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# IMMUNITY IN HUMAN PARASITOSIS. PART I: ESSENCE OF IMMUNE RESPONSE AND TYPES OF IMMUNE REACTIONS

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**ABSTRACT**

Innate immunity is not a result of previous invasion and interaction between host and parasite and is not associated with actively acquired antibodies. It is a quality acquired in the course of evolution. Acquired immunity in still ongoing invasion is directed against superinvasion. Acquired immunity against helminths is even less effective than protosoic infection. These features of immunity hamper the establishment of vaccine which explains their absence in our days. Antigenic variation is observed in many protozoa, as well as stage specific antigens. That is why the malaria vaccine is not available. The acquired immunity to some invasion (toxoplasmosis) plays a crucial role in control the disease. Monoclonal antibodies are increasingly applied in diagnostics of parasite infection.

**Key words:** immunity, parasitosis, invasion, complement, antibody

Immunity is the organism's ability to protect itself from other living bodies which contain the signs of alien genetic information (R. V. Petrov, 1982). That information can be introduced into the body via microorganisms, foreign cells and tissue or the body's original cells that are changed as a result of somatic mutations. This genetic defensive ability of the host organism (macroorganism) that makes it capable of counteracting the spread and development of the parasite (the microorganism), as well as its pathogenic influence on the body is called immunity. The immunity is the result of the combination of innate, inherited and acquired defensive capabilities in the macroorganism forming the immuno-biological condition ( Moshkovski S D).

In multicellular organisms, specialized cells and tissues are responsible for these highly specific defensive mechanisms. Their function is to identify alien or original antigenic stimuli and to respond to them accordingly. Basic elements of this immune response are high differentiation and specificity. This complex system is only a part of the defensive mechanisms of the organism. The non-specific protection is formed before the birth and also includes: the barrier functions of the skin and the mucosa, phagocytes, the complement's system, interferons and other elements of the non-specific protection (1, 2, 3 , 9 ,10, 11, 12).

The meeting of the organism with genetically foreign antigen forms specific protection after delivery which is performed by specialized branches of T and B lymphocytes responsible for cellular and humoral immune response. In the overall immune response involved additional cellular systems – the complement and the nature killers (NK cells). Their action in the immune defense is regulated by certain genes.

The main structures of lymphatic tissue are lymph nodes, spleen, bone marrow, thymus, tonsils and Payer's patches which are

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functionally subordinate. Central lymphoid organs are thymus and bone marrow and peripheral – lymph nodes, spleen, non-capsulated lymphoid tissue (Payer's patches, tonsils and lung lymphoid tissue). Besides these organs and tissues the elements of the immune processes include more cells (T and B lymphocytes, NK cells, macrophages) and molecules (immunoglobulins, cell membrane molecules - HLA, receptors, thymus hormones, cytokines).

The development of lymphoid cells begins after the first month of embryonic phase from stem cell in the fetal liver. All hemopoetic cells originate from the stem cell. From the third month of embryogenesis these stem cells colonize the bone marrow and lead to the development of two types of lymphoid cells.

