Lymphatic System

- Consists of:
  - Lymphatics (lymph vessels/ducts)
  - Lymphatic tissue
    - involved in cleansing and immunity
      - Lymph nodes
      - Spleen
      - Thymus
      - Bone marrow
      - Other
Lymphatic System Functions

- reclaims excess fluid pushed out by systemic capillaries that is not taken up by capillaries
  - Lymph fluid

- Tissue fluid accumulation would amount to 3L/day

- Edema could destroy tissue
  - Elephantitis – caused by parasitic worm infection which blocks lymphatics
Lymphatic System: Overview

Regional lymph nodes:
- Cervical nodes
- Axillary nodes
- Inguinal nodes

Entrance of right lymphatic duct into right subclavian vein
- Internal jugular vein
- Entrance of thoracic duct into left subclavian vein
- Thoracic duct
- Aorta
- Cisterna chyli
- Lymphatic collecting vessels

Figure 20.2a
Lymphatic System: Overview

One way conduction toward the heart via merging with major veins.
Lymphatic Vessels

- One-way system, lymph flows toward the heart

- Lymph vessels (lymphatics) include:
  - Lymphatic capillaries
    - More permeable than blood capillaries
  - Lymphatic collecting vessels
  - Lymphatic trunks and ducts
Lymphatics

Filaments anchored to connective tissue

Endothelial cell

Flaplike minivalve

Fibroblast in loose connective tissue
Succession of lymph vessels

Lymphatic capillaries → lymphatic collecting vessels → lymphatic trunks → lymphatic ducts → major blood veins
Lymphatic anatomy

- Anatomically similar to veins; have the same three tunics as veins
- Have thinner walls, with more valves
- Like veins - require skeletal muscle movement to return lymph to blood
- Along the way lymph is filtered through lymph tissue (mostly nodes)
Lymphatic System:

Figure 20.2a

- **Regional lymph nodes:**
  - Cervical nodes
  - Axillary nodes
  - Inguinal nodes

- **Entrance of right lymphatic duct into right subclavian vein**
- **Internal jugular vein**
- **Entrance of thoracic duct into left subclavian vein**
- **Thoracic duct**
- **Aorta**
- **Cisterna chyli**
- **Lymphatic collecting vessels**
Lymphatic system:

Lymphatic Tissue

- Composed of reticular connective tissue and contains several cell types involved in activating the immune response

- Types of tissues/Organs:
  - Lymph nodes
  - Spleen
  - Thymus
  - Bone marrow
  - Other: Tonsils, Peyer’s patches, appendix
Lymphoid Organs

- Tonsils (in pharyngeal region)
- Thymus (in thorax; most active during youth)
- Spleen (curves around left side of stomach)
- Peyer’s patches (in intestine)
- Appendix

Figure 20.5
Lymph Nodes

- Clustered along lymphatic vessels
- Main functions:
  - filter/cleanse lymph
  - Contain cells that help activate a complex immune system—cells are B lymphocytes, T lymphocytes, Macrophages and dendritic cells – to mount an attack against antigens
    - T cells – manage immune response; attack and destroy foreign cells
    - B cells – produce plasma cells which secrete antibodies
Other Lymphoid Organs

- The spleen, thymus gland, and tonsils
- Peyer’s patches and bits of lymphatic tissue scattered in connective tissue
- All are composed of reticular connective tissue
- All help protect the body
- Only lymph nodes filter lymph
Lymphoid Organs: Spleen

- Largest lymphoid organ

- Functions:
  - Primarily Immune “surveillance” and response
  - Cleanses the blood (removes pathogens, old RBCs, debris)
  - Stores breakdown products of RBCs (i.e. iron) for later use; stores blood platelets
Lymphoid Organs: Thymus

- **Function:**
  - T lymphocyte maturation
  - Important in immune response

- **Size with age**
  - Active in infants – partially overlies heart
  - Increases in size & most active during childhood
  - Stops growing during adolescence and then gradually atrophies
Other Lymphoid Organs

- **Bone Marrow**: site of B lymphocyte maturation
- **Tonsils**
  - specialized lymph nodes
  - have invaginations called crypts
    - Trap and destroy bacteria & particulate matter
- **Peyer’s patches & appendix**
  - Peyer’s patches: Isolated clusters of lymph tissue in ileum of small intestine
  - Appendix: houses some immune response cells
  - Both destroy bacteria, preventing them from breaching the intestinal wall
    - Generate “memory” lymphocytes
CHAPTER 21

