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## THE EFFECT OF INTRAVENOUS ANTIBIOTIC THERAPY ON INFLAMMATORY MARKERS IN BRONCHIAL SECRETIONS FROM PATIENTS WITH CYSTIC FIBROSIS.

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In cystic fibrosis, *Pseudomonas aeruginosa* colonization leads to a progressive destructive chronic bronchitis and despite antibiotic treatment, eradication is not attained and inflammation usually persists. However, in recent years the survival rate of these patients has been markedly improved by repeated, elective i.v. antibiotic treatment. In this study we asked the question how two-weeks antibiotic treatment modified lung functions and several inflammatory markers in the bronchial secretions of seven patients in a total of 12 such treatments.

The lung functions (FEV<sub>1</sub> and FVC) improved and the number of circulating WBC decreased significantly after each treatment period. In spite of this, no change was observed for the neutrophil chemotactic activity (NCA) of sputum, or for the mean sputum concentrations of IL-8, and human leukocyte elastase (HLE) activity. The total amount of sputum and IL-8 however, had decreased significantly:

	N	Before (± SD)	After (± SD)
Sputum weight (g)	7	39.1 ± 24.2	10.95 ± 6.7*
Elastase (mg)	7	14.02 ± 11.7	7.57 ± 11.76
IL-8 (nmol)	7	228.7 ± 169.3	56.14 ± 30.52*

\* p < 0.05, Wilcoxon

In summary, the quality of the sputum remained unchanged, while the quantity decreased significantly together with the general clinical improvement of the patients.

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## A RECOMBINATION EVENT CAUSING A DE NOVO DELETION OF THE STEROID 21-HYDROXYLASE GENE CYP21.

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Steroid 21-hydroxylase deficiency is the most prominent cause of congenital adrenal hyperplasia (CAH). Patients suffer from virilization, and in severe cases, from salt loss caused by lack of aldosterone. The CYP21 gene, encoding steroid 21-hydroxylase, and the highly homologous pseudogene CYP21P are located within the human MHC on chromosome 6p21.3, the usual arrangement being centromere - HLA-DP, -DQ, -DR - CYP21-complement C4B-CYP21P-complement C4A - tumour necrosis factor (TNF) genes - HLA-B, -C, -A. We investigated a CAH family (father, mother, patient, three healthy sibs) using 21-hydroxylase and complement C4 probes and allele specific oligonucleotides to detect specific mutations. Oligonucleotide hybridization showed that the patient inherited the Ile172->Asn mutation, characteristic of "simple virilizing" CAH, from the mother. On the other chromosome, the CYP21 gene was deleted; however, this defect was not found in DNA from the father. Paternity was confirmed using VNTR probes. Establishment of HLA-B, TNF and HLA-DQα markers showed that the patient had the HLA-B and TNF genes from one paternal chromosome and the HLA-DQα gene from the other. Apparently, a paternal meiotic recombination event has eliminated the CYP21 gene (as well as the adjacent C4B gene), contributing to steroid 21-hydroxylase deficiency in the patient.

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## THE SIGNIFICANCE OF BLOOD LACTATE IN CRITICALLY ILL NEONATES

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Although arterial blood lactate (ABL) is regarded as a competent indicator of the severity, and predictor of outcome of critical illness in adults, little is known about its significance in acutely ill neonates.

We have, therefore, studied the prognostic value of serial ABL and acid-base changes in 65 consecutive ill, ventilated neonates with median (range) gestation 29 (23-40) weeks and birthweight 1330(550-4080) g, with indwelling arterial catheters. Lactate concentrations were measured in 40 ul of deproteinised blood by a specific enzymatic method. Hyperlactatemia was defined as ABL > 2.5 mmol/L. The overall mortality was 20% (13/65). Hyperlactatemia was strongly associated with mortality. While 6/48 babies with peak lactate concentrations (PLC) < 2.5 mmol/L died, 3/12 babies with PLC 2.5-4.9 mmol/L and 4/5 babies with PLC > 5 mmol/L died. None with persistent hyperlactatemia survived. The median (Q1-Q3) % reduction from PLC was significantly lower in non-survivors than in survivors { 3.6(0-16.4) vs 32.1(17.6-48); p=0.001}. The acid-base changes were not related to outcome. ABL was also superior to CRIB scores in predicting mortality.

ABL, therefore, appears to be a useful indicator of the outcome in critically ill neonates. Blood lactate levels that are rising, show little reduction or are > 5mmol/L carry a bad prognosis.

