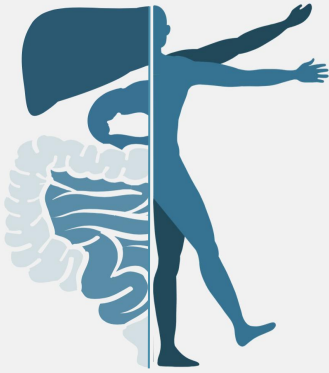


Revised & Approved



Reticuloendothelial system and function of the spleen

Special thanks to Rand Al Refai & Mona Al Omiriny

Objectives:

- ❖ At the end of this lecture you should be able to:
- ❖ 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.

Color index:

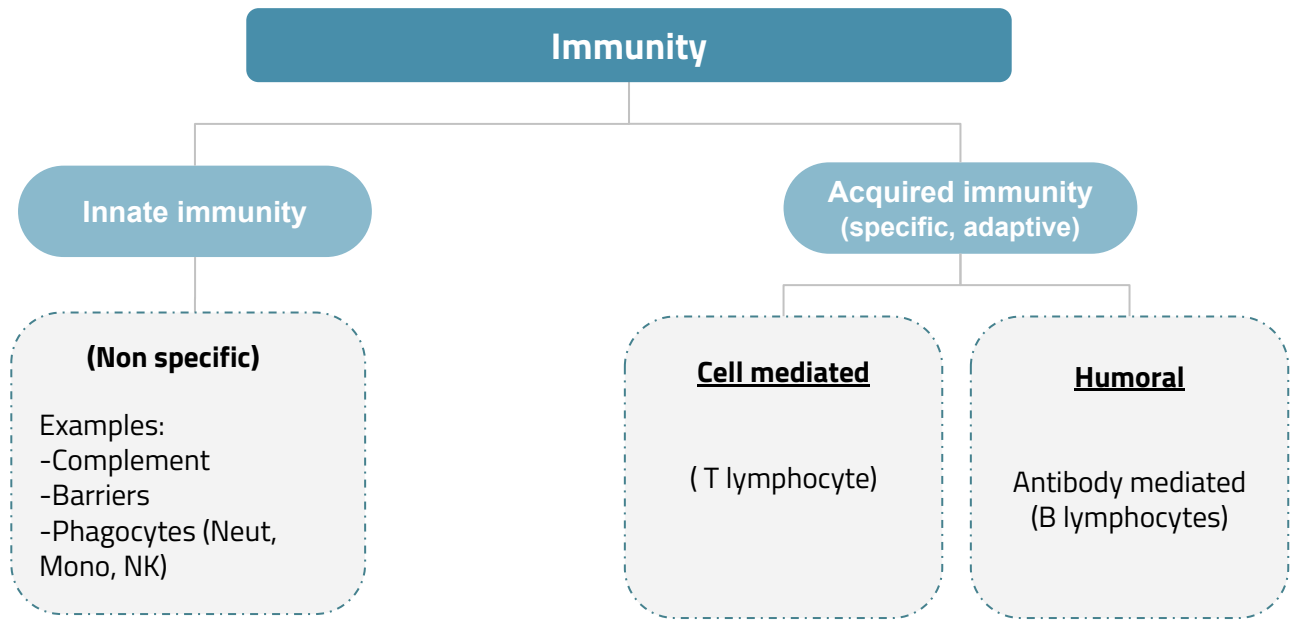
- ❖ **Important.**
- ❖ **Girls slide only.**
- ❖ **Boys slide only.**
- ❖ **Dr's note.**
- ❖ **Extra information.**



Editing File

Overview of the immune system

Only in boys' slides



Note:

Macrophages are key components of the innate immunity & activate adaptive immunity by transforming into antigen presenting Cells

Reticuloendothelial system (RES)

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.
- ❖ Reticuloendothelial system is an older term for the mononuclear phagocyte system.
- ❖ It's a collection of cells united by the common property of phagocytosis.
- ❖ Is an essential component of the immune system
- ❖ RES term is old: reticulo refers to the propensity of these large phagocytic cells in various organs to form a network of reticulum by cytoplasmic extensions: endothelial refers to their proximity to the vascular endothelium.
- ❖ Therefore, the term reticuloendothelial system is not used nowadays since they are neither reticular nor of endothelial origin.
- ❖ Most endothelial cells are not macrophages.



