



Reticuloendothelial system & functions of spleen

Objectives :

- ❖ Describe monocyte macrophage system RES
- ❖ Functions of monocytes/ macrophages in different tissues.
- ❖ Mechanism of chemotaxis, phagocytosis and microbial killing.
- ❖ Explain functions of spleen.
- ❖ Understand the basic concept of the indications and risks of splenectomy.

Done by :

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Colour index:

- Important
- Numbers
- Extra

Immunity

Innate immunity

- Non-specific

- phagocyte
(Neutrophils, monocytes, NK)
- complement
- Barriers

Note: Macrophages are key components of the innate immunity and activate adaptive immunity by transforming into Antigen Presenting Cells

Acquired immunity

- Specific
- Adaptive

Cell mediated

-T lymphocytes

Humoral

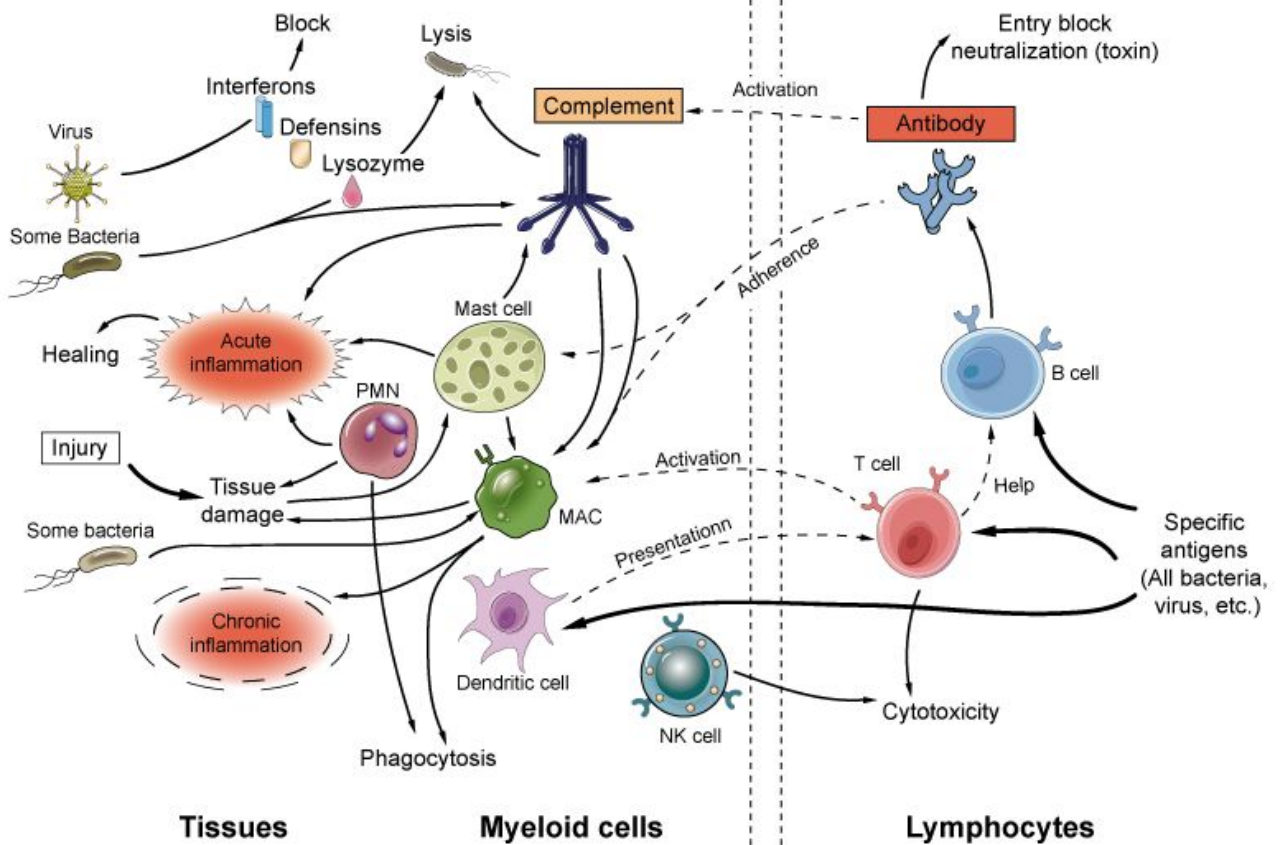
-antibody mediated
-B lymphocytes

Extra :

The Origin of NK is lymphocyte
Origin of dendritic cell is monocyte
All have similar function from different origin (morphology & properties)

Innate immunity

Adaptive immunity



Reticuloendothelial system (monocyte/macrophage system)

It is a network of connective tissue fibers inhabited by phagocytic cells such as macrophages ready to attack and ingest microbes.

