

# RETICULOENDOTHELIAL SYSTEM AND FUNCTIONS OF THE SPLEEN

## Nonspecific Host Defenses

*DR SYED SHAHID HABIB*  
MBBS DSDM PGDCR FCPS  
Professor & Consultant Clinical Physiology  
Dept. of Physiology  
College of Medicine & KCUH

# 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.**

# IMMUNITY

```
graph TD; A[IMMUNITY] --> B["Innate immunity  
(non specific)"]; A --> C["Acquired immunity  
(specific, adaptive)"]; B --> D["Phagocytes  
(Neut, Mono, NK)"]; B --> E["Complement"]; B --> F["Barriers"]; C --> G["Cell mediated  
T lymphocytes"]; C --> H["Humoral  
Antibody  
mediated  
B lymphocytes"];
```

## Innate immunity

(non specific)

Examples:

- Phagocytes  
(Neut, Mono, NK)
- Complement
- Barriers

## Acquired immunity

(specific, adaptive)

**Cell mediated**  
T lymphocytes

**Humoral**  
Antibody  
mediated  
B lymphocytes

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

# RETICULOENDOTHELIAL 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: Reticulo refers to the propensity of these large phagocytic cells in various organs to form a network or a 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.

# Monocyte/Macrophage System

## TISSUE MACROPHAGE SYSTEM COMPONENTS

- Monocytes in **Blood** circulate for about 72 hours after leaving the Bone Marrow
- Mobile & Fixed Macrophages in **Tissue** (Life Span 3 months)
- **Specialized endothelial cells** in bone marrow, spleen and lymph nodes

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

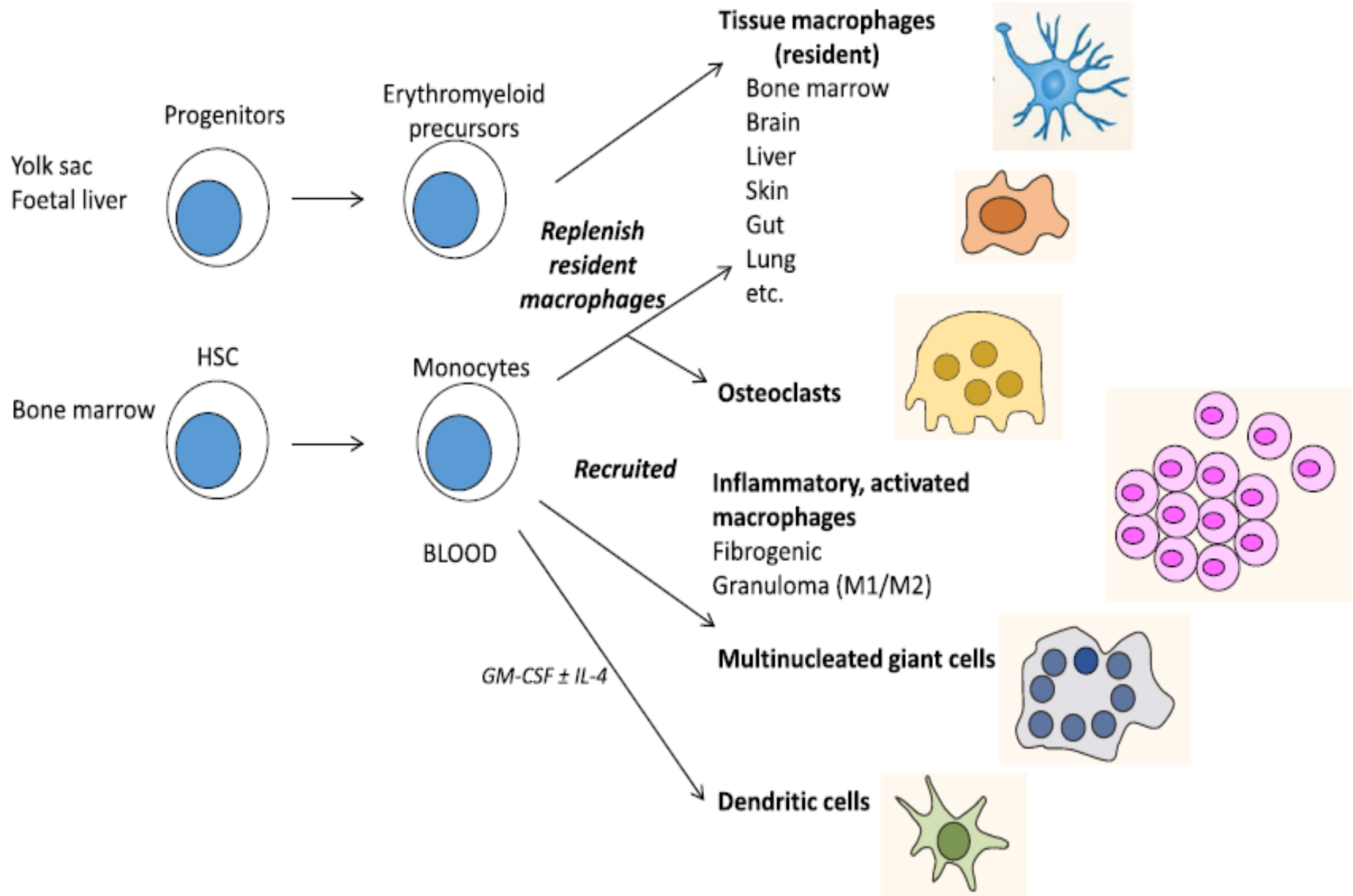
# MONOCYTES



- **Size:** 15-20  $\mu\text{m}$  (active cells 60-80  $\mu\text{m}$ )
- **Small Granules (azurophilic) & Vacuoles**
- **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...& in tissues?
- **Two types:** Mobile & Fixed
- **Lysosomes contain lipases** unlike Neutrophils.
- **Acts as Antigen Presenting Cells**

