INTRODUCTION

At the 1987 meeting of the European Pediatric Respiratory Society (EPRS), invited lectures and free papers presented a cross-sectional overview of European activities in one of the youngest subspecialties of pediatrics. The researchers—a multilingual group with widely differing professional, national, and cultural backgrounds—convened for presenting their work, exchanging ideas, educating each other, and, thereby, serving the common goals represented by the Society.

The following Abstracts of the free papers read at the meeting, while fairly accurately presenting current European research activities with lung diseases in children, also feature a certain lack of scientific homogeneity. This reflects the marked differences in the state of development of pediatric pulmonology in various countries and at their respective institutions. In an increasing number of teaching centers the subspecialty is gaining recognition and support, and is thus prospering; but the majority of European pediatric institutions still lack highly educated personnel as well as specialized diagnostic and therapeutic facilities. There are many reasons for this. Basic structural differences in health care services and educational programs between various countries, together with factors related to more fundamental differences between the peoples of the continent, often hamper the exchange of ideas and dissemination of expertise, which would be the prerequisite for the development of uniform professional standards. Also, frequently voiced misgivings about further subspecialization within pediatrics are, at times, aimed at pediatric pulmonology. However, by holding back progress in any subsegment of pediatrics, even some of the most influential leaders of the conservative pediatric establishment may, in fact, weaken what they intend to protect: the integrity of pediatrics itself. Last, but not least, pediatric pulmonology is struggling to establish itself in a period of wide-spread reductions in medical and academic budgets.

Yet, against all these odds, the new subspecialty is thriving in most of Europe, pioneered and supported by a modest number of dedicated, dynamic young researchers. To date, this lively crowd congregates in two societies: the EPRS and the more physiologically oriented Pediatric Group of the European Society for Clinical Respiratory Physiology (SEPCR). The two organizations have established close ties and share the leaders in the field among their membership. In addition, national societies and working groups have been established, providing momentum on the local scenes of different countries. The recent growth of all these organizations provides the pleasure of witnessing a steadily increasing expertise, improving academic standards, and dedicated research, that are gaining in both quantity and quality. The Helsinki meeting can rightfully be considered as a milestone in this ongoing development.

—MAXIMILIAN ZACH, MD
Graz, Austria
 European Assistant Editor
Progress in our understanding of pulmonary immunopathology will help to lower the risks of disease, to improve the treatment of infections and possibly to develop pharmacological means of stimulating compromised or compensatory immune mechanisms. As a rule, selective defects of pulmonary immune mechanisms will lead to infection if additional defects develop or coexist, e.g. IgG subclass deficiencies in addition to IgA deficiency. Combined humoral immunodeficiencies predispose to recurrent or chronic infections with purulent bacteria. In congenital T-cell deficiency viral, fungal, protozoal and mycobacterial organisms prevail. Immunodeficiencies following HIV, EBV or other viruses result in clinical syndromes resembling congenital immunodeficiency. In contrast, immunosuppression causes a wide spectrum of immunodeficiency depending on the treatment regimen. Most respiratory infections in such patients result from aspiration or hematogenous spread of endogenous organisms. Reactivation of Herpes Virus or Cytomegalovirus and acquisition of Measles, Legionella and Pneumocystis carinii are important other causes of infection. In contrast, Mumps, Rubella, Hepatitis B, EBV and Parainfluenza Type I, Polio, Echo and Coxsackie viruses appear of little significance in this respect. Analysis of several series of pulmonary infections in immunosuppressed children has shown Pneumocystis to be the most frequent organism followed by viruses, mixed infections, fungi and bacteria. This type of analysis underestimates common bacteria which respond to the usual treatment regimen. All types of immunodeficiency are characterized by decreased inflammatory responses and accordingly by the absence or by delayed appearance of radiological signs.
SUCCESSFUL TREATMENT OF INVASIVE ASPERGILLUS INFECTIONS IN TWO CHILDREN WITH CHRONIC GRANULOMATOUS DISEASE.

H.J. Neijens, S.M.P.P. de Muijnck Keizer-Schraa, G. Dzele-Danilovic. Department of Pediatrics, Sophia Children's Hospital/University Hospital Rotterdam, Gouda

Chronic granulomatous disease (CGD) is characterised by impaired neutrophil function which is often accompanied by Staphylococcal and sometimes by fungal infections. The treatment of the fungal infections is difficult and a high mortality rate is the rule. We treated two children with CGD and Aspergillus infection of the respiratory system plus other sites, using itraconazole, a new broad spectrum, orally active triazole antifungal.

Patient RH is 14 years old, having x-linked CGD with absent O2 consumption and cytochrome B, developed Aspergillus infection in the lung and bone. Treatment with aphotericin B in normal and twice normal dose was unsuccessful, as judged by clinical observation and persistent presence of the fungus. Itraconazole was found to suppress the inflammatory process, as judged by clinical response, X-ray and antibody level. A serum level of ≥2000 ng/ml was needed for this effect which required an oral dose of ≥400 mg/24h. A decrease in dose resulted in resolution of pain which faded away after reestablishment of a serum level above 2000 ng/ml. No side effects with respect to biochemical or endocrinological variables were encountered, notwithstanding a three year treatment period.

Patient CT is 7 years old, having x-linked CGD with a decreased O2 consumption and cytochrome B inactivity. A right upper lobe infiltration was found from which Aspergillus could be cultured. After failure with aphotericin B, treatment with itraconazole with serum levels between 600-1600 ng/ml resulted in gradual disappearance of the inflammatory process in about six months, without side effects. Thus, Aspergillus infection in two CGD patients could be treated with itraconazole without side-effects. Relationships of dose and concentrations in serum, leucocytes and tissue will be discussed.

ETIOLOGY OF CHRONIC SUPPURATIVE LUNG DISEASES IN CHILDHOOD

M. Nikolaizik, J. O. Warner

Bronchiectasis is only a descriptive label and must have the consequence of further investigations to evaluate the predisposing causes of the illness. We are now presenting 40 children with supportive lung diseases who were referred during the last 5 years (aged 15–15 yr), included are only patients with irreversible damage of bronchial walls shown by bronchography, other histology, or in cases of known etiology a persistent radiological changes and matched ventilation defects on isotope scanning.

Six children (15%) had a congenital malformation (William- Campbell syndrome, absent pulmonary valve syndrome, lung sequestrations, cystic adenomatoid and hamartomatous malformations). Six children (15%) suffered from primary dyskinetasia, and one child from a cystic fibrosis-like illness, however with negative sweat test results (otherwise CF excluded). One child had a history of pain, and one of a nut aspiration. Nine children (22.5%) had an immune defect (neutrophil defects of chemotaxis, migration or phagocytosis, T-cell defect, hypergammaglobulinemia, Hyper-IGE syndrome and AIDS; however in a total of 16 children (40%) at least slight abnormalities of immune function were found including three children with bronchiolitis obliterans and one with bronchiectasis post-pertussis.

In 11 children no predisposing factors were detectable. One child suffered from Warner-Marshall syndrome, and ten (25%) had a history of severe pneumonia. In 7/10 Haem. influenzae was cultured from sputum with three Ampicillin resistant strains.

A diligent search for the underlying cause of bronchiectasis (excluding cystic fibrosis) is likely to be fruitful if 75% of cases.

BACTERIAE AND VIRUSES IN RECURRENT RESPIRATORY INFECTIONS AFTER BRONCHIOITIS

Carlsen KH, Eng J, Ørstavik I.
Department of Pediatrics and Microbiological laboratory, Ullevål Hospital, Oslo, Norway.

After acute bronchiolitis in infancy 51 children were prospectively followed until two years of age and clinically examined at all cases of respiratory infection and wheezing, and at regular control examinations at 1, 1 1/2 and 2 years of age. At all occasions nasopharyngeal swabs were taken for bacteriological cultures, and at all respiratory infections nasopharyngeal aspirates were drawn for virological examination by rapid immunofluorescence and cell cultures. A virus infection was diagnosed in 68 of 158 infections examined, 31 with wheezing. Possible positive bacterial culture findings were found in 63 of 141 infections examined, and in 52 of 139 control examinations (P<0.2). More positive bacterial culture findings were done in otitis media than in other infections (P<0.005), but not more often in infections with wheezing, and not in children with especially frequent wheezing and infections. Staphylococcus pneumoniae and Haemophilus influenzae were the bacteriae most often isolated. Positive bacterial culture findings did not occur more often in cases with positive virological findings (P<0.2). RS virus and parainfluenza virus infections were more often related to wheezing then than influenza virus and adenovirus. The most frequent viruses among nursery children were adenovirus and parainfluenza virus. The role of respiratory virus infections in small children with recurrent respiratory infections is well established. Apart from in otitis media, bacterial infections seem to play a minor role, and the bacteriae isolated probably represent colisation of the nasopharyngeal space in many cases. This is an important question for children who often receive frequent courses of antibiotics.

A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF DEXAMETHASONE AND RACEMIC EPINEPHRINE IN THE TREATMENT OF GROUP A STREPTOCOCCAL POST-ABSCESIONS AND PNEUMONIA IN INFANTS AND CHILDREN

Kuusela A-L, Vaestkari T
Department of Paediatrics, Tampere University Central Hospital, and Department of Clinical Sciences, University of Tampere, Tampere, Finland.

Despite of study the treatment of acute viral group A Streptococcus post-infections examined, with randomized amplified and not in children with especially frequent wheezing and infections. Staphylococcus pneumoniae and Haemophilus influenzae were the bacteriae most often isolated. Positive bacterial culture findings did not occur more often in cases with positive virological findings (P<0.2). RS virus and parainfluenza virus infections were more often related to wheezing then than influenza virus and adenovirus. The most frequent viruses among nursery children were adenovirus and parainfluenza virus. The role of respiratory virus infections in small children with recurrent respiratory infections is well established. Apart from in otitis media, bacterial infections seem to play a minor role, and the bacteriae isolated probably represent colonisation of the nasopharyngeal space in many cases. This is an important question for children who often receive frequent courses of antibiotics.

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Kuusela A-L, Vaestkari T
Department of Paediatrics, Tampere University Central Hospital, and Department of Clinical Sciences, University of Tampere, Tampere, Finland.
BRONCHIAL HYPERREACTIVITY

EFFECTS OF EXPOSURE TO IRRITANT GASES ON LOCAL ALLERGIC SENSITIZATION IN THE GUINEA PIG

F. Riedel, M. Kramer, C. Scheibenbogen, C.H.L. Rieger
Section of Pediatric Pulmonology and Immunology, Department of Pediatrics, Philippus-University Marburg, FRG

Exposure to irritant gases causes inflammatory reaction of bronchial epithelium and increased permeability for macro- molecules. This condition facilitates access of antigens to immunocompetent cells of the bronchial mucosa. We studied the effect of sulphur dioxide (SO2) inhalation on local bronchial sensitization to inhaled antigen in the guinea pig. Exposure to SO2 (0.1 - 4.3 - 16.6 ppm) was performed in a 20 ltr. exposure chamber for 8 hours on 5 consecutive days while temperature, moisture and concentration of SO2 were monitored and kept constant. On the last 3 days SO2-exposure was followed by inhalation of 0.1% ovalbumin for 45 min. After 7 days of rest specific bronchial provocation with inhaled ovalbumin (0.1%) followed by plethysmographic measurements of compressed air (Dorsch et al., Pflügers Archiv 391:126, 1981) were performed. Specific antibodies against ovalbumin were measured in serum and bronchoalveolar fluid by ELISA inhibition assay before exposure and at the end of investigation.

The SO2 exposed group (n = 20) showed in 16 - 100% positive bronchial reactions (obstruction) to inhaled ovalbumin, depending on the concentration of SO2, while the control group without SO2-exposure (n = 12) showed no reaction (p < 0.05). Compressed air after antigen inhalation (as measurement of bronchial obstruction) was significantly higher in the exposed group compared to the control group (p < 0.001). For all SO2-concentrations, ovalbumin specific antibodies increased in bronchoalveolar fluid and serum in the SO2 exposed group compared to the control group (p < 0.05). It is concluded from these results that damage of bronchial mucosa induced by low and medium concentrations of SO2 facilitates local allergic sensitization in the guinea pig.
INCIDENCE OF TUBERCULOSIS AMONGST LOW BIRTHWEIGHT CHILDREN AT SCHOOL AGE

Ming Chan, Charles Noble-Jamieson, Michael Silverman
Department of Paediatrics, Royal Postgraduate Medical school, Hammersmith Hospital, London

Asthma-like symptoms are common following preterm birth. Increased non-specific airway responsiveness has been described in small groups of prematurely born children at school age. Its prevalence amongst these children remains unknown. We aim to determine its prevalence and its relationship to perinatal and subsequent health.

We are currently doing detailed lung function studies on a cohort of children at 7 years, whose birthweight was below 2000g. We employed the rapid method described by Zan (Thorax 1983; 38:760-5) to measure the airway response to histamine. Doubling doses of histamine were administered until the fall in peak expiratory flow rate (PEFR) exceeded 20% or until a maximum cumulative dose of 600µl had been given. The dose required to cause a 20% fall in PEFR (PD20) was obtained by linear interpolation from the dose-response curve constructed by plotting PEFR against the log of cumulative dose of histamine. Of the first 98 children in the cohort, 87 completed the tests satisfactorily. A cohort of 110 pupils of equivalent age (mean 6.95, range 6.1 - 8.0 years), recruited from three local schools, formed the reference population.

