

## #8 Reticuloendothelial system and function of the spleen



### objectives :

- Define the term Reticuloendothelial system (RES).
- Describe the cellular components of RES.
- Describe the functions of the RES.
- Define the structural function of the spleen.
- Describe the functions of the spleen.
- Understand the basic concept of the indication and risks of splenectomy.

■ Doctors' notes

■ Extra

■ Important

Revised by  
خولة العماري & هشام الغفيلي

**Resources:** 435 Boys' & Girls' slides | Guyton and Hall 12<sup>th</sup> & 13<sup>th</sup> edition

[Editing file](#)

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## ► Reticuloendothelial system (RES)

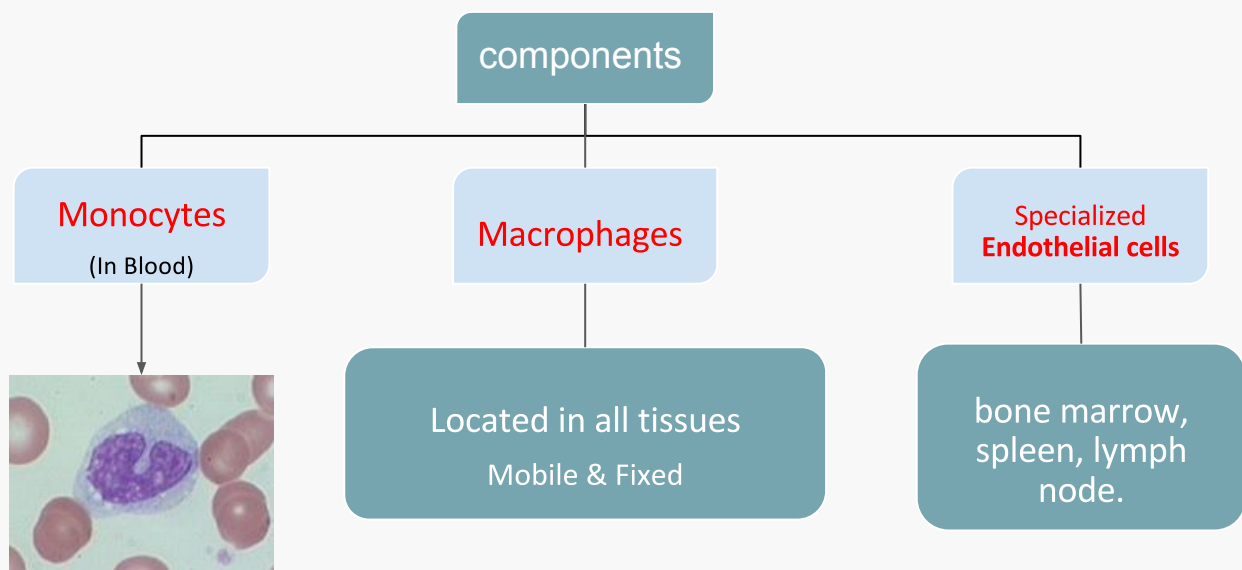
Also called : **Mononuclear phagocyte system** الاسم الجديد

### ❖ Definition:

- It's a network of connective tissue fibers inhabited by phagocytic cells such as macrophages ready to attack and ingest microbes. مراكز دفاع
- **Reticuloendothelial system (RES)** is an older term for the **mononuclear phagocyte system**, but it is used less commonly now, as it is understood that they neither have endothelial origin nor have a reticular appearance (Most endothelial cells are NOT macrophages ).
- The spleen is the largest unit of the mononuclear phagocyte system.
- RES is an **essential** component of the **immune system**.
- Monocytes transform themselves into macrophages in tissue & this system of phagocytes is called as Monocyte-Macrophage Cell System ( : تسمية دكتور شاهد حبيب )

Another definition : The aggregate of the phagocytic cells, including certain cells of the bone marrow, lymphatic system, liver, and spleen, that have reticular and endothelial characteristics and function in the immune system's defense against foreign bodies. RES is located in reticular connective tissue, which is found around the kidney, the spleen, and lymph nodes, as well as in bone marrow.

## ► Cellular components of RES



**Guyton corner :** The total combination of monocytes, mobile macrophages, fixed tissue macrophages, and a few specialized endothelial cells in the bone marrow, spleen, and lymph nodes is called the reticuloendothelial system. However, all or almost all these cells originate from monocytic stem cells; therefore, the reticuloendothelial system is almost synonymous with the monocyte-macrophage system. Because the term reticuloendothelial system is much better known in medical literature than the term monocyte-macrophage system, it should be remembered as a generalized phagocytic system located in all tissues, especially in the tissue areas where large quantities of particles, toxins, and other unwanted substances must be destroyed.

## ► Macrophages: (2-8% of total WBC)

**Function:** They **filter** and **destroy** objects which are foreign to the body, such as **bacteria**, **viruses**.

**Location:** Macrophages differ depending on the organs in which they reside, and often remain **fixed** to their organs.

Macrophages can be:  
1- Fixed in tissues (often)  
2- Mobile: to ingest large particles

**What if the foreign particle is larger ?**

Some macrophages are **mobile**, and can group together to become **one big phagocytic cell** in order to ingest larger foreign particles.

## ► Types of macrophages

Type	Tissue Histiocytes	Reticular	Microglia	Kupffer	Alveolar
Location	Fixed macrophages in subcutaneous tissues. Differentiate into langerhans	lymph nodes, bone marrow, spleen	Brain	liver	lungs

Others:

\*Hofbauer cells in Placenta.

\*Langerhans cell in Skin, mucosa and Subcutaneous tissues.

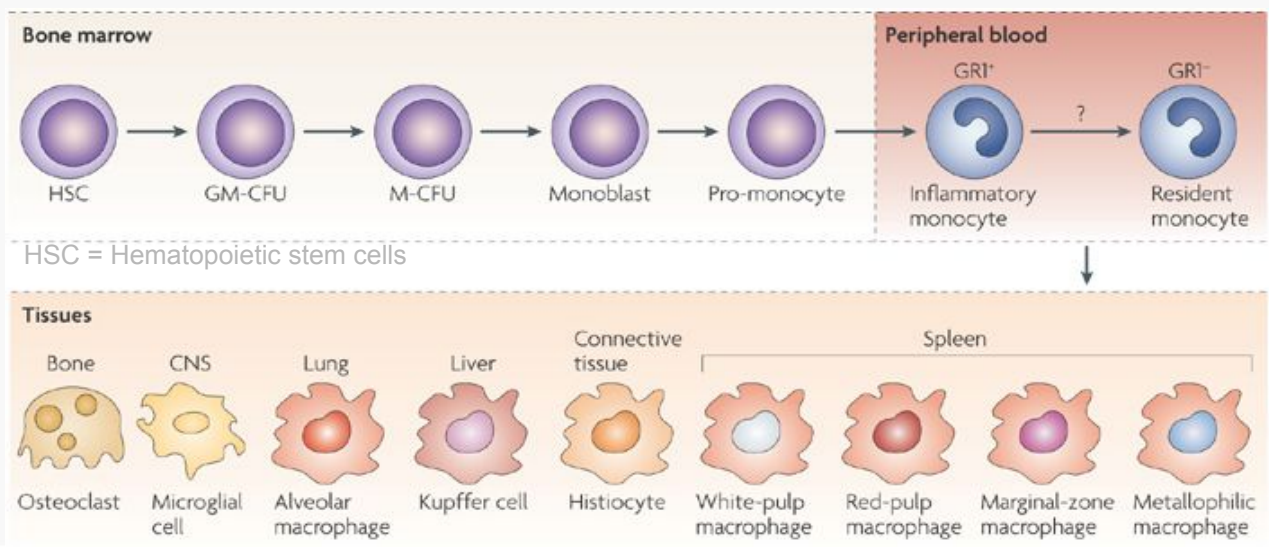
\*Osteoclasts in bone.

