Title: Serology and immunity

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A. Blood plays a role in respiration, nutrition, waste elimination, thermoregulation, immune defense, water and acid-base balance, and internal communication.

B. Blood is a connective tissue with plasma and formed elements.
1. Formed elements include red blood cells (erythrocytes), platelets, and white blood cells (leukocytes).
2. After centrifugation erythrocytes make up 45% of the total blood volume, and plasma makes up nearly 55% of the volume, with leukocytes and platelets making up the rest.

I. Plasma

A. Proteins
1. Blood plasma is a complex mix of proteins, enzymes, nutrients, wastes, hormones, and gases.
2. The three major types of plasma proteins
a. Albumins are the smallest and most abundant of the plasma proteins. They make major contributions to viscosity and osmolarity, and changes in their abundance can influence blood pressure, flow, and fluid balance.
b. Globulins are divided into three subclasses: alpha, beta, and gamma globulins.
c. Fibrinogen is the soluble precursor of fibrin, a protein involved in clotting.
3. The liver produces all plasma proteins with the exception of gamma globulins, which are produced by cells of the immune system.

B. Nutrients
1. Various nutrients absorbed by the digestive tract are transported by plasma.
2. These include glucose, amino acids, fats, cholesterol, phospholipids, vitamins, and minerals.

C. Gases
1. Plasma transports a portion of the carbon dioxide and oxygen circulated by the blood, and also carries dissolved nitrogen.

D. Electrolytes
1. The plasma electrolytes and their concentrations - see water-ions balance chapter.

II. Blood Types

A. The ABO Group
1. The ABO blood group was discovered in 1900 by Karl Landsteiner.
2. Surfaces of blood and body cells possess antigens. The antigens of RBCs that determine blood type are called agglutinogens because of their role in agglutination during blood transfusions. Plasma antibodies that react against agglutinogens are agglutinins.
3. The ABO blood group consists of blood types A, B, AB, and O. The presence of ABO antigens determines the person's blood type, as determined by genetics.
4. Type A blood has type A antigen on the surface of its RBCs, and anti-B antibody in its plasma. Type B blood has type B antigens and anti-A antibody. Type AB has both antigens but no antibodies, while type O has no antigens, but both anti-A and anti-B antibodies.
B. The Rh Group
1. The Rh blood group is so called because of the rhesus monkey in which it was first discovered.
2. If antigen D of the Rh system is present on the RBCs, the person is Rh positive. If there is no antigen D on the RBCs, the person is Rh negative.
3. Anti-Rh antibodies are normally absent, unlike the situation for the ABO blood groups. They may be produced as a result of immunization to Antigen D.
4. Problems arise when an Rh-negative person receives a transfusion from an Rh-positive person, and starts to produce antibodies against the Rh factor (Antigen D). The next time Rh-positive blood is received, the recipient's plasma antibodies agglutinate the donor's RBCs.
5. A similar situation occurs when an Rh-negative woman is carrying an Rh-positive fetus. The first fetus goes unharmed and mother starts to produce anti-Rh antibodies; the production usually begins with parturition. When a second Rh-positive fetus begins to grow, the mother's anti-Rh antibodies cause a severe anemia in the infant, called hemolytic disease of the newborn (HDN). This can be prevented by administering an anti-Rh gamma globulin injection the mother shortly after the first, and subsequent, Rh-positive babies are delivered.

C. Other Blood Groups
1. At least 300 other blood groups are known, but most do not cause transfusion reactions.

III. The Lymphatic System

A. The lymphatic system's network of capillaries and vessels drains excess tissue fluid and returns it to the bloodstream.
B. The principal components of the lymphatic system are lymph, lymphatic vessels, lymphatic tissue, and lymphatic organs.
C. Lymph and the Lymphatic Vessels
1. Once tissue fluid has entered lymphatic vessels, it is called lymph.
2. Lymph is usually clear and colorless and is similar in composition to blood plasma but contains less protein and no RBCs.
D. Lymphatic Tissue
1. Diffuse lymphatic tissue occurs throughout the mucous membranes and connective tissues of many organs.
2. In the small intestine at its junction with the large intestine, lymphatic nodules take the form of Peyer patches.
E. Lymphatic Organs
1. Lymph nodes are numerous and embedded within connective tissue.
   a. Lymph nodes are especially concentrated in the cervical, axillary, thoracic, abdominal, pelvic, and inguinal regions.
   b. Macrophages are concentrated in the medulla of the lymph node. Lymphocytes are located in the cortex, where germinal centers arise when fighting off a pathogen.
   c. Lymph nodes filter lymph. Lymph flows through several nodes in series before returning to the bloodstream.
2. The tonsils are patches of lymphatic tissue at the entrance to the pharynx.
3. The thymus is an organ located in the superior mediastinum.
4. Within the spleen, red pulp consists of sinuses filled with erythrocytes, and white pulp consists of lymphocytes and macrophages.
   a. The spleen produces blood cells in the fetus, serves as a blood reservoir, acts as an erythrocyte graveyard where macrophages engulf their remains.
IV. Nonspecific Resistance

A. Immune defenses fall into two categories: (1) nonspecific defenses that guard against a wide variety of pathogens and (2) immunity, composed of mechanisms whereby lymphocytes recognize and destroy specific pathogens.

