IMMUNOLOGY

V 1.0 2024-25

SEM IV

K HARISH BABU

PS GOVT COLLEGE PENUKONDA

SEMESTER-IV

COURSE 11: IMMUNOLOGY

Theory Credits: 3 3 hrs/week

LEARNING OBJECTIVES

- To promote critical thinking among students.
- To provide students with a foundation in immunological processes
- To provide students with knowledge on how the immune system works building on their previous knowledge
- To clearly state the role of the immune system.
- To compare and contrast the innate versus adaptive immune systems.
- To provide an overview of the interaction between the immune system and pathogens.

LEARNING OUTCOMES:

The overall course outcome is that the student shall develop deeper understanding of concepts of immunology. This course will provide students with a deep knowledge in immunology by the completion of the course the graduate shall able to

- Articulate the roles of innate recognition receptors in immune responses
- Compare and contrast humoral versus cell-mediated immune responses
- Distinguish various cell types involved in immune responses and associated functions;
- Distinguish and characterize antibody isotypes, development, and functions
- Understand the role of cytokines in immunity and immune cell activation;
- Understand the significance the Major Histocompatibility Complex in terms of immune response and transplantation

SYLLABUS:

UNIT – I: Overview of Immune system

1.1 Introduction to basic concepts in Immunology
1.2 Innate and adaptive immunity
1.3 Cells of immune system
1.4 Organs of immune system

UNIT II : Antigens

2.1 Basic properties of antigens
2.2 B and T cell epitopes, paratopes
2.3 Haptens and adjuvants
2.4 Factors influencing immunogenicity

UNIT III: Antibodies

3.1 Structure of antibody
3.2 Classes of antibodies
3.3 Functions of antibodies
3.4 Monoclonal antibodies

UNIT IV: Working of Immune system

4.1 Structure and functions of major histocompatibility complexes
4.2 Exogenous pathway of antigen presentation and processing
4.3 Endogenous pathway of antigen presentation and processing
4.4. Basic properties and functions of cytokines

UNIT V: Immune system in health and disease

5.1 Gell and Coombs' classification and brief description of various types of hypersensitivities
5.2 Introduction to concepts of autoimmunity and immunodeficiency
5.3 General introduction to vaccines Types of vaccines, Immunization programme
5.4 Organ transplantation- Graft rejection, immune suppressors

SEMESTER-IV

COURSE 11: IMMUNOLOGY

Practical Credits: 1 2 hrs/week

LEARNING OBJECTIVES

- To acquire knowledge on the distribution of lymphoid organs
- To study the histology of lymphoid organs
- To acquaint with the process of blood grouping with kit
- To acquaint with the ELISA test
- To acquaint with the Widal test

SYLLABUS:

1. Demonstration of lymphoid organs (as per UGC guidelines)
2. Histological study of spleen, thymus and lymph nodes (through prepared slides)
3. Blood group determination
4. Demonstration of ELISA
5. Demonstration of Immunoelectrophoresis
6. Testing for Typhoid antigens by Widal test.
7. Differential Leukocyte Count
8. Isolation of monocytes from blood.
9. Rapid Plasma Reagin (RPR) Test

RFERENCE WEB LINKS:

- https://vlab.amrita.edu/?sub=3&brch=69
- https://ivl1-au.vlabs.ac.in/List%20of%20experiments.html
- https://ivl2-au.vlabs.ac.in/List%20of%20experiments.html
- https://www.medicine.mcgill.ca/physio/vlab/immun/vlabmenuimmun.htm
- http://www.zoologyresources.com/uploadfiles/books/dc64b77d8769325515d17c945e461b45.pdf
- http://www.lucp.net/books-pdf/Lab%20Manual%20Dr.%20Idris%20Adewale%20Ahmed/15.%20BASIC%20IMMUNOLOGY.pdf
- https://www.avit.ac.in/lab/immunology_bioprocess_engineering_lab/download/17BTCC89/lab_manual.pdf
- https://www.urmc.rochester.edu/MediaLibraries/URMCMedia/labs/frelinger-lab/documents/Immunology-Lab-Manual.pdf
- https://webstor.srmist.edu.in/web_assets/downloads/2021/18BTC106J-lab-manual.pdf

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1.1. Introduction to basic concepts in Immunology

Immunology is the branch of biology that focuses on the immune system, which protects the body from infections, diseases, and foreign invaders. Here's a brief introduction to some fundamental concepts in immunology:

The Immune System

The immune system is a complex network of cells, tissues, and organs that work together to defend the body against harmful substances. It can be broadly divided into two types: innate immunity and adaptive immunity.

Innate Immunity

Innate immunity is the body's first line of defense and provides immediate, non-specific protection against pathogens. Key components include:

- **Physical Barriers**: Skin, mucous membranes, and other barriers that block pathogen entry.
- **Phagocytes**: Cells like macrophages and neutrophils that engulf and destroy invaders.
- **Natural Killer (NK) Cells**: Destroy infected or cancerous cells.
- **Complement System**: A group of proteins that assist in destroying pathogens.
- **Inflammatory Response**: A response that involves swelling, heat, redness, and pain to isolate and repair affected tissues.

Adaptive Immunity

Adaptive immunity is a more specific and delayed response, involving the activation and clonal expansion of lymphocytes (B cells and T cells).

- **B Cells**: Produce antibodies that neutralize or mark pathogens for destruction.
    - **Plasma Cells**: B cells that produce antibodies.
    - **Memory B Cells**: Provide long-term immunity by remembering previous infections.
- **T Cells**: Attack infected cells and regulate immune responses.
    - **Helper T Cells (CD4+)**: Activate other immune cells.
    - **Cytotoxic T Cells (CD8+)**: Kill infected or cancerous cells.
    - **Regulatory T Cells**: Suppress immune responses to maintain homeostasis and prevent autoimmunity.
    - **Memory T Cells**: Provide long-term immunity.

Antigens and Antibodies

- **Antigens**: Substances (usually proteins) on the surface of pathogens that are recognized by the immune system.

- **Antibodies**: Y-shaped proteins produced by B cells that specifically bind to antigens, neutralizing them or marking them for destruction.

The Lymphatic System

The lymphatic system supports immune functions and includes lymph nodes, the spleen, thymus, and bone marrow.

- **Lymph Nodes**: Filter lymphatic fluid and trap pathogens.
- **Spleen**: Filters blood, removes old red blood cells, and provides a site for immune cell interactions.
- **Thymus**: Site of T cell maturation.
- **Bone Marrow**: Produces all blood cells, including immune cells.

Immune Response

The immune response involves several steps:

1. **Recognition**: Immune cells recognize antigens.
2. **Activation**: Lymphocytes are activated and proliferate.
3. **Effector Phase**: Immune cells and molecules eliminate pathogens.
4. **Resolution**: The response is downregulated to prevent excessive damage.
5. **Memory**: Memory cells remain to provide faster and stronger responses to future exposures to the same pathogen.

Immunological Memory

One of the hallmarks of adaptive immunity is the development of immunological memory, which allows for a more rapid and effective response upon subsequent exposures to the same pathogen.

Vaccination

Vaccination leverages immunological memory by introducing a harmless form of a pathogen to stimulate an immune response, thereby providing protection against future infections.

Autoimmunity and Allergies

- **Autoimmunity**: The immune system mistakenly targets the body's own cells.
- **Allergies**: The immune system overreacts to harmless substances (allergens).

Understanding these basic concepts provides a foundation for exploring more complex immunological processes and their implications for health and disease.