- Monocytes transform themselves into macrophages in tissue & this system of phagocytes is called as Monocyte-Macrophage Cell System
- RES term is old although they are neither reticular in appearance nor they have endothelial origin just these phagocytic cells are located in reticular connective tissue
- Therefore, the term reticuloendothelial system is not used nowadays.

TISSUE MACROPHAGE SYSTEM COMPONENTS

Monocytes in Blood

Mobile & Fixed
Macrophages in Tissue

Specialized endothelial
cells in bone
marrow, spleen and
lymph nodes

General Functions of RES

Phagocytosis (**direct**)

- Bacterial
- Dead cells
- Foreign particles

Immune function(**indirect**)

Processing antigen and
antibodies production

Breakdown
Of aging RBC

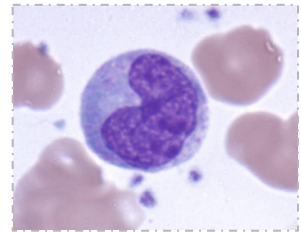
Storage
Of RBCs and recycling **iron**

MONOCYTES

- **Size:** 15-20 μm (active cells 60-80 μm)^{largest WBC}
- Small Granules (azurophilic) & Vacuoles¹
- More Efficient Phagocytosis than Neutrophils (100 bacteria vs 3-20 by Neutr, larger particles like RBCs & malarial parasites)
- Life span: 10-20 hours in blood.
- Two types: Mobile & Fixed
- Lysosomes contain lipases² unlike Neutrophils. Acts as Antigen Presenting Cells

Azurophilic granules of monocytes are primary lysosomes or storage granules. Lysosomes contain Acid hydrolases, MPO, HOCl, Defensins³

For your knowledge.. There are three types of granules:
 1- primary granules which is found in all WBCs "very small it's called azurophilic"
 2- secondary granules
 3- tertiary granules



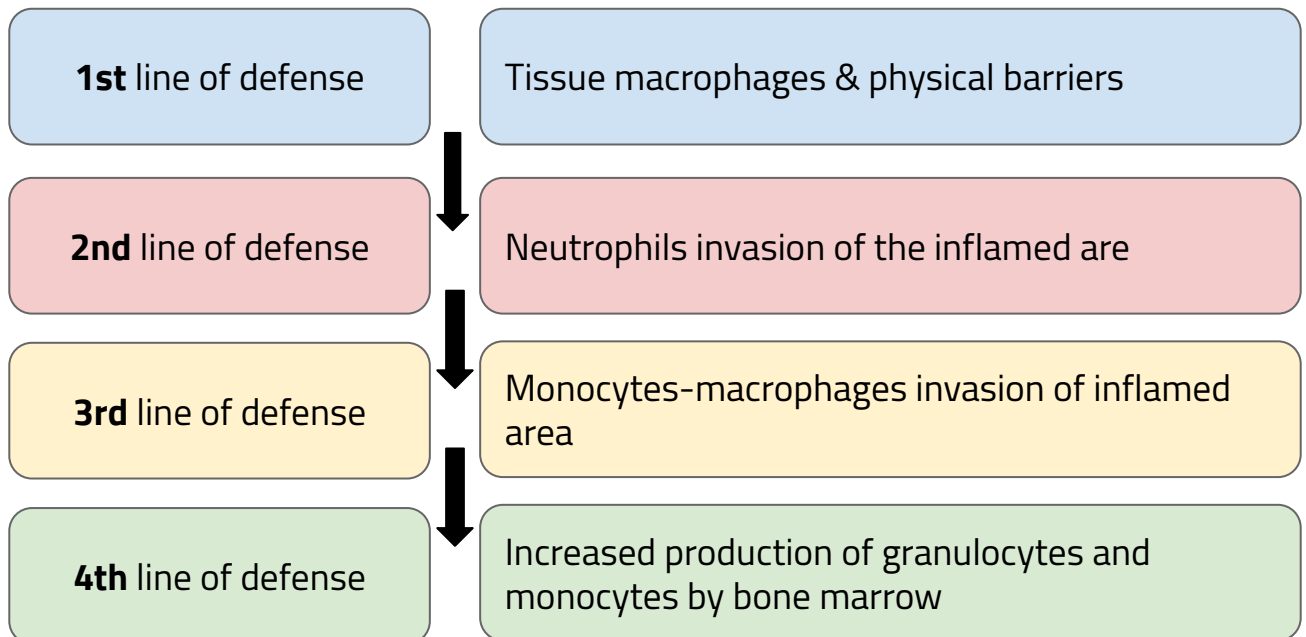
Under microscope you won't see clear granules as in neutrophils or eosinophils.

