Review Article

A Concise Review of Immune System and Natural Immune Modulators

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ABSTRACT

Immunity is defined as resistance offered by the host against microbes and other foreign substances that prevent them from illness caused by these offending agents. The immune system is responsible for the identification and elimination of pathogens that invade the body before sickness and prevent the damage caused by them. Immunity to a particular disease is obtained by the presence of specific antibodies against that disease. Antibodies are proteins that the body produces to neutralize or kill pathogens or species carrying diseases. Antibodies are unique to diseases. A healthy immune system is highly essential and to strengthen the immunity, several dietary and lifestyle changes can reinforce the natural defences of the body and help fight injurious pathogens or organisms that cause sickness. Being a vast topic, full details of all mechanisms of the immune responses and immune therapies are beyond the scope of this article. This article aimed to provide the basic information and mechanisms involved in functioning of the immune system and its importance in health and disease. This review article highlights on basics of immunity and substances that can act as natural immunity boosters.

Keywords: Immunity, Antibodies, Immunoboosters, Natural immunity enhancers.

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INTRODUCTION

The word immunity is derived from the Latin word "immunitas" whose literal meaning is freedom from disease.[1] Immunity is defined as resistance offered by the host against microbes and other foreign substances which can potentially cause harm to the host. Two kinds of immunity exist: innate and adaptive. The immune system that has been active since birth is innate immunity. It works as first line of our body's defences against pathogens and other foreign substances. It requires physical obstacles, such as mucous membranes and skin, and some special proteins and cells that can identify and destroy them.[2] Adaptive immunity is defence gained by the body in the lifetime. This type of immunity is long lived as it bears immunological memory and in case of re infection body induces rapid immune response and forms antibodies to clear the antigen. Two types of adaptive immunity exist: active and passive. In active immunity, antibodies are formed by an individual's immune system when the body is exposed to an antigen via a disease or after immunization.[3] But in passive immunity, pre formed antibodies are given to a person for the prevention of disease or to treat the disease after the body is exposed to an antigen. Passive immunity can be natural as mother-to-child transmission of antibodies via placenta prior to birth and through breast milk after birth.[4]The passive immunization can also be given therapeutically by antibody-containing blood products, such as immunoglobulin. This form of immunity works rapidly, but only lasts for a few time periods. Although innate and adaptive immunity are not exclusive mechanism of the host defence rather they complement each other's functions.[5-7] The aim of the article is to provide the basic information and mechanisms involved functioning of the immune system with its importance in health and disease.

Innate immunity and its components

Innate immunity is the resistance to infection that an individual possesses since birth. It is the first line of defence mounted by the body against any pathogen or foreign substance. The unique feature of this type of immunity is that it does not require prior exposure to the antigen for action and the immune response is prompt which occurs within few minutes after exposure to the antigen, however this type of immunity is non-specific with limited diversity and the immune response do not possess any immunological memory. Therefore, on subsequent exposure to the same antigen the immune response will be same unlike adaptive immunity where re exposure of the

same antigen will result in rapid and more intense secondary response.[8]

Following the exposure to a pathogen, several cells that confer innate immunity are recruited via a chain reaction of various cytokines to the site of infection. The microbe must possess conserved site with repeat patterns which are commonly present on the surface of most microbes these are known as microbe associated molecular pattern (MAMP). Peptidoglycan, lipopolysaccharide and teichoic acid present in the bacterial cell wall are common example of MAMP.[9] While on the host cell there are unique receptor molecules known as pattern recognition receptor (PRR) which recognize microbe associated molecular pattern (MAMP's). Following the interaction between microbe associated molecular pattern (MAMP) and pattern recognition receptor (PRR) signals are generated which activate transcription of genes encoding for various cytokines and enzymes that helps in destruction of the pathogen. Toll like Receptor (TLR) are classical example of pattern recognition receptor (PRR).[10]

