Chapter II: Immunology

Doc 1: HLA : a major self marker.

HLA: Human Leukocyte Antigen.

MHC: Major Histocompatibility cmplx:

HLA or MHC molecules: are self membrane markers expressed on membrane of all nucleated body cells.

- They are the expression of 6 genes located on chrm n°6, ~~where~~ A, B, C, Dp, Dq, DR, each 2 alleles of gene are codominant.
- They are involved in graft rejection, where graft rejection depends on the degree of compatibility of HLA between donor & receptor.

The role of HLA is: is the expression of self & non-self antigens on the membrane of nucleated body cells.

- self HLA + self antigen → immunological self.
- self HLA + non-self antigen → modified self.

+ Classification of HLA:

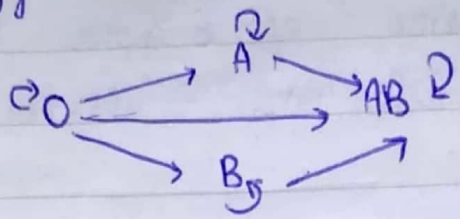
1) HLA I on A, B, C ~~correspond~~ to expressed on all nucleated body cells.
2) HLA II on Dp, DQ, DR expressed on leukocytes "immune cells".

Doc 2: Blood Grp: Another marker.

1) The blood group of an individual depends on ⊕se or ⊖se of antigen ~~of~~ expressed on membrane of RBC. (anucleated cells).
2) Antigens on RBCs are of 2 types: glycoproteins or Oligo Saccarides.
3) Blood tissue is composed of 2 types:
- plasma (serum) it contains water, minerals & organic substances such as antibodies A & B.
- cellular part: Blood cells: Erythrocytes RBC.
  Leukocytes WBC
  Thrombocytes or platelets.

Blood transfusion depends on antigens of donor & antibodies of recipient.

To be on safe side, there must not be a complementary rxn between antigens of donor & antibodies of recipient that leads to Hemagglutination



- Rhesus system: Determines whether the blood grp of an individual is Rh^+ or Rh^- depending on presence or absence of antigen of Rh on membrane of R.B.C.

* Body of a person has no anti-Rh antibodies in the plasma of RBC, but, Rh antigen is considered as a non-self antigen that induces immune system to fabricate anti-Rh antibodies.

Hence indiv having Rh antigen can't donate for one having no Rh antigen.

Hence: O^- : universal donor,

AB^+ : universal recipient.

- antigen: agglutinogen.
- antibody: agglutinin / globulin / immunoglobulin.
- Hemagglutination: is a complementary rxn done between agglutinogen & agglutinin.

* Differences between ABO & RH system.

Doc 3: The non self:

Non-self: Any foriegn element that invades human body.
It's of 2 kinds:

1) pathogen: infectious organism that infects human body cells & causes diseases.

a) microorganism such as: viruses, bacteria, protozoans, fungi.

b) Multicellular organism: worms, tania.

KB. Koch Bacillus (bacteria) ⇒ TB (Tuberculosis disease).

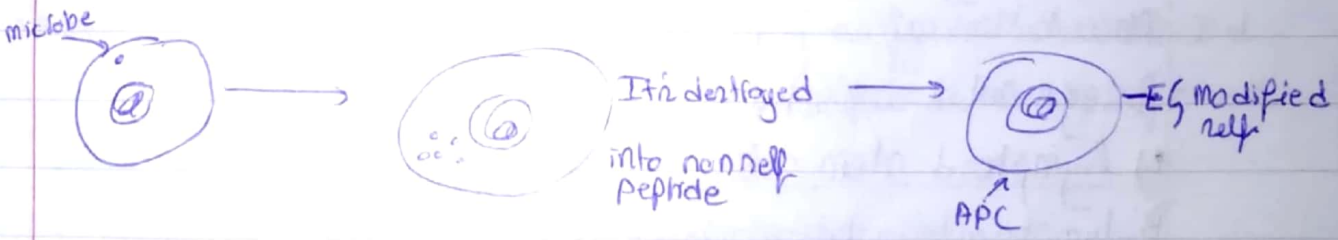
Ameba protozoan:

False feet (cytoplasmic extensions)
pseudo-podia

It deforms its shape & make a shape of fingers, it infects small intestine.

