innate immunity and immune organs

Dr.Eman Albataineh,
Associate Prof. Immunology
College of Medicine, Mu'tah university
Immunology, 2nd year students

Innate immune cells 1-Mononuclear phagocyte system (macrophages)

- have rounded or kidney-shaped nuclei with finely granular cytoplasm
- Mononuclear phagocyte's primary function is phagocytosis
  – Originate in BM, and first to leave. When monocyte becomes settled in tissue they are called macrophages. Some mononuclear cells may differentiate to dentritic cells. some joint to form multi-nucleated giant cells
- 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.

2-Neutrophils

- Granulocytes contain nucleus segmented into 3-5 connected lobes, hence the name polymorphonuclear leukocyte and cytoplasmic granules. **Neutrophils (95% of granulocytes)** respond w/I 24 hours of stimulus (the earliest). have 20 times as many receptors as macrophages. They have Fc receptor to IGG and IGA as well as complement receptors.

- Intracellular killing by azurophil lysosomal granules and specific granules.

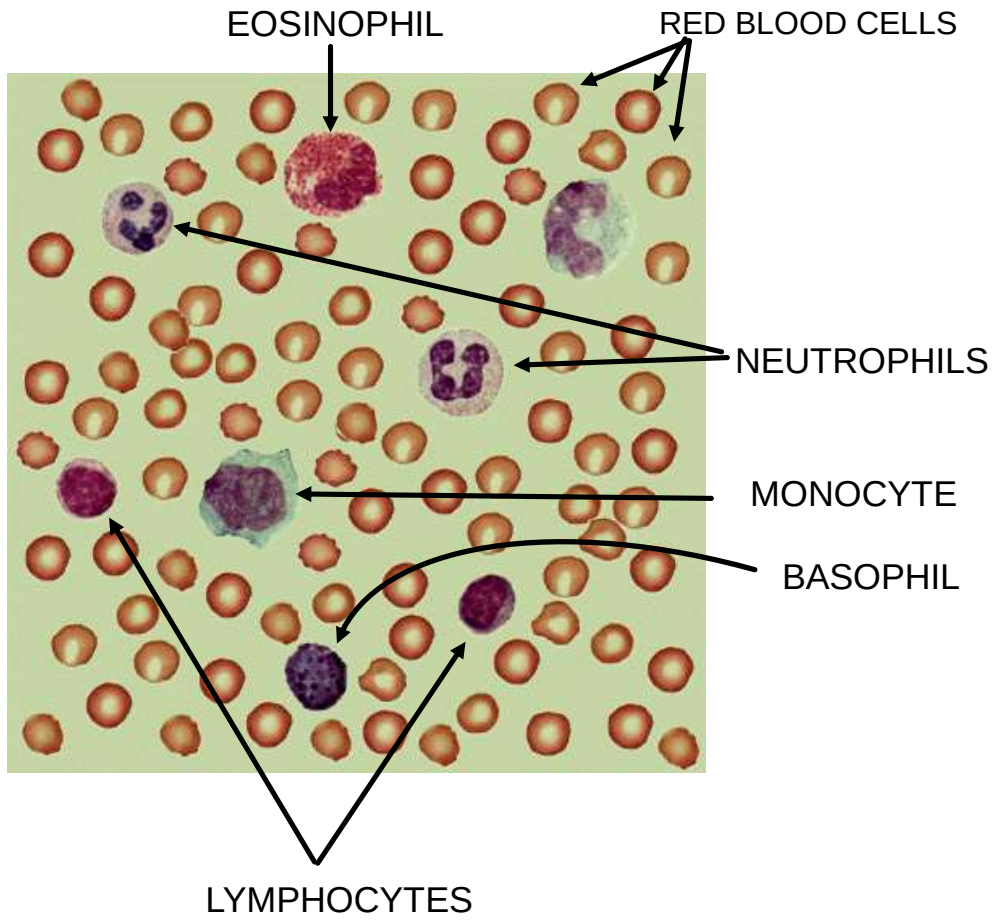
EOSINOPHILS

- These cells are eosinophilic or "acid-loving" as shown by their affinity to coal tar dyes: Normally transparent, it is this affinity that causes them to appear brick-red after staining with eosin, a red dye,
- There are many hydrolytic enzymes present in the granules 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).

