●1201 OSTEOCALCIN PLASMA LEVELS IN OSTEOGENESIS IMPERFECTA: AN INDEX OF SEVERITY OF THE DISEASE. Salvador Castells, Maria A. Fusi, Seiichi Yasumura, Sam Smith, Charles Colbert, Richard S. Bachtell, and Caren Gundberg, SUNY, Downstate Med. Ctr., Depts of Ped. and Phys., Brooklyn, N.Y., Clin. Radiol. Test. Lab., Yellow Springs, OH, and Children's Hospital, Boston, MA.

Octeocalcin (OC) a calcium binding protein of bone matrix, appears to play a role in the regulation of mineral deposition and remodeling of bone. Elevated plasma levels of OC have been reported in some metabolic bone diseases with high bone turnover. We have reported an increase in bone turnover in osteogenesis imperfecta (OI). Plasma OC and serum Ca, P, Alkaline phosphatase concentrations drawn at 8-9 am were studied in 17 untreated OI patients (Ages 0.6-11 y.), and 22 normal controls (Ages 2-9 y.). OC was measured by RIA using rabbit-antiserum to bovine OC and purified bovine OC. Osteoporosis was quantitated by measurements of bone density using the method of radiographic photodensitometry, and compared to age and sex-matched normals. OC plasma levels in OI were 81.6±34.3 mean ± SD compared to 25.0±12.5 ng/ml in control subjects. The difference is significant at $p<0.001$. Bone density, normalized for age and sex was significantly correlated to plasma OC concentrations, $r=0.49$, $p<0.05$, but it did not correlate with serum alkaline phosphatase levels. The elevated plasma levels of OC in OI is the first reported biochemical index to correlate with the severity of osteoporosis in OI.

●1202 TRANSCRIPTION OF THE INSULIN GENE IN THE BRAIN AND SUBMANDIBULAR GLAND OF THE RAT. David L. Cooper, Derrel W. Clarke (Spons. by Arlan L. Rosenbloom), Univ. Florida Coll Med., Dept. Pediatrics, Gainesville, FL.

Analysis of RNA from day old rat brain neuronal cell cultures and adult salivary gland tissue revealed a 2.4Kb polyA+ RNA species that hybridized to both cloned human and rat insulin genomic probes. Hybridization was not observed between glial cell RNA and either insulin DNA probe. The abundance of the 2.4Kb RNA species was 83 copies/neuronal cell and 14.5 copies/cell in the submandibular gland. Mature preproinsulin mRNA (PPImRNA) was not detected in either tissue. The 2.4Kb RNA was present in the adult pancreas at very low levels (<10 copies/cell vs. 1600 copies/cell for the PPImRNA). Immunofluorescent studies with purified anti-insulin antibodies detected a subpopulation of neuronal cells (5%) and scattered ductal epithelium in the submandibular gland as sources of extrapancreatic insulin synthesis.

Others have postulated the extrapancreatic synthesis of insulin based on the presence of low but detectable levels of protein in various tissues. Most controversial has been the discussion centered on the brain as a site of insulin synthesis. Our results suggest that two distinct tissues, the brain and the submandibular gland, possess unique cell types that contain both (i) a 2.4Kb RNA species that hybridizes with an insulin gene and (ii) positive anti-insulin immunofluorescence staining patterns. This may indicate that the insulin gene(s) is expressed in brain and salivary gland and that both tissues are potential de novo synthetic sites.

●1203 α ADRENERGICS STIMULATE NEONATAL GLUCOSE PRODUCTION LESS THAN β ADRENERGICS. Richard M. Cowett, Brown University, Department of Pediatrics, Providence, RI

Catecholamines are important in maintenance of neonatal glucose homeostasis. The relative contribution of α versus β adrenergics in control of neonatal glucose kinetics has not been established. Twenty-three term lambs [birth weight 4.4±0.2 kg (M±SEM) and age 3.8±0.4 days] were infused with 0.9% NaCL at 0.06 ml·kg^{-1}·min^{-1} plus 100 μCi/kg D[6-^{3}H] glucose by prime plus constant infusion. Ra (production)(mg·kg^{-1}·min^{-1}) was measured during infusion of variable doses of epinephrine (Epi) (ng·kg^{-1}·min^{-1}) with or without variable doses of propranolol (Prop) (ug·kg^{-1}·min^{-1}), a competitive β-adrenergic antagonist, to isolate α adrenergic effects. All basal kinetic data was comparable. Kinetic data is shown from the experimental period:

(Epi)+ (Prop)	N	Pl.Glu mg/dl	Pl. Ins μU/ml	Ra	(Epi)	N	Pl.Glu mg/dl	Pl.Ins μU/ml	Ra
0	6	95±8	10±2	5.3±0.5					
(50)+(1.1)	5	122±12*	13±2	4.8±1.0	(50)	4	129±18*	16±3	6.5±1.6
(500)+(11)	4	134±12*	5±1	6.7±0.5	(500)	4	253±8*	8±2	18.5±3.0*

*p <.0001 by ANOVA with repeated measures design

There was a rise in pl. glucose in all groups infused with both epinephrine + propranolol and epinephrine alone compared to controls. While there was no significant rise in Ra with either dose of epinephrine + propranolol, there was a rise in Ra in response to the higher dose of epinephrine alone compared to controls. We conclude that α adrenergics are less important than β adrenergics in control of neonatal glucose production.

