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CIRCADIAN PULMONARY RHYTHMS IN ASTHMATIC CHILDREN AFTER WITHDRAWAL OF MEDICATION.

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Three days after withdrawal of maintenance treatment, peak expiratory flow rate (PEFR) was measured in 38 asthmatic children every four hours during 24 hours on three consecutive days. In all children a circadian rhythm, with a nocturnal fall in PEFR existed. The interindividual amplitude varied from 2 to 65%. Two groups of 9 patients each, were selected from the total study population based on a difference in PEFR values between 16.00 and 04.00 hours of more then 20% or less then 15% on three study days. The remaining children did not fit in both subgroups because the 16.00 and 04.00 hour difference in PEFR values was not persistent. The clinical data of this group, however, were comparable with both subgroups.
In the group with a 16.00 - 04.00 hours difference of more then 20% (mean ± SD: 31.5 ± 8.5) both the mean PEFR value and the PEFR value measured at 04.00 hours on day 6 was significantly decreased as compared to the values obtained on day 4. Moreover the amplitude of the PEFR still increased significantly from day 4 to day 6. In the group with 16.00 - 04.00 hours difference of less then 15% (mean ± SD: 6.4 ± 2.7) no increase in amplitude and decrease in mean PEFR values during day 4 and day 6 were observed. With regard to FEV_1/FEV_1 predicted, PC_{20} Histamine and skintests no significant differences were observed between both subgroups. In retrospect the group of children with the large amplitude seems to be more inhaled steroid dependent.

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CIRCADIAN ENDOCRINE FUNCTION IN CHILDREN SUFFERING FROM NOCTURNAL ASTHMA

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In 28 children (5-15 years, 15 with noct. asthma, 13 without asthma) epinephrine, norepinephrine, dopamine and C-AMP from the blood, and cortisol, histamine from the urine was tested between 4.00 p.m. and 8.00 a.m. in 4 hrs. intervals. We found signifikant more epinephrine and signifikant less dopamine in children with nocturnal asthma. C-AMP was also decreased, but not statistical different. There was more histamine in children with nocturnal asthma, individual different data did not allow statistic evaluation. No different results were found in norepinephrine, C-AMP and cortisol in asthmatic and non - asthmatic children. There was a phase shift of the cortisol decrease from 12.00p.m. to 8.00 p.m. compared to adult persons.
These results could be understood as a reaction to a ß-2 receptor dysfunction in the bronchial system of asthmatic children. The increase of dopamine might be the result of a modulated synthesis of katecholamines in children suffering from nocturnal asthma bronchiale.

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RECOVERY OF LUNG FUNCTION FROM HISTAMINE CHALLENGE IN ASTHMATIC CHILDREN.

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Recovery of lung function with time after challenge with histamine was studied in 45 asthmatic children (14 girls and 31 boys) aged 8 to 15 years. The children were allergic to house dust mite and had an increased bronchial reactivity to histamine. Lung function tests and histamine challenge were performed under standardized conditions. Baseline FEV_1, the provocation concentration producing a 20% fall in FEV_1 (PC_{20}) for histamine, the fall in FEV_1 after inhaling histamine and age were compared with time of complete recovery of FEV_1. A significant correlation was found between PC_{20} (histamine) and time of complete recovery ($p=0.023$). No significant correlation was found between total recovery time and the other parameters. Baseline FEV_1 was compared with PC_{20} for histamine. A significant correlation could be demonstrated between pretest bronchial obstruction (baseline FEV_1) and the PC_{20} for histamine ($p=0.028$). FEV_1 recovered within 75 min. to pretest values in all but two children. Conclusions:
The response to histamine is related with pretest bronchial obstruction. In a few children recovery from histamine challenge is prolonged. In these children further provocation test on the same day should be avoided. The recovery time is related with the dose of histamine administered.

