

306 EFFECT OF INCREASED F_2O_2 ON IUGR FETUS. Rita A. Vileisis (spon. by J. Bfazy) Duke Univ. Med. Ctr.; Department of Pediatrics; Durham, N. C.

Since the growth retarded fetus (IUGR) is subjected to chronic hypoxia, we tested the effect of \uparrow inspired oxygen concentration in the maternal environment. The uterine artery of 29 pregnant rats was ligated at 17 days gestation; the other horn was left untouched resulting in AGA littermates. Rats were placed in cages designed to deliver either a constant f_2O_2 of 0.40 (O_2) or room air (RA). Both groups of rats gained weight equally. On day 21 the pregnant rat was injected ip with 3H_2O to evaluate fetal fatty acid synthesis and returned to the same cage. Four hours later, fetuses were delivered. All fetuses from the ligated horn were resorbed in 5 of 17 RA rats, while all 12 O_2 rats had ≥ 2 surviving pups from the ligated horn. Survival was significantly \uparrow ($p < .05$) in IUGR- O_2 fetuses (57 \pm 8%, m+sem) compared to IUGR-RA group (33 \pm 6%). Data from IUGR fetuses are expressed as percentages of AGA littermates exposed to the same maternal environment. (Table) Fetal weight was significantly \uparrow in the IUGR- O_2 group compared to IUGR-RA fetuses, without a concomitant \uparrow in the AGA- O_2 group. 3H -fatty acid specific activity (SA) was significantly \uparrow in IUGR-RA fetal liver, lung and carcass. Maternal O_2 therapy resulted in a slight, although not statistically significant \uparrow in fatty acid SA in all 3 organs.

	IUGR-RA*	IUGR- O_2
Fetal weight	67 \pm 2 [†]	74 \pm 2 [†]
Liver SA	63 \pm 5	77 \pm 6
Lung SA	76 \pm 4	87 \pm 7
Carcass SA	90 \pm 5	94 \pm 9

*percentage of AGA counterpart; [†] $p < .05$ compared to O_2 group

307 DEVELOPMENTAL CEREBROVASCULAR RESPONSE TO SYMPATHETIC NERVE STIMULATION IN NEWBORN PIGLETS. L. Craig Wagerle,* Savitri P. Kumar,* and Maria Delivoria-Papadopoulos. University of Pennsylvania School of Medicine, Departments of Physiology and Pediatrics, Philadelphia, PA.

Previous studies suggest that sympathetic nerves may affect cerebral blood flow (CBF) more profoundly in neonates than adult animals. Data regarding developmental aspects of adrenergic mechanisms and CBF regulation are not available. The present study investigates the functional development of sympathetic vasoconstriction in the cerebral circulation. In 16 anesthetized (30% N_2O) newborn piglets (4 to 15 days), the right sympathetic trunk was electrically stimulated for 60s (16 Hz, 15v, 3 msec) while the left side served as control and blood flow to each hemibrain was measured (microspheres). Blood pressure and blood gases were not altered by sympathetic nerve stimulation. During baseline (no stimulation) CBF was 78 \pm 5 and 77 \pm 5 ml/min/100g in the left and right hemibrain respectively. Electrical stimulation of the sympathetic trunk decreased flow to the right hemibrain by 10 \pm 2% compared to the left side. Flow to the right cerebrum (CBM) was reduced by 15 \pm 3% while flow to cerebellum and brainstem regions were unaffected. The efficacy of sympathetic vasoconstriction appears to be related to age where flow to the right CBM was reduced by 14 \pm 3 in piglets less than 6 days old, 19 \pm 5% in 7-9 day old piglets and 6 \pm 3% in piglets over 9 days of age. The developmental pattern was most profound in the choroid plexus where sympathetic vasoconstriction reduced flow by 45 \pm 7, 83 \pm 5, and 58 \pm 8% in the respective age groups. These data suggest that there is a critical time during postnatal development when sympathetic activation may significantly alter CBF. (NIH T33-HD-07217-10A1 and NIH-HD-15973-01.)

308 LONG TERM PROSTAGLANDIN SYNTHESIS INHIBITORS (PGSI) AND TRACHEAL FLUID (TF) PRODUCTION IN FETAL SHEEP. L.D. Wallen, D.T. Murai, C.H. Lee, and J.A. Kitterman. Univ. of California, Cardiovascular Res. Inst., San Francisco.

In fetal sheep, TF production is relatively constant during the last month of gestation; it decreases in the few days before birth, a time when fetal plasma PGE_2 concentrations ($[PGE_2]$) are rising. Short term (12 h) infusions of PGE_2 decrease TF production, suggesting that the rise in endogenous $[PGE_2]$ may be responsible for the prepartum decrease in TF production. To investigate the possible role of PGE_2 in the control of TF production before birth, we studied 5 chronically catheterized fetal sheep from 131-150d gestation. In 4 animals, we infused meclofenamate (Mec), a PGSI, at 1.4-2.8 mg/h (a dose previously shown to decrease $[PGE_2]$); the infusion was continued until birth or fetal demise (5-13d). A control animal received an infusion of vehicle only, for 11d. Each day we collected tracheal fluid from a tracheal cannula and a soft, intrauterine collection bag. TF production in experimental and control animals was similar to previously reported normal values. During the 2 days prior to birth TF production progressively decreased in all animals to 30% of the usual rate; this decrease is similar to that previously reported. Thus, Mec did not prevent the prepartum decrease in TF production. We conclude that in the last few days before birth, the rise in $[PGE_2]$ does not cause the fall in TF production. (Supported by USPHS Grant HL 27356 (Pulmonary SCOR) and ALA Fellowship Grant.)

