Types of Immunity: Innate Immunity

Innate Immunity

Immunity is the power of an individual to fight against diseases. It is the sum total of all mechanisms which help the host's body to resist against invading infectious organisms or harm causing substances. Our body defenses work at different levels by different mechanisms. Broadly these mechanisms can be divided into two categories: -

I. Non Specific Host Defense Mechanism
II. Specific Host Defense Mechanism

Non Specific Host Defense Mechanisms do not discriminate between the types of invading agent and responds in the similar manner to all of them. It is not specific for a particular agent but exhibits generalized reaction. It also does not need prior exposure to the infectious organism to exhibit resistance against it. This is also termed as **Innate** or **Inborne** or **Native Immunity**. This type of immunity is present in the host by birth. It is said so because, the anatomical structure and physiological components of the body provides Innate immunity to the host. They comprise of physical and chemical barriers.

Specific Host Defense Mechanism is exhibited by the host only after the body experiences the infectious agent. Immunity provided by this method is known as **Adaptive Immunity**. This segment of host defense works through cell mediated and antibody mediated immunity. Specific defense first recognizes the foreign substance then prepares against it and mounts an exclusive response which is also stored in it's memory.

The immunity prevailing in the population is usually referred by following terms.

Species Immunity

This refers to the inability of a pathogen to infect any member of the species. All the members of the species are inherently immune to specific pathogens. Example human beings are not affected by plant pathogens or some animal diseases. This inability may be due to varied host susceptibility. The physiological and biochemical differences in the host tissues accounts for differed host susceptibility.A pathogen can cause disease inside any host only if it gets suitable conditions to establish and multiply.

Racial Immunity

Some races among the species are not affected by the pathogens, which commonly infect other members of the species. The cause of this variation is not very clear [Human Races]. A well-known example of immunity against *Plasmodium falciparum* is observed among human beings in some parts of Africa. These individuals posses sickle shaped RBCs which is not suitable for malarial parasite survival. Some individuals of Negroid origin in USA are more prone to tuberculosis than Caucasians. Such examples highlight the presence of resistance or susceptibility among some group of individuals against some diseases.

Individual Immunity

The difference in immunity exhibited by the individuals of a given species against infectious agents is individual immunity. All the members of a species respond to varying extents against the pathogen's entry. Their responsiveness depends on numerous factors, which include individual's anatomical, physiological, metabolic and immunological differences. These differences are due to the genetic constitution of the individual.

Factors Influencing immunity

The power of host response depends on various factors such as-

Age

Effectiveness of immune system is at its best between adolescent and middle age group. Very young and old individuals are more prone to infections. This is

appropriately accounted by the immature working of immune system in infants and young children [Age Animate graph, S6]. They get exposed to numerous disease causing agents for the first time and do not have preexisting immunity towards it. These recurrent exposures provide them immunity as they grow up. The effects of aging are obvious on all the body systems which is also exhibited in the form of the reduced ability of immune system to protect against infections in old age people.

Hormonal influence

The cells of immune system are highly influenced by the endocrine systems. They possess receptors for the hormones produced by adrenal and thyroid gland. Their multiplication, activity and suppression of functions are influences by the hormones. Immune cells also respond to the physiological consequences of over or underproduction of these hormones. Eg. diabetes and hypothyroidism increases the host's susceptibility to infections.

Nutrition

Immune system does not work efficiently in malnourished individuals. The body is not able to combat diseases in deficiency of proper supply of proteins, carbohydrates, vitamins and minerals. Malnutrition causes significantly, the impairment of cell-mediated immunity, phagocyticactivity, complement pathway functioning, secretory immunoglobulin A antibody concentrations, and production of cytokines. Overnutrition and obesity is also found to be associated with reduced immune response. At the same time it is also observed that some infections are not apparent in case of undernourished individuals.

