Innate immunity and immune organs

Lab1

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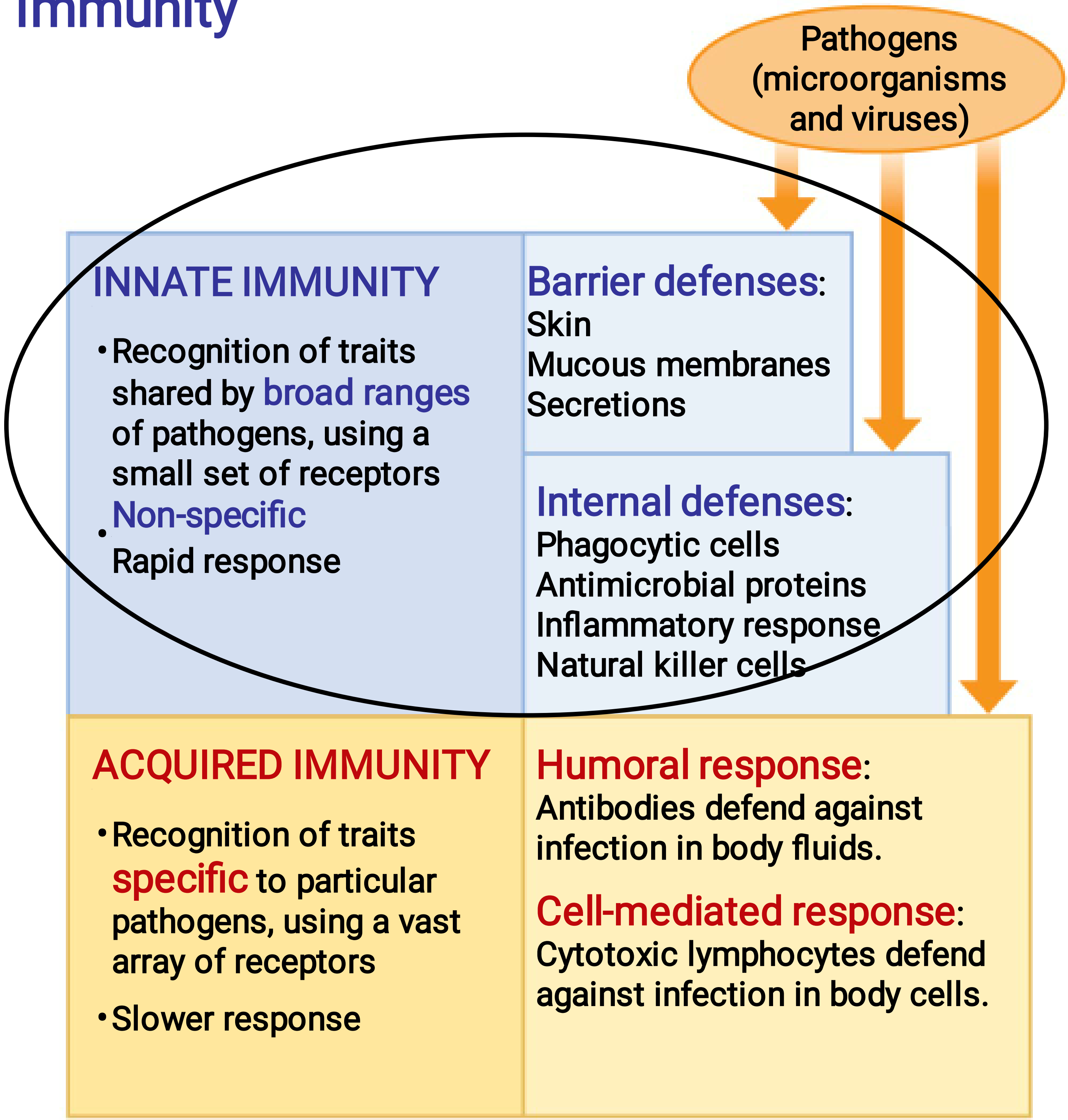
Animal Immunity