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

# Origins and distribution of Tissue Macrophages



## 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



# General Functions of RES

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

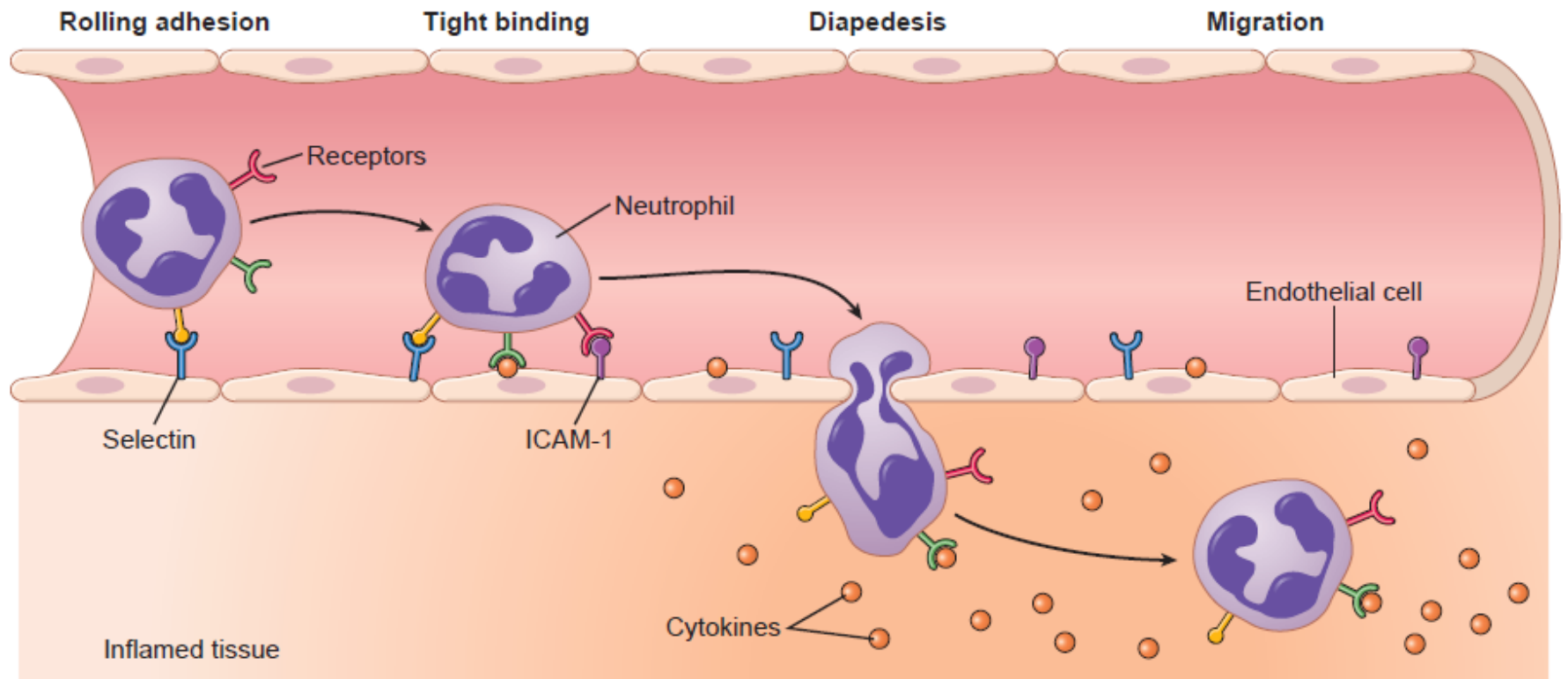
# Responses During Inflammation

## Macrophage and Neutrophil

- ❑ **1<sup>st</sup>** line of defense – **Tissue macrophages & Physical Barriers**
- ❑ **2<sup>nd</sup>** line of defense – Neutrophil Invasion of the inflamed area
- ❑ **3<sup>rd</sup>** line of defense – **Monocytes –macrophage invasion of inflamed area**
- ❑ **4<sup>th</sup>** line of defense – Increased production of granulocytes and Monocytes by Bone marrow

# DEFENSIVE PROPERTIES OF MACROPHAGES & NEUTROPHILS

- **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



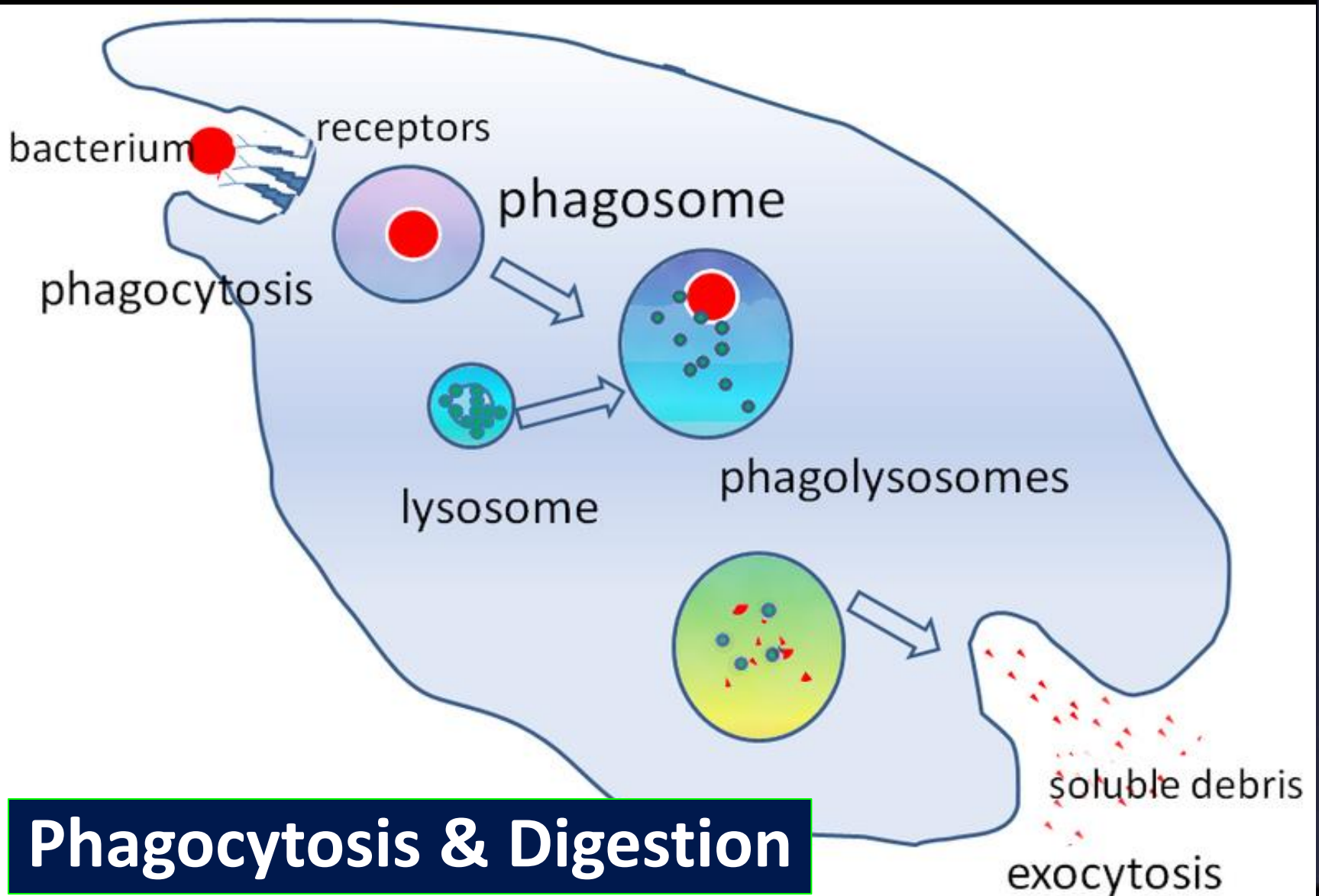
**Figure 34-6.** Migration of neutrophils from the blood into inflamed tissue. Cytokines and other biochemical products of the inflamed tissue cause increased expression of selectins and intercellular adhesion molecule-1 (*ICAM-1*) in the surface of endothelial cells. These adhesion molecules bind to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

A scanning electron micrograph (SEM) of an activated macrophage. The cell is shown in a highly spread, flattened state, with a prominent, long, and thin lamellipodium extending from its main body towards the bottom right. The surface of the cell is covered in a complex network of microvilli and ruffles. The background is a dark, reddish-brown color, and there are some small, bright, irregular shapes scattered around the cell, possibly representing other cells or debris.

macrophage = *big eater*

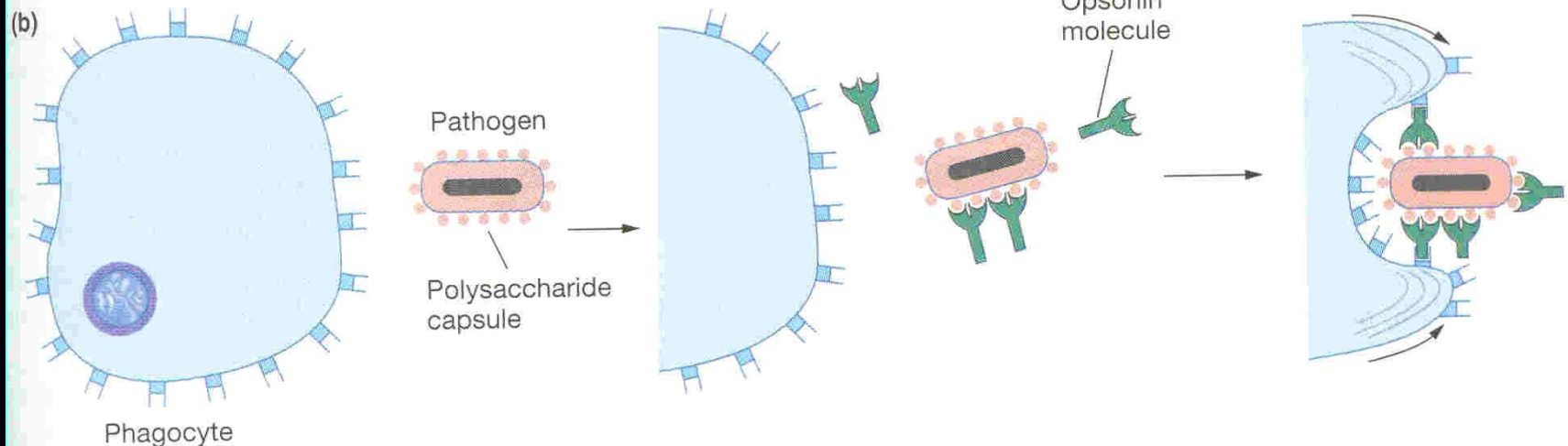
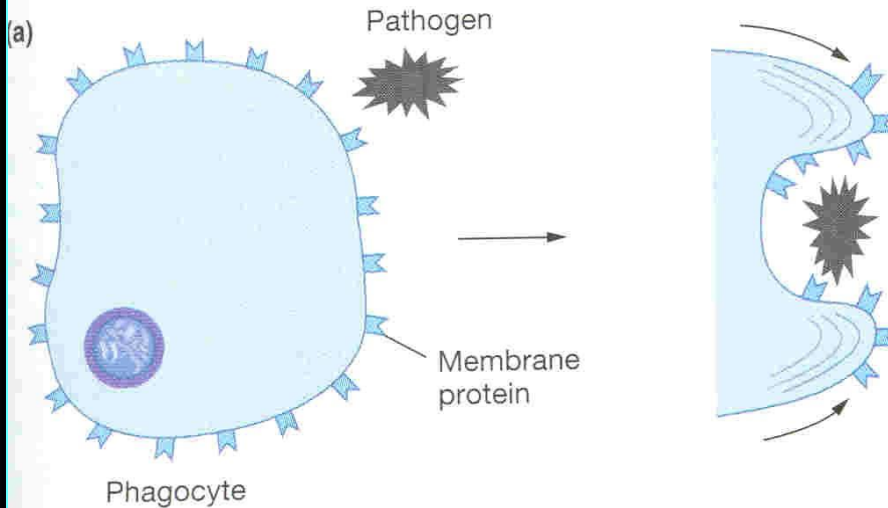
**ACTIVATED  
MACROPHAGE**

