nova

Charting New Horizons in Education

innate immunity and immune organs

02

Immunology
+
Lab

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Innate immunity cells

(part 1)

Charting New Horizons in Education

Cellular Components of the Immune System (Percentages)

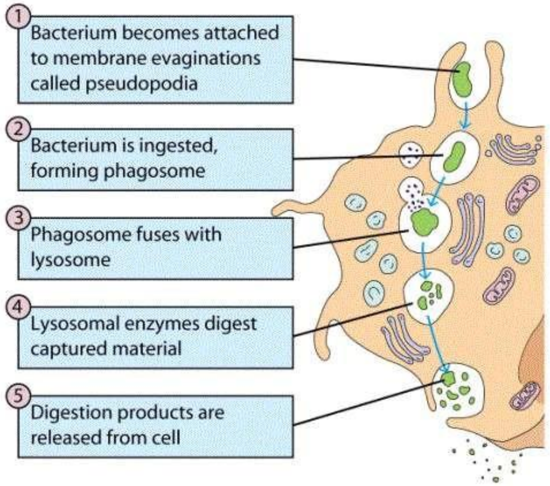
- **Lymphocytes (30%)**:
  - **T cells**: 60%
  - **B cells**: 30% (High nucleus-to-cytoplasm ratio)
  - **Natural Killer (NK) Cells**: 10% (Low nucleus-to-cytoplasm ratio, granular)
- **Mononuclear Phagocytes**:
  - **Macrophages**: 5.3%
- **Granulocytes**:
  - **Neutrophils**: 62%
  - **Eosinophils**: 2.3%
  - **Basophils**: 0.4%

TABLE 41.2 Differential White Blood Cell Count

Cell Type	Normal Value (percent)	Elevated Levels May Indicate
Neutrophil	54–62	Bacterial infections, stress
Lymphocyte	25–33	Mononucleosis, whooping cough, viral infections
Monocyte	3–9	Malaria, tuberculosis, fungal infections
Eosinophil	1–3	Allergic reactions, autoimmune diseases, parasitic worms
Basophil	<1	Cancers, chicken pox, hypothyroidism

Mononuclear Phagocyte (Macrophages)

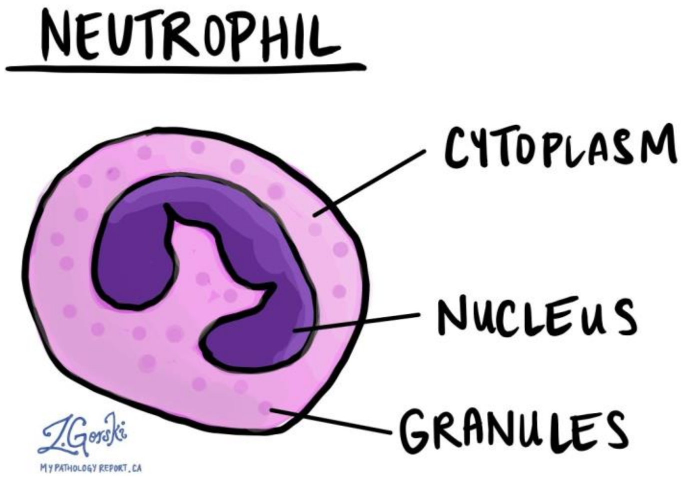
- **Characteristics**:
  - Have rounded or kidney-shaped nuclei.
  - Contain finely granular cytoplasm.
- **Primary Function**:
  - Phagocytosis.
- **Origin and Differentiation**:
  - Originate in the bone marrow (BM).
  - When monocyte becomes settled in tissue; they are called macrophages
  - Some differentiate into dendritic cells, while others join to form multinucleated giant cells.



- **Names in Different Tissues**:
  - Kupffer cells in the liver.
  - Histiocytes in connective tissues.
  - Macrophages in bone marrow, spleen, and lymph nodes.
  - Langerhans' cells in the skin.
  - Osteoclasts in bone.
  - Mesangial cells in the kidney.
  - Microglial cells in the brain.
  - Monocytes in the blood.

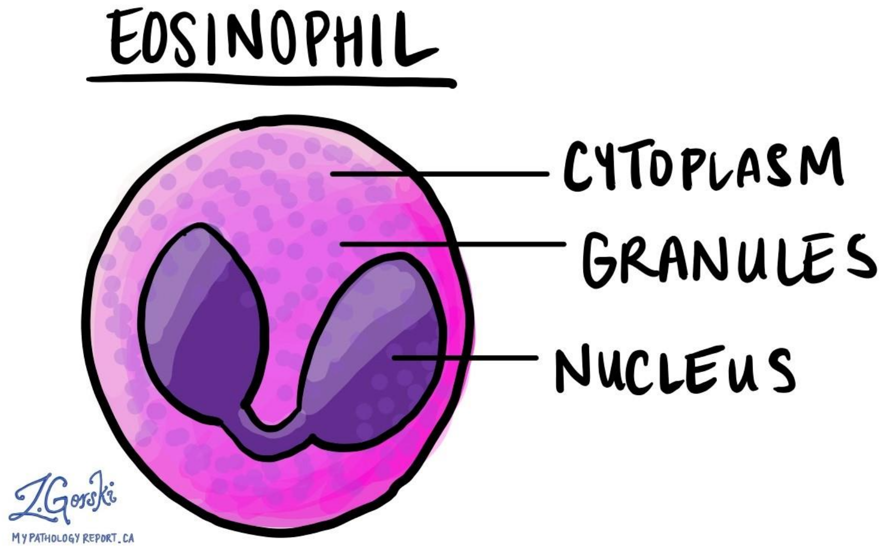
Neutrophils

- **Characteristics**:
  - Granulocytes with a nucleus segmented into 3-5 connected lobes (polymorphonuclear leukocytes).
  - Contain cytoplasmic granules.
  - Neutrophils make up 95% of granulocytes.
  - Respond within 24 hours (earliest responders).
- **Receptors**:
  - Have 20 times more receptors than macrophages.
  - Possess Fc receptors for IgG and IgA.
  - Contain complement receptors.
- **Intracellular Killing**:
  - Mediated by azurophilic lysosomal granules and specific granules.



