Cytokine profiles, infections and IgE sensitisation in childhood.

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Background: The etiologic factors behind development of IgE-mediated allergy are incompletely understood although the interaction between allergic heredity and exposure to various environmental factors seems to be most important.
Objective: The overall aim of this thesis was to study the associations between allergic heredity, environmental factors like viral infections and IgE sensitisation and the development of allergic diseases during childhood.
Methods: A cohort of 281 infants, with different patterns of family history for allergic disease (both parents, maternal or neither parent) was followed prospectively from birth to 2 years of age using questionnaires, clinical examinations, blood sampling and skin prick tests.
Results: The associations between the number of IFN-γ, IL-4 and IL-12-producing cord blood mononuclear cells (CBMC) and parental allergic history were evaluated by the ELIspot method in 57 children. Children with two allergic parents had a statistically significantly higher IL-4/IFN-γ ratio ($p < 0.05$) than children without allergic parents. The number of IL-12-producing CBMC was statistically significantly higher among children without allergic parents compared to the children with only maternal allergic disease ($p < 0.01$). These findings suggest a strong genetic influence on the cytokine pattern in CBMC, where having a father with allergic disease has at least as much influence as a mother with allergy.
The association between the number of IFN-γ, IL-4 and IL-12-producing CBMC in 82 children and allergic outcome at 2 years of age was investigated. Compared with non-sensitised children, the IgE-sensitised children had lower number of IL-12-producing CBMC after stimulation with allergens, and this was statistically significant for cat ($p = 0.002$). Children with eczema had statistically significantly lower numbers of IFN-γ producing CBMC after stimulation with ovalbumin ($p = 0.017$) and cat ($p = 0.01$) compared to children without eczema. These results might indicate that different cytokine profiles in cord blood are associated with different allergic phenotypes.
The association between serostatus against 13 selected viral infections and IgE sensitisation was evaluated among 246 children at 2 years of age. IgE sensitisation (24%) was statistically significantly less prevalent at 2 years of age among infants who were seropositive against Epstein-Barr virus (EBV), ($OR_{adj} = 0.34$; 95% CI 0.14 - 0.86). Seropositivity against both cytomegalovirus (CMV) and EBV gave a further reduction in the risk for IgE sensitisation, indicating an interaction between the viruses. Thus, acquisition of EBV infection during the first two years of life seems to be associated with a reduced risk of IgE sensitisation and this effect is enhanced by CMV co-infection.
The association between the phytohaemagglutinin (PHA) -induced cytokine-profile in peripheral mononuclear blood cells (PBMC), serostatus against CMV and EBV and IgE sensitisation was evaluated among 75 children at 2 years of age. CMV seropositive children had higher numbers of IFN-γ-producing PBMC (OR_{adj} 37.48 95% CI 5.71 - 246.15) and lower number of IL-4-producing PBMC (OR_{adj} 0.05; 95% CI 0.01 - 0.46) than seronegative children. The IgE sensitised children more often had high numbers of IL-4-producing PBMC than the non-IgE sensitised (OR 13.50; 95% CI: 1.56 - 117.13). These data support the idea that persistent viral infections may affect the immune system for a considerable period of time.
Conclusion: Our findings illustrate the complex traits of allergy in infancy where the different allergic phenotypes are influenced by both genetic and environmental factors like viral infections.

***Keywords**: allergy, allergic heredity, childhood, cytokines, IgE-sensitisation, Epstein-Barr virus, interleukin-12, viral infections.*

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