# Direct function of RES



**Phagocytosis & Digestion**

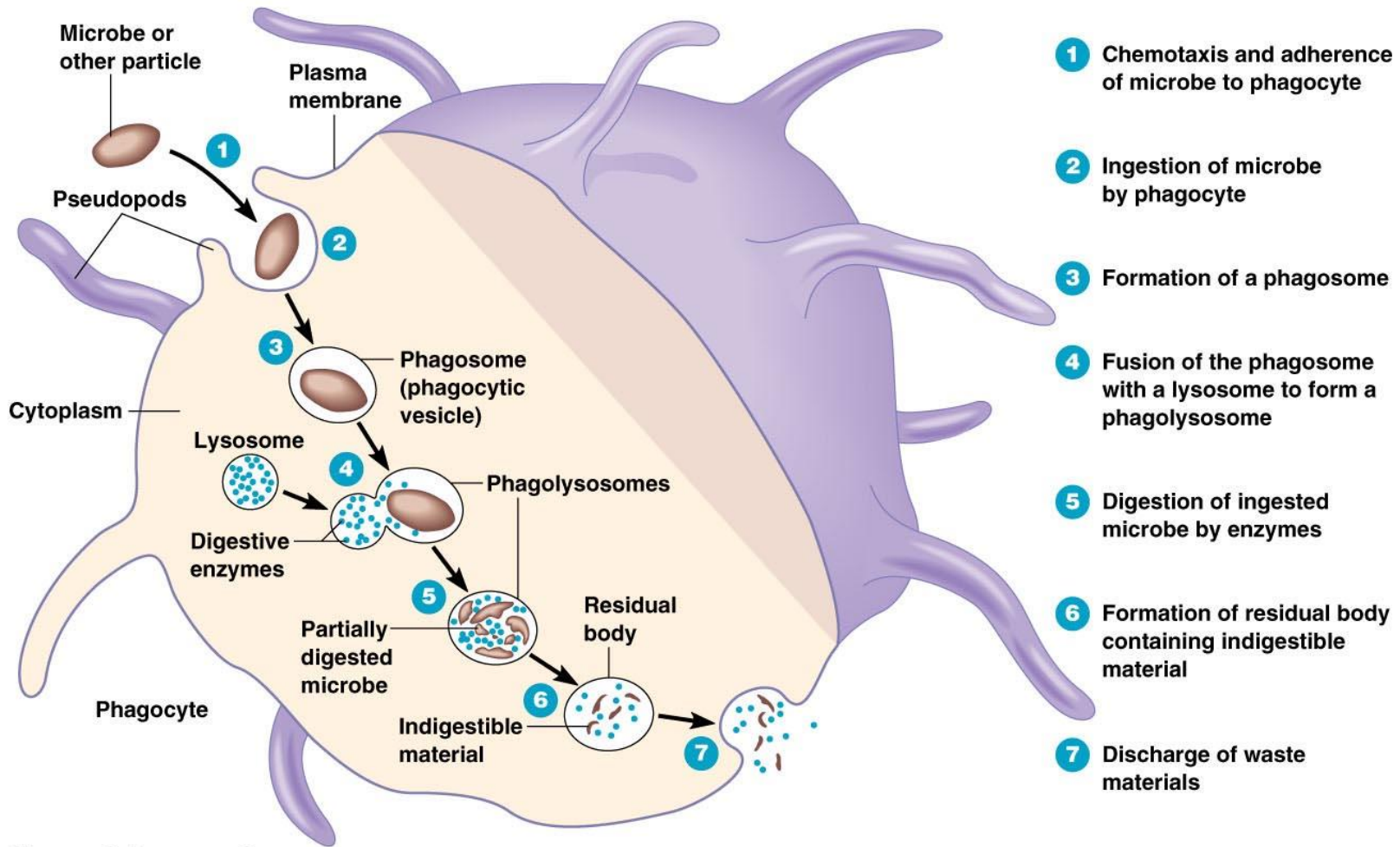
# Opsonization & Phagocytosis



Phagocytosis is increased by certain substance a process called **OPSONIZATION**

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

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



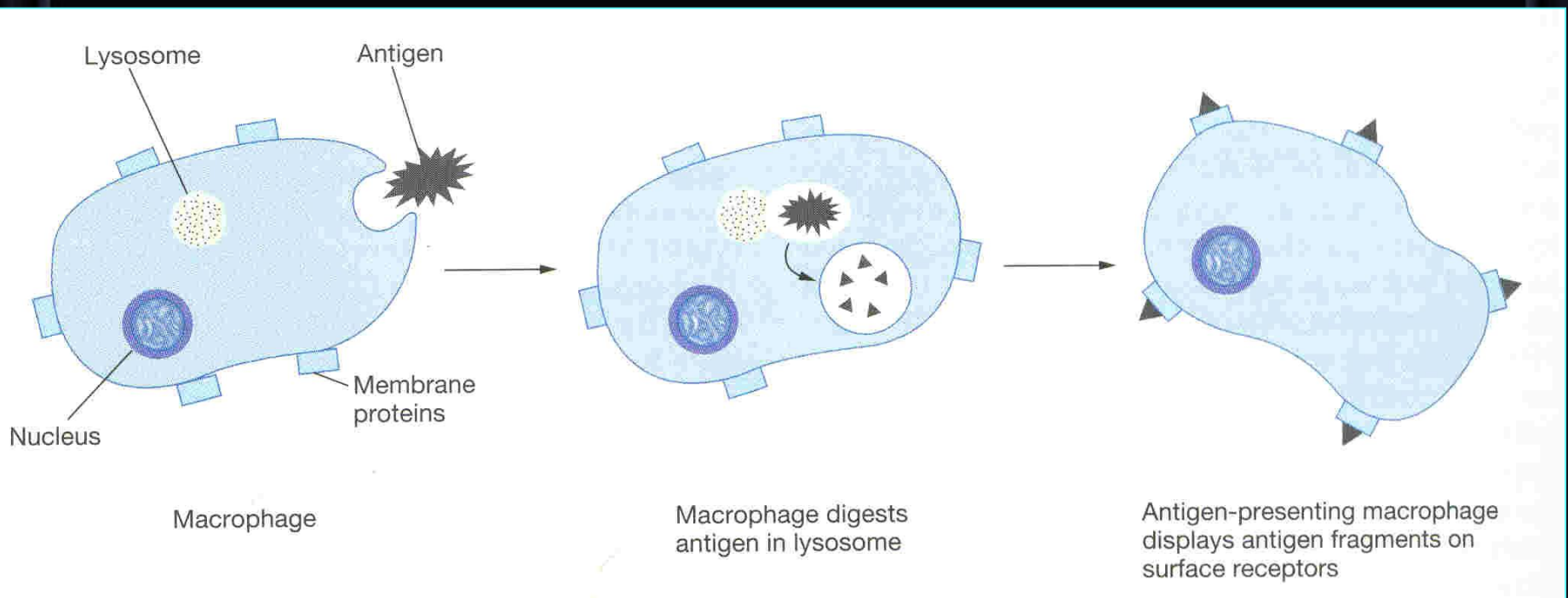
Phases of phagocytosis



# Indirect Immune function Of RES

## Antigen Presenting Cells

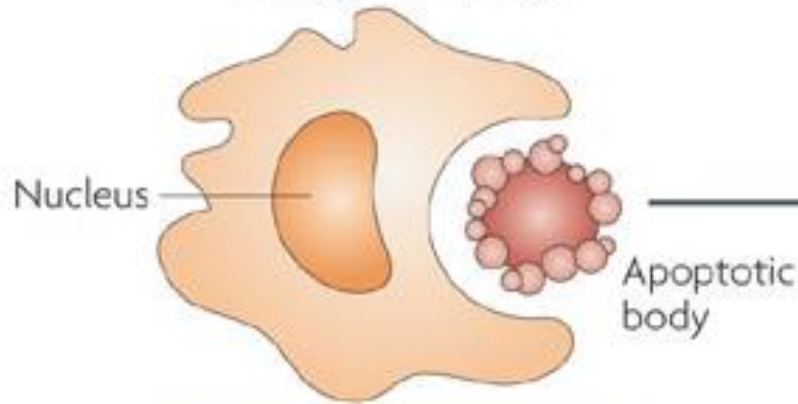
Displaying it attached to an MHC class II molecule



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

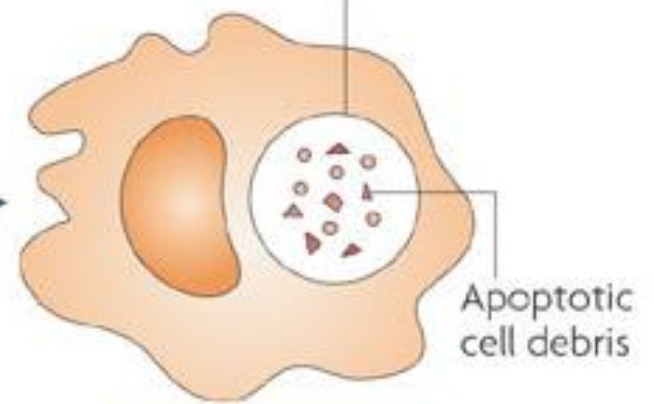
**a**

Resting macrophage



No inflammatory signals

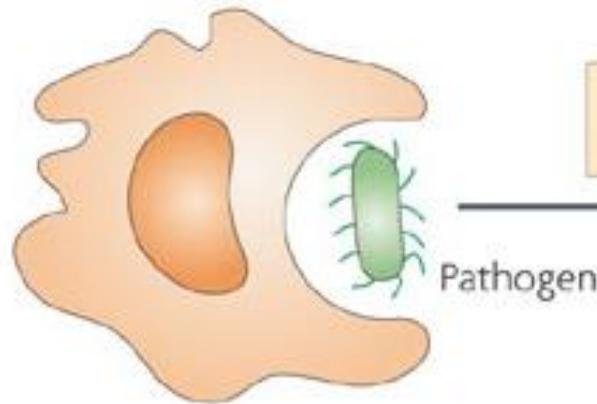
Highly degradative phagosome



