Introduction

Immunology is an area of science which helps in understanding the way by which animals gained protection from disease causing agents. It also includes the use of antibody-antigen reaction or other laboratory work i.e. serology and immunochemistry.

History of Immunology-

The Nobel Prize in Physiology or medicine (1908) was awarded to llya llytic Metchni-Koff(1845-1916) with Paul Elich in recognition of their work in immunity.

Late 18th century

Jernner, Edward introduces cowpox vaccine for protection against smallpox (1798).

Late 19th century

- Pasteur; germ theory, attenuated & killed vaccines i.e. anthrax vaccine, developed rabies vaccine.
- Kock (1882) described tubercule bacillus and produced killed vaccine.
- Metchnikoff (1884) described phagocytosis.
- Pasteur (1885) developed rabies vaccine.
- VouBehring & Kitasato (1890) prepared killed vaccine.
- Bordet, Pfeiffer (1895) discovered complement activity.
- Ehrlich (1891) standardized diphtheria toxin so that its potency can be assessed and antitoxin measured against it.
- Durhan- bacterial agglutination.

Mid 20th Century to date

1902 –Landsteiner discovered blood group.
1903 - Wright and others discovered antibody in the blood of immunized animals.
1903 –Antigenic determinant – Landsteiner ,Heidegerger, Murrack
1903 –Electrphoretic separation of gammaglobulin by Kabat & Tiselius
1903 – Antiglobulin test – Coobs, Mourant and Race
1903 – Recognition of immunity.
1955 –Clononal selection theory of immunity – Burnet & Jerae
1953 –Medabear – discovered immune tolerance
1962 – Porter – propose basic structure for immunoglobin G molecule
Transplant immunology, tumor immunology, Rhesus immunization, Deficiency states and role of thymus

Relationship between structure and biological activities of immunoglobin Molecules and genetic control mechanism

-Determinant of immunogenicity of antigen molecule
-Immunogenetic and evolution of immune system
-Lymphocyte activation and cell cooperation.
-Role of macrophages – antibacterial and cytotoxiceffects.

1975 – Monoclonal antibody production technique by Kholer & Milstein
1983-1984 –Mullis developed Polymerase Chain Reaction (PCR)
1986 -First vaccine (Hepatitis B vaccine) produced by genetic Engineering approved for human use.
1986 -Chickenpox vaccine approved for use in U. S

IMMUNOLOGY CONCEPT

Immunology is the study of host immune system from the moment o birth and sometimes even before that, the body exists in an environment filled with potentially harmful organisms and agents. Over the course of thousands of years of evolution, protective mechanism have developed in human – animal immune system reflects many aspect of this evolution ranging from the innate immunity afforded by the skin and mucous membranes to the highly complex specific response of T -cells and antibodies which recognizes invading pathogens if they are encountered again.

TERMINOLOGIES

Antibody (AB): A protein produced as a result of interaction with an antigen. The protein has the ability to combine with the antigen that stimulated its production.

Antigen (Ag): A substance that can react with an antibody. Not all antigens can induce antibody production; those that can are also called immunology.

B cell (also B lymphocyte): Strictly, a bursa–derived cell in avian species and, by analogy, a cell derived from the equivalent of the bursa in nonavian species. B cells are the precursors of plasma cells that produce antibody.

Cell – mediated (cellular) immunity: Immunity in which the participation of lymphocytes and macrophages is predominant. Cell–mediated immunity is a term generally applied to the type IV hypersensitivity reaction (see below).

Chemokines: low–molecular–weight protein that stimulate leukocyte movement.

Chemotaxis: A process whereby phagocytic cells are attracted to the vicinity of invading pathogens.

Complement: A set of plasma proteins that is the primary mediator of antigen-antibody reactions.

Cytolysis: The lysis of bacteria or of cells such as tumor or red blood cells by insertion of the membrane attack complex derived from complement activation.

Cytotoxic T cell: T cells that can kill other cells infected with intracellular pathogens.

Endotoxins: Bacterial toxins released from damaged cells.

Epitope: Site on an antigen recognized by an antibody. Also known as an antigenic determinant

Hapten: A molecule that is not immunogenic by itself but can react with specific antibody.