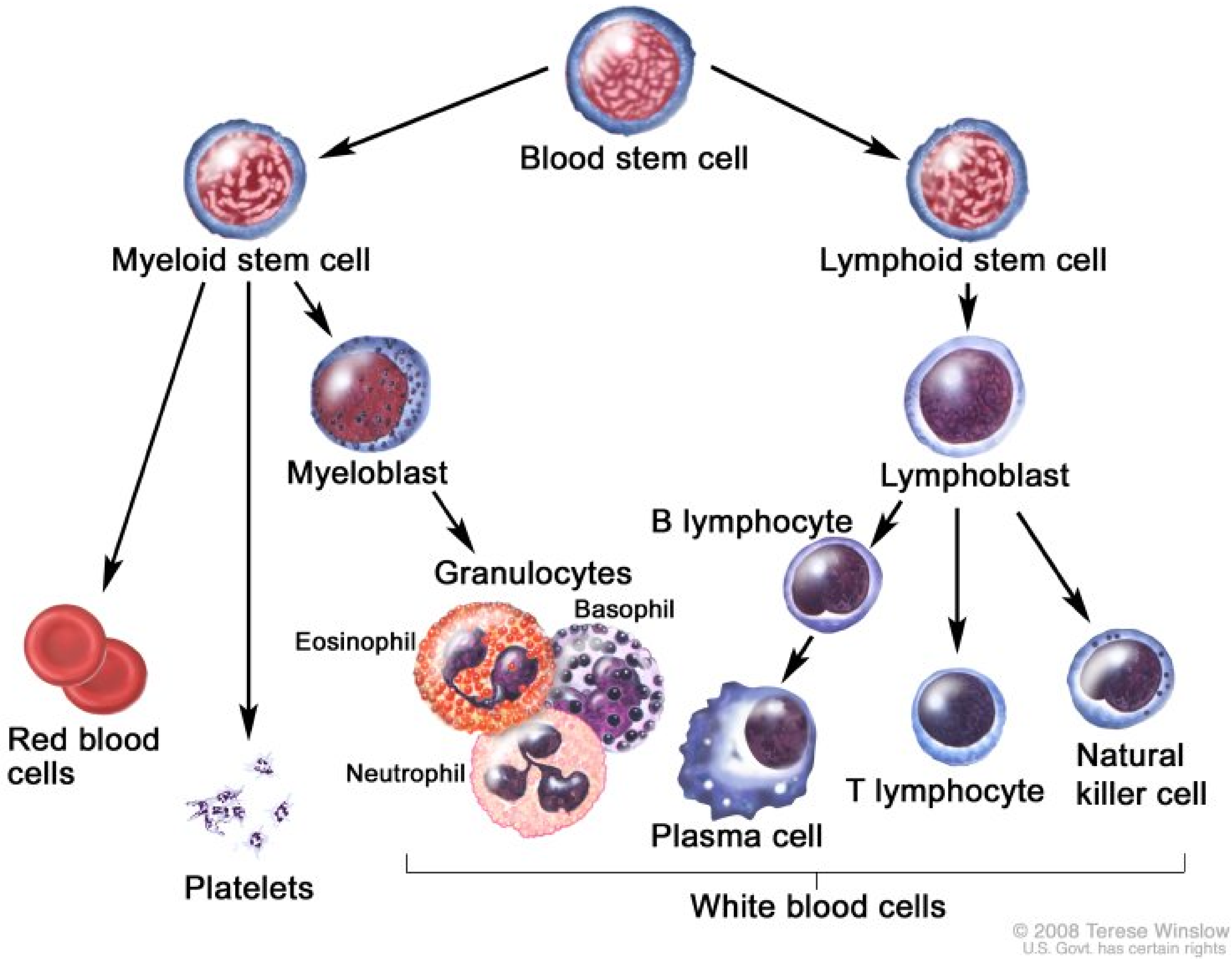
Barrier Defenses

- ***Barrier defenses*** include the ***skin*** and ***mucous*** *membranes* of the respiratory, urinary, and reproductive tracts.
- *Mucus* traps and allows for the removal of microbes.
- Many ***body fluids*** including saliva, mucus, and tears are hostile to microbes.
- The *low pH* of skin and the digestive system prevents growth of microbes.

Cellular Innate Defenses

- *White blood cells* = ***leukocytes*** engulf pathogens in the body via *phagocytosis*.
- A white blood cell engulfs a microbe, then fuses with a lysosome to destroy the microbe.
- There are different types of WBCs:

1. Mononuclear phagocyte system(macrophages).
2. Polymorphonuclear leukocyte.


Blood stem cell
Myeloid stem cell
Lymphoid stem cell
Myeloblast
Lymphoblast
B lymphocyte
Granulocytes
Basophil
Eosinophil
Neutrophil
Red blood cells
Platelets
Plasma cell
T lymphocyte
Natural killer cell
White blood cells
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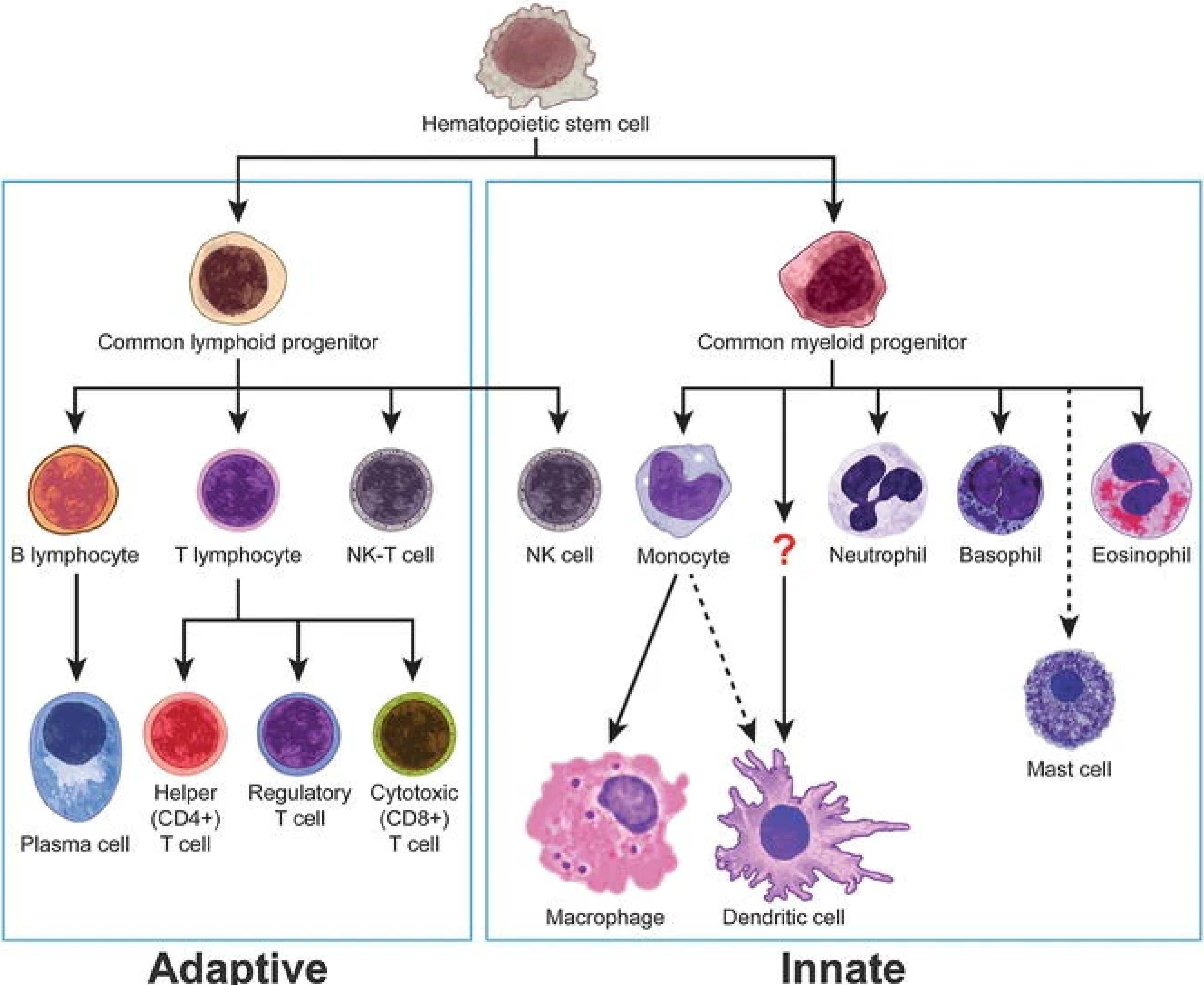
1-Mononuclear phagocyte system (macrophages) -Monocytes-

- Have rounded or kidney-shaped nuclei.
- Originate in BM, and first to leave.
- When monocyte becomes settled in tissue, they are called macrophages.
- Some mononuclear cells may differentiate to dendritic cells.
- Phagocytic, and help in acquired immune response.
- They have many names; kupffer cells in liver, histiocytes in connective tissues, macrophage in bone marrow, spleen and lymph nodes, langerhans' cells in skin, osteoclast in bone, mesangial cell in kidney, microglial cells in brain and monocytes in blood.


Hematopoietic stem cell
Common lymphoid progenitor
Common myeloid progenitor
B lymphocyte
T lymphocyte
NK-T cell
NK cell
Monocyte
?
Neutrophil
Basophil
Eosinophil
Plasma cell
Helper (CD4+) T cell
Regulatory T cell
Cytotoxic (CD8+) T cell
Macrophage
Dendritic cell
Mast cell
Adaptive
Innate

2. Polymorphonuclear leukocyte.

A. **Neutrophils**

- In case Bacterial infection.
- (95% of granulocytes) respond w/I 24 hours of stimulus (the earliest). Have 20 times as many receptors as macrophages.