Basophils and mast cells

- Granulocytes, have acidic proteoglycan, Lobed nucleus--more variable, large coarse granules stain blue with basic dye methylene blue.
- Mast cells is the cessile form whereas basophils is the circulating form

Cells of the blood



Cellular Components of all immune system in percents

1. Lymphocytes(30%); T cells (60%), B cells (30%) (high N:C ratio) and large granular lymphocytes called natural killer cells(10%) low N:C ratio and granular)
2. Mononuclear phagocytes; macrophages (5.3%)
3. Granulocytes; neutrophils (62%), eosinophils(2.3%) and basophils (0.4%)

(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 milllimeter (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.

women of child-bearing age and during pregnancy. Counts also vary in different populations with lower total WBC and neutrophil counts being found in Africans

WBC reference range

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

- Children at one year — 6.0-18.0 X 10^9 / L
- Children at 4-7 year — 5.0-15.0 X 10^9 / L
- Adults — 4.0-10.0 X 10^9 / L
- Pregnant women — up to 15.0 X 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:

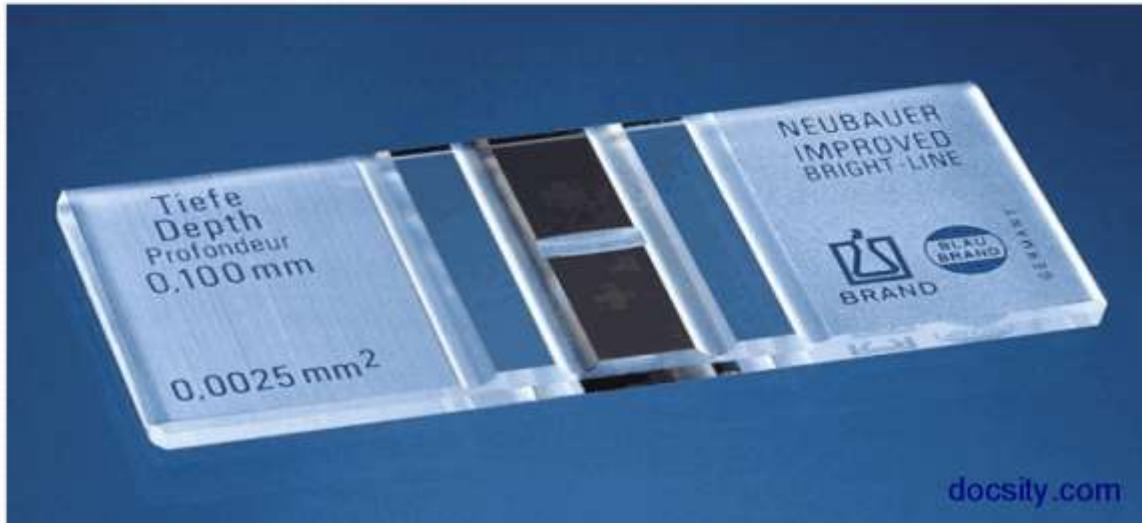
- Viral, bacterial, parasitic infections, e.g. HIV, viral hepatitis, measles, rubella, influenza rickettsial infections, overwhelming bacterial infections such as military T.B, relapsing fever, typhoid fever , brucellosis, ,parasitic infections including leishmaniasis and malaria.
- Hypersplenism.
-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

