RETICULOENDOTHELIAL SYSTEM AND FUNCTION OF THE SPLEEN

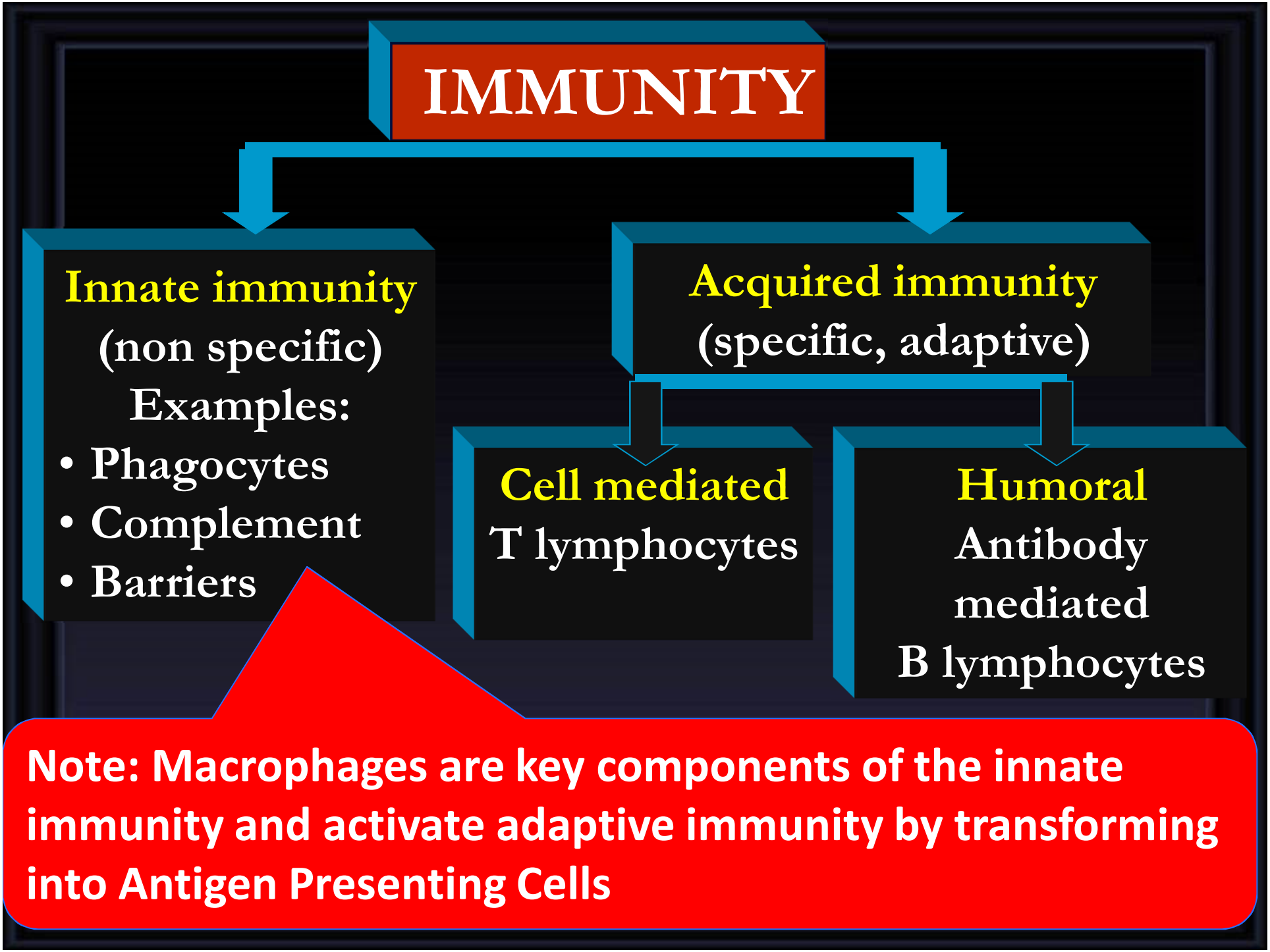
Nonspecific Host Defenses

DR SYED SHAHID HABIB
MBBS DSDM PGDCR FCPS
Professor
Dept. of Physiology
College of Medicine & KKUH

OBJECTIVES

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

- Classify immune systems
- Describe Monocyte macrophage system
- Functions of monocytes/macrophages in different tissues
- Mechanism of chemotaxis, phagocytosis and microbial killing
- Know the feedback control of macrophages & neutrophils and Pus formation
- Explain functions of spleen


IMMUNITY
Innate immunity
(non specific)
Examples:
• Phagocytes
• 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

BARRIERS

(Chemical barriers)

- Sweat
- Tears
- Saliva

Trachea / Cilia
(Physical barrier)

Skin
(Physical barrier)

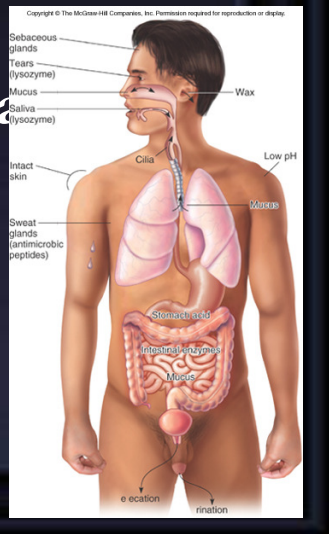
Stomach acid
(Chemical barrier)

Physical or Anatomical Barriers:

First Line of Defense

Skin and mucous membranes of respiratory, urogenital, eyes and digestive tracts;

- outermost layer of **skin** is composed of epithelial cells compacted, cemented together and impregnated with keratin; few pathogens can penetrate if intact
- flushing effect of **sweat glands**
- damaged cells are rapidly **replaced**
- **mucous coat** impedes attachment & entry of bacteria
- blinking and **tear** production
- stomach **acid**
- **nasal hair** traps larger particles



Nonspecific Chemical Defenses

- Sebaceous secretions
- Lysozyme, an enzyme that hydrolyzes the cell wall of bacteria, in tears
- High lactic acid and electrolyte concentration in sweat
- Skin's acidic pH
- Hydrochloric acid in stomach
- Digestive juices and bile of intestines
- Semen contains antimicrobial chemical.
- Vagina has acidic pH.

RETICULOENDOTHELIAL SYSTEM

- Monocytes transform themselves into macrophages in tissue these macrophages are mononuclear cells, & this system of phagocytes is called as **Monocye-Macrophage Cell System**
- This system of cells was known as reticuloendothelial system although neither they are reticular in appearance nor they have endothelial origin
- Therefore, the term reticuloendothelial system is obsolete.

Reticuloendothelial System
Monocyte/Macrophage System

TISSUE MACROPHAGE SYSTEM

- Monocytes
- Mobile macrophages
- Fixed tissue macrophages
- Specialized endothelial cells in bone marrow, spleen and lymph nodes

WBC TYPES (CLASSIFICATION)

- **Granulocytes**
  - Polymorphonuclear leukocytes (PMNs)
  - Neutrophils
  - Eosinophils
  - Basophils
- **Agranulocytes**
  - Lymphocytes
    - T lymphocyte
    - B lymphocyte
  - Monocytes → macrophage system

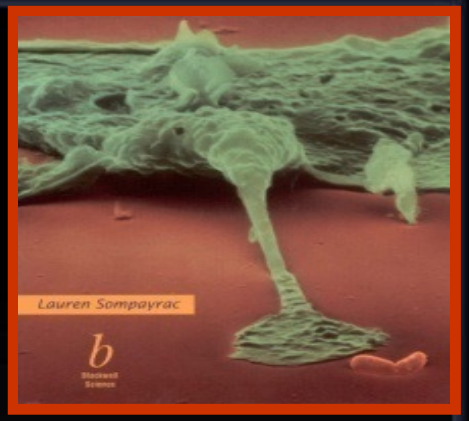
Concentration (Normal Counts)

Cells	Approximate Normal range (/µL)	Percentage of Total WBC	Life Span
Total WBC	4000-11000	- - -	
Granulocytes •Neutrophils • Eosinophils • Basophils	3000-6000 150-300 0-100	50-70 1-4 0.4	4-8 hours in blood and 4-5 days in tissues
Lymphocytes	1500-4000	20-40	Weeks-months
Monocytes (macrophages)	300-600	2-8	10-20 hours (months)

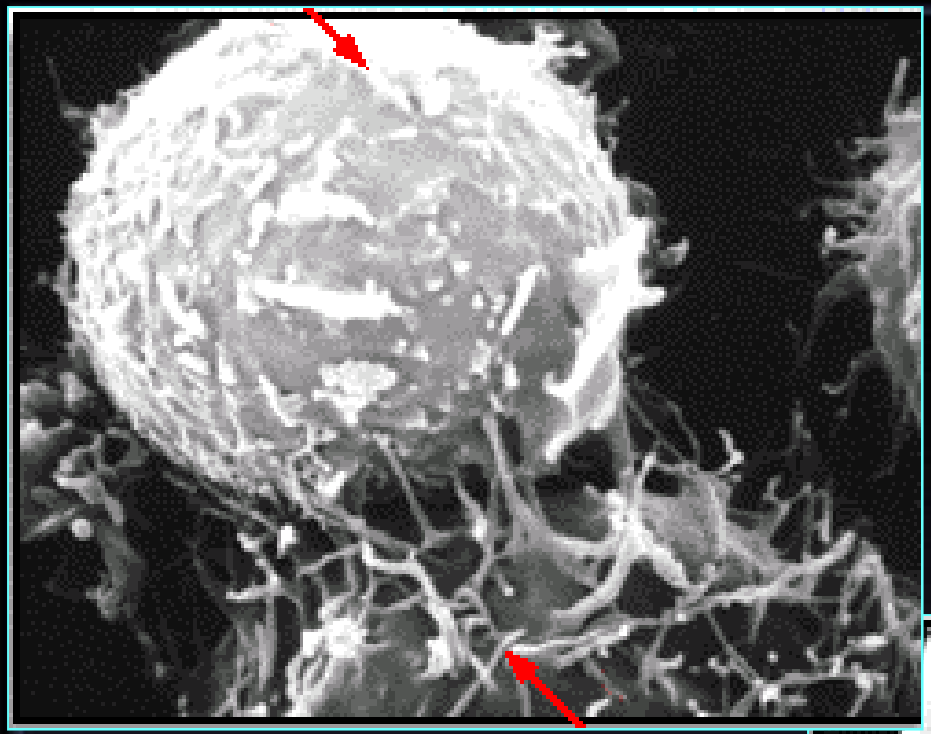
Macrophage and Neutrophil Responses During Inflammation

