IMMUNOLOGY

Introduction

- Humans and animals have survived on earth for hundreds of thousands of years because they have many built-in or naturally occurring mechanisms of defense against pathogens and infectious disease they cause.

IMMUNOLOGY

- The ability of any animal to resist these invaders and recover from disease is due to many complex interacting functions within the body.

Immunology cont'd

Immunology :-

is the scientific study of the immune system and immune responses, including the active and passive acquired immunity to infectious agents, antibody production, cell-mediated immune responses, and allergic responses, other types of hypersensitivity reactions, autoimmune disorders and immunodiagnostic procedures.

Immunology cont'd

- The immune system is the third line of defense against pathogens; it is a specific host defense mechanism. **Definition of terms**
- **Host defense mechanisms**:-are ways in which the protects itself from pathogens.

Definition of terms

- **Non-specific defense mechanisms**:- are ways in which the attempts to destroy all types of substances that are foreign to it including pathogens.
- **Specific host defense mechanisms**:-is the immune response ,very specific – because antibodies(special proteins) are usually produced in the body in response to the presence of foreign substances(antigens).
- **Antigens** :- are foreign substances.

NONSPECIFIC HOST DEFENSE MECHANISMS

These are general and serve to protect the body against many harmful substances.

FIRST LINE OF DEFENSE

a) **Mechanical and physical factors**

i. **Skin:-**

- intact, unbroken skin that covers our bodies serves as a physical or mechanical barrier to pathogens.
- very few pathogens are able to penetrate the skin.
- the dryness of most areas of skin inhibits colonization by many pathogens

ii. Mucous membranes:-

- they serve as physical and mechanical barriers to pathogens.
- most pathogens can only pass when these membranes have are cut or scratched.

ii. Mucous membranes:-

- the sticky mucous produced by the goblet cells within the mucus membranes serve to entrap invaders(pathogens). They can be removed by normal reflex like coughing or sneezing.
- Such areas include nose (respiratory tract), mouth, and vagina

b). Cellular and Chemical factors:-

- Body temperature -<37°c and acidity of the skin inhibit the growth of pathogens.
- the oily sebum that is produced by sebaceous glands in the skin contains fatty acids which are toxic to some pathogens.

b). Cellular and Chemical factors cont'd

- Perspiration (sweat) aids in flushing organisms from pores and surface of skin.
- Sweat contains enzyme-lysozyme which degrades peptidoglycan in bacteria cell walls.
- Sloughing off of dead skin cells removes potential pathogens from the skin.

b). Cellular and Chemical factors cont'd

- Sticky mucus produced by the mucous membranes contains lysozyme,lactoferin,and lactoperoxidase that kill bacteria or inhibit growth.
- Lactoferrin binds with iron, a mineral that is required by all pathogens;because they are unable to compete with lactoferrin for free iron,the pathogens are deprived of these essential nutrient.

b). Cellular and Chemical factors cont'd

- Lactoperoxidase is an enzyme that produces superoxide radicals, highly reactive forms of oxygen which are toxic to bacteria.
- Because mucosal cells are among the most rapidly dividing cells in the body, they are constantly being produced and released from the mucous membranes. Bacteria that is adhering to the cells are often expelled along with the cells they are attached.

b). Cellular and Chemical factors cont'd

- The hair, mucous membranes and irregular chambers of the nose serve to trap much of the inhaled debris.
- The cilia present on the epithelial cells of the posterior nasal membranes, nasal sinuses, bronchi and trachea sweep the trapped dust and microbes upward toward the throat where they are swallowed or expelled by sneezing and coughing.

b). Cellular and Chemical factors cont'd

- Swallowing of saliva can be thought of as a non-specific defense mechanism ,because thousands of bacteria are removed from the oral cavity every time we swallow. Humans swallow approximately 1 litre of saliva per day.
- Digestive enzymes, acidity of the stomach (approx.PH 1.5), alkalinity of the intestines protects the digestive system from bacteria colonization.

b). Cellular and Chemical factors cont'd

- Peristalsis and expulsion of feces serve to remove bacteria from the intestine. Bacteria make up 50% of feces.
- Microorganisms are continually flushed from the urethra by frequent urination and expulsion of mucus secretions.

b). Cellular and Chemical factors cont'd

- The low PH of vaginal fluid usually inhibits colonization of the vagina by pathogens.

c). Microbial antagonism:-

- The indigenous microflora prevent colonization by new arrivals to a particular anatomical site through competition for colonization sites, nutrients and production of substances that kill other bacteria.