TABLE 41.2 Differential White Blood Cell Count

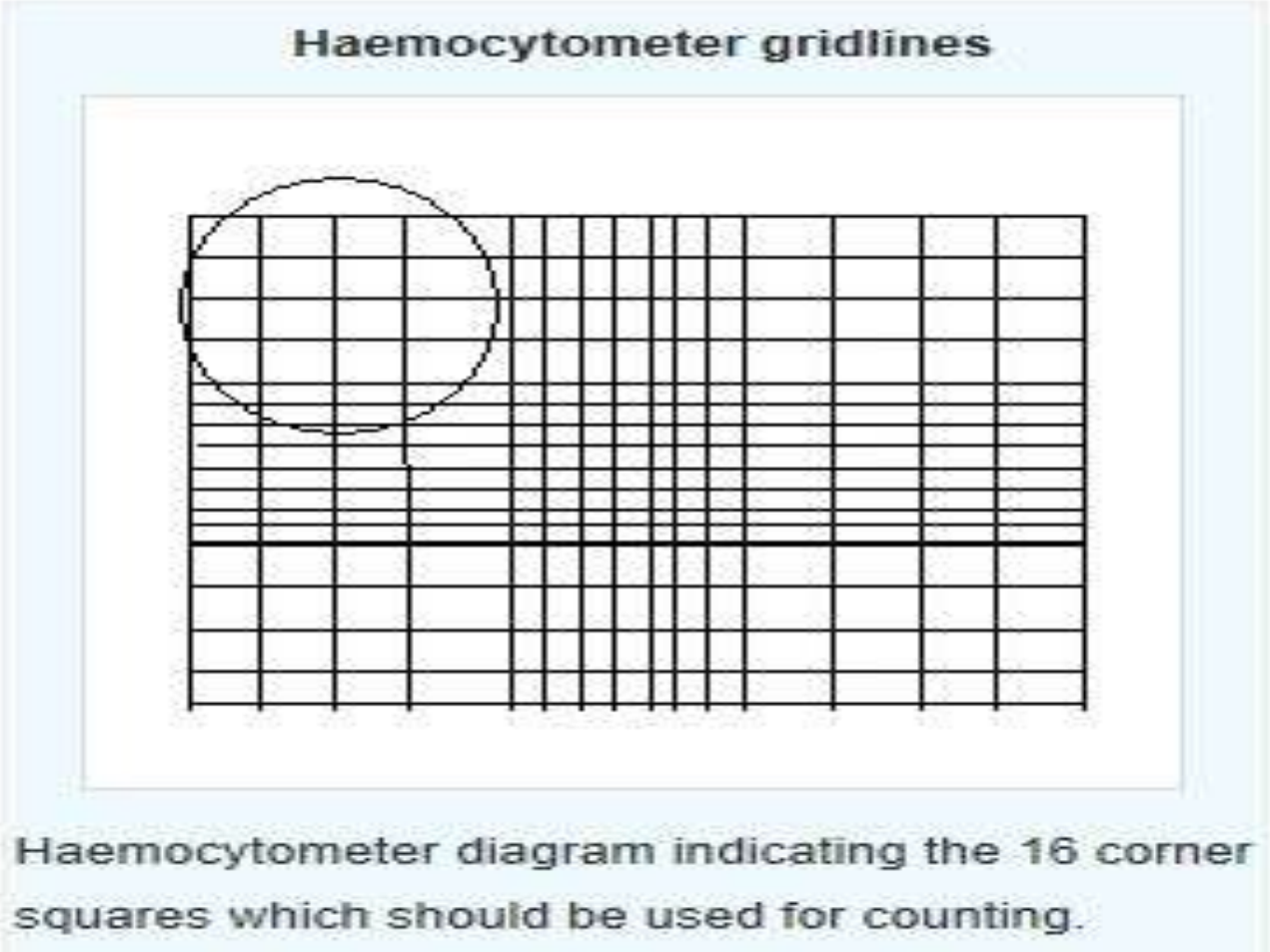
Cell Type	Normal Value (percent)	Elevated Levels May Indicate
Neutrophil	54–62	Bacterial infections, stress
Lymphocyte	25–33	Mononucleosis, whooping cough, viral infections
Monocyte	3–9	Malaria, tuberculosis, fungal infections
Eosinophil	1–3	Allergic reactions, autoimmune diseases, parasitic worms
Basophil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

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.



