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MATURATION OF THE HYPOTHALAMO-PITUITARY-OVARIAN AXIS IN PRETERM GIRLS. G Sedin, C Bergquist, PG Lindgren, T Andersson and L Wide.
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We have earlier reported on oestradiol producing ovarian cysts and high serum concentrations of oestradiol in four very preterm infants at a postconceptional age (PCA) that slightly precedes the expected time of birth.

To determine the maturation of the hypothalamo-pituitary-ovarian axis in preterm girls we measured the serum concentration of luteinizing hormone (LH) and follicle stimulating hormone (FSH) before and after an i.v. injection of luteinizing hormone releasing hormone (LHRH). At a PCA of 33 weeks all preterm girls born at a PCA of 27 weeks and less had high basal serum concentrations of FSH and LH (15.4 and 5.2 g/l respectively) and had a postpubertal type of response to LHRH. At the same PCA preterm girls born at a PCA of 28-32 weeks showed the same type of response.

When the LHRH test was repeated at a PCA of 40 weeks, preterm girls with a low serum concentration of FSH showed a transient increase in oestradiol from 309 to 453 pmol/l (mean values). Almost all girls had a prepubertal type of response, which is normal for that age. Thus maturation of the hypothalamo-pituitary-ovarian axis occurs late in fetal life.

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IMMUNE RESPONSE AND BRONCHOPULMONARY BACTERIAL CLEARANCE AFTER MUCOSAL IMMUNIZATION WITH OUTER MEMBRANE PROTEINS (OMP) OF P.AERUGINOSA
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Averting initial colonization of the respiratory tract with P.aeruginosa would be of great benefit for patients with cystic fibrosis (CF). Our approach to this problem is mucosal immunization with a vaccine prepared from the OMP fraction of a PAO-1 strain of P.aeruginosa. Sprague-Dawley rats were given 5 intragastric doses of the vaccine on 5 consecutive days and an intranasal booster dose 21 days later. Immunized animals developed high titers of OMP-specific IgG antibodies in serum and a specific IgA response in bronchoalveolar and small intesinal lavage samples, all determined by ELISA. When challenged 7 days after the booster (day 28) by intratracheal injection of live bacteria of a heterologous strain of P.aeruginosa the immunized rats showed enhanced bronchopulmonary bacterial clearance compared to nonimmunized controls, as indicated by bacterial counts from homogenized lung tissue taken 4 hrs after challenge. Thus, mucosal immunization with OMP vaccines might hinder initial colonisation of the lungs with P.aeruginosa.

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STRETCH RECEPTOR ACTIVITY CHANGES AFTER LUNG INJURY IN CATS. Anders Jonzon and Peter Radell.
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In infants with severe pulmonary disease spontaneous breathing is usually inhibited when the infants are adequately ventilated (chemo-inhibition). During recovery spontaneous breathing may return despite adequate artificial ventilation. This may be due to changes in activity from pulmonary receptors.

Activity in single afferent fibers from slowly adapting pulmonary stretch receptors (PSR) was recorded before and after lung injury in anaesthetized cats. Lung injury was induced by intratracheal instillation of xanthine oxidase.

Six PSR:s were analyzed. Total activity decreased after lung injury ($p<0.05$). During inspiration the mean increase in afferent activity was 7.8 impulses/cm H_2O before lung injury, after lung injury the mean increase was 5.0 impulses/cm H_2O i.e. a decrease and change in spatial distribution. This occurred in spite of higher airway pressures after lung injury ($p<0.025$).

We speculate that the decrease in activity and change in spatial distribution influence the reflex control of breathing during IPPV.

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HIGH FAT FORMULA (HFF) FOR INFANTS WITH BRONCHOPULMONARY DYSPLASIA (BPD). G.R. Pereira, S. Baumgart, V. Stallings, M. Georgieff, M. Hamosh.
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CO_2 production ($\dot{V}CO_2$) and elimination by the lungs can be reduced by lowering the respiratory quotient (RQ) using high fat diets. We studied 6 premature infants (1.46-2.80 kg, 4-14 wks) with BPD fed HFF (67% fat, 22% carbohydrate, 11% protein), and Special Care with Polycose (SC + P) (37% fat, 52% carbohydrate, 11% protein) over alternate weeks at similar intakes (120-125 kcal/kg/day).

