# IMMUNITY



- Animal body is always exposed to various harmful invaders like viruses, bacteria, fungi and parasites and toxic substances.
- It has been noticed that the persons who had been suffering from certain diseases like measles and mumps, are not attacked in future by the pathogens of the same disease. It is due to the fact that these people have become immune to the concerned disease.
- The human body has the ability to resist almost all types of organisms or toxins that damage the tissues and organs. This capacity is called **immunity**.
- In other words, immunity refers to the resistance of a host to pathogens and their toxic products.
- The system of animal body, which protects it from various infectious agents and cancer, is known as **immune system**.
- The study of the immune system is called **immunology**.

- The credit for having first observed and described bacteria goes to **Antony van Leeuwenhoek**. In 1683, he made accurate descriptions of various types of bacteria and communicated them to the Royal Society of London.
- **Edward Jenner** (1796) observed that milkmaids did not get small pox infection apparently because they were exposed to a similar but milder form of disease called cowpox. Edward Jenner infected first James Phipps, a healthy boy of 8 years with cowpox and two months later he infected the boy with small pox. The boy did not suffer from small pox; Jenner proposed that an induced mild form of a disease would protect a person from a virulent form. Edward Jenner was the first to discover a safe and effective means of producing artificial immunity against small pox. Edward Jenner is regarded as "*Father of Immunology*".
- The decisive step in human immunization was made in 1885, when **Louis Pasteur** administered the anti-rabies vaccine to the young Joseph Meister, severely bitten by a rabid dog. That was for the first time in history that the rabies treatment was done by a cultured vaccine.
- **Robert Koch** discovered the bacteria of tuberculosis (1882) and the cholera (1883). Koch formulated **Koch's postulates** which are as follows:
    - (i) The organism (pathogen) must be regularly found in the body of the animal that is suffering from a disease.
    - (ii) The organism must be isolated that grow in pure culture on artificial media.
    - (iii) The same disease must be produced when the cultured organisms are injected into other healthy animals.
    - (iv) The same organism must be recovered from the injected animals.
- These postulates originally were applied for animal diseases but are equally applicable for human diseases. However, *Koch's postulates are not applicable to viral diseases*

because viruses cannot be cultured on artificial media. *Koch's postulates are also not applicable to bacteria of leprosy* because it has not been possible to grow these bacteria in culture media.

- **Emil Adolf von Behring** (1891) discovered the technique of passive immunization by injecting diphtheria pathogen into sheep preparing serum from its blood after some time. He got the 1901 Nobel Prize for serum therapy for giving acquired passive immunity against diphtheria.
- **Shephard** (1960) described that *Lepra bacilli* (bacteria of leprosy) could multiply in the foot of mice kept at a low temperture 20°C. The nine banded armadillo is highly susceptible to infection with *Lepra bacilli.*



# TYPES OF IMMUNITY

**1. INNATE IMMUNITY (NON-SPECIFIC IMMUNITY)**

- Innate immunity is the resistance to infection, which an individual possesses by virtue of his/her genetic and constitutional make up. Thus innate immunity comprises all those defence elements with which an individual is born, and which are always available to protect a living body.

- One form of innate immunity comprises various types of barriers which prevent entry of foreign agents into the body. When pathogens enter into the body, they are quickly killed by some other components of this system.
- This is the **first line of defence** of most animals and plants. Innate immunity consists of the following four types of barriers: physical, physiological, cellular and cytokine barriers.

- **Physical Barriers.** These barriers prevent the entry of organisms into the body.
  (a) **Skin.** The skin is physical barrier of body. Its outer tough layer, the **stratum corneum** prevents the entry of bacteria and viruses.
  (b) **Mucous Membrane.** Mucus secreted by mucous membrane traps the microorganism and immobilizes them. Microorganisms and dust particles can enter the respiratory tract with air during breathing which are trapped in the mucus. The cilia sweep the mucus loaded with microorganisms and dust particles into the pharynx (throat). From the pharynx it is thrown out or swallowed for elimination with the faeces.

- **Physiological Barriers.** Body temperature, *pH* of the body fluids and various body secretions prevent growth of many diseases, causing microorganisms. Some of the important examples of physiological barriers are as follows:
  (a) Acid of the stomach kills most ingested microorganisms.