Innate Immunity (First Line of Host Defense Mechanism)

Innate immunity is present in the body since birth by the virtue of anatomical and physiological of our body. It is also known as Inborne or Native immunity. It consists of numerous components, which work through various mechanisms. These components can be divided into two sub-categories:-

I. First Line of Host Defense Mechanism
II. Second Line of Host Defense Mechanism

First Line of Host Defense Mechanism

First Line of Host Defense Mechanism includes physical and chemical barriers. It consists of body covering, body linings and body secretions. Each and every part of the body is safeguarded by specialized strategies. The components can be broadly listed as:-

i. Skin
ii. Mucous membrane
iii. Antibacterial secretions
iv. Normal Flora

These components are supported by the physiological activities of the body.

Skin

Skin is the most important physical barrier for the invading pathogens. It forms a strong cover over soft and moist internal body organs and surfaces. The inner body tissues can be very easily colonized by infectious agents but not the outermost covering skin because of following reasons: -

- Dermis layer of skin contains fibrous connective tissue which makes it tough and strong[Skin Dermis].
- The keratin content in skin makes it water proof and unfavourable for microbial growth.
- Sebaceous glands secrete oily sebum which contains fatty acids and lactic acid[Skin Dermis].
- Acidic secretions maintain acidic pH, which hinders the growth of microbes.
- Salt produced by sweat glands also inhibits microbial growth.
- Desquamation-Outermost dead layer of epidermal cells is regularly removed which in turn removes the adhering microorganisms.

These functions of skin resist the penetration and establishment of infectious microorganisms. Any cut, wound or burn in the skin destroys the obstruction and

provides easy entry for invading agents. Breaks in this barrier can also be created by insects like mosquitoes, which can insert pathogens inside our body.

Mucous Membrane

Mucous membrane covers all the body openings i.e. respiratory, digestive, urinary and genital tract. This consists of mucous cells, which produces a slimy secretion known as mucous. This serves as a sticky trap for incoming pathogens. These secretions are rich in antimicrobial substances such as lysozyme and lactoferrin.

Our body is a hollow tube, which has numerous openings. Inner body parts which appear to be away from external environment are actually completely exposed to it. The digestive tract starts from mouth and ends at anus, but in between it passes through various organs. All these organs must be protected from the innumerable substances present in food, water and air. Microbes which enter mouth are bathed in saliva which entraps them; and the digestive juices exert inhibitory action on them. Most of the organisms reaching stomach are destroyed by the acidic pH.The mucous membranes in the intestine expel microbes outwards by the peristaltic movements. The whole of inner body lining of mucous membrane possess cilia which propels the contents in required direction. This mucociliary blanket protects the breaching of internal epithelial layers below the mucous layer.

Nostrils serve as openings for inlet of air which leads to lungs. The nostrils possess nasal cilia which enmeshes the dust particles and interferes in the entry of the invading agents. The mucous lining along with this protects the upper and lower respiratory tract by trapping unwanted matter and pushing it outwards by sneezing and coughing action.

Eyes are continuously washed with tears, which contain the antimicrobial agent lysozyme.

Earwax produced in ear is a thick waxy secretion, which contains antimicrobial substances and traps the microbes present in dust.

Urinary tract also lined by mucous membrane. Urethral opening is freed from microbes of the environment by regular flushing action of urine.

Antimicrobial Secretions

Our body is protected from microbes by numerous antimicrobial substances for eg. high salt concentration on skin, lysozyme, peroxidase, lactoferrin, transferrins and defensins. They are present on skin, in saliva, tears and mucous which covers most of the body. Lysozyme and peroxidase are bactericidal for microbes whereas lactoferrinand transferring creatsunfavourable conditions for microbes by sequestering iron. Defensins are antimicrobial peptides which disrupt the cell integrety.

Normal Flora

Microorganisms routinely found growing on healthy human body are termed as normal microbiota or normal microflora. These organisms colonize on body surfaces and prevent the establishment of pathogens by creating a competition for them. They block the receptors on host's surfaces which can bind to pathogens for causing infections. They also secrete certain antimicrobial substances which kill or inhibit the growth of pathogenic microbes, for instance *E.coli* secretes colicins in gastrointestinal tract which inhibits other strains of bacteria, *Lactobacillus* in vagina creates acidic pH due to production of lactic acid and inhibits the growth of pathogens. Usage of antimicrobial therapy destroys the normal microbiota and renders the body surfaces free for incoming pathogens.

