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DIFFERENTIAL BINDING OF ARACHIDONIC ACID (AA) BY NEONATAL AND ADULT PLASMA. P.D. Sadowitz, R.W. Walenga, D. Clark, M.J. Stuart. SUNY, Upstate Medical Center, Syracuse, New York.

AA metabolites including both thromboxanes and leukotrienes have recently been implicated in neonatal pulmonary pathology, including respiratory distress syndrome and pulmonary hypertension. We have previously shown that neonatal platelet rich plasma (PRP) produces more thromboxane B_2 than adult PRP when stimulated with low levels of exogenous AA. If neonatal plasma binds less AA than adult plasma in vivo, more substrate (AA) availability could lead to the increased production of these products. The present study was thus undertaken to determine if neonatal plasma had less capacity to bind AA than adult plasma. Thirteen adult and 13 neonatal plasma samples (0.5ml) were dialyzed against 10 ml of 400 μ M 3 H-AA (0.1 μ Ci/ μ M) for 24 hrs at room temperature. Bound AA was calculated from the radioactivity present in the dialyzed plasma minus the radioactivity in an equal volume of dialysate. Neonatal plasma bound significantly less AA than adult plasma 2064 nmol/ml $\pm$ 60.7 (1SD) vs 2776 $\pm$ 92.6 ($p < .01$). When AA binding was expressed as nm AA bound/nm albumin, neonatal and adult plasma bound nearly equivalent amounts 4.75 $\pm$ 0.8 nm AA/nm albumin vs 4.35 $\pm$ 0.35; ($p = ns$). We have shown that neonatal plasma has a significantly decreased binding capacity for AA when compared to the adult. This difference appears to be due to the decreased albumin levels in neonatal plasma. Increased availability of AA in neonatal plasma, especially in the hypoalbuminemic premature infant, may be important in neonatal pathophysiological states involving thromboxanes and leukotrienes.

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UMBILICAL ARTERY (UA), UMBILICAL VEIN (UV) AND MATCHED PLACENTAL CONCENTRATIONS OF HUMAN EPIDERMAL GROWTH FACTOR (hEGF) IN FULL TERM (FT) AND PREMATURE INFANTS (PT). S.M. Scott, D. Orth, B. Larson and D.A. Fisher, UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. of Pediatrics, Torrance, CA and Vanderbilt University Medical Center, Dept. of Medicine, Nashville, TN

To help elucidate the role of hEGF in perinatal growth and development, we examined UA/UV serum levels in 23 AGA FT infants and 7 PT infants (1/7 on a respirator). Matching amniotic membrane (AM) and fetal (FP) and maternal (MP) placental tissue concentrations were measured in 10/23 FT and 7/7 PT. Tissue samples were collected within 1 hr of delivery and stored at -20°C . Tissues were homogenized 1:5 (W:V) in cold PBS. Blood was kept at 4°C for 4-6 hr to allow release of EGF from platelets. Serum was frozen at -70°C after centrifugation at 3000 xg for 20 min. Human EGF concentrations (pg/ml serum and pg/mg wet weight tissue) were measured in a homologous RIA and expressed as mean $\pm$ SEM:

	UA	UV	UA/UV	AM	FP	MP
FT	1527 $\pm$ 158 ^a	1434 $\pm$ 195*	1.1 $\pm$ 0.1 [†]	425 $\pm$ 90*	222 $\pm$ 40	<200 ^a
PT	492 $\pm$ 140	585 $\pm$ 143	0.8 $\pm$ 0.1	380 $\pm$ 70	350 $\pm$ 60	<200 ^b

FT vs PT ($\Delta p = .004$, $*p = .03$, $†p = .02$); AM vs FP $p = .04$; AM vs MP ($a p < .009$, $b p < .005$)

In summary: 1) FT vs PT hEGF serum levels suggest values increase with age; 2) similar UA and UV levels do not support secretion of hEGF from placenta into the fetal circulation; 3) AM $\gg$ FP $\gg$ MP hEGF may reflect secretion from AM or a concentration gradient established by hEGF secretion in fetal urine during the second half of gestation.

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THE α_2 -ADRENERGIC RECEPTORS IN BROWN ADIPOCYTES OF DEVELOPING RATS. Josef P. Skala & Iqbal M. Shaikh. The University of British Columbia, Department of Paediatrics, Vancouver, B.C., Canada. V5Z 1L7

We have previously described a link between cyclic GMP and α -adrenergic stimulation in vivo of brown fat of developing rats. Subsequent in vitro experiments showed that cyclic GMP content of brown adipocytes is influenced by pharmacologically defined α_2 -adrenergic receptors. Since these thermogenic cells are known to possess predominantly the β_1 -adrenoreceptors, we have undertaken a series of in vitro binding studies. Partially purified cell membrane fragments from brown fat of 7-day-old rats exhibited a large proportion of non-specific binding for both yohimbine and rauwolscine. However, evidence was obtained for the presence of a relatively small number of high-affinity (α_{2H}) binding sites for the α_2 -adrenergic antagonists, which seem to readily interconvert to a low affinity form (α_{2L}). The age of the animals, the purity of the membrane fraction, and the ionic composition of the incubation media were found to influence the relative proportions of these two affinity forms of the α_2 -receptors. Preliminary results indicated that the existence of the two states of the α_2 -receptors may add another dimension to the regulation of both the functional and the proliferative responses of the brown adipocytes during perinatal development of the rat. The mechanism of the apparent link between the α_2 -adrenergic receptors and the guanylate cyclase activity in brown adipose tissue remains to be established.

