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Immunity in Medically Important Parasitic Infections

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Review Article

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Abstract

Immunity is the rule. It is often incomplete and takes many years to develop and fade away quickly. Human life is a battlefield in which we are like soldiers attacked from all sides by bacteria, viruses, fungi and parasites. Our body is bestowed with a defense mechanism in the form of an immune system It has long been recognized that infections with parasites, such as intestinal worms, are often accompanied by blood eosinophilia, and this is due to an immunological process. Conditions in which blood eosinophilia is common include intestinal infections with *Ancylostoma duodenale*, *Ascaris lumbricoides*, *Trichuristrichiura*, various forms of *Wuchereria bancroft*, *Brugiamalayi*, *loaloa*, *Dracunculus medinensis*, mite infection of the lungs (including at least some cases of tropical eosinophilia);and hydrated disease is due to *Echinococcus granulosus*. Eosinophilia, in large numbers invades tissues in which antigen-antibody reaction has taken place. They appear to be attracted by some product of the antigen-antibody reaction and it has been shown that if tissues from sensitized guinea -pigs mixed with antigen in vitro, or tissues from guinea-pigs which have died from anaphylaxis, are transferred to the peritoneal cavity of normal guinea-pigs, the recipient develops very marked eosinophilia within 24 hours. The active agent has not been infected, but it is probably not histamine. The eosinophils of rodents are very actively phagocytic, and ingest cellular debris, mast cell granules, etc, but it is not certain whether this is true of eosinophils from other species, nor it is known what functions the eosinophils serve in these reactions. A multitude of defensive mechanisms are involved in parasitic infection. A humoral response develops when parasites invade blood stream (Malaria, Trypanosoma), whereas cell-mediated immunity is elicited by parasites that grow within the tissues (Eg: *Cutaneous leishmaniasis*). In protozoal infections, IgG, and IgM are produced. In Addition, IgA also produced in intestinal infection. With helminthic infections, IgG, IgM and IgE antibodies are produced.

Keywords: Anti-Inflammatory Cytokines; Phagocytes; Dendritic Cells and T Cells; CD4; CD8; Humoral Immunity; B Cells; Memory Cells; Tropical Eosinophilia; Immune Response; Immunoglobulin's; Macrophages; Prostaglandins; Leukotrienes; Thromboxane; Igg; Igm; Ige

Introduction

Extensive research shows that parasitic worms have the ability to deactivate certain immune system cells, leading to a gentler immune response [1]. During the erythrocyte stage of malaria infection, IFNγ production from CD4+ Th1-cells and CD4+ T-cell help for the B-cell response are each required for effective control and elimination of the parasitaemia [2]. Helminth infections can promote the secretion of IL-10 by regulatory T –cells [3,4]. A study of Senegal children similarly showed that those with *S. haematobium* infection had lower burdens of *P. falciparum* [5]. It is possible that the reduced levels of regulatory T cells or a Th2-polarized cytokine milieu in *S. haematobium* infected children may provide protection against falciparum malaria by modulating systemic expression of Th1 cytokines [6]. These chronic infections are often associated with the development of systemic and mucosal CD4+ T helper cell type 2 (Th2) polarized immune responses. These are typically characterized by increased expression of cytokines such as interleukin-4, IL-13, eosinophilia, production of immunoglobulin E (IgE) [7].

Infections with helminth parasites often cause significant pathology, as they migrate through host tissues via the skin (e.g., schistosomes), or feed on the gut epithelium (e.g., Trichuris spp.) [8]. A study of 3-year-old children in the Quininde district of Ecuador has shown that helminth *Ascaris lumbricoides* had plasma cytokine profiles indicative of an increased Th2/Th1 cytokine bias, and significantly lower plasma levels of IL-2 and TNF-Alfa [9].

Studies from mouse models have shown that expression of TNF-Alfa is essential for resistance to G. lamblia infection [10]. Macrophages are innate immune cells present in every tissue and necessary for homeostasis. Macrophages sense and respond to pathogens and other environmental challenges and participate in tissue repair after injury [11]. The mega eaters bind the bacteria, engulf and digest intracellularly wit hydrolytic enzymes. During emergency, more macrophages and neutrophils are initiated in digestion [12].

