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CHARACTERIZATION OF CHRONIC HEPATITIS B IN CHILDHOOD USING MOLECULAR BIOLOGY TECHNIQUES. Stefan Wirth, Elmar Schaefer, Klaus-Michael Keller and Bernhard Zabel. Department of Pediatrics, Johannes Gutenberg University, Mainz, Germany

The introduction of molecular biology techniques in the diagnostics of chronic hepatitis B virus infection proved HBV DNA to be the most sensitive marker of viral replication and infectivity. The aim of our study was to characterize the HBV DNA status in children with chronic hepatitis B with various molecular biology techniques in relation to conventional HBV markers.

Methods: 206 sera of 172 and liver tissue of 108 children with chronic hepatitis B infection were investigated by dot blot-, Southern blot-, and in situ hybridization. In dot blot and Southern blot negative specimens polymerase chain reaction (PCR) was performed.

Results: 111 of the 206 sera were positive for HBV DNA by dot blot hybridization. 78% of these patients had HBeAg and 7.7% anti-HBe. In 60 (92.3%) of the anti-HBe positive sera no HBV DNA could be detected. 83.9% of the dot blot negative children were HBV DNA positive by PCR comprising all HBeAg positive and 80% of the anti-HBe positive cases. HBV DNA studies in liver tissue by Southern blot revealed free HBV DNA in 74/103 (71.8%). HBV DNA integration was present in 2 children (1.9%). PCR in the Southern blot negative tissue specimens confirmed the presence of viral sequences in all HBeAg and in 63% of anti-HBe positive cases. In situ hybridization was applied to tissue sections of 63 children. HBV DNA was detected in 48 patients. 40 were HBeAg- and 6 anti-HBe positive. The distribution of HBV DNA in the tissue was classified as homogeneous, inhomogeneous with focal patches and focal.

Conclusions: In conclusion our results demonstrate that all HBeAg- and most of the anti-HBe positive children show viral sequences in serum and liver. Integration of HBV DNA into the liver cell genome can occur at an early stage of chronic disease but is not a very frequent event. Finally, in situ hybridization is a reliable method to detect HBV DNA in small amounts of liver tissue and to provide informations about the distribution of replicative viral sequences.

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NUTRITIONAL THERAPY FOR ACUTE MILD GASTROENTERITIS AS EMPLOYED BY PRACTISING PEDIATRICIANS

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A representative survey was conducted to ascertain the extent to which the modifications in scientifically based therapeutic measures over the last 10-15 years have been utilized by pediatricians in private practice. In the first 6 months of 1990, 427 practising pediatricians selected by random sampling were asked to complete a detailed questionnaire entitled "Treatment of acute mild infant gastroenteritis in your practice". The questionnaires of 350 pediatricians (83%) were suitable for evaluation.

Results: 97% of all pediatricians prescribe a tea period (ORT) of < 6 hours in 54% and 6-12 hours in 26% of cases. Only 65% recommend the use of any form of electrolyte solution additionally! A transitional diet based on rice or carrot soup is still recommended by 75% of all pediatricians for 6-48 hours or even longer. In 73% of cases re-feeding itself takes place in the form of "Heilnahrungen" for 3-6 days, which also contrasts with recent inverstigations, which indicate that direct transition from ORT to previous nutrition is adequate. Surprisingly, there have been very few changes in the treatment of acute infant gastroenteritis as compared with the findings of the survey conducted by Scharf and Schaub 15 years ago - apart from an increase in the use of OR solutions. Information on modern, targeted therapy through suitable counselling measures for practising pediatricians is meaningful and necessary.

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ONTOGENY OF TRACHEAL IMMUNITY IN THE FETAL PERIOD AND THE FIRST YEAR OF LIFE. Lauritz Stoltenberg, Per S Thrane, Torleiv O Rognum. Institute of Forensic Medicine, Laboratory for Immunohistochemistry and Immunopathology, The National Hospital, N-0027 Oslo 1, Norway.

Immunoglobulin (Ig)-producing cells, T cells (CD 3) and epithelial expression of secretory component (SC) and major histocompatibility complex (MHC) class II (HLA-DR, -DP and -DQ) were studied by immunohistochemistry to obtain information on the ontogenesis of the tracheal mucosal immune system. Fourteen fetal and 13 postnatal carina specimens obtained at autopsi were examined. SC was present in the tracheal wall in small amounts during the fetal period and showed increased expression towards delivery. A few IgM- and IgG-producing cells were present in 40% of the fetal specimens wheras no IgA-producing cells were seen. Intraepithelial CD3+ T-cells were found in 4 prenatal specimens. They increased rapidly in number after birth with a concomitant increase in IgA-, IgM-producing cells and epithelial SC expression. Epithelial MHC class II expression was absent in fetal specimens. In the postnatal specimens, HLA-DP and -DQ were absent wheras HLA-DR was extensively expressed on the apical border of the surface epithelium from the first week of life.