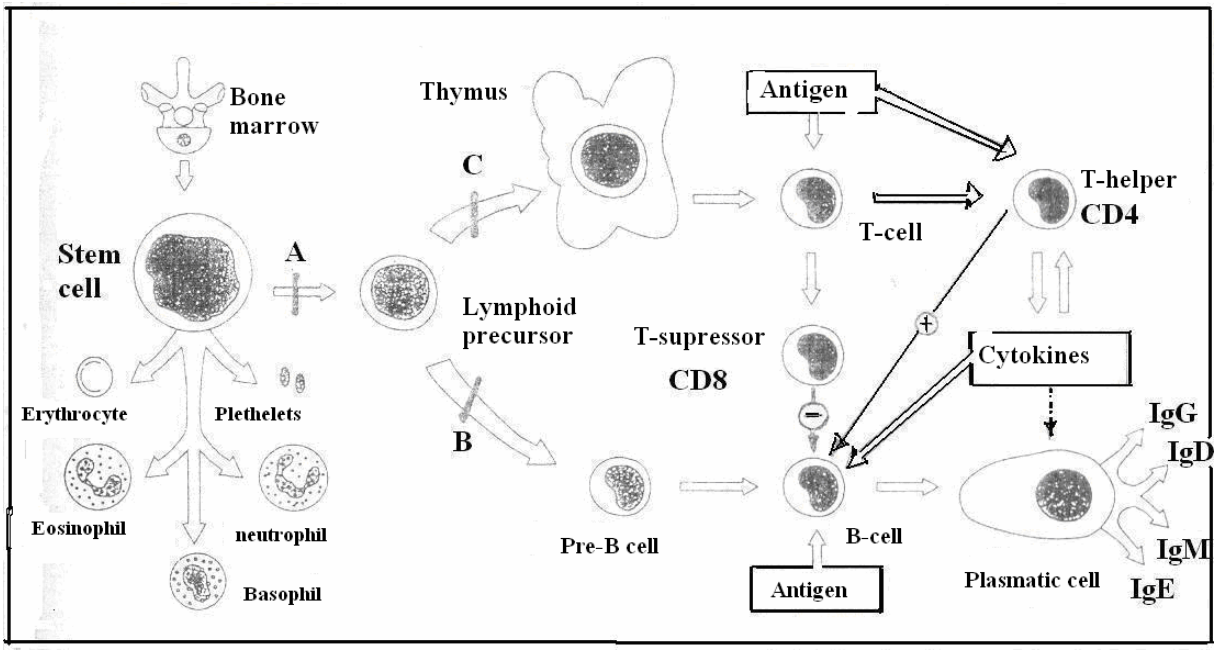


**Fig. 1.** Ontogenesis of T and B lymphocytes.

The block A leads to a combined immunodeficiency. Block B leads to a deficiency of antibodies while preserving cellular immunity. Block C leads to a cellular immunity deficiency. T-helpers stimulate differentiation of B cells and T-suppressors supress it. Cytokines are produced by activated lymphocytes and include interleukins and interferon.

***Essence and course of the immune response***. According Burnet's clonal-selection theory each lymphocyte is capable for reacting with specific antigen before meeting with it. Binding of antigen receptor activates the cell and causes its reproduction and maturity. Thus the antigen stimulates only those cells which have specific receptors for it – ***antigen specific immune response***.

There are two types of immune response – primary (at first meeting of body with antigen) – slow, low amplitude and long duration of action and secondary (after repeated contact with same antigen) – a fast, high amplitude and fast dwindling. The immunological memory can be accounted for the secondary immune response, which is provided by the specific B and T lymphocytes. The last have already had the meeting with the antigen (memory cells). These cells circulate in peripheral blood and does not divide a long life and repeated contact can differentiate into effectors realizing the final stage if the immune response.

Receptor molecules on the surface of T and B lymphocytes associate with antigens specifically. The monocyte - macrophageal system realizes combined immune response. Macrophages fix the antigenes (opsonization) on its surface. Their role in antigen process includes ingestion, digestion and partial expression of antigen. After the binding of antigen with immunocompetent cells the process of cellular differentiation starts and ends with formation of effector branches T and B lymphocytes (2, 5, 8, 10, 11, 12, 15, 17, 18)

Cytokines are important mediators in supporting the intercellular interactions. They are secreted mainly by T lymphocytes and macrophages, but is also possible to be separated from B lymphocytes, fibroblasts and vascular endothelial cells. Cytokines are two types: undifferentiated (chemotaxis factors for eosinophils, monocytes and neutrophils, migration inhibitory factors and suppressor transfer factors); specific or interleukins (IL). The last include interferon (IFN) in three classes: α (produced by leucocytes), β (produced by fibroblasts) and γ (immune IFN, synthesized only by T lymphocytes and NK cells) (2 ,8, 10, 11, 12) **(Fig. 2 and 3)**.