There was a significant difference between the low birthweight cohort and the reference population (p<001).

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Results:

| Total responders | PD20 | PD60 |
|-----------------|------|------|
| Non-normal      | 110  | 64%  |
| Low birthweight | 87   | 20%  |

There was a significant difference between the low birthweight cohort and the reference population (p<001).

The results of our study carried out so far suggested that the frequency distribution of the airway response to histamine is shifted to the left compared to that of the reference population.

AIRWAY HYPERREACTIVITY CAN BE ATTENUATED BY ACUPUNCTURE

U.Wagner, M.Götz
Department of Paediatrics, University of Vienna, Vienna Austria

Bronchial hyperreactivity is characterized by bronchoconstriction induced by stimuli such as exercise, airway cooling and pharmacologic agents. The aim of this presentation is to establish the possibility of reduction of bronchial hyperreactivity by acupuncture.

In ten children, clinically manifesting as a stable exercise induced asthma, with reversible bronchial hyperreactivity established by methacholin inhalation challenge (PD20 182.1 mg/ml), ten laser acupuncture sessions were administered to specific acupuncture points. Clinical symptoms were scored throughout sessions and methacholin inhalation challenges were repeated at the end of these and also two weeks after the end of acupuncture treatment. With the exception of initial short-term disodiumcromoglicate (BASC) treatment in one patient no antiobstructive treatment was administered.

Clinical improvement was observed in nine patients (exercise tolerance, rhinitis). Both Raw and FEV1 showed statistically significant diminished increases/decreases at the end of treatment (Raw % increase p = 0.01; Raw absolute p = 0.001; FEV1 absolute p = 0.02; n=10. P02 p = 0.05; n = 6) and two weeks after cessation of acupuncture (Raw % increase p = 0.02; Raw absolute p = 0.001; n = 6). The P02 was increased after two weeks after ending acupuncture treatment vs. initial values (182.1 vs. 295 mg/ml; p = 0.02; n = 8).

These findings suggest a positive influence of acupuncture in treatment of childhood asthma.

ASTHMA, BRONCHIOLITIS AND LUNG FUNCTION

COMPARISON OF MAST WITH RAST, SKIN TEST AND CLINICAL HISTORY RELATED TO ENVIRONMENTAL FACTORS IN ASTHMATIC CHILDREN

Jill A Price, J Reiser, Joan L Longbottom and J O Warner
Cardiothoracic Institute, Brompton Hospital, London, U.K.

Thirty three children with asthma were selected for comparison of MAST, RAST and skin test with clinical history. Results from the MAST profile were compared with 8 skin test antigens and 4 individual RAST complexes. Quantitation of two domestic environmental allergens was performed on vacuum dust from the children's mattresses. The overall sensitivity for MAST was 65%, Alternaria 64%, Aspergillus 85%, Cladosporium 64%, Penicillium 94%. The overall sensitivity for MAST was 65% and for RAST was 90%. However, there was a good percentage agreement: grass 70%, cock 85%, dog 61%, house dust mite 85%, Alternaria 64%, Aspergillus 85%, Cladosporium 64%. Sensitivity for MAST repeasted.

Comparison of MAST with RAST showed a change between positive and negative results. The presence of Fel dI, Der fI and viable moulds were compared with the MAST and RAST results in relation to skin tests. Ten patients were selected at random and the MAST repeated. 85% of tests were reproducible (r = 0.977) and only 4% showed a change between positive and negative results.

MAST is a simple test performed simultaneously in vitro for up to 35 different allergens. It compared favourably with RAST and skin test, but in some cases appeared to support the clinical history more accurately than either test in the paediatric group.

INCREASED PREVALENCE OF AIRWAY HYPER-RESPONSIVENESS TO HISTAMINE AMONGST LOW BIRTHWEIGHT CHILDREN AT SCHOOL AGE

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The differences in steady state serum concentration of theophylline are dependent on individual rate and extent of absorption and elimination. The assessment of individual pharmacokinetic parameters in asthmatic children is often difficult while the number of collected blood samples is insufficient. The noninvasive collection of saliva samples offers advantages above all in children. Saliva reveals the concentration of free pharmacologically active form of most drugs. In our study the estimation of theophylline disposition in blood serum and saliva during a 3-week treatment of 20 asthmatic children with sustained release theophylline /Euphylline CA/ was performed. A significant and linear correlation between serum and saliva was found. The ratio saliva:serum is constant and stable for every patient. The salivary concentration of theophylline can be used to predict the serum drug concentration. Theophylline estimation in saliva permits the assessment of all pharmacokinetic parameters. It is a convenient and noninvasive alternative with important advantages for children.

The role of recurrent respiratory viral infections in the manifestation of childhood asthma

T. Nicolai, A. Pohl, Universitäts-Kinderklinik, München, FRG

Infections with respiratory viruses can induce bronchial hyperreactivity and precipitate asthmatic attacks. It has been speculated that asthmatic children are more prone to such infections than other children, but this is controversial. Some researchers believe that childhood asthma is mainly allergic in origin.

Four groups of children with recurrent wheeze/asthma (A), n=59, recurrent respiratory infection without wheeze (B) n=30, neurodermitis without asthma (N) n=33 and a control group with no history of asthma (C) n=48 were examined for the presence of IgE antibodies against 5 important respiratory viruses.

Serum was tested by immunofluorescence and slides covered with RSV, Adenovirus and Paramyxovirus type 1-3 infectious indicator cells. Titers were measured for each virus and a mean titer for all five viruses was calculated for every patient. The mean titer was thought to reflect frequency and intensity of contact with common respiratory viruses, although an increased immunological reaction in asthmatics can not be excluded.

A clearcut age dependency of this titer was found in all patient groups with the steepest increase between age 2 and 5. This increase was more marked and occurred earlier in groups A and B. The mean titer was significantly higher in A (4.89) than in C (2.96) and N (3.00), p<0.001. No significant difference was found between A and B (5.19).

Mean serum IgE (% of reference values) was significantly higher in A (308%) than in C (91%) p<0.001 and B (125%) p<0.01. If age related values of control patients (mean±SD) were used as cutoff points 25% of asthmatics had elevated mean antiviral antibodies only, 22% elevated IgE only, and 21% both. Atopic patients without asthma (N) with very high IgE did not show serological signs of recurrent viral infections.

These results suggest that respiratory viral infections are relevant triggers of asthma in genetically disposed children. This raises the question if asymptomatic children with genetic risk factors would benefit from the prevention of such infections.

METOCLOPRAMID IN THE TREATMENT OF CHILDREN WITH BRONCHIAL ASTHMA AND GASTROESOPHALIC REFLUX (GER)

Bauer M, Mustala L, Vesikari T
Department of Paediatrics, Tampere University Central Hospital, Tampere, Finland

30 children with bronchial asthma were found to have a significant GER, defined as pH less than 4 for 5 minutes or longer in esophageal pH long-term registration during sleeping time. All the children were receiving appropriate treatment for asthma at the time of entering the study. The children were randomized to receive either metoclopramid 0.5 mg/kg (n=14) or no metoclopramid (n=16) before sleeping time. Both groups were comparable for age, number of hospital days before the study, and severity and frequency of GER. The treatment with metoclopramid was continued for 6 months, and the follow-up time was 3.7 and 1.6 years, respectively, in the two groups. During and after the 6 months' treatment period there were no differences in the need of asthma medication or of hospitalization between the two groups. However, the occurrence of night cough decreased significantly more (p<0.01) in the metoclopramid group than in the controls. We conclude that GER should be actively sought in children with bronchial asthma, and, when found, treated with metoclopramid.

EXTRINSIC ALLERGIC ALVEOLITIS IN CHILDREN.

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In order to evaluate the clinical picture and radiological, immunological as well as pathophysiological changes forty cases of Allergic Alveolitis /AA/ diagnosed and treated at our Institute have been analysed.

On the basis of symptoms, three clinical forms of the diseases were being diagnosed: acute AA - 27 cases /67.5%, subacute AA - 8 cases /20% and chronic AA - 5 cases /12.5%.

Radiological lesions were classified into: miliary - like /22 cases/, focal /14 cases/ and band-shaped /32 cases/. Contrary to generally accepted views, we observed X-ray lesions also in lung apices in 57.5% of cases and no lesions in the pleura.

The most frequent positive precipitation tests were found against antigens prepared from pigeons excreta/54.5%,/ and from chicken, pigeon and duck sera /39%. The leukocyte inhibition migration tests were also most frequently positive using antigens from chicken and pigeon sera.

Lung function testing included spirometric examination, gas exchange and static lung compliance were carried out in all children and abnormal results of lung function parameters were observed mainly in children with acute and subacute clinical forms of the diseases.
LUNG FUNCTION AFTER RESECTION OF PULMONARY METASTASES IN CHILDREN AND ADOLESCENTS

K. Paul (+), L. Swoboda (++), I. Vogt-Maykopf (++); University Children's Hospital, Heidelberg, FRG; ++ Klinik Schillerhöhe, Garlingen, FRG; +++ Krankenhaus Rohrbach, Heidelberg, FRG.

In order to evaluate respiratory impairment and the time course of recovery after thoracotomy for suspected metastatic lesions of the lung we studied lung function prior and following 24 surgical explorations in 15 patients (13-18 years). Median sternotomy was chosen in 21 operations. 1-28 metastases or suspected areas were removed mostly by wedge resection. 11 operations (op) were repeated thoracotomies (2-6).

Lung function studies were performed before the operation and at different intervals ranging from 8 days to 14 months postoperatively. As expected, vital capacity (vc) proved to be diminished postoperatively. In order to evaluate respiratory impairment and the time course of recovery after thoracotomy for suspected metastatic lesions of the lung we studied lung function prior and following 24 surgical explorations in 15 patients (13-18 years). Median sternotomy was chosen in 21 operations. 1-28 metastases or suspected areas were removed mostly by wedge resection. 

The operation was usually well tolerated with a mean duration of the postoperative hospital care of 14 days.

CELL-MEDIATED IMMUNE RESPONSE IN ACUTE AND CONVALESCENT PHASE OF BRONCHIOLITIS:

A.K. Zicari MD, F. Signoretti MD, F Ippoliti MD, T Granato MD, G. Antognini MD, F. Tosi MD, F. Midulla MD, R Ronchetti MD, Pediatric Clinic, Rome University "La Sapienza," Italy.

It has been reported that in patients with bronchiolitis, the percentage of OKT8-positive lymphocytes (suppressor) decreases during convalescence and that this may represent a diminution of the control on IgE synthesis and a cause of the wheezing syndrome associated with the illness (Nelliver 1984). To confirm this hypothesis, we studied 30 infants admitted with mild to severe bronchiolitis. The subjects ranged in age from 1 to 23 months (X7.75±7.51); males were 17 (56.7%). In all patients T-lym.

PHASE

Tab. 1

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TRACHEAL STENOSIS AND BRONCHIAL STENOSIS IN CHILDREN

C. Wiechert, H. von der Hardt, M. Müller, J. Seidenberg

Tracheal stenosis and bronchial stenosis are relatively rare malformations in children. Treatment and clinical outcome were discussed controversially.

We report on 73 infants and children with these malformations out of a group of 468 patients, in which a bronchoscopy has been undertaken between 1978 and 1983. The term "tracheomalacia" and "bronchomalacia" is used if a congenital dysplasia of the trachea or bronchi is observed. A clinical follow-up study could be realized in 54 cases. Stenosis (or malacia) was most frequently seen in the trachea (n=25) and in the left main bronchus (n=25). In 42 cases, the mucosa shows signs of a chronic inflammation, more frequent in bronchial stenosis than in tracheal stenosis. The predominant clinical symptoms were stridor and/or frequent bronchitis/obstructive bronchitis (n=49). The clinical symptoms were stridor and/or frequent bronchitis/obstructive bronchitis (n=49). In 38 cases the first clinical symptom could be observed in the first 3 months of life. In further 24 cases within the first 12 months. Szintigraphy has been done in 51 cases and pathological results were observed in 49 cases. In 29 infants and children, the ventilation/perfusion disturbance was seen only in the post-stenotic area.

The analysis of the pressure/flow curves (whole body plethysmography) revealed characteristic patterns for supra- and subglottic stenosis or malacia. After diagnoses a long term treatment programme was proposed with daily inhalation of isotonic solution and with physiotherapy. Antibiotics were given in acute infections. The clinical follow-up was excellent and clinical symptoms disappeared in 80% within the first 24 months after diagnosis. Diagnosis and treatment were discussed in respect to literature and to the probable natural course of the clinical symptoms.

Lit.: B.H. Landing

Congenital malformations and genetic disorders of the respiratory tract. Am. Rev. Resp. Dis. 120, 151 (1979)
LONG-TERM INTUBATION FOR PHARYNGEAL AIRWAY COLLAPSE IN CHILDHOOD.

N. MEERS, J. RAMET, M. DELREE, I. DAB and L. SACRE.
Dept. of Pediatrics (Prof. H. LEBE) and Radiology (Prof. M. OOSTAUK) Antwerp, Belgium.

A fine balance exists between the inspiratory opening and closing forces controlling the patency of the upper airway. If the collapsing forces predominate, acute asphyxia rapidly leads to asphyxial coma and finally death.

We report on a child with long-term tracheal and pharyngeal intubation for upper airway obstruction during the first two years of life.