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

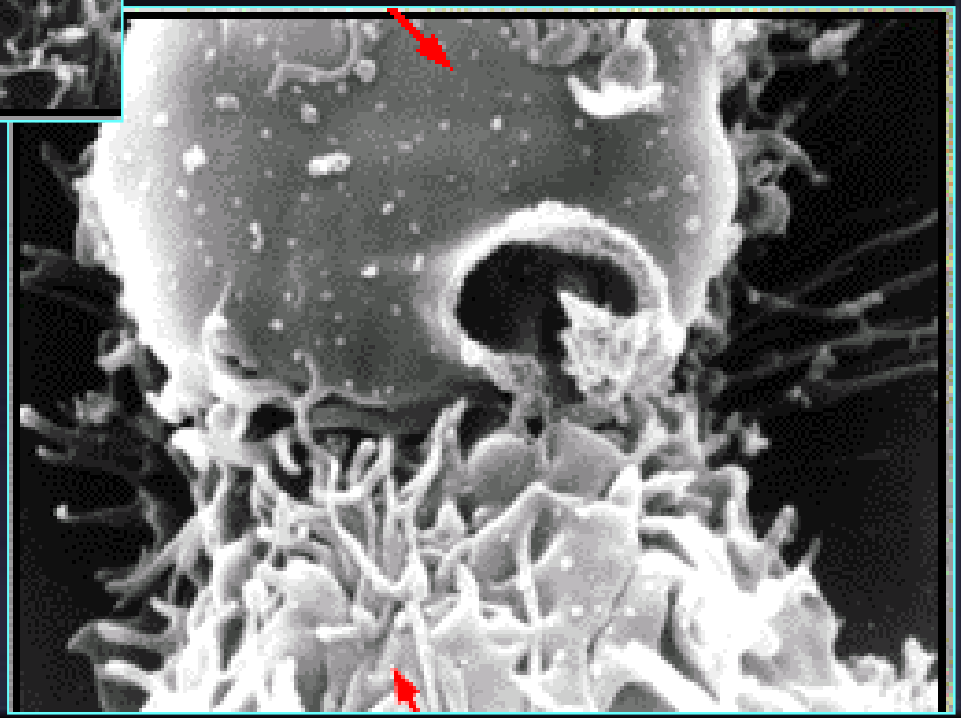
MONOCYTES



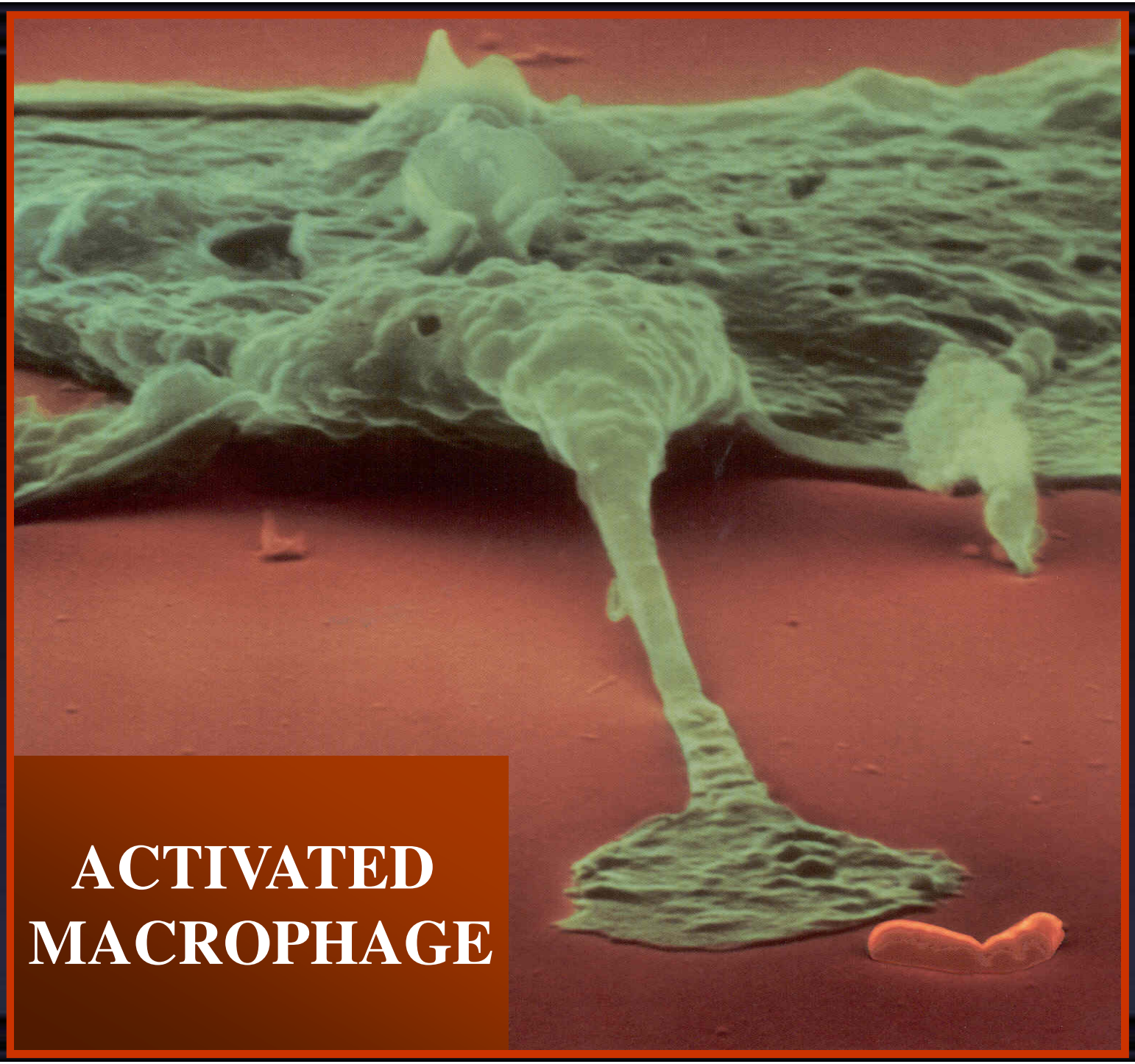
- No Granules but Vacoules
- Size: 15-20 μm (active cells 60-80 μm)
- More Efficient than Neutrophils (100 bacteria vs 3-20 by Neutr, larger particles like RBCs & malarial parasites)
- Life span: 10-20 hours in blood
- Two types: Mobile & Fixed
- Lysosomes contain lipases unlike Neut.



