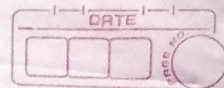


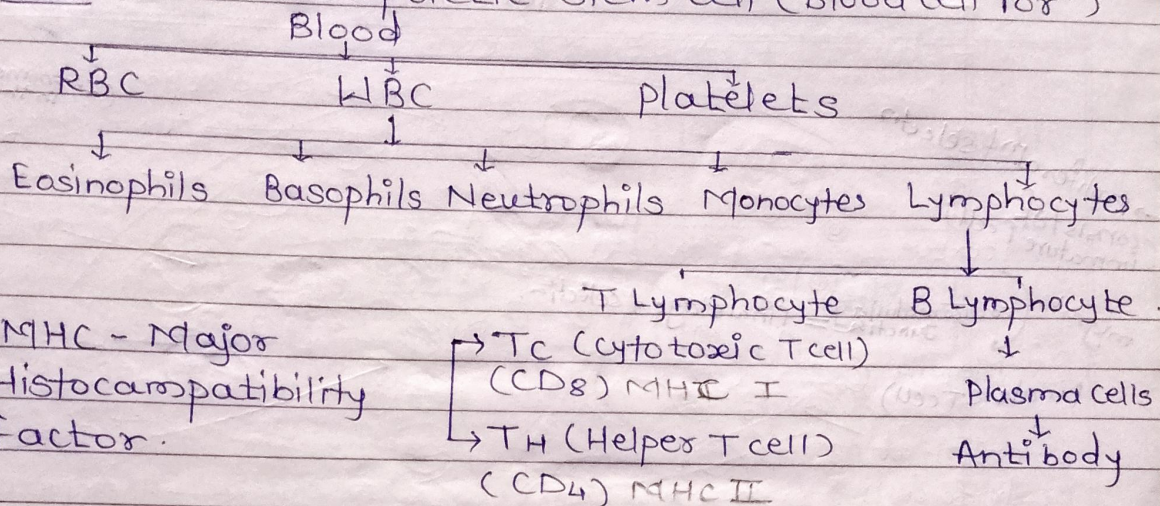
21/9/22
Friday



• Unit 1 :- Lymphoid Organs.

* Lymphoid Organs :-

- HSC - Haematopoietic Stem cell (Blood cell for)



Lymphoid Organs.

Primary Lymphoid organ
(Central)

Secondary Lymphoid organ.
(Peripheral)

— function → formation of Blood cells

• function → Training of cells.

eg.

(i) Bone marrow
(forms B cells)

eg. (i) Spleen

(ii) Tonsils

(ii) Thymus
(forms T cells)

(iii) MALT (Mucous associated Lymphoid tissue)

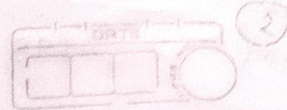
(iv) GALT (Gut associated Lymphoid tissue)

(v) Lymph node

— Cells that forms & mature in bone marrow called as B Lymphocytes.

— Recognition of self & non-self antigen training done in Secondary Lymphoid organs.

31/9/22
Saturday



* Primary Lymphoid Organs :-

1) Thymus :- thymosine - a hormone necessary for T cell development & prod

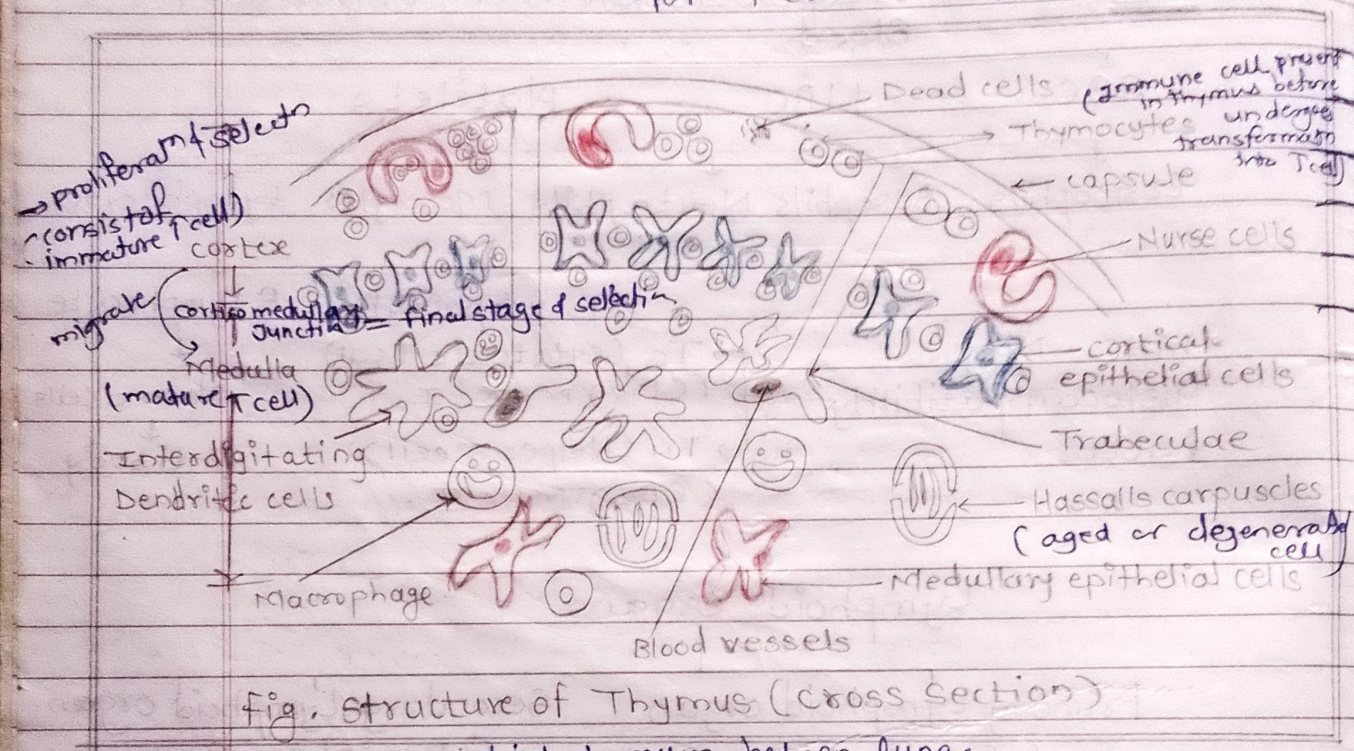


fig. Structure of Thymus (cross section)

behind sternum, between lungs.

- location : Above heart & behind breast bone.
 - bilobed organ ; each lobe called lobule.
 - Large in infancy (weighing 25g at birth & reaches a maximal weight in adolescence 12-19 year (35g))
- * Thymic Education - Positive and Negative Selection :-

(i) Positive Selection :-

- takes place in cortical region of thymus.
- moderate or weak binding of MHC & antigen resulting cell survive.

(ii) Negative Selection :-

- strong binding of MHC & self antigen resulting into cell death by apoptosis.