Second line of defense

- Pathogens able to penetrate the first line of defense are usually destroyed by non-specific cellular and chemical responses(second line of defense).
- A complex sequence of events develops involving production of fever, interferons, activation of the complement system, inflammation, chemotaxis, and phagocytosis

a). Transferrin:-

- is a glycoprotein synthesized in the liver has a high affinity for iron.
- Its normal function is to store and deliver iron to the host cells.
- Transferrin serves as a nonspecific host defense mechanism by sequestering iron and depriving pathogens of these essential nutrient.

b) Fever:-

- normal body temperature fluctuates between 36.2c and 37.5c.Average 37.2c.
- A body temperature greater than 37.8c is generally considered to as be fever.
- substances that stimulate production of fever are called pyrogens or pyrogenic substances
- Fever acts as a body nonspecific host defense mechanism by:-

b) Fever cont'd

- Stimulating white blood cells(leukocytes) to deploy and destroy invaders
- Reducing the available free plasma iron ,which limits growth of pathogens that require iron for replication and synthesis of toxins.
- Inducing the production of interleukin-1 (IL-1) which causes the proliferation,maturation,and activation of lymphocytes in the immunologic response.

c). interferons:-

- are small antiviral proteins produced by virus-infected cells .
- They are called interferons because they "interfere" with viral replication.
- There are three types of interferons – **alpha**, **beta** and **gamma** induced by different stimuli, including viruses ,tumors, bacteria and other foreign cells.

c). Interferons cont'd

- Alpha-interferon -are produced by B lymphocytes(B cells),monocytes, macrophages.
- Gamma-interferon -activated by T lymphocytes(T cells) and Natural killer cells(NK cells).
- Beta-interferon -by fibroblasts and other virus-infected cells.

c). Interferons cont'd

- Interferons produced by a virus-infected cell are unable to save that cell from destruction, but once they are released from that cell, they attach to the membranes of surrounding cells and prevent viral replication from occurring in those cells.
- Thus the spread of infection is inhibited ,allowing the body to fight the disease more effectively.

d). The complement system:-

- is not a single entity, but rather a group of approximately 30 different proteins(including nine proteins designated as C1-C9) that are found in normal blood plasma.
- Proteins of the complement system sometimes collectively referred to as complement components, interact with each other in a step-wise manner called complement cascade.

d). The complement system cont'd

- The complement system assists in the destruction of many different pathogens by
  - Initiation and amplication of inflammation
  - Attraction of phagocytes to the sites where they are needed(chemotaxis).
  - Activation of leukocytes
  - Lysis of bacteria and other foreign cells
  - Increased phagocytosis by phagocytic cells(opsonization).

e). Inflammation:-

- the body normally responds to local injury,irritation,microbial invasion or bacterial toxin by a complex series of events collectively referred to as inflammation or inflammatory response.

e). Inflammation cont'd

- The 3 major events in acute inflammation are:-

i). An increase in the diameter of capillaries , which increases blood flow to the site.

ii). Increased permeability of the capillaries ,allowing the escape of plasma and plasma proteins.

iii). Egress(exit) of leukocytes from the capillaries and their accumulation at site of injury.

e). Inflammation cont'd

- The primary purpose of the inflammatory response

  -Localize an infection

  -Prevent the spread of microbial invaders

  -Neutralize any toxins being produced at the site

  -Aid in the repair of any damaged tissue.

f). Phagocytosis:-

- is the process by which phagocytes surround and engulf (ingest) foreign material.
- The phagocytic white blood cells are called phagocytes.
- The three major categories of leukocytes found in blood are-

  -monocytes

  -lymphocytes and

  -granulocytes.

f). Phagocytosis cont'd

- The three types of granulocytes are:- eosinophils,basophils and neutrophils.
- The two most important groups of phagocytes in the human body are macrophages and neutrophils; sometimes called 'professional phagocytes ' because their major function is phagocytosis.

f). Phagocytosis cont'd

- Phagocytes serve as a 'clean-up crew' to rid the body of unwanted and often harmful substances such as dead cells, unused cellular secretions, debris and microorganisms.
- Granulocytes –are named from the prominent cytoplasmic granules that they posses. The phagocytic granulocytes include neutrophils and eosinophils .
- Neutrophils are much more efficient in phagocytosis than eosinophils .

f). Phagocytosis cont'd

- Macrophages-develop from monocytes during the inflammatory response to infections.
- Those that leave the blood stream and migrate to infected areas are called wandering macrophages. Fixed macrophages remain in the tissues and organs and serve to trap foreign debris.
- Macrophages are extremely efficient phagocytes. They are found in tissues of the reticuloendothelial system(RES).

g). Chemotaxis:-

- phagocytosis begins when phagocytes move to the site where they are needed. The directed migration is called chemotaxis and is the result of chemical attraction called chemotaxic agents.
- Chemotaxic agents produced that are produced by various cells of the human body are called chemokines.

g). Chemotaxis cont'd

- Chemotaxic agents are produced during the complement cascade and inflammation.
- The phagocytes move along the concentration gradient, meaning they move from areas of low concentration of chemotaxic agents to the area of the highest concentration.
- The area of highest concentration is the site where the chemotaxic agents are being produced or released-often the site of inflammation.

