Life science course

Grade 12 Life science section

2020

Teacher: Hussein Abdallah

Chapter1: Basic mechanisms of sexual reproduction.

Doc 3 page: 22 Meiosis

Meiosis: cell division for sex stem cell only.

-it takes place in the gonads.

-it transforms single diploid cell into 4 haploid gametes.

-it consists of 2 cell divisions:

1st meiotic division (reductional division): includes: prophase1\metaphase1\anaphase1\telophase1.

2nd meiotic division (equational): includes: prophase2\metaphase2\anaphase2\telophase2.

-there is no DNA replication (duplication) during meiosis; it takes place only during S-phase of interphase prior to meiosis.

Mechanism:

Replication (Interphase).

Meiosis1: Metaphase1\anaphase1\telophase1\end of telophase1.

Meiosis2: prophase2\metaphase2\anaphase2\telophase2\end of telophase2.

Doc 5 page: 27 Oogenesis

Documents (a, b) for study.

Folliculogenesis: development of the epithelial layers that surround the oocyte. In which primordial follicles (oocyte that is surrounds by a layer of epithelial cells) are formed during fetal life, they remain as primordial after birth and during childhood. Before puberty (1st cycle) with 4 months, the primordial follicles develop into primary then secondary and then into cavitary (tertiary) follicles, during follicular phase (0 tell 14 days of the cycle) certain number of cavitary follicle try to complete their development into Graafian follicle, but one of them become mature, and then it is subjected to rupture in a process called ovulation that occurs at the middle of the cycle approximately (14+ or – 1), then this ruptured follicle, during the luteal phase (14 till 28 days) transforms into yellow body. In case of no fertilization, it transforms into white body and then degenerate at the end of cycle. If fertilization occurs the yellow body survives for 3 months and then degenerates as white body.

Oogenesis:

-it takes place in the ovary.

-it leads to the production of only a single female gamete (ootid) from every oogonium.

-it consists of 4 stages: **1-Multiplication**

2-Growth

3-Maturation (meiosis with 2 arrests)

4-Very short differentiation

Doc 6 page:30 Fertilization

Document (b) for study.

Fertilization capacity: is a biochemical change in the cytoplasmic membrane of sperm cell in order to recognize and adhere to the zona pellucida of oocyte2.The sperm cell acquires its capacitation (fertilization capacity) during the passage in the female reproductive system.

Steps of fertilization page: 30 (doc.c) for study.

-The sperm cell forces its head between the follicular cells (pedunculated cells) and then adheres to the zona pellucida (due to fertilization capacity).

-It releases the acrosomal enzymes (acrosomal reaction) that digest the zona pellucida.

-The motility and the propulsion of the flagellum enable the sperm cell to penetrate into the periovocytar space.

-Oocyte2 (blocked at metaphase2) get activated, it releases the content of the cortical granules (cortical reaction) that lead to the formation of the fertilization membrane which in turn blocks (prevents) polyspermy (penetration of more than 1 sperm cell).

-Oocyte2 resumes meiosis2 it, releases the 2^{nd} polar body and becomes ootid.

-The whole sperm cell is absorbed into the cytoplasm of the ootid.

-The flagellum and the mid piece of the sperm are separated.

-The male and the female rule: approach to each other and swell forming the pronuclei.

-DNA replication takes place in each pronucleus (each chromosome becomes consist of 2 chromatids).

-The two pronuclei fuse, the nuclear membrane breaks down between them, and then the paternal and maternal chromosomes mix together (karyogamy or amphimixy) the ootid becomes a zygote.

-Mitosis starts.

Chapter: 2 Transmission of genes and genetic recombination

Doc 1 page 42 Hereditary traits and genes

Gene:-DNA fragment that encodes for a certain protein.

- Efficient DNA unit.

Allele: new version of a gene.

For example:-the gene that determines the coat color in mice has many alleles: gray, black and white.

-only two alleles (of the same gene) are present in a single individual.

-the two alleles (of the same gene) most occupy the same position on the same pair of chromosome.

Dominant allele: Is the allele that is expressed in homozygous and heterozygous states.

Recessive allele: expressed in homozygous state only.

Homozygote: *organism having two identical alleles (for a certain trait).*

Heterozygote: organism having two different alleles

True- breading line: the offspring's always have the same phenotype (and genotype) as parents.

Hybridization: experimental crossing between two true-breading lines that differ in one or more traits.

Doc (a) page: 42

Objective: the experiment was done in order to determine exactly the localization of genetic information.

Problem: where is the genetic information localized?

Hypothesis: may be the genetic information is localized in the nucleus.

Doc 2 page *44* Transmission of Alleles

Monohybridism*:* experimental crossing between two true breeding lines parent that differ in a single traits.

Case of complete dominance.

Test cross: experimental crossing to determine the real genotype of the dominant parent (heterozygous or homozygous) and the types of the produced gametes.

Note: it is performed by the crossing of the dominant parent with recessive one.

Intermediate heredity:

First cross: Red male cross white female

Result: 100% pink

Second cross: pink cross pink.

Result: 25% red, 25% white, 50 %pink.

Deduce from first cross:

New phenotype (pink) which is intermediate between the parents (red and white) was expressed in the offsprings.

Hence this is the case of intermediate heredity (incomplete dominance).

Codominance:

First cross: Black with white.

Result: 100% black with white spots.

Second cross: Black with white spots cross Black with white spots.

Result: 25% black 25% white 50% black with white spots.

Deduce from first cross: Both phenotypes (black and white) of the parents are expressed equally in the phenotype of each offspring hence it is the case of Codominance.

Case of lethal allele:

It is an allele that leads to the death of the homozygous carrier. If the death occurs before birth the ratio (proportion of phenotype) would be modified.

Chapter3: Genetic variation and polymorphism

Doc 2 page: 60 Mutations and multiple alleles

Types of mutations:

1-Substitution: one or more nucleotides are replaced by another.

2-Deletion: one or more nucleotides are deleted from the sequence.

3-Insertion: one or more nucleotides are inserted to the sequence of DNA.

Note: point mutation: mutation that affect (changes) the sequence by a single nucleotide.

Transcription: takes place in the nucleus by the action of RNA polymerase (for transcribed strand only).

In order to write the sequence of mRNA:

1- If the given strand of the DNA (gene) is non-transcribed (coding) write the same sequence but replace T by U.
2- If the given strand is transcribed (non- coding, template) write the complementary sequence.

Multiple allele: gene subjected to many different mutations leads to the production of many forms of gene (many alleles) as a consequence many phenotypes for the same trait is obtained (Case of polymorphism).

Doc 4 page: 64 Detection of genetic polymorphism

Restriction enzyme: found in bacteria.

-Specific enzyme for cutting DNA at specific sites.

-The recognition site for these enzymes consists of 4 to 8 base pairs.

Electrophoresis:

- Separation technique for DNA fragments.

- It needs electric supply.

- If mutation occurs in the restriction sites the restriction enzyme would not recognize the site, and hence different DNA fragments for the same gene would be produced.

Doc 5 page: 67 Genetic identity of individuals

FISH: fluorescence in situ hybridization. It is useful to determine the exact localization of the genes on the chromosomes.

Steps:

- Denaturation (DNA strands are partially separated).

- Hybridization with specific probe that binds to the DNA of single location.

- Observation with specific microscope.

Genetic map: map for the distribution of all genes and their location on the chromosomes.