Histocompatible: Sharing transplantation antigens.

Humoral immunity: Pertaining to immunity in a body fluid and used to denote immunity mediated by antibody and complement.

Immune response: Development of resistance (immunity) to a foreign substance (e.g., infectious agent). It can be antibody-mediated (humoral) ,cell-mediated (cellular), or both.

Innate immunity: Nonspecific resistance not acquired through contact with an antigen. It includes skin and mucous membrane barriers to infectious agent and a variety of non specific immunologic factors, and it may vary with age and hormoral or metabolic activity.
Adaptive immunity: Protection acquired by deliberate introduction of an antigen into a responsive host. Active immunity is specific and is mediated by either antibody or lymphoid cells (or both)

Immunoglobulin: A glycoprotein, composed of H and L chain, that functions as antibody. All antibodies are immunoglobulin, but not all immunoglobulin have antibody function.

Inflammation: Local accumulation of fluid and cells after injury or infection.

Interferon: One of a heterogeneous group of low-molecular-weight proteins elaborated by infected host cells hat protect noninfected cells from viral infection. Interferons, which are cytokines, also have immunomodulating functions.

Leukocyte: General term for a white cell.

Lymphocyte: A molecule cell 7-12pm in diameter containing a nucleus with densely packed chromatin and a small rim of cytoplasma, lymphocytes include the T cells and B cells, which have primary roles in immunity.

Macrophage: A phagocytic mononuclear cell derived from bone marrow monocyte and found in tissues and at the site of inflammation. Macrophages serve accessory roles in immunity, particularly as antigen presenting cells (APCs).

Major histocompatibility complex(MHC): A cluster of genes located in close proximity eg, on human chromosomes 6, that encoded the histocompability antigens (MHC molecules)

Membrane attack complex: The end product of activation of the complement cascade, which contains C5, C6, C7, and C8 (and C9). The membrane attack complex makes holes in the membrane of gram-negative bacteria killing them and, in red blood or other cells, resulting in lysis.

Monoclonal antibodies: Each B lymphocyte produces antibody of a single specificity. However, normal B cells do not grow indefinitely. If B cells hybridization and fused cells that secret the desired antibody-producing cell line, known as a hybridoma, is contained, and these hybrid cells produce monoclonal antibodies.

Monocyte: A circulating phagocytic blood cell that develops into tissue macrophages.

Natural killer (NK) cells: Large lymphoid cells with no known antigen-specific receptors. They are able to recognize and kill certain abnormal cells, e g tumor cells.

Opsonin: A substance capable of enhancing phagocytosis. Antibodies and complement are the two main opsonins

Opsonization: The coatings of an antigen or particle (e.g., infectious agent) by substances, such as antibodies, complement components, fibronectin, and so forth, that facilitate uptake of the foreign partile into a phagocytic cell.

Immunology

Immunology is the study of immunity or protein against infectious or other agents and conditions arising from the mechanisms involved in immunity. Immunity is the protection against infectious agents and other substance.
There are two types of immunity,

1. Non adaptive immune response or Innate immunity. This is the immunity that is not affected by prior contact with the infectious agent or other material involved and is not mediated by lymphocytes.
2. Adaptive immune response/ specific immune response/Acquired immunity. This is the immune response that depends on the recognition and the elimination of antigens specific lymphocytes.

Adaptive/acquired Immunity can be natural or artificial, active or passive

	Active	Passive
Natural	Exposure to antigen induces an immune response s	Transfer of antibodies or cells produced by others as

	immunity that follows attacks of measles or canine distemper	temporary immunity from antibodies of the mother transferred to infant across the placenta or in milk.
Artificial	Deliberate exposure to antigen induces an immune response e.g. immunization of children or young animals.	Antibodies in immune serum are introduced into body e.g. injection of rabies immune globulin after dog bite.

The Innate Defenses

1. The innate defense system is composed o first-line defenses, sensor systems such as toll-like receptors and complement, and phagocytes. Inflammation is a coordinated response that involves many aspects of the innate defenses.