History

Parasite association with the human body was known from antiquity. First parasite discovered in 18th century.1758- Linnaeus discovered many Helminths.1782- Isolation of tapeworm. 1817- Term “Protozoa” was used by a German –Gold- fuss 1836- Alfred Donne showed that flagellates responsible for vaginal discharge. 1880- Alphonso Laveran observed malarial parasites in blood. 1908-Paul Ehrlich explained theory of immunity 1908—Metchnikoff—phagocytosis 1913—Richet—Anaphylaxis 1919-Bordet—immunity 1960- Bordet—Immunological Robert Koch’s proofs, awarded a Nobel Prize in 1905, that microorganisms were confirmed as the cause of infectious disease Viruses were confirmed as human pathogens in 1901, with the discovery of the yellow fever virus by Walter Reed Immunology made a great advance towards the end of the 19th century, in the study of humoral immunity and cellular immunity [13-16].

In 1974, Jerne NK, et al. developed the immune network theory; he shared a Nobel Prize in 1984 with Georges JF Kohler and César Milstein for theories related to the immune system [17,18]. The immune system has the capability of self and non-self-recognition. An antigen is a substance that ignites the immune response [19]. Antibodies are specific proteins released from a certain class of immune cells known as B lymphocytes it’s now getting clear that the immune responses contribute to the development of many common disorders [20,21].

a. Innate Immunity

Non-specific, Limited diversity and no memory

b. Adaptive Immunity

Also called acquired immunity Mediated by either B cells (antibody) or T cells (cell-mediated immunity) Recognize antigenic molecules Antigens can be “foreign” or “self” Produce cytokines (messenger boys) Takes 7-10 days to mobilize on first encounter Mobilize much faster on second encounter (memory). They use antigen recognition molecules, antibodies on B cells (BCRs), T cell recognition (TCR) on T cells. Major histocompatibility antigens (MHC on antigen-presenting cells) Adaptive immunity can be active or passive The B or T cell encounters the antigen for which it is specific Reaction with the antigen causes cytokines to be produced Cytokines affect other cells AND the cell which produced the cytokine. The cell proliferates a clone of cells all with the same specificity as the original cell thus the response to the antigen is augmented [22-24].

c. Active Immunity

The immunity which results from exposure to an antigen Natural infection, Vaccination, Passive immunity Immune components from an exposed individual are transferred to and individual without immunity. Usually antibody occasionally cellular.

d. Macrophages

Macrophages are the large eaters. These are the long lived phagocytes. These cells move over alveolar surfaces, scavenger dust particles, microorganisms and other debris. The attachment of antigens to macrophage is specific. All the macrophages have specific receptors for C3 component of complement as well as Fc component of antibody. The C3 receptor promotes the adherence of antigen to macrophage by way of opsonization antigen by the complement whereas

the Fc receptors help in binding within the antibody there by promoting the phagocytosis of antigen antibody complex. When the antigen adheres with lymphocyte processing, receptors for the antigen, recognition takes place and thus the lymphocytes are induced to produce immunity [25-28].

The macrophages that present antigens to T-helper cells (Th) should have MHC determinant of class 11 on the surface whereas macrophage that present antigens to T-cytotoxic cells (Tc) cells should have the MHC determinant, it cannot cooperate and thus antigen presentation cannot occur, which is known as MHC restriction Macrophages are important secretory cells producing and secreting a number of substances such as components of complement system, hydrolytic enzymes, toxic forms of oxygen and the monokines. The monokines have regulatory effects on lymphocyte function. Each cell type expresses characteristic surface molecules (CD3, CD4, CD8.) These cells scavenging the dust particles, microorganisms and other debris. The primary function of macrophage is phagocytosis. The macrophages, by their property of amoeboid movement, put forth pseudopodia which help in engulfing any solid particle such as the invading microorganisms. The attachment of antigens to macrophage is specific. All the macrophages have surface receptors for C3 component of complement as well as for Fc component of antibody.

e. Neutrophils

Neutrophils only migrate into tissue if there is inflammation. Monocytes cruise normal tissue when macrophages encounter a signal (infection), they recruit neutrophils to the site! Example, mediate selectins and adhesins which cause neutrophils to stop and migrate into tissue the term 'left shift' indicates that the neutrophils present in the blood are at a slightly earlier stage of maturation than usual. Inflammatory signaling Mediators produced by macrophages and neutrophils are Prostaglandins.

