Microbiology 1

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ACADEMY

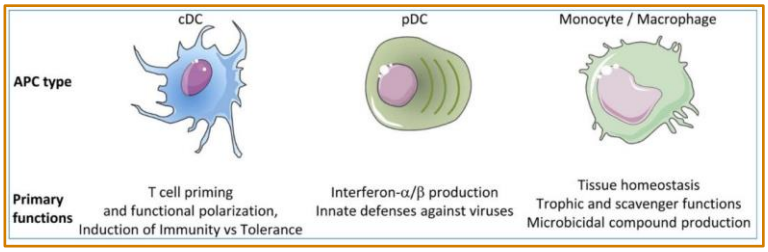
Cells and tissue of the immune cells

- Although most of these cells are ***found in*** the blood, their responses to microbes are usually localized to tissues and are generally not reflected in changes in the total numbers of circulating leukocytes
- ***Phagocytes including*** neutrophils and macrophages, are cells whose primary *function* is to identify, ingest, and destroy microbes.
- Phagocytes also *communicate* with other cells in ways that promote or regulate immune responses.

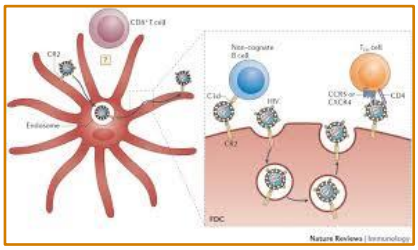
- **Cells of the immune system:**
  - Phagocytes
  - Mast Cells, Basophils, Eosinophils
  - Antigen-Presenting Cells
  - Lymphocytes

- **Antigen presenting cells:**
  - *Function: APCs* are specialized cells that capture and display microbial and other antigens to lymphocytes. They also provide signals that stimulate the proliferation and differentiation of lymphocytes, linking the innate immune system to the adaptive immune system.
  - *Types of APCs:*
    - ✓ Dendritic Cells: The primary APC involved in initiating T cell responses. They are highly effective at antigen presentation.
    - ✓ Macrophages: Present antigens to T lymphocytes during various immune responses.
    - ✓ B Cells: Can also present antigens to T cells in certain immune responses.
  - *Role in Immunity:* APCs are essential for bridging the innate and adaptive immune responses, acting as components of both immune systems.

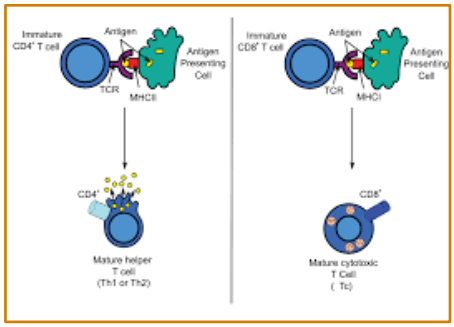
- **Dendritic Cells** (APC)
  - *Key Role*: Dendritic cells are the most important APCs for activating naive T cells and linking innate and adaptive immune responses.
  - *Structure & Distribution*: They have long membranous projections (dendrites) and are phagocytic. They are widely found in lymphoid tissues, mucosal epithelium, and organ parenchyma.
  - *Activation & Migration*: Upon activation by microbes, conventional dendritic cells (cDC) in tissues like the skin, mucosa, and organs migrate to lymph nodes, where they present microbial antigens to T cells.
  - *Types* of Dendritic Cells:
    - ✓ Plasmacytoid DC (pDC): Specialized in producing type *I interferons* in response to viral infections.
    - ✓ Conventional DC (cDC): Specialize in *antigen capture*, processing, and presentation for T-cell priming and activation.



- **Follicular Dendritic Cells** (APC)
  - *Location & Structure:* FDCs are found in germinal centers of lymphoid follicles in lymph nodes, spleen, and mucosal lymphoid tissues. They have membranous projections and are intermingled with activated B cells.
  - *Origin:* Unlike most dendritic cells, FDCs are not derived from bone marrow precursors; they have a mesenchymal origin and are non-migratory.
  - *Function:* FDCs trap antigens that are complexed to antibodies or complement products. They display these antigens on their surfaces for recognition by B lymphocytes, playing a crucial role in B cell activation and antibody production.



