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The role of immune system in the newborn

Abstract

The transition made by the newborn when pass through intra-uterine medium to a new world, will determinate new changes of the immune system against harmful environment. These changes can renders newborns to many pathogens which could lead to some pathologies like pre-term delivery. The immune system works with adaptive immunity response which requires previous contact with antigens and with innate system response without requiring immune experience. Therefore, a better understanding of the cell mechanisms of the immune system which start to develop from newborn to childhood and then adulthood will help physicians to improve the sites of different infections during this period of life. This review focuses mainly on the role of T and B-cells activation in newborns, innate and adaptive immunity, and the changes from newborn to childhood and adulthood.
Keywords: *immune system, newborn, innate, adaptive, childhood, vaccines*

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Introduction

The stability of the immune system of a newborn has been showed to have less trigger effects against different pathogens from the environment. Therefore, the infections could become a real enemy against the system that the newborn has it at birth[1].

When the newborn see the light of the world too early in the premature period comparing with normal gestational period, the immune system is less developed, and the rate of infections could arise about 5-10 times higher at less than 28 weeks prematurity. The ability of the newborn immunity to detect antigen IgE especially from the umbilical blood showed that neonatal B and T cells have an antigen-specific response[1].

The primary site of infection is still effective until around 3 month of age, which is the duration when the immune system start to develop[2]. At the first months, the newborn is still dependent on the maternal antibodies, and the development will be achieved only in childhood progressing in time[1]. In newborns, there are some basic factors which influence such maturation from the immune system features. Furthermore, vaccines should be optimized for immune system of neonates by harnessing the power of new technologies advanced[3].

The milk also contains secretory immunoglobulin (Ig) which is found in the gastrointestinal and respiratory pathways, phagocytes, lymphocytes, cytokines, lyzozyme, lactoferin and lipids. Although the newborn immune system renders a complex set of immunoglobulins, the response can lead to pre-term delivery facing in the same time a new environment rich in foreign antigens[4].

The liver represent the first hematopoietic organ in the first months were the lymphoid and myeloid progenitors are found. After this period, they migrate to spleen, thymus and bone marrow[1]. Therefore, after the spreading of the specified cells and start to differentiate the immune system is split into specific or adaptive and nonspecific or innate, which comprise the cellular and humoral response based on mice experiments[5].

Both cellular and humoral immunity act through lymphocites and antibodies cascade. The antibodies can be serum or secretory antibodies which stop the entry of the microorganism in the human body.

T-cell activation in newborn immune system

T-cells are dividing into two T cell receptors (TCRs), γ/δ and α/β proteins. The receptor expressing γ/δ cells is can't be found in thymus, although it present an important role against inflammatory action. These kinds of receptors are being developed by the dendritic cells and further it began to secrete chemokines which represent part of the adaptive triggers[6]. In brestmilk the concentration of maternal T lymphocytes are low and their role is still unknown. In this case, newborns are mostly dependent on that immune system against different types of infections[7].

One study suggested that the activation of T-cell response leads in the end in more reduced immune defense system. This attempt was sustained by the fact that into umbilical blood TCR showed to slower the expression of the tyrosine kinase protein, named Lck. In the case when Lck is not early phosphorilated, the TCR was associated with lowering expression[8]. The same study sustained the molecular defect linked to limited signaling ability of umbilical cord T cells, providing in such case the bases for future research on T cell maturation[8].

Another study shows that when cluster of differentiation (CD)4 of TCR is affected, because of the Cb1-b, and ubiquitin ligase higher expression, it will reduce the anti-CD3 and anti-CD29 expression[9].

Interestingly, micro-ribonucleic acid improve the calcium flux from the phosphorylation of some signaling cells, reducing the activation of interleukin-2 and interferon[9]. Therefore, the mechanism of these cells which positively regulate the immune response will develop in

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the future new strategies in order to enhance the newborn immune response.

B-cell activation of newborn immune system

B-cells from early ages have partially developed in the meaning of the surface of the Ig repertoire. B-cells are made two parts, B1 and B2 cells based on CD5 expression. B1 cell is differing from B2 playing an important role in early bacterial and viral infection downstream. B2 cell present a different phenotype on the surface comparing with B1 cell[10].

The lower efficiency of the antibody in neonates and younger ages can depend on the fact that B-cells are still immature, or the signal of the B-cell receptor (BCR) is too slow. The activation of the receptor with different dependent T-cell antigens starts to intercalate the surface of Ig cells. After that linking, some process like the Src-related kinases protein phosphorylation are activated. Some studies showed that neonatal B cells are deficient in producing T-cell independent antigen together with type 4 polysaccharide[11]. Those limited strength features of B cells at lower antigen stimulation can be attributed to regulators in negative way. Therefore, the lower ability of neonatal B cells, especially in crossing the receptor with polysaccharides can be the results of the higher density of IgM molecules[12]. Furthermore, the results of the study showed that T1 antigens lower the BCR signaling through down-regulation of CD22, which require B cell response and premature apoptosis[12].

The negative BCR regulator can be increased by the stimulation of adult B-cell with a T cell dependent antigen[13]. The immature neonatal B cells was also attributed to some defects in nuclear signaling pathway and some isotype switching in response to T cell dependent antigens[14]. Although the signals necessary for the formation of B-2 cells and the stages at which cells are develop have been defined, some events required in the maturation of B1 cells has still merely to be discovery[14].

