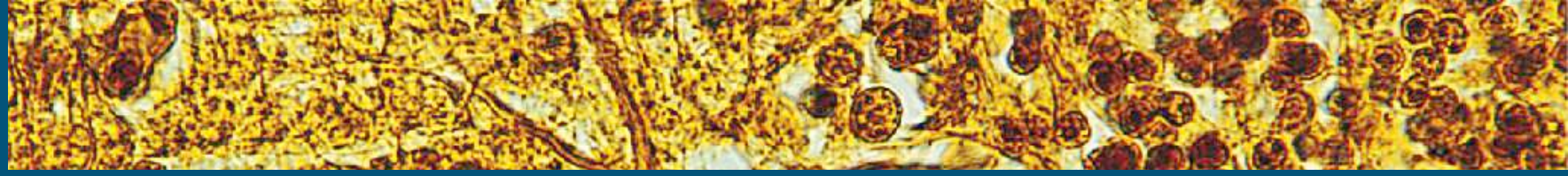


Blood and Lymphoid system

Textbook of Histology, 4th ed.

Gartner

https://gestioneval.unibo.it

BLOOD

Blood, a *specialized type of connective tissue*, consists of plasma the fluid component (the extracellular matrix) and cells.

These components may be separated by centrifugation when blood is collected in the presence of anticoagulants.

The sedimented red blood cells (RBCs) constitute about **42%–47%** of blood volume.

This percentage of erythrocyte volume is the **hematocrit**. Sitting on top of the erythrocyte layer is the **buffy coat** layer, which contains **leukocytes** (Greek *leukos*, white; *kytos*, cell) and **platelets**. The translucent supernatant fraction above the packed RBCs is plasma. Normal adult blood volume measures **5** to **6 L**.

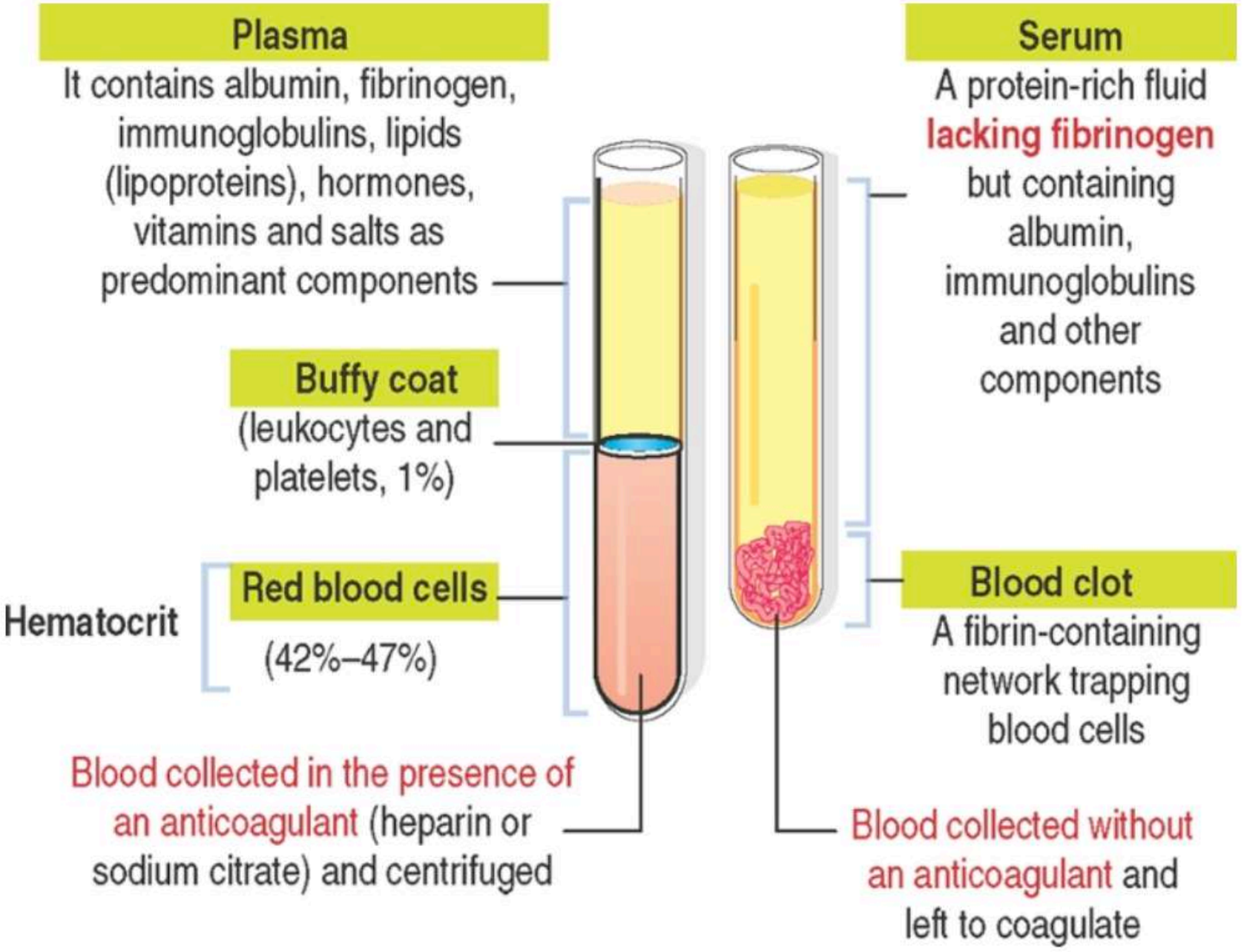


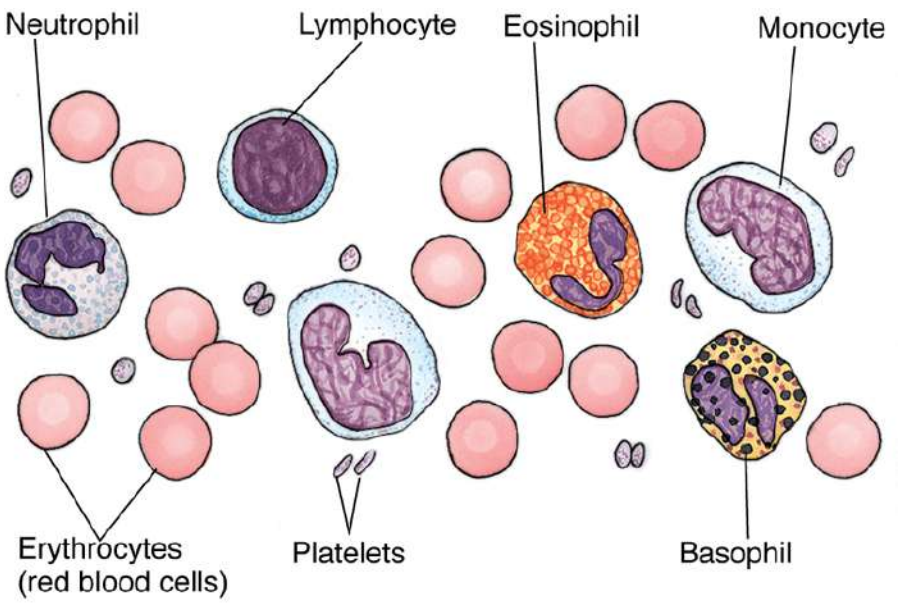
FIGURE 6.1 Blood: Plasma, serum and cells

Plasma

Plasma is the fluid component of blood. Plasma contains salts and organic compounds (including amino acids, lipids, vitamins, proteins and hormones).

In the absence of anticoagulants, the cellular elements of blood, together with plasma proteins (mostly **fibrinogen**), form a clot in the test tube. The fluid portion is called **serum**, which is essentially *fibrinogen-free plasma*.

Circulating Blood Cells



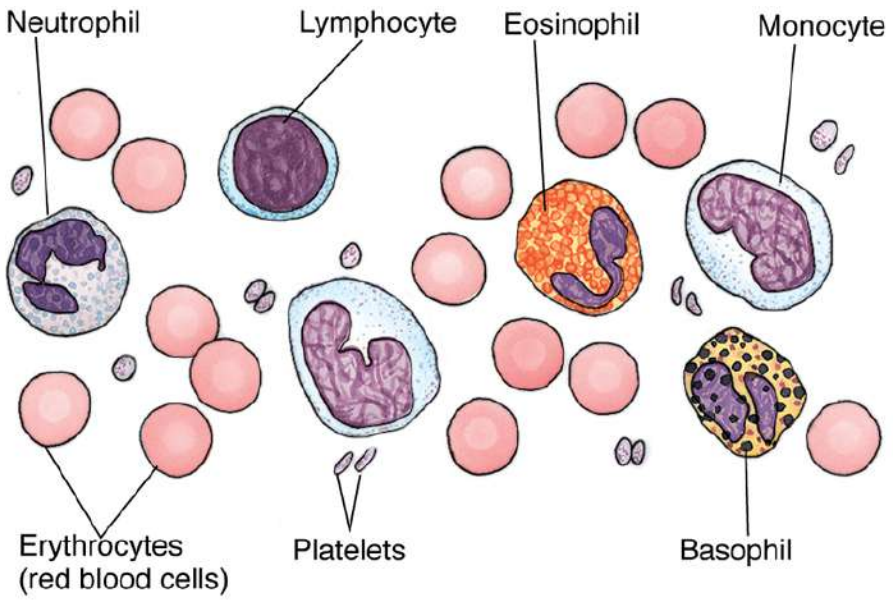
Cells and platelets of circulating blood.

The total volume of **blood** of an average adult is about 5 L, and it circulates throughout the body within the confines of the circulatory system.

The formed elements are composed of cells and cell fragments, known as platelets.

Light microscopic examination of the formed elements is performed using either the Wright or Giemsa stains, and identification of blood cells is based on the colors produced by these stains.

Circulating Blood Cells



Cells and platelets of circulating blood.

The cells of blood are subdivided into two major components:

- **red blood cells** (RBC)
- **white blood cells** (WBCs, leukocytes).

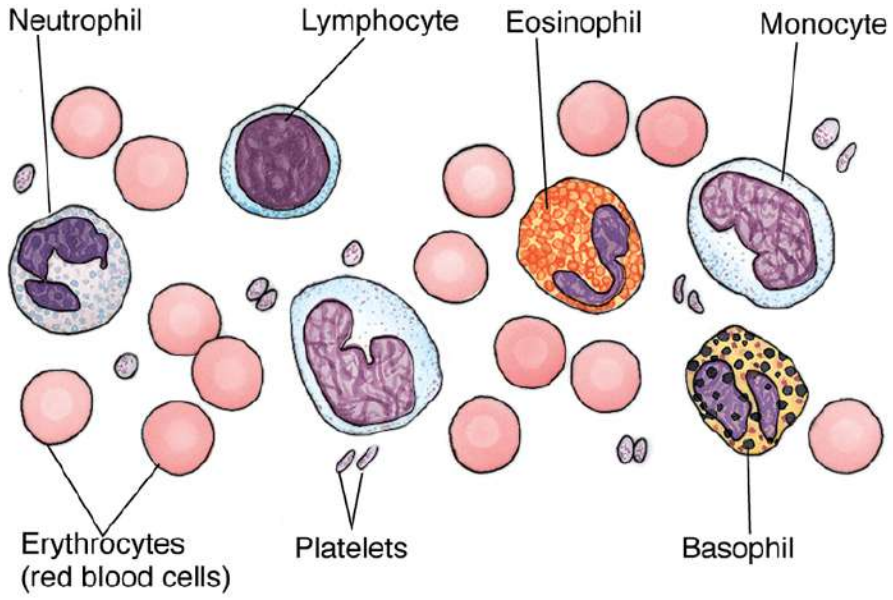
Red blood cells lose their nuclei and organelles during development, therefore mature, circulating RBC are anucleated cells whose cytoplasm is filled with hemoglobin.