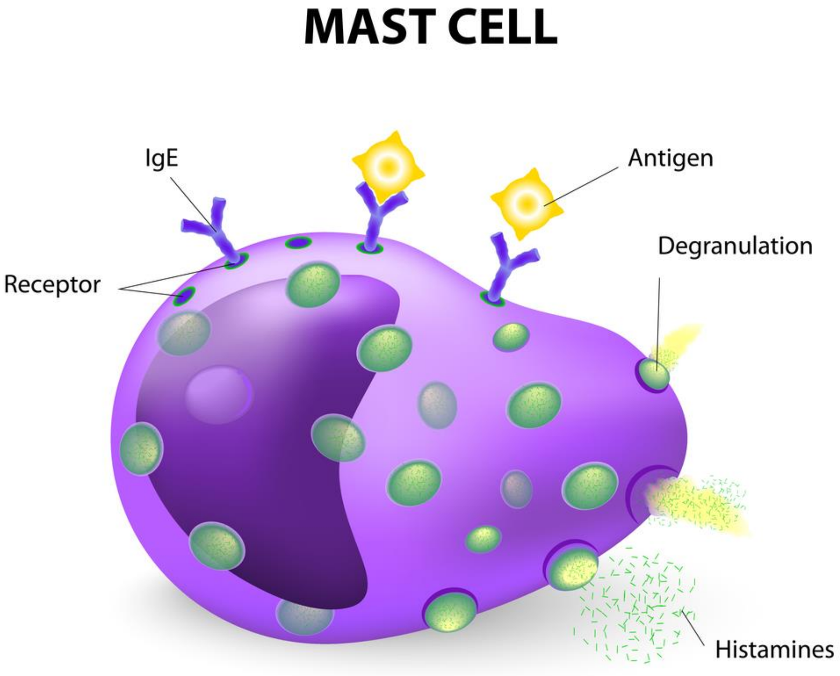
Eosinophils

- **Staining**:
  - Eosinophilic or "acid-loving" cells.
  - Show affinity to coal tar dyes, appearing brick-red after staining with eosin (a red dye).
- **Granules and Enzymes**:
  - Contain hydrolytic enzymes responsible for anti-helminthic activity.
- **Major Basic Protein (MBP)**:
  - Unique to eosinophils.
  - Highly toxic to worms.