Innate Immunity (Second Line of Host Defense Mechanism)

Second Line of Host Defense Mechanism is also a non specific defense mechanism and does not discriminate between different pathogens. If the infectious agent is successful in crossing the first line of defense then it confronts second line. Infections may follow the breaching of physical barriers which are prevented by following components of second line: -

White blood cells

White blood cells [WBCs] are very important components of immunity[White blood cells]. A repertoire of these cells is recruited to work by different mechanisms. All the blood cells [RBCs and WBCs] arise from the stem cells present in bone marrow. The formation and development of these stem cells takes place in liver and spleen during the development of fetus. Eventually these cells move to bone marrow where differentiation and primary maturation of these cells take place under the influence of hematopoietic-inducing microenvironment. The hematopoietic stem cells give rise to myeloid lineage and lymphoid lineage. Myeloid lineage cells differentiate into red blood cells, granulocytes, monocytes and platelets. Lymphoid lineage gives rise to T cells, B cells and natural killer cells [Hematopoiesis].T and B cells have the ability of recognition of self/non self, diversity, memory and specificity which are the hallmarks of adaptive immunity. All the other cells work for innate immunity and as a part of the effector mechanism in adaptive immunity. Neutrophils among the granulocytes, monocytes and natural killer cells play significant role in innate immunity.

Neutrophils are the prime phagocytic cells, which work, in the second line of host defense. They constitute more than 50% of the circulating WBCs. Monocytes in blood and their matured forms; the macrophages in tissues are also involved in scavenging foreign invaders. Natural killer cells destroy the tumor cells or intracellularly infected cells. Two important strategies followed by these cells are:-

i. **Phagocytosis**
ii. **Inflammation**

Phagocytosis

EliMetchnicoff Neutrophils and macrophages both are recruited for engulfing the foreign substances. Phagocytosis involves following major steps: -

i. Chemotaxis
ii. Recognition and Attachment
iii. Engulfment
iv. Digestion
v. Exocytosis

Chemotaxis

Chemotaxis means migration under the influence of chemicals. At the time of injury, pharmacologically active substances are produced by the affected host cells, or the products of pathogens such as LPS. These serve as chemo attractants for recruiting phagocytes to the site of injury.

Recognition and Attachment

The phagocytic cells recognize the foreign particles on reaching the site of injury, and adhere to it. Specific receptors are present on phagocytes, which can identify the patterns associated with compounds present on pathogens. Coating of target molecules or bacteria with complement components or antibodies enhances their recognition.

Engulfment

The attachment of phagocytes to the target leads to the formation of pseudopodia around it. The captured foreign particles are endocytosed in a membrane bound vacuole and are known as phagosome.

Digestion

These phagosomes are moved inwards and fused with the lysosomes. This complex is known as phagolysosome. The lysosome contains hydrolytic enzymes for the destruction of the invading agent. The degradative mechanisms completely destroy the infectious agent.

Exocytosis

The debris of the infectious agent at the end of digestion is expelled out of the cell by exocytosis. The membrane bound vesicle containing degraded matter fuses with the plasma membrane for its removal from the cell.

Inflammation

Inflammation is a mechanism of response against the tissue injury, which helps in restricting the spread of infection. The inflammation at any site is marked by following signs:-

i. *rubor* - reddness
ii. *tumor* - swelling
iii. *calor* - heat
iv. *dolor* - pain
v. *functiolaesa* - loss of function

Initiation of Inflamation

The inflammatory process is initiated by the destruction of tissue and entry of microbes. Foreign substances like LPS, flagellin, and DNA derived from microorganisms bind to the receptors on macrophages, which get activated and release pro-inflamatory cytokines. This initiates a cascade of reactions.

Vasodialation

The local blood vessels near the site of injury are dialated. This increases the flow of blood near the destroyed tissue which inturn causes redness and heat. As the blood vessels are dialated, gaps are created between the endothelial cells of the vessel walls.

This increase in permeability is to allow fluid and cells to move out of the vessel and reach the area of action. Accumulation of fluid in the tissue leads to swelling.

