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Immunology concept and terms

***Immunology**

Science that study immune responses in body and the cellular and molecular events that occur .after an organism encounters microbes and other foreign macromolecules enter the body

Immunity*

The latin term immunis ,meaning "exempt" in English immunity ,which refers to all mechanisms used by the body as protection against environmental agents that are foreign to the .body

Immune system*

The cells and molecules responsible for immune response , The immune system has a multi- .layered organization that provides immunity to infectious organisms

Immune response*

the collective and coordinated response from the immune system to the foreign molecules

Antigens*

substances that bind to specific lymphocyte receptors, whether or not they stimulate immune .responses

Immunogens*

substances that stimulate immune responses are called immunogens

Innate immunity*

Is conferred by all those elements with which an individual is born and that are always present .and available at very short notice to protect the individual from foreign antigens

Characteristic of Innate immunity

does not involve specific recognition of a microbe*

provides a rapid, early response*

innate immunity does not have a memory response*

.No more rapid and stronger immune reaction to the same microbe at a later date*

Among the components of innate immunity are the first line of defense (skin and mucous *

membranes) and the second line of defense (natural killer cells and phagocytes, inflammation, (fever, and antimicrobial substances

Acquired immunity *

acquired immunity is more specialized than innate immunity , the individual is born with the capacity to mount an immune response to a foreign invader , this immunity is acquired by . contact with the invader and is specific to that invader only

:Acquired immunity is induced by immunization ,which can achieved in several ways

.Active immunization : refers to immunization of an individual by administration of an antigen

Passive immunization :refers to immunization through the transfer of specific antibody from an .immunized individual to a nonimmunized individual

.Adoptive immunization: refers to the transfer of immunity by the transfer of immune cell

: Characteristics of the acquired immune response

specificity: is the ability to discriminate among different molecular entities and to respond only - .to those uniquely required rather than making a random

Adaptiveness: is the ability to respond to previously un seen molecules that may in fact never - . have naturally existed

Discrimination between self and non self :is ability to recognize and respond to molecules that - .are foreign (nonself) and to avoid making a response to those molecules that are self

Memory :is the ability to recall previous contact with a foreign molecule and respond to it in .learned manner , that is with a more rapid and larger respond

:Humoral immunity

is mediated by molecules in the blood and mucosal secretions called antibodies which is (produced by cells called B lymphocytes (also called B cells

(Cell-mediated immunity (Cellular immunity

is mediated by T lymphocytes (also called T cells). Intracellular microbes such as viruses and some bacteria, survive and proliferate inside phagocytes and other host cells, where they are not attached to circulating antibodies. Defense against such infections is a function of cell-mediated immunity, which promotes the destruction of microbes residing in phagocytes or the killing of infected cells to eliminate reservoirs of infection

Immune cell , Primary and secondary lymphoid organs

:Immune cell include

-١ Polymorphonuclear Leukocytes (polymorphonuclear(PMN:((

Leukocytes are a populations of cells also referred to as granulocytes ,these include the basophils, mast cell,eosinophils and neutrophils ,granulocytes are short lived phagocytic

cell which contain enzyme-rich lysosomes which play important role to destructions the infectious microorganisms and produce superoxide radicals which toxic to microorganisms .(,some lysosomes contain antibacterial proteins (lactoferrin

-٢Macrophages:

Macrophages are phagocytes derived from blood monocytes ,macrophages is included in the reticuloendothelial system ,the functions of RES is phagocytize microorganisms and foreign substances in blood stream and various tissues.

-٣Natural killer cells

The role of these cell limited in the viral infection or cancer cells which recognized by cytotoxic or killer cell that destroy target cells by releasing biological potent molecules that kill target cells . ,such killer cells include : antigen specific cytotoxic T lymphocytes

-٤Narural Killer T lymphocytes

The functions of these cell is similar to Natural Killer cells ,this cell is derived from thymus ,following activation of this cell they secrete cytokines (interleukins and interferon. (

-٥Antigen-Presenting Cells

Antigen-presenting cells (APCs) are cells that capture microbial and other antigens, display them to lymphocytes, and provide signals that stimulate the proliferation and differentiation of the lymphocytes. By convention, APC usually refers to a cell that displays antigens to T lymphocytes .

