THE COMPLEMENT SYSTEM

THE COMPLEMENT SYSTEM

- The complement system consists of plasma proteins that play important roles in defending the host and regulating inflammation.

- The complement system consists of more than 20 proteins produced by various cells in blood serum including hepatocytes, macrophages and intestinal epithelial cells.
- Some of the complement proteins attach to immunoglobulins or components of cell membrane.
- Other proteins are present as proenzymes and when they are activated, they break down to compose one or more complement proteins.

Substitute for activation of the complement which is inactive in serum.

One is the antigen-antibody reaction.

When the antigen reacts with the specific antibody molecule, the "complement binding region" in the Fc region of the antibody is exposed. the serum component binds to this region. Complement cannot be bound because the "complement binding region" is not in the appropriate position in the antibody molecule which is normally free and bound with no antigen.

Another factor that activates complement is the ability to directly bind to the surface of some microorganisms.

The final step of complement reactions is known as the terminal pathway. In this final stage, an end product called "membrane attack complex" is formed. This complex has the function of lysing the target cell.

FUNCTIONS OF THE COMPLEMENT SYSTEM

- **The opsonization:** C3b and C4b bound covalently to a microbial surface effectively tag it as foreign and so serve as very potent and effective opsonins.

- **Chemotaxis:** C5b is chemotactic for neutrophils and eosinophils, whereas C5a attracts not only neutrophils and eosinophils but also macrophages.

- **Inflammation:** The anaphylatoxins, C3a and C5a, enhance TLR-induced production of the three proinflammatory cytokines, TNF-α, IL-1β, and IL-6.

CYTOKINES

CYTOKINES

- Cytokines are small proteins secreted by the cells of the immune system and they affect the behaviour or the functions of other cells.

Cytokines by their Origin

- Macrophages ⇒ monokine
- Lymphocytes ⇒ lymphokine
- Leukocytes ⇒ interleukin

Monokines: Cytokines synthesized by mononuclear phagocytic cells

Lymphokines: Active Lymphocytes

Interleukins: Cytokines acting as mediators among leukocytes

Properties of Cytokines

They may, for example, bind to receptors on the cell that produced them and thus have an autocrine effect.

Alternatively, they may bind only to receptors on nearby cells; this is called a paracrine effect.

Some cytokines may spread throughout the body, affecting target cells in distant locations, and thus have an endocrine effect.

