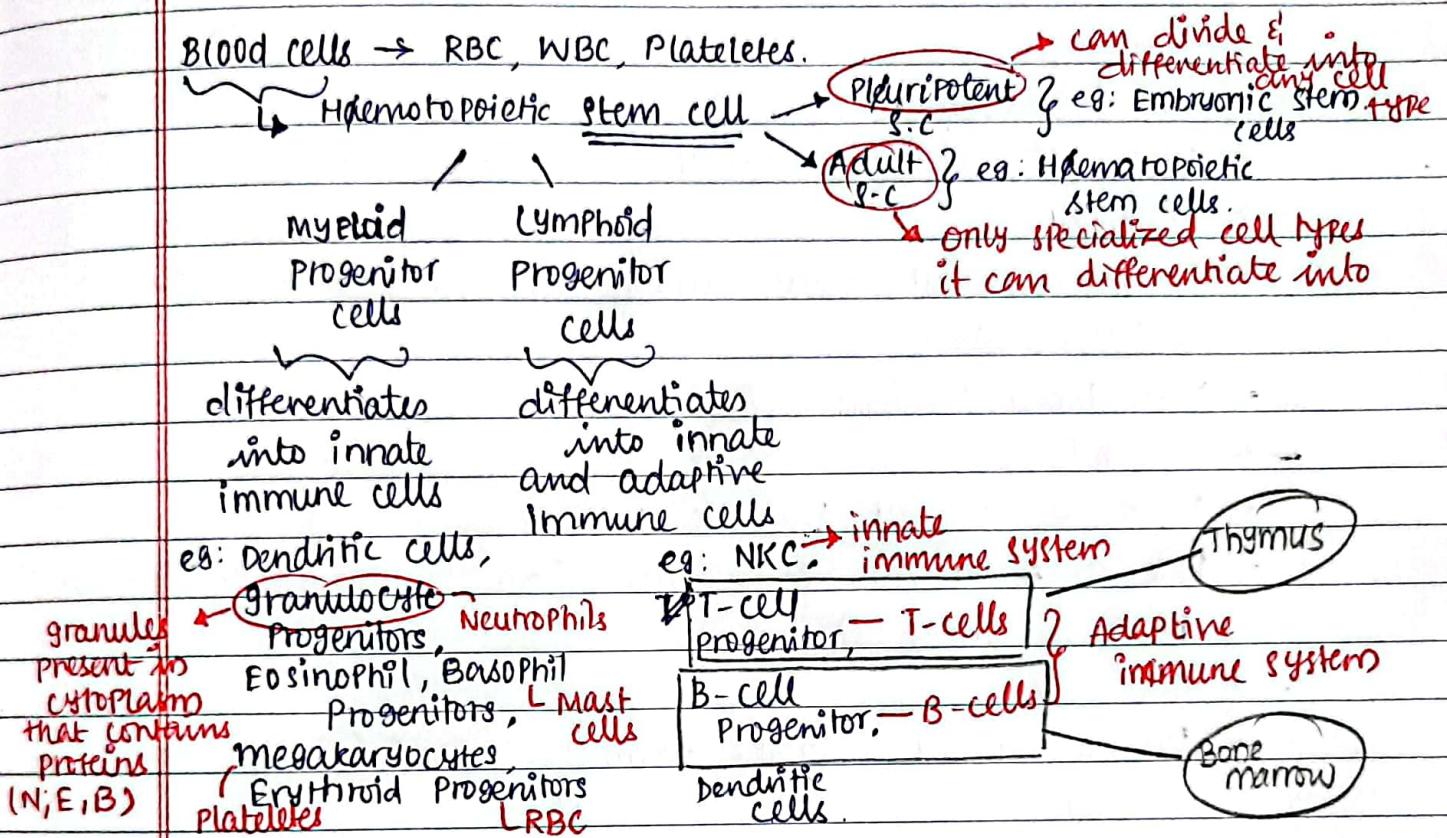


CELLS & ORGANS OF THE IMMUNE SYSTEM

Cells of the immune system :-



NOTE: Neutrophils are the MOST ABUNDANT Leukocyte present in the blood.

during infection, Neutrophils levels increase since they form 1st line of defense and thus can be used as an indicator of infection.

Myeloid lineage :-

- Granulocytes**
- Presence of granules in the cytoplasm
 - Multi-lobed (mostly bilobed) nucleus
 - 4 types of Granulocytes : Neutrophils, Basophils, Eosinophils, Mast cells.