White blood cells are subdivided into two categories, those without specific granules, **agranulocytes** and those housing granules, **granulocytes**.

Lymphocytes and **monocytes** belong to the **agranulocytes** and **neutrophils, eosinophils**, and **basophils** belong to the latter category, **granulocytes**.

Platelets are round to oval cell fragments derived from megakaryocytes.

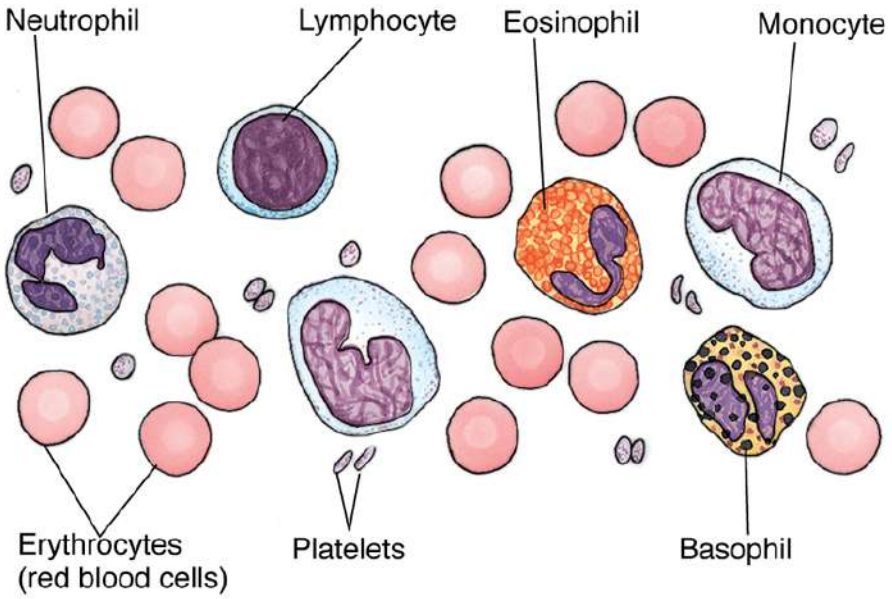
Red blood cells (RBC; erythrocytes)



Cells and platelets of circulating blood.

RBCs, also called erythrocytes (Greek *erythros*, red; *kytos*, cell), are non-nucleated, biconcave-shaped cells measuring about **7.8 µm** in diameter. RBCs lack organelles and consist only of a plasma membrane, its underlying cytoskeleton, hemoglobin and glycolytic enzymes.

Red blood cells (RBC; erythrocytes)



Cells and platelets of circulating blood.

RBCs **4 to 6 × 10^6 per mm^3** circulate for **<u>120 days</u>**.
Senescent RBCs are removed by phagocytosis or destroyed by **hemolysis** in the spleen.
RBCs are replaced in the circulation by **reticulocytes**, which complete their hemoglobin synthesis and maturation 1 to 2 days after entering the circulation.
Reticulocytes account for **1%** to **2%** of circulating RBCs. RBCs transport oxygen and carbon dioxide and are confined to the circulatory system.

Red blood cells (RBC; erythrocytes)

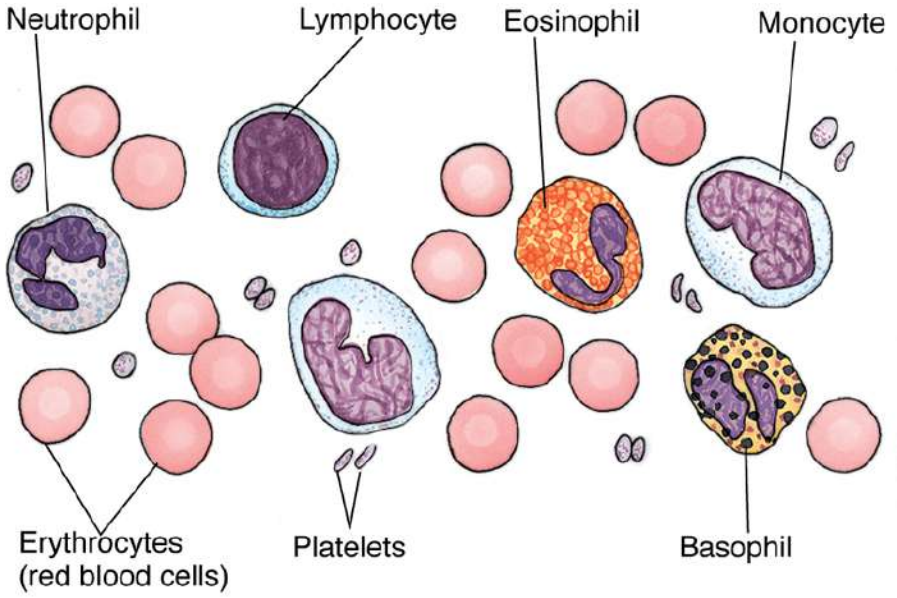
Red blood cells are packed with **hemoglobin,** a large tetrameric protein composed of four polypeptide chains, each of which is covalently bound to an iron containing **heme.**

The hemoglobin provides the *unstained* cell with its pale yellow color.

The globin moiety of hemoglobin releases CO_2, and the iron binds to O_2 in regions of high oxygen concentration, as in the lung.

However, in oxygen-poor regions, as in tissues, hemoglobin releases O_2 and binds CO_2. Hemoglobin carrying oxygen is known as **oxyhemoglobin,** and hemoglobin carrying carbon dioxide is called **carbaminohemoglobin.**

Circulating Cells of Blood (cont.)



Cells and platelets of circulating blood.

The extracellular surface of the red blood cell plasmalemma has specific inherited carbohydrate chains that act as antigens and determine the blood group of an individual for the purposes of blood transfusion. The most notable of these are the **A** and **B antigens,** which determine the four primary blood groups, **A, B, AB,** and **O.**

Another important blood group, the **Rh** group, is so named because it was first identified in rhesus monkeys. Three of the Rh antigens (C, D, and E) are so common in the human population that the erythrocytes of 85% of Americans have one of these antigens on their surface, and these individuals are thus said to be **Rh^+.**

Leukocytes

Leukocytes **(6 to 10 × 10^3 per mm^3)** are categorized as either **granulocytes** or **agranulocytes**.

- Granulocytes **contain primary and specific or secondary, cytoplasmic granules**.

- Agranulocytes **contain only primary granules**.

Blood cells/uL or mm3

Erythrocytes	4-6 × 10^6	
Leukocytes	6000 to 10,000	
Neutrophils	5000	**(60% to 70%)**
Eosinophils	150	**(2% to 4%)**
Basophils	30	**(0.5%)**
Lymphocytes	2400	**(28%)**
Monocytes	350	**(5%)**
Platelets	300,000	
Hematocrit	42%–47%	

Granulocytes

Granulocytes are phagocytic cells with a **multilobed nucleus** and measuring **12** to **15 µm** in diameter. Their average life span varies with cell type. Three types of granulocytes can be distinguished by their cytoplasmic granules:

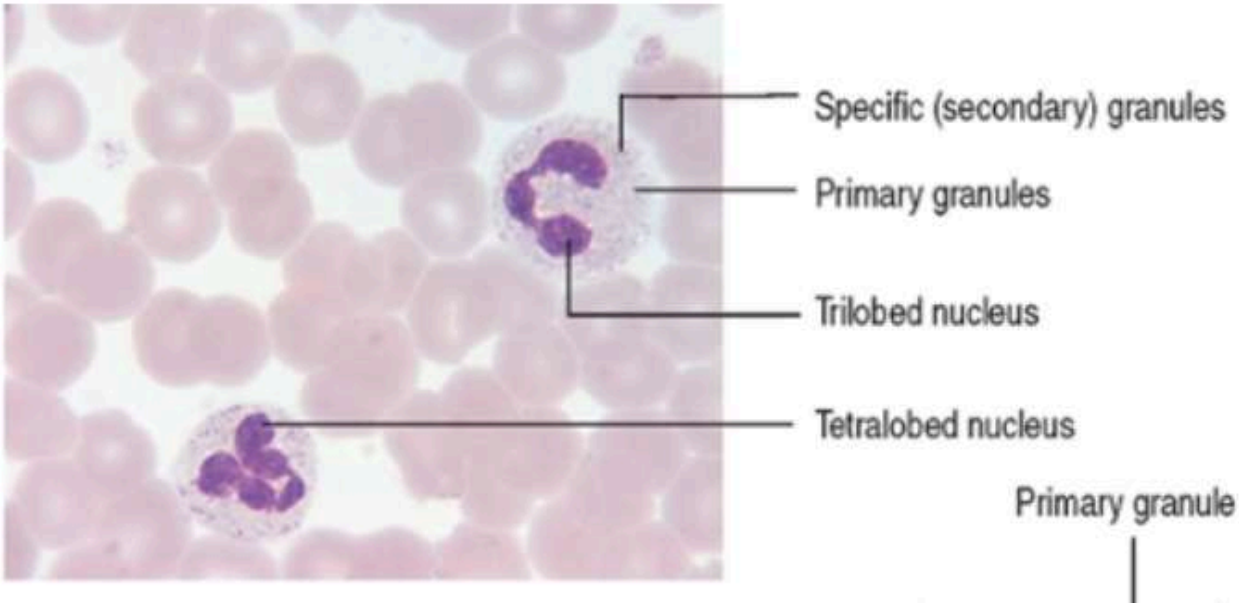
Neutrophils

Eosinophils

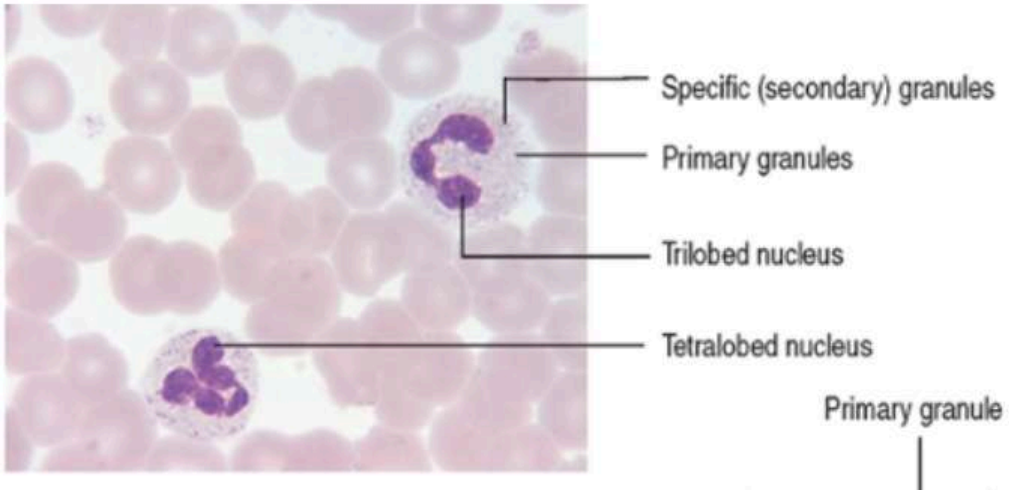
Basophils

Granulocytes Neutrophils

Neutrophils have a multilobed nucleus. Their cytoplasm contains secondary (specific) and primary granules. In stained smears, neutrophils appear very pale pink. Neutrophils, which constitute **50%** to **70%** of circulating leukocytes, have a life span of **6** to **7 hours** and may live for up to **4 days** in the connective tissue.



