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AUTOIMMUNITY AND PRIMARY IMMUNE DEFICIENCIES (PID)

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A total of 172 autoimmune disorders was recorded in 262 children with some major PID (hypogammaglobulinemia (X-linked, with hyper-IgM, common variable), IgA-deficiency, chronic mucocutaneous candidosis (CMCC) and Wiskott-Aldrich syndrome), while no autoimmunity was manifest in 103 patients with several other PID (ataxia-telangiectasia, chronic granulomatous disease, hyper-IgE syndrome). Rheumatoid-like arthritis (29%) and granulocytopenia (23%) were typical features of hypogammaglobulinemic states and often responded to pathogenetic therapy. Autoimmune endocrinopathy developed in most patients with CMCC (70%), while a variety of other less common autoimmune disorders (haemolytic anemia - 2, Sjogren's syndrome -1, keratopathy -2, alopecia - 1), also occured. IgA - deficient patients had typical arthritis (5%), scleroderma (6.5%) and vitiligo (5%) which required routine antiinflamatory and immunosuppressive therapy.

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Prevalence of Allergic Disorders and Sensitisation to Common Allergens at age Four Years

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Preliminary results are presented on 940 consecutively born children at the age of four years. One hundred and thirty seven, 14.6%, 95% confidence interval (CI) (12.3%, 16.8%) had asthma (recurrent cough and wheezing), One hundred and nine, 11.6%, 95% CI (9.6%, 13.6%) had atopic eczema, fifty eight, 6.2%, 95% CI (4.7%, 7.9%) had allergic rhinitis, forty five, 4.8%, 95% CI (3.5%, 6.4%) had food intolerance and eighteen, 1.9%, 95% CI (1.1%, 3.0%) had urticaria. The prevalence of latent atopy (positive skin prick test to common allergens without history suggestive of atopy was 7.4%, 95 CI (5.8%, 9.2%).

Skin prick tests (SPTS) were positive (wheal size $\geq$3 mm) to one or more common allergens in 170 out of 814 children (20.9%). SPTS were not done in 126 children. 107 (13.1%) were sensitive to housedust mite (HDM), 64 (7.9%) to grass, 46 (5.7%) to cat, 44 (5.4%) to alternaria, 23 (2.8%) to dog, 18 (2.2%) to cladosporium, 14 (1.7%) to milk, 11 (1.4%) to peanut, 9 (1.1%) to egg, 4 (0.5%) to wheat, 2 (0.2%) to soya and 10 (1.2%) to other plants, animals and foods. Only 163 (20.0%) reacted positive to histamine.

Conclusion(s) : This ongoing study looks at the evolution of atopic sensitisation in a cohort of 1250 children from birth. Positive reactions to foods are uncommon but a 1.2% positive rate for peanut is alarming in view of its persistence and potential fatality. The importance of HDM is emphasized by the substantial sensitisation to it. Moulds (Alternaria and Cladosporium) are significant allergens after dog and cat. Next follow up will be at age 7.

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GENETIC ANALYSIS OF CORD BLOOD IgE IN UNSELECTED LIKE-SEXED MONOZYGOTIC AND DIZYGOTIC TWINS

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Both genetic and environmental factors have been implicated in the determination of serum IgE levels. We measured cord blood-IgE (CB-IgE) in twins by a sensitive radioimmunoassay with detectable levels of IgE in all samples. Samples with contamination by maternal blood were identified by IgA determination and excluded. CB-IgE was evaluated in 29 monzygotic (MZ) and 28 dizygotic (DZ) otherwise unselected like-sexed twin pairs. By analysis of variance with subsampling the among-pair, within-pair and analytical variance components were calculated. A significant genetic dependence ($p<0.005$) was oberved by comparison of MZ and DZ within-pair variances (mean squares). The genetic variance and the intra-class coefficients were used to obtain heritability estimates of 0.30 and 0.34, respectively. The levels of CB-IgE were significantly dependent on genetic factors, but a substantial component seemed to be derived from the intra-uterine environment.