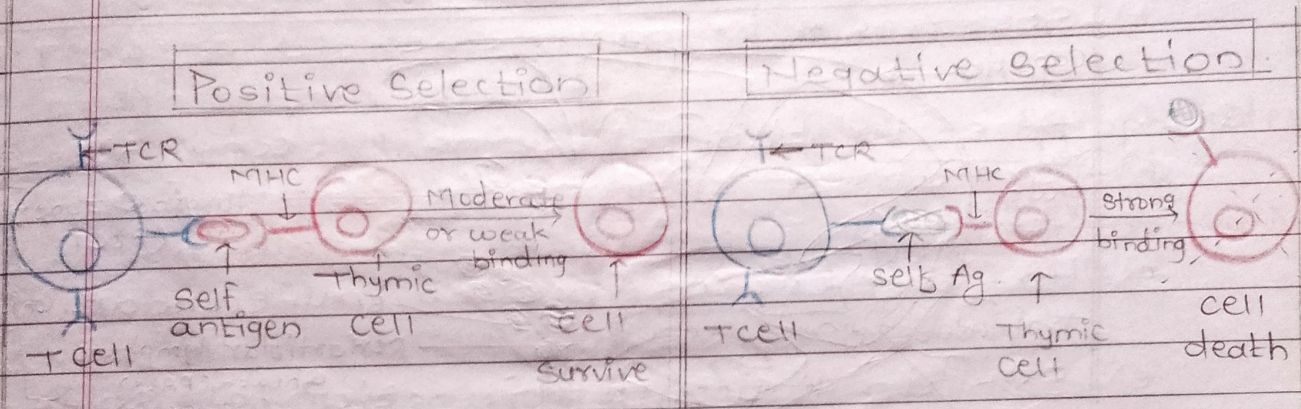
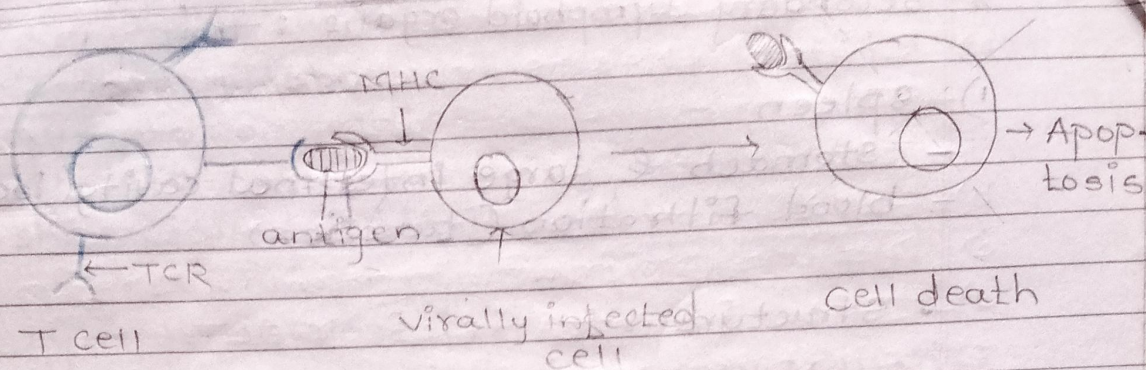


fig. Thymic education - positive & Negative Selection

16/9/22

*) Bone Marrow :-

- Bone marrow located in center of bone.
- In adults mostly in ribs, vertebrae, sternum & bones of pelvis.
- It consists of haematopoietic stem cells which forms all blood cells.

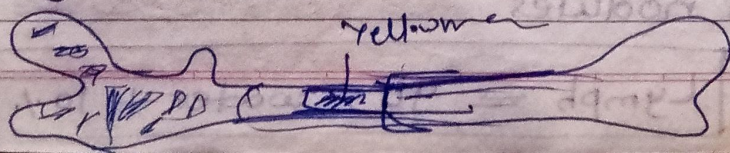
- Two types :

flat bones

(i) Red marrow → contain haematopoietic cells.

(ii) Yellow marrow → fatty cell, produce stem cell which turn into our body cartilage bone & fat cell.

- Bone marrow consists of long trabeculae inside. sponge-like reticular framework.

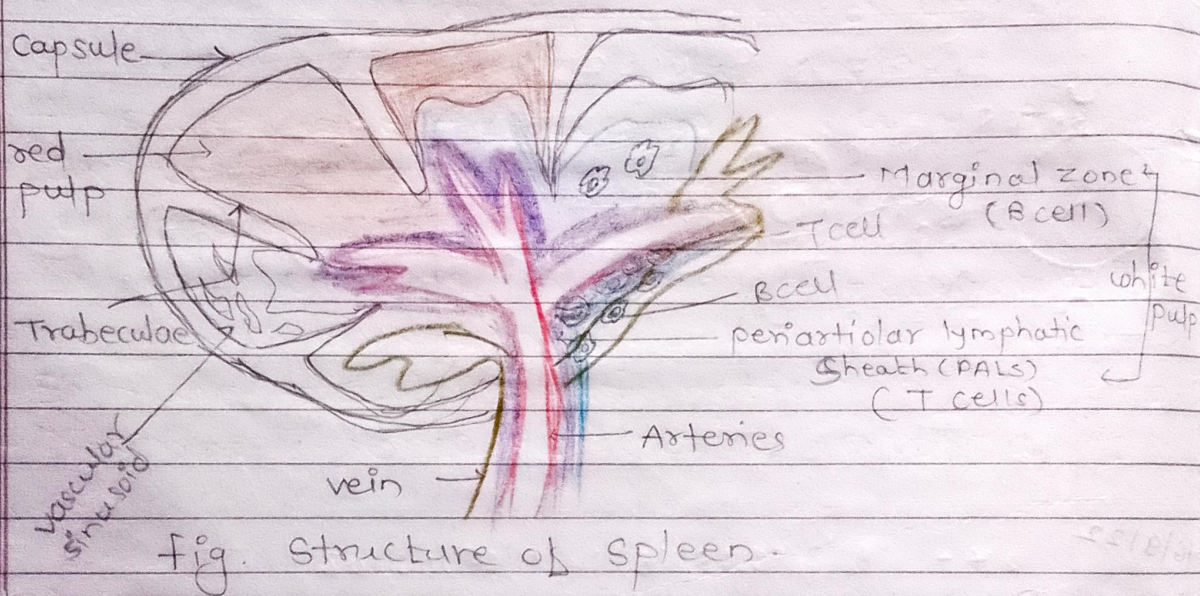


* Secondary Lymphoid organs :-

i) Spleen -

- Stomach & large intestinal cavity (location)
- blood filtration (function)

• Structure :-



17/1/22
Saturday

* Mucous Associated Lymphoid tissue (MALT) :-

* GALT

* CALT

* Lymphatic System :-

- Lymph capillaries - thin walled, dead end.
- Lymph veins / vessels.
- Lymph node
- Lymph duct
- Lymph nodules

Lymph = 90% water + 10% proteins/minerals

2) Lymphatic vessels —
Disease collects lymph from capillaries.
cells

2) Lymphatic node -

Disease cell $\rightarrow$ Lymph collection $\rightarrow$ vessels $\rightarrow$ Lymph nodes $\downarrow$
more microorganism
i.e. Training of B & T cells.

