*Journal of Advances and Scholarly Researches in Allied Education*
*Vol. 16, Issue No. 6, May-2019, ISSN 2230-7540*

# Factors Affecting Immune Response System

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***Abstract – Dysregulated serum proteins (cytokines) profiles relate to several immune mediated disorders. Strong correlation exists between cytokine genes and immune mediated diseases, i.e., SLE are dominated by interferon-inducible gene within the blood however, the pathological influence of such genetic associations is already difficult to understand.***

***Recent inter-individual variations studies on APC and T-cells results estimated about 22% variation as genetically heritable factors and suggest its moderate contribution to affect blood transcriptomes. All these information gave us an estimation of variations among the individuals within a population.***

***Keywords: Immune, Blood, Cells***

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## INTRODUCTION

During acute infections white blood cell (WBC) count increased with a moderate heritability of 0.38 (0.14 basophils; 0.4 monocytes) and the reason to the inter-individual variations could be the specific loci, i.e., chromosome 2 loci are associated with coeliac disease and monocyte count. Similarly with the help of high dimensional Flow Cytometry approach about 24 additional loci that affect >20 immune cells populations were identified.

Similarly, GWAS also deal in with the finding of individual immune system measurements with the specific genetic loci that are responsible for the disease prevalence specially the autoimmune conditions (genetic risk variants >80) which have been widely studied over the past and affecting humans in many ways. Therefore, more considerations have been placed on the heritable factors that influence the immune system components including immune cells frequencies and serum protein concentration, in the current scenario while some of the studies performed on immune cell functions give analysis of the discern heritable influences.

To maintain their efficiency over time immune system serves as a sensory and regulatory system for external or internal stimuli. Suggesting that these stimuli can alter the composition and functional property of an individual's immune system. These non-heritable factors are typically, infections and vaccines, as well as de novo mutations and stochastic epigenetic variations, in addition to pathogenic and symbiotic microorganism influence. Stochastic epigenetic changes occur during an immune cells division and influence immune cell phenotypes.

The development of the immune system also depends on the encounter of microorganisms' types and their threshold, i.e., GIT bacterial strains (E. coli) interaction with lymphoid tissues promotes their normal development, while in germ free animal functional deficiencies are observed, suggest the co-evolution. The controlled animal facility environment has positive as well as negative effects on the study of the relationship between microbiota and immune system. On the other hand microbiota in human GIT has been associated with inflammation and diseases complications like Ulcerative Colitis and Crohn Diseases.

Similarly, humoral response between microorganisms and non-adjuvant vaccines, i.e., bacterial flagellin sensors as a vaccines stimulus is responsible for plasma cell activation and antibody production. Therefore, differences in gut microbiota may depict different responses in specific individuals. Likewise, many viruses became the cause of chronic disease while some are integrated into our genome, i.e., cytomegalovirus (CMV) acts as modulators for human immune systems. About 10% CMV specific T cell and NK cells change their phenotypes to CMV stimulus. CMV analysis within 20-30 year age groups was associated with beneficial flu vaccine mediated immune response in immune compromised people. Constant infection

with low grade virulence viruses induces immune response and promotes immune mediated pathologies.

Environmental factors like other units deeply affect individual immune system development and regulation. Beside microorganisms, many environmental factors influenced the development and reshaping our immune system.

## FACTORS AFFECTING IMMUNE RESPONSE SYSTEM

One of the most harmful factors is the cigarette smoking along with its >4000 components which damage human's lungs and systemic system that result in increased leukocyte count and reduced serum immunoglobulin's and NK-cells activity. Similarly Smoking further leads to altered antibody specificity that produces modified peptides, i.e., citrullinated peptides, which have a clinical importance in various autoimmune diseases including rheumatoid arthritis. Furthermore, industrial west, heavy metals, vehicle smoke, plastic fire, acid rain and animal debris etc. also affect badly immune system development.

The immune system is designed to detect and destroy foreign invaders inside the body like bacteria and viruses. When working optimally, the immune system can prevent sickness when we're exposed to germs. Several factors like sleep, diet, stress and hygiene can affect the immune system's performance, and any offsets in these behaviors can cause havoc on immune function.

Often times the impact of these factors go unnoticed, but if you tend to get sick after a big project at work or during finals at school, it's likely because your immune system has suffered due to stress, lack of sleep, binge eating or unhygienic behaviors.