An apparently healthy newborn presented episodes of obstructive apneas during sleep, increasing in number and severity during the first 6 months of life, leading finally to repeated spells of respiratory distress, cyanosis, bradycardia, cerebral hypoperfusion and convulsions and necessitating first tracheal, then pharyngeal intubation for a period of 14 months. No signs of autonomic dysfunction were present.

The respiratory disturbances were sleep-related, more severe in supine than in prone position and not due to central causes.

The patient was successfully detubated and discharged at the age of 18 months with a normal polysomnographic recording. Relaxation of the coniocleidal muscle and/or the mandible during sleep in children might lead in certain predisposing circumstances to upper airway obstruction. Hypoplasia of the tongue against the soft palate or the epiglottis. This anatomical and physiological problem can disappear spontaneously with growing age.

In conclusion, we propose long-term pharyngeal intubation especially during sleep in infants with obstruction secondary to pharyngeal collapse; complications related to tracheostomy can thus be avoided.

CHILDHOOD MAXILLARY SINUSITIS TREATED BY ANTORSTOMY

P. Ruoppi
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One hundred and three children up to 12 years of age underwent antrostomy in the Kuopio University Central Hospital between 1960 and 1979. Ninety-two of them attended for check-up after the operation, 6 years later, on average.

Allergy proved to be the commonest and most important factor predisposing to sinusitis, as was the obvious cause of persistent, non-acute sinusitis. After 6 years of antrostomy, the estimated annual notification rates being much higher in the latter group, namely 40 per 100,000 compared with 10,000.

No immediate complications were associated with antrostomy, nor were there any serious late complications.

STRIDOR - DIAGNOSIS AND MANAGEMENT

C. Martin Bailey
The Hospital for Sick Children, Great Ormond Street, London, England.

Stridor will be defined, and the discussion put in perspective by a brief consideration of the common causes of stridor in children, based on the experience at Great Ormond Street with 752 cases over the last 5 years.

A systematic approach to the assessment of children with stridor will be presented, incorporating history, physical examination, and special investigations including endoscopy.

Emphasis will be given to the findings encountered in children with subglottic stenosis, laryngeal, vocal cord palsy, tracheomalacia, foreign body, subglottic haemangioma and respiratory papillomatosis. The treatment of these conditions will be outlined in principle.

CHILDHOOD TUBERCULOSIS TODAY

CHILDHOOD TUBERCULOSIS IN THE UNITED KINGDOM COMPARED WITH DEVELOPING COUNTRIES

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The incidence of tuberculosis in the technically advanced countries has been declining for many years, but no such decline is apparent in most developing countries where tuberculosis remains a cause of considerable childhood morbidity and mortality.

We have undertaken surveys of tuberculosis notifications in England and Wales in 1963 and in Kenya in 1984, which provide an opportunity to compare childhood tuberculosis in the 2 countries. In England and Wales 9% of patients were children (aged less than 15 years) compared with 27% in Kenya. Nearly all the children in England and Wales were of White (48%) or Indian, Pakistani or Bangladeshi (40%) ethnic origin, the estimated annual notification rates being much higher in the latter group, namely 40 per 100,000 compared with 2,440 for the White group. The estimated annual registration rate for African children in Kenya was 30 per 100,000.

Bacteriological confirmation of respiratory tuberculosis was obtained in only 19% of children in England and Wales and 17% in Kenya; however, about half of those with a culture result were positive. A higher proportion of children in Kenya had a chest radiograph considered to be within normal limits at independent assessment, 24% compared with 10% of those in England and Wales. However, of those with a pulmonary lesion, the disease was, on average, more extensive in Kenya, 20% having disease involving a total area of more than 1 lung and 22% cavitation, compared with 10% and 5% respectively in England and Wales. In both countries lymph node disease was the commonest non-respiratory lesion and about 15% of children with a non-respiratory lesion had meningitis.

In England and Wales nearly all the children received isoniazid plus rifampicin daily, 40% with ethambutol or pyrazinamide or both drugs, the median duration being 9.0 months. In Kenya nearly all the children were treated with the nationally recommended regimen of isoniazid and thiacetazone daily, supplemented by streptomycin initially, although many failed to collect the recommended 12 months' duration.
CHILDHOOD TUBERCULOSIS IN EUROPEAN COUNTRIES

Dr. Herbert Landmann
Research Institute for Pulmonary Diseases and Tuberculosis Berlin-Buch / GDR

At the beginning of this century childhood tuberculosis was a heavy load especially for the families of sweated industrial workers. In the postwar years there was an epidemic of tuberculosis in most of the European countries. Such high incidences of childhood tuberculosis we find today only in developing countries linked with a high prevalence of bacillary lungtuberculosis and a low level of social and hygienic conditions. In European industrial countries in general low tuberculosis prevalence is existing, but there are remarkable differences in the rate of tuberculosis in childhood. We see the reason for it in the different preventive measures taken against tuberculosis in general and in children, especially in form of BCG-vaccination of the newborns.

Examples for the effectiveness of BCG-vaccination in low prevalence countries are given. Some ideas about the future of measures for protecting children against tuberculosis are presented.

PRESENT AND FUTURE OF BCG VACCINATION AND TUBERCULIN DIAGNOSTICS IN CHILDREN

T.B. Jablogoiva, N.N. Piesaronko, D.T. Levy

Our studies were aimed at the development of a preparation with dosed antigenic content due to a lesser number of killed particles. A preliminary experimental study was performed in various biological test systems; controlled clinical investigations were carried out in more than 400,000 newborns. The proposed preparation, i.e. BCG-R, is intended mainly for vaccination of newborns and high risk groups of children. BCG-R vaccine contains in one vaccinating dose of 0.025 mg 500,000 to 750,000 countable particles, while one vaccinating dose of the commercial vaccine equal to 0.05 mg contains 500,000 to 1,100,000 countable particles. The use of BCG-R allows to increase the coverage of infants with vaccination by 10-12% and to reduce the number of postvaccinal complications thrice.

The improvement of tuberculins preparations and the development of new tuberculins with higher specificity for the vaccinated organism are also of great importance. The work in this direction was started in the USSR. Thus, FP-BG that was proposed as a substitute for FPB but proved to be unsuitable for this purpose is now successfully used for assessing the efficiency of BCG immunization. The use of FP-BG in a dose of 2 TU allows to reveal 30-35% more tuberculins positive persons. Besides, the preparation gives more informative results when used for screening children of 7-8 years before the first booster injection.

In view of the increased risk of infectious agents transmission with injectors and syringes, epikutaneous tests performed by means of Finn Chambers on Scanpor are preferable. They show good correlation with the intradermal Mantoux test in infants and preschool children.

VALUE OF FLEXIBLE BRONCHOSCOPY IN CHILDREN UNDER THREE YEARS WITH PRIMARY TUBERCULOSIS

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Tuberculosis is still a frequent pediatric problem. In young children the primary tuberculous process (PT), mediastinal lymphadenopathy, emphysema and/or atelectasis are particularly frequent. During four years (1983-1986), we have assessed the value of flexible bronchoscopy (FB) in 28 children under 3 years (13/28 were <1 year). Fifty five were performed. Fourteen children had PT. FB was normal in 11 children (12 FB): 8 with normal chest Xray, 3 with abnormal chest Xray (1 non compressive lymph node enlargement, 1 hilar calcification, 1 consolidation of the right upper lobe). Culture of tubercle bacillus (TB) was positive only in the child with the mediastinal adenopathy.

FB was abnormal in 17 children:

10 children (30 FB) had endobronchial granuloma. All of these children received antituberculosis and glucocorticosteroid (GCS) treatment. In 6/10, regression of granuloma with medical treatment alone was confirmed by FB. Among these, 2 had a right late rostracheal compressive lymph node. In 4/10, bronchoscopic resection was necessary (1 had a persistent bronchial stenosis).

6 children (12 FB) had bronchial compression by hilar lymphadenopathies without granuloma. FB showed regression of lymph node enlargement under medical treatment.

1 child had an inflammation of the left lower lobar bronchus. Bronchoalveolar lavage was performed in all children, TB culture was positive in 7.

For a simple, well tolerated procedure even in young children, FB should be performed in all children with PT and abnormal chest Xray. FB allows a) to determine whether the obstructive lesion is extra and/or intraluminal; b) to indicate when a GCS and/or a bronchoscopic resection should be combined with antituberculosis drugs; c) and finally, to control the evolution.
SECOND IUAT STUDY ON COMPLICATIONS INDUCED BY INTRA-DERMAL BCG VACCINATION

A. Lotte (Unité de Recherches 179, INSERM, Paris), O. Wasz-Höckert (University Children's Hospital, Helsinki), N. Potson (U.179, INSERM) and the national Coordinators for Denmark (H.), Germany (J. Landmann) Federal Republic of Germany (U. Quast), Hungary (B. Andrafoszky, L. Lugosi, I. Vadasz), Romania (F. Mihalache), Yugoslavia (R. Pal, D. Sudic).

Intra-dermal BCG vaccination being still largely used in young children (its efficacy is not questionable), post-vaccination complications are a current problem. On the basis of the 1st retrospective study, we proposed a classification of serious post-vaccinal lesions and estimated risks in cohorts vaccinated from 1948 to 1974; but the number of registered cases was an underestimate and the diagnosis criteria were not always well documented. To improve the notification system, we undertook prospectively a 2nd study. The group delineated the complications to be studied and prepared standard cards for recording the diagnosis of each case. The national coordinators had to: register the vaccinated population by age, inform all the responsible specialists, collect and send the cards to at least one to each national register, in close connection with the international register. Six European countries participated in the new study (Spain, Germany, Sweden and Greece). In these countries, 80% of the cases were vaccinated from 1979 to 1981 and followed-up to 1983. The risks of BCG disseminated infections relative to new-borns (4.29 per million) and older subjects (3.58) are higher than those estimated in the retrospective study (1.75 and 1.95) which indicates an improvement of the notification system. They are similar in the different territories. The risks of local regional abscesses (388 per million in new-borns and 26 in other subjects) show discrepancies in the 6 countries, probably related to the different "virulence" of the BCG substrains.

OSTEOMYELITIS AS A COMPLICATION OF BCG-VACCINATION

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All over the world an increased number of BCG-vaccination complications is observed. The BCG-osteomyelitis is a serious one and many cases are present in Scandinavia. The interval between vaccination and symptoms in majority of cases is 7 to 18 months. The pathological finding is frequent limited to one bone, oft it is sternum, clavicle, ribs, long and small bones of limbs, femur, tibia, fibula, tarsus, rib and finger. The diagnosis is proved histologically, in about one half of cases bacteriologically, too.

In Czechoslovakia the BCG-osteomyelitis was not observed till 1980. From this year a new vaccine with a higher virulence is used. In the last 6 years we have cured 28 cases, it represents an incidence of 3.5/100,000 vaccinated newborns, 19 cases are boys, 9 cases girls. Except two all were vaccinated after birth. The interval between vaccination and first symptoms was 10 to 41 months, on the average 17.8 months. In most cases one bone was affected, in two cases there were 2 bones, in 9 cases it was femur, in 6 cases tibia, in 4 cases humerus, in 3 cases spine, in 2 cases clavicle andcalcaneous and in 1 case fibula, tarsus, rib and finger. The diagnosis was proved in 25 cases histologically, in 9 cases the BCG stem was standardised. The tuberculin test was in all but one case positive 6 to 22 MM in diameter, on the average 13 MM. Immuno-deficiency was not proved in our patients, but we cannot rule out some defect of the local immunity, because the vaccination on the vaccination place was very small or absent.

To decrease the number of complications we have from 1985 diminished the vaccination dose to one half. From that time we didn't seen some new case of BCG-osteomyelitis, but the interval is short.

NEONATAL BCG VACCINATION AND MYCOBACTERIAL CERVICAL ADENITIS

M.L. Katila*, E.Brandt**, A. Backman***, Kuopio University Central Hospital, Public Health Institute**, Helsinki University Children's Hospital***, Finland.

A retrospective study on mycobacterial cervical adenitis among Finnish children in 1977-86 was performed to gain information on incidence, etiologic mycobacteria and clinical data of the disease. The material was based on the tuberculosis registries of the National Board of Health and on the records of the reference tuberculosis laboratory**.

The number of cases registered in the 10 year period was 33, where 25 girls and 8 boys gave an incidence of the order of 0.3 cases / year / 100 000 children. Lymphadenopathy was usually developed in connection with upper respiratory infection tonsillitis or otitis, but when taken to examinations, the child was lacking signs and symptoms of infection. In all cases, the diagnosis was based on histopathological changes typical of tuberculosis. Microbial cultures of the biopsy material were positive for mycobacteria in 40%. Atypical mycobacteria, predominantly M. avium-intracellulare, outnumbered tuberculosis by 1 to 10 as etiologic microbes. A wide local excision of the affected lymphnodes seemed to be the therapy of choice. Antituberculous drugs seemed to be of little value in treatment of atypical mycobacterial infections.

25 (81%) of the children had been vaccinated with BCG as newborn. Tuberculin tests by Mantoux technique were positive in 50% of the confirmed cases with atypical mycobacteria and in 28% of the cases based on histopathology alone. Neonatal BCG vaccination seemed to protect children against atypical mycobacteria, especially at 1-4 years of age. A comparison to Swedish data on cervical adenitis due to atypical mycobacteria confirms this observation.