Number of cell
cells in 16 corn
sequare*10*di



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

White cell count by heamocytometer

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

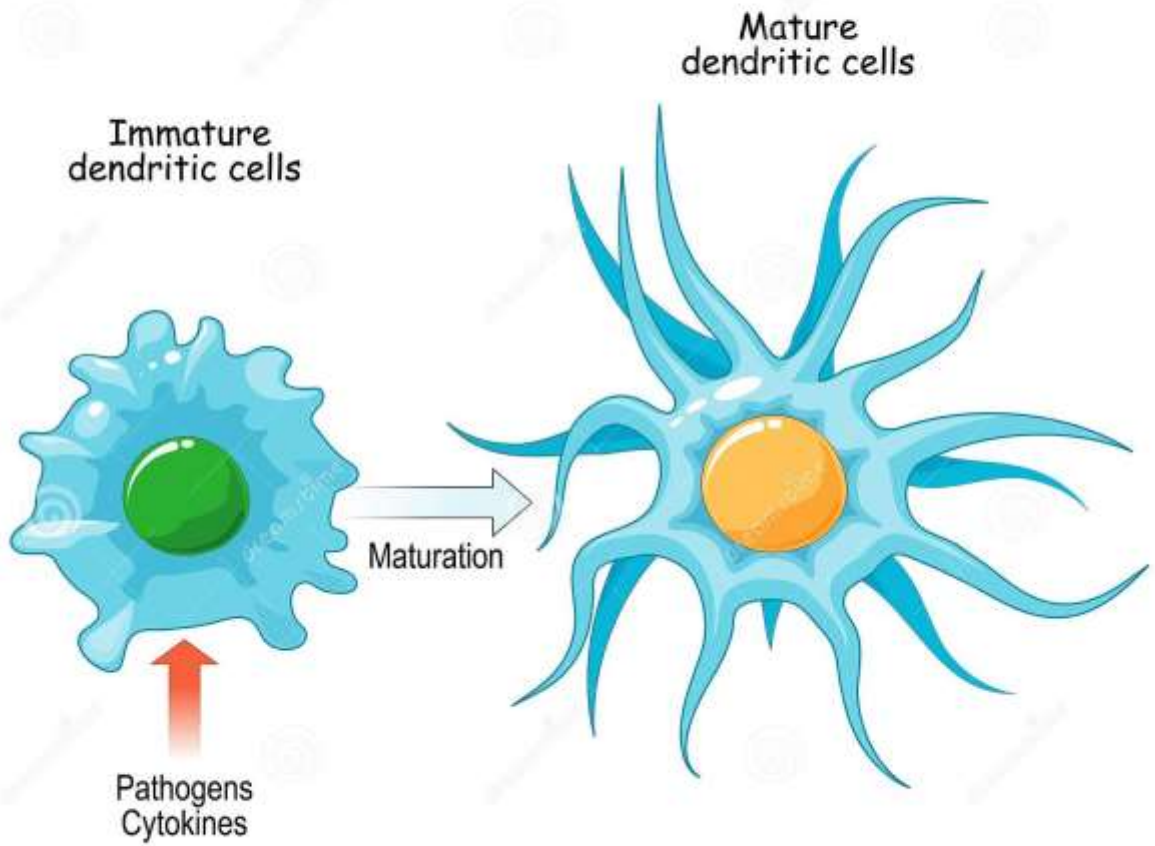
Dendritic cells (DCs)

- Their main function is to phagocytose antigen material and present it on the surface to lymphocytes, thus functioning 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. They can also be found in an immature state in the blood.
- Once activated, they migrate to the lymphoid tissues where they interact with T cells and B cells to initiate and shape the adaptive immune response. they grow branched projections for that they are called DC,

DC or dendritic cells

- 4 types
  - Myeloid DC, macrophage origin, common, diffuse localization, phagocytose antigen and activate T cells
  - Lymphoid DC, lymphocyte origin, recruit cells to site of infection
  - Follicular DC, mesenchymal origin, present in peripheral lymph nodes, do B cell activation.
  - plasmacytoid dendritic cells, are early cellular responders to viral infection. They have potent antiviral activities.

Dendritic cells



Organs of the immune response

- Primary lymphoid organs
  A. Bone marrow; where the immune cells originate
  B. Thymus; where T cells differentiation to mature
- Secondary lymphoid organs
  - maintain mature naive lymphocytes and initiate an adaptive immune response.
  - the sites of lymphocyte activation by antigen.
  - It is exemplified by the lymph nodes, and the lymphoid follicles in tonsils, Peyer's patches, spleen, adenoids, skin, etc. that are associated with the mucosa-associated lymphoid tissue (MALT).

