



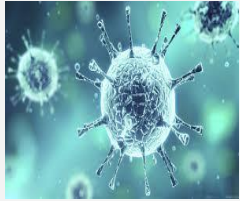
Immunology team - 437

## 2- Natural Defense Mechanisms

### Objectives :

- 1- To know first (non-specific immunity) and second (adaptive immunity) lines of defense.
- 2- To understand the Complement system, its activation and how it involves in pathogen killing.
- 3- To recognize the importance of accumulation of inflammatory cells for clearance of infection.
- 4- To Know the role of Cytokines as mediators which regulate inflammation.

## The main function of the immune system is to protect from infections:



Viruses e.g.  
Influenza  
Polio



Parasites e.g.  
Tapeworms, Malaria



Fungi e.g.  
*Candida albicans*



Bacteria e.g.  
*Tubercule bacillus*  
*Staphylococci*

## First and the second lines of defense:

NONSPECIFIC DEFENSE MECHANISMS		SPECIFIC DEFENSE MECHANISMS (IMMUNE SYSTEM)
First line of defense	Second line of defense	Third line of defense
<ul style="list-style-type: none"> <li>• Skin</li> <li>• Mucous membranes</li> <li>• Secretions of skin and mucous membranes</li> </ul>	<ul style="list-style-type: none"> <li>• Phagocytic white blood cells</li> <li>• Antimicrobial proteins</li> <li>• The inflammatory response</li> </ul>	<ul style="list-style-type: none"> <li>• Lymphocytes</li> <li>• Antibodies</li> </ul>

First line of defense	Biochemical barriers	Physical and mechanical barriers
<p>1- Natural (Innate) Immunity</p> <p>2- Physical (skin/ mucous membranes )</p> <p>3- Mechanical (Coughing, sneezing, vomiting, action of cilia in trachea)</p> <p>4- Biochemical barriers (antimicrobial peptides, lung secretions, mucus, saliva, tears)</p>	<p>1- Body secretions contain anti-bacterial substances e.g. saliva, tears and sweat.</p> <p>2-Antimicrobial peptides. (e.g., defensins, hepcidins)</p> <p>3-Normal bacterial flora.</p> <p>4- (Compete with pathogenic bacteria for nutrients)</p>	<p>A) Skin, impermeable to microbes.</p> <p>B) Mucous membranes lining the gastrointestinal, genitourinary and respiratory tracts.</p> <p>Other protective mechanisms:</p> <p>1-Shedding of outer skin layers.</p> <p>2-Coughing and sneezing.</p> <p>3-Flushing of urine.</p> <p>4-Vomiting.</p> <p>5-Mucus and cilia in respiratory tract.</p>

# Inflammation

## Definition

Inflammation is the first response of the immune system to infection or irritation.

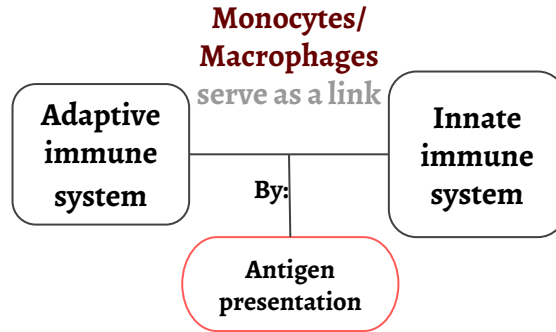
(Part of innate immunity)

It consists of a series of vascular and cellular changes that occur in response to various stimuli.

Many things can cause inflammation, for example: infections, injury, radiation etc.

## Goals

- Prevent and limit infection and further damage.
- Interact with adaptive immune system:



- Prepare the area of injury for healing

Microbial infection initiates inflammation;

As bacteria possess (تملك) an array (ترتيب) of pro-inflammatory molecules: Lipopolysaccharides (LPS)

Dr.'s note:

Innate immunity has Pattern Recognition Receptors, that are nonspecific (recognize general characteristics) -unlike adaptive immunity-, when the receptors detect LPS; inflammation starts.