* Lymph :-

Prevent accumulation of excess blood plasma between two cells.

* Path of Lymphs —

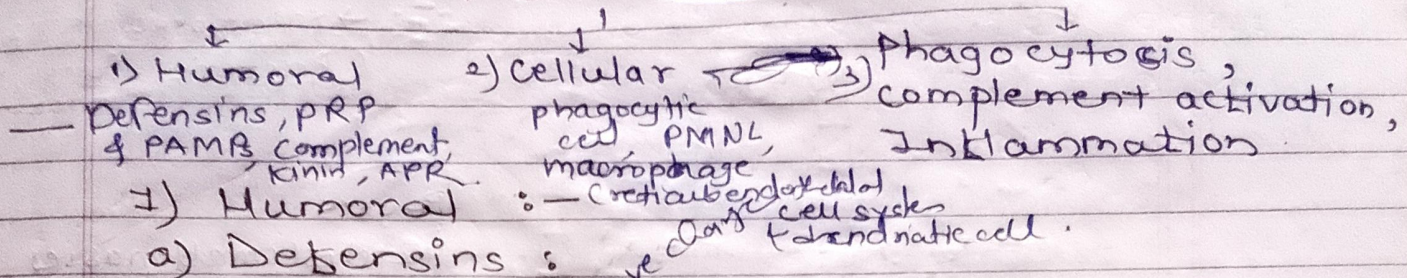
* Path of Lymph :-
Lymph - Lymph capillaries → Lymph vessel ↓

medullary sinus ← trabecular sinus ← cortex sinus ← lymph node ← lymphatic vessel

Efferent lymphatic vessel $\rightarrow$ lymph duct

* Innate Immunity : - / Non specific mechanism of defence
Second line of defence.

Defensins



a) Defensins : - Small cationic peptides

- Broad spectrum antimicrobial.

(Kills all types of microorganisms like fungi, virus, protozoa, Gram +ve & -ve)

• Mechanism :-

- Defensins forms pores to bacterial cells & cytoplasm comes out & cell shrinks & die.

- Selective toxicity:

bacterial cell → phospholipid, peptidoglycan
Human cell → cholesterol

• Structure :-

- Hydrophobic β sheets stabilized by 8 disulfide bonds.

• Class :- 2 class

(i) α defensins :-

(ii) β defensins :-

* α defensins :-

- presynthesize
- stores in granules
- WBC

* β defensins :-

- Not presynthesize
- No storage
- Gene to gene signal
- Leader sequence and acidic region

• Secretion of Defensins :-

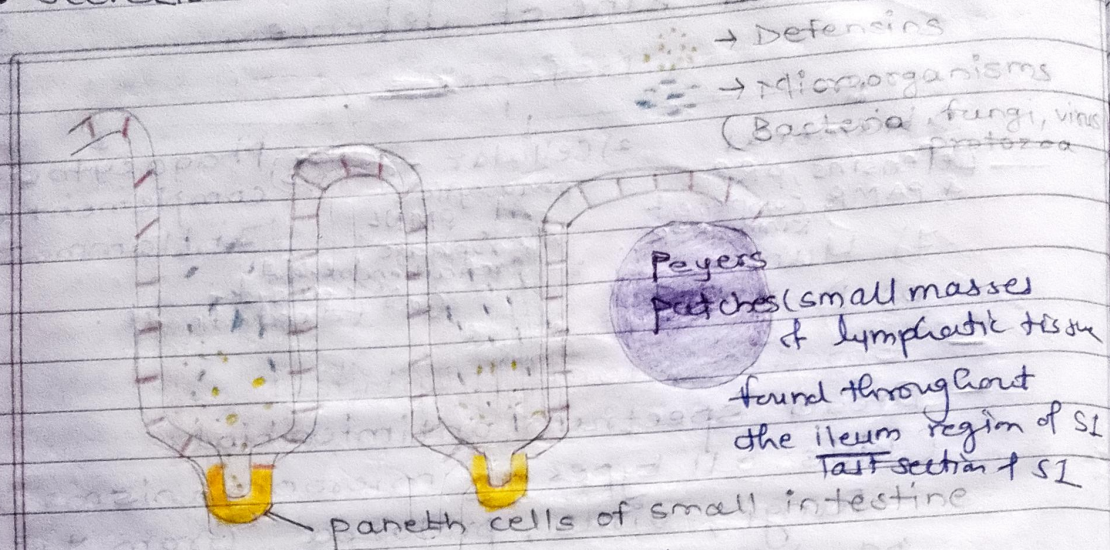


fig. Secretion of Defensins.

b)* PAMP → Pathogen Associated Molecular pattern
OR (MAMP)
Microbial Associated Molecular pattern

c)* PRR → Pathogen Recognition Receptor
Pattern Recognition Receptor.

✓ Immunity in plants

- Entry route of microorganisms in plants by root, leaf & bark.
- PAMP & PRR activity
- PTI immunity.
(Pathogen Associated Molecular pattern Triggered immunity)
- Microorganism → Effector protein binds with plant cell → Effector receptor generate ETI
Effector triggered Immunity.

Cytokinin is the chemical secretory agent of a cell.

C₁, C₂, C₃, C₄, C₅, C₆, C₇, C₈, C₉

Thursday

29/9/22

- d)* Complement :- C₁ — C₉.
- protein molecule
 - present in plasma or blood.
 - kill microorganisms by opsonization process
 - Opsonization → formation of pore through bacterial cell through membrane attack complex (MAC) & kill microorganisms.
 - Enzymes involved → C₃ convertase
C₅ convertase.
 - Each complement divided into a & b subunit
b subunit is large than 'a' except C₂.
- | | |
|---|---|
| b
(large subunit)
↓
opsonization | a
(small subunit)
↓
Anaphylotoxin
(helps in inflammation) |
|---|---|

e)* Kinins :-

- It is a protein
- secreted by leucocytes (WBC)
- present in blood plasma and tissue
- Neutrophils → complete synthesis process.
 - plasma - plasma kinin forming system
 - Tissue - kallikrein system.
- ↳ Kininogen - enzyme responsible for synthesis of kinin.

4/10/22
Tuesday

⊙ APR - Acute phase reactant :-
(Acute phase protein)

- protein in nature
- when APR increases in reactions → called acute phase reactant.
- role in inflammation.
- APR ↓ ses → called negative acute phase reactant.

- Mechanism process :-
 - Injured part $\rightarrow$ cardinal signs $\rightarrow$ redness, Hot, pain
 - cardinal signs + WBC + interleukins $\rightarrow$ liver
 - Inflammation $\rightarrow$ APR

Acute phase reaction

Positive (APR $\uparrow$)

- Help immune system
- Increase vascular permeability
- Trap microbe in clot.
- eg. CRP (C-Reactive protein)

Negative (APR $\downarrow$)

- If there is no inflammation
- Inflammation is cure
- eg. Albumin.

