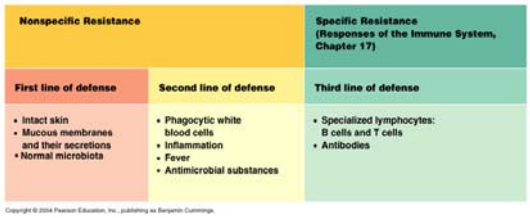
NON-SPECIFIC IMMUNE RESPONSE

CHAPTER 16

Overview of the Defense System



Physical barriers that protect the body

- Skin
- Mucus membranes
- Fluids

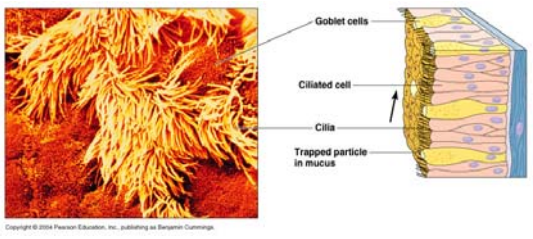
Skin as the first line of defense

- Intact skin protects
  - Epidermis
  - Dermis
- Largest organ
- Epidermis consists of tightly packed cells with
- Keratin, a protective protein: Dryness
- shedding

Physical Barriers

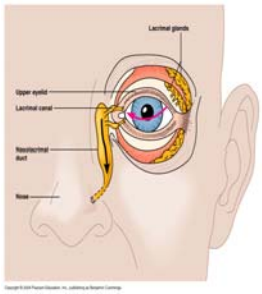
- Mucous membranes
- Ciliary escalator: Microbes trapped in mucus are transported away from the lungs
- Fluids
- Lacrimal apparatus: Washes eye
- Saliva: Washes microbes off
- Urine: Flows out
- Vaginal secretions: Flow out

Mucus membranes have ciliated cells



Fluids help to wash and cleanse

- Tears flush the eye
- lysozyme present in tears, saliva



Chemical Factors

- **Fungistatic fatty acid in sebum in Sebaceous (oil) glands**
- **Low pH (3-5) of skin**
- **Lysozyme in perspiration, tears, saliva, and tissue fluids**
- **Low pH (1.2-3.0) of gastric juice: toxic to bacteria and most toxins (not Clostridia and Staph aureus): Food protects**
  - **Helicobacter pylori: neutralizes acid→ulcers**

Microbial Barriers

- Normal flora play a role in keeping the body protected
  - Competitive exclusion
  - *E. coli* produce bacteriocins which kill *Salmonella* and *Shigella*
- Opportunistic organisms: usually harmless organisms that can cause infections when the environment changes

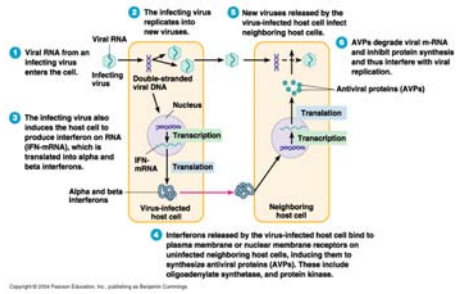
Proteins in the blood protect

- NO (Nitric Oxide) Released from blood vessels and macrophages appear to kill microbes
- Iron binding proteins known as transferrins; Inhibit bacteria by reducing amount of iron
- Interferons (IFNs): anti-viral proteins
- Complement proteins

Interferons

- Three types of glycoproteins
  - Alpha: diffuses to neighboring cells
  - Beta
    - induce mRNA to synthesize enzymes to disrupt viral multiplication
  - Gamma
    - Produced by lymphocytes to induce phagocytes
- Host cell specific
- Recombinant IFNs: to treat disease

Interferons inhibit viral replication

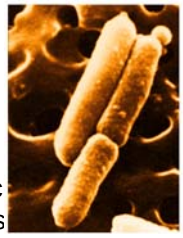


Complement Proteins

- Consists of a collection of 30 interacting proteins found in blood and tissues
- These proteins promote
  - Opsonization: C3b coats surface/enhance phagocytosis
  - Inflammation
  - Cell lysis