The importance of atypical mycobacteria as etiologic pathogens has to be recognised. Contrary to tuberculosis which always has to be treated with specific drugs, atypical mycobacterial infections need proper surgical excision of the affected lymph nodes, which preferably is performed in connection of the primary biopsy, and antituberculous drugs are needed only exceptionally.

TREATMENT AND SELFMANAGEMENT OF ASTHMA

BEHAVIOR ABNORMALITIES AND POOR SCHOOL PERFORMANCE DUE TO ORAL THEOPHYLLINE (T) USAGE

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Studies evaluating adverse effects of oral T on learning/behavior have been performed on children with asthma receiving chronic T therapy. To further differentiate the effects of asthma itself from the drugs used, we evaluated 20 asthmatic children (6-12 yr) who had always to be treated with specific drugs, atypical mycobacterial infections need proper surgical excision of the affected lymph nodes, which preferably is performed in connection of the primary biopsy, and antituberculous drugs are needed only exceptionally.

Thus, the short term administration of T to asymptomatic asthmatic children previously off chronic oral bronchodilators can adversely affect school performance, behavior and memory. Since this population represents the majority of asthmatic children, one may cautiously in this age group, monitor school performance closely, or seek other treatment modalities.
M. Zach, U. Karner; Pediatric Department, University of Graz, Austria

BRONCHIAL REACTIVITY AND LUNG FUNCTION IN TWO CASES

Asthma deaths in children aged 1-16 years were investigated by reviewing all available documentation and by interviewing their parents. 27 deaths (20.6%) were apparently unexplained. The remaining 27 deaths (79.4%) might have been prevented with one or more of the following factors having been identified in the management:

1) Failure to diagnose asthma: 2 cases (6%).
2) Poor long-term supervision and sub-optimal treatment: 15 cases (56%).
3) Delayed referral to hospital: 12 cases (32.2%).
4) Sub-optimal management of the first illness in hospital: 7 cases (20%).

If future deaths are to be prevented, greater efforts need to be made to alert all parents to the potential danger of acute or deteriorating asthma. They should be given the means to initiate early treatment with oral corticosteroids and to maximize bronchodilator therapy. They should be given clear guidelines as to when to seek medical help.

Hospitals should have a clear management policy for children suffering from asthma and should permit open access.

SUDDEN DEATH IN ASThma: COMPARATIVE OBSERVATIONS ON BRONCHIAL REACTIVITY AND LUNG FUNCTION IN TWO CASES

M. Zach, U. Karner; Pediatric Department, University of Graz, Austria

Measuring bronchial reactivity by cold air challenge (CACH) is the prerequisite for assessing the "functional dimensions" of childhood asthma. Two girls with asthma, 10 and 14 years old, died suddenly in the winter 1985/86. Both had been classified by clinical criteria as moderately severe asthma; had given the impression of a well-stabilized disease course, and had shown good compliance and relatively low expenditure. In summary both girls with later occurring sudden death demonstrated a high degree of reactivity, only partial recovery of function after bronchodilator, and a markedly reduced perception of bronchoconstriction.
Clinical and socio-cultural factors associated with asthma self-management (ASM) program. L. Indirimmo MD, F. Midulla MD, M. Hindi Alexander PhD, A.M. Zicarelli MD, F. Fritsenga MD, A. Lo Tosoniere MD, M.P. Villa MD, R. Ronchetti MD.

Pediatric Clinic, University “La Sapienza,” Rome, Italy; *Suffalo NY, USA; **Pediatric Clinic, Bologna, Italy.

We performed a study to determine in which way socio-cultural level of the family and the severity of asthma can influence the acceptance of ASM program in two non-industrialized regions. In the first region a population of 5817 children 6-15 was surveyed by questionnaires through the schools. The response rate was 91% (5308). 2.5% (136) of whom had an asthma episode within the past year. Of those 222 (29) completed: a) the 1st interview on personal and family medical histories; b) the 2nd interview assessing knowledge (k); c) the 3rd interview assessing co-reactivity with carbacol. The children were divided into two groups: E=14 and C=10. The children who followed the whole program were affected by a more severe asthma and were brought up in a higher socio-cultural environment than children who dropped out. Short-term outcome measures demonstrated statistically significant improvement in k for all. The results showed that ASM programs may have some success.

Exercise induced asthma (EIA) is a very frequent clinical problem in asthmatic children. Its prevention is important in order to assure these patients of as nearly normal life as possible. The present study was undertaken to determine the bronchodilation and EIA-preventive effect of oral clenbuterol (OCL) and inhaled clenbuterol (ICL) during 240 minutes after OCL or ICL or placebo (PL) in a double blind randomized manner. Flow-volume curve parameters, arterial blood pressure and heart rate were tested in basal conditions 15,30,60,120,180,240 minutes after the drug, and 1,5,10,15,20 minutes after the exercise test. During the exercise test the cardiorespiratory parameters (VE, Vo2max, VCO2, HR, O2 pulse) were monitored. The time course of the change observed in FEV1 (expressed in % of predicted) was: Basal 77% 60 min 89% 240 min' PL 86.5±6.4 91.4±5.1 90.2±4.5 91.1 ±4.8 91.7±4.6 OCL 84.3±3.4 90.7±3.6 92.4±3.8 92.9±4.3 93.5±3.4 91.3±3.4

The mean percent fall of FEV1 after exercise test was 29.0±5.2 SE for PL, 13.9±2.1 SE for OCL and 17.9±1.0 SE for ICL. The degree of protection (FEV1 fall > 20% than before exercise FEV1) obtained was 25% for PL, 67% for ICL and 92% for OCL. The analysis of cardiorespiratory parameters didn’t reveal differences in VO2max and O2 pulse in the 3 tests. We often noted a significant increase in VE/Min test protected by OCL and ICL. We conclude that: OCL provides significant protection against EIA compared to the PL. The lower degree of protection of ICL than OCL is possibly due to a relative ineffective inhaled dose in the ICL (30% of oral dose).

Effect of inhaled budesonide on lung volume in young children with asthma. J.G.A. Gleeson, J. Pool, A. Greenough, J.F. Price.

Paediatric Respiratory Laboratory, King’s College Hospital, London, England.

We have previously demonstrated that the majority of young asthmatic children are hyperinflated even when asymptomatic. We have subsequently studied the effect of an inhaled steroid on lung volume in asthmatic children aged 2-6 years with frequent symptoms. The trial was double-blind and after a two week “run-in” patients were randomised to receive either budesonide 200ug or placebo twice daily via the nebulizer for 6 weeks. Functional residual capacity (FRC) was measured by helium gas dilution before and after the treatment period and expressed as a percentage predicted for height. Results are available on 23 children, mean age 4.6 years; 13 have received budesonide and 10 have received placebo. In the majority of children FRC was increased before treatment; the mean FRC was higher in the budesonide group (140%, range 96-169%) than the placebo group (123%, range 97-155%). This did not reach statistical significance. The change in FRC after budesonide (mean 17.1%) was significantly greater than after placebo (mean 4.2%, p < 0.05 Wilcoxon rank sum test). The magnitude of change in FRC after budesonide correlated with the pretreatment FRC (r = 0.5, p < 0.05).

These results suggest that long term steroid inhalation may be useful in reducing hyperinflation in young asthmatic children.
BRONCHOPULMONARY DYSPLASIA
PREVENTION OF BRONCHOPULMONARY DYSPLASIA
M Hallman, University of Helsinki, Department of Pediatrics, Helsinki, Finland

BPD is a problem of infants who are born before 32 weeks of gestation, and have acute neonatal respiratory failure. The prevention of this chronic debilitating and life threatening disease involves: 1. prevention of the prematurity, 2. prevention of functional immaturity or infection that cause acute respiratory failure, and result in progressive lung damage. 3. prevention of complications of respiratory care, especially pulmonary air-leak syndromes. 4. reduction of the severity of respiratory failure. 5. prevention and early treatment of patent ductus arteriosus, with left to right circulatory shunt. 6. treatment that improves the resistance against lung injury and promotes the healing. Uncertainty about the pathophysiology of BPD limits preventive measures. There are few randomized clinical trials. Perhaps the most promising is the reported decrease in the incidence of BPD following exogenous human surfactant. Antioxidants, and other micro-/macronutrients that improve healing/growth (for instance vitamins E, A, superoxide dismutase, and insulin) are being studied. In addition, a multitude of other clinical factors that are related to a high risk of BPD in the neonatal period (birth until age 4 weeks) not only increases diagnostic opportunities but also assists early indications for appropriate treatment, and the critical assessment of treatment results. In the immediate postnatal stage, analysis of respiratory mechanics also offers the possibility of showing the functional state of the surfactant system, and provides information about fluid resorption in the lungs.

Furthermore, the study of neonatal respiratory mechanics is an integral part of the search on the respiratory stress syndrome (RDS). Such studies (postnatally and under spontaneous or artificial ventilation) enable objective assessment of the action of substances (administered both in utero and immediately after birth) that affect the surfactant system, or assessment of changes in pulmonary mechanics following surfactant instillation.

RESPIRATORY PHYSIOLOGY IN THE NEWBORN
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For successful post-natal pulmonary adaptation some minimum requirements are necessary, including: initiation of regular, rhythmic and controlled breathing pattern; rapid resorption of fetal pulmonary fluid combined with the establishment of proper static and dynamic pulmonary mechanics to permit easy ventilation and sufficient gas exchange; and establishment of the respiratory failure influence the outcome. Treatment of BPD differs in the acute and late phase. When still on ventilator the patient shall receive optimal oxygenation with lowest possible pulmonary pressures. Failure or treatment with low oxygen partial pressure and high pressure may be harmful. This is especially true for prematures with left to right circulatory shunt. Knowledge of these functional values in the neonatal period (birth until age 4 weeks) not only increases diagnostic opportunities but also assists early indication for appropriate treatment, and the assessment of treatment results. In the immediate postnatal stage, analysis of respiratory mechanics also offers the possibility of showing the functional state of the surfactant system, and provides information about fluid resorption in the lungs.

The pathogenesis of bronchopulmonary dysplasia is still unclear. We have hypothesized that the acute and chronic lung injury seen in preterm babies ventilated artificially is caused by production of oxygen radicals produced by the hypoxanthine-xanthine oxidase system. Hypoxanthine is a potential oxygen radical generator. In hypoxic tissues, as in the low compliant lung ventilated with positive pressure, hypoxanthine is accumulated. Whereas extra oxygen in gas mixtures with high oxygen concentrations'of oxygen radical scavengers are lower in preterm babies than in term babies, preterm babies are more susceptible to the damaging effects of oxygen radicals in their lungs than in term babies. To test this hypothesis we have performed a series of animal experiments: 1) Young rats were infused with hypoxanthine intravenously while breathing 100 % oxygen. Compared with control animals their lungs were edema- tosous and hemorrhagic. Their surfactant function was destroyed in spite of a normal surfactant phospholipid pattern. 2) Xanthine oxidase was instilled into the trachea of young guinea pigs. A dramatic decrease in lung-thorax compliance was measured. This effect came rather acute and could partly be prevented by giving a superoxide radical scavenger, superoxide dismutase. A chronic effect was observed as well since lung-thorax compliance was lowered even two weeks after one single instillation of xanthine oxidase. 3) Xanthine oxidase was instilled into the trachea of fetal rabbits at gestational day 27-29. Lung-thorax compliance was affected most in the most mature animals. Morphologic changes as hemorrhage and edema was by contrast significantly more manifest in the least mature animals. Does the presence of mature surfactant protect the lungs from oxygen radical injury?

The present findings support the hypothesis that the hypoxanthine-xanthine oxidase system can damage the lung. We believe we are dealing with a broad-spectrum mechanism of lung tissue damage in a series of different clinical conditions, one of the manifestations of such damage is bronchopulmonary dysplasia.

Several follow-up studies have reported frequent respiratory problems, growth retardation and retarded psychomotor development in BPD patients. In a long-term follow-up study up to the age of 10 years we have followed 46 low birth weight infants surviving after ventilator treatment in the newborn period. Fourteen had BPD. Pulmonary mechanics shortly after discharge showed low compliance and high resistance. Re-examination one year later showed no significant difference in both parameters. However, at the age of 10 the BPD-patients in many respects showed signs of impaired lung functions e.g. abnormal FEV1, FRC and VCo.

Lower respiratory tract disorders were common in many BPD patients during the first two years but later subsided. Weight and length development were retarded during the first years but at the age of 6 the patients had normal growth. All patients were treated with Griffith developmental test. The BPD- and non-BPD patients did not differ from a normal population. However, clumsiness and concentration difficulties were relatively common in both groups.

Treatment of BPD differs in the acute and late phase. When still on ventilator the patient shall receive optimal oxygenation with lowest possible pulmonary pressures. Failure or treatment with low oxygen partial pressure and high pressure may be harmful. This is especially true for prematures with left to right circulatory shunt. Knowledge of these functional values in the neonatal period (birth until age 4 weeks) not only increases diagnostic opportunities but also assists early indication for appropriate treatment, and the assessment of treatment results. In the immediate postnatal stage, analysis of respiratory mechanics also offers the possibility of showing the functional state of the surfactant system, and provides information about fluid resorption in the lungs.