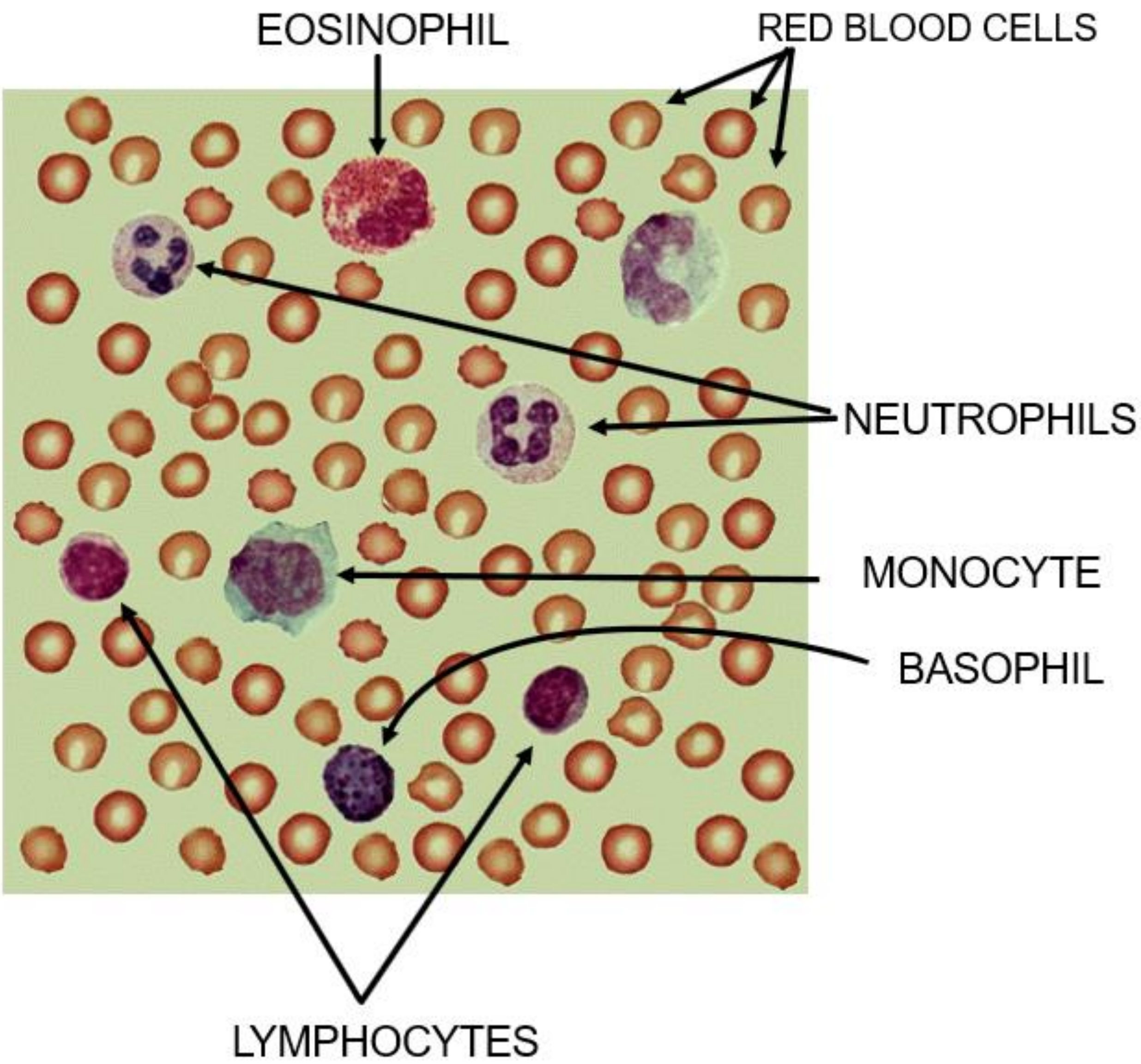


Basophils and Mast Cells

- **Characteristics**:
  - Granulocytes with acidic proteoglycans.
  - Lobed nucleus (more variable in shape).
  - Large, coarse granules that stain blue with the basic dye, methylene blue.
- **Forms**:
  - **Mast Cells**: Sessile (stationary) form.
  - **Basophils**: Circulating form.

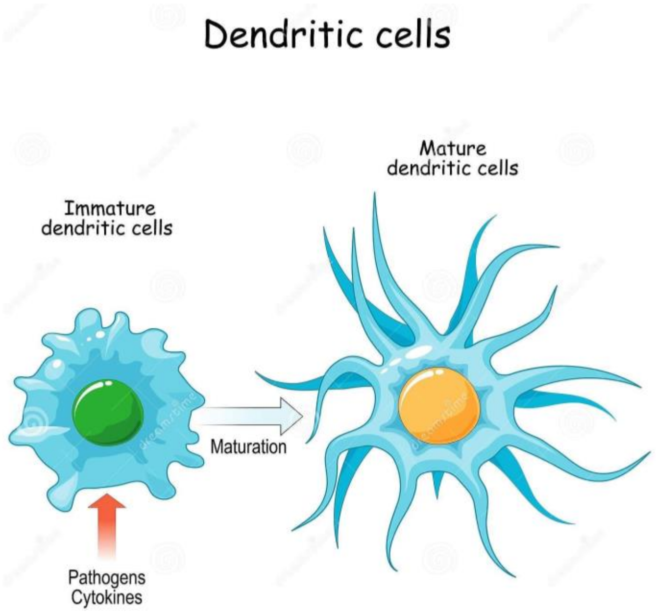


Cells of the blood



Dendritic Cells (DCs)

- **Main Function**:
  - Phagocytose antigen material and present it to lymphocytes, acting as **antigen-presenting cells (APCs)**.
- **Location**:
  - Present in tissues in contact with the external environment, including:
    - **Skin** (specialized type: **Langerhans cells**).
    - Inner lining of the **nose**, **lungs**, **stomach**, and **intestines**.
  - Found in an immature state in the **blood**.
- **Activation and Migration**:
  - Once activated, migrate to **lymphoid tissues**.
  - Interact with **T cells** and **B cells** to initiate and shape the adaptive immune response.
- **Structure**:
  - Grow branched projections, which gives them the name **dendritic cells**.



Types of Dendritic Cells (DCs)

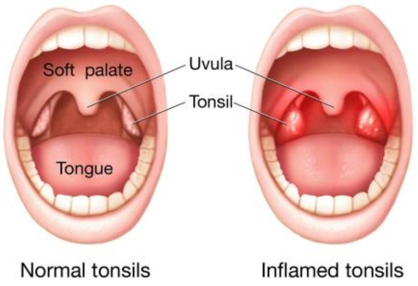
1. **Myeloid DC**
    - Origin: **Macrophage**.
    - Function: Phagocytose antigens and activate **T cells**.
    - Localization: Common and diffuse throughout the body.
2. **Lymphoid DC**
    - Origin: **Lymphocyte**.
    - Function: Recruit immune cells to the site of infection.
3. **Follicular DC**
    - Origin: **Mesenchymal**.
    - Location: Present in **peripheral lymph nodes**.
    - Function: Activate **B cells**.
4. **Plasmacytoid DC**
    - Function: Early responders to viral infection.
    - Special Role: Potent **antiviral** activities.

