

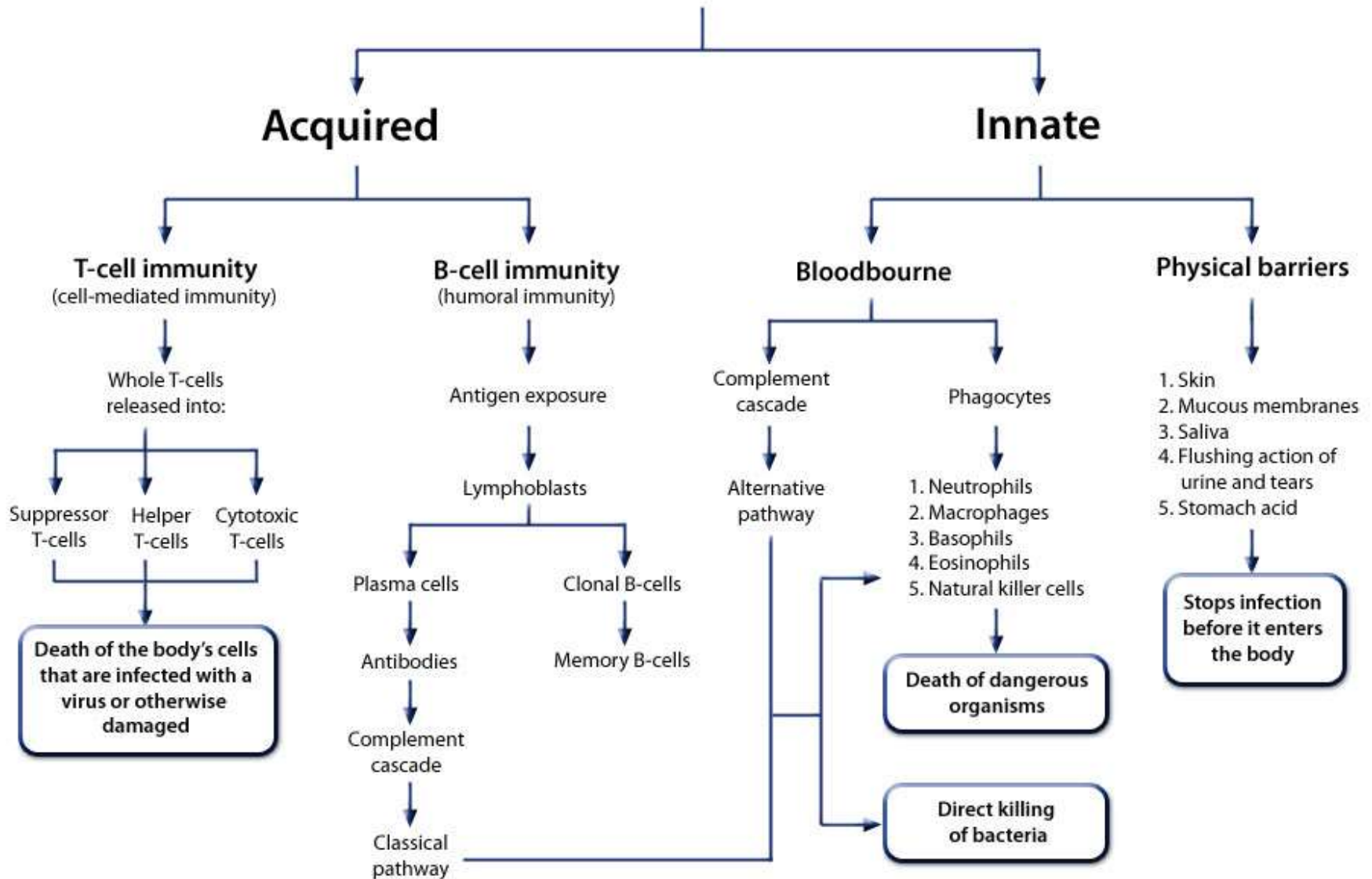
# immunity and innate immunity

Dr.Eman Albataineh,  
Associate Prof. Immunology  
College of Medicine, Mu'tah university  
Immunology, 2<sup>nd</sup> year students

# History

- Immunity: protection from infectious microbes or foreign macromolecules; proteins and polysaccharides
- Immune system constitutes of cells, tissues and small molecules
- The first application in immunology is done by Edward Jenner's vaccination against smallpox when he injected parts of cowpox microbe into a small boy who later became resistant to smallpox disease in 1798 (vaccine)
- This was crowned in 1980 when the WHO announced the smallpox has been eradicated worldwide.