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## IRON INDUCED LIPID PEROXIDATION AND REPERFUSION INJURY AFTER SEVERE BIRTH ASPHYXIA Caroline A. Dorrepaal, Manon J.N.L. Benders, Ernst Houdkamp, Margot van de Bor, Frank van Bel, Dept. of Pediatrics, University Hospital Leiden, The Netherlands

Iron-induced oxidative stress may play a role in postasphyxial reperfusion injury. We serially measured free iron (bleomycin assay) and TBARS (index of lipid peroxidation) in plasma of 50 term neonates in the first 24 h after birth. We compared 20 healthy newborns (HN) with 15 moderately asphyxiated newborns (MAN), and 15 severely asphyxiated newborns (SAN) with abnormal neurological signs in the first 24 h of life. Results: Cord pHs were 7.29±0.09, 7.02±0.08 and 6.87±0.10 for HN, MAN and SAN. All HN, 14 MAN and 7 SAN had normal neurological examinations at discharge. Eight SAN had brain damage, 5 died in the neonatal period. Liver and renal functions were abnormal in 10 SAN and 4 MAN. Free iron was not detectable in 66% of HN, 20% of MAN, and 12% of SAN. Results are summarized in table:

GROUP	1-6H	7-12H	13-18H	19-24H
	FI/TBARS	FI/TBARS	FI/TBARS	FI/TBARS
HN	13±26/7.5±3.1	21±26/7.7±1.6	18±19/8.3±1.5	12±28/8.6±1.3
MAN	14±16/6.5±1.5	64±39/7.9±3.2	48±43/9.5±2.4	34±33/9.6±1.4
SAN	41±38/6.4±1.3	67±43*/10.5±6.5	61±38*/9.9±3.7	62±41*/11.8±3.4*

ANOVA, \*p<0.05 vs HN, Free Iron (FI) and TBARS are expressed in μM

Conclusion: Neonates with severe birth asphyxia, neurological abnormalities, and abnormal liver and renal tests had increasing plasma levels of free iron and TBARS in the first 24 h of life. This suggests a role for iron-induced lipid peroxidation in the etiology of reperfusion injury after severe birth asphyxia.

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## FACTORS ASSOCIATED WITH THE RESPONSE TO SURFACTANT REPLACEMENT THERAPY IN NEONATES WITH RDS

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Objective: Identification of factors associated with the response to surfactant replacement therapy in preterm neonates with RDS.

Material - Methods: We prospectively studied 37 preterm neonates, 26 males and 11 females, ranging in GA from 23 to 34 weeks, with RDS. None neonate had received steroids prenatally and all had a score of radiographic severity >2. After initial stabilization they were treated with bovine surfactant (Alvofact\*) at a dose of 100 mg/kg. Additional doses (each, 50mg/kg) were given if the neonate had an a/APO<sub>2</sub><20, 12 and 24 h later. Neonates were classified into responders (a/APO<sub>2</sub>≥30 or extubation at 24 h after the 1st dose and non responders (a/APO<sub>2</sub><30 or need for additional doses). This response pattern was analysed in relation to GA, BW, sex, perinatal asphyxia, pH on admission and at initiation of treatment, a/APO<sub>2</sub>, FiO<sub>2</sub>, ventilatory requirements and complications of RDS.

Results: 20 neonates (GA=29.1±2.4 wk) were classified as responders and 17 (GA 29.8±2.0 wk) as non responders. Surfactant was given at a mean age of 7.7±8h and 11.3±6h to the two groups, respectively (>0.5). The non responders had significantly lower mean pH on admission and mean a/APO<sub>2</sub> before surfactant administration and higher incidence of PDA. There was also a trend for higher incidence of asphyxia, higher mean FiO<sub>2</sub>, mean airway pressure and peak inspiratory pressure in the group of the non responders. No difference was found with regard to GA, BW, sex, arterial pressure and pH at the time of surfactant administration.

Conclusions: 1) The response is adversely affected by the low pH on admission, even when corrected before surfactant administration. 2) This response is also associated with the a/APO<sub>2</sub> reflecting the severity of the disease, and the patency of ductus arteriosus.

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## HAEMORRHAGIC-ISCHAEMIC LESIONS OF THE NEONATAL BRAIN:

## CORRELATION BETWEEN CEREBRAL VISUAL IMPAIRMENT,

## NEURODEVELOPMENTAL OUTCOME AND MRI IN INFANCY.

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A group of sixty-five at-risk neonates was enrolled in a prospective follow-up study in order to assess the relationship between the degree of Cerebral Visual Impairment, established using the Acuity Card Procedure, and the extent of neurological sequelae. Furthermore, MR- and CT-scans were performed in all infants with severe neurological sequelae to study whether characteristic lesions occurred in the central visual pathway.

Eleven out of twelve infants with an acuity on or below the 10<sup>th</sup> centile at 18 months developed cerebral palsy; the underlying condition was extensive cystic leukomalacia in all. However, an acuity above the 10<sup>th</sup> centile was no guarantee for a normal development, as ten out of 52 infants developed cerebral palsy; six had a large peri/intraventricular haemorrhage, four had cystic leukomalacia.

MR- and CT-scans showed, that periventricular high signal intensity in the occipital area was found to be a non-specific finding with regards to visual function. Very extensive periventricular white matter loss and involvement of the striate/parastriate cortex was found in the most severely visually impaired infants.

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