Lymphatic and Immune Systems

- Homeostatic role of defense against pathogens, injury, diseased body cells, and toxins
  - Requires both lymph and immune systems to be effective
- Three levels of defense
  1. Skin, mucous membranes (non-specific)
  2. Inflammation, complement protein cascade (non-specific)
  3. Immune response (specific)

Early Advances

- Edward Jenner developed the first immunization in 1796
- The term “vaccine” comes from the practice of using Vaccinia virus (cow pox) to inoculate against smallpox (Variola virus)
- Smallpox remains the only infectious disease successfully eradicated
Early Advances

- Ignaz Semmelweis (1840s) was frustrated by the high rates of maternal death from childbirth fever (15%).
- He demonstrated that hand washing prevented the spread of childbirth fever.

Early Advances

- Louis Pasteur demonstrated that heating could kill microorganisms in food and beverages (1860s)
- “Germ Theory of Disease” was first described by Pasteur
- Theory states that a specific disease (set of symptoms) is caused by a specific kind of microorganism
Early Advances

- Robert Koch developed a sequence of experimental steps for directly relating a specific microbe to a specific disease
- “Koch’s Postulates” (1882) were the basis of microbiology for years

Lymphatics

- Lymph
  - formed from excess filtration at capillaries
  - similar to interstitial fluid, but has increased concentration of lymphocytes
Lymphatics

- **Lymph Functions**
  - drain excess interstitial (extracellular) fluid
  - remove filtered proteins
  - transport dietary fats
  - **Identify and remove pathogens (immune responses and nonspecific defenses)**
Lymphatics

- **lymphatic vessels** allow for one-way flow of lymph
- **lymph nodes** trap foreign substances and attack using lymphocytes

Lymphatic Flow

- one way valves
- muscle pump
- thoracic pump
- ultimately drains into left brachiocephalic and right subclavian veins
Lymphatic Tissues

- red marrow: produces B & T lymphocytes (cells)
- thymus: pre-T cells develop into mature T cells, begins to atrophy after puberty

Lymphatic Tissues

- Lymph nodes
  - Pathogens, chemicals, are picked up along with excess fluid
  - Everything passes through nodes before returning to blood
  - Nodes are screening areas, and are frequently the site for identifying a new infection
Lymphatic Tissues

- Tonsils: fight ingested or inhaled pathogens
  - Function is similar to lymph nodes, though structure is different

Spleen
- white pulp: B cells become plasma cells here (plasma cells make antibodies)
- red pulp: phagocytosis of bacteria, RBC, and platelets
- reservoir of monocytes (rapid response to injury or infection)
Immune System

- Provides the ability to resist damage from foreign substances (microorganisms, harmful chemicals, and diseased body cells)
- Two categories
  - Innate/non-specific
  - Adaptive/specific (acquired)

Immune system lines of defense

1. Non-specific: external barriers
2. Non-specific
   - Phagocytes
   - Antimicrobial proteins
   - Complement system
   - Inflammation
3. Specific: immune response
1\textsuperscript{st} Line of Defense

- Mechanical protection
  - Epidermis of skin
  - Mucous membranes (mucus and cilia)
  - Lacrimal apparatus
  - Saliva
  - Urine (washes urethra)

1\textsuperscript{st} Line of Defense

- Chemical protection
  - Sebum
  - Perspiration (contains lysozymes)
  - Gastric juice (acid and mucus)
  - Vaginal secretions (acidity may help prevent spread of certain sexually transmitted infections)
2nd Line of Defense

• Phagocytosis
  – Carried out by specific leukocytes and macrophages working together
  
  – Leukocytes
    • Neutrophil: recent bacterial infection
    • Basophil: attract neutrophils and increase blood flow (histamine)
    • Eosinophils: parasitic worm infections, allergies, inflammation
  – Macrophages: monocytes transform into macrophages in damaged/inflamed tissues

2nd Line of Defense

- Anti-microbial substances
  - interferons (an example of a cytokine): small proteins released by lymphocytes and macrophages, they prevent viral infection of cells, stimulate phagocytosis and natural killer cells
  - complement system: 20 normally inactive proteins that help nonspecific immunity in variety of ways
2nd Line of Defense