# Immune system



# Immunity in practice

- The innate immune system ( the first to act;),
  - consists of physical, chemical and cellular defenses against pathogens( complements and cells)
  - present and act the same in all people against general antigens.
  - it is monotonic; the same magnitude and speed of response each time,
  - not specific, act against common microbial antigens..
- The second is adaptive immune system (T and B cells),
  - it is specific act against certain antigen,
  - increasing in magnitude and speed of response in re-exposure to the same antigen (memory)

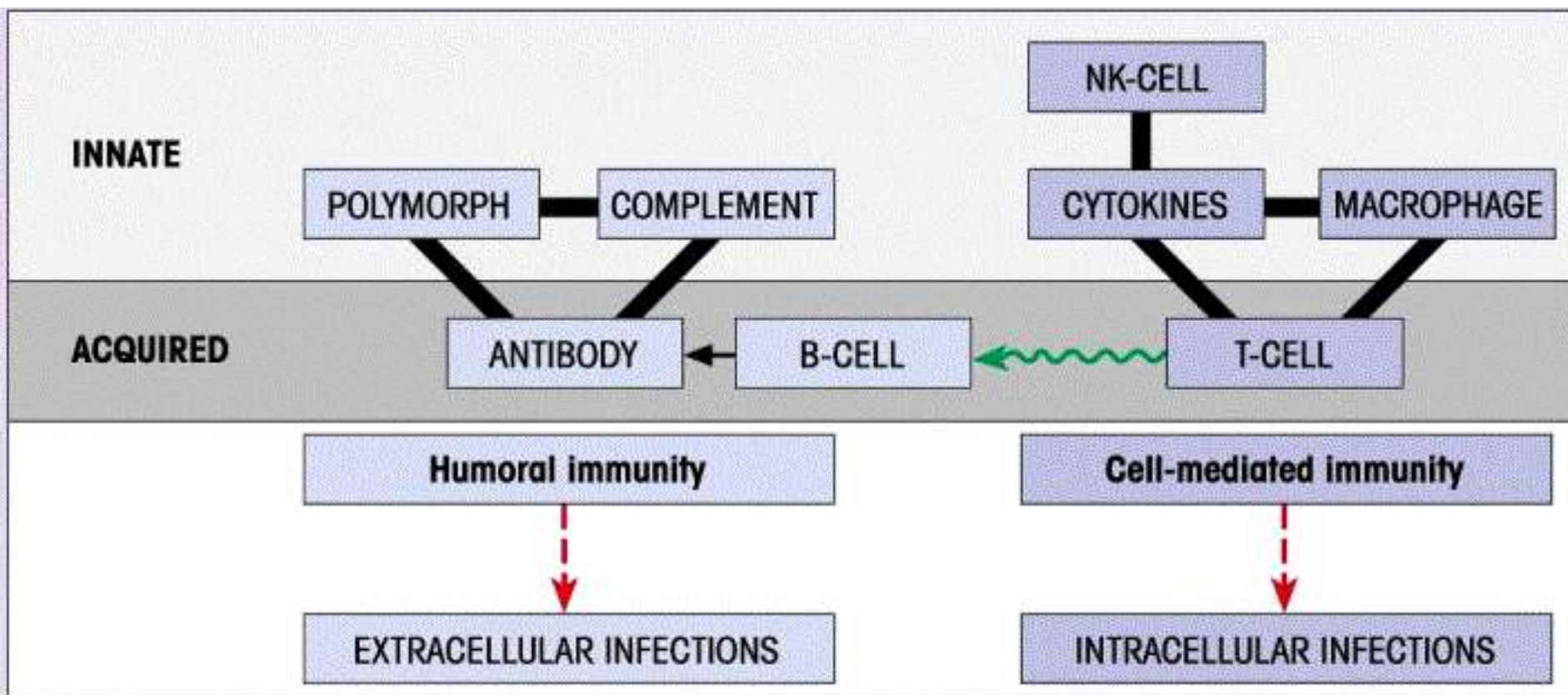
- The first line of defense is provided by
  - barriers , Mechanical; skin, Chemical; acidic stomach,
  - Enzymes and anti-microbial peptides as defensins and surfactants
  - Complements and cytokines, Phagocytes and natural killers (Innate immune system)

# Innate immunity

- Innate immunity is the initial response to microbes that prevents, controls, or eliminates infection, eliminate damaged cells and initiate the process of tissue repair.
- Innate immunity stimulates adaptive immune responses
- the major responses of the innate immune system that protect against microbes is started by inflammation in local tissue, innate cells activation, complements activation and production of cytokines.

