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PROSTAGLANDINS (PGs) SYNTHESIS IN THE ISOLATED HUMAN UMBILICAL ARTERY (UA). James T. Courtney, Harilyn Smith, Frank Sun, Zvi Friedman, Baylor College of Medicine, Department of Pediatrics, Houston, Texas & Upjohn Research Laboratories, Kalamazoo, Michigan.

The role of PGs in the maintenance and the control of fetal and placental hemodynamics was suggested. Umbilical vessels having smooth muscle that is not innervated may be particularly responsive to vasoactive agents such as PGs. Six UA were freshly obtained from normal term pregnancies. Biosynthesis of PGE₂, PGF_{2α}, thromboxane A₂ (analyzed as TxB₂) and prostacyclin (PGI₂) (Measured as 6-keto PGF_{1α}) was studied by incubating UA microsomes with (¹⁴C) arachidonic acid (AA) and with (¹⁴C) cyclic PG endoperoxide (PGH₂), separation by thin layer chromatography and scintillation counting. Percent recovery of (¹⁴C) AA and (¹⁴C) PGH₂ as PGs was 1.73 and 36.4 respectively. The relative percent PGs recovered was ($\bar{x} \pm \text{SEM}$):

No. Samples	Substrate	PGE ₂	PGF _{2α}	TxB ₂	6-keto PGF _{1α}
4	(¹⁴ C) AA	20.2±4.2	29.5±2.7	21.3±1.7	29.0± 6.6
5	(¹⁴ C) PGH ₂	10.1±3.8	32.0±6.2	9.7±3.4	48.2±10.5

In addition, PGI₂ synthesis by UA microsomes was determined by the degree of inhibition of platelet aggregation compared with inhibition by known PGI₂ standards and was 7μg/mg protein. Azo analog I inhibited PGs biosynthesis in duplicate incubations. The results suggest that PGs synthesis by the vascular wall of the UA may contribute to the regulation of vascular tone and platelet vessel wall interaction, thus, modulating fetoplacental blood flow. PGs inhibitors may alter balanced homeostasis in the fetus and the placenta.

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INSULIN SECRETION RATE IN PREMATURE FETAL AND NEONATAL LAMB. J. Creswell, R.M. Cowett, J. Susa, W. Oh. Brown Univ. Program in Medicine, Women & Infants Hospital, Dept. of Ped., Providence, RI.

To compare the insulin secretory response to glucose between fetal and neonatal subjects, steady state insulin turnover studies were performed with ¹³¹I insulin in 6 chronic fetal lamb preparations (gestation = 123 days and weight of 2.8 kg) and 3 clinically well, 1-2 day old premature lambs of similar gestational age. The insulin turnover measurements were made during a 0.45% saline infusion and repeated following a glucose infusion to double the prior plasma glucose concentration. Plasma glucose, insulin, and immuno-precipitable insulin were measured during the steady state and post-hepatic insulin secretion rates (PHISR) and metabolic clearance rates (MCR) were calculated.

Group	Pl. Glucose (mg/dl)	Pl. Insulin (μU/dl)	PHISR (μU/kg/min)	MCR (ml/kg/min)
Fetal Saline	18± 2	16± 4	146±31	10.4±1.9
Fetal Glucose	34± 4*	35± 8	196±22	6.4±1.1
Prem. Saline	108±18	17± 4	69± 7	4.5±1.1
Prem. Glucose	202±33*	29±20	224±55	6.9±1.8

*p<.05 compared with corresponding saline infusion group. M±SEM. Both fetal and neonatal (Prem) subjects doubled their plasma glucose concentrations during glucose infusion (p<.05). With this glucose challenge, the PHISR were unchanged in both fetal and neonatal lambs. The data suggest that in spite of the difference in glucose control in the intra and extrauterine states, the responsiveness of insulin secretion rate in the fetus is similar to that of the neonate.

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AN OVINE MODEL OF FETAL (F) HYPERINSULINEMIA - EFFECTS ON GLUCOSE (G) KINETICS. S. Devaskar, S. Ganquili, U. Devaskar and M. Sperling, Dept. of Peds. Univ. of Cincinnati.

We used the chronically catheterized pregnant sheep in late gestation (130 ± 2D; term ~150D) and simultaneous infusion of labeled G to mother (²⁻³H) and F (^{U-14}C) to assess the effects of short term insulin (I) infusion on glucose kinetics across the placenta. After achieving steady state, I was infused to F at 0.05 U/kg/hr. (group A; n=10) or 0.1U/kg/hr (group B; n=4) for 3 hrs. F pH, pO₂ and Hb did not change throughout. M glucose kinetics and plasma insulin (IRI) remained unchanged in all studies. In A, IRI rose from 18 ± 1 to 80-100 uU/ml after 60 min; glucagon levels were unchanged. Fetal G turnover (GT), production (Ra) and utilization (Rd) dropped from 31 ± 2 to 20 ± 2 mg/min at 3 hrs; no change in GT occurred until IRI was ~100 uU/ml. Similarly fetal G fell by 25% after 2 hrs. In contrast, in B, F GT, Ra and Rd dropped by 50% within 15 min when IRI rose to 157 ± 5 although G levels remained unchanged. These effects were transient, so that by 90 min all had returned to pre-insulin values. The fall in Ra and Rd in the absence of a change in G concentration suggested a reduction of the glucose space. This was assessed by infusing U-¹⁴C inulin along with insulin; the radioactivity increased. In neither group was there any evidence of endogenous F Ra, all of F G being derived from M. Conclusions: (i) I at high normal concentrations reduces F glucose flux. (ii) At even higher doses, continuous I infusion exerts only a transient effect on GT. (iii) Failure to show an increase in F Rd may be a consequence of ignoring placental changes, since only M and F were sampled.