Granulocytes Neutrophils



The lobes of their **multilobed nucleus** are connected to each other by slender chromatin threads.

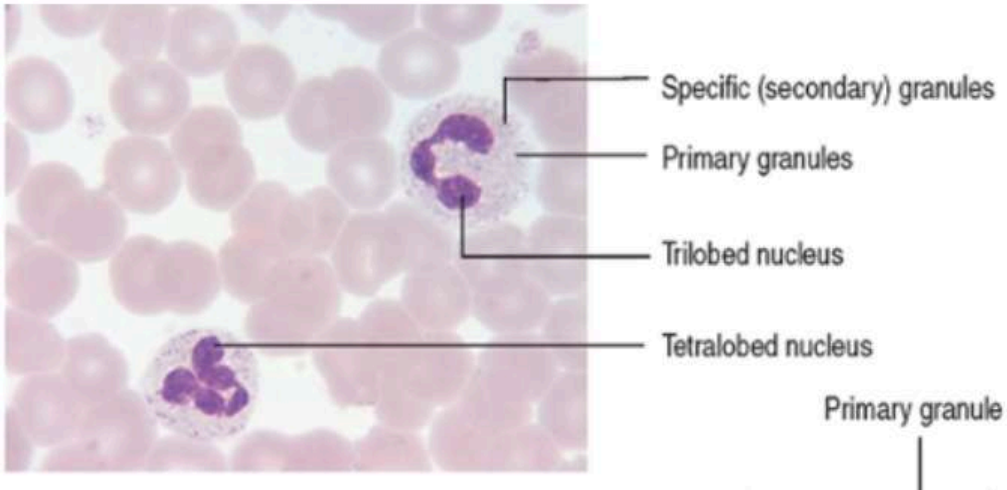
In females, the nucleus presents a characteristic small appendage, the "drumstick," which contains the condensed, inactive second X chromosome, but is not always evident in every cell.

Neutrophils are among the first cells to appear in acute bacterial infections. They possess very small specific granules.

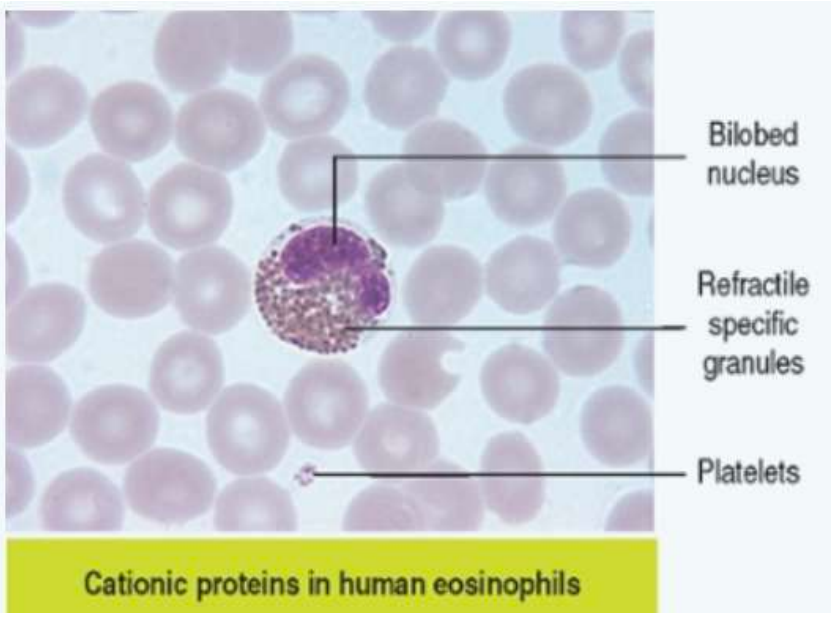
Granulocytes Neutrophils

After leaving the circulation, neutrophils act to eliminate bacteria or limit the extent of an inflammatory reaction in the connective tissue.

- **Elastase, defensins** and **myeloperoxidase** are enzymes contained in the primary granules.
- **Lactoferrin, gelatinase, lysozyme** and other **proteases** are seen in secondary granules. **L-selectin** and **integrins** in neutrophils bind to endothelial cell ligands **intercellular-adhesion molecules 1** and **2 (ICAM-1** and **ICAM-2)**. These ligands enable the antibacterial and antiinflammatory function of neutrophils in the extravascular space.



Granulocytes Eosinophils



Cationic proteins in human eosinophils

Eosinophils constitute less than 4% of the total white blood cell population.

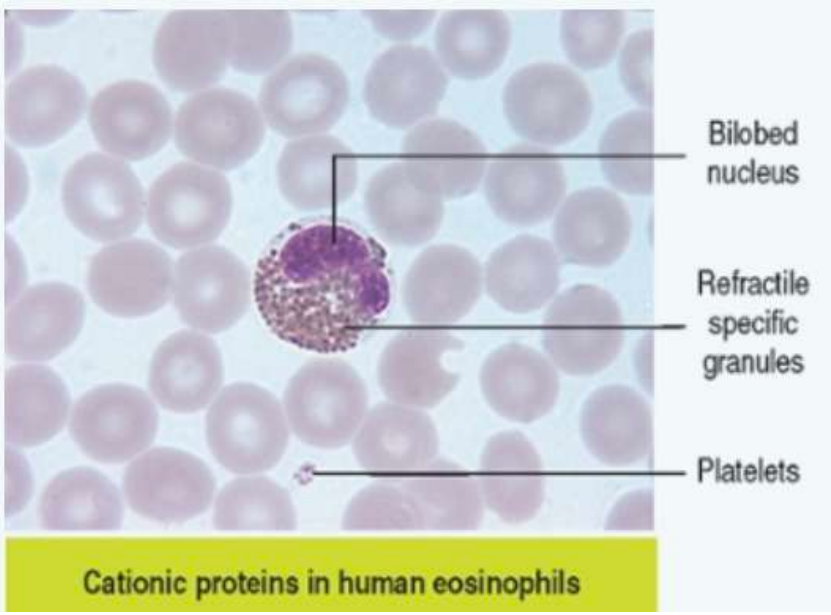
They are round cells containing large, salmon pink colored specific granules.

They have a sausage-shaped, bilobed nucleus in which the two lobes are connected by a thin chromatin strand and nuclear envelope.

Eosinophils function in parasitic infections and phagocytosing antigen-antibody complexes.

Granulocytes Eosinophils

Eosinophils have a characteristic **bilobed nucleus**. Their cytoplasm is filled with large, refractile granules that stain red in blood smears and tissue sections.

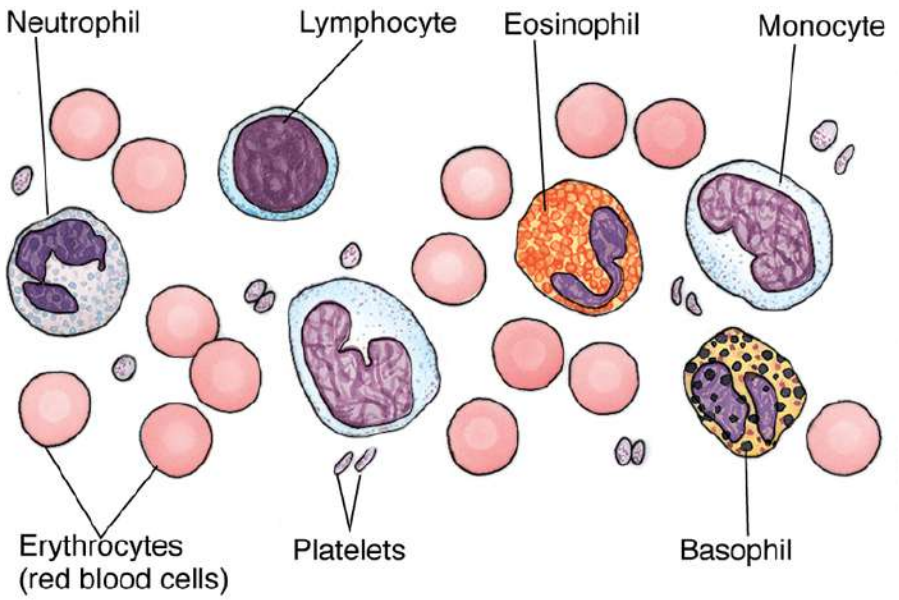


Cationic proteins in human eosinophils

Eosinophils constitute **1%** to **5%** of circulating leukocytes and have a half-life of about 18 hours. Eosinophils leave the circulation, recruited to the connective tissue by IL-5.

These cells are the first line of defense against **parasites** and also participate in triggering **bronchial asthma. Eosinophilic esophagitis**, associated with eosinophilia, is clinically defined by dysphagia and abdominal pain.
This condition is triggered by fungal and insect allergens

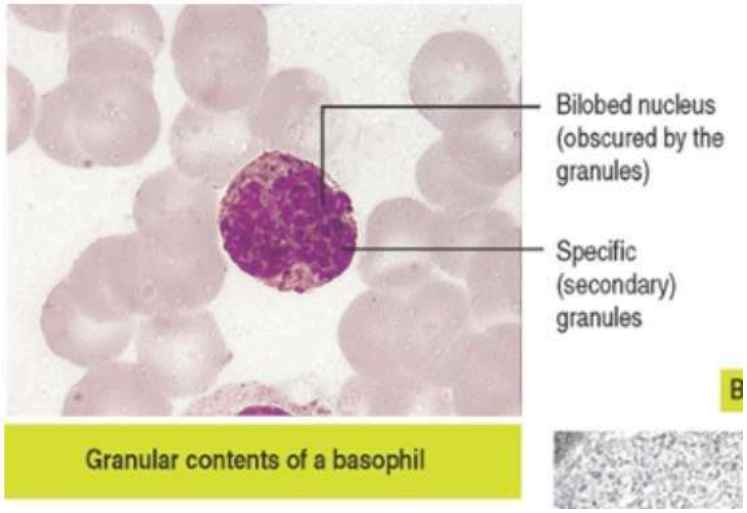
Circulating Cells of Blood (cont.)



Cells and platelets of circulating blood.

Basophils constitute less than 1% of the total leukocyte population. They are round cells and have an **S**-shaped nucleus, which is commonly masked by the large dark blue to black specific granules present in the cytoplasm. Basophils have several surface receptors on their plasmalemma, including **immunoglobulin E (IgE) receptors.** Their function is very similar to those of mast cells.