No inflammation

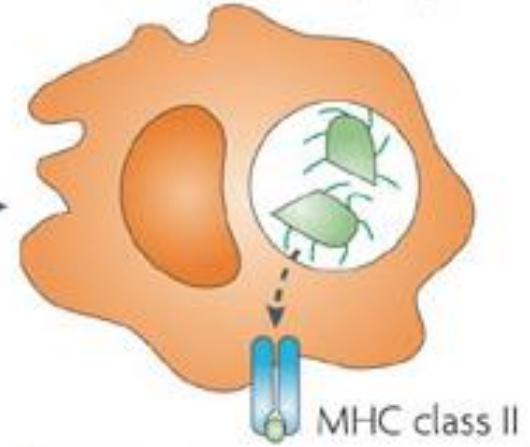
**b**

Activated macrophage



Inflammatory signals such as LPS and IFN $\gamma$

↑ Superoxide burst  
↓ Proteolysis



Inflammation and enhanced antigen presentation

# 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**

**Examples are: -**

1. Skin, mucosa and Subc tissues (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

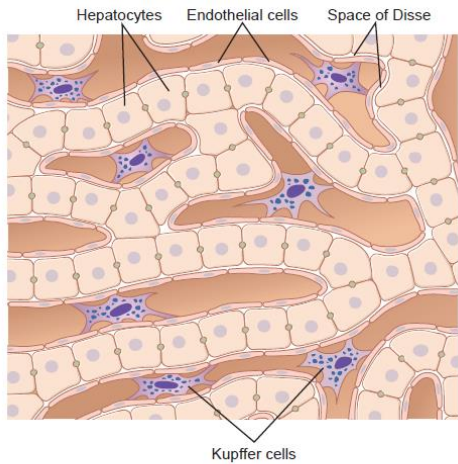
8. Kidneys (Mesangial Cells)

9. Bone (Osteoclasts)

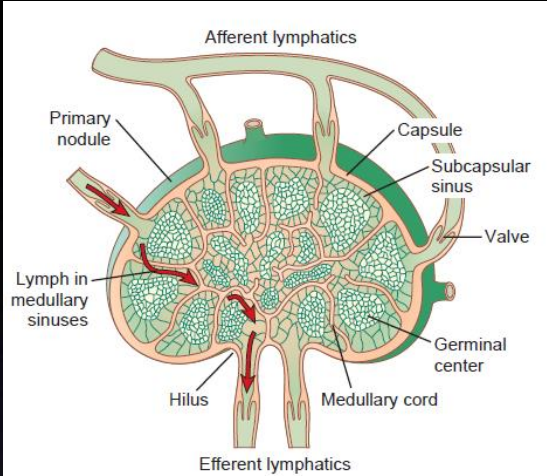
Hofbauer cells in Placenta

Epithelioid cells in Granulomas

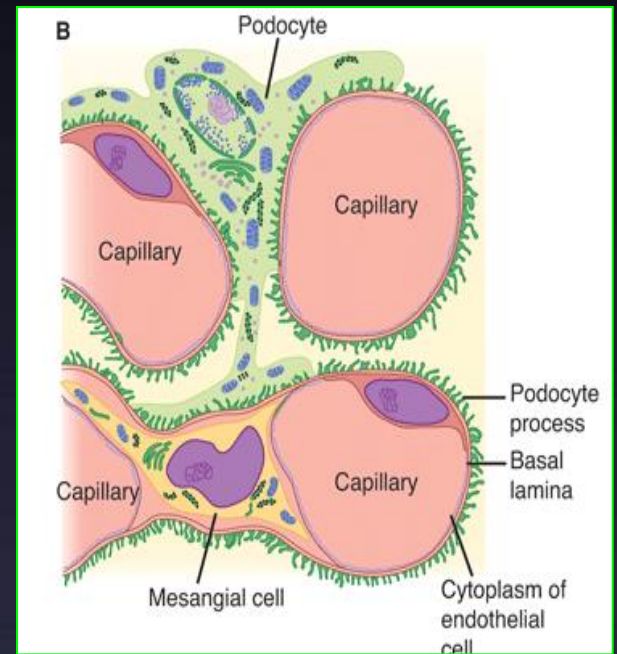
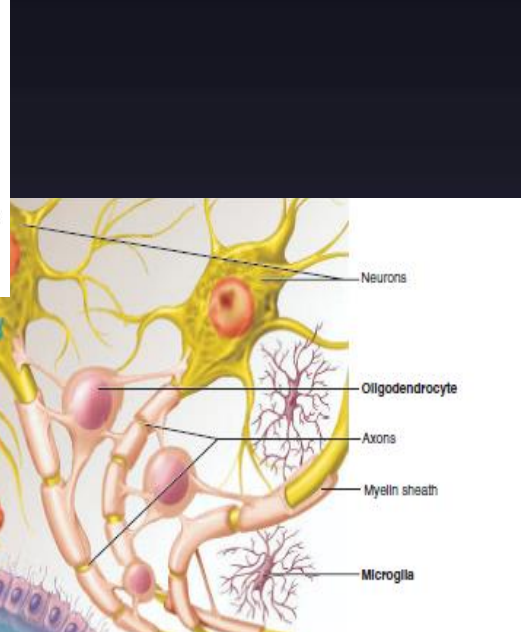
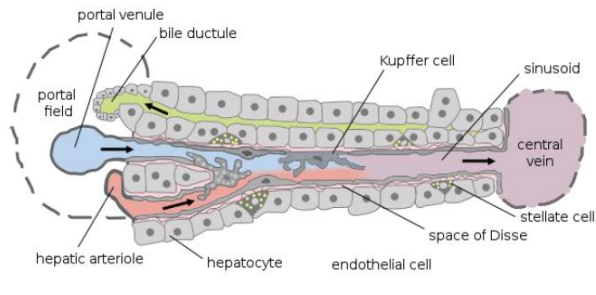
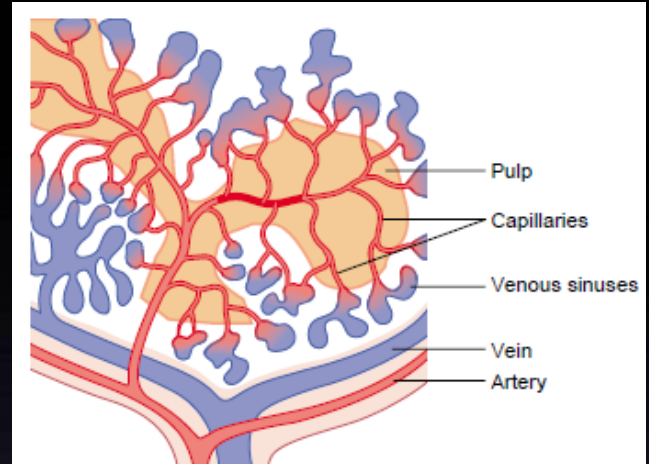
# Tissue macrophages



