● **295** FETAL DEVELOPMENT IN THE DIABETIC MOUSE, A MODEL OF GENETIC MATERNAL DIABETES. H.C. Nielsen, C. Gebhardt, J.B. Warshaw, Dept. of Pediatrics, Southwestern Med. School, Dallas, Texas.

The heterozygous diabetes mouse (db/+) has been found to have glucose intolerance during pregnancy. To determine if fetal growth and metabolism were affected we studied fetal weights, lung, liver and placenta protein, DNA and glycogen (G) content, and lung and liver phospholipids. Controls were from pregnancies of the same genetic background without the diabetes gene (misty). Fetuses were studied on day 18 of gestation (19=term). Fetuses of (db/+) pregnancies weighed more than controls (1091±12 mg vs. 1022±20 mg; mean±SE; p<.005) and placentas and lungs also weighed significantly more. Glycogen content was higher in liver (1340±54 mg G/gram prot vs 623±42 mg G/gram prot; mean±SE; p<.001) and placenta (228±16 mg G/gram prot vs 106±8 mg G/gram prot; p <.001) of (db/+) fetuses but was not different in lung. Significant differences were found in liver and placenta protein and DNA content consistent with fewer but larger cells. Fetuses of (db/+) pregnancies had higher phosphatidylcholine content of lung and liver, with significantly less phosphatidylglycerol and more phosphatidylinositol in lung. These data show that fetal growth and development is abnormal in (db/+) pregnancies consistent with abnormal fuel metabolism. This provides a useful model for studying fetal growth and development during genetic maternal diabetes.

● **296** IN VITRO SYNTHESIS OF SURFACTANT ASSOCIATED APOLIPOPROTEIN A: DEVELOPMENTAL ASPECTS. Lawrence Nogee, Carol Dion, D. Lorow, Jeffrey Whitsett. University of Cincinnati College of Medicine of Medicine, Ohio

Apolipoprotein A is a major surfactant associated protein localized to Type II cells in adult lung. We now demonstrate in vitro synthesis of apo A in lung slices, adult Type II epithelial cells and fetal epithelial cells in organotypic culture. Synthesis and secretion of apo A was assessed in cells and media after ^{35}S-methionine labelling; apo A was immunoprecipitated with antisera and identified by 2D-IEF-SDS-PAGE. Fully sialated apo A (Mr=26-36,000) was identified in media from adult rat lung slices and purified adult Type II cells. Apo A synthesis by adult Type II cells was optimal in freshly isolated cells: labelling was undetectable after 24 hrs. in culture. Intracellular forms of apo A were less acidic, Mr=30-34,000, representing partially glycosylated peptides. Apo A synthesis was undetectable in slices of fetal rat lung (day 18 of gestation). However, organotypic cultures of fetal epithelial cells isolated on day 19 of gestation, synthesized fully glycosylated forms of apo A after culture for 3-4 days. These studies demonstrate that apo A synthesis and secretion is developmentally regulated in Type II epithelial cells. Apo A synthesis is rapidly lost in primary culture of adult Type II cells but maintained in organotypic cultures of fetal cells. Major intracellular forms of apo A lack complete glycosylation and only a small fraction of cellular apo A exists as the mature secreted form.

297 PROTEIN KINASE C (PK-C) IN THE DEVELOPING RAT LIVER AND HEART. Akihiko Noguchi, John DeGuire, and Paul Zanaboni. St. Louis University, School of Medicine, Pediatric Research Institute, Cardinal Glennon Memorial Hospital for Children, St. Louis, MO.

Ca dependent, phospholipid regulated protein kinase (PK-C) serves a crucial role for receptor activation by substances such as α-adrenergic agonists which stimulate phosphatidylinositol breakdown. Ontogeny of α_1-receptors is known to be organ specific and distinct from β-receptors. To assess receptor-protein kinase relationship, ontogeny of PK-C and cAMP dependent protein kinase (PK-A) activities were compared to cytosol from rat liver and heart:

		f17d	f21d	1d	5d	28d	Adult
Liver	PK-C	78	124*	150*	200*	129*	53
	PK-A	94§	126§	143§	86§	55	53
Heart	PK-C	154*	176*	124*	198	111	63
	PK-A	159	137	86	135	155	116

means of 6-8 samples (pmol P transferred/min/mg protein)
*, §: different from adult P < 0.05 to 0.001

Cytosol/particulate ratio of PK-C at 21d fetus were 0.72 & 2.41 for liver and heart and similar to adult. DEAE cellulose column separation of PK-C showed a major and a minor peak, & the minor peak was Ca and phosphatidylserine independent in liver and heart. This pattern did not change with age qualitatively. We conclude that PK-C activity is higher perinatally, its subcellular distribution does not seem to change with age, and it is not correlated with PK-A activity or previously reported α_1-receptor density in these organs. We speculate that PK-C is not rate limiting in the receptor activation perinatally.

298 ALTERED PERINATAL GLUCAGON-PHOSPHOENOLPYRUVATE CARBOXYKINASE (PEPCK) RELATIONS IN THE GROWTH RETARDED RAT. Edward S. Ogata, Mary E. Bussey, Sandra Finley and Andrew LaBarbera, Northwestern University Medical School, Depts of Pediatrics, OB/Gyn and Physiology, Chicago, IL.

