

Host Defense Mechanisms (non-specific)

BIO162 Microbiology for Allied Health
Chapter 15
Page Baluch

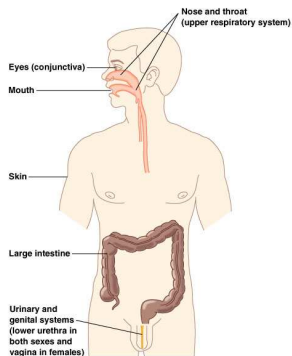
Host Defenses

- **Resistance**
 - Ability to ward off disease
 - Varies among organisms and individuals within the same species
- **Immunity** - mechanisms used by the body as protection against microbes and other foreign agents; self vs. non-self
- **Nonspecific** immunity (innate, natural, inborn)
 - Defenses against any pathogen
- **Specific** immunity
 - Resistance to a specific pathogen

Host Defenses

Nonspecific Resistance		Specific Resistance (Responses of the Immune System,
First line of defense	Second line of defense	Third line of defense
<ul style="list-style-type: none">• Intact skin• Mucous membranes and their secretions• Normal microbiota	<ul style="list-style-type: none">• Phagocytic white blood cells• Inflammation• Fever• Antimicrobial substances	<ul style="list-style-type: none">• Specialized lymphocytes: B cells and T cells• Antibodies

First line of defense – physical & chemical barriers



First line of defense – physical & chemical barriers

- **Intact, unbroken skin** (Broken skin = port of entry)
 - Almost all bacteria are incapable to penetrate a few helminths (hookworm & schistosoma) may
 - skin predominantly inhabited by *Staphylococcus epidermidis*
 - How?
 - Dryness
 - temperature
 - Low pH (acidic) of skin;
 - bacteriocidal secretion by the sebaceous glands
 - Desquamation – sloughing of epithelium
 - Perspiration (sweat contain lysozymes – attack bacterial cell wall)
 - Exception: *Staphylococcus aureus* in moist area

First line of defense – physical & chemical barriers

- **Eyes**
 - Blinking of eyelids
 - Tears containing lysozymes
- **Outer ear canal**
 - Wax contains antibacterial components

First line of defense – physical & chemical barriers

- **Mucus membranes** – layers of mucosal cells that line body cavities that open to the outside (digestive, genitourinary and respiratory tracts)
 - Mucus is produced by the mucosal cells
 - Contains antimicrobial substance such as lysozymes, lactoferrin (sequester iron)
 - Mucosal cells are rapidly dividing → flush out of body along with attached bacteria

First line of defense – physical & chemical barriers

- **Digestive tract**
 - Mouth and lower digestive tract – lots of bacteria (mostly anaerobes e.g. *Bacteroides*, anaerobic streptococci [*Streptococcus mutans* in mouth] and *Clostridium* in colon)
 - How?
 - Mucus
 - Saliva (contains lysozyme)
 - Bile (alkaline) in small intestine
 - Stomach acids
 - Defecation (feces contains up to 50% bacteria !)
 - Mucus contain antibacterial agents, antibodies and immune cells called phagocytes

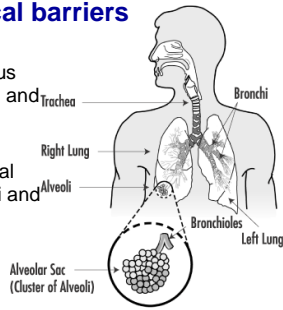
First line of defense – physical & chemical barriers

- **Genitourinary tract**
 - Urinary tract is sterile in a health person except the distal urethra
 - How?
 - Urination
 - Secretion (vaginal and seminal fluid)
 - Low pH of vagina (presence of several *Lactobacillus* sp., *Candida albicans*)

First line of defense – physical & chemical barriers

• Respiratory tract

- Nose - nasal hair, mucus secretions (phagocytes and antibacterial enzymes), irregular chambers
- ciliated epithelium (nasal cavity, sinuses, bronchi and trachea)
- Cough reflexes
- Alveolar macrophages



First line of defense – physical & chemical barriers

• Microbial antagonism

- Normal flora vs. invaders
 - Compete for colonization sites
 - Compete for nutrients
 - Produce bacteriocins
- Administration of broad spectrum antibiotics may kill only certain members of the normal flora, leaving the others to overgrow → **superinfection**
 - e.g. yeast in vagina – yeast vaginitis
 - Clostridium difficile* in colon – diarrhea and colitis

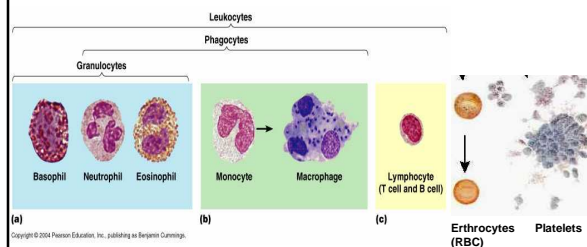
Second line of defense

- Once beyond the protective outer barrier of the body, the invading microbes will encounter a series of nonspecific cellular and chemical defense mechanisms
- Mechanisms:
 - **Inflammation** – a series of events that removes or contain the offending agent and repair the damage
 - **Chemotaxis** – movement of cells toward a chemical influence (**chemokines** or **chemotatic agents**)
 - **Phagocytosis** – process in which cell ingest foreign particulate matter e.g. microbes
- Many are carried out by the white blood cells in blood