RESTING MACROPHAGE



ACTIVATED MACROPHAGE

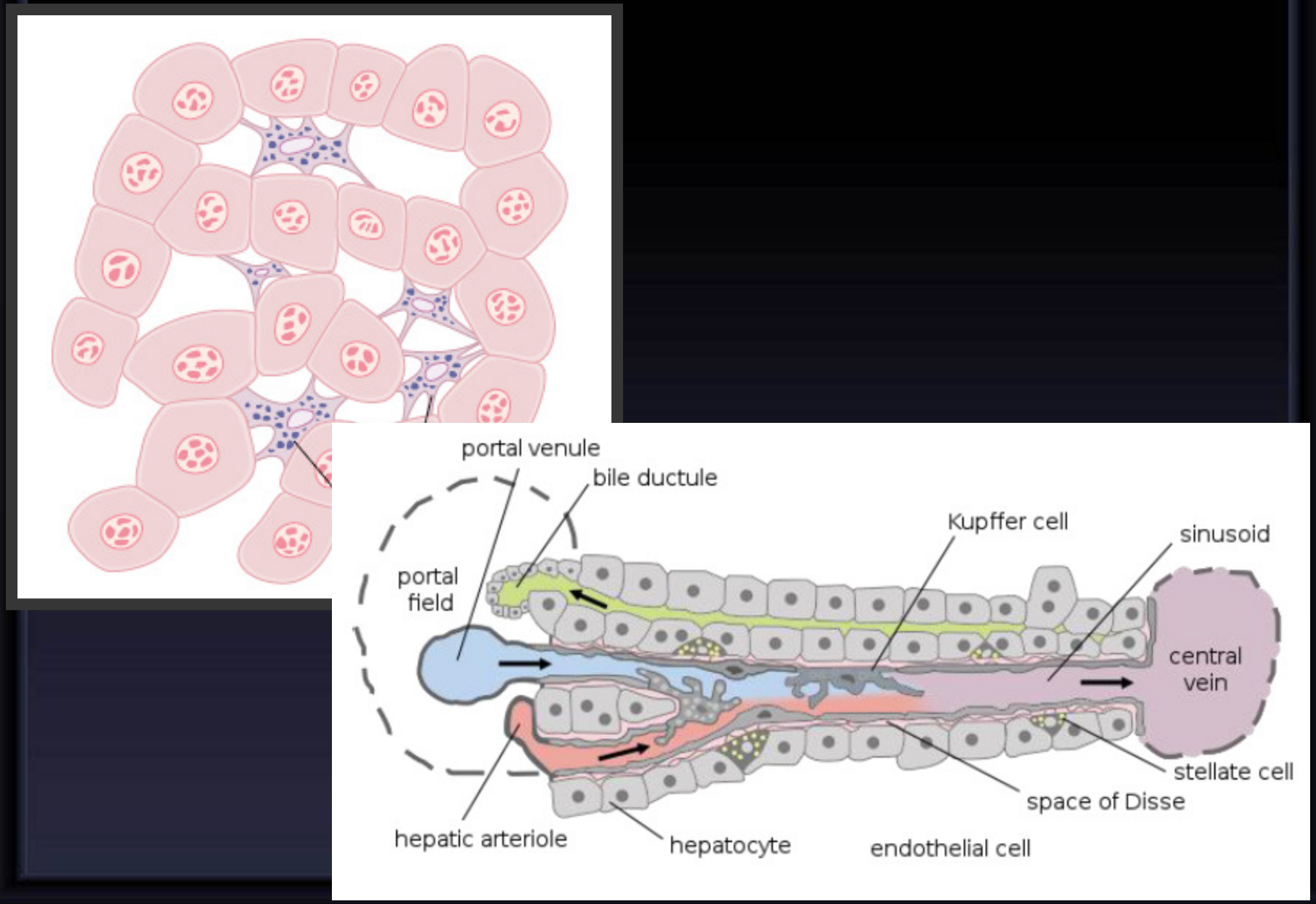

ACTIVATED
MACROPHAGE

Reticuloendothelial System
Monocytes/Macrophage System

Examples are: -

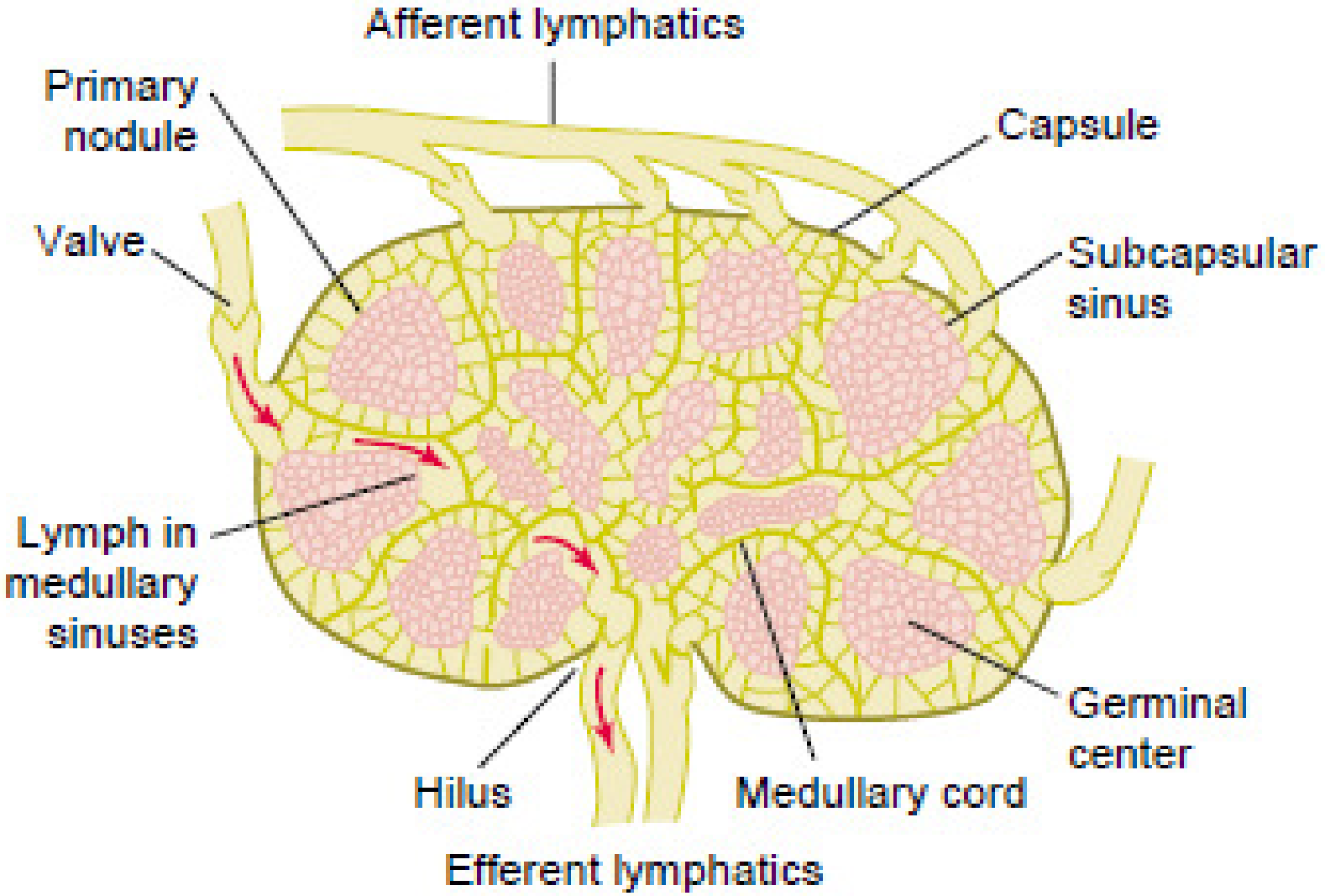
1. Skin and Subc tissues (Histiocytes)
2. Lymph Nodes
3. Alveolar macrophages
4. Liver sinuses (Kupffer Cells)
5. Spleen & Bone marrow
6. Microglia in Brain