Influx of phagocytes

The neutrophils moving in high speed are slowed down near the site of invasion. They start getting accumulated near the capillary wall, this is known as margination. Eventually they make their way out of the gaps between the cells of capillary walls. This is known as diapedesis or extravasation.

Degradation of invaders

The phagocytes reach at the site and engulf all the foreign invaders. They release hydrolytic enzymes, which damage the bacteria and nearby infected and healthy cells. The exudates consisting of dead cells and digested material is known as pus.

The fluid released out of the vessels contains clotting factors, which forms fibrin network and cuts off the infected material from the rest of the healthy tissue. This

prevents the spread of infection. Once the inflammatory response subsides completely and tissue debris is cleared, repair and regeneration of tissue takes place.

This short-term inflammatory response is known as **acute inflammation.** If the process continues for a longer period, may be more than a few months it is known as **chronic inflammation.**

Fever

Our normal body temperature is maintained at 37ºC. In case of invasion by pathogens, cytokines are released by the infected cells and our temperature is set above this. An oral temperature above 37.8ºC is regarded as fever. The increase in temperature is body's defense mechanism facilitating;-

i. Retardation of pathogen's growth at elevated temperature as 37ºC is optimum for it's growth.
ii. Increase in the rate of enzymatic reactions.
iii. Enhancing inflammatory response and phagocytic killing.

The substances responsible for rise in body temperature are known as **pyrogen**. Cytokines released by host cells are **endogenous pyrogens**, which induce the host defense mechanisms. Endotoxins produced by pathogens are the **exogenous pyrogens**.

Interferon's and Complements

Alick Isaacs and Jean Lindenmann described Interferon for the first time in 1957 at the National Institute for Medical Research in London. They interfere in viral replication therefore named as interferon's. They are the glycoproteins produced in response to pathogenic presence inside a cell. They are also known as antiviral proteins. Virus, bacteria or protozoan infected cells or tumor cells produce them. They belong to a category of molecules named as cytokines. Cytokines are substances, which help in communication between cells for enhancing or suppressing activities. Interferon's are the signaling molecules which are involved in activating or up regulating the cells of immune system. A virus infected cell produces interferon's, which are sent to the neighbouring cells for signaling. Interferon's stimulate other cells for initiating antiviral activities. These cells

produce antiviral proteins in response to the stimulus and are protected from viral infection. The interferon's enhance the expression of MHCs; activate natural killer cells and macrophages to clear off the infectious organism. Their biological activities lead to fever and pain. They are basically involved in clearing the infectious agents or tumor cells from the host.

They are divided into three categories:-

i. Type I INF
ii. Type II INF
iii. Type III INF

Complements

Complements are heat labile serum proteins which are present in blood in inactive form. They are a group of 20 components. They are activated by a nonself structure or an immune complex. Their activation by a non self structure is a part of innate immunity or non specific host defense mechanism whereas their activation by immune complex serves as an effector mechanism of adaptive immunity [Complements1]. Complement components get activated and proceeds in a chain reaction. The complement components are denoted by 'C'. Presence of nonself surface activates the complement by splitting it into two fragments. The fragments are denoted by small alphabets for eg. C3 on activation is cleaved into C3a and C3b. One of the fragment attaches to the foreign nonself structure and the other one performs the effector function. The target foreign substance is destroyed by phagocytosis as a result of the effector functions.

The complements can be activated by one of the following methods: -

Alternative pathway

Complement component C3 has the capacity to differentiate between self and nonself. As soon as C3 comes in contact with a nonself surface, it gets activated and initiates alternative pathway. A cascade of events takes place, which ultimately destroys the target for example a bacterium.

Lectin Pathway

Mannan, a polymer of mannose is usually present on microbial cells and rarely on mammalian cells. Lectins bind to them and inturn activates the complements of the host cells. This further initiates the chain reaction of complements.

Classical Pathway

Complement components of classical pathway are activated by the formation of immune complexes. Antigen-antibody complex formation activates complement component C1q, which further activates C1r, then C1s and then rest of the chain reaction starts.

All these pathways lead to the formation of membrane attack complex, which creates pores leading to the destruction of the target [MAC, MAC1]. Any of the above pathways is basically to clear off the invading agent from the host.