Blood Components

- **Fluid portion**
 - Serum: liquid portion of clotted blood
 - Plasma: liquid portion with clotting factors
 - “Plasma can clot; Serum cannot”
 - Contains antibodies & other proteins
- **Clotting factors** (proteins)
 - Fibrinogen
 - Prothrombin
- **Formed elements**
 - Erythrocytes – red blood cells (RBC) – carry oxygen and carbon dioxide; no nucleus
 - Leukocytes – white blood cells (WBC) - defense
 - Platelets – thrombocyte particles – clotting; no nucleus

Second line of defense – formed element in blood



Wright's stain of the peripheral blood cells can identify granulocytes based on properties of the granules. It contain two dyes:

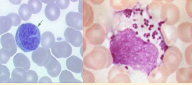

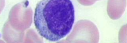
- Eosin dye stains basic cell components → reddish
- Methylene blue dye stain acidic cell components → blue-ish

Formed Elements In Blood

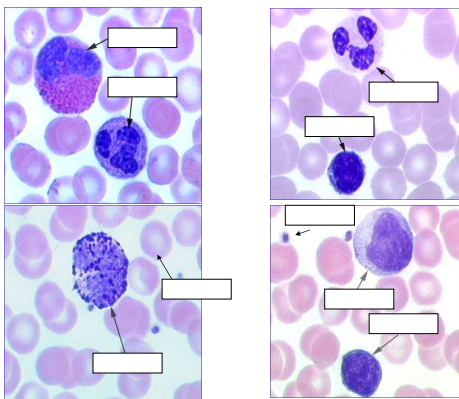
Type of Cell	Numbers per microliter (μl) or cubic mm (mm^3)	Function
Erythrocytes (Red Blood Cells)	4.8–5.4 million	Transport of O_2 and CO_2
Leukocytes (White Blood Cells)	5000–10,000	Phagocytosis
A. Granulocytes (stained)		
1. Neutrophils (PMNs) (60–70% of leukocytes)		Phagocytosis
2. Basophils (0.5–1%)		Production of histamine
3. Eosinophils (2–4%)		Production of toxic proteins against certain parasites; some phagocytosis

Formed Elements In Blood

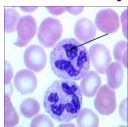
TABLE 16.1 (continued)

Type of Cell	Numbers per microliter (μl) or cubic mm (mm^3)	Function
B. Agranulocytes (stained) 1. Monocytes (3-8%)		Phagocytosis (when they mature into macrophages) Wandering or Fixed
2. Lymphocytes (20-25%)	 Lymphocyte	Antibody production (descendants of B lymphocytes); cell-mediated immunity (T lymphocytes)*
Platelets	150,000-400,000 	Blood clotting

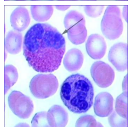
Can you identify these leukocytes?



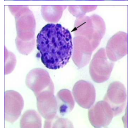
Granulocytes



- Neutrophils** (aka polymorphonuclear cells or PMN)
- Most common leukocytes in the blood. Granules unstained.
 - mobile cells and can pass through capillaries and engulf bacteria by phagocytosis
 - secrete a fever inducing agent called pyrogen which also helps the body fight infection.



- Eosinophils**
- the granules of cytoplasm are stainable with eosin (red)
 - The exact function of eosinophils has been a mystery for many years, but research has pointed to its role in allergy, asthma and parasitic (helminth) infection; some phagocytosis.

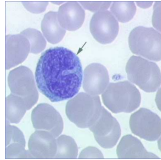


- Basophils**
- rarest WBC in normal blood
 - Blue granules contain histamine
 - play a role in immediate hypersensitivity reactions and in some cell-mediated delayed reactions, such as contact hypersensitivity in humans, skin graft or tumor rejections

Monocyte (Macrophage)

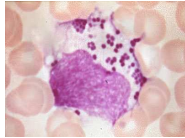
Monocytes (the blood form)

- the largest WBC's normally found in blood
- horseshoe or "U" shape nucleus, or it may be folded
- travel to different tissue to mature into specific macrophage



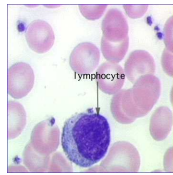
Macrophage

- As it developed from monocytes, its size can increase 2-3 times
- **Wandering** – motile and travel in bloodstream; found throughout body
- **Fixed (histiocytes)** – attached and remain in the tissue
- Removal and engulfment of foreign particles and useless body cells/material