Probe: single stranded DNA of short complementary sequence.

- Known sequence.
- It can be **monolocus** probe complementary only to a single DNA sequence.

Multilocus probe: complementary to repetitive sequence (DNA sequence frequently repeated in non-coding regions of DNA), thus this type of probe binds to many sites on the DNA. Used in DNA fingerprint.

-
- DNA fingerprint: same steps as DNA analysis except the use of Multilocus probe to generate many bands.(doc.c page:68)
- **Observation:** unique distribution of bands for each individual that represents the genetic identity (genetic fingerprint)
- **Identical twins:** have identical DNA fingerprint.
- Use of DNA fingerprint: paternity test, criminology…

Chapter 5: Human genetics

Doc 2 page 94 **Autosomal Disease**

Traits (phenotype) are:

-morphological and anatomical traits (like skin color…..)

-physiological traits (like synthesis of normal structural or functional protein)

-pathological (like synthesis of abnormal protein =>causing disease)

Doc. a page 94

Indication whether the allele responsible for the disease is dominant or recessive:

Couple (1 and 2) is normal but they have affected children, thus affected allele is marked in the parent, hence it is recessive.

Localization of the gene:

-The pedigree shows that both sexes are affected, probably the gene responsible for the disease is located on an autosomal.

If the allele is located on the non-homologous segment of gonosome Y, then every affected boy should have an affected father, but this is not the case.

If the allele is located on the non-homologous segment of gonosome X then the affected girl should take X^c from father (that should be affected, but he is normal), then this is not the case

If the gene is located on the homologous segment of X and Y then the affected boy should take Y^c from his father and his affected sister should take X^c from her father that should be affected but he is normal then this is not the case.

Hence the allele responsible for disease is located on an autosome.

Doc-b page 95:

Huntington disease

The allele responsible for the disease is dominant since every affected individual has at least one of his \her parent affected

Symbols: Normal n

- Disease D

The pedigree shows that both sexes are affected, probably the allele responsible for the disease is autosomal

If the allele responsible for the disease is located on the non-homologous segment of the gonosome Y then the affected boy should take affected allele from the father that should be affected also but he is normal then this is not the case .

If the allele responsible for the disease is located on the non-homologous segment of the gonosome X then the girl should take X^n from her father that should be normal but he is affected then this is not the case

If the allele of the disease is located on the homologous segment of X and Y gonosome then the normal girl should take X^n from her father and the normal boy should take Y^n from father, then this father should be normal but he is affected then this is not the case.

Hence the allele responsible for the disease is located on an autosomal.

Doc 3 page 96 sex – linked diseases

Doc .b page 97:

Duchene muscular dystrophy

Symbols: -normal n

-disease m

The pedigree shows that only some of boys are affected (no affected female), thus most probable is that the diseased allele is sex linked

I f the disease allele is carried by the non-homologous segment of gonosome Y then every affected boy should have an affected father, but this is not the case.

Hence the allele responsible for the disease is X- linked.

Doc 4 page 98 Chromosomal Mutation

- **Chromosomal mutations:**
  1. Numerical abnormality (trisomy, monosomy, …).
  2. Structural abnormality (in certain homologous pair one chromosome is longer than the other due to translocation for example).

Numerical Abnormality:

Example: case of trisomy 21(familial or free trisomy 21) doc (a) page: 98

-chromosomal formula: 2n+1 =47, XY

=45 +XY

-autosomal abnormality since there is an error in the number of autosomes (45) instead of (44) and pair 21 is an autosomal pair.

Origin of free trisomy 21

First case: non-disjunction of chromosomes 21 at anaphase 1.

Second case: non disjunction of the 2 sister chromatids of chromosome 21 at anaphase 2

Doc (c): linked trisomy 21 (Translocation)

The extra copy of chromosome 21 had been translocated (linked, attached) to one of the chromosomes 14.

Doc (f):

- Klinefelter syndrome.

-numerical gonosomal: existence of 3 gonosomes (X, X and Y) instead of 2 (X and Y).

-Sterile man.

Chromosomal formula: 2n+1=47, XXY

=44 + XXY

Structural abnormality:

Example: “Cri du chat “or cry of the cat syndrome

Characteristic: Deletion of DNA fragment of one of the chromosomes number 5.

Doc 5 page 101 Prenatal Diagnosis

Methods used in prenatal diagnosis:

- Amniocentesis: sampling of the amniotic fluid that contains cells that have sloughed off the fetus skin (16^{th} week)
- Chorionic villus biopsy: sampling of the chorionic cells (8^{th} week)
- Blood sampling: sampling of the fetal blood withdrawn from the umbilical cord (20^{th} week).

Analysis of the fetal cells:

- Karyotype: detection of the chromosomal mutations (numerical or structural abnormalities).
- DNA analysis: detection for genetic or hereditary diseases (detection of gene mutations, doc (b) page: 101).
- Biochemical analysis: detection for protein or enzyme alterations (change in the structure or function).

DNA analysis:

- Denaturation: partial separation of the 2 DNA strands by the breaking down of the H-bonds between the base pairs.
- Hybridization: binding (fixation) of the radioactive probe with its complementary sequence on the denatured DNA fragment.
  (Probe: single stranded, and short known sequence of nucleotides that are complementary to a specific sequence on the DNA (it is called cDNA).

Chapter 6: Role and components of the immune system.

Doc 1: page 114 HLA major self-marker

Doc (a) **auto graft**: tissue graft between two different sites of the same individual

Iso graft: tissue graft between two individuals of the same lineage (same genetic information)

_identical twins in human

_same line (breeding or strain in animals)

Allograft: tissue graft between different individuals of same species (even relatives)

Interpret doc a: after performing the grafting (in the 3 crosses) same aspect was obtained 2 days later (vascularization, pinkish aspect) but one week later graft is integrated into neighboring cells in autograft and isograft but in allograft redness, and edema appear around the graft, this shows that the body's reaction toward the graft starts after 1 week. 15 days' later graft is rejected only in case of allograft (black and dry aspect), this proves that the rejection of the graft needs 15 days and it occurs only in case of allograft. Therefore, the acceptance or rejection of the graft depends on the type of the grafts and needs 15 days to be confirmed.

Expression of MHC (HLA molecules)

Expression of MHC is controlled by 6 genes (DP, DQ, DR, B, C, A) that are highly polymorphic (multi allelic genes), these genes are located on chromosome 6

_the alleles of each gene are codominant

_the genes B, C, A encode for the synthesis (upon transcription + translation) of HLA class I that is expressed on all nucleated cells.

The genes DP, DQ, DR encode for the synthesis of HLA class II that is expressed only on certain immune cells

(Note; immune cells express HLA I and HLA II)

Immunological self: HLA associated to self-peptide leading to the formation of HLA self-peptide complex and then it is expressed on the surface of the cells

Note; self-peptide is obtained by the fragmentation (digestion) of self-protein inside the cell

The acceptance or rejection of the graft depends on the compatibility of immunological self between the donor and recipient

Doc 3: page 119 The non self

Non self: element, component, molecule or a cell related to a foreign body that invade our body

For example:

_ Pathogenic agents (virus, bacteria, protozoa fungi, worms, bacterial toxins)

_ modified self (turnoral or cancerous cells)

_ Vaccine (contains attenuated microbe)

_ Red blood cells from incompatible blood group

In case of modified self or infected cell: the immunological self is modified in which the self-peptide is replaced by non self-peptide and associated to self HLA

Antigen: is a large molecule usually protein or complex carbohydrate that provokes immune response against it

It could be: _ soluble (free antigen, circulating in blood like bacterial toxin or venom).