(b) Bile does not allow growth of microorganisms.
(c) Cerumen (ear wax) traps dust particles, kills bacteria and repels insects.
(d) Lysozyme is present in tissue fluids and in almost all secretions except in cerebrospinal fluid, sweat and urine. Lysozyme is in good quantity in tears from eyes. Lysozyme attacks bacteria and dissolves their cell walls.
(e) A rise of temperature (fever) due to infection is a natural defence mechanism and helps not only to accelerate physiological processes but may, in some cases, destroy the infecting pathogens.
(f) Certain kinds of cells, when infected within a virus, release interferons (glycoproteins). Interferons (IFNs) make the cells resistant to viral infections.
(g) Bicarbonate ions in saliva neutralize the acids in food.

- **Cellular Barriers.** Certain types of leukocytes (WBC) like polymorphonuclear leucocytes (PMNL), neutrophils and monocytes and natural killer (type of lymphocyte) in the blood and macrophages in tissues can engulf microbes, viruses and cellular debris etc. The phenomenon of phagocytosis was discovered and named by Metchnikoff (1883). He proposed the phagocytic response as the prime defence against the microbial invasion of tissue. Metchnikoff and Paul Ehrlich got the 1908 Nobel Prize for their work on body resistance.

- **Cytokine Barriers.** Virus infected cells secrete proteins known as interferons which protect non infected cells from further viral infection.
- Fever may be brought about by toxins produced by pathogens and a protein called endogenous pyrogen (fever producing substance), also called interleukin released by macrophages. When enough pyrogens reach the brain, the body's thermostat is reset to a higher temperature, allowing the temperature of the entire body to rise. Mild fever strengthens the defence mechanism by activating the phagocytes and by inhibiting the growth of microbes. A very high temperature may prove dangerous. It must be quickly brought down by giving antipyretics.

- In addition to the above mentioned barriers, natural killer cells and the complement system also provide innate immunity.
- **Natural Killer Cells (NK Cells)**. Besides the phagocytes, there are natural killer cells in the body which kill virus-infected and some tumour cells. Killer cells produce perforins which create pores in the plasma membrane of the target cells. These pores allow entry of water into the target cells, which then swell and burst. Cellular remains are eaten by phagocytes.
- **The Complement System.** The complement system is a defensive system consisting of plasma proteins that attack and destroy the microbes. The term 'complement' (c) refers to a system of factors occurring in normal serum that are activated characteristically by antigen antibody interaction, and subsequently mediate a number of biologically

significant consequences. This system participates in both innate and acquired immunities. The complement system consists of over 30 proteins that act in various ways to protect the individual from invading microbes. Complement proteins create pores in the plasma membrane of the microbes. Water enters the microbes. The latter burst and die. Some components of the complement system form a coat over the invading microbes. This coating attracts phagocytes (neutrophils and macrophages) for engulfing them. The complement system also causes agglutination of microbes, neutralisation of viruses, activation of mast cells and basophils and has some inflammatory effect.

- **Second Line of Defence.** Phagocytes, interferons, inflammatory reactions, fever, natural killer cells and complement system constitute the second line of defence.

- **Third line of defence** is provided by specific defence mechanism which includes (i) antibodies and (ii) lymphocytes.

**2. ACQUIRED IMMUNITY (= ADAPTIVE OR SPECIFIC IMMUNITY)**

- The resistance that an individual acquires during life is called acquired immunity. Acquired or adaptive or specific immunity has the following properties:
  **(i) Specificity.** It is the ability to differentiate between various foreign molecules.
  **(ii) Diversity.** It can recognize a vast variety of foreign molecules.
  **(iii) Discrimination between Self and Non-self.** It can recognise and respond to foreign molecules (non-self) and can avoid response to those molecules that are present within the body (self) of the animal.
  **(iv) Memory.** When the immune system encounters a specific foreign agent, *(e.g.,* a microbe) for the first time, it generates immune response and eliminates the invader. This is called first encounter. The immune system retains the memory of the first encounter. As a result, a second encounter occurs more quickly and abundantly than the first encounter.

- **Cells involved in Acquired Immunity.** Two major groups of cells are involved in acquired immunity: Lymphocytes and Antigen presenting cells.