7/10/22
Friday

* Phagocytosis :-

- (i) Polymorphonuclear leukocyte (Neutrophils)
 - (ii) Dendritic cell
 - (iii) Macrophage
- } Phagocytic cells.

• Phagocytic process stages :-

- Activation
- Chemotaxis
- Migration, Margination, rolling & Adhesion
- Diapedesis
- Recognition & attachment
- Phagocytosis :
 - oxygen dependant (oxidative burst)
 - oxygen independant

1) Activation :-

- Activating resting phase phagocytes with help of cytokine & inflammatory substance or bacterial endotoxins.

2) Chemotaxis :-

- Migration of phagocytic cell towards injury.

3) ^{Migration} Margination, rolling & Adhesion :-

- Migrates phagocytic cells rolls & compactly attached at another end near injury.

4) Diapedesis :-

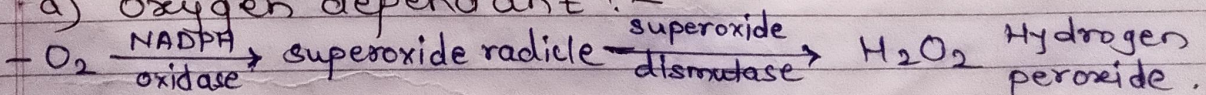
- Phagocytic cells comes out of blood vessel by help of collagen present at blood vessels gets break by collagenase secreting cells by collagenase enzyme.
- Removing phagocytic cells out of blood vessel towards injury by interstitial space.

5) Recognition & attachment :-

- Recognized required phagocytic cell & attach at injury point.

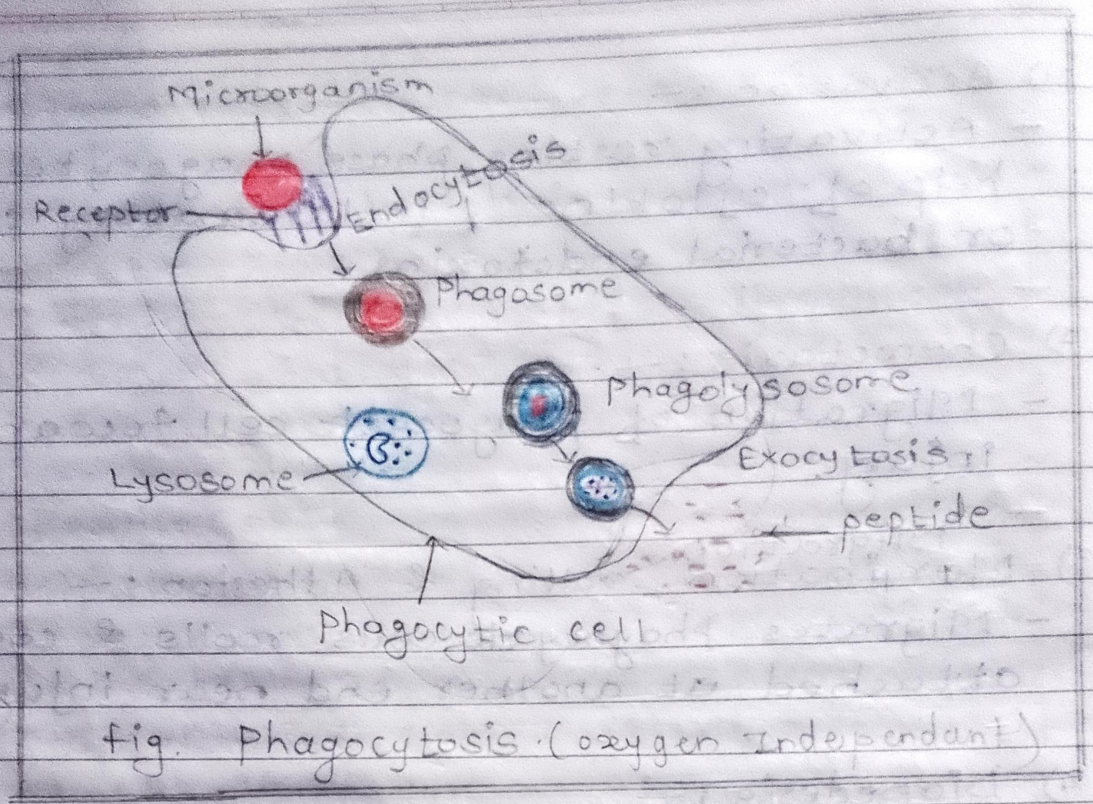
6) Phagocytosis :-

a) Oxygen dependant :-



b) oxygen independant :-

- Kill with enzyme → phospholipase, nuclease, lysozyme, peptidoglycan breaking enzyme.



14/10/22
Friday

Imp * Complement Pathway :-

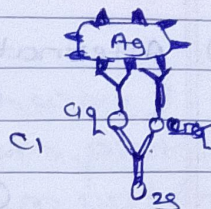
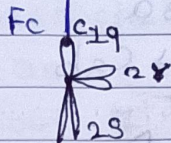
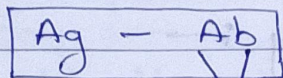
- 1) classical pathway
- 2) Alternative pathway
- 3) MBL pathway

1) Classical pathway :-

- Ag - Ab binding dependant.

Ag - Ab

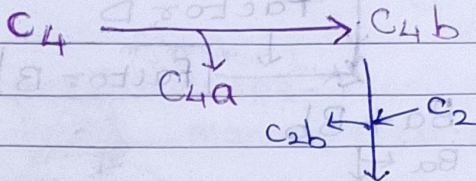
• classical pathway :-



① complement system is a part of innate immune system.

function -

- ① Lysis
- ② opsonization
- ③ Inflammation
- ④ Immune clearance



- C2 & C3 helps to cleave other C proteins.

- proteins from C1 - C9

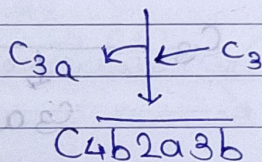
② - these C1 - C9 protein are in inactive state

- Complement divides into 2 fragments: (Cleared)

- ① a - small (inactive)
 - ② b - large (active)
- except for C2 protein

- Antibody dependant pathway (usually IgG or IgM Ab presents)

C3 Convertase

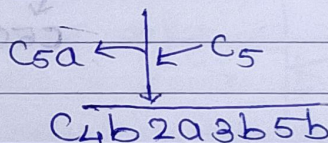


③ * Complement → Enhances or complements our immunity (protein)

- formed in liver & widely distributed among body tissues & fluids.

- complement system shows effect only when it is activated.