Conclusion: SC synthesis is independant of the B-cell system. Epithelial HLA-DR determinantes, CD3+ T-cells and IgA immunocytes apparently reflect a respons to environmental factors.

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NEUTROPHIL ELASTASE IN TRACHEAL ASPIRATES OF INFANTS WITH RESPIRATORY DISTRESS SYNDROME (RDS). Christian P. Speer[1], Egbert Herting[1], Karsten Harms[1], Dorothea Rosinski[1] and Olaf Gefeller[2]. [1]Dept of Pediatrics and [2]Medical Statistics, University of Göttingen, Germany

Neutrophil Elastase (E) seems to play an important role in the pathogenesis of chronic lung disease (CLD) in premature infants; acute effects of this neutral protease on neonatal pulmonary disease have not been evaluated. In this prospective study we have analyzed E and α_1-Proteinase-activity (α_1-PI) in tracheal aspirates of 140 neonates with severe RDS ($FiO_2 > 0.6$, mechanical ventilation) during the first day of life; all infants were treated with natural porcine surfactant (Curosurf).

Results: In 42 infants (30 % [group 1]) a considerable activity of E was detected (0.8 - 253 µg/mg albumin, range); in 98 neonates (70 % [group 2]), who had protective levels of α_1-PI, no E was found. Characteristics and disease severity were identical in both groups. Gestational age: 29.3 ± 2.3 weeks (group 1); 29,7 ± 2,2 (group 2). Using logistic regression analysis, 28 day outcome data of both groups showed an increased incidence of pulmonary interstitial emphysema (PIE) in patients with E-activity in tracheal aspirates (31.7 % vs. 17.5 %, group 1 vs. group 2, $p < 0.05$). The incidence of pneumothorax, CLD and non-pulmonary complications was identical in both groups.

We conclude that Elastase present in the bronchoalveolar space of infants with RDS is associated with an increased risk of PIE.

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GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR (GM-CSF) SUPPRESSES BOTH SPONTANEOUS AND LIPOPOLYSACCHARIDE-STIMULATED BIOSYNTHESIS OF COMPLEMENT COMPONENT C3 IN CULTURED MONOCYTES.
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At extravascular sites, monocyte/macrophage synthesis of complement protein is thought to be quantitatively important. Lipopolysaccharide(LPS) stimulates the production of C3 and other complement components.

In the present study human monocytes were isolated from peripheral blood and cultured for 1-5 days under serum-free conditions. GM-CSF or LPS was added both alone and in combination to selected monocyte populations on day 0. Supernatants were harvested on day 2 and day 5 and analysed for total C3 content in a sensitive enzyme-linked immunoassay.

C3 conc.(ng/ml) in cell supernatants:(Mean ±SD of 7 exp)

	control	GM-CSF 100 ng/ml	LPS 1 ng/ml	GM-CSF 100ng/ml + LPS 1ng/ml
Day 2	2,4±1,0	1,7±0,7	4,6±2,2*	2,4±1,2 †
Day 5	6,8±1,9	3,7±1,6 **	26,4±10,1**	7,3±3,4 ††

*p<0,05 and **p<0,01 vs.control cells.
†p<0,05 and ††p<0,01 vs. LPS-stimulated cells.

Conclusion: GM-CSF is thought to increase resistance to infections, but the described effect may reduce complement opsonization and phagocytosis of pathogens in the tissues.

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INTERLEUKIN-6 LEVELS IN NEONATAL SEPSIS. J. David Edgar*, David C. Wilson**, Stanley A. McMillan*, Alistair D. Crockard*, Henry L. Halliday**, Thomas A. McNeill*. *Regional Immunology Laboratory, Belfast City Hospital and **Royal Maternity Hospital, Belfast, Northern Ireland.

Neonatal sepsis is a major cause of morbidity and mortality in preterm infants. Clinical diagnosis is difficult and no reliable diagnostic test exists. Interleukin-6 (IL-6) is a central mediator of the sepsis syndrome. In this study we examined the diagnostic value of plasma IL-6 in preterm infants thought to be septic.

Normal plasma IL-6 levels were established in cord bloods of sixty preterm infants at a range of gestational ages. 50 infants suspected of congenital (n=14) or acquired (n=36) infection were then studied. Samples were taken at the time of blood culture. IL-6 levels were determined by ELISA. The study group had a mean (SD) gestational age of 29.8 (3.6) weeks, and birth weight of 1361 (735)g.

Results: Dependent on clinical course 36 babies were considered septic (20 blood culture positive, 16 blood culture negative) and 14 non-septic. IL-6 levels were significantly ($p < 0.001$) elevated in both blood culture positive and culture negative sepsis. For sepsis, plasma IL-6 >0.235ng/ml had a sensitivity of 33%, specificity of 89%, +ve predictive value 60%, -ve predictive value 73%, figures for blood culture positive sepsis were 35%, 86%, 35%, and 86% respectively.

Conclusions: Plasma IL-6 levels have been shown to be significantly elevated in septic preterm infants . However predictive values of this test are insufficient to warrant the replacement of existing diagnostic tests.