1.2. Innate and adaptive immunity

Innate and adaptive immunity are the two main components of the immune system, each playing distinct roles in defending the body against pathogens. Here's a detailed comparison and explanation of each:

A. Innate Immunity

i. Characteristics:

- **Non-specific:** Responds to a wide range of pathogens without specificity.
- **Immediate Response:** Acts quickly, often within minutes to hours of an infection.
- **No Memory:** Does not provide long-lasting immunity or memory of the pathogen.

ii. Components:

1. Physical and Chemical Barriers:

*** Skin and Mucous Membranes:** Act as a physical barrier to prevent entry of pathogens.

*** Secretions:** Such as saliva, mucus, and stomach acid, which can destroy or inhibit pathogens.

2. Cellular Defenses:

*** Phagocytes:** Cells like macrophages and neutrophils that engulf and digest pathogens.

*** Dendritic Cells:** Capture antigens and present them to T cells, bridging innate and adaptive immunity.

*** Natural Killer (NK) Cells:** Destroy infected or cancerous cells without prior sensitization.

3. Soluble Factors:

*** Complement System:** A group of proteins that can lyse pathogens or mark them for destruction.

*** Cytokines and Chemokines:** Signaling molecules that mediate and regulate immunity, inflammation, and hematopoiesis.

*** Antimicrobial Peptides:** Such as defensins that directly kill microbes.

4. Inflammatory Response:

Characterized by redness, heat, swelling, and pain. It isolates and controls infection and initiates tissue repair.

B. Adaptive Immunity

i. Characteristics:

- **Specific:** Targets specific pathogens based on recognition of unique antigens.
- **Delayed Response:** Takes longer to activate (days to weeks) but is more precise.
- **Memory:** Provides long-lasting immunity through memory cells, leading to a faster and stronger response upon subsequent exposures to the same pathogen.

ii. Components:

1. Lymphocytes:

B Cells:

*** Plasma Cells:** B cells differentiate into plasma cells that produce antibodies specific to the antigen.

*** Memory B Cells:** Long-lived cells that remember the antigen for faster future responses.

T Cells:

*** Helper T Cells (CD_4^+):** Activate other immune cells, including B cells and cytotoxic T cells.

*** Cytotoxic T Cells (CD_8^+):** Kill infected or cancerous cells by inducing apoptosis.

*** Regulatory T Cells:** Suppress immune responses to prevent autoimmunity and maintain immune homeostasis.

*** Memory T Cells:** Provide long-term immunity by remembering past infections.

iii. Antibodies:

Produced by B cells, these proteins specifically bind to antigens to neutralize them or mark them for destruction by other immune cells.

iv. Antigen Presentation:

Major Histocompatibility Complex (MHC): Molecules that present antigen fragments on the surface of cells. MHC class I molecules present to CD8+ T cells, while MHC class II molecules present to CD4+ T cells.

Interaction between Innate and Adaptive Immunity

- **Activation:** The innate immune system often initiates the adaptive immune response. For example, dendritic cells capture antigens and present them to T cells, leading to their activation.
- **Enhancement:** Components of the adaptive immune system, such as antibodies, can enhance the effectiveness of the innate immune system. For instance, antibodies can opsonize pathogens, making them easier for phagocytes to ingest.
- **Regulation:** Cytokines produced by both innate and adaptive immune cells help regulate the intensity and duration of the immune response.

1.3. Cells of immune system

The immune system consists of a variety of specialized cells that play key roles in defending the body against infections, diseases, and foreign substances. Here's an overview of the main types of immune cells and their functions:

A. Innate Immune Cells

1. Phagocytes:

Macrophages: These large cells are found in tissues and are responsible for engulfing and digesting cellular debris, pathogens, and other foreign substances. They also play a role in alerting the adaptive immune system by presenting antigens on their surface.

Neutrophils: The most abundant type of white blood cell, these cells are the first responders to microbial infection. They quickly migrate to infection sites and ingest and destroy pathogens.

Dendritic Cells: These cells are key antigen-presenting cells (APCs). They capture antigens and migrate to lymph nodes to present them to T cells, bridging innate and adaptive immunity.

2. Granulocytes:

Eosinophils: These cells combat multicellular parasites and are also involved in allergic reactions.

Basophils: These cells release histamine and other chemicals that contribute to inflammation and allergic responses.

Mast Cells: Found in tissues, particularly around blood vessels and nerves, these cells release histamine and other mediators involved in allergy and anaphylaxis.

3. Natural Killer (NK) Cells: These cells can recognize and destroy infected or cancerous cells without prior sensitization. They play a critical role in the early defense against viral infections and tumor formation.

4. Complement System: Though not cells, the complement system consists of proteins that enhance the ability of antibodies and phagocytic cells to clear microbes and damaged cells, promote inflammation, and attack the pathogen's cell membrane.

B. Adaptive Immune Cells

1. Lymphocytes:

*** B Cells**: Responsible for producing antibodies. When activated, they differentiate into plasma cells, which secrete large quantities of antibodies, or memory B cells, which provide long-lasting immunity.

*** T Cells**: These cells mature in the thymus and are critical for adaptive immunity. There are several types:

Helper T Cells (CD4+ T cells): They coordinate the immune response by secreting cytokines that activate other immune cells, including B cells, cytotoxic T cells, and macrophages.

Cytotoxic T Cells (CD8+ T cells): These cells directly kill infected cells, cancer cells, and cells that are damaged in other ways.

Regulatory T Cells: These cells help maintain immune system homeostasis and prevent autoimmune responses by suppressing excessive immune reactions.

Memory T Cells: They remain in the body long-term after an infection has been cleared, providing a quicker response if the same antigen is encountered again.

2. Antigen-Presenting Cells (APCs):

*** Dendritic Cells**: As mentioned, these cells capture and present antigens to T cells.

*** Macrophages**: Also function as APCs in addition to their phagocytic activities.

*** B Cells**: Can present antigens to helper T cells as part of the process of activation and differentiation.

C. Hematopoietic Stem Cells (HSCs)

All immune cells originate from hematopoietic stem cells found in the bone marrow. These stem cells differentiate into either myeloid progenitor cells (which give rise to most innate immune cells, including phagocytes and granulocytes) or lymphoid progenitor cells (which give rise to lymphocytes and NK cells).

1.4. Organs of immune system

The immune system consists of various organs and tissues that collaborate to produce, mature, and deploy immune cells. These organs can be broadly categorized into primary and secondary lymphoid organs.

i. Primary Lymphoid Organs

These organs are where immune cells are produced and mature.

1. Bone Marrow:

The primary site of new blood cell (including immune cell) production. All blood cells originate from hematopoietic stem cells found in the bone marrow. Immune Cells Produced are B cells, T cells (precursors), NK cells, granulocytes, and macrophages. B cells mature in the bone marrow before migrating to secondary lymphoid organs.

2. Thymus:

The site of T cell maturation. Precursor T cells migrate from the bone marrow to the thymus, where they mature and differentiate. It is located in the upper chest, behind the sternum. The thymus is most active during childhood and gradually shrinks with age.

ii. Secondary Lymphoid Organs

These organs are where immune responses are initiated and regulated. They provide sites for antigen capture and presentation, and for the interaction between immune cells.

1. Lymph Nodes:

They are small, bean-shaped structures that filter lymphatic fluid and trap pathogens. They provide a site for interaction between antigens, APCs, and lymphocytes. They are located and distributed throughout the body, particularly in the neck, armpits, groin, and abdomen. Lymph nodes swell during infections due to the proliferation of immune cells.

2. Spleen:

It filters blood, removing old or damaged red blood cells and pathogens. It also facilitates interactions between antigens and immune cells. It is located in the upper left abdomen, near the stomach. The spleen has white pulp (rich in lymphocytes) and red pulp (involved in filtering blood).

3. Mucosa-Associated Lymphoid Tissue (MALT):

It protects mucosal surfaces such as the gastrointestinal, respiratory, and urogenital tracts from pathogens. It includes structures like the tonsils, Peyer's patches (in the small intestine), and the appendix. MALT contains specialized cells that capture antigens from mucosal surfaces and initiate immune responses.

4. Tonsils:

They trap and process antigens from inhaled or ingested substances. They are located at the back of the throat and nasal cavity. Tonsils are part of the larger MALT system.