# Innate and Adaptive

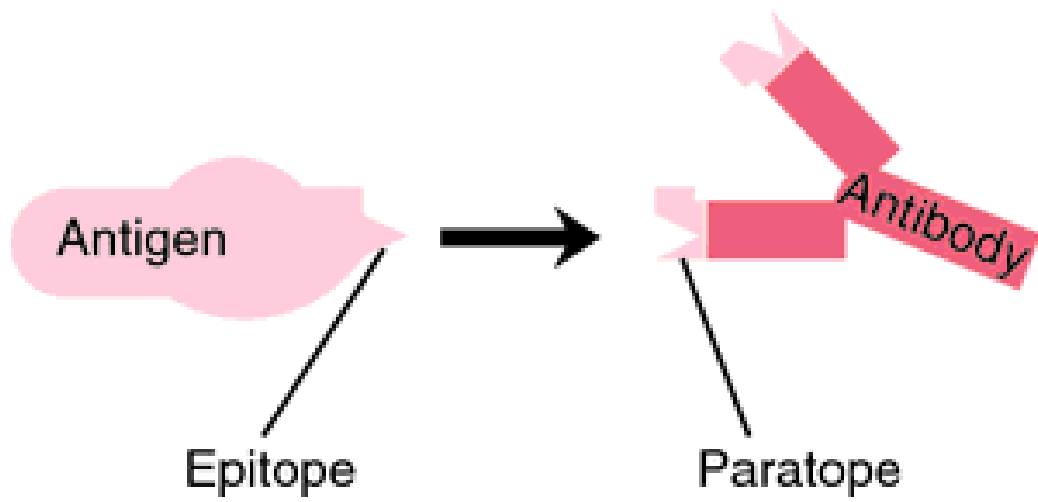
- Innate immune response is better than adaptive in recognizing self from non-self.
- Innate immune responses to a foreign microbe are immediate and do not require prior exposure to the microbe
- effective adaptive immune responses to a newly introduced microbe develop over several days as T and B lymphocytes are activated by some activated innate cells and they undergo expansion and differentiate into functional effector Th and Tc cells and antibody producing B cells.
- The targets of the innate immune response is essential for the survival of the microbes





# Antigen and immunogen

- Any particle (organism, molecule or part of molecule) that is recognized by the immune system called antigen
- antigen that does not stimulate the immune response called (hapten, tolerogen)
- antigen that stimulate the immune response called (immunigen)
- Each antigen contain one or more antigenic determinant that are specific for binding to immune components; called epitopes
- Epitopes are the smallest part of an antigen that is seen by antigen receptors on adaptive immune cells, or antibodies.



# Haptens

- Very low molecular weight antigen need to conjugate to a carrier protein to induce the immune response, then the immune response will direct against both the carrier and the hapten
- Examples
  1. Drugs as penicillin
  2. Food additives, lipids, nucleic acids, small peptides and carbohydrates

# tolerogen

- Antigen that induce tolerance. Tolerance (antigen- insensitive) can develop later in life to antigens present frequently as cat fur or antigens that administered orally or exposed to in early life (immunotherapy to house dust mite). Tolerogens induce negative or diminished immune response.

# Factors increase the antigenicity

1. More Foreignness more response

2. More Chemical complexity

Proteins are most potent, polysaccharides are both antigenic or non antigenic whereas nucleic acids and lipids are non antigenic but can be antigenic when bind protein carriers

3. High molecular weight antigen, whereas haptens have very low molecular weight

4. Higher Biodegradable

5. Mode of contact more response in Intra venous than subcutaneous or Intramuscular injections.

6. More different Host genetics like HLA type in organ transplant

# Types of antigens

- Auto-antigen
- Iso-antigen; found in genetically identical twins, like HLA antigens
- Allo-antigens; found in members of the same species; blood groups in human
- Xeno-antigen; found in different species like animals and human