1 engulf and keep the bacteria that cannot kill " mycobacterium TB" in their layers, so at least prevent further spreading of infection

2 some bacteria have lipid coat so lipase is needed.

3 it kills bacteria by oxidative burst .. MPO: myeloperoxidase HOCl : hypochlorous

Responses During Inflammation Macrophage and Neutrophil



DEFENSIVE PROPERTIES OF MACROPHAGES & NEUTROPHILS

Margination:

WBC Roll, Bind and then stick along the walls of blood capillaries *it's also called pavementation (endothelial perspective)*



Diapedesis:

WBC squeezes itself through endothelial holes leaving blood capillaries



Chemotaxis:

WBC move by amoeboid motion towards inflammation area following chemotactic substances (Bacterial toxins, Complement [C5a], LKB4) are released from site of infection



Phagocytosis:

Upon reaching the site of infection neutrophils start to engulf infecting organism

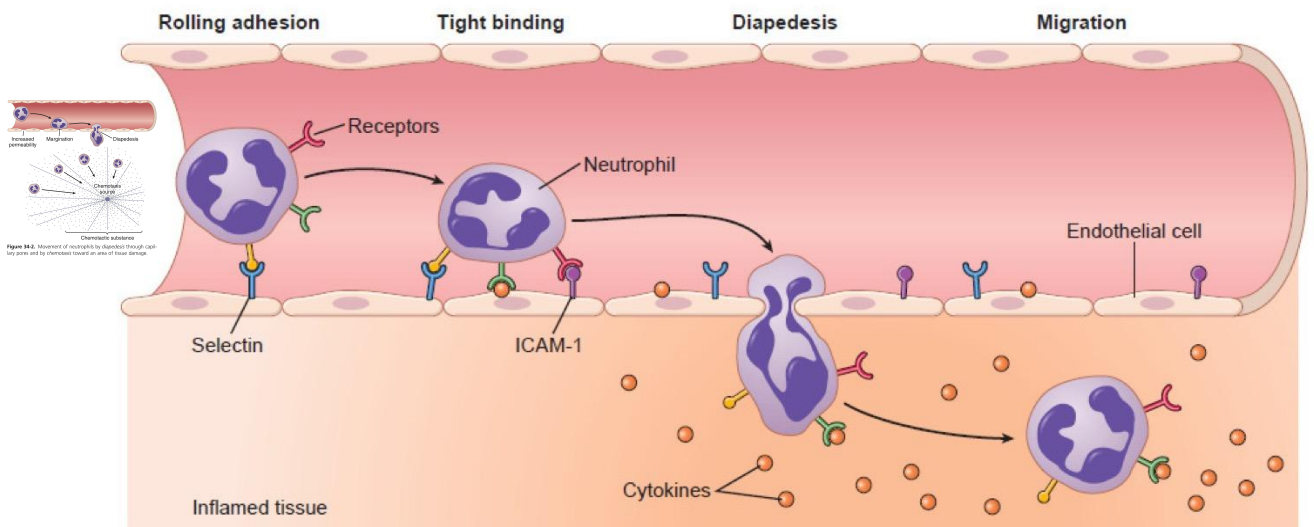
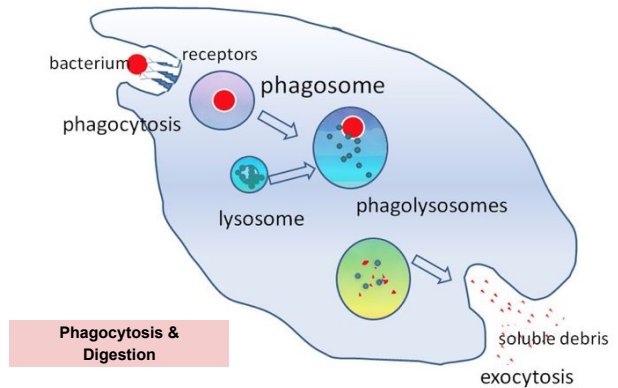
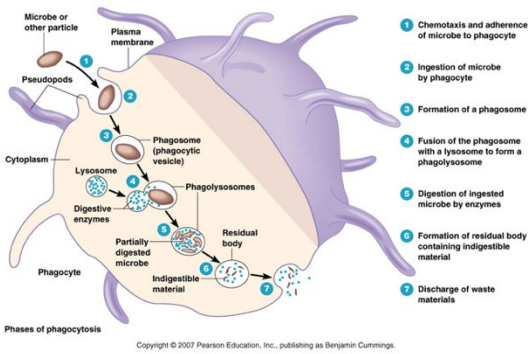