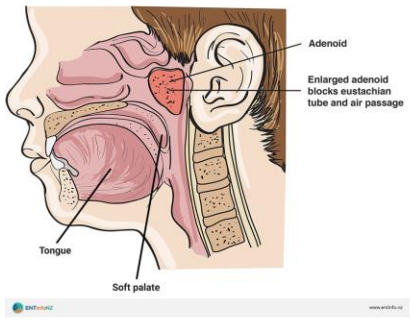
Immune organs

(part 2)

Organs of the Immune Response

- **Primary Lymphoid Organs**:
  - **Bone Marrow**: Where immune cells originate.
  - **Thymus**: Site where T cells differentiate and mature.
- **Secondary Lymphoid Organs**:
  - Maintain mature naive lymphocytes and initiate an adaptive immune response.
  - Sites of lymphocyte activation by antigen.
  - It is exemplified by: (**mucosa-associated lymphoid tissue**, MALT).
    - Lymph nodes
    - **Lymphoid follicles in tonsils**
    - **Peyer's patches**
    - Spleen
    - **Adenoids**
    - **Skin**



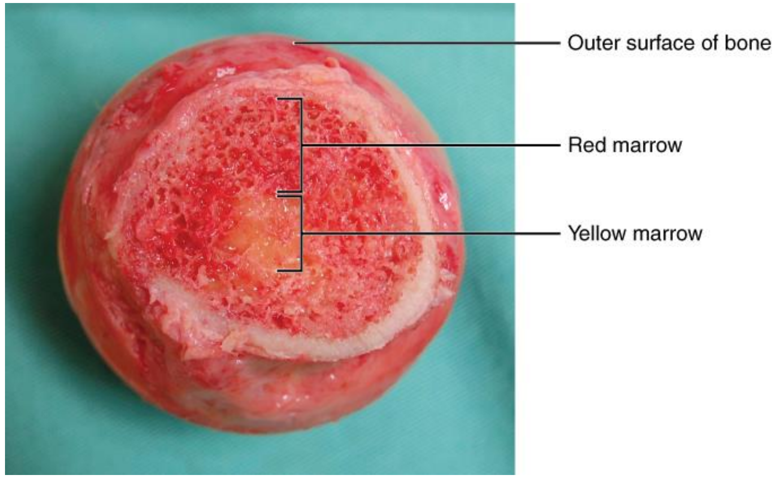


Bone Marrow and Thymus

- **Bone Marrow Functions**:
  - **Leukocyte Production**.
  - **B Cell Maturation**.
  - **Hematopoiesis**:
    - Starts in childhood (yolk sac and mesenchyme)
    - Then in the liver and spleen
    - Finally, in the bone marrow during puberty, reaching maximum levels in adulthood.
  - **Common Sites in Bone Marrow**:
    - Sternum
    - Vertebrae
    - Iliac bones
    - Ribs.
  - **Extramedullary Hematopoiesis**: In cases of excess demand, the liver and spleen assist the bone marrow.
- **Thymus Functions**:
  - **T Cell Maturation**.
  - **Formation of T Cell Antigen Receptors**.

Components of bone marrow

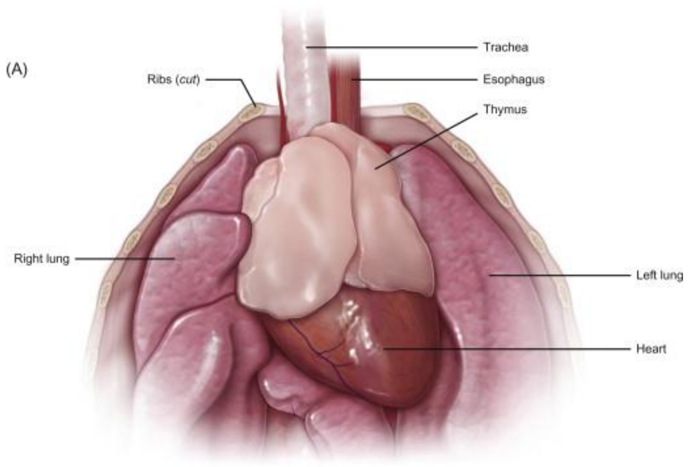
- **Red Marrow**:
  - Consists mainly of hematopoietic tissue.
  - Produces red blood cells, platelets, and most white blood cells.
  - **Location**: Found mainly in flat bones, including:
    - Pelvis // Sternum // Cranium // Ribs // Vertebrae // Scapulae
    - Epiphyseal **ends** of long bones (e.g., femur and humerus).



- **Yellow Marrow**:
  - Mainly composed of fat cells.
  - At birth, all bone marrow is red; as a person ages, more marrow is converted to yellow, with around half of adult bone marrow being red.
  - **Location**: Found in the hollow interior of the middle portion of long bones.
  - In cases of severe blood loss, the body can convert yellow marrow back to red marrow to increase blood cell production.

- **Stroma**:
  - Any tissue not associated with blood production, including:
    - Fatty marrow // Fibroblasts // Osteoclasts // Osteoblasts.

Thymus



- **Location**:
  - Found in the thorax, specifically in the **anterior mediastinum**.
- **Development**:
  - Gradually enlarges during **childhood**.
  - Undergoes **involution** after puberty, leading to a reduction in the functioning mass of the gland.
  - Continues to function throughout life.
- **Vascular Supply**:
  - Has a rich vascular supply.
  - Contains efferent lymphatic vessels that drain into **mediastinal lymph nodes**.
- **Embryological Origin**:
  - Derived from invaginations of the **ectoderm** in the developing neck and chest of the embryo.
  - Forms structures called **branchial clefts**.

