

Chapter 14

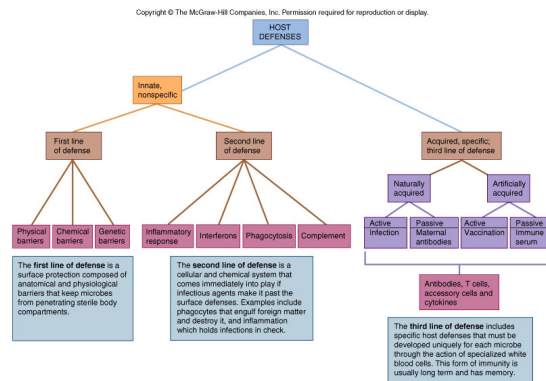
Topics

- Defense Mechanisms
- Non-specific immunity

Defense Mechanisms

- **Innate - Non specific**
 - First line of defense
 - Second line of defense
- **Acquired - Specific**
 - Third line of defense

Summary of the major components of the host defenses.



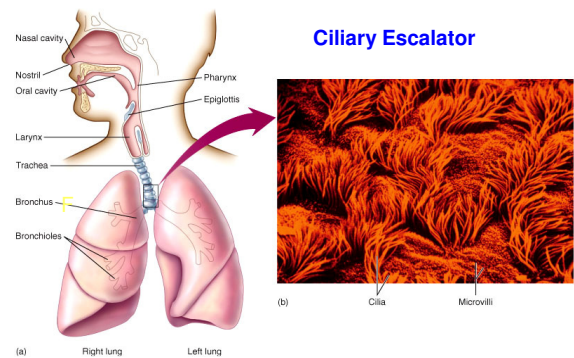
First line of defense

- **Barriers**
 - Anatomical
 - Chemical

Anatomical barriers

- **Skin**
 - Outermost layer
 - Hair follicles
 - Skin glands
 - Dequamation
- **Mucous membrane**
 - Digestive
 - Urinary
 - Respiratory
 - Eye

The trachea contain cilia that entrap and propel particles out of the respiratory tract



Chemical barriers

- Sebaceous secretions
- Tears and saliva – lysozyme
- Acidic pH
 - Sweat
 - Stomach
 - Skin
 - Semen
 - Vagina - mediated by presence of *Lactobacillus*

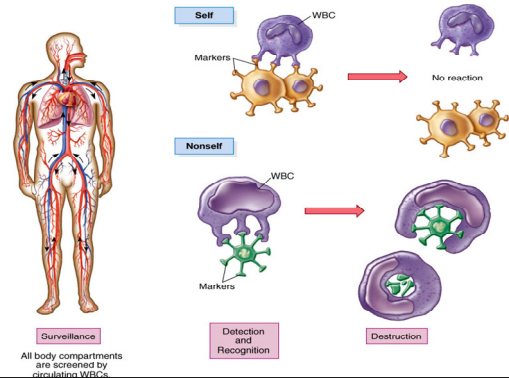
Immunology

- Study of the development of resistance to infectious agents by the body
 - Surveillance of the body
 - Recognition of foreign material
 - Destruction of foreign material or agent
- Involve nonspecific (**Second line**) and specific (**Third line**) immune defense systems
- White blood cells (WBC) or leukocytes are involved

WBC

- WBC recognize "self" markers on the host cell
 - Do not attack or do not respond to host cell
- WBC recognize non-self markers on the invading microbe
 - Attack or respond to microbe