The Immune System
Immune System

- Resistance to disease

- Has 2 intrinsic systems
  - Innate (non-specific) defense system
    - surface barriers & inflammatory response
  - Adaptive (specific) defense system
    - attack particular foreign substances
      - through T cells & B cells
Innate (Non-Specific) Immunity

- First line of defense
  - Surface membrane barriers (Skin and mucous membranes)

- Second line of defense
  - Non-specific cellular & chemical defenses
    - Phagocytes: monocytes → macrophages, neutrophils etc
      - Engulf invader; some use lysosomes or respiratory bursts
    - Natural Killer (NK) cells - Large “lymphocytes”
      - Secrete potent chemicals – preforins - and cause lysis
    - Inflammatory response: prevents spread of injury
    - Antimicrobial proteins
      - Interferon- block viral replication
      - Complement proteins- cause cell lysis after opsonization
    - Fever: inhibits (somewhat) bacterial growth; speeds body repair
## Innate Immunity: First Line of Defense

### Table 21.2: Summary of Innate Body Defenses

<table>
<thead>
<tr>
<th>CATEGORY/ASSOCIATED ELEMENTS</th>
<th>PROTECTIVE MECHANISM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Line of Defense: Surface Membrane Barriers</strong></td>
<td></td>
</tr>
<tr>
<td>Intact skin epidermis</td>
<td>Forms mechanical barrier that prevents entry of pathogens and other harmful substances into body</td>
</tr>
<tr>
<td>- Acid mantle</td>
<td>Skin secretions (sweat and sebum) make epidermal surface acidic, which inhibits bacterial growth; also contain various bactericidal chemicals</td>
</tr>
<tr>
<td>- Keratin</td>
<td>Provides resistance against acids, alkalis, and bacterial enzymes</td>
</tr>
<tr>
<td>Intact mucous membranes</td>
<td>Form mechanical barrier that prevents entry of pathogens</td>
</tr>
<tr>
<td>- Mucus</td>
<td>Traps microorganisms in respiratory and digestive tracts</td>
</tr>
<tr>
<td>- Nasal hairs</td>
<td>Filter and trap microorganisms in nasal passages</td>
</tr>
<tr>
<td>- Cilia</td>
<td>Propel debris-laden mucus away from nasal cavity and lower respiratory passages</td>
</tr>
<tr>
<td>- Gastric juice</td>
<td>Contains concentrated hydrochloric acid and protein-digesting enzymes that destroy pathogens in stomach</td>
</tr>
<tr>
<td>- Acid mantle of vagina</td>
<td>Inhibits growth of most bacteria and fungi in female reproductive tract</td>
</tr>
<tr>
<td>- Lacrimal secretion (tears); saliva</td>
<td>Continuously lubricate and cleanse eyes (tears) and oral cavity (saliva); contain lysozyme, an enzyme that destroys microorganisms</td>
</tr>
<tr>
<td>- Urine</td>
<td>Normally acid pH inhibits bacterial growth; cleanses the lower urinary tract as it flushes from the body</td>
</tr>
</tbody>
</table>

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## Innate Immunity: Second Line of Defense

### Second Line of Defense: Innate Cellular and Chemical Defenses

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phagocytes</td>
<td>Engulf and destroy pathogens that breach surface membrane barriers; macrophages also contribute to adaptive immune responses</td>
</tr>
<tr>
<td>Natural killer (NK) cells</td>
<td>Promote apoptosis (cell suicide) by direct cell attack against virus-infected or cancerous body cells; do not require specific antigen recognition; do not exhibit a memory response</td>
</tr>
<tr>
<td>Inflammatory response</td>
<td>Prevents spread of injurious agents to adjacent tissues, disposes of pathogens and dead tissue cells, and promotes tissue repair; chemical mediators released attract phagocytes (and other immune cells) to the area</td>
</tr>
<tr>
<td>Antimicrobial proteins</td>
<td></td>
</tr>
<tr>
<td>- Interferons ($\alpha$, $\beta$, $\gamma$)</td>
<td>Proteins released by virus-infected cells and certain lymphocytes that protect uninfected tissue cells from viral takeover; mobilize immune system</td>
</tr>
<tr>
<td>- Complement</td>
<td>Lyses microorganisms, enhances phagocytosis by opsonization, and intensifies inflammatory and immune responses</td>
</tr>
<tr>
<td>Fever</td>
<td>Systemic response initiated by pyrogens; high body temperature inhibits microbial multiplication and enhances body repair processes</td>
</tr>
</tbody>
</table>
Innate (Non-Specific) Immunity:
Inflammatory Response