Granulocytes Basophils

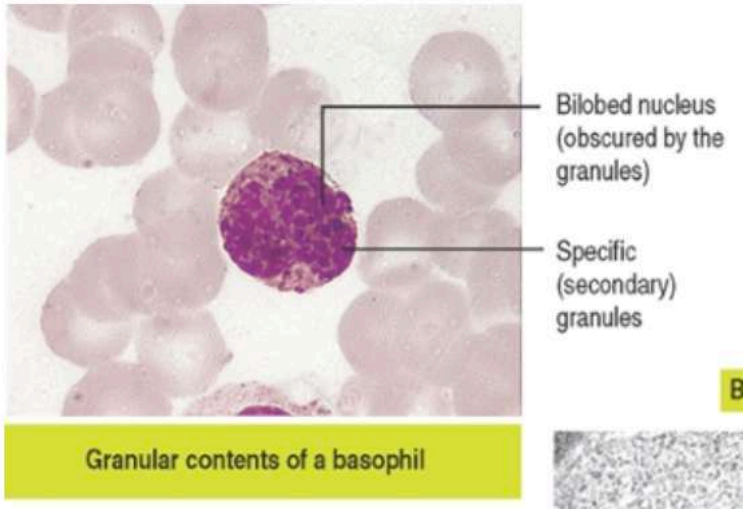


Granular contents of a basophil

Their specific granules are large and stain dark blue or purple. The nucleus is often obscured by the specific Granules.

Basophils have a short life span (about 60 hours), whereas mast cells survive for weeks and months.

Granulocytes Basophils



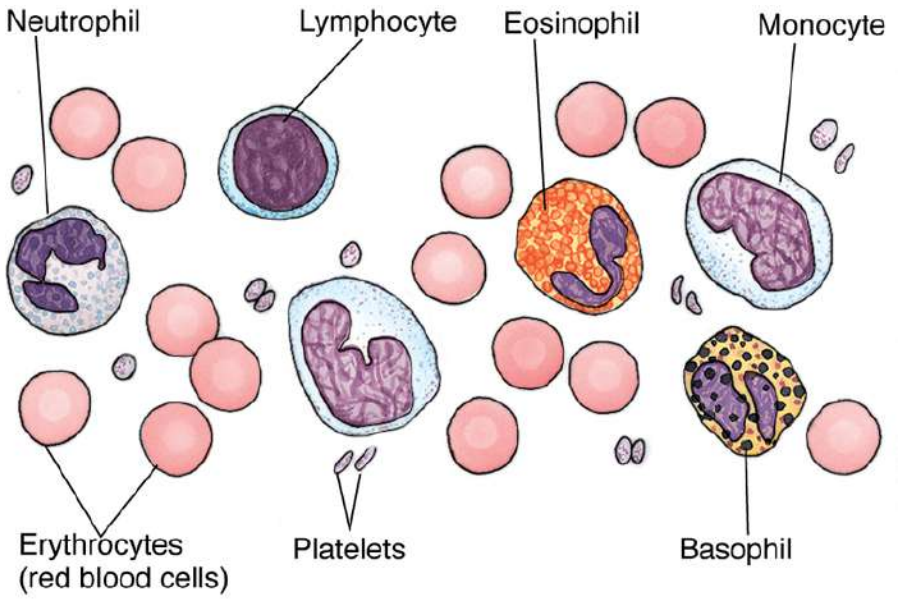
Granular contents of a basophil

Basophils complete their maturation in the bone marrow. Similar to Mast cells in the connective tissue, express on their surface IgE receptor.
In contrast, mast cells enter the connective tissue or mucosae as immature cells lacking cytoplasmic granules.

In addition, basophils and mast cells differ in the presence of c-kit receptor and CD49b but share FcεR1.
Basophils are c-kit^{-}FcεR1^{+} CD49b^{+};
mast cells are c-kit^{+}FcεR1^{+}CD49b^{-}.

Basophils play a role in **bronchial asthma** and **type 2 immunity** in response to allergens **(allergic skin reaction)** and parasitic worms **(helminths)**.

Lymphocytes



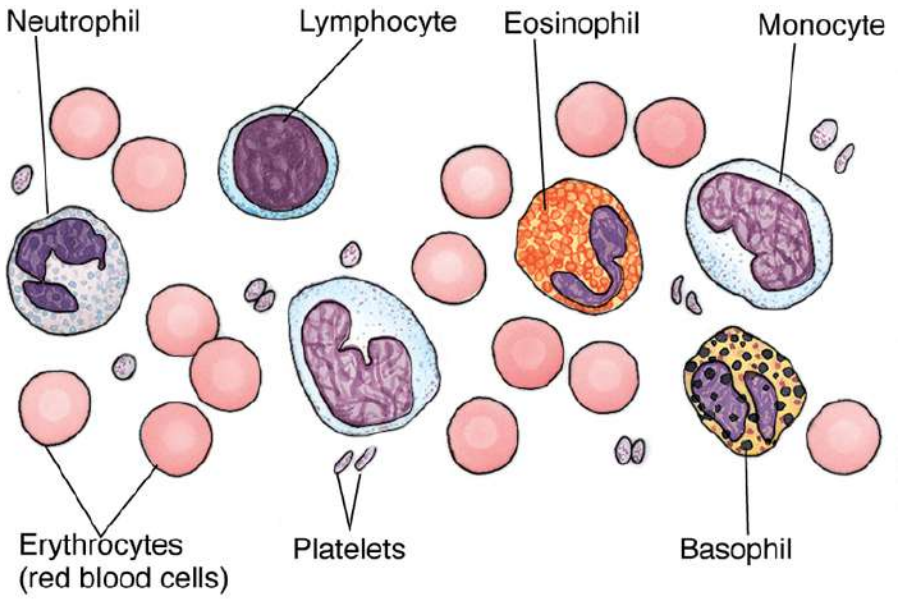
Cells and platelets of circulating blood..

Lymphocytes are either large **(3%** of lymphocytes; **7** to **12 μm)** or small **(97%** of lymphocytes; **6 to 8 μm** cells.

Lymphocytes constitute 20% to 25% of the total circulating leukocyte population.

They are round cells, somewhat larger than RBCs, and have a slightly indented, dense, round nucleus that occupies most of the cell. The cytoplasm is basophilic, often appearing as a thin rim around the nucleus. A few primary granules may be present. Lymphocytes may live for a few days or several years.

Lymphocytes



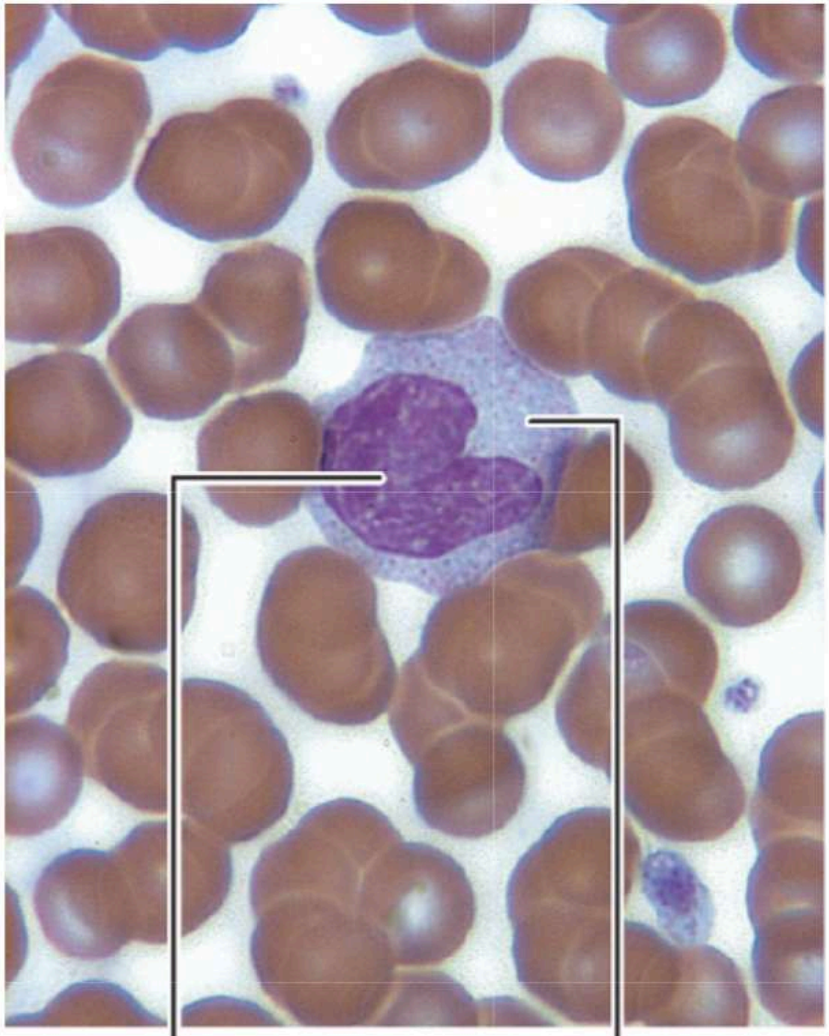
Cells and platelets of circulating blood..

Lymphocytes are divided into two categories:

B lymphocytes (also called **B cells)** are produced and mature in bone marrow. Antigen-stimulated B cells differentiate into antibody-secreting **plasma cells**.

T lymphocytes (also called **T cells)** are produced in bone marrow but complete their maturation in the **thymus**. Activated T cells participate in **cell-mediated immunity.**

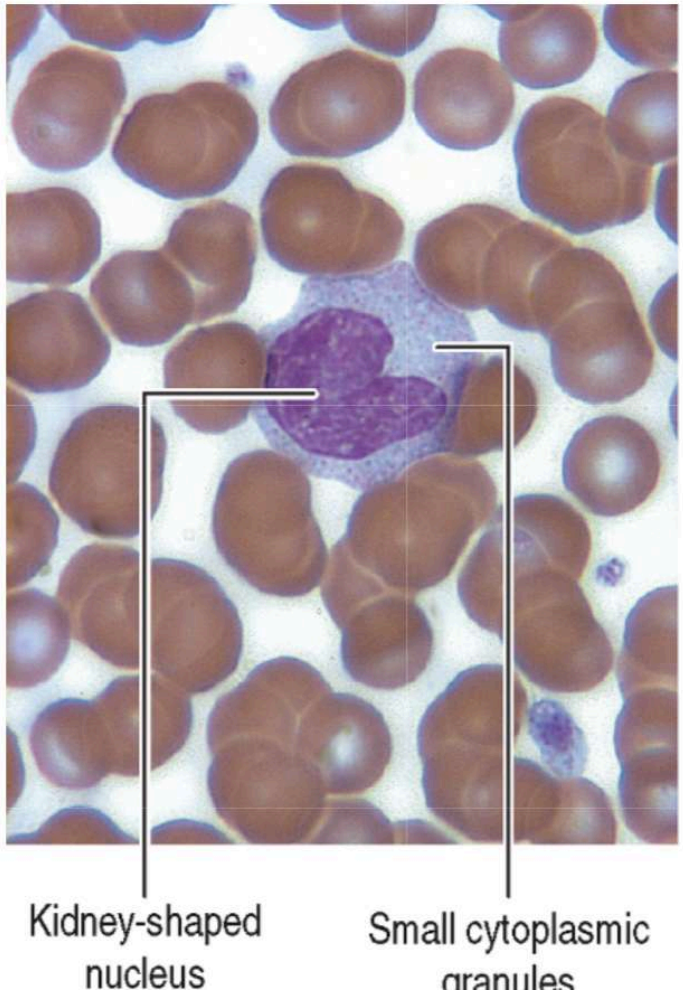
Monocytes



Monocytes are the largest leukocytes, with sizes ranging from 15-20 um. Monocytes travel briefly (**12** to **100 hours**) in the bloodstream and then enter the peripheral tissues where they become macrophages and survive a longer time.