1204 INSULIN IS THE PRIMARY HORMONE FOR CONTROL OF NEONATAL GLUCOSE HOMEOSTASIS. Richard M. Cowett and Denis G. Tenenbaum Brown University, Women & Infants Hospital, Department of Pediatrics, Providence, Rhode Island

Immprecise control of neonatal glucose homeostasis may be partially due to hepatic insensitivity for insulin. In prior kinetic studies, the degree of insensitivity could not be determined because the hormonal effects of insulin could not be differentiated from that of glucagon. Somatostatin (SRIF) suppresses secretion of both and has been used to differentiate the hormonal effects. Eighteen term lambs [birth weight 4.0±0.2 kg (M±SEM) and age 4.2±0.3 days] were infused with 0.9% NaCL at 0.06 ml·kg^{-1}·min^{-1} plus 100 μCi/kg D[6-^{3}H] glucose by prime plus constant infusion. Ra (production) and Rd (utilization) were measured during infusion of SRIF or SRIF plus replacement insulin. All basal kinetic data was comparable. Kinetic data is shown from the experimental period:

(M±SEM)	N	Pl.Glucose mg/dl	Pl.Insulin μU/ml	Ra mg·kg^{-1}·min^{-1}	Rd mg·kg^{-1}·min^{-1}
CONTROL	6	95±8	10±2	5.3±0.5	5.3±0.5
SRIF	6	119±10*	7±1*	13.2±4.1*	11.3±3.0*
SRIF+INSULIN	6	101±10	10±2	5.5±0.8	5.6±0.8

* p<0.05 or less by ANOVA with repeated measures design

There was a rise in pl. glucose ($p<.0001$), a fall in pl. insulin ($p<.004$), a rise in Ra ($p<.05$) and Rd ($p<.05$) in SIRF compared to controls. All pertubations were eliminated when replacement insulin plus SRIF produced control insulin levels. We suggest that insulin is the primary hormone for control of neonatal glucose homeostasis.

1205 LACTATE TURNOVER IS INCREASED IN THE NEONATE RELATIVE TO THE ADULT. R.M. Cowett, M.H. Wolfe, & R.R. Wolfe, Brown Univ., Dept. of Peds., Women & Infants Hosp., Prov., RI and UTMB & Shriners Burns Institute, Galveston, TX.

Gluconeogenesis is a major component of glucose production. The contribution of specific gluconeogenic precursors has not been studied in the newborn relative to the adult. Glucose production and lactate production have been evaluated by prime constant infusion of 45 ug·kg^{-1}·min^{-1} D-[6,6-^{2}D]glucose and 20 ug·kg^{-1}·min^{-1} [3-^{13}C]lactate in 3 AGA premature(PT) [BW 2088±174 gm (M±SEM) & GA 34.3±0.9 wks] & 4 AGA term infants(T) [BW 3316±175 gms & GA 41±0.4 wks] at 31±7 hrs after birth & compared to studies in 4 adults(A). Ra(production) was measured during infusion of 0.9% NaCL at 0.06 ml·kg^{-1}·min^{-1} and analyzed by Gas Chromatograph Mass Spectometry(GCMS). Turnover period results are shown:

Group	Pl.Glucose mg/dl	Ra(Glucose)$_1$ mg·kg^{-1}·min	Ra(Lactate)$_1$ mg·kg^{-1}·min	Ra(Lactate)/ Ra(Glucose)
Premature(PT)	67±15	8.1±1.2**	7.3±1.2**	0.92±0.13*
Term(T)	87±7	7.7±1.6*	6.4±1.4+	0.83±0.09*
Adult(A)	84±5	3.2±0.2	1.9±0.2	0.60±0.04

(M±SEM) * p <0.05, + p <0.02, ** p <0.01 by unpaired t-tests

Ra(Glucose) & Ra(Lactate) were ↑ in both PT & T relative to A, but not between PT & T. There was an ↑ ratio of Ra(Lactate) to Ra (Glucose) in both PT & T relative to A but not between PT & T. This is consistent with the relationship of Ra(Glucose) measured by the non-recycling tracer D-[6,6-^{2}D]glucose in these studies compared to Ra(Glucose) measured with the recycling tracer D-[U-^{13}C]glucose in prior studies. Availability of lactate due to recycling may be a mechanism for sparing of gluconeogenic amino acid precursors in the anabolic newborn.

1206 GLUCOSE OXIDATION IN THE HUMAN NEWBORN INFANT. Scott C. Denne and Satish C. Kalhan. Case Western Reserve University at Cleveland Metropolitan General Hospital, Div. of Pediatr. Metabolism, Cleveland, Ohio.

The contribution of glucose to oxidative metabolism was quantified in the human newborn using [U-^{13}C]glucose and indirect respiratory calorimetry. Six infants, gestational age 39.9 ± 0.5 wks (mean ± SD), birth weight 3.06 ± 0.13 kg were studied at 43.7 ± 5.0 hrs of age following a 9.3 ± 0.4 hour fast. A primed constant rate infusion of the tracer was given for 4 to 5 hours. $\dot{V}O_2$ (ml/kg·min), $\dot{V}CO_2$ (ml/kg·min) and RQ were measured during the last 2 hours of the study. The fraction of glucose turnover oxidized (FGO) was calculated from the rate of U-^{13}C glucose infused and the change in ^{13}C enrichment of CO_2 above baseline. Plateau was achieved after approximately 3½ hrs. The fuel mixture was calculated from $\dot{V}O_2$ and RQ data assuming an 8% protein contribution.

FGO	$\dot{V}O_2$	$\dot{V}CO_2$	RQ	Fuel Mixture (kcal/kg·day)		
				Cho	Fat	Protein
0.370 ± 0.034	6.80 ± 0.74	5.61 ± 0.64	0.826 ± 0.022	18.9	24.6	3.8

Conclusions: Only half of the carbohydrate calories can be accounted for by oxidation of glucose turnover. These data suggest that in the fasting newborn, local tissue oxidation of glycogen makes a significant contribution to calories derived from carbohydrate.