B. External Barriers
1. The skin, except in a few areas, is relatively dry and lacks the nutrients to support microbial growth.
2. The mucous membranes of the digestive, respiratory, urinary, and reproductive tracts protect them from invasion. Mucous traps microbes and contains protective chemicals.
3. Certain bodily secretions inhibit the survival of pathogenic microorganisms. Stomach acid, acid in the urethra and vagina, lysozyme in tears, saliva, and mucus all serve to destroy pathogens.

C. Leukocytes (Neutrophils, Eosinophils, Basophils, Monocytes, Natural Killer Cells) and Macrophage System
a. Lymphocytes fall into several functional types. Large lymphocytes called natural killer (NK) cells attack cells of your own body that are infected by viruses or have turned cancerous.
D. Inflammation
1. Inflammation is a response to tissue injury, and is characterized by four cardinal signs: redness, swelling, heat, and pain.
2. The general purposes of inflammation are to limit the spread of the pathogen and destroy it, to remove the debris of damaged tissue, and to initiate tissue repair.

E. Antimicrobial Proteins
1. **Interferons** are polypeptides secreted by cells that have been invaded by viruses. They diffuse to neighboring cells and prevent viruses from attaching to them.
   a. Interferons activate natural killer cells and macrophages, which destroy infected host cells before they release more viruses.
   b. Interferons also stimulate the destruction of cancer cells.
2. The **complement** system is a group of 20 or more beta globulins of blood that aid nonspecific resistance and immunity.
   a. Complement helps destroy pathogens in three ways:
      - by enhanced inflammation
      - by opsonization (making bacteria easier to phagocytize by coating their surfaces)
      - by cytolysis (leading to the rupture of target cells).

F. Fever
1. Fever (pyrexia) can result from trauma, drug interactions, infection, and other causes.
2. Fever is beneficial in that it promotes interferon activity, elevates metabolic rate and accelerates tissue repair, and inhibits the reproduction of bacteria and viruses.

V. General Aspects of Specific Immunity

A. The immune system consists of widely distributed cells that recognize foreign substances and act to neutralize or destroy them.
1. Two characteristics that distinguish immunity from nonspecific resistance are specificity and memory.
2. Two types of immunity are recognized.
   a. **Humoral** (antibody-mediated) immunity is based on the action of antibodies. Circulating antibodies bind to bacteria, toxins, and extracellular viruses and destroy them.
   b. **Cellular** (cell-mediated) immunity is based on the action of lymphocytes that directly attack foreign cells, cells infected with viruses or parasites, and cancer cells.

B. Antigens
1. An antigen (Ag) is any molecule that is able to start an immune response.
   a. Antigens are generally large, complex molecules, such as proteins, polysaccharides, glycoproteins, and glycolipids.
   b. An antigen molecule has multiple antigenic determinants that can stimulate formation of a variety of antibodies.
2. Some molecules are too small to be antigenic alone; these are called haptens.
   a. Haptens can stimulate an immune response by binding to a host macromolecule.
   b. Cosmetics, detergents, industrial chemicals, poison ivy, and animal dander act as haptens.

C. Antibodies
1. An antibody (Ab), or immunoglobulin, is a gamma globulin.
2. An antibody is composed of four polypeptide chains linked by disulfide bonds. Two are heavy chains, and two are light chains; all four have a variable region (V region) that gives an antibody uniqueness. The rest of each chain is a constant region (C region).

3. The V regions of a heavy and light chain combine to form an antigen-binding site on each arm.

4. There are five classes of antibodies, named for the structures of their C regions: IgA, IgD, IgE, IgG, and IgM.

D. Lymphocytes

1. The major cells of the immune system are lymphocytes and macrophages.
2. Macrophages are active in nonspecific resistance but are also crucial in immunity.
3. Most lymphocytes can be classified as T lymphocytes (T cells) or B lymphocytes (B cells).

a. T Lymphocytes

- During fetal development, the bone marrow releases undifferentiated stem cells into the blood. Some of these colonize the thymus, where they are stimulated to become T (thymus) lymphocytes. Under the influence of thymosin, each cell develops numerous plasma membrane proteins that serve as antigen receptors.
- An immunocompetent T cell divides rapidly, forming a clone of T cells with identical receptors.
- Clonal deletion leaves only the T cells capable of responding to foreign antigens destroying any that are self-reactive.
b. B Lymphocytes
- Fetal stem cells also settle into other regions of the body where they become B lymphocytes. ("B" stands for the bursa of Fabricius, a lymphatic organ in chickens.) B cells synthesize their antigen receptors, divide rapidly, and produce immunocompetent clones. Each clone can react to only one antigen.
- Immunocompetent B cells disperse through the body and colonize the same organs as T cells.