5. Peyer's Patches:

They monitor intestinal bacteria populations and prevent the growth of pathogenic bacteria in the intestines. They are located in the lining of the small intestine, particularly the ileum. Peyer's patches are covered by a layer of epithelial cells that capture and present antigens to immune cells.

iii. Additional Components

1. Lymphatic Vessels:

They transport lymph, a fluid containing immune cells, throughout the body. They connect lymph nodes and provide a pathway for lymphocyte circulation. The lymphatic system also helps in the removal of waste and excess fluids from tissues.

2. Blood Circulation:

They transports immune cells throughout the body, allowing them to patrol for pathogens and respond to infections. The spleen and liver filter the blood and remove pathogens and dead cells.

2.1. Basic Properties of Antigens

Antigens are substances that can trigger an immune response, leading to the production of antibodies or the activation of T cells. They are typically recognized as foreign by the immune system. Here are the basic properties of antigens:

1. Immunogenicity

The ability of an antigen to provoke an immune response. Factors Influencing Immunogenicity:

Foreignness: The more foreign an antigen is to the host, the more likely it is to be immunogenic.

Size: Larger molecules are generally more immunogenic.

Complexity: More complex molecules (e.g., proteins with multiple epitopes) are more likely to be immunogenic.

Degradability: Antigens that can be processed and presented by antigen-presenting cells (APCs) are more likely to provoke an immune response.

Dose and Route of Administration: The amount of antigen and the route through which it enters the body can affect its immunogenicity.

2. Antigenicity

The ability of an antigen to specifically bind to the products of the immune response (antibodies or T cell receptors). Factors Influencing Antigenicity:

Epitopes (Antigenic Determinants): Specific regions on the antigen that are recognized by immune cells. Each antigen can have multiple epitopes.

Accessibility: Epitopes must be accessible to antibodies or T cell receptors to be recognized.

3. Foreignness

The degree to which the antigen is perceived as non-self by the immune system. The more different the antigen is from the host's own molecules, the stronger the immune response. Self-antigens are usually tolerated by the immune system, while non-self antigens trigger responses.

4. Molecular Size

Larger molecules are generally more effective as antigens. Typically, molecules with a molecular weight above 10,000 Daltons are good antigens. Small molecules, called haptens, need to be attached to larger carrier molecules to become immunogenic.

5. Chemical Composition and Complexity

Proteins are usually the most immunogenic due to their complexity and diversity of amino acid sequences and structures. Polysaccharides can also be immunogenic, while simple molecules like lipids and nucleic acids are usually less immunogenic unless complexed with proteins or other molecules.

6. Degradability

The ability of an antigen to be processed by APCs and presented to T cells. Antigens must be degradable into smaller fragments that can be presented on MHC (Major Histocompatibility Complex) molecules for T cell recognition. Stable, non-degradable molecules are less likely to be immunogenic.

7. Specificity

The precise molecular interaction between an antigen and the specific receptors on B cells or T cells. This property ensures that each antigen elicits a response that is tailored specifically to its unique structure.

8. Epitope Density and Distribution

The number and distribution of epitopes on an antigen. Antigens with multiple epitopes can cross-link receptors on B cells, leading to stronger and more effective immune responses. Epitopes that are too sparse or hidden may not be effectively recognized.

2.2. B and T cell Epitopes, Paratopes

B and T cell epitopes are specific regions on antigens that are recognized by the receptors of B cells (antibodies) and T cells (T cell receptors), respectively. Paratopes are the corresponding regions on the B cell receptor (BCR) or T cell receptor (TCR) that bind to the epitopes. Here's an explanation of each:

I. B Cell Epitopes and Paratopes

i. B Cell Epitopes:

B cell epitopes are specific regions on antigens that are recognized by the variable regions of B cell receptors (BCRs), which are antibodies secreted by B cells.

Characteristics:

Linear Epitopes: Continuous sequences of amino acids on the antigen.

Conformational Epitopes: Discontinuous regions brought together by protein folding.

Importance: Recognition of B cell epitopes by BCRs initiates the activation of B cells, leading to their differentiation into plasma cells that produce antibodies.

ii. B Cell Paratopes:

Paratopes are the antigen-binding sites on the variable regions of B cell receptors (BCRs) that specifically interact with B cell epitopes. The paratope is formed by the variable regions of the heavy and light chains of the BCR.

Function: Paratopes determine the specificity of the BCR, allowing it to recognize and bind to specific epitopes on antigens.

II. T Cell Epitopes and Paratopes

i. T Cell Epitopes:

T cell epitopes are specific regions on antigens that are recognized by the T cell receptors (TCRs) expressed on the surface of T cells.

Characteristics:

* Usually short peptides derived from antigen processing.

* Presented on the surface of antigen-presenting cells (APCs) bound to major histocompatibility complex (MHC) molecules.

Importance: Recognition of T cell epitopes by TCRs, in conjunction with MHC molecules, leads to T cell activation and the initiation of cellular immune responses.

ii. T Cell Paratopes:

Paratopes are the antigen-binding sites on the T cell receptors (TCRs) that specifically interact with T cell epitopes presented on MHC molecules.

Structure: The paratope of the TCR is formed by the variable regions of the α and β chains in the case of αβ TCRs, or γ and δ chains in the case of γδ TCRs.

Function: Paratopes determine the specificity of the TCR, allowing it to recognize and bind to specific epitopes presented by APCs.

III. Interaction Between Epitopes and Paratopes

* The interaction between epitopes and paratopes is highly specific, analogous to a lock-and-key mechanism.

* Binding of the paratope to the epitope is crucial for initiating immune responses.

* The specificity of the interaction ensures that immune cells selectively recognize and respond to pathogens and foreign substances while avoiding self-reactivity.

Understanding the interaction between epitopes and paratopes is fundamental for comprehending antigen recognition by the immune system and the subsequent activation of immune responses.

2.3. Haptens and Adjuvants

A. Haptens:

* Haptens are small molecules that are not inherently immunogenic but can become immunogenic when they bind to carrier molecules, forming a complex. Alone, haptens are too small to elicit an immune response, but when attached to larger carrier molecules, they can trigger an immune reaction.

*** Characteristics**:

- Haptens typically have a molecular weight of less than 1,000 Daltons.
- They are usually non-immunogenic because they cannot activate T cells directly.
- Examples of haptens include drugs, certain chemicals, and small molecules found in allergens.

*** Mechanism of Action**:

- Haptens bind covalently to carrier proteins in the body, forming hapten-carrier complexes.
- The immune system recognizes these complexes as foreign and mounts an immune response against them.
- The carrier protein acts as an antigen, while the hapten serves as an epitope, stimulating the production of antibodies specific to the hapten.

*** Applications**:

- Haptens are used in research to study immune responses and antibody production.
- They are also used in diagnostic tests to detect the presence of specific antibodies in blood samples.
- In medicine, haptens are utilized in the development of vaccines and allergy treatments.

*** Examples**:

- Penicillin: A common example of a hapten. Penicillin binds to proteins in the body, forming a complex that can trigger allergic reactions in susceptible individuals.
- Poison Ivy: The oil from poison ivy contains a hapten called urushiol, which can cause allergic reactions when it binds to skin proteins.

II. Adjuvants:

***** Adjuvants are substances that are added to vaccines to enhance the body's immune response to the antigen (usually a protein or polysaccharide). They help improve the effectiveness and longevity of the immune response, allowing for smaller doses of antigen to be used.

*** Characteristics**:

- Adjuvants are often molecules that stimulate innate immune responses by activating pattern recognition receptors (PRRs) on antigen-presenting cells (APCs).

- They can enhance the production of cytokines and chemokines, promote the recruitment and activation of immune cells, and increase the uptake and presentation of antigens by APCs.

*** Mechanism of Action**:

- Adjuvants work by providing signals to the immune system that help promote a robust and long-lasting immune response.
- They can enhance the activation and maturation of APCs, leading to improved antigen presentation and T cell activation.
- Adjuvants also help stimulate the production of antibodies and promote the formation of memory immune cells, leading to enhanced protection against future infections.