First-Line Defenses

Physical Barriers:

1. The skin provides the most difficult barrier for microbes to penetrate, it is composed of two main layers- the dermis and the epidermis.
2. The cells of the mucous membrane are constantly bathed with mucous and other secretion that help wash microbe from the surfaces. Some mucous membranes have mechanism that propel microbes, directing them towards areas where hey can be eliminated more easily.

Antimicrobial Substances:

1. Lysozyme, peeoxidase, enzymes, lactoferrin, and defensins re antimicrobial substances that inhibit or kill microorganisms

Normal Flora:

1. Members of the normal floral competitively exclude pathogens and stimulate the host defenses.

The Cell of the Immune System

1. There are three types of granulocytes- neutrophils, basophila and consinophilis.

Mononuclear Phagocytes:

1. Monocytes differentiate into either macrophages or dendritic cells.

Lymphocytes

1. Lymphocytes, which include B cells, T cells and Natural Killer (NK) cells, are involved in adaptive immunity.

Cell Communication
Surface Receptors bind ligands that are on the outside of the cell, enabling the cell to detect that the ligand is present.

Cytokines:

1. Cyrokines include interleukins (LLs), colony-stimulating factors (CSFs), tumor necrosis factors (TNFs), chemokines, and interferons.

Adhesion Molecules

1. Adhesion molecules allow cells to adhere to other cells.

Sensor Systems

Toll-Like Receptors

1. Toll-like receptor enables cells to detect molecules that signify the presence of microbe.

The Complement System

1. Complement proteins circulate in the blood and the fluid that btches tissues, in response to certain stimui that indicate the presense of foreign material, they become activated.
2. The major protective outcomes of complement activation include opsonizatio,lyisof foreign cells, and initiation of inflammation.

Phagocytosis

The Process of Phagocytosis

1. The step of phagocytosis includes chemotaxis, recognition and attachment, engulfiment, destruction and digestion, and exocytosis.

Specialized Attributes of Macrophages:

1. Macrophages are always present in tissues to some extent, but are able to call in reinforcements when needed.
2. A macrophage can increase its killing power, becoming an activated macrophage.
3. Macrophage, giant cells, and T- helper cells form concentrated groups called granulomas that wall off and retain organisms or other material that cannot be destroyd by mcrophages.

Specialized Attributes of Neutrophils

1. Neutrophils play a critical role during the early stages of inflammation, being the first cell type recruited from the blood stream to the site of damage.

Inflammation-A Coordinated Response to Invasion or Damage

1. Swelling, redness, heat, and pain are the signs of inflammation, the attempt by the body to contain a site of damage, localized the response, and restore tissue function.

Factors that Initiate the Inflammatory Response:

1. Inflammation is initiated when pro inflammatory cytokines or other inflammatory mediators are released as a result of the engagement of tells like receptors or activation complement by invading microbes, or when tissue damage occurs.

The Inflammatory Process

1. The inflammatory process leads to a cascade that result in dilation of small blood vessels, leakage of fluids from those vessels, and the migration of lculocytes out of the bloodstream and into the tissues.
2. Acute inflammation is marked by a preponderance of neutrphils, chronic inflammation is characterized by the prevalence of macrophages, giant cells, and granulomas.

Outcomes of Inflammation

1. Inflammation can contain an infection, but the process itself can case damage, a system response can be life threatening.

Apoptosis –Controlled Cell Death that Circumvent the Inflammatory Process.

1. Apoptosis is a mechanism of eliminating self-cells without evoking an inflammatory response.

Interferons

1. One of the roles of interferons is to induce cells in the vicinity of a virally infected cell to prepare to cease protein synthesis in the event they become infected with a virus, double, stranded RNA signifies to the cell that it has been infected.

Fever

1. Fever occurs as a result of certain pro-inflammatory cytokines released by macrophages when their toll-like receptors bind microbial products.
2. Fever inhibits the growth of many pathogens and increases the rate of various body defenses.

Strategy of the Adaptive Immune Response

The Humoral Immunity

Humoral immunity is mediateds by B.cells; in response to extracellular antigens, these maybe triggered to proliferate and then differentiate into plasma cells that function as antibody producing factories.

Cellular Immunity
Effector T- cytotoxic cells are able to induce apoptosis in 'self" cells
that present abnormal protein that signify danger. Effctor T-helper orchestrates the various response of cellular and humoral immunity.