Effects of Complement Activation

- Opsonization or immune adherence: enhanced phagocytosis
- Membrane attac complex: cytolys
- Attract phagocytes



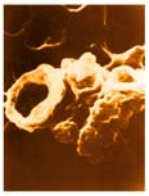


Figure 16.11

Effects of Complement Activation

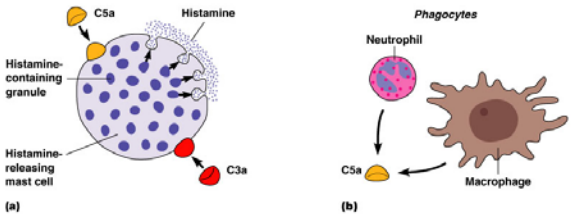
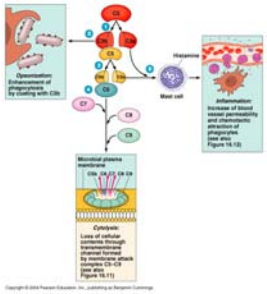


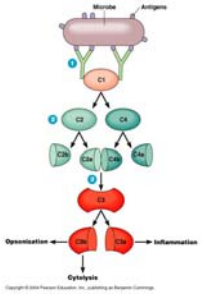
Figure 16.12

Overview of complement activation



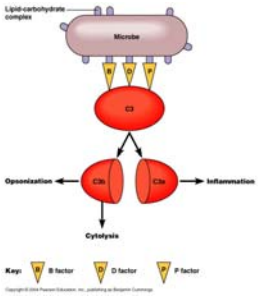
Classical Activation of complement

- Requires an antigen-antibody complex to bind C1
- C2b and C4b combine to activate C3



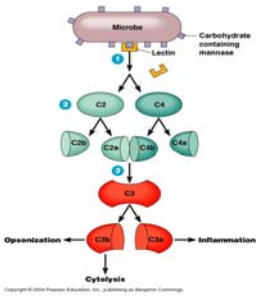
Alternative activation of complement

- Proteins in the blood, Factor B, D and P bind to pathogen
- Activates C3



Mannose Binding proteins activate complement

- Lectin binds to mannose found in the bacterial cell wall
- Activates C2a and C4b



Some bacteria evade complement

- Capsules prevent C activation
- Surface lipid-carbohydrates prevent MAC formation
- Enzymatic digestion of C5a

Cell Communicaton

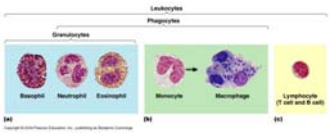
- Surface receptors on cells: on membrane; when binds to specific compound, signals cell to respond
- Cytokines: cell messengers; proteins made by cells to communicate with other cells
- Adhesion molecules: on surface of cell that allows cell to adhere to other cell

Cell Communication

- Toll-like receptors (TLRS): enable cell to see certain molecules that indicate presence of microorganisms or viruses
  - 10 recognized
  - Eg. TLR-2 recognizes peptidoglycan
  - Others recognize flagella, bacterial nucleotide sequences, LPS of gram-neg (triggers TLR on monocytes and macrophages and causes cell to produce chemokines (cytokine for chemotaxis) to attract other phagocytes to site

Cells involved in the nonspecific immune response

- Phagocytes
  - Neutrophils
  - Macrophages



Differential White Cell Count

- Percentage of each type of white cell in a sample of 100 white blood cells

Neutrophils	60-70%
Basophils	0.5-1%
Eosinophils	2-4%
Monocytes	3-8%
Lymphocytes	20-25%

White Blood Cells

- Neutrophils: Phagocytic
- Basophils: Produce histamine
- Eosinophils: Toxic to parasites, some phagocytosis
- Monocytes: Phagocytic as mature macrophages
- Fixed macrophages in lungs, liver, bronchi
- Wandering macrophages roam tissues
- Lymphocytes: Involved in specific immunity