Tissue macrophages in Liver sinuses



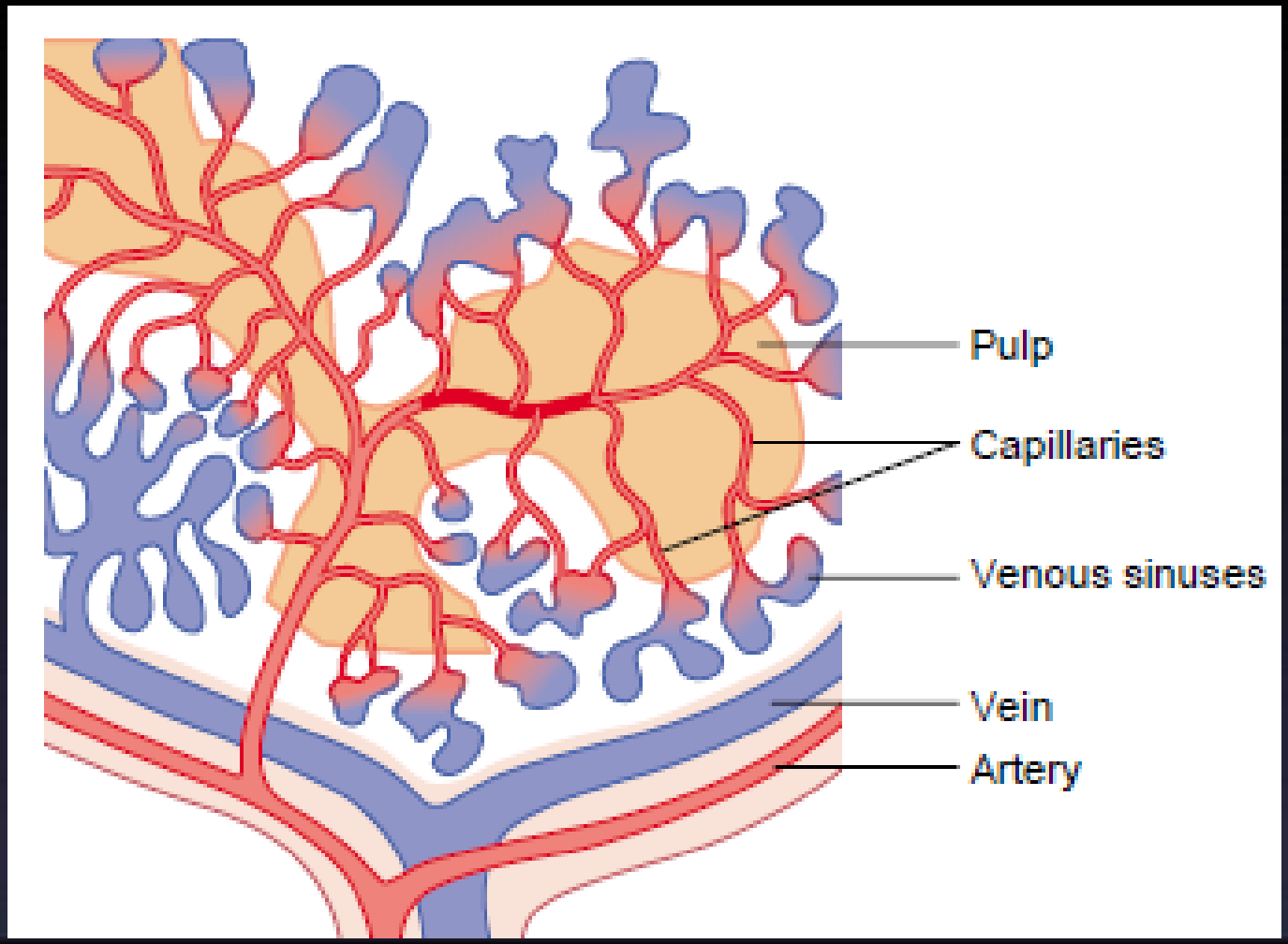
Tissue macrophages in Lymph Nodes

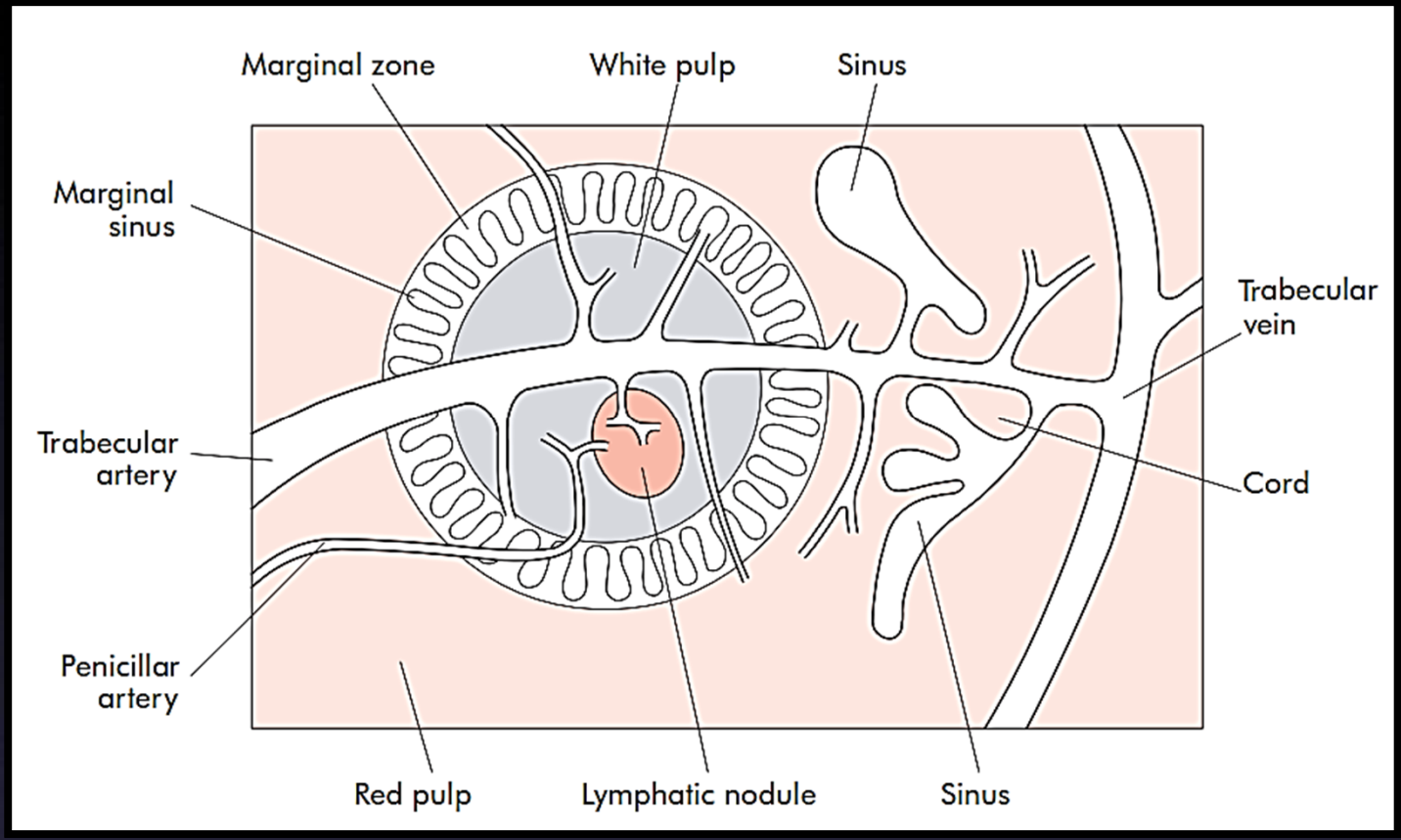
Macrophages line nodal medullary sinuses



Tissue macrophages in Spleen

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




Marginal zone
White pulp
Sinus
Marginal sinus
Trabecular vein
Trabecular artery
Cord
Penicillar artery
Red pulp
Lymphatic nodule
Sinus

FUNCTIONS OF SPLEEN

Red Pulp- Red Pulp- filtering function

- **RBC's able to deform through sinusoidal wall and endothelium Culling**
- **Macrophage activation - macrophages filter and destroy foreign material in blood Macrophage activation**

White pulp - immunologic functions

– trapping and processing of antigens

– the major site of antibody synthesis

– key role in removal of encapsulated bacteria (Strep pneumo)

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

- **Formation of blood cells**

–play in important role in the hemopoieticfunction in embryo

–during the hepatic stage, spleen produces the blood cells along with liver

- **Destruction of blood cells**

–the older RBCs, lymphocytes & thrombocytes are destroyed in spleen

- **Reservoir function**

–a large number of RBCs and platelets are stored in spleen

–RBCs are released form spleen into circulation during the emergency conditions like hypoxia & hemorrhage

- **Role in defense of body**

–spleen filters the blood by removing the microorganism

–macrophages in splenic pulp phagocytose microorganisms & foreign bodies

–spleen contains about 25% of T lymphocytes & 15% of B lymphocytes & form the site of antibody production mainly IgM

FUNCTIONS OF SPLEEN

•Role in defense of body

—Immune function:spleen filters the blood by removing the microorganism. Macrophages in splenic pulp phagocytose microorganisms & foreign bodies

- **spleen contains about 25% of T lymphocytes & 15% of B lymphocytes**
- **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.**
- **These antibodies are of B- and T-cell origin and bind to the specific receptors on the surface of macrophages and leukocytes, stimulating their phagocytic, bactericidal and tumoricidal activity.**

SPLENOMEGALY

INFECTIVE

- BACTERIA: Typhoid, Paratyphoid, TB, Pyogenic, Abscess
- VIRUS: IMN
- SPIROCHETES: ?
- PARASITES: Bilharziasis, Hydatid cyst, Malaria, Kala azar

BLOOD DISEASE

- Leukemia
- Anemia
- Polycythemia
- ITP
- Hemolytic anemia

NEOPLASTIC

MOST COMMON IS LYMPHOMA

- Hemangioma
- Fibro-sarcoma

CONGESTIVE

Portal Hypertension

METABOLIC

- Gaucher's disease
- Amyloidosis
- Rickets

NON-PARASITIC & COLLAGEN

- Felty's disease
- Still's disease

HUGE SPLENOMEGALLY

(Enlargement of spleen Crossing Umbilicus)

- Myeloid leukemia, Chronic leukemia
- Thalassemia Major
- Amyloidosis

HYPERSPLENISM

PRIMARY HYPERSPLENISM

- ETIOLOGY: Idiopathic
- CLINICAL PICTURE:
  1) ↓WBCs ... Fever, Frequent infection, Oral Ulcers
  2) ↓Platelets ... Petichae, Ecchymosis
  3) ↓RBCs ... Pallor
- INVESTIGATIONS:
  - CBC→ Pancytopeni a, ↑Reticulocytosis
  - BM → Hyperplasia
- TREATMENT: Splenectomy

SECONDARY HYPERSPLENISM

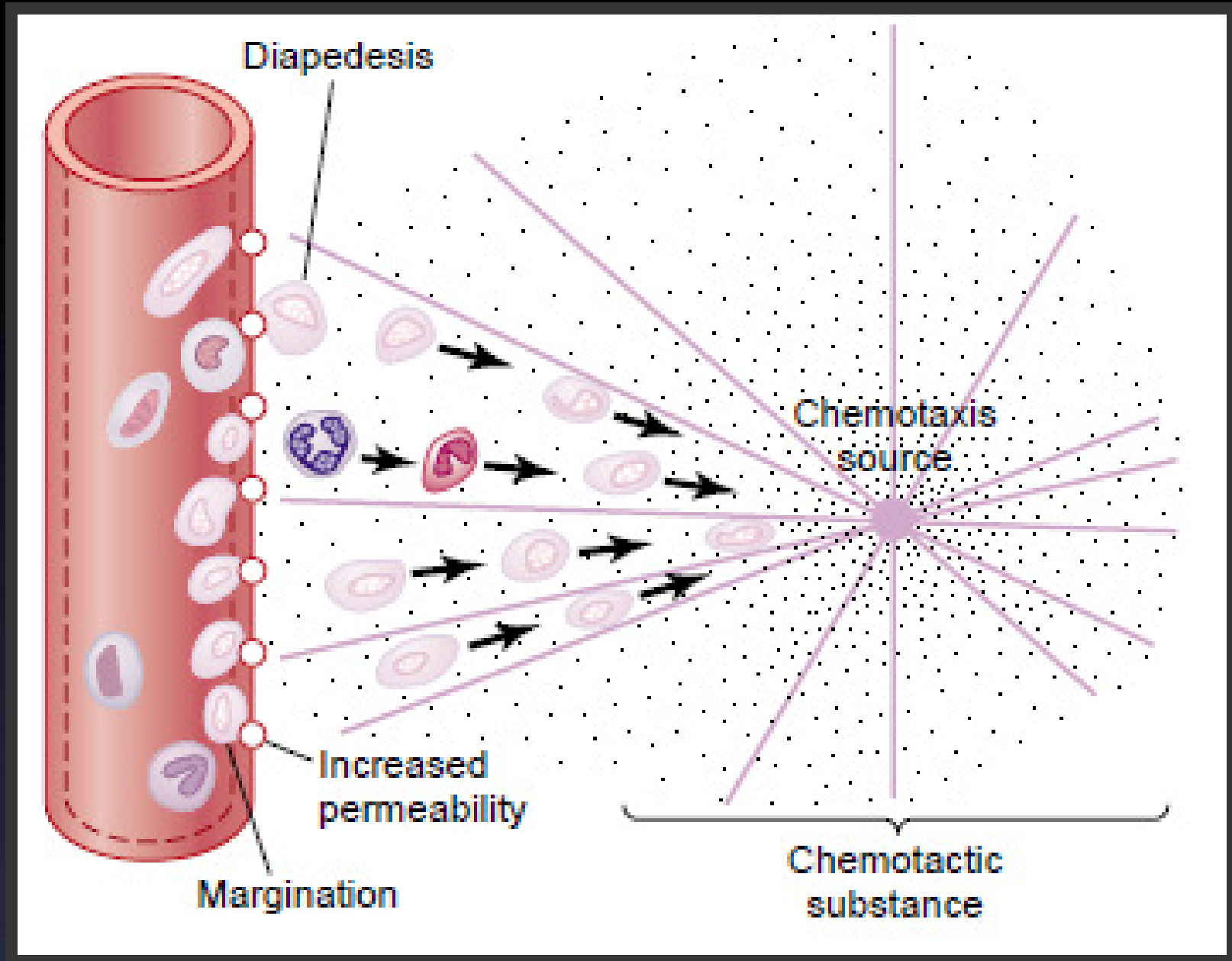
- ETIOLOGY: Secondary to portal hypertension
- TREATMENT: Splenectomy + Vasoligation