Examples of Reticuloendothelial System (RES):

1. skin, mucosa and Subc tissue (langerhans cell)
2. Lymph Nodes (Sinus histiocytes)
3. Alveolar macrophages
4. Liver sinuses (Kupffer Cells)
5. Spleen (Sinus histiocytes)
6. Bone marrow
7. Microglia in Brain
8. Kidneys (Mesangial Cells)
9. Bone (Osteoclasts)

-Hofbauer cells in placenta

-Epithelioid cells in granulomas

Tissue Macrophages:

Liver sinuses

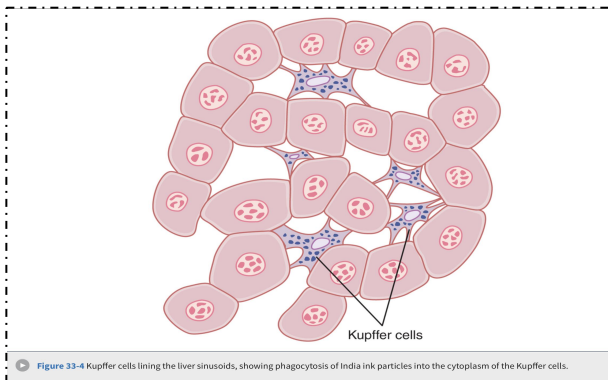
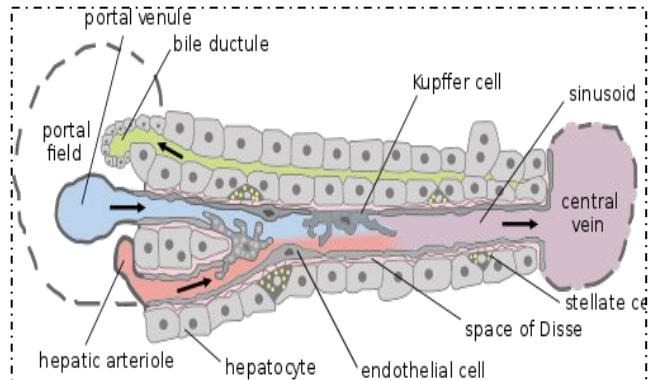


Figure 33-4 Kupffer cells lining the liver sinusoids, showing phagocytosis of India ink particles into the cytoplasm of the Kupffer cells.



Lymph nodes

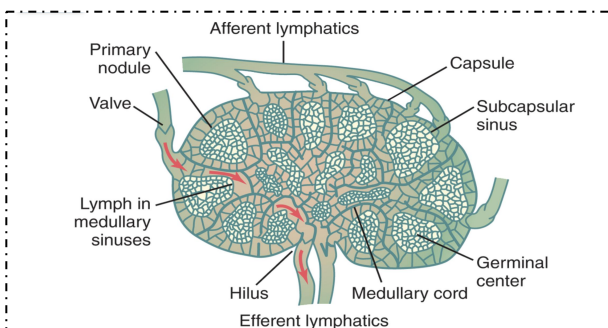


Figure 33-3 Functional diagram of a lymph node. (Redrawn from Ham AW: Histology, 6th ed. Philadelphia: JB Lippincott, 1968.)

- ❖ Macrophages line medullary sinuses.
- ❖ Subcapsular sinus macrophages (ssms)
- ❖ Medullary sinus macrophages (msms)
- ❖ Medullary cord macrophages (mcms)

Spleen

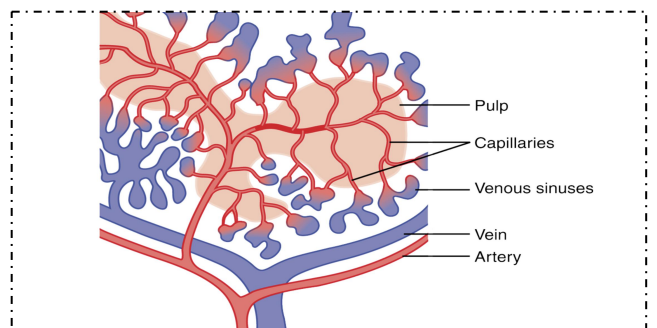


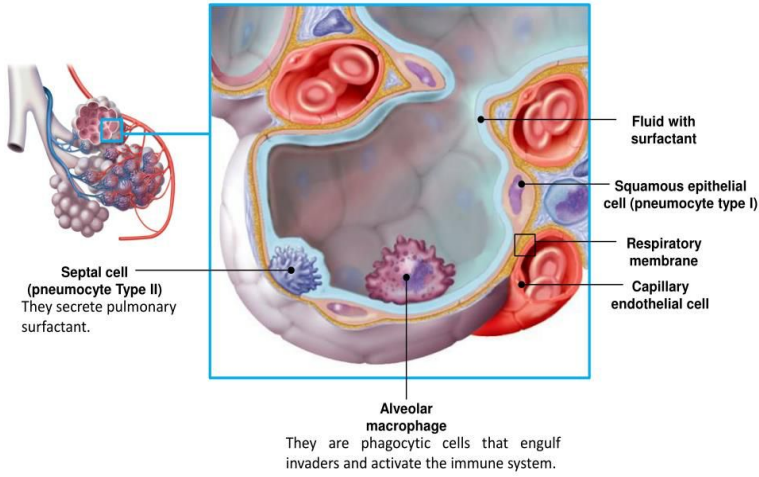
Figure 15-13 Functional structures of the spleen.