2) Antigen: Cmplx organic substance (mainly protien nature):

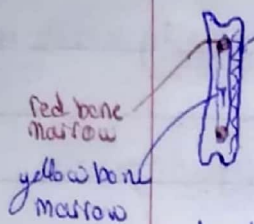
ex: - Toxins (☠ Venum)
- pollen of flowers ⇒ hypersensitivity.
- vaccines: dead or particle microbe
- body cells of another organism.
- modified protien.



APC: antigen-presentic cell: an infected body cell that presents the non-self peptide on its membrane by self HLA molecule.

Doc 4: Cells of the immune system:

All blood cells are produced by bone marrow:



Red bone marrow: pluripotent stem cell: grandmother of all ~~body cell~~ leukocytes.

- Leukocytes: → Myloid stem cells.
  → lymphoid stem cells.

1) Myloid stem cells: secreted in blood:

* Granulocyte:
  - Eosinophils
  - Basophils
  - Neutrophils

It's polynucleated: its nucleus consists of lobes.

It's called granulocyte since its cytoplasm is rich with granules.

Role: phagocytosis: Absorbtion of foriegn solid elements.

* Monocyte:

It's activated by the introduction of non-self → it becomes: macrophage.

Role: phagocytosis: Absorbtion of foriegn solid elements.

* Mast cell:

granulated: has membrane receptors that bind to other membrane receptor clan E, it releases histamine in case of allergy.

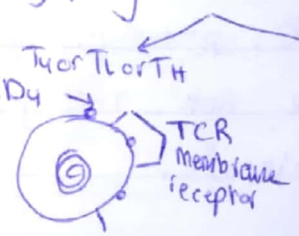
{ T4 is mistrook immune system.

2) lymphoid stem cells:

B-lymphocytes: has membrane receptor called antibody.

- It's activated by introduce of non-self.
- It becomes plasma cell or plasmocyte. it develops its organelles & secrete high amount of clones of antibodies in plasma.

T-lymphocytes:



Role: help other immune cells.

Role: cellular cytotoxicity: Kills infected cells.

Both TS & BLs have huge nucleus & restricted cyto.

Doc5: Lymphoid organs:

They are of 2 types:
1) primary lymphoid organs.
2) secondary lymphoid organs.

1) primary lymphoid organs → bone marrow
→ thymus.

* bone marrow:
- In the site of production of all blood cells including BL & TL.
- In the site of maturation of only BLs.
- maturation of BL: is done by monoselection
- BLs having membrane receptors that recognize self antigen ⇒ they must be eliminated.
- BLs having membrane receptors that recognize non self antigens ⇒ they must be preserved.

* thymus: is the site of maturation of TL:
maturation of TL is done by double selection:
1st selection - TLs that have membrane receptors that recognize non self HLA molecules ⇒ ~~eliminated~~ (eliminated)
- TLs that recognize self HLA molecule (preserved).
2nd selection: TLs that recognize self antigens ⇒ eliminated.
" " " non-self " ⇒ preserved.

2) Secondary lymphoid organs → lymph nodes
→ spleen.

* lymph node: connected by lymphatic vessel through yellowish fluid called lymph.
Its role: Site of IR against non-self coming from infected tissues of extra-cellular fluid.
* spleen: Site of IR against agressors circulating in blood.

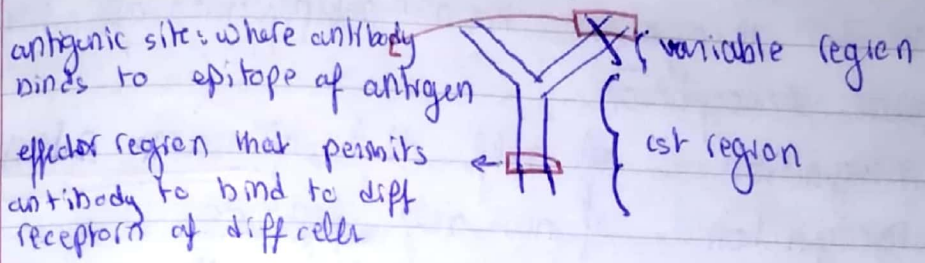
- Maturation: is agenetic mechanism during which lymphocyte become immuno-compitent (ready to defend body against the agrenors (non-self).

Irradiation: destruction of bone marrow.

- Lymphocyte maintain permenant surviellance of the body by circulating through lymph nodes & blood stream of 2ndary lymphoid organs to invade aggrenors.

Doc.6: Antigen Recognition By BLs

- Upon the introduction of a non-self, inactive B lymphocyte develops its organelles (Mitochondria, Golgi body...) and secretes clones of antibodies that are similar in the plasma of the blood ~~cells~~, & becomes plasma cells or plasmocyte.
- Antibody is composed of 3 segments (Y & U peptide chains) connected by disulfure.