B. Eosinophils

- On skin and respiratory ducts.
- These cells are eosinophilic or "acid-loving" as shown by their affinity to coal tar dyes and appear brick-red after staining with eosin, a red dye.
- They have many hydrolytic enzymes responsible for the anti-helminthic activity. One component which is unique to the eosinophils - and highly toxic to worms is a substance known as Major Basic Protein (MBP).

Phagocytic cells…

C- Basophils and mast cells

- In case of stress and Allergy.
- Granulocytes have acidic proteoglycan, Lobed nucleus- more variable, large coarse granules stain blue with basic dye methylene blue.

D- Mast cells is the sessile form whereas basophils is the circulating form.

E- Lymphocytes (NK-Cells)

-Dendritic cells

- stimulate development of acquired immunity.
- The main function as antigen-presenting cells.
- Dendritic cells are present in tissues that are in contact with the external environment, mainly the skin (where there is a specialized dendritic cell type called Langerhans cells) and the inner lining of the nose, lungs, stomach and intestines.

DC or dendritic cells

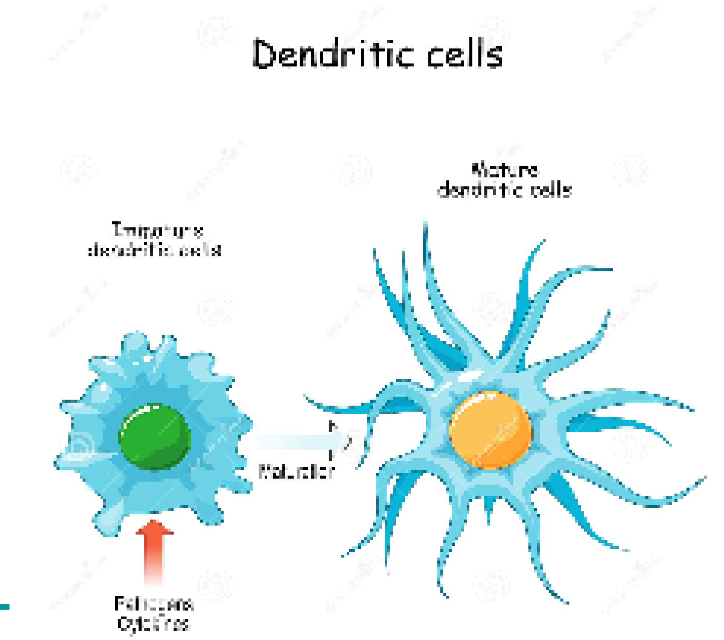
4 types:

✓Myeloid DC, macrophage origin, common, phagocytose antigen, and activate T cells.

✓Lymphoid DC, lymphocyte origin, recruit cells to the site of infection.

✓Follicular DC, mesenchymal origin, present in peripheral lymph nodes, activate B cells.

✓Plasmacytoid DC, are early cellular responders to viral infection. They have potent antiviral activities. Rare type cells secrete large quantity of type 1 interferon.



Cells of the blood

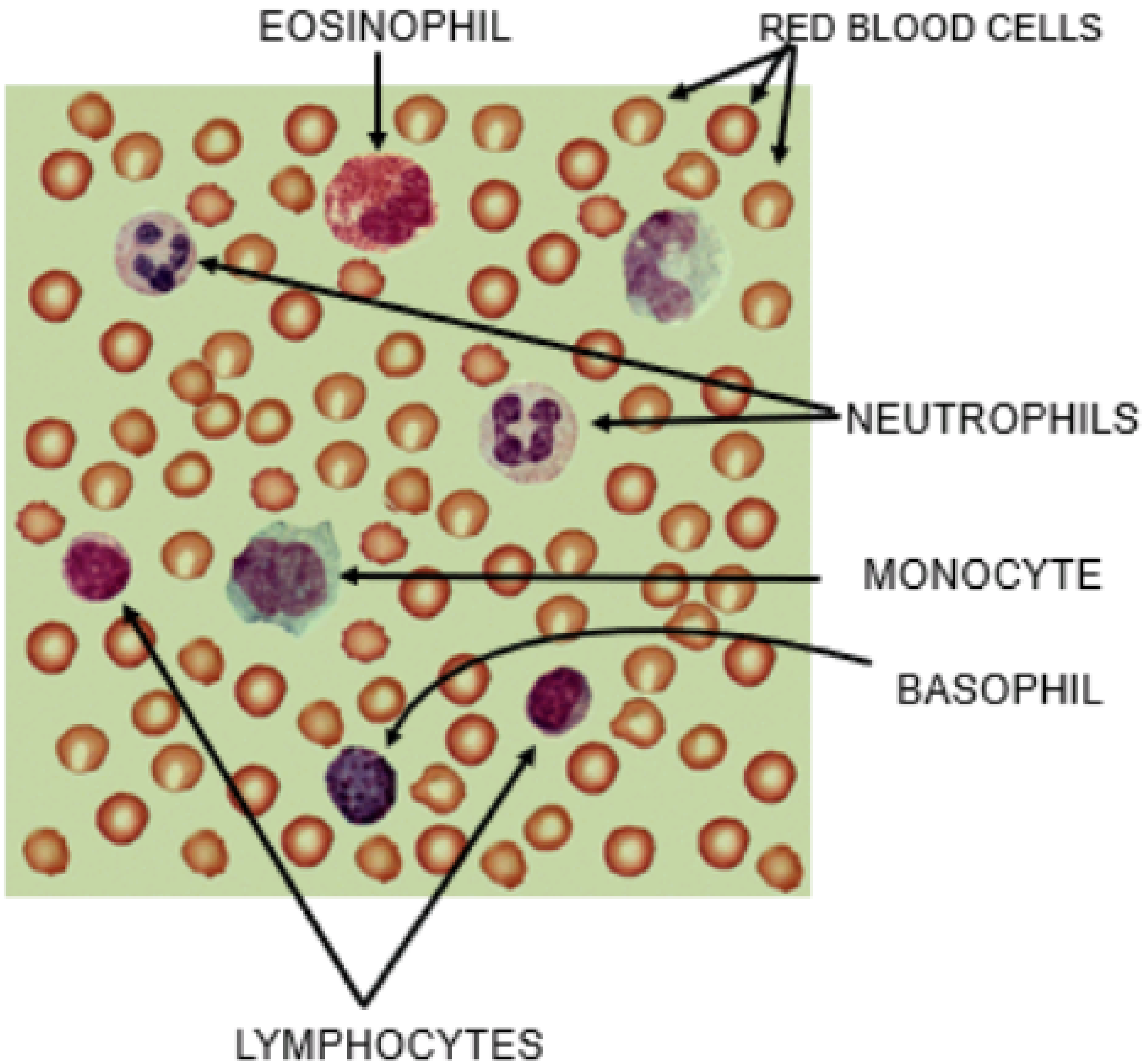


TABLE 41.2 Differential White Blood Cell Count

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

(3)

WHITE CELL COUNT (LEUKOCYTE COUNT)

The white cell count is the number of the white cells in 1.0 cubic millimeter of blood. In the total leukocyte count no distinction is made among the six normal types (neutrophils. bands, lymphocytes, monocytes, eosinophils).