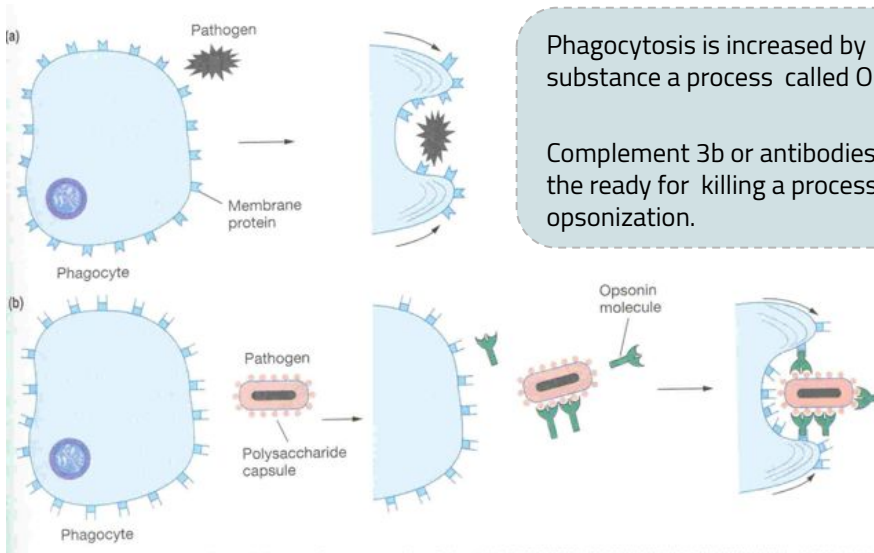
Figure 34-6. Migration of neutrophils from the blood into inflamed tissue. Cytokines and other biochemical products of the inflamed tissue cause increased expression of selectins and intercellular adhesion molecule-1 (ICAM-1) in the surface of endothelial cells. These adhesion molecules bind to complementary molecules/receptors on the neutrophil, causing it to adhere to the wall of the capillary or venule. The neutrophil then migrates through the vessel wall by diapedesis toward the site of tissue injury.

Direct immune function of RES



Macrophage: a wandering, walking cell. "Big eater" capable of phagocytosis. Is a modified monocyte in tissues

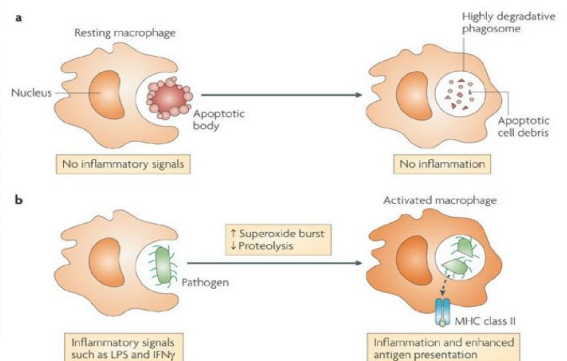
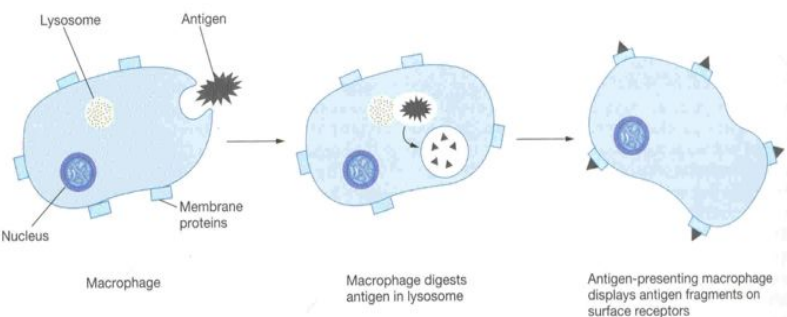
Opsonization & Phagocytosis



Indirect immune function of RES

Displaying it attached to an MHC class II molecule.

