1207 THE INSULIN RECEPTOR (IR) IS INTERNALIZED IN THE FETAL BRAIN CELLS. S. Devaskar and L. Karycki (Spons. by W. Keenan), St. Louis Univ. School of Medicine, Cardinal Glennon Pediatric Research Institute, Dept. of Peds., St. Louis, Mo.

We studied ^{125}I-insulin total and non-specific binding(IB) and ^{3}H-deoxyglucose uptake (Gu) by 30d isolated fetal rabbit-brain cells (viability of >93%;n=8), to define the significance of the IR in the fetal brain. IB and Gu by brain cells were also assessed in the presence of 10mM phenylarsine oxide (PA) (n=4; prevents IR internalization) and 10μM chloroquin (CQ) (n=5; a lysosomotropic agent), to study the internalization and intracellular degradation of the IR (extracellular degradation was constant throughout the study). Peak specific IB per $6.4x10^5$ cells was achieved by 1-3 min (2.74±0.18%, X±SEM), declining by 20 min (0.48±0.15;p<0.001). A decrease in the peak binding was observed with PA (0.40±0.08;p<0.001), whereas CQ resulted in a peak IB of 1.32±0.19, with no decline in IB at 20 min (2.11±0.49;p<0.01). $1x10^{-6}$M insulin increased the Gu from 0.03±0.002 to 0.05±003nM/$6.4x10^5$ cells (p<0.01). PA inhibited Gu and the insulin induced increase in Gu by the brain cells, while CQ inhibited the insulin induced increase in Gu alone (0.02±0.0007;p<0.01). Summary: 1)In the presence of PA, IB is decreased 2)CQ delayed the decline in peak IB secondary to its lysosomotropic effects and decreased intracellular IR degradation 2)Insulin augmented Gu by fetal brain cells 4)Inhibition of IR internalization by PA or lysosomotropic effects by CQ interfered with the insulin induced Gu by the brain cells. We conclude that the insulin induced Gu by fetal brain cells is associated with internalization of the IR.

1208 GALACTOSE-1-PHOSPHATE URIDYL TRANSFERASE SCREENING. Chandradhar Dwivedi and Saburo Hara (Spon. by Festus O. Adebonojo) Department of Pediatrics, Meharry Medical College, Nashville, TN. 37208

Galactose-1-phosphate uridlytransferase (Gal-1-PUT) deficiency is an inborn error of metabolism transmitted as an autosomal recessive trait. Gal-1-PUT Screening was performed in all the newborns delivered at Hubbard Hospital of Meharry Medical College for an early detection of this deficiency. The appearance of fluorescent NADPH after incubating the blood spot with Gal-1-P, UDPG and NADP was used as a screening test. 2134 newborns were screened during May 1979-Sept. 1984. Three abnormal tests were detected initialy. After repeating the screening test and quantitating the Gal-1-PUT, one case of this deficiency was established. Two false positives were presumably due to insufficient blood on the spot. This patient is a full term first born male to a Black mother. Gal-1-PUT was quantitated in erythrocytes by UDPG consumption test. The patient had 1.6 units of activity, however, mother and her brother had 10.7 and 6.4 units respectively. Utilization of one micromole of UDPG per gram hemoglobin per hour is defined as one unit. Patient was placed on modified galactose free diet and successfully treated. His growth and development are within normal limits for his age. Several variants of Gal-1-PUT deficiency have been reported. The black variant of this deficiency has an extensive capacity for the galactose metabolism. Incidence of this variant is extremely rare. Identification of a black patient at our hospital, which serves a predominantly black community is an interesting observation. (Supported by Maternal and Child Health Care Grant No. 440).

1209 INCREASED ACCUMULATION OF SORBITOL IN EMBRYOS OF MANIFEST DIABETIC RATS. Ulf J. Eriksson, Peter Naeser and Sven E. Brolin, (Spon. by Joseph B. Warshaw), Department of Medical Cell Biology, University of Uppsala, Biomedicum, P.O. Box 571, S-751 23 UPPSALA, Sweden.

Intracellular accumulation of sorbitol is known to be associated with many complications of diabetes mellitus. It is not known if increased levels of this polyol are involved in the teratogenic effects of diabetic pregnancy or whether embryos of diabetic mothers have the capacity to generate and accumulate sorbitol during organogenesis.

Sorbitol content was determined, by bioluminiscence assay, in offspring of normal (N) and manifest diabetic (MD; serum glucose exceeding 20 mmol/l) rats during gestational days 11-15. This animal model of (streptozotocin-induced) diabetic pregnancy exhibits a 15-20 % rate of fetal malformations (Biochem. Soc. Trans. 13:79,1985). Furthermore, the embryos of MD rat mothers of this model show a growth retardation in early pregnancy, similar to that reported in other rat strains (Diabetes 33:281,1984).

The sorbitol accumulation in the MD embryos was increased compared to the N embryos at all times studied (gestational days 11-15). Moreover, sorbitol levels appeared to be further increased (not statistically significant) in the malformed compared to the non-malformed embryos from the MD rats.

This study demonstrates that offspring of diabetic mothers may accumulate high levels of sorbitol during organogenesis, indicative of a functioning aldose reductase system. This animal model may therefore serve as a useful tool to further investigate the possible relationship between disturbed metabolism of polyols and teratogenesis in diabetic pregnancy.

1210 GLUCOSE-LACTATE RELATION IN THE HUMAN NEWBORN. Carol A. Gilfillan, Kou-Yi Tserng, and Satish C. Kalhan. Case Western Reserve University at Cleveland Metropolitan General Hospital, Div. of Pediatr. Metabolism, Cleveland, Ohio.