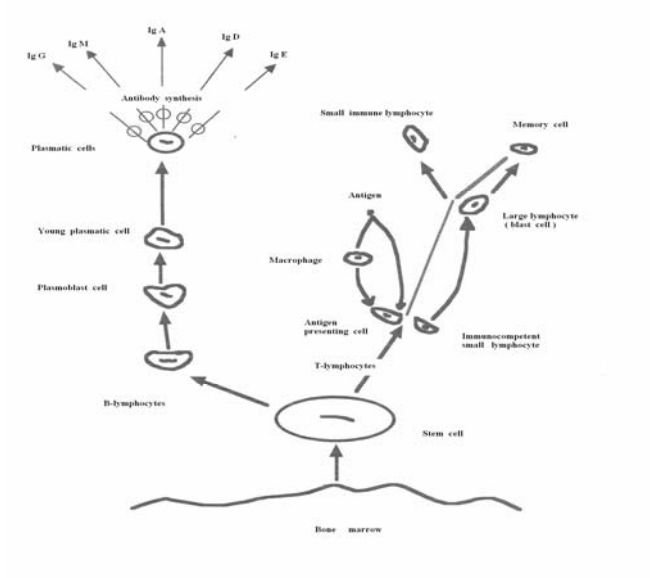


**Fig. 2.** Scheme of diferentiation of immunocompetent cells (by Leikina E S, 1975)

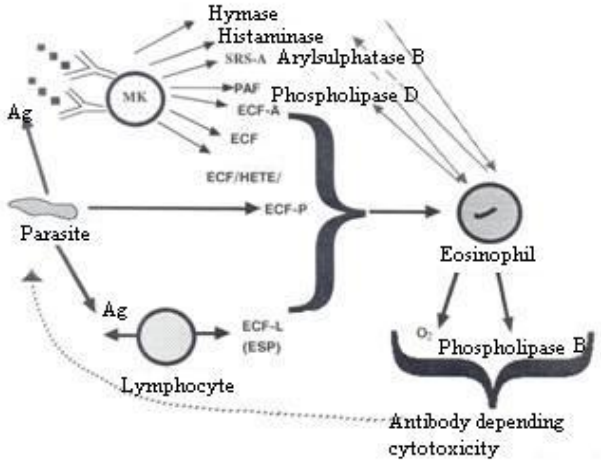


**Fig. 3.** Scheme of eosinophilic reaction after invasion of the parasite (by Goetz E G, Austen K F, 1977)

Ag-antigen; MC- mast cell; ECF-P – eosinophilic chemotaxis factor secreted by parasite; ECF-L – the same factor secreted by lymphocytes; RCF, ECF-A – the same factors released by mast cells; ESP – stimulator of eosinophilic activity present in lymphocytes. Continuous arrows – production or releasing, dotted lines – inactivation, cellular attack or cytotoxicity.

Innate immunity is called by Moshkovski SD, (1973) primary and nonspecific (11). It is not a result of previous invasion and interaction between host and parasite and is not associated with actively acquired antibodies. It is a quality acquired in the course of evolution. It varies from total unsusceptibility to partial or lack of immunity. The absolute resistance of rodent to malaria is a example for total unsusceptibility to this invasion.

The innate immunity to malaria is very well studied. The invasion of parasite in malaria tropica is lower in people with glucose-6-phosphate dehydrogenase deficiency, hemoglobin S and thalassemia. It is known that P. vivax and P. ovale are implemented primarily in young erythrocytes and P. malariae – in older ones. The innate immunity among natives in Africa to P.vivax is also genetically determined. Africans with Duffy negative erythrocyte antigen are unsusceptible to P. vivax because it invades only Duffy positive erythrocytes. Normal serum of some vertebrates has destructive agents against Schistosoma mansoni. The complement of the host in some cases penetrates the wall of the hydatic cysts and leads to lysis of the protoscolex. (3, 7, 9, 11, 14, 15,16)

The innate immunity is absolute and relative. The organisms have relative (natural) immunity to parasites in cases these hosts are not mandatory, but facultative. Manifestations of this type of immunity are: 1. reducing infectivity of animals 2. reducing the size and the time of invasion 3. extension of the developmental course 4. reduction of the vitality of helminthic ova and cysts.

There is also individual immunity which is relative. Not all individuals of a host species are equally resistant. Unfavorable factors can affect the resistance of organisms.

Age plays a great role in natural host resistance to parasitic infection. Young animals, unlike old ones, are generally more susceptible to parasites which results in frequent and massive invasion.

