ROLE OF IMMUNITY AND IMMUNOGLOBULINS IN DIFFERENT AILMENTS; A COMPREHENSIVE REVIEW

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ABSTRACT: Immunity is the capacity of the body to resist invading organisms. Immunity works by immunoglobulins and white blood cells. Healthy subjects protect themselves by various ways such as physical barriers, phagocytosis mechanism of leukocytes, natural killer cells and various other blood molecules. The immune system provides protection against various organisms from invading pathogens in body. The body provides immunity by overcoming various strategies of infectious agents such as bacteria and virus etc. This is commentary on the basics of immunity and an introduction to the field. In present commentary, role of immunity and immunoglobulins in human ailment has been discussed. It was concluded that defective immunity may be the origin of various infections. Immunoglobulins i.e. IgG, IgA, IgM, IgE and IgD are involved actively in immunity. Immune system components originating in the bone marrow circulate in the blood.

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INTRODUCTION

Immunology deals with complex defense mechanism of the body & also with equally complex invading agent. Immunology is used in immunization program, in hypersensitivity & adverse reactions, inforecasting epidemics, in serological diagnosis & blood grouping and carrier detection. The toxins or pathogens that are harmful to tissues and body organs are resisted by our body and this capability is termed as immunity. Skin is an important component of immune system. Saliva has anti-bacterial activity. Polymorph nuclear leukocytes including neutrophils, eosinophils, and basophils are component of defense mechanism in the body. Spleen destroys foreign bodies and stimulates different types of immune system cells. Kumari et al has reported the immuno-modulatory effect of herbal extract of *Asparagus racemosus* willd [1]. Immunoglobulins are antibodies that protect the body against antigens. Immunoglobulins are of 5 types including IgG, IgA, IgM, IgE and IgD [2,3]. Innate immunity is modified by factors like species and strains, age, hormonal influence, and nutritional factors. Malnutrition is associated with increased susceptibility to bacterial infections due to decreased phagocytosis and leucopenia. Limitations of artificial immunization include faulty preparation, contamination, faulty technique, and hypersensitivity reaction and carrier state. It has been observed that breastfed children have high level of immunoglobulins as compared to formula fed children [4]. Immune responses are stimulated by white blood cells [5]. WBC arises from a pluripotent hematopoietic stem cell. Granulocytes circulate in the blood. Macrophages phagocytose bacteria and kill

them [6]. There are two types of lymphocytes i.e. B and T lymphocytes whichmature in bone marrow and in the thymus, respectively [7]. There are 3 primary types of T lymphocytes including helper, regulatory and cytotoxic cells [8]. Constituents of immune system are thymus, lymphatic system, spleen, white blood cells, antibodies, hormones, bone marrow and complement system [9]. Immunity may be artificial or natural and either active or passive. Active natural immunity (contact with infection): produces slowly but it is longterm and antigen specific. Active artificial immunity (immunization): also develops slowly and lasts for several years, it is particular to the antigen for which the immunization was given [10]. Passive natural immunity (transplacental mother to child): develops instantaneously is temporary, and it affects all the antigens to which the mother has immunity. Passive artificial immunity (injection of gamma globulin): impermanent and develops immediately and affects all donor immune antigens [11]. Generally immune system is self-tolerant and does not response the cells or proteins of self. But sometimes due to several causes, the immune system fails to differentiate between self and non-self. Due to this reason the cells or tissues of the body are attacked. This phenomenon is called autoimmunity and the diseases associated to these are referred as autoimmune diseases [12-14]. It has been observed that side effect of rifabutin is leucopenia. Rifabutin is usually prescribed for treatment of atypical mycobacterial infections. Immunity fights against all kinds of microorganisms that damage body tissue and organs. Skin is an important organ in immune system [15]. Thymus is involved in immune system [16]. Saliva has anti-bacterial activity [17]. Spleen destroys foreign bodies and stimulates different types of immune system cells [18]. T Cells are of two types. CD4 is involved in stimulating other immune system components while CD8 directly kill the foreign bodies [19]. Cells that are involved in immune system include monocytes, leukocytes, lymphocyte, B and T cells, helper T-cells, killer suppressor T- cells, Granulocytes, plasma cells, natural killer cells, eosinophils, basophils, neutrophils, macrophages and phagocytes. Anatomical barrier include skin, gastrointestinal tract, respiratory airwaysand lungs [20], nasopharynx and eyes. When an infectious agent can cross the anatomic defenses then acute inflammation starts. The humoral factors (complement system and interleukin-1) are important in the inflammation associated with arthritis [21]. Cellular barriers include neutrophils, macrophages, dendritic cells, natural Killer (NK) and NKT cells. Immune system disorders [22] include immunodeficiency and autoimmunity. Autoimmune disorder occurs due to irregular function of immune system by attacking and destroying healthy body tissue. There exists more than 80 different types of autoimmune disorders [23]. Some types of autoimmune diseases are autoimmune hepatitis, alopecia areata, diabetes type 1, celiac disease, guillain- Barre syndrome, grave`s disease, hemolytic anemia, hashimoto's disease, idiopathic thrombocytopenic purpura, crohn's disease,ulcerative colitis, inflammatory boweldisease (IBD), myasthenia gravis, inflammatory sympathies, rheumatoid arthritis, multiple sclerosis, primary biliary cirrhosis, psoriasis, scleroderma. , sjogren's syndrome, systemic lupus erythematosus and vitiligo [24]. It is widely accepted that autoimmunity generally occurs as a consequence of body s response against bacterial, viral or any foreign antigen. Few epitopes of foreign antigens and host proteins are similar (homologous) [25]. Due to this cross reaction of antigens and