Normal values:

In health the Whit cell count varies between 4,500 and 11,000 cells per cubic millimeter ($4.5 - 11.0 \times 10^9$ L). These variations are caused by some activities done by the persons such as bath, exercise, digestion and others. The white cell count rises and falls to indicate the cause of a disease or progress of infection.

1. The leukocyte count rises above the normal values in some diseases which may rise to 20,000 cells per cubic millimeter, (leukocytosis). It is due to a stimulation of the white cell factories in the bone marrow, this stimulation may be caused by such factor as bacteria and invading organisms.

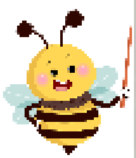
2. The white cell counts drop below the normal values in other diseases which may drops to 3.000 cell/cubic millimeter (leukopenia), this is due to a depression of the white cell factories in the bone marrow. The depression may be caused by such agents as viruses and undesirable chemicals.

Methods used for the white cell counts, 2 main methods are used:

- **Microscopic methods**
- **Automatic method.**

Microscopic method:

Principle of the test: white blood is diluted 1 in 20 in an acid reagent which caus haemolysis to the red cells, leaving the white cells to be counted by usi haemocytometer.



WBC reference range

(N.B. These are guideline figures which should be checked locally)

- Children at one year — $6.0\text{-}18.0 \times 10^9$ / L
- Children at 4-7 year — $5.0\text{-}15.0 \times 10^9$ / L
- Adults — $4.0\text{-}10.0 \times 10^9$ / L
- Pregnant women — up to 15.0×10^9 / L

Leukocytosis: the main causes of a raised WBC count are:

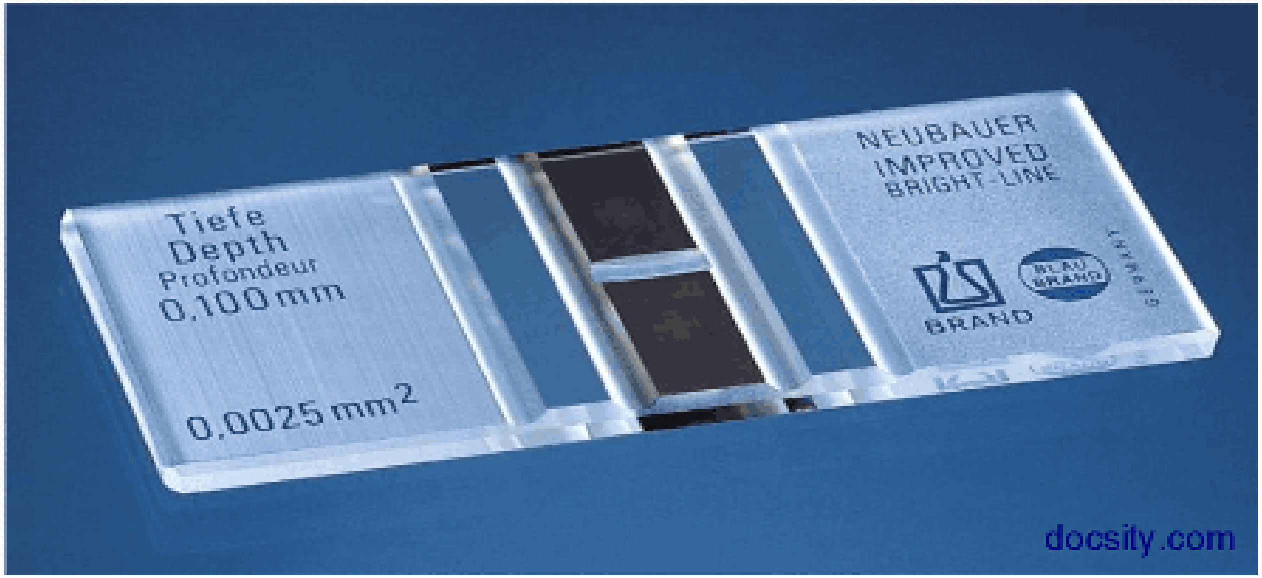
- Acute infections: e.g. pneumonia , meningitis , abscess tonsillitis , cholera. septicemia....etc Appendicitis, leukemia, meningitis, rheumatic fever, newborn, pregnancy, chickenpox,....
- Inflammation and tissue necrosis e.g. burns, ,trauma, arthritis , tumors,...etc
- Acute hemorrhage
- Stress, menstruation, exercise,

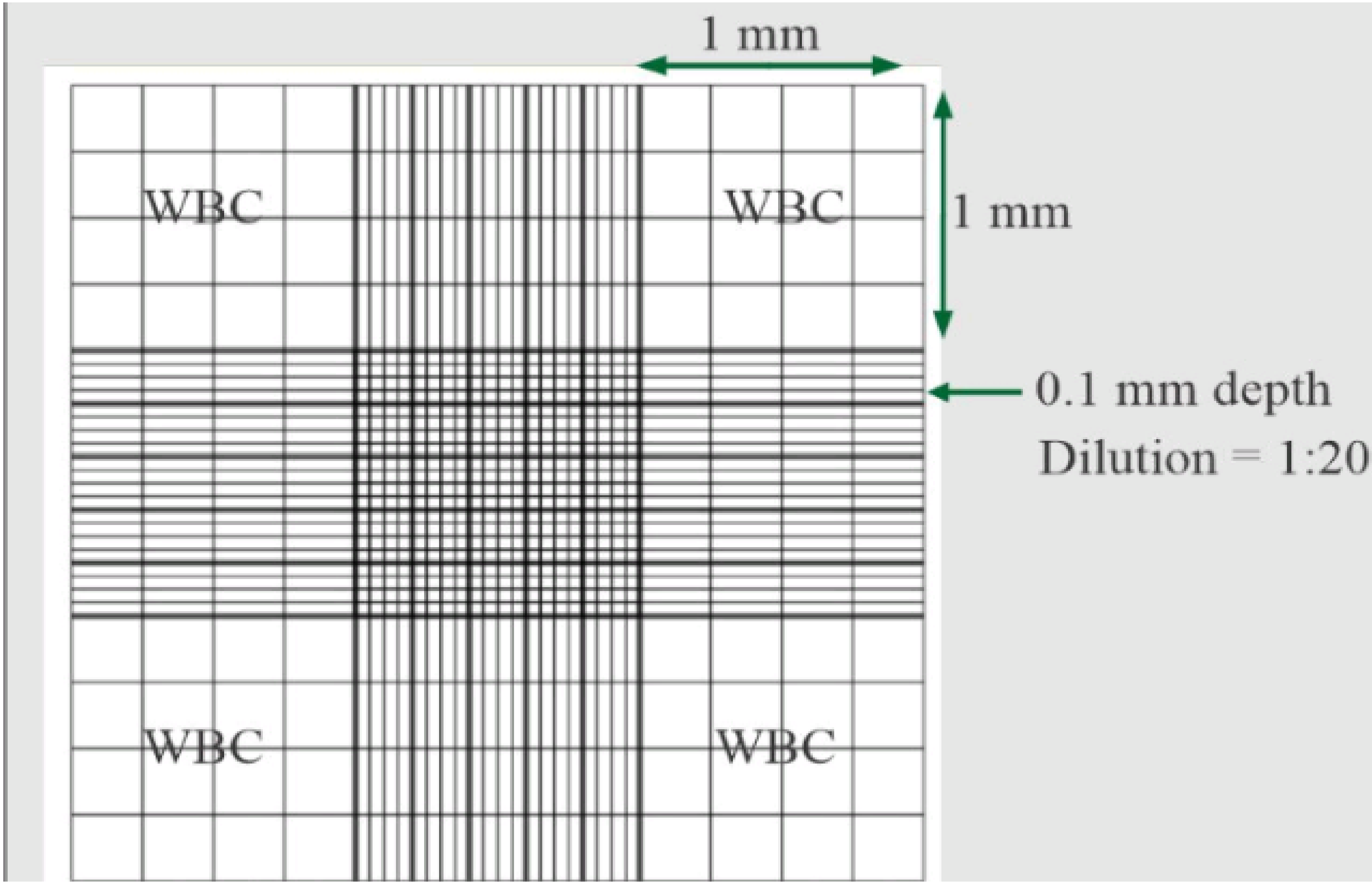
Leukopenia: the main causes of a reduced WBC count are:

- Viral, bacterial, parasitic infections, e.g. HIV, viral hepatitis, measles, rubella, influenza rickettsial infections, overwhelming bacterial infections such as military T.B, relapsing fever, typhoid fever , brucellosis, ,parasitic infections including leishmaniasis and malaria.
- Hypersplenism.
- Bone marrow infiltration.
- Ionizing radiation.

The Haemocytometer

The simplest, most convenient and cheapest mean of accurately determining the numbers of cells in a sample is to use a Haemocytometer and a microscope. A Haemocytometer is a specialised slide that has a counting chamber with a known volume of liquid.





1 mm
WBC
WBC
1 mm
0.1 mm depth
Dilution = 1:20
WBC
WBC

The white cell count is the number of white cells in 1.00 cubic millimeter of undiluted blood. So we have 2 correction factors: dilution factor and volume factor.

Dilution factor: The blood has been diluted 1 in 20

Volume factor: the chamber has an area of 1 square millimeter and depth of 0.1
So the volume of the chamber"is = area X depth
=1 X 0.1 =0.1 cumm

Number of cells / cmm = number of cells in chamber X dilution factor X volume factor
= N X 20 X 10

Organs of the immune response

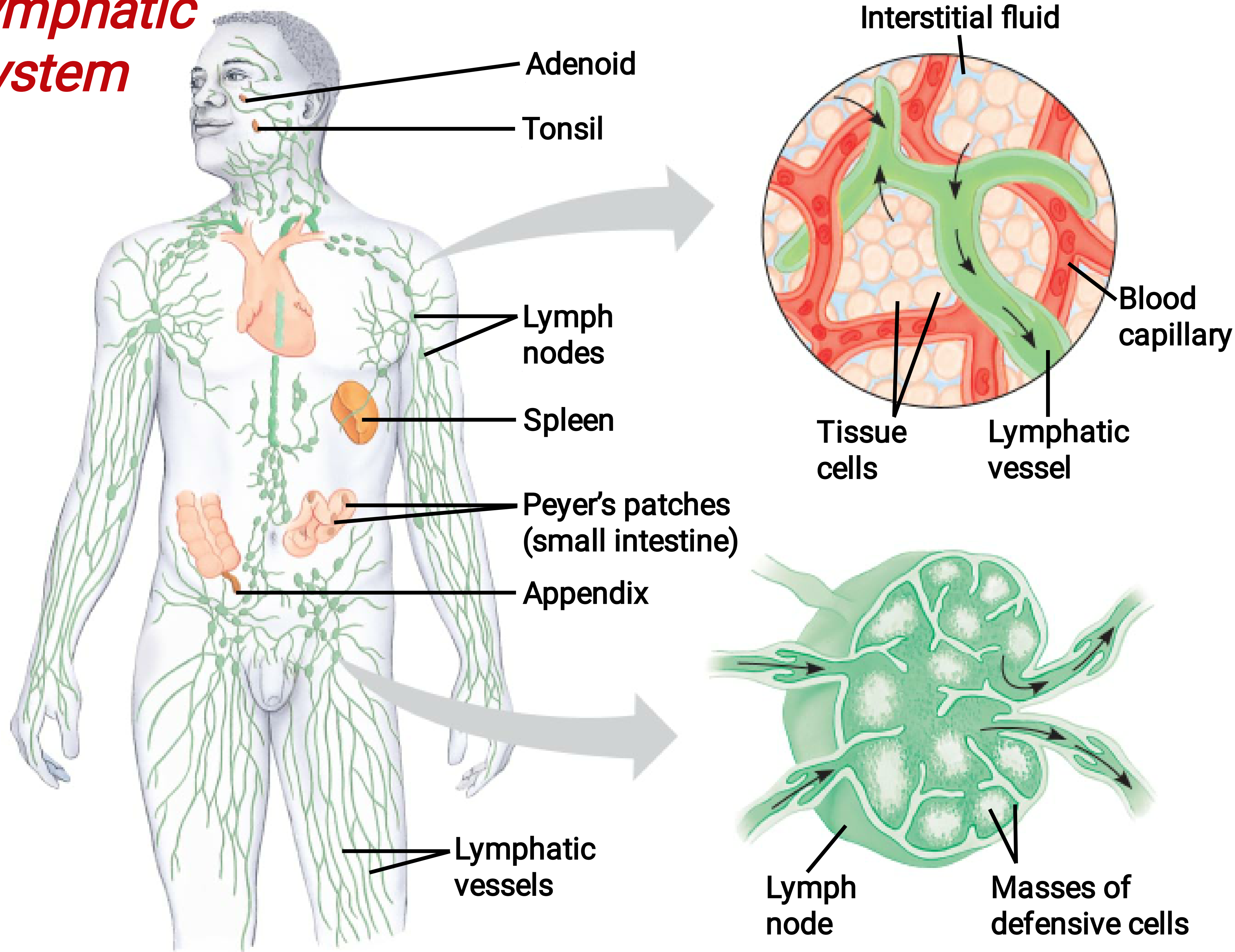
✓ Primary lymphoid organs

- Bone marrow; where the immune cells originate
- Thymus; where T cells differentiation to mature.

