

† **235** INFLUENCE OF EPIDERMAL GROWTH FACTOR AND DEXAMETHASONE ON THE MATURATION OF BRUSH BORDER ENZYMIC ACTIVITIES OF THE FETAL MOUSE SMALL INTESTINE IN ORGAN CULTURE. J.-F. Beaulieu, R. Calvert, Département d'anatomie et de biologie cellulaire, Université de Sherbrooke, Sherbrooke, Québec, Canada (sponsored by M. R.-Pleszczynski).

We have shown that Epidermal Growth Factor (EGF) as well as dexamethasone (Dx) exert a direct positive influence on the maturation of some brush border enzymic activities in the fetal mouse small intestine in organ culture. We report herein the effect of a combination of these two hormones. Mouse duodenal explants resected at 17 days of gestation were cultured during 48 h at 37°C in Leibovitz L-15 serum-free medium alone or supplemented with EGF (100 ng/ml) and/or Dx (300 ng/ml). Maturation of absorptive cells was evaluated by measuring alkaline phosphatase (ALP), maltase (M), lactase (L), trehalase (T) and sucrase (S) activities. In control explants, protein and DNA contents and the level of the ALP, M, T and S specific activities remain comparable to the values measured in 17-day explants at the beginning of the culture period except for L activity that falls drastically. In explants cultured in presence of EGF and Dx, protein contents and the level of ALP, M, T and S activities increase significantly but only at levels comparable to those obtained with EGF or Dx separately while DNA contents remain unchanged and L activity remains under the level observed at the beginning of the culture period. These results suggest that EGF and glucocorticoids can influence the maturation of some brush border enzyme at a similar level in the small intestine during the fetal period.

† **236** METABOLIC STUDIES DURING EARLY FETAL LIFE. Alan Bell, Jan M. Kennaugh, Frederick Battaglia, Edgar L. Makowski, and Giacomo Meschia, Division of Perinatal Medicine, University of Colorado School of Medicine, Denver, CO.

Previous studies of fetal metabolism were confined to the last 20% of gestation. This report presents data on 11 fetal lambs chronically catheterized at 71-81 days (mid-gestation). Mean fetal weight was 210 ± 20 g. Umbilical and uterine blood flows, and the AV differences of substrates were determined. Oxygen (V_{O2}) glucose (G.U.) and lactate (L.U.) uptakes by the fetus were calculated. V_{O2} was slightly higher (%) on a wet weight basis than at term. But this represented a 250% increase expressed on a dry weight basis. Fetal G.U. was also increased relative to the term fetus but L.U. was decreased.

Fetal Gestation	Umbilical Blood Flow	Fetal V _{O2}	Fetal G.U.	Fetal L.U.
	ml/kg/min	uM/kg/min	uM/kg/min	uM/kg/min
Mid (71-81 days)	468 ± 57	485 ± 26	52.3 ± 7	12.6 ± 7.6
Late (120-150 days)	200	353	30	30

At mid-gestation placental weight is significantly greater than at term (486 ± 22 vs 302 ± 12 g). Nevertheless, the rates of placental oxygen and glucose metabolism were significantly less than in late pregnancy and placental lactate production was also reduced. Developmental aspects of fetal metabolism and physiology can now be studied under unstressed steady-state conditions.

† **237** EFFECTS OF HYPOXIA ON FETAL AND PLACENTAL GROWTH. Wm Berman, Jr., Robert Greenberg, John Johnson, UNM, Dept Ped, Alb, NM.

The effect of hypoxia (H) on fetal (F) and placental (P) growth during pregnancy was studied by placing rats in a hypobaric chamber (P_{chamber} = 400 torr). Ambient PO₂ (torr) of control (C) animals was 123; ambient PO₂ of H animals was 74. All animals resided in normoxic environments for the first 6 days of gestation. On day 7, H animals were placed at a barometric pressure 50 torr < atmospheric: the vacuum was increased in 50 torr increments over 4 days to achieve a barometric pressure of 400 torr by day 10 of gestation (term=21 days). At 20 days, the following variables were measured for 118 C and 69 H fetuses: litter size (L); F wt (gm); P wt (gm); and the quantities of protein (Prot-mg), DNA and RNA (microgm) per placenta. Mean results are shown below:

	L	Fetal				Placental		
		F wt	P wt	F/P	Prot	DNA	RNA	
C	12	3.74	0.64	6.67	48.8	998	2.0	
H	7	3.33	0.69	4.82	50.4	980	2.0	

Hypoxia reduces F wt and increases the ratio of P/F. Placental composition of Prot, DNA and RNA did not change. This suggests: 1) hypoxia affects fetal but not placental weight gain during pregnancy, 2) fetal and placental growth are not inextricably correlated, and 3) maternal circulatory adjustments to hypoxia may maintain placental weight.

238 RIBOFLAVIN INFLUENCE ON HEPATIC AND BRAIN RESPONSES TO TRYPTOPHAN IN NEONATAL GERBILS. Jatinder Bhatia, David K. Rassin, Audelio Rivera, Jr., and Holda A. Brown, Department of Pediatrics, University of Texas Medical Branch, Galveston, Texas.