Components of innate immunity includes- anatomical barrier like skin and mucosa, physiological barrier like body temperature and low pH, phagocytes like neutrophils, monocytes and macrophages, natural killer cell, Normal resident flora of the body, complement pathway (alternate and mannose binding pathway), acute phase reactant. Cytokines like IL-1, IL-6, IL-8, IL-12, IL- 16, IL-18, INF-α, INF-β, INF-γ and TGF-β. Other cells included in innate immunity are dendritic cell, mast cell and some rare classes of lymphocytes like γ δ T cells, N-K T cells, B-1 cells, and marginal zone B cells are also included in innate immunity.[10]

Immune cells like neutrophils, monocytes and macrophages, in addition to phagocytic action also possess granules and enzymes which help in elimination of the pathogen. Among the phagocytes neutrophils are short lived while macrophages have long life span and act as antigen presenting cell (APC) to T cells thus act as a bridge between innate and acquired immunity. While natural killer cells play major role in destruction of cells infected with virus or tumour cells by release of perforins and granzymes and by inducing apoptosis.[11]

The main function of innate immunity is directing the immune cells to the site of infection and inflammation by the help of cytokines produced due to interaction of microbe associated molecular pattern (MAMP) and pattern recognition receptor (PRR).[9] Cytokines like IL-1, IL-6, Il-8, IL-12, IL- 16, IL-18, INF-α, INF-β, INF-γ and TGF-β activate local cellular response to infection and complement cascade which results in opsonization and increase susceptibility of the pathogen for phagocytosis which subsequently result in clearance of the pathogen.[12]

Acquired/ Adoptive immunity and its components

It is the resistance to infection that an individual acquires during the lifetime. This type of immunity is specific and more diverse as it develops against antigen specific for each microbe. It develops after antigenic exposure and immune response may occur in days. The hallmark feature of this type of immunity tends to be immunological memory. Therefore, later on, exposure to the same antigen in the host will result in more rapid and intense immunological response. T and B cells play pivotal role in adoptive immunity. Host cells possess specific T-cell receptor (TCR) and B-Cell immunoglobulin receptor.[5]

Active immunity is produced actively by the host immune system in response to infection (natural) or vaccination (artificial). It is long lasting as it bears immunological memory. Booster doses are useful as secondary antibody response is more intense and long lasting. It is not useful in immunodeficient persons while in passive immunity, immunoglobulins are received passively either from mother to the foetus (natural) or in the form of readymade immunoglobulins (artificial). Action is short lived as there is no immunological memory therefore booster doses are less effective. It is useful in immunodeficient persons.[6, 7]

Component of adoptive immunity are T and B cells, classical complement pathway, antigen presenting cell (APC), cytokines like IL-2, IL-4, IL-5, INF-γ. Adoptive immunity can be active or passive or artificial or natural.

T-cells of the adoptive immunity are derived from hematopoietic stem cells located in the bone marrow but later they migrate and mature in the thymus. The B-cells are also derived in the hematopoietic stem cells of bone marrow where they mature and later released in the circulation.[13] The T- cells bear unique receptors known as T cell receptor (TCR), which has ability to proliferate and differentiate when appropriate signals are received. T cell requires action of antigen presenting cell to recognize an antigen. Therefore, TCR interact with a group of proteins known as major histocompatibility complex (MHC) present on the surface of the antigen presenting cell (APC).[14] These MHC are also called as human leukocyte antigen (HLA). They are classified as MHC-I which are found on all nucleated cells and MHC-II is seen on macrophages, dendritic cells and B-cells. For induction of appropriate immune response antigen has to be presented by an APC to the TCR. MHC-I presents endogenous/intracellular peptides to the TCR, while MHC-II presents exogenous peptides derived from an extracellular antigen. The interaction of MHC molecule of APC to the TCR activates the T-cell which secretes cytokines and control the immune response.[14] The activated T-cell differentiates into cytotoxic T cells (CD8+) or T-helper cells (CD4+). CD8+ cytotoxic T cells are mainly involved in destruction of tumour cells and virus infected cell. While CD4+ T cells secrete various cytokines to activate B cells, cytotoxic T cells and other immune cells.[15]

There are several types of T helper cells (Th) responses that can be induced by an antigen presenting cell. Among all Th-1, Th-2 and Th-17 are the most important. Th-1 induces the production of interferon gamma which activates macrophages and also enhances anti-viral activity.[16] The Th-2 induces release of cytokines like IL-4 and IL-5 which

are responsible for production of IgE antibody from B cells while Th-17 is found to be associated with inflammatory response in chronic infections. Apart from all the above foresaid T cells, there is one unique subset of CD4+ T cells known as the T regulatory cells while control and prevent the immune system from destruction of self-antigens and thus prevent auto immunity.[17]