Lymphocytes

- The lymphocyte nucleus is usually round to slightly indented with a sharply defined edge, and deep, dense purple. Cytoplasm may be scant or form a narrow rim around the nucleus.
- Cornerstone of the immune system: antibodies production & cell-mediated immunity



Second line of defense

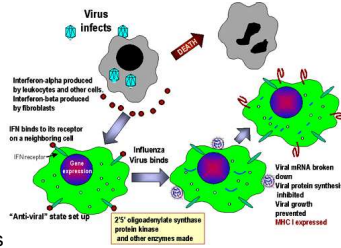
- **Acute phase proteins**
 - set of plasma proteins whose level increases during infection to enhance host defense mechanisms
 - e.g. complement proteins, coagulating factors, transferrins
- **Cytokines**
 - small secreted proteins produced by cells
 - Communication between different defense systems
 - Examples: interleukins, interferons

Second line of defense

- **Fever**
 - **Pyrogens** are substances that stimulate fever
 - External, e.g. bacterial endotoxin
 - Internal (endogenous), e.g. interleukins (IL-1)
 - Body temperature increases in response to pyrogens to:
 - Stimulate WBC to deploy & destroy microbes
 - Increase in immunological response (e.g. proliferation and activation of lymphocytes)
 - Slow down growth of or kill pathogens

Second line of defense

- **Interferons**
 - Anti-viral proteins produced by virus-infected cells (eventually died)
 - Alert system to prevent virus from infecting other cells and to stimulate certain lymphocytes
 - Has been used as an experimental therapy (nowadays, many are genetically engineered) for viral infections and cancers
 - Species-specific for host cells

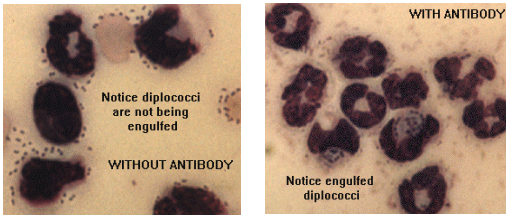


Second line of defense

- **The complement systems**
 - Consists of ~30 proteins that complement the action of the immune system
 - Functions:
 - Inflammation
 - Stimulate leukocytes
 - Lyse bacteria
 - Increase phagocytosis by opsonization

Opsonization

- Process by which phagocytosis is facilitated by deposition of **opsonins**
- Opsonins can be complement proteins, or antibodies
- e.g. encapsulated bacteria
- Deficiency in complement system may lead to increase susceptibility to certain infections.

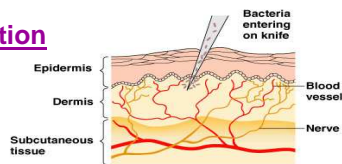


Inflammation

- **Four cardinal signs**
 - Redness
 - Heat
 - Swelling
 - Pain
- **Primary functions**
 - Localize infection
 - Neutralize toxins at injury site
 - Repair damage tissue
- **Major events**
 - Vasodilation
 - Increase permeability of capillaries
 - Mobilization of leukocytes to site of injury (chemotaxis & emigration)
 - Phagocytosis

Second Line of Defense

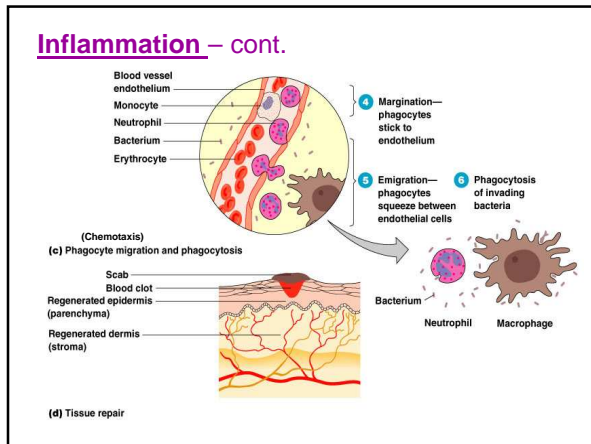
Inflammation



(a) Tissue damage

- 1 Chemicals such as histamine, kinins, prostaglandins, and leukotrienes (represented as blue dots) are released by damaged cells
- 2 Blood clot forms
- 3 Abscess starts to form (yellow area)

(b) Vasodilation and increased permeability of blood vessels



Phagocytosis is the ingestion of microorganisms or other matter by a cell. Many white blood cells engulf invasive microorganisms by the process of phagocytosis. The steps in phagocytosis are:

1. **Chemotaxis** is the process by which phagocytes are attracted to microorganisms.
2. **Attachment**. The phagocyte then adheres to the microbial cell. This adherence may be facilitated by *opsonization* – coating the microbe with plasma proteins.
3. **Ingestion**: Pseudopods of phagocytes engulf the microorganism and enclose it in a phagosome to complete ingestion.
4. **Digestion**: Lysosomes fuse with the phagosome to form a digestive vacuole. The microbe is killed and digested.