- **Lymphocytes.** A healthy person has about a trillion lymphocytes. Lymphocytes are of two types: T lymphocytes or T cells and B lymphocytes or B cells. Both types of lymphocytes and other cells of the immune system are produced in the bone marrow. The process of production of cells of immune system in the bone marrow is called haematopoiesis.

- **T Lymphocytes (= T cells).** Certain stem cells in the bone marrow give rise to immature lymphocytes. These lymphocytes migrate via blood to the thymus. Once these cells

enter the thymus, they are called thymocytes. In the thymus these cells mature as T lymphocytes (T cells).

- **Types of T -Cells and their functions.**

  **(a) Helper T cells.** They are numerous. These cells stimulate the B-cells to produce antibodies. They also stimulate the killer T cells to destroy the nonself cells. Their role is overall regulation of immunity. They do this function by forming a series of protein mediators, called lymphokines that act on other cells of the immune system as well as on bone marrow cells.

  **(b) Cytotoxic T cells (= Killer Cells or K Cells).** These cells directly attack the foreign cells. The cytotoxic T cells secrete a protein perrorin which punctures the invader's cell membrane. Water and ions flow into the nonself cell, which swells up and finally lyses. The cytotoxic T cells also destroy the cancer cells. The cytotoxic cells are responsible for cell mediated immunity.

  **(c) Suppressor T Cells.** They are capable of suppressing the functions of cytotoxic and helper T cells. They also inhibit the immune system from attacking the body's own cells.

  **(d) Memory T Cells.** These cells remain in the lymphatic tissue *(e.g.,* spleen, lymph nodes) and recognize original invading antigens, even years after the first encounter. These cells keep ready to attack as soon as the same pathogens infect the body again.



- **B Lymphocytes (= B-Cells).** Certain cells of the bone marrow produce B lymphocytes. These cells mature in the bone marrow itself. The B cells produce specialised proteins called antibodies and, therefore, generate antibody mediated or humoral immunity.
- The B lymphocytes give rise to :

  **(a) Plasma Cells (Effector B cells).** Some of the activated B cells enlarge, divide and differentiate into a clone of plasma cells. Although plasma cells live for only a few days, they secrete enormous amounts of antibody during this period. A few days after exposure to an antigen, a plasma cell secretes hundreds of millions of antibodies daily and secretion occurs for about 4 or 5 days until the plasma cell dies.

  **(b) Memory B Cells.** Some activated B cells do not differentiate into plasma cells but rather remain as memory cells. They have a longer life span. The memory cells remain dormant until activated once again by a new quantity of the same antigen.

- **Antigen Presenting Cells (APCs).** These specialized cells include macrophages (monocytes as blood macrophages and histocytes as tissue macrophages), B-lymphocytes and dendritic *(e.g.,* Langerhans cells of epidermis of skin). They are distinguished by two properties: (i) they express class II MHC molecules on the membrane, and they are able to deliver a co-stimulatory signal that is necessary for helper T cell activation.

**ACTIVE AND PASSIVE IMMUNITY**

- **1. Active Immunity.** This involves the active functioning of the person's own immune system leading to the synthesis of antibodies and/or the production of immunologically active cells. Active iminunity may be natural or artificial.
- **(i) Natural active immunity**. It results either from a subclinical or clinical infection, The large majority of adults in the developing countries possess natural active immunity to poliomyelitis due to repeated subclinical infections with poliovirus during childhood, A person who has recovered from an attack of *small pox* or measles or mumps develops natural active immunity,
- **(ii) Artificial active immunity.** Artificial active immunity is the resistance induced *by vaccines.* Vaccines are preparations of live or killed microorganisms or their products used, for immunisation. Examples of vaccines are as follows:
- Bacterial vaccines. (a) Live- BCG vaccine for tuberculosis (b) Killed- TAB vaccine for enteric fever.
- Viral vaccines. (a) Live- sabin vaccine for poliomyelitis, MMR vaccine for measles, mumps, rubella. (b) Killed- salk vaccine for poliomyelitis, neural and non-neural vaccines for rabies.
- Bacterial products. Toxoids for Diphtheria and Tetanus.