Since diminished gluconeogenic enzyme activity is a cause of hypoglycemia in the growth retarded neonate, we characterized the relation of glucagon, an inducer of gluconeogenic enzymes, to the appearance of hepatic PEPCK, a key gluconeogenic enzyme. Fetal and neonatal rat pups were rendered growth retarded by maternal bilateral uterine artery ligation (L) on day 18.5 (term 21.5). Pups of L, sham (S), and nonoperated (N) mothers had significantly different body and placental mass on days 19.5 - 21.5 (L< S <N). Glucose availability was limited in L on day 19.5 since fetal glucose (L 37±5; S 65±6; N 72±5 mg/dl; p <.01) and fetal/maternal glucose ratios differed (L< S< N). Despite this, glucagon and PEPCK were not stimulated in L fetuses. Glucagon (516-552 pg/ml), insulin, and hepatic PEPCK (.078-.096 μmoles PEP/g liver/min) did not differ between L, S, and N fetuses. At birth, L pups had significantly greater glucagon surge than S and N, but did not increase PEPCK as S and N did (120 min: L .147±.019; S .223±.031; N .201±.019 μmoles PEP/g liver/min; p <.01). Exogenous glucagon induced PEPCK equivalently in L, S, and N (day 20.5) fetuses and newborns but not in day 19.5 fetuses. Little PEPCK induction occurs during late fetal life, and exogenous glucagon can induce PEPCK on day 20.5 and at birth. L newborns, despite excessive glucagon surge, cannot induce PEPCK due to either limited secretory capability or relative insensitivity to glucagon.

† **299** NEONATAL ADAPTATION: SYMPATHOADRENAL AND ENDORPHIN (END) RESPONSES TO DELIVERY IN TERM AND PRETERM LAMBS. J.F. Padbury, Y. Ogata, D.L. Wang, D.H. Polk, C.C. Callegari and R.W. Lam, UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. of Pediatrics, Torrance, CA.

A marked increase in plasma catecholamines (CAT) at birth has been described in animals and man. This study was conducted to determine whether the magnitude and duration of the CAT surge are similar in preterm (130 days, n=4) and term lambs (145 days, n=6), and to correlate plasma CAT and plasma END levels in the acutely exteriorized fetal lamb. CAT were measured by radioenzymatic assay and END by specific radioimmunoassay. Preterm lambs were maintained physiologically stable by administration of natural sheep surfactant intratracheally prior to the first breath. Baseline CAT & END were similar in the term and preterm lambs. Following umbilical cord cutting there was a marked increase in circulating norepinephrine (NE) and epinephrine (E) levels. Peak preterm NE (2.2±0.6 ng/ml at 1 hr) was greater than peak term NE (1.0±0.2 ng/ml, at 5 min). Peak preterm E also later and greater than peak term E (2.9±0.9 ng/ml at 1 hr vs 0.9±0.2 ng/ml at 15 min, respectively p<.01). Similarly, peak plasma END in preterm animals (2.2±0.1 ng/ml at 3 hrs) was later and greater than at term (1.1±0.2 ng/ml at 15 min). END was positively correlated with NE and E in both term and preterm animals (p<.05). Conclusions: 1) Preterm animals have a delayed, exaggerated CAT surge following delivery, 2) The peak plasma END response parallels the peak of plasma CAT. Speculation: The CAT surge at birth is an important adaptive phenomenon and may be modulated by changes in the END system.

300 LACK OF DRUG EFFECT ON OXYGEN INDUCED RETINAL ARTERY CONSTRICTION IN THE KITTEN Dale L. Phelps University of Rochester School of Medicine, Strong Memorial Hospital, Departments of Pediatrics and Ophthalmology, Rochester, New York

The initial injury in the animal model of oxygen induced retinopathy is thought to be irreversible arteriolar constriction. Since vitamin E is beneficial in this model, its effect on early arteriolar constriction, as well as the effect of prostaglandin inhibitors (as used in the beagle model) were tested. 3 day old kittens were placed in 80% oxygen and their retinas perfused with india ink 48hrs later. Pretreatment from day 1 with free tocopherol (vitamin E) 200 mg/kg/day IM, aspirin 20 mg/kg/day orally, or indomethacin 0.5 mg/kg/day orally was compared to no drug treatment in oxygen and room air controls. 5 kittens were randomly assigned to each group. Additionally, the effects of 8% carbon dioxide in combination with 21% oxygen (room air), 80% oxygen, or aspirin plus 80% oxygen was studied.

All treatments except room air control and 8% carbon dioxide in room air O2 resulted in near total obilteration of patent retinal vessels, as demonstrated with the india ink perfusions. Kittens in 8% carbon dioxide with only 21% oxygen had moderate attenuation of the smallest vessels and partial closure of the arterioles. This unexpected failure of carbon dioxide to cause vasodilitation is unexplained.

Vitamin E does not exert its beneficial effect on oxygen induced retinopathy in the kitten by maintaining vessel patencey during hyperoxia.