The major type of APC that is involved in initiating T cell responses is the dendritic cell. Macrophages and B cells present antigens to T lymphocytes in cell mediated and humoral .immune responses, respectively

:Lymphatic organs

Lymphatic organs are those organs in which lymphocytes maturation , differentiation ,and . proliferation take place

-: They are generally divided into two categories

: a-Primary (Central)lymphoid organs

are those in which the maturation of T and B lymphocytes into Antigen –recognizing . lymphocytes occurs

mature T and B lymphocytes migrate from the bone marrow and thymus through blood stream and peripheral lymphoid tissues including lymph nodes ,spleen and gut associated lymphoid . tissues

: b-Secondary (peripheral)lymphoid organs

. are those organs in which the antigen –driven proliferation and differentiation take place

Primary (Central)lymphoid organs

-١Thymus:

Thymus is a lymphoepithelial organ and consist of epithelial cells organized into cortical (outer) and medullary (central) areas that are infiltrated with lymphoid cells (thymocytes. (

Maturation T lymphocytes involves the commitment of a given T cell to recognize and respond.

Lymphocytes in thymus are mainly responsible for mounting cell- mediated immune responses. They are called thymus-derived lymphocytes or T cells. T-cell precursors originate in the bone marrow but then enter the thymus. Once within the thymus, the cells (called thymocytes) divide rapidly. Of the new cells produced, where as remain in the thymus for 4 to 5 days before leaving the thymus as mature T cells, circulate in the bloodstream, and colonize the secondary lymphoid organs

-٢bursa of Fabricius in bird and it equivalent in mammal

Bursa of Fabricius is found only in birds. the bursa is a primary lymphoid organ that functions as a maturation and differentiation site for the cells of the antibody-forming system. Lymphocytes originating in the bursa are therefore called B cells. The bursa acts like the thymus . the immature cells produced in the bone marrow migrate to the bursa. These cells then proliferate rapidly, Once their maturation is completed, B cells emigrate to secondary lymphoid .organs

bone marrow

is the primary lymphoid organ for B cells in mammals (ruminants, pigs, and dogs)..There is no exclusive B cell development with in the bone marrow, although it is suggested that precursor B cells develop at the outer edge of the marrow and migrate to the center as they mature and .multiply

Secondary lymphoid organ include

-١spleen

spleen can be considered a specialized lymph node for blood-born removes antigenic particles such as blood-borne microorganisms, cellular debris, and aged blood cells. This filtering function, together with highly organized lymphoid tissue, makes the spleen an important component of the immune system.

the spleen consists of two forms of tissue. One is used predominantly for blood filtering called the red pulp. It contains large numbers of antigen-presenting cells, lymphocytes, and plasma cells. The other is rich in both B and T cells where immune responses occur and is called the white pulp. The white pulp is separated from the red pulp by a region called the marginal zone. This zone contains numerous macrophages and dendritic cells and a large population of B cells.

-٢payer's patches

Peyer's patches are lymphoid organs located in the walls of the small intestine. The ileal PPs of some species function in a manner similar to the avian bursa. as sites of rapid B cell proliferation , release into the circulation

-٣ tonsils and lymph node

lymph nodes. Lymph nodes are round or bean-shaped filters. placed on lymphatic vessels in such a way that they can sample antigens carried in the lymph, The lymph node thus acts as a .filter for lymph fluid

The interior of lymph nodes is divided into three discrete regions: a peripheral cortex, a central medulla, and an defined region in between, called the paracortex

B cells predominate in the cortex, where they are arranged in aggregates called follicles. In lymph nodes that have been stimulated by antigen, some of these follicles form specialized . structures called germinal centers

Lymph node are rich in antigen-trapping follicular dendritic cells T cells and dendritic cells ، predominate in the paracortex

If we have foreign body entering the lymph node we get a phagocytosis. Then if Ag stimulate humeral immunity , we will get a mitotic activity in cortex and we con- find the production of Ab .in germinal center, so the Ab and Ig are found in the germinal center

But if we have Ag stimulate cell mediated immunity, we will get hyperatrophy of paracortex and trabeculae and this hyperatrophy represented by enlargement of paracortical zone and .trabeculae , this indicator for cell mediated immune response

The cause of hyperatrophy is due to the mitotic activity of T- cell that transform to lymphoblast .((T- cell transformation

So in the lymph node we have three types of cells participate in immune response

-١humeral immunity cells.

-٢Cell mediated immunity cells.

