P. G. III rd Semester By Dr. Sushma Kumari

Innate Immunity

Immunity is the state of protection from infectious disease. The word immunity is said derived from Latin term 'immunis' meaning exempt. Immunity provides a well adaptive defence system in animals to protect them from invading antigen or allergens.

Innate immunity of an animal is also known as Natural, native, inherited or inborn immunity. It pertains to the first line of defence mechanism of an organism. It concerns with the general or nonspecific type of resistance to a particular pathogens or antigens. The extent of this natural immunity differs in different organisms. This level of natural or innate immunity may vary not only between species but also between races or strains and sexes. This may also be controlled by nutrition, hormones and many other factors. The innate immunity is accomplished by phagocytic neutrophil and macrophages with various antimicrobicidal agents like NK cell, complement proteins, lysozyme, interferon etc. The innate immunity does not involve antibody or immunoglobulin.

Innate immunity as first line of defence mechanism comprises four kind of defensive barrier are as follows-

(1) Anatomic
(2) Physiologic
(3) Phagocytic
(4) Inflammatory

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(1) Anatomic barriers :-

Anatomic or physical barriers prevent the entry of pathogens into the body. Examples: Skin mucous lining of the alimentary canal, nasal tract respiratory tract vaginal tract etc

Low pH (3 to 5) inhibits most bacterial growth. Low pH of skin is maintained by lactic acid and fatty acid of Sebum produced by sebaceous gland. The epithelial cells of skin, respiratory tract, urinogenital tract, nasal tract and gastrointestinal tract secrete a proteolytic polypeptide - defensin. The defensin rupture bacterial cells, fungi and capsulated virus. Lysozyme of tear and saliva degrade bacterial cell wall.

The E coli of gastrointestinal tract secrete an antibacterial called colicins which prevent the gut from colonization of colic bacteria.

Mucous membrane also acts as defensive barrier. Adherence of bacteria to mucous membrane is due to interaction between hairlike protrusion on a bacterium called fimbriae of pilli and certain glycoproteins or glycolipids of the mucous membrane.

Physiologic barriers :→

The physiologic barriers under innate immunity are Temperature, pH and various soluble factors. High Temperature of the body inhibits the growth of the bacteria.

Gastric acidity is an innate Physiological barrier to infection because very few microorganism can survive the low pH of the stomach contents.

A number of soluble factors like lysozyme, interferon and complement contribute to the innate immunity. Lysozyme a hydrolytic enzyme cleave the peptidoglycan layer of the bacterial cell wall. Interferon synthesized by virus infected cells and complement protein damage the membrane of the pathogens.

Phagocytic barriers:→

Most phagocytosis is conducted by specialized cells such as blood monocytes, neutrophils and tissue macrophages. Both macrophages and neutrophil are very rich in proteolytic enzymes like myeloperoxidase, defensin, lactoferrin, alkaline phosphatase etc.

The macrophages are found in entire connective tissue and skin. These macrophages are named differently depending on the site of occurrence. For example macrophage of liver, Kupffer cell, Microglial cell in brain, osteoclast in bone marrow.

For effective phagocytosis, the antigen bearing pathogens must bind with the surface of either macrophages or neutrophil. The microorganisms are ingested by actin and myosin contractile system which forms pseudopodia like structure around the microbe mediated by receptors. As soon as a pathogen enters the host there is an immediate increase in hexose monophosphate shunt. It further reduces NADPH which influence electron transport through FAD cytochrome b-558 oxidase.

$$NADPH + O_2 \xrightarrow{\text{cytochrome b558}} NADP^+ + O_2^-$$

$$2\,O_2^- + 2H^+ \xrightarrow[\text{Dismutase}]{\text{superoxide}} H_2O_2 + O_2$$

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Cytochrome-b-558 oxidase mediate reductions of molecular O_2 to superoxide anion. This superoxide anion is transformed to free radical hydrogen peroxide (H_2O_2) catalyzed by superoxidase dismutase and finally to hydroxyl free radicals (-OH). The H_2O_2 with others compound and ions form an a strong neutralizing agent to kill viruses and bacteria.

Inflammatory barriers! →

Tissue damage caused by any means induce a complex sequence of events collectively called inflammatory response. The cardinal signs of inflammation are redness, swelling, heat and pain to that particular place. This event involve three steps- Vasodilation, capillary permeability and finally influx of phagocytes from the capillary into the tissues.

Vasodilation! → An increase in the diameter of blood vessels near the damage site result in engorgement of the capillary network. The engorged capillaries are responsible for tissue redness and an increase in tissue temperature.

(2) An increase in capillary permeability promotes influx of fluids and cells from the engorged capillaries into the tissue. Accumulated fluid is rich in protein content and contribute to tissue swelling or edema.

(3.) Increased capillary permeability facilitates emigration of phagocytes. It includes adherence of the cells to the endothelial wall of the blood vessels (marginations) followed by diapedesis and finally chemotaxis.

As phagocytic cell accumulate at the site and begin to phagocytose bacteria, they release lytic enzymes, which can damage nearby healthy cells. The accumulation of dead cells, digested material and fluid forms a substance called pus.

Mechanism of Innate Immunity:

The innate immunity is mediated by alternative complement pathway. It does not involve antigen recognition and their removal by antigen and antibody reactions.

In alternative complement pathway, the complement protein C_3 is directly activated which binds with protected surface of bacteria containing lipopolysaccharide. The activation of C_3 in alternative pathway is completed in 3 steps –

(1) Tickover activation
(2) Activation of Protected Surface
(3) Amplification of alternative pathway.

(1) **Tickover activation:** →

The native C_3 is converted into active C_{3i} by the spontaneous hydrolysis of internal thioester bond of former. This process is known as tick-over activation. The C_{3i} bends with factor B forming

a large immune complex C3iBb which is further cleaved by factor D into a small Ba and a large C3iBb fragments. The C3iBb is fluid phase C3 convertases. Most of the C3 convertases are lost in fluid phases. They upon hydrolysis these are inactivated

(2) Activation of Protected Surface :→

The bacterial surfaces remain protected after binding with C3b complement proteins. Such surfaces are protected from proteolytic degradation. It has higher affinity for factor B protein than factor H. Factor B acts as an accelator whereas factor H is a strong inhibitor of convertase activity. The protected bacterial surface provides stable surface for C3 convertase activity. The initial activity of C3b initiates amplification.

Amplification of alternative pathway :→

The surface bound C3b binds to factor D to form C3bBb. The C3bBb is unstable compound but it quickly stabilized on cell membrane by properdin forming immune complex C3bbP which constitutes C3 convertase ready to enter terminal complement pathway. The terminal complement pathway for the formation of membrane attack complex is initiated by C3 convertase. It binds to complement protein C5 forming a smaller C5a and a larger C5b fragments. The C5b binds to complement protein C6, 7 and 8 in stepwise manner forming C5b678 complex on

which changes from hydrophyllic to hydrophobic state. The C5b678 complex finally binds with complement protein C9 to form C56789 complex which undergoes polymerization. All the polymerised component on the surface of the cell form membrane attack complex (MAC). MAC is a 660 to 850 KDa tubular hole or tunnel like structure like a doughnut. The central hole of this tunnel is the site of osmotic lysis of antigen bearing pathogens. There is a influx of water through the tunnel. The tunnel is large enough to permit the water and ions but impermeable to cascade enzymes hence the cell swells and bursts killing bacterial cell or pathogens.