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ANTIBODY RESPONSE TO PNEUMOCOCCAL POLYSACCHARIDES BY ADULT AND NEONATAL B LYMPHOCYTES IN VITRO

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Bacteria carrying capsular polysaccharides (Str. pneumonia, H. influenza) are major causal agents for infections in infants and children, especially during the first 2 years of life. Immunisation with polysaccharide vaccines (eg. Pneumovax) does not result in production of specific antibodies nor does it confer clinical protection. We have initiated in vitro studies with Pneumococcal polysaccharides (PS) to address the cellular basis of the relative late appearance in ontogeny of anti-PS responsiveness. Type 4 PS (PS4) can provisionnally be classified as a TI-2 antigen in humans based on the observations that purified B cells cultured in vitro with 10^{-8} µg/ml PS4 are able to generate an antibody response and that this response is augmented by the addition of T cells and growth factors. Even in this latter system, neonatal B cells isolated form cord blood fail to respond to PS4. The culture system used does however allow the differentiation of B cells reactive with T dependent antigens like eg. ovalbumin. In order to evaluate the concept that in man the anti-PS response is derived from a particular B cell subset we have separated adult peripheral blood B cells on basis of expression of FMC7. The anti-PS4 response is found mainly, but not exclusively, in the $FM7^{+ve}$ B cell subset. The selective unresponsiveness of neonatal B cells to TI-2 antigens is however not due to the absence of $FMC7^{+ve}$ B cells because, unlike adult B cells of which about 50% are $FMC7^{+ve}$ 100% of neonatal B cells are $FMC7^{+ve}$

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ANTIPNEUMOCOCCAL VACCINATION DURINGGAMMAGLOBULIN REPLACEMENT THERAPY

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We want to report the preliminary results of an ongoing study documenting the beneficial effects of active pneumococcal vaccination during gammaglobulin replacement therapy in young children, with low IgG_2 subclass levels. Four children suffering from early chronic rhinitis and from respiratory problems were representing abnormal low levels of plasma IgG_2 and an absence of salivary IgA (twice checked). Surinfection was relapsing twice a month and streptococcus pneumoniae was isolated at least on four occasions from cultures of nasal secretions. The allergic check-up was non-contributive, nor the evaluation of plasma immunoglobulin levels, complement system and neutrophil function. Repeated IM injections of gammaglobulins every three weeks, subjectively improved the patient status but did not modify the frequency of relapsing infections, nor the IgG_2 levels sequentially reassessed before each injection. With the consent of the parents, antipneumococcal vaccination then was given simultaneously to the last gammaglobulin injection. In all cases, we observed a total remission on the recurrent infections and a significative increase of their IgG_2 levels ($p<.001$) that was sustained at least in the next two months in spite of the arrest of gammaglobulin treatment. These results suggest that low levels of IgG_2 are associated to a pneumococcal induced paralysis and that vaccination can be efficient when performed during gammaglobulin therapy.

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RECURRENT INFECTIONS OF RESPIRATORY TRACT WITH $GRAM^-$ BACTERIA DUE TO OPSONIC DEFECT IN FACTOR D-DEFICIENCY.

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Three siblings, two boys and one girl, suffered from recurrent infections of the respiratory tract, almost exclusively caused by H.influenzae, from todler's age onwards. Non-immunological causes, e.g. immotile cilia syndrome, were excluded. Extensive testing of the immunological defence capacities revealed consistently an impaired alternative complement pathway(AP_{50}) and serum levels of all major immunoglobulin classes at the lower borderline of normal. There was no absence of one of the IgG subclasses. The impaired AP_{50} was due to a functional deficiency of complement factor D. However, antigen factor D, as determined by a sandwich ELISA technique, revealed normal levels. Opsonic activity of serum from the three patients for S.aureus was similar to that of serum from healthy adults, but E.coli, opsonized by the patients' sera were ingested at abnormally decreased rate. It is hypothesized that to combat $Gram^-$ infections C_{3b}-mediated opsonisation is attained via the alternative pathway in case insufficient IgG antibodies are available. The latter might have been the case in these children, in association with an impaired alternative pathway-mediated opsonisation. The discrepancy between the antigenic and functional factor D levels needs further investigation.