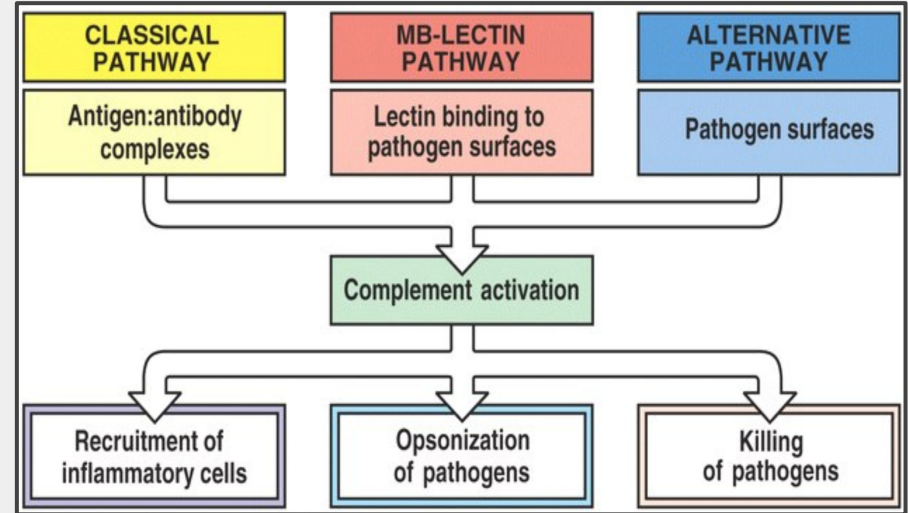
# The Complement System

- Consists of a group of serum proteins initially present in **inactive form**.
- Activation occurs in **cascade** (one component or more activating another) after enzymatic cleavage.
- Once components become activated they produce important biological effects that **initiate inflammation**.
- This system plays an important role in linking **Innate** and **Adaptive immunity**.



## 3 Pathways of activation :

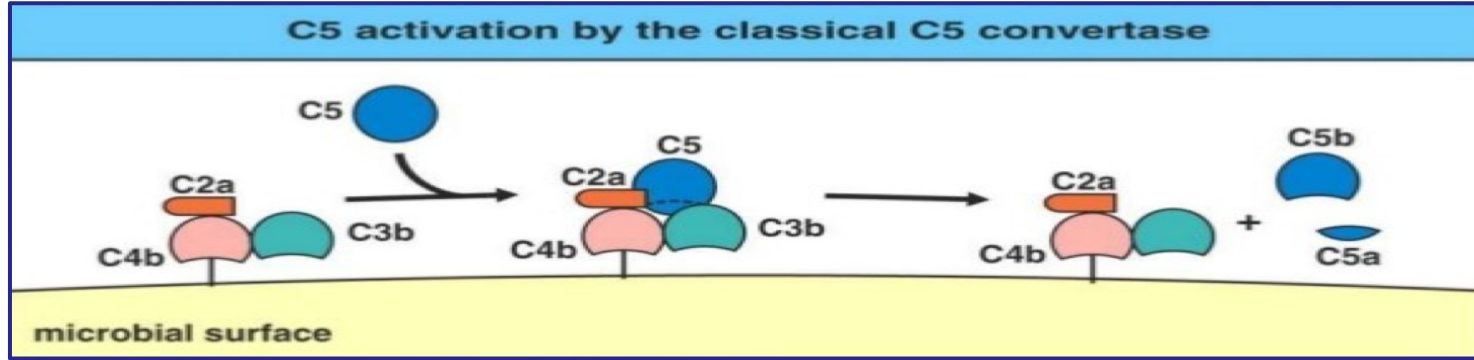
- **Classical** (Requires antigen-antibody binding)
  - (C1,C4,C2,C3,C5,C6,C7,C8,C9)
- **Lectin** (Activated by mannan binding protein binding mannose groups of bacterial carbohydrates)
  - (C4,C2,C3,C5,C6,C7,C8,C9)
- **Alternative** (Activated by bacterial products)
  - (C3,C5,C6,C7,C8,C9)



# The complement system

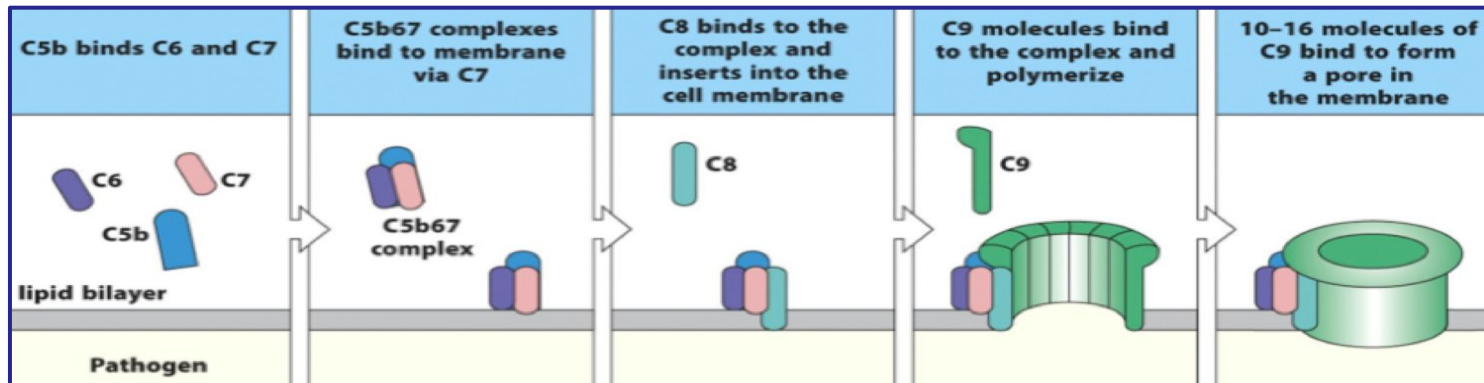
C5 activation:

Team 436



## Membrane Attack Complex Formation:

Insertion of lytic complex into cell membrane



# Biological effects of complement activation

## 1. Anaphylatoxin functions (e.g. C3a, C5a):

- Trigger degranulation (release of substances) of endothelial cells, mast cells or phagocytes.
- Induce smooth muscle contraction and increased vascular permeability.
- Attract additional inflammatory cells to the site of activation.

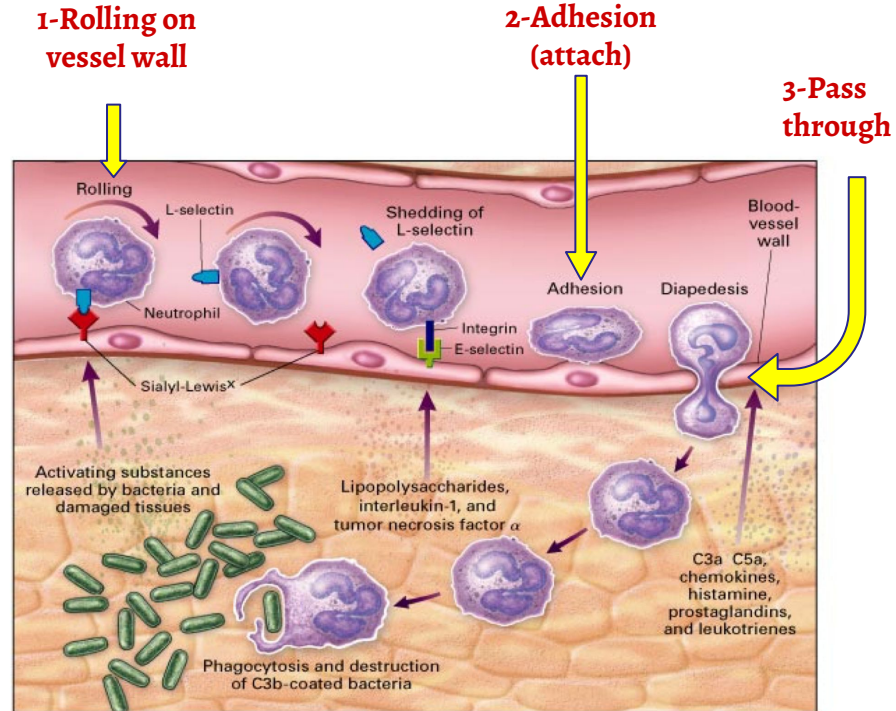
## 2. Opsonization: C3b is the main opsonin and to a lesser extent C4b.

- Coating of bacteria enhances phagocytosis

## 3. Direct cell lysis: lytic complex

- Destruction of bacteria.