Search, recognize, and destroy is the mandate of the immune system

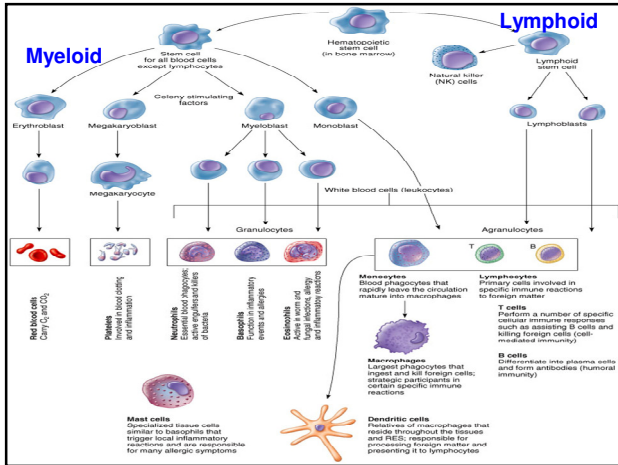


Blood

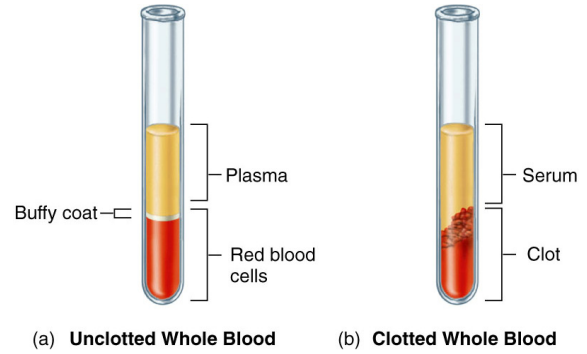
- Stem cells precursors
- Hemopoiesis
- Components

Hemopoiesis

- Production of blood
 - Starts at the embryonic stage
 - Yolk sac and liver
 - Continues during adult stage
 - Hematopoietic stem cells in **bone marrow**



The macroscopic composition of whole blood



White blood cells

- **Leukocytes**
 - **Granulocytes** (large cytoplasmic granules)
 - Neutrophils
 - Basophils
 - Eosinophils
 - **Agranulocytes**
 - T cells
 - B cells
 - Monocytes

Neutrophils

- Present in high numbers in blood and tissue
- Phagocytizes bacteria – granules contain digestive enzymes
- First to arrive during an immune response (inflammation)

Eosinophils

- Contain granules with hydrolytic enzymes
- Attach and destroy large eucaryotic pathogens (**worms**)
- Associated with **inflammation** and **allergies**

Basophils

- Present in low in number in the body
- Function is similar to eosinophils. Involved in **allergic reactions** due to cytoplasmic granules
- Localized basophils are called **mast cells**

Lymphocytes

- **Specific immunity**
 - T cells → cellular immunity
 - B cells → humoral/antibody immunity
- Third line of defense
- Present throughout the body

Monocytes

- Agranulocyte
- Differentiate into macrophages (**circulation and lymphatics**) and **dendritic cells** (tissue associated)
- Phagocytosis

Lymphatic system

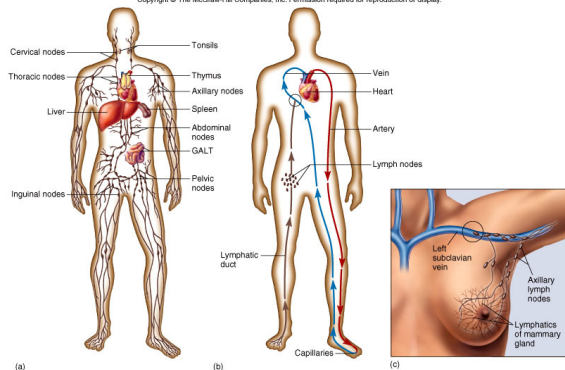
- Network of vessels, cells, and tissues that extend to most body areas
- Connected to the blood system
- Provides an auxiliary route for the **return of extracellular fluid** to the circulatory system
- “Drain off” system for inflammatory response
- Contains lymphocytes, phagocytes and antibodies

Lymphatic system

- Fluids
- Vessels
- Nodes
- Spleen
- Thymus
- Miscellaneous (GALT)

Representation of the lymphatic system.

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Gut-associated lymphoid tissue (GALT)

- Recognized incoming microbes from food
- Supply lymphocytes for antibody response
- Ex. Appendix, lacteals, Peyer's patches

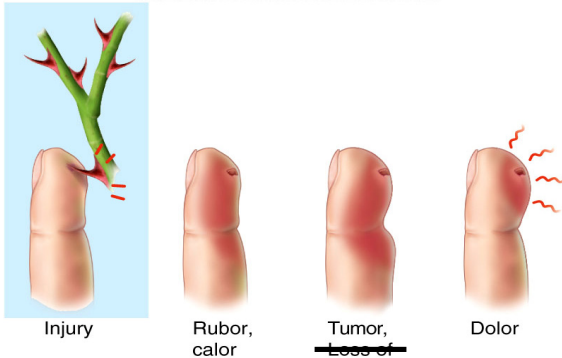
Non-specific Immunity Second Line of Defense