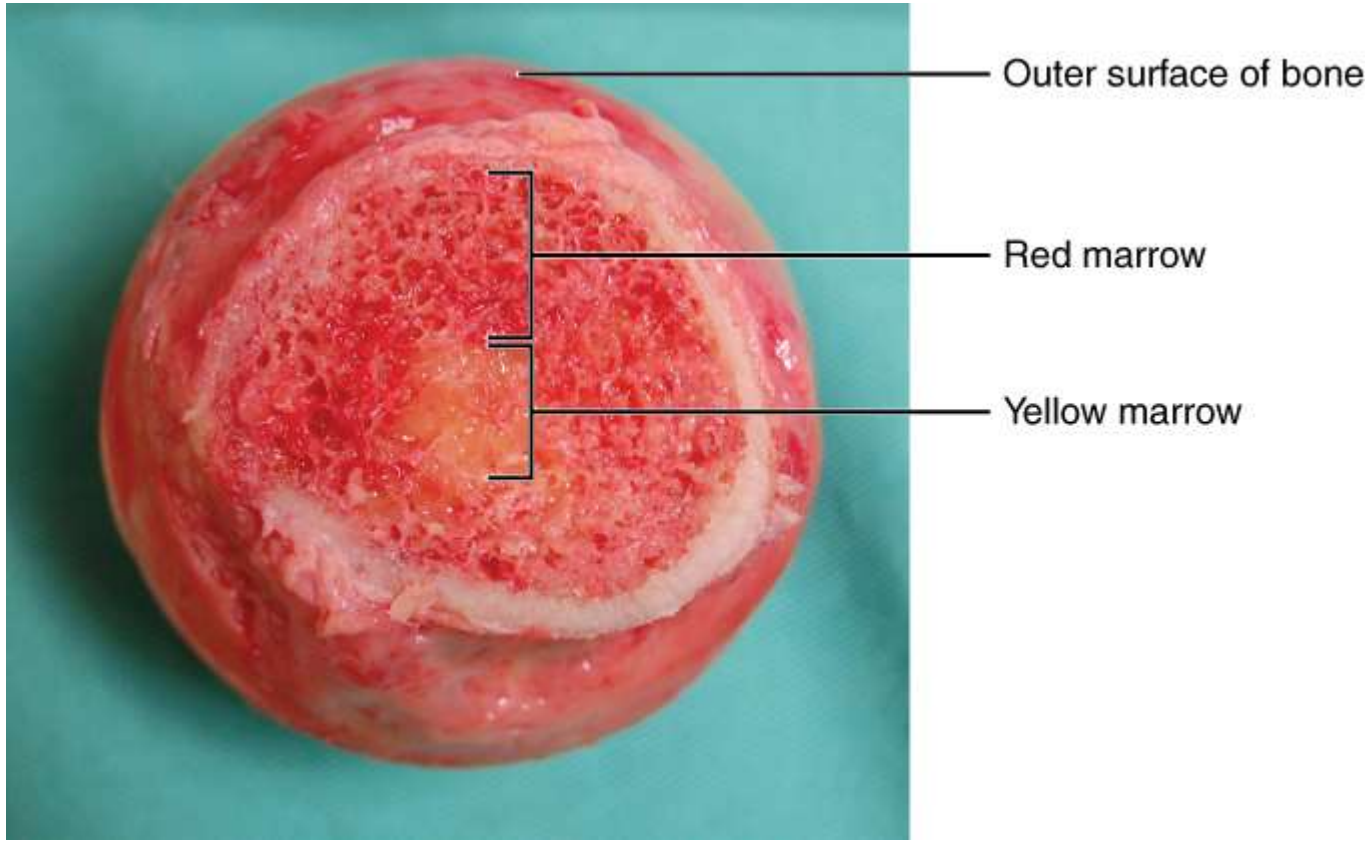
Primary immune organs; Bone marrow and thymus

- Bone marrow functions
  - Leukocytes production, B cells maturation. hematopoiesis start in childhood (YOLK SAC AND mesenchyme, then liver and spleen and finally the bone marrow in puberty) and get maximum in adult age, most common site of BM is sternum, vertebrae, iliac bones and ribs.
  - In cases of excess demand liver and spleen help the BM (the extramedullary 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 Red marrow is found mainly in the flat bones, such as the pelvis, sternum, cranium, ribs, vertebrae and scapulae, and at the epiphyseal ends of long bones such as the femur and humerus
  - and "**yellow marrow**", which is mainly made up of fat cells. At birth, all bone marrow is red. With age, more and more of 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 fatty marrow, fibroblast, osteoclast and osteoblast.