Lipid derivatives of arachidonic acid they Inhibit platelet aggregation, increase vascular permeability, induce smooth muscle contraction Leukotrienes Lipid derivative of arachidonic acid slow reactive substance of anaphylaxis – SRS-A –But long-term inflammation (chronic) is controlled by macrophages –If not cleared, chronic inflammation turns into a granuloma .

f. Mast cells and Basophils Cells

These concentrated within the respiratory and gastrointestinal tract, and within the deep layers of skin. Influenced by TH2, and IL-13 and IL-4 Reside in submucosa, skin, connective tissue Numbers in tissue increase during worm infection IgE binds to Fc receptors on the surface of mast cells Binds to IgE Even though Ig is not bound to antigen Receptor is FceRI One mast cell has multiple specificities Cross-linking of IgE molecules à activation (Mast cells also activated by C3a, C5 and certain drugs, STAY TUNED) Activation à degranulation and synthesis of mediators Mast cell proteolytic enzymes = tryptase and chymotrypsin These enzymes Increase mucus production –Increase smooth muscle contraction .Cleave and activate complement components and kinin components à inflammation Histamine (à pruritus) .Smooth muscle contraction –Increased vascular permeability .Chemotactic for white cells Cytokines to promote and extend inflammation .TNF àlfa enhanced diapedesis à inflammation –IL-4 stimulates TH2 responses – IL-3 and IL-5 stimulates eosinophil production and activation Eosinophils These cells contain Blobbed Nucleus These are granulocytes. Phagocytic. Granules contain hydrolytic enzymes. Primary defense against helminth infections (MBP) Eosinophils contains Toxic substances in granules. Derived from same precursor as PMNs. Influenced by IL-3 and IL-5 (secreted by TH2 cells) Leukotriene are produced by mast cells. Provokes bronchospasm Cationic protein à damages worm plus damages worms nervous system (a neurotoxin)

g. Tropical Pulmonary Eosinophilia

It is by *Brugia malayi* and *Wuchereria bancroft* TPE is pervasive in endemic regions of the world. Patients suffer from fever, cough and massive eosinophilia. This is described as a pseudo-Tuberculosis condition. It is called Weingarten syndrome [29]. In TPE, microfilariae larvae antigens rapidly cleared from the bloodstream by large eater cells in some patients trapping of microfilariae and other reticuloendothelial organs can cause hepatomegaly, splenomegaly or lymphadenopathy.

h. Research on Inflammatory Response

The only thing certain is uncertainty. The change is life's one constant. Your ability to accept and tolerate the consistent uncertainty may be one of your most useful skills a person could cultivate.

Tissue injury such as that following the establishment and multiplication of microorganisms, call forth an inflammatory response. This begins with local arterioles and capillaries, from which plasma escapes. Edema fluid accumulates in the area of injury, and fibrin forms a network and occludes the lymphatic channels, tending to limit the spread of organisms. Polymorph nuclear leukocytes in the capillaries stick to the walls, and then migrate out of the capillaries towards the irritant.

This migration is stimulated by substances from the inflammatory exudate (chemotaxis). The phagocytes engulf the microorganisms and intracellular digestion begins. Soon the PH of the inflamed area becomes more acid, and the cellular proteases tend to induce lyses of the leukocytes. 15 Large mononuclear macrophages arrive on the site and,

in turn, engulf leukocyte debris as well as microorganisms and pave the way for resolution of the local inflammatory process.

Drugs that inhibit the synthesis of prostaglandins (by blocking the enzyme cyclooxygenase) act as inflammatory agents. Recent studies of human Plasmodium falciparum malaria emphasize due importance of the balance between pro and anti-inflammatory cytokines. In any event, pro-inflammatory cytokines such as INF gamma,IL-1,IL-6 and others may be protective by inducing parasite killing by monocytes/macrophages and other cells, contributes to protection against pre erythrocyte and blood infection by initiating a Th-1 anti-malaria response in mice as well as in monkeys. In contrast the anti-inflammatory cytokines such as IL-10 counteract the production and possible cytopathic effects of pulmonary cytokines. The cytokine which has central role for both protection and malaria pathogenesis is TNF-alfa. TNFalfa does not kill parasites directly but exerts protection by activating the anti-parasitic effects of the various leucocyte effector cells. With regards to pathogenesis, TNFalfa levels are positively correlated with disease severity as well as with malaria fever.