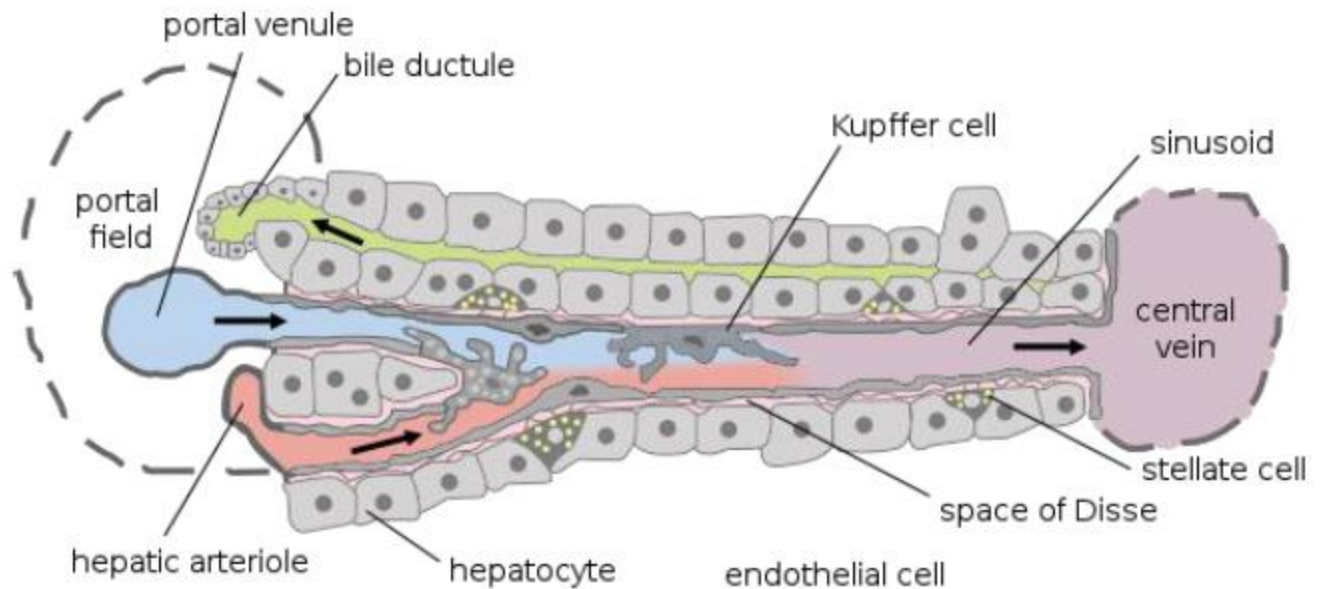
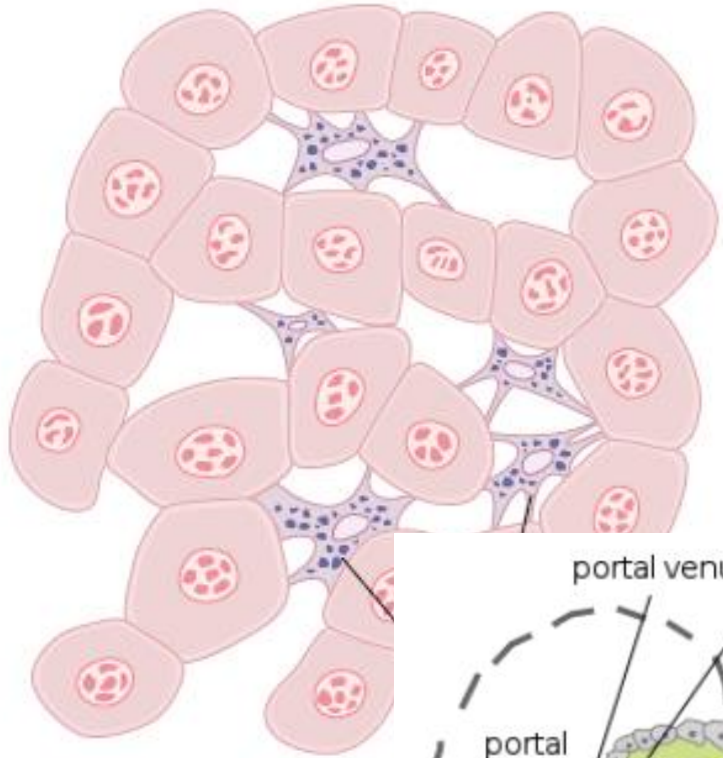
**Figure 34-4.** Kupfer cells lining the liver sinusoids, showing phagocytosis of India ink particles into the cytoplasm of the Kupfer cells.