The blood squeezes through the trabecular cords meshwork or red pulp

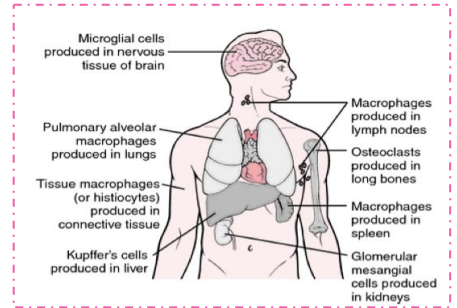
Tissue Macrophages: *Only in boys' slides*

Lungs

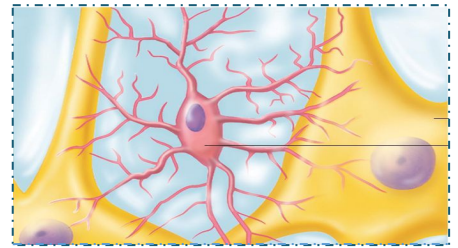
Alveolar Ducts and Alveoli



"Dust cells" because of their content of intracellular carbon particles.

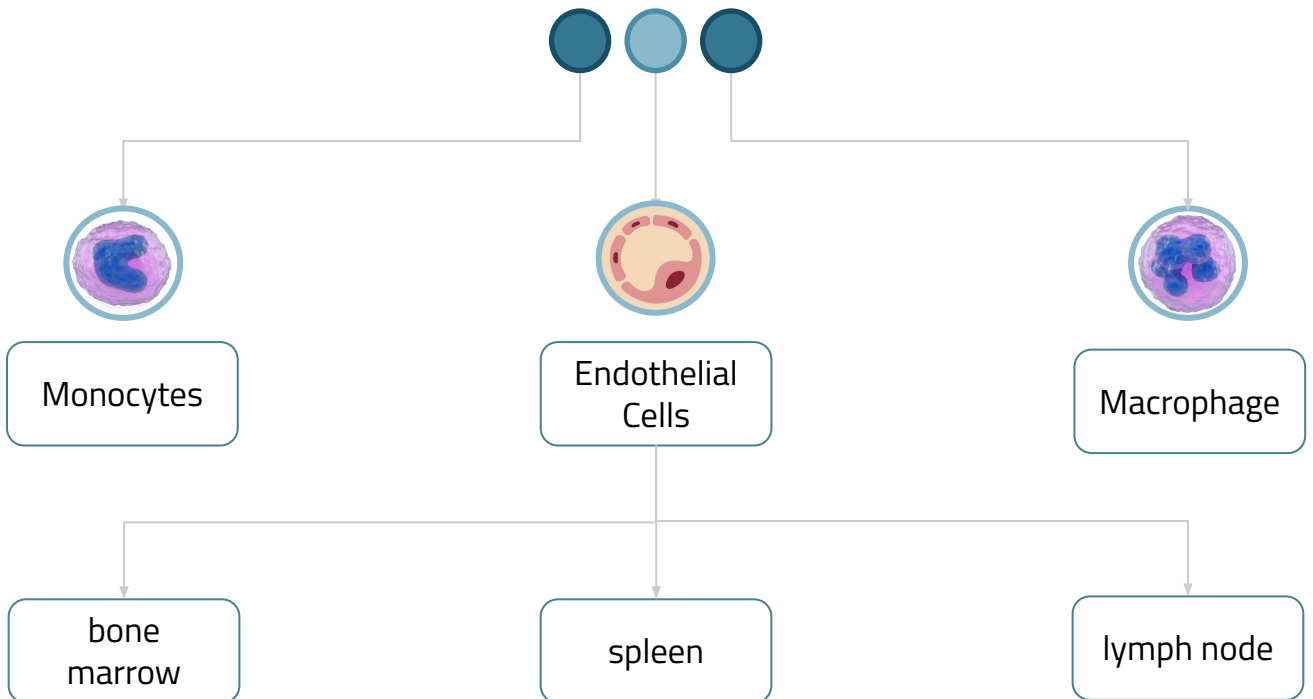


CNS



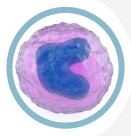
Microglial cells.

Cellular components of RES



Some may end up as the multinucleated giant cells seen in chronic inflammatory diseases such as tuberculosis.