Tryptophan (T) photooxidized in the presence of riboflavin (R) alters hepatic function in developing animals. Solutions of T (48 um/ml) were either exposed to (+L) or protected from (-L) light for 12 hours (in the presence, +R, or absence, -R, of 1 mg/dl of R). Two-week old suckling gerbils were randomly assigned to daily intraperitoneal injections of T+R+L, T+R-L, T+L, T-L or were untreated for 7 d (4 mM/kg⁻¹d⁻¹ of T). Animals were killed on day 8 and assessed for: serum γ-glutamyl transferase; serum, liver and brain T conc; body, brain & liver weight. Data (X̄±SD):

Group	N	γ-GT U/ml	Serum T (um/dl)		Tryptophan Conc (um/100g)	
			Brain	Liver		
T+R+L	9	2.19±1.07	15.20±7.51	10.24±3.55	13.65±4.38	12.63±5.01
T+R-L	7	2.67±2.09	12.85±8.47	7.13±3.38	12.63±5.01	10.91±4.53
T+L	8	0.84±0.29	7.38±2.18	3.13±0.41	10.91±4.53	10.32±2.81
T-L	7	0.72±0.25	6.81±5.39	2.00±0.79	10.32±2.81	5.94±0.78
Untreated	4	0.62±0.03	7.04±1.53	2.36±0.39	5.94±0.78	

γ-GT activity and brain T conc were significantly increased in the presence of R and either +L or -L. Serum and liver concentrations of T were similar amongst the treatment regimens. Liver T was greater in the treated animals than in those untreated. Our data suggest the role of R in the alteration of hepatic function; further, both R and L alter brain conc of T in the developing gerbil. The clinical implications of the infusion of amino acids in the presence of R and L must be considered.

239 BEHAVIOURAL AND CARDIOVASCULAR CHANGES DURING MECHANICAL LUNG VENTILATION IN FETAL SHEEP IN UTERO. Carlos E. Blanco¹, Chester B. Martin Jr.², Jane A. Crevels² and Theo H. Arts³ (Spon. by Henrique Rigatto). ¹Dept. of Pediat., Univ. of Limburg, NL. ²Dept. of Ob-Gyn and ³Central Animal Laboratory, Catholic Univ., Nijmegen, NL.

We questioned whether the prevailing fetal PaO₂ conditions the distribution and organization of states and responses in the fetus and newborn. To investigate this we mechanically ventilated the fetal lungs in chronically instrumented fetal sheep. Electrodes (for ECoG, ECG, ECG and EMG of diaphragm - DP, posterior neck and biceps brachii muscles), catheters (carotid artery, jugular vein, trachea and amniotic cavity), and the endotracheal tube and ventilator tubes were placed at 122-127 days GA. Experiments were begun 3 to 5 days later. Thus far 12 ventilation experiments have been carried out in 5 fetal sheep 3 to 13 days after operation. At the onset of mechanical ventilation both the FHR and fetal blood pressure (BP) decreased abruptly. Ventilatory arrhythmia appeared and its amplitude varied inversely with frequency. During ventilation with either O₂ or N₂ the proportion of high voltage (HV) ECoG increased. Fetal movements decreased during mild hypoxaemia, continuous tonic neck EMG was not observed. End-inspiratory bursts of DP EMG activity were observed more often during LV at normal and elevated PaO₂'s and did not become continuous in either state and it varied with PaO₂. Switching abruptly to N₂ after up to 4 h of hyperoxia did not result in stimulation of phasic DP EMG. At end of experiments PaO₂ and PaCO₂ returned rapidly to normal fetal levels and normal fetal state-cycling was resumed. Occlusion of the umbilical cord with a constant flow of O₂ through the tubes resulted in the initiation of sustained, continuous breathing in only one of 4 such trials.

Conclusions: 1. Mechanical ventilation appears to increase HV state. 2. Elevation of PaO₂ does not result in 'arousal', continuous breathing, or tonic activity in the antigravity muscles. 3. Fetal response to hypoxemia is not modified and 4. umbilical circulation remained open.

240 HEMODYNAMIC RESPONSES OF LAMBS AND ADULT SHEEP TO HEMORRHAGE. Steven M. Block and James C. Rose, (Spon. by William B. Lorentz), Bowman Gray School of Medicine of Wake Forest University, Depts. of Pediatrics and Physiology/Pharmacology, Winston-Salem, NC.

Hemorrhage stimulates the secretion of catecholamines by newborns and adults. This study directly compares the response of newborn and adult sheep to hemorrhage after alpha-blockade. We chronically instrumented 11 newborn lambs and 8 adult sheep for continuous measurement of blood pressure (BP), heart rate (HR), and thermodilution cardiac output (CO). After pretreatment with prazosin (P), an alpha-1 blocker, or vehicle (V) in a randomized, crossover fashion, each animal was hemorrhaged 20% of its blood volume. Cardiac output was measured at baseline; 20 mins after drug administration; after hemorrhage; at 100 mins, after which the animal was retransfused; and at 150 mins. Stroke volume (SV) and total peripheral resistance (TPR) were calculated. The effects of treatment with P and V on the measurements are shown in the table. All deviations from baseline were significant (p<.05). There were greater decreases in BP, CO, SV and TPR in P-treated versus V-treated ewes (indicated by *, p<.05). This difference was not seen in the lambs. (NC denotes no change.)

		BP	HR	CO	SV	TPR
Ewes	V	↓	↑	↓	↓	↑
	P	↓*	↑	↓*	↓*	↓*
Lambs	V	↓	NC	↓	↓	NC
	P	↓	NC	↓	↓	NC

We conclude that catecholamines do not play a major part in the response to hemorrhage in the lamb. (Supported by NIH Grant HD 17644.)