234 PROSTAGLANDINS (PGs) SYNTHESIS IN THE ISOLATED HUMAN UMBILICAL ARTERY (UA).

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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 PGE_2, $PGF_2\alpha$, thromboxane A_2 (analyzed as TxB_2) and prostacyclin (PGI_2) (Measured as 6-keto $PGF_1\alpha$) was studied by incubating UA microsomes with (^{14}C) arachidonic acid (AA) and with (^{14}C) cyclic PG endoperoxide (PGH_2), separation by thin layer chromatography and scintillation counting. Percent recovery of (^{14}C) AA and (^{14}C) PGH_2 as PGs was 1.73 and 36.4 respectively. The relative percent PGs recovered was ($\bar{x}$ ± SEM):

No. Samples	Substrate	PGE_2	$PGF_2\alpha$	TxB_2	6-keto $PGF_1\alpha$
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, PGI_2 synthesis by UA microsomes was determined by the degree of inhibition of platelet aggregation compared with inhibition by known PGI_2 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.

235 INSULIN SECRETION RATE IN PREMATURE FETAL AND NEONATAL LAMB.

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To compare the insulin secretory response to glucose between fetal and neonatal subjects, steady state insulin turnover studies were performed with ^{131}I 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-precepitable 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.

236 AN OVINE MODEL OF FETAL (F) HYPERINSULINEMIA - EFFECTS ON GLUCOSE (G) KINETICS.

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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 ($U\text{-}^{14}C$) 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,pO_2 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 $U\text{-}^{14}C$ 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.

237 TRANSFER OF 3H-1-25 DIHYDROXYVITAMIN D_3 (3H-1,25 D_3) FROM THE FETUS TO THE MOTHER IN OVINE MODEL.

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Maternal plasma 1-25 dihydroxyvitamin D_3 (1-25 D_3) levels increase during pregnancy; the source of this increase remains unclear and could be the fetus. Transfer of 3H-1,25 D_3 from fetus to mother was studied in chronically catheterized ewes (n=5, gestation 125-146 days). Ten µCi of 3H-1,25 D_3 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 D_3 in the fetal and maternal plasma at 4 hrs was assessed by high pressure liquid chromatography (HPLC). Plasma 1,25D (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 D_3 was rapid (t 1/2 <15 min) followed by a gradual decline over 6 hrs. Appearance of 3H-1,25 D_3 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 D_3. We conclude that 1) clearance of 1,25 dihydroxyvit D_3 in the fetus is curvilinear suggesting more than two pools, and 2) 1,25 dihydroxyvit D_3 may cross the placenta from the fetus to the mother.

238 THE EFFECTS OF COMBINED HYPOTHERMIA AND HYPOXIA ON REGIONAL PERFUSION IN THE NEONATAL PIGLET.

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Radioisotope labeled (^{85}Sr and ^{141}Ce) 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 neontal 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	

239 THE EFFECT OF INTRAUTERINE GROWTH RETARDATION (IUGR) UPON HEPATIC AND RENAL PHOSPHOENOL PYRUVATE CARBOXYKINASE (PEPCK) ACTIVITY IN THE NEONATAL RAT.

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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).

	N	Weight (g)	Glucose at 4 hr (mg/dl)	Hepatic PEPCK (µmol/min/g)	Renal PEPCK (µmol/min/g)
Control	17	5.5±0.1	106±6	0.336±.049	0.251±.019
IUGR	10	4.5±0.2	77±12	0.267±.048	0.363±.052
		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.