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Treatment of neonatal neutropenia with recombinant human granulocyte colony-stimulating factor (rhG-CSF).
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Background: The outcome of neonatal septic neutropenia is poor.
Methods Uncontrolled pilot study of rhG-CSF as adjuvant therapy in 12 neutropenic preterm infants (24-35 weeks gestation). All received appropriate antibiotics.
Results Median (range) values shown

Absolute counts	Pre-treatment	Peak post-treatment	p
Neutrophils $x10^9/L$	0.7 (0.1-1.2)	6.6 (0.8-61)	<0.01
Platelets $x10^9/L$	136 (34-235)	39 (19-103)	<0.05

Six infants recovered from acute, severe illness (4 with confirmed and 2 with probable sepsis). Four infants died from respiratory distress syndrome; 2 others were moribund pre-treatment and died after their first doses of rhG-CSF.
Conclusions RhG-CSF may correct neutropenia; prophylactic use is likely to be of more benefit than interventional use; thrombocytopenia may be a side effect.

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DIFFICULTIES IN DIAGNOSIS OF SECONDARY LEUKEMIA IN PATIENTS TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Despite major improvements in the treatment of acute lymphoblastic leukemia (ALL) patients during the last two decades, 20-30% of children with ALL still relapse. In 5-10% of these relapses a secondary leukemia is diagnosed. Most secondary leukemias are myeloid in origin and only 5-10% are lymphoid.

Fourty ALL patients were analyzed for their cytomorphology, immunophenotype and immunogenotype at diagnosis and relapse. Immunogenotypic studies included the analysis of immunoglobulin heavy chain (IgH), Igκ, Igλ, T-cell receptor-β (TcR-β), TcR-γ, and TcR-δ genes. In two precursor B-ALL cases an interlineage shift to acute myeloid leukemia (AML) occurred, suggesting the development of a secondary leukemia. In one of them, a complete change in immunogenotype at relapse was found, supporting the diagnosis of secondary leukemia. However, in the other case, seven identically rearranged IgH and TcR alleles were still present at relapse, indicating that the AML was related to the precursor B-ALL at diagnosis and thereby excluding the development of a secondary leukemia. In a third precursor B-ALL, the immunophenotype at diagnosis and relapse was identical, but a completely different immunogenotype (on at least ten Ig and TcR alleles) was found at relapse, suggesting a secondary ALL. Unfortunately, no cytogenetic data at diagnosis and relapse were available for confirmation of this assumption.

These three cases demonstrate the difficulties in defining a secondary leukemia based on cytomorphology and immunophenotype and emphasize the importance of immunogenetic studies as well as cytogenetic analysis of malignant cell samples to determine the clonal relation or clonal evolution between diagnosis and relapse.

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ARE THERE CHANGES IN CARDIO-PULMONARY HEMODYNAMICS AFTER A THERAPEUTIC DOSE OF INDOMETHACIN? Manon J.N.L. Benders, Margot van de Bor, Frank van Bel. Dept of Pediatr, Univ Hosp Leiden, The Netherlands.

Previous studies showed an early increase in systemic vascular resistance and a decrease in the perfusion of brain, kidneys and intestines for at least 2 h. The effect of Indo on cardio-pulmonary hemodynamics was studied in 14 preterm infants. PDA was diagnosed clinically and confirmed by echocardiography. We measured LV-output (mL/mL.min.$^{-1}$ kg^{-1}) and the resistance in the ascending aorta (RAO; mmHg/mL.min.$^{-1}$ kg^{-1}) before Indo and during the first 12 h after a single i.v. dose 0.1 mg/kg at 1 h, 4 h and 12 h. To assess changes in ductal patency and postductal pulmonary flow we measured peak velocities at the ductal-pulmonary opening (D-PV) and in the left pulmonary artery (P-PV) in m.sec^{-1}. Results: All 14 infants had clinical signs of PDA at 1 h after Indo, this number was reduced to 9 at 4 h after Indo but in only 1 infant ductus closure was definite. Measurements are summarized in the table:

	Pre-Indo	1 H after	4 H after	12 H after
LV output	386±54	248±38*	250±36	275±34
MABP	37±3	41±2	38±12	41±3
RAO	0.11±0.01	0.21±0.02*	0.16±0.02	0.16±-0.16
D-PV	1.33±0.09	1.52±0.11	0.84±0.15#	0.99±0.12#
P-PV	0.84±0.07	0.87±0.04	0.86±0.07	0.88±0.05

ANOVA, *p<0.05 vs pre-Indo, #p<0.05 vs previous values

Conclusions: At 1 h after, 0.1 mg Indo caused constriction of the systemic vascular bed with a concomitant decrease in LV-output. Ductal patency and pulmonary vascular resistance seemed not to be affected at this early stage. Afterwards Indo had a constrictive effect on the ductus, whereas its systemic vascoconstrictive effect subsided.

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HEMODYNAMIC CONSEQUENCES OF PHOTOTHERAPY (PT) IN PRETERM INFANTS. Manon N.J.L. Benders, Frank van Bel, Margot van de Bor. Dept. of Pediatrics, Univ. Hosp. Leiden, The Netherlands.

