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THE DEPENDENCY OF FUNCTIONAL RESIDUAL CAPACITY (FRC) ON POSITIVE ENDEXSPIRATORY PRESSURE (PEEP) AND MEAN AIRWAY PRESSURE (MAP).

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In mechanically ventilated preterm infants, adequate FRC must be maintained in order to avoid collapse of alveoli and ensure adequate oxygenation. PEEP as well as mean airway pressure may play a role in establishing and maintaining FRC. We have investigated 1) how adjustments of PEEP correlate to changes of FRC, 2) how long FRC takes to stabilize after adjustments of PEEP and 3) whether FRC depends more on PEEP or on MAP. **Methods:** 8 neonates ventilated because of respiratory distress syndrome (n=6) or recurrent apnea (n=2) were studied (gest. age 26-34 wks (range), 28 wks (median), birthweight 550-2150g, 780g, age at measurement 2-35 days, 7 days, weight 880-2040g, 1020g). FRC was measured by means of the SF_6-washout technique. PEEP was systematically varied, starting from the clinically selected value. Further, MAP was changed independently of PEEP by adjusting inspiratory time. **Results:** 1) With variable PEEP, FRC was between 5.7 and 36.0 ml/kg of body weight (median 16.5). 2) Adjustments of PEEP correlated well with changes of FRC (2.3 ml kg^{-1} cmH_2O^{-1}, r=0.81). 3) Changes of MAP also showed a good correlation with changes of FRC (2.7 ml kg^{-1} cmH_2O^{-1}, r=0.77), because PEEP and MAP are interrelated. 4) When MAP was changed independently of PEEP by adjusting inspiratory time, no significant effect could be demonstrated. 5) After adjustments of PEEP, FRC took between 2 and 16 minutes for stabilization on a new level (median 8). This time could not be predicted from any other value. **Conclusions:** 1) PEEP had a much stronger influence on FRC than MAP. 2) Stabilization of FRC after adjustments of PEEP took up to 16 minutes. 3) Investigating pulmonary function, the selected PEEP and the time needed for stabilization of FRC after modification of PEEP has to be considered.

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MEASUREMENT OF OXYGEN FREE RADICALS (OFR) IN A RABBIT SHOCK LUNG INJURY MODEL: EFFECT OF SUPEROXIDE DISMUTASE (SOD) AND VITAMIN A.

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Lung injury by oleic acid (OA) or phorbol myristate acetate (20ng/ml) plus polymorphonuclear cells (PMA-PMN) in an ex vivo rabbit shock lung model has been suggested to be caused by OFR production. Using a standard heart/lung preparation with New Zealand rabbits (2.4-4.5 Kg), baseline mean pulmonary artery pressure (PAP) was maintained at 15mmHg and mean airway pressure (MAP) at 10mmHg. Experimental perfusates were infused over 30 minutes followed by Krebs solution. Dimethyl pyroline oxide (DMPO, infused over 30 min) captured OFR which were measured by electron spin resonance. Lung injury was assessed by light and scanning electron microscopy, and lung weight.

A five-fold increase in MAP and PAP occurred with both OA and PMA-PMN (p less than 0.003). SOD (20,000 U/kg), but not Vit.A (2,000 IU), prevented lung injury and the increase in OFR with PMA-PMN.

Maximum Increase In OFR (nM)

Control	0	(5)	PMA+PMN+SOD	0	(5)
OA	0	(5)	PMA+PMN+Vit.A	108±18	(5)
PMN+PMN	112±22	(5)*			

Means±SE; (n), no. of animals; *p less than 0.0003

We conclude that 1) the mechanism of PMA-PMN lung injury is via OFR because SOD prevents both the rise in OFR and lung injury; 2) Vit.A does not prevent lung injury; 3) OA does not produce injury by increase in OFR but by other unknown mechanisms. We speculate that lung damage by OA and PMA-PMN models have different mechanisms.

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EFFECTS OF EARLY POSTNATAL RECOMBINANT HUMAN GROWTH HORMONE (rhGH) TREATMENT ON PROTEIN METABOLISM IN INTRA UTERINE GROWTH RETARDED (IUGR) PRETERM INFANTS: a pilot study.

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Treatment with rhGH has direct anabolic effects in catabolic adult intensive care patients. Preceding a randomised double blind placebo controlled investigation, a pilot study was performed in 10 type II (non-symmetric) IUGR preterm infants (birthw. 920±155 g., gest. age 30±2 wks.) (SDS≤-2) regarding possible early postnatal anabolic effects of rhGH on protein metabolism. 5 infants received a daily subcutaneous injection with 0.5 (n=2) or 1.0 (n=3) IU.kg^{-1}.d^{-1} rhGH and 5 IUGR infants were studied as controls. Daily rhGH was started one week after birth and stopped 6-8 weeks later. At postnatal age 41 ± 15 d. protein metabolism was studied during indirect calorimetry using 1-^{13}C-leucine turnover studies. All infants received continuous special formula feeding via a nasogastric drip (120 kcal.kg^{-1}.d^{-1}). Results of protein intake, turnover, synthesis, breakdown, and accretion in g.kg^{-1}.d^{-1} as means ± S.D. (sign. of diff. tested by Mann-Whitney U test):

GH	Prot.Intake	Turnover	Synthesis	Breakdown	Prot.Accretion
-	3.4±0.1	9.8±1.9	8.6±1.7	5.3±2.0	3.3±0.4
+	3.3±0.6	13.7±5.3	12.2±5.0	9.6±5.1	2.5±0.4
	NS	NS	NS	NS	NS

Conclusions: These results indicate a stimulatory effect of rhGH in IUGR preterm infants on protein turnover, synthesis and breakdown not resulting, however, in a significant rise of net-protein accretion. Additional studies are necessary to give conclusive evidence of a non-anabolic or possibly even catabolic effect of daily rhGH treatment in these infants.