**TABLE 1-3****Comparison of adaptive and innate immunity**

	<b>Innate</b>	<b>Adaptive</b>
Response time	Hours	Days
Specificity	Limited and fixed	Highly diverse, improves during the course of immune response
Response to repeat infection	Identical to primary response	Much more rapid than primary response

# Phases of innate immune cells response

- Antigen enter tissue cause **inflammation** which activate the local innate cells ( mast cells, macrophages)
- Movement of the cells from all body toward the site of infection called **chemotaxis**, and mediated by molecules secreted from local innate cells.
- **Functional activities** of the immune cells
  - Recognition of the foreign antigen through cell receptors
  - Response
    - Effector or activated cells
    - Memory ( only in adaptive response)



# Inflammation

- Inflammation is the process by which local immune cells produce signals (cytokines) or local complement activated so that recruit circulating immune cells to sites of infection in the tissues and are activated to destroy and eliminate the offending agents.
- Inflammation is also the major reaction to damaged or dead cells and to accumulations of abnormal substances in cells and tissues.
- It is the major way by which the innate immune system deals with infections and tissue injury

# Changes in inflammation

- A. Increased blood supply to the area
- B. expression of endothelial adhesion molecules on blood vessel lining
- C. Increase capillary permeability
- D. Activation of local innate cells to secrete chemotactic factors that recruit leukocytes,

# inflammation

- Signs of inflammation
  1. Swelling
  2. Pain
  3. Redness
  4. Loss of function
  5. Heat
- Cells of inflammation
  - Local macrophages and Mast cells that secrete mediators (cytokines) or local complement activation that help in chemotaxis of other innate cells and increase vascular permeability



# Cell chemotaxis

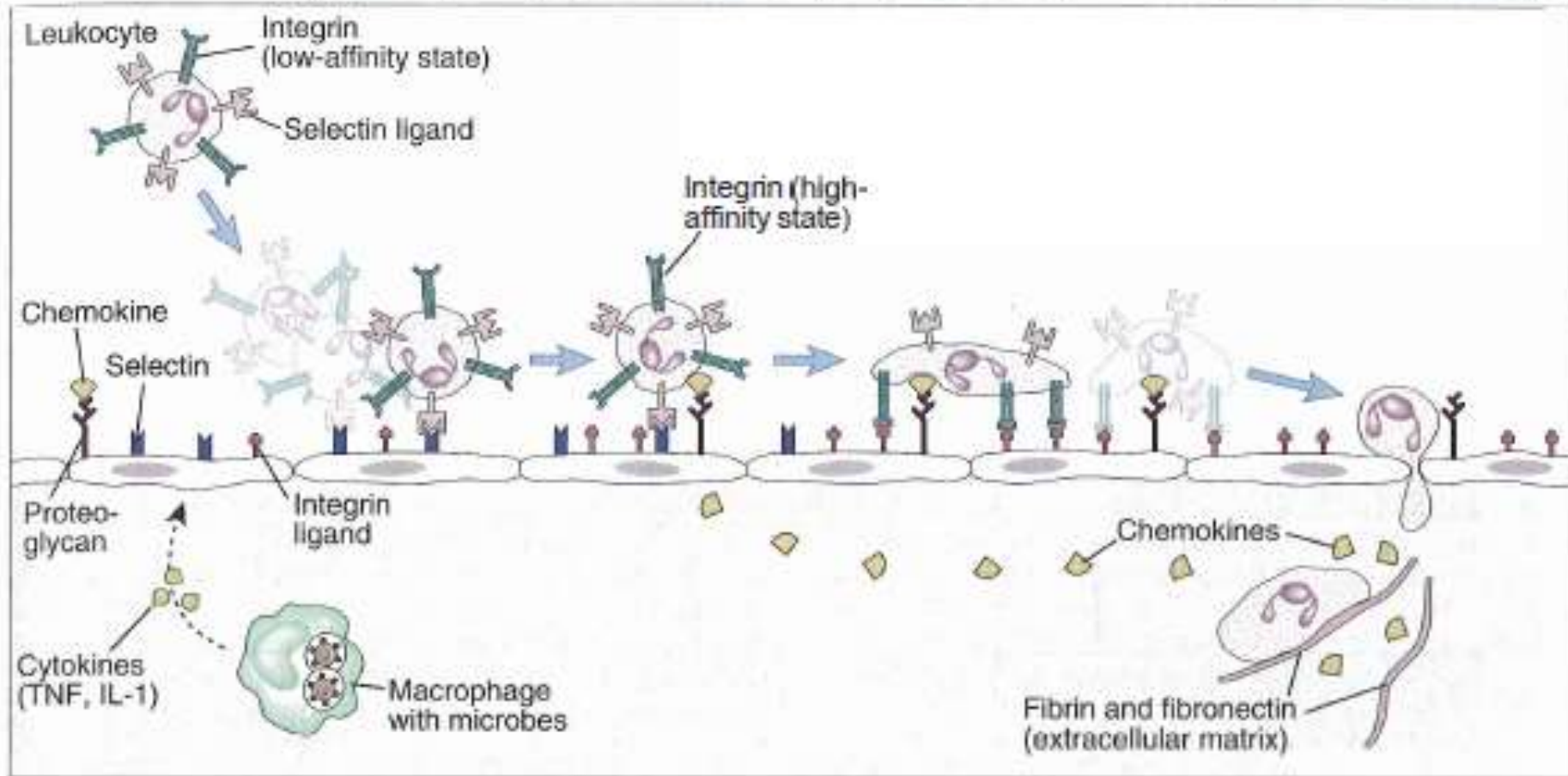
- ❖ Recruitment of phagocytes to site of infection
  - Follow chemotactic factors gradient(cytokines) produced by resident macrophages and (complements) activated by peptides of bacteria, they migrate by
    - Capture and rolling; enhance adhesion molecules on both endothelial and innate immune cells
    - enhance the strength of binding of interacting molecules on both endothelium and leucocytes that make the leukocyte flatten
    - Extravasation to site of infection. First neutrophils then macrophages. activated T cells migrate in the same way