_ attached (cellular): part of the cell

Doc:4 page 121 Cells of the immune system

Blood:

Blood cells: _ red blood cells (erythrocyte): numerous, and small

_ White blood cells (leukocytes): less in number and large in size

Plasma serum: (liquid containing water, salts, protein, lipid)

Origin of leukocyte:

Bone marrow: contains stem cells called pluripotent stem cells that are the origin of all the populations of leukocytes

Pluripotent stem cells: it gives rise for two types of stem cells:

Myeloid stem cells: _ granulocyte: neutrophil, eosinophil, basophil.

_ Monocyte: in blood and it becomes macrophage in tissue.

_ Mast cell

Lymphoid stem cells: B-lymphocyte

T-lymphocyte: T4-cell (TH-cell), T8-cell (TC-cell)

Characteristics of WBCs:

_ Granulocytes (polymorph nuclear cells): has multilobed nucleus

_ Monocyte: has horse shoe shaped nucleus

_ Mast cells: round nucleus, cytoplasm filled with granules containing histamine

_ Lymphocytes: round large nucleus

Certain characteristics of lymphocytes

B-lymphocyte: expresses membrane receptor molecule called: antibody (single B-lymphocyte expresses only a single type of antibodies).

T-lymphocytes: expresses a membrane receptor molecule called TCR

T-lymphocyte: T4- cell: expresses in addition to TCR, a marker co-receptor molecule called CD4

: T8-cell: expresses in addition to TCR, a marker molecule called CD8

Doc 5: page 123 lymphoid organs

Lymphoid organs:

1- Primary organs: responsible for the production and maturation of leukocytes (especially lymphocytes) bone marrow and thymus

Bone marrow: is responsible for production of all leukocytes including B and T lymphocytes and maturation of B-lymphocytes only

Thymus: site of maturation of T-lymphocytes

2- **Secondary organs**: site of immune reactions (responses) against non-self antigens (spleen and lymph nodes)

Spleen: site of immune reactions against antigens circulating in the blood

Lymph node: site of reactions against non-self antigens drained by lymph from infected tissues

Maturation: is a genetic mechanism that enables lymphocytes (B and T) to become immunocompetent that is able to distinguish between self and non-self antigens

1_Maturation of B-lymphocyte: takes place in the bone marrow.

1st step: production of expressed antibodies due to transcription and translation of certain gene (takes place in the bone marrow)

2nd step: all the B-cells whose antibodies can recognize and bind to self antigens are eliminated. Other B-cells that cannot recognize self antigens are preserved

As a consequence of B-cells maturation all B-cells become immunocompetent can bind only to non-self antigens

2_ T-lymphocyte maturation: takes place in the thymus.

1st step: production of TCR in the T-cells (due to transcription and translation of a certain gene)

2nd step: all the T-cells whose TCR (and coreceptor CD4 and CD8) can recognize self HLA (class I and class II) are preserved. T-cells that can't recognize to self HLA are eliminated

3rd step: all T-cells whose TCR can recognize and bind to self-peptides (associated to self HLA expressed on APC are eliminated).

As a consequence, mature T cells can recognize self HLA associated to non self-peptides (double recognition) so they are immunocompetent.

Doc.6 p: 125 Antigen Recognition by B-lymphocytes

Structure and classes of Antibodies:

Antibody:

.Y-shaped protein, consists of 2 heavy chains and 2 light chain (doc. c)

.It can be expressed on B-cells or circulating in the plasma.

.It consists of variable and constant regions: The variable region constitutes the binding site (each antibody has 2 similar binding sites).

.The constant region presents slight variation (5 differences), so the immunoglobulins (Ig or antibodies) are classified into 5 classes according to these differences: IgG, IgA, IgM, IgE and IgD (GAMED).

.Ig can act as monomer or polymer (dimer as secretory IgA or pentamer IgM).

Note: Each B-cell expresses a high number of identical antibodies on its surface.

Specificity:

.The binding site of the antibody can bind either soluble or cellular (attached) antigen.

.The binding site doesn't bind to the whole antigen (which is a complex macromolecule) but to a small part of this antigen called antigenic determinant of epitope.

.The binding site and the epitope have complementary structures and fit together in a key and lock relationship (high chemical affinity derived from non-covalent bond).

Cross-Reaction:

Similar antibodies can bind to different antigens that share common epitopes. (Doc f)

Remark:

Immuno-complex: Fixation or binding of an antibody with an antigen.

Doc 7 p: 127 Antigen Recognition by T-lymphocyte

Structure of TCR:

-Always expressed on T-cells.

-Consists of 2 polypeptide chains, each has a constant region (without differences) and variable region (the terminals of the variable regions constitute the binding site).

- Has a single binding site.

Double Recognition of TCR (and the co-receptor CD4 or CD8):

TCR can't bind to an antigen (whether soluble or cellular), it can bind only to non self-peptide associated to HLA (MHC) molecule (HLA, non-self-peptide complex) (this is referred to double recognition).

Expression of MHC (HLA) genes:

HLA_I encoded by A, B and C genes is expressed on all nucleated cells including immune cells.

HLA_II encoded by DP, DQ, and DR is expressed on some immune cells (mainly macrophage).

Doc d (p. 128): All the details.

Note:

HLA_I associated to non-self-peptide (ex: viral peptide) activates only Tc-cells.

HLA_II (expressed on macrophage) associated to non-self-peptide (ex: bacterial peptide) activates only TH-cells (T4-cells).

Chapter 7 : The immune Response

Doc 1 p: 138 Non-specific Immune Response

Natural Barriers: Doc a. study.

Non-specific immune response:

1- Inflammation: set of the physiological events that lead to the signs (manifestation): pain, redness, and swelling (edema).

Pain: due to the stimulation of nerve endings found in the site of lesion (for example: skin lesion).

Redness: due to the dilation of the blood capillaries, this leads to increased blood flow in the site of inflammation.

Edema (swelling): due to leaking out of plasma to the tissue.

Mechanism of inflammation:

> The damaged cells release variety of chemical messengers (substances) called cytokines. This substance causes local dilation of the capillaries, and also an increase in vascular permeability (that causes leaking out of plasma).

> Some cytokines are chemo tactic factors that attract leukocyte to the site of inflammation, mainly phagocytes (neutrophil, macrophage).

> Phagocytes can cross the capillary wall by a process called diapedesis, and thus migrate into the site of inflammation.

Note: monocytes migrate into the tissue and become macrophage.

2- Phagocytosis: Essential process of the non-specific immune response that can eliminate a lot of invaders.

Steps:

_The macrophage approaches and surrounds the bacterium (adhesion).

_The macrophage absorbs (engulfs) the bacterium into the cytoplasm, and surrounds it with a vesicle (called phagosome: vesicle in addition to the lysosomes).

_Bacterium is fragmented or digested (infection is stopped).

_In case of enzymatic deficiency or resistant bacterium, the infection continuous (The bacterium remains in stationary state or it multiplies and disintegrates the macrophage leading to the formation of pus).

Doc 2 p: 140 The Specific Immune Response

Doc (a):

Exp.1: injection of killed salmonella, 10 days later, also injection of live salmonella, and the chicken survives.

