†224 EFFECT OF MURINE AND HUMAN YOLK SACS ON THE DEVELOPMENT OF THE FETAL MOUSE DUODENUM IN ORGAN CULTURE. Guy Bordeleau, Raymond Calvert, François Bouthillier, Jean-Guy Lehoux. (Spon. by Marek R.-Pleszczynski). Département d'anatomie et de biologie cellulaire, Faculté de médecine, Université de Sherbrooke, Sherbrooke, Québec, Canada.

When 15-day fetal mouse duodenum is cultured for 48 hours in Trowell T8 medium, villi do not form and crypts or crypt-like structures are scanty. In vivo villi differentiate at 16 days of gestation and crypts appear three days later. If the same culture medium is supplemented with an organic extract of 19-day rat amniotic fluid well differentiated crypts are present in the explants after 48 hours of culture. This effect was attributed to the presence of a crypt differentiation factor (CDF) in the amniotic fluid. When fetal duodenum is cultured with immersed fragments (25 mg) of 19-day fetal rat visceral yolk sac (VYS) or with T8 medium conditioned by a 24 hour incubation with VYS fragments, a high CDF activity is observed. VYS incubated for 6 hours in T8 medium is completely degranulated and the medium exhibits a strong CDF activity. Subcellular fractionation of VYS by differential centrifugation in sucrose reveal that the most active fraction showing CDF activity is the richest in large granules. Human yolk sac was taken from a 38-39 day embryo following a preventive abortion (tubal implantation). When 15-day fetal mouse duodenum is cultured in presence of half of the human yolk sac (HYS), villi and crypts differentiate in the duodenal segments. It appears that HYS also has a CDF activity. (Supported by grant No. MT-6069 from the Medical Research Council of Canada)

†225 EFFECT OF HYPOXIA ON OXYGEN CONSUMPTION OF AND BLOOD FLOW TO THE PELVIC LIMB OF FETAL SHEEP. David W. Boyle, Randall B. Wilkening, Giacomo Meschia (spon. by F. Battaglia) Depts of Pediatrics and Physiology University of Colorado School of Medicine, Denver, CO.

Previous studies have demonstrated a constant fetal cerebral $O_2$ consumption over a range of arterial $O_2$ content ($CaO_2$) from 5 to 1 mM. To determine the effect of such hypoxia on the "non-vital" tissues, we measured hindlimb $O_2$ consumption ($\dot{V}O_2$) in 5 fetal sheep (8-16 days post-op). Four to six sample sets for hemoglobin concentration expressed as oxygen capacity and $O_2$ saturation were drawn from the external iliac artery (IA) and vein during a control period and after equilibration at progressively decreasing levels of arterial $O_2$ saturation ($SaO_2$, %). Hypoxia was produced by maternal common internal iliac artery occlusion yielding fetal $CaO_2$ from 4.93 to 0.95 mM. Blood flow (F, ml/min) to the pelvic limb was measured continuously with an ultrasonic blood flow transducer(Transonics Systems, Inc) placed around the IA. $CaO_2$ (mM) and $\dot{V}O_2$ (µm/min) were calculated for each set. Hindlimb F had a tendency to increase while $\dot{V}O_2$ remained constant to a $CaO_2 \sim 1.5$ mM ($SaO_2 \sim 25\%$), below which both F and $\dot{V}O_2$ fell sharply. We compared control with severe hypoxia ($CaO_2$ <1.5 mM) by paired t-test. Results for the 5 animals expressed as mean ± sem are as follows:

| | $SaO_2$ | $CaO_2$ | F | $\dot{V}O_2$ |
|---|---|---|---|---|
| Control | 53.4 ± 2.1 | 3.48 ± 0.21 | 46 ± 5 | 42.1 ± 2.4 |
| Hypoxia | 18.4 ± 1.0 | 1.24 ± 0.06 | 28 ± 5 | 15.9 ± 2.9 |
| | p < 0.001 | p < 0.005 | p < 0.01 | p < 0.001 |

We conclude that 1) the fetus decreases F and $\dot{V}O_2$ to the pelvic limb in the face of severe hypoxia in order to preserve $\dot{V}O_2$ of vital organs such as brain, and 2) this decrease occurs at a well-defined level of fetal oxygenation.

