Chapter 15

Innate immunity

What is nonspecific host resistance?

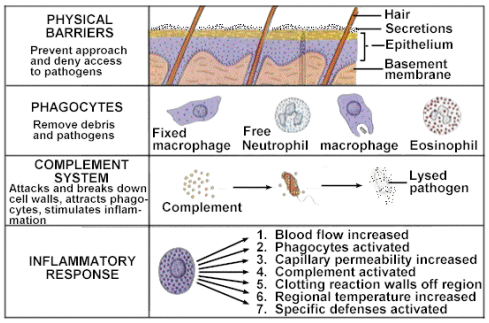
- Mechanisms that are not directed at any one specific pathogen.

•A Global Shield

Nonspecific defenses

- Physical barriers
  - Skin, mucous membranes and chemicals
- Chemical barriers
  - Substances in saliva, gastric juices, iron limitation
- Cellular defenses
  - Phagocytosis
- Inflammation
  - Reddening, swelling, localized temperature increases
- Fever
  - Hostile environment, toxin inactivation
- Molecular defenses
  - Interferon, complement

Non-specific defenses



Other resistance factors

- Physical and emotional stress.
- Age.
- General health and state of nutrition.
- Socioeconomic conditions.
- Occupational hazards.
- Personal hygiene.

Species, Racial, Individual Resistance

- Physiological and anatomical characteristics.
- Genetic or racial factors.
- Individual susceptibility to disease.

Physical Barriers

- Skin
- mucous membranes
- Chemical secretions
- Hairs in the nose
- Cilia on the trachea
- Coughing and sneezing
- Urine flow
- Normal flora.

Skin and mucous membranes

- Mechanical barrier.
- Low moisture.
- Low pH.
- Inhibitory secretions.
- Secretion of mucus.

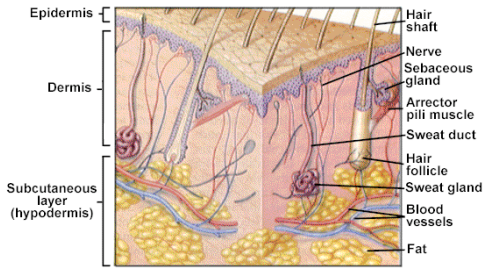
Normal flora

- Prevent colonization of pathogens.
  - Out compete for nutrients
  - Release of toxic substances that inhibit pathogens
- Stimulate the production of cross-reactive antibodies
- Stimulate the development of certain tissues, i.e. Peyer's patches

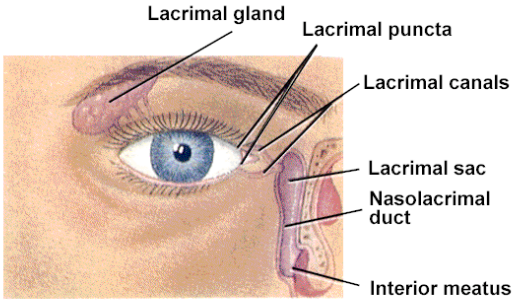
Chemical barriers

- Lysozyme is an enzyme that breaks down peptidoglycan.
- Sebum is an oily secretion from the sebaceous glands of the skin.
- Gastric juice contains hydrochloric acid.
- Lactoferrin is protein found in body secretions that binds iron.