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PREDICTION OF BEHAVORIAL AND EMOTIONAL OUTCOME IN CHILDREN OPERATED UPON FOR CONGENITAL HEART DISEASE.

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Behavorial/emotional outcomes, at least nine years after surgical correction for congenital heart disease (ConHD) in childhood, were predicted by variables concerning: 1)biographical status 2)medical history 3)heart surgery 4)direct and 5)late postoperative course 6)number of previous surgeries and comorbid anomalies, using regression analysis. Parents of 144 9-15-year-old ConHD-children completed the Child Behavior Checklist (CBCL). For 115 patients complete medical data were available. The outcomes on the CBCL-total problem score and on "Externalizing" (i.e. agressive and delinquent behavior) were predicted by: number of previous surgeries and preoperative complaints ($p<0.05$; mult.R's resp. 0.31 and 0.28). According to parents' reports, higher total problem and externalizing scores were associated with a higher number of previous surgeries and presence of preoperative complaints. Higher internalizing scores (i.e. withdrawal, somatic complaints, anxiety/depression) were associated with a higher number of previous surgeries, a shorter duration of pregnancy, systemic oxygen saturation < 80%, and having a congenital heart defect other than pulmonal stenosis ($p<0.05$, mult. R=0.40).

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PREFERENTIAL USAGE OF INCOMPLETE REARRANGEMENTS IN PRECURSOR B-ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL)

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Southern blot analysis of T-cell receptorTCR genes rearrangements is usefull for diagnostic studies on the clonality of lymphoproliferative diseases and for a better assigment of the cell lineage of leukemic cells.

We analyzed 26 cases of precursor B-ALL in aim to detect the presence of TCR-δ gene rearrangements. In fact lineage crossover of gene rearrangements have been osserved quite frequently in neoplastic cells. We found 6/26 patients in germline configuration, 5/26 deleted and 15/26 with at least one allele rearranged. Taking into account previous studies (Breit et al. 1993) we were able to define exactly in 8/26 cases the gene segments involved in the rearrangement; DNA extracted from bone marrow samples was digested with Eco RI, Hind III and Bgl II restriction enzymes. The hybridization with TCRJδ 1 probe showed that the majority of the rearrangements were Vδ2Dδ3 and Dδ2Dδ3.

It is possible that the crossover rearrangements reflect the earliest steps of recombinational event in rearranging antigen-receptor gene loci. Besides the Vδ2Dδ3 rearrangement, the most frequently observed in precursor B-ALL , may be the earliest recombinational event in TCR-δ gene during normal T-cell ontogeny. Amplification by PCR technique, using specific primers revealed the presence of a specific band of leukemic clone and in one case we found the sequence of junctional region between Vδ2 and Dδ3 gene segments. In this particular case, the insertion of 6 nucleotides creates a unique clonal marker of leukemic cells that can be used for the detection of minimal residual disease (MRD).

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BIOCHEMICAL LUNG IMMATURITY IN EXPERIMENTAL CONGENITAL DIAPHRAGMATIC HERNIA.

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Background: Clinical and experimental evidence supports the hypothesis that there is an alteration of pulmonary surfactant system (PSS) in congenital diaphragmatic hernia (CDH) with pulmonary hypoplasia (PH). In fact, several authors have reported the exogenous surfactant administration in human newborns with CDH.

Methods: CDH was induced in fetal rats by Nitrofen® administration on 9.5 day of gestation. Fetuses were recovered at term and lungs dissected and weighted. They were divided in 3 groups (n=6): untreated controls (Control) and Nitrofen-treated fetuses with (CDH) or without left-sided diaphragmatic hernia (no-CDH). DNA, protein, total phospholipids (PL) and disaturated PC (DSPC) contents were individually measured.

Results:	Control	no-CDH	CDH
Lung / Body weight ratio (mg/g)	28.1±3.3	21.6±1.9 *	19.2±1.1 * #
total DNA (μg)	889±123	599±50 *	554±57 *
Protein / DNA (μg/μg)	9.31±0.85	9.11±0.31	7.69±0.60 * #
total PL / DNA (μg/μg)	1.31±0.17	1.10±0.04 *	0.73±0.03 * #
DSPC / DNA (μg/μg)	0.38±0.05	0.32±0.04	0.26±0.03 *

(*) significative vs. controls, $p<0.05$. (#) significative vs. no-CDH, $p<0.05$.

Conclusions: There is a marked PH (low lung/body weight ratio and DNA content) in Nitrofen-treated fetuses and cellular atrophy in those with CDH (low Protein/DNA). At term, a decreased PL/DNA ratio and particularly DSPC/DNA are consistent findings with immaturity of PSS. Studies of the early fetal PSS maturation pattern could clarify that issue.

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