antibodies occur causing autoimmune diseases.

Vaccination and Immunization

Vaccines contain living, attenuated or killed organism and are used as inoculation to stimulate the production of antibodies. Primary active immunity from vaccination develops more slowly than the incubation period of most infection and must be induced prior to exposure to the infection agent; therefore, the general action of vaccines should be considered prophylactic. Nonliving vaccines provide protection for only a limited time, and repeated vaccinationis required to maintain protection against typhoid fever, cholera, plague, and typhus. Allergic reaction may result either from the organism constituting the vaccines or from a protein incorporated into the vaccine during manufacture (vaccination schedule in children has been shown in Fig. 1). A vast majority of the 11 million deaths every year in children under five years are causedby infections and over two third of thesetake place in developing countries. Many of these can be prevented by vaccines. The expanded program on immunization initiated by the world health organization in 1974 has improved coverage for BCG, DPT, polio and measles to about 80% of children in developing countries. Immunization in childhood is carried out to prevent specific infections. For this purpose, vaccines (antigens) are given at an age when the infant is capable of producing antibodies (Table 1). There are various types of vaccines.

1. Bacterial vaccines
2. Viral vaccines
3. Conjugate vaccines
4. DNA/RNA/Nucleic acid vaccines

Innate Immunity

It is a natural, inborn and nonspecific immunity considered as first line of defense without antigenic specificity. This is the natural resistance of the body to various bacteria, toxins and other foreign agents without any specific immune process. This immunity is present in both vertebrates and invertebrates. Impairment of innate immunity results in appearance of severe infections [26-28]

Factors for Modification of Innate Immunity Species and Strains

The man and guinea pig are highly susceptible to diphtheria while rats are resistant. Infectious diseases are often more severe in early childhood and old age. Patients having diabetes mellitus, hypothyroidism and adrenal dysfunction are more prone to infectious diseases. Malnutrition is associated with increased susceptibility to bacterial infections due to decreased phagocytosis and leukopenia[29].

Acquired Immunity

The ability of human body to develop extremely powerful specific immunity against invading agentries called theacquired immunity. Two kinds of cells (B- lymphocytes and T-lymphocytes) generates specific immune responses by two specific cell populations having clonally distributed receptors. B-lymphocytes synthesize and secrete immunoglobulins (antibody) of the same specificity and T lymphocytes express a surface antigen receptor with clonal specificity [30].

Humoral (Antibody-mediated) Immunity The type of immunity in which body develops circulating antibodies from B-lymphocytes that are capable of attacking the invading agents is called humoral immunity. Humoral immunity is effective against extracellular bacteria while its role against intracellular[31].

Passive Immunization

Immunoglobulin is given for prevention whena patient has been exposed to an infectious disease. This provides temporary protectionimmediately [32].

Functions of Immunoglobulins

IgG is mostly responsible for humoral immunity. IgA protects the body surfaces. IgM serves as first line of defense. IgD may function as B-cell receptor. The IgE molecule bind with mast cells which release histamineand cause allergy [33].

Immunoglobulin IgM

Increase level of IgM is found in actinomycosis, rheumatoid arthritis, carrión's disease, malaria, Walden storm's macroglobulinemia, trypanosomiasis,infectious mononucleosis and lupus erythematosus. Decrease level of IgM is found in gammaglobulinemia, IgG and IgA myeloma, chronic lymphoblastic leukemia, lymphoproliferative disorders and lymphoid aplasia [34].