- **Purpose:** Prevents spread of damage; dispose of pathogen; begin repair

- **Injury →** triggers release of “inflammatory chemicals” at site
  - Causes localized arterioles to vasodilate (causes redness)
  - Increased capillary permeability → leakage of exudate – proteins, clotting factors, antibodies (causes edema)

- **Initiates phagocyte mobilization** (neutrophils & macrophages)
  1. Leukocytosis- mobilization from the bone marrow (4-5 fold increase in WBC)
  2. Margination- leukocytes adhere to capillary wall in inflamed area via CAMs
     - Cell adhesion molecules
  3. Diapedesis- leukocytes (neutrophils) flatten & squeeze through capillary wall
  4. Chemotaxis- chemicals direct movement of leukocytes toward injury

- **Reabsorption of debris/ clean up**
Tissue injury

Release of chemical mediators (histamine, complement, kinins, prostaglandins, etc.)

Vasodilation of arterioles

Increased capillary permeability

Attract neutrophils, monocytes, and lymphocytes to area (chemotaxis)

Leukocytes migrate to injured area

Margination (leukocytes cling to capillary walls)

Diapedesis (leukocytes pass through capillary walls)

Phagocytosis of pathogens and dead tissue cells (by neutrophils, short-term; by macrophages, long-term)

Pus may form

Area cleared of debris

Healing

Release of leukocytosis-inducing factor

Leukocytosis (increased numbers of white blood cells in bloodstream)

Locally increased temperature increases metabolic rate of cells

Heat

Local hyperemia (increased blood flow to area)

Redness

Increased capillary permeability

Exudate formation

Leaked protein-rich fluid in tissue spaces

Temporarily fibrin patch forms scaffolding for repair

Temporary fibrin patch forms scaffolding for repair

Healing

Possible temporary limitation of joint movement

Exudate formation

Leaked clotting proteins form interstitial clots that wall off area to prevent injury to surrounding tissue

Leukocytes pass through capillary walls

Phagocytosis of pathogens and dead tissue cells (by neutrophils, short-term; by macrophages, long-term)

Area cleared of debris

Pain

Swelling

Initial stimulus

Physiological response

Signs of inflammation

Result
Innate defenses

1. Leukocytosis. Neutrophils enter blood from bone marrow.

Inflammatory chemicals diffusing from the inflamed site act as chemotactic agents.
Adaptive (Specific) Immunity

- Specific, as in ANTIGEN specific
  - Antigen
    - any substance that causes an immune response
    - “antibody generator”
  - Amplifies the inflammatory response
    - Programmed for specific antigens
    - Is systemic & has a memory
- 2 types of adaptive immunity:
  - Humoral (antibody-mediated) immunity
  - Cellular (cell-mediated) immunity
Immunity Terms:

- **Antigen**
  - “antibody generator”
  - Anything the body perceives as foreign can trigger an immune response
    - Bacteria & their toxins, viruses, mismatched RBCs or cancer cells

- **Pathogen**: disease causing organism

- **Self antigens**: ID as self “biochemical fingerprint”
  - Protein molecules on the surface of cells; unique in every person
  - Human Leukocyte Associated (HLA) antigen system
    - MHC Proteins (major histocompatibility complex)
      - Class I: found on all body cells
      - Class II: found on certain immune specific cells
Cells of Adaptive Immunity

- **Lymphocytes**
  - Originate in red bone marrow
    - B lymphocytes (B cells)
      - Mature in red bone marrow
      - Involved in humoral (antibody-mediated) immunity
    - T lymphocytes (T cells)
      - Mature in the thymus
      - Involved in cell-mediated immunity

- **Antigen-presenting cells (APCs)**
  - Do not respond to specific antigens
  - Engulf antigens then present fragments to T cells
    - Dendritic cells, macrophages, B lymphocytes
Red bone marrow: site of lymphocyte origin

Primary lymphoid organs: site of development of immunocompetence as B or T cells

Secondary lymphoid organs: site of antigen encounter, and activation to become effector and memory B or T cells

1. Lymphocytes destined to become T cells migrate (in blood) to the thymus and develop immunocompetence there. B cells develop immunocompetence in red bone marrow.