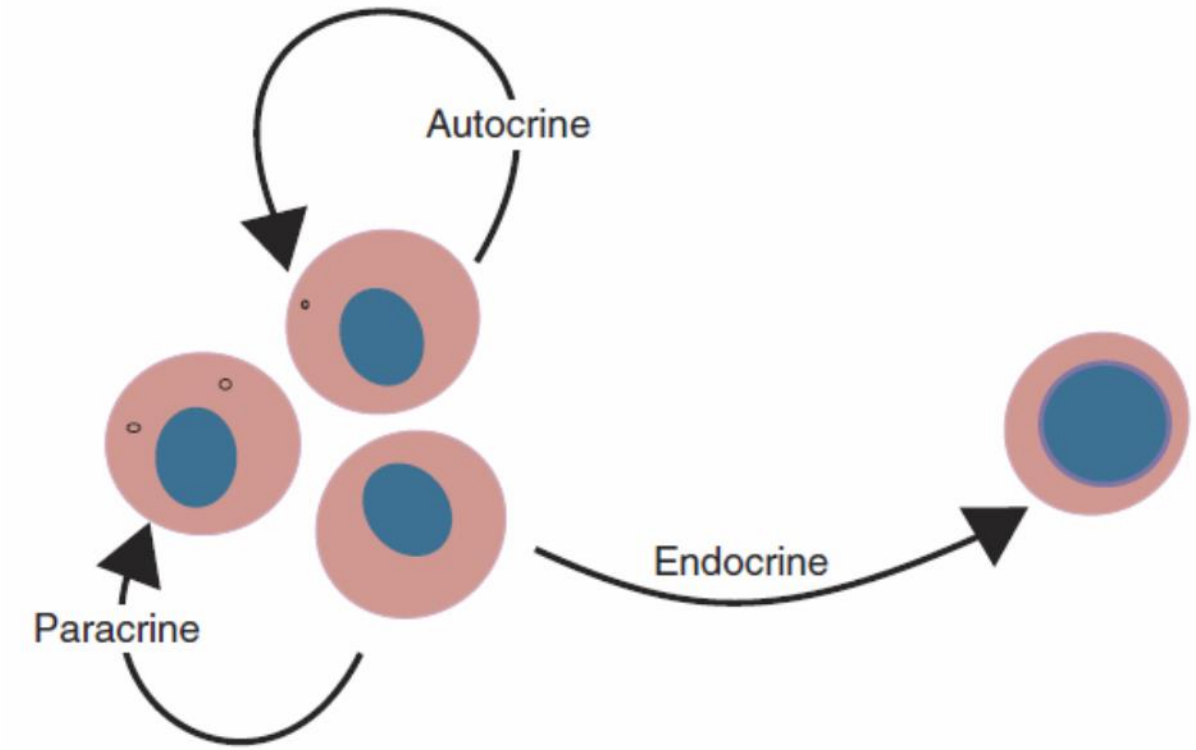
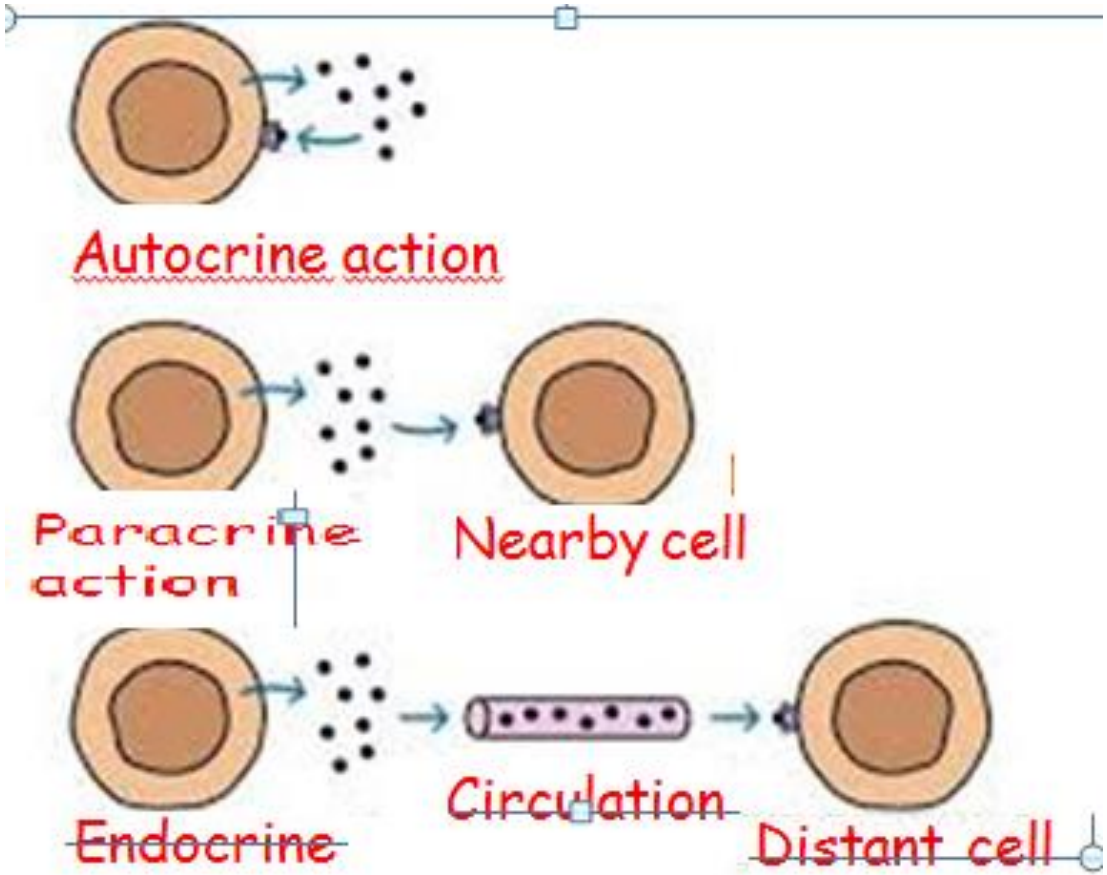


FIGURE 8-2 The distinction among autocrine, paracrine, and endocrine effects. Cytokines differ from hormones in that most of their effects are autocrine or paracrine, whereas hormones usually act on distant cells in an endocrine fashion.