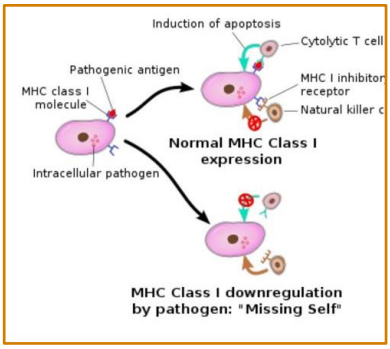
- **Antigen-Presenting Cells for Effector T Lymphocytes:**
  - ***Macrophages***:
    - ✓ Macrophages present antigens to helper T lymphocytes at the site of infection.
    - ✓ This activates helper T cells, which, in turn, produce molecules that further activate the macrophages.
    - ✓ This activation cycle is crucial for eliminating microbes that are ingested by macrophages but resist killing.
  - ***B Cells***:
    - ✓ B cells also present antigens to helper T cells, but this occurs in the lymph nodes and spleen.
    - ✓ This interaction is key for cooperation between helper T cells and B cells, especially in humoral immune responses to protein antigens.



- **Major Histocompatibility Complex I (MHC I)**
  - *Function*: MHC I displays peptide fragments from intracellular proteins to cytotoxic T cells. This triggers an immune response against the non-self antigen.
  - *Proteasome Role*: The proteasome breaks down proteins within the cell into peptides, which are then displayed on MHC I.
  - *Constant Process*: Cells continually degrade proteins and present the resulting peptides via MHC I, helping cytotoxic T cells monitor for abnormal or infected cells.

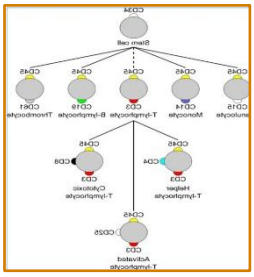
- **Major Histocompatibility Complex II (MHC II):**
  - *Location:* MHC II is found on professional antigen-presenting cells (APCs) such as dendritic cells, macrophages, B cells, and some endothelial cells.
  - *Function:* MHC II presents peptides derived from extracellular proteins (unlike MHC I, which presents intracellular proteins).

- **Natural killer (NK) cells (lymphocyte)**
  - *Type*: NK cells are a type of lymphocyte, distinct from T and B cells.
  - *Function*: NK cells play a crucial role in the innate immune response, particularly against intracellular viruses and bacteria. They are important for early defense before the adaptive immune system kicks in.
  - *Killing Mechanism*: NK cells are capable of killing infected or abnormal cells without requiring clonal expansion or differentiation. They can act quickly and effectively.
  - *Inhibitory Receptors*: Most NK cells have inhibitory receptors that recognize MHC I molecules, which are present on healthy cells. These receptors help NK cells differentiate between healthy cells and abnormal or infected cells.
  - *Balance*: The NK cell's ability to attack or not attack is determined by a balance between activating and inhibitory signals. If the inhibitory signals (from MHC I) are not detected (as in infected or cancerous cells), NK cells can initiate killing.

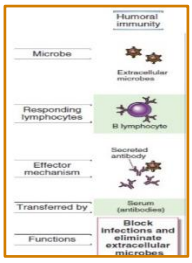


- Cells of the immune system / ***Lymphocytes***
  - **Types of Lymphocytes**: Lymphocytes are a type of white blood cell and consist of distinct subsets, each with different functions and protein products, but they are morphologically similar. These subsets include B cells, T cells, and natural killer (NK) cells.
  - **B Lymphocytes:**
    - ✓ Originate in the bone marrow.
    - ✓ Early maturation occurs in the bone marrow itself.
    - ✓ Involved in humoral immunity by producing antibodies (immunoglobulins) that bind to specific antigens.
  - **T Lymphocytes**:
    - ✓ Also originate in the bone marrow but mature in the thymus.
    - ✓ Involved in cell-mediated immunity, including the destruction of infected or cancerous cells and helping other immune cells respond.
    - ✓ Markers: Lymphocytes can be distinguished based on membrane proteins, which act as phenotypic markers. These markers help identify the specific population of lymphocytes (e.g., CD4+ for helper T cells, CD8+ for cytotoxic T cells, etc.).
  - Lymphocytes are crucial to both the adaptive immune response and play central roles in fighting infections, recognizing abnormal cells, and producing antibodies for future immunity.