\*Mesangial Cells in kidneys.

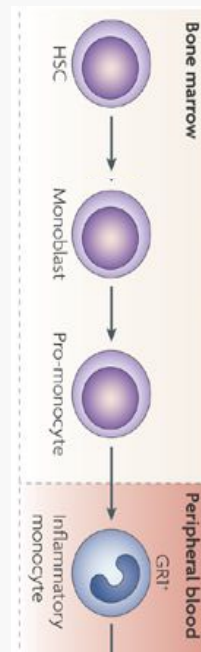
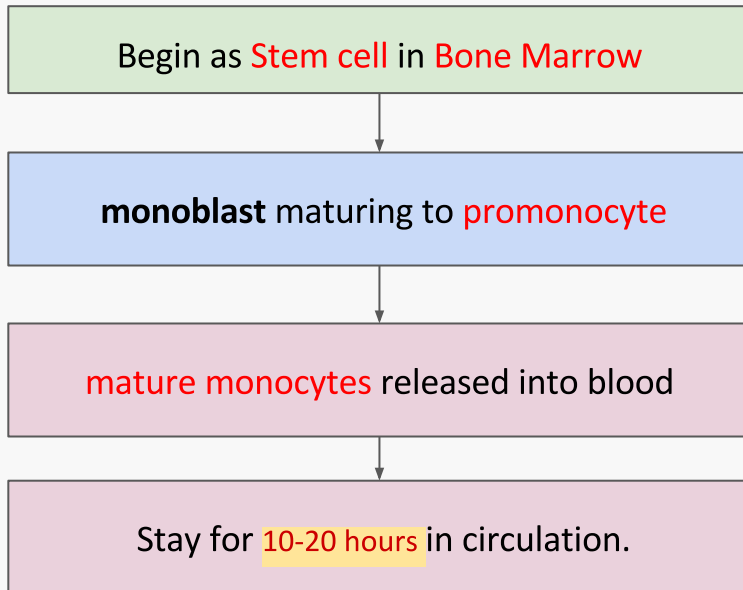
**Chemotaxis > Margination > Diapedesis > Phagocytosis**

Diapedesis: the passage of blood cells through the intact walls of the capillaries

Extra:



## ► Formation of Macrophages

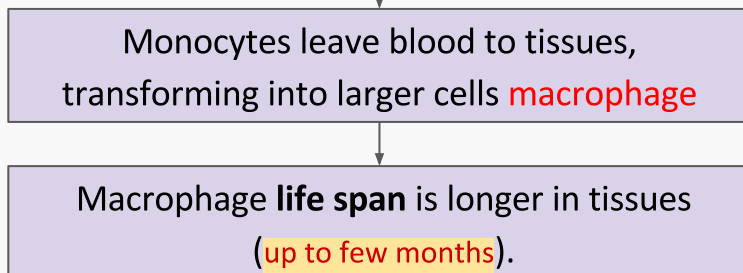


### How can monocytes transform into macrophages ?



Acting as antigen presenting cell (APC) requires an **increase** in: (to increase potency of the cell)

- 1- Cell **size**.
- 2- Number and complexity of intracellular **organelles**: **Golgi**, **mitochondria**, **lysosomes** (which Contain **Lipase** unlike Neutrophils).
- 3- Intracellular **digestive enzymes**.



**Guyton corner** :Tissue Macrophages Provide a **First Line of Defense** Against Infection.

Within minutes after inflammation begins, the macrophages already present in the tissues immediately begin their phagocytic actions. When activated by the products of infection and inflammation, the first effect is rapid enlargement of each of these cells. Next, many of the previously sessile (immobile) macrophages break loose from their attachments and become mobile, forming the first line of defense against infection during the first hour or so. The numbers of these early mobilized macrophages often are not great, but they are lifesaving.



\*Boys slides only.

## ► Neutrophils

- **Most Abundant WBCs** 60-70 %.
- **Size:** 15-20  $\mu\text{m}$ .
- **Nucleus:** Multilobed (2-5 lobes).
- **Life span:** 6-8 hours.
- While Monocyte contains **only** primary granules, Neutrophils also contain Glycogen stored in a granules for anaerobic glycolysis.
- Neutrophils work as the fastest and the most potent chemotactic properties, while the slower triggered monocytes are stronger in response to the inflammatory process.

## ► Neutrophils' granules

Primary granules	Secondary granules	Tertiary granules
<ul style="list-style-type: none"><li>● Non specific.</li><li>● Azurophilic</li><li>● Has <b>lysosomes</b> Contain:<ul style="list-style-type: none"><li>- Acid hydrolase.</li><li>- MPO (Myeloperoxidase)</li><li>- HOCl (Hypochlorite acid)</li><li>- defensins.</li></ul></li><li>● Represent 33%</li></ul>	<ul style="list-style-type: none"><li>● Specific</li><li>● Represent 67%</li><li>● Granules contain:<ul style="list-style-type: none"><li>- Lysozyme(not lysosome)</li><li>- Lactoferrine</li><li>- Alkaline Phosphatase</li><li>- Gelatinase</li><li>- Bacteriostatic and bactericidal products</li></ul></li></ul>	<ul style="list-style-type: none"><li>● help to digest tissues.</li><li>● Granules contain:<ul style="list-style-type: none"><li>- Collagenase.</li><li>- Hyaluronidase.</li><li>- Gelatinase.</li></ul></li></ul>
<ul style="list-style-type: none"><li>● All of them get activated only when needed, so in case of infection, primary granules will get activated. If it's not enough secondary granules will be activated (in acute infection) and then tertiary.</li><li>● When All mechanisms don't work then Monocytes will start to invade that area.</li></ul>		