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PULMONARY FUNCTION TESTING IN BPD

LUNG VOLUMES, DISTRIBUTION OF VENTILATION AND LUNG MECHANICS DURING MECHANICAL VENTILATION IN INFANTS WITH BPD

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A multiple breath nitrogen washout method was developed to study lung function in very low birth weight infants (< 1 500 g) during ongoing mechanical ventilation. To measure ventilatory flow, the baby was placed in a whole body plethysmograph with its face outside. During an expiration the breathing gas was instantaneously changed to 100% oxygen, with maintained respirator setting, and the nitrogen washout course was followed. By computerized methods the functional residual capacity (FRC), nitrogen elimination pattern (distribution of ventilation) and nitrogen clearance were calculated. The use of body plethysmography also enabled simultaneous measurement of lung mechanics.

So far, five VLBW infants requiring mechanical ventilation longer than during their first month of life were studied repeatedly.

During mechanical ventilation there was a progressive increase in FRC in combination with an increase in lung resistance (Rl). The nitrogen clearance was also increased.

We conclude, that the changes in FRC, nitrogen washout course and Rl reflect a progressive airway damage in infants developing BPD.

MEASUREMENT OF COMPLIANCE OF THE TOTAL RESPIRATORY SYSTEM IN INFANTS WITH BRONCHOPULMONARY DYSPLASIA

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This study was designed to determine the usefulness of the passive compliance of the total respiratory system (Cra) measured by the occlusion technique in infants with bronchopulmonary dysplasia (BPD). Twenty-one infants (136, 60) with BPD were tested in intensive care units. Some infants were tested two or three times at intervals of at least 15 days. A total of 29 measures was obtained. Gest. age : 28 ± 2 wk (25-32): postnatal age 11 ± 8 wk (6-38); body weight (BW): 2460 ± 1060 g (1240-2670). Occlusions were performed during the first 2/3 of expiration. Cra was calculated as the slope of the regression line of airway pressure against the volume at occlusion. At the moment of the test, 16 infants were intubated and mechanically ventilated but able to breathe spontaneously through the endotracheal tube for short periods of time. During Cra determination continuous monitoring of heart rate and Pco2 was performed. The mean Pco2 was 35 ± 13 mmHg (0.1-0.72). Cra in the whole group of infants is significantly decreased when compared to predicted Cra values normalized for body weight (0.26 ± 0.20 ml/cmH20/kg versus 1.15 ± 0.26 ml/cmH20/kg; p<0.001). A significant relationship was found between Cra values and Fij02 needed for maintaining Pa02 > 60 mmHg (r = -0.70; p<0.001). When arterial/alveolar Q2 ratio is plotted against Cra normalized for BW a significant relationship was found (r=0.47; p<0.05). Furthermore, a significant difference was observed between Cra in intubated and ventilated infants compared to extubated infants (0.44 ± 0.16 ml/cmH20/kg versus 0.70 ± 0.16 ml/cmH20/kg; p<0.001). We conclude that 1) Cra measurements are useful in assessing lung mechanics in BPD, 2) Cra decreases are significantly related to gas exchange impairment 3) Cra measurement could provide useful information for guiding oxygen therapy and mechanical ventilation adjustment.

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PERSISTENT ABNORMALITIES OF LUNG FUNCTION AFTER BPD

The pulmonary function testing of 13 out of 56 children who developed broncho-pulmonary dysplasia between 1964 and 1973 was evaluated 10 to 20 years later (mean: 15 years). All subjects were premature (gestational age: 28-35 weeks) and had been intubated and ventilated (IPPV) for an extended period of time (mean: 49 days) receiving high oxygen concentrations (FiO2 > 0.75).

The pulmonary function testing included spirometry, body-plethysmography, helium flow-volume curves and methacholine-provocation.

The degree of pulmonary dysfunction of these patients was correlated to the duration of IPPV and the oxygen concentration. A significantly high proportion of these survivors showed small airways disease and/or bronchial hyperreactivity which changes could predispose to the development of chronic obstructive pulmonary disease in the adult.

RELIABILITY OF TRANSCUTANEOUS PO2 MEASUREMENT WITH ADVANCING AGE IN INFANTS WITH BRONCHOPULMONARY DYSPLASIA

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In infants with bronchopulmonary dysplasia, monitoring of oxygenation is of the first importance. Previous report of few patients suggested unreliability of transcutaneous PO2 (TcPO2) due to systematic underestimation of arterial PO2 (PaO2) after 6 weeks (wk) of postnatal age (PNA) (Peditricle 1984; 74: 217). We thus tested the reliability of TcPO2 in a group of 19 patients with bronchopulmonary dysplasia 12 were studied once at 16 wk (4-43) of PNA; the 7 others were tested longitudinally from 5 wk (2-11) to 12 wk (6-16) of PNA. At the time of the test mechanical ventilation was necessary in 22 occasions and mean FiO2 was equal to 75% (25-100%). Twenty-eight simultaneous PaO2 and TcPO2 measurements were done. The transcutaneous electrode (Radiometer, 44°C) was fixed close to a peripheral arterial line and the cutaneous temperature around the electrode was monitored (36°C ± 0.5°C). Under stable hemodynamic conditions (mean heart rate = 152 [126-166], mean arterial pressure : 39 - 80 mmHg) and during behavioral stage 1, arterial blood samples were collected and simultaneous PaO2 was recorded. From 28 measurements, TcPO2 was found to be significantly related to PaO2 (TcPO2 = 0.81 PaO2 (mmHg) + 5.2; r = 0.73, p<0.01). Relationship between PaO2 - TcPO2 difference and PNA and PaO2 was studied; results are in the table.

| PNA | SD | Coefficient of regression |
|-----|----|----------------------------|
| PaO2 | 9.8 | 10.5 |
| TcPO2 | r = 0.24 | r = 0.08 |

PaO2-TcPO2 values were not related to PNA nor PaO2. We conclude that in infants with bronchopulmonary dysplasia 1) TcPO2 does not underestimate PaO2 with advancing age 2) TcPO2 is a reliable way for monitoring PaO2.

(Supported by CNRS and Fac Med Paris XI).
**Fetal Therapy to Reduce Postnatal Respiratory Morbidity**

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Improved antenatal ultrasound facilitates both diagnosis and treatment of fetal anomalies. Pleural effusions may now be diagnosed early in gestation and this raises the possibility that chronic drainage by pleuro-amniotic shunting may allow normal lung growth and reduce problems at resuscitation.

We describe 9 cases of antenatally diagnosed pleural effusion in whom pleuro-amniotic shunts were inserted, gestations from 24-35 weeks (2 cases were bilateral). In all 9 cases there was successful drainage of the effusion without fetal distress. In 2 cases the effusion reaccumulated two weeks later, following probable fetal removal of the shunt, further shunts were inserted.

One infant delivered 24 hours after the second shunting procedure at 30 weeks gestation, she developed respiratory distress syndrome but had no pleural effusion at birth. One infant delivered 6 weeks after shunting (35 weeks gestation), required minimal resuscitation but later died of pseudomonas septicaemia, there was no evidence of pulmonary hypoplasia at postmortem examination. The remaining 7 infants delivered between 32-35 weeks requiring minimal or no resuscitation and none required drainage of pleural effusion postnatally.

At follow-up there were no respiratory problems. In 8 infants measurements of lung function demonstrated normal lung growth. The infant delivered prematurely who had respiratory distress syndrome initially had low lung compliance but when seen at 1 year of age had functional residual capacity within the normal range. These preliminary results suggest antenatal insertion of pleuro-amniotic shunts results in chronic drainage of pleural effusions reducing problems at birth and permitting normal lung growth.

**Bronchial Hyperreactivity II**

**Selective Histamine Blockade in childhood asthma: the effect of Terfenadine on Resting Bronchial Tone and Exercise Induced Bronchospasm (EIB).**

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Histamine is an important mediator of bronchoconstriction but conventional antihistamines only weakly antagonize its effects at bronchial muscle H1 receptors; they are not effective in the prevention of exercise induced asthma. Terfenadine is a potent selective H1 antagonist devoid of side effects. We have investigated the effect of histamine blockade by terfenadine on resting bronchial tone and EIB in 49 asthmatic children, aged 8 to 14 years, a histamine provocation test was performed at 00:00 hours on 2 consecutive days.

From the dose-response curves the PC21 and PC22 were calculated and log-transformed. The mean PC21-values were 2.50 and 2.12 and the PC22-values were 3.04 and 2.76 on day one and day two respectively. The coefficient of repeatability was for PC21 2.70 and for PC22 2.13 (analysis according to Bland).

After de PC21 determination in 5 children an additional inhalation step was necessary to induce a 20% fall in FEV1. We calculated the variance of PC21 and PC22 with one way analysis of variance. The variances were 1.60 and 1.29 on day one and 1.30 and 1.16 on day two respectively. The variances were not statistically different.

These data show that in asthmatic children the PC21 and PC22 -histamine are interchangeable. The PC21-histamine is preferred in children with severe bronchial obstruction.

**Histamine Threshold Value: PC21 or PC22?**

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The provocation concentration of histamine causing a 20% fall in FEV1 (PC21) is nowadays a generally used method to assess bronchial hyperreactivity. This test is well established but its conclusion is more or less the same. Especially in children with severe bronchial obstruction. We investigated whether a PC21-histamine is as useful and as reliable as a PC22-histamine.

In 14 asthmatic children, aged 8 to 14 years, a histamine provocation was performed at 00:00 hours on 2 consecutive days. From the dose-response curves the PC21 and PC22 were calculated and log-transformed. The mean PC21-values were 2.50 and 2.12 and the PC22-values were 3.04 and 2.76 on day one and day two respectively. The coefficient of repeatability was for PC21 2.70 and for PC22 2.13 (analysis according to Bland).

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These data show that in asthmatic children the PC21 and PC22 -histamine are interchangeable. The PC21-histamine is preferred in children with severe bronchial obstruction.

**Study on the Connection Between Flow-Volume and FEV1: PEF Values in Acetylcholine Challenge of Children**

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In bronchial challenge tests the increase over 20% of initial PEF value is a common sign of positivity. In the course of acetylcholine challenge of children the connection between the changes of PEFlmax and FEV1 max values and those of flow-volume curve values have been studied.

In the follow-up of children having had obstructive bronchitis before 2 years of age acetylcholine challenge with 0.5% solution inhalation for max 3 mins/ was performed for studying bronchial hyperreactivity. The criterion of positivity was a decrease over 20% of initial PEF and/or FEV1 values. After the challenge of 186 children and 30 healthy controls, the flow-volume curve values /max75, %max50, %max25/ were also measured.

After the 0.5% solution 26 children have shown positivity, but none of the controls. The SD of PEF and PEFlmax was 12.9, while the SD of flow volume results 17.1. PEFlmax was /mean -10% .-0.3%/ and %max75 was /mean -12.9%/.

On the basis of correlation coefficient in all the challenges a significant correlation was found between the changes of flow-volume results and of PEFlmax values. Evaluating, however, only the positive cases - decrease over 20% in PEF and PEFlmax over 30% in flow-volume results - significant correlation can be stated between values of PEF and PEFlmax, %max75 and %max50 and the changes of %max50, %max25 and of PEF, PEFlmax values could be detected.
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EFFECT OF BRONCHODILATORS ON AIRWAY MECHANICS IN ASTHMA

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Twenty-five asthmatic children aged 5-14 attended the respiratory laboratory for routine pulmonary function testing. The children had been trained from using bronchodilators for at least four hours prior to testing. We measured thoracic gas volume and airways resistance in a whole body plethysmograph, and performed routine spirometry. We then recorded a cough sequence from all subjects. Each child was seated, wearing a noseclip, and breathing quietly through a pneumotachograph. When the end-expiratory level was stable, he inspired fully, then coughed out as forcefully as possible to residual volume without intervening inspirations between the individual cough efforts. Signals of flow and volume were stored and subsequently plotted at 1 speed on an X-Y chart recorder. Each child then took his routine dose of bronchodilator and all measurements were repeated 10 minutes after medication. The flow-volume profile of each cough effort showed a rapid rise in flow to a transient peak, followed by a period of lower flow rates, and a proportionally greater increase in cough flow caused by bronchodilator is brought about by differences in the relative influences of these two factors.

THE CORRELATION OF AIR TRAPPING, HYPERINFLATION, AND AIRFLOW LIMITATION IN 54 ASTHMATIC CHILDREN.

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Recently Desmond et al. (Ped. Pulm. Monol. 1986; 2: 126-134) have demonstrated very good correlations between trapped gases and RV/TLc, TGV, FEF25-75, MEF50 and MEF25 in patients with Cystic Fibrosis. In 13 asthmatic patients however, with the same degree of lung function impairment, they did not find any correlation between trapped gases and other parameters of hyperinflation and of airflow limitation. We therefore decided to check these relationships again in a small pilot study with 13 asthmatic children and found good correlations between trapped gases (in % of TLC = TSTLC/TLc) and TGV(r=0.705, p<0.01) as well as RV(r=0.716, p<0.01). For confirmation of these results we increased the number of patients to 54 and found these correlations still significant, although much weaker (TSTLC/TLV=r=0.382, p<0.01; TSTLC/RV=r=0.363, p<0.01). We also got significant correlations between MEF50 and RV(r=0.443, p<0.01) and MEF50 and TGV(r=0.323, p<0.01), whereas there was no relationship between the parameters of airflow limitation and air trapping. Preliminary analysis could not define significant differences between the pilot study group and the whole group of 54 patients. However the ongoing study includes clinical parameters to find out subgroups of asthmatics with a very good or no correlation between the lung function parameters mentioned above.