The turnover rate of glucose (GPR), lactate (LPR) and incorporation of lactate carbon into glucose were quantified on the first post-natal day in 10 normal, 4 small-for-gestational age (SGA) and 3 infants of diabetic mothers (IDM). They were either studied prior to feeding or at least 4 hours after the last feed. ul[^{13}C]Lactate and [$^{2}H_2$]glucose were administered as a prime-constant rate infusion for 4 hours and turnover rates calculated by tracer dilution (mean ± SD).

	Lactate mM	LPR uM/kg·min	Glucose mM	GPR uM/kg·min
Normal				
Unfed (7)	1.8 ± 0.32	43.6 ± 10.00	2.9 ± 0.41	23.1 ± 2.04
Fed (3)	1.7 ± 0.19	25.9 ± 2.86	3.3 ± 0.98	17.6 ± 1.36
SGA Fed (4)	2.3 ± 0.29	32.5 ± 5.74	3.4 ± 1.84	17.5 ± 3.75
IDM (3)	2.1 ± 0.61	44.8 ± 12.9	2.7 ± 0.68	20.9 ± 1.14

The lactate turnover in the human newborn is increased compared with adults, reflecting increased glycolysis and increased oxygen consumption. Maternal diabetes and intrauterine growth retardation did not effect lactate turnover or its incorporation into glucose. Lactate incorporation into glucose represents only a small component of total glucose produced in the human neonate.

●1211 THE EFFECT OF FETAL INSULINOPENIA ON FETAL GLUCOSE AND OXYGEN METABOLISM. William Hay, Jr., Huei Mezнarich, Frederick C. Battaglia. University of Colorado School of Medicine, Division of Perinatal Medicine, Denver.

To measure the effect of a reduction of insulin concentration on ovine fetal glucose and oxygen metabolism, we measured glucose (G), insulin (I), oxygen (O_2) concentrations (n=11), oxygen (O_2Up) and glucose (GUp) uptakes from the placenta (n=11), glucose production (GPr) and utilization (GUt) (n=10), and glucose oxidation (GOx)(n=8) rates before and after reducing fetal insulin concentration with streptozotocin.

	G mg/dl	I uU/ml	O_2 mM/L	GUp	GUt	GPr	GOx	O_2Up mmol/min/kg
				---mg/min/kg---				
Control, X̄	20.4	21	4.3	6.13	6.08	-0.05	2.75	0.338
SEM	0.9	2	0.2	0.43	0.52	0.34	0.25	0.021
Low I, X̄	33.9	10	4.0	1.98	4.73	2.75	1.99	0.335
SEM	4.4	1	0.2	1.17	0.53	1.02	0.35	0.016

These results demonstrate that a reduction in fetal insulin concentration results in: reduced fetal glucose utilization (p< 0.05) accounted for by a fall in both glucose oxidation (0.91 mg/min/kg) and the disposal of glucose by non-oxidative pathways (0.44 mg/min/kg); increased fetal endogenous glucose production (p< 0.01) producing hyperglycemia; and reduced fetal glucose uptake from the placenta (p < 0.001). Thus the basal level of insulin suppresses fetal endogenous glucose production, increases glucose utilization, decreases fetal glucose concentration, and increases fetal glucose uptake from the placenta.

† 1212 MINERAL METABOLIC PARAMETERS IN THE SERUM OF TERM INFANTS FOLLOWING THEIR SUPPLEMENTATION WITH VITAMIN D_2, D_3 or 25-HYDROXY VITAMIN D_3. BW Hollis, WB Pittard. CWRU, Depts Peds & Nutr, Cleve, OH.

Mineral metabolic parameters were studied in 14 term infants supplemented from birth with vitamin D_2,D_3 or 25OHD$_3$ for 16 wks. Serum was collected at 0,1,2,3,4,6,8,10,12,14 and 16 wks. Samples were analyzed for: vitamin D_2;D_3;25OHD$_2$;25OHD$_3$;24,25(OH)$_2$D$_2$;24,25(OH)$_2$D$_3$;1,25(OH)$_2$D$_2$;1,25(OH)$_2$D$_3$;Ca^{++};PO_4;PTH and alkaline phosphatase(AP). Bone mineral content(BMC) and bone width(BW) were determined on the radius at 8 and 16 wks. Serum levels of PO_4, PTH,1,25(OH)$_2$D and AP increased in infants following birth and remained elevated throughout the study. Infants supplemented with vitamin D_2,D_3 or 25(OH)D$_3$ demonstrated a corresponding rise in the 25(OH) and 24,25(OH)$_2$ metabolites. However, supplemental vitamin D_2,D_3 or 25(OH)D$_3$ demonstrated different abilities to elevate the infant's 25OHD status. On a weight basis, 25OHD$_3$ was most effective at increasing the infant's 25OHD status(11.6ng 25OHD$_3$/ml serum/1μg 25OHD$_3$ intake) followed by D$_3$(2.10ng 25OHD$_3$/ml serum/1μg D$_3$ intake) and D$_2$(1.15ng 25OHD$_2$/ml serum/1μg D$_2$ intake). The infants demonstrated a substrate-product relationship for D$_3$ vs 25OHD$_3$(r=.7,p<.001), D$_2$ vs 25OHD$_2$(r=.8,p<.001), 25OHD$_2$ vs 24,25(OH)$_2$D$_2$(r=.7,p<.001) and 25OHD$_3$ vs 24,25(OH)$_2$D$_3$(r=.6, p<.001). 25OHD and 1,25(OH)$_2$D serum levels did not correlate in infant serum. Serum Ca^{++} levels demonstrated an inverse correlation(-.22,p<.05) with serum 24,25(OH)$_2$D levels indicating a possible role of this metabolite in Ca homeostasis of the rapidly growing infant. BMC remained constant in all infants although BW increased between 8 and 16 weeks.