Hemodynamic effects were determined in 18 preterm infants undergoing blue-light PT for hyperbilirubinemia using 2D/pulsed Doppler ultrasound. Mean±SD birth weight and gestational age were 1475±757 g and 30.0±4.5 wks respectively. The mean age at which PT was initiated was 4.4±3.7 days. Left ventricular output (LVO), blood flow velocities in the left pulmonary artery (PBFV), right internal carotid artery (CBFV), and the right renal artery (RBFV) were studied in all infants just prior to the onset of PT, 1/2 h, 2 h, 12 h after initiation of PT and before and 12-24 h after discontinuation of PT. Patency of the ductus arteriosus (PDA) was assessed at all ultrasound examinations. Mean CBFV increased significantly (15.3%; $p<0.05$) and mean RBFV decreased significantly (19.2%; $p<0.05$) during the first 12 h of PT. After discontinuation of PT, CBFV as well as RBFV values returned to baseline values. LVO and mean PBFV increased significantly $\geq$12 h of PT: 26.3%; $p<0.05$ and 22.6%; $p<0.01$ respectively. LVO as well as mean PBFV remained at higher levels after the withdrawal of PT than they had been before the onset of PT. It appeared that 9 of the 18 infants developed PDA during PT. These infants had a significantly higher mean PBFV $\geq$12 h of PT than the infants without PDA had.

Conclusion: PT in preterm infants increased left cardiac output, PBFV and CBFV and decreased RBFV. The changes in CBFV and RBFV were however not associated with simultaneous changes in left cardiac output and PBFV. Furthermore, PT appeared to affect the patency of the ductus arteriosus, which resulted in a higher PBFV. This effect was more pronounced if PT lasted > 12 h.

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PROSPECTIVE RANDOMIZED MULTICENTER TRIAL COMPARING SYNCHRONIZED AND CONVENTIONAL INTERMITTENT MANDATORY VENTILATION (SIMV vs IMV) IN NEONATES.

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At 6 centers, 306 infants with significant lung disease were randomized at 7.5 ± 6 hrs of age to SIMV or IMV. SIMV was performed with the InfantStar ventilator and Star Sync module. Infants on each mode had similar BW, GA, Apgar scores, arterial-alveolar oxygen (a/A) ratio at time of randomization, # surfactant doses and rates of sepsis and PDA. The rates of mortality, IVH and pharmacologic paralysis were similar. The median duration (95% confidence interval) of mechanical ventilation of survivors was:

BW < 1 kg (n=73)		BW 1-2 kg (n=120)		BW > 2 kg (n=93)	
SIMV	IMV	SIMV	IMV	SIMV	IMV
874 hr	929 hr	107 hr	122 hr	72 hr *	96 hr
(359-1098)	(596-1090)	(98-171)	(91-167)	(64-78)	(73-106)

(* SIMV vs. IMV, p < 0.02)

In infants with BW < 1 kg, the need for supplemental O_2 at 35 weeks corrected age was less for SIMV (46%) than IMV (77%), p < 0.05. In infants with BW 1-2 kg there was more rapid improvement on SIMV with lower average FiO_2 and higher a/A ratio during the first 12 hours (p < 0.05), and a trend for less sedation with benzodiazepines (p = 0.08) and morphine (p = 0.1) during the first 10 days. In infants with BW > 2 kg, there were trends toward decreased pneumothorax occurrence and need for ECMO on SIMV (both p = 0.1). SIMV compared to IMV in sick newborns can improve oxygenation, shorten the duration of ventilation and reduce chronic lung disease. (Funded in part by Infrasonics, Inc.)

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DELETERIOUS EFFECT OF ALUMINIUM CONTAMINATION OF INTRAVENOUS FEEDING SOLUTIONS ON LONG TERM DEVELOPMENTAL OUTCOME FOR INFANTS BORN PRETERM. NJ Bishop, A Lucas, R Morley. University Department of Paediatrics and MRC Dunn Nutrition Unit, Cambridge, UK.
Aim. To investigate the possibility that aluminium contamination of intravenous feeding solutions in routine use for preterm infants is associated with adverse long term developmental outcome.
Methods. 240 infants were randomly assigned to receive either the standard or aluminium-depleted solutions (typical exposure of 40-50 vs 4-5 mcg/kg/day of aluminium). Detailed monitoring of all aspects of perinatal care was undertaken in order to evaluate confounding influences. Developmental follow-up of the 193 survivors was undertaken at 18 months post-term using the Bailey motor and mental scores.
Results. Mean scores for the non-handicapped survivors in depleted vs standard groups were 100.1 (18.4) vs 95.6 (22.3), t=1.42, p=0.16. In a regression model which adjusted for the unequal distribution of sex between the groups, the effect of receiving the standard as opposed to depleted solutions was to reduce IQ at 18 months by 0.6 points per day of intravenous feeding (t=3.96, p=0.0001). Reduction of aluminium contamination of these feeding solutions would be of long term benefit.