HYPOXAEAMIA FOLLOWING BRONCHODILATOR THERAPY IN WEEZY INFANTS

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Nebulised beta-2 adrenerceptor agonists are still used in the treatment of infantile wheezing in spite of the evidence that they may be ineffective. We have recently shown that they may cause deterioration in peripheral airway function (Prendiville A, Green S, Silverman M). Paradoxical response to nebulised salbutamol in wheezy infants assessed by partial expiratory flow volume curves. Thorax 1987; 42:86-91).

The aim of this study was to assess changes in oxygenation and airway calibre in response to nebulised salbutamol in recurrently wheezy infants.

Nebulised saline 20ml and preservative free nebulised salbutamol 2.5mg were given to 5 recurrently wheezy infants on nine occasions. Changes in oxygenation (measured by pulse oximeter Ohmeda Biox 3700 and transcutaneous PO2 monitor Kontron Cutan 820) and PtcO2 (Radiometer TCM 20) were measured in the five minute interval prior to and at 0-5 and 15-20 minutes after saline and salbutamol administration.

A significant mean drop in SaO2 of 2% (p<0.01) and PtcO2 of 1.3 kPa (p<0.001) was seen at 0-5 minutes after salbutamol administration. The maximum drop in SaO2 of 4% and in PtcO2 of 1.8 kPa occurred at a mean time of 11 min after salbutamol.

Twenty min after the end of nebulisation, the mean value of PtcO2 of 7.1 kPa was still significantly lower than the mean value of 8.4 kPa pre salbutamol administration (p<0.01). There were no significant changes in PtcCO2. Nebulised saline had no significant effect.

This study shows that hypoxaemia, lasting for at least 20 min, can follow bronchodilator therapy. Because of its duration, the effect is unlikely to be due simply to the pH or osmolarity of the preparation.

OBSERVATIONS OF NOCTURNAL COUGH AND ROOM TEMPERATURE AND HUMIDITY IN ASTHMATIC CHILDREN

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The timing of nocturnal cough was documented in 17 asthmatic children (mean age 5-6 yrs) in their own homes. The relationship between nocturnal cough and changes in ambient temperature (17 children) and changes in relative humidity (8 children) during the night was assessed. Studies were performed on three nights, with the same duration and relative humidity and recorded every five minutes throughout the night on a Grant Squirrel Data Logger. A voice-activated system with electronic time signal recorded cough.

Sixteen children coughed on 44 nights with a median of 6 bouts of coughing per night (range 0-272). The cough rate in the two hours after going to bed was significantly higher than the cough rate in the middle of the night (z=+4.11, p<0.01). Peak coughing times were 7-9 p.m. and 6-8 a.m. The mean ambient temperature in the children's rooms was 18.4°C (+2.1°C). The minimum temperature occurred between 5 and 7 a.m. There was great variation from room to room in relative humidity - overnight median 53% (range 26.5-68%). There was no significant alteration in cough rate during periods of either rapid temperature change (>1°C per hour) or rapid change in relative humidity (>2% per hour).

The timing of night-time cough observed in this study differed from the known bathophase of circadian cycles described in adults and children. The interpretation and possible therapeutic implications of these findings are discussed.
PLASMA ATRIAL NATRIURETIC PEPTIDE AND PLASMA ALDOSTERONE IN ASTHMATIC CHILDREN

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To investigate whether chronic airways obstruction stimulates secretion of atrial natriuretic peptide (ANP) we measured plasma ANP levels in 24 consecutive asthmatic children (group A, mean age 7.9 yrs, range 4.6 to 15.7 yrs) compared to a control group of 19 healthy children. Blood samples were taken from 8.30 to 12.00 a.m. in the recumbent position after a normal breakfast. ANP was measured by direct radioimmunoassay (RIA) from unextracted plasma as described earlier. In addition, plasma aldosterone was measured in 19 asthmatic children with a commercially available RIA (DPC).

In Group A, mean ANP levels were increased compared to normal children (180 ± 124 pg/ml, p<0.01). Mean plasma aldosterone concentration was 253 pg/ml (range 50 to 932 pg/ml) in asthmatic children. There was a strong correlation between ANP-1 and aldosterone (r=0.70, p<0.001). Small airways obstruction measured by trapped gas was associated with higher ANP-levels (r=0.64) and lower aldosterone values (r=0.76 with 1/aldosterone, p<0.01). Moreover, there was a positive correlation between aldosterone and serum IgG (r=0.61, p<0.01). These results suggest that chronic hyperinflation leads to ANP secretion, probably by increasing right atrial pressure. Lower aldosterone levels can be explained by the inhibitory effects of ANP on the renin-angiotensin-aldosterone axis. The clinical implications of these observations for the treatment of asthmatic children remains to be determined.

POSTERS

CHANGE IN FEV1 AFTER SALBUTAMOL: UPPER NORMAL LIMIT IN CHILDREN.

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During an epidemiologic study of respiratory health, 554 children (aged 6 to 15 years) attending three schools in Pisa (Italy) were enrolled. Sixty-seven of them refused to participate to the study. Remaining 487 children answered a questionnaire on respiratory symptoms and underwent pulmonary function tests (PFT) in baseline conditions and 10 min after the inhalation of 200 mcg of salbutamol. PFT were considered acceptable when at least 2 trials were obtained in which FEV1 differed by 5% or less both in baseline and post-salbutamol sessions: accordingly PFT from 127 children that did not meet this criterion were excluded from analysis. Three-hundred-three children, among those with acceptable PFT, were considered normal on the basis of absence of past conditions and 10 min after the inhalation of buffered saline solution and increasing cumulative doses of carbachol. The test was stopped when a fall of FEV1 of 30% or more from post-saline value was reached. Dose-response curve was obtained plotting the dose of drug (logarithmic scale) versus the corresponding fall in FEV1 from post-saline value. By manual interpolation, the dose responsible for a decrease of 15% of FEV1 (PD15FEV1) was calculated. The slope of dose-response curve was obtained through linear regression analysis. PD15FEV1 was then used to evaluate bronchial sensitivity and the coefficient b from the formula y=a+bx to express reactivity. Curvilinear regression analysis showed a highly significant correlation between these values (r=-.95). Our results suggest that bronchial sensitivity and reactivity cannot be considered as different phenomena. In clinical practice, the measurement of bronchial sensitivity should be considered sufficient for patients characterization.

COMPARISON BETWEEN BRONCHIAL SENSITIVITY AND REACTIVITY IN CHILDREN.

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We carried out this study to evaluate whether bronchial sensitivity (i.e. the threshold dose of bronchoconstrictor drug that causes a significant fall in pulmonary function), and reactivity (i.e. the slope of dose-response curve beyond this threshold dose) could be considered as distinct aspects of bronchial hyperresponsiveness, as suggested. Fourteen children aged 8 to 14 years underwent a bronchial challenge test. Forced expiratory volume in 1 sec (FEV1) was measured in baseline conditions and 1 min after the inhalation of buffered saline solution and increasing cumulative doses of carbachol. The test was stopped when a fall of FEV1 of 30% or more from post-saline value was reached. Dose-response curve was obtained plotting the dose of drug (logarithmic scale) versus the corresponding fall in FEV1 from post-saline value. By manual interpolation, the dose responsible for a decrease of 15% of FEV1 (PD15FEV1) was calculated. The slope of dose-response curve was obtained through linear regression analysis. PD15FEV1 was then used to evaluate bronchial sensitivity and the coefficient b from the formula y=a+bx to express reactivity. Curvilinear regression analysis showed a highly significant correlation between these values (r=-.95). Our results suggest that bronchial sensitivity and reactivity cannot be considered as different phenomena. In clinical practice, the measurement of bronchial sensitivity should be considered sufficient for patients characterization.

SELFMANAGEMENT IN CHILDHOOD ASTHMA: PISA IN "ITALIA PROJECT".

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"ITALIA PROJECT" is a multicenter study on selfmanagement in childhood asthma conceived to assess the effectiveness of different programs in italian children. At the University of Pisa the program "living with asthma" was tested and its original form (8 lessons) was compared with a shortened form (4 lessons). Thirty-six children, aged 7 to 14 years, and their parents entered the study; ten families were assigned to the original course, 8 to the shortened form and 18 to the control group. The severity of asthma was assessed in baseline conditions; children and their parents answered a questionnaire on knowledge about asthma; parents also answered a questionnaire on anxiety. Lessons were delivered by physicians separately for children and parents in 8 or 4 weeks for long and short course, respectively. The same questionnaires were administered at the end of course. At the end of the two experimental groups and showed inversely related to the baseline level; no substantial improvement was shown in the control group.
The possible effects resulting from interactions of a used medicine with the components of lung surfactant must be taken into consideration while applying inhalation with broncho dilators. It thus seemed useful to study "in vitro" of aerosols containing Berotec and Salbutamol on surface activity of a monolayer of DPL /dipalmitoyllecithin/, the main component of lung surfactant. The measurements were performed in Langmuir trough: aerosols containing the studied medicines in concentration applied for inhalations were introduced to gaseous phase above a DPL monolayer. Surface activity of the monolayer was measured during successive processes of monolayer expansion. The results demonstrate that both substances considerably increase the surface activity of DPL monolayer.

Simultaneously the study "in vivo" was performed on 20 children aged from 1 - 7 yrs. The surface activity of secretion of the respiratory tract of the children was measured before inhalation with bronchodilators and 20 minutes after it. There was found a considerable increase in surface activity of the secretion after the inhalation.

EFFECT OF INHALED STEROIDS ON BRONCHIAL HYPERREACTIVITY INDUCED BY BRONCHIOLITIS.

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Previous studies at our department and elsewhere have shown that bronchial responsiveness is increased after an attack of bronchiolitis, thus a substantial number of such children develop recurrent episodes of bronchopulmonary obstruction. The beneficial effect of inhaled steroids on bronchial hyperreactivity in childhood asthma has been well documented. The aim of this study was to investigate whether the same beneficial effect may be obtained in children below the age of two years, suffering from repeated episodes of bronchopulmonary obstruction. The children were observed.

The inhalation was performed prophylactically and double blind. Admitted to the trail were children below the age of two years who had had one attack of bronchiolitis previously and afterwards suffered at least from one episode of bronchopulmonary obstruction. The children were randomly allocated to receive either placebo or beclomethasone dipropionate solution given in a nebulised form. This was given over an eight week period, and the patients were followed up for one year. The results showed that the placebo-group (P) during this year had more respiratory infections, more bronchopulmonary obstructions and used more symptomatic treatment than the group receiving active treatment (B).

The two groups were matched in all respects except that children in P-group were somewhat older than those in the B-group. The results demonstrate that beclomethasone dipropionate given in a nebulised form influences the number of respiratory infections children contract after an initial episode of bronchiolitis. And it also influences the number of bronchopulmonary obstructions they get after the initial bronchiolitis.

THE INTERACTION BETWEEN SELECTED MUCOLYTIC AGENTS AND MONOLAYER OF DPL - MAIN COMPONENT OF LUNG SURFACTANT "IN VITRO".

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This study was designed to estimate the interactions between mucolytic agents used in form of syrup /mucosolvan/, ambroxol and mucodyne - s-carboxymethylcysteine and DPL /di-Palmitoyl-Lecithin/ monolayer. The investigations were performed in a Langmuir trough with movable barrier. The changes of surface activity were measured during compression and expansion of DPL monolayer. The examined substances were introduced under such a monolayer and possible effects resulting from monolayer and possible effects were measured. The results demonstrated that mucosolvan, ambroxol and mucodyne - s-carboxymethylcysteine do not change the surface activity of DPL monolayer, whereas ambroxol in mucosolvan syrup throughly changes the properties of both water-air interface and the DPL monolayer. These results are in a good agreement with those obtained for aerosols of ambroxol and s-carboxymethylcysteine.
visaged as a mechanism capable of limiting the bronchoconstriction introduced by hypoxia and hypercapnia, i.e., a mechanism for optimizing the conflicting influences of dead space and airway resistance on alveolar ventilation.\textsuperscript{79} It should also be noted that the neuromuscular mechanisms controlling airway tone are less effective in the newborn.\textsuperscript{77}

In the adult the majority of vagal respiratory fibers originating from the lung and airways are unmyelinated, the ratio of unmyelinated to myelinated fibers being 11:1.\textsuperscript{79} The mechanosensitivity of these receptors, and thus any clear modulation of their activity during respiration, is more difficult to demonstrate due to a higher $P_{tp}$ threshold than that of the SAR and RAR.\textsuperscript{79,80} The properties of these receptors are usually studied by stimulating their activity with extraneous substances like capsaicin and phenylbiguanide. As yet little is known about the location of these endings, although some have been found to be directly associated with the airways.\textsuperscript{81} Two groups of C-fiber receptors have been distinguished on the basis of their circulatory accessibility: “pulmonary” receptors, which, after injection of a challenging drug, are reached with shorter latency periods via the pulmonary vs the systemic circulation and “bronchial receptors,” which are reached with shorter delays via the systemic vs the pulmonary circulation. Another difference between the two groups of endings is the relatively greater mechanosensitivity of the “pulmonary” endings, which have a lower $P_{tp}$ threshold.\textsuperscript{79,80} These receptors might be identifiable with the J receptors of Paintal.\textsuperscript{82} An interesting feature is their different chemosensitivity to extraneous or naturally occurring substances. Among the latter, bradykinin, histamine, serotonin, and prostaglandins (of the F or E series) stimulate “bronchial” C-fiber receptors, while only prostaglandins of the E series stimulate “pulmonary” C-fiber endings.\textsuperscript{80} At present
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there are no specific data for corresponding receptors in the newborn.