Monocyte: Only in boys' slides



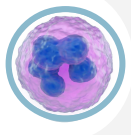
- **Size:** 15-20 µm (active cells 60-80 µm)
- Small granules (azurophilic) & vacuoles
- More efficient ^{macrophage} Phagocytosis than Neutrophils (100 bacteria vs 3-20 by neutr larger particles like RBCs & malarial parasites)
- **Life span: 10-20 hours in blood & in tissues** ^{3m?macrophage}
- **Two types:** mobile & fixed ^{macrophage} because monocytes is **mobile** in blood
- Lysosomes contain lipases (digest lipid coat of some bacteria like *mycobacterium tuberculosis*) unlike neutrophils
- Acts as antigen presenting cells



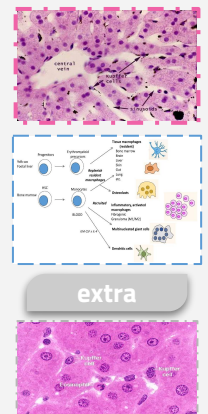
Azurophilic granules of monocytes are primary lysosomes or storage granules. Lysosomes contain acid hydrolases, MPO, HOCL, Defensins **Doctor Q: What are azurophilic granules? primary lysosomes**

- **Monocytes** in blood circulate for about **72 hours** after leaving the bone marrow and then convert to macrophage & stay in blood for 10-20h then enter to tissue for 3 months

Macrophage:



- Macrophages located in all tissues such as skin (histiocytes), liver (kupffer), spleen, bone marrow, lymph nodes, lung.
- Often remain fixed to their organs.
- They filter and destroy objects which are foreign to the body, such as bacteria, viruses.
- Some macrophages are mobile, and they can group together to become one big phagocytic cell in order to ingest larger foreign particles. Some may end up as the multinucleated giant cells seen in chronic inflammatory diseases such as tuberculosis.
- **Mobile & fixed macrophages in tissue (life span 3 months)**

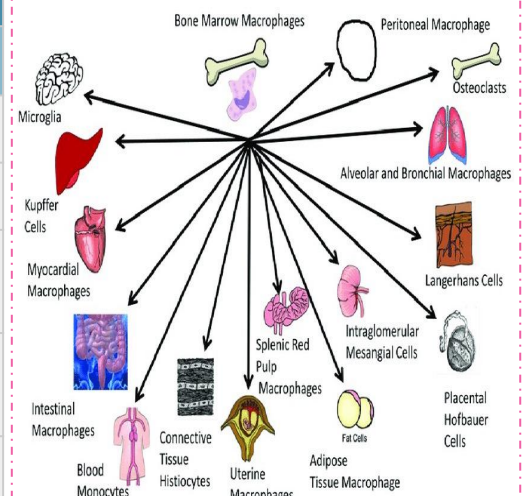


Types of Macrophages Only in girl's slides

Macrophage differ depending on the organs in which they reside.

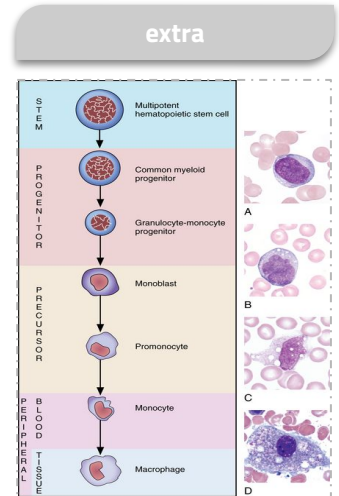
Cell	Organ
Kupffer cells	liver
Microglia	brain
Reticular cells	lymph nodes, bone marrow, spleen
Tissue histiocytes (fixed macrophages)	subcutaneous tissues
Alveolar cells	lungs

Examples of Specialized Macrophage Populations



Formation of Macrophages Only in girl's slides

- 1** **Begin by Stem cell in Bone Marrow:**
monoblast maturing to promonocyte and mature monocytes released into blood
- 2** Stay for 10-20 hours in circulation.
- 3** Then leave blood to tissues transforming into larger cells macrophage.
- 4** Macrophage lifespan is longer up to few months in tissues.



Only in boys' slides

Quick review: Cells of the RES or Tissue Macrophage System

Descriptions	Locations
Fixed macrophages: (reticulum cells) large cells, small nucleus	Spleen, lymph nodes, bone marrow, liver, skin (histiocytes), lungs (macrophages), etc.
Free macrophages: large wandering cells	Spleen, lymph nodes, lungs, many other tissues
Circulating monocytes: large, motile cells with indented nuclei	Blood

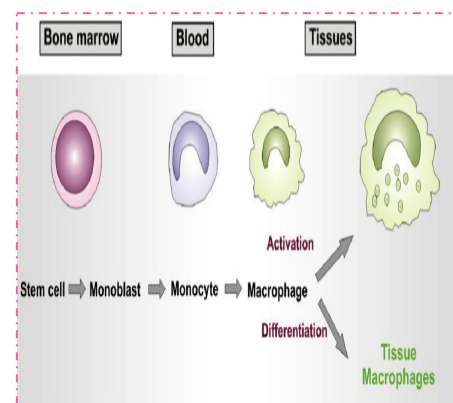
Transformation of Monocytes to Macrophage Only in girl's slides

Characterized by an increase in

Cell size.

Number and complexity of intracellular organelles Golgi, mitochondria, lysosomes.