Phagocytosis cells-٣

Also secondary lymph organs contain many lymphoid tissue found in various submucosal membrane sites (mucosa-associated lymphatic tissue)(MALT) of the body, such as the gastrointestinal tract, thyroid, breast, lung, salivary glands, eye, and skin. MALT is populated by lymphocytes such as T cells and B cells, as well as plasma cells and macrophages

the components of MALT are sometimes subdivided into the following

GALT (gut-associated lymphoid tissue. Peyer's patches are a component of GALT * .found in the lining of the small intestines

(BALT (bronchus-associated lymphoid tissue*

NALT (nasal-associated lymphoid tissue*)

(CALT (conjunctival-associated lymphoid tissue*

(LALT (larynx-associated lymphoid tissue*

(SALT (skin-associated lymphoid tissue*

(VALT (vulvo-vaginal-associated lymphoid tissue*

Differences between primary and secondary lymphoid organs

Secondary	Primary	Different
Ag dependent	Ag independent	Lymphpoiesis
Postnatal life	Prenatal life	Development
Participate directly	Do not participate directly	Participation in immune response
-	+	Induration and atrophy
-	+	Differentiation of lymphocyte

(Already differentiate)

(Innate (Nonspecific Immunity

innate immunity is present from birth and consists of many factors that is relatively non-specific , it is against any substance that threatens the body , it is play importance role an early response . ,nonspecific , 1st line defense mechanisms against antigen

:innate immunity include

Physical and Chemical Barriers*

Most organisms and foreign substances cannot penetrate intact skin but can enter the body if the skin is damaged. Some microorganisms can enter through sebaceous glands and hair follicles. However, the acid pH of sweat and sebaceous secretions and the presence of various .fatty acids and hydrolytic enzymes (e.g., lysozymes) all have some antimicrobial effects

In addition, soluble proteins, including the interferon and certain members of the complement system found in the serum . contribute to nonspecific immunity. Interferon are a group of proteins made by cells in

response to virus infection, which essentially induce a generalized antiviral state in surrounding .cells

Activation of complement components in response to certain microorganisms results in a controlled enzymatic cascade which targets the membrane of pathogenic organisms and leads to .their destruction

mucous membrane barrier traps microorganisms which are then swept away, by ciliated epithelial cells, toward the external openings. The hairs in the nostrils and the cough reflex are .also helpful in preventing organisms from infecting the respiratory tract

some microorganisms that have penetrated the mucous membrane barrier can be picked up by macrophages or otherwise transported to lymph nodes

Gastrointestinal tract is made of many factors that are destroy many

microorganisms by other innate mechanisms including the hydrolytic enzymes in saliva, the low pH of the stomach, and the proteolytic enzymes and bile in the small intestine. The low pH of the .vagina serves a similar function

Cellular Defenses*

Once an invading microorganisms has penetrated the various physical and chemical barriers, _ the next line of defense consists of various

.specialized cells whose purpose is to destroy the invader

Phagocytosis and Extracellular Killing

As part of its innate immunity, the body has developed defenses

mediated by specialized cells that destroy the invading microorganisms

by first ingesting and then destroying it (phagocytosis) or by killing it extracellularly (without (ingesting it

.Endocytosis and phagocytosis

Two innate immune mechanisms result in the internalization of foreign

macromolecules and cells and can lead to their intracellular destruction and elimination. These .involve processes called endocytosis and phagocytosis

Endocytosis

Endocytosis is the process whereby macromolecules present in extracellular tissue fluid are ingested by cells. This can occur either by pinocytosis. which involves nonspecific membrane invagination

or by receptors mediated endocytosis a process involving the selective binding of macromolecules to specific membrane receptors

in both cases, ingestion of the foreign macromolecules generates

endocytic vesicles filled with the foreign material which then fuse with acidic compartments .called endosomes

Endosomes then fuse with lysosomes containing degradative enzymes (e.g., nucleases, lipases, .(proteases

Phagocytosis

.phagocytosis is the ingestion by individual cells of invading foreign particles, such as bacteria

.Many microorganisms release substances that attract phagocytic cells

Phagocytosis may be enhanced by a variety of factors that make the foreign particle an easier .target

These factors collectively referred to as opsonins (Greek word meaning "prepare food for,,), . consist of antibodies and various serum components of complement

Phagocytes can also damage invading pathogens through the generation of toxic products in a process known as the respiratory burst . Production of these toxic metabolites is induced during phagocytosis of pathogens such as bacteria and catalyzed by a set of interrelated enzyme pathways. The most important of these are nitric oxide (inducible nitric oxidase synthase), (hydrogen peroxide and superoxide anion (phagocyte NADPH oxidase

:Normal flora*

:Its not consider apart of body defense , but flora helps the body to prevent infection by

-١Competing with them for nutrient

--٢Changing the condition that effect survival of pathogen as pH or oxygen availability (alter of vagina pH by action of lactobacillus bacteria prevent infection by candida(

-٣Produce substance that harmful to pathogen .(bacteriocins produced by E.coli prevent salmonella infection(

Complement

The complement system, made up of approximately 30 circulating and membrane-expressed proteins, is an important effector arm of both the innate and antibody-mediated acquired .immune responses

Named from some of the earliest observations of its activity-a heat-sensitive material in serum that"complemented" the ability of antibody to kill bacteria-we now know that complement plays .a major role in defense a-against many infectious organisms

The most important of these functions are

(١) the production of opsonins, molecules that enhance the ability of macrophages and neutrophils to phagocytose material

(٢)the production of anaphylatoxins, peptides that induce local and systemic inflammatory responses

(٣)direct killing of organisms

(٤)enhancing antigen-specific immune responses and maintaining homeostasis (the maintenance of stability within the body) by removing immune complexes and dead or dying cells.

