Introduction

Immunology is the scientific study of the immune system and immune responses.

The primary functions of the immune system are to:
- Differentiate between “self” and “non-self”
- Destroy that which is “non-self”

Cells involved in immune responses originate in bone marrow; 3 lines of lymphocytes are derived from lymphoid stem cells of bone marrow: B lymphocytes (or B cells), T lymphocytes (or T cells) and natural killer cells (NK cells)

Introduction, cont.

There are 2 categories of T cells:
- Helper T cells and Cytotoxic T cells

There are 2 major arms of the immune system:
- Humoral immunity; where special glycoproteins called antibodies are produced by B cells to destroy specific microbes
- Cell-mediated immunity; involves a variety of cell types, with antibodies only playing a minor role, if any

The Two Major Arms of the Immune System

Immunity

Acquired immunity = immunity that results from the active production or receipt of antibodies during one's lifetime
- Active acquired immunity:
  - Antibodies are produced within the person
  - Usually provides long lasting protection
- Passive acquired immunity:
  - Antibodies are received that were produced by another person or persons or by an animal
  - Usually provides only temporary protection

Active Acquired Immunity

- Two types of active acquired immunity:
  - Natural active acquired immunity – occurs naturally
  - Artificial active acquired immunity – artificially induced

- Artificial active acquired immunity results when a person receives a vaccine.
  - A vaccine is defined as material that can artificially induce immunity to an infectious disease, usually following injection or ingestion of the vaccine.
  - Most vaccines are made from living or dead pathogens or the toxins that they produce.

How Vaccines Work

- Vaccines stimulate the recipient’s immune system to produce protective antibodies (i.e., antibodies that will protect the person from disease).

- Types of available vaccines:
  - Attenuated vaccines
  - Inactivated vaccines
  - Subunit vaccines
  - Conjugate vaccines
  - Toxoid vaccines

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Passive Acquired Immunity

- Antibodies produced in one person are transferred to another person to protect the latter from infection – provides temporary protection.

- Two types:
  - Natural passive acquired immunity
  - Small antibodies, IgG, present in mother’s blood cross the placenta to reach the fetus
Artificial passive acquired immunity

- Antibodies from an immune person are transferred to a susceptible person; example, hepatitis B immune globulin

Humoral Immunity

- Antigens
  - Foreign organic substances that are large enough to stimulate the production of antibodies
  - Substances capable of stimulating antibodies are said to be antigenic
  - A bacterial cell has many molecules (antigenic determinants) on its surface that are capable of stimulating the production of antibodies

Humoral Immunity, cont.

- Antigens, cont.
  - The processing of either T-dependent or T-independent antigens results in B cells developing into plasma cells, which are capable of secreting antibodies.
  - The initial immune response to an antigen is called the primary response; it takes 10-14 days for antibodies to be produced.
  - The increased production of antibodies following the second exposure to a particular antigen is called the secondary response.

Humoral Immunity, cont.

- Where Do Immune Responses Occur?
  - Immune responses to antigens in the blood are usually initiated in the spleen; responses to microbes and other antigens in tissues are generated in lymph nodes located near the infected area.

- Antibody Structure and Function
  - Antibodies are a class of glycoprotein called immunoglobulins; 5 types = IgA, IgD, IgE, IgG, IgM.
  - All antibodies are immunoglobulins, but not all immunoglobulins are antibodies!

Antigen-Antibody Complexes

- When an antibody combines with an antigen an antigen-antibody complex (or immune complex) is formed.
- Antigen-antibody complexes are capable of activating the complement cascade; results in some of the following effects:
  - Activation of leukocytes
  - Lysis of bacterial cells
  - Increased phagocytosis as a result of opsonization

Cell-Mediated Immunity

- Antibodies are unable to enter cells.
- Cell-mediated immunity (CMI)
  - A complex system of interactions among many types of cells and cellular secretions (cytokines)
  - An arm of the immune system capable of controlling chronic infections by intracellular pathogens (e.g., certain bacteria, protozoa, fungi, and viruses)
  - Examples of cells that participate in CMI: macrophages, T_{H} cells, T_{C} cells, NK cells, and granulocytes

Cell-Mediated Immunity, cont.

- NK (Natural Killer) Cells
  - NK cells are in a subpopulation of lymphocytes called large granular lymphocytes.
  - They resemble lymphocytes, but lack typical T or B cell surface markers.
  - Do not proliferate in response to antigen and appear not to be involved in antigen-specific recognition.
  - NK cells kill target cells, including foreign cells, host cells infected with viruses or bacteria, and tumor cells.

Hypersensitivity and Hypersensitivity Reactions

- Hypersensitivity refers to an overly sensitive immune system.
- Different types of hypersensitivity reactions:
  - Immediate-type: occurs from within a few minutes to 24 hours after contact with a particular antigen; 3 types: type I, II and III hypersensitivity reactions
  - Delayed-type: usually takes more than 24 hours to manifest themselves
    - Also known as Type IV hypersensitivity reactions.