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TRANSFER OF 3H-1-25 DIHYDROXYVITAMIN D₃ (3H-1,25 D₃) FROM THE FETUS TO THE MOTHER IN OVINE MODEL. U. Devaskar, M. Ho, S. Devaskar, R.C. Tsang, U. of Cincinnati, Department of Pediatrics

Maternal plasma 1-25 dihydroxyvitamin D₃ (1-25 D₃) levels increase during pregnancy; the source of this increase remains unclear and could be the fetus. Transfer of 3H-1,25 D₃ from fetus to mother was studied in chronically catheterized ewes (n=5, gestation 125-146 days). Ten μCi of 3H-1,25 D₃ was given by bolus in the fetal jugular vein. Fetal and maternal carotid arterial blood was collected at -10, 1, 5, 15, 30, 45, 60, 120, 180 and 240 min and at 24 and 48 hrs. Radioactivity in 0.1 ml of plasma was quantitated as CPM and DPM. Recovery of 3H-1,25 D₃ in the fetal and maternal plasma at 4 hrs was assessed by high pressure liquid chromatography (HPLC). Plasma 1,25D₃ (HPLC-protein binding assay) in fetuses and ewes was 29-82 and 26-45 pg/ml respectively. In all fetuses, initial disappearance of 3H-1,25 D₃ was rapid (t 1/2 <15 min) followed by a gradual decline over 6 hrs. Appearance of 3H-1,25 D₃ in the ewe was observed within 15 min, with a gradual increase over 4 hrs in 4 pregnancies of 125-142 days, but not in the 145 day pregnancy. >90% of radioactivity recovered at 4 hrs was 1,25 D₃. We conclude that 1) clearance of 1,25 dihydroxyvit D₃ in the fetus is curvilinear suggesting more than two pools, and 2) 1,25 dihydroxyvit D₃ may cross the placenta from the fetus to the mother.

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THE EFFECTS OF COMBINED HYPOTHERMIA AND HYPOXIA ON REGIONAL PERFUSION IN THE NEONATAL PIGLET. David L. Dudgeon, Donna A. Spoon, Patricia A. Randall, (Spon. by Roger E. Spitzer) SUNY Upstate Medical Center, Syracuse

Radioisotope labeled (⁸⁵Sr and ¹⁴¹Ce) 15±3μ microspheres were injected into the left atrium of 9 anesthetized neonatal piglets during normoxia and normothermia, N/N, and after 30 minutes of mild hypothermia (4.5-5.0°C reduction in core temperature) and hypoxia (mean PAO₂ reduction 38.7%), H/H. The cardiac index was not significantly changed. (N/N 150.8±18.1cc/kg/min, H/H 133.5 ±15.1 cc/kg/min). Most tissue blood flows appeared to be reduced; however only renal blood flow and flow to the separated mucosa with H/H and submucosa of the distal small intestine (DSI) and colon (C) were significantly reduced with p>.05. Hypoxia or hypothermia alone does not produce both the DSI and C mucosal changes with H/H. The blood flow reduction with H/H occurs in the same areas as the necrosis seen in neonatal necrotizing enterocolitis (NNEC). Differential blood flow due to shunting at the submucosal and mucosal levels during H/H may be an etiologic factor in NNEC.

	N/N (cc/kg/min)	H/H
Right/left kidney	6.50±.70, 7.15±.86	4.15±.85, 4.91±.43 p>.05
DSI mucosa	3.20±.76	2.13±.55 p>.02
submucosa	4.13±.90	2.69±.60 p>.05
seromuscularis	1.09±.17	1.05±.19
Colon mucosa	1.44±.29	.91±.14 p>.05
submucosa	5.69±.77	3.94±.60 p>.02
seromuscularis	3.81±.73	3.75±.63

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THE EFFECT OF INTRAUTERINE GROWTH RETARDATION (IUGR) UPON HEPATIC AND RENAL PHOSPHOENOL PYRUVATE CARBOXYKINASE (PEPCK) ACTIVITY IN THE NEONATAL RAT. Deborah V. Edidin, Lynne L. Levitsky, Amy Bryan, Nanci Hackl, Lee-Chin L. Hsieh, Pritzker School of Medicine, Univ. of Chicago, Michael Reese Hosp., Dept. of Pediatrics, Chicago.

The contribution of renal gluconeogenesis to glucose homeostasis in the newborn has been neglected despite its well-established role in fasting glucose homeostasis. We have studied the activity of the key gluconeogenic enzyme PEPCK (forward spectrophotometric reaction) in normal and IUGR rat neonates (uterine vessel ligation) fasted for 4 hours postpartum (34°C).

	Weight (g)	Hepatic PEPCK (μmol/min/g)	Renal PEPCK (μmol/min/g)
Control	17 5.5±0.1	106±6	0.336±.049
IUGR	10 4.5±0.2	77±12	0.267±.048
	p<.001	p<.05	NS
			p<.05

Neonatal PEPCK activity was lower than maternal hepatic (1.14±.11 μmol/min/g) and renal (0.99±0.10 μmol/min/g) activity. Hepatic PEPCK activity was diminished in IUGR animals, but this was not significant. In contrast, renal PEPCK activity was significantly increased in IUGR neonates. This suggests independent regulation of neonatal renal and hepatic gluconeogenesis. The compensatory increase in renal PEPCK activity in growth-retarded newborns may contribute significantly to gluconeogenic capacity since PEPCK is the rate-limiting enzyme in the system.