✓ Secondary lymphoid organs

- Maintain mature naive lymphocytes.
- Initiate an adaptive immune response.

Lymphatic System



Primary immune organs; Bone marrow and thymus

Bone marrow functions

- Leukocyte production, B cells maturation.
- Hematopoiesis start in childhood (YOLK SAC and mesenchyme, then liver and spleen, and finally the bone marrow in puberty).
- Common site of BM is sternum, vertebrae, iliac bones and ribs.
- In cases of excess demand on BM, liver and spleen help the (hematopoiesis).

Thymus

- T cell maturation and formation of T cell antigen receptors.

Bone marrow components

The two components of bone marrow are

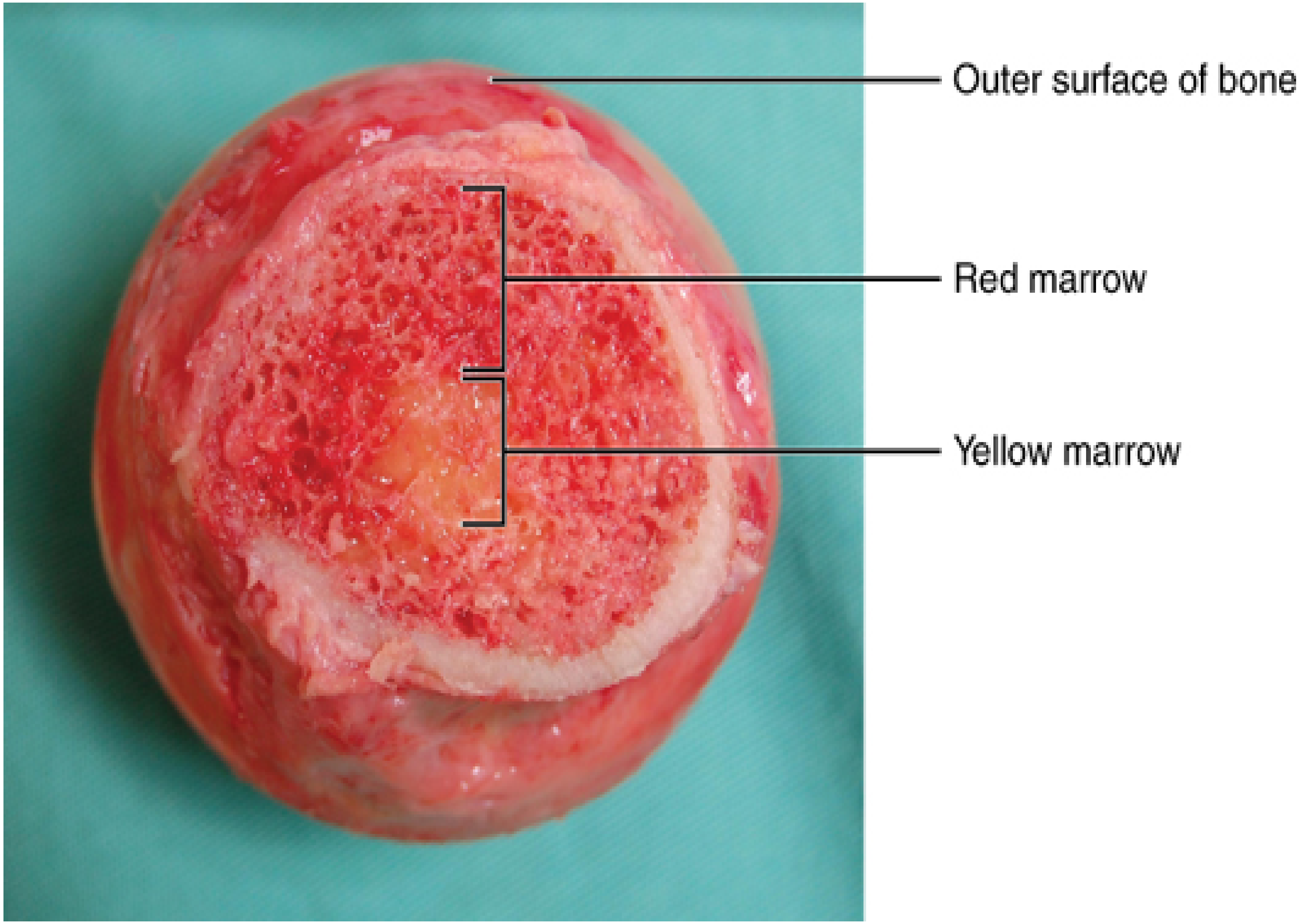
✓Red marrow which consists mainly of hematopoietic tissue, Red blood cells, platelets, and most white blood cells arise in red marrow.

✓Yellow marrow which is mainly made up of fat cells. At birth, all bone marrow is red and with age, it is converted to the yellow type; only around half of adult bone marrow is red.

- Yellow marrow is 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 to blood production as fibroblast, osteoclast and osteoblast.

BM



Thymus

- The thymus gland is found in the thorax in the anterior mediastinum.
- It gradually enlarges during childhood but after puberty, it undergoes a process of involution (reduction in the functioning mass of the gland).
- However, It continues to function throughout life.
- The thymus is derived from invaginations of the ectoderm in the developing neck and chest of the embryo, forming structures called branchial clefts.

Thymus

A. Anatomy: The thymus is composed of two identical lobes and is in the anterior superior mediastinum, in front of the heart and behind the sternum