Exp.2: injection of killed salmonella, followed by injection of live vibrio cholera (after 10 days), the chicken dies.

-> This proves that the immune response mounted (induced) against killed salmonella (after 10 days) protects only against live salmonella (and not vibrio cholera).

-> Therefore, the immune response mounted against any intruder (after 10 days) is specific.

Doc (b):

Fig. (a): **Interpret:** Sampling of blood from mouse A1, after being injected with tetanus toxoid, then separation it into serum and blood cells, the cells are then injected into mouse A3, in addition to tetanus toxin, the mouse A3 dies. Whereas in case of injection of the serum in mouse A2 along with tetanus toxin, the mouse A2 still survives.

-> This proves that the serum (of mouse A1) contains effector molecules (substance) that protects mouse A2 against tetanus (the cells didn't protect against the tetanus toxin).

The serum is then introduced into a solid matrix containing attached tetanus toxoid; the filtrate is transmitted into mouse A4 that dies after the injection of tetanus toxin.

→ This indicates that the effector molecules that protects against tetanus toxin had been specifically bound to the attached tetanus toxoid in the matrix.

Fig (b): **Interpret:**

Separation of blood into serum and cells, the cells are injected into mouse B3 in addition to KB, the mouse dies, whereas the injection of cells into mouse B2 along with KB, the mouse B2 stays alive, **this proves** that the cells are the effectors that protect against KB (and not the serum).

Separation of cells into B and T lymphocytes, B cells are injected into the mouse B, whereas T-cells injected into mouse B5 along with KB (in the two cases), mouse B4 dies and mouse B5 is still alive.

This signifies that T-cells are the effector cells against KB and not B-cells.

Deduce the type of the immune response in each case fig. A and fig. B:

Knowing that the immune response against tetanus had been mounted by serum and that of KB had been mounted by T-cells:

The immune response is **humoral** in case of tetanus and **cellular (cell-mediated)** in case of KB.

Immune Response :

Non-Specific Immune Response:→Natural Barries

→Inflammation
→Phagocytosis
} Immediate

Specific Immune Response:

- Mounted after 10 days (or 2weeks).

→ **Humoral S.I.R**: mounted by circulating antibodies in the serum (plasma).

→**Cellular (cell-mediated S.I.R):** mounted by T-lymphocytes.

Doc 3 p: 142 Induction of the specific Immune Response

Mosier Experiment: Induction of the specific immune response (doc a, page 142).

Objective: The experiment was done to demonstrate the important role of macrophages in the induction of a specific immune response.

Interpret: Culturing macrophages alone in the presence of SRBC, no antibodies were produced, whereas in case of culturing macrophages with SRBC in addition to lymphocytes, anti-SRBC antibodies were produced.

This proves that lymphocytes are responsible for the secretion of anti-SRBC.

In case of culturing lymphocytes alone with SRBC, no antibodies were produced; **this indicates** that the existence (presence) of macrophage is indispensible (necessary) for the production of anti-SRBC antibodies by the lymphocytes.

Therefore, macrophages induce (stimulate the induction of) antibodies secretion (specific immune response) by the lymphocytes.

Role of Macrophage in the induction phase:

In case of engulfment of bacterium (for example) by the macrophage (process of **phagocytosis**), the bacterial peptides are associated to HLA-II in the macrophage and then presented on the cell surface (macrophage in this case is called **Antigen presenting cell: APC**), then it migrates to the nearest lymph node, and leads to the activation of the suitable T4-cell, that expresses the compatible TCR that recognizes and binds to HLA- II peptide complex, in this situation the T4-cell gets activated.

Fate of activated T4-cell:

The activated T4-cells are then subjected to proliferation:

1_ Multiplication: The activated T4_cell divide and multiply into high number of T4-cells that express identical TCR (clonal selection).

2_Differention: The clone of T4-cells transforms into 2 types of cells:

→**Memory cells**: less differentiated and survive for many years.

→**Interleukin secreting cells:** highly differentiated, survive for few days. The secreted interleukins induce the specific immune response (humoral and cellular).

Doc 4 p: 144 Role of TH Cells in the Specific Immune Response

Interpret: Doc (b)

Introducing macrophages and Th-cells in tow beakers, then add killed CGB in the first and tetanus toxoid in the second, after certain time, high levels of IL-2 appear in the first beaker and high levels of IL-4 in the second.

This proves that Th-cells secrete different types of interleukins according to the type of the non-self (CGB or tetanus).

Transfer of IL-2 and IL-4 into two different beakers, each contains B and Tc cells. Proliferation of Tc-cells takes place in the medium containing IL-2 whereas proliferation of B-cells takes place in the medium containing IL-4.

This indicates that IL-2 induces the proliferation of Tc-cells and IL-4 induces the proliferation of B-cells.

Therefore, Th-cells induce the proliferation of B and Tc cells through the secretion of different types of interleukins.

Fate of activated B-cells:

B-cells, whose antibodies recognize and bind the antigen, get activated and due to the stimulation of IL4, B-cells proliferate:

1- Multiplication: Activated B-cells divide.

2-Differentiation:

-Some of B-cells keep their Ig (antibodies) and become memory cells (long lived cells).

-High number of B-cells completes their differentiation, lose their antibodies and become plasma cells (plasmocytes), they are short lived cells and secrete high amounts of antibodies (soluble circulating) that are identical to the expressed antibodies of the activated B-cells.

Fate of activated Tc-cells:

Activated Tc-cells (whose TCR can recognize and bind the non-self peptides associated to HLA_I undergo proliferation (clonal selection).

1- Multiplication: Division of activated Tc-cells due to stimulation by IL-2.

2- Differentiation: Some Tc-cells become memory cells (long lived cells), they do not complete their differentiation, other cells complete their differentiation and become cytotoxic (killer) cells (Tc-Killer cells) (Tc-cytotoxic cells) which are short lived effector cells.

Doc 5 p: 146 Specific Humoral Immune Response

Specific Humoral immune response: Elimination of antigens (cellular or soluble) by circulating antibodies (immunoglobulins) secreted by plasma cells (plasmocytes).

1-Elimination by macrophage:

First step: **Neutralization:** The circulating antibodies bind the antigens (formation of antibody- antigen complexes or Immuno-complexes) and inhibit their effect, thus prevent the binding of antigens on the body cells.

Second step: **Opsonization:** The antibodies create a molecular bridge between the antigens and the phagocytes (neutrophils and macrophages), in which the constant region of the antibodies bind to specific receptors on the phagocytes.

2- Elimination by complement cascade:

Note: Complements are plasma proteins (enzymes circulating in plasma and called C1, C2…….. C9).

First step: **Neutralization:** The circulating antibodies bind to cellular antigens.

Second step: The constant region of antibodies (bounded to cellular antigen) activates C1 which in turn activates the other complements (chain of enzymatic reactions that activates the complements from C1 to Cg.

This chain of activation reactions is called complement cascade. The cascade then leads to the formation of membrane attack complex that perforate the cell (coated with antibodies and expressing the antigens) causing its death.

Doc 6 p: 148 Specific Cell-mediated Immune Response

Mode of action of Tc-cells (Mechanism of elimination of target cells or infected cells by Tc-cells) (doc a page 148).

First step: Tc-cells bind to the infected (target cell) through its TCR, that recognizes and binds to HLA-I-peptide complex expressed on the infected cells.