Classical APCs include macrophages, dendritic cells, Langerhans cells and B cells.



Immune Functions of the Spleen

The spleen processes foreign antigens and is the major site of specific immunoglobulin M (IgM) production.

Spleen acts as reservoir of lymphocytes (contains about 25% of T cells & 15% B cells)

The non-specific opsonins, properdin and tuftsin, are synthesized that bind to the specific receptors on the surface of macrophages and other leukocytes, stimulating their phagocytic, bactericidal and tumoricidal activity.

Spleen filters the blood by removing the microorganism. Macrophages in splenic pulp phagocytose microorganisms & foreign bodies

Splenectomy

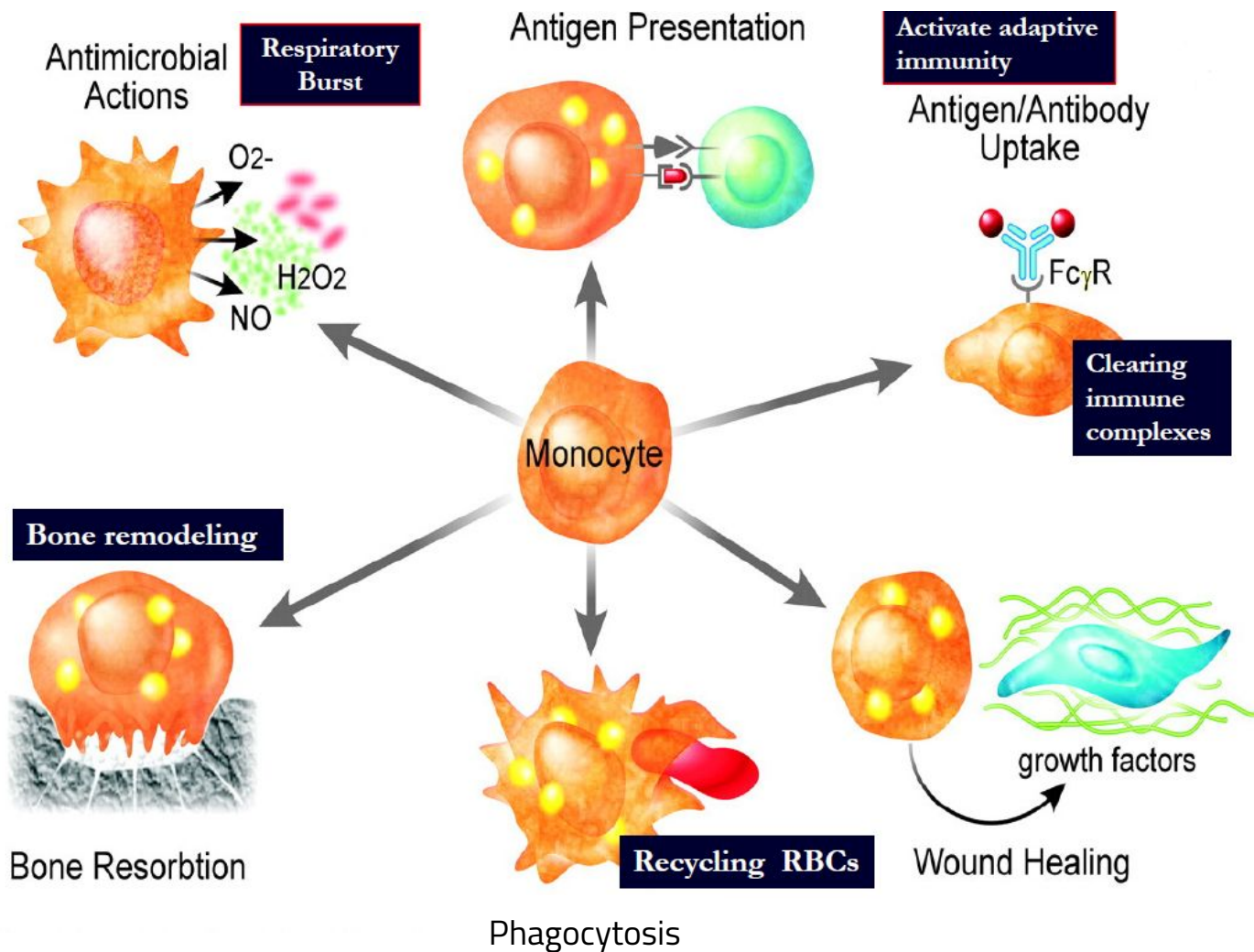
A splenectomy is the surgical procedure that partially or completely removes the spleen.