C5 convertase

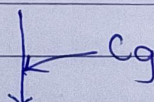


① opsonization →

C3b activates Neutrophils, macrophages

↓ phagocytosis
kills foreign microorganism

Membrane Attack complex (MAC)



② Cell Lysis →

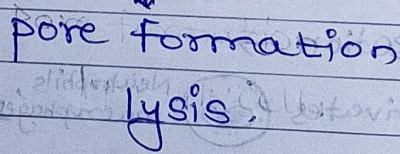
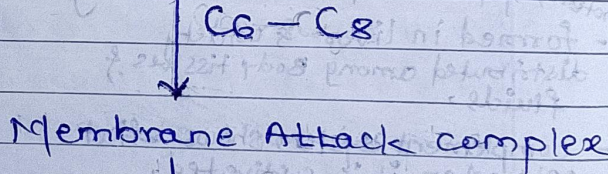
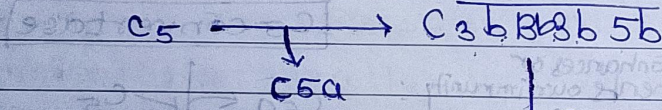
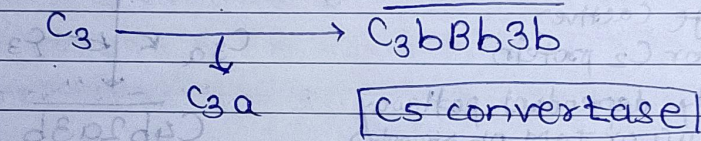
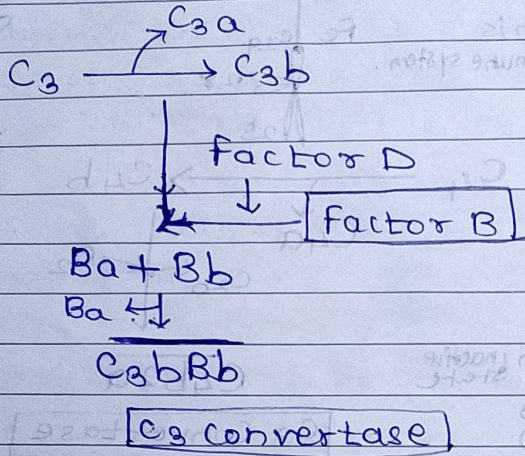
MAC (C5b6789)

↓
Ruptures B's cell wall & destroys it.

pore formation takes place
lysis of cell.

③ Inflammation → release of inflammatory substances, & destruction of pathogen.

2) Alternative pathway :-



Lectin pathway

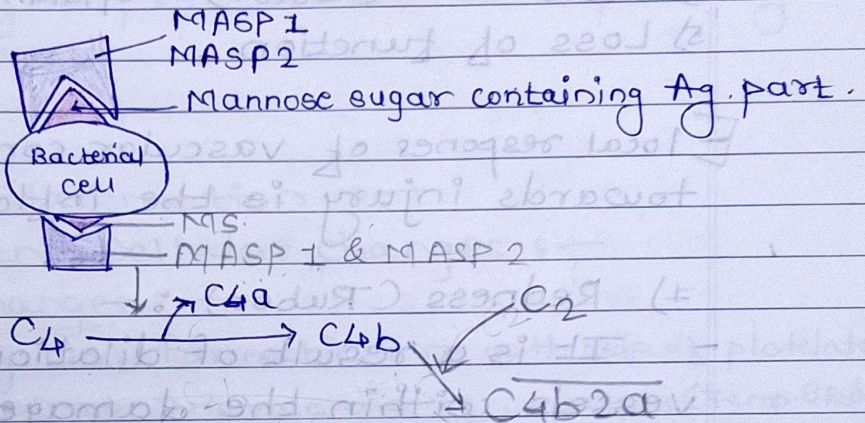
3) MBL pathway :-

(Mannose binding Lectin pathway)

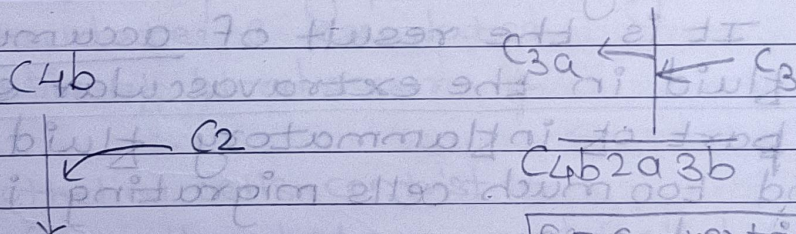
MAASP 1 → MBL associated serum protein 1

MAASP 2 → MBL associated serum protein 2

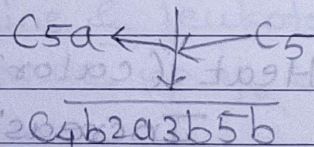
MBLP → Mannose binding Lectin protein



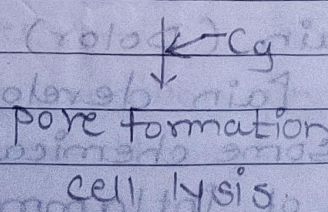
C3 Convertase



C5 Convertase



Membrane Attack complex



* Inflammation :-

• Cardinal Signs :-

- 1) Redness (Rubor) → blood vessels dilates & blood flows
- 2) Swelling (Tumor) → cells, serum & exudates comes out
- 3) Heat (calor) → Blood Flows.
- 4) Pain (Dolor) → cytokinin irritates the nerve tissue so pain starts.
- 5) Loss of function

[Local responses of vascular connective tissue towards injury is the inflammation]

1) Redness (Rubor) :-

- It is a result of dilations of small blood vessels within the damage area.

2) Swelling (Tumor) :-

- It is the result of accumulation of a fluid in the extravascular space as a part of inflammatory fluid exudates. and too much cells migrating into injured area.

3) Heat (calor) :-

- Increasing temperature detected is due to increased blood flow towards injured area.

4) Pain (Dolor) :-

- Pain develops due to swelling or due to some chemical mediators produced at a site of inflammation which irritate nerve endings.

- chemical mediators like kinin & prostaglandins are play major role in pain.

5) Loss of function :-

- After certain time inflammed area is inhibited by a pain either consequently consciously.

14/11/22

Monday

* Inflammation :-

- Vascular and cellular changes :-

* Vascular changes :-

- (i) Temporary clot formation → with help of platelets.
- (ii) Vasodilation → Increase dia. of vessels (Temp. & Redness)
- (iii) Endothelial cell constrict.
- (iv) Increase capillary permeability.
- (v) Transudates & exudates
- (vi) Stasis of blood occur.

(iii) Endothelial cells constrict :-

- Gap formation between endothelial cells.
- histamine, prostaglandins & leukotriens.
- Inner layer of vessels made up of endothelial cells.

(iv) Increase capillary permeability :-

(v) Transudates & exudates :-

- Transudates → pressure condition protein go out
- Exudates → protein go out through constiction.

(vi) stasis of blood occur :-

- Blood cells stops, working at injury site.

• Cellular changes :-

* Steps -

(i) Margination -

- Marginal WBC cells comes flows in marginal area & makes contact with endothelial cells.

(ii) Rolling through receptors -

- Receptors present on Macrophages (any WBC) binds to receptors of endothelial cell & rolling occurs.

(iii) Adhesion -

- Adhesion occurs with help of leukotriens of WBC & CAM on adhesion.

(iv) Diapedesis -

- squeezing out of WBCs through intracellular spaces between two endothelial cells.