Second step: The Tc-cells release its perforin content that assembles on the membrane of the target cells leading to the formation of hollow channel called poly perforin channel.

Third step: Tc-cell release granzymes that penetrate through poly perforin channels, and then trigger chain of enzymatic reactions that leads to DNA degradation, and thus causing cell death.

Fourth step: Tc-cell detaches and recirculates, and it is ready to kill another target cell (expressing the same HLA I_peptide complex).

Cancer and Immunity: doc a (page 149).

Doc 7 p: 150 Immunological Memory

Doc a (page: 150)

Primary response: specific immune response triggered after the first encounter with an antigen.

Secondary response: specific immune response triggered after the second encounter with the same antigen.

Characteristics of primary and secondary immune response:

→**Latency:** delay in antibody production (amount that is sufficient for protection, at least equal to protection threshold).

→**Persistent:** duration of protection.

Table for the characteristics:

	Primary Response	**Secondary Response**
Amount of antibodies	Low	High
Latency	Long time (10 days)	Short time (2 day)
Persistence	Short time (1 week)	Long Time (months)

Immunological memory:

The proliferation of B and T-cells leads to the formation of memory cells (due to the 1st encounter with the antigen), these cells are numerous, less differentiated and long lived, thus in Case of second encounter with the

same antigen, these cells are more efficient (for example: in case of Humoral specific immune response, high amount of antibodies with short time latency and long persistence are produced), and thus the secondary response is stronger, amplified, durable, faster and persistent.

Vaccination: administration (introduction) of the attenuated (weak) microbe into the body in order to produce active immunity, represented by immunological memory (that is efficient against the microbe for a long time).

-Serotherapy:

- Treatment by serum that contains ready antibodies (against certain microbe or toxin).

-Efficient for a short time (about 20 days), thus it provides passive immunity.

Doc: 8 p:152 Diagnostic application of antibody properties

Antibody properties that help for diagnostic application (detection for disease):

1- Specificity: The binding site of the antibody only binds specific antigen (epitope).

2-Production of soluble antibodies (circulating in blood plasma or serum) takes place only in case of microbe entrance (in case of infection).

***Applications:**

1-Serological reaction:

a-**Agglutination reactions:** the serum of the suspect patient is mixed with the microbe (for example bacteria) if the bacteria are agglutinated (as shown in doc (a) figure) it means that the antibodies specific for the bacteria are present in the serum, thus the patient is seropositive **(his serum contains specific antibodies against the given bacteria),** hence the patient is infected **(the diagnosis is confirmed).**

If the bacteria remain free (doc. a fig.2), the patient is seronegative, does not certain antibodies specific for the given bacteria.

b- **Immunodiffusion in gel:** The serum of the suspected patient and the given antigens **(these antigens are determined according to the symptoms of the disease)** are placed in hollow wells in the agar gel, they can migrate in all direction.

The appearance of gray arc between the serum and a given antigen reveals the formation of Immuno-complex **(binding of antibodies for antigen).**

Thus the patient is seropositive.

2- Immunomarking Test: (doc.c page: 153)

ELISA technique used to detect the presence of anti-HIV antibodies in the serum of the patient.

Used tools: - Antibody coupled to an enzyme, which is specific for the binding of human anti-HIV antibodies.

-Colorless substrate specific for the enzyme.

3- Immunofluorescence test. Doc d Page: 153

Chapter: 9 Function of Neurons

Doc1 page: 182 Resting potential

Resting potential: potential difference between the intracellular and the extracellular media of a non-stimulated neuron is called resting potential (or membrane potential).

Interpret: doc (a)

Fig(1) : The two microelectrodes of the voltmeter are on the extracellular surface. 0mv was recorded.

Fig(2) : One of the microelectrodes is in the intracellular medium and the other on the extracellular medium (surface), a certain value was recorded (deviation of the needle of the voltmeter).

This proves that the 2 surfaces of the neuron (extracellular and the intracellular) have opposite charges. Thus the neuron is polarized, and has potential difference at rest.

Origin of Resting Potential: (value= **-70mv**)

Resting potential is originated from the unequal distribution of positively and negatively charged ions between the extracellular and the intracellular media.

As a consequence of this distribution of ions the extracellular and intracellular medium becomes positive and the intracellular medium becomes negative.

Normally the plasma membrane is permeable for the flow of ions; this diffusion takes place through membrane channels (channel protein).

Passive Diffusion: takes place through membrane channels and the concentration gradient, thus this ion diffuses normally (without energy consumption) from medium of high concentration into a medium of low concentration.

. Na+ diffuses inside (inflow)

. k+ diffuses outside (outflow)

If the passive diffusion continues, the internal and the external media would have the same ion concentration, and leads to state of electric neutrality (or electric balance or equilibrium) that disturbs resting potential, thus in order to prevent this state, and maintain the resting potential, active transport is performed.

Maintaining the Resting Potential:

Resting potential is maintained by active transport in which ions diffuses against the concentration gradient (from medium of low concentration to a medium of high concentration), through specific channels called Na+ / k+ pump.

This transport needs ATP (energy) consumption.

. Na+ diffuses outside (outflow of Na+).

. K+ diffuses inside (inflow of k+).

Principle of Na+ / K+ pump: doc. h page: 184

Experiment: p: 184 (4th paragraph)

Addition of DNP (that blocks metabolism, and thus prevents the phosphorylation of ATP) leads to gradual decrease of Na+ and then stops completely.

ATP is then added (under the effect of DNP) Na+ ions are observed to flow outside again.

This proves that the outflow of Na+ needs the consumption of the ATP.

Note: ATP is an energy molecule that is used by the Na+ / k+ pump (or Na+/K+ ATPase).

Doc 2 page: 185 Action Potential

Action Potential: is a momentary change (in resting potential) of amplitude **100mv.**

Phases of action Potential:

1-Depolarization

2-Inversion of polarity

3-Repolarization

4-Hyperpolarization

Ionic Interpretation:

1-Depolarization: due to Na+ inflow (stimulation provokes a change of the membrane potential, thus the opening of the Na+ voltage dependent channels).

2-Inversion of polarity: End of depolarization (complete reverse of charge between the extracellular and the intracellular medium).

3-Repolarization: due to K+ outflow (opening of K+ voltage (gated) dependent channels).

4-Hyperpolarization: due to continuous outflow of k+ (delay in the closure of k+ voltage dependent channels leads to the increase of electro negativity in the intracellular medium.

Doc 3 page 187 Nerve Impulse and Action Potential

Characteristics of the nerve impulse in a nerve fiber:

Analyze (Recording by O1):

With intensities I1, I2 and I3 ($I < I4$), a potential difference below the threshold of depolarization was recorded, thus no action potential was recorded.

With intensities I4, I5 and I6 ($I \geq I4$), an action potential with constant amplitude was recorded.

_What can you draw out (about the law of all or none):

Knowing that the amplitude of the action potential was constant ($I \geq I4$) and no action potential was recorded in case of intensity $I < I4$, then the response of the nerve fiber obeys the law of all or none.

Hence the nerve impulse of the nerve fiber is characterized by the obeisance of the law of "all or none".

Characteristic of the nerve impulse in the nerve:

_Same experiment as doc. (a), but replace the nerve fiber by nerve.

Explain: doc. (e) fig *(1)* p:188

With the intensities I1, I2, I3, I4, I5, the amplitude of the global potential increases, due to increased number of excited nerve fibers (that constitute this nerve).