Reflex Responses from the Tracheobronchial Tree and Lungs

There is convincing evidence that SARs are responsible for the classical Hering-Breuer inflation reflex (i.e., the termination of inspiration and prolongation of expiratory time on lung inflation) which, in anesthetized animals, provides the predominant mechanism for regulating the depth and rate of breathing. In fact the activity of SARs related to lung volume, together with the output from bulbopontine neurons, determines the duration of the respiratory cycle and the tidal volume of anesthetized animals. A volume threshold, which depends on a given SAR activity, must be achieved to terminate inspiration, and the magnitude of this threshold decreases with time from the onset of inspiration, i.e., larger volumes are needed to switch off inspiration at shorter inspiratory durations. In the absence of volume feedback inspiratory duration is determined only by the bulbopontine mechanism. Expiratory duration is dependent on the duration of the preceding inspiration. The inverse relationship between cycle duration and tidal volume results in an increase in both the rate and depth of respiration when the drive to breathe increases. Without vagal afferents, only the tidal volume will increase in most hyperventilatory circumstances.

However, this model does not satisfactorily explain the experimental observations in humans or conscious animals. The observation of a reduced vagal feedback in the newborn, commonly held view that the Hering-Breuer reflex is stronger in the newborn, is based primarily on the presence of inflation apnea in the sleeping newborn human and the lack of Hering-Breuer reflexes in conscious adults. To be consistent with the hypothesis of a stronger Hering-Breuer reflex, the newborn should have an increased sensitivity of the “respiratory centers” to volume-related feedback resulting in a greater reflex effect even if afferent input is reduced compared with the adult. This might reflect an absence of well-developed higher influences that in the adult might inhibit the effect of volume feedback. On the other hand, as Cross et al. pointed out, differences in mechanical properties of the lung might be responsible for the apparent differences in reflex behavior. Indeed, recent comparisons of apnea in newborns and adults of several species following lung inflation and tilting, based on the same P_t, stimulus, would suggest weaker volume-related vagal reflexes. Moreover, when assessing the importance of the Hering-Breuer mechanism in the newborn, particular attention should be paid to the potential influence of afferents from the rib cage, which undergoes far greater distortion than in the adult. Indeed, during distortion, rib cage afferents are known to provide an additional off-switch mechanism.

SARs also play a role in the reflex regulation of smooth muscle tone and, in the adult, an increase in SAR activity leads to a reduction in the efferent vagal excitatory activity to airway smooth muscle. This results in a negative feedback mechanism, which, it has been proposed, may serve to optimize the reciprocal relationship between dead space and airway resistance. There is no information concerning this in the newborn except for the observations that the neuromuscular mechanism activating tracheobronchial smooth muscle is weaker in the newborn and that smooth muscle contraction may excite SARs.

The observation that RAR activity increases as lung compliance is reduced, together with the fact that they function to promote inspiration, supports the hypothesis that RARs are important in the generation of augmented breaths or sighs. Indeed, in premature infants the ability to provoke an augmented breath is inversely related to dynamic compliance. Furthermore the increase in compliance that occurs with growth is accompanied by a decrease in the frequency of sighing (figure 15). Once again we are faced with an apparent discrepancy between the above observations and the scant RAR data.
ASPECTS OF PATHOGENESIS

BRONCHIAL PATHOGENESIS OF ASTHMA

M.A. ASTHMA CARE TRAINING (ACT) FOR KIDS.
G. S. Rachelefsky, M.D., C. Lewis, M.D., A. de la Sota, M.A.

Use of emergency room and hospitals was determined by reviewing the records of these patients (all members of the Los Angeles Kaiser Permanente health care system) for the period of 1 year prior to and 1 year after treatment. Results include 1) equivalent increases in knowledge and changes in beliefs in both groups, 2) significant changes in the self-reported compliance behaviors of the experimental group only, and 3) significant reductions in emergency room visits and days of hospitalization among those receiving the experimental treatment compared to the control group. These changes represent an estimated savings of approximately $180 per child per year for those in the experimental group.

ASPECTS OF PATHOGENESIS AND MANAGEMENT OF BRONCHIAL ASTHMA

PATHOGENESIS OF ASTHMA

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Asthma is a chronic disease characterized by increased bronchial responsiveness. Such bronchial hyperreactivity may lead to airway obstruction which at one extreme is easily reversible and at the other is only partially reversible. Clinical asthma is characterized by smooth muscle contraction, hypersecretion and mucosal swelling.

Two main mechanisms leading to airway obstruction are recognized. Neurogenic mechanisms produce obstruction either by direct reflex action or as a result of abnormalities in the non-adrenergic non-cholinergic system. The other major mechanism is the release of mediators from sensitized cells. A further mechanism, mucosal inflammation in the airways is in many cases related to the other two, but can occur independently.

A popular scheme for the pathogenesis of asthma suggests that epithelial damage exposes afferent nerve endings in the airway epithelium which become irritated by mediators released from inflammatory cells. Stimulation of these nerve endings causes a variety of effects including smooth muscle contraction, leakiness of the bronchial vessels and mucosal hypersecretion. The number of inflammatory cells in the mucosa seems to correlate with asthma severity, is increased during the late stage of the asthmatic reaction to bronchial antigen challenge, and is raised in necropises of patients that had died in an asthma attack.

To conclude in the pathogenesis of asthma the emphasis is put on the neurogenic mechanisms and the inflammation of the airways. These mechanisms may be of great importance, because they may have implications for the treatment of the disease. It seems that the bronchial inflammation of asthma patients should be treated at early stages of the disease more vigorously than it is done at present.

ANTI-INFLAMMATORY TREATMENT OF ASTHMA

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Asthma has at least two major pathologial components: bronchospasm of airway smooth muscle and airways inflammation. It is increasingly apparent that asthma is essentially an inflammatory disease with a component of airflow obstruction. The new way of thinking has important therapeutic implications. It is the inflammatory process in the airways which is the primary goal for prophylaxis and treatment, not the bronchospasm.

We have shown that epithelial damage, as a result of inflammation, is found in fresh bronchial biopsy specimens from asthmatics, even with mild disease and in disease which has lasted only a few months (Laitinen et al. 1985). Experimentally, it has been shown that airways inflammation is related to increased bronchial responsiveness, which is the hallmark of asthma. We have now data, which show that epithelial destruction is associated with bronchial hyperresponsiveness and epithelial recovery is followed by loss of hyperresponsiveness in man in life (Haahtela et al. 1987).

Chronic inflammation can lead to persistent airflow limitation. Thickening of the basement membrane and hyperplasia of bronchial smooth muscle contribute to the development of irreversible component of bronchial obstruction. This may be prevented with a more aggressive anti-inflammatory therapy at the early stages of the disease.

Sypathonemetics and anticholinergics do not have any significant effect on the inflammatory elements of asthma. Theophylline may have prophylactic anti-inflammatory effects in addition to relieving bronchospasm. OCS prevent inflammation and symptoms but has no immediate symptomatic effect and does not significantly resolve established inflammation. Corticosteroids prevent development of inflammation but are unique in their capability to resolve established inflammation.

In order to control asthma adequately we need to suppress the airway inflammation and reduce hyperresponsiveness.

A MODERN THERAPEUTIC APPROACH FOR CHILDHOOD ASTHMA IN THE UNITED STATES OF AMERICA

Clifton T. Furukawa, M.D., Clinical Professor of Pediatrics, University of Washington School of Medicine, Seattle, Washington, USA

Recent comparative studies have shown subtle behavioral and learning problems associated with acute and chronic theophylline treatment. Additionally, frequent use of beta-adrenergic bronchodilators have been associated with delayed in critical medical care and the development of increased bronchial hyperreactivity. Disodium cromoglycate has now been shown to be equivalent to theophylline for chronic therapy in children, and has no behavioral or adverse effects upon learning. The current pharmacologic therapy for chronic asthmatic children has thus changed to a primary use of cromolyn with use of beta-adrenergic drug for acute wheezing. Theophylline therapy is avoided in children with possible behavioral or learning deficits. Steroids are still reserved for severely affected asthmatics. Inhaled steroids do not protect against the immediate asthmatic reaction so they remain a secondary form of therapy to the use of cromolyn.

Thus, in the USA a clear trend has developed towards prophylaxis of the asthmatic episode with environmental manipulations and the use of cromolyn. The interest is much more in favor of long-term stability and safety, rather than short-term acute relief.
RAPID DIAGNOSIS OF BACTERIAL PNEUMONIA IN CHILDREN.

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The definite etiological diagnosis of bacterial pneumonia in children can be achieved only by isolation of bacteria from blood or lung aspirate. However, blood cultures are positive only in a very few patients and invasive techniques like lung puncture cannot be recommended for routine use. Pneumococcus (PC) is considered to be the most common causative bacterium both in children and adults and the demonstration of PC antigen in the sputum obtained from adults with pneumonia has been shown to be a useful tool for rapid diagnosis. In the present study we wanted to investigate, if the demonstration of PC in nasotracheal aspirates (NTA) could be used for the rapid diagnosis of PC pneumonia in children. NTA samples, collected by suction through a catheter inserted through the nostril so deep that it elicited a vigorous cough reflex, were obtained from 198 children (1 month to 6 years of age) with X-ray positive pneumonia. PC antigen was detected in the NTA samples by counterimmunoelectrophoresis and latex agglutination. PC antigen was found in 30.5% of the NTA samples studied. When PC antigen findings were correlated to CRP-concentrations in the acute sera of these children, PC antigen was positive in 18% of NTA specimens of children with CRP > 25 mg/l (probably non-bacterial pneumonia) and in 46.5% of those with CRP > 200 mg/l (probably bacterial). The results suggest that PC antigen detection as an only diagnostic test is not suitable for etiological diagnosis in individual patients. However, when combined with a high CRP-level, it is suggestive of PC etiology.

RAPID DIAGNOSIS OF RESPIRATORY VIRUS INFECTIONS

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Since 1980 rapid diagnosis of respiratory virus infections (adenovirus, influenza A and B, parainfluenza 1, 2 and 3, respiratory syncytial viruses) have been extensively tested in Turku. Indirect radioimmunoassay, enzyme immunoassay and recently time-resolved fluoroenzymoimmunoassay have been used to detect the virus antigen in the nasopharyngeal mucus. Currently used fluoroenzymoimmunoassay was tested. 160 nasopharyngeal samples were tested and 30% were positive. Since the illness onset 20-30% of Children younger than 24 months in the period from 1981-1986 (11%), compared to 3.4% in the years before and less children younger than 24 months during the same periods (37.6% compared to 73.5%). There were more boys (67%) than girls suffering from a foreign body aspiration. From 1981 to 1986 in 58.8% of all cases, we found different nuts in the bronchial system compared to 75% from 1986 to 1980. There was an periodic increase of the foreign body aspiration during february - april and october to december. Most of the foreign bodies were found in the bronchial system of the right lung. Until 1980, in 4.6% more than one bronchoscopy was necessary to remove the foreign body, compared to 1.2% between 1981 and 1986. In 73% of all cases, the children were sent to the hospital with the correct diagnosis. Characteristic signs of the chest were seen in 99% by X-ray diagnostic. During and after the extraction of the foreign body, pneumonia, fever, bronchitis etc. occurred in 27%, when cefotaxim and methylprednisolone was given some hours until one day before, the rate of such complications could be reduced to 8%. In most of the foreign body was removed from the bronchial system 30 minutes after the anaesthesia was started. The technique of the foreign body extraction and the evaluation of different parameters from the blood will be discussed.

FOREIGN BODY ASPIRATION IN INFANTS AND CHILDREN

Th. Zimmermann, K. Steen, Department of Pediatrics, University of Erlangen-Nürnberg, West-Germany.

During the past 25 years, we observed 172 cases of foreign body aspiration in infants and children. The definite etiological diagnosis of bacterial pneumonia in children will be discussed.

FIBEROPTIC BRONCHOSCOPY.

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Fiberoptic bronchoscopy is widely practiced in adults under sedation, without the need for a general anaesthetic. In children a general anaesthetic is required which removes one of the major advantages of this method. The size of the bronchoscope reduces the available tracheal lumen for anaesthesia and the 4.9 mm fiberoptic bronchoscope is only suitable for children down to approximately 3 years old. The main advantages of the flexible bronchoscope is its manouevrability. The upper lobe bronchi are easily visualised merely by flexing and advancing the bronchoscope. Microbiological samples are easy to obtain from chosen peripheral sites and are of good quality provided adequate precautions are taken to avoid contamination with pharyngeal bacteria. Biopsies can be taken but because of the size of the biopsy channel (2 mm) the specimens are small and require careful processing.