There are also reverse individual immunity against helminths. For example the trihinelic invasion in lambs is significantly shorter than in adult sheep (experimentally determined by Matt K, 1942) (3, 5).

B. Acquired immunity. Unlike congenital one, it is a result of a prior infection and can be maintained for a long time limiting or totally preventing the pathological reaction after superinfection.

Active immunity develops after spontaneous invasion and vaccination as well. There are two types of active acquired immunity: immunity gained as a result of a passed invasion and to a previous but still existing invasion.

Active immunity, directed against reinvasion, is the after-result of a passed invasion. It occurs in the same way as with innate immunity. There is a number of authors who have succeeded in the induction of artifitial immunity by injectiing live or dead helminths or their extract (dictiocaulosis, moniesiosis, methastrongiloidosis and ctr.). Shulz RS and Shihobalova called this type of immunity postvaccination. (3, 8)

Acquired immunity in still ongoing invasion is directed against superinvasion. It is known as non-sterile because of the resistance against the second invasion as a result of parasite presence in the body. Thus Matov K observed acquired immunity in dogs with E.granulosus. Acquired immunity against helminths is even less effective than protosoic infection. These features of immunity hamper the establishment of vaccine which explains their absence in our days.

**Antigens** – high molecular substances able to cause a specific immune response of the body which occurs with formation of specific antibodies, sensitized lymphocytes, development of tolerance and immunological memory. There are lots of determinant groups on the surface of the protein molecule. There are different antigen types: group, species or organ specific . There are also functional and somatic antigens (2, 3, 5, 8, 10, 11, 12). They differ in immune response: thymus-dependent antigens - the response is implemented with participation of thymus origin cells; and thymus–independent antigens – the response comes without the participation of T lymphocytes.

Antigenic variation is observed in many protozoa, as well as stage specific antigens (these are found in studies of preparation of malaria vaccine). For example the antigenic structure of sporosoite, merosoite, shisont, gametocyte is different (13). That is why the sporosoite's vaccine is active only against sporosoite; shisont's vaccine is active in erythrocyte stage etc.

Secretory and excretory somathic antigens of helminths significantly differ in their chemical properties and structures. This explains why lactatdehydrogenase is the antigen of A.suum and also an enzym that facilitates the lysis of collagen and is an antigen of S.mansoni. The somatic and secretory antigens sensitisize the host organism. There are heterogeneous antigens that are responsible for cross-reacting immunity. Antigen affinity between some helminths and ABO

erythrocyte antigens is established in people. Such antigen has been isolated from A.suum, F.hepatica and S.mansoni. It is assumed on this basis that individuals with certain blood types are exposed to a higher risk of certain parasitic diseases. The theory of "molecular mimicry" explains this affinity. Some authors consider that antigens are produced in the process of evolution.

The presence of common host and parasite antigens can cause development of three categories of immunological phenomena:

- increasing the pathogenicity of the agent
- lack of reactivity of the host and development of autoimmune process
- host tolerance to parasite

Parasite rarely causes the death of the host because the latter is necessary for their survival. This is one of the reasons parasitic infection usually occurs chronically.

**Antibodies**. They are globulins capable to bind specifically to the antigens. According to the WHO nomenclature immunoglobulins are divided into five classes: IgA, IgM, IgG, IgD and IgE.

The acquired immunity is responsible for the resistance against reinfection (1, 2, 3, 5, 8, 10, 11). Resistance in volunteers against reinfection with Trichinella is described (6). Acquired immunity in cutaneous, visceral leishmaniosis and American trypanosomiasis is life-long. The acquired immunity to toxoplasmosis plays a crucial role. Severe course of disease in humans is rare. Primary infection with low virulent strain prevents a fatal course after high virulent strain infection.

Combined antigenic composition of parasites, which includes heterologous antigen fractions determine the heterogeneity of the antibodies. The immunity is species-specific, strain-specific and stage-specific depending on predominant antibodies.

Monoclonal antibodies are increasingly applied in diagnostics of parasite infection. They are derived from in vitro cultures of hybrid cells from lymphocytes and cancer cells.

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