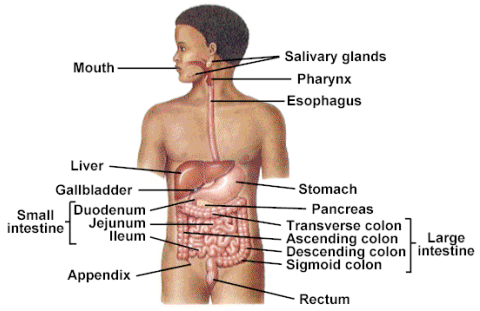
Skin



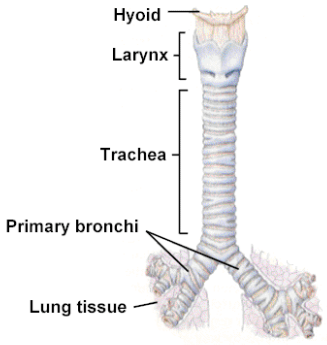
Lysozyme is excreted in tears



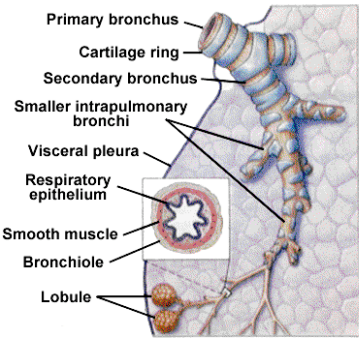
Other tissues



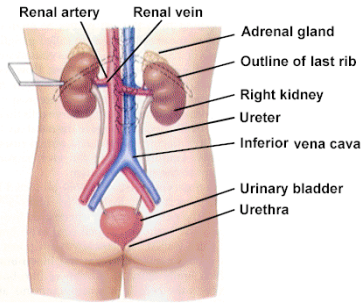
Trachea



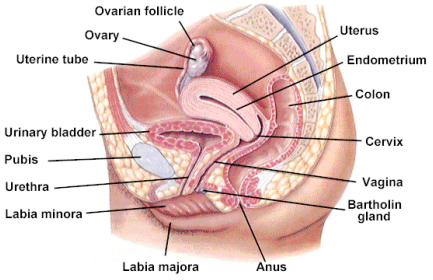
Bronchi



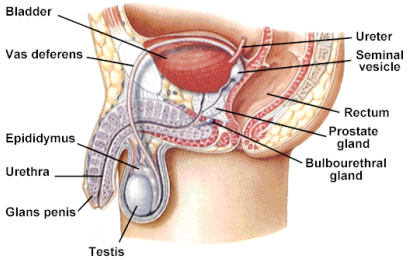
Distance of ureters prevents infection



Female are more prone to UTI



Male urethra is 20 cm vs 5 cm

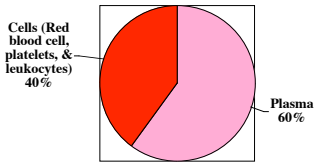


Internal Defense Mechanisms

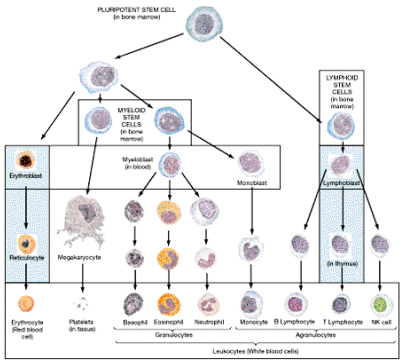
- Inflammation.
- Fever.
- Natural killer cells.
- Phagocytic cells.
- Soluble mediators

Cellular defenses

- Introduction
  - Blood
    - 60% plasma
    - 40% cells (RBC, platelets, WBC or leucocytes)



Cellular elements of the blood



Cellular defenses

- Leucocytes
  - Granulocytes - granular cytoplasm & lobed nucleus
  - Agranulocytes

Granulocytes

- Neutrophils
  - Polymorphonuclear leucocytes (PMNs).
  - Phagocytic cells
  - Can leave blood and enter tissues.
- Eosinophils
  - Weakly phagocytic, can leave blood
  - Associated with allergies - release histamine
- Basophils
  - Release heparin, serotonin, histamine.
  - Become mast cells and associated with allergies
  - Not phagocytic.

Agranulocytes

- Monocytes
  - Monocytes become macrophages when induced by lymphokines and are phagocytic
  - Macrophages are big eaters
  - May wonder or may reside in a tissue
- Lymphocytes
  - Lymphocytes have role in specific immunity.
- NK cells - extracellular killing

Phagocytic cells

- All phagocytes are leucocytes.
- Not all leucocytes are phagocytes.
- Two main types: granulocytes and agranulocytes.

Macrophages in their tissues

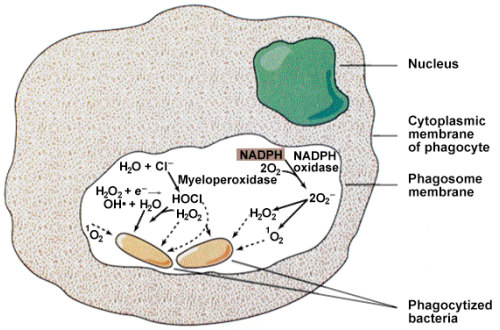
➢ Table 16.2 **Names of fixed macrophages in various tissues**

Name of macrophage	Tissue
Alveolar macrophage (dust cell)	Lung
Histiocyte	Connective tissue
Kupffer cell	Liver
Microglial cell	Neural tissue
Osteoclast	Bone
Sinusoidal lining cell	Spleen