BM



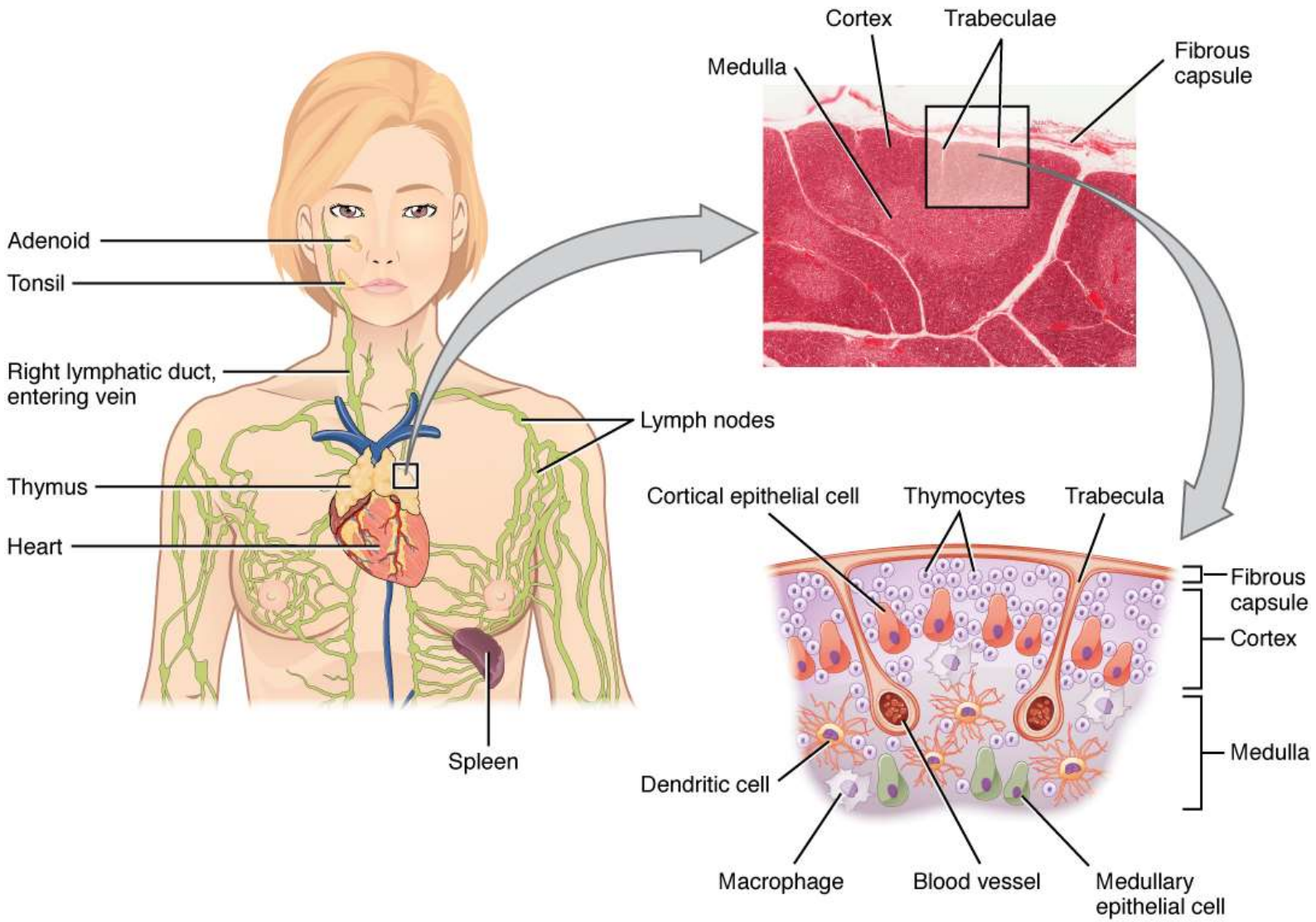
Thymus

- 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 resulting in a reduction in the functioning mass of the gland. It continues to function throughout life, however.
- The thymus has a rich vascular supply and efferent lymphatic vessels that drain into mediastinal lymph nodes. 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 located anatomically 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 thymocytes or T cells mature, they migrate toward the medulla, then to circulation
  - Epithelial cells
  - Macrophages and lymphoid dentritic cells
- Digeorge syndrome (genetic defect in development of 3rd pharyngeal pouch in embryo); T cell deficient as a result of impaired thymus development, plus parathyroid gland defect