E. Antigen-Presenting Cells (APCs).
1. The role of an APC is to phagocytize an antigen, digest it into molecular fragments, and "display" some of these fragments on its surface. Wandering T cells regularly inspect APCs for displayed antigens.

F. Interleukins
1. Interleukins are hormonelike messengers between leukocytes.
2. Those produced by lymphocytes are called lymphokines, and those produced by macrophages are called monokines.

VI. Humoral Immunity

A. In humoral immunity, the essential stages are recognition, attack, and memory.

B. Recognition
1. The process of recognition involves five steps.
   a. Since an antigen is a large molecule with numerous copies of each antigenic determinant, it binds to several receptors on a B cell and links them together. This capping process activates the cell.
   b. The capped receptors of the B cell become drawn into a cluster, culminating in receptor-mediated endocytosis of the antigen-receptor complex.
   c. The internalized antigen is digested into fragments, linked to MHC proteins, and displayed. This alerts helper T cells to become active.
   d. A helper factor stimulates the B cell to divide repeatedly into a battalion of identical cells in a process known as clonal selection.
   e. Most cells of a clone differentiate into plasma cells that can produce antibodies at a rate of 2,000 molecules per second.
2. The first time you are exposed to a particular antigen, your plasma cells produce mainly \textbf{IgM}. In later exposures to the same antigen, they produce mainly \textbf{IgG}.
3. The immune system is thought to be able to produce 2 million different antibodies.

C. Attack
1. Once released by a plasma cell, antibodies use four different mechanisms to destroy antigens.
   a. Neutralization occurs as antibodies mask sites that bind to human cells destroying them
   b. Complement fixation occurs when antibodies bind complement, then bind with an antigen and expose its complement binding site. This binds the complement to the antigen, leading to destruction of the pathogen.
   c. Agglutination occurs as antibody molecules bind to several antigen molecules at once sticking them together.
   d. Precipitation occurs as antibodies interact with antigens, binding them in groups, and the complex precipitates out of solution.
D. Memory
1. The primary response is generated the first time a person is exposed to an antigen.
a. During clonal selection, some members of the clone become memory cells that are long-lived. They are more abundant than the original virgin lymphocyte pool, and thus are able to produce a much quicker secondary immune response.

VII. Cellular Immunity

A. In cellular immunity, lymphocytes directly attack and destroy foreign cells and diseased host cells.
1. This involves cytotoxic T cells that carry out the attack, helper T cells that promote defense mechanisms, suppressor T cells that regulate the attack, and memory T cells that lie in wait for the next time the antigen is encountered.

B. Recognition
1. Recognition involves antigen presentation and T cell activation.
2. Antigen Presentation
   a. T cells respond only to antigen fragments displayed by APCs, not to free antigens.
   b. Both helper and cytotoxic T cells are involved in surveillance, and they examine the MHC proteins of all cells.
   c. MHC-I (class I) proteins occur on all body cells; MHC-II (class II) proteins occur only on the surfaces on APCs, including B cells, macrophages, and some T cells. An MHC-II protein displaying an antigen stimulates helper T cells.

C. Attack
1. When a helper T cell recognizes a MHC-antigen complex, it secretes a variety of lymphokines that attract neutrophils and promote inflammation. One of the lymphokines, macrophage-activating factor (MAF), enhances the phagocytic activity of macrophages.
2. Cytotoxic (killer) T cells are the only T lymphocytes that directly attack and kill other cells. When a cytotoxic T cell recognizes a complex of antigen and MHC-I protein, it destroys pathologic cells.
   a. Cytotoxic T cells degranulate and release perforin that is inserted into the enemy plasma protein.
   b. Other ways that cytotoxic T cells kill by release of lymphotoxin, which destroys the target cell's DNA, and tumor necrosis factor, which kills cancer cells.
3. Suppressor T cells release lymphokines that inhibit T cell and B cell activity.

D. Passive and Active Immunity
1. When antibodies or lymphocytes are given from one person or source, the recipient acquires passive immunity. Passive immunity lasts only 2–3 weeks.
2. Active immunity refers to the production of one's own antibodies or lymphocytes against an antigen. It can be induced by natural exposure or artificially induced by vaccination and generally lasts a long time.
VIII. Immune System Disorders

A. Hypersensitivity
1. Hypersensitive people produce antibodies to substances that most people tolerate, such as bee venom.

B. Autoimmune Diseases
1. Autoimmune diseases are failures of the immune system to distinguish self from foreign antigens.
2. The immune system produces autoantibodies that attack the body's own tissues as a result of cross-reactivity (some foreign antigens are similar to those of the body, causing antibodies to direct their attack against the body).