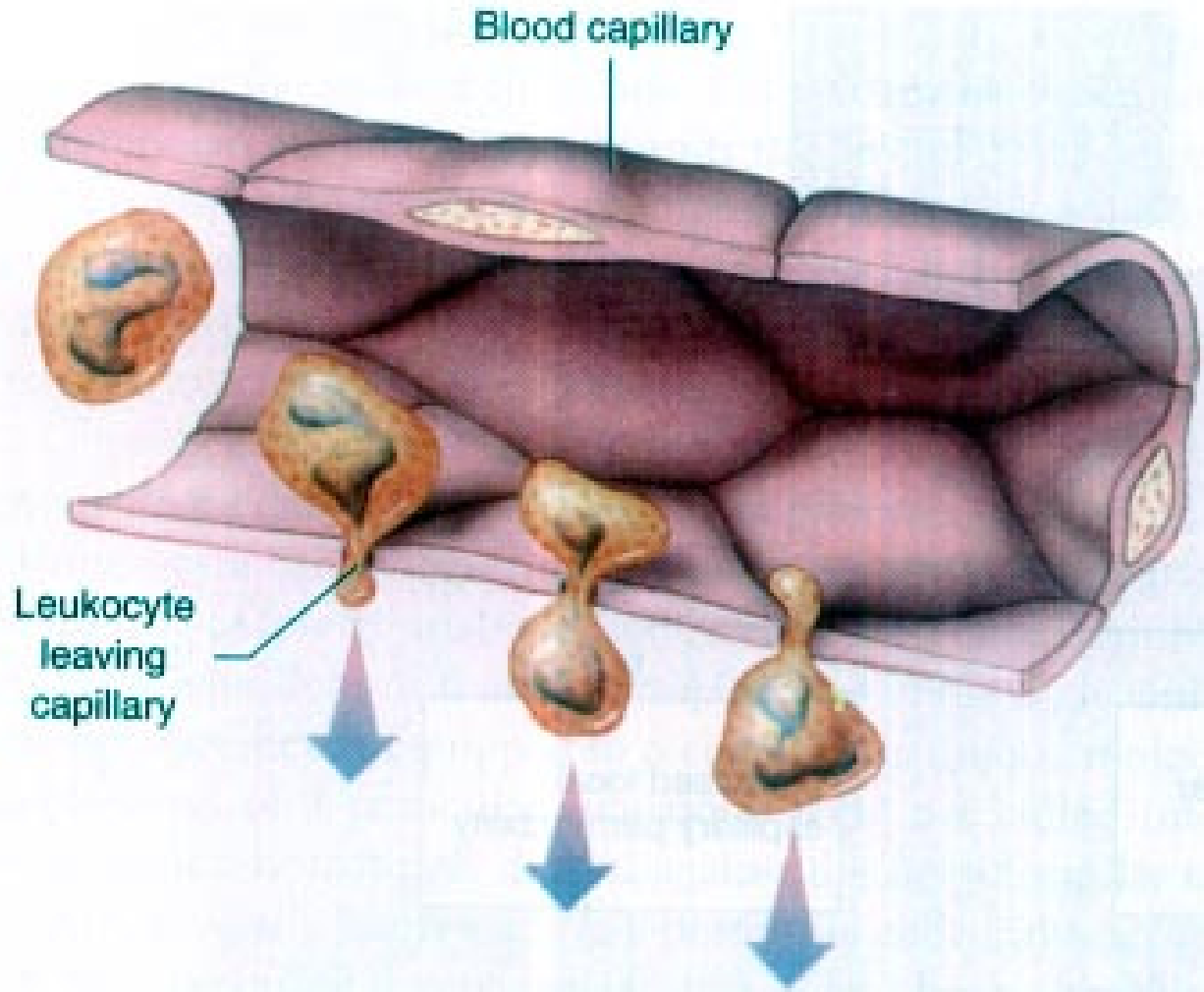
NEUTROPHILS

- Most Abundant WBCs 60-70 %
- Size: 15-20 μm
- Nucleus: Multilobed 2-5 lobes
- Life span: 6-8 hours

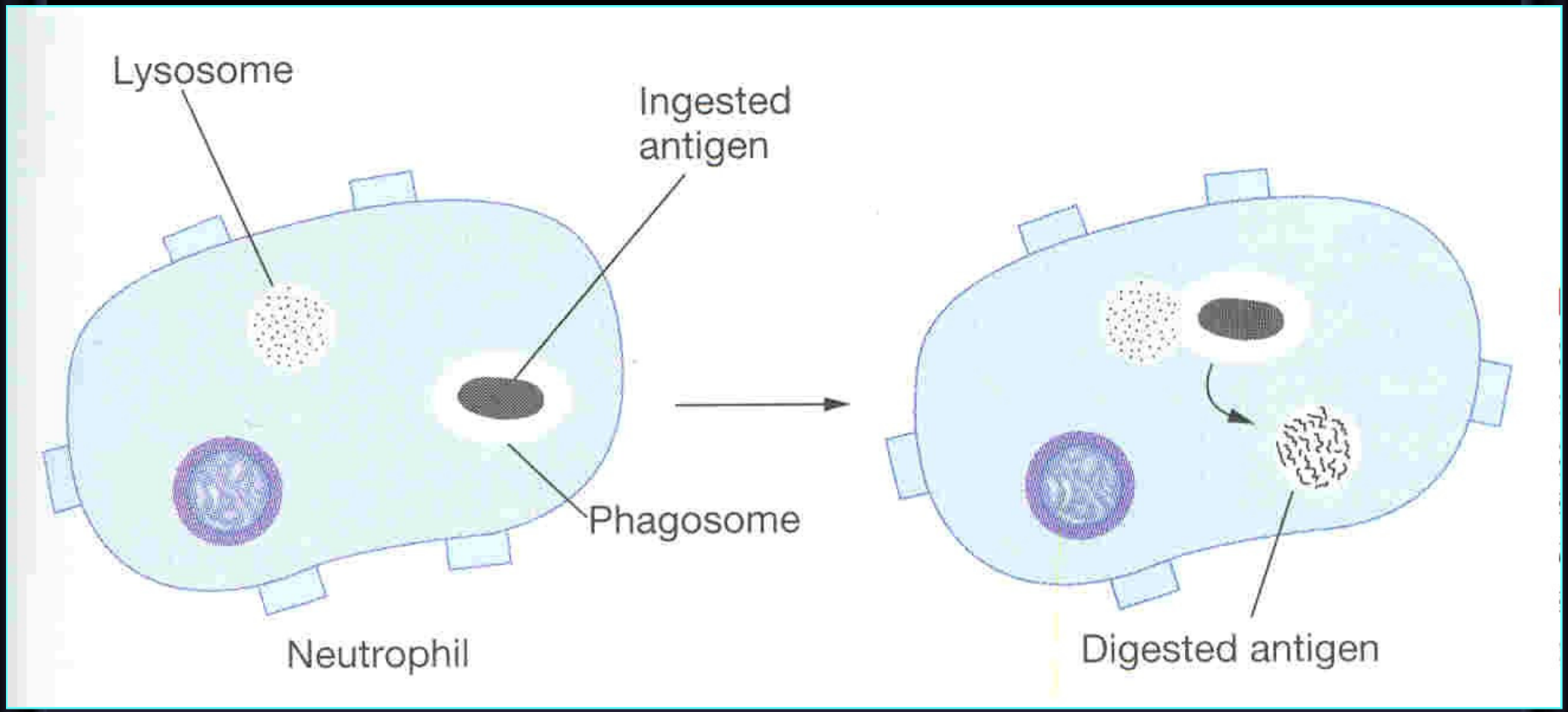
DEFENSIVE PROPERTIES OF
MACROPHAGES & NEUTROPHILS