2. Immunocompetent but still naive lymphocytes leave the thymus and bone marrow. They “seed” the lymph nodes, spleen, and other lymphoid tissues where they encounter their antigen.

3. Antigen-activated immunocompetent lymphocytes (effector cells and memory cells) circulate continuously in the bloodstream and lymph and throughout the lymphoid organs of the body.

Figure 21.8
Lymphocytes

- T cells and B cells protect the body against antigens
- When mature, have immunocompetence – can recognize and bind a specific antigen
  - Have self-tolerance > unresponsive to self-antigens
- Naïve B and T cells are exported to lymph nodes, spleen, and other lymphoid organs
Lymphocytes

- **T cells**
  - Manage the immune response
  - Attack and destroy cancer and infected cells

- **B cells**
  - Produce plasma cells, which secrete antibodies
    - Antibodies immobilize antigens — whole bacteria cells, toxins
There are a variety of different types of T cells (know these)

- **Helper T cells**
  - function to mediate the immune response (both T and B cell mediated responses)

- **Cytotoxic T cells**
  - attack and destroy infected cells/ or tumor cells

- **Regulatory (suppresor) T cells**
  - involved in suppression of the immune system—may be involved in prevention of autoimmune disorders

- **Memory T cells**
  - function to circulate in the blood stream until subsequent exposure to antigen
Adaptive (Specific) Immunity

- Humoral (antibody-mediated) immunity
  - Provided by antibodies present in bodily fluids
  - Antibodies produced by lymphocytes

- Cellular (cell-mediated) immunity
  - Lymphocytes act against targets directly by killing, or indirectly by releasing chemicals to enhance inflammatory response
Humoral Immune Response

- Antibody or B cell mediated immunity
- Produces progeny through clonal selection:
  - Plasma cells → antibodies
  - Memory B cells
- Requires:
  - Helper T
When B-cells first encounter foreign antigen, they divide rapidly forming a colony of progeny B-cells. Some of the colony will become plasma cells and produce antibodies against the antigen immediately others will become Memory B cells that will circulate in wait for the next exposure. T cells go through a similar process to form cytotoxic and memory T cells. Both the formation of B and T cells requires T-helper cells.
Humoral Immune Response:

B Cells and Plasma cells

- **Plasma cells**
  - B cells that produce antibodies

- **Antibodies** (also called immunoglobulin or gamma globulin) produced are specific for a particular antigen (pathogen)
  - They can work by:
    - Causing agglutination (clumping)
    - Marking the cells as a target for macrophages
    - Activation of complement system/ complement fixation
      - System of proteins activated by the presence of antibodies that basically punch holes in the bacteria causing it to lyse
Antibodies and complement

- Complement fixation
  - main mechanism for antibody mediated destruction
  - Triggers cell lysis

- Opsonization
  - helps C3b protein coats bacterial surface >>> target for phagocytosis
Antibodies

- Aka: immunoglobulins (Igs)
- Five major classes of Igs (each has different role)
  - IgM: 1st to be released by plasma cells
  - IgA: found in mucus & other secretions; prevents pathogens entering body
  - IgD: acts as B cell surface receptor
  - IgG: most abundant; only one that crosses placental barrier
  - IgE: “troublemaker antigens” involved in allergies; least abundant
Adaptive Immunity: Humoral Immunity

Humoral immunity

Active
- Naturally acquired
  - Infection; contact with pathogen
- Artificially acquired
  - Vaccine; dead or attenuated pathogens

Passive
- Naturally acquired
  - Antibodies pass from mother to fetus via placenta; or to infant in her milk
- Artificially acquired
  - Injection of immune serum (gamma globulin)
Cell-Mediated Immune Response

- T cell mediated immunity
- Requires:
  - Antigen presenting cells
  - T helper cells
- Produces progeny:
  - Memory T cells
  - Cytotoxic T cells
Imbalances of Immunity

- **Immunodeficiencies**
  - Any condition that causes immune cells to behave abnormally
    - Exs. SCID, AIDS, HIV

- **Autoimmune diseases**
  - Immune system loses its ability to recognize itself
    - Exs. Multiple sclerosis, Type 1 Diabetes Mellitus, Lupus, Rheumatoid Arthritis, Grave’s Disease

- **Hypersensitivities**
  - Immune system causes tissue damage as it fights off threats
    - Exs. Pollen & animal dander allergies