The rigid bronchoscope is superior for the removal of foreign bodies.
Since rigid bronchoscopy had been introduced in our pediatric clinic in 1979, 122 bronchoscopies have been carried out for suspected foreign bodies. Up to March 1987, 100 foreign bodies were found (82 %) and extracted in almost all cases (thoracotomy was needed in one child). Mucosal granulations as a hint for a foreign body that had been coughed up and expectorated spontaneously were found in an additional number of 11 cases. The duration of the extraction procedure did not correlate to the similar procedures already done or to the elapsed time interval between suspected aspiration and extraction. A prolonged time interval (up to 2h) or repeated endoscopies (up to 3) were, however, needed in cases of multiple inhaled nut-pieces or small foreign bodies lodging in more peripheral Airways. 12 children presented with signs of pneumonia (12 %). Median time interval up to extraction was 70 days in this sub-group, as compared to 20 days in children without pneumonia. Severe morbidity was only seen in cases with pneumonia (lobectomy in 3, bronchiectasis in 4, recurrent pneumonia in 3; 6/12-65 %). Thus delayed diagnosis of pulmonary aspiration of foreign bodies in childhood remains a major problem in pediatrics. The awareness of such an event of parents, pediatricians and GP's has to be reawakened continuously. A clear-out history of aspiration together with any observed clinical sign is an indication for radiologic examination (x-ray during inspiration and expiration, fluoroscopy if doubtful). The majority of children will have to undergo endoscopy then. A falsely positive figure of 18 % of children, where a foreign body is already visible to the endoscopist, seems justified in the light of the prevention of severe morbidity as seen in chronic foreign body aspiration. 

EFFICIENCY OF BRONCHOALVEOLAR LAVAGE (BAL) FOR DIAGNOSIS OF ACUTE RESPIRATORY INFECTIONS.

U. Ehrentreich, I. Dab, A. Walfroot, D. Pierard, Department of Pediatrics and Microbiology, Academic Hospital Free University of Brussels (A.Z.-VUB) Belgium.

We compared the diagnostic information obtained by bronchoscopy in an unselected group of children with a respiratory infection before treatment and in a previously untreated information in children with persistent respiratory infection, mostly despite antibiotic treatment.

Over the last 13 months 82 respiratory endoscopies were performed in children, aged 6 week to 12 years, admitted with radiological and/or clinical evidence of a respiratory infection, preferably before treatment was instituted. Bronchoscopy, including simple bronchial aspiration (BA) and bronchoalveolar lavage (BAL), was performed on these patients. The BA and BAL were submitted for bacterial, viral and fungal culture, including techniques for possible identification of Mycoplasma pneumoniae, Chlamydia trachomatis and CMV. Positive bacterial cultures were obtained in 28 cases (35%): 64% Hemophilus influenzae (of which 16% were β-lact.+), 14% Staph. a. and the remaining consisted of Klebsiella pneumoniae, Streptococcus pneumoniae, E. coli, Branhamella catarrhalis, each in an average of 4%. Fungal infection with Aspergillus fumigatus was found in one child with cystic fibrosis and in another child the culture of the BAL was positive for a respiratory syncytial virus. Interestingly, whereas bacterial infection couldn’t be diagnosed by cultures of other body fluids, including blood cultures, viral cultures were positive in 9 children (11%), but only once in BAL, 4 in throat, 3 in nose and 1 in urine. Rigid and flexible bronchoscopy were performed in equal proportion, avoiding positive bacterial cultures in an unselected group of children with acute respiratory infection as in a selected group with persistent infection and will lead sooner to a correct choice of therapy in at least half of the patients, some of them harbouring resistant strains for classic antibiotics. Since positive viral cultures seem to be less frequent on BA and BAL, we suggest to combine cultures on BA and BAL with those on nasopharyngeal aspiration, mainly for the possible diagnosis of a viral etiology.

THE CROSS-OVER LUNG SEGMENT

A new congenital malformation associated with a variant of scimitar syndrome.

B.S. Clements, J.W. Marver.

Three cases of a congenitally misplaced segment of lung were described. In one case the abnormal segment was identified at thoracotomy extending from an origin in the right upper lobe, across the mid-line into the left lower hemithorax. The remaining two cases with identical radiographic features (utilising pulmonary angiography, bronchography and CT scans) were identified in a review of 24 cases of broncho-vascular malformation. In all three patients, the cross-over segment was associated with a variant of the scimitar syndrome: right lung hypoplasia with dextrocardia, aberrant systemic arterial supply to the right lower lobe, anomalous venous drainage of the whole of the right lung, and (in two cases) extracardiac of the right hemi-diaphragm.
SMOKING, POLLUTION AND EXERCISE

CHILDREN AND TOBACCO

Knol K, Colombijn M, and Knol E. Department of Pediatrics, University Hospital Groningen, The Netherlands.

In the absence of cigarette smoking clinically significant chronic obstructive lung disease in adults would be rare. An important way to influence a population's smoking habits is to reduce the incidence of the current infections. The ultrasonographic evaluation (ATL Mark GDD, 5 MHz) demonstrated a homogenous tumor above the diaphragm. We found pulsatile flow patterns by the pulsed doppler sonography within the arteries feeding the sequestration. Aortography finally clearly showed the anomalous arteries leading from the descending aorta to the sequestrum.

Bronchoscopy and bronchography demonstrated, that the sequestered area of the lung had no connexion to the bronchial tree.

Surgical treatment is the only possible method to remove the individual cause of the recurrent infections. The sonographic investigation of the diaphragm could be a useful tool in the diagnosis of malformations of the lung. The doppler technique allows the detection of pulsatile flow patterns in doubtful cases.

Table 1. Smokers(%) in the first two classes of two secondary schools.

| Age | % class | % sex | % type of school | % |
|-----|---------|-------|-----------------|---|
| 12  | 14.6    | 14.2 boys | 21.7 | school I | 26.2 |
| 13  | 16.0    | 27.7 girls | 21.5 | school II | 17.1 |

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Table 1.

| Smokers(%) in the first two classes of two secondary schools. |
|---------------------------------------------------------------|
| n=722                                                          |

COTININE AND PASSIVE-SMOKING IN ITALIAN SCHOOL-CHILDREN AGED 9-15.

G. Antonogoni MD, G. Ciofetta MD, N. Haley MD, K. Axelrade MD, E. Porro MD, G. S. Covini MD, S. Russo MD, R. De Blasio MD, R. Ronchetti MD, Pediatric Clinic, Rome Univ. "La Sapienza", Italy; Am. Health Found. Valhalla, N.Y.

We studied saliva cotinine concentrations, bronchial reactivity and flow-volume curves in 216 schoolchildren aged 9-15 (47% males) to assess the relationship between these parameters and parents' smoking habits. The latter were established in parents and children by two different and standardized questionnaires. All children performed a basal flow-volume curve and carbachol-challenge test. Cotinine was determined by aRIA method. The correlation between the cigarettes smoked by both parents and cotinine levels is shown in the table:

Table 2. Parents smoking.

| Cotinine | PARENTS SMOKING |
|----------|------------------|
| 0 cig.   | <29 cig.         |
| >29 cig. |                  |
| absent   |                  |
| 1-7 ng/ml|                  |
| >7 ng/ml |                  |

Similar tendency was seen especially for mothers. 12 children (13.3%) aged 9-14 of no smoking-parents had measurable concentrations of saliva cotinine and we suppose that they were smokers themselves. We did not find a significant correlation between cotinine saliva and bronchial reactivity. The mean F51 (CI limits) values were 9812, 9425, 93±12 for not detectable, 1-7 ng/ml and >7 ng/ml cotinine levels respectively (p<0.06). These data suggest that passive smoking can be correlated with decreased respiratory function tests.

EDSINOPHIL COUNTS (EC) AND PASSIVE-SMOKING IN CHILDREN.

R. Ronchetti MD, E. Bonchi MD, F. Macri MD, G. Ciofetta MD, G. De Castro MD, F. Lalia MD, D. Capotosti MD, F. Martinez MD, Pediatric Clinic, Rome University "La Sapienza", Italy.

EC and EC% have been shown to be significantly increased in adult smoking subjects independently of atopy. EC have also been found to be negatively correlated with lung function tests in adults. Passive smoking in children as assessed by the number of cigarettes smoked by parents has been shown to be negatively correlated with lung function tests in children. No study has addressed the issue of the possible correlation of passive smoking and EC in children.

As a part of a cross-sectional study on determinants of respiratory function and diseases in children this relationship was studied in 159 boys and girls aged 9 yrs: EC were estimated by a culter counter. As a part of standardized questionnaire on respiratory health, the total number of cigarettes smoked by both parents was estimated and added. Five smoking categories (0, 1-10, 11-20, 21-30, >30 cig/day) were established. Data are shown in the table:

Table 3.

| Ec/day | N | Ec | Leuc. | Cases and % with cig/day |
|--------|---|----|------|-------------------------|
| 0-1    | 43 | 145±14 | 1.99±15 | 4 (9%) |
| 1-10   | 22 | 161±21 | 2.25±39 | 4 (18%) |
| 1-20   | 28 | 185±27 | 2.45±32 | 9 (24%) |
| 21-30  | 29 | 215±34 | 2.82±41 | 7 (24%) |
| >30    | 30 | 225±39 | 2.50±43 | 10 (37%) |

p trend <0.01 <0.01 <0.01

It was concluded that EC and EC% are significantly correlated with the totol numbers of cigarettes smoked by parents and suggested that this can be an important pathway in the previously described effects of passive smoking upon lung function in children.

1. Targets For Health For All, WHO, Copenhagen, 1985.

Erlangen.
When compared with children of non-smoking parents, the more than 10 cigarettes per day) showed smaller increases in passive smoking can impair lung growth. In order to significantly decrease perform and data from literature are scanty. Epidemiologic evidence suggests that in children bronchial reactivity decreases with age and that factors like passive smoking can impair lung growth. In order to contribute to this field, 75 non-asthmatic children, of the initial age of 11 years (40 females, 35 males) randomly chosen from a school population of Bologna (Italy) performed annually for three consecutive years a spirometric evaluation before and after an exercise test (free maximal running for 6 minutes). Results showed that:

1) Spirometric parameters consistently increased during the three years according to predicted values: however, children with passive smoking (one or both parents smoking more than 10 cigarettes per day) showed smaller increase when compared with children of non-smoking parents. The difference was statistically significant for PEF (p < 0.01) and PEF 25-75 (p < 0.001).
2) Bronchial reactivity expressed by exercise induced fall of PEF and lability index (fall + increase of PEF), significantly decreased (p < 0.01) during the three years. The reduction was not significantly influenced by passive smoking.

**The Interrelationship Between Residual Airway Obstruction and Exercise Induced Response in Childhood Asthma**

D. Linna

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To study whether bronchial reactivity to exercise is dependent on baseline lung function, 84 asthmatic children aged 7-16 years were investigated. The percent age fall in PEF values after a standard exercise running test was 9.4 ± 8.6% in those 39 children with an attack rate of less than 10 per year and 29.6 ± 23.3% in those 45 children with an attack rate of 10 or more per year (p < 0.001). A significant negative correlation (r = -0.46, p < 0.001) was found between pre-exercise MMEF as well as between other sensitive and reproducible tests of airway calibre and the response to exercise. Such a correlation was not found between the baseline PEF or SGaw values and the exercise response (r = -0.16 and -0.20, respectively, p < 0.05). These results show that bronchial hyperreactivity to exercise is dependent on the residual airway obstruction, but a wide variety of reactivity can occur.

If baseline flow-values less than three standard deviations below predicted are found, however, a clinically significant response to exercise is predicted.

**Values of Vital Capacity in Children Staying in Areas With and Without Air Pollution**

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We have studied pulmonary function tests in five groups of children from different cities with known high pollution levels of sulphur dioxide and soot. Vital capacity (VC) and forced expiratory volume in one second (FEV1), at rest measurements (by Electronic Pneumoscreen, Jager), were found to be 20-30% lower than normal in approximately 19-47% of the exposed children. The disturbed function of ventilation (decreased VC and FEV1) was caused by the irritant effect of air pollution. Bronchospasm was not registered in any of the groups, not even after exercise testing. According to illness history, these children had problems with respiratory illnesses more often than children from a control group living in areas without air pollution. The control group of children had VC and FEV1 values normal or above normal. By statistical analysis of VC in the control group and the group of children from air polluted areas, a significantly high difference was obtained (t = 22.53; p < 0.01). The children from high polluted areas were sent on a two-week recreative stay to a mountain climate free of air pollution. Lung function disorders of these children were reversed VC and FEV1 values with or above normal. By statistical analysis of VC in the control group and the group of children from air polluted areas, a significantly high difference was obtained (t = 13.46; p < 0.01).

**The Effect of Swimming Exercises on Bronchial Reactivity**

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Children’s Asthma and Allergy Institute, Voksenteroppen and The Norwegian College of Physical Education and Sport, Oslo, Norway.

Seven asthmatic and 18 elite children swimmers without bronchial asthma, swam intervals at a speed 5% below, at the calculated aerobic capacity, and 5% above. Bronchial reactivity was measured by PC-20 histamine 15 minutes before and 15 minutes after the swimming exercises. Lung function, blood gases and blood lactate were measured before swimming, in each interval during swimming and afterwards. Heart rate was recorded electronically during the entire exercise period. Maximal VO2 was measured by the Douglas bag method on swimming in a counter-current swim-mill with variable speed of the water flow. PC-20 ranged from 0.143 to 32 mg/ml. Bronchial reactivity increased from before to after swimming (P < 0.0005), both in children with and without asthma (P < 0.03). A positive correlation was found between decrease in log PC-20 and blood-lactate after maximal load (r = 0.88, P < 0.001), and a negative correlation between decrease in log PC-20 and Base excess (r = -0.70, P < 0.01).

The increase in bronchial reactivity provoked by intensive physical exercise, and correlating to the magnitude of exercise, may possibly be important also on a long time scale, when reports of increased incidence of bronchial hyperreactivity in elite athletes are taken into account.