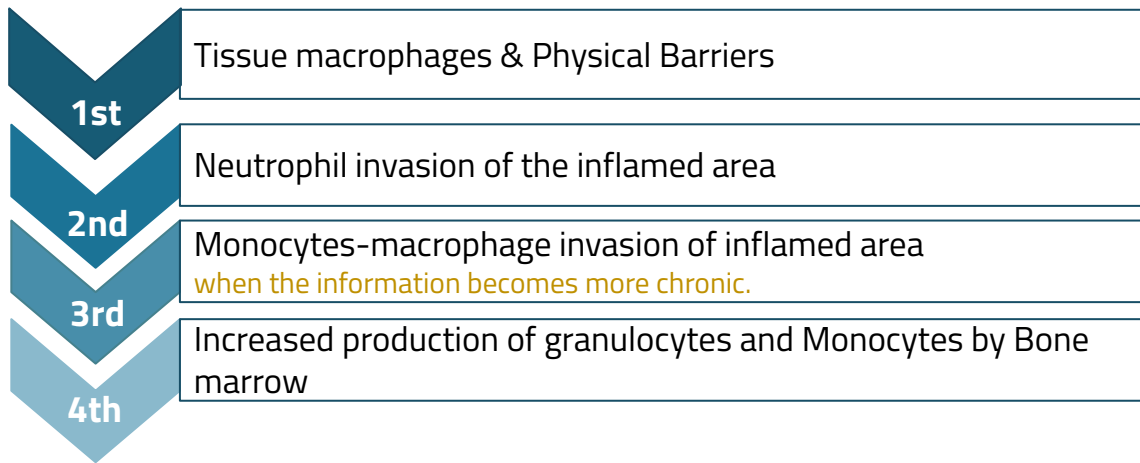
Intracellular digestive enzymes



Macrophage and Neutrophil

Responses During Inflammation

lines of defenses:



Defense properties

SAQ: Enumerate the defensive properties of macrophages and neutrophils IN ORDER

Margination	WBC Roll, Bind and then stick along the walls of blood capillaries
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

The inflamed area will release some substance that neutrophils can detect from the BV then it brined to the wall of BV and squeeze *تحشر نفسها* & enter to the tissue between the cells and move by amoeboid *الاقدام* to the inflamed area and ingest, eat the microbes 🦠

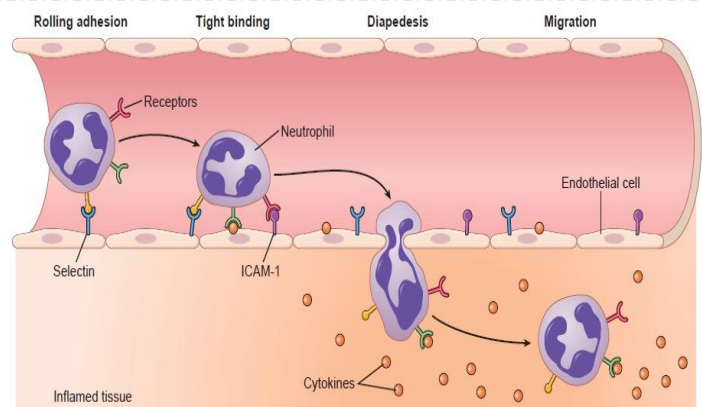


Figure 34-6. Migration of neutrophils from the blood into inflamed tissue. Cytokines and other biochemical products of the inflamed tissue cause increased expression of selectins and intercellular adhesion molecule-1 (ICAM-1) in the surface of endothelial cells. These adhesion molecules bind to complementary 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.

General functions of RES

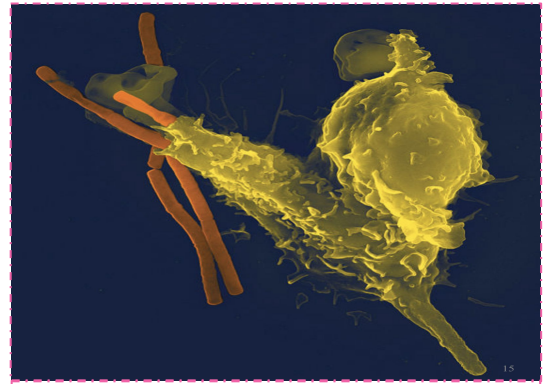
Phagocytosis	Bacteria, dead cell, foreign particles (direct)
Immune functions	Processing antigen and antibodies production (indirect) they act like Antigen Presenting Cells
Breakdown	of aging RBCs
Storage	of RBCs and circulation of iron. iron that come from the broken RBCs