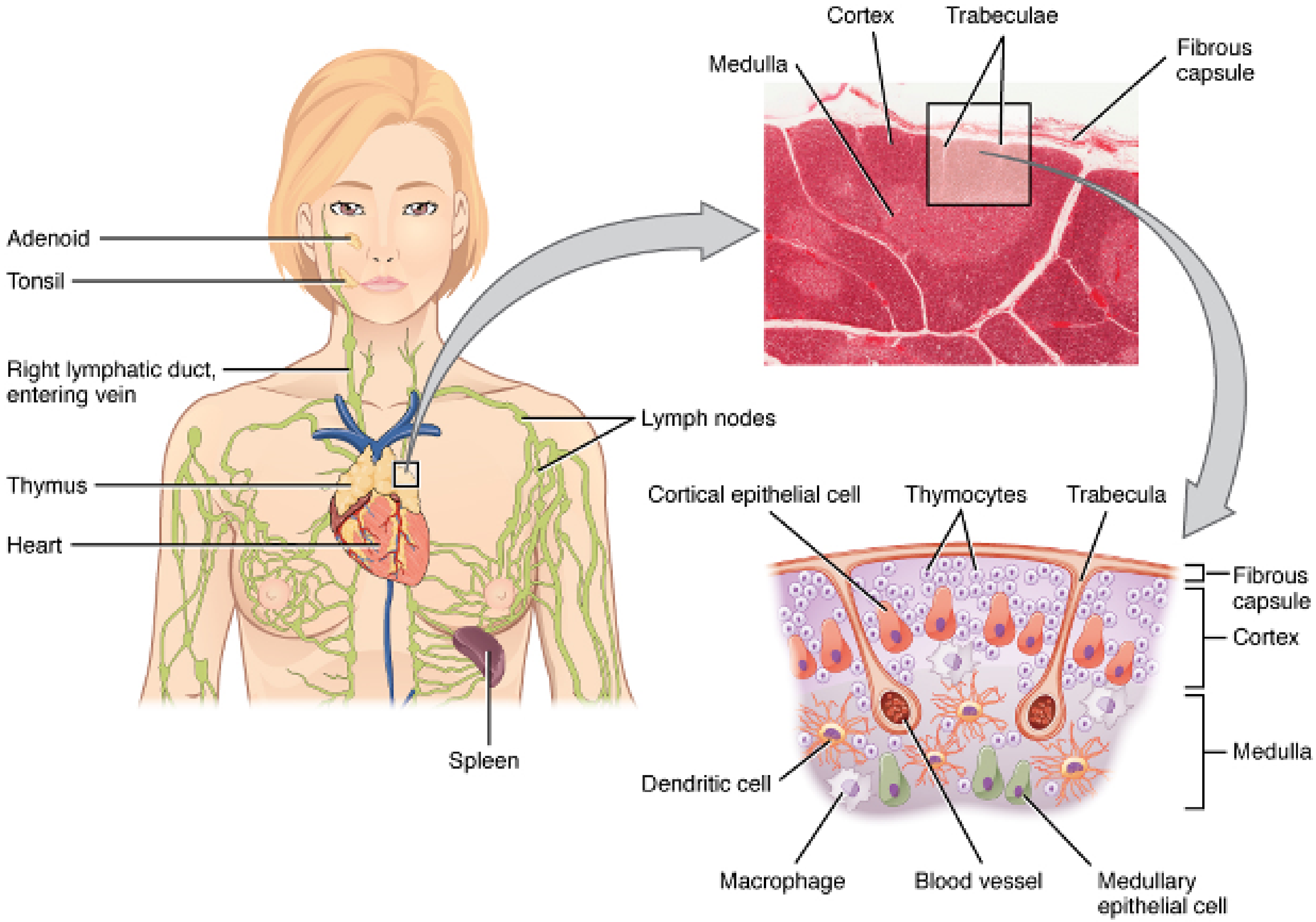
B.Histology: The thymus gland is surrounded by a fibrous capsule, and arranged into an outer, more cellular, cortex. and an inner, less cellular, medulla.

Cells involved:

- The most immature T cells in the cortex. As T cells mature, they migrate toward the medulla, then to circulation.
- Epithelial cells
- Macrophages and lymphoid dendritic cells

✓Digeorge syndrome (genetic defect in development of 3rd pharyngeal pouch in embryo); T cell deficient, plus parathyroid gland defect

Thymus



Adenoid
Tonsil
Right lymphatic duct, entering vein
Thymus
Heart
Spleen
Lymph nodes
Medulla
Cortex
Trabeculae
Fibrous capsule
Cortical epithelial cell
Thymocytes
Trabecula
Fibrous capsule
Cortex
Medulla
Dendritic cell
Macrophage
Blood vessel
Medullary epithelial cell

Secondary lymphoid tissues consist of

- Lymph nodes, which are clustered at sites such as the groin, armpits and neck and along the small intestine, and collect antigen from the tissues.

- The spleen, which collects antigen from the bloodstream.

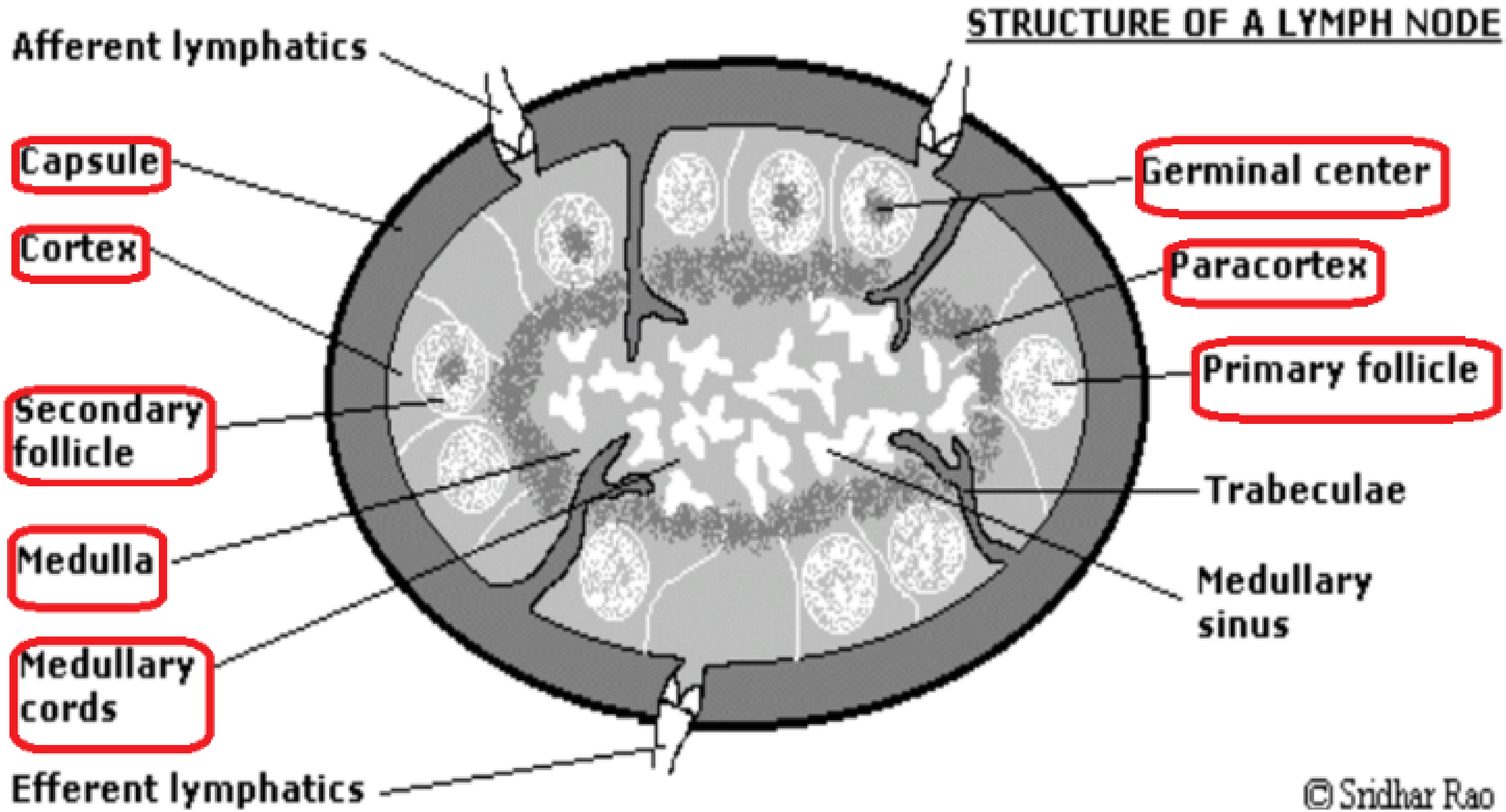
- The mucosa-associated lymphoid tissues (MALT), which collect antigen from the respiratory, gastrointestinal and urogenital tracts and are particularly well organized in the small intestine, in structures known as Peyer's patches.