Limitations of Artificial Immunization

Faulty preparation, contamination, faulty technique, hypersensitivity reaction andcarrier state [35].

Immunoglobulin IgA

It is synthesized by plasma cells. It is found in mucus membranes of the gastrointestinal tract, respiratory tract, urinary tract and excretory organs. It is also found in secretions such as sweats, nasal fluids and tears. IgA protects against invasion by bacteria. IgA is found in colostrum that provides immunity to the new born [36].

Research Study

The ingenuity of Infection Receptive Serum Immunoglobulin M Counter Acting Agent in Affirmed West Nile Infection Encephalitis Cases

In a study, 60% of patients were having anti-WNV Ig Malong with bleeding afterapproximately 500 days of onset. It was also suggested that physicians should be carefulwhile detecting serologic results from WNV IgM-positive patients in the early season [37].

Anti-inflammatory Action of IVIG (Mediated through the Inhibitory FC Receptor)

It was observed in a study that autoantibody-mediated thrombocytopenia was inhibited by IVIG through inducing inhibitory FcRIIB receptors on macrophages. The main factor in the regulation of macrophage phagocytosis is balance between inhibitory (FcRIIB) and activating (FcRIII) Fc receptors. So, it was concluded that various new medicines that inhibit macrophage phagocytosis could be used to treat autoantibody-triggered inflammatory diseases [38].

Anti-inflammatory Action of IgG: Intravenous IgG Paradox

In a study, it was noticed that limited concentration of sialic acid–bearing IgGglycoform can be cause of IVIG activity that offers the rationale for the preparation of sialic acid–enriched IVIG product that would confer greater anti-inflammatory activity at dose rates of 1/10 to 1/100 required currently. It also suggests that a fully recombinant IVIG composed of hyper sialylated IgG would be an effective anti-inflammatory agent for therapeutic use in autoimmune diseases. The identity of the macrophage receptor involved in the characterization of the inhibitory pathways induced by diallylated IgG and binding of diallylated IgGwill give insights into the normal biological functions of sialylated IgG in vivo and the homeostatic pathways that regulate IgG effector activity [39].

Intravenous Immunoglobulin Ameliorates itp via Activating Fc Gamma Receptors on Dendritic Cells

Monoclonal CD44 antibodies (total 8) were tested in murine ITP. It was found that 4 antibodies could successfully ameliorate ITP; out of it, two antibodies function at a full 3-log fold lower dosage compared with IVIg. Further studies of two more antibodies (5035–41.1D and KM114) revealed that, similar to IVIg: (1) for their ameliorative function of these the presence of the inhibitory IgG receptor FcγRIIB was prerequisite (2) mice that were complement-deficient responded to anti- CD44 treatment,

and (3) mice that were human transgenic FcγRIIA-expressing also responded to the CD44 therapeutic modality. The Fc portion of the CD44 antibody was not required IVIg. This information revealed that CD44 antibodies can function therapeutically in murine ITP and could potentially provide a very low-dose recombinant therapy for the amelioration of human ITP.

Mechanisms of Action of Intravenous Immunoglobulin in Autoimmune and Inflammatory Diseases

The symptoms of the rare disease Nemaline rod myopathy are muscle weakness andpresence of rod-shaped structures in musclefibers. During adulthood, numerous acquiredconditions were found associated with slow-progressing presentation. In adults, HIV infection has been detected in many cases. In a study, two patients with HIV-related nemaline rod myopathy responded successfully to IVIG therapy [40].

CONCLUSION

Immunology deals with the study of immunityand the immune system of vertebrates. Immunity involves the resistance shown, and protection offered by the host against the infectious organism. Immunoglobulins, a specific group of plasma globular proteins, are actively involved in immunity. IgG and IgM are primarily concerned with humoral immunity while IgE is associated with allergic reactions. Components of the immune system originate in the bone marrow and circulate in the blood. Defects in the immune system result in various ailments. Skin is the most important component of the immune system. White blood cells (WBCs) including monocytes, leukocytes, lymphocytes, granulocytes, B- cells and T-cells, suppressor T-cells, helper killer T-cells, natural killer cells, plasma cells, basophils, neutrophils, eosinophils, phagocytes, and macrophages are also important components of the immune system.

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Table 1: Vaccination schedule for children