_With intensity $I > I5$, the amplitude of the global potential remains constant, since all the nerve fibers are excited.

_ what can you draw out (about the law of "all or none"):

Knowing that the global potential recorded with increasing intensity had variable amplitude, thus the response of the nerve doesn't obey the law of all or none.

Fig: (2) page: 188

Explain: Upon increasing the distance between S2 (stimulus) and R1 (recording electrode) 2 global potential were recorded. This can be explained by the existence of 2 different groups of nerve fibers (that constitute this nerve: they can differ by nature or diameter).

Each group would conduct the nervous message with certain speed.

Propagation of the nerve impulse in a:

1-Non-myelinated fiber: The wave of depolarization moves along the fiber step by step (it covers all the distance).

2-myelinated fiber: Depolarization jumps from one node of Ranvier to another. This conduction for the nerve impulse is called saltatory conduction.

Note: saltatory conduction is faster than the conduction of nerve impulse in the non-myelinated.

Doc 4 page 190 Sensory receptor and nerve impulse

Sensory Receptor: specific structures for receiving different types of stimulation. It transforms any type of stimulation (light, sound, chemical substance…) into potential difference (electrochemical energy).

Classification of Sensory Receptor:

1-According to their location*:*

a- Exteroceptor: that receive information form external medium (light, sound).

b- Interceptor: that provides information about the internal medium.

2-According to the type of energy of stimulation: Doc.a page: 190

Receptor Potential: potential difference (change in resting potential) at the level of the sensory receptor due to the applied stimulation. The intensity of stimulation and the period (for this stimulation) affect the value of this receptor potential.

Doc.b page: 191

Applying pressure (13 g/cm^2) on the pacinian corpuscle (mechanoreceptor) leads to the difference in the resting potential (-70) above the threshold of depolarization, this is called receptor potential recorded by R1 which in turn causes the generation of a train of action potentials (4 A.P) at the level of the sensory fiber (recorded by R3).

DOC.C page: 191

Interpret: Applying pressure (0.9 g/cm^2) for 2 ms, leads to receptor potential below the threshold of depolarization, no A.P was recorded at the level of the nerve fiber, this proves that this pressure (intensity of stimulation) is ineffective.

Applying pressure (0.7 g/cm^2) for the same period of time, leads to receptor potential above the threshold of depolarization (for approximately 1 ms), this in turn is translated into 6 A.P (of constant amplitude), whereas 13 A.P (of constant amplitude) were recorded in case of receptor potential of higher value (above the threshold of depolarization for a longer period of time (approximately 2ms) due to pressure (2.5 g/cm^2).

This indicates that there is a relationship between the intensity of the stimulus, receptor potential and the frequency of action potential (at the level of the fiber).

Deduce the code of the nervous message. Knowing that the amplitude of action potentials remains constant, but the recorded number (frequency) was variable, hence the nervous message is coded by the frequency of A.P (and not the amplitude.

Doc 5 page 192 Synapse: Structure and Function

Synapse: zone of junction between the terminal bud of an axon and another structure (neuron or effector cells like muscle and gland cells).

Types of synapse:

1-Neuro-neuronal synapse:

a- Electric synapse: direct contact between the 2 neurons (no synaptic cleft).

b-Chemical synapse: existence of synaptic cleft between the two neurons.

Neuro-neuronal synapse can be: axo-axonal, axo-dendritic and axo-somatic.

2-Neuro-muscular synapse: chemical synapse between a neuron and a muscle.

3-Neuro-glandular*:* chemical synapse between a neuron and a gland.

Synaptic Function:

Interpret page 192

Exp1: A.P was recorded in the pre-synaptic neuron A and post-synaptic neuron B. Upon effective stimulation for neuron A, but in case of the stimulation for neuron B, A.P was recorded only in neuron B.
This proves that the A.P was transmitted in single direction from pre-synaptic neuron A to post-synaptic neuron B and didn't transmit from neuron B to neuron A.
Note: Deduce the property of synaptic transmission.
The transmission of the A.P along the synapse is unidirectional always from the pre-synaptic neuron to the post-synaptic neuron.
Exp 2: Upon removing Ca2+ from the medium, A.P was recorded only in neuron A in case of stimulation of neuron A.
This proves that the existence of Ca2+ (in the medium) is indispensible for the transmission of A.P along the synaptic cleft, and it is not related to the generation of A.P at the level of the nerve fiber (neuron A).
In case of Ca2+ injection inside the pre-synaptic terminal bud (and without stimulation), a response was recorded in neuron B, this confirms that the existence of Ca2+ inside the terminal bud provokes the response at the level of the post-synaptic neuron B.

Exp 3: The injection of small dose of acetylcholine at the level of the synaptic cleft causes the generation of a response at the level of the post-synaptic neuron B (even without stimulation), and the response varies (increases) in case of deposition of increasing doses of acetylcholine.
This indicates that acetylcholine is a chemical mediator that induces the change of resting potential (response of doc.d), and this change depends on the applied dose (quantity).

Mechanism of the transmission of nerve impulse (message) along a chemical synapse (synaptic function):
The arrival of A.P to the pre-synaptic terminal bud allows the opening of Ca2+ channels (which are voltage dependent channels), the entrance of Ca2+ into the synaptic bud causes the fusion of some synaptic vesicles with the pre-synaptic membrane, leading to the release or liberation of the neurotransmitter (chemical mediator contained in the synaptic vesicle) into the synaptic cleft by a process called exocytosis, once released, neurotransmitter binds to specific receptor (chemical dependent channels) located on the pots-synaptic membrane, this will modify the membrane potential by opening ion channels (Na+, Cl- , K+) thus creating a post-synaptic potential (PSP), later the neurotransmitter is rapidly degraded by a specific enzyme or recaptured (absorbed) by the terminal bud.

Doc 6 page: 194 Integrating Properties of Nerve Centers

Nature of Chemical Synapse:
***1-Excitatory Synapse*:**
The binding of the neurotransmitter on its receptor causes the opening of Na^+ channels this causes Na+ inflow, which in turn causes the generation of EPSP (depolarization).
2-Inhibitory Synapse:
The binding of the neurotransmitter on its receptor (chemical dependent channel), cause the opening of Cl- (inflow) or K+ (outflow) which in turn causes the generation of IPSP (inhibitory post-synaptic potential which is hyperpolarization).

Integration: Algebraic summation of afferent information (more than a single afferent message) done by the Motor neuron of the nervous centers.

1-Temporal Summation (integration): 2 or more afferent (sensory) messages received by the motor neuron due to successive stimulations for the same fiber, are integrated into a single efferent (motor) messages, this is called Temporal Summation.

2-Spatial Summation (integration): 2 or more afferent (sensory) messages that are resulting from the stimulation of 2 or more different fibers (or similar) simultaneously are integrated into single efferent (motor) messages (by the Motor neuron).

For example: in case of the excitatory effect (EPSP) is stronger than the inhibitory (IPSP), the resultant potential difference (PSP) would be EPSP.

Chapter 12: Neurotransmitters and medical applications

Doc 1 page 236 Neurotransmitters and Membrane Channels

Classification of Neurotransmitters:

1- According to the location of the synthesis:

a- Some of the Neurotransmitters are synthesized at the level of the terminal buds but their conversion enzymes are synthesized at the level of the cell body, these Neurotransmitters are called classical Neurotransmitters.

b- Other Neurotransmitters are synthesized directly at the level of the cell body; these are called neuropeptides that are formed from many amino-acids.