Rolling

Integrin activation  
by chemokines

Stable  
adhesion

Migration through  
endothelium



# Recognition by innate immune cells

## ❖ Recognition phase

-Innate immune cells recognize structures found only on microbes called pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRR). The PAMPs may be;

1. double stranded RNA in viruses
2. DNA in bacteria
3. Lipo-polysaccharides or endotoxins in G- bacteria
4. Teichoic acid in g+ bacteria
5. Mannose rich oligo-saccharides

-The innate immune system also recognizes endogenous molecules that are produced by or released from damaged and dying cells. These substances are called damage-associated molecular patterns (DAMPs)

# Receptors

- The receptors on the surface of the innate immune cells are fixed in all human being and encoded by inherited (germline) genes present from early life
- Whereas the genes encoding receptors of adaptive immune cells are variable and generated by a process called somatic recombination of gene segments in the precursors of lymphocytes throughout the life
- In Innate cells the receptors are present in nature, and are less in number ( $10^3$ ) and less variety than adaptive cells receptors



# Receptors of innate immune cells

- Via Pattern recognition receptors (PRR).
  - They are proteins expressed by cells of the innate immune system to identify pathogen-associated molecular patterns (PAMPs), which are associated with microbial pathogens or cellular stress, as well as damage-associated molecular patterns (DAMPs), which are associated with cell components released during cell damage
  - PAMP is general conserved microbial molecules as sugar, protein, lipid and nucleic acids.
  - the receptors are similar in all humans,
  - And bind to the target :
    1. directly through cell surface receptors binding to the antigen
    2. indirectly by binding to soluble molecules that engage the microbe( opsonins as complements)

# Receptors of innate immune cells (PRR)

PRR are 3 types

1. Toll like receptors (TLR), binding results; signaling; phagocyte activation and secretion of immune mediators called cytokines
2. Scavenger receptors they help in internalization of bacteria in the phagocytic cells

