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DUST MITE ALLERGY AND RESTRICTION BY HLA-CLASS II IMMUNE RESPONSE GENES - V. Stephan', V. Schmid', V. Wahn' and J. Kuehr". University Children's Hospital 'Düsseldorf and "Freiburg, Germany

From a population-based study cohort of 1812 elementary school children we selected 129 nine year old unrelated children to investigate the clinical relevance of HLA-class II molecules in the regulation of immune response to the dust mite allergen Der p I. Individuals were selected on the basis of skin prick test results which were validated by measurement of specific IgE (sIgE). Three different groups were defined according to sIgE determinations: Group I (n=20) included controls without detectable sIgE; in group II (n=22) were patients with sIgE to antigens other than Der p I; group III patients (n=85) had sIgE to Der p I and other allergens. In total, 43 different HLA class II alleles were determined by sequence specific oligonucleotide typing with PCR amplified patient DNA. Gene frequencies were determined for every allele in the three study groups and no statistically significant difference could be demonstrated between children sensitized to Der p I and controls. In addition, the association of HLA class II haplotypes with clinical phenotypes was investigated. A positive association was found between DRB *0100/*0300/ *1100 and/or DPB *0201/*0401 in patients suffering from asthma, hay fever or atopy ($p \leq 0.01$). Detection of a rising number of the above mentioned alleles was associated with an increasing risk of presenting with a clinical history of allergic disease. Similarily, there is evidence for a negative association between the presence of DQB *0303/*0503 and/or DRB *0200/*0700 and a clinical history of eczema, hayfever and atopy ($p \leq 0.01$). Thus, the findings of our epidemiological study do not confirm the clinical relevance of HLA-class II molecules for IgE responses to dust mite allergen. However, certain HLA haplotypes were clearly associated with a significantly increased risk for the presence of allergic disease.

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IGG SUBCLASSES AND ANTIBODIES TO STREPTOCOCCUS PNEUMONIAE IN IMMUNODEFICIENT CHILDREN WITH CHRONIC LUNG SUPPURATIONS

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We studied 17 immunodeficient children 4-14 years old (9 with hypogammaglobulinemia, 8 with selective IgA deficiency) all having chronic lung suppurations. The highest rate of *S.pneumoniae* colonization was in children with IgA deficiency (up to 50%) with noncapsular *H.influenzae* found in 43%. Antibody levels to *S.pneumoniae* capsular polysaccharides, C-polysaccharide, protein antigens were studied in serum, saliva and bronchoalveolar lavage fluid by ELISA; IgG subclasses in serum - by radial immunodiffusion. All patients had absent or very low levels of pneumococcal IgA-antibody in secretions. In spite of the presence of serum IgG-antibody (even their high levels in selective IgA deficiency) all children had severe suppurations indicating the major role of local immune response in bacterial clearance from the respiratory tract. It also suggests that serum IgG antibodies do not pass in sufficient quantity into bronchial secretion due to a peribronchial fibrosis. Low serum IgG-antibody levels were found in children with hypogammaglobulinemia, however two patients with combined IgA - IgG subclass deficiency (IgA plus IgG1,IgG3,IgG4 and IgA plus IgG4) had almost normal serum antibody level probably due to the relation of pneumococcal antibody to IgG2. Clinical data indicate that different rate of hypogammaglobulinemia expression may explain the diversity in manifestations of primary humoral immunodeficiency.

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THE RESULTS OF VARIOUS LUNG FUNCTION TESTS AMONG ATOPIC AND NON-ATOPIC ESTONIAN SCHOOLCHILDREN

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Four-step methacholine provocation test (cumulative doses of methacholine, respectively 100, 300, 700 and 1100 µg), exercise challenge test and assessment of peak expiratory flow variability (four times daily for two weeks) were used in the cross-sectional study in order to reveal the prevalence of bronchial hyperreactivity among the Estonian schoolchildren. The study included 458 children from Tallinn (industrialized capital, situated on the cost) and 653 children from Tartu (inland, university town) aged 10-12 years. The prevalence of positive skin prick test was 13% in Tallinn and 8.3% in Tartu. Surprisingly the number of positive responses in the methacholine challenge tests was significantly higher in Tartu than in Tallinn (31% and 19% respectively). Similarily, decrease of FEV_1 value more than 15% was observed in exercise challenge tests (18% and 6% respectively). There was a good correlation between the data obtained in the methacholine and exercise challenge tests (p=0.006). The findings show that other factors than sensitization to allergens are important for bronchial hyperreactivity.

