Lecture 4 **Dr. Basim Mohammed Hanon**

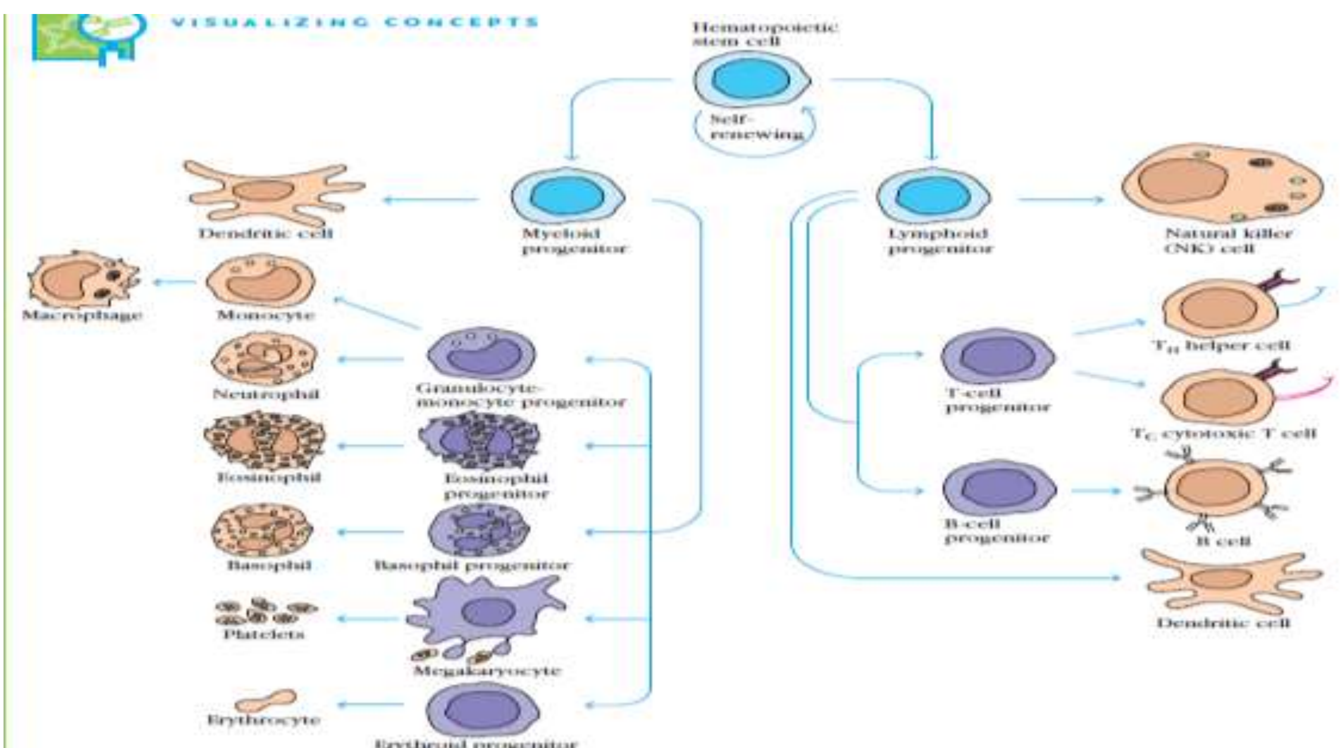
Cells and Organs of the Immune System:-

The immune system may consist of many different organs and tissues that are found throughout the body. These organs can be classified functionally into two main groups. These are **central lymphoid tissue** (bone marrow, thymus) and **peripheral lymphoid tissue** (lymph nodes, spleen, and mucosa-associated lymphoid tissue):

- **The primary** lymphoid organs are the **bone marrow** and the **thymus.**
- **The secondary** lymphoid organs include: **lymph nodes, spleen and mucosa-associated lymphoid tissue (MALT)**
- **The tertiary** lymphoid tissue consists of areas that generally have few lymphoid cells but which can import them during a local inflammatory response – for example, **cutaneous-associated lymphoid tissue (CALT).**

