895 GLUCAGON RESPONSES IN LEUCINE-SENSITIVE HYPOGLYCEMIA. Thomas F. Roe,(Spon. by Maurice D. Kogut) USC School of Medicine, Childrens Hospital of Los Angeles, Dept. of Pediatrics, Los Angeles, California.

To determine the role of glucagon in idiopathic leucine-sensitive hypoglycemia (LSH) and the effects of oral diazoxide (D), responses to oral L-leucine (L) were studied in 3 LSH children and in 6 controls. In controls mean plasma insulin (IRI), glucose (G) and glucagon (IRG) values were unchanged after L, 150 mg/kg. In LSH children after L, 50 mg/kg, mean±SEM plasma IRI rose from 14±3 to 41±5 μU/ml, mean plasma G fell from 72±4 to 35±3 mg/dl, mean plasma IRG increased 48±8%; each significantly different from baseline (P<0.025). Maximum changes in mean IRI, G and IRG values were at 15, 30 and 45 min.,respectively. In LSH children given L, while on D, 10 mg/kg/day, baseline values were similar, mean peak IRI was significantly lower and mean nadir G was significantly higher (P<0.05 and <0.025 respectively) compared to no D therapy; mean IRG rose less, but not significantly. One LSH child given L while on D, 20 mg/kg/day, showed minimal changes in IRI, G and IRG values. Following arginine infusions in another LSH child, ΔG values were 1 and 12 mg/dl, ΔIRI values were 56 and 21 μU/ml and ΔIRG values were 252 and 254 pg/ml, off and on D therapy, respectively. Peak changes were at 30 min.

Conclusions: 1) In LSH children, given L orally, a rise in IRI precedes the fall in G and the rise in IRG. 2) D therapy blunts all of these changes in proportion to the D dose. 3) D does not directly inhibit IRG release. 4) The rise in IRG following L is secondary to the fall in G.

896 CALCIUM HOMEOSTASIS IN CHILDREN WITH THYROID OR PITUITARY DYSFUNCTION: EFFECT OF EDTA INFUSION. A. Root, E. Reiter, J. Weisman, and G. Duckett. Dept.Ped.,Univ.S.Fla., All Children's Hosp.,St.Petersburg, Fla.

In order to investigate calcium homeostasis in patients with hypothyroidism (HO), hyperthyroidism (HY), and hyposomatotropism (HS), serum levels of Ca, Ca^{++} and iPTH were measured prior to, during and for 4 hours following infusion of EDTA (50 mg/kg/2 hr) in 11 children with normal mineral metabolism (C), 5 with HO, 3 with HY and 4 with HS.

	Ca**		Ca^{++}**		iPTH***		
Group	Basal	Nadir	Basal	Nadir	Basal	Peak	%
C	9.4	8.2	4.25	3.06	110	168	167
HO	9.9*	7.4*	3.92	2.44	106	228	257
HY	9.6	7.7	4.64	2.54	105	194	185
HS	9.0*	7.6	4.20	1.82*	68	126	182

* p < 0.05 compared to C. ** mg/dl. *** pg/ml.

In C 4 hours after completion of the infusion Ca (8.9) was still significantly (p<.01) below basal levels,although Ca^{++} and iPTH had returned to basal values by 2 and 1 hours respectively. In HO serum Ca and Ca^{++}were significantly below values in C subjects 4 hours after the infusion. In patients with HS, treatment with growth hormone for 12 months did not consistently alter the iPTH response to EDTA. Conclusions: 1) EDTA infusion is a useful procedure for evaluation of calcium metabolism in children; 2) children with HO have prolonged hypocalcemia after EDTA infusion despite normal or supranormal secretion of iPTH,suggesting that such subjects may have end organ unresponsiveness to iPTH or may secrete a biologically less effective form of PTH.