In contrast to T cells which recognize antigen with the help of antigen presenting cell, B cells possess antibodies present on their surface, antigens directly interact with these surface antibodies. Once activated, the B cells differentiate into short lived plasma cells which later produce antibodies. These cells undergo apoptosis once the stimulus is removed while memory B cells are long lived. On subsequent exposure these cells promptly produce antibodies and remove the antigen.[18]

T cells play a major role in cell mediated immunity which does not involve antibodies. In cell mediated immunity (CMI), on interaction with the antigen with the help of APC, the T cells are activated; these differentiate in to either cytotoxic T cell which induces cell apoptosis or T helper cells which secrete various cytokines to activate B cells, cytotoxic T cells and other cells which mediate effective immune response.[15]

Antibody mediated immunity on the other hand is mediated by B cells. The receptors present on the B cells directly bind to the antigen and transform in to activated B cells which differentiate into plasma cells which produces antibodies or memory B cells. B cells produce five different antibodies Activated B cells promotes phagocytosis by neutralization, opsonization, activation of complement cascade.[10, 11]

Hypersensitivity reaction

These reactions are undesirable injurious responses that are produced by the normal immune system in a sensitized individual following subsequent contact with specific antigen. There are four types of hypersensitivity reaction.[19] Type-I hypersensitivity reaction or immediate type of hypersensitivity reaction is mediated by IgE antibodies. Examples of type-I hypersensitivity reaction are asthma, anaphylaxis, and atopic dermatitis. Type-II hypersensitivity reaction/cytotoxic/antibody dependent hypersensitivity reaction is mediated by IgG antibodies. Most common examples of Type II hypersensitivity reaction are transfusion reaction, Rh incompatibility and hemolytic anaemia. Type III hypersensitivity reaction is also known as immune complex disease. Most common examples of Type III hypersensitivity reaction are localized- Arthus reaction and generalized- Serum sickness. Type IV hypersensitivity reaction is also known as delayed type of hypersensitivity. It is only type of hypersensitivity reaction which is T cell dependent. Most common examples of Type IV hypersensitivity reaction are granuloma formation in tuberculosis and leprosy. This type of reaction can also be manifested in Lepromin test, Tuberculin test.[20, 21]

Autoimmunity

It is a condition in which body's own immunologically competent cells act against self-antigen resulting in either structural or functional damage. Auto immunity can be cell or organ specific as seen in various auto immune anaemia, Idiopathic thrombocytopenic purpura, Good Pasture Syndrome, Grave's disease, myasthenia gravis etc. Auto immunity can also involve several organs and may result in systemic manifestation as seen in Systemic Lupus erythematosus (SLE), Rheumatoid arthritis, and Multiple sclerosis etc.[22]

Immunodeficiency

It is a condition where the defence mechanism of body is compromised which results in increased susceptibility to infections or even cancer. Immunodeficiency may be result of primary genetic defect or secondary immunodeficiency which occurs secondary to some disease, malnutrition or aging. Primary immunodeficiency may occur either due to defect or deficiency of specific immunity like humoral or cellular or both (like B cells, T cells or both) or due to defect in protective mechanism like phagocytosis or complement cascade.[23, 24]

Maintaining a healthy and competent immune system is very crucial in order to maintain a healthy body. A strong and effective immune system can be achieved by various ways and one of the effective options is natural immune boosting products. These are certain substances that provide immunity in natural ways these are also known as immunoboosters.

The table 1 tries to summarize the possible various natural immunity boosters.