Thymus

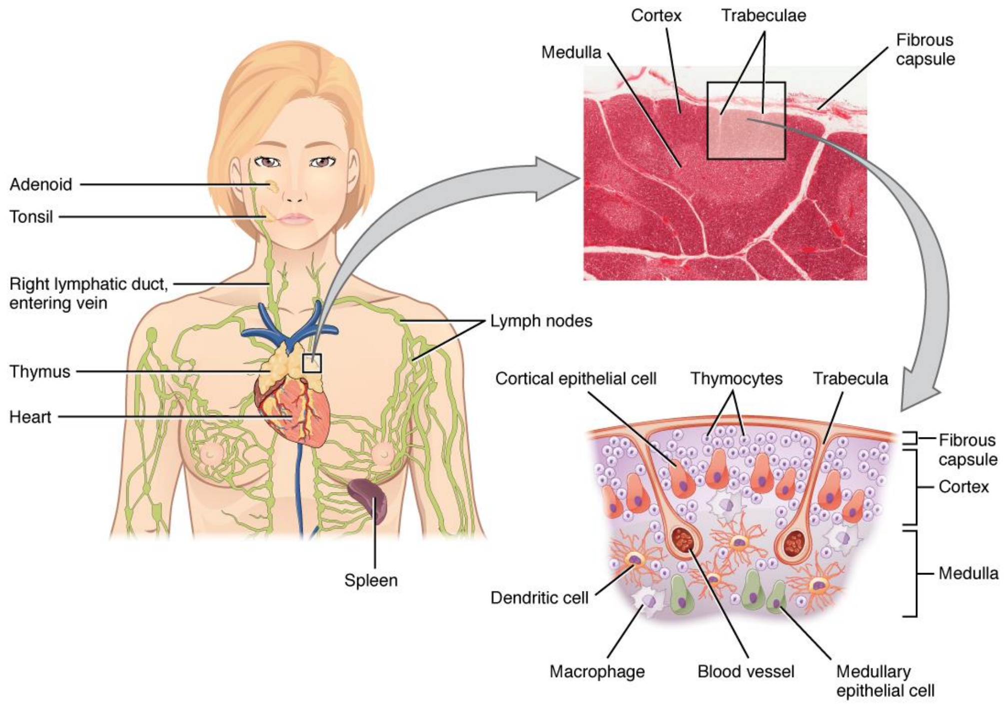
A. Anatomy;

- **Structure**: Composed of **two identical lobes**.
- **Location**: Anterior superior mediastinum, located in front of the heart and behind the sternum.

B. Histology

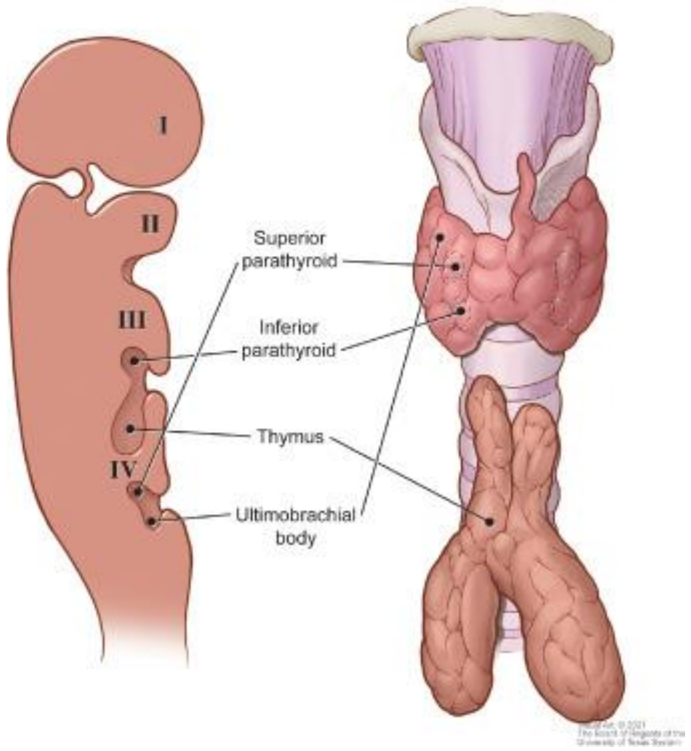
- **Capsule**: Surrounded by a **fibrous capsule**.
- **Arrangement**:

  Organized into:
    - **Outer Cortex**: More cellular.
    - **Inner Medulla**: Less cellular.
- **Cell Types;**
  - **Thymocytes**: Immature T cells found in the cortex; they mature and migrate toward the medulla and then to circulation.
  - **Epithelial Cells, Macrophages** & **Lymphoid Dendritic Cells**



DiGeorge Syndrome

- Genetic defect in the development of the **3rd pharyngeal pouch** in the embryo.
- Results in T cell deficiency due to impaired thymus development, along with a parathyroid gland defect.



Lymph Nodes and Lymphatic System (Peripheral or Secondary Lymphatic System)