- **2. Passive Immunity.** In passive immunity, there is transfer of immune products, like antibodies, etc. to a recipient in a ready-made-form. Passive immunity is also of following two types.
- **(i) Natural passive immunity.** This is the resistance passively transferred *from the mother to the foetus through placenta.* IgG antibodies can cross placental barrier to reach the foetus. After birth, immunoglobulins are passed to the newborn through the breast milk. Human colostrum is rich in IgA antibodies. Mother's milk contains antibodies which protect the infant properly by the age of three months.
- **(ii) Artificial passive immunity**. Artificial passive immunity is the resistance passively transferred to a recipient by adminstration of antibodies. This is done by administration of hyperimmune sera of man or animals. Serum contains antibodies. For example, antitetanus serum (ATS) is prepared in horses by active immunisation of horses with tetanus toxoid, bleeding them and separating the serum. ATS is used for passive immunisation against tetanus. Similarly antidiphtheric serum (ADS) and anti-gas gangrene serum (AGS) are also prepared.

# ANTIGENS

- Antigens are substances which, when introduced into the body, stimulate the production of antibodies. Most antigens are proteins but some are carbohydrates, lipids or nucleic acids.

- **Antigenic determinants or epitopes** are those sites on antigens that are recognised by antibodies and receptors present on T and B cells.
- In fact the *smallest units of antigenicity are the antigenic determinants.* Each determinant can stimulate the formation of a particular kind of *antibody or effector cell*. Thus a pure protein antigen may give rise to many distinct antibodies and effector cells.
- Based upon the ability of antigens to carry out their functions, antigens are of two types: **complete antigens** and **incomplete antigens (haptens)**.
- A complete antigen is able to induce antibody formation and produce a specific and observable reaction with the antibody so produced.
- Haptens (partial antigens) are substances which are incapable of inducing antibody formation by themselves, but can be capable of inducing antibodies on combining with larger molecules (normally proteins) which serve as carriers.

- **H antigen.** Red blood corpuscles of all ABO blood groups possess a common antigen; the H antigen, which is a precursor for the formation of A and B antigens. Due to universal distribution, H antigen is not ordinarily important in grouping or blood transfusion. However, Bhende *et al* (1952) from Mumbai reported a very rare example in which A and B antigens and H antigens were absent from the red blood corpuscles. This is known as Bombay or Oh blood group. Such individuals will have anti A, anti B and anti H antibodies. Therefore, they can accept the blood only from their own group.