## So what is the general functions of RES?

PMNs and APCs

### 1. Direct immune function (Phagocytosis)

- ★ **Direct**
- ★ Ingest bacteria, dead cells, foreign particles .
- ★ is part of the natural or innate immune process.
- ★ **Macrophages** are powerful phagocytic cells:
  - Ingest **up to 100** bacteria.
  - Ingest **larger particles** such as old RBC.
  - Get rid of **waste products**.
  - **Macrophages are more potent phagocytes than neutrophils**

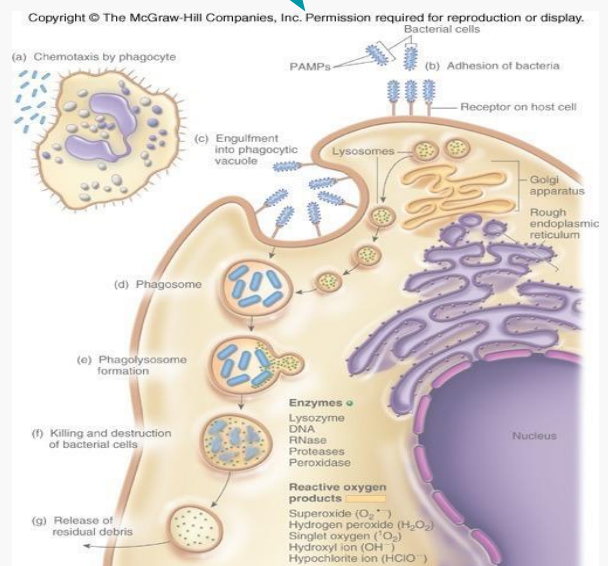
### 2. Indirect Immune function

- ★ **Indirect**
- ★ It is **processing antigen and antibodies production**
- ★ Ingest foreign body, process it and present it to **lymphocytes**.

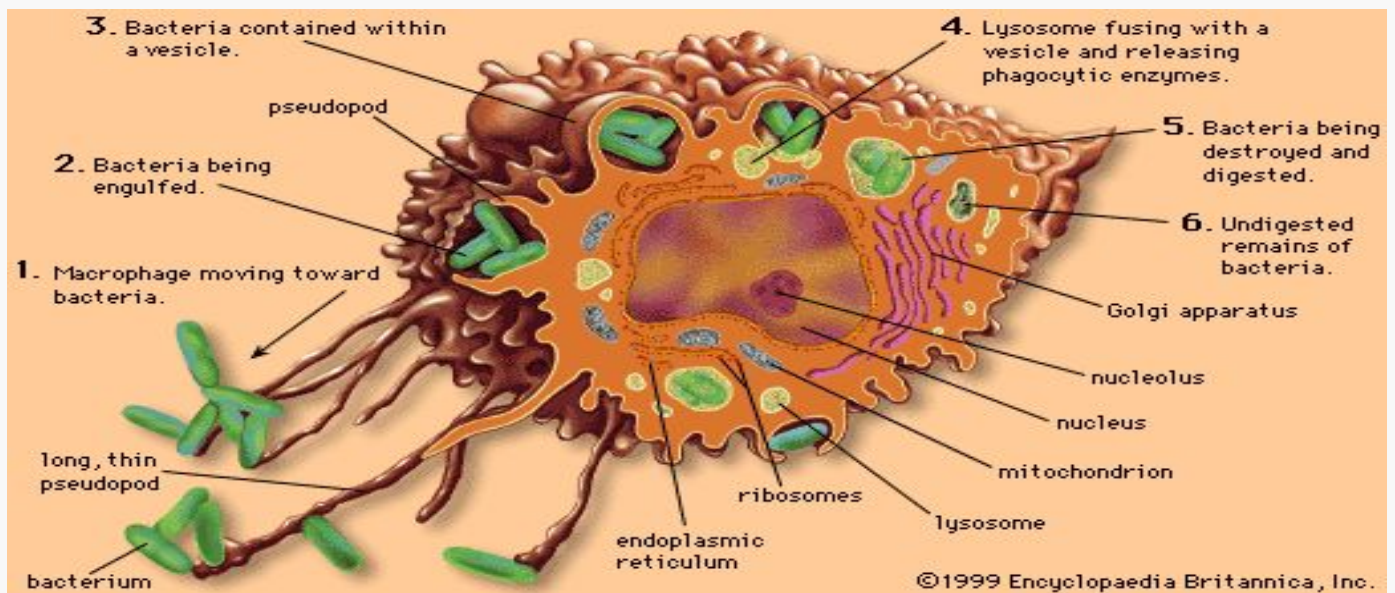
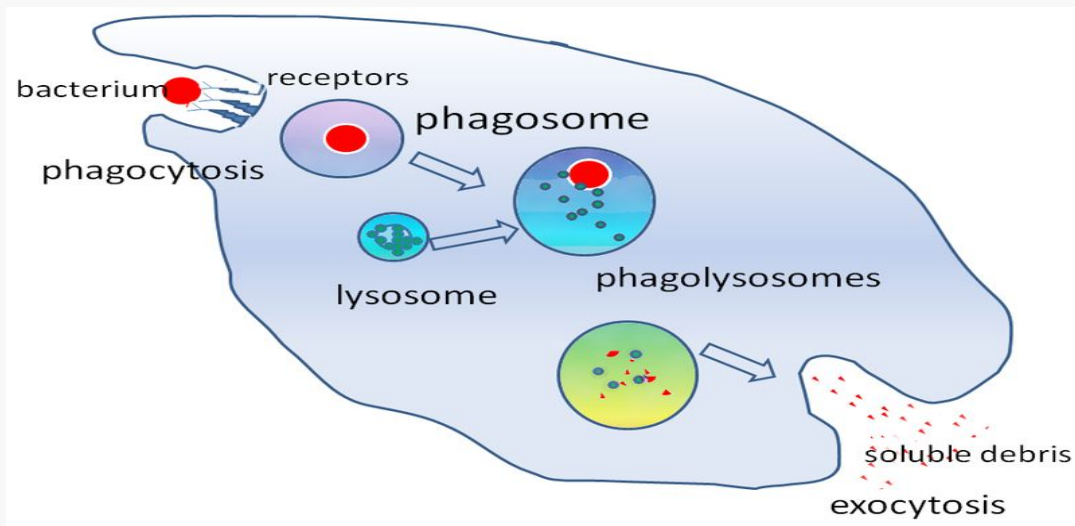
In the spleen