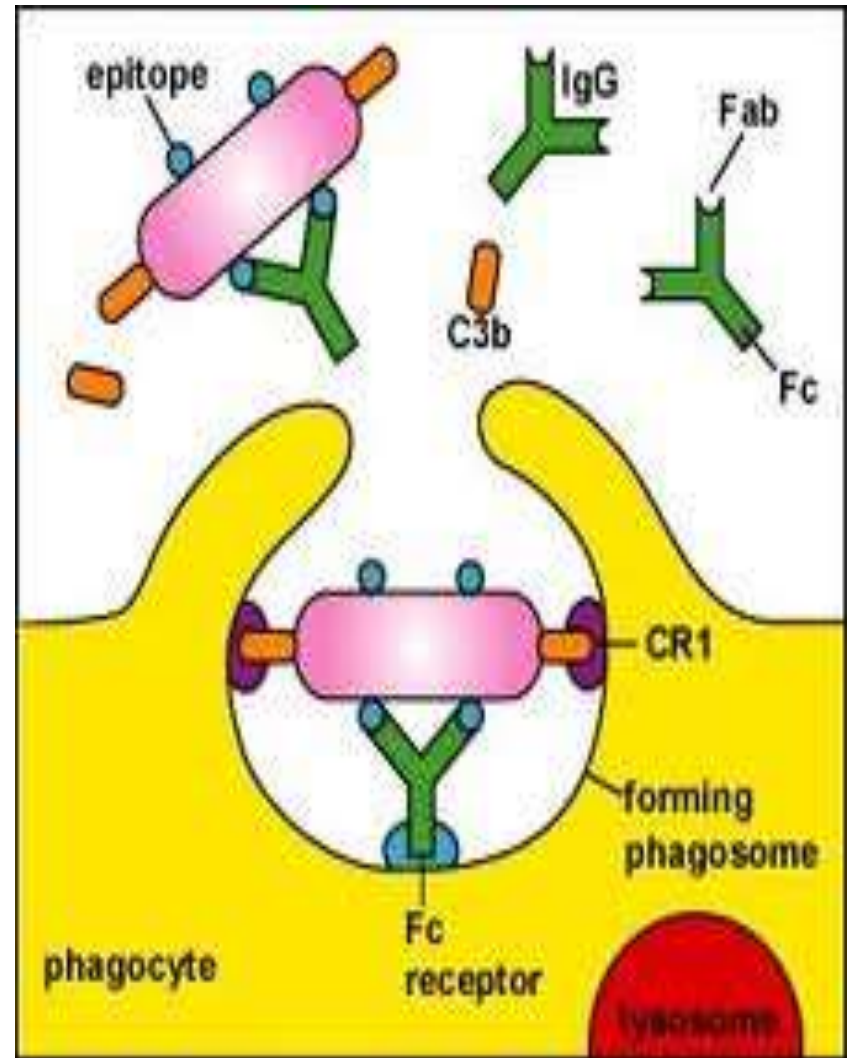
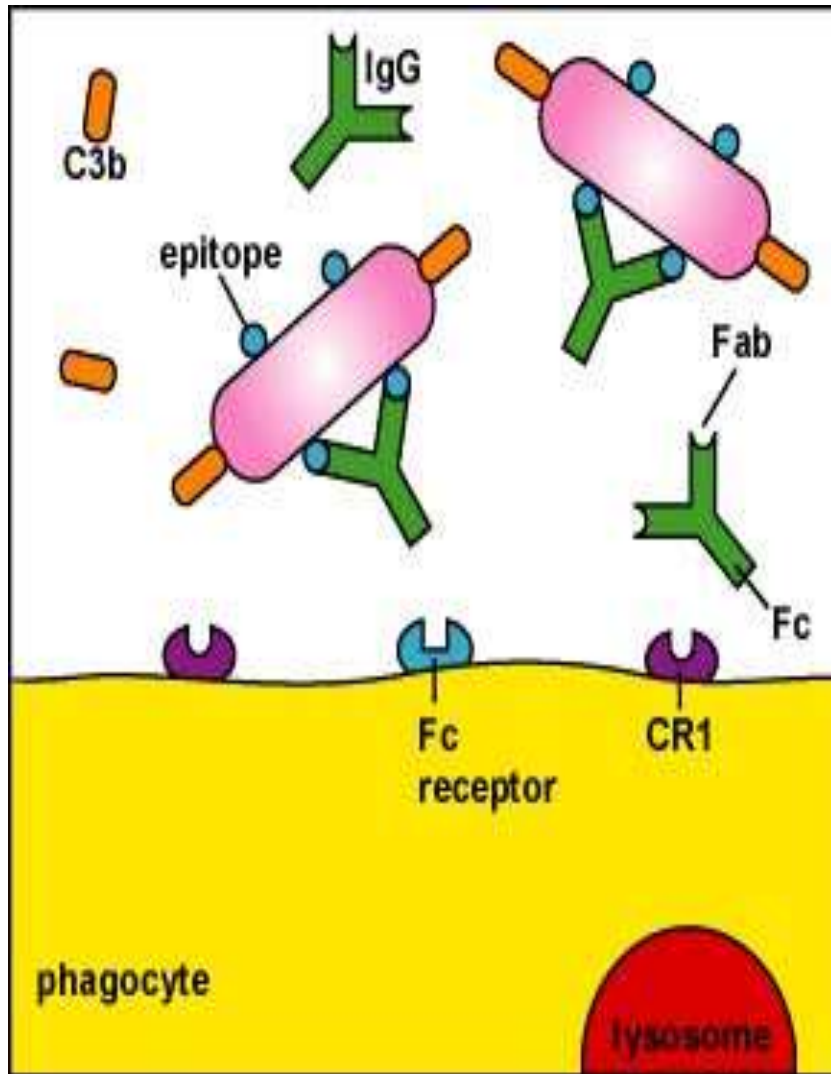
# Receptors of innate immune cells (PRR)