- Inflammation
- Phagocytosis
- Interferon
- Complement

Inflammation

- Four major symptoms
 - Redness
 - Warmth
 - Swelling
 - Pain
- That result in **Cellular Damage**

Inflammation - 1



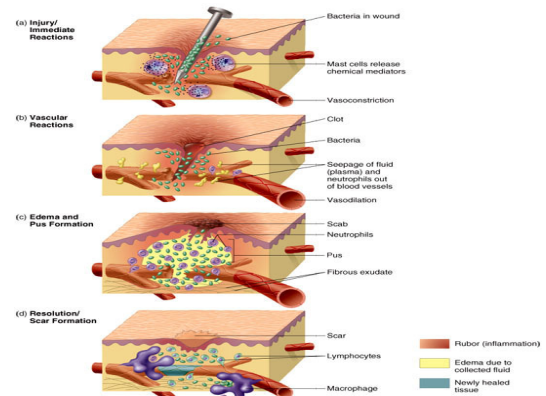
Causes

- Trauma
- Tissue injury due to physical or chemical agents
- Reaction to foreign pathogens or bodies (ie medical implants)

Function

- Mobilize and attract immune components to the site of injury
- Localized and remove harmful substances
- Destroy microbes and block their invasion
- Aid in the repair of tissue damage

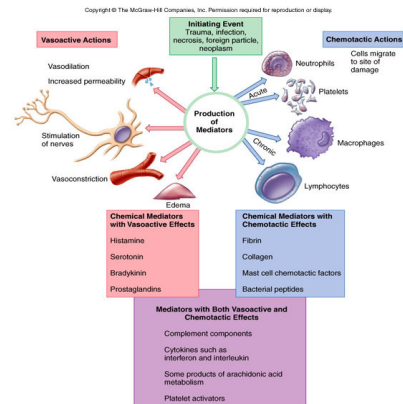
Inflammation - 2



1. Vascular changes

- Blood cells, tissue cells, and platelets release **chemical mediators** and **cytokines**
- Chemical mediators
 - **Vasoactive**
 - Affect endothelial cells, smooth muscles of blood vessels
 - **Chemotactic (chemokines)**
 - Affect WBC

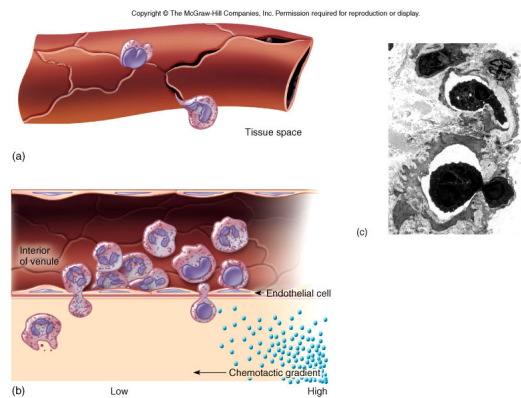
Chemical mediators during inflammation.



2. Edema

- Leakage of vascular fluid (**exudate**) into tissue
- Exudate - plasma proteins, blood cells (WBC), debris, and pus
- Migration of WBC is called diapedesis or transmigration
 - Chemotaxis

The transmigration of WBCs is followed by chemotaxis.



3. Fever

- **Caused by pyrogens**
 - reset the **hypothalamic** thermostat (increase temperature)
- **Pyrogens**
 - Microbes and their products (ex. LPS)
 - Leukocyte products (ex. Interleukins)
 - **IL-1 resets the thermostat**
- **Inhibits microbe and viral multiplication, reduces nutrient availability, increases immune reactions**

Phagocytosis

Neutrophils and monocytes/macrophages (and dendritic cells) are called professional phagocytes

Eosinophils

Phagocytosis

Neutrophils - First to arrive during an immune response (inflammation)

- Neutrophils are primary components of pus

Monocytes/Macrophages -

Differentiate into **macrophages** (circulation and lymphatics) and **dendritic cells** (tissue associated)