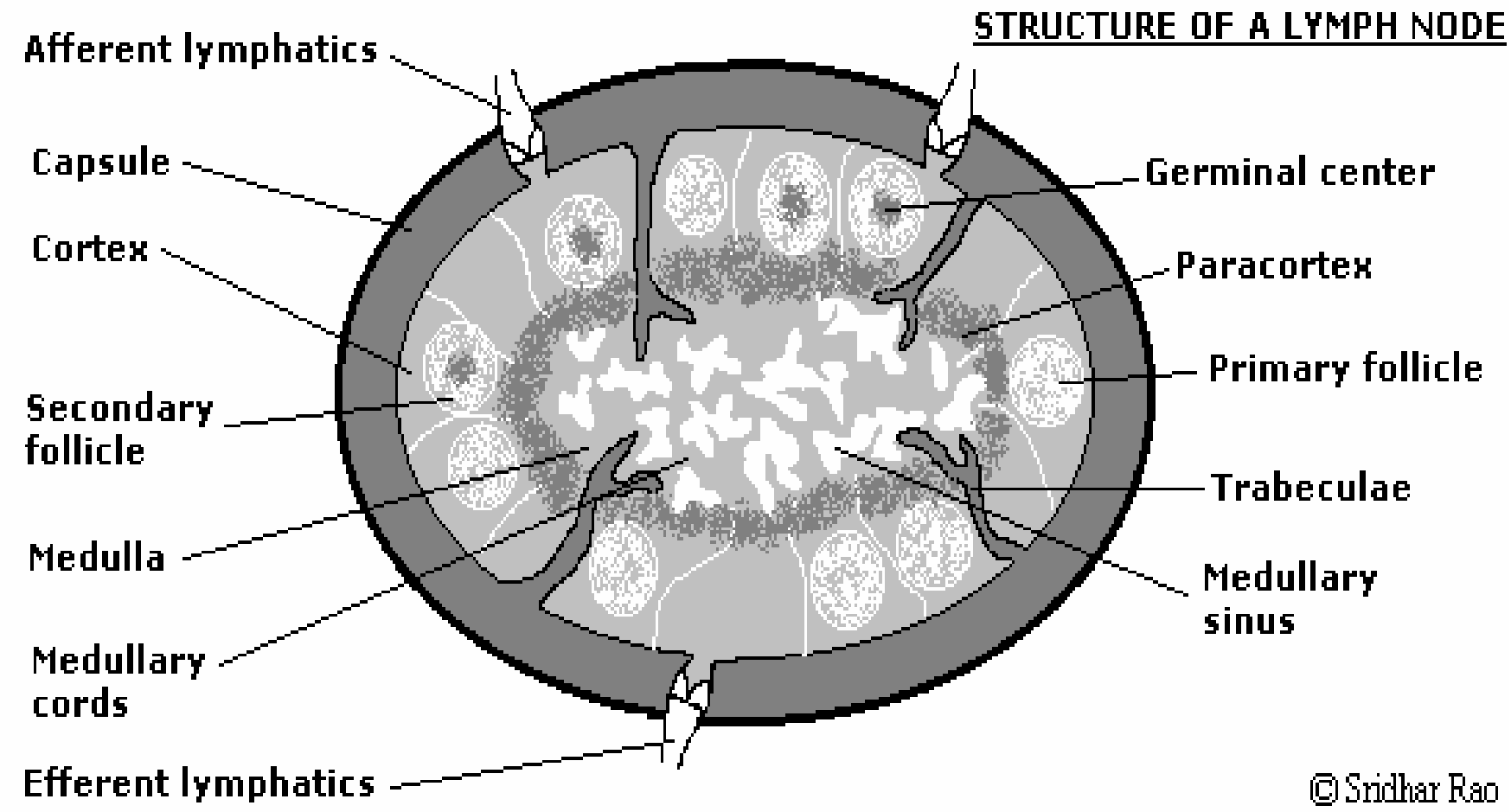
Thymus


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

Lymph nodes and lymphatic system (peripheral or 2nd lymphatic sys.)

- function to concentrate antigens that are introduced through the common portals of entry (skin and gastrointestinal and respiratory tracts).
- They Are places where the innate cells carry the antigen and present it to the adaptive immune system
- Site of lymphocyte activation by antigen

- Secondary lymphoid tissues consist of the
  - **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;
  - and 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**
- The node is made up of three components:
  - lymphatic sinuses the Lymph flows from afferent vessels cortical sinuses, into the medullary sinuses and into efferent lymphatic vessels
  - , blood vessels
  - parenchyma (cortex, paracortex, medulla)


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

Structure of the lymph node

Cortex

- Cortex consists of primary follicles and secondary follicles (with germinal center).
- Germinal center formed from stimulated B cells and follicular dendritic cells. whereas primary follicles have only mature but not activated B cells
- Stimulated mature B cells change into plasma cells or memory B cells which reside in medulla and antibody that move to the circulation.

- **Paracortex**
- The paracortex contains T lymphocytes and macrophages
- **T cells:** The various types of T cell enter the node from the blood via the HEVs. When activated they form lymphoblasts which divide to produce a clone of T cells responding to a specific antigen. Activated T cells then pass into the circulation to reach peripheral sites.