*** Applications**:

- Adjuvants are commonly used in vaccines to improve their efficacy and potency.
- They are particularly useful for vaccines composed of weakly immunogenic antigens or for vaccines targeted at vulnerable populations, such as infants, elderly individuals, or immunocompromised individuals.
- Adjuvants are also used in research to study immune responses and develop new vaccine formulations.

*** Examples**:

- Aluminum salts (alum): One of the oldest and most widely used adjuvants in vaccines. It enhances antibody production and is included in many vaccines, including those for diphtheria, tetanus, and hepatitis B.
- MF59 and AS03: Oil-in-water emulsions that have been used in influenza vaccines to enhance immune responses.
- CpG oligodeoxynucleotides: Synthetic DNA sequences that activate toll-like receptors (TLRs) and stimulate innate immune responses. They are being investigated as adjuvants for various vaccines, including those for cancer and infectious diseases.

2.4. Factors influencing immunogenicity

Immunogenicity refers to the ability of a substance to provoke an immune response. Several factors influence the immunogenicity of antigens, including:

1. Foreignness:

Degree of Foreignness: Antigens that are more foreign to the host organism are typically more immunogenic. This is because the immune system recognizes non-self antigens as potential threats and mounts a stronger response against them.

Cross-Species Reactivity: Antigens from other species are often highly immunogenic because they are perceived as foreign by the host immune system.

2. Molecular Size:

Larger Molecules: Larger antigens are generally more immunogenic than smaller ones. This is because they can provide more epitopes for immune recognition and induce a stronger immune response.

3. Complexity and Structure:

Complexity: Antigens with greater structural complexity, such as proteins with multiple epitopes, are usually more immunogenic.

Conformational Epitopes: Antigens with conformational epitopes (formed by the folding of the antigen) can be highly immunogenic, as they mimic the natural structure of pathogens.

Linear Epitopes: Linear epitopes (continuous sequences of amino acids) also contribute to immunogenicity.

4. Degradability and Processing:

Ability to Be Processed by Antigen-Presenting Cells (APCs): Antigens that can be efficiently processed and presented by APCs are more immunogenic. APCs digest antigens into smaller peptides and present them on their surface to activate T cells.

Uptake by APCs: Antigens that are readily taken up by APCs, such as dendritic cells, are more likely to induce an immune response.

5. Route of Administration:

Route of Exposure: The route through which antigens enter the body can influence their immunogenicity. For example, antigens delivered via intramuscular or subcutaneous injection may be more immunogenic than those delivered orally or intranasally.

Adjuvants: Adjuvants added to vaccines can enhance the immunogenicity of antigens by promoting inflammation, increasing antigen uptake by APCs, and prolonging antigen presentation.

6. Dose and Frequency of Exposure:

Dose: The amount of antigen administered can impact its immunogenicity. Higher doses may induce stronger immune responses.

Frequency of Exposure: Repeat exposure to an antigen can lead to immune tolerance or memory, depending on the context and timing of exposure.

7. Genetic Factors:

Genetic Variation: Genetic factors can influence an individual's immune response to antigens. Variations in genes encoding immune receptors, cytokines, and other immune-related molecules can affect immunogenicity and vaccine responsiveness.

8. Adjuvants and Co-Stimulatory Signals:

Adjuvants: Certain substances, known as adjuvants, are added to vaccines to enhance their immunogenicity by providing additional signals to the immune system.

Co-Stimulatory Signals: Co-stimulatory molecules expressed by APCs and other immune cells play a crucial role in antigen recognition and immune activation.

3.1 Structure of Antibodies

Antibodies, also known as immunoglobulins (Igs), are Y-shaped proteins produced by B cells and plasma cells in response to the presence of specific antigens. They play a crucial role in the immune system by recognizing and neutralizing pathogens, toxins, and other foreign substances. The basic structure of an antibody molecule consists of several components:

1. Variable Region (Fab):

- **Antigen-Binding Site**: Located at the tips of the Y-shaped antibody molecule.
- **Specificity**: Determines the antibody's ability to recognize and bind to a specific antigen.
- **Composed of**: Composed of variable domains from both the heavy (H) and light (L) chains.
- **Diversity**: The variable region exhibits high diversity among different antibodies, allowing them to recognize a wide range of antigens.

2. Constant Region (Fc):

- **Effector Functions**: Determines the antibody's effector functions, such as complement activation, phagocytosis, and binding to cell surface receptors.
- **Composed of**: Composed of constant domains from the heavy chains.
- **Subclasses**: Antibodies can belong to different subclasses (e.g., IgG1, IgG2, IgA1, IgA2), which have distinct effector functions.

3. Heavy Chains (H):

- **Structure**: Each antibody molecule contains two identical heavy chains.
- **Domains**: The heavy chain consists of multiple domains, including variable (VH) and constant (CH1, CH2, CH3, CH4) domains.
- **Disulfide Bonds**: Formed between cysteine residues stabilize the structure of the heavy chain.

4. Light Chains (L):

- **Structure**: Each antibody molecule contains two identical light chains (either kappa or lambda).
- **Domains**: The light chain consists of variable (VL) and constant (CL) domains.
- **Disulfide Bonds**: Formed between cysteine residues stabilize the structure of the light chain.

5. Glycosylation:

- **Attachment of Sugars**: Antibodies are often glycosylated, meaning that sugar molecules are attached to specific sites on the heavy chains.

- **Role**: Glycosylation can influence the stability, solubility, and effector functions of antibodies.

6. Disulfide Bonds:

- **Stabilization**: Disulfide bonds form covalent links between cysteine residues in the heavy and light chains, stabilizing the overall structure of the antibody.

7. Isotypes and Subclasses:

- **Isotypes**: Antibodies can belong to different isotypes (e.g., IgM, IgG, IgA, IgE), which have distinct structural and functional properties.
- **Subclasses**: Within each isotype, antibodies can further be classified into subclasses based on differences in the constant regions of the heavy chains.

3.2. Classes of antibodies

Antibodies, also known as immunoglobulins (Ig), are glycoproteins produced by B cells and plasma cells in response to specific antigens. They are a crucial component of the immune system and play diverse roles in defending the body against pathogens. Antibodies can be classified into several classes (or isotypes), each with distinct structural and functional properties. The five main classes of antibodies in humans are:

1. IgM (Immunoglobulin M):

Structure: IgM antibodies are pentameric molecules, with five monomeric units joined by disulfide bonds and a J chain.

Location: They are primarily found in the blood and lymphatic system.

Functions:

*** First Response**: IgM is the first antibody class produced during the primary immune response to an infection.

*** Complement Activation**: IgM is highly efficient at activating the complement system, leading to pathogen lysis and opsonization.

*** Agglutination**: IgM antibodies can agglutinate pathogens, facilitating their clearance by phagocytes.

2. IgG (Immunoglobulin G):

Structure: IgG antibodies are monomeric molecules composed of two heavy chains and two light chains.

Location: They are the most abundant antibodies in the blood and are found in other body fluids and tissues.

Functions:

*** Neutralization**: IgG antibodies can neutralize pathogens by binding to their surface and preventing them from infecting host cells.

*** Opsonization**: IgG can opsonize pathogens, marking them for phagocytosis by macrophages and neutrophils.

*** Complement Activation**: IgG can activate the complement system, leading to pathogen lysis and inflammation.

*** Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)**: IgG antibodies can bind to target cells and recruit immune cells (such as natural killer cells) to kill them.

3. IgA (Immunoglobulin A):

Structure: IgA antibodies exist in two forms: monomeric IgA and dimeric IgA. Dimeric IgA molecules are joined by a J chain and a secretory component.

Location: IgA is found primarily in mucosal secretions, such as saliva, tears, and breast milk, as well as in the blood.

Functions:

*** Mucosal Immunity**: IgA plays a crucial role in protecting mucosal surfaces from pathogens, toxins, and allergens.

*** Neutralization**: IgA can neutralize pathogens and toxins in mucosal secretions, preventing their entry into the body.