COMPLEMENT ACTIVATION PATHWAYS

The early steps in complement activation involve a sequential activation-a cascade-of successive components. In this part of the activation pathway, the activation of one component induces enzymatic function that triggers the activation of the next component in the sequence. Because ،one active enzyme molecule can cleave multiple substrate molecules

Three pathways of complement activation are known the classical, lectin, and alternative pathways. The initiation of each pathway involves distinct recognition events and components, but the later stages of all three pathways use the same components. The characteristics of each pathway

The Classical Pathway

The classical pathway was so named because it was the first complement pathway to be worked out. The component proteins are designated Cl, C2,...C9. The numbers designate the order in which the components were discovered rather than their position in the activation sequence Antigen-antibody complexes are the predominant activators

of the classical pathway; thus this pathway is a major effector pathway of the humoral adaptive immune response. Other activators include some viruses, necrotic cells and subcellular (membranes (e.g., from mitochondria

The classical pathway is initiated when C1 binds to the antibody in an antigen-antibody complex; for example, antibody bound to an antigen expressed on the surface of a bacterium

C I is a complex of three different proteins C1q (made up of six identical subunits) combined .with two molecules each of C1r and C1s

To activate C1, the globular head regions of C1q subunits bind to C1q-specific receptors on the . Fc regions of either one IgM or two closely spaced IgG molecules bound to the antigen

As a consequence of C 1 binding to the antigen-antibody complex, C1s becomes enzymatically active. This enzymatically active form, known as C1s esterase, cleaves the next component in the classical pathway, C4, into two pieces, C4a and C4b. C4a, the smaller piece, remains in the fluid phase but C4b binds covalently to the surface of the bacterium or

.other activating substance

The C4b bound to the cell surface then binds C2, which is cleaved by C1s. Cleavage of C2 generates the fragments C2b, which remains in the fluid phase and C2a. C2a binds to C4b on the surface of the cell to form a complex, C4b2a. The C4b2a complex is known as the classical

The Lectin Pathway

The lectin pathway is activated by terminal mannose residues Of proteins and polysaccharides .found on the surface of bacteria

These terminal mannose residues are not found on the surface of mammalian cells, and so the lectin pathway of complement activation may be thought of as discriminating between self and .non-self

Because this pathway is activated in the absence of antibody, it is part of the innate immune .defenses

bacterial mannose residues bind to a circulating complex of mannose-binding lectin (MBL structurally homologous to that of C1q in the classical pathway) and two associated proteases, known as mannose associated serine protease 7 (MASP-I) and 2 (MASP-2 Binding activates MASP-1 to sequentially cleave the classical complement pathway components C4 and C2 to form C4b2a, the classical pathway C3 convertase, on the surface of the bacterium. MASP-2 appears to be able to cleave C3 directly. Thus the lectin pathway converges with the classical .pathway at the activation of C3

The Alternative Pathway

The alternative pathway of complement activation is triggered by almost any foreign substance. The most widely studied include lipopolysaccharide (LPS; also referred to as endotoxin, from the cell walls of gram-negative bacteria the cell walls of some yeasts, and a protein present in .cobra venom, known as cobra venom factor

Some agents that activate the classical pathway-viruses, aggregated immunoglobulins and .necrotic cells-also trigger the alternative pathway

Activation of the alternative pathway occurs in the absence of specific antibody. Thus the .alternative pathway of complement activation is an effector arm of the innate immune defenses

C3b is generated in the circulation in small amounts by the spontaneous cleavage of a reactive thiol group in C3 This "preformed" C3b can bind to hydroxyl groups of proteins

The deposition of C3b on the cell surface initiates the alternative pathway , C3b deposition can .occur on either foreign or host cells, so in a sense the alternative pathway is always occur

host cells regulate the progression of the alternative pathway, whereas foreign cells lack these regulators and cannot prevent the development of the subsequent steps in the alternative pathway