1. Diapedesis
2. Chemotaxis
3. Opsonization
4. Degranulation
5. Phagocytosis & Digestion

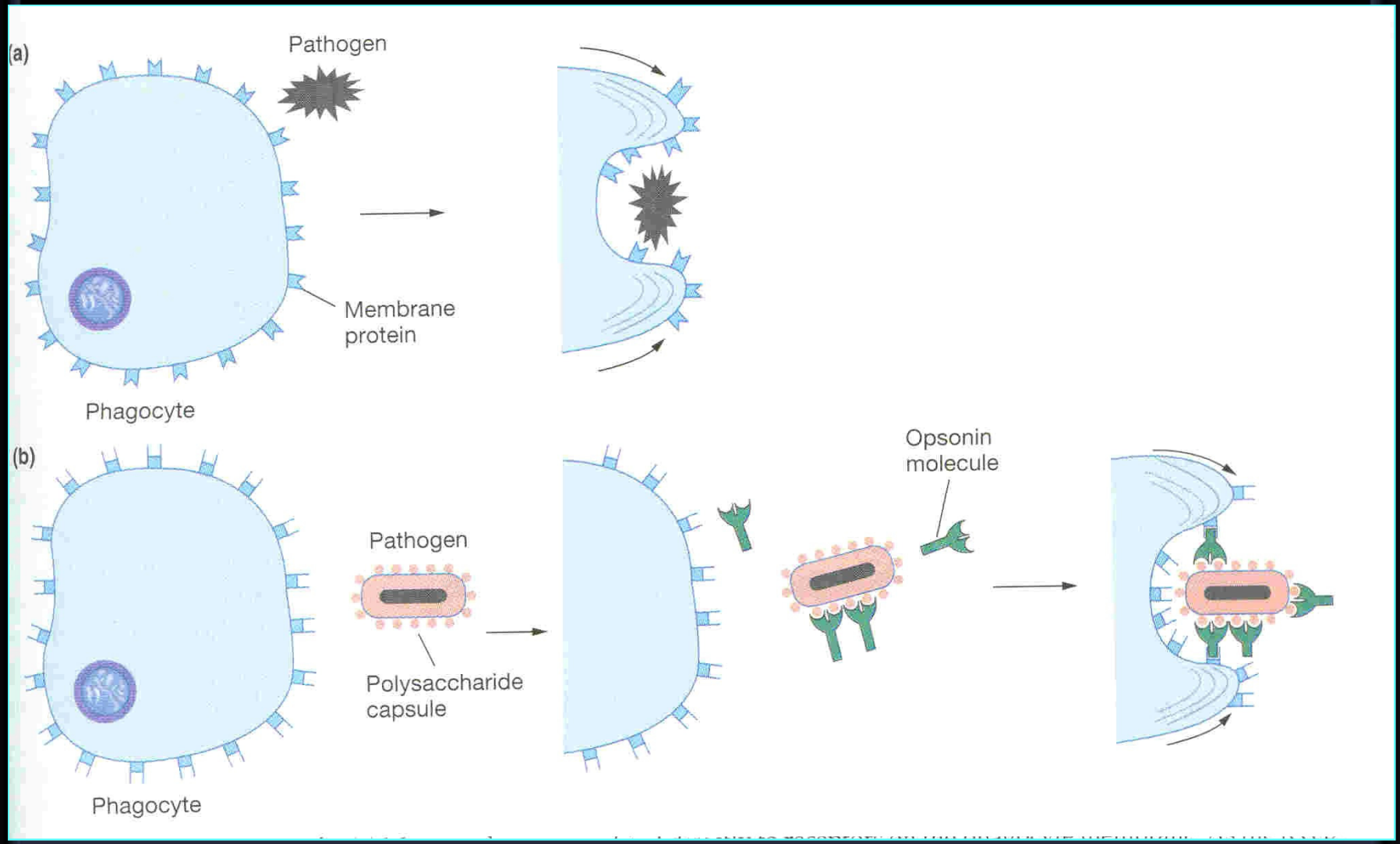

Diapedesis
Chemotaxis source
Increased permeability
Margination
Chemotactic substance