Properties of Cytokines

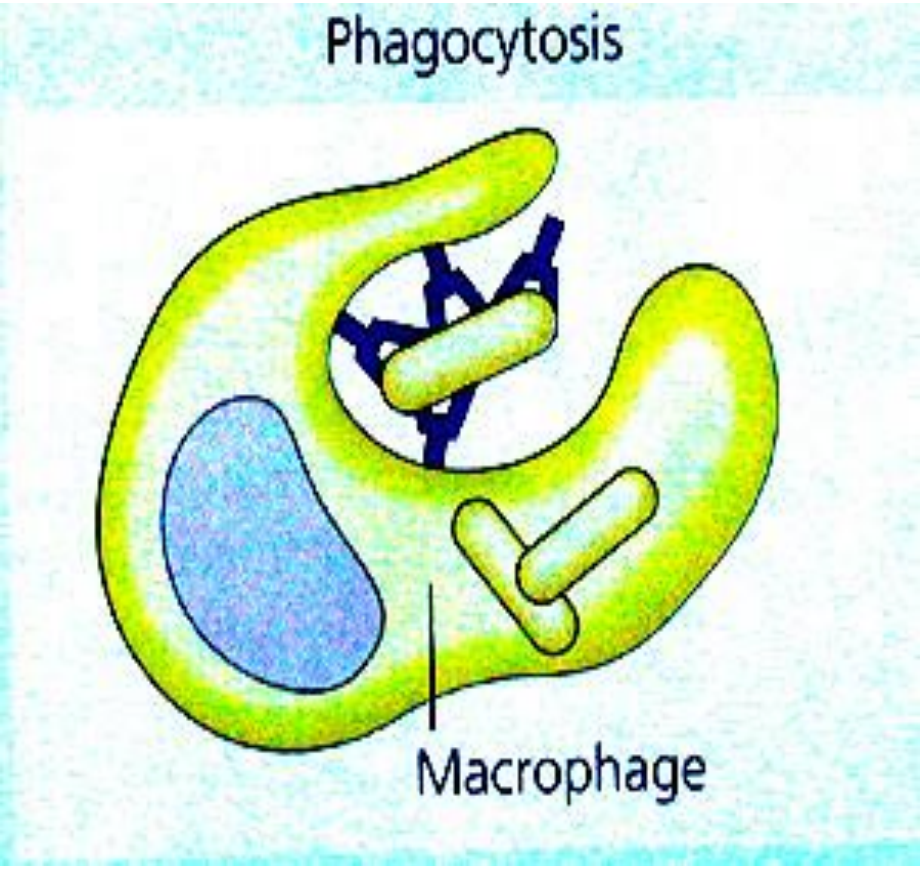


Functions of Cytokines

- **Cytokines involved in natural immunity:** This group has functions such as macrophage activation, dendritic cell activation, chemotactic factor. For example: TNFα, IFNy, IL1, IL10, IL12
- **Cytokines involved in specific immunity**: B lymphocyte differentiation, antibody synthesis.. For ex: IL2, IL4, IL5, TGFb
- **Hematopoesis:** Some cytokines are responsible for the formation and maturation of immune system cells in the bone marrow. For example: GM-CSF, G-CSF, M-CSF, IL3, IL7,IL9, IL11

PHAGOCYTOSIS

PHAGOCYTOSIS



- Phagocytosis: Foreign molecules that penetrate in to body phagocytized by special immune system cell
- Once they reach sites of microbial invasion, neutrophils eat and destroy invading bacteria through phagocytosis.
- Although a continuous process, phagocytosis can be divided into discrete stages: activation, chemotaxis, adherence, ingestion, and destruction.

PHAGOCYTOSIS

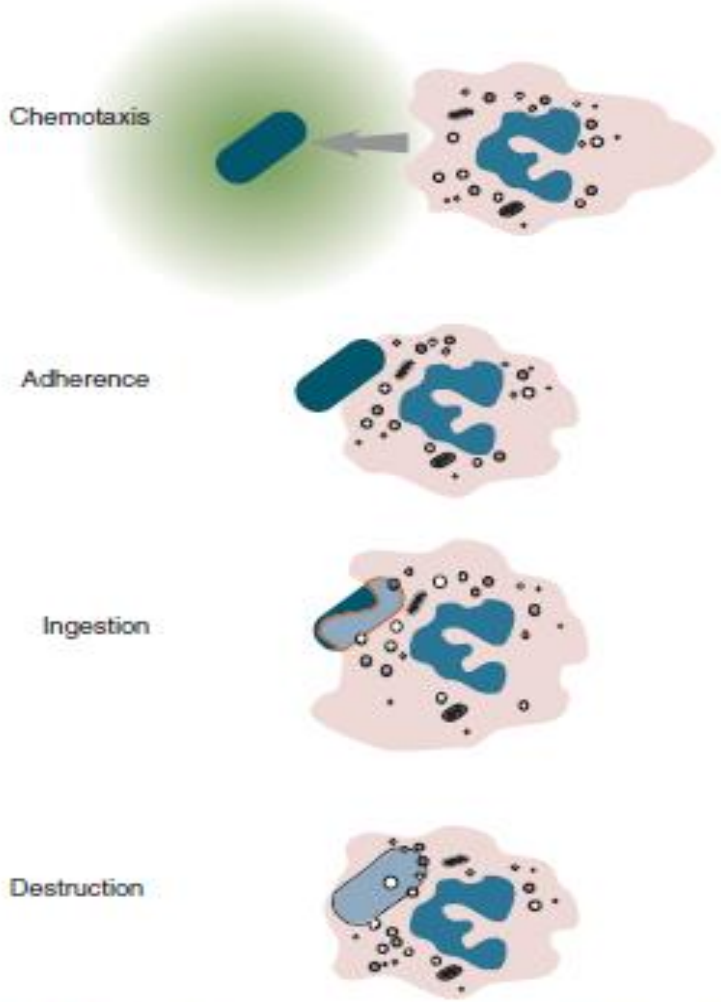


FIGURE 4-9 The different stages in the process of phagocytosis. While in fact a continuous process, this division into stages provides a useful method of analyzing the process.