Phagocytosis Only in girl's slides

Part of the natural or innate immunity

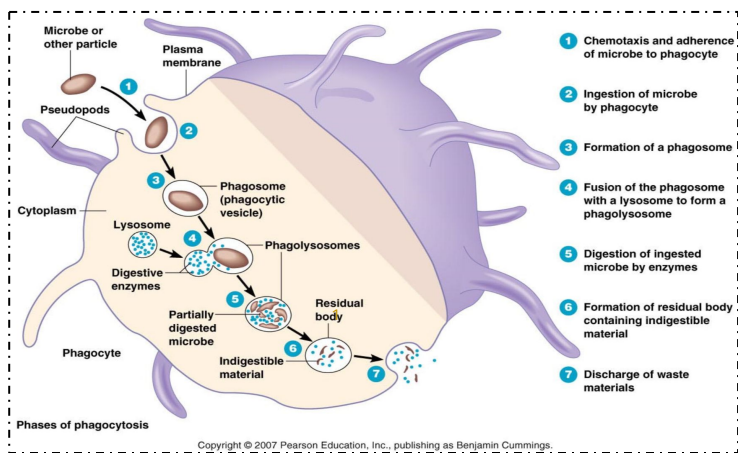
Macrophages are a powerful phagocytic cells:

- Ingest **up to 100 Bacteria**
- ingest **larger particles** such as old RBCs
- get rid of **waste products**



A scanning electron microscope image of a single neutrophil (**yellow**), engulfing anthrax bacteria (**orange**).

Microbial Killing



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

1) Residual bodies contain indigestible material only

Direct functions of RES

Only in boys' slides

Phagocytosis

Opsonization and phagocytosis

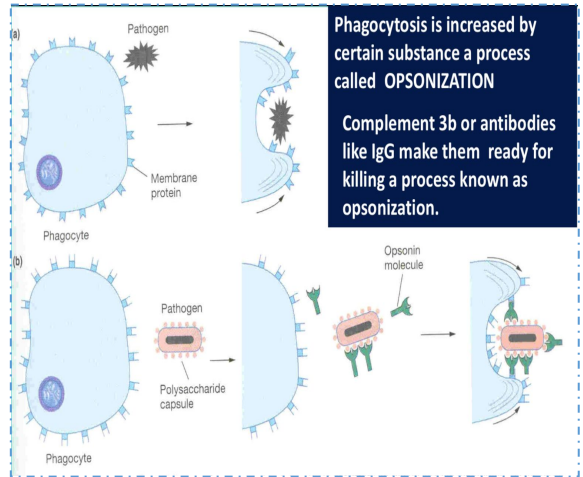
Phagocytosis is increased by certain substance a process called OPSONIZATION.

opsonization: "to make something more tasty"

Complement 3b or antibodies like IgG make them ready for killing a process known as opsonization.

For some reason the macrophage can't eat this microbe so it enhances this substance (IgG...) to engulf and coat that microbe and make it easy to be ingested

كانت مو حلو طعمها وبعد الاضافات صارت احلى واكلها



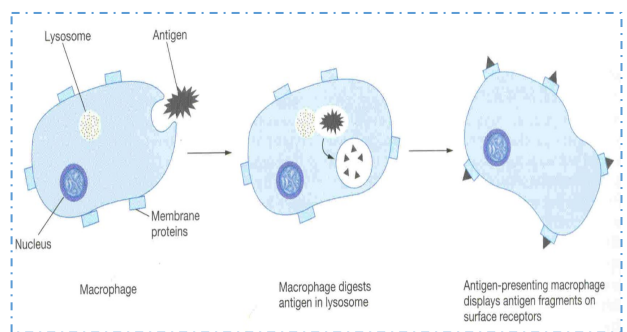
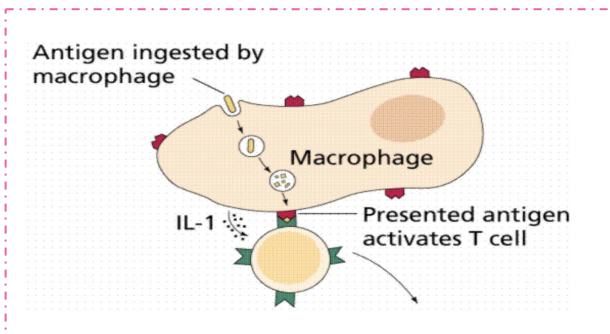
indirect functions of RES

Ingesting foreign bodies

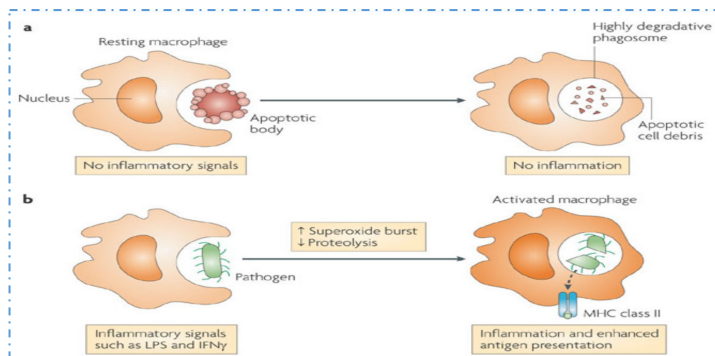
Process it

Present it to lymphocyte

APCs; displaying it attached to MHC II molecule



Classical APCs include Macrophages, dendritic cells, Langerhans cells and B cells. Doctor Q: name 4 APCs



Lymphoid organs Only in girl's slides

1

Thymus

High rate of growth and activity until puberty, they begins to shrink; site of T-cell maturation.