**Figure 34-3.** Functional diagram of a lymph node.

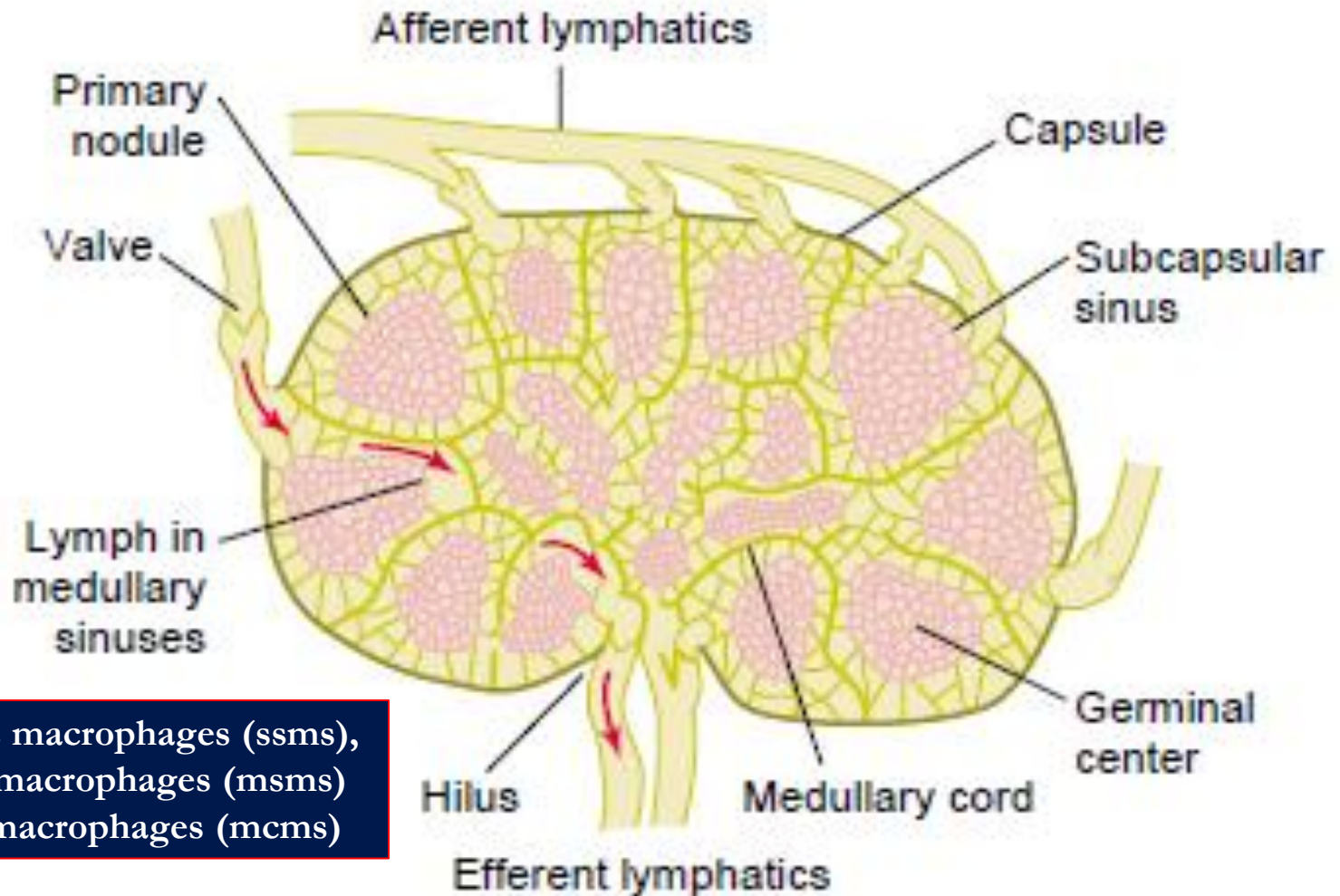


# Tissue macrophages in Liver sinuses



# Tissue macrophages in Lymph Nodes

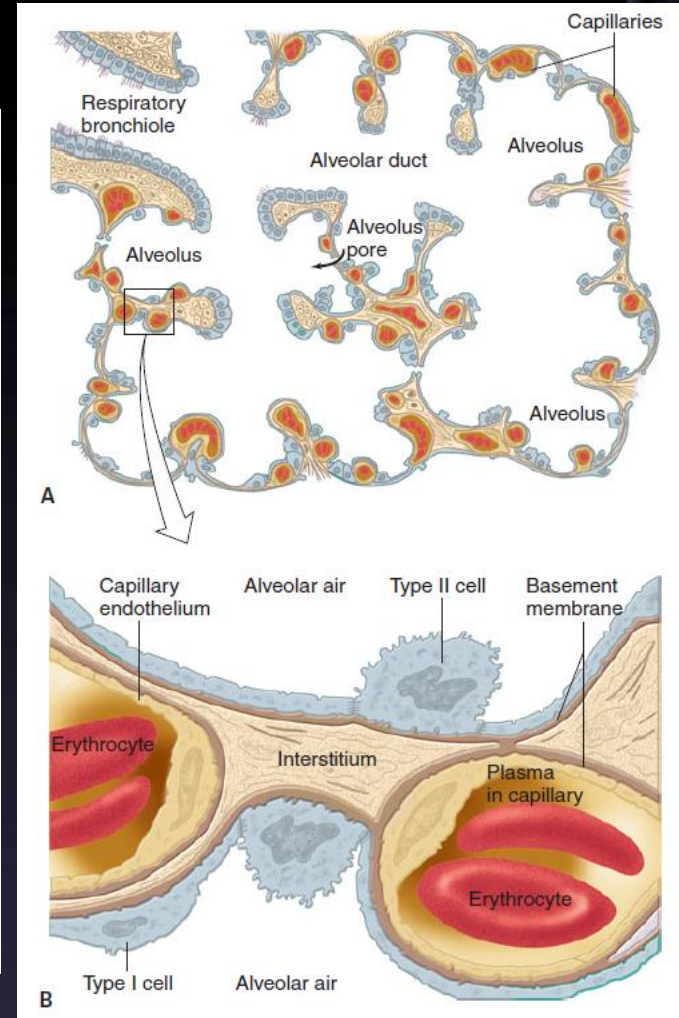
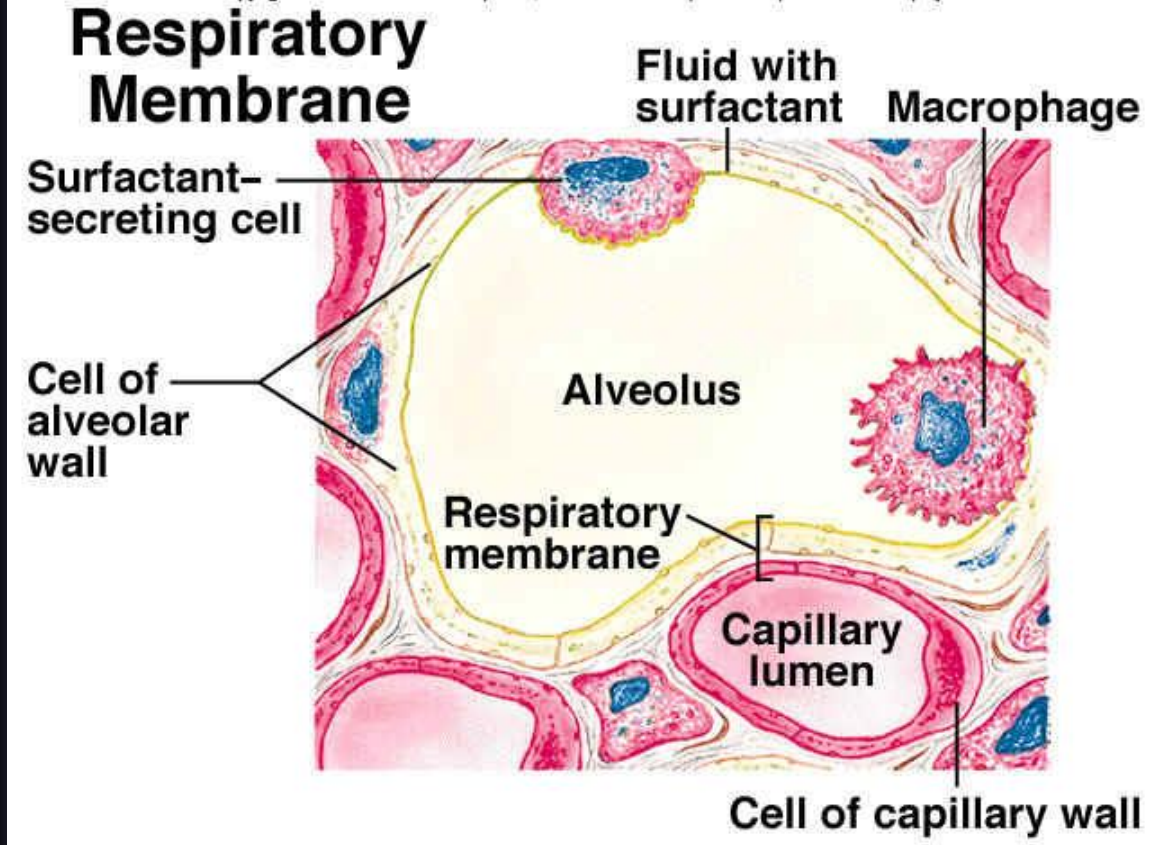
Macrophages line nodal medullary sinuses



Subcapsular sinus macrophages (ssms),  
Medullary sinus macrophages (msms)  
Medullary cord macrophages (mcms)