309 GLYCOGEN METABOLISM OF FETAL LAMB LUNG IS MODIFIED BY CHRONIC HYPERGLYCEMIA AND HYPERINSULINEMIA. David Warburton (Spon. by Robert McAllister).

Neonatal Respiratory Disease Division, Childrens Hospital of Los Angeles, Dept. Pediatrics, University of Southern California School of Medicine, Los Angeles.

I studied the developmental profile of glycogen, glycogen synthase and phosphorylase in the lungs of control fetal lambs at 123, 131, and 142d gestation (term 150d) and in the lungs of their twins given intravenous glucose (16 \pm 2 mg/kg/min, M \pm SE) from 112d onwards. Serum glucose (34 \pm 2 mg/dl) and insulin (47 \pm 11 μ U/ml) in the glucose treated fetuses were higher than serum glucose (19 \pm 3 mg/dl $P < 0.01$) and insulin (14 \pm 2 μ U/ml $P < 0.01$) in the controls.

	123d	131d	142d	
Glycogen content	153	83	39	Control
μ g/mg prot	240	95	62	Glucose
Synthase A	0.41	1.19	1.25	Control
Nmole/min/mg prot	0.35	1.14	0.63	Glucose
Synthase A+B	4.90	5.46	5.82	Control
Nmole/min/mg prot	5.39	10.20	4.81	Glucose
Phosphorylase A	0.30	0.15	0.17	Control
Nmole/min/mg prot	0.25	0.22	0.16	Glucose
Phosphorylase A+B	3.8	0.8	0.9	Control
Nmole/min/mg prot	1.7	1.4	1.0	Glucose

Fetal lung glycogen was higher in the glucose treated fetuses and fell more slowly towards term than in the controls. The enzyme activities were also modified by chronic hyperglycemia and hyperinsulinemia.

310 APPEARANCE OF c-AMP DEPENDENT ACTIN PHOSPHORYLATION IN RAT LUNG AND TYPE II EPITHELIAL CELLS Jeffrey A. Whitsett, James Lessard, Children's Hospital, University of Cincinnati, Ohio

c-AMP enhances surfactant release from Type II epithelial cells, presumably by activation of protein kinases (PK) and increased protein phosphorylation. cAMP dependent (dep) phosphorylation of endogenous proteins was therefore assessed in rat lung during development and in adult Type II epithelial cells. Protein Mr=43,000 was the major substrate of c-AMP-PK in cytosol from postnatal lung and in purified adult Type II cells. Evidence that $[^{32}P]43,000$ is the cytoskeletal protein, actin, includes migration on 2-D SDS-PAGE and phospho-peptide mapping. $[^{32}P]$ Serine was the only phosphoamino acid detected. Phosphorylation was reversible and entirely cAMP dep, $EC_{50}=5 \times 10^{-7}$ M. cAMP dep ^{32}P -actin was barely detectable until 21d gestation and increased 25-fold during the perinatal period. cAMP dep protein kinase activity did not correlate with developmental increase in ^{32}P -actin. cAMP-PK was higher in fetal than adult preparations, $p < .01$. Lung actin content did not change with age. Addition of purified actin but not cAMP-PK to fetal cytosol enhanced ^{32}P -actin. Actin is a major endogenous cytosolic substrate of c-AMP-PK in Type II epithelial cells and in postnatal lung. Actin phosphorylation is developmentally regulated in association with other aspects of lung maturation. Mechanisms that might account for the developmental changes in lung ^{32}P -actin include 1) availability of actin to serve as substrate of c-AMP-PK, 2) new actin forms, or 3) ontogenic appearance of specific c-AMP dependent actin kinase activity.

311 EFFECT OF MAGNESIUM SULFATE Tocolysis ON MATERNAL SERUM TOTAL AND IONIZED CALCIUM. Heidi Winkler, Paul Y.K. Wu and Raul Artal. Univ. of So. Calif. Sch. of Med., LAC-USC Med. Ctr., Depts. of Peds and OB/GYN, Los Angeles.

The appearance of "Gap junctions" in the myometrium permits the initiation of parturition, and terminate pregnancy by providing large areas of low resistance between cells and allowing spread of electrical information. Ionized calcium (Ca^{++}) plays an essential role in modulating this function. Magnesium sulfate ($MgSO_4$) displaces Ca^{++} in the conduction of nerve impulse thus blocking its transmission. Although the depressant action of $MgSO_4$ on myometrial excitation-contraction coupling is well known, little is known of its effect on serum Ca^{++} concentration. We studied 18 pregnant women who were in active premature labor (fetal GA \leq 34 wks) in whom $MgSO_4$ was used as a tocolytic agent. The patients received a loading dose of 4 g of $MgSO_4$ followed by a constant infusion of 2 g/h. Maternal serum total Mg, Ca and Ca^{++} were measured sequentially prior to $MgSO_4$, at 4, 8-12, every 12 h during the infusion and 24 h after cessation of infusion. Serum Mg rose from 1.5 \pm 0.17 mg (M \pm SD) to 3.9 \pm 0.8 mg at 4 h and remained elevated during the infusion. Total Ca and Ca^{++} fell significantly ($p < .01$) from 9.0 \pm 0.5 to 7.5 \pm 0.4 mg/dl and 1.16 \pm 0.05 to 1.09 \pm 0.07 mM/dl respectively. Both total Ca and Ca^{++} returned to pre $MgSO_4$ level 24 h after cessation of infusion. Conclusion: Contraction of the myometrium is dependent on Ca^{++} in extracellular fluid, the fall in serum Ca^{++} may be an added factor in reduced myometrial excitation-contraction coupling during $MgSO_4$ tocolysis.