The immune system is influenced by the sleep-wake cycles of our circadian rhythms. Studies suggest that while we're sleeping we have decreased levels of the stress hormone cortisol, which can suppress immune function, and increased signals that activate the immune system.

Even though we know that sleep is important, it can be difficult to get enough, especially during busy times of the year. According to a Gallup survey, 56% of adults say they get enough sleep. However, 7 hours is the minimum recommended amount of sleep for adults and only 40% of us are averaging 6.8 hours of sleep per night.

Many factors influence immune responses to vaccines; these include the quality of the vaccine program, vaccine type, e.g. live versus subunit vaccines, age at priming time, intervals between doses, vaccine potency, formulation, and stability, vaccine administration and scheduling, host-related factors, including sex, genetic factors, psychological stress, nutrition, smoking, microbiota, breastfeeding, maternal antibodies, environment agents, including prenatal, perinatal, and postnatal environments, and infections. Although some of these factors are not directly involved in the vaccine response, they should be considered as confounding factors.

In general, stress and anxiety reduce antibody responses to vaccines. Glaser et al. observed that stress affects the primary response, and the response to HBV vaccine occurred later in stressed than in healthy individuals. It was also observed that IgG levels were lower in stressed than in normal individuals eight weeks post-immunization with keyhole limpet hemocyanin antigen.

Genetic factors play an important role in the modulation of antibody responses to environmental antigens in early life; however, the role of genetics in immune responses to vaccines is not yet fully understood. The impact of genetic diversity is specific for each vaccine; heritability was estimated to be about 90%, 39%, and 46% for MMR, measles, and rubella vaccines, respectively.

The HLA DRB1 locus is significantly involved in all vaccine responses, and less for other HLA class II genes. The HLA class II locus has been shown to play an important role in antibody responses and vaccine failure, especially following HBV and measles vaccinations.

Davila et al. reported that polymorphisms in loci of HLA DRB1* alleles 1, 11, and 15 are associated with strong responses to HBV vaccination, whereas HLA-DR3 and DR7, which are in linkage disequilibrium with HLADQ2, are important in non-responsiveness.16 Alleles associated with immune responses are shown in Table I. Non-HLA genes also have roles in the induction of antibody responses following vaccinations and cytokine responses to vaccines; for example, antigen-specific IL-13 and IFN responses to tetanus and pertussis antigens are controlled by non-HLA genes.

Toll-like receptors (TLRs) are important in the initiation and activation of responses to vaccines. The activation of these receptors leads to activation of immune cells, induction of cytokines, and vaccine antigen recognition.

Toll-like receptor polymorphisms are also associated with immune responses to the BCG vaccine in newborns. Overall, genetic factors play important roles in regulating responses to vaccines, and identification of the genes involved in the responses will likely help in effective vaccine development.

Microbial colonization begins at birth, but the bacterial diversity before two years of age is not

sustainable. Studies showed that environmental exposure influences the microbiota, and this affects vaccine immune responses.

Environmental factors that affect the childhood microbiota include diet (breast fed vs. formula fed), delivery mode (vaginal vs. caesarean section), hygiene, gestational age, hospitalization, and antibiotic use.

## DISCUSSION

Several studies show that flora of breastfed children contain probiotics including Lactobacillus, Streptococcus, and Bifidobacterium. In contrast, formula-fed infants have relatively high numbers of Bacteroides and Enterobactericeae. These findings indicate that diet directly affects the microbiota. In addition, the mother's diet and antibiotic use before and during pregnancy can affect the baby's microbiota.

The delivery mode is the first major determinant of gut microbiota in early life; infants delivered vaginally are colonized by the mother's fecal and vaginal bacteria, whereas infants delivered by Cesarean section are exposed to hospital bacteria.

Infants delivered by cesarean section have lower Bifidobacteria and B. fragilis-group species and higher C. difficile and E. coli counts than those delivered vaginally. In general, children born in developing countries have higher exposures to pathogens than children in developed countries, and this affects the microbiota.

Age and immune responses to antigens are strongly correlated. The immune system matures considerably from birth until age two. In young children, the immune system is not able to respond to polysaccharide antigens.

In infants, antibody responses are low due to the absence of a survival factor produced by bone marrow stromal cells. This limited vaccine response is also observed in the elderly. In adults, the antibody response is maintained by long-lived plasma cells in bone marrow.

