

I. Immune System

A. Our bodies defense systems to disease can be divided into 2 categories: our **nonspecific resistance (innate defenses)** which are defense mechanisms we are born with that provide immediate protection against any foreign substance; and **specific resistance (immunity)** which is a system that recognizes specific foreign microbes and mounts an attack to destroy them.

1. Nonspecific resistance (innate defenses) includes **physical** and **chemical barriers** we are born with to protect us from microbial invasion.

a. External barriers (1st line of defense)

i. The **epidermis** of the skin.

(a) The thickness of the skin is difficult to penetrate.

(b) The continuous sloughing removes microbes at the surface.

ii. **Mucous membranes** lining cavities open to the external environment.

(a) Mucous traps microbes and foreign substances.

(b) Respiratory tract also contains cilia to propel the mucous towards the throat.

iii. **Tears, saliva, urine**

(a) Help to flush microbes off the surfaces of the body.

(b) Tears and saliva also contain the enzyme **lysozyme** which can break open bacterial walls.

iv. **Gastric juice** in the stomach.

(a) Destroys most bacteria and bacterial toxins.

b. Internal defenses (2nd line of defense)

i. **Interferon**

(a) Proteins produced by certain cells when they have been infected with a virus.

(b) The interferon diffuses to uninfected neighboring cells to stimulate them to produce **antivirals**, protecting the neighboring cells.

ii. **Complement** system

(a) A group of 20 proteins that when activated result in immune, allergic and inflammatory reactions.

(i) Can break open bacterial walls.

(ii) Attract phagocytes to the area to phagocytize microbes.

(iii) Mark microbes for phagocytosis.

iii. **Natural killer cells**

(a) A lymphocyte found in the blood, spleen, lymph nodes and red bone marrow.

(b) Can kill many microbes and certain tumor cells.

iv. **Phagocytes**

(a) Leukocytes such as neutrophils and macrophages that can ingest microbes and other particles.

v. **Inflammation**

(a) Occurs in response to tissue damage caused by things such as a cut, burns or microbial invasion.

(b) Stimulates vasodilation of vessels to the area to increase blood flow and bring in more leukocytes and antibodies. Results in warmth and redness at the area.

- (c) Stimulates increased permeability of the vessels so antibodies, cells and chemicals can easily enter the tissue from the blood. The increase in fluid in the tissue results in swelling and pain.

vi. Fever

- (a) A high body temperature that occurs during infection and inflammation.
 - (b) The high temperature inhibits replication of some microbes and speeds up body reactions for recovery.
2. Specific resistance (immunity) involves the production of cells and antibodies that are directed toward **antigens** (microbes, foods, drugs, pollen or tissue the body recognizes as foreign).
- a. Cell-mediated immunity
 - i. Involve **T lymphocytes (T-cells)** that originate in the bone marrow but migrate as immature cells to the **thymus** to complete their maturation.
 - (a) Involves learning **self-tolerance** so T-cells will not attack our own cells.
 - (b) T-cells also receive **antigen receptors** which allow the cells to recognize and bind to specific antigens. Note: your T-cells will get antigen receptors that can identify any antigen you could encounter in your life (flu virus, ebola virus, E. coli bacteria), even if you never come into contact with it.
 - (c) These cells migrate to lymphatic organs once they have matured.
 - (d) These cells will divide into **Helper T cells** and **Cytotoxic T cells**.
 - ii. Involve **B lymphocytes (B-cells)** that originate in the bone marrow and complete their maturation within the bone marrow.
 - (a) The maturation process for B-cells is similar to T-cells.
 - (b) Also migrate to lymphatic organs once they have matured.
 - (c) These cells will be able to divide into **plasma cells** for the production of **antibodies**.
 - iii. Involves **antigen presenting cells (APCs)**
 - (a) Includes cells such as macrophages, B cells and dendritic cells (similar to macrophages).
 - (b) These cells are placed within tissues where microbes are likely to penetrate.
 - (c) Will ingest a foreign antigen, break it into pieces and present a fragment of the antigen on their plasma membrane.
 - (d) The cell then migrates to the lymphatic organs where it can present the antigen to waiting T-cells that have a matching antigen receptor.
 - b. Antibody-mediated immunity
 - i. Upon activation by a foreign antigen B-cells divide to form plasma cells, which produce and secrete antibodies.
 - (a) Antibodies can bind to and inactivate specific antigens.
 - (b) Are also known as **immunoglobulins**.
 - (c) There are five different classes of antibodies that differ structurally and functionally.
 - (i) **IgG** antibodies protect against bacteria and viruses. Can cross the placenta from mother to fetus.