Phagocytosis occurs mainly in four stages

Phagocytosis-Chemotaxis

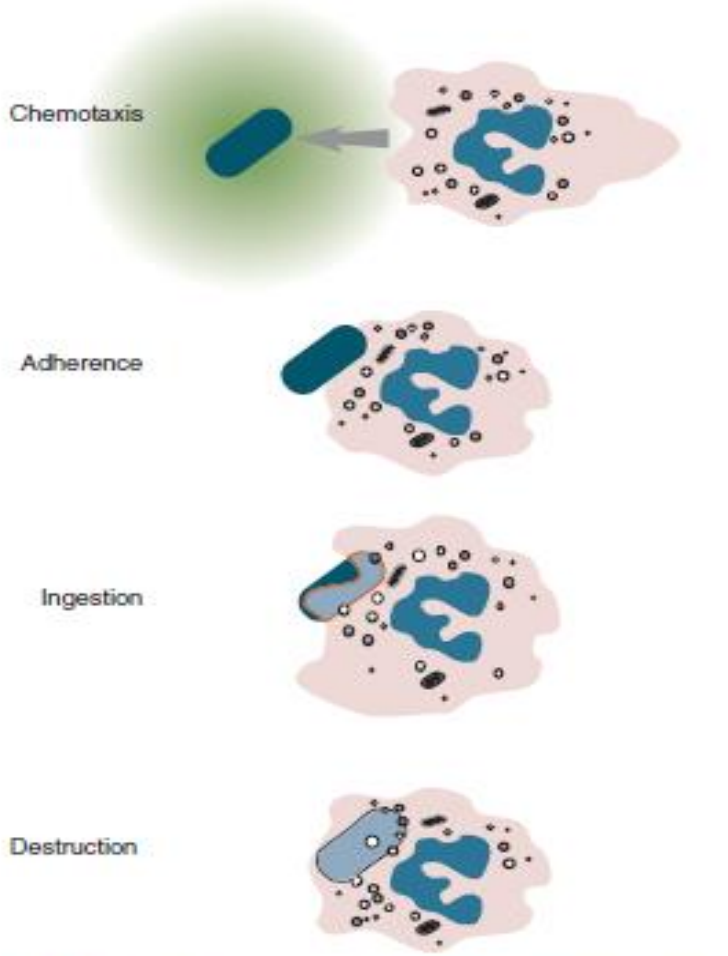


FIGURE 4-9 The different stages in the process of phagocytosis. While in fact a continuous process, this division into stages provides a useful method of analyzing the process.

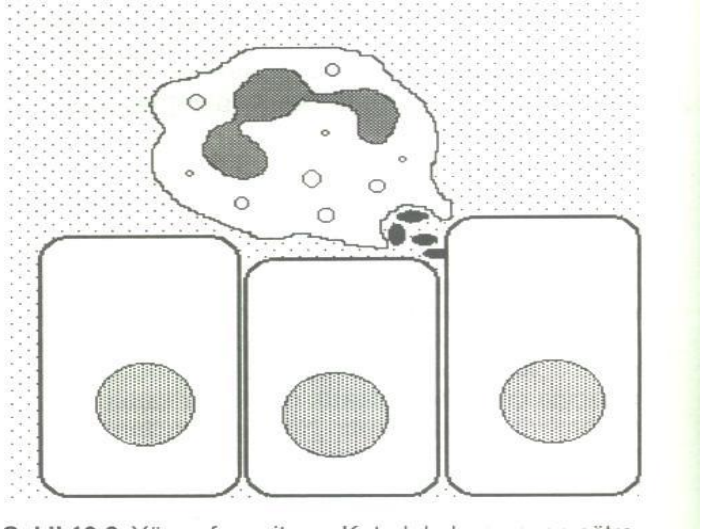
Chemotaxis: Moving neutrophils towards self-stimulating substances

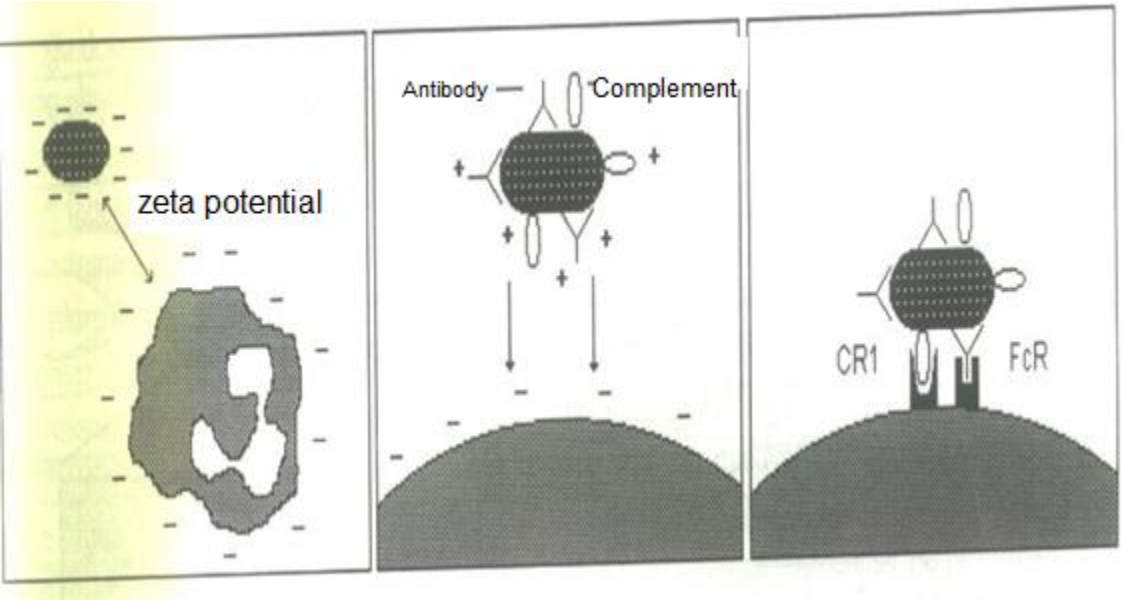
Chemotactic substances are released from damaged tissues and attract phagocytic cells towards damaged tissue