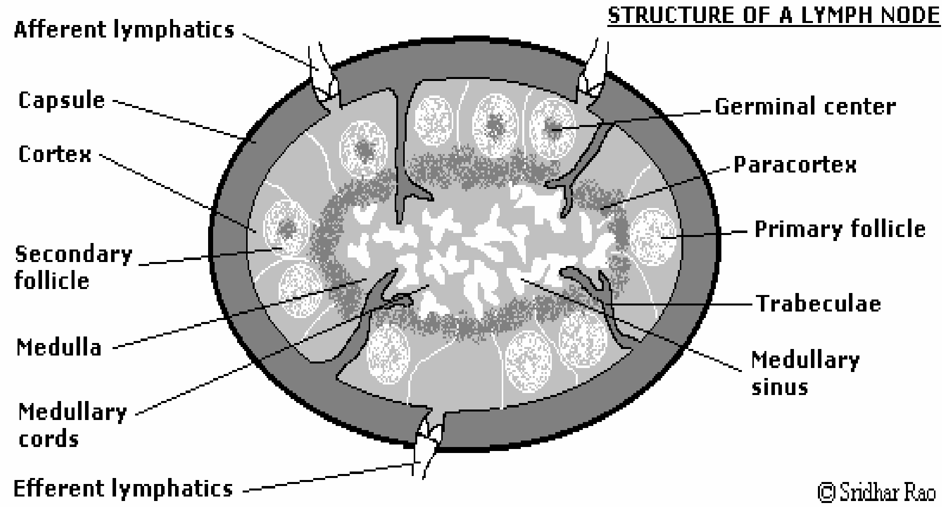
- **Functions**:
  - **Concentrate antigens** introduced through common portals of entry: (Skin Gastrointestinal tract Respiratory tract.)
  - **Antigen Presentation**: Innate immune cells carry antigens to the lymph nodes and present them to the adaptive immune system.
  - **Lymphocyte Activation**: Site of activation of lymphocytes by antigen.

Secondary Lymphoid Tissues

- **Components**:
  - **Lymph Nodes**:
    - Clustered at sites such as the **groin**, **armpits**, **neck**, and along the **small intestine**.
    - Collect antigens from the tissues.
  - **Spleen**:
    - Collects antigens from the bloodstream.
  - **Mucosa-Associated Lymphoid Tissues (MALT)**:
    - Collects antigens from the respiratory, gastrointestinal, and urogenital tracts.
    - Well-organized in the small intestine as **Peyer's patches**.

Lymph Node Structure

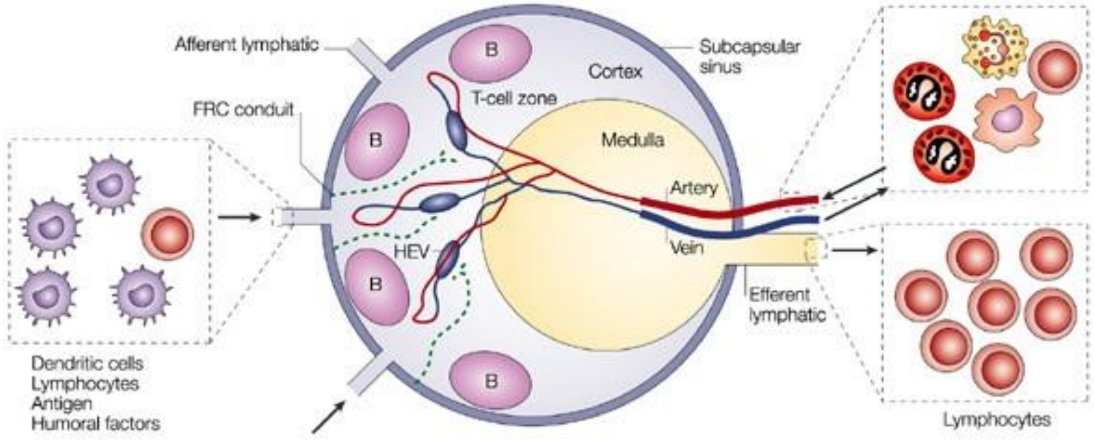
- **Three Components**:
  - **Lymphatic Sinuses**:
    - Lymph flows from afferent vessels, through cortical sinuses, into medullary sinuses, and exits via efferent lymphatic vessels.
  - **Blood Vessels**
  - **Parenchyma**:
    - Includes the **cortex**, **paracortex**, and **medulla**.



Lymph Node Structure

Cortex

- **Primary Follicles**:
  - Contain mature but **not activated B cells**.
- **Secondary Follicles**:
  - Contain **germinal centers**, formed from **stimulated B cells** and **follicular dendritic cells**.
  - **B Cell Activation**:
    - Stimulated B cells transform into **plasma cells** or **memory B cells**.
    - Plasma cells reside in the medulla and produce antibodies that enter circulation.



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Lymph Node Structure

Paracortex

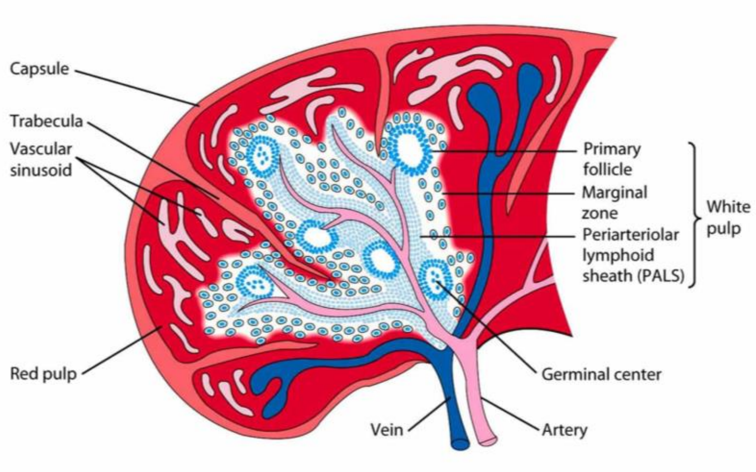
- Contains **T lymphocytes** and **macrophages**.
- **T Cell Activation**:
  - T cells enter the node via **high endothelial venules (HEVs)**.
  - Upon activation, they form **lymphoblasts** and divide, creating clones of T cells responding to specific antigens.
  - Activated T cells move into circulation to reach peripheral sites.