- (ii) **IgA** antibodies are found mainly in body secretions (sweat, tears, saliva, breast milk, etc.).
 - (iii) **IgM** antibodies are the first antibodies to be secreted after exposure to an antigen, short lived.
 - (iv) **IgD** antibodies are embedded within the surface of B-cells.
 - (v) **IgE** antibodies are imbedded in the plasma membrane of mast cells and basophils and are involved in allergic reactions.
3. T lymphocytes (T-cells) and the immune response
- a. When an APC ingests a microbe and presents it on its surface it will travel to the lymphatic organ to present it to waiting T-cells.
 - b. Only T-cells with an antigen receptor that matches the presented antigen can be activated by the APC. So if the APC is carrying an antigen for the cold virus, only T-cells that have an antigen receptor for that specific cold virus can respond.
 - c. In order for activation of the T-cell to occur, the T-cells must also be stimulated by the chemical **interleukin-2** (released by other cells of the immune system). This is referred to as **costimulation**.
 - d. Once the T-cell has been activated it begins to enlarge and divide producing clones of itself. All of these clones will also be able to identify the specific antigen that was presented.
 - e. These clones can differentiate into:
 - i. Helper T cells**
 - (a) These cells produce and release many different types of chemicals (**lymphokines**) that facilitate the actions of other cells of the immune system.
 - (b) For example, these cells release **interleukin-2**.
 - (c) These are the cells attacked by the HIV virus.
 - (d) Without the action of Helper T cells the immune response is minimal.
 - ii. Cytotoxic (Killer) T cells**
 - (a) These cells will leave the lymphatic organs to search for self-cells infected by microbes with the matching antigen. Are also effective against tumor cells.
 - (b) Release the protein **perforin** to form holes in target cells, rupturing and killing the cells.
 - iii. Memory T cells**
 - (a) These are the “best of the best” helper and cytotoxic T cells that will remain after the immune response is over.
 - (b) If the same antigen invades the body these cells will have a “memory” for it and can initiate an immune response much quicker than the first time.
 - (c) These cells are maintained for years to provide extended immunity.
4. B lymphocytes (B-cells) and the immune response
- a. Like T-cells, B-cells can respond to APC’s presenting antigens to them. However, the antigen receptor present on B-cells also allows the cell to detect whole antigens themselves.
 - b. When a B-cell detects or is presented with an antigen it will ingest the antigen.
 - c. The antigen is broken down and presented on the surface of the B-cell.

- d. The B-cell then presents this antigen to Helper T cells in order to help activate them.
 - e. In response, the Helper T cells will release interleukin-2 which is needed to costimulate the B-cell.
 - f. Once the B-cell is stimulated it will begin to enlarge and divide producing clones of itself.
 - g. These clones will differentiate into **plasma cells**.
 - i. Plasma cells will secrete hundreds of millions of **antibodies** daily.
 - (a) Antibodies can **neutralize** bacterial toxins.
 - (b) Can also **immobilize** bacteria so they cannot infect cells.
 - (c) Can **agglutinate** (clump) antigens so they can be easily phagocytized.
 - (d) Can initiate a **complement reaction**.
 - (e) Can **mark** antigens for phagocytosis.
 - h. Some of the “best of the best” plasma cells will remain after the immune response is over as **Memory B cells** should the same antigen appear at a future time.
5. Immunological memory
- a. The first time you encounter an antigen results in a **primary immune response** where T-cells and B-cells are activated and memory cells remain after the immune response is over.
 - i. The memory cells can remain for decades in case of second exposure.
 - ii. The antibodies produced only remain for a few days.
 - b. With a second encounter to the same antigen the **secondary immune response** (anamnestic response) is initiated.
 - i. The memory cells initiate the production of new T-cells, B-cells and antibodies within hours.
 - ii. The response is much larger and much more prolonged than the primary response.
 - iii. Usually dispose of the antigen before you even feel symptoms.
6. Types of immunity
- a. Naturally acquired immunity
 - i. Active
 - (a) Occurs when you encounter a “wild-type” antigen and an immune response is generated.
 - (b) You generate your own T-cells, B-cells and antibodies.
 - ii. Passive
 - (a) There is no actual exposure to an antigen and no immune response.
 - (b) Occurs when a fetus or infant acquires antibodies from their mother via the placenta or breastmilk and is temporarily protected.
 - b. Artificially acquired immunity
 - i. Active
 - (a) Occurs when a person is immunized with a dead or living antigen.
 - (b) Results in an immune response that generates memory cells.
 - (c) Later, when a person encounters the “wild” version of the antigen they produce a strong secondary immune response to fight of the antigen.
 - ii. Passive
 - (a) Occurs when a person is given an injection of antibodies (often from a horse).