→ Neutrophils

- First cells to arrive at site of infection
- High levels - indication of infection
- Phagocytize pathogens and can generate antimicrobial agents
- Most abundant leukocytes.
- Usually defense against bacteria

→ Eosinophil

- Defense against multi-cellular infection (e.g. parasitic if pathogens)

- Multi-lobed Nucleus

→ Basophil

- Defense against parasitic pathogens

- Role in allergic reactions (due to presence of Histamines in their granules)

→ Mast cells

- Defense against parasitic worm pathogens (such as parasitic worms)

- Takes part in allergic reactions.

Professional APCs :

①

②

③

Macrophages, Dendritic cells and B-cells,

Myeloid origin

Lymphoid origin

Myeloid APCs are cellular bridges b/w innate and adaptive immune system.

These APCs will have MHC → presents a part of Phagocytizes pathogen and co-stimulatory molecules expressed on them.

→ Macrophages

- Monocytes differentiate into it.
- TYPES : 1) Tissue - resident Embyronic origin
Monocytic origin
- Phagocytic
- Phagosomes fuse with ~~two~~ lysosomes to form Phago-lysosomes that destroys the engulfed pathogens.
- Involves in inflammatory response
 - ↳ due to dilation of Blood vessels near site of ~~an~~ infection since it requires more blood flow to supply the immune cells.
- Dendritic cells
- Extensive tentacles-like structure
- Most imp. APC.

Lymphoid Lineage :-

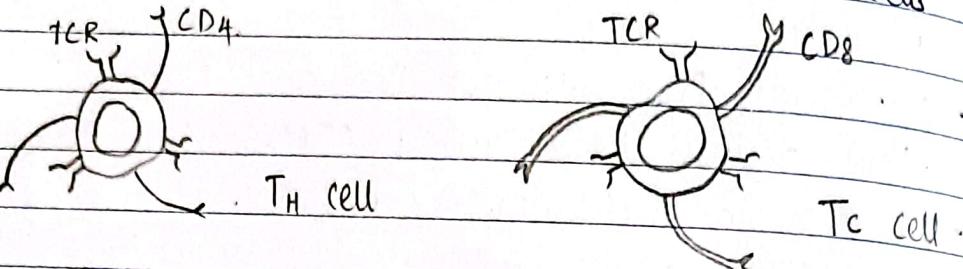
- Natural killer cells, B-cells, T-cells.
- Lymphocytes possess diff. types of surface markers known as CD (cluster of differentiation).
- CDs can be used to distinguish b/w diff. types of lymphocytes.
 e.g: $CD_4 \rightarrow$ diff. b/w T_H and T_c (Present in T_H only)
 $CD_8 \rightarrow$ diff. b/w T_H and T_c (Present in T_c only)
 $CD_{45} \rightarrow$ diff. b/w lymphocytes from other cells (Present in all lymphocytes)
 $CD_{28} \rightarrow$ diff. b/w T and B (Present only on T cells)

NOTE: Any nucleated cell can behave as APC however some class of cells are specialized in presenting: Professional APCs.

→ T-lymphocytes

- Progenitors arise in bone marrow but mature in Thymus.

- TYPES: T_H — T helper cells, T_c — T cytotoxic cells



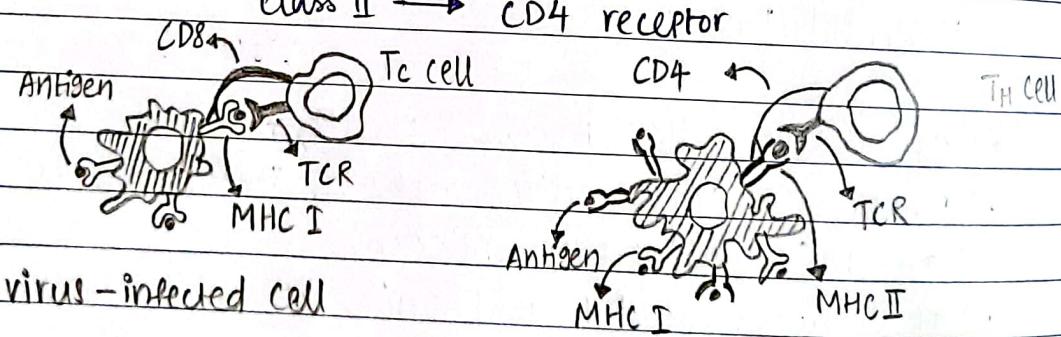
- All T-lymphocytes will express a T-cell receptor (TCR).