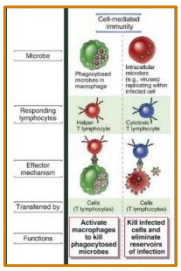
- **Cluster of differentiation**
  - *Definition*: A system used for identifying and classifying cell surface molecules for immunophenotyping of cells.
  - *Function*:
    - ✓ Acts as receptors or ligands.
    - ✓ Functions as adhesion molecules.
    - ✓ Immunophenotyping:
  - *Used* in flow cytometry to analyze cell populations.
  - CD *markers* are numbered (e.g., CD4, CD8, CD19).
  - *Examples*:
    - ✓ CD4: Found on helper T cells.
    - ✓ CD8: Found on cytotoxic T cells

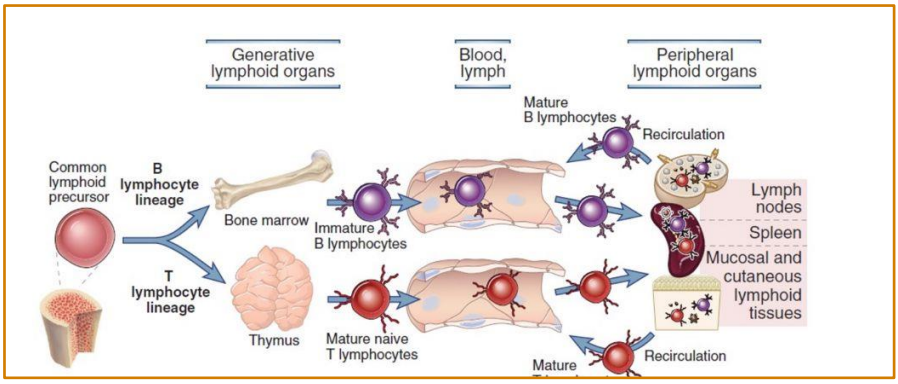


- ***B-lymphocytes***
  - *Function*: The only cells capable of producing antibodies.
  - *Antigen Recognition*: They recognize extracellular antigens (including cell surface antigens).
  - *Differentiation*: Differentiate into plasma cells, which secrete antibodies.
  - *Role*: Mediators of humoral immunity.



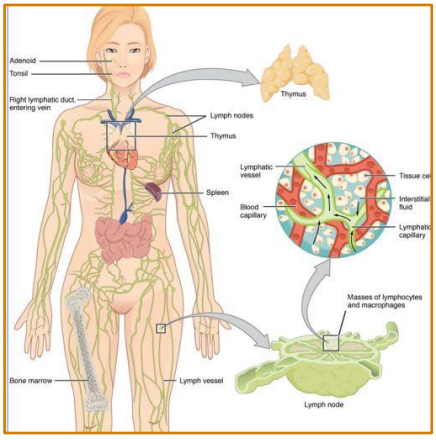
- **T-lymphocytes**
  - *Function*: Cells of cell-mediated immunity, recognizing antigens from intracellular microbes.
  - *Action*: Help phagocytes destroy microbes or directly kill infected cells by Perforin enables the entry of granzymes into the target cell's cytoplasm, triggering the caspase cascade, which leads to apoptosis (programmed cell death).
  - *Antibody Production*: Do not produce antibodies.
  - *Antigen Receptors*: Membrane molecules distinct from, but structurally related to, antibodies.





- **Lymphocytes**
  - Lymphocytes are the *unique cells* of adaptive immunity and are the only cells in the body that express clonally distributed antigen receptors, each with *specificity* for a different antigenic determinant.
  - Each clone of lymphocytes consists of the *progeny* of one cell and expresses antigen receptors with a single specificity.
  - There are millions of lymphocyte clones in the body, allowing recognition and response to millions of foreign antigens.
  - Q. How is the enormously diverse repertoire of antigen receptors (millions) generated from a small number of genes in the germline?
    - ✓ Germline DNA: DNA in germ cells (egg and sperm) that forms the source for all other cells in the body.
  - The *genes encoding* antigen receptors are formed by the *recombination* of DNA segments during lymphocyte maturation. This somatic recombination has a random aspect, resulting in millions of receptor genes and a highly diverse antigen specificity.
  - The antigen receptors are essentially antibodies bound to the cell surface.
  - Unlike most organs, the immune system adapts to an ever-changing environment by using random changes in receptor genes, which preserves responsiveness despite creating *some inefficiency* or "waste".