In the connective tissue, monocytes differentiate into **macrophages**, which are involved in bacterial phagocytosis, antigen presentation and clean-up of dead cell debris.
In bone, monocytes differentiate into **osteoclasts** under the control of osteoblasts

Monocytes



Monocytes are the largest of the circulating blood cells and constitute 3% to 8% of the leukocyte population.

They have a large, **kidney-shaped nucleus** whose lobe-like extensions seem to overlap one another.

The chromatin network is coarse but not overly dense, their cytoplasm is bluish gray and has numerous azurophilic granules, (lysosomes) and occasional vacuole-like spaces, but no specific granules.

Macrophages are avid phagocytes, and as members of the **mononuclear phagocyte system** they phagocytose and destroy dead cells as well as antigens and foreign particulate matter (such as bacteria). They also have a major role in the immune response.

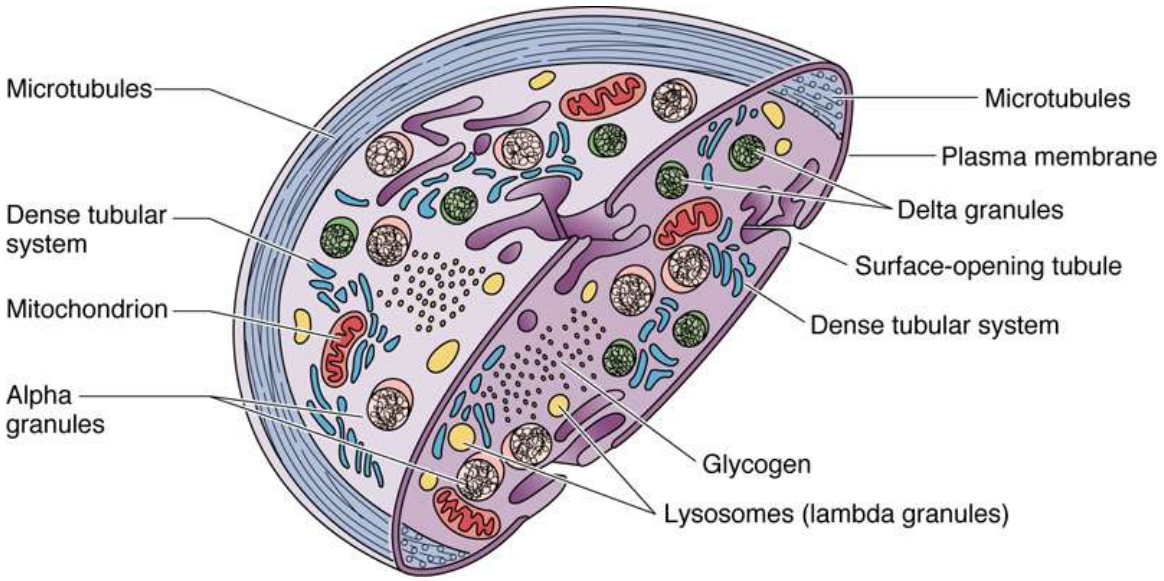
Platelets

Platelets are small **(2 to 4 μm)** cytoplasmic discoid fragments derived from the **megakaryocyte** under the control of **thrombopoietin**, a 35- to 70-kd glycoprotein produced in the kidneys and liver.

Megakaryocytes develop cytoplasmic projections that become **proplatelets**, which fragment into platelets. This differentiation process takes 7 to 10 days.

Platelets bind and degrade thrombopoietin, a mechanism that regulates platelet production.

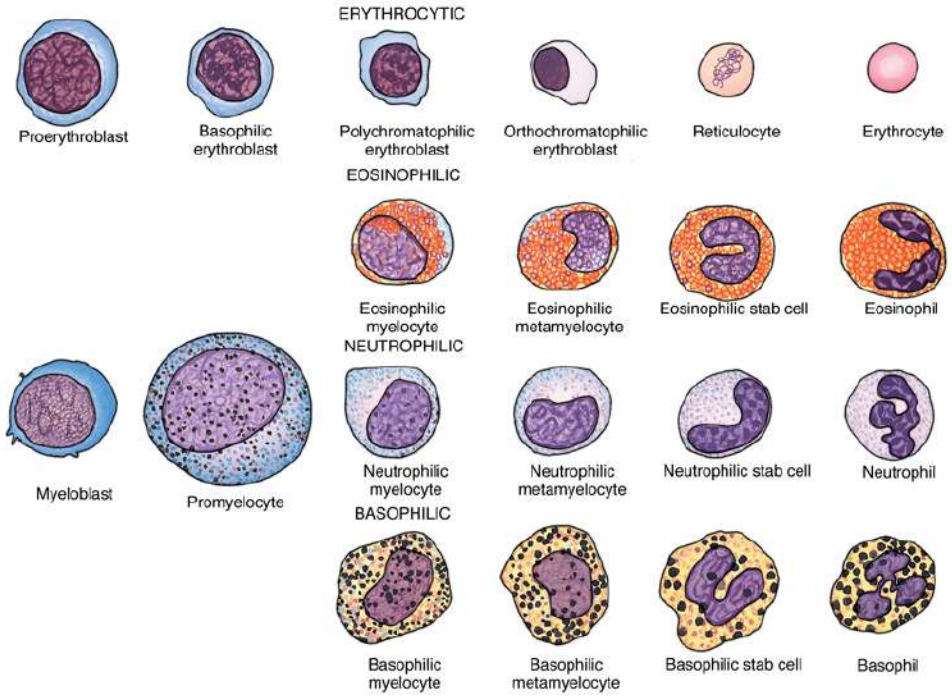
Platelets



Platelet ultrastructure. Note that the periphery of the platelet is occupied by actin filaments that encircle the platelet and maintain the discoid morphology of this structure.

If the endothelial lining of a blood vessel is disrupted and platelets come in contact with the subendothelial collagen, they become **activated,** release the contents of their granules, adhere to the damaged region of the vessel wall **(platelet adhesion),** and adhere to each other **(platelet aggregation).** Interactions of tissue factors, plasma-borne factors, and platelet-derived factors form a blood clot.

Cells of Bone Marrow

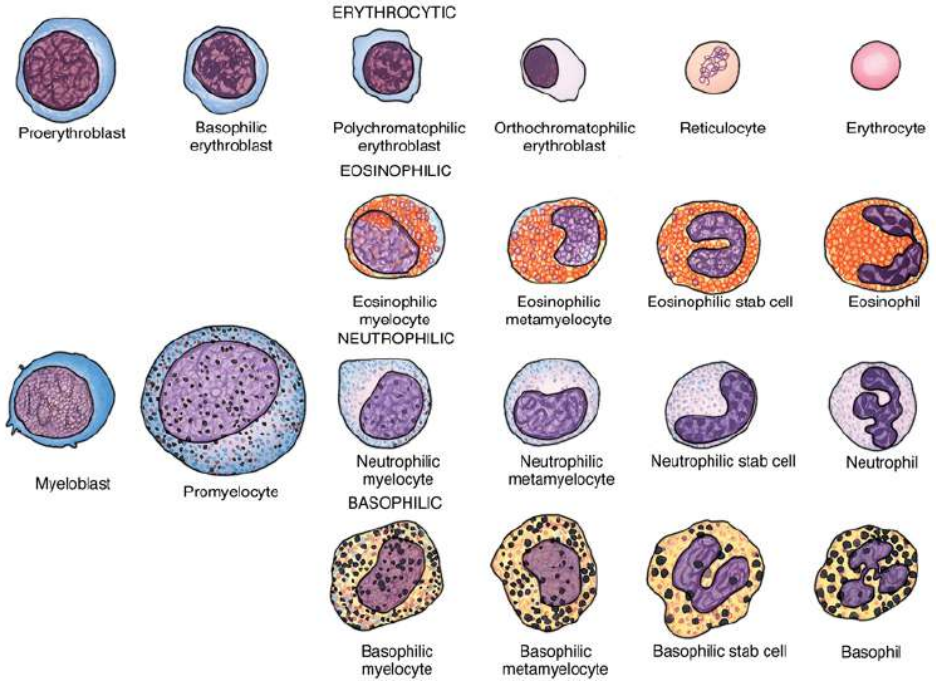


Precursor cells in the formation of erythrocytes and granulocytes. The myeloblast and promyelocyte intermediaries in the formation of eosinophils, neutrophils, and basophils are indistinguishable for the three cell types.

Bone marrow, a gelatinous, vascular connective tissue located in the marrow cavity, is richly endowed with cells that are responsible for hemopoiesis.

The marrow of the newborn is called **red marrow** because of the great number of erythrocytes being produced there. By age 20 years, however, the diaphyses of long bones house only **yellow marrow** because of the accumulation of large quantities of fat and the absence of hemopoiesis in the shafts of these bones. The marrow cavities of most cancellous bone contains red marrow even in the adult and hemopoiesis occurs there.

Cells of Bone Marrow



Precursor cells in the formation of erythrocytes and granulocytes. The myeloblast and promyelocyte intermediaries in the formation of eosinophils, neutrophils, and basophils are indistinguishable for the three cell types.

CFU-GEMM

All blood cells arise from **pluripotential hemopoietic stem cells (PHSCs),** which give rise to more PHSCs as well as to two types of **multipotential hemopoietic stem cells (MHSCs).** The two populations of MHSCs, **CFU-GEMM, colony forming unit-granulocyte, erythrocyte, monocyte, megakaryocyte**. and **colony-forming unit–lymphocyte (CFU-Ly),** are responsible for the formation of various progenitor cells.

CFU-GEMM cells are predecessors of the **myeloid cell lines** (erythrocytes, granulocytes, monocytes, and platelets); CFU-Ly are predecessors of the **lymphoid cell lines** (T cells and B cells). Both PHSCs and MHSCs resemble lymphocytes and constitute a small fraction of the population of circulating blood.

The accompanying diagram illustrates the provenance of RBCs and granulocytes.

Hematopoiesis

Hematopoiesis is the process of blood formation. The initial wave of hematopoiesis (Greek *haima*, blood; *poiein*, to make) in the **fetus** starts during the first trimester in islands of hematopoiesis found in the **yolk sac**.

The islands develop from **hemangioblasts**, the common progenitors of hematopoietic and endothelial cells.

Hematopoiesis

Fetal hematopoiesis continues after the second trimester in the **liver** and then in the **spleen** as a second definitive wave.

During the seventh month of intrauterine life, the **bone marrow** becomes the primary site of hematopoiesis, where it remains during adulthood.

In the adult, an approximate volume of 1.7 L of marrow contains 10^{12} hematopoietic cells, producing about 1×10^9 RBCs and about 1×10^8 leukocytes every hour.

The bone marrow consists of two microenvironmental domains, called **niches:**

- The **vascular niche**.
- The **endosteal niche**.

Niches provide physical support, soluble factors and cell-mediated interactions to regulate cell self-renewal, differentiation and quiescence of hematopoietic stem cells (HSCs). Under normal conditions, niches enable the balanced, or homeostatic, cell self-renewal and differentiation of HSCs. Under pathologic conditions, such as **myelodysplasia, aging** or **bone marrow malignancies**, niches can alter or restrain normal hematopoiesis.