Major Advances in and Discoveries

a. Immunology in Plasmodium vivax

Tumor necrosis factor and functionally related proteins such as the interleukins are produced as a normal part of the host response to infection.

West African Blacks and their descendants in the Americans and elsewhere possess a relatively immunity to *Plasmodium vivax.*

b. Immunology in Leishmania Donovani

A direct relationship between elevated TNF levels and death from cerebral malaria has been found. Sera from patients with a variety of infections and neoplastic diseases contain elevated levels of TNF in two thirds of those with malaria and Kala Azar but in fewer than 8 of healthy subjects or persons with neoplastic disease.

c. Immunology in Trypanosome cruzi

Serum antibodies develop in *Trypanosomacruzi* infection but as the parasite continues to grow as amastigote form inside the RE cells and parenchyma cells they are not exposed to the action of these antibodies [30].

d. Immunology in Entamoeba Histolytica

Entamoeba. Histolytica trophozoites secrete potent chemokines, such as IL-8, resulting in immune cell recruitment [31]. Neutrophils activated by interferon-gamma (IFN-gamma) [32,33]. Depletion of neutrophils with anti-Gr-1 antibodies resulted in exacerbated intestinal disease in murine models; supporting the protective role of neutrophils in amebiasis [34]. Macrophages also play a crucial role in the host response against intestinal amebiasis [35,36]. Several amebic antigens are known to activate these cells via pattern recognition receptors. *Entamoeba. Histolytica,* triggering pro-inflammatory cytokine production via NF-kB activation Macrophages that lack TLR-2 and TLR-4 displayed impaired response *to Entamoeba. Histolytica* [37,38]. Additionally, *Entamoeba histolytica* DNA can activate macrophages through interacting with TLR-9 39 Amebicidal activity of macrophages is contributed to by the production of nitric oxide (NO) from L-arginine, which is mediated by macrophage nitric oxide synthase [39,40].

e. Immunology in *Ascaris Lumbricoides*

A partial immunity may be acquired by man, induced by the larvae and produce protective antibodies which lower the worm burden and play a part in the immune response. A severe allergic reaction occurs when the larvae reach the small intestine for the second time. Eosinophil count is increased at the time of tissue invasion. Specific antibodies can be demonstrated in *Ascaris lumbricoides* infection. Hyper sensitivity to Ascaris is demonstrated by skin test [41].

f. Immunity in Strongyloides Stercoralis

The immunity may be diminished in immunosuppressive states which reduce the resistance of the body, leading to an extensive tissue invasion by the adult worm. An infected individual when exposed to reinfection responds by tissue hypersensitivity with eosinophilia and giant urticarial rash. Serum antibody develops in strongyloidiasis and gives a cross reaction with filarial complement fixation test [42].

g. Immunology in *Wuchereria* Bancroft

Asymptomatic microfilaremic individuals generally have a marked Th1 hypo responsiveness but a strong Th2 response. This may suggest a protective effect of IgE, because the highest ratios of specific to total IgE are found in patients with tropical pulmonary eosinophilia [43].

h. Immunology in *Schistsoma Haematobium*

Mouse models have been used extensively to investigate the protective immune response to schistosome infection primarily with *S. mansoni* as the infecting species [44]. A single exposure to attenuated cercariae induces partial protection, primarily associated with production of IFN- γ Treatment of infected mice with praziquantel confers similar levels of resistance to reinfection [45,46].

- Immune Response
- Intestinal Amoeba
- Invasive amoebiasis

Transient secretary response, Production of serum

antibodies CMI---Chemokines, Cytokines by damaged epithelial cells, mediators like NO

i. Evasion

Degradation of IgG and secretory IgA Resistant complement analysis Change in surface antigen Lyse in immune response cell---Insertion of Amoeba Pores Production of IL-4,IL-10 and block IL-18 and inhibition of CMI

j. Intestinal Flagellates

Acquired immunity and genetically controlled Spontaneous clearance and resistant to reinfection Chronic infection in immunosuppressed Specific IgA --- In Acute Giardiasis A gammaglobulinemic--in chronic Giardiasis

k. Evasion: Antigenic variation Protecting them from interstitial proteases Acquired immunity genetically controlled Spontaneous clearance and resistant to reinfection Chronic infection in immunosuppressed Specific IgA in acute Giardiasis Hypogammaglobinemia in chronic Giardiasis Protozoa inhabiting.