Chemotactic agents: C5a, fibrinopeptide B, platelet factor 4, methionine and the like.

Chemotactic agents also enhance the ability of vascular endothelial cells to adhere to neutrophils. DIAPEDEZIS

Phagocytosis-Adherence

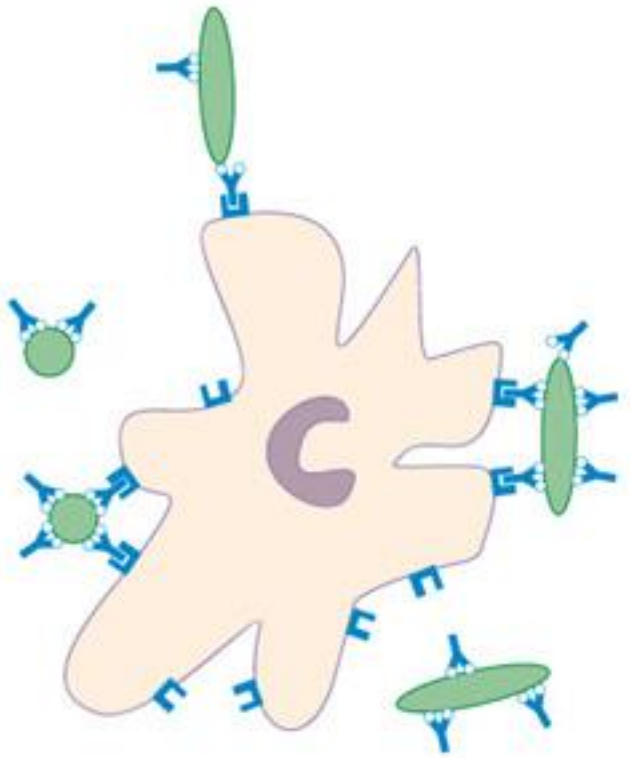




- Surface phagocytosis - solid environments
- Zeta potential in liquid environments the opsonization

Opsonins: antibody (immunoglobulin) and C3b component of complement

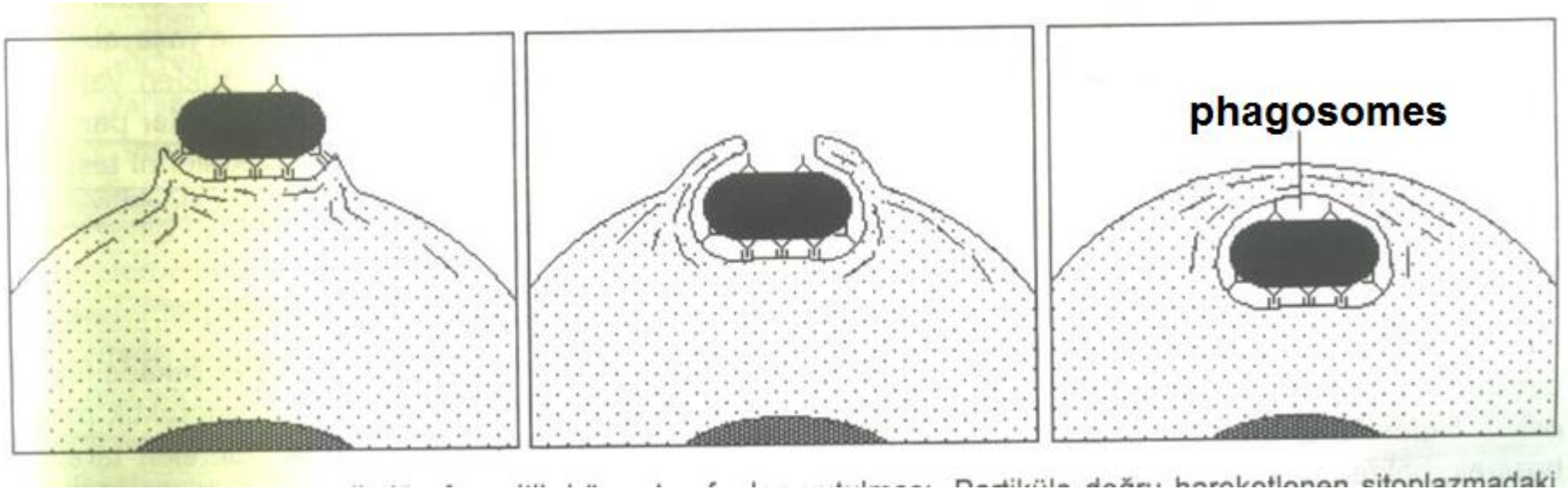
Phagocytosis-Adherence



- The opsonization
- FcR and complement receptor presence required
- Opsonin is “flavoring “ Yunan in the Greek alphabet