Indications:

1. Hypersplenism: enlargement of the spleen (splenomegaly) with defects in the blood cells count.
2. Primary spleen cancers.
3. Haemolytic anaemias: Sickle cell anaemia, Thalassemia, hereditary spherocytosis (HS) and elliptocytosis
4. Idiopathic thrombocytopenic purpura (ITP).
5. Trauma.
6. Hodgkin's disease.
7. Autoimmune hemolytic disorders.

Risks & complications of Splenectomy

- Overwhelming bacterial infection or post splenectomy sepsis. Bc it has large no. of macrophages
- Patient is prone to malaria.
- Inflammation of the pancreas and collapse of the lungs.
- Excessive post-operative bleeding (surgical).
- Post-operative thrombocytosis and thrombosis.



Extra :

	Macrophage/Monocyte	Neutrophil
Morphology	Large mononuclear cells with granular cytoplasm	Smaller cells with multi-lobed nucleus and neutral cytoplasmic granules
Location	Often resident in tissues (remove routine cell debris)	Blood - requires recruitment to site of infection
Killing ability	Require activation by bacterial molecules \pm $IFN\gamma$	Activated during recruitment, then able to kill internalised bacteria automatically
After killing	Migrate to local lymph nodes	Die at site by apoptosis (then taken up by macrophages)
Antigen presentation	Can present antigen (Class II up-regulated by $IFN\gamma$)	Cannot present antigens (don't normally express class II)

Reticuloendothelial System Monocytes/Macrophage System

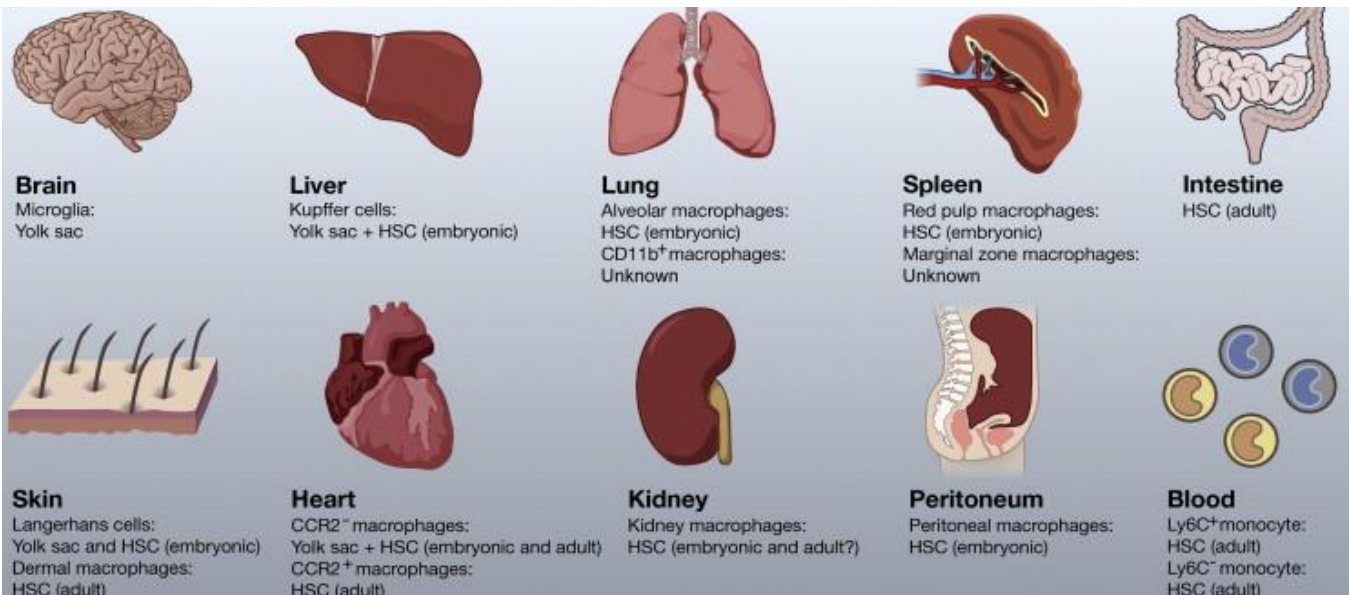
Monocytes when enter the tissues they transform themselves into macrophages this system of phagocytes is called as **Monocyte-Macrophage Cell System**

Types of Macrophages:

Macrophage differ depending on the organs in which they reside.