Table 1: Natural immunity booster

S NO.	AGENT	PROCESS	Remarks	Reference
1.	Adequate and proper sleep	Getting enough rest will improve your natural immunity. You can also sleep extra while you're sick to allow your immune system to combat the sickness better.[25]	Insufficient sleep and improper rest may raise the risk of becoming ill. Most of the adults must sleep approximately seven hours a night.	25
2	Whole plant food product	Whole plant foods are rich in nutrients and antioxidants. These are fruits, vegetables, nuts, seeds, and legumes, which can give you an advantage against harmful pathogens. By opposing reactive compounds called free radicals,	There are antioxidants, fiber, and vitamin C in some whole plant foods, which can reduce your susceptibility to disease.	26

		antioxidants in these foods help minimize inflammation.[26]		
3	Healthy oils and omega 3 fatty acids	Beneficial fatty acids, found in salmon and olive oil can boost the immune response against the pathogens by diminishing inflammation. Though inflammation even in minimal level is a cardinal response to any stress or injury, chronic inflammation can further worsen the immune response.[27]	Omega 3 containing oils like Olive oil have anti-inflammatory properties. Chronic inflammation is well known to weaken immune system; hence these fatty acids might prove helpful in naturally combating illnesses.	27
4	Fermented food products or probiotic supplement	Fermented food products have valuable bacteria which are known as probiotics that colonize the intestinal tract.[28] The food products that contain probiotics include kimchi, yogurt, sauerkraut, kefir, and natto. Evidence reveals that a good and healthy quantity of favorable gut bacteria might help our immune cells distinguish between innate normal cells from intruder microbes.[29]	Gastrointestinal tract normal health and immune milieu are very profoundly interrelated. Foods prepared by fermentation and probiotics might be helpful in reinforcing the immune system by identifying the offending pathogens.	28,29
5	Limited extra sugar	Evolving evidence reveals that overweight and obesity are closely related to increased consumption of added sugars and refined carbohydrates.[30,31] Minimizing the intake of sugar can help in minimizing the inflammatory process hence aiding weight loss and curbing the risk of type 2 diabetes mellitus, heart disease and other chronic health disorders.[32,33]	Decreased sugar intake may reduce associated inflammation and further reducing risk of various chronic diseases.	30-33
6	Mild to moderate exercises	Even though sustained exercise in intensive form can suppress the immune response, however, moderate exercise can be beneficial in improving it. Evidence suggests that moderate exercise sessions can enhance the vaccine efficacy in people with weak immune systems.[34] Regular sessions of moderate exercise might be helpful in minimizing the inflammation and assist in regeneration of immune cells regularly.[34]	Moderate exercise like Jogging, brisk walking, swimming and running can prove helpful in reducing inflammation and boosting immunity.	34
7	Water hydrated body	Adequate hydration is crucial in maintain a healthy system even though it might not necessarily protect us from microbes. Dehydration might cause headache, loss of focus, altered mood, improper digestion and can also hamper the physical performance which can further enhance the susceptibility to diseases.[35]	Dehydration can make the body more susceptible to sickness. Adequate hydration can be maintained by drinking enough fluid daily.	35
8	Stress management	The process of relieving anxiety and stress is a crucial in maintaining immune health. Chronic stress enhances inflammation and disrupt the functioning of immune cells.[27, 36]	Minimizing the stress levels through various activities like meditation, yoga, exercise, jogging, music and other practices can help maintain a sound immune system.	27, 36
9	A well balanced diet	A healthy fulfilled balanced diet can support keep us healthy. Eating multicolored fruits and vegetables on daily basis can help us in getting a variety of nutrients. Lean proteins and complex carbohydrates which are present in brown rice and quinoa, etc. are also a part of healthy diet.[37]	Eat healthy food and minimize processed foods, sugar and beverages that are deficient in nutrients, like carbonated drinks.	37
10	Quit smoking and consume limited alcohol	Smoking and excessive drinking weaken your immune system.[38]	Smoking is injurious to health.	38

CONCLUSION

Immunity plays integral part in an individual's health. The innate and acquired immunity do not work independently, rather they work in collaborative manner. Although innate immunity is the body's first line of defence but there are certain immune components that bridge both type of immunity and work in highly interactive manner and bring about highly efficacious and more effective combined response that help in fighting various pathogens. Defects or imbalances in either system may result in immunopathological disorders like hypersensitivity reactions, autoimmune diseases or immunodeficiency disorder. This article briefly overviews basics of immunity and mechanisms involved functioning of the immune system with its importance in health and disease.

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