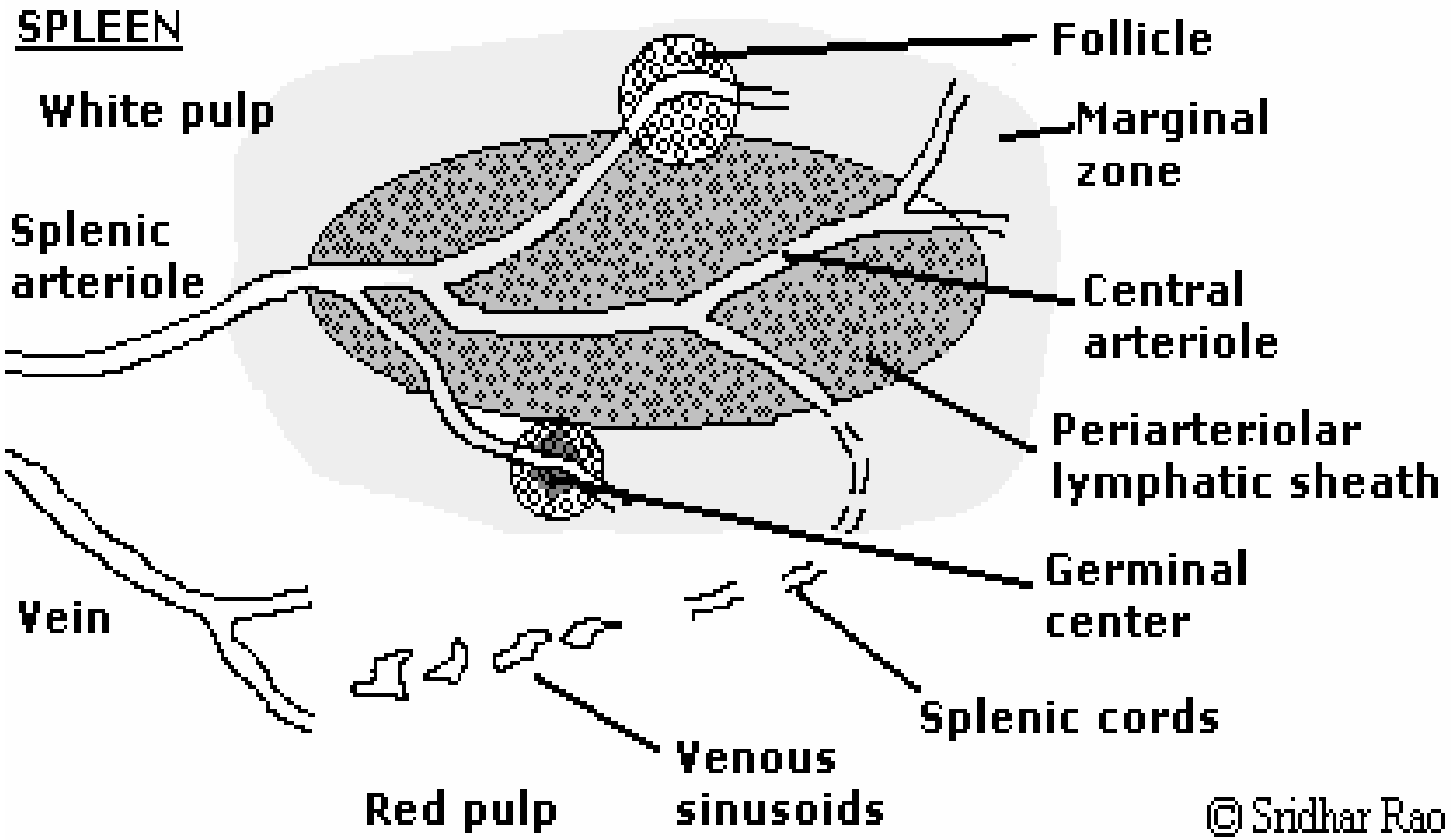
- **Medulla**
- The medulla comprises:
  - large blood vessels
  - medullary cords and sinuses
  - plasma cells

spleen

- Weigh 150g, in left upper quadrant
- Immune response against blood borne antigens
- Consist of 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.
- Red pulp; outer, splenic artery, vascular sinusoid, splenic vein. 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.

Spleen functions

- Functions
  - It is the major site for killing antibody coated microbesand destroying the damaged RBC
  - 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


SPLEEN
White pulp
Follicle
Marginal zone
Splenic arteriole
Central arteriole
Periarteriolar lymphatic sheath
Germinal center
Vein
Splenic cords
Venous sinusoids
Red pulp
© Sridhar Rao