### Breakdown of aging RBC

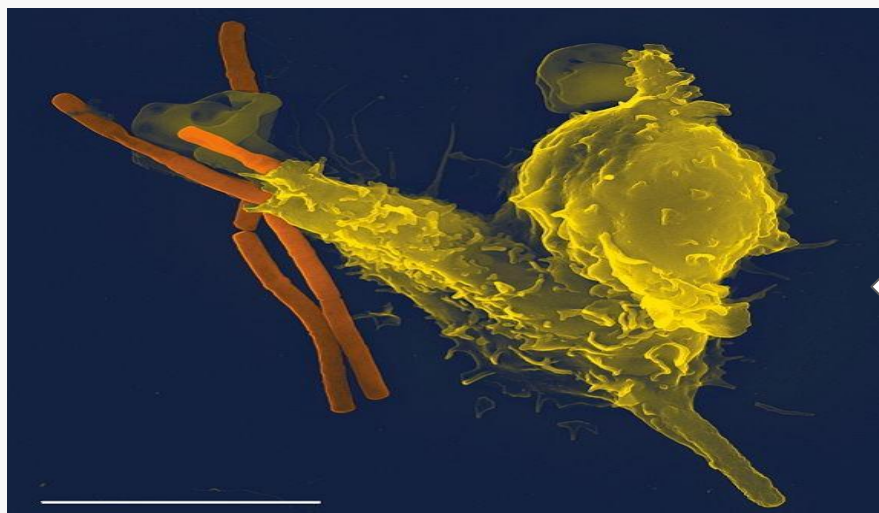
### Storage and circulation of iron



► **Direct anti-inflammatory function (phagocytosis):**

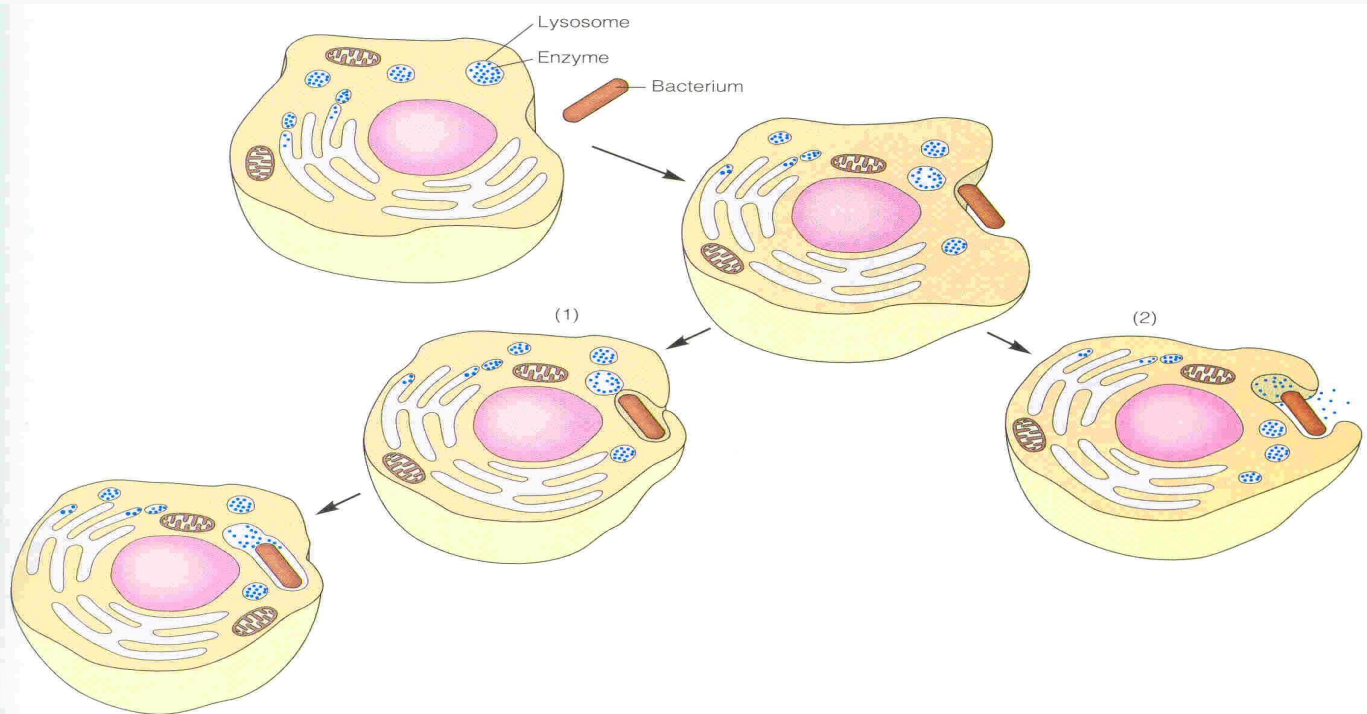


Bacteria vs. Macrophage - 3:14 min



A [scanning electron microscope](#) image of a single [neutrophil](#) (yellow) engulfing [anthrax](#) bacteria (orange)

## ► Phagocytosis (cont.)

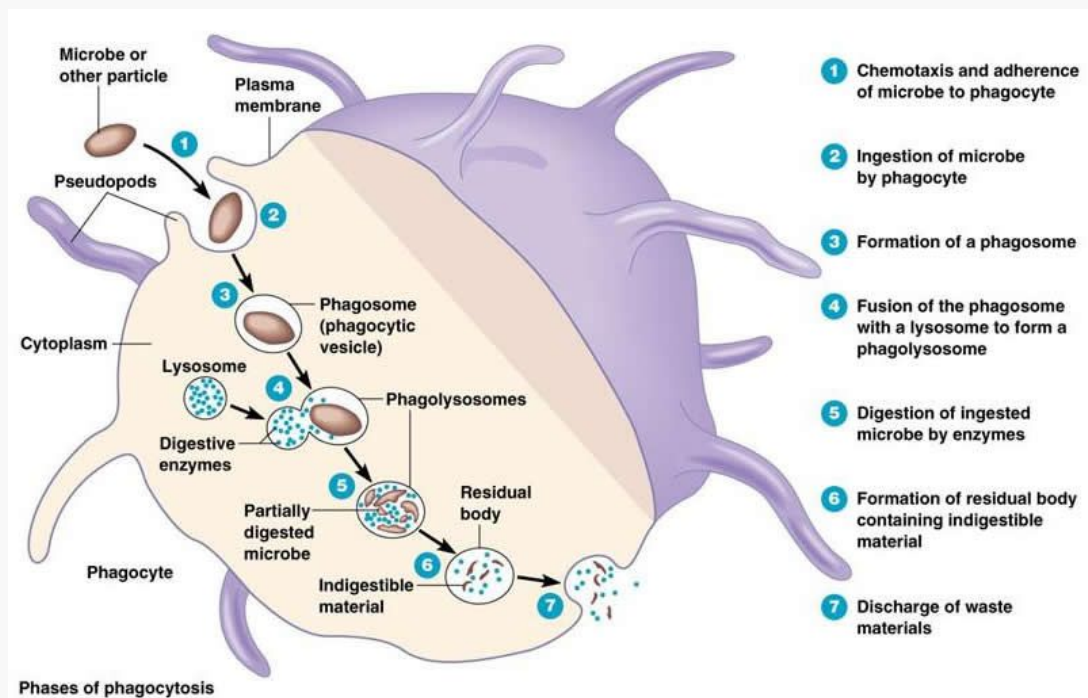


**Figure 15.2**

Phagocytosis by a neutrophil or macrophage. A phagocytic cell extends its pseudopods around the object to be engulfed (such as a bacterium). (Blue dots represent lysosomal enzymes.) (1) If the pseudopods fuse to form a complete food vacuole, lysosomal enzymes are restricted to the organelle formed by the lysosome and food vacuole. (2) If the lysosome fuses with the vacuole before fusion of the pseudopods is complete, lysosomal enzymes are released into the infected area of tissue.