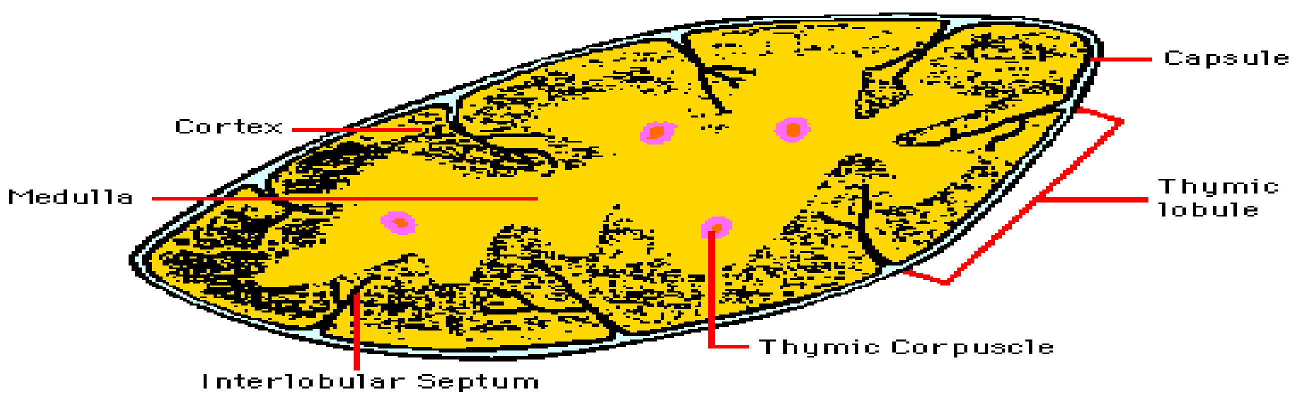
Bone marrow:-

All cells of the immune system have their origin in the bone marrow. They include **myeloid** (neutrophils, basophils, eosinophils, macrophages, and dendritic cells) and **lymphoid cells** (B lymphocytes, T lymphocytes, and natural killer cells) (Figure 1).



Thymus:-

- In the thymus gland **lymphoid cells undergo a process of maturation** and education prior to release into the circulation.
- This process allows **T cells to develop** the important attribute known as **self-tolerance**.
- The thymus gland is arranged into an **outer, more cellular, <u>cortex</u> and an inner, less cellular**, **<u>medulla</u>**.
- **Immature lymphoid cells enter the cortex proliferate**, **mature and pass on to the medulla**. From the medulla mature T lymphocytes enter the circulation.



Lymph nodes:-

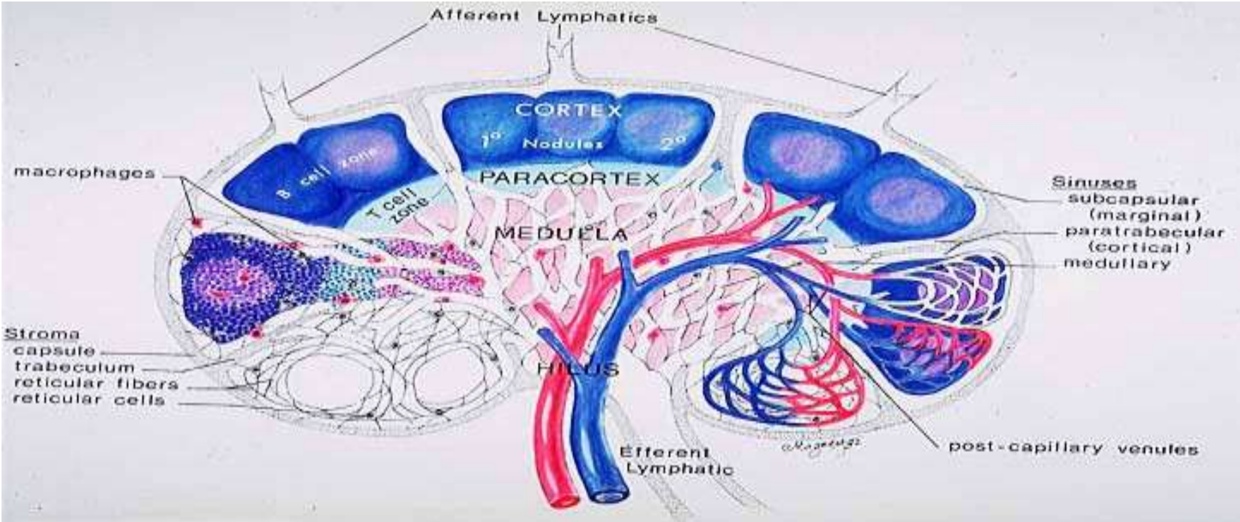
Lymph nodes are **small bean shaped** structures lying along the course of lymphatics. They are aggregated in **particular sites such as the neck, axillae, groins and para-aortic region**.

<u>Lymph nodes have two main functions</u>:-

- Phagocytic cells act as filters for particulate matter and micro-organisms.
- Antigen is presented to the immune system.

<u>The node is made up of three components:-</u>

- lymphatic sinuses
- blood vessels
- parenchyma (cortex, paracortex, medulla)



Hematopoiesis:-

- The process begins in **yolk sac of embryo is 1st week**. In month 3, **stem cells** migrate to **fetal liver and then spleen**.
- During **months 3-7**, both organs play major role. By birth, **bone marrow BM is site of hematopoiesis**.
- Most of the cells involved in the immune system are derived as part of **hematopoiesis**. The key cell in this process is the **hematopoietic stem cell (HSC).**
- Ability to purify HSCs is a major benefit in **bone marrow transplantation**.
- HSCs give rise to progenitors that give rise to **lymphoid** and **myeloid** series.

Many growth factors exist. The direction of differentiation in any one area depends on:

- The factors that are being **secreted by stroma**
- The factors secreted by the **cells themselves**
- The receptors **expressed on the cells**

B lymphocytes: –

- The series of cells that will actually **synthesize antibodies.**
- They have a **number of surface molecules** that distinguish them, but the most important one is **surface immunoglobulin**.
- B cells are generated in the **bone marrow of an adult**, and seed the rest of the body.