(v) Chemotaxis -

- Chemotaxis with help of chemical secretions.

(vi) Phagocytosis -

- Microorganisms engulfed & destroyed.

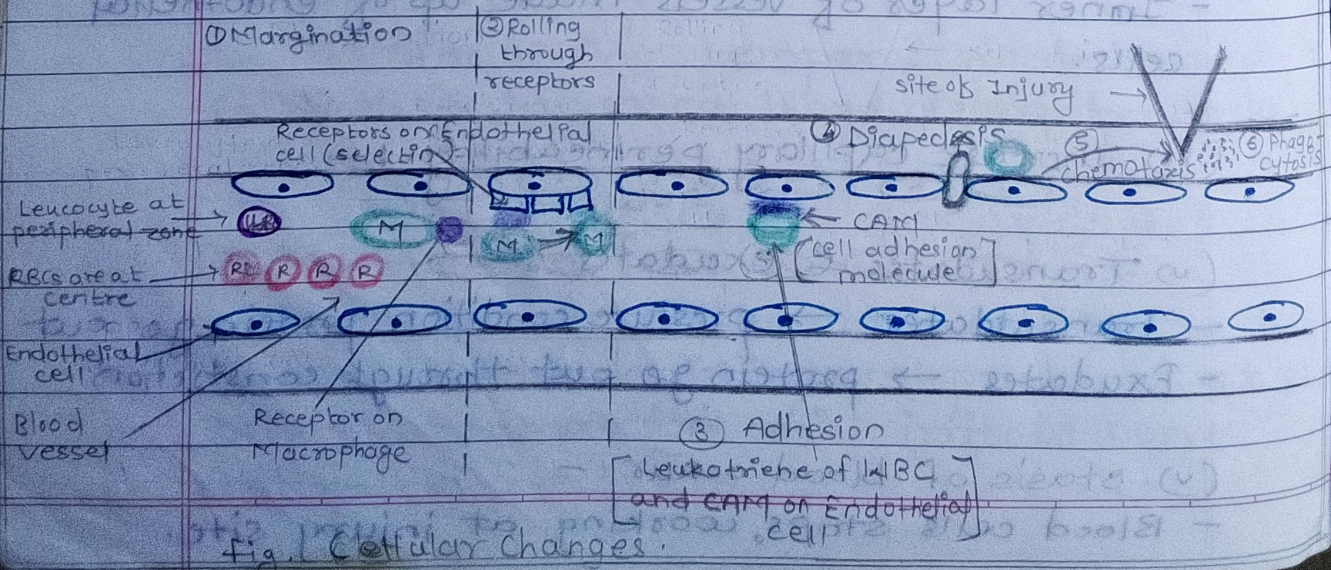


Fig. Cellular Changes.

- Tuesday
DATE 15/11/22
- Phagocytic cells → Macrophage
Neutrophils
Dendritic cells. { antigen presenting cells }

* Cellular components :-

- 1) Macrophage (Reticulo-endothelial system)
- 2) Dendritic cells
- 3) PMNL (Polymorphonuclear Lymphocyte)

1) Macrophage (Reticulo-endothelial system) :-
(Mononuclear phagocytic system)

- Reticulo-endothelial cell system is also known as macrophage system or mononuclear phagocytic system.

- Location : spread throughout the body in different organs & tissue.

It also present in the blood stream.

- Their location often dictate their size & specific shape and sometime known by a special name.

~~ex~~ e.g. (i) Kupffer's cell in liver.

(ii) Microglia in brain.

(iii) Reticular cells in Lymph node, Bone marrow and spleen.

(iv) Alveolar cells in Lungs

(v) Tissue Histocyte or fixed macrophage in subcutaneous tissue.

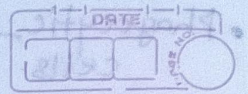
● Functions :-

1) Filter out dead toxic particles in blood & tissue.

- Reticuloendothelial cells filter & destroy particles.

- Recognize foreign substance for presentation is also called as destroyer who able to engulf whole cells preventing them from causing harm to the body.

• spleen → clutter house of RBCs



2) Recognize foreign substance and attack on foreign substance —

- Macrophage attack on viruses, bacteria and other microorganism, neutralising their power to infect and cause damage.

3) Immune presentation —

- Macrophage Recognize and describe nature of a antigen to the next immune cells.

4) Most Macrophage are inactive and motionless it means that they attach themselves to one place and perform their filtering and destruction in that area only.

5) It plays spleen special role i.e. filtration of blood.

- old cells are eliminate from circulation and broken down while maintaing haemoglobin count in blood.

2) Dendritic cells : —

It is accessory cell.

Antigen



Antigen pre. cell



TH



B cell



plasma



Ab

- The another name for dendritic cell is Antigen-presenting cell.

- Dendritic cells are the immune cells that provide link between innate & adaptive immunity.

- Dendritic cells present in those tissue that are in contact with the external environment such as skin, Nose, etc.

- special dendritic cells e.g. Langerhan's cell mainly present in stomach, lungs, etc.

- Dendritic cells get activate & migrate to lymph node interact with T-Lymphocyte to initiate immune response.

3) Polymorphonuclear Lymphocyte (PMNL) (Neutrophils, Basophils, Eosinophils)

- It is also called as granulocyte. It have two or three lobes of nucleus. It have various shape & size.
- It contains granules.

PMNL

① Neutrophil

- 3 to 5 lobes
- Neutrophils**
- active phagocyte cell (first leukocyte to arrive at site of infection)

② Eosinophil

- Bilobed
- after staining nucleus gain red or dark pink colour.
- kill parasite & moderate local inflammation

③ Basophil

- S-shape nucleus
- after staining gain dark blue or purple colour
- Work in allergic conditions.

- After staining nucleus gain light pink colour

- Contains two types of granules :

- (i) primary granules -
- Azurophilic granules

- (ii) Secondary granules -
- specific granules.

- Azurophilic → resemble like lysosome.
- protease, antimicrobial activity.

- specific → Regulation function outside the cell.

Antigen (Immunogen)

* factors affecting on Immunogenicity :-

a) Chemical composition & heterogeneity —

- chemical composition & heterogeneity plays significant role in immunity.
- If there is no heterogeneity antigen fails to stimulate immune response.
- Different amino acid at different site makes it immunogenic.
- Eg. proteins are good immunogen because of high molecular density.

b) Size :-

- Substance with molecular weight about 1 lakh dalton considered as best immunogenicity.
- Substance with molecular weight less than 5000 - 10,000 dalton are considered as poor immunogenicity.

c) Foreignness :-

- It is very important & necessary character.
- phylogenetic distance between two species produce inequality between antigen except collagen & cytochrome C highly conserved throughout evolution.

quality of being easily ~~heart~~ attacked.

d) Vulnerability to Antigen presenting & processing —

- Antigen presentation to T-helper cells through antigen presenting cells after processing is important for both humoral & cell mediated immunity.
- Therefore molecules that cannot be process and presentate to T cells become poor antigenic.