Structure of the lymph node

1. **Cortex**

- Cortex consists of primary follicles (mostly B cells) and secondary follicles (with a germinal center).

- Germinal center is formed from stimulated B cells and follicular dendritic cells.
- Stimulated mature B cells change into plasma cells or memory B cells which reside in medulla and antibody that move to the circulation.



STRUCTURE OF A LYMPH NODE
Afferent lymphatics
Capsule
Cortex
Secondary follicle
Medulla
Medullary cords
Efferent lymphatics
Germinal center
Paracortex
Primary follicle
Trabeculae
Medullary sinus
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2. Paracortex

The paracortex contains (mostly T cells).

3. Medulla

The medulla comprises:

- Large blood vessels.
- Medullary cords mostly (Macrophages, plasma cells)
- and sinuses

Spleen

- Weigh 150g, in left upper quadrant.
- Immune response against blood borne antigens
-Consist of:

1.White pulp (inner)

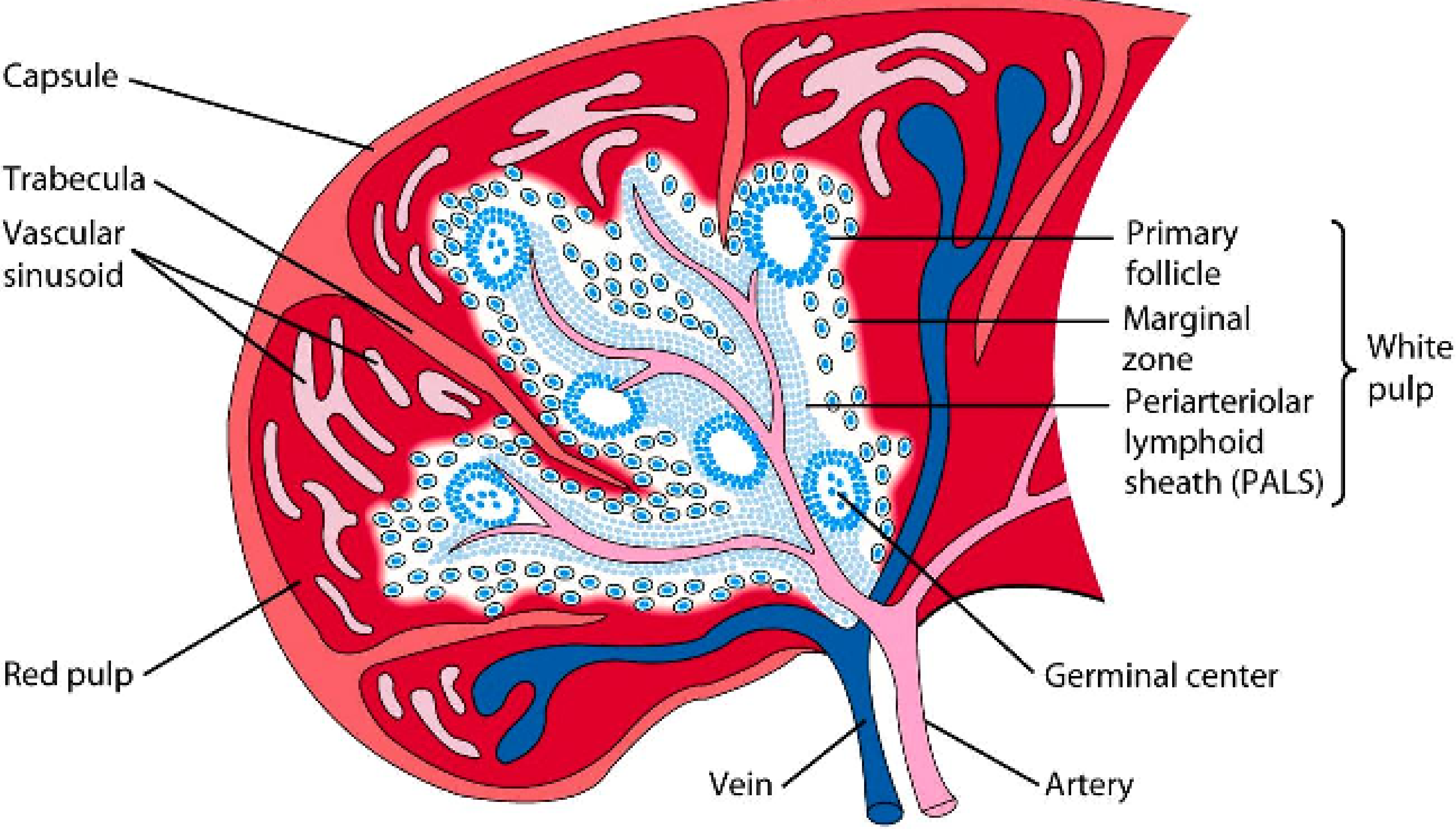
•Peri-arteriolar lymphoid sheath; PALS (T cell Zone).
•Follicles (B cells zone).
•Marginal zone in between red and white pulp, have both B and T cells and macrophages.

2.Red pulp (outer),

•Consist of old erythrocytes and macrophages, it is the place where aged RBC is destroyed by macrophages

The splenic artery enters the red pulp through a web of small blood vessels, and blood-borne microorganisms are trapped in this loose collection of cells until they are gradually washed out through the splenic vein

No afferent lymphatic vessel in spleen.


Capsule
Trabecula
Vascular sinusoid
Red pulp
Primary follicle
Marginal zone
Periarteriolar lymphoid sheath (PALS)
White pulp
Germinal center
Vein
Artery

Spleen functions

- ✓ It is the major site for killing antibody coated-microbes and destroying the damaged RBCs.
- ✓ Storage of RBCs and lymphocytes.
- ✓ Individuals lacking a spleen are extremely susceptible to infections with encapsulated bacteria such as pneumococci and meningococci because such organisms are normally cleared by opsonization and phagocytosis, and this function is defective in the absence of the spleen.