Vascular niche

The **vascular niche** consists of **blood vessels** surrounded by a distinct population of non-hematopoietic stromal cells, including **mesenchymal stem cells, adipose cells, endothelial cells, reticular stromal cells and macrophages**.

The vascular niche provides a microenvironment for the short-term proliferation and differentiation of HSCs.

The endosteal niche

The **endosteal niche**, located at the endosteum–bone marrow interface, consists of preosteoblasts (osteoprogenitor cells), osteoblasts and osteoclasts interacting with HSCs. Type I collagen is the most abundant extracellular component of the endosteal niche. The endosteal niche is regarded as a site for long-term storage of quiescent HSCs.

Osteoblasts produce multiple hematopoietic cytokines, including **G-CSF** (granulocyte colony-stimulating factor), **M-CSF** (macrophage colony-stimulating factor), **GM-CSF** (granulocyte-macro-phage-colony stimulating factor), **IL-1, IL-6** and **IL-7**.

Hematopoietic cell populations

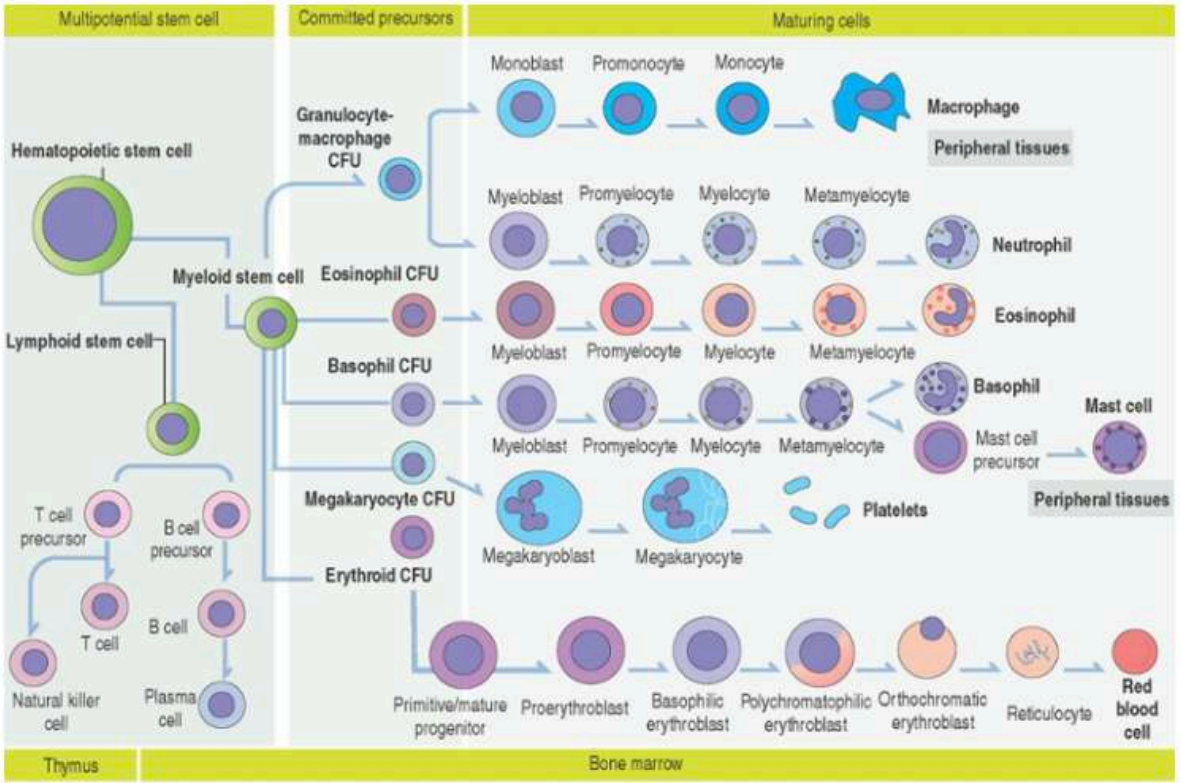
The bone marrow consists of three major populations:

- **HSCs**, capable of **self-renewal**.
- **Committed precursor cells**, responsible for the generation of distinct cell lineages.
- **Maturing cells**, resulting from the differentiation of the committed precursor cell population.

Hematopoietic cell populations

HSCs can self-renew and produce two committed precursor cells that develop into distinct cell progenies:

- The **myeloid stem cell**.
- The **lymphoid stem cell.**



The bone marrow consists of: (1) **hematopoietic stem cells (HSCs)**, multipotential cells capable of self-renewal; (2) **committed precursor cells (myeloid stem cell and lymphoid stem cell)**; (3) **maturing cells**. Maturing cells develop from cells called **colony-forming units (CFUs)**.

The **myeloid stem cell** gives rise to CFUs responsible for the regeneration of red blood cells (**erythroid CFUs**), platelets (**megakaryocyte CFUs**), basophils and mast cells (**basophil CFUs**) and eosinophils (**eosinophil CFUs**). Monocytes and neutrophils derive from a common committed progenitor cell (**granulocyte-macrophage CFU**). The **lymphoid stem cell** generates the **B cell progeny** in the **bone marrow** and **T cell progenies** in the **thymus**. They are discussed in detail in Chapter 10, Immune-Lymphatic System.

Hematopoietic cell populations

- **Self-renewal** is an important property of HSCs. Self-renewal preserves the pool of stem cells and is critical for feeding common myeloid progenitor and common lymphoid progenitor into the differentiation or maturation pathway.
- HSCs are difficult to identify, mainly because they represent approximately 0.05% of total hematopoietic cells (about 10^6 to 10^7 stem cells). In bone marrow transplantation, **only 5%** of the normal hematopoietic stem cells are needed to repopulate the entire bone marrow.

HSCs cannot be identified by morphology. They can be recognized by specific cell surface markers (c-kit receptor and Thy-1).

The primary lymphoid organs produce the cell components of the immune system. They are:

- The **bone marrow**.
- The **thymus**.

The secondary lymphoid organs are the sites where immune responses occur. They include:

- The **lymph nodes**.
- The **spleen**.
- The **tonsils**.
- Aggregates of lymphocytes and antigen-presenting cells in the **lung** (bronchial-associated lymphoid tissue, BALT) and the mucosa of the **digestive tract** (gut-associated lymphoid tissue, GALT), including **Peyer's patches**.

The **two key cell components of the immune system** are **lymphocytes** and **accessory cells.**

Lymphocytes include two major cell groups:

- **B cells**, responding to cell-free and cell-bound antigens.
- **T cells**, subdivided into two categories: **helper T cells** and **cytolytic** or **cytotoxic T cells**. T cells respond to cell-bound antigens presented by specific molecules.

Types of immunity

Immunity in general is the reaction of cells and tissues to foreign (non-self) substances or **pathogens**, including bacterial, viral and parasite antigens. Two types of immunity are distinguished:

- Innate or natural immunity.
- Adaptive or acquired immunity.

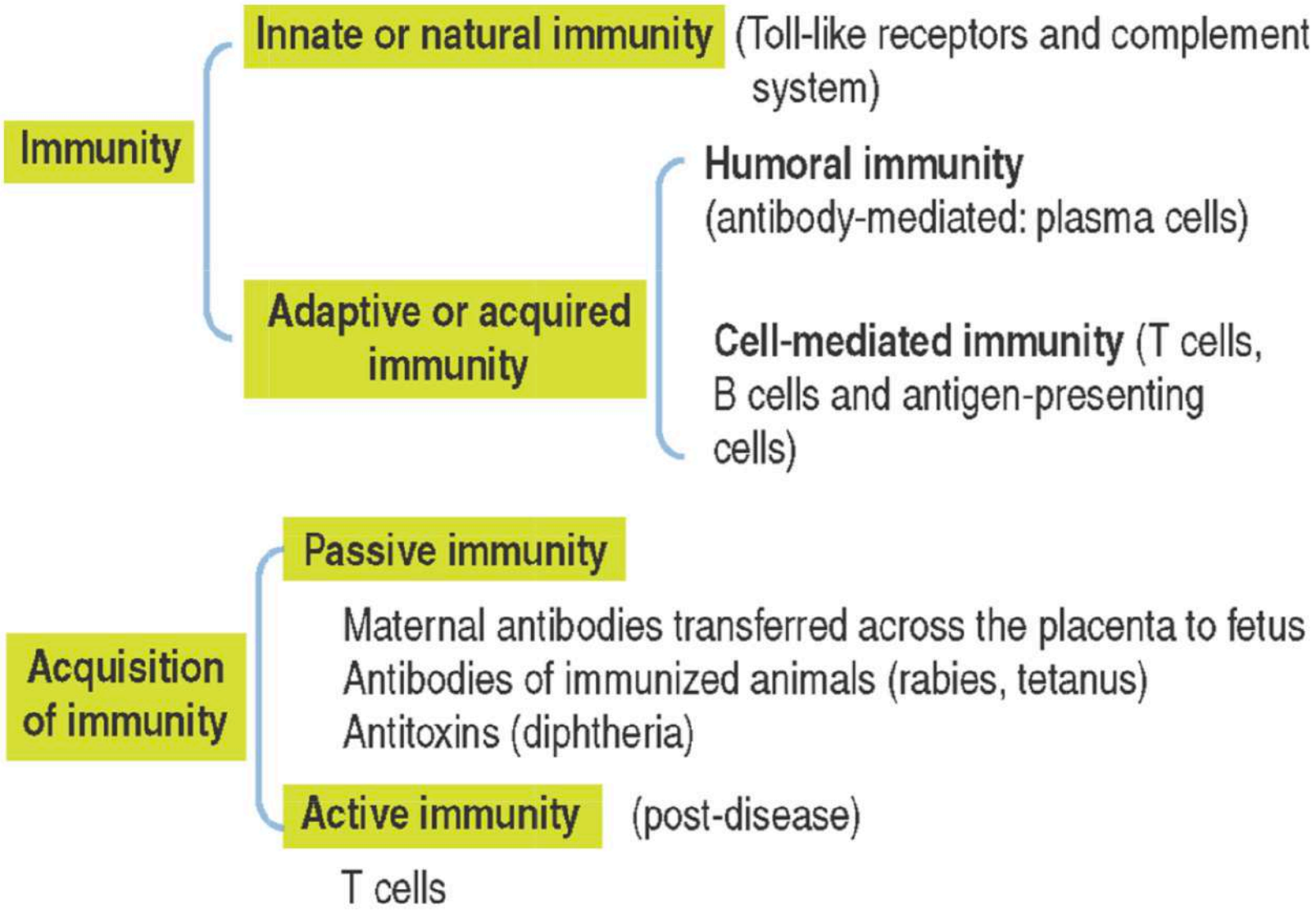
Innate or **natural immunity of the newborn** is the simplest mechanism of protection. It does not require previous exposure to a pathogen and elicits rapid responses by ***macrophages and dendritic cells***.

Toll-like receptors (TLRs) initiate innate immunity against components of invading pathogens (such as nucleic acids, proteins, lipids and polysaccharides). Different TLRs recognize distinct types of conserved microbial structures, a condition that provides specificity to the innate response

Adaptive or acquired immunity develops when an individual is exposed to a pathogen with the aims of eliminating the pathogen as well as the generation of immunologic memory.

To achieve adaptive or acquired immunity, it is necessary to select lymphocytes **(clonal selection)** from a vast repertoire of cells bearing antigen-specific receptors generated by a mechanism known as **gene rearrangement**.