Macrophages

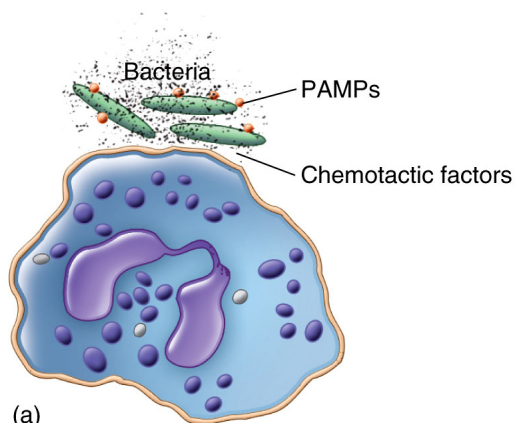
- Monocytes/macrophages → motile
- Specialized/Residents:
 - Alveolar → lungs
 - Langerhan cells → skin
 - Kupffer cells → liver
- 1) Responsible for phagocytosis
- 2) Interact with B and T cells

Mechanism of Phagocytosis

- Chemotaxis
- Ingestion
- Phagolysosome
- Destruction

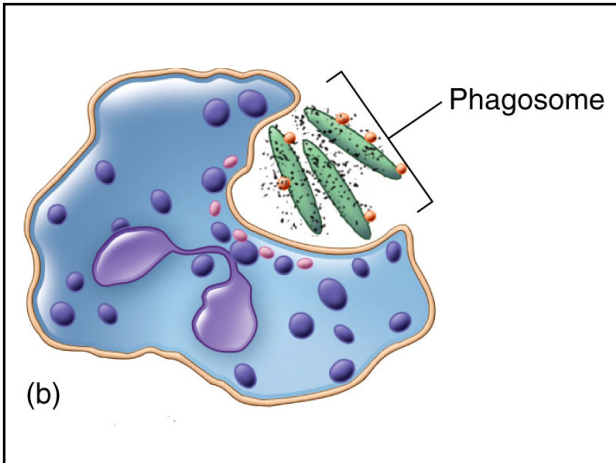
1. Chemotaxis & binding

- Directed by
 - Pathogen-associated molecular patterns (**PAMPs**)
 - Peptidoglycan
 - LPS
 - Foreign debris



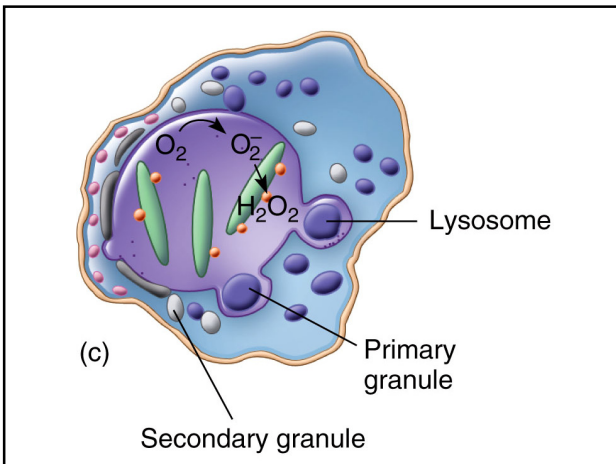
2. Ingestion

- Pseudopods enclose the pathogen or foreign material
- Form a **phagosome** or **phagocytic vacuole**



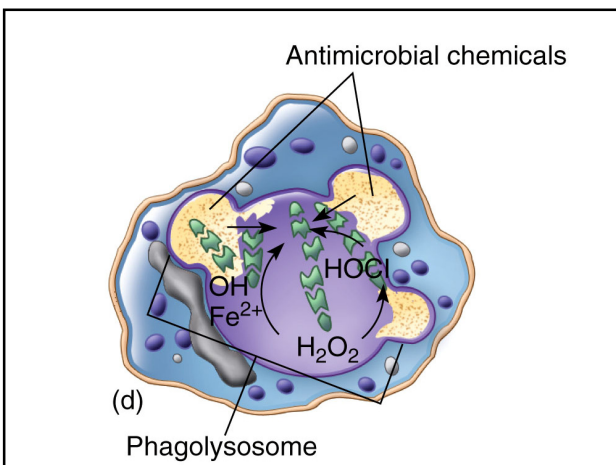
3. Phagolysosome

- **Lysosomes** fuse with the phagosome
- Other antimicrobials chemicals are released into the phagolysosome



4. Destruction

- Within the phagolysosome
 - A) **Oxygen-dependent mechanisms** – Similar to byproducts of respiration
 - B) **Oxygen-independent mechanisms** – due to numerous hydrolytic enzymes
- Undigestible debris are released