*** Immune Exclusion**: IgA antibodies can exclude pathogens from mucosal surfaces by binding to them and preventing their adherence to epithelial cells.

4. IgE (Immunoglobulin E):

Structure: IgE antibodies are monomeric molecules similar in structure to IgG.

Location: IgE is found in low concentrations in the blood and tissues.

Functions:

*** Allergic Responses**: IgE antibodies play a central role in allergic reactions by binding to allergens and triggering the release of histamine and other mediators from mast cells and basophils.

*** Parasite Defense**: IgE is involved in defense against parasitic infections, particularly helminths.

5. IgD (Immunoglobulin D):

Structure: IgD antibodies are monomeric molecules similar in structure to IgG.

Location: IgD is found in low concentrations in the blood and tissues.

Functions:

*** Antigen Receptor**: IgD is expressed on the surface of mature B cells, where it acts as a receptor for antigens.

*** Role in B Cell Activation**: IgD may play a role in the activation and regulation of B cell responses, although its precise functions are still being elucidated.

Each class of antibody has unique properties and functions, allowing the immune system to mount diverse and effective responses against a wide range of pathogens and foreign substances.

3.3. Functions of Antibodies

Antibodies, also known as immunoglobulins (Igs), play diverse roles in the immune system. They are produced by B cells and plasma cells in response to specific antigens and contribute to the defense against pathogens and foreign substances. The functions of antibodies include:

1. Neutralization:

Definition: Antibodies bind to pathogens (such as viruses or bacteria) and prevent them from infecting host cells by blocking their attachment to cell surface receptors or inhibiting their entry into cells.

Mechanism: Antibodies can neutralize pathogens by binding to surface antigens or toxins, thereby preventing their interaction with host cells.

2. Opsonization:

Definition: Antibodies coat pathogens, marking them for phagocytosis by immune cells such as macrophages and neutrophils.

Mechanism: Antibodies bind to antigens on the surface of pathogens, facilitating their recognition and engulfment by phagocytes through interactions with Fc receptors (FcγRs) on the phagocyte surface.

3. Complement Activation:

Definition: Antibodies activate the complement system, a group of proteins that can destroy pathogens directly or enhance their clearance by phagocytes.

Mechanism: Antibodies bound to pathogens can activate the classical pathway of the complement system by interacting with complement component C1q, leading to the formation of the membrane attack complex (MAC) and pathogen lysis.

4. Antibody-Dependent Cellular Cytotoxicity (ADCC):

Definition: Antibodies recruit immune cells, such as natural killer (NK) cells, to kill target cells (e.g., infected or cancerous cells) by inducing their lysis.

Mechanism: Antibodies bind to antigens on the surface of target cells, and the Fc region of the antibody interacts with Fc receptors (FcγRs) on the surface of NK cells, triggering their activation and release of cytotoxic granules.

5. Immune Exclusion:

Definition: Antibodies prevent the adherence of pathogens to host cells or mucosal surfaces, thereby excluding them from invading the body.

Mechanism: Antibodies, particularly IgA, bind to pathogens or toxins, preventing their attachment to epithelial cells and promoting their clearance from mucosal surfaces through mechanisms such as mucociliary clearance.

6. Allergic Responses:

Definition: IgE antibodies play a central role in allergic reactions by binding to allergens and triggering the release of histamine and other mediators from mast cells and basophils.

Mechanism: IgE antibodies bind to allergens, leading to cross-linking of IgE receptors (FcεRI) on mast cells and basophils, which triggers the release of inflammatory mediators.

7. Maternal Immunity:

Definition: Antibodies transferred from mother to offspring (e.g., through breast milk or placental transfer) provide passive immunity to the newborn, protecting against infections until their own immune system matures.

Mechanism: Maternally-derived antibodies, particularly IgG, provide immediate protection to the newborn by neutralizing pathogens and enhancing their clearance.

3.4. Monoclonal Antibodies

Monoclonal antibodies (mAbs) are laboratory-produced antibodies that are designed to target specific antigens. Unlike polyclonal antibodies, which are derived from different B cell clones and recognize multiple epitopes, monoclonal antibodies are derived from a single B cell clone and recognize a single epitope with high specificity.

1. Production:

Hybridoma Technology: Monoclonal antibodies are typically produced using hybridoma technology. This involves fusing a specific antibody-producing B cell with a myeloma cell, creating a hybrid cell line called a hybridoma. These hybridomas can proliferate indefinitely, producing large quantities of identical antibodies.

Recombinant DNA Technology: In addition to hybridoma technology, recombinant DNA technology can also be used to produce monoclonal antibodies. This involves cloning the genes encoding the antibody of interest and expressing them in host cells, such as bacteria, yeast, or mammalian cells.

2. Properties:

Specificity: Monoclonal antibodies are highly specific, binding to a single target molecule with high affinity. This specificity allows for precise targeting of antigens, cells, or tissues in various applications.

Homogeneity: Monoclonal antibodies are homogeneous, meaning they are identical copies of one another. This ensures consistency in their binding properties and therapeutic effects.

Stability: Monoclonal antibodies are relatively stable molecules, allowing for long-term storage and transportation under appropriate conditions.

Low Immunogenicity: Due to their human or humanized nature, monoclonal antibodies typically exhibit low immunogenicity, reducing the risk of triggering an immune response in patients.

3. Applications:

i. Therapeutics:

Cancer Therapy: Monoclonal antibodies are used in cancer treatment to target specific proteins expressed on cancer cells, inhibiting their growth or promoting their destruction.

Autoimmune Disorders: mAbs can modulate the immune response in autoimmune diseases by targeting immune cells or inflammatory cytokines.

Infectious Diseases: Monoclonal antibodies can neutralize pathogens such as viruses or bacteria, offering passive immunity against infections.

ii. Diagnosis:

Diagnostic Tests: Monoclonal antibodies are used in various diagnostic tests, including ELISA, immunohistochemistry, and lateral flow assays, to detect the presence of specific antigens or antibodies in patient samples.

Imaging: Labeled monoclonal antibodies can be used for in vivo imaging techniques, such as PET or SPECT, to visualize specific targets in the body.

iii. Research:

Protein Function Studies: Monoclonal antibodies are valuable tools for studying the function and localization of proteins in cells and tissues.

Drug Development: mAbs are used in preclinical and clinical research to validate drug targets, screen potential therapeutics, and assess drug efficacy and safety.

iv. Immunotherapy:

Immune Checkpoint Inhibitors: Monoclonal antibodies targeting immune checkpoints, such as PD-1 or CTLA-4, enhance anti-tumor immune responses in cancer patients.

Allergy Treatment: Monoclonal antibodies can neutralize allergens or block allergic reactions, providing relief for patients with allergies.

4.1. Structure and Functions of Major Histocompatibility Complexes (MHC)

Major Histocompatibility Complexes (MHC) are cell surface proteins that play a crucial role in the immune system, particularly in antigen presentation and immune recognition. There are two main classes of MHC molecules, Class I and Class II, each with distinct structures and functions.

A. Structure:

Class I MHC Molecules:

Structure: Class I MHC molecules are heterodimers composed of two polypeptide chains: an alpha chain (encoded by the HLA-A, HLA-B, or HLA-C genes in humans) and a non-covalently associated beta-2 microglobulin (β2m) chain.

Peptide Binding Groove: Class I MHC molecules have a peptide-binding groove formed by the alpha-1 and alpha-2 domains of the alpha chain, where short peptide fragments (usually 8-10 amino acids in length) derived from intracellular proteins can bind.

Class II MHC Molecules:

Structure: Class II MHC molecules are also heterodimers consisting of two polypeptide chains: an alpha chain (encoded by the HLA-DP, HLA-DQ, or HLA-DR genes in humans) and a beta chain (encoded by the HLA-DP, HLA-DQ, or HLA-DR genes).

Peptide Binding Grooves: Class II MHC molecules have two peptide-binding grooves formed by the alpha-1 and beta-1 domains of the respective chains, allowing them to bind longer peptide fragments (typically 13-25 amino acids) derived from extracellular proteins.