Process of phagocytosis

- Find
  - Chemotaxis to chemical signals
    - Cytokines
- Adhere
  - Capsule prevents adherence
  - Antibodies
  - Complement
- Ingest -
  - Phagosome
- Digest
  - Phagolysosome - fusion of a phagosome and a lysosome

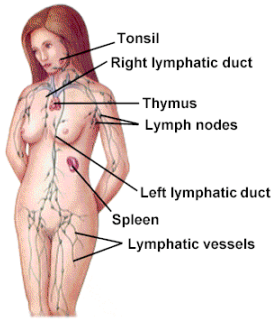
Phagosome/phagolysosome



Natural killer cells

- NK cells are large lymphocytes that kill virus-infected cells or tumor cells.
- NK cells bind to target cells and release proteases and phospholipases.
- Maturation of NK cells is stimulated by interferon.
- Main role is surveillance.
- Not phagocytic.

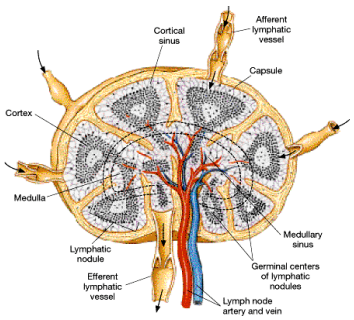
Lymphatic system drains tissues



Acts as a filtering system for microbes

Many cellular defenses are located in the lymphatic system

Lymph node



Inflammation

- A vascular and cellular response to presence of invading microorganisms or inanimate irritants.
- Symptoms include redness, swelling and pain and increased temperature.
- Symptoms are due to vasodilation.

Process of inflammation

- Initiation.
- Tissue response.
  - Histamines, TNFα, bradykinin, prostaglandins released.
  - Vasodilation occurs
- Leucocyte response.
  - Vasodilation allows movement of phagocytes (diapedesis).

Inflammation

- pus formation
  - Dead phagocytes, damaged cells, dead organisms
  - *Streptococcus pyrogenes* produces leukocidins that kill phagocytes
  - Abscesses - hollowed out due to tissue damage
    - Boils
    - Pimples

Inflammation

- Harmful effects
  - Meninges
  - Airways
  - Walling off
  - Chronic inflammation
    - Granuloma

Fever

- Normal body temperature is 98.6°F (37° C)
  - 100.5°F (37.8°C) orally
  - 101.5°F (38.4°C) rectally
- Fever is a systemic response to chemicals
- Endotoxins (pyrogens) cause fever because they affect the hypothalamus.
- Other substances raise the metabolic activity of the body
- Often associated with bacterial and viral infection.

Benefits of fevers

- Body temp. is higher than optimum for pathogens
- Microbial enzymes and toxins are inactivated
- Increase immune response
- Patient feels ill and rests

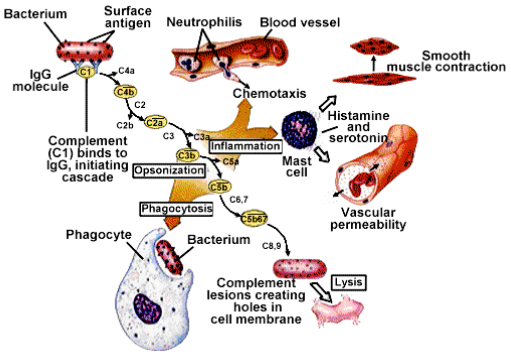
Soluble mediators

- Complement
- Lymphokines
- Interferon

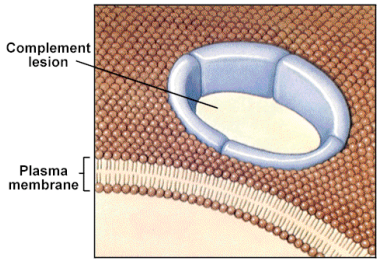
Complement

- A group of ~20 proteins that act in a cascade in response to an antibody-antigen interaction.
  - Enhance phagocytosis by phagocytes.
    - opsonization
  - Lyse invading bacterial cells and some viruses
    - membrane attack
  - Stimulates inflammatory response
    - Releasing of histamines and other substances by basophils and mast cells