Constant region varies slightly between antibodies which permits us to classify them into 5 classes & 3 forms:

1) Monomer: 1 antibody of any class.
2) Dimer: 2 antibodies binding of same class.
3) Polymers: more than 2 antibodies of same class.

* Specificity of antibody:

Antibody doesn't bind to the antigen at whole, it binds to a part of the antigen that's called epitope or antigenic determinant.

Immuno complex: molecular aggregation of diff antibodies binding to diff antigens.

* Cross rxn: Complementary rxn done between same antibody of 2 similar epitopes of ~~two~~ diff antigens.
- Binding between antibody & ~~antig~~ epitope depends on the complementary shapes between both.
- Antibodies can recognize cellular or soluble antigens.

- If the antigen enters to the cell, then it ~~the~~ the function job of antibody stops.

Doc 7: Antigen recognition by Tlymphocyte.

TLs have a membrane receptor called TCR. TCR is of chemical nature formed of 2 peptide chainn

- variable region
- constant region.

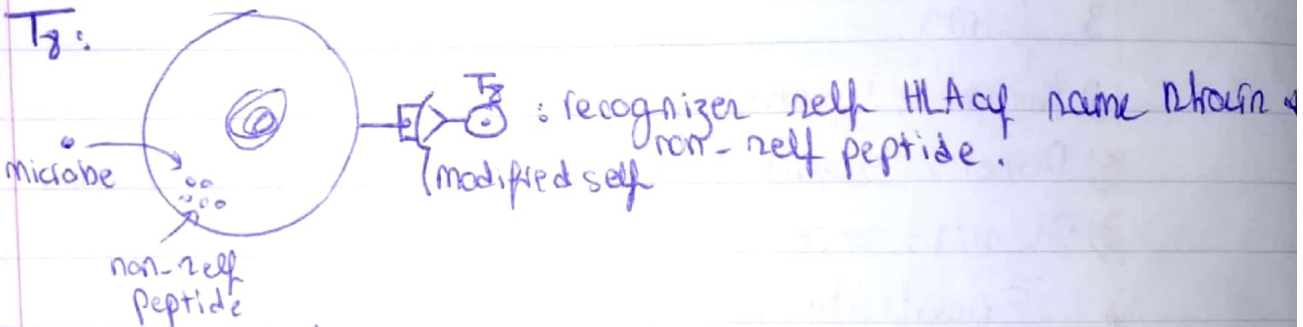
- Tlymphocyte recognizer the non self peptides of infected cells by double recognition.

1st: recognition of self HLA of same strain.

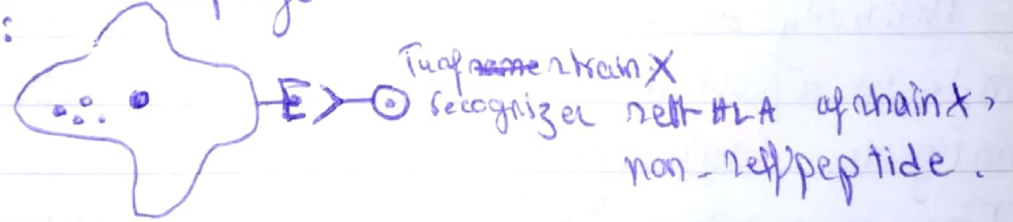
2nd recognition of non-self peptide

non-self peptide is represented on the membrane of APC represented by HLA molecules

T_γ:



T_4:



T_c binds on infected cells.

T_4 binds on immune cells.

Chapter 7: The immune response:

Doc1: non-specific IR.

Non-specific IR: is the immediate IR against non-self ~~without~~, where phagocytes (Granulocytes & Monocytes), attack any non-self without recognition.

- Native barriers of the body:

They are the first line of defense of the body against invadors. They are of 2 types:

Chemical barriers:
- Nasal mucus & hair in nose
- Gastric juice: very acidic
- vaginal secretionn in woman & semen in man.
- sweat: it's very acidic destroy bacteria.
- saliva and tears: they contain enzyme that destroy bacteria

Mechanical Barriers:
- skin it prevents entrance of bacterium, but, when it's injured, it becomes totally permiable to introduction of bacterium
- vibratory cilia in the bronchus
- commensal flora on endometrium
-

- Upon the injury of the skin, ~~to~~ non-self bacteria inter the internal body causing: redness hotness, edema & pain.