B. Functions:

Antigen Presentation:

Class I MHC: Present antigens derived from intracellular pathogens (such as viruses) or proteins (such as tumor antigens) to CD8+ cytotoxic T cells (CTLs). This process allows CTLs to recognize and eliminate infected or aberrant cells.

Class II MHC: Present antigens derived from extracellular pathogens (such as bacteria) to CD4+ helper T cells. Helper T cells play a central role in coordinating immune responses by activating other immune cells and facilitating antibody production.

Immune Recognition and Activation:

Class I MHC: Recognized by CD8+ cytotoxic T cells (CTLs) via their T cell receptors (TCRs). Binding of the TCR to the peptide-MHC complex, along with co-stimulatory signals, activates CTLs, leading to their proliferation and cytotoxic activity against target cells.

Class II MHC: Recognized by CD4+ helper T cells via their TCRs. Binding of the TCR to the peptide-MHC complex, along with co-stimulatory signals, activates helper T cells, which then provide help to B cells for antibody production and to other immune cells for enhanced immune responses.

Self and Non-Self Discrimination:

MHC molecules play a crucial role in distinguishing self-antigens from non-self antigens. T cells are educated in the thymus to recognize self-MHC molecules and ignore self-antigens presented by self-MHC, while they are activated by non-self antigens presented by foreign MHC molecules.

5.2. Exogenous pathway of antigen presentation and processing

The **exogenous pathway of antigen presentation and processing** is a mechanism by which professional antigen-presenting cells (APCs), such as dendritic cells, macrophages, and B cells, process extracellular antigens and present them on Major Histocompatibility Complex (MHC) class II molecules. This process is crucial for the activation of CD_4^+ helper T cells, which are essential for coordinating various immune responses.

Steps in the Exogenous Pathway

1. **Antigen Uptake**:
    - **Phagocytosis**: APCs engulf large extracellular particles, such as bacteria or dead cells, into phagosomes.
    - **Endocytosis**: Smaller extracellular molecules and soluble antigens are internalized into endosomes via receptor-mediated endocytosis or pinocytosis.
2. **Antigen Degradation**:
    - The internalized antigens are contained within endosomes or phagosomes, which fuse with lysosomes to form phagolysosomes or endolysosomes.
    - The acidic environment and proteolytic enzymes within these vesicles degrade the antigens into peptide fragments.
3. **MHC Class II Synthesis and Transport**:
    - MHC class II molecules are synthesized in the endoplasmic reticulum (ER) of APCs.
    - In the ER, MHC class II molecules bind to a protein called the invariant chain (Ii), which blocks the peptide-binding groove and prevents premature binding of peptides.
4. **Invariant Chain Processing**:
    - The MHC class II-invariant chain complexes are transported from the ER through the Golgi apparatus to the endosomal/lysosomal compartments.
    - In these compartments, the invariant chain is progressively degraded by proteolytic enzymes, leaving a small fragment called CLIP (Class II-associated invariant chain peptide) in the peptide-binding groove of the MHC class II molecule.
5. **Peptide Loading**:
    - The MHC class II-containing vesicles fuse with the endosomal/lysosomal compartments containing the degraded antigen peptides.
    - The protein HLA-DM facilitates the removal of CLIP and the binding of antigenic peptides to the MHC class II molecules.
    - This ensures that only the appropriate peptides bind to MHC class II molecules.

6. **Transport to the Cell Surface**:
    - The peptide-loaded MHC class II molecules are transported to the cell surface via exocytic vesicles.
    - Once on the surface, the MHC class II-peptide complexes can be recognized by CD4+ T cells.
7. **T Cell Activation**:
    - CD4+ T cells, through their T cell receptors (TCRs), specifically recognize the antigenic peptides presented by MHC class II molecules.
    - This recognition, along with co-stimulatory signals provided by the APC, leads to the activation of CD4+ T cells.
    - Activated CD4+ T cells proliferate and differentiate into various subsets (e.g., Th1, Th2, Th17, Treg) that coordinate different aspects of the immune response, including B cell help for antibody production, macrophage activation, and regulation of immune responses.

4.3. Endogenous pathway of antigen presentation and processing

The **endogenous pathway of antigen presentation and processing** is a mechanism by which cells present intracellular antigens, typically from proteins synthesized within the cell, on Major Histocompatibility Complex (MHC) class I molecules. This process is essential for the immune system to monitor and respond to intracellular pathogens, such as viruses, and to identify and eliminate cancerous or otherwise abnormal cells.

Steps in the Endogenous Pathway

1. **Protein Synthesis and Degradation**:
    - Proteins within the cell, whether they are normal cellular proteins or abnormal proteins produced by viruses or mutations, are continuously synthesized and degraded.
    - These proteins are tagged for degradation by ubiquitin, a small regulatory protein.
2. **Proteasome-Mediated Degradation**:
    - Ubiquitinated proteins are directed to the proteasome, a large proteolytic complex that degrades them into peptide fragments.
    - The proteasome generates peptides typically 8-10 amino acids in length, which are suitable for binding to MHC class I molecules.
3. **Peptide Transport into the Endoplasmic Reticulum (ER)**:
    - The generated peptides are transported from the cytosol into the ER by the Transporter associated with Antigen Processing (TAP) proteins.

- TAP is a peptide transporter that preferentially translocates peptides of appropriate length and sequence for MHC class I binding.

4. **MHC Class I Synthesis and Peptide Loading**:
    - MHC class I molecules are synthesized in the ER, where they initially associate with several chaperone proteins that assist in their proper folding and stability.
    - The MHC class I heavy chain associates with β2-microglobulin to form a stable MHC class I complex.
    - The peptide loading complex, which includes TAP, tapasin, ERp57, and calreticulin, facilitates the loading of peptides onto MHC class I molecules.
5. **Peptide Binding and Maturation**:
    - Once a suitable peptide binds to the peptide-binding groove of the MHC class I molecule, the MHC class I complex undergoes conformational changes that stabilize it.
    - Properly folded and peptide-loaded MHC class I molecules are released from the chaperone proteins and transported through the Golgi apparatus to the cell surface.
6. **Transport to the Cell Surface**:
    - The peptide-MHC class I complexes are transported to the cell surface in exocytic vesicles.
    - Once on the surface, these complexes are displayed for recognition by CD8+ cytotoxic T cells.
7. **T Cell Recognition and Activation**:
    - CD8+ cytotoxic T cells, through their T cell receptors (TCRs), specifically recognize the antigenic peptides presented by MHC class I molecules.
    - This recognition, along with co-stimulatory signals, leads to the activation of CD8+ T cells.
    - Activated CD8+ T cells proliferate and differentiate into effector cells that can directly kill infected or abnormal cells by inducing apoptosis.

4.4. Basic Properties and Functions of Cytokines

Cytokines are small proteins secreted by cells that play crucial roles in cell signaling, especially in immune responses. They are involved in the regulation of immunity, inflammation, and hematopoiesis (the formation of blood cellular components). Cytokines can act on the cells that produce them (autocrine action), nearby cells (paracrine action), or distant cells (endocrine action).

Basic Properties of Cytokines

1. **Pleiotropy**:
    - A single cytokine can act on different cell types, producing multiple effects. For example, interleukin-4 (IL-4) can promote B cell differentiation and class switching, and also affect T cells and macrophages.
2. **Redundancy**:
    - Different cytokines can have overlapping functions. Multiple cytokines can elicit similar responses, which provides a backup mechanism in case one cytokine is absent or dysfunctional.
3. **Synergy**:
    - Cytokines can work together to produce a combined effect that is greater than the sum of their individual effects. For instance, IL-12 and IL-18 can work synergistically to enhance the production of interferon-gamma (IFN-γ) from T cells and natural killer (NK) cells.
4. **Antagonism**:
    - Some cytokines can inhibit the effects of others. For example, IL-10 can suppress the inflammatory responses mediated by cytokines such as IL-1 and TNF-α.
5. **Cascade Induction**:
    - Cytokines can induce the production of other cytokines, creating a cascade effect that amplifies the immune response. For instance, IL-1 can induce the production of IL-6 and TNF-α.