# Tissue macrophages in Lungs

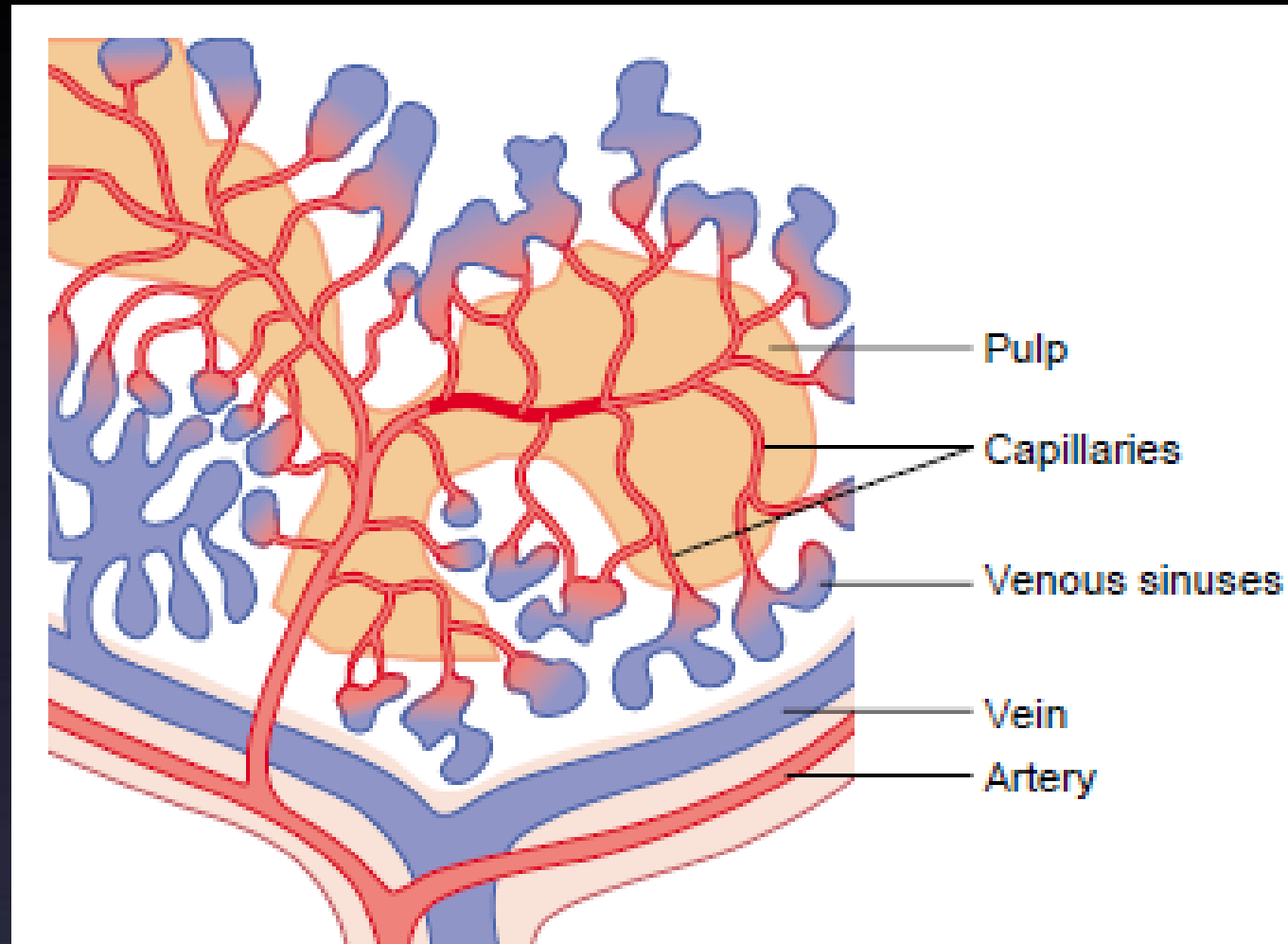
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“dust cells” because of their content of intracellular carbon particles

# 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).

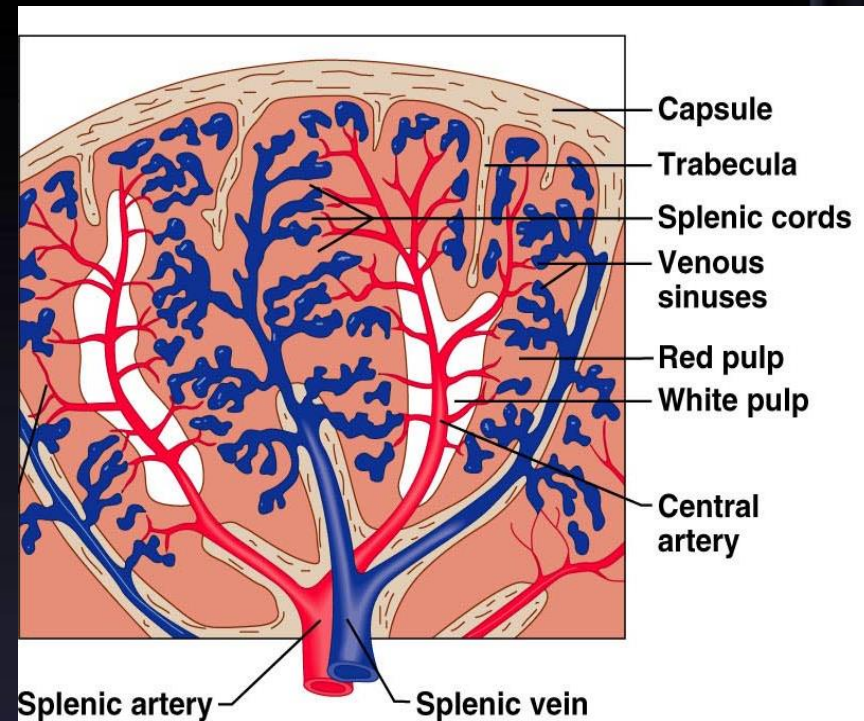
# SPLEEN

- 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.