# Process of chemotaxis



# Types of Cells attracted to the site of infection that mediate inflammation:

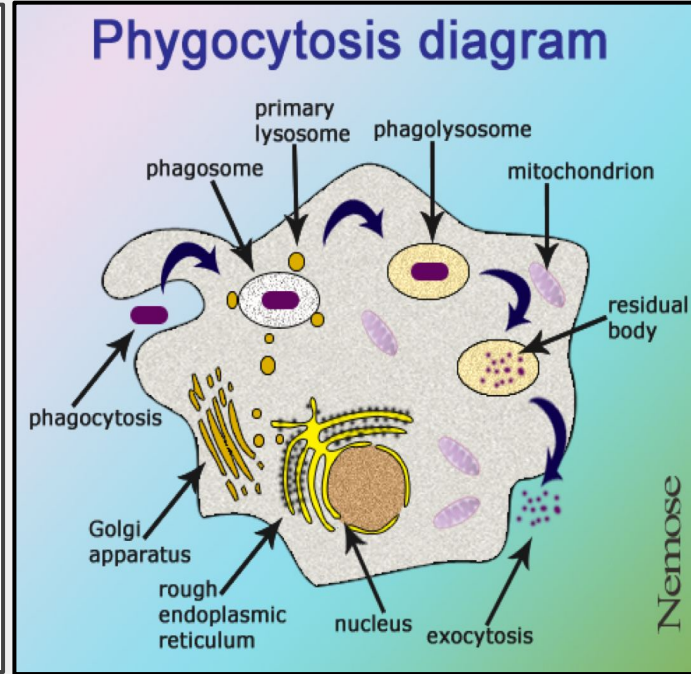
1- **Monocytes:** Become **Macrophages** when they leave the blood and enter the tissues.

2- **Neutrophils:** (Phagocytic cells).

3- **Eosinophils:** (Allergy and Parasitic infections).

4- **Natural Killer (NK) cells:** (Kill tumor cells and virus infected cells).

Phagocytic cells (neutrophils & macrophages) at site of infection start the process of **phagocytosis** which is the process by which a cell engulf a solid particle such bacteria to form internal vesicle known as **phagosome**.





# Cytokines

**Soluble molecules, produced by different cells, that control cell functions**

e.g. differentiation, proliferation activation or inhibition.

**\*Information vector: when the cell is not able to send the information it will send cytokines instead.**

**More explanation:**

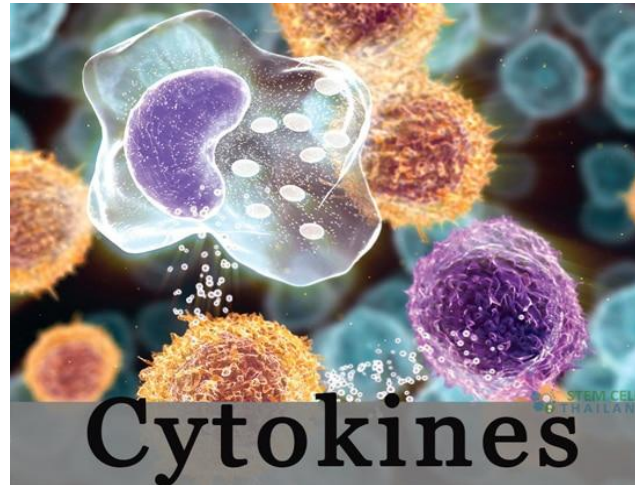
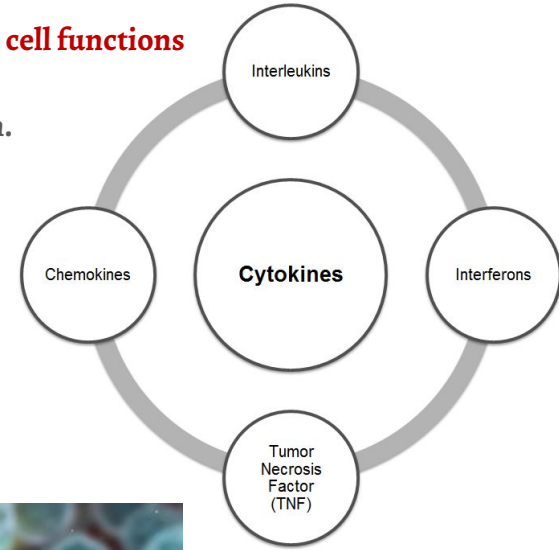
**When the cell is infected by a virus it will secrete some of the interferons \* type of Cytokines\* to the near cells that the cell has been infected and the other cells to protect itself.**

