

Changes in leukocyte counts and soluble ICAM1 and E-selectin during cardiopulmonary bypass in children

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A consequence of cardiopulmonary bypass (CPB) in young children is postoperative capillary leak and associated pulmonary dysfunction. Neutrophils sequester in the lungs during CPB and may contribute to functional endothelial damage. Endothelial adhesion molecules E-selectin and ICAM1 mediate sequential steps in adhesion by binding to leukocyte ligands. Circulating forms of these proteins have recently been identified. We therefore studied changes in the plasma concentrations of soluble E-selectin and soluble ICAM1 using fixed phase immunoassays, and associated leukocyte counts in 10 paediatric patients undergoing CPB for corrective cardiac surgery. Preoperative concentrations of soluble E-selectin and soluble ICAM-1 consistently fell during CPB from 89±27ng/ml (mean±2SE) and 218±70ng/ml respectively, to 39±12ng/ml and 84±28ng/ml respectively at the beginning of maximum hypothermia during CPB. The haemodilution that occurred during CPB largely explained this fall, but not a more marked decrease in white cell counts that also occurred over this period (6.66±1.23 to 1.73±1.73x10<sup>9</sup>/l) which may reflect increased leukocyte sequestration. By 24 hours postoperatively, levels of both soluble adhesion molecules approached preoperative concentrations, as did lymphocyte counts. In marked contrast neutrophil counts rose appreciably at the end of CPB and during the immediate post-operative period and remained at these elevated levels 24 hours later. Major consistent changes in circulating leukocyte numbers which occur early in CPB may reflect changes in adhesion to endothelium and consequent sequestration. Alterations in the levels of soluble adhesion proteins may influence these processes.

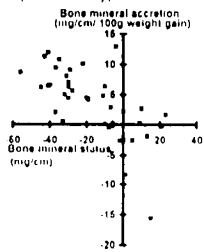
MINERAL METABOLISM

CATCH-UP BONE MINERAL ACCRETION IN OSTEOPENIC PRETERM INFANTS AFTER SUFFICIENT SUPPLEMENTATION OF CALCIUM AND PHOSPHORUS.

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VLBW infants often develop bone mineral deficiency but the intrauterine bone mineral accretion (BMA) rate (4.5 mg/cm 100 g weight gain) can be achieved postnatally if the mineral supplementation is increased up to the point that both calcium and phosphorus are simultaneously excreted with the urine. The wide range of bone mineral accretion (-2.2 to 13.3) observed in a previous study prompted us to look for variables that contribute to this variation. **Methods:** From a longitudinal study of 74 VLBW infants (birth weight range 430 - 1.580 g, median 970; gestational age 24 - 33, 28 weeks), who received stepwise increased supplements of Ca/P, 37 three-weeks-periods were selected when urine samples (2/week) contained both Ca and P. BMA during those periods, measured by single photon absorption densitometry at the right humerus, was related to the bone mineral status (actual bone mineral content minus weight related 50th centile BMC at birth) at the beginning of each period (Postnatal age range 1.8 - 28 weeks, median 11; body weight range 1455 - 5685 g, median 2380). **Results:** BMA was directly proportional to the degree of bone mineral deficiency. The highest BMA was found in the infants with the lowest mineral status.

**Conclusion:** Osteopenic VLBW infants show catch-up mineralization when they are sufficiently supplemented with Ca/P.



CHANGES IN BONE ALKALINE PHOSPHATASE PARALLEL CHANGES IN HEIGHT VELOCITY DURING GROWTH HORMONE TREATMENT OF SHORT NORMAL CHILDREN

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We have compared bone alkaline phosphatase (ALP, by lectin affinity electrophoresis) and height velocity (HV), measured at 3-monthly intervals over one to two years, in three groups of short, healthy children treated with growth hormone. Group A were 12 prepubertal children with a bone age <8 years, Group B were 11 prepubertal boys with a bone age >8 years and a chronological age <14 years, and Group C were 4 boys older than 14 years, in puberty or early puberty. Analysis of variance showed that all groups had significant increments in HV and bone ALP during the first year of treatment (P<0.05), but the pattern of response was different for the different age groups. Group A had a maximal response at 3-6 months (P<0.001, paired t-test), decreasing thereafter to a nadir at 18 months. Group B also had a maximal response at 3-6 months (P<0.01), which was maintained at constant levels up to 2 years. Group C showed an increase at 3 months (P<0.05), with a further gradual increase up to 12 months. In all groups, changes in bone ALP mirrored the observed changes in HV. By contrast, a control group of 6 children treated with placebo for one year showed no significant change in HV or bone ALP. For groups A, B and C combined, the increments in HV and bone ALP at 3 months were significantly correlated (r = 0.49, P<0.01). We conclude that different patterns of growth may be observed in response to growth hormone in short normal children, and that there is a close temporal and quantitative relationship between changes in bone ALP and growth. Bone ALP is therefore a useful short-term marker of growth in children.