	$\dot{V}CO_2$ (ml/kg/min)	RQ	% Fat Absorbed	N retained (g/kg/day)	ΔWeight (g/day)	TG (mg/dl)
HFF	6.1 ± .5*	.8 ± .02*	85 ± 4.6*	.37 ± .03	27 ± 3	90 ± 14
SC+P	8.1 ± .9	.9 ± .02	97 ± .4	.44 ± .02	33 ± 5	94 ± 7

*$p<0.05$, M ± SEM

Significant reduction in $\dot{V}CO_2$ and RQ were seen with HFF. Both formulas 1) were well-tolerated despite lower coefficient of HFF absorption; 2) promoted comparable weight gain (ΔWeight) and nitrogen retention (N retained); 3) maintained normal serum biochemistries including triglycerides (TG). HFF may relieve respiratory CO_2 load while promoting adequate growth in premature infants with BPD.

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THE EFFECT OF CYCLOOXYGENASE INHIBITION ON RETINAL (RBF) AND CHOROIDAL (ChBF) BLOOD FLOW DURING HYPERCARBIA IN NEWBORN PIGLETS. Tom Stiris, Cleide Suguihara, Dorothy Hehre, and Eduardo Bancalari.
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The effect of cyclooxygenase inhibition on ChBF and RBF during hypercarbia was investigated in tracheotomized, paralyzed and mechanically ventilated newborn piglets. The animals were assigned to a placebo group (n=5) or an indomethacin (Indom) group (n=6). The results were (flow expressed as ml/min/100g tissue $\bar{X}$ ± SEM):

		RBF		ChBF	
		Placebo	Indom	Placebo	Indom
Basal	Room air	36±1	39±3	1720±155	1475±250
Post treat	Room air	38±2	28±3**	1621±146	1267±299
Post treat	CO_2	83±8*	31±6#	2796±429	1618±569

*$p<0.01$ (Room air vs post treat CO_2), **$p<0.05$ (Basal room air vs post treat Room air), #$p<0.01$ (between groups).

Indomethacin reduced RBF and eliminated the RBF increase in response to hypercarbia. The effect on ChBF was similar but less marked. The results suggest that the changes in RBF and ChBF in response to hypercarbia are mediated by arachidonic acid metabolites and that these metabolites are involved in maintaining normal occular vascular tone. These findings may have implications regarding the use of indomethacin in children with respiratory failure and hypercarbia.

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MATERNAL PKU SYNDROME IN COUSINS CAUSED BY MILD, UNRECOGNIZED PHENYLKETONURIA IN THEIR MOTHERS HOMOZYGOUS FOR THE PHENYLALANINE HYDROXYLASE 261 ARG → GLN MUTATION

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Microcephaly observed at birth in 2 first cousins lead to the recognition of phenylketonuria in their mothers, 24- and 23-year-old sisters with blood phenylalanine around 1,2 mmol/l who had never been treated and had no overt mental retardation. PCR amplification and direct sequencing of exon 7 of the phenylalanine hydroxylase gene in one sister revealed a homozygous G → A transition leading to a ARG → GLN substitution at codon 261, a mutation which has recently been associated with mild PKU (Y. Okano et al., Am J Hum Genet 46:18-25, 1990). A positive/negative PCR amplification system employing wild type and 3'end-mutation specific primers was used to confirm homozygosity for this mutation in both sisters with PKU and heterozygosity in their parents and an unaffected sister. We conclude that (1) homozygosity for the 261 ARG → GLN mutation indeed can result in a mild variant of PKU with little or no mental retardation, but that (2) elevation of blood phenylalanine in such individuals suffices to cause the maternal PKU syndrome.