Interferon

- Produced due to viral infections, microbe infections, RNA, immune products, and antigens

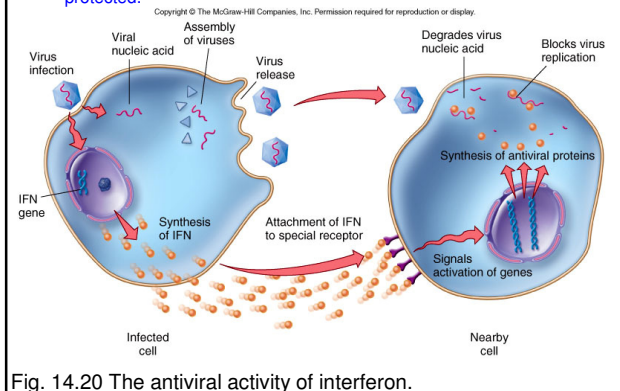
Classes

- Interferon alpha
 - Product of lymphocytes and macrophages
- Interferon beta
 - Product of fibroblasts and epithelial cells
- Interferon gamma
 - Product of T cells

Activity

- Ex. Virus - binds to host cell
- A signal is sent to the nucleus to synthesized (transcription and translation) interferon
- Interferon is secreted
- Binds to other host cells
- Host cells produce antiviral proteins
 - inhibit viral multiplication or translation
 - Not virus-specific

Interferon is produced, released, and taken-up by a near-by cell, where by original cell is not protected but the recipient cell is protected.



Other Roles of Interferon

- Activates and instructs T and B cell development
- Inhibits cancer cells
- Activates macrophages

Complement

- Consist of ~26 blood proteins
- **Produced** by liver hepatocytes, lymphocytes, and monocytes
- Pathways
- Cascade reaction
- Stages

Pathways

- **Classical**
 - Activated by the presence of antibody bound to microbes
- **Lectin**
 - Activated when a host serum protein binds a sugar (mannan) in the wall of fungi and other microbes
- **Alternative**
 - Activated when complement proteins bind to cell wall or surface components of microbes

The three complement pathways, their activators, and the complement proteins involved.

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Pathway	Activators	Host Components That Initially Bind	Complement Proteins Involved
Classical (Rapid, efficient)	Complement-fixing antibodies (IgG, IgM) (sometimes microbe surface components)	C1 complex	C1 complex C4 C2 C3
Lectin	Mannans	Mannose-binding lectin	C5 C6 C7 C8 C9 Membrane Attack Complex
Alternative (Slower, less efficient)	Bacterial or fungal cell wall Viruses Parasite surfaces	C3	C3 Factor B Factor D Properdin

Table 14.1 Complement pathways

Stages

- Initiation
- Amplification and cascade
- Polymerization
- Membrane attack

Fig. 14.21a

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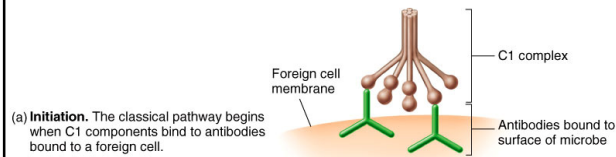


Fig. 14.21b

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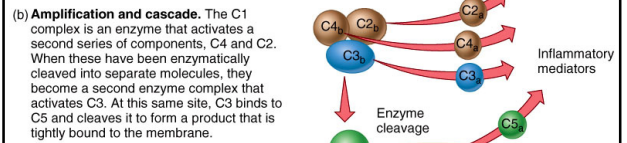
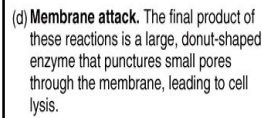
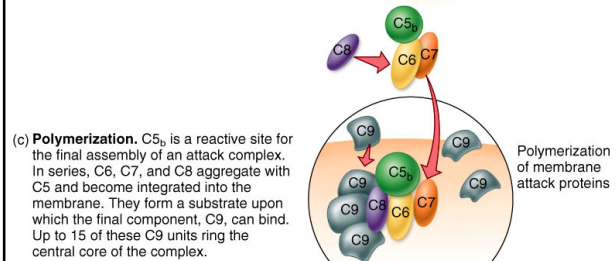


Fig. 14.21d

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Complement does 3 things

- **Inflammation** → C3a, C4a, C5a
- **Opsonization** → C3b
- **MAC killing** → C5-C9