- Large insoluble molecule are more immunogenic than small molecule because large molecule are easily recognized by phagocytic cells.

e) degradability & solubility :-

- The substance which is soluble in the body fluid stimulate the immune response properly.

E.g. Pneumococcal polysaccharide are greater immunogen in mice but not in rabbit because pneumococcal molecules are highly soluble in mice body but not in rabbit.

16/11/22

Wednesday

* Antigenic Determinants :-

- Antigenic determinants are also known as epitopes on antigen.

- Antigenic determinants classified into three types :-

* Antigenic Nature of immunoglobulins -

(i) Isotype

(ii) Allotype

(iii) Idiotype

(i) Isotype -

- found in all normal individual (Iso means same in all members of the species).

- Define subclass & class of a heavy chain and types & subtypes of light chain.

✓ Isotypes are constant region determinants defining types & subtypes of a antibody in given species.

Ab. Types.	Heavy chain
Ig M	μ
Ig G	γ
Ig D	δ
Ig E	ϵ
Ig A	α

(ii) Allotype :-

- Allotype characterized slight difference in the amino acid sequence of a heavy chain and light chain of different individual in same species.
- Even single amino acid difference can give rise to an allotype determinant.
- This are the variation of constant region due to allelic difference of the gene encoding them among the members of the species.
- Allotype is a individual specificity.

Eg.

Antigen

one type

Inject in same species but
diff. individual
(Mice or human)

Mice 1

production
of
antibody

Mice 2

Ig G

Ig G

Antibodies are almost same but the slight difference on constant region because of allelic difference.

(iii) Idiotypic :-

- ✓ Unique antigenic determinant present on individual antibody.
- ✓ These are the variation of variable region among the antibodies in the given individual.
- These variation defines specificity of antibody.

one type of (antigen) which have two epitopes → differ in structure

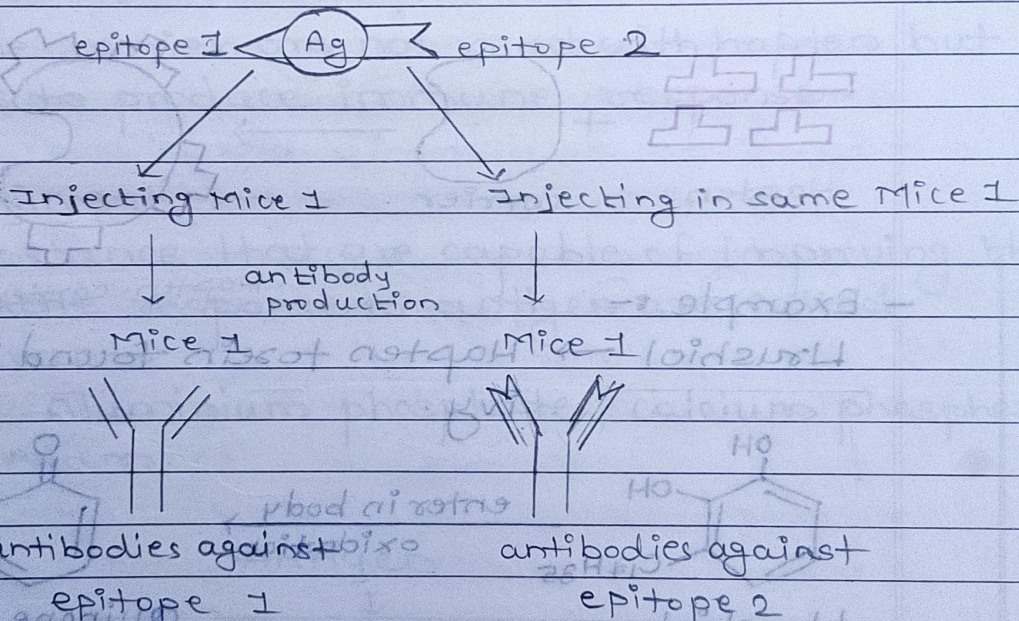
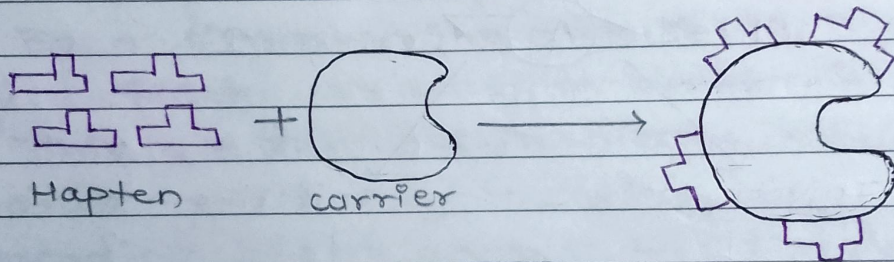


Fig. Idiotypic Determinants.

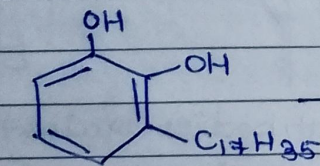
* Hapten :-

- Haptens are the minute molecule that elicit an immune response only when attach to a large carrier such as protein.
- (The carrier ~~ma~~ that does not elicit an immune response itself)
- Not Immunogenic but antigenic.
- Low molecular weight compound cannot activate helper T cells due to inability to bind with MHC molecule.



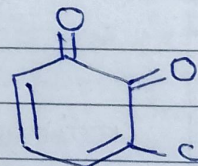
- Example :-

Urushiol $\rightarrow$ Hapten toxins found in poison ivy.



Urushiol

enters in body
oxidation



Quinone derivative
highly reactive.

Production of
Antibodies

Present
to
lymphocyte

Recognized
by langerhans
& other DC

React with skin
protein & form

Urushiol-protein conjugate

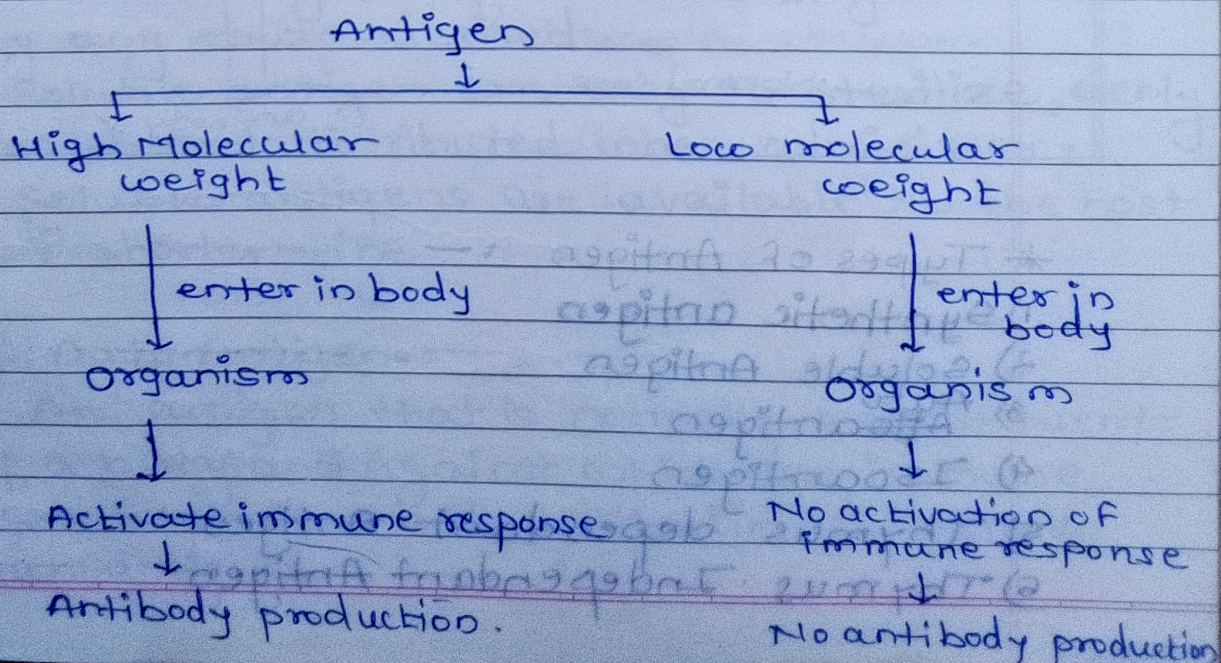
- Eg. Penicillin, Dinitrophenol, Urushiol.