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## ► Microbial killing





Just read them to insure that you understand all of the phagocytic function

### ► Direct phagocytic function of RES (explanation)

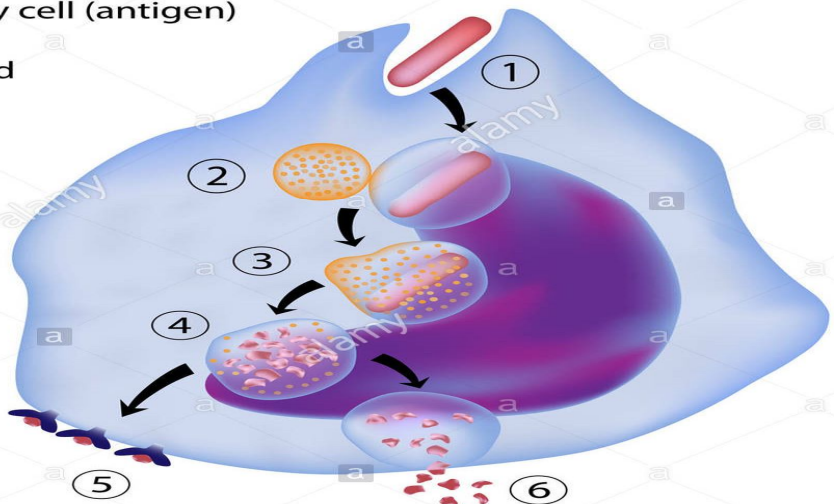
1. Macrophage moves toward the pathogen which will be engulfed in a phagosome.
2. The lysosome will bind to the phagosome and release its substances.
3. Now it becomes a phagolysosome which will digest the pathogen.
4. The residual part of the digested pathogen will be released out of the cell by exocytosis.
5. The residual part contains indigestible material which will be cleared from the tissue gradually through the blood circulation.

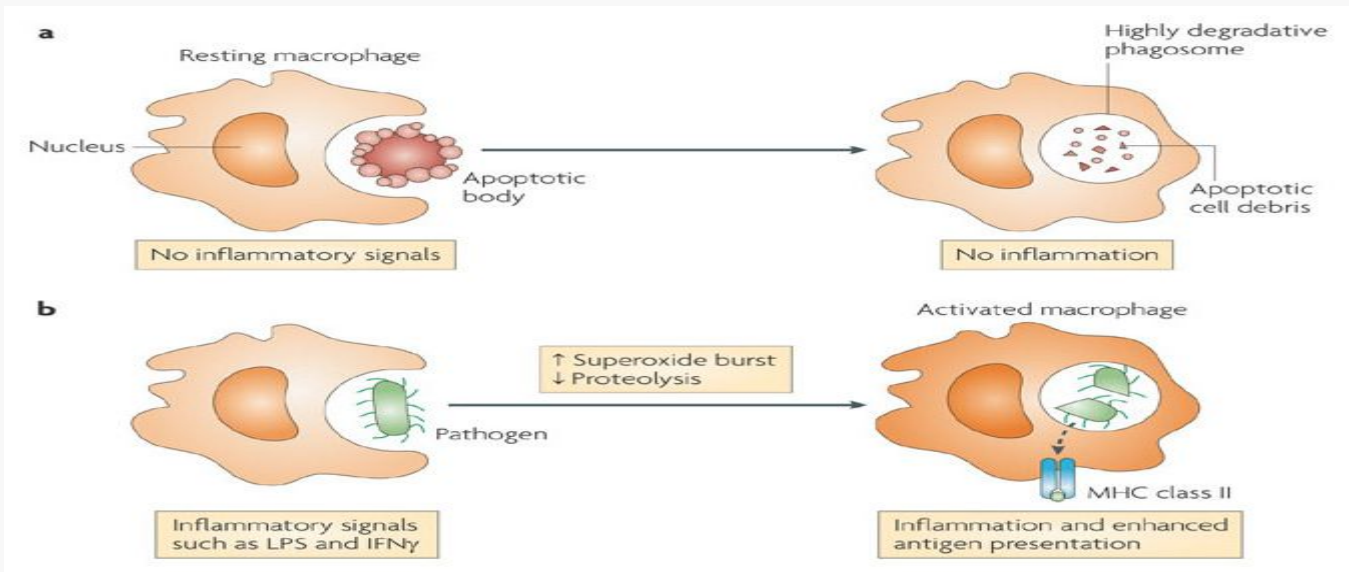
### ► Indirect phagocytic function of RES

- Same as the further steps in (Direct function) .
- But here after it get digested(pathogen), a copy of the protein structure of antigen is taken and exposure on the surface of the cell and this is what we call it **Antigen presenting cell (APC)** .
- This is expressed by MHC class II.

## Role of an Antigen-Presenting Cell

- ① Phagocytosis of enemy cell (antigen)
- ② Fusion of lysosome and phagosome
- ③ Enzymes start to degrade enemy cell
- ④ Enemy cell broken into small fragments
- ⑤ Fragments of antigen presented on APC surface
- ⑥ Leftover fragments released by exocytosis



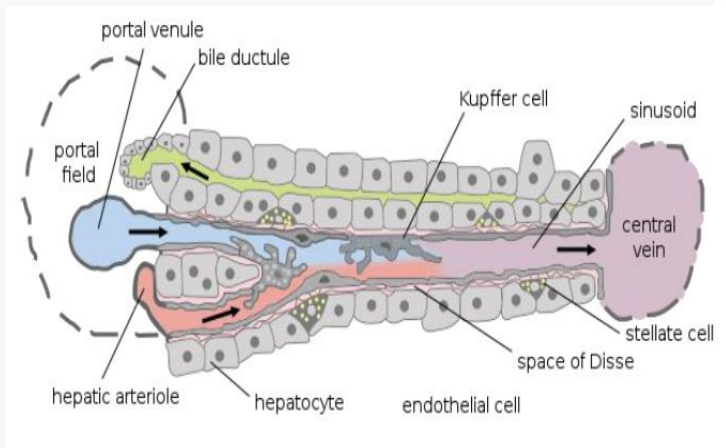


Here guys i want to tell you that phagocytosis is either due to inflammatory response or apoptotic bodies that get ingested from macrophage and degraded to be cleared from the body