IMMUNOGENS AND ANTIGENS

Immune responses arise as a result of exposure to foreign stimuli. The compound that evokes the .response is referred to either as antigen or as immunogen

An antigen is any agent capable of binding specifically to components of the immune response, such as the B cell receptor (BCR) on B lymphocytes and soluble antibodies. By contrast, an immunogen is any agent capable of inducing an immune response and is therefore .inmmunogenic

The distinction between the terms is necessary because there are many compounds that are incapable of inducing an immune response, yet they are capable to binding with components of the immune system that have been induce specifically against them. Thus all immunogens are .antigens, but not all antigens are immunogens

REQUIREMENTS FOR IMMUNOGENICITY

A substance must possess the following characteristics to be immunogenic

(١)foreignness; (2) high molecular weight

(٣) chemical complexity (4) degradability،

and (5)interaction with host major histocompatibility, complex

.(MHC)

Foreignness

Animals normally do not respond immunologically to self Thus, for example, if a rabbit is injected with its own serum albumin, it will not mount an immune response; it recognizes the albumin as self. By contrast, if rabbit serum albumin is injected into a guinea pig, the guinea pig recognizes the rabbit serum albumin as foreign and mounts its immune response against it. To prove that the rabbit, which did not respond to its own serum albumin, is immunologically 'competent

it can be injected with guinea pig albumin' The competent rabbit will mount an immune response to guinea pig serum albumin. because it recognizes the substance as foreign' Thus the first requirement for a compound to be immunogenic is foreignness. The more foreign substance, the more immunogenic

In general, compounds that are part of self are not immunogenic

to the individual. However, there are exceptional cases in which an individual mounts an .immune response against his or her own tissues. This condition is termed autoimmunity

High Molecular Weight

The second requirement for being immunogenic is that the compound must have a certain minimal molecular weight. In general, small compounds with a molecular weight < 1000 Da

:e.g., penicillin, progesterone, aspirin) are not immunogenic

those of molecular weight between 1000 and 6000 Da e.g insulin, adrenocorticotropic hormone may or may not be immunogenic; and those of molecular weight >6000Da e.g albumin, tetanus toxin are generally immunogenic

.So small substances have decreased immunogenicity.

.whereas large substances have increased immunogenicity

Chemical Complexity

The third characteristic necessary for a compound to be immunogenic is a certain degree of physicochemical complexity. Thus, for example, simple molecules such as homopolymers of amino acids (e.g., a polymer of lysine with a molecular weight of 30,000 Da) are seldom good immunogens

Similarly, a homopolymer of poly-y-o-glutamic acid

the capsular material of Bacillus anthracis) with a molecular weight of 50,000 Da is not .immunogenic

The absence of immunogenicity is because these compounds, although of high molecular weight, .are not sufficiently chemically complex

However, if the complexity is increased by attaching various moieties-such as dinitrophenol or -other low molecular weight compounds

In general, an increase in the chemical complexity of a compound is accompanied by an increase in its immunogenicity. Thus copolymers of several amino acids, such as polyglutamic, alanine, and lysine tend to be highly immunogenic

Degradability

For antigens that activate T cells to stimulate immune responses interactions with MHC .molecules expressed on antigen-presenting cells (APCs) must occur

APCs must first degrade the antigen through a process known as antigen processing (enzymatic degradation of antigen) before they can express antigenic epitopes (small fragments of the .inmmunogen) on their surface

.these epitopes stimulate the activation and clonal expansion of antigen-specific effector T cells

:A protein antigen's susceptibility to enzymatic degradation largely depends on two properties

l) It has to be sufficiently stable so that it can reach the site of interaction with B cells or T cells) necessary for the immune response and

II)the substance must be susceptible to partial enzymatic degradation that takes place during) .antigen processing by APCs

Peptides composed of D-amino acids, which are resistant to enzymatic degradation. are not .immunogenic, whereas their r--isomers ale susceptible to enzymes and are immunogenic

By contrast, carbohydrates are not processed or presented and are thus unable to activate T cells, although they can activate B cells

In general, a substance must have all four of these characteristics to be immunogenic; it must be foreign to the individual in whom it is administered, have a relatively high molecular weight, . .possess a certain degree of chemical complexity and be degradable

Haptens

As noted earlier, substances called haptens fail to induce immune responses in their native form .because of their low molecular weight and their chemical simplicity

These compounds are not immunogenic, unless they are conjugated to

.high molecular weight, physiochemical complex carriers

Thus an immune response can be evoked to thousands of chemical compounds-those of high molecular weight and those of low molecular weight, provided the latter is conjugated to high .molecular weight complex carriers