* Carrier :-

- It may be immunogenic or non-immunogenic protein to which an incomplete antigen known as 'Hapten' get bind & form a conjugate.
- While hapten is not immunogenic by itself conjugation to the carrier makes it immunogenic.
- When self protein are appropriately modified by the hapten they may serve as carriers in vivo a mechanism is operating in allergy to drug.
- The carrier are not react with hapten but helps to produce immune response.

* Adjuvant :-

- Substance that are capable of improving the immune response to antigen are called adjuvant.
- Eg. Aluminium phosphate, calcium phosphate, Alum.

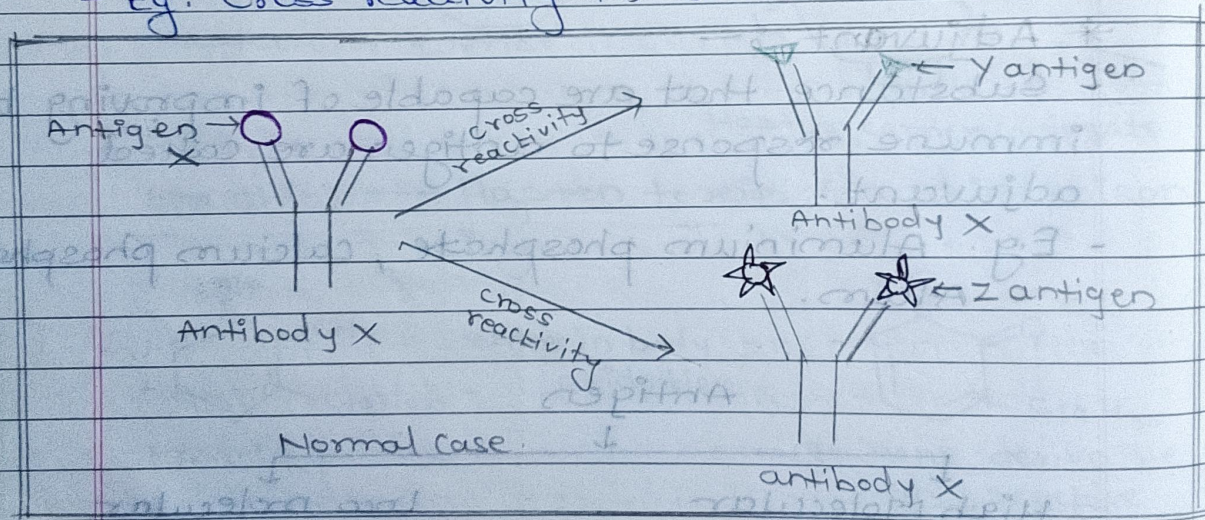




Low. molecular + Adjuvant → production of Antibody
wt. antigen

*** Cross Reactivity :-**

- one antibody can bind with unrelated antigen but ~~he~~ it have a same epitope.
- Antigen - antibody reaction are highly specific but in some cases antibody generated by one antigen can cross reactive with unrelated antigen. Such cross reactivity occurs if two different antigens are highly specific and share a very similar epitope.
- Eg. Cross reactivity in blood.



*** Types of Antigen :-**

- 1) Synthetic antigen
- 2) Soluble Antigen
- 3) Auto ~~Ant~~ antigen
- 4) Isoantigen
- 5) Thymus dependant Antigen
- 6) Thymus Independant Antigen

1) Synthetic Antigen —

- Derived exclusively by laboratory synthesis and not obtain by living cells.
- Synthetic antigens are polypeptide in nature and having a backbone containing amino acid generally include Lysine.
- Contributed much more to our knowledge of epitopic structure & function.
- Have well defined specificities by specific arrangement, number, nature of amino acid.
- Size of a molecule is less important with synthetic antigen compared to natural antigen.

2) Soluble Antigen —

- Antigen that remain in solution after the foreign particles have been removed with the help of centrifugation is called soluble antigen.
- Can be more easily measured, characterized & purified.
- It is easily store can be safely administer by any route desired.
- Soluble antigen can easy to sterilize, evenly absorb and distributed when administer.
- Soluble antigens are available to the host ~~for~~ shorter time

3) Auto-Antigen —

- An antigen that is normally a constituent of a body and against which the immune system produce autoantibodies is called auto-antigens.

- It is normal protein & sometime DNA or RNA i.e. identified by the immune system of a patient suffering from autoimmune disease.
- Under the normal condition, this antigen should not be target of the immune system but due to genetic or environmental factor the normal immunological tolerance for such antigen has lost in this patient.

4) Isoantigen —

- Antigen found in a members of a species that stimulates immune response if injected into genetically different members of the same species are known as iso-antigen.
- These are the antigens carrying similar determinants in a given individual,
- An iso-antigen is a antigen for isograft

Thymus Dependant Antigen

- An antigen that requires interaction between T and B cells to initiate antibody production is called Thymus dependant antigen.
- Soluble antigens

Thymus Independant Antigen.

- The antigen that not requires interaction between T cells to initiate antibody production is called Thymus independant antigens.

- Bacterial cell wall components.
e.g. lipopolysaccharide, flagella, capsular polysaccharide.

- | | |
|---|--|
| <ul style="list-style-type: none"> • Immunogenic memory present • Antigen processing and presentation is needed. • Immunogenic over a wide range of dose | <ul style="list-style-type: none"> • No Immunogenic memory. • Antigen presenting & processing is not needed. • Dose dependant immunogenic response. |
|---|--|

* Immunoglobulin 2 -

a) Characteristics of domain structure -
 of light chain and heavy chain - domain and antigenic nature of immunoglobulin molecule.

b) Molecular basis of antibody diversity -
 (kappa - lambda & heavy chain)

a) Characteristics of domain structure -
 Immunoglobulin domain is type of protein domain that contains -