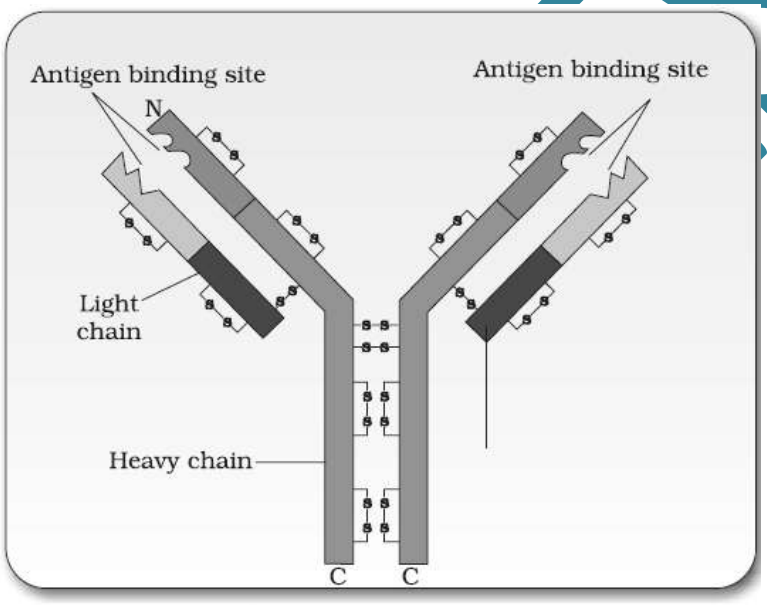
# ANTIBODIES

- Antibodies are immunoglobulins (Igs) which are produced in response to antigenic stimulation. Thus all antibodies are immunoglobulins but all immunoglobulins are not antibodies.
- The antibodies may be bound to a cell membrane or they may remain free. Antibodies are produced by **B lymphocytes and plasma cells**.
- In fact B-lymphocytes get transformed into plasma cells. The mature plasma cell produces antibodies at an extremely rapid rate- about 2000 molecules per second. Antibodies direct the **antibody-mediated immunity (= humoral immunity).**
- On the basis of physicochemical and antigenic structure human Igs are grouped into five classes or isotypes namely **Ig A, Ig D, Ig E, Ig G**, and **Ig M**. They differ from each other in size, charge, carbohydrate content and amino acid composition. A = Alpha *(a),* D = Delta *(0,)* E = Epsilon (f), G = Gamma *(y),* M = Mu (μ).

| Differences between Antibodies and Antigens | |
|---|---|
| *Antibodies (Immunoglobulins)* | *Antigens (Immunogens)* |
| 1. Antibody is a protein molecule.<br>2. It is synthesized by an animal to combat foreign material.<br>3. Antibody occurs on the surface of a plasma cell and also in body fluids.<br>4. Antibody directly joins an antigen to destroy the latter. | 1. Antigen is a protein or polysaccharide molecule.<br>2. It is usually a foreign material that stimulates antibody formation.<br>3. Antigen may occur on the surface of a microbe or as a free molecule.<br>4. Antigen binds to a macrophage to reach a helper T-cell to initiate immune response. |



- ***Ig* G has been studied extensively and *serves as a model of basic structural unit of all Igs.***




Structure of an antibody molecule

- It is made up of 4 peptide chains. Of the four chains, there are two long chains, called **heavy or H Chains** and two short chains, called **light or L Chains**, which may be either **lambda or Kappa type.** The four peptide chains are held together by disulphide bonds to form a Y -shaped molecule. Two identical fragments of Y -shaped molecule possess the antigen-binding sites and are thus named fragment-antigen binding (Fab). The antigen-binding sites bind to the specific antigens in a lock and key pattern, forming an antigen-antibody complex. The third fragment which lacks the ability to bind to antigen and can be crystallized, is, therefore, known as fragment crystallizable (Fc).

- Five classes of antibodies are described below:
- (i) **IgA.** It is the *second most abundant class,* constituting about 10 per cent of serum immunoglobulins. There is an additional peptide chain called joining (J) chain. It is the major immunoglobullin in **colostrum** (the first milk secreted by a nursing mother), saliva and tears. *It protects from inhaled and ingested pathogens.* Thus it protects the body surface. When Ig A is excreted through faeces, it is called **coproantibody.**

- (ii) **IgD.** It is *present on the surface of B lymphocytes* which are destined to differentiate into antibody-producing plasma cells. Thus *IgD activates B cells to secrete other antibodies.*
- (iii) **IgE.** This immunoglobulin was discovered in 1966 by Ishizaka. It exhibits unique properties such as heat lability (inactivated at 56°C in one hour). IgE mediates type I hypersensitivity (anaphylaxis). Prausnitz and Kustner in 1921 demonstrated transmission of IgE-mediated type I hypersensitivity by injecting serum containing IgE antibodies from allergic person into the skin of a normal or non allergic person. It is called.Prausnitz-Kustner (PK) reaction. Thus *IgE* acts as *mediator in allergic response.*
- (iv) **IgG.** This is the *most abundant class of Ig* in the body constituting approximately 75% of the total Igs. IgG is the only maternal immunoglobin that is normally transported across the placenta and *provides natural passive immunity in the foetus and the new born.* Thus, IgG is present in the milk. IgG protects the body fluids. *IgG* also *stimulates phagocytes and complement system.*
- (v) **IgM. It** is the *largest Ig.* It is so named because it is a macroglobulin atleast five times larger than IgG. **It** also has J chain. IgM is the oldest immunoglobulin class. It activates the B cells. It is also *the earliest immunoglobin to be synthesised by the foetus,* beginning about 2 weeks of age. **It** cannot cross the placental barrier. Ig M is 500-1000 times more effective than Ig G in opsonisation, a 100 times more effective in bacterial action and 2, times in bacterial agglutination. But in neutralization of toxins and viruses, it is less active that Ig G. Thus Ig M protects the blood stream.