Types of immunity



Lymphoid Organs

Lymphoid organs are the sites where immune protective responses occur when the body is confronting immunological challenges.

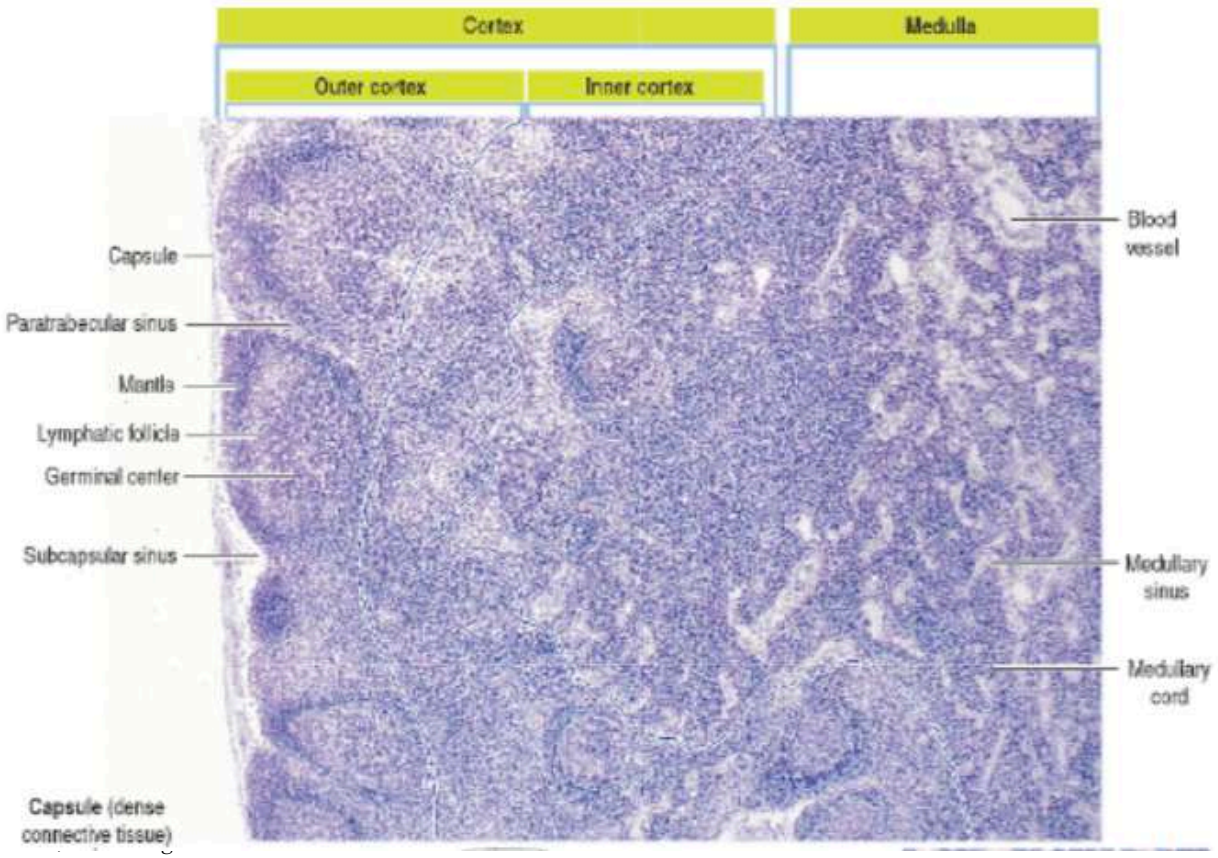
The major lymphoid organs are:

- The **lymph nodes**.
- The **thymus**.
- The **spleen**.

Lymph nodes

The function of lymph nodes is to filter the lymph, maintain and differentiate B cells and house T cells.

Lymph nodes detect and react to lymph-borne antigens.



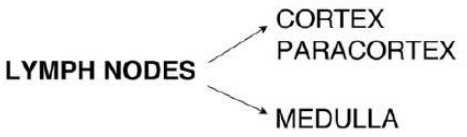
A lymph node is surrounded by a capsule and the parenchyma is divided into a **cortex** and a **medulla**. The **capsule** consists of dense irregular connective tissue surrounded by adipose tissue. The capsule at the convex surface of the lymph node is pierced by **afferent lymphatic vessels**. Afferent lymphatic vessels have **valves** to prevent the reflux of lymph entering a lymph node. The stroma, or parenchyma, of a lymph node consists of interconnected fibroblastic **reticular cells** and **fibers** forming an open network, which enables B-cell and T-cell compartmentalization and survival, as well as the transport of antigens and signaling molecules deep in the lymph node. Cell compartmentalization ensures adaptive immune responses to antigen and inflammation.

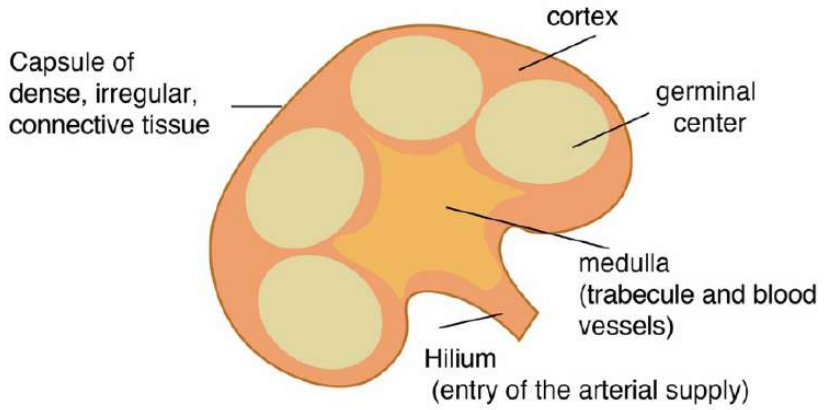
The **cortex** has two zones:

- The **outer cortex**, containing **lymphoid follicles,** rich in **B lymphocytes**.

- The **deep or inner cortex**, housing **$CD4^+$ helper T cells** and **venules** lined by **high endothelial cells**.

The deep or inner cortex is a zone in which mainly $CD4^+$ helper T cells interact with B cells to induce their proliferation and differentiation when exposed to a specific antigen.





Lymphoid follicle consists of:

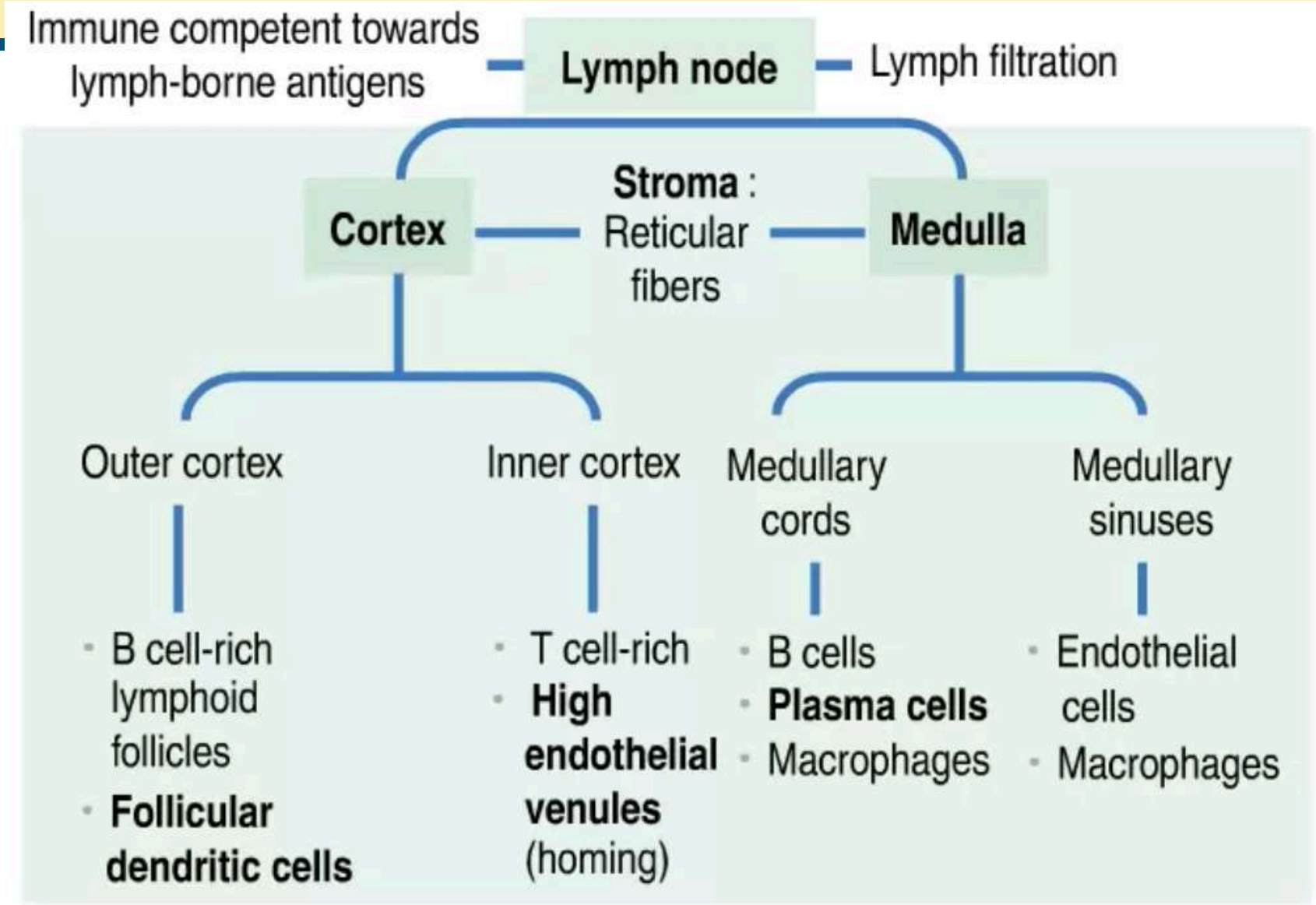
A **mantle** (facing the cortex),

A **germinal center** containing mainly proliferating B cells or **lymphoblasts**, resident **follicular dendritic cells (FDCs)**, migrating **dendritic cells, macrophages** and supporting **reticular cells**, which produce reticular fibers (type III collagen).

The **medulla** is surrounded by the cortex, except at the region of the **hilum**. The hilum is a concave surface of the lymph node where **efferent lymphatic vessels** and a single **vein** leave and an **artery** enters the lymph node.