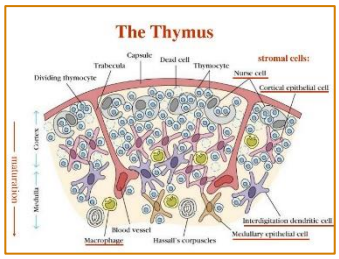
- **Tissues of the immune system:**
  - To optimize the cellular interactions necessary for antigen recognition and lymphocyte activation in adaptive immune responses, ***lymphocytes*** and ***APCs*** are *localized* and *concentrated* in anatomically defined *tissues* or *organs*, which are also the sites where foreign antigens are transported and concentrated
  - Lymphoid tissues are classified as:
    - ✓ Generative organs, also called *primary* or *central lymphoid organs*, where lymphocytes first express antigen receptors and attain phenotypic and functional maturity
    - ✓ Peripheral organs, also called secondary lymphoid organs, where lymphocyte responses to foreign antigens are initiated and develop



- **Bone Marrow** (primary lymphoid tissue)
  - Bone marrow is the *site of production* for most mature circulating blood cells, including red blood cells, granulocytes, monocytes, and early B cell maturation.

- *Hematopoiesis*, the process of blood cell generation, begins in the yolk sac and para-aortic mesenchyme during fetal development, shifts to the liver around the third to fourth month, and gradually moves to the bone marrow.
- At birth, hematopoiesis occurs throughout the skeleton but becomes increasingly restricted to the marrow of flat bones as the individual matures.

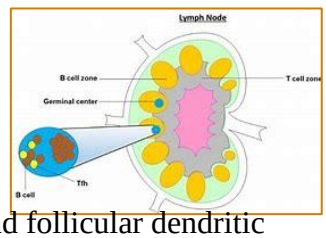
- **Thymus** (primary lymphoid tissue)
  - The thymus is where *T cell maturation* occurs. It is a bilobed organ located in the anterior mediastinum, with each lobe divided into lobules containing an outer cortex and inner medulla.
  - Thymic medullary epithelial cells (*TMECs*), found in the medulla, present self-antigens to developing T cells, leading to the deletion of self-reactive T cells.
  - T cell maturation *starts* in the cortex, and as thymocytes *mature*, they *migrate* toward the medulla, where most mature T cells are found.



  - Associated Conditions:
    - ✓ ***DiGeorge syndrome***: A condition resulting from mutations in genes needed for thymus development, leading to T cell deficiency.
    - ✓ ***Nude mice***: A strain used in immunology research with a mutation in a transcription factor gene that impairs thymus and hair follicle development, causing a lack of T cells and hair

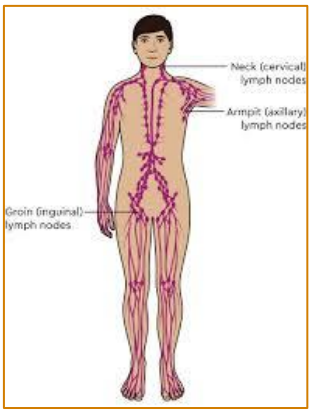
- **The lymphatic system**
  - The lymphatic system consists of *specialized vessels* that drain fluid *from* tissues, *passing* it through lymph nodes and eventually *into* the blood.
  - It plays a *crucial role* in tissue fluid homeostasis and immune responses.
  - It *collects* microbial antigens from entry points and transports them to lymph nodes, where they stimulate adaptive immune responses.
  - Microbes, antigens, dendritic cells, and inflammatory mediators from tissues reach the lymph *nodes* to initiate immune activation.

- **Lymph nodes** (Secondary lymphoid tissue)
  - Lymph nodes are *encapsulated*, *vascularized* organs that facilitate the **initiation** of adaptive immune responses by filtering antigens carried from tissues via lymphatics.