Urogenital Tract

a. Trichomonas vaginalis

Secretary IgA-- vaginalis-Vaginal Secretion Antibodies diminish with time Reinfection frequent No acquired immunity Specific immune response insignificant

Evasion: Antigenic Variation Macrophage inhibiting protozoa Inhibit Macrophage at some stage in their life cycle *Leishmaniadonovani, Trypanosomacruzi, Toxoplasmagondii* They possess enzymes to counteract toxic molecules of phagosome Leishmania spp Infect macrophage of skin and viscera. Survive and multiply in resting macrophage Protective immune response--Classical Th-1 type CMI response Evasion---IL-4,IL-13, TGF-Beta-Inhibit macrophage activation.IL-10 Regulate macrophage activity The net result is--NO inhibition and Parasite Killing *Toxoplasma gondii* No mediated parasite killing

Evasion: TGF-Beta inhibits no production, Increases replication op parasite Il-6 and IL-10 promote parasitic proliferation *Toxoplasma gondii* activates transcription factors START-1 and NFKB but blocks to their translocation and macrophage can't produce IL-12 and TNF-alpha Blood inhabiting Protozoa *Trypanosomagambiense* Glycoprotein coat-Variant glycoprotein (VSG).

IgM class facilitates agglutination complement mediated lysis phagocytosis by macrophage and neutrophils

Evasion: Interferon Gamma growth factor for *Trypanosoma Brucei* and cytotoxic immune *Trypanosoma brucei* inhibits lymphocyte and lymphocyte activation.

Immunosuppressive: Macrophages, NO, prostaglandins. *Trypanosomacruzi*-Chagas disease Partially effective strong immune response. Response to all classes of Igs. T-Cell dependent immunity

Evasion: Inhibition of antibody binding by non-protective IgM. Inhibition of complements by surface glycoprotein. *Plasmodium falciparum* Malaria immune response Circumsporozoite protein (CSP) highly antigenic and strong antibody response. Immunity---Gradually builds up and fades quickly. PfEMP-1 on late infected RBC—Antigenic variation Immune response to helminths

Immune response: Multiple interactions between parasite surfaces and inflammatory cells. Mediated by complement and antibodies. ADCC is the most common response. Interaction of abs and parasitic enzymes help in prevention of invasion, migration and growth of the worm death.

Evasion: Adults are several meters but larvae less than 1 mm. Ability to move actively. Structural and antigenic make up may change. Intestinal nematodes Antibody induce the metabolic change. Expulsion by activated lymphocytes. Immediate and delayed hypersensitivity Evasion---Immunosuppression Ascaris lumbricoides Immune response--Elevated levels of IgE. Hypersensitivity reaction in the lung of previously infected host. Ascaris induces anaphylactic shock and death.

Evasion: Immune suppression by immune modulators Filarial Nematodes *Wuchereria bancroft* and Brugia malayi ---lymphatic tissue---T-Cell dependent immunity Evasion--Immune Suppression Flukes--*Paragonimuswestermani, Clonorchissinensis, Schistosoma haematobium* Schistosomiasis

Immune Response: Penetration of skin produces dermatitis. Developmental stage produces allergy. Granuloma formation around trapped eggs. Balance between Th-1 and Th-2 is critical.

Evasion: Secrete antioxidant enzymes.

Cestodes*: Taeniasolium, Taeniasaginata, Diphillobothriumlatum ,Echinococcusgranulosus* Adult cestodes are less pathogenic, but larvae are highly pathogenic Immune response two types A. Directed against intestinal lumen dueling adult tapeworms. Eg: *Taeniasolium, Taeniasaginata*. B. Directed against migratory tissue encysting larval Cestodes Eg: *Echinococcus granulosus.*

Evasion: Tissue cyst formation protection from immune response Echinococcusgranulosus ---IgE is elevated, CMI plays

a role in initial clearance of the larvae. Anaphylaxis is due to ruptured cyst fluid Evasion-- Connective tissue capsule.