## ► Reticuloendothelial System Monocytes/Macrophage System in different tissues.

### 1. Tissue macrophages in Liver sinuses.

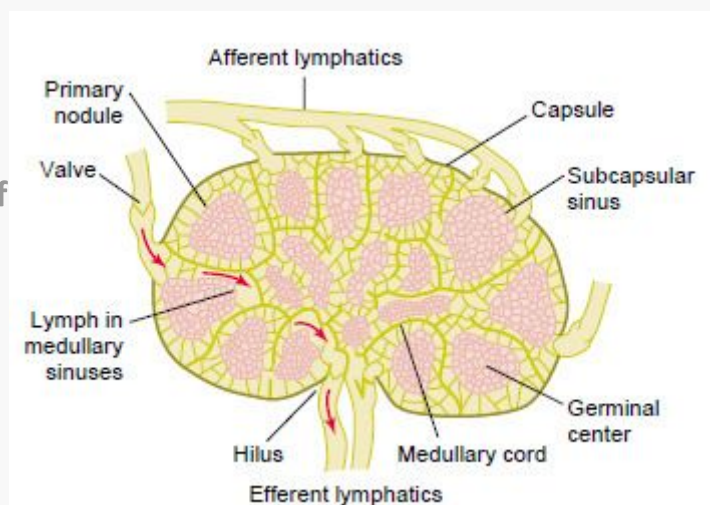
Sinusoid is covered by endothelium and the **Kupffer cells** between them. They are facing and protect the hepatocyte from anything that comes from the circulation (Portal = GIT)



### 2. Tissue macrophages in Lymph Nodes.

Lymph node is the primary site for storage and activation of lymphocyte. Germinal centers are the site of generating lymphocyte. At every step of the lymph node there are gates for macrophages:

1. subcapsular sinus macrophages.
2. medullary sinus macrophages.
3. medullary cord macrophages.

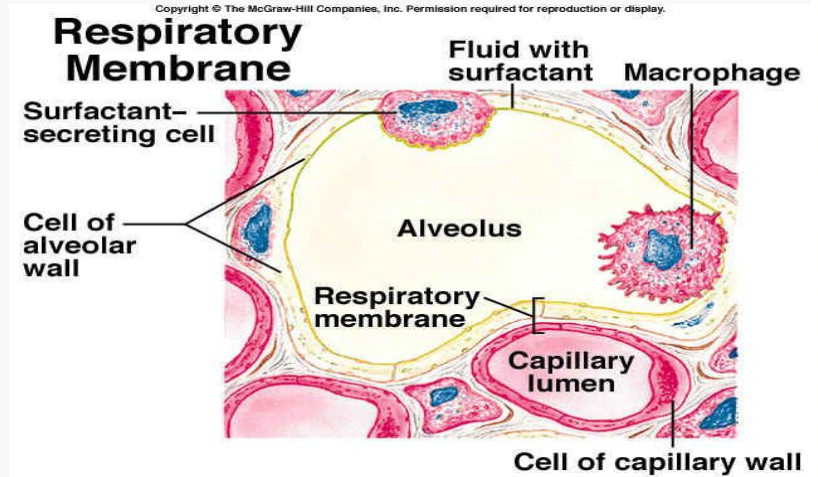




### 3. Tissue macrophages in Lungs

Here there is two important type of cells: type one cell secrete surfactant.

**Type two cell: it is the macrophage of the alveoli and Also they called “dust cells”** because of their content of intracellular carbon particles.



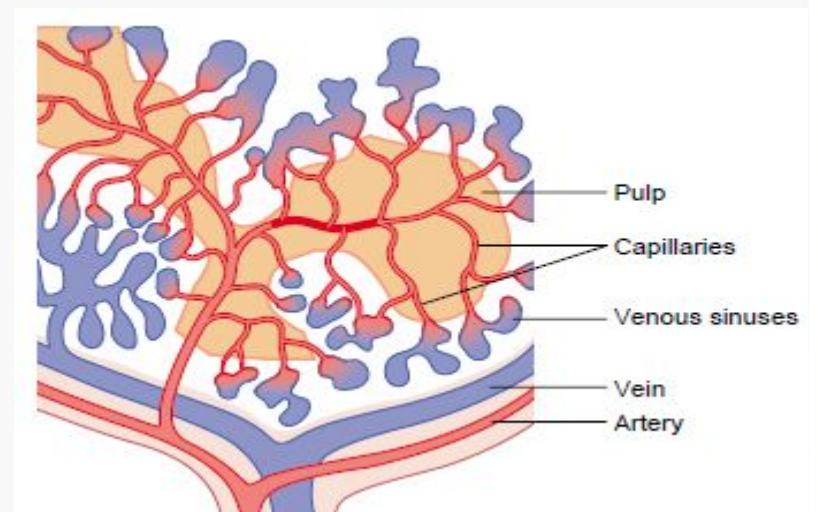
### 4. Tissue macrophages in Spleen

Here we have two part of the spleen :

1.white pulp that contain lymphoid part.

2.red pulp that surround white pulp by its venous sinuses.

\*so the blood that come from the red pulp drained into these venous sinuses all of this system called reticular connective tissue.



\*so if there is an old RBCs Or a bacteria or abnormal RBCs , they ruptured in the spleen.

\*the red pulp cords are lined by macrophages also which called splenic macrophages .

In case of abnormal production of RBCs there will be a splenomegaly because the RBCs are going to die there. So in this case we can't do anything to the genesis of the blood because it is hereditary but we can do splenectomy to decrease the the destruction of platelet and RBCs

# Lymphoid Organs

## Thymus:

It has a high rate of growth and activity **until puberty**, then begins to shrink.

The Thymus is the site of T-cell maturation.

T-cells (Thymus dependent cells)

## Lymph nodes:

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

## Spleen:

structurally similar to lymph node

which is why it is okay to do splenectomies as LN can compensate

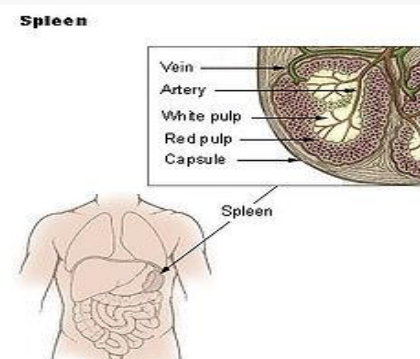
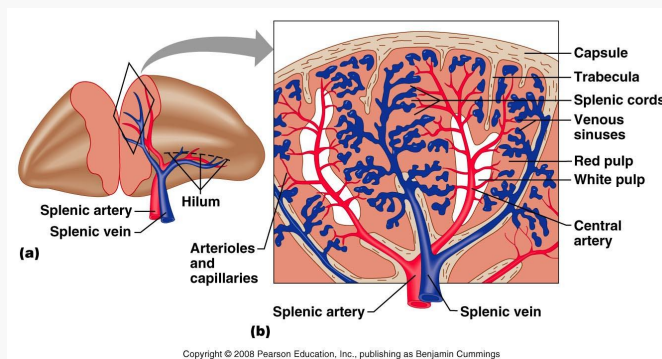
It filters circulating blood to remove worn out RBCs and pathogens.