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ATOPIC MANIFESTATIONS OF PRIMARY IMMUNE DEFICIENCIES

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During screening of 367 children with primary immune deficiencies (PID) for allergic manifestations the most frequent atopic finding was dermatitis, established in all patients with Wiscott-Aldrich syndrome (n=11) and hyper-IgE syndrome (n=20), in 25 from 108 patients with selective IgA deficiency (sIgAd) and in 2 from 19 patients with chronic granulematous disease. Bronchial asthma or wheezing bronchitis were diagnosed in 26 patients with sIgAd. Among the patients with other PID, including 113 patients with hypogammaglobulinemia (congenital X-linked, common variable, with elevated IgM), 66 patients with ataxia-teleangiectasia and 30 patients with chronic mucocutaneous candidiasis atopy was absent, apparently due to inability of such patients to produce IgE-antibodies. The occurence of urticaria, predominantly based on non-specific phenomenon of histamine liberation, and non-atopic dermatitis was the same in different forms of PID.

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ONCE VERSUS TWICE DAILY DOSING OF CEFTAZIDIME IN THE PRETERM INFANT. John N. van den Anker, Rik C. Schoemaker, Henriette M. Broerse, Wim C.J. Hop, Herman J. Neijens, Ronald de Groot. University Hospital Rotterdam/Sophia Children's Hospital, Departments of Pediatrics and Epidemiology & Biostatistics, Rotterdam, and Centre for Human Drug Research, Leiden, The Netherlands.

Ceftazidime (CAZ) pharmacokinetics were studied on day 3 of life in 28 preterm infants who were randomized at birth to receive once or twice daily 25 mg/kg CAZ. Thirteen infants were treated once daily, 15 infants twice daily. Blood samples were collected from an arterial catheter at 0, 0.5, 1, 2, 4, 8, 12h after the CAZ dose in both groups and an additional sample at 24h in the once daily group and analyzed by HPLC-assay. The results were (mean ± SD):

	Once daily	Twice daily	p-value
Gestational age (wks)	29.1 ± 2.0	29.6 ± 2.2	NS
Birth weight (g)	1168 ± 309	1141 ± 400	NS
Serum half life (h)	8.15 ± 1.18	7.09 ± 1.66	NS
Volume of distribution (ml)	376 ± 120	350 ± 138	NS
Total body clearance (ml/h)	32.4 ± 10.9	35.7 ± 16.8	NS
Trough levels (mg/l)	13 ± 5	42 ± 13	<0.001

Conclusions. 1. Twice daily dosing of 25 mg/kg CAZ results in high serum trough levels of CAZ. 2. Dosage reduction from twice to once daily results in a significant decrease of serum trough levels of CAZ to more desired levels. 3. The frequency of CAZ administration may be adjusted after the efficacy of once daily 25 mg/kg CAZ has been studied.

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THE VALUE OF THE LATERAL CHEST RADIOGRAPH IN THE DIAGNOSIS OF PULMONARY TUBERCULOSIS IN CHILDREN.

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The aim of the study was to assess the value of the lateral chest radiograph in children being investigated for tuberculosis (TB). Material and Methods: In a prospective study of 449 children the chest radiographs (PA and lateral) were assessed. The children were drawn from 2 groups. Firstly, those with symptomatic disease and secondly, asymptomatic children in contact with an adult with active pulmonary TB. Results: In 13% of the children with proven TB and 19% of children with probable TB (WHO criteria) the hilar glands were visible on the lateral chest radiograph only. Hilar glands were present only on the lateral chest radiograph in 11% of asymptomatic children in contact with an adult with active TB. Conclusion: These data suggest that lateral chest radiographs are essential in the evaluation of children suspected of having PTB and in children in contact with an adult with active disease.