Anatomy of the lymphoid system

Lymphatic Vessels.

Lymph, which may contain antigens that have entered tissues, flows in the lymphatic vessels to the lymph nodes.

Secondary lymphoid organs

Secondary lymphoid organs are the sites at which lymphocytes gather to contact antigens; they facilitate the interactions and transfer of cytokines between the various cells of the immune system.

Primary Lymphoid Organs

1. Primary lymphoid organs are the sites where B.cells and T.cells mature.

The Nature of Antigens

1. Antigens are molecules that react specifically with an antibody or lymphocyte, immunogen refers specifically to an antigen that elicits an immune response.
2. The immune response is directed to antigenic determinant, or epitopes, on the antigen.

The Nature of Antibodies

Structures and Properties of Antibodies

1. Antibodies monomers have a Y shape with an antigen-binding site at the end of each arm of the Y. The tail of the Y is the Fc region.
2. The antibody monomer is composed of two identical heavy chains and two identical light chains; each chain forms several domains. The variable region contains the antigen binding site; the constant region encompasses the entire Fc region as well as part of the Fab regions.

Protective Outcomes of Antibody-Antigens Binding

1. Antibody-antigens binding result in neutralization, immobilization and prevention of adherence, agglutination and precipitation, opsonization, complement activation, and antibody-dependent cytotoxicity.

Immunoglobulin Classes

1. There are five major antibody classes, IgM, IgG, IgA, IgD, and IgE, and each has distinct functions.

Clonal Selection of Lymphocytes

1. When antigens enter a secondary lymphoid organ, only the lymphocytes that specifically recognize the antigen will respond; the antigen receptor they carry on their surface governs this recognition.
2. Lymphocytes may be immature, naïve, activated, effector, or memory cells.

B. Lymphocytes and the Antibody Response

The Response to T-Dependent Antigens

1. B.cells present antigen to effector T-helper cells for inspection. If an effector T-helper cell recognizes the antigen, it will deliver cytokines to the cell, initiating the process of clonal expansion, which ultimately forms plasma cells that produce antibody.
2. Under the direction of effector T-helper cells, the expanding B-cell population will undergo affinity maturation and class switching, and form memory cells.
3. In the primary response, a lag period occurs before antibodies can be detected; memory cells are responsible for the swift and effective secondary response, eliminating invaders before they cause noticeable harm.

The Response to T-Independent Antigens

1. T-independent antigens include polysaccharides that have multiple identical evenly spaced epitopes and LPS.

T Lymphocytes: Antigen Recognition and Response

1. The T-cell receptor recognizes antigen presented by major histocompatibility (MHC) molecules.
2. T-cytotoxic cells are referred to as CD8 T cell; T-helper is referred to as CD4 T-cells.

Functions of Effctor T-Cytotoxic (CD8) Cells

1. T-cytotoxic cells induce apoptosis in cell that produce proteins associated with danger, they also produce cytokines that allow neighboring cells to become more vigilant against intracellular invaders.
2. All nucleated cells present peptides from endogenous protein in the groove of MHC class molecules.

Functions of Effector T-helper (CD4) Cells

1. T-helper cells respond to exogenous antigen, which are presented to MHC class II molecules.
2. ThI cells judge antigens presented by macrophages, a responding ThI cell activates that particular macrophage and secrete cytokines that help orchestrate the immune response.
3. Th2 cells judge antigen presented by B.cells; a responding Th2 cell activates that particular B. cell and supports actions that enhance its effectiveness

Activation of T Cells

1. Naïve T-cells require signals to become activated, upon activation the cell stimulates ti own proliferation and ten gain its effector functions.
2. Dendritic cell sample material in tissues and the travel to the secondary lymphoid organs to present the antigen to naïve T-cells. Those that detect molecules associated with danger produce co stimulatory molecules and are able to activate both subcots of T-helper-cells

Natural Killer (NK) Cells

1. NK cells mediate antibody-dependent cellular-cytotoxicity (ADCC).
2. BK cells kill host that are not bearing MHC class I molecules on their surface.

Lymphocyte Development

Generation of Diversity