226 EPIDERMAL GROWTH FACTOR DEGRADATION BY GASTROINTESTINAL FLUID FROM SUCKLING AND WEANLING RATS. John R. Britton and Otakar Koldovský, Univ. of Arizona Hlth. Sciences Ctr., Dept. of Pediatrics, Tucson, AZ.

Epidermal growth factor (EGF), present in the milk of a number of species, may be trophic for the gastrointestinal tract in the perinatal period. Previous studies from our laboratory have demonstrated intact luminal survival of enterally-administered EGF in suckling rats with subsequent absorption from the gut. Since the capacity for survival and absorption may be influenced by digestive processes within the gastrointestinal lumen, we evaluated the development of EGF degradative activity by measuring the release of trichloroacetic acid soluble radioactivity from human $^{125}$I-EGF incubated in vitro with fluid flushed from the lumen of the stomach and small intestine of 12-day old suckling and 31-day old weanling rats. In the stomach at pH 3.2, minimal luminal degradation of EGF was demonstrable in both suckling and weanling rats. By contrast, fluid from all small intestinal segments at both ages showed EGF degradative capacity at neutral pH, although hydrolytic activity of the weanling was twice that of the suckling. We conclude that EGF may be degraded in the lumen of the small intestine of the rat and that luminal digestive capacity toward this growth factor increases after weaning.

227 DEVELOPMENTAL CHANGES IN COLONIC MYOELECTRIC ACTIVITY IN THE INFANT PRIMATE. RA Cannon, J Meadows* and ATW Cheung*, (Spon. R. Chesney). Department of Pediatrics and Primate Research Center, University of California, Davis, CA.

Developmental changes in gastrointestinal motility are poorly understood in the human. We have utilized the infant Rhesus to investigate developmental responses of the distal colon to feeding.

Colonic myoelectric activity in 3 newborn (<24 hrs), 6 infant (ages: 4-7 mos) and 6 adult Rhesus was studied using intraluminal Ag-AgCl electrodes. Slow waves and spike potentials were recorded during fasting and following administration of liquid meal of 10 cc/kg of infant formula (6.7 cal/kg). Slow wave frequency spectra were determined from Fast Fourier transforms (FFT) of digitized signals; spike activity by visual analysis of paper recordings. Results: 1) both infant and adults exhibit increased colonic spike activity within 10 - 15 min following feeding, compared to fasting periods. 2) Newborns show a significantly reduced spike response to feeding compared to older animals (2.3 vs 14.2 mean spikes / 5 min, $p < .05$) at 15 minutes postprandial. 3) Slow wave activity is well developed at 24 hours of age; frequency spectra are similar in all age groups following a meal.

Conclusions: Infant rhesus manifest increases in meal stimulated colonic spiking similar to that seen in human adults. Newborns exhibit a diminished spike response to feeding even though slow wave activity is well defined. This decreased spike response may account for altered colonic motility during adaptation to enteral nutrition.

†228 THE DIABETIC BB RAT - A SUITABLE MODEL OF DELAYED FETAL LUNG MATURATION. Kathleen S. Carlson, Barry T. Smith, Alan D. Stiles, George A. Franco and Martin Post (Spon. by Ivan D. Frantz III). Tufts Univ. School of Medicine, New England Med. Center, Dept. of Pediatrics, Boston, MA and Univ. of Toronto, The Hosp. for Sick Children, Dept. of Pediatrics, Toronto, Ontario.