**the near cells will produce a defence mechanism against the infection**

**Dr's Note:**

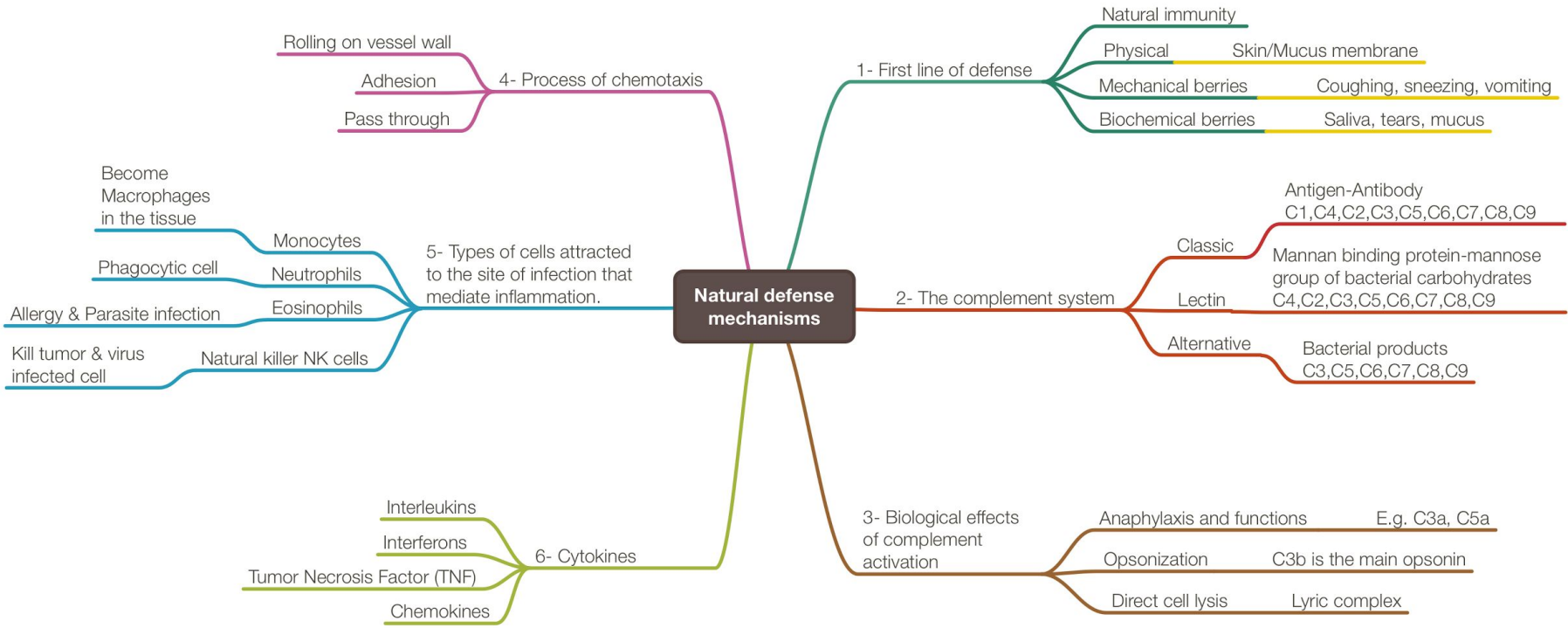
**\*Cytokines are glycoproteins used by cells in the immune system to communicate between each other.**

**So, cytokines are important in the innate immunity**



# Cytokines

Interleukins	Interferons	Tumor necrosis factor (TNF)
<p>1- Produced primarily by macrophages and lymphocytes in response to a pathogen.</p> <p>2- Many types Examples... IL-1, IL-2, IL-3 ...</p>	<p>1- Protects against viral infections.</p> <p>2- Produced and released by virally infected cells in response to viral infections.</p>	<p>-Secreted by macrophages.</p> <p>-Induces fever by acting as an <b>endogenous pyrogen</b> (a substance released from inside the body that produces fever).</p> <p>- Increases synthesis of inflammatory serum proteins.</p> <p>- Increase expression of adhesion molecules on endothelial cells and vascular permeability.</p>



# MCQ

1-Example of Specific defense mechanisms (second line of defense ) is

- A- skin                      B- phagocytic white cells  
C-antimicrobial proteins   D-lymphocytes

2-it is lining the gastrointestinal genitourinary and respiratory tracts.

- A- blood vessel              B- muscles  
C- mucous membranes   D- endothelial cells

3- if the Body is secreting contain anti-bacterial substances that's called

- A- inflammation            B- physical barrier  
C- biochemical barriers   D- mechanical barriers

4-the first response of the immune system to infection or irritation is called

- A- mechanical barriers    B-inflammation  
C-biochemical barriers    D-physical barrier

5-What is the system that plays an important role in linking Innate & Adaptive immunity

- A- circulations system    B-complement system  
C-immune system          D-cardiovascular system

6-Pathways of activation from C2 until C9 is called

- A-Classical pathway    B-Alternative  
C-Lectin                      D-complement pathway

7-which of the following cells exist in Allergy and Parasitic infections

- A-Monocytes                B-Neutrophils  
C-Natural Killer (NK) cells   D-Eosinophils

8-internal vesicle known as

- A-phagocytosis            B-phagosome  
C-lysosomes                D-endocytosis

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