Will be explained further in this lecture.

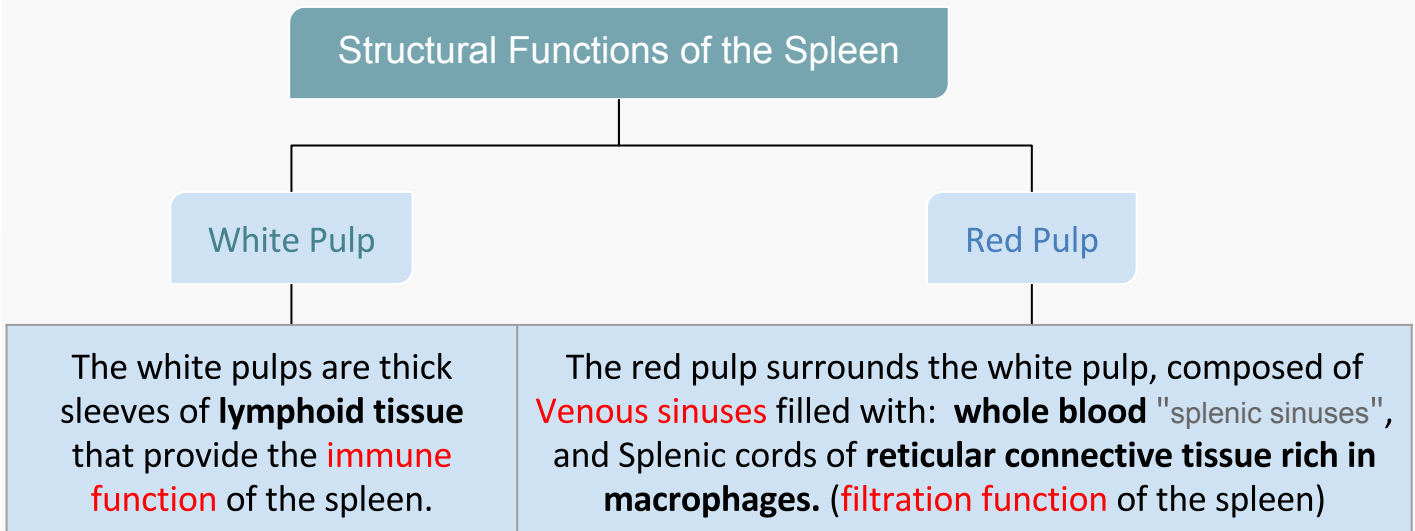
## ► Spleen

### ❖ Main Characteristics:

- It is soft, purple gray in color, and located in the **left upper quadrant** of the abdomen.
- It is a **highly vascular** lymphoid organ.
- It plays an important role in **red blood cells** integrity and has **immune function**.
- It holds a **reserve** of blood in case of **hemorrhagic shock**. It will release its **reserved 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**. Like pneumococci, give vaccine in case of splenectomy.
- Despite its importance, there are **no tests** specific to splenic function. **CBC** is done to assess splenic function, but it's not specific.



## ❖ Structural Functions of the Spleen:



### Immune Functions of the Spleen:

<ol style="list-style-type: none"> <li>1. <b>Reservoir of lymphocytes.</b></li> <li>2. Site of <b>B cell maturation</b> into plasma cells, which synthesize antibodies (mainly IgM) and initiate <b>humoral response</b>.</li> </ol>	<ol style="list-style-type: none"> <li>1. Site for <b>Phagocytosis</b> of bacteria and worn-out blood cells (<b>Slow blood flow</b> in the red pulp cords allows foreign particles to be phagocytosed)</li> <li>2. It contains (in its blood reserve within the red pulp) half of the body <b>monocytes</b>, upon moving to injured tissue (such as the heart), turn into <b>dendritic cells</b> and <b>macrophages</b> that promote <b>tissue healing</b>.</li> </ol>
<ol style="list-style-type: none"> <li>1. <b>Destruction and processing</b> of antigens (<b>mainly by White pulp</b>): Because the organ is <b>directly connected to blood circulation</b>, it responds faster than other lymph nodes to <b>blood-borne antigens</b>.</li> <li>2. Removes antibody-coated bacteria (encapsulated e.g. <i>S.pneumoniae</i>) (<b>mainly by white pulp</b>), along with <b>antibody-coated blood cells</b>.</li> </ol>	

### General Functions of the Spleen:

<ol style="list-style-type: none"> <li>1. <b>Haematopoiesis (Hemopoiesis)</b>: fetal life <sup>(1)</sup></li> <li>2. Spleen is a main site for <b>destruction of RBCs, lymphocytes and thrombocytes</b> specially old and abnormal e.g. spherocytosis. <sup>(2)</sup></li> <li>3. Blood is <b>filtered</b> through the spleen.</li> <li>4. <b>Reservoir of thrombocytes</b> and immature erythrocytes. (released during emergency)</li> <li>5. Recycles <b>iron</b>. <b>Stores and reuses iron</b></li> </ol>
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(1) While the bone marrow is the primary site of hematopoiesis in the adult, the spleen has important hematopoietic functions up until the fifth month of gestation. After birth, erythropoietic functions cease, except in some hematologic disorders. As a major lymphoid organ and a central player in the reticuloendothelial system, the spleen retains the ability to produce lymphocytes and, as such, remains a hematopoietic organ.

(2) Spherocytes are sphere-shaped RBCs rather than bi-concave disk shaped. Found in all hemolytic anemias to some degree.

**Guyton corner : THE SPLEEN AS A RESERVOIR FOR STORING RED BLOOD CELLS**

The spleen has two separate areas for storing blood: the venous sinuses and the pulp.

The sinuses can swell the same as any other part of the venous system and store whole blood.

In the splenic pulp, the capillaries are so permeable that whole blood, including the red blood cells, oozes through the capillary walls into a trabecular mesh, forming the red pulp. The red cells are trapped by the trabeculae, while the plasma flows on into the venous sinuses and then into the general circulation. As a consequence, the red pulp of the spleen is a special reservoir that contains large quantities of concentrated red blood cells. These concentrated red blood cells can then be expelled into the general circulation whenever the sympathetic nervous system becomes excited and causes the spleen and its vessels to contract. As much as 50 milliliters of concentrated red blood cells can be released into the circulation, raising the hematocrit 1 to 2 percent.

In other areas of the splenic pulp are islands of white blood cells, which collectively are called the white pulp. Here lymphoid cells are manufactured that are similar to those manufactured in the lymph nodes. They are part of the body's immune system.