Blood capillary
Leukocyte leaving capillary

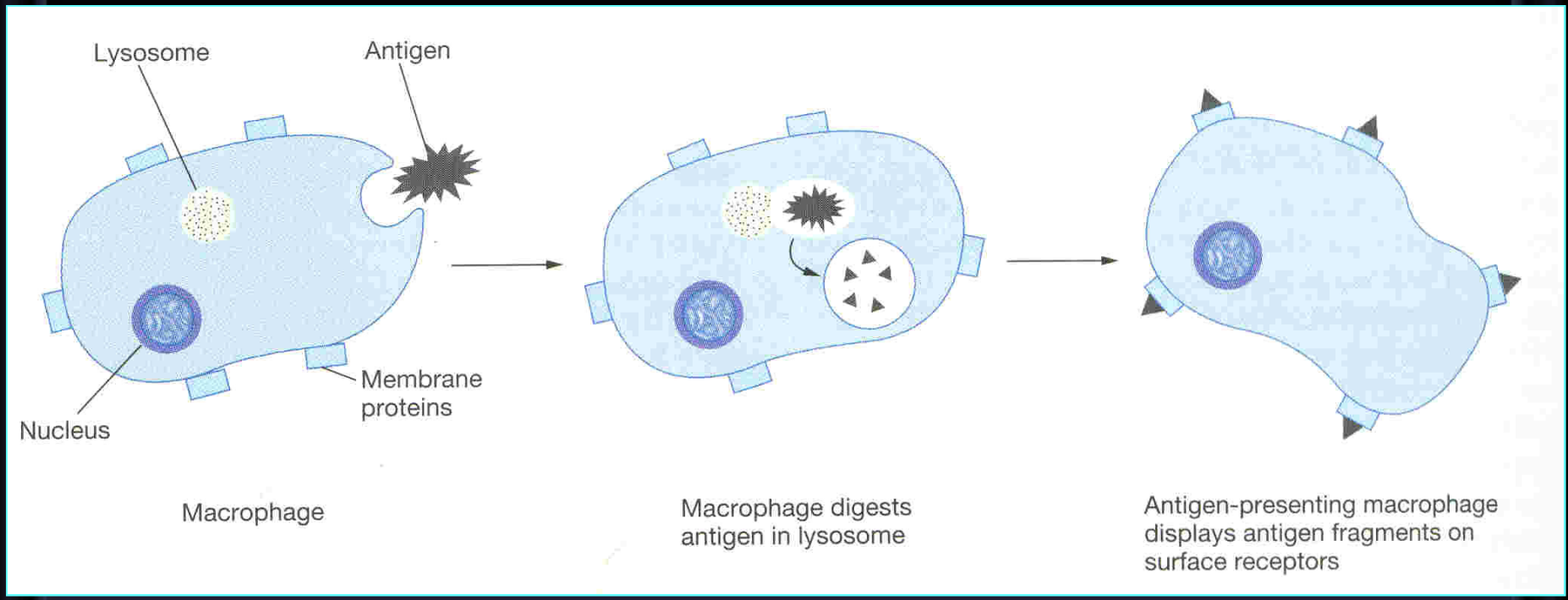
Phagocytosis & Digestion

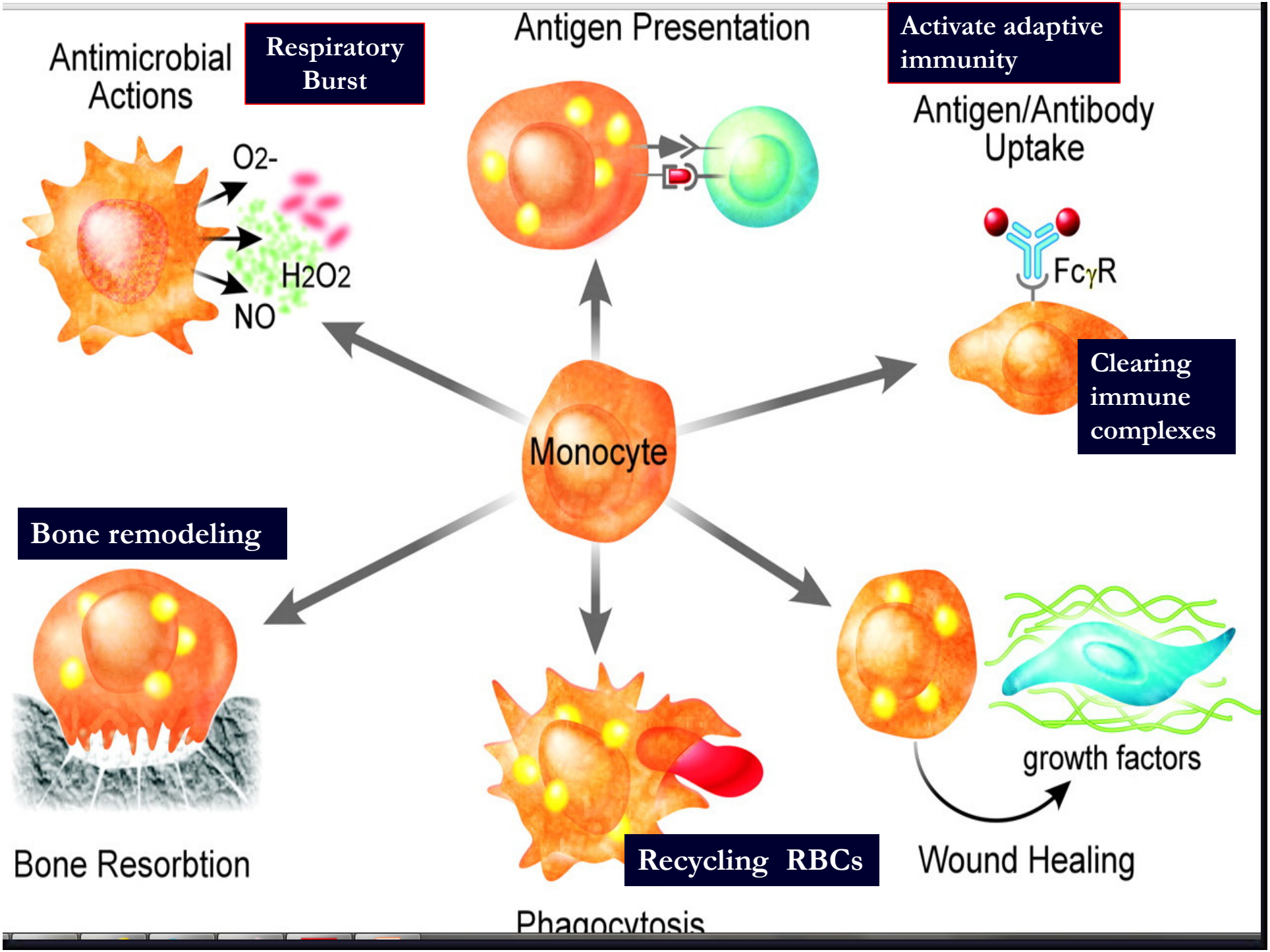


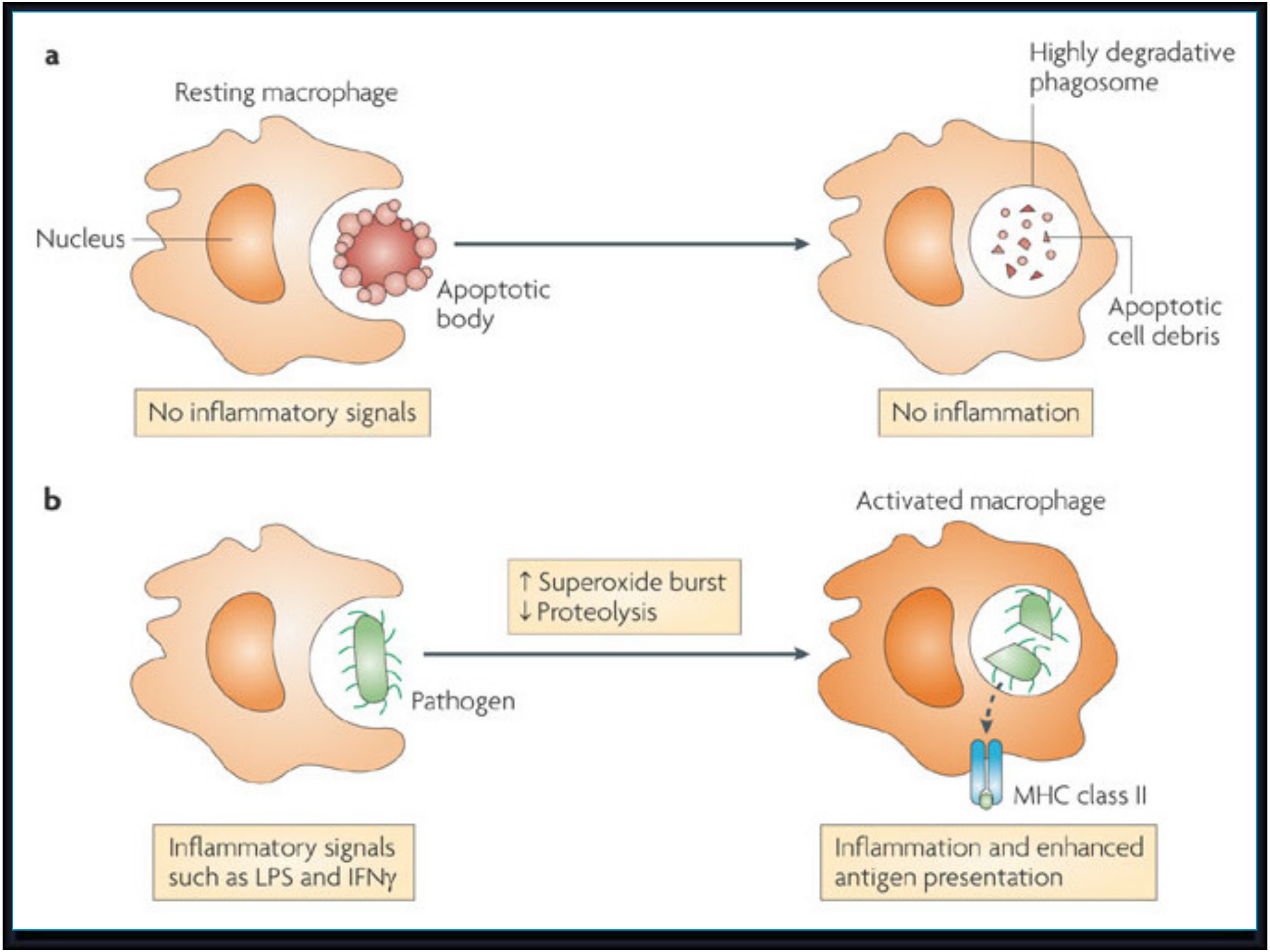
Opsonization & Phagocytosis

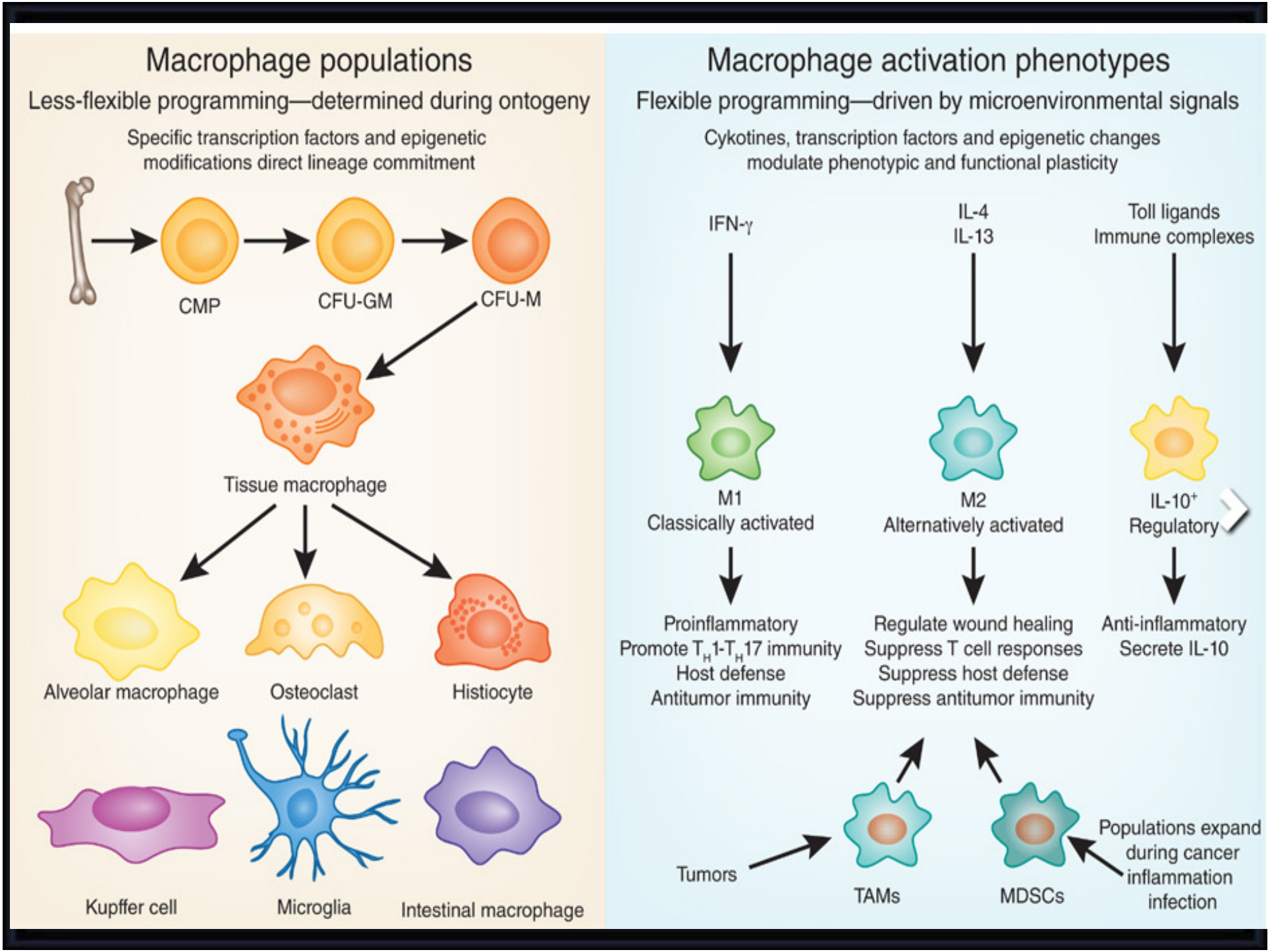


Antigen Presenting Cells




Antimicrobial Actions
Respiratory Burst
O2-
H2O2
NO
Antigen Presentation
Activate adaptive immunity
Antigen/Antibody Uptake
FcγR
Clearing immune complexes
Monocyte
Bone remodeling
Bone Resorbtion
Recycling RBCs
Phagocytosis
growth factors
Wound Healing