2

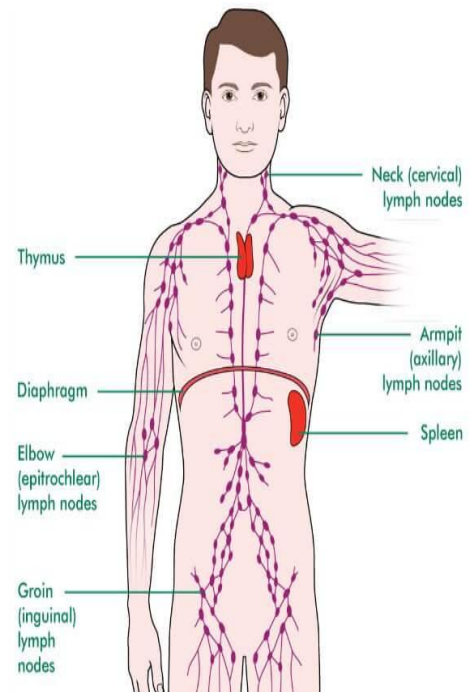
Lymph nodes

Small, encapsulated, bean-shaped organs stationed along lymphatic channels & large blood vessels of the thoracic and abdominal cavities .

3

Spleen

Structurally similar to lymph nodes, it filters circulating blood to remove worn out RBCs and pathogens.



Only in boys' slides

Primary Lymphatic Organs

Are where lymphocytes are **formed** and **matured**. They provide an environment for stem cells to divide and mature into B and T cells.

These include: Red **bone marrow** and **thymus gland**.

Both B and T 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 fluid, 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).**

MCQ: which of the following is a Primary/Secondary lymphatic organ?

Spleen

Is a soft purple gray in color located in the left upper quadrant of the abdomen

It is a highly vascular lymphoid organ **If the spleen is damaged in trauma it has to be removed because sutures will make it bleed more**

It plays an important roles in: red blood cell integrity and has an immune functions

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.

Functions of the spleen Only in girl's slides

- 1 Hematopoiesis (hemopoiesis): during **fetal life**.
- 2 Spleen is a main site for **destruction of RBCs** specially old and abnormal e.g. spherocytosis.
- 3 **Blood is filtered** through the spleen
- 4 Reservoir of thrombocytes and immature erythrocytes.
- 5 Recycles iron

Reservoir function:

- A large number of RBCs and platelets are stored in spleen and recycles iron
- RBCs are released from spleen into circulation during the emergency conditions like hypoxia & hemorrhage

Structural functions of Spleen

White pulp

Thick sleeves of lymphoid tissue, that provides the **immune function** of the spleen.

Immunologic functions:

- trapping and processing of antigens
- initiates immunologic response (APC)
- the major site of antibody synthesis
- **key role in removal of encapsulated bacteria (Strep pneumo) imp if the spleen is removed, the patient will need anti streptococcal vaccines annually.**

-Macrophage activation
-Site of B cell maturation into plasma cells, which synthesize antibodies initiates white pulp and initiates humoral response.

Red pulp

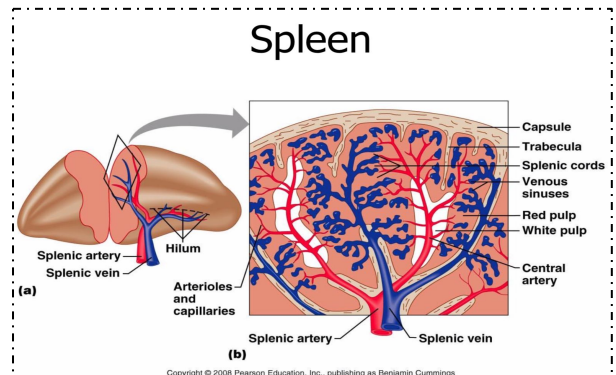
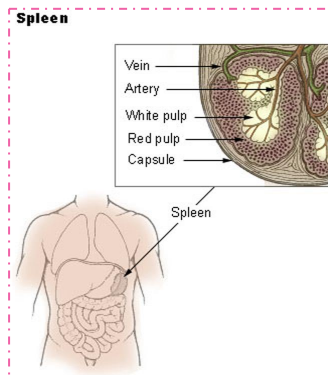
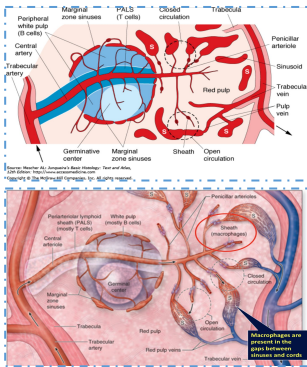
Surrounds white pulp, composed of **venous sinuses** filled with whole blood and splenic cords of reticular connective tissues rich in **macrophages**.

Hematological functions (filtering function):

- RBC's able to deform through sinusoidal wall and endothelium Culling (Increased in hereditary spherocytosis).
- Retrieve iron for the body

Cytopenias:

- 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. **adults with these diseases spleen begin to produce RBCs like fetal life**

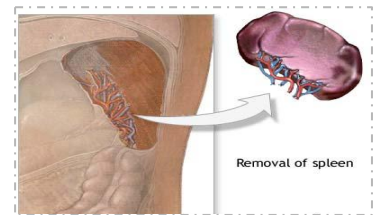
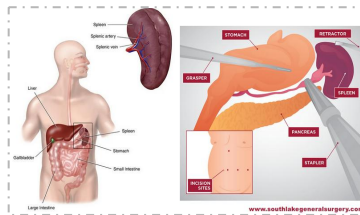
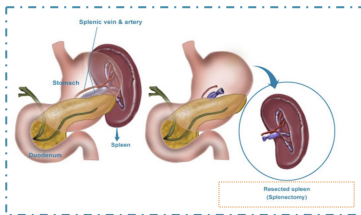


Immune functions of the spleen

- 1 *Because the organ is directly connected to blood circulation, it responds faster than other lymph nodes to **blood-borne antigens**, filters the blood by removing the microorganisms & foreign bodies
- 2 **Destruction and processing** of antigens, and is the major site of IgM production.
- 3 **Reservoir of lymphocytes** in white pulp, contains about 25% of T-cells and 15% of B-cells.
- 4 *Site for **Phagocytosis** of bacteria and worn-out blood cells (Slow blood flow in the red pulp cords allows foreign particles to be phagocytosed)
- 5 *the non-specific opsonins, properdin and tuftsin, are synthesized that bind to the receptors on the surface of macrophages and other leukocytes, stimulating their phagocytic, bactericidal, tumoricidal activity.
- 6 *Site of **B cell maturation** into plasma cells, which synthesize antibodies in its white pulp and initiates humoral response.
- 7 *Removes antibody-coated bacteria along with **antibody-coated blood cells**
- 8 *It contains (in its blood reserve) half of the body **monocytes** within the red pulp, upon moving to injured tissue (such as the heart), turn into **dendritic cells** and **macrophages** that promoting **tissue healing**.

Splenectomy Indications

- 1 Hypersplenism** Enlargement of the spleen (splenomegaly) with defect in the blood cells count.
- 2 Primary spleen cancer**
- 3 Hemolytic anemias** Sickle-cell anemia, Thalassemia, Hereditary spherocytosis (HS) and elliptocytosis.
- 4 ITP** Idiopathic thrombocytopenic purpura
- 5 Trauma**
- 6 Hodgkin's disease**
- 7 Autoimmune hemolytic disorder**



Risks & complications of splenectomy

Overwhelming **bacterial infection**/ post splenectomy **sepsis**.

Inflammation to the **pancreas** and collapse of the **lungs**

Patient prone to **Malaria**

Post-operative **thrombocytosis** and **thrombosis**

Excessive post-operative **bleeding** (Surgical)

MCQ & SAQ:

Q1: Key components of the innate immunity & activate adaptive immunity by transforming into APCs

- A. Natural Killer cells
- B. Macrophage
- C. Eosinophils
- D. Neutrophils

Q3: in thymus:

- A. T cell maturation
- B. B cell maturation
- C. RBCs
- D. Destruction of pathogenic antigen

Q5: What does the white pulp of the spleen contain?

- A. Venous sinuses
- B. Splenic cord
- C. Lymphoid tissue
- D. Reticular connective tissue

Q2: Which of the following is true about Thymus

- A. Small, encapsulated, bean-shaped organ
- B. Has a high rate of growth and activity until puberty
- C. Structurally similar to lymph nodes
- D. Low rate of growth and activity until puberty

Q4: Thick sleeves of lymphoid tissue, that provides the immune function of the spleen.

- A. Lymph node
- B. Red pulp.
- C. White pulp
- D. Thymus

Q6: One of the general functions of RES

- A. Digestion
- B. Presenting Antigens
- C. Breakdown of aging RBCs
- D. Hematopoiesis

6: C
5: C
4: C
3: A
2: B
1: B
key:
answer

1- What are the cellular of RES?

2- Write 4 indications splenectomy

3-Mention three complications of splenectomy.

4- Mention briefly the indirect functions of RES

A1: Monocytes, Endothelial cells, Macrophages

A2: Hypersplenism, Primary spleen cancer, Haemolytic anemia, Trauma

A3: Overwhelming **bacterial infection**, post splenectomy **sepsis**, Post-operative **thrombocytosis** and **thrombosis**

A4: Ingesting foreign bodies > Process it > Present it to lymphocytes.

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- Saud Alhasani
- Muneerah Alsadhan