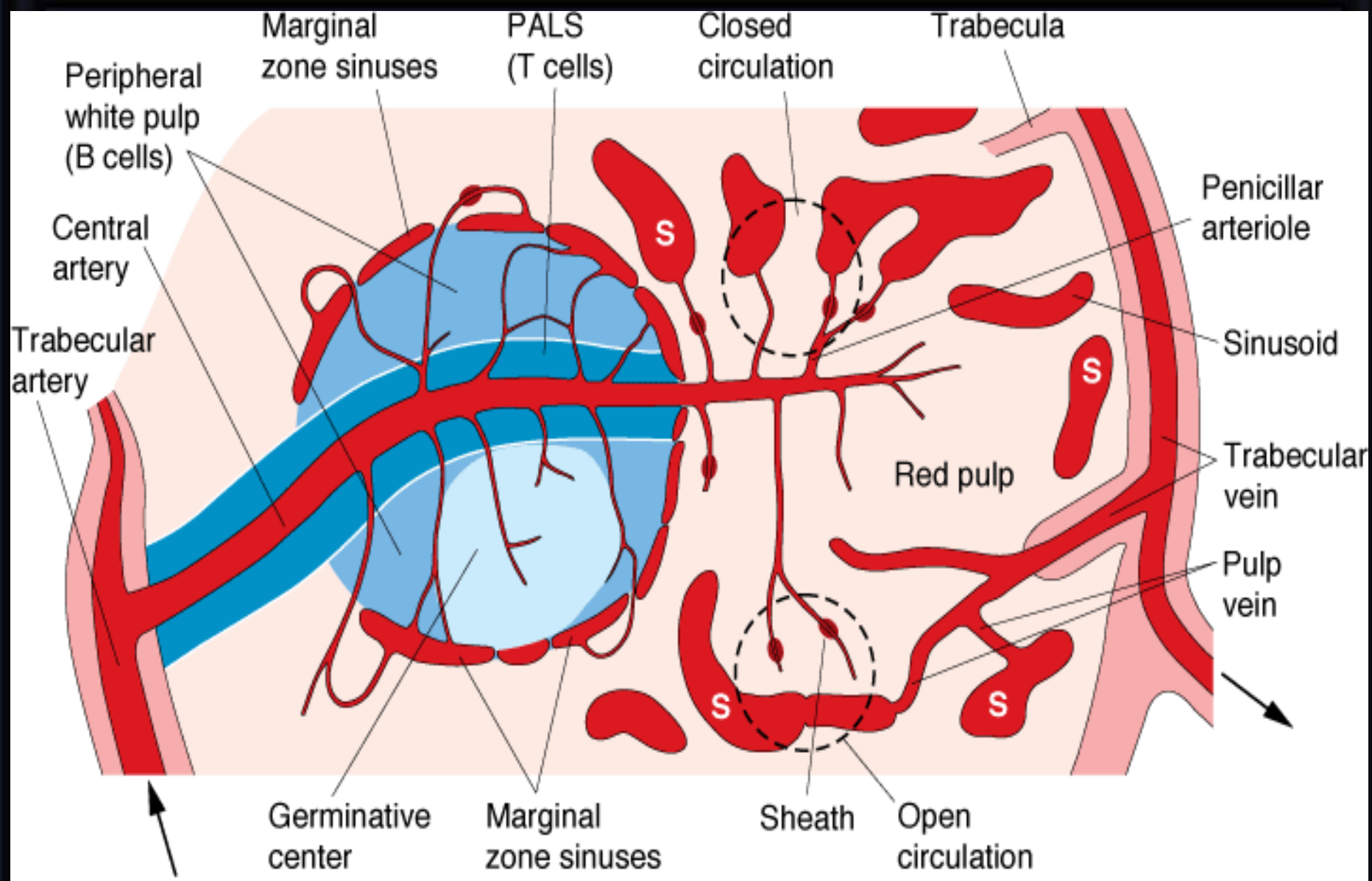
# STRUCTURE OF SPLEEN

**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.

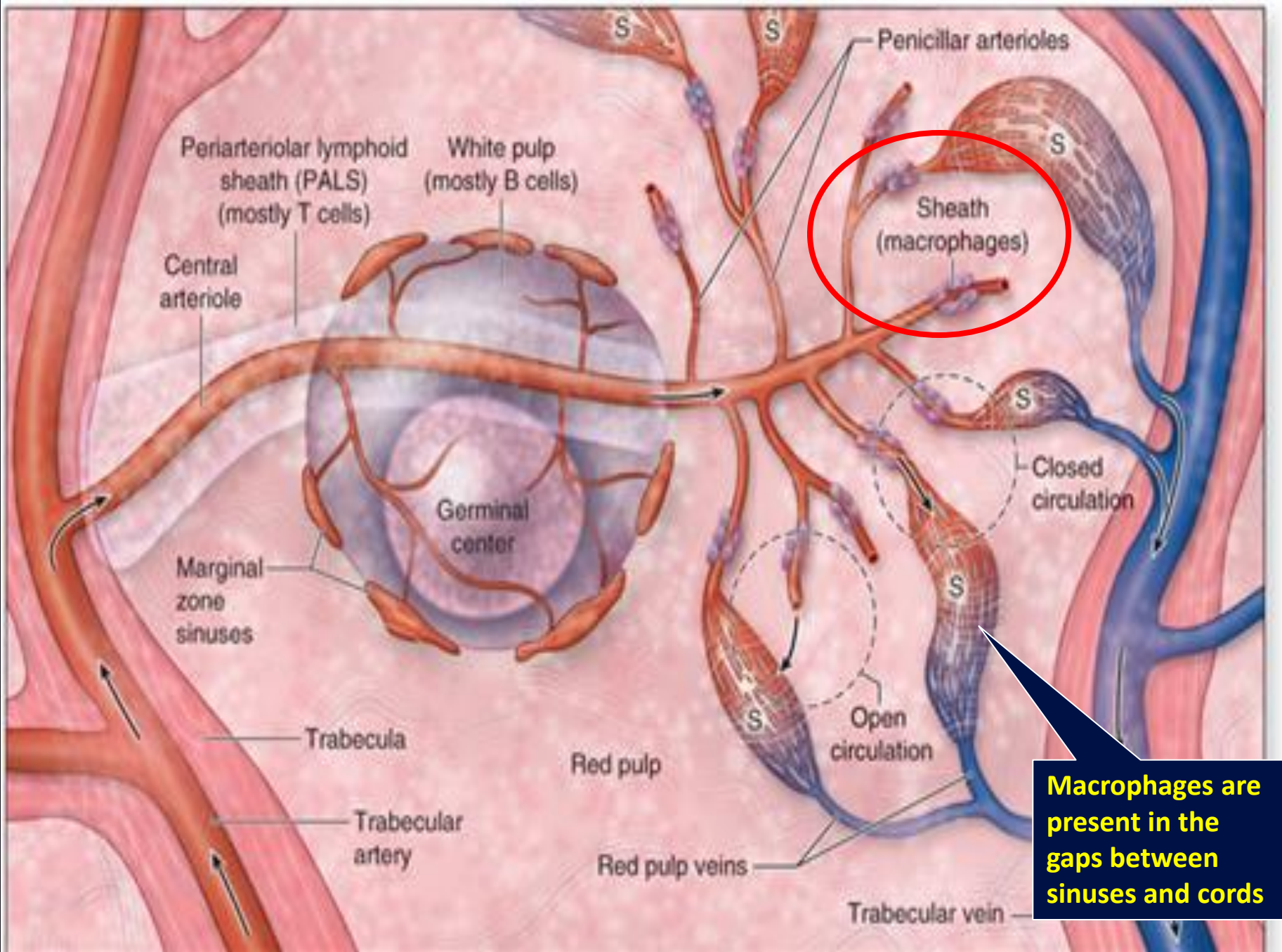


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**Macrophages are present in the gaps between sinusoids and cords**

# FUNCTIONS OF SPLEEN

## **Red Pulp- Red Pulp- Hematological functions (filtering function)**

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

## **White pulp - 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)**

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

## **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.

# FUNCTIONS OF SPLEEN

## 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

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

- Spleen acts as reservoir of lymphocytes (contains about 25% of T cells & 15% B Cells)
- The spleen processes foreign antigens and is the major site of specific immunoglobulin M (IgM) production.
- 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.

# Splenectomy

## 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.

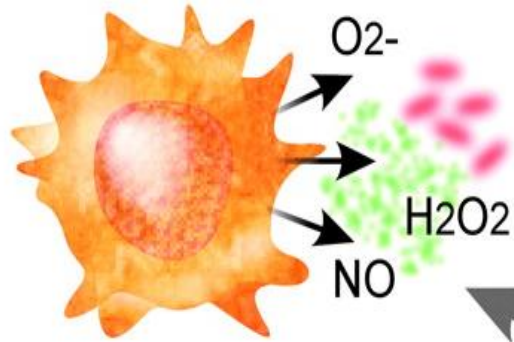


# Risks & Complications of Splenectomy

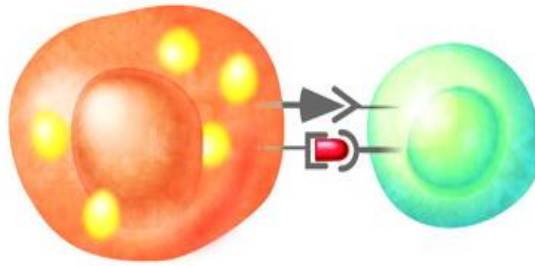
- ❖ Overwhelming **bacterial infection** or post splenectomy **sepsis**.
- ❖ Patient is prone to **malaria**.
- ❖ Inflammation of the **pancreas** and collapse of the **lungs**.
- ❖ Excessive **post-operative bleeding** (surgical).
- ❖ Post-operative **thrombocytosis** and thrombosis.

Antimicrobial  
Actions

**Respiratory  
Burst**



Antigen Presentation



**Activate adaptive  
immunity**

Antigen/Antibody  
Uptake



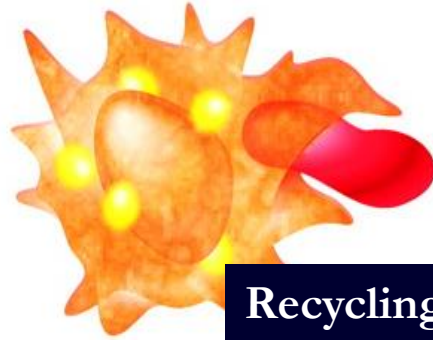
**Clearing  
immune  
complexes**

Monocyte

**Bone remodeling**

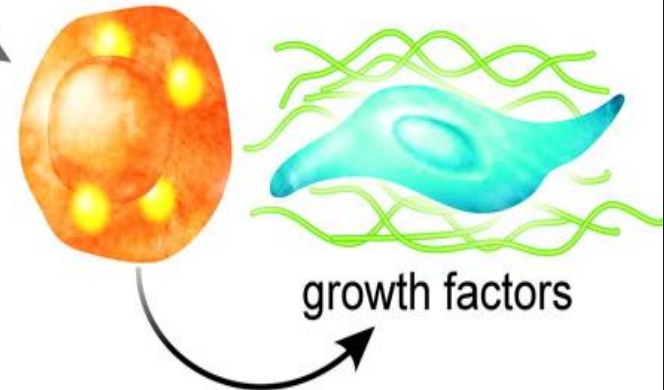


Bone Resorbtion



**Recycling RBCs**

Phagocytosis



Wound Healing

growth factors

**THANKS**