Medulla

- Comprises:
  - **Large Blood Vessels**
  - **Medullary Cords and Sinuses**
  - **Plasma Cells**

Spleen

- **Location**: Weighs **150g**, located in the **left upper quadrant**.
- **Function**: Immune response against **blood-borne antigens**.



Structure;

- **White Pulp (Inner)**:
  - **Peri-Arteriolar Lymphoid Sheath (PALS)**: T cell zone.
  - **Follicles**: B cell zone.
  - **Marginal Zone**: Between red and white pulp, contains both **B and T cells** and **macrophages**.
- **Red Pulp (Outer)**:
  - Contains the **splenic artery**, **vascular sinusoids**, and **splenic vein**.
  - Site where **old erythrocytes** are destroyed by macrophages.
  - **Blood-borne microorganisms** are trapped in a web of small blood vessels and gradually washed out through the splenic vein.
- **No afferent lymphatic vessels** in the spleen.

Spleen Functions

1. **Killing of Antibody-Coated Microbes**:
2. **Destruction of Damaged RBCs**:
3. **Storage**: (reservoir for red blood cells and lymphocytes.)

- **Clinical Significance**:
  - Individuals lacking a spleen are highly susceptible to infections from encapsulated bacteria (e.g., **pneumococci** and **meningococci**).
  - These bacteria are normally cleared by **opsonization** and **phagocytosis**, which is compromised in the absence of the spleen.

Leukocyte (White Cell) Count

(LAB)

Leukocyte (White Cell) Count

- **Definition**:
  - The number of white cells in 1.0 cubic millimeter of blood.
  - Total leukocyte count does not distinguish among the six normal types (neutrophils, bands, lymphocytes, monocytes, eosinophils).
- **Normal Range**:
  - Varies between **4,500 and 11,000 cells per cubic millimeter** ($4.5–11.0 \times 10^9$/L).
  - Variations can be influenced by activities such as bathing, exercise, and digestion.
  - The white cell count rises and falls to indicate the cause of a disease or progress of infection.
- **Clinical Significance**:
  - **Leukocytosis**:
    - White cell count rises above normal, up to **20,000 cells/cubic millimeter**.
    - Caused by stimulation of white cell production in the bone marrow due to bacteria or invading organisms.
  - **Leukopenia**:
    - White cell count drops below normal, down to **3,000 cells/cubic millimeter**.
    - Caused by depression of white cell production in the bone marrow, often due to viruses or harmful chemicals.

Leukocytosis

- **Main Causes of Elevated WBC Count**:
- **Acute Infections**:
  - Pneumonia, meningitis, abscess, tonsillitis, cholera, septicemia, appendicitis, etc.
  - Also seen in leukemia, rheumatic fever, pregnancy, newborns, chickenpox.
- **Inflammation & Tissue Necrosis**:
  - Burns, trauma, arthritis, tumors, etc.
- **Other Causes**:
  - Acute hemorrhage, stress, menstruation, exercise.

Leukopenia

- **Main Causes of Reduced WBC Count**:
- **Infections**:
  - Viral (HIV, viral hepatitis, measles, rubella, influenza).
  - Bacterial (miliary TB, typhoid fever, brucellosis).
  - Parasitic (leishmaniasis, malaria).
  - Overwhelming bacterial infections (e.g., relapsing fever).
- **Other Causes**:
  - Hypersplenism, bone marrow infiltration, ionizing radiation.

WBC Reference Range by Population

- **Children (1 year)**: 6.0–18.0 × 10^9/L
- **Children (4–7 years)**: 5.0–15.0 × 10^9/L
- **Adults**: 4.0–10.0 × 10^9/L
- **Pregnant Women**: Up to 15.0 × 10^9/L

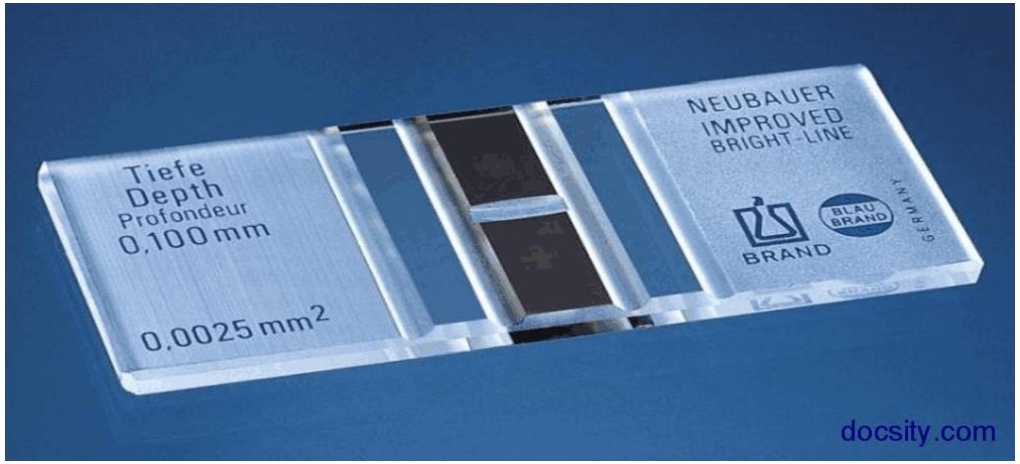
- *counts also vary in different populations with lower total WBC and neutrophils counts being found in Africans