Phagocytosis - Ingestion

- Fluid structure of cytoplasm (actin and myosin) Pseudopod formation
- Phagosome formation
- Hydrophobic surface (Mycobacterium tuberculosis) Hydrophilic surface (encapsulated bacteria) - <u>opsonization</u>



Phagocytosis-Killing and Destruction

- Respiratory destruction and enzymatic (lysozimal) digestion
- Respiratory destruction:
- -oxidative reactions
- - Latest products: hydrogen peroxide and hypochlorite

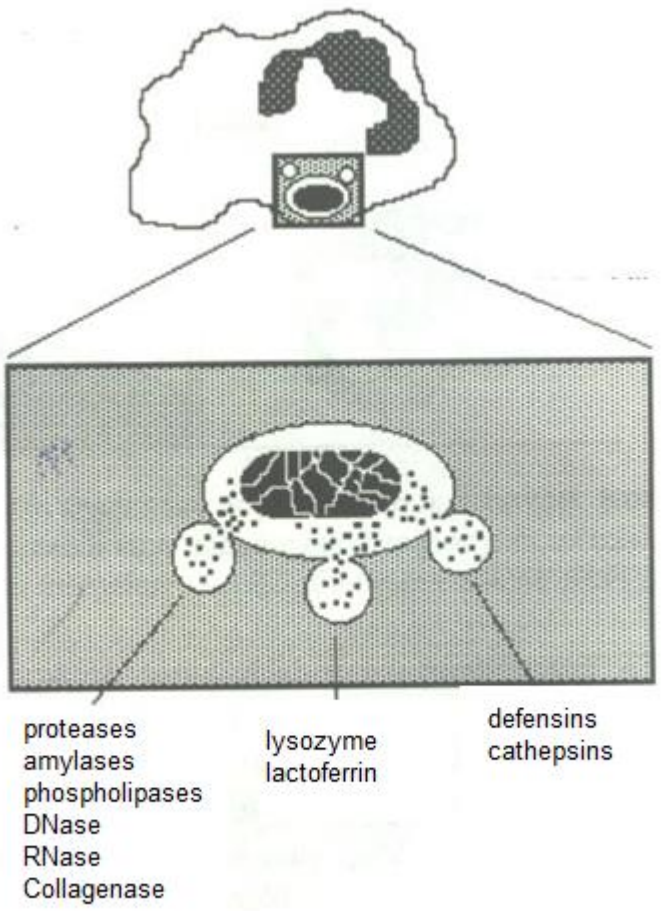
for neutrophil

- nitrate, nitrite and ozone

for macrophages

- - Effects: oxidizes bacterial proteins and increases lysosomal enzyme activity.

Phagocytosis-Killing and Destruction



- Enzymatic digestion
- Phagolysosomes,
- Effects:

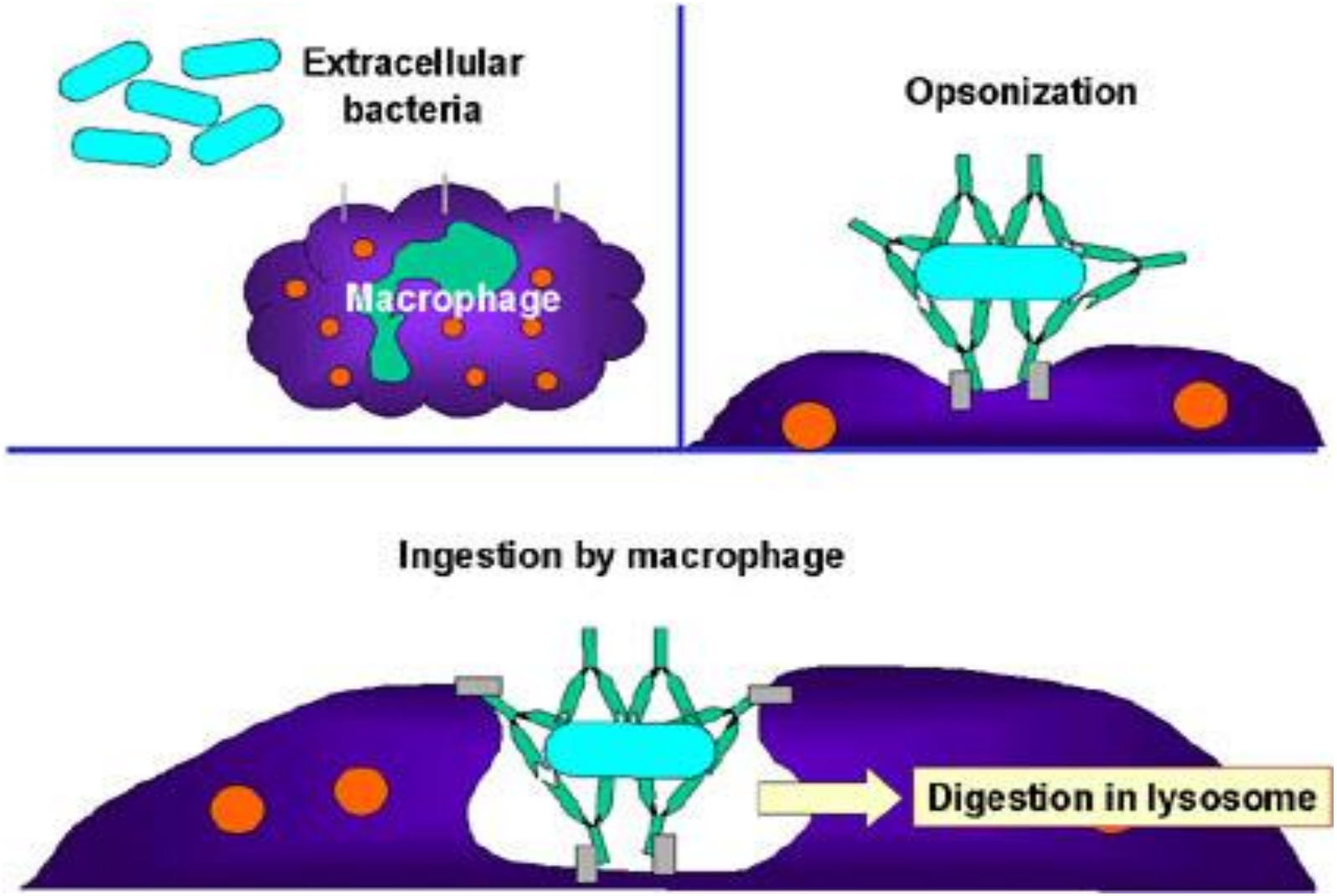
- * Breaking down the wall of bacteria (Gr + bacteria)
- * Iron holding
- * disintegration of lipid layer
- Eosinophils can kill parasites by their enzymes outside the cell

