

NEONATAL METATARSUS ADDUCTUS, JOINT MOBILITY, AXIS AND ROTATION OF THE LOWER EXTREMITY IN TERM AND PRE-TERM BORN CHILDREN AT 5 YEARS OF AGE.

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To compare the development of attitude and joint mobility of the lower extremity in 111 normal term born (TB) with that of 128 preterm born (PTB) children, orthopedic examinations were carried out at birth and the age of 5 years. 21/128 (16%) PTB children had cerebral palsy (CP) requiring physiotherapy for 6 to 24 months ( $m = 12.5, 1SD = 5.1$ ). At birth, the incidence of metatarsus adductus (MA) was identical in single born TB and PTB infants (12% vs 16%), but higher in twins compared to single born infants (41% vs 16%,  $p < .05$ ). At 5 years, MA had resolved in all TB but only in 83% of the PTB children. In the PTB group, incomplete resolution of neonatal MA occurred in 5/7 (71%) children with CP compared with 2/18 (11%) without CP [ $p < .05$ ]. Passive joint mobility did not differ between the groups except abduction (56 vs 45°) and extension (22 vs 9°) of the hip which were both smaller in the PTB group [ $p < .01$ ]. When PTB children with CP were excluded from analysis, abduction and extension of the hip were identical in TB and PTB children. Median gait angle, tibia torsion and genu valgum were comparable in both groups.

In conclusion, neonatal MA is more frequent in twins because of intrauterine space constraint. At 5 years, incomplete resolution of MA and impaired hip mobility are more likely to be the expression of neurological impairment than of prematurity.

STERIOD EFFECTS ON LUNG COLLAGEN (C) AND ELASTIN (E) ARE DEPENDENT ON GESTATIONAL AGE. Harris C. Jacobs, David M. Lima, Mark R. Mercurio, John M. Fiascone (Spon. by Ian Gross). Dept. of Ped., Yale Med Sch, New Haven, CT.

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C and E, the major lung structural proteins, increase as a fraction of dry lung weight throughout development. Since connective tissue metabolism is known to be effected by corticosteroids, we sought to determine the effect of antenatal exposure to betamethasone (B) on the C and E content of the lungs of prematurely delivered fetal rabbits. Pregnant does were injected with either saline (control) or B (0.2 mg/kg) at 48 and 24 hours prior to sacrifice which was at 24, 27, or 29 days gestation (term = 31). Fetuses were delivered by hysterotomy and weighed, after which their lungs were removed and lyophilized. E was isolated from aliquots of dried lungs by hot alkali digestion. Total lung hydroxyproline (OH-PRO) and E OH-PRO were determined by a colorometric assay and expressed as ug OH-PRO/100 mg dry lung. The difference between these two values was taken as a measure of lung C. C (ug OH-PRO/100 mg dry lung) in control fetuses increased from a mean of 262 at 24 days to 375 at 29 days ( $p < .01$ ). Over the same period, E (ug OH-PRO/100 mg dry lung) increased from a mean of 4 to 11 ( $p < .01$ ). Note that a steroid effect was demonstrated at 24, 27, and 29 days by a decrease in body weight (vs. controls) of 25%, 34%, and 33% respectively. At 24 days B increased C by 25% and E by 100%; at 27 days B increased C by 20% but had little effect on E; at 29 days B had little effect on C or E. These preliminary results suggest that steroid effects on lung connective tissue are significant but only at certain gestational ages.

CENTRAL HYPOVENTILATION SYNDROME RESULTS FROM THE ANOMALOUS DEVELOPMENT OF THE RHOMBENCEPHALIC NEURAL CREST. Dana E. Johnson and Barbara A. Burke, University of Minnesota Medical School, University of Minnesota Hospital, Departments of Pediatrics and Pathology, Minneapolis.

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Central hypoventilation syndrome, a rare disorder of unknown etiology, can be associated with other manifestations of autonomic maldevelopment, chiefly Hirschsprung's disease. A 35 week gestational age female with a small jaw and cleft hard palate was evaluated for central hypoventilation syndrome over the course of one month. The child had little response to CO<sub>2</sub> which was only minimally enhanced by therapeutic levels of caffeine and progesterone. In addition, she also had further evidence of diffuse autonomic dysfunction which included; electrophysiologic studies which suggested a denervated heart, unresponsive persistently dilated pupils and an exceptionally prolonged small intestinal transit time (2-3 weeks). Following her death, an autopsy revealed reduced numbers of ganglion cells in the enteric plexuses in the esophagus, stomach and duodenum and none distal to this point. With the exception of the rectum, the pelvic viscera (bladder and uterus) had normal numbers of ganglion cells. While the intracardiac conduction system was normal, no ganglion cells could be demonstrated in the cardiac plexus. Compared to other infants of the same developmental age, her thyroid gland had a noticeable decrease in calcitonin immunoreactive cells. Her brain and brainstem were normal except for a mild diffuse increase in microglia in the medulla. The quail-chick chimera technique has provided data on the derivatives of rhombencephalic neural crest. All of the abnormalities in this child, and perhaps other children with central hypoventilation syndrome, can be explained by postulating an early developmental defect in neural crest migration from this area.

PROTEIN TURNOVER IN TISSUES OF THE FETAL RAT FOLLOWING MATERNAL PROTEIN RESTRICTION. John D. Johnson and Tracy Dunham, University of New Mexico, Department of Pediatrics, Albuquerque, NM.

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We previously reported that maternal starvation late in gestation results in relatively unperturbed protein synthesis in fetal striated muscle and brain. We have now studied protein turnover in fetal tissues after restriction of maternal protein intake throughout gestation.

