energy
- Active transport requires energy to get done.

Diffusion: the Simple and the Facilitated

Diffusion is the movement of particles down their gradient. A gradient is any imbalance in concentration, and moving down a gradient just means that the particle is trying to be evenly distributed everywhere

When water undergoes simple diffusion, it is known as **osmosis**.

Simple diffusion: molecules move down their gradients through the membrane. Molecules that practice simple diffusion must be small and nonpolar*, in order to pass through the membrane.

Transport	Molecules moved	Uses energy?
Simple diffusion	Small, nonpolar	No
Facilitated diffusion	Polar molecules, larger ions	No
Active transport	Molecules moving against their gradient coupled to the hydrolysis of ATP	Yes

Facilitated diffusion is diffusion that is helped along (facilitated by) a membrane transport channel. These channels are glycoproteins (proteins with carbohydrates attached) that allow molecules to pass through the membrane.

Active Transport: Sometimes the body needs to move molecules against their gradient, and requires energy from the cell.

Cell organelles

Organelle	Function	Factory part
Nucleus	DNA Storage	Room where the blueprints are kept
Mitochondrion	Energy production	Powerplant
Smooth Endoplasmic Reticulum (SER)	Lipid production; Detoxification	Accessory production - makes decorations for the toy, etc.
Rough Endoplasmic Reticulum (RER)	Protein production; in particular for export out of the cell	Primary production line - makes the toys
Golgi apparatus	Protein modification and export	Shipping department
Peroxisome	Lipid Destruction; contains oxidative enzymes	Security and waste removal
Lysosome	Protein destruction	Recycling and security

Extra

Polymerase chain reaction (PCR)

is a laboratory technique used to amplify DNA sequences.
The method involves using short DNA sequences called primers to select the portion of the genome to be amplified. (And by amplifying that DNA, it allows us to study that DNA molecule in detail in the laboratory.)
The temperature of the sample is repeatedly raised and lowered to help a DNA replication enzyme copy the target DNA sequence.
The technique can produce a billion copies of the target sequence in just a few hours.
A primer is a short, single-stranded DNA sequence used in the polymerase chain reaction (PCR) technique

Regulation of glycemia

The reactions that take place in the liver, muscles and adipose tissue:

In case of hyperglycemia or after a meal

In the liver and muscles:

- Glycogenesis : Glucose → glycogen

In the adipose tissue:

- lipogenesis: Glucose → lipids.

In case of Hypoglycemia or after a fast Liver

In the liver and muscles:

- Glycogenolysis : glycogen → Glucose

In the adipose tissue:

- lipolysis: lipids. → fatty acids + glycerol

- Neoglucogenesis: amino acids or lipids → glucose (only in liver, it means production of glucose from sources other than glycogen)

Remarks:

- The liver is the only organ capable of releasing glucose directly since it contains an enzyme called glucose 6 phosphatase. This enzyme can remove the phosphate from the glucose resulting from the hydrolysis of glycogen. As a result. Glucose, void of phosphate, can leave the liver toward blood.
- The muscles: The enzyme G6Pase is absent in the muscles. That's why the muscles cannot release glucose directly in the blood. Instead, it releases amino acids that pass into the liver to be transformed there into glucose (neoglucogenesis).
- The adipose tissue: it cannot release glucose directly. Instead, lipids are hydrolyzed into fatty acids and glycerol, the glycerol is transformed in the liver into glucose (neoglucogenesis).

The pancreas: a mixed gland: exocrine and endocrine.
Exocrine function of the pancreas: the exocrine pancreas is formed of exocrine cells called acini that present an excretory duct through which they secrete the pancreatic juice (it contains enzymes important for digestion).
Endocrine function of the pancreas: the endocrine pancreas is formed of clusters of cells called Islets of Langerhans void of excretory ducts and rich with blood vessels. These Islets contain two types of cells:
• α cells that secrete glucagon, a hyperglycemic hormone that leads to the increase in glycemia.
• β cells that secrete insulin, a hypoglycemic hormone that leads to the decrease in glycemia.

Diabetes is a disorder characterized by a permanent hyperglycemia greater than 1.2 g/l.
Types of diabetes: They are divided into two groups:
- IDD or insulin dependant diabetes: this type can be treated by insulin injections since it is due to either a low number or absence of β cells (juvenile diabetes) or it is due to the production of abnormal insulin (mutated insulin gene).
- NIDD or non –insulin-dependant diabetes: this type cannot be treated with insulin since it is due to the presence of very few insulin receptors or 6 even the absence of insulin receptors. This is the case of maturity-onset diabetes.