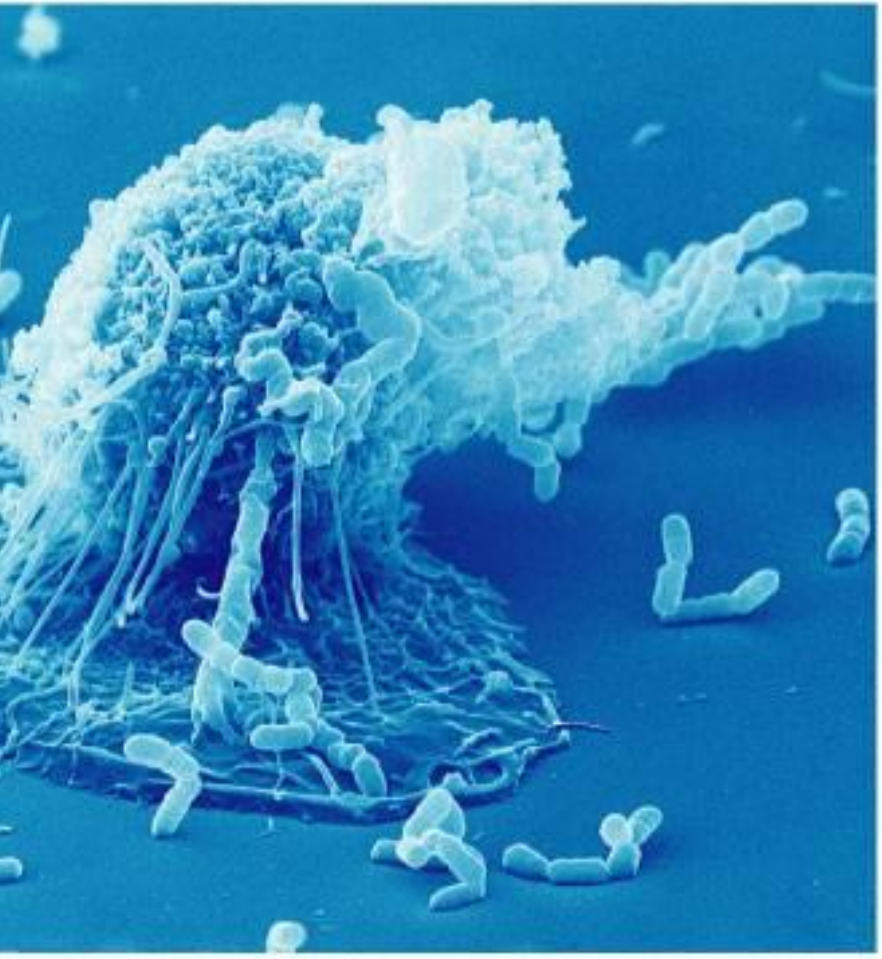
Phagocytosis

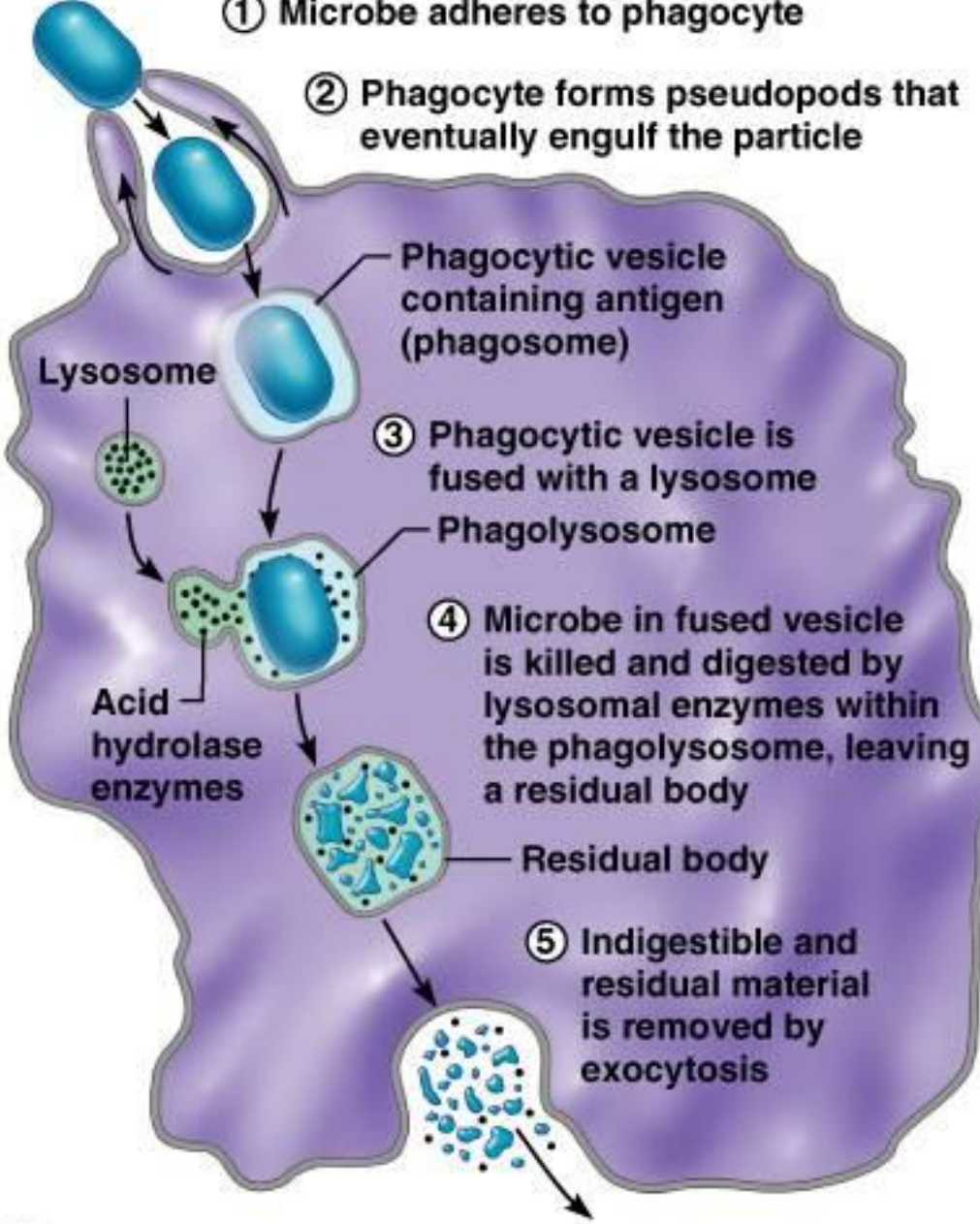
Neutrophil Phagocytosis	Macrophage Phagocytosis
Makes the first attack on the foreign substance entering the body	They are activated late and begin to phagocytosis after neutrophils
They can only phagocytize foreign molecules	In addition to foreign molecules, they phagocytize old, damaged and dead cells, residues and inorganic substances.
They are kill microorganism more powerful which they are phagostosed	They power of killed and digestion is less than neutrophil.The phagocytosis power is increased with cytokine stimulation.
They have a limited number of phagocytosis because of their limited energy	They perform phagocytosis continuously and repeatedly throughout their lives
No antigen processing and presentation functions	Antigen processing and presentation
End product of oxidative metabolism: hydrogen peroxide and hypochlorite (oxidizes bacterial proteins)	The final products of oxidative metabolism are nitrate, nitrite and ozone. They are also cause of tissue damage

Functions of Macrophages

- Phagocytosis
- Antigen processing and presentation
- Wound healing
- Enzyme (lysozyme, collagenase, protease),
- Cytokine (IL1, IL6, IL12) synthesis


Extracellular bacteria
Macrophage
Opsonization
Ingestion by macrophage
Digestion in lysosome





(b)

Phagocytosis Resistance

- Resistance to ingestion
- Live on the phagolysosome
- Stay Escape from phagosome
- Development in phagosomes