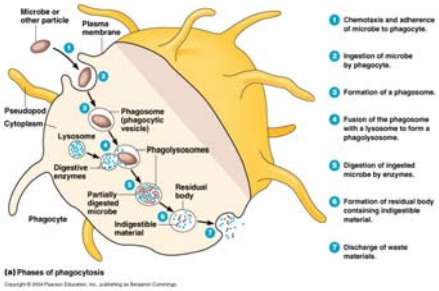
Phagocytosis

- *Phago*: eat
- *Cyte*: cell
- Ingestion of microbes or particles by a cell, performed by phagocytes
- Phagocytic cells
  - Neutrophils (segs, polymorphonuclear;,polys)
  - Monocytes: enlarge and develop into macrophages (Fixed in tissue or Wandering)

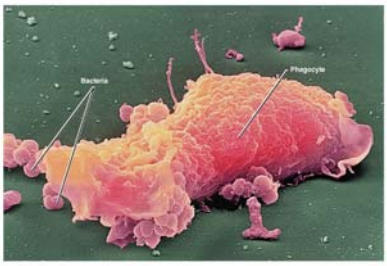
Steps of Phagocytosis

- Chemotaxis
- Adherence
- Ingestion
- Digestion
- Residual body discharged from cell

Process of Phagocytosis



(a) Phases of phagocytosis



(b) A phagocyte engulfing bacteria (*Neisseria gonorrhoeae*)

Microbial Evasion of Phagocytosis

- Inhibit adherence: M protein, capsules: *Strep pneumoniae and pyogenes; Haemophilus influenzae;*
- Kill phagocytes: Leukocidins: *Staph aureus*
- Lyse phagocytes: Membrane attack complex: *Listeria*
- Escape phagosome: *Shigella*
- Prevent phagosome-lysosome fusion: *HIV* and *Mycobacterium TB*
- Survive in phagolysosome: *Yersinia pestis*

Symptoms of inflammation

- Redness
- Swelling
- Heat
- Pain

- Apoptosis: programmed cell death; does not trigger inflammation

Purpose of inflammation

- Contain site of infection
- Localize response
- Restore tissue function

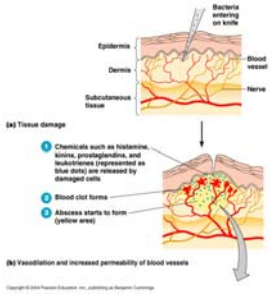
Inflammation

Acute-phase proteins activated (complement, cytokine, kinins, CRP)

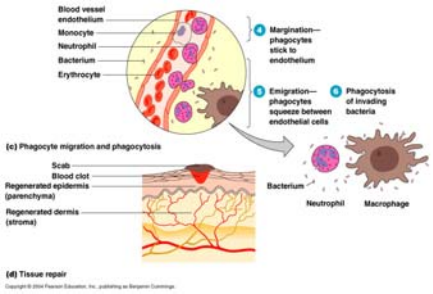
Process:

- Vasodilation (histamine, kinins, prostaglandins, leukotrienes)
- Phagocytic migration: chemotaxis-attracted by cytokines
- Phagocytosis
- Tissue repair

Inflammation begins with tissue damage



Phagocytes migrate to damaged area

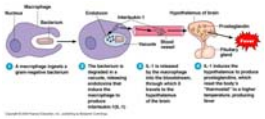


Fever: Abnormally High Body Temperature

- Hypothalamus normally set at 37°C
- Pyrogens (Gram-neg endotoxin/cytokines) cause phagocytes to release interleukin 1
- Hypothalamus releases prostaglandins that reset the hypothalamus to a high temp
- Body increases rate of metabolism and shivering to raise temperature
- When IL-1 is eliminated, body temperature falls. (Crisis)

Fever is a nonspecific response

- Il-1 increases T lymphocytes
- Decreases available iron
- Increases cellular reactions



Results of Fever

- Enhances natural defenses
- Stimulates phagocytosis
- Accelerates reaction rates
- Intensifies interferon
- Reduces iron content of body
- Increases T cell production