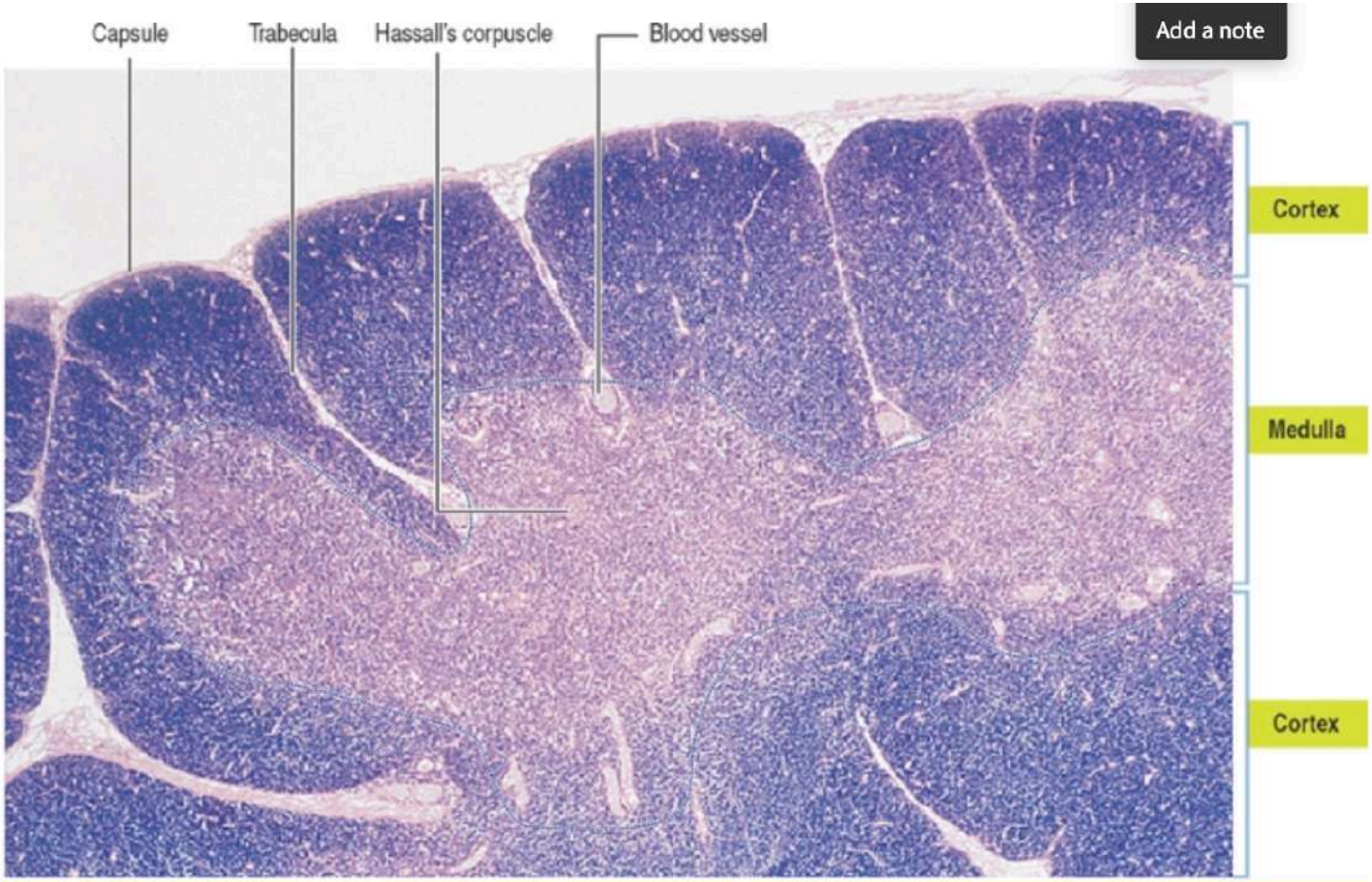
The medulla consists of two major components:

- **Medullary sinusoids**, spaces lined by endothelial cells surrounded by reticular cells and macrophages.
- **Medullary cords**, with B cells, macrophages and **plasma cells.** Activated B cells migrate from the cortex, enter the medullary cords and become plasma cells. This is a strategic location, because plasma cells can secrete immunoglobulins directly into the lumen of the medullary sinuses without leaving the lymph node.



Thymus

The thymus consists of **two lobes** subdivided into several **incomplete lobules**, each consisting of an independent **cortex** and a shared **medulla**



The medulla contains **mature thymocytes** migrating from the cortex. Maturation of the thymocytes is completed in the medulla and functional thymocytes enter postcapillary venules in the corticomedullary junction to exit the thymus.

The medulla harbors **medullary thymic epithelial cells (mTECs)** and a subset of them form **Hassall's corpuscles**. Hassall's corpuscles are present only in the medulla of the thymus.

Hassall's corpuscles are aggregates of terminally differentiated cornified mTECs

Note that **the blood-thymus barrier is not present in the medulla** and that **Hassall's corpuscles can be seen only in the medulla**. In addition, be aware that specialized cTECs and mTECs provide the required checkpoints for thymocyte selection.

Development of the thymus

The **mesenchyme** gives rise to the capsule, trabeculae and vessels of the thymus. The **thymic epithelial rudiment** attracts **bone marrow–derived thymocyte precursors, dendritic cells** and **macrophages** required for normal thymic function.

During **fetal life**, the thymus contains lymphocytes derived from the liver. T-cell progenitors formed in the bone marrow during hematopoiesis enter the thymus as **immature thymocytes** and mature to become (predominantly **CD4**$^{+}$ or **CD8**$^{+}$**)**, which are carried into lymph nodes, spleen and other lymphatic tissues.

The thymus in humans is fully developed before birth. The production of T cells is significant before puberty. After puberty, the thymus begins to involute and the production of T cells in the adult decreases. The progenies of T cells become established and immunity is maintained without the need to produce new T cells.

A significant difference from the lymph node and the spleen is that **the stroma of the thymus consists of thymic epithelial cells (TECs)** organized in a dispersed network to allow for intimate contact with developing **thymocytes**, the cell precursors arriving from bone marrow. In contrast to the thymus, the stroma of the lymph node and the spleen contains reticular cells and reticular fibers. Stromal epithelial cells are absent.

Spleen

The spleen is the largest secondary lymphoid organ of the body. The spleen **lacks a cortex and a medulla**.

The spleen has two major components with distinct functions:

The **white pulp**.

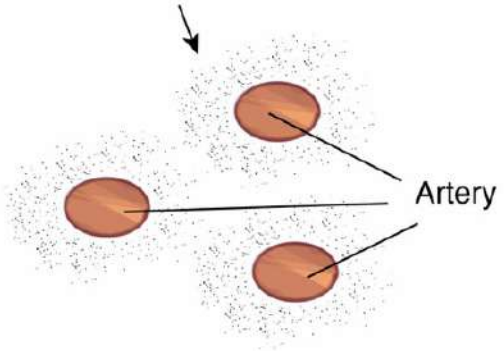
The **red pulp**.

The **white pulp is the immune component of the spleen**.
The cell components of the white pulp are similar to those of the lymph node, except that antigens enter the spleen from the blood rather than from the lymph.
The red pulp is a **filter, which removes aged and damaged red blood cells and microorganisms from circulating blood**.
It also is a **storage site for red blood cells**. Bacteria can be recognized by macrophages of the red pulp and removed directly or after they are coated with complement proteins (produced in the liver) and immunoglobulins (produced in the white pulp).

Pulp → Red Pulp (mostly of venous sinuses)

Pulp → White Pulp (mostly lymphocytes)

lymphocytes surrounding the artery will form a follicolar structure



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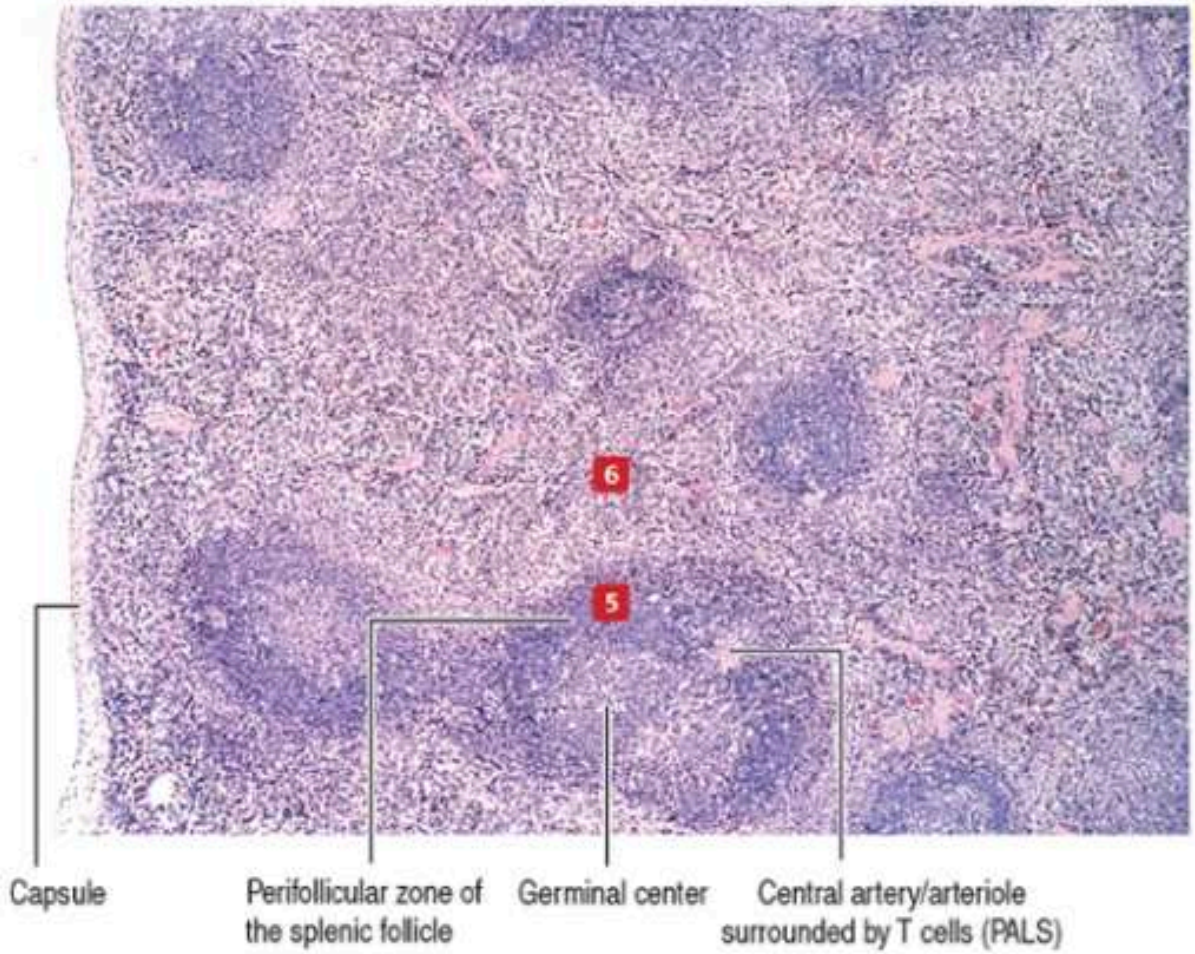
Spleen



White and red pulp

5 The white pulp consists of four components: (1) the central/artery arteriole; (2) the periarteriolar lymphoid sheath (PALS); (3) a splenic follicle formed by B cells (found in the perifollicular zone), reticular cells and antigen-presenting cells; and (4) a germinal center.

6 The red pulp surrounds the white pulp. As discussed later, the white and red pulp interact at the marginal channel, a permeable gate between the red pulp compartment and the white pulp compartment.

The red pulp receives a significant blood supply, including antigens entering the spleen from the blood. This differs from the lymph node, where antigens enter through the afferent lymphatic vessels. Although the splenic follicle mimics a lymphatic nodule of the lymph node cortex, the central artery/arteriole is a distinctive feature. The spleen has no afferent lymphatic vessels.

The spleen has two major components with distinct functions:
The **white pulp**.
The **red pulp**.