Blocking of Complements and Antibodies Immunodiagnostic Methods in Parasitology: Immunodiagnostic Skin Test

a. Amoebic Liver Abscess

ELISA, detecting antibodies against 170 kDa of lectin antigen. Visceral leishmaniosis: Detecting antibodies to rK-39 antigen by immunochromatographic test (ICT) Toxoplasmosis: (i) Sabin-Feldman dye test- a complement mediated neutralization test, which detects antibodies, (ii) Detection of specific IgM or IgA or IgG antibodies by ELISA Cysticercosis: ELISA, detecting antibodies against purified glycoprotein antigens, (ii) Western blot, detecting antibodies against highly specific 50–13 kDa lentil lectin-purified seven glycoprotein (LLGP) antigenic fractions.

b. Hydrated Disease

ELISA, detecting antibodies against B2t or 2B2t antigen, (ii) DIGFA (Dot immunogold filtration assay) Lymphatic filariasis: (i) Flow-through assay, detecting antibodies against recombinant filarial antigen (WbSXP-1), (ii) Brugia Rapid, detecting antibodies against Recombinant B. malayi antigen (Bm-14). Antigen detection tests: Amoebiasis: ELISA, detecting 170 kDa of lectin antigen in blood and stool. Triage parasite panel: It is an ICT, that detects three antigens in stool*: Giardia lamblia* (alpha-1 giardin antigen) *Entamoeba histolytica*/ *Entamoeba dispar* (29 kDa Ag*) Cryptosporidium* (isomerase Ag) Malaria: ICT format available detecting: Histidine rich protein-2 (Pf. HRP 2)— P. falciparum specific Parasite lactate dehydrogenase (pLDH) and aldolase - common to all species Lymphatic filariasis: ELISA and ICT formats are available detecting filarial antigens by using monoclonal Ab against Og4C3 and AD12 antigens.

c. Serological Tests

Enzyme immunoassay Indirect fluorescence test Latex agglutination Immune electrophoresis Radioimmunoassay Complement fixation test Direct Immunofluorescence test Immunoblot Bentonite flocculation test Hem agglutination test Antigen detection It indicates active or recent infection and parasitic load.

d. Serum

Amoebiasis, Malaria, Toxoplasmosis, Filariasis, Schistosomiasis, Echinococcosis Coagulation, Rapid tests, Dye tests, EIA, ELISA Faeces-Giardiasis-DFA, EIA and Rapid tests.

e. Urine

Trichinosis, IA CSF-Cysticercosis-ELISA Cyst fluid-Echinococcosis-ELISA Anaphylaxis-Tests The two commercially available lab tests include Tryptase (a mast cell marker) and SC5b-9 (terminal complement complex).

Mast cells release tryptase during anaphylaxis. These lab tests can show transient elevation shortly following a severe allergic reaction. The ideal time window to collect blood for these tests is between 30 minutes and 90 minutes after the reaction begins. These blood tests might still be elevated up to 6 hours after the reaction began. A second sample for tryptase could be taken 24 hours or more after the severe allergic reaction, or even weeks after the reaction. The tryptase level obtained 24 hours or more following the severe allergic reaction indicates the patient's typical tryptase level and can help assess the allergic reaction. (CDC) [47].

f. Mediators of Acute Inflammation

Metabolism of phospholipids is required for production of prostaglandins and leukotrienes both of which enhance inflammatory response by promoting increased vascular permeability and vasodilation. Prostaglandins are 20-carbon fatty acid derivatives containing a cyclopentane ring and an oxygen containing functional group; leukotrienes are 20 carbon fatty acid derivatives containing three conjugated double bonds and hydroxyl groups.

Conclusion

Prepare and prevent rather than repair and repent Humans evolved with a unique immune system consisting of innate and adaptive immunity. Cell-mediated immunity provides protection using different cells such as white blood cells (WBC), Macrophage, Phagocytes, Dendritic cells and T cells (CD4 and CD8), etc. Humoral immunity is a function of B cells, memory cells and antibodies. The immune response in human and other higher vertebrates consist of activity of different cells and immune players for identification of the foreign substance, presentation to the immune system followed by killing/removal. There is growing research evidence demonstrating that the animal-based bioactive molecules are being tested and used clinically for various purposes such as antiparasitic, antimicrobial, anti-inflammatory, clot buster and antiviral etc. The clot-dissolving enzyme, peptides, and proteolytic enzyme are classic examples studied tremendously in past from various sources.

References

1. Osada Y, Kanazawa T (2010) Parasitic Helminths: New Weapons against Immunological Disorders. Journal of Biomedicine and Biotechnology (1): 1-9.