Functions of Cytokines

1. **Regulation of Immune Responses**:
    - **Pro-inflammatory Cytokines**: These include IL-1, IL-6, TNF-α, and IFN-γ. They promote inflammation, enhance the activity of immune cells, and increase the expression of adhesion molecules on endothelial cells, facilitating leukocyte migration to infection sites.
    - **Anti-inflammatory Cytokines**: Examples are IL-10 and TGF-β. They help to resolve inflammation and limit immune responses to prevent tissue damage.

2. **Cell Growth and Differentiation**:
    - Cytokines such as IL-2, IL-4, and IL-7 play vital roles in the growth, proliferation, and differentiation of various immune cells. IL-2 is crucial for T cell proliferation, while IL-7 is important for B and T cell development.
3. **Hematopoiesis**:
    - Cytokines like colony-stimulating factors (CSFs), including granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF), stimulate the production of white blood cells from bone marrow progenitor cells.
4. **Antiviral Responses**:
    - Interferons (e.g., IFN-α, IFN-β) are critical in antiviral defense. They inhibit viral replication, activate NK cells, and increase the expression of MHC class I molecules, enhancing the presentation of viral antigens to CD8+ T cells.
5. **Chemotaxis**:
    - Chemokines are a subgroup of cytokines that direct the migration of immune cells to sites of infection or injury. For instance, IL-8 (CXCL8) attracts neutrophils, while CCL2 (MCP-1) recruits monocytes and T cells.
6. **Apoptosis**:
    - Some cytokines can induce programmed cell death (apoptosis). TNF-α and Fas ligand (FasL) are involved in apoptosis, which is essential for eliminating infected or damaged cells and maintaining immune homeostasis.

5.1. Gell and Coombs' classification – brief description of various types of hypersensitivities

Gell and Coombs' classification, also known as the Coombs and Gell classification, is a system used to categorize hypersensitivity reactions, which are exaggerated or inappropriate immune responses to antigens (foreign substances). These reactions are classified into four main types:

Type I: IgE-mediated Hypersensitivity (Immediate Hypersensitivity)

Mechanism: This type of hypersensitivity is mediated by immunoglobulin E (IgE) antibodies. When an allergen (a harmless substance) encounters an individual with a predisposition to allergies, it triggers the production of specific IgE antibodies that bind to mast cells and basophils (immune cells) in tissues. Upon re-exposure to the allergen, it binds to the IgE antibodies on these cells, triggering the release of inflammatory mediators like histamine.

Symptoms: Symptoms typically develop rapidly (within minutes to hours) and can include:

- Runny nose, sneezing, and itchy eyes (hay fever)
- Wheezing and difficulty breathing (asthma)
- Skin reactions like hives and itching (anaphylaxis in severe cases)

Examples: Allergies to pollen, dust mites, peanuts, shellfish, insect stings, and some medications.

Type II: Cytotoxic Hypersensitivity (Antibody-mediated Cytotoxic)

Mechanism: This type involves antibodies (IgG or IgM) directly targeting antigens on the surface of host cells. The antibodies can trigger various mechanisms to damage or destroy the cells, including complement activation and phagocytosis.

Symptoms: Symptoms vary depending on the affected tissue. Examples include:

- Autoimmune hemolytic anemia (destruction of red blood cells
- Goodpasture's syndrome (attack on lung and kidney tissues)
- Graves' disease (hyperthyroidism)

Examples: Certain blood transfusions (incompatibility), autoimmune diseases like Graves' disease, and some drug reactions.

Type III: Immune Complex-mediated Hypersensitivity

Mechanism: This type of hypersensitivity occurs when immune complexes (antigen-antibody aggregates) form in the circulation or tissues. These complexes can activate the complement system, leading to inflammation and tissue damage.

Symptoms: Symptoms can develop within hours to days and can vary depending on the location of the immune complexes. Examples include:

- Serum sickness (fever, rash, joint pain)
- Glomerulonephritis (inflammation of the kidneys)
- Systemic lupus erythematosus (SLE, a complex autoimmune disease)

Examples: Serum sickness (reaction to foreign proteins), some allergic reactions to medications, and some autoimmune diseases.

Type IV: Cell-mediated Hypersensitivity (Delayed Hypersensitivity)

Mechanism: This type is mediated by T lymphocytes (specifically T cells) rather than antibodies. Upon exposure to an antigen, T cells become sensitized. Later re-exposure to the same antigen leads to activation of these T cells, which can directly attack antigen-presenting cells or release inflammatory mediators that damage tissues.

Symptoms: Symptoms typically develop after a longer period (24-72 hours) and can include:

- Skin reactions like allergic contact dermatitis (redness, itching, blisters)
- Tuberculin skin test (positive reaction indicates prior exposure to tuberculosis)
- Transplant rejection (immune response against transplanted tissue)

Examples: Allergic contact dermatitis (poison ivy rash), tuberculin skin test, and transplant rejection.

5.2. Introduction to concepts of autoimmunity and immunodeficiency

Autoimmunity and immunodeficiency are two important concepts in immunology that represent disorders of the immune system. These conditions can lead to significant health problems due to improper immune responses.

i. Autoimmunity

Definition: Autoimmunity occurs when the immune system mistakenly targets and attacks the body's own cells and tissues, considering them as foreign. This leads to a variety of autoimmune diseases.

Mechanisms:

Loss of Self-Tolerance: Normally, the immune system can distinguish between self and non-self antigens. In autoimmunity, this self-tolerance is lost.

Genetic Factors: Certain genes increase the susceptibility to autoimmune diseases.

Environmental Triggers: Infections, drugs, and other environmental factors can trigger autoimmune responses in genetically predisposed individuals.

Molecular Mimicry: Pathogens may possess antigens that resemble self-antigens, leading to an immune response against both the pathogen and the body's own tissues.

Examples of Autoimmune Diseases:

Type 1 Diabetes: The immune system attacks insulin-producing beta cells in the pancreas.

Rheumatoid Arthritis: Immune cells attack the synovium (lining of the joints), causing inflammation and joint damage.

Multiple Sclerosis: The immune system attacks the myelin sheath of nerve cells in the central nervous system.

Systemic Lupus Erythematosus (SLE): A systemic autoimmune disease where antibodies target various tissues and organs, including the skin, kidneys, and joints.

ii. Immunodeficiency

Definition: Immunodeficiency refers to conditions where the immune system's ability to fight infections and diseases is compromised or entirely absent. Immunodeficiency can be congenital (primary) or acquired (secondary).

a. Primary Immunodeficiency:

Genetic Origin: These are often inherited and result from genetic mutations that affect the development or function of the immune system.

Examples:

Severe Combined Immunodeficiency (SCID): A group of rare, life-threatening disorders caused by mutations that affect both T cells and B cells.

Common Variable Immunodeficiency (CVID): Characterized by low levels of serum immunoglobulins and an increased susceptibility to infections.

b. Secondary Immunodeficiency:

Acquired Factors: These are not inherited but occur as a result of other conditions or treatments.

Examples:

HIV/AIDS: Caused by the Human Immunodeficiency Virus (HIV) which targets and destroys CD4+ T cells, weakening the immune system.

Cancer and Chemotherapy: Certain cancers and treatments can suppress bone marrow function, reducing the production of immune cells.

Malnutrition: Severe deficiencies in essential nutrients can impair immune function.

Consequences:

- Increased susceptibility to infections.
- Greater risk of developing certain cancers.
- Complications from infections that would otherwise be manageable in individuals with a normal immune system.

5.3. General introduction to vaccines, Types of vaccines, Immunization programme

i. General Introduction to Vaccines

Vaccines are biological preparations that provide immunity to a specific infectious disease. They work by stimulating the immune system to recognize and combat pathogens (viruses, bacteria, or other microorganisms). Vaccines are one of the most effective tools in preventing infectious diseases and have significantly reduced the incidence of many life-threatening diseases.