The diabetic BB rat was examined to determine its suitability as a model for the study of the effects of maternal diabetes on fetal lung development. 18 to 22 day fetuses of diabetic BB rats were evaluated for the presence of macrosomia, hyperglycemia, hyperinsulinemia and delayed lung maturation.

| Group | Day 22 Body Weight (gm±S.E.) | Serum Glucose (mg/dl±S.E.) | Serum Insulin (µU/ml±S.E.) |
|---|---|---|---|
| Control (N) | 5.02±0.06 (54) | 29.7± 6.0[b] (6) | 35.0±16.9[c] (5) |
| Diabetic (N) | 5.48±0.18[a] (22) | 190.2±28.2[b] (5) | 112.5±16.4[c] (4) |

a. P<0.01 b. P<0.0001 c. P<0.001

Macrosomia was observed at term in the diabetic fetuses. The diabetic fetuses were hyperglycemic and hyperinsulinemic when compared to controls. Whole lung homogenates from the diabetic fetuses exhibited increased glycogen and decreased saturated phosphatidylcholine and phosphatidylglycerol contents compared to controls (P<0.05) on Day 21. These findings are consistent with a delay in the onset of augmented synthesis of the major surfactant-associated phospholipids in fetuses of diabetic BB rats. The spontaneous development of the maternal diabetic state and the coexistence of fetal hyperglycemia and hyperinsulinemia are features of the BB rat which may make it more useful than existing animal models in elucidating the mechanisms of delayed fetal lung maturation in the diabetic pregnancy.

229 ABNORMAL PATTERNS OF POLYUNSATURATED FATTY ACIDS (PUFA) IN PLASMA PHOSPHOLIPIDS (PL) IN PREMATURE INFANTS FED MEDIUM CHAIN TRIGLYCERIDE (MCT) DIET. V.Carnielli, M.Dunn, A.T.Shennan, M.Skidmore, A. Ohlsson, E.Hoskins, M.Rapp, and T.Heim. Depts.Pediat. Obst.Gynecol, Nutr.Sci.,Univ.Toronto,Regional Perinat. Center,Women's College Hosp.,& Res.Inst.,Hosp. for Sick Child., Toronto, Ont. M5G 1X8, Canada.

During early human development the requirement for essential fatty acids (EFA) is increased. In order to establish normative data, we studied the fatty acid composition of the major plasma lipid classes every week from the second to the fifth week of life in two groups of "healthy" appropriate for gestational age (AGA) premature infants fed either own mother's milk (OMM) n=12, Bwt=1420±71, Gest.age 30.7±0.7) or medium chain triglyceride formula (MCTF) n=16, Bwt=1385±52, Gest.age 30.7±0.5). Macronutrient, energy and individual fatty acid balances were determined at the same time intervals. Results: Significant differences in the fatty acid composition of the plasma phospholipids were found between the MCTF or OMM fed infants. Linoleic acid was significantly higher in the MCTF group (28.8±0.67 vs. 18.8±0.57%*), and the linolenic acid lower (0.19±0.03 vs. 0.32±0.03%*). Striking differences were found in the longer chain PUFA. (see Table: M±SE; %; *p<0.05).

| Postnatal age (wks) | | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Arachidonic Acid (%) | OMM | 12.63±2.0 | 12.91±0.7 | 12.24±0.7 | 12.48±0.6 |
| | MCTF | 11.62±0.8 | 10.28±0.5* | 10.01±0.6* | 10.50±0.5* |
| Docosahexaenoic Acid(%) | OMM | 4.82±1.1 | 3.49±0.3 | 3.66±0.3 | 3.78±0.3 |
| | MCTF | 2.09±0.3* | 1.60±0.2* | 1.20±0.1* | 0.83±0.1* |

Conclusions: 1) The competition of medium chain fatty acids for the same chain elongating enzyme system of the essential fatty acids and/or the trace amounts of PUFA in the OMM diet may have elicited these differences. 2) The long term sequelae of this distorted phospholipid fatty acid profile on the developing brain and retina has to be seriously considered.