Complement system



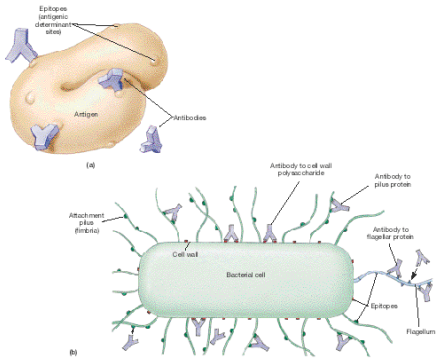
Complement forms pores in the pathogen



Complement system

- Classical pathway
  - Antibody-antigen stimulation
- Alternative pathway
  - Pathogen surface stimulation
- Opsonization -
  - coating of the pathogen with antibody/complement complex
  - Stimulates phagocytosis

Antibodies bind to the cell surface



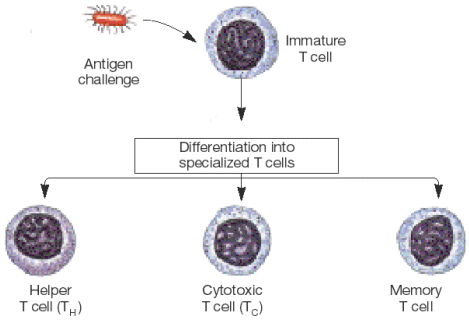
Deficiencies in complement lead to disease susceptibilities

DISEASE STATE	COMPLEMENT DEFICIENCIES
Severe recurrent infections	C3
Recurrent infections of lesser severity	C3, C2, C5
Systemic lupus erythemotosus (a bodywide immunologic disease)	C1, C2, C4, C5, C8
Glomerulonephritis (an immunologic disease of the kidneys)	C1, C8
Gonococcal infections	C6, C8
Meningococcal infections	C6

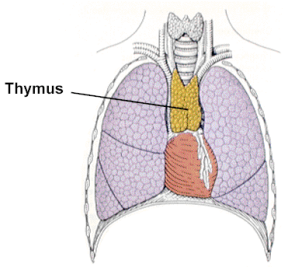
Lymphokines

- Soluble proteins secreted by activated T lymphocytes.
  - Inhibit macrophage migration.
  - Activate macrophages.
  - Poison foreign cells or virus-infected cells.
  - Can damage tissue in inflammation.

T-cells



T-cells mature in the thymus



Interferon

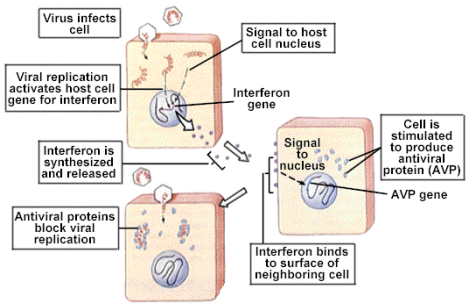
- Inhibits intracellular viral replication.
- Protein in nature.
- Secreted by infected cells and alerts other uninfected cells.
- Are not virus-specific.
- Are species specific.

Interferons

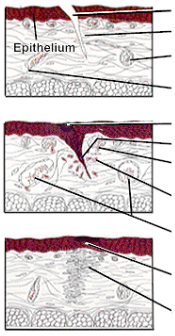
Table 16.3 Properties of type I and type II human interferons

Class	Cell source	Subtypes	Stimulated by	Effects
Type I				
Alpha-interferon (INF-α)	Leukocytes	20	Viruses	Production of antiviral proteins in neighboring cells
Beta-interferon (INF-β)	Fibroblasts	1	Viruses	Same as INF-α
Type II				
Gamma-interferon (INF-γ)	T lymphocytes and NK cells	1	Viruses and other antigens	Activates tumor destruction and killing of infected cells

Antiviral effect of interferon



Repair and regeneration



1. Cut allows bacteria to get beneath surface of skin.
2. Damaged cells release histamine and bradykinin.
3. Capillaries dilate, bringing more blood to the tissue. Skin becomes reddened and warmer.
4. Capillaries become more permeable, allowing fluids to accumulate and cause swelling.
5. Blood clotting occures, and a scab forms.
6. Bacteria multiply in cut.
7. Phagocytes enter tissue by moving through the walls of blood vessels (diapedesis).
8. Phagocytic cells are attracted to bacteria and tissue debris (chemotaxis) and engulf them.
9. Larger blood vessels dilate, further increasing blood supply to tissue and adding to heat and redness.
10. As dead cells and debris are removed, epithelial cells proliferate and begin to grow under the scab.
11. Scar tissue (connective tissue) replaces cells that cannot replace themselves.