How Vaccines Work

When a vaccine is administered, it introduces an antigen derived from the pathogen into the body. The immune system responds to this antigen by producing specific antibodies. If the vaccinated individual later encounters the actual pathogen, their immune system can recognize and fight it off more effectively.

ii. Types of Vaccines

Vaccines can be broadly classified into several types based on how they are made:

1. **Live Attenuated Vaccines**:
    - **Description**: Contain a weakened form of the live pathogen that is unable to cause disease in healthy individuals.
    - **Examples**: Measles, Mumps, and Rubella (MMR) vaccine, Varicella (chickenpox) vaccine, Oral Polio Vaccine (OPV).
    - **Advantages**: Strong and long-lasting immune response.
    - **Disadvantages**: Not suitable for immunocompromised individuals.
2. **Inactivated (Killed) Vaccines**:
    - **Description**: Contain pathogens that have been killed or inactivated so they cannot cause disease.
    - **Examples**: Inactivated Polio Vaccine (IPV), Hepatitis A vaccine, Rabies vaccine.
    - **Advantages**: Safe for immunocompromised individuals.
    - **Disadvantages**: Often require multiple doses or boosters for effective immunity.
3. **Subunit, Recombinant, Polysaccharide, and Conjugate Vaccines**:
    - **Description**: Contain only parts of the pathogen (e.g., protein, sugar) that stimulate the immune system.
    - **Examples**: Hepatitis B vaccine (recombinant), Human Papillomavirus (HPV) vaccine (subunit), Haemophilus influenzae type b (Hib) vaccine (conjugate).

- **Advantages**: Target specific components, reducing the risk of side effects.
- **Disadvantages**: May require boosters for long-term immunity.

4. **Toxoid Vaccines**:
    - **Description**: Contain inactivated toxins (toxoids) produced by the pathogen.
    - **Examples**: Tetanus vaccine, Diphtheria vaccine.
    - **Advantages**: Induce immunity to the toxin rather than the pathogen itself.
    - **Disadvantages**: Often require boosters.
5. **mRNA Vaccines**:
    - **Description**: Use messenger RNA to instruct cells to produce a protein that triggers an immune response.
    - **Examples**: COVID-19 vaccines (Pfizer-BioNTech, Moderna).
    - **Advantages**: Rapid development, strong immune response.
    - **Disadvantages**: Newer technology, long-term data still being gathered.
6. **Viral Vector Vaccines**:
    - **Description**: Use a modified virus (vector) to deliver genetic material from the pathogen to stimulate an immune response.
    - **Examples**: COVID-19 vaccines (AstraZeneca, Johnson & Johnson).
    - **Advantages**: Strong immune response, versatile platform.
    - **Disadvantages**: Preexisting immunity to the vector can reduce effectiveness.

iii. Immunization Programmes

Immunization programmes are public health initiatives aimed at increasing vaccine coverage to prevent infectious diseases. These programmes can be national, regional, or global and are designed to protect individuals and communities through vaccination.

Key Components of Immunization Programmes

1. **Routine Immunization**:
    - Regular administration of vaccines according to a schedule to infants, children, and adults.
    - Examples: DTP (Diphtheria, Tetanus, Pertussis), MMR, Polio, and Hepatitis B vaccines.
2. **Mass Vaccination Campaigns**:
    - Targeted efforts to vaccinate large populations in a short period, often in response to outbreaks or to achieve high coverage quickly.
    - Examples: Polio eradication campaigns, measles immunization drives.

3. **School-based Immunization**:
    - Vaccination programmes conducted in schools to reach children and adolescents.
    - Examples: HPV vaccine, Meningococcal vaccine.
4. **Maternal and Neonatal Immunization**:
    - Vaccination of pregnant women to protect them and their newborns.
    - Examples: Tetanus toxoid vaccine, Influenza vaccine.
5. **Outreach Services**:
    - Vaccination efforts aimed at reaching remote, underserved, or high-risk populations.
    - Mobile clinics and community health workers often play a critical role.

Goals of Immunization Programmes

- **Disease Eradication**: Complete and permanent worldwide reduction to zero new cases through deliberate efforts (e.g., smallpox).
- **Disease Elimination**: Reduction to zero of the incidence of a specified disease in a defined geographical area (e.g., polio in certain regions).
- **Disease Control**: Reduction of disease incidence, prevalence, morbidity, or mortality to a locally acceptable level.

5.4. Organ transplantation- Graft rejection, immune suppressors

i. Organ Transplantation

Organ transplantation is a medical procedure in which an organ is removed from one body and placed into another to replace a damaged or missing organ. The success of organ transplantation has significantly improved the quality of life and survival rates for patients with end-stage organ failure. However, one of the major challenges in organ transplantation is graft rejection, which is the recipient's immune response against the transplanted organ.

ii. Graft Rejection

Graft rejection occurs when the recipient's immune system recognizes the transplanted organ as foreign and mounts an immune response against it. This response can damage or destroy the transplanted organ. Graft rejection can be categorized into three main types:

1. **Hyperacute Rejection**:
    - **Timing**: Occurs within minutes to hours after transplantation.
    - **Mechanism**: Pre-existing antibodies in the recipient’s blood recognize and attack antigens on the donor organ’s endothelial cells. This leads to rapid and severe damage to the organ.
    - **Outcome**: Often results in immediate failure of the transplanted organ and necessitates its removal.
2. **Acute Rejection**:
    - **Timing**: Occurs within days to weeks after transplantation.
    - **Mechanism**: T lymphocytes recognize foreign antigens on the donor organ and initiate an immune response. This involves direct cytotoxic T-cell-mediated damage and recruitment of other immune cells.
    - **Outcome**: Can be managed with immunosuppressive therapy, but if not controlled, it can lead to significant organ damage.
3. **Chronic Rejection**:
    - **Timing**: Occurs over months to years after transplantation.
    - **Mechanism**: Involves both immune and non-immune factors leading to chronic inflammation and fibrosis of the transplanted organ. The exact mechanisms are complex and involve both antibody-mediated and cell-mediated responses.
    - **Outcome**: Progressive loss of organ function, and often irreversible.

iii. Immune Suppressors

To prevent graft rejection, recipients are treated with **immunosuppressive drugs**. These medications suppress the immune response, reducing the likelihood of rejection. However, they also increase the risk of infections and other complications due to the generalized suppression of the immune system.

Common Immunosuppressive Drugs

1. Calcineurin Inhibitors:

Examples: Cyclosporine, Tacrolimus.

Mechanism: Inhibit the activity of calcineurin, a protein involved in the activation of T cells. This reduces the proliferation and activity of T cells.

Side Effects: Nephrotoxicity, hypertension, neurotoxicity, increased risk of infections.

2. Antiproliferative Agents:

Examples: Azathioprine, Mycophenolate mofetil.

Mechanism: Inhibit the proliferation of T and B cells by interfering with DNA synthesis.

Side Effects: Bone marrow suppression, gastrointestinal disturbances, increased risk of infections.

3. mTOR Inhibitors:

Examples: Sirolimus, Everolimus.

Mechanism: Inhibit the mammalian target of rapamycin (mTOR) pathway, which is essential for cell growth and proliferation.

Side Effects: Hyperlipidemia, delayed wound healing, increased risk of infections.

4. Corticosteroids:

Examples: Prednisone, Methylprednisolone.

Mechanism: Suppress inflammation and immune responses by affecting multiple signaling pathways involved in immune activation.

Side Effects: Hyperglycemia, osteoporosis, weight gain, increased risk of infections.

5. Biological Agents (Monoclonal Antibodies and Fusion Proteins):

Examples: Basiliximab, Alemtuzumab, Belatacept.

Mechanism: Target specific components of the immune system. For example, Basiliximab blocks the interleukin-2 receptor on T cells, preventing their activation.

Side Effects: Vary depending on the specific agent but can include infusion reactions, increased risk of infections, and specific organ-related toxicities.