Type I Hypersensitivity Reactions
Type I hypersensitivity reactions are also known as anaphylactic reactions; they include:
- classic allergic responses such as hay fever symptoms, asthma, hives, and gastrointestinal symptoms that result from food allergies
- allergic responses to insect stings and drugs
- anaphylactic shock

Type I Hypersensitivity Reactions, cont.
- The Allergic Response
  - Type I immediate hypersensitivity is probably the most common type of hypersensitivity.
  - People prone to allergies (atopic persons) produce IgE antibodies when exposed to allergens (antigens that cause allergic reactions).
  - The allergic reaction results from the presence of IgE antibodies bound to basophils in the blood or to mast cells in connective tissues – IgE antibodies that were produced in response to the person’s first exposure to the allergen.

Factors in the Development of Type I Hypersensitivity

Events That Occur in Type I Hypersensitivity Reactions

Type I Hypersensitivity Reactions, cont.
- Type I hypersensitivity reactions may be localized or systemic.
  - Localized reactions involve mast cell degranulation; they result in allergic reactions, such as hay fever symptoms, asthma, and food allergies.
  - Systemic reactions involve basophil degranulation; they occur throughout the body, can lead to anaphylactic shock, and can be life-threatening.

Type I Hypersensitivity Reactions, cont.
- Systemic Anaphylaxis
  - Results from the release of chemical mediators from basophils in the bloodstream
  - Occurs throughout the body – much more serious than localized anaphylaxis
  - Common allergens involved are drugs or insect venom

- Latex Allergy
  - Latex can trigger any of 3 types of reactions: irritant contact dermatitis, allergic contact dermatitis, and immediate type hypersensitivity

Type I Hypersensitivity Reactions, cont.
- Allergy Skin Testing and Allergy Shots
  - Anaphylactic reactions can be prevented by avoiding known allergens, which is often difficult to do.
  - Skin tests (scratch tests) are used to identify offending allergens in patients.
    - A positive test is indicated if cutaneous anaphylaxis occurs at the site of the scratch.
    - Immunotherapy (i.e., allergy shots - IM doses of the allergen) may be used to treat the patient.
    - IgG blocking antibodies are produced in response to allergy shots.

Type II Hypersensitivity Reactions
- Type II hypersensitivity reactions are cytotoxic reactions, meaning that body cells are destroyed during these reactions.

  Sequence of events in a Type II hypersensitivity reaction:
  1. A particular drug binds to the surface of a cell.
  2. Anti-drug antibodies then bind to the drug.
  3. Complement activation on the cell surface is initiated.
  4. The complement cascade leads to lysis of the cell.

Type III Hypersensitivity Reactions
- Type III hypersensitivity reactions are immune complex reactions – such as those that occur in serum sickness and certain autoimmune diseases (e.g., systemic lupus erythematosus and rheumatoid arthritis).
- Involve IgG or IgM antibodies, complement and neutrophils
- Some complications of untreated or inadequately treated strep throat and other Streptococcus pyogenes infections are the result of type III hypersensitivity reactions (e.g., rheumatic fever and glomerulonephritis).

Type IV Hypersensitivity Reactions
- Type IV hypersensitivity reactions are delayed-type hypersensitivity (DTH) or cell-mediated immune reactions, and are part of cell-mediated immunity.
  - Reactions are usually observed 24-48 hours or longer after exposure or contact
• DTH is the prime mode of defense against intracellular bacteria and fungi.
• DTH involves a variety of cell types, including macrophages, cytotoxic T cells, and NK cells - antibodies do not play a major role.
• A classic example of DTH is a positive TB skin test.

Autoimmune Diseases
• Autoimmune diseases result when a person’s immune system no longer recognizes certain body tissues as “self” and attempts to destroy those tissues as if they were “non-self” or foreign.
• May occur with certain tissues that are not exposed to the immune system during fetal development and, thus, are not recognized as “self.”
• There are more than 80 recognized autoimmune diseases.
• Can be classified as organ-specific or non-organ-specific.
• Examples: Hashimoto’s thyroiditis, Graves disease, etc.

Immunosuppression
• Persons whose immune systems are not functioning properly are said to be immunosuppressed.
• Acquired immunodeficiencies may be caused by drugs (e.g., cancer therapeutic agents), irradiation, or certain infectious diseases (e.g., HIV infection).
• Inherited immunodeficiency diseases can be the result of deficiencies in antibody production, complement activity, phagocytic function, or NK cell function; examples – DiGeorge syndrome and Wiskott-Aldrich syndrome.
• People born lacking the ability to produce antibodies (i.e., gamma globulins) have agammaglobulinemia; persons not producing a sufficient amount of antibodies are said to have hypogammaglobulinemia.

Immunodiagnostic Procedures
• Immunodiagnostic procedures (IDPs) help diagnose infectious diseases by detecting either antigens or antibodies in clinical specimens; test results are usually available on the same day!
• 3 possible reasons for the presence of antibodies to a particular pathogen: present infection, past infection, vaccination.
• A variety of different laboratory tests have been designed to observe the presence of an antibody-antigen reaction.

• Examples of these tests include agglutination, precipitin tests, immunofluorescence, and enzyme-linked immunosorbent assays (ELISAs).

Immunodiagnostic Procedures, cont.
• Skin Testing
  – Performed in vivo
  – Antigens are injected within or beneath the skin
  – Example: the tuberculosis skin test
• Procedures Used in the Diagnosis of Immunodeficiency Disorders
  – For assessment of patient’s immune status and evaluation of immunodeficiency disorders
  – Include B-cell deficiency states, cell-mediated immunodeficiencies, complement deficiencies, etc.