**Guyton corner : Blood-Cleansing Function of the Spleen — Removal of Old Cells**

Blood cells passing through the splenic pulp before entering the sinuses undergo thorough squeezing. Therefore, it is to be expected that fragile red blood cells would not withstand the trauma. For this reason, many of the red blood cells destroyed in the body have their final demise in the spleen. After the cells rupture, the released hemoglobin and the cell stroma are digested by the reticuloendothelial cells of the spleen, and the products of digestion are mainly reused by the body as nutrients, often for making new blood cells.

## ► 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<sup>(1)</sup> .
4. Idiopathic thrombocytopenic purpura (**ITP**)<sup>(2)</sup>. To prevent continuous breakdown of platelets.
5. **Trauma**. Which cause spleen rupture. (the most common indication for splenectomy)
6. Hodgkin's disease. Because it's lymphoid tissue and hodgkin's lymphoma is a malignancy of the lymph nodes.
7. Autoimmune hemolytic disorders. To protect against continuous hemolysis

### ❖ Risks and Complications:

1. Overwhelming **bacterial infection** or postsplenectomy **sepsis**.
2. Patient prone to **malaria**.
3. Inflammation of the **pancreas** and collapse of the **lungs**.
4. Excessive postoperative **bleeding** (surgical).
5. Postoperative **thrombocytosis** and **thrombosis**. Because of removal of platelet reservoir. ( count is around 700,000 ! )

(1) Hereditary elliptocytosis, also known as ovalocytosis, is an inherited blood disorder in which an abnormally large number of the patient's RBCs are elliptical rather than the typical biconcave disc shape

(2) Idiopathic thrombocytopenic purpura (ITP) is a disorder that can lead to easy or excessive bruising and bleeding. The bleeding results from unusually low levels of platelets. Splenectomy is typically performed only after other treatments have failed to reduce the symptoms.

- There are two diseases for which a splenectomy is the only treatment—primary cancers of the spleen and a blood disorder called hereditary spherocytosis (HS). [Read more](#)

## Summary

<ul style="list-style-type: none"><li>● RES: It's a network of connective tissue fibers inhabited by phagocytic cells such as macrophages ready to attack and ingest microbes.</li></ul>
<ul style="list-style-type: none"><li>● <b>Composed of 3 component:</b> monocyte, macrophages &amp; specialized endothelial cell.</li></ul>
<ul style="list-style-type: none"><li>● Have 4 main function: immune (direct &amp; indirect), destruction of old RBC, storage of iron.</li></ul>
<ul style="list-style-type: none"><li>● monocyte formed by stem cell in bone marrow</li></ul>
<ul style="list-style-type: none"><li>● Monocyte stay at the circulation for 10-20 hours compare to macrophages which stay in the tissue up to several months.</li></ul>
<ul style="list-style-type: none"><li>● Monocyte contain the enzyme Lipase unlike neutrophils.</li></ul>
<ul style="list-style-type: none"><li>● Spleen is located at the left hypochondrium</li></ul>
<ul style="list-style-type: none"><li>● It reserve blood in case of emergency e.g. hemorrhagic shock</li></ul>
<ul style="list-style-type: none"><li>● Its absence will lead to predisposition for certain infection</li></ul>
<ul style="list-style-type: none"><li>● There is no test to measure the function of the spleen.</li></ul>
<ul style="list-style-type: none"><li>● Spleen is composed of 2 main structural function:     White pulp: immune function     Red pulp: filtration function</li></ul>
<ul style="list-style-type: none"><li>● Splenectomy has a great be considered unless it's necessary</li></ul>

# Summary

## General Function Of RES

Direct immune function	Indirect immune function	Storage	Breakdown
Ingest bacteria, dead cells, foreign particles .	processing <b>antigen and antibodies production</b>	For circulating Iron	For <b>aging RBCs</b>
is part of the <b>natural or innate immune</b> process.	Ingest foreign body, process it and present it to lymphocytes.		Platelets

### Neutrophils

- **Most Abundant WBCs** 60-70 %.
- **Life span: 6-8 hours.**
- Monocyte contains **only** primary granules.

### Neutrophil granules

Primary granules	Secondary granules	Tertiary granules
<ul style="list-style-type: none"> <li>• <b>Non specific.</b></li> <li>• Has <b>lysosomes.</b></li> <li>• Represent <b>33%</b></li> </ul>	<ul style="list-style-type: none"> <li>• Specific</li> <li>• Represent <b>67%</b></li> <li>• <b>Lysozyme</b></li> </ul>	<ul style="list-style-type: none"> <li>• help to digest tissue.</li> </ul>

## Types of macrophages

Kupffer	Reticular	Macrogelia	Alveolar	Mesangial
Liver	lymph nodes spleen	Brain	Lung	Kidney
<b>Histiocyte</b>	Langerhans cell	Osteoclast	Hofbauer	
subcutaneous tissues	Skin	Bone	Placenta	



# MCQs

**1-Which of the following is Agranulocyte:**

- A- Eosinophil
- B- Neutrophil
- C- T- lymphocyte
- D- Basophil

**2-In thymus:**

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

**3-Macrophages in the liver called:**

- A- Kupffer
- B- Histiocytic
- C- Stellate
- D- Reticular

**4-which of the following is function of spleen:**

- A- Destruction and processing of antigens
- B- Reservoir of lymphocytes
- C- B cell maturation
- D- All of them

**5-Which of the following structures primarily can hold a reserve of blood in case of hemorrhagic shock:**

- A- Liver
- B- Spleen
- C- Pancreas
- D- Thymus

**6-Which of the following is lymphoid organ :**

- A- Thymus
- B- Spleen
- C- Lymph node
- D- All of them

**7-Macrophage participate in which of the type of immunity :**

- A- Natural
- B- Adaptive
- C- A&b
- D- None of them

**8-Monocyte life span :**

- A- 10-20 min
- B- 10-20 h
- C- 10-20 day
- D- Months

**9-Macrophages can ingest bacteria up to:**

- A- 10
- B- 100
- C- 1000
- D- 10000

عمر آل سليمان  
عبدالعزیز الحماد  
عبدالرحمن السیاری  
محمد أبونیان  
عبدالرحمن البركه  
إبراهیم النفیسه  
محمد البشر  
عمر العتیبي  
حمزة الفعر  
عبدالله الجعفر  
عبدالله الضحیان  
حسن البلادي  
حسن الشماسي  
محمد الفواز  
محمد السحیبانی  
وائل العود  
رواف الرواف  
عمر الشهري

خولة العمّاري  
نجدود الحیدري  
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لولوة الصغیر  
لجین السواط  
رزان السبتي  
ربی السليمي  
ديما الفارس  
خولة العريني  
ملاك الشریف  
منيرة الحسيني  
مروج الحربي  
أفنان المالكي  
دلال الحزيمي  
رناد القحطاني  
سارة الخليفة  
فرح مندوزا  
مي العقيل  
نورة الخراز  
سارة الخليفة  
نورة الخيال  
رغد النفیسة  
منيرة السلولي  
نوف العبدالكريم  
سها العنزي  
نورة القحطاني