2- According to their function:

a- Excitatory it binds to Na^+ channels (or receptors) and this depolarizes the post-synaptic membrane.

b- Inhibitory: if it binds to Cl^- or K^+ channels (or receptors) and thus hyperpolarizes the pre-synaptic membrane (ex: GABA is an exclusively inhibitory neurotransmitter that always binds to Cl^- channels).

3- According to the speed of their effects:

a- Ionotropic Neurotransmitter: has instant effect, since it binds directly on the ion channel (ex: GABA binds to receptor that is Cl^- channel).

b- Metabotropic Neurotransmitter: has delayed effect, it binds to receptors coupled to enzymes (enzymatic activation reactions) that allow the synthesis of second messengers which in tum stimulate the opening of on channel.

Doc 4 page 242 Action of drugs on synapses.

Motor end plate: Neuro-muscular synapse (between neuron and skeletal muscle).

- The binding of acetylcholine on the past-synaptic receptors (on the muscle), causes the inflow of Na^+ (excitatory effect), and thus the contraction of the muscle.

(Note: Acetylcholine is degraded by an enzyme called Acetylcholinestrase).

Mode of action of curare:

Curare is a competence substance for Acetylcholine, so it blocks (occupy) Acetylcholine receptors, and has anti-effect, it doesn't cause the contraction of the muscle.

Curare has partially similar 3D structure as Acetylcholine.

Pleasure Sensation:

Stimulation for the neuron releasing dopamine causes its release and thus binding on the post-synaptic receptor. It has excitatory effect, causes the generation of EPSP (A.P.) in the post-synaptic neuron, and thus pleasure feeling. Later, dopamine is recaptured into the terminal buds through specific pumps located in the pre-synaptic membrane (doc.b).

Mode of Action of Cocaine:

Cocaine blocks the dopamine pumps, thus inhibits the recapture of dopamine, this leads to high concentation of dopamine in the synaptic cleft. This amplifies the effect of dopamine (more intense and more durable).

Mode of action of amphetamine:

Amphetamine causes the release of dopamine, even without stimulation (doc.c) thus leads to a state of euphoria.

If the treatment with amphetamine is prolonged irreversible destruction of neuron releasing dopamine would be observed (this leads to a state of depression).

Mode of action of benzodiazepine:

Benzodiazepine binds to the same receptor as GABA, which is Cl^- channels; it causes the inflow of Cl^- (IPSP) and has inhibitory effect as GABA.

Therefore, it reduces the concentration of GABA needed to hyperpolarizes the past-synaptic membrane. (Benzodiazepine is an anxiolytic medicine that is anti-anxiety).

Classification of drugs according to their effect:

1- Agonistic substance (drug): it amplifies the effect of the neurotransmitter by:

- The more release of the neurotransmitter.
- The inhibition of the neurotransmitter recaptures.
- Occupying the same receptors and achieving the same effect.

Example: - Amphetamine causes the release of dopamine, so amphetamine is agonistic substance for dopamine.

- Cocaine prevents the recapture of dopamine, so cocaine is agonistic substance for dopamine.
- Morphine: agonistic for encephalin, since it binds to encephalin receptors and has the same effect which decreases the release of substance P.

- Benzodiazepine: agonistic for GABA, it binds to GABA receptor (or different site), and causes the inflow of Cl^- as GABA.

2- Antagonistic substance: it reduces or prevents the action of the neurotransmitter.

Example: Curare blocks Acetylcholine receptors and prevents muscle contraction.

Chapter 15 Regulation of the female sexual hormones

Doc 1 page 294 The sexual cycle

Female genital (reproductive) system consists of:

1- Ovaries: site of oogenesis (production of oocytes).

2- Genital tracts: it ensures sperm cells reception, fertilization, implantation, and fetus development.

Uterus consists of 3 layers (Doc a and doc b)

1- Serous external layer

2- Myometrium

3- Endometrium: consists of basal and superficial functional layer.

The tightly constricted cervix and the mucus (secreted from the cervical glands that are located in the cervical mucosa) form a barrier to infection between the vagina and the uterus, and also hinder the passage of sperm cells throughout most of the cycle (it facilitate the passage only at ovulation days).

Ovarian cycle:

During preovulatory phase, certain number of cavitary follicles will develop (< 15 cavitary follicles per cycle) and one of them becomes Graafian, which is ready for ovulation. During ovulation the Graafian follicle ruptures and releases the oocyte II (blocked at metaphase II). During postovulatory phase the ruptured follicle that remains in the ovary develop into corpus luteum (yellow body), without fertilization, the corpus luteum will subsequently regress (shrink), leaving a nonfunctional corpus albicans (white body) that degenerates at the end of the cycle.

Menstrual cycle (endometrial or uterine cycle):

During menses (menstruation 0 to 5 days), part of the endometrial superficial layer degenerates in which the bleeding is due to the actual sloughing off of the superficial layer of the endometrium, that exposes the blood vessels below and leads to bleeding.

During proliferative phase (follicular phase 5 to 14 days) the superficial layer (degenerated part) begins to thicken and develop, and the tube like glands begin to enlarge, and also the development of the injured blood vessels occurs.

During the secretory phase (luteal phase 14 to 28 days) maximum thickening of the endometrium, spiral form of blood vessels and glands occur leading to the formation of uterine lace (these glands secrete a liquid containing nutrients like glycogen).

Thermal cycle:

Before ovulation, the female's body temperature fluctuates between 36.7 and 37; it rises after ovulation and fluctuates between 37 and 37.2

Doc f: Cyclic changes in the vagina also occur during the cycle (change in the % of differentiated cells reveals these cyclic changes).

Doc 2 page 296 Cyclic evolution of the ovarian hormones

Doc a Interpret:

Exp 1 and 2: this proves that ovaries are responsible for the induction of the cyclic development of the endometrium or the existence of the ovaries is indispensible for the cyclic development of the endometrium.

Exp 3: this indicates that ovaries perform their function via blood.

Exp 4: this proves that certain chemical substances in the ovarian extracts cause the development of the endometrium, and their constant level prevents or inhibits the cyclic variation.

Therefor variable and cyclic secretion of these chemical substances (hormones) into blood by the ovaries controls the cyclic development of the endometrium.

Ovarian hormones include:

1- **Estrogen (estradiol**): secreted from the granulosa and theca interna (of the follicles) during the follicular phase and from the corpus luteum during the secretory (luteal phase). It has important peak before ovulation and less important peak at day 21.

2- **Progesterone**: secreted from the corpus luteum during the secretory phase only. It has important peak at day 21.

Effect of ovarian hormones:

1- Estrogen: it causes the proliferation (thickening) of the endometrial (superficial layer) and vaginal mucosa and also the development of the tube like glands and blood vessels**. It** induces the development of the cervical glands and triggers the endometrial cells to produce more specific receptors for progesterone (make the endometrium more sensitive and ready for receiving progesterone).

2- Progesterone: it triggers the formation of uterine lace (and preserves it) and thus complete development of endometrial glands and blood vessels and their transformation into spiral form. It causes slight increase in body temperature and stimulates gland secretion in the endometrial mucosa and the cervix. Finally, it inhibits the uterine contractions during pregnancy.