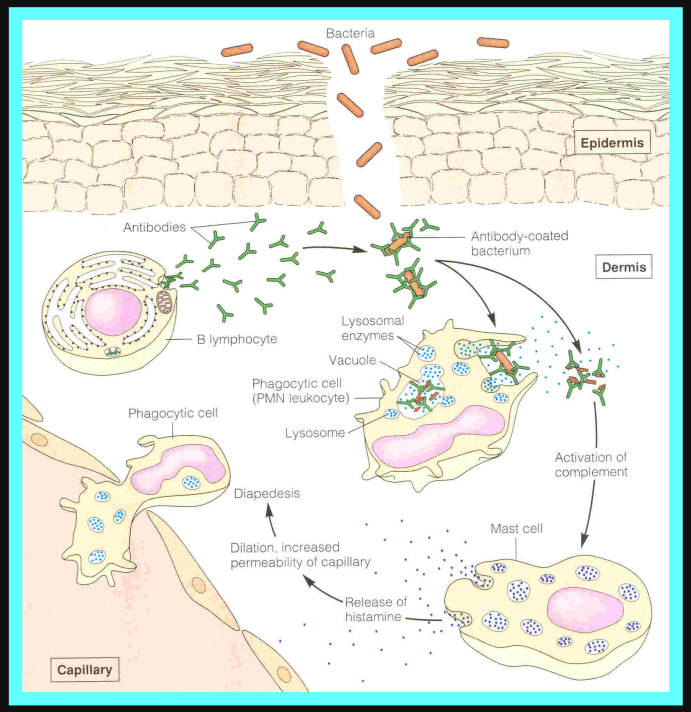

a
Resting macrophage
Nucleus
Apoptotic body
No inflammatory signals
Highly degradative phagosome
Apoptotic cell debris
No inflammation
b
Activated macrophage
↑ Superoxide burst
↓ Proteolysis
Pathogen
MHC class II
Inflammatory signals such as LPS and IFNγ
Inflammation and enhanced antigen presentation


Macrophage populations
Less-flexible programming—determined during ontogeny
Specific transcription factors and epigenetic modifications direct lineage commitment
CMP
CFU-GM
CFU-M
Tissue macrophage
Alveolar macrophage
Osteoclast
Histiocyte
Kupffer cell
Microglia
Intestinal macrophage
Macrophage activation phenotypes
Flexible programming—driven by microenvironmental signals
Cykotines, transcription factors and epigenetic changes modulate phenotypic and functional plasticity
IFN-γ
IL-4
IL-13
Toll ligands
Immune complexes
M1
Classically activated
M2
Alternatively activated
IL-10+
Regulatory
Proinflammatory
Promote TH1-TH17 immunity
Host defense
Antitumor immunity
Regulate wound healing
Suppress T cell responses
Suppress host defense
Suppress antitumor immunity
Anti-inflammatory
Secrete IL-10
Tumors
TAMs
MDSCs
Populations expand during cancer inflammation infection

PMNs Digestive System (Antimicrobial system)

ENZYMATIC Granules

- Heparin
- Histamine
- Bradykinin
- Serotinin
- Defensins
- Lysosomal enzymes
- Slow reacting substance of anaphylaxis



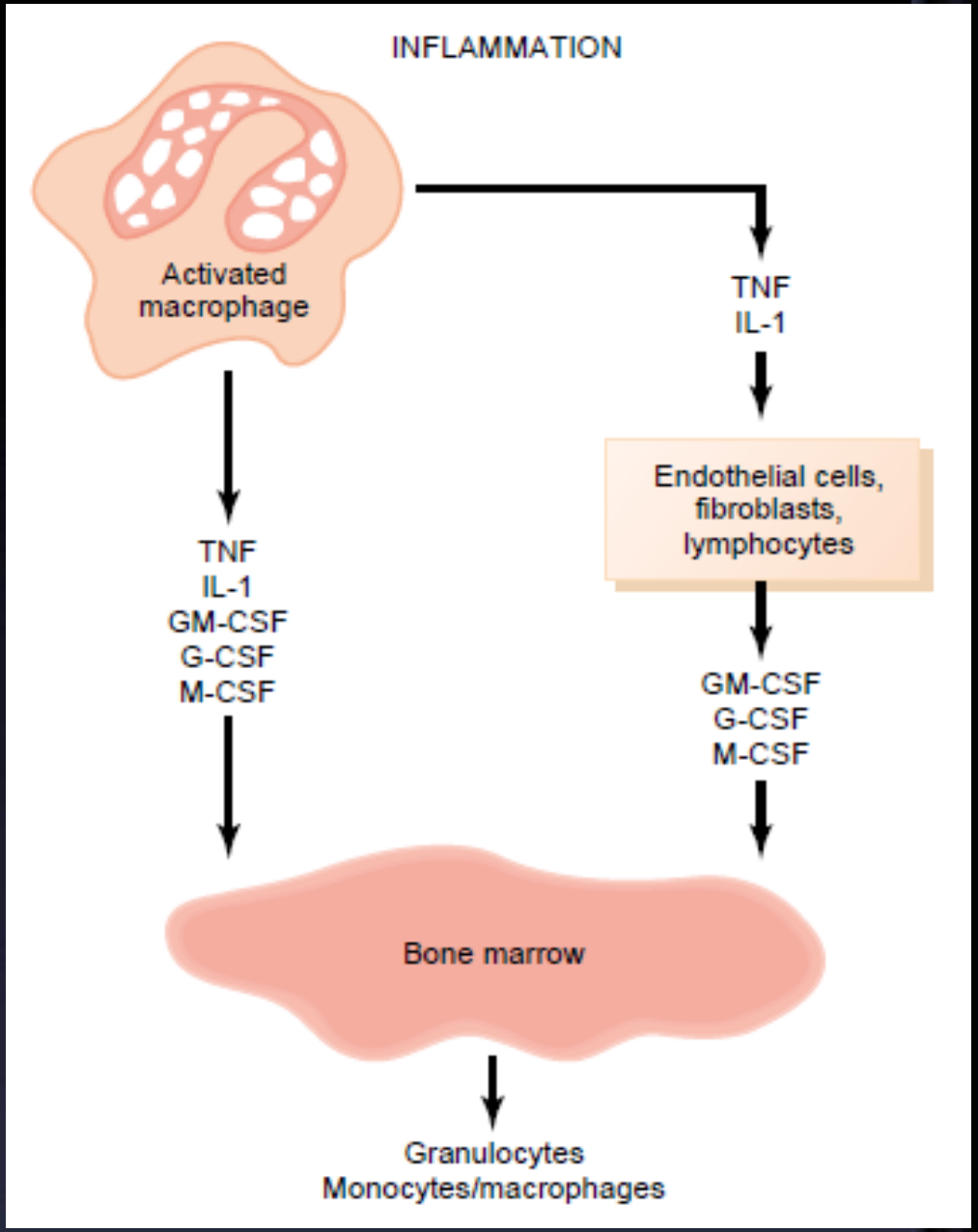
PMNs Digestive System (Antimicrobial system)

NON ENZYMATIC

respiratory burst

- **O2 Free Radicals (O-2, H2O2, -OH)**
- **NADPH-oxidase**
- **Myeloperoxidase**
- **Cl- → HoCl**
- **Hypochlorous acid "very toxic"**

Feed Back Control of Macrophage & Neutrophil response



IMPORTANT TERMS

- **Pus** (necrotic tissue, dead neutrophils, dead macrophages and tissue fluid → Autolyze)
- **Leukocytosis**
- **Neutrophilia**
- **Leukopenia**
- **Leukemias**

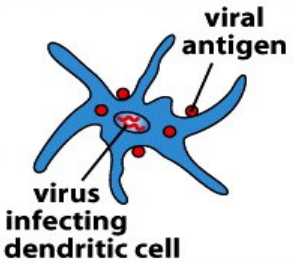
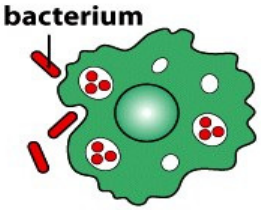
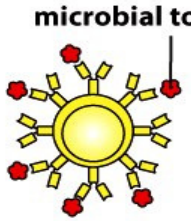
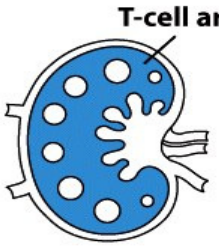
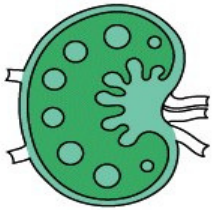
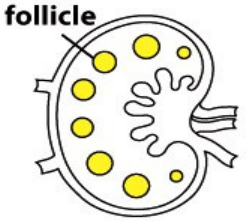
	Professional antigen-presenting cells		
	Dendritic cell	**Macrophage**	**B cell**
Cell type			
Location in lymph node			
Antigen uptake	+++ Macropinocytosis and phagocytosis by tissue dendritic cells Viral infection	Phagocytosis +++	Antigen-specific receptor (Ig) ++++
MHC expression	Low on tissue dendritic cells High on dendritic cells in lymphoid tissues	Inducible by bacteria and cytokines – to +++	Constitutive Increases on activation +++ to ++++
Co-stimulator delivery	Constitutive by mature, nonphagocytic lymphoid dendritic cells ++++	Inducible – to +++	Inducible – to +++
Antigen presented	Peptides Viral antigens Allergens	Particulate antigens Intracellular and extracellular pathogens	Soluble antigens Toxins Viruses
Location	Ubiquitous throughout the body	Lymphoid tissue Connective tissue Body cavities	Lymphoid tissue Peripheral blood

Figure 8.11 The Immune System, 3ed. (© Garland Science 2009)


THANKS