- TCR can recognise ONLY an antigen present on the MHC in an APC.

- CD4 and CD8 helps binding of TCR with Antigen.

- MHC TYPES: Class I → Present in all nucleated cells.
 Class II → Present only on Professional APCs.

- Recognition: Class I → CD8 receptor
 Class II → CD4 receptor



NOTE:

Professional APCs have both class I & class II MHC.

- T_{reg} — T regulatory cells

They suppress immune response after clearing pathogens.

→ B-lymphocytes

- Site of maturation is in Bone marrow.

- Display membrane-bound immunoglobulin (Antibody)

- Upon encounter with antigen, B-cells differentiate into :
 - Plasma cells: Antibodies are secreted, short-lived
 - Memory cells: Long-living, Differentiates into effector cells upon future pathogenic encounters
- Natural killer cells (NK cells)
- Innate immune cell response
- Large, granular
- (ix) - recognise tumor or /and virus-infected cells.

Organs of the immune system :-

- primary lymphoid organs: immune cells mature and develop.
eg: Thymus, Bone marrow
- secondary lymphoid organs: site of action of immune cells; they travel through blood and lymph systems.
eg: spleen, MALT (mucosa associated lymphoid tissue), Appen Peyer's patch, Tonsil, lymph nodes
- Lymphatic system carries extracellular fluids from peripheral tissue and forms the colourless lymph fluid. The lymph carries its fluids to the lymph nodes where lymphocytes act on pathogens/infected cells.

THYMUS:

(inner) (outer)

- can be divided into : Medulla, Cortex
- Naive and immature T-cells are called Thymocytes.
- Thymus is connected to blood circulatory system : The blood vessel is present in the cortico-medullary region.
- T-cells enter Thymus via the blood vessels.

- Thymocytes are called DN (double negative) T-cells because they lack either of the two markers: CD8, CD4. They still haven't differentiated into TH or Tc cells.
 - Upon maturation, they become DP (double positive) T-cells since they possess both markers.
 - (X) - DP T-cells undergoes Thymic selection to induce tolerance in them.
 - It will interact with Cortical Epithelial cells (self cells). Indicates lack of tolerance: inability to recognize self cells
 - If DP T-cells binds very strongly with Cortical Epithelial cells, they will die out: Negative Selection.
 - If DP T-cells binds intermediate with Cortical Epithelial cells, they will be selected: Positive Selection.
 - The selected cells would then complete maturation and be selected for any one of the surface marker (the other marker will randomly be removed). This single positive SP (SP) T-cells (which would now be differentiated into either TH or Tc cells depending on the marker present), will move to the Medullary Epithelial cells.
 - In the Medullary Epithelial cells, the T cells will undergo a second set of Thymic selection for any negative selection, in order to ensure any escaped T-cells from 1st negative selection will be destroyed in the 2nd selection.
 - The selection of TH or Tc cells is random, however, often $\text{TH} : \text{Tc}$ ratio is 2 : 1. Since it's imp. for activation of exceptions arise in cases of - other lymphocytes.
 - High infection rate — too high levels of Tc cells are produced
 - AIDS — Attacks TH cells, so TH levels drop.
 - The naive mature T cells enter the blood vessels to encounter any antigens.
 - If has a T-cell receptor
- still no encounter with antigen

Experimental models \Rightarrow Nude mouse \rightarrow Prone to infections!
[compromised immune system]

SECONDARY LYMPHOID ORGANS :-

Site of interaction b/w naïve B/T cells and antigens/APCs.
Present around mucosal lining of gut & respiratory tract

Mainly - • Lymph nodes (most specialised)
 • Spleen
 • MALT

Lymphatic system (carries antigens to lymph nodes) \leftrightarrow Circulatory system (carries naïves T/B cells to nodes for antigen encounter)

\downarrow connected to circulatory system — Blood-related antigens are dealt

Tissue lymphatics \rightarrow Lymph capillaries that creates a mesh-like network around the tissues. The lymph (extracellular fluids leaked by the tissue) is collected by them.

Lymph nodes \rightarrow populated with naïve B & T cells are present and lymph gets send to these sites.