- (b) Since these antibodies have half-lives they only provide temporary protection.

II. Lymphatic system

A. Functions of the lymphatic system

1. Drain excess interstitial fluid from tissues.
2. Transport lipids from the digestive system.
3. Storage of lymphocytes involved in the immune response.

B. Lymphatic vessels

1. Lymphatic capillaries

- a. Tiny, blind-ended capillaries located within tissues.
- b. Composed of simple squamous epithelia.
 - i. Cells loosely overlap allowing fluid to easily enter the capillaries.
 - ii. Once fluid enters a lymphatic capillary it is referred to as **lymph**.
 - iii. Will have **valves** within them to assist in the one-way flow of lymph.
 - iv. Capillaries unite to form larger lymphatic vessels.

2. Lymphatic vessels

- a. Resemble veins in structure.

b. Thoracic duct

- i. Major lymphatic vessel draining lymphatic fluid from left side of the head, neck and chest; left upper limb and entire body below the ribs.
- ii. Returns the lymph to the circulatory system by emptying into the left subclavian vein.

c. Right lymphatic duct

- i. Major lymphatic vessel draining lymphatic fluid from the upper right side of the body.
- ii. Returns the lymph to the circulatory system by emptying into the right subclavian vein.

d. Factors assisting lymphatic flow

- i. The contraction of skeletal muscles compressing lymphatic vessels.
- ii. Pressure changes during respiration compressing lymphatic vessels.

3. Edema

- a. If the lymphatic vessels are obstructed it allows for excess interstitial fluid to accumulate within the tissues, resulting in edema.
- b. May also be the result of increased blood pressure at the capillaries causing excessive fluid to lead out of the capillaries into the tissues, overwhelming the lymphatic vessels.

C. Lymphatic organs and tissues

1. Thymus

- a. A bi-lobed organ located superior to the heart.
- b. T cell maturation occurs here.
- c. Has its functional peak during childhood.
- d. Reaches maximum size at puberty and then shrinks.
- e. **Severe combined immune deficiency (SCID)** results if the thymus is missing.

2. Lymph nodes

- a. Located along lymphatic vessels.
- b. A bean shaped structure surrounded by a capsule.

- c. Filter lymph.
 - d. Contain B cells, T cells, dendritic cells and macrophages.
3. Spleen
- a. Located between the stomach and the diaphragm.
 - b. Surrounded by a thin capsule.
 - c. Consists of white pulp and red pulp.
 - i. White pulp
 - (a) Lymphatic tissue consisting of lymphocytes and macrophages.
 - (b) Responsible for the immune functions of the spleen.
 - ii. Red pulp
 - (a) Red blood cells and macrophages in venous sinuses.
 - (b) Has 3 functions:
 - (i) Macrophages destroy old or damaged red blood cells.
 - (ii) Storage of platelets.
 - (iii) Production of fetal red blood cells.
4. Lymph nodules
- a. Unencapsulated mass of lymphatic tissue.
 - b. Located within mucous membranes, aggregated in the tonsils, Peyer's patches (ileum) and the appendix.
 - c. Contain lymphocytes and dendritic cells.