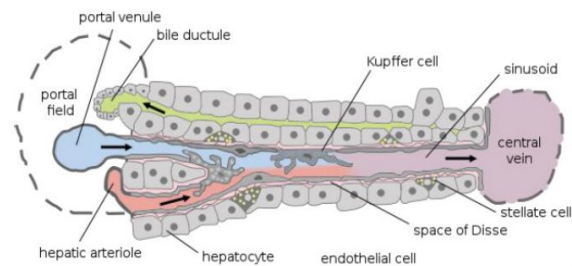
Types	Langerhans cell	Sinus histiocytes	Alveolar macrophages	Kupffer Cells	Reticular cells
Location	-Skin -mucosa Subcutaneous tissues.	Lymph Nodes	Lung	Liver sinuses	-Spleen -Bone marrow

Types	Microglia	Mesangial Cells contractible control GFR	Osteoclasts	Hofbauer cells	Epithelioid cells
Location	Brain	Kidneys	Bone	Placenta	Granulomas



Tissue macrophages in Liver sinuses

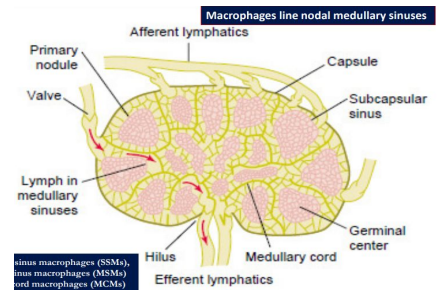
The liver is one of the immune and lymphoid tissues so They line the liver sinuses to catch anything unwanted pass



Tissue macrophages in Lymph Nodes

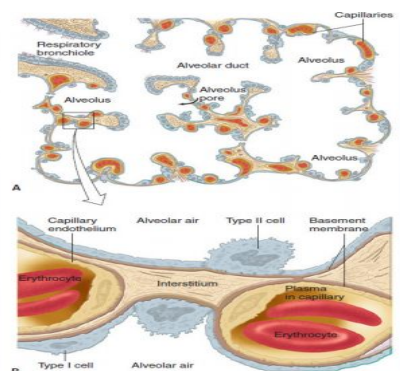
Macrophages Line Nodal Medullary sinuses:

1. subcapsular sinus macrophages (SSMs).
Below the capsule
2. medullary sinus macrophages (MSMs).
3. medullary cord macrophages (MCMs).



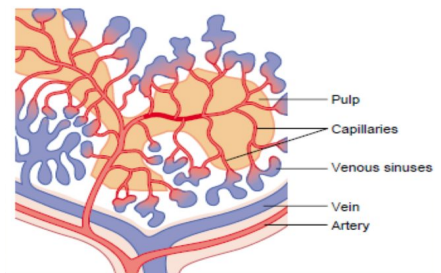
Tissue macrophages in Lungs

"dust cells" because of their content of intracellular carbon particles



Tissue macrophages in Spleen

The blood squeezes through the trabecular cords meshwork of red pulp.



Lymphoid Organs

Primary lymphatic organs

-Primary lymphatic organs are where lymphocytes are formed and mature. -They provide an environment for stem cells to divide and mature into B- and T- cells:

These include:

- red bone marrow and the thymus gland.
- Both T-cell and B-cells are 'born' in the bone marrow. However, whereas B cells also mature in the bone marrow, T-cells have to migrate to the thymus, which is where they mature in the thymus.

Secondary lymphatic organs

-Secondary lymphoid tissues are arranged as a series of filters monitoring the contents of the extracellular fluids, i.e. lymph, tissue fluid and blood.

-Secondary lymphoid tissues are also where lymphocytes are activated.

These include:

lymph nodes, tonsils, spleen, Peyer's patches and mucosa associated lymphoid tissue (MALT).