RATIONALE FOR A SECOND DOSE SURFACTANT TREATMENT IN SEVERE RESPIRATORY FAILURE. Frans B. Plötz, Henk Stevens, Alle Heikamp, Sidarto Bambang Oetomo, Dept. of Pediatrics, University Hospital, Groningen.

Newborn infants with respiratory distress who fail to respond to surfactant treatment receive a second dose surfactant. The effect of this strategy on the distribution of surfactant to the lung is unknown. We therefore investigated the distribution of the first (100 mg/kg) and second dose (50 mg/kg body weight) of surfactant (Alvofact®) in 6 lung lavaged rabbits. We used Ce and Ru microspheres that were mixed with the surfactant. Arterial PO<sub>2</sub> increased from 5.7±0.5 to 10.6±1.2 kPa (mean±SEM) after the first and from 20.1±6.4 to 30.1±6.2 kPa (p<0.05) after the second dose. Thereafter the rabbits were killed and the lungs were cut in 200 pieces (10-50 mg). The radioactivity of Ce and Ru microspheres were measured and distribution histograms were obtained. Histograms of the first, second, and, total dose of surfactant showed similar non-uniform distribution. Correlation coefficients of the Ce and Ru radioactivity in the different lung lobes ranged from 0.03 to 0.28. This indicates that the second dose is directed both to areas that initially received surfactant and to areas that were still surfactant deficient that were aerated by this second dose, resulting in a further rise in PO<sub>2</sub>. We conclude that a second dose surfactant does not lead to homogenous distribution of surfactant but results in a significant rise in PO<sub>2</sub>.

SYSTEMIC INFLAMMATION (SI) IN THE SEVERE IDIOPATHIC RESPIRATORY DISTRESS SYNDROME (IRDS). Frank Brus, Wim van Oeveren, Sidarto Bambang Oetomo, Albert Okken. Dept. of Pediatrics, University Hospital Groningen, The Netherlands

SI occurs during several clinical disorders and primarily affects the lung. To determine whether SI exists in IRDS we measured activation of clotting (thrombin-antithrombin III complex, T-AT III), fibrinolysis (tissue plasminogen activator, t-PA; fibrin degradation products, FDP's), kinin-kallikrein (kallikrein inhibition, KKI), and complement (C3a) and the leukocyte and platelet count in 10 premature infants with severe IRDS on day 1, 3, and 5 (see table).

	reference group	IRDS patients	
		day 1	day 5
T-AT III (ng/ml)	13±3	247±137**	70±55*
t-PA (ng/ml)	5.6±3.4	12.3±1.6*	4.5±0.4
FDP's (mg/ml)	0.7±0.2	5.0±1.8**	3.5±0.9**
C3a (ng/ml)	399±35	1860±915**	1481±386**
KKI (%)	42±5	46±7	53±4
platelets (x10 <sup>9</sup> /l)	235±13	206±31	144±27*
leukocytes (x10 <sup>9</sup> /l)	8.1±0.9	4.3±0.8*	5.8±0.9*

\*p<0.05, \*\*p<0.01 for IRDS vs reference group. Data shown as mean ± SEM

We conclude that SI including a low leukocyte and platelet count and activation of clotting, fibrinolysis and complement occurs in premature infants during the early phase of severe IRDS. This likely contributes to lung injury.

CAUDAL EPIDURAL REGIONAL ANESTHESIA AND ANALGESIA IN NEONATES WITH ABDOMINAL DEFECTS

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**INTRODUCTION:** In this study we reviewed our experience with caudal epidural catheters in newborns with abdominal wall defects who were less than 48h (hours) of age.

**Methods:** After receiving IRB approval, charts of 5 former newborns who underwent abdominal wall defect (gastroschisis and omphalocele) repair were reviewed. Either a 20 or 24g catheter was inserted 3-6cm into the epidural space, via the caudal route. After a test dose of lidocaine an infusion of 0.5-2.0% lidocaine with 1-2mcg/ml of fentanyl was begun.

**RESULTS:** Results of the review are listed in Table 1. Five infants less than 48h of age weighing 1.92-2.70 kg had caudal epidural catheters placed easily. The catheters remained in situ for 3-20 days. No infections from the catheters occurred. Plasma lidocaine levels were <0.5-5.8 mcg/ml.

**Discussion:** No adverse effects to the local anesthetic or opiate were observed. The use of epidural infusions in neonates with abdominal wall defects provides a useful alternative to the standard sedation and paralysis currently used at our institution.

NUMBER OF PATIENTS	WEIGHT (KG)	TOTAL INFUSION DAYS	INFUSION RATE (ml/kg/hr)	LIDOCAINE LEVELS (mcg/ml)
5	1.92-2.7	3-20	0.16-0.79	<0.5-5.8