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RESPIRATORY SYMPTOMS AND ATOPIC SENSITIZATION AMONG ESTONIAN 10-12 YEARS OLD CHILDREN.

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For establishing asthma prevalence among Estonian schoolchildren 753 10-12 years old children in Tallinn (Tln) and 766 in Tartu (Ta) were investigated in a cross-sectional study, including parental questionnaires, skin prick tests (SPT), serial PEF-measurements and provocation tests with metacholine and exercise tests.

Allergic respiratory symptoms were less common among Estonian children than among children in West- and North-European countries. 5.1% of children in Tln and 4.1% in Ta had nocturnal cough without signs of cold; 9.4% of children in Tln and 5.8 in Ta had wheezing in the chest during cold, physical exertion or in contact with animals. The corresponding figure in Sundsvall in Central-Sweden was 13.1% . 13% of children in Tln and 8.3% in Ta had at least one positive SPT (in Urban Sundsvall - 35.3%). 10% had common cold > 6 times a year and coughing bouts for more than 2 weeks after a common cold - respectively 18.8% in Tln and 13.8% in Ta.

Estonian schoolchildren have a low prevalence of atopic sensitization but symptoms of respiratory infections and hyperreactivity are frequent.

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QUALITATIVE AND QUANTITATIVE DIFFERENCES IN THE IMMUNE SYSTEM OF ALLERGIC CHILDREN

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In allergic diseases serum IgE levels are elevated. It has been suggested in many studies that this is due to a shift in the balance between IFN-γ producing Th1 cells and IL-4/IL-10 secreting Th2 cells. The period between 0 - 4 years is very important in the development of allergy, due to qualitative and quantitative differences in the immune system of children as compared to adults. The aim of this study is to examine the isotype switching potential of purified B cells and the cytokine profiles of purified T cells of allergic children. Therefore peripheral blood samples were collected of children (0-4 years), with allergic asthma or atopic dermatitis and healthy age-matched controls. Stimulation of purified B cells in vitro, revealed a decreased production of IgG4 and IgA, but not of IgE in atopic dermatitis. The production of these isotypes by B cells in asthma did not differ from healthy controls. Purified T cells were polyclonally stimulated in vitro and analyzed for cytokine (IL-4, IL-5, IL-10, IL-13 and IFN-γ) production by semi-quantitative reverse transcription PCR analysis and cytokine specific ELISA. The IFN-γ production by T cells in atopic dermatitis was lower than in asthma and healthy controls, whereas the IL-4 production was comparable in the examined groups. By means of FACS-analysis of peripheral blood mononuclear cells (PBMC), we found that the relative amount of T cells was increased and the NK-cells relatively decreased in children with atopic dermatitis, which has been described in adult patients with atopic dermatitis. Furthermore the fraction of CD4CD45RO positive cells (memory T cells) tended to be higher in atopic dermatitis. The data obtained show more profound differences in cytokine pattern, isotype production and cell distribution in small children with atopic dermatitis than in children developing asthma.

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DIAGNOSIS OF ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS (ABPA) IN CYSTIC FIBROSIS (CF)

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In patients with CF the importance of serological investigations are increased as the clinical diagnostic features of ABPA resemble those of pulmonary bacterial infections. However elevated specific IgE to Aspergillus fumigates (Af) while being sensitive, gives false positives as non ABPA patients may develop asymptomatic Type I sensitivity. We previously identified and isolated a 66KD allergenic protein of AF. An Enzyme Linked Immunosorbant Assay (ELISA) was used to detect specific IgE to this 66KD protein, and IgE to the un-fractioned AF extract was detected using a Radio Immunoassay. Serum was obtained from patients with ABPA (14), no ABPA but type I sensitive (27), and no ABPA & non allergic (38) who attended the paediatric cystic fibrosis clinic. Elevated IgE detection using the un-fractioned extract was 92.9% sensitive and 58.5% specific for diagnosis of ABPA while the new ELISA using the 66KD allergen maintained the 92.9% sensitivity but increased specificity to 78.5%. It is hoped that the use of this protein will aid in the diagnosis of ABPA particularly in patients with CF.