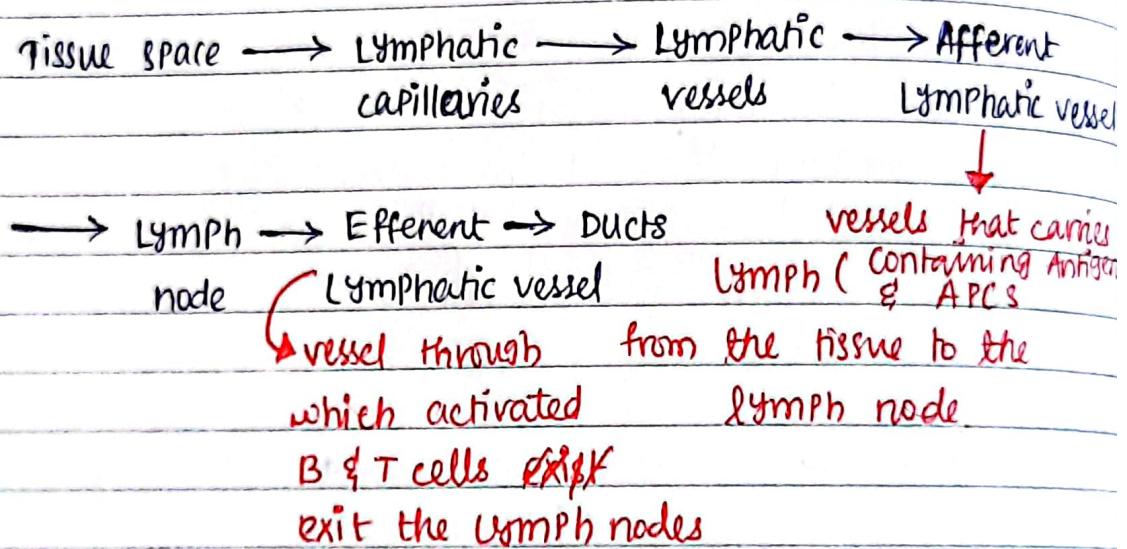
Lymph ducts \rightarrow Thoracic duct [collect lymph from all parts of the body except from right arm & right head]
 \rightarrow Right lymphatic duct [lymph from right arm & right head is collected by it]

Lymph from Thoracic duct enters the heart through left subclavian vein while lymph from Right lymphatic duct will enter the heart from right subclavian vein.

NOTE:  The lymphatic system of our body is connected to our blood circulatory system.

Naïve mature T/B cells gets activated upon encounter with antigens at the lymph nodes and undergoes clonal selection, where only a particular type of B or T cells are selected, mature and divide.

Lymphatic System:-



The lymph nodes are circulated with blood capillaries allowing entry of naïve mature B/T cells.

Lymph nodes

NOTE : In all secondary lymphoid organs, they have a specific site for maturation of B or T cells.

NOTE : Often they mature in a group called follicles.

(i) Lymph nodes :

Entry \Rightarrow via Afferent Lymphatic vessel

Exit \Rightarrow via Efferent Lymphatic vessel

3 layers of lymph node -

1) Cortex \rightarrow Site of maturation for B-cells

2) Para-cortex \rightarrow Site of maturation for T-cells

3) Medulla → Region where activated B & T cells exit via Efferent lymphatic vessel.

Follicular Development - [mostly for B-cells]

Primary lymphoid follicle → Secondary lymphoid follicle → Effector cells (with Germinal center)

Germinal center: Site of B-cell Activation.

(*) Somatic Hypermutation → B-cells undergoes further random mutation to generate more affinity for the antigen.

Paracortex region is concentrated with APCs such as Dendritic cells. When naïve T-cells encounter Antigens presented by Dendritic cells, they get activated into effector cells. They do not undergo SOMATIC HYPERMUTATION.

(ii) Spleen :

- The largest 2° lymphoid organ.
- It is not connected with lymphatic system rather with the circulatory system.
- It only encounters blood-circulated antigens.

2 regions of Spleen -

- 1) Red pulp → High levels of RBC Blood vessels.
- 2) White pulp → Higher levels of lymph vessels.

Periarteriolar lymphoid sheath (PALS) → maturation site for T-cells
Marginal zone → site of maturation for B-cells

(iii) Mucosa associated lymphoid tissue (MALT):

- Found along mucosal lining.
- Gut-associated lymphoid tissue (GALT)
- Bronchus-associated lymphoid tissue (BALT)

e.g: Peyer's patches (Present in intestine).

M cells connected to Peyer's Patches present on the intestine lining. M cells can be distinguished by absence of microvilli.