Rats were maintained on isocaloric diets containing either 6% or 27% protein throughout pregnancy. Growth curves ( $K_G$ ) for protein content of fetal diaphragm, heart, liver and brain were constructed from days 19-22 gestation. Fetal protein synthesis ( $K_S$ ) was determined after i.v. injection of "massive" amounts of [<sup>3</sup>H]-phenylalanine to the mothers on day 21 gestation. Protein degradation ( $K_D$ ) was calculated from the equation,  $K_D = K_S - K_G$ . Fetal body weight was reduced significantly on days 19-22 when pregnant rats were fed the low protein (LP) diet.  $K_S$  (days<sup>-1</sup>) in fetal tissues is shown in the table:

	Diaphragm	Heart	Liver	Brain
27% protein	0.414(.131)*	0.523(.063)*	0.889(.0054)*	0.394(.061)
6% protein	0.257(.034)*	0.406(.055)	0.353(.179)	0.339(.021)

+ means ± S.D. \* <.05 vs. 27% protein diet (by t-test)

Reduced  $K_S$  in tissues of fetuses from LP rats was accompanied by reduced  $K_D$  values in all tissues. Thus, protein restriction in pregnant rats throughout gestation results in fetal growth retardation; protein turnover in fetal striated muscle and liver is characterized by decreased  $K_S$  and  $K_D$ . These results correspond to trends in protein turnover observed in young adult rats subjected to protein restriction.

IMMATURITY ALTERS THE ENDOGENOUS LIPID LEVELS IN PLASMA LIPOPROTEINS (PLP) OF NEWBORN INFANTS. B. Koletzko, T. Maragi, H. White, R.M. Filler, M. Rapp, T. Heim, Depts. Pediat., Surg. & Nutr. Sci., Univ. Toronto, & Res. Inst., Hosp. Sick Child., Toronto, Ont. M5G 1X8, Can.

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In infants on intravenous (I.V.) alimentation with glucose and amino acid (GL/AA), PLP lipids reflect endogenous fat synthesis and metabolism. We determined the composition of PLP (mg lipid/dl; M±SE) after 5.4±0.4 days of I.V. alimentation with GL/AA in 28 full term (F) appropriate for gestational age (AGA; Gest. age 39.5±0.2 wks) and 17 preterm (P) AGA infants (Gest. age 34.4±1.0 wks). We have found that, in plasma very low density lipoproteins (VLDL) of the P infant there was a marked reduction of total lipids (TL), triglycerides (TG), esterified (CE) and free cholesterol (CH), but not of phospholipids (PL).

LIPIDS	IN	V L D L	PL	CE	CH
					(mg/dl; *p<.05)
Fullterm	40.3±5.8	12.3±1.9	6.8±0.9	17.3±4.1	3.9±1.0
Pretermure	18.8±4.9*	6.3±1.9*	5.6±1.8	6.0±2.1*	0.9±0.3*

Levels of chylomicrons (CHYL) and low density lipoproteins (LDL) were similar. High density lipoproteins (HDL) were increased in P (85.9±9.1 vs. 63.5±8.9\*) and carried more PL (42.2±5.9 vs. 24.9±4.4\*). The HDL/LDL cholesterol ratio was significantly higher in the preterm, than in the fullterm infant (0.55±0.04 vs. 0.28±0.03\*).  
Conclusions: PLP profile reflects significant metabolic differences between F and P infants such as: 1) endogenous synthesis of TG, CE and CH and their secretion as VLDL by the liver is reduced in P infants, possibly due to immaturity of the synthetic pathways and/or low substrate availability. 2) In contrast, synthesis of PL appears to be increased in prematurity, possibly in order to meet the high PL requirement for membrane and surfactant synthesis during this vulnerable period of human development. 3) In the P infant HDL seems to be a major vehicle for CH and PL transport to the peripheral tissues.

THE PROSTACYCLIN ANALOG CARBACYCLIN INCREASES TRANSFER IN PLACENTAE FROM PATHOLOGICAL PREGNANCIES.

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The vasodilator prostacyclin (PGI<sub>2</sub>) is involved in the maintenance of blood flow in the placental vascular bed. Inhibition of PGI<sub>2</sub> synthesis reduces diffusional transfer and increases vascular pressure in the perfused human placental lobe. Reduced umbilical PGI<sub>2</sub> synthesis is characteristic of pregnancies complicated by pre-eclampsia, IUGR or maternal smoking. We have, therefore, assessed the effect of a PGI<sub>2</sub> analogue, carbacyclin, on antipyrine (AP) clearance in dual-perfused placental lobes from normal and pathological pregnancies. Carbacyclin (1 and 10µM), administered in the maternal afferent circulation, had no effect on AP clearance or fetal afferent perfusion pressure in normal placentae. However, in placentae from pathological pregnancies (4 pre-eclampsics, 6 smoking mothers), administration of carbacyclin (1 and 10µM) resulted in a significant increase (19%,  $p < .01$  and 35%,  $p < .001$  respectively) in AP clearance over baseline values. Increased AP clearance in placentae from smoking mothers was accompanied by a decrease in fetal afferent pressure (2-3 mm Hg). Finally, subsequent perfusion of carbacyclin-free perfusate resulted in a return of both AP clearance and fetal afferent perfusion pressure to baseline values. These results suggest that maternally-administered carbacyclin effects blood flow and nutrient transfer in the pathological human placenta and could be considered in the therapeutic approach to pathological pregnancies associated with fetal growth retardation.