3. opsonin receptors (Opsonization of microbe :coating the microbe to make it obvious)

- Act indirectly by binding to soluble molecules that engage the microbe The result is microbe internalization to the cell.

1. complements receptors C4b, C3b and C3bi complements receptors
2. or antibodies receptors. using IGG or IGM. 2 types
  1. Direct opsonization by IGG, IGA
  2. Indirect opsonization by IGM + complement

# Opsonins



PAMP	PRR	Biological Consequence of Interaction
Microbial cell wall components	Complement	Opsonization; Complement activation
Mannose-containing carbohydrates	Mannose-binding protein	Opsonization; Complement activation
Polyanions	Scavenger receptors	Phagocytosis
Lipoproteins of Gram + bacteria Yeast cell wall components	TLR-2 (Toll-like receptor 2)	Macrophage activation; Secretion of inflammatory cytokines

# The job of innate cells; 1-Ingestion in macrophages and neutrophils

- Intracellular killing, mechanisms of lysosomal killing
  - O<sub>2</sub> dependent; the process called respiratory burst. O<sub>2</sub> metabolites are; hydrogen peroxide, singlet oxygen, hydroxyl radical, hypochlorite (OCl or OI) and nitric oxide
  - O<sub>2</sub> independent; using granules contents as proteases, hydrolases and nucleases

## 2-Secretion of cytokines

- Help in attraction of cells to site of infections
- Induce signs of inflammation as high temperature

# 3- activation of the adaptive immune sys.

- Mediated by mainly Macrophages
- By either
  - Indirect way; secretion of molecules that attract adaptive cells to site of infection
  - Direct way; present antigen to T cells.



# Innate immune cells

## A. phagocytic cells

- **Neutrophil polymorphs, main**
- **Mononuclear phagocytes**, phagocytic, and help in acquired immune response. They have many names; kupffer cells in liver, histiocytes in connective tissues, macrophage in bone marrow, spleen and lymph nodes, langerhans' cells in skin, osteoclast in bone, mesangial cell in kidney, microglial cells in brain and monocytes in blood.

## B. Non phagocytic cells; Extracellular killing

- **Eosinophils and basophils**
- **Natural killer cells,**

# Innate immune cells 1-Mononuclear phagocyte system (macrophages)

- have rounded or kidney-shaped nuclei with finely granular cytoplasm
- Mononuclear phagocyte's primary function is phagocytosis
  - Originate in BM, and first to leave. When monocyte becomes settled in tissue they are called macrophages. Some mononuclear cells may differentiate to dendritic cells. some joint to form multi-nucleated giant cells

# Activation and function of macrophages

- Functions in Natural and adaptive Immunity
- 1. Phagocytosis of foreign particles the same as neutrophils**
    - Scavenger receptors
    - opsonin dependant phagocytosis; engulf antigen antibody complex as in viruses via **receptor for opsonizing IgG and complement C3b, No receptors for IGM**
  - 2. Secretion of enzymes and oxidative metabolites if antigen is big, cause tissue damage**  
(respiratory burst- oxygen radicals, NO, prostaglandins)
  - 3. Cytokine production which recruit other inflammatory cells,**
  - 4. Antigen-Presentation to T cells,**

# 2-Neutrophils

- Granulocytes contain nucleus segmented into 3-5 connected lobes, hence the name polymorphonuclear leukocyte and cytoplasmic granules. **Neutrophils (95% of granulocytes)** respond w/i 24 hours of stimulus (the earliest). have 20 times as many receptors as macrophages. They have Fc receptor to IGG and IGA as well as complement receptors.
- Intracellular killing by azurophil lysosomal granules and specific granules.
- Cytokine production which recruit other inflammatory cells,

# phagocytosis