Causes of inflamation:
- Upon the introduction of non-self, phagocyte leukocyte ~~& neon cells~~ secrete cytokines in the site of infection.
- Role of cytokine:
- it enlarges the blood ~~capillary~~ vessel diameter, then more volume of blood is coming causing redness.
- increases permiability of blood capillary that leads to leakage of plasma towards the site of infection causing edema.

- edema induce the pain nerve fibers to create a pain message to brain ⇒ feeling pain.
- It's a chemeotactic substance that attracts phagocyte to the site of inflamation.
- Diapedesis: is the migration of phagocyte from its internal medium in blood to site of inflamation, where, it passes through 2 neighboring cells of blood wall capillary.

* steps of phagocytosis:

- Adhesion: where phagocyte comes beside bacterium.
- Absorbtion: invagination of ~~cyt~~ membrane of phagocyte, where phagocyte phagocytes bacterium & stores it in the phagosome.
- Digestion: one of the 3 cases:

1) Phagocyte produces digestive enzymes that digest the bacteria & destroys it ⇒ infection stops.
2) the amount of enzyme produced by the phagocyte is very deficit, so bacteria stays in the stationary state
3) the bacteria multiplies & destroys nucleus of ~~mac~~ phagocyte & ~~comes up~~ forming pus lipidic granules, ~~the~~ phagocyte dies ⇒ infection continues.

Doc 2: Specific IR:

* Specific immune response: immune cells recognize non self & then attack it.
- Humoral IR: effectors are: - cells: BLs
  - molecules: antibodies.

  Its so called since effectors are ~~close~~ in the plasma of blood.
- Cell mediated IR: by TC: cellular cytotoxicity.
- latency time: is the time ~~between~~ taken from introduction of vaccine to beginning of IR.

Doc 3: Induction of Specific IR:

Clones: are grp of cells having same membrane receptors that recognize same antigen.
lymph nodes: site of IR against intruders coming from infected tissues: contains all types of leukocyte.

Non-specific IR induces specific one.

Steps of induction:

- ~~Macroph~~ Phagocyte phagocytes the ~~intr~~ bacteria & digests it, and it presents it by self HLA II on its membrane, and it becomes APC.
- APC moves by ameboid movements towards nearest lymph node.
- T_H found in the lymphe node that have TCR that recognizes by double recognition the modified self, T_H binds to modified self of APC through its TCR: this binding: Activates T_H.

Activation of T_H passes in 2 main stages:

* Proliferation: during which T_H replicates mitotically producing clones of TH.
* Differentiation: T_H differentiates into:

1) memory cells: that live for many years, they are activated by the reintroduction of same antigen within hrs.
2) Interleukin secreting cells: it secrets IL_4 or IL_2 that activates BL or TL respectively.

* BL: Activation of BL passes in 2 main stages.
- proliferation.
- Differentiation: It differentiates into:
- activated BL (plasma cell), antibodies in plasma of blood.

- Tc : proliferation: multiplication
  differentiation → memory cells.
  → effector Tc that destroys infected cells by cellular cytotoxicity.

Serotherapy : immediate therapy through injection of ready made antibodies.

Doc 5: Specific Humoral I.R.

Mechanism of antibody:

1) Neutralization: binds to non-self antigens before entering the cell membrane, then, neutralizi

2) Elimination of intruders by:

* opzinization: binding to a specific microbe facilitating the adherence by macrophage, through their binding to macrophage on membrane receptor through their cst region.
* Activation of complement cascade:
* complement: is a set of protiens "complements" that activate each other.

- Mechanism: antibody binds to the antigen of infected cells, where E_1 binds to it through its cst region, which activates other enzymes forming complement cascade, which perforates the membrane of the cell entering the cytoplasm & destroys its nucleus.

Doc 6: Specific Cell Mediated:

Tc recognizes through TCR modified self by double recognition to non self peptide & self HLA of same strain.

Cellular cytotoxicity:

1) Tc recognizes by TCR modified self.
2) Perforin is secreted by secretory vesicles perforates the cellular membrane of the infected cell causing poly-perforin hole.
3) Granzymes are released by exocytosis enter the cytoplasm of the cell & digests its nucleus causing its death.

Same Tc is used to destroy other infected cells.

Tumor cell: is a modified self cell during which a

mutation happens to a gene causing synthesis of abnormal protien that's considered non-self represented on the HLAI of cell,