Doc 3 page 298 Hypothalamo-pituitary axis and ovarian secretions

The hypothalamo-pituitary axis (doc a)

Certain secretory neurons in the hypothalamus secrete Gonadotropin releasing hormone (GnRH) into blood stream of the hypo-physeal vascular duct (main duct or stem connecting the hypothalamus with the pituitary gland). GnRH stimulates the anterior pituitary to secrete the Gonadotropin stimulating hormones (gonadotropic hormones) FSH and LH.

FSH (follicular stimulating hormone) stimulates the development of follicles (the development and maturation of the cavitary into Graafian follicle during the preovulatory phase).

LH (luteinizing hormone) induces the rupture of the Graafian follicle and the releasing of the oocyte II (ovulation). Also promotes the transformation of the ruptured follicle into yellow body (corpus luteum).

Doc c: normal levels of FSH and LH (for study).

Interpret (Doc b): the experiment shows that the ablation of the anterior pituitary leads to the atrophy of the ovaries and inhibits the cyclic activity, whereas the graft in the area of the pituitary reestablishes the cyclic activity of the ovary, this proves that the anterior pituitary controls the development and the cyclic activity of the ovaries, and this control is ensured through blood.

Interpret (Doc d):

Exp 1: analyze + this proves that these hypothalamic neurons are responsible for the stimulation of the anterior pituitary to secrete FSH and LH.

Exp 2: this confirms that these neurons stimulate the anterior pituitary secretions.

Exp 3: this indicates that the control exerted by the hypothalamus neurons on the anterior pituitary is ensured through the pituitary stem (hypo-physeal vascular ducts).

Exp 4: the presence of highly active substance called GnRH confirms that the exerted control is chemical; at the level of the pituitary stem (duct) the hypothalamic neuron secretes GnRH into the blood which in turn stimulates the secretion of FSH and LH.

Interpret (Doc e):

The experiment shows that a selective lesion in the posterior part of the hypothalamus leads to an abrupt (strictly) fall (from 30 $\mu g.L^{-1}$ to approximately nil in one day) for LH (graph 1) and FSH (from 350 to 50 $\mu g.L^{-1}$ in two days, then it becomes nil in the 6^{th} day graph 2), this proves that the control exerted on the anterior pituitary by the posterior part of the hypothalamus is indispensible for the secretion of FSH and LH.

Interpret (doc f):

This indicates that the lesion of the hypothalamic posterior part can be corrected by the injection of discontinuous and variable (pulsatile) amounts of GnRH.

Deduce: the pituitary gland secretions of FSH and LH are stimulated by the posterior part of the hypothalamus that releases GnRH in a pulsatile (discontinuous) manner.

Doc 4 page 301 Ovarian feedback control on the hypothalamo- pituitary axis

The ovarian hormones (estrogen and progesterone) exert a feedback control on the hypothalamo-pituitary axis which always detects the variations in the blood levels of these ovarian hormones.

First negative feedback: takes place at the beginning of the follicular phase, in which the low level of estrogen causes a slight increase in FSH and LH levels.

Second negative feedback: takes place from 7^{th} to 12^{th} day of the cycle, the moderate level of estrogen (secreted from the developing follicle) induces a decrease in FSH and LH.

Positive feedback: at the end of the follicular phase (before ovulation) the rise of estrogen concentration (peak) exerts a positive feedback on the hypothalamus and the anterior pituitary causing a peak (surge) of LH, which in turn provokes ovulation.

Third negative feedback: during the luteal phase, the high level of estrogen and progesterone induce a fall (decrease) in the blood level of FSH and LH.

Chapter 16: Birth control

Doc 1 page 312 Contraceptive methods

Contraceptive methods: any method of birth control whose primary mode of action is the prevention of procreation**.**

Contraception can be either permanent (irreversible) or temporary (reversible).

Permanent contraception that prevents fertilization includes:

1- Vasectomy: it involves the ligation of the spermiduct (vas deferens) , thus preventing the passage of the sperm cells from the testis to the penis.

2- Tubal ligation: the oviducts are surgically blocked.

Temporary contraception that prevents fertilization includes:

1- Male condoms.

2- Diaphragm: placed in the vagina.

3- Cervical caps and vaginal sponges.

Contraception that prevents ovulation (temporary): using of combination pills that contain synthetic estrogen and synthetic progesterone, this pill would increase the level of estrogen and progesterone that lead to a negative feedback control, thus inhibits the secretion of GnRH, FSH, and LH, hence the peak of LH which normally appears in the middle of the cycle doesn't occur, therefor ovulation doesn't occur.

Mini- pill (temporary): Contains low doses of synthetic progesterone only. It makes the cervical mucus thick and viscous, and thus prevents the passage of sperm cells (it also interferes with ovulation).

Contraception that prevent implantation (temporary): using of **intra uterine device (IUD**): highly effective, in which IUD (flexible plastic) is placed in the uterine cavity, causing the release of large number of

phagocytic white blood cells, thus the endometrium is maintained in chronic state of low grade inflammation, hence the endometrium can't accept the process of implantation.

Doc 2 page 314 Contragestive Methods

Contragestive Methods: Any methods used to interrupt pregnancy (induce abortion) it includes:

1- **Mechanical Methods** (Embryonic suction): terminate pregnancy by curettage in which cannula (already attached to suction pump) is passed into the uterine cavity.

-Note: the risk of maternal death due to induced abortion increases as pregnancy advances (induced abortion up to 12^{th}) week is relatively safe.

2- **Abortion pill (RU486):** Oral pill that contains a molecule (RU486) that is similar in part to progesterone, but it has anti -effect (inhibits the action or effect of progesterone) for progesterone, in which Ru486 can bind to progesterone's receptors, block them and stops the synthesis of the protein that maintains and preserves the thickening of the endometrial uterine lace ,so sloughing off the endometrial superficial layer took place and abortion occurs .

Doc. c: Interpret

Analyze +

Exp.1 and 2: This proves that the combination of estradiol and progesterone is indispensable for the development of the endometrium (complete development to become uterine lace.

Exp 3; same result as exp 1, this indicate that RU486 has no effect on estradiol.

Exp 4: with the increase of the introduced quantity of Ru486 (1 to 5 and then to 30m kg^{-1}), the size and the development of the endometrium had decreased as compared to the endometrium of exp: 2. This proves that RU486 had reduced the development of the endometrium, and has anti-effect for progesterone.

Mode of action of progesterone

The secreted progesterone from the follicular cells of the corpus luteum into blood penetrate the cytoplasmic and nuclear membrane of the target cells (endometrial cells) and binds to specific receptors inside the nucleus (which are considered as transcription factors) stimulating the transcription of a gene and then its translation into a protein that maintains and preserves the thickening of the endometrial lining (uterine lace).

Doc 3 page 316 Medically assisted procreation

1- Artificial insemination (AI): is a technique by which spermatozoa are delivered directly into the uterus (doc a).
AIH: the sperm cells come from the husband; it is helpful mainly in case of cervical troubles or low sperm count.
AID: the sperm cells come from a donor, it is used in case of the husband infertility cannot be treated (for instance no sperm cells in the ejaculate).

2- In vitro fertilization (IVF) and embryo transfer (ET): it is mainly used in case of the blockage in the oviduct that prevents the passage of gametes (doc b page 317).

Note: super ovulation is the growth and maturation of multiple follicles in the woman's ovary due to FSH injections.