2. Perez Mazliah D, Langhorne J (2015) CD4 T-cell subsets

in malaria: TH1/TH2 revisited. Front Immunol 5: 671.

3. Hartmann W, Haben I, Fleischer B, Breloer M (2011) Pathogenic nematodes suppress humoral responses to third-party antigens *in vivo* by IL-10-mediated interference with Th cell function. J Immunol 187(8): 4088-4099.

4. Metenou S, Dembele B, Konate S, Dolo H, Coulibaly YI, et al. (2011) Filarial infection suppresses malaria-specific multifunctional Th1 and Th17 responses in malaria and filarial coinfections. J Immunol 186(8): 4725-4733.

5. Lemaitre M, Watier L, Briand V, Garcia A, Le Hesran JY, et al. (2014) Coinfection with *Plasmodium falciparum* and *Schistosoma haematobium*: additional evidence of the protective effect of schistosomiasis on malaria in Senegalese children. Am J Trop Med Hyg 90(2): 329-334.

6. Lyke KE, Dabo A, Arama C, Daou M, Diarra I, et al. (2012) Reduced T regulatory cell response during acute *Plasmodium falciparum* infection in Malian children co infected with *Schistosoma haematobiu.* PLoS ONE 7(2): e31647.

7. Gerbe F, Sidot E, Smyth DJ, Ohmoto M, Matsumoto I, et al. (2016) Intestinal epithelial tuft cells initiate type 2 mucosal immunity to helminth parasites. Nature 529(7585): 226-230.

8. Inclan Rico JM, Siracusa MC (2018) First responders: innate immunity to helminths. Trends Parasitol 34(10): 861-880.

9. Weatherhead J, Cortes AA, Sandoval C, Vaca M, Chico M, et al. (2017) Comparison of cytokine responses in Ecuadorian children infected with *Giardia, Ascaris*, or both parasites. Am J Trop Med Hyg 96(6): 1394-1399.

10. Zhou P, Li E, Shea Donohue T, Singer SM (2007) Tumour necrosis factor α contributes to protection against *Giardia lamblia* infection in mice. Parasite Immunol 29(7): 367-74.

11. Wynn TA, Chawla A, Pollard JW (2013) Macrophage biology in development, homeostasis and disease. Nature 496(7446): 445-455.

12. Dezube R (2019) Pneumomediastinum. Lung and airway disorders, MSD manual consumer version.

13. Plotkin SA (April 2005) Vaccines: past, present and future. Nature Medicine 11(4S): S5-11.

14. (2009) The Nobel Prize in Physiology or Medicine 1905.

15. (2007) Major Walter Reed, Medical Corps, U.S. Army Walter Reed Army Medical Center.

16. Metchnikoff E (1905) Immunity in Infectious Diseases (Full Text Version: Internet Archive). Translated by Binnie FG. Cambridge University Press. LCCN 68025143. History of humoral immunity.

17. Niels K Jerne (2020) The Nobel Prize.

18. Yewdell J (2003) He put the Id in Idiotype. *EMBO Reports* (Book review) 4(10): 931.

19. (2019) Transplant rejection: T-helper cell paradigm British Society for Immunology.

20. Goldsby RA, Kindt TK (2003) Immunology. In: 5th (Edn.), San Francisco: WH Freeman and Company USA, pp: 24-56.

21. Jaspan HB, Lawn SD, Safrit JT, Bekker LG (2006) The maturing immune system: implications for development and testing HIV-1 vaccines for children and adolescents. AIDS 20(4): 483-494.

22. Colley DG, LoVerde PT, Savioli L (2001) Medical helminthology in the 21st century. Science 293(553): 1437-1438.

23. Kennedy MW, Harnett W (2001) Parasitic nematodes. CAB International. In: Littlewood DTJ, Bray RA, et al. (Eds.), Interrelationship of the Platyhelminthes. Taylor & Francis, London, United Kingdom, 60.

24. MacDonald AS, Araujo MI, Pearce EJ (2002) Immunology of Parasitic Helminth Infections,American Society of Biology. Infect Immun 70(2): 427-433.

25. Maizels RM, Yazdanbakhsh M (2003) Immune regulation by helminth parasites: cellular and molecular mechanisms. Nat Rev Immunol 3(9): 733-744.

26. Kreider T, Anthony RM, Urban JF, Gause WC (2007) Alternatively activated macrophages in helminth infections. Curr Opin Immunol 19(4): 448-453.