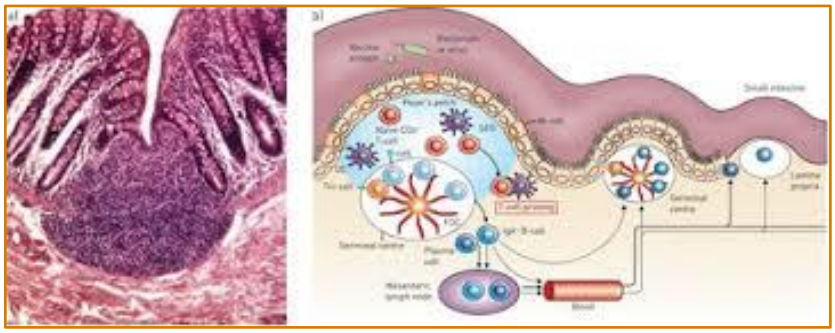


  - Follicles in the lymph node *cortex* are the zones for B cells, organized around follicular dendritic cells (FDCs), which form a reticular network.
  - T cells reside in the *parafollicular cortex*.

- *The segregation* of B and T cells in distinct areas is driven by chemokines, cytokines that act as chemoattractants, guiding the migration of lymphocytes to their respective areas.
- This segregation ensures that T cells are in close contact with dendritic cells and B cells with FDCs.
- *Macrophages* in the sinuses capture and present high-molecular-weight antigens to B lymphocytes
- *Dendritic* cells in the node capture low-molecular-weight soluble antigens for T cell activation.
- The initial immune response often involves antigen delivery by dendritic cells to the node, with larger and sustained responses requiring tissue-specific *antigen delivery.*

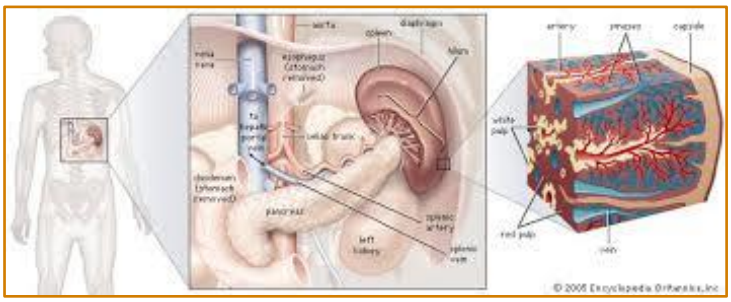


- **Spleen** (Secondary lymphoid tissue)
  - The spleen is a highly vascularized organ that removes *aging* and *damaged* blood cells, *immune complexes*, and *opsonized microbes* from circulation, while initiating adaptive immune responses to blood-borne antigens.
  - It consists of two main parts: the red pulp, made up of blood-filled vascular sinusoids, and the white pulp, which is rich in lymphocytes.
  - Blood enters the spleen through the splenic artery, which branches into smaller vessels surrounded by protective fibrous trabeculae.
  - *Macrophages* in the red pulp filter the blood, removing damaged cells and microbes.
  - Individuals *without a spleen* are more vulnerable to infections, especially from encapsulated bacteria.
  - The spleen is *located* in the left upper abdomen and weighs around 150g in adults.
  - The white pulp *promotes* immune responses to blood-borne antigens and is organized around central arteries, which are distinct from the *vessels* in the red pulp. The marginal zone, surrounding the marginal sinus, separates the red and white pulp.



- **Regional Immune Systems**

- Each major epithelial barrier (e.g., skin, gastrointestinal mucosa, and bronchial mucosa) has its *own system of lymph nodes*, *non-encapsulated* lymphoid structures, and *immune cells* that coordinate to provide specialized immune responses against pathogens entering through these barriers.
- Mucosa-associated lymphoid tissue (*MALT*) is crucial for immune responses to ingested and inhaled antigens and microbes.
- Example: Immune Response in the Gut (***Peyer's Patches***):
  - ✓ Microfold (*M*)-cells in the small intestine take up antigens and process them to resident dendritic cells (DCs) in the Peyer's patches.
  - ✓ T-follicular helper (*TFH*) cells interact with B-cells and follicular dendritic cells (FDCs) to form a germinal center.
  - ✓ Antigen-specific plasma cells and memory B-cells are generated, and these migrate through the blood and mesenteric lymph nodes



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