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INCREASED ACETAMINOPHEN GLUTATHIONE METABOLITE FORMATION IN CHILDREN - ROLE IN DECREASED CHILDHOOD ACETAMINOPHEN HEPATOTOXICITY. Wayne R. Snodgrass, David Nyman and Avinoam Rachmel (Spon. by Michael A. Linshaw). Departments of Pediatrics and Pharmacology-Toxicology, University of Kansas Medical Center, Kansas City, Kansas.

To test the hypothesis that children may be at less risk than adults for acetaminophen (APAP) hepatotoxicity due to increased liver glutathione turnover rate, 11 children with rectal temperature greater than 38.5°C , were given a single 10, 20, or 30 mg/kg oral dose. Urine was collected for 12 hours. Glutathione conjugates, APAP-mercapturic acid and APAP-cysteine, were quantitated by high pressure liquid chromatography. Per cent dose was calculated on the basis of a urine creatinine excretion of 12 mg/kg/24 hours. The data are:

Dose	% URINARY EXCRETION $\pm$ S.D. (N)	APAP-Mercapturic Acid + APAP-Cysteine
10 mg/kg	(3)	14.7 $\pm$ 7.0
20 mg/kg	(3)	24.2 $\pm$ 10.9
30 mg/kg	(5)	21.4 $\pm$ 10.9

These data demonstrate that children excrete glutathione conjugate metabolites of APAP. The conclusions are: 1. children given therapeutic doses of APAP produce greater amounts of the glutathione conjugate metabolites than published for adults at therapeutic doses; 2. this may explain observations of less APAP hepatotoxicity in children compared to adults following overdose.

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INCREASED SURVIVAL IN HYPEROXIA OF STREPTOZOTOCIN (SZ) RAT OFFSPRING IS NOT ASSOCIATED WITH LUNG ANTIOXIDANT ENZYME (AOE) OR SATURATED PHOSPHOLIPID LEVELS. Ilene Sosenko and Lee Frank. Univ. of Miami School of Medicine, Depts. of Pulmonary Research and Pediatrics, Miami, FL.

Diabetic offspring (IDMs) have delayed functional and morphologic lung maturation. Biochemical delay of lung maturation in IDMs is controversial, with several studies reporting no differences in disaturated phosphatidylcholine (DSPC) compared to controls (C). We have previously reported increased survival in hyperoxia of newborn rats born to (SZ)-treated mothers (79% vs. 20% for C) (Peds. Res. 17:142A, 1983). To determine whether developmental differences in AOE (superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GP)) or DSPC in IDMs could explain their improved survival in hyperoxia, pregnant rats were injected with 65 mg/kg SZ or saline (SAL), i.p., 24 hrs after mating. Mean blood sugar was 537 in SZ rats. SZ and SAL were sacrificed on gestational days 19, 20, 21 and 22 (term) and fetal lung tissue was analyzed for DSPC, SOD, CAT and GP. Results are expressed SAL/SZ; 2-4 experiments/age group, n=2-5 samples/expt.; *only observation significantly different, SZ vs. SAL, $p < .05$.

Gestation	DSPC (mg/g lung)	SOD	CAT	GP (μ g/DNA)
Day 19	58/60	26.8/25.3	398/349	1.49/1.63
Day 20	86/93	34.8/29.5	431/351*	1.43/1.24
Day 21	110/84	50.9/48.9	438/445	2.00/1.84
Day 22	183/178	67.1/59.3	672/617	3.05/2.69

We conclude that protective mechanisms other than DSPC content or accelerated development of AOE are responsible for the increased survival in 100% O_2 in newborns of SZ-treated rats.

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ENDOTOXIN ALTERS MORPHOMETRIC PATTERN OF LUNG REGROWTH IN PNEUMONECTOMIZED RATS. Ilene Sosenko and Lee Frank. Univ. of Miami School of Medicine, Depts. of Pulmonary Research and Pediatrics, Miami, FL.

We have previously demonstrated that a low dose of endotoxin (ENDO) alters the biochemical response of adult rats postpneumectomy (PX) towards the pattern seen post-PX in young animals (i.e. increase in lung RNA and RNA/DNA ratio) (Peds. Res. 17:390A, 1983). To determine whether ENDO also alters the morphologic pattern of lung regrowth, we performed left pneumectomies on adult rats, followed 24 hrs later by ENDO (250 μ g/kg) or saline injection, i.p. Lungs were formalin-fixed (20cmH $_2$ O inflation pressure) at 3 days post-op. The percent increases in right lung volume at 3 days post-PX was 48 $\pm$ 10% for ENDO-PX compared to a control group and 23 $\pm$ 14% for saline-PX, $p < .05$. Microscopically the ENDO-PX lungs had obviously enlarged terminal air spaces compared to controls or the saline-PX group. Morphometric evaluations confirmed this impression:

Group	Lm (mean linear intercept, mm X 10^{-2})	% Air Space	ISA (internal surface area, m^2)
ENDO-PX	6.99 $\pm$ 0.31	77.9 $\pm$ 0.5	.322
Saline-PX	5.70 $\pm$ 0.32	73.0 $\pm$ 1.0	.327
p	<0.001	<0.001	NS

Saline pressure-volume curves, with volume expressed as percent of total lung capacity (at 20cmH $_2$ O) were not different between ENDO-PX and saline-PX rats. We conclude that adult rats subjected to PX followed by ENDO treatment have an altered pattern of lung regrowth (consisting of large air spaces without a decrease in ISA), not explained by differences in tissue compliance.