SPECIFIC IMMUNITY or THIRD LINE OF DEFENSE

- Micro-organisms that overcome non-specific are faced with specific immunity
- The antigens of the invading micro-organisms comes into contact with cells of immune system (macrophages and lymphocytes) and initiate a response
- The response takes two ways:-
- **humoral immunity** and **cell-mediated immunity**

Humoral immunity

- Humoral(antibody-mediated) immunity is directed primarily against
- Exotoxin-mediated diseases such as tetanus and diphtheria
- Infections in which virulence is related to polysaccharide capsules (e.g meningococci, pneumococci, haemophilus influenzae).
- Certain viral infections.

Antibody synthesis is by

- The primary response
- Secondary response

The primary response

- When an antigen is first encountered, antibodies are detectable in the serum after a long period.
- The lag period is typically 7-10 days but can be longer depending on the nature and dose of the antigen and the route of administration(oral or parenteral).
- A small clone of B cells and plasma cells specific for the antigen is formed.
- Serum antibody concentration continues to rise for several weeks,then drops to low levels.

The secondary response

- When there is a second encounter with the same antigen or closely related one, months or years after the primary response, there is a rapid antibody response(in 3-5 days) to higher levels than primary response.
- This is due to persistence of antigen-specific memory cells after the first contact.
- In the secondary response the amount of IgM produced is qualitatively similar to

ANTIBODIES

- **Antibodies(immunoglobulins)** are formed by B lymphocytes-each individual has a large pool of different B lymphocytes that have a lifespan of days or weeks and are found in the bone marrow, lymph nodes, and gut associated lymphoid tissues
- B cells display immunoglobulin on their surface.
- They serve as receptors for specific antigen

Antibodies or immunoglobulins

IgG:-

- It has two identical antigen binding sites
- Is the predominant antibody in secondary responses and constitutes an important defense against bacteria and viruses.
- It is the only antibody that can pass the placenta barrier and is the most abundant immunoglobulin in newborns.

IgM:-

- Is the main immunoglobulin produced early in the primary response
- It is present in the surface of virtually all

Antibodies cont'd

IgA:-

- is the main immunoglobulin in secretions such as milk, saliva, and tears and secretions of the respiratory, interstinal and genital tract.
- It protects the mucous membranes from bacteria and viruses.

IgE:-

- It binds to the receptor on the surface of mast cells, basophils, and eosinophil

IgD:-

CELL-MEDIATED IMMUNITY

- This depends on development of lymphoid cells which are specifically sensitized to the inducing antigen and which react directly with the antigen to bring about cytotoxic effects
- Development of activated macrophages can also result from this process
- Antibody response is a physiological reaction to the introduction into the body of foreign materials, irrespective of whether it is harmful or not

types of immunity

Immunity

Natural — Artificial

Active — Passive — Active — Passive

Sickness — breast milk — vaccination — antiserum

or

via placenta

Active immunity:-

- is induced after contact with foreign antigens. This contact may consist of clinical or sub-clinical infections, immunization with live or killed infectious agents or antigen exposure to microbial products e.g toxins, toxoids
- The host actively produces antibodies and lymphocytes acquire the ability to respond to the antigens.
- Advantages:

Active immunity can be acquired naturally or artificially e.g

- The production of antibodies in response to a pathogen that has entered the body is an example of natural active acquired immunity.
- The production of antibodies in response to a vaccine is an example of artificial active acquired immunity.

- **Passive immunity:-**is transmitted by antibodies or lymphocytes performed in another host.
- Advantage:-

  -prompt availability of large amounts of antibodies.
- Disadvantages:-

  -short lifespan of antibodies

  -Possible hypersensitivity reactions if antibodies from

- A fetus receiving antibodies that were produced by the mother is an example of natural passive acquired immunity.
- A soldier receiving antibodies contained in a shot of gamma globulin is an example of an artificial passive acquired immunity

Herd immunity

- When a large proportion of people are immunized in a community, even those few people who have not been vaccinated also get some protection because the disease becomes so uncommon. This is called herd immunity.
- It is mainly effective for those diseases that pass from man to man e.g measles, polio and pertusis.

Immunizing agents and clinical importance

- **Immunization:-** is the process of protecting a person from a particular disease.
- It happens when a vaccine against a disease has been given. This is called active immunization.
- Some vaccines are made from live bacteria or viruses that have been modified enough not to cause a severe infection, but they are still similar to the original bacteria or viruses for the body