Aaby et al. suggested that non-specific effects of vaccines to diphtheria, influenza, hepatitis A and B, pneumococcus, measles, rubella and yellow fever are less pronounced in boys than girls.

The mechanisms responsible for this difference are not yet known, but are not related to sex hormones nor just restricted to females. Males had greater serological responses than females to pneumococcal, diphtheria, yellow fever, Venezuelan equine encephalitis, and rabies vaccines.

Nutrition affects the immune system and its responses to vaccines. Malnutrition impairs immune responses to yellow fever, smallpox, tuberculosis, and polio vaccines.6 Rikimaru et al. showed that serum levels of IgA1, IgA2, and C4 were higher, and C3 and B cell counts lower, in severely malnourished than in normal children.

Malnutrition occurs for various reasons in children. Bacterial and parasitic infections can cause diarrhea and loss of electrolytes and minerals, resulting in impaired host immune responses. Malaria in pregnant women increases the risk of low-birth weight babies, and zinc deficiency impairs immune responses to intestinal nematodes. Infections that cause diarrhea and enhance zinc loss.

Overall, malnutrition can occur via several mechanisms that lead to changes in the composition of the normal flora and impair host immune response to pathogens. Micronutrients important for vaccine efficiency include zinc, iron, selenium, and vitamins. Lack of adequate macronutrients or selected micronutrients, especially zinc, selenium, iron, and the antioxidant vitamins, can lead to clinically significant immune deficiencies and infections in children. Antioxidants and cofactors are involved in cytokine regulation. Iron and zinc deficiencies impair host immune responses.

Maternal exposure to pathogens increased levels of Th1 and proin flammatory cytokines in cord blood. Chronic infections during pregnancy with helminths, Plasmodium spp., and HIV affect fetal immunity, including responses to vaccines.

The effect of these environmental exposures on the postnatal response of children to vaccines is not yet clear; however, the prenatal environment can have long-term effects on responses to vaccines. Current evidence suggests that schistosomiasis, filariasis, and other helminthic infections during pregnancy can suppress subsequent immune responses to standard childhood immunizations.

Kizito et al. reported that malaria and HIV infections in mothers during pregnancy, and their infants after birth, reduced the infants' humoral immune responses to the measles vaccine. In contrast, other helminthic infections showed no correlations with infant measles-specific antibodies. Therefore, vaccination of both mothers and children is important for the formation of protective responses in children.

The vaccination of mothers during gestation leads to transplacental transfer of antibodies and immune protection in the neonate. In this active transfer, IgG1 and IgG3 subclasses transport via the FcRn receptor. The efficiency of the transfer is dependent on multiple factors including the IgG concentration in maternal blood, the vaccine type,

placental integrity, the timing of the vaccination during pregnancy, the gestational age of the fetus at birth, and the IgG subclass.48 Another study showed that in children born to mothers with the highest anti-influenza antibody titers, the onset of influenza symptoms occurred later and the illness was shorter than in children born to mothers with lower titers.

Delivery mode, birth weight, season of birth and season of vaccination all influence postnatal immune development. During vaginal delivery, the acute phase reaction causes cytokine production following TLR stimulation in cord blood.

## CONCLUSION

Children who are delivered vaginally have more beneficial gastrointestinal microbiota than those delivered by Cesarean section, which has a positive effect on immune system development and subsequent immune responses.

Birth season and weight predict immune responses in both children and adults. Belderbos et al. reported that babies born in the winter have less TLR3-mediated IL-12p70 and grater IL-10 production upon stimulation of TLR7 than those born in other seasons.

The season of vaccination is associated with specific antibody to HBV vaccine. In this study, the antibody response was greater in winter than summer at both the first and second vaccinations. The authors proposed that increased exposure to ultraviolet radiation reduced antibody titers after vaccination. A cohort study demonstrated that birth weight is not associated with a rabies vaccine response, but is correlated with a typhoid vaccine response.

Postnatal exposure to infectious pathogens or microbiota can affect immune responses to vaccines. Postnatal exposure to microbes results in cross-reactions with specific antigens and specific modulation of immune responses.

Both animal and human model studies suggest that chronic parasitic infections can decrease vaccine efficacy. Chronic infections with protozoa reduced specific antibody titers to tetanus, influenza type B, and typhoid vaccines, and caused adverse effects following vaccinations. Exposure to parasitic infections during the first years of life also can influence subsequent immune responses to vaccinations.

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