T lymphocytes:-

- The series responsible for cellular immunity and also for providing the "second opinion" needed before B cells leave the resting state, eventually to secrete antibody.
- They also have a characteristic set of surface molecules, most important of which is the αβ**-T cell receptor (TCR).** This determines what antigen they recognize.
- Particularly important additional surface molecules that distinguish mature T cells are **CD8** (on cytotoxic T cells, CTLs) and **CD4** (on helper T cells)

Myeloid cells:-

These descend from the **myeloid stem cell** that gives rise to a number of progenitors.

Monocytic cells:-

- These circulate in the blood and give rise to **macrophages** when they leave blood stream and enter tissues.
- Differentiation to tissue macrophage involves a great increase in size and elaboration of factors that help them deal with organisms or other antigens that they **phagocytose**.

1. Alveolar macrophages – lung
2. Kupffer cells – liver
3. Microglial cells – brain
4. Histiocytes – connective tissue
5. Mesangial cells – kidney
6. Osteoclasts – bone

Granulocytic cells:-

These myeloid cells contain obvious staining granules that are **mobilized to attack and destroy bacteria and foreign antigens.**

Neutrophils:-

- Their granules stain with both acid and basic dyes. They are generally the **first cells to arrive at site of inflammation.**
- They **extravasate** from the blood vessels in response to chemotactic factors.
- They phagocytose antigen and introducing lytic enzymes via lysosomes, they store them in granules.
- Also kill by reactive oxygen and nitrogen intermediates, and show a **respiratory burst** when activated.

<u>Eosinophils</u>:-

- These are stained with the acid dye, eosin red. They also phagocytose – **main function appears to be against parasites.**

<u>Basophils</u>:-

- These stain with the basic dye, methylene blue. They do **not** phagocytose, and they function in **immediate hypersensitivity response** – **allergy.** The granules contain **histamine** and other potent mediators.

<u>Mast cells:-</u>

- These are non-motile cells that populate various tissues of the body. Like basophils, they play a role in **allergy by releasing histamine** and other pharmacologically active compounds from granules.

<u>Dendritic cells:-</u>

- Their name of "dendrites" of neurons – long processes extending from cells. These are the best **presenters of antigen**.

- **Langerhans cells** – epidermis and mucus membranes
- **Interstitial dendritic cells** – heart, lungs, liver, kidney, GI tract
- **Interdigitating dendritic cells** – thymus medulla, T cell areas of 2o lymphoid.
- **Follicular dendritic cell -** located in the B-cell rich areas of the lymph nodes.

They are **MHC class II-positive** (i.e., specialized for antigen presentation), and they have receptors for **antibodies and complement components**. They are thought to present antigen/antibody complexes over a very long period.

<u>Mucosa-associated lymphoid tissues (MALT):-</u>

- **Respiratory, gastrointestinal (GI) and urogenital tracts** have mucosal lining. These are major sites for pathogen entry, and there is much 2 lymphoid tissue associated with these sites. The GI tract is a major site with 3 regions:

1. **<u>Mucosal epithelial layer</u>** adjacent to lumen. Contains **intraepithelial lymphocytes** (IELs) which are poorly understood in that they have an alternative type of T cell receptor (γδ**TCR**).

2. <u>The **lamina propria**</u> which contains many **B cells, plasma cells**, activated **Th cells and macrophages** in loose clusters.
3. <u>The **submucosal layer**</u> which contains organized follicles called **Peyer's patches.**

- ❒ **<u>M cells</u>** in the outer mucosal layer transport Ag from the lumen via endocytosis across the cell into a large **basolateral pocket filled with B and T cells and macrophages.**
- ❒ The M cells overlay organized lymphoid follicles in the lamina propria.
- ❒ Activated B cells mature into plasma cells and secrete a **specialized type of antibody** called **IgA** that is transported across the epithelial cells and is secreted into the lumen..
- ❒ Some pathogens exploit the M cells to enter the body, since they cannot penetrate the physical barrier set by the tight junction between mucosal epithelial cells.

  Vibrio cholerae , Some *Salmonella* species , Polio virus

<u>Cutaneous-associated lymphoid tissue (CALT):-</u>

- ❒ The outer epidermal layer is made up of epithelial cells called **keratinocytes**. They **secrete cytokines** in response to penetration that non-specifically can promote a **local inflammatory response.**
- ❒ They can also be induced to express **class II**, keratinocytes may **function as APCs**.
- ❒ **Langerhans cells** (resident macrophages in epidermis) can **pick up the antigen**, and transport it via lymphatic drainage to draining lymph nodes. There they present antigen to T cells.
- ❒ The epidermis also contains **interepithelial lymphocytes** that are mostly CD8-positive and have γδ**TCRs**. Much as the case in the IELs in the gut mucosa, their function is poorly understood.
- ❒ In the dermis (deeper), there are macrophages and both CD4- and CD8-positive T cells in the dermis (deeper) that contain γδ**TCRs**. These T cells have properties that suggest they were previously activated, and they may be memory cells.