Leukocyte (White Cell) Count

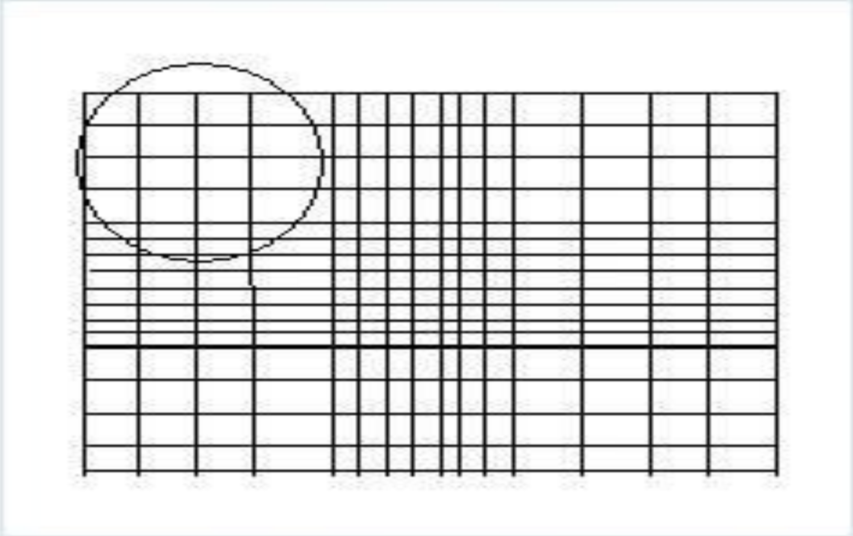
- **Methods of White Cell Count**:
  - Microscopic Method
  - Automatic Method
- **Microscopic Method**
  Principle of the Test:
  - White blood cells are diluted **1 in 20** in an **acid reagent**.
  - The acid reagent causes **hemolysis of red cells**, leaving white cells to be counted.
  - White cells are counted using a **haemocytometer**.

Haemocytometer

- **Purpose**:
  - A simple, convenient, and cost-effective tool for accurately determining the number of cells in a sample.
- **Description**:
  - A haemocytometer is a specialized slide with a counting chamber that holds a known volume of liquid.
- **Usage**:
  - Requires a microscope for cell counting. **(Microscopic Method)**
- **Cell Count Formula**:
  - **Number of cells/cmm** = (Counted cells in 16 corner squares) × volume factor × Dilution factor.



Haemocytometer gridlines



Haemocytometer diagram indicating the 16 corner squares which should be used for counting.

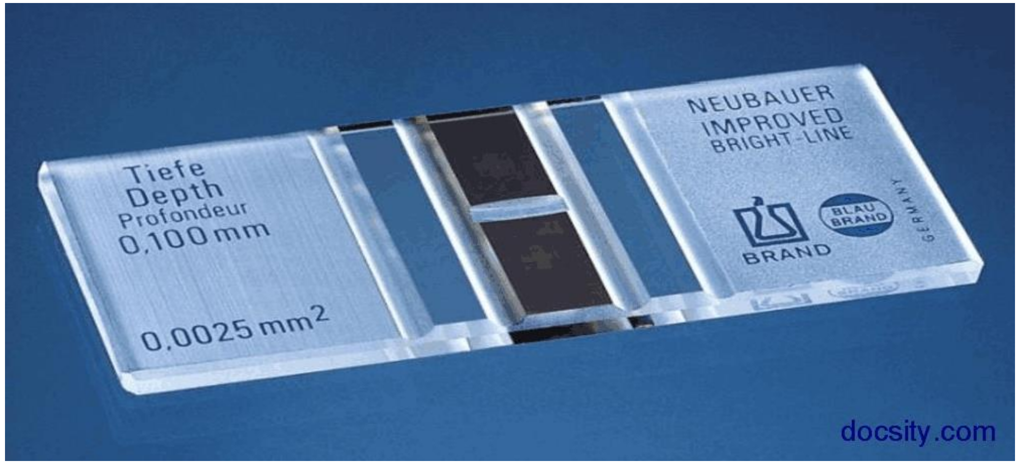
White Cell Count: Correction Factors

- **White cell count** is the number of white cell in 1 cubic millimeter of undiluted blood, so we have **two correction factors**; Dilution & volume
- **Dilution Factor**:
  - The blood is diluted **1 in 20**.
- **Volume Factor**
  - The haemocytometer chamber has an area of **1 square millimeter** and a depth of **0.1 mm**.
  - **Volume of the chamber** = Area × Depth = **1 × 0.1** = **0.1 cubic millimeters (cmm)**.

- **Number of cells/cmm** = (Number of cells in chamber) × Dilution factor × Volume factor.
- **Number of cells/cmm** = (Number of cells in chamber) × 20 × 10.

Practice

- **You counted 80 cells in the 16 corner squares of a haemocytometer grid. If the dilution factor is 5, calculate the total number of cells per cubic millimeter (cmm).**



Practice

- **A sample was diluted by 10 times, and 60 cells were counted in the 16 corner squares.**
  What is the final concentration of cells in the original sample?
  What does the number indicate?

Practice

1. **If you counted 300 cells in 16 corner squares and the sample was diluted by 6, what is the final concentration of cells per cubic millimeter?** Based on this result, indicate your finding.

Answers;

- 1) 4,000 (normal)
- 2) 3,000 (leukopenia)
- 3) 18,000 (leukocytosis)

Thank you

Charting New Horizons in Education