897 SERUM CA AND MG DECLINE DURING ORAL GLUCOSE TOLERANCE TESTING (OGTT) IN PRE-CLINICAL DIABETES MELLITUS (DM) IS LESS THAN IN NORMALS. Arlan L. Rosenbloom (Spon. by Owen M. Rennert). University of Florida College of Medicine, Department of Pediatrics, Gainesville, Florida.

Changes in serum [Ca], [Mg] and [P] during 4 hr OGTT in 54 normal children and adolescents (N) were compared to borderline (B), chemical diabetes (C) and normal (AN) tests in 69 youngsters who had had at least one abnormal test. 38 of the pts. had siblings with overt DM and the rest were ascertained through the finding of glucosuria or hyperglycemia. Mean maximal % decline in [Ca] in 49 AN tests (7.4 ± .7 SEM), 28 B tests (7.2 ± .8) and 53 C tests (6.3 ± .6) differed at the <.005 level from N (12.9 ± 1.02). [Mg] average % maximal decline was similar to that of Ca for each group (N-11.8 ± 1.2, AN-7.1 ± 1.0, B-6.7 ± 1.0, C-5.3 ± .6). There were no significant differences in maximum [P] decreases (N-17.1% ± 1.4, AN-16.4 ± 1.2, B-15.9 ± 1.9, C-17.8 ± 1.5). Analysis of average % decline at each sampling time in the OGTT also revealed significantly less decline for Ca and Mg at all points after glucose intake, except 4 hr for Mg, during AN, B and C tests. [P] declined to a significantly *greater* degree at ½ hour in B and C tests and at 3 and 4 hours in C tests than N, consistent with known inverse relationship between glycemia and phosphatemia. None of these differences could be attributed to initial Ca, Mg and P levels, which were significantly low only in C tests. Marked *diminution* in hypocalcemic and hypomagnesemic effect of normal OGTT in persons presumed to have preclinical diabetes implies a metabolic derangement that precedes inappropriate maintenance of glycemia in DM.

898 DO CULTURED FIBROBLASTS (CFB) FROM YOUNGSTERS WITH DIABETES MELLITUS (DM) DEMONSTRATE PRECOCIOUS AGING (PA)? Arlan L. Rosenbloom and Edith K. Rosenbloom. University of Florida College of Medicine, Department of Pediatrics, Gainesville, Florida.

The donor's inherent program of biologic aging is performed *in vitro* by CFB. Goldstein *et al.* demonstrated PA of CFB from persons thought to have genetic prediabetes, as decreased numbers of cells able to establish colonies at low density inoculation (plating efficiency). We studied CFB from 10 controls (N) age 10-52 with normal OGTT and no known family history of diabetes and from 4 pts. age 12-20 with duration of insulin dependent DM of 2 wks, 4, 6 and 12 yrs. Two had the syndrome of joint contracture, tough skin and growth failure. In N, days-to-confluency correlated significantly with donor age at 20, 30 and 40 *in vitro* generations (G) and cell density at confluence was donor-age correlated at 30 and 40 G (r=.81,.71). Plating efficiency was significantly age correlated only at 30 G (r=.84 p<.001) but not when performed at 20 (r=.49) or 40 G (r=.35). Compared to 5 N 10-20 yrs old, DM had normal time to confluency and confluent cell density at 20, 30 and 40 G. Plating efficiency did not differ between N (10.2%±.8/20G, 9.5±.2/30G, 6.2 ±.7/40G) and DM (11±.6, 9.8±.4, 6.5±.5). Failure to demonstrate *in vitro* PA despite inclusion of subjects with *in vivo* growth failure indicates either more subtle genetic factors in the expression of long-term complications of DM or that genetic factors play a relatively minor role compared to the non-insulin dependent population previously studied by Goldstein *et al.*

899 INFANTILE HYPOGLYCEMIA (HG) FROM FAMILIAL HYPERPROINSULINISM (HPI). Arlan L. Rosenbloom, Arthur H. Rubenstein and William