- Anti-microbial substances
  - Natural killer cells: specialized lymphocytes of spleen, lymph nodes, red marrow, blood that destroy microbes and especially tumor cells by producing cytotoxic chemicals (e.g., perforins)

- Inflammation
  - Response to tissue injury
  - Local symptoms: redness, heat, swelling, pain, loss of function
  - Systemic symptoms: increased neutrophils, pyrogen production, widespread increased vascular permeability
Inflammation

- Mast cells (similar to basophils) release histamine
- Capillaries dilate and leak
- Complement proteins attack bacteria
- Phagocytes attack invaders and clean up

3rd Line of Defense: Specific Resistance

- Specific resistance: the immune response or immunity
- Characteristics of “immune response”
  - Self vs. non-self recognition
  - Specificity
  - Diversity
  - Memory
Immune Response

- Includes cell mediated and antibody mediated immunities
  - Cell-mediated immunity directly kills infected or diseased cells
  - Antibody-mediated immunity uses antibodies to identify and agglutinate pathogens, which then are usually phagocytized

Key Components of Immune Response

- Antigen-presenting cells (APCs)
- Major histocompatibility complex (MHC) proteins
- T cells
- B cells
- Natural killer cells
B and T Cells (Lymphocytes)

- B cells acquire unique antigen-binding receptors in bone marrow
- T cells acquire unique antigen-binding receptors in thymus (before puberty)

Specific Resistance: Immunity

- Recognition of danger
  - antigens: “non-self” markers on foreign agents and altered body cells such as tumors
  - when specialized macrophages called antigen-presenting cells (APCs) are activated, they present the antigen (via MHC molecule)
  - alternatively, an infected cell itself can present an antigen
  - self vs. non-self recognition occurs
  - immune system recognizes specific antigens
Types of Immune Response

- Cell-mediated immune response
  - Cytotoxic T cells or NK cells
  - Useful in eliminating threats from body cells infected by bacteria, protozoans, or viruses; or tumor cells
  - Intracellular pathogens or dangerous body cells

![Diagram of immune response](image)
Cell Mediated Immunity

- APCs activate helper T cells and cytotoxic T cells
- Helper T cells (CD4 cells) stimulate mitosis of $T_C$ cells
- Defense against viral infection mostly involves the action of cytotoxic T cells, natural killer (NK) cells, and interferons

Specific Resistance: Immunity

- Cytotoxic T cells directly destroy target cells
  - Stimulate apoptosis
  - Perforins
  - Shut off metabolism
Types of Immune Response

- Antibody-mediated immune response
  - Carried out by B cells
  - B cells produce antibodies that bind to antigens promoting recognition and elimination
  - Antibodies mark targets for destruction by phagocytes and complement proteins
  - Useful in eliminating threats from bacterial cells, fungal cells, toxins circulating in blood or tissue fluid (extracellular pathogens and toxins)
Antibody Mediated Immunity

- Antibodies work in the following ways
  - neutralization: antibodies block the binding sites for bacterial entrance into cells
  - agglutination and precipitation: antibodies clump pathogens together, making them an easier target for phagocytes
  - activation of complement system, which destroys the antigen
Antibody Mediated Immunity

- Antibodies work in the following ways
  - direct attraction of phagocytes
  - opsonization: coating the antigen so that it's not slippery, allowing phagocytes to work
  - stimulation of inflammation
  - prevention of bacterial adhesion to cells: antibodies are in sweat, saliva, and mucus
Immunological Memory

- A second infection will provoke a much quicker and larger response than an initial infection.

![Graph showing primary and secondary immune responses](image)

Organ Rejection

- Cytotoxic T cells can contribute to rejection of transplanted tissue.
- A portion of the donor cell’s MHC complex is recognized as self, and another portion as foreign.
- T cells treat the combination as an antigen-MHC complex and attack donor cells.
Allergies

- Immune reaction to a harmless substance
- IgE responds to antigen by binding to mast cells and basophils
- These cells secrete the substances that cause symptoms
- Hygiene hypothesis: allergies and other autoimmune diseases related to under-training of IgE