In the different contexts, the relationships between the viruses and viral proteins have been focused on homologies between different amino acids, but the cross-reactivity of the T cell recognition could not be dependent on the amino acids sequences. Both T and B lymphocytes seems to have different action in newborn comparing to adults. In newborn, the lymphocytes are more immature along with higher rate of thymic cells and reduced in BCR signaling[15].

Although some researchers sustain the fact that newborn immunity can have similar responses in T and B cells, primarily infections of the organism showed some differences.

Innate immunity

Innate immunity is activated after exposure of the human body to the first contact with different antigens, representing the first line of defense. It consists from the large barrier like skin, mucosa, and proteins from the complement system. Moreover, toll-like receptors showed to play a role in detection of different pathogens and the induction of innate immune system[16].

In newborns the barriers like skin- are still in develop stages, most probably because of the lower production of the free fatty acids. The newborn skin is in this way more susceptible to pathogens, representing a week defense bridge at this age. Although until present only a few data regarding the host-defence capability in newborn exist, more recent advances in immunology will better provide new inside underlying the mechanism of infection[17].

In newbonrs, the monocytes and macrophages alter phagocytosis process, based on the reduced function. Therefore, in newborns are seen more often the deterioration of the features like chemotaxis, adhesion and in the end migration at the infection surface. Interestingly, the number of circulating neutrophils into blood stream is less comparing with adults, sometimes being compared with septic conditions[18].

Taken together, the innate system from newborns showed to be partially responsible of the reduce ability in different site of infections in terms of monocytes and polymorphonuclears.

Adaptive immunity

The decreased function of the innate immunity is in concordance with the decreased adaptive immunity, considering the fact that the two systems are interconnected. This system comprises the cell-mediated response and antibody-mediated response with T lymphocytes being the main effectors cells. Furthermore, polymorphonuclear neutrophils defects and other parameters of neonatal immune deficiency lead to sepsis and other infections representing the major causes of morbidity and mortality[19].

T lymphocytes represent mainly the cellular immunity. Those subtypes are Th cells (i.e. CD3 and CD4) and T cytotoxic cells (i.e. CD3 and CD8). Another type of T lymphocytes family is represented by the Th cells which is divided into two patterns: Th1 which represent cellular immunity response and Th2 which represent the humoral response[20]. T lymphocytes present a major shortcoming by the fact that it recognizes only the antigens which are presented by the cells from 1st and 2nd class of major histocompatibility antigens[20].

Although the quantitative expression of the T cells at birth is higher, it's expression and action is decreased comparing to adults and only few are beginning to differentiate into memory cells. In the same context, the experiment on different bacterial type involved in the pathway of this immune system together with its mechanism will further elucidate the complex host-commensal interactions which will allow for different therapeutic manipulation of this process[21].

The immunity from newborn to childhood till adulthood

From the beginning, at newborns, the risk of pathogen invasion still exists. During childhood, the immune system starts to develop, primarily the innate and after a period the adaptive system.

The risk is nowadays represented more by the undeveloped countries, in which a screening methods and new vaccines should be integrated in order to prevent the infections. The results of the study sustain the fact that new generation of more effective vaccines should be developed which elicit T-cell memory in the optimal combination required especially in the neonate protective immunity against infectious pathogens[22].

Although the immune system is only at the starting point to be developed, in these countries the accent is mainly on the extreme genetic polymorphism in the major histocompatibility complex (MHC). The MHC which is one of the important key regulators in immune system works by a peptide presentation to T cells. Because of the vaccination, these risks are now more decreased, stimulation in this way the protective immune responses. In these directions, many antigens stimulation may become important key players in the memory of immune cells[23].

Taken together, the rebuild of the immunological memory in the child organism represent a better adaptation of the immune system. Moreover, the memory of the implicated cells still resists at any age and reaching at senescence, they start to decreased.

The newborn is every time exposed to many foreign antigens. Passing from an almost sterile environment from in utero outside, the newborn is rapidly exposed to pathogens. First exposure is represented at the birth, then through the skin and respiratory tract. Interestingly, some bacteria which are normally colonize the mucosal sites are playing an important role not only for the survival functions, but also into development of the immunity[24]. In the future new era of technologies will be able to identify human symbiotic bacteria with different anti-inflammatory effects, which will suggest that some features aspects of human health could depend on the microbiota "health"[24].

About one third from the lymphocytes comes from the gut[25], which influences the development of the memory T cells[26]. In newborns, the proportion of the T cells which carry CD45RA which is a glycoprotein, are increased along with Tregs cells. Therefore, looking at the T cell memory it was showed that the memory populations are still maintained following pathogens exposure or vaccination considering the dynamic point of view. In the same direction, these cells may be activated by the responses at other infections[27].

Taken into account the complex evolution of the T and B cells, and considering the mechanisms which are involved into a stimulus response, the composition and properties of such cells will be different in each individual, depending also on the immunological load received by the mother.

Conclusions

The immune system of the newborns presents some features which make it very particular in the meaning of defense barrier against different pathogens. This fact sustains the involvement of viruses and bacteria in primarily infection even in the first month of life, named the immune weakness period. When the newborn immunity start to develop, many factors like cytokines, monocytes, antigen exposure or lymphocytes are come in order to achieve its finally aim. Some researched have been shows that the maturation of the system came most from B and T cells responses. Therefore, it is important in newborn stages to understand the mechanisms of these factors which will pave the new era of more efficient and protective vaccines against different pathogens. ■

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