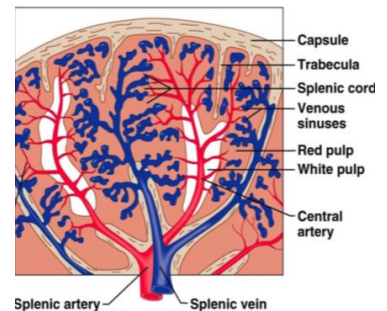
SPLEEN

- Is soft **purple gray** in color located in the **left upper quadrant** of the **abdomen**.
- It is a **highly vascular** lymphoid organ.
- It plays an important roles in: **red blood cells** integrity and has **immune function**.
- It holds a **reserve** of blood in case of **hemorrhagic shock**. " It is one of the centers of activity of the **RES** and its **absence** leads to a **predisposition** toward certain **infections**.
- Despite its importance, there are **no tests** specific to splenic function.

Structure of spleen

➔ White pulp: Thick sleeves of lymphoid tissue, that provides the immune function of the spleen.

➔ Red pulp: surrounds white pulp, composed of Venous sinuses filled with whole blood and Splenic cords of reticular connective tissue rich in macrophages



son Education, Inc., publishing as Benjamin Cummings

Functions of spleen

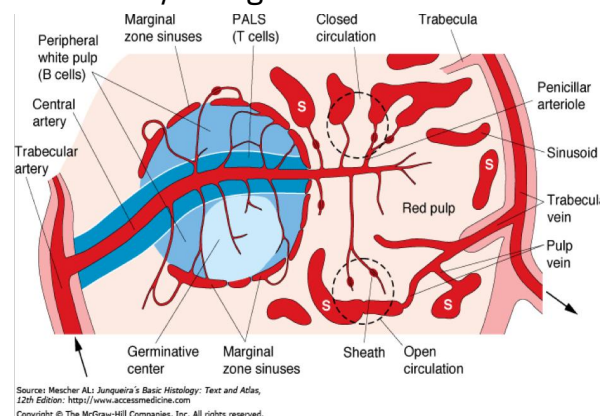
1-Red Pulp ➔ filtering function :

- RBC's able to deform through sinusoidal wall and endothelium Culling (Increased in hereditary spherocytosis).
- Macrophage activation ➔ macrophages filter and destroy foreign material in blood.

2-White pulp ➔ immunologic functions :

Site of B cell maturation into plasma cells, which synthesize antibodies in its white pulp and initiates humoral response

- trapping and processing of antigens .
- the major site of antibody synthesis .
- key role in removal of encapsulated bacteria (Strep pneumo) .



Sources: Mascher AL; Junqueira's Basic Histology: Text and Atlas, 12th Edition; <http://www.accessmedicine.com>
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3-Cytopoiesis

- From the fourth month of intrauterine life, some degree of hemopoiesis occurs in the fetal spleen.
- Stimulation of the white pulp may occur following antigenic challenge, resulting in the proliferation of T and B cells and macrophages.
- This may also occur in myeloproliferative disorders, thalassaemias and chronic haemolytic anaemias.

MCQs

1-Which condition of the following most likely can cause low platelets count:

- A- Splenomegaly
- B- Hepatomegaly
- C- Hypersplenism
- D- A&C

2-Macrophages in the liver called:

- A.Alveolar cell.
- B.Histiocyte.
- C.Microglia.
- D.Kupffer's cell.

3-In thymus:

- A. B cell maturation.
- B. RBC storage.
- C. T cell maturation.
- D. destruction of pathogenic antigen.

4- which of the following is primary lymphatic organ :

- A.thymus
- B.tonsils
- C.spleen
- D.lymph nodes

5-which of the following is not indication of splenectomy:

- A.Trauma.
- B.Hodgkin's disease.
- C.Autoimmune hemolytic disorders.
- D.infection.

6-What does the white pulp of the spleen contain :

- A.venous sinuses
- B.vitamin A
- C.lymphoid tissue
- D.splenic cord

SAQ

1- what is the general function of RES: Ans:

- 1.Phagocytosis: Bacterial,dead cells or foreign particles (direct).
- 2.Immune function: processing antigen and antibodies production (indirect).
- 3.Breakdown of aging RBC.
- 4.Storage and circulation of iron.

Answers:
1. D
2. D
3. C
4. A
5. D
6. C