27. Jeffrey K (2012) Actor, Immunology and Microbiology. Elsevier's integrated review, Elsavier Saunders. In: 2nd (Edn.).

28. Nutman TB, Weller PF (2013) Harrison's Principles of internal medicine, Vol-1McGraw Hill Education Infect Dis Poverty 2: 15.

29. David T John, Willium A, Petri J, Markel (2020) Voges Medical Parasitology. In: 9th (Edn.), South Asia.

30. Yu Y, Chadee K (1997) Entamoeba histolytica stimulates

interleukin 8 from human colonic epithelial cells without parasite-enterocyte contact. Gastroenterology 112(5): 1536-1547.

31. Denis M, Chadee K (1989) Human neutrophils activated by interferon-gamma and tumour necrosis factor-alpha kill Entamoeba histolytica trophozoites in vitro. J Leukoc Biol 46(3): 270-274.

32. Guerrant RL, Brush J, Ravdin JI, Sullivan JA, Mandell GL (1981) Interaction between Entamoeba histolytica and human polymorphonuclear neutrophils. J Infect Dis 143(1): 83-93.

33. Asgharpour A, Gilchrist C, Baba D, Hamano S, Houpt E (2005) Resistance to intestinal Entamoeba histolytica infection is conferred by innate immunity and Gr-1+ cells. Infect Immun 73(8): 4522-4529.

34. Lin JY, Seguin R, Keller K, Chadee K (1994) Tumor necrosis factor alpha augments nitric oxide-dependent macrophage cytotoxicity against Entamoeba histolytica by enhanced expression of the nitric oxide synthase gene. Infect Immun 62(5): 1534-1541.

35. Ghadirian E, Denis M (1992) Entamoeba histolytica extract and interferon-gamma activation of macrophage-mediated amoebicidal function. Immunobiology 185(1): 1-10.

36. Kammanadiminti SJ, Mann BJ, Dutil L, Chadee K (2004) Regulation of Toll-like receptor-2 expression by the Gal-lectin of Entamoeba histolytica. FASEB J 18(1): 155-157.

37. Maldonado Bernal C, Kirschning CJ, Rosenstein Y, Rocha LM, Rios Sarabia N, et al. (2005) The innate immune response to Entamoeba histolytica lipopeptidophosphoglycan is mediated by toll-like receptors 2 and 4. Parasite Immunol 27(4): 127-137.

38. Ivory CP, Prystajecky M, Jobin C, Chadee K (2008) Toll-like receptor 9-dependent macrophage activation by Entamoeba histolytica DNA. Infect Immun 76(1): 289-297.

39. Seydel KB, Smith SJ, Stanley SL (2000) Innate immunity to amebic liver abscess is dependent on gamma interferon and nitric oxide in a murine model of disease. Infect Immun 68(1): 400-402.

40. Chatterjee KD (2020) Parasitology (Protozoa and Helminthology) in relation to clinical medicine. In: 12th (Edn.).

41. Dakshinamoorthy G, Samykutty AK, Munirathinam G, Reddy MV, Kalyanasundaram R (2013) Multivalent fusion protein vaccine for lymphatic filariasis. Vaccine 31(12): 1616-1622.

42. Jankovic D, Wynn TA, Kullberg MC, Hieny S, Caspar P, et al. (1999) Optimal vaccination against *Schistosoma mansoni* requires the induction of both B cell- and IFN-γ-dependent effector mechanisms. J Immunol 162(1): 345-351.

43. Kelly EA, Colley DG (1988) In vivo effects of monoclonal anti-L3T4 antibody on immune responsiveness of mice infected with Schistosoma mansoni. Reduction of irradiated cercariae-induced resistance. J Immunol 140(8): 2737-2745.

44. Wilson MS, Cheever AW, White SD, Thompson RW, Wynn TA (2011) IL-10 blocks the development of resistance to re-infection with *Schistosoma mansoni*. PLoS Pathog 7: e1002171.

45. Aggarwal KK (2020) CMAAO, Coronavirus Facts and Myth Buster: Anaphylaxis, medinexus.

46. Jeffrey K (2012) Actor, Elsevier's integrated review, Immunology and Microbiology. In: 2nd (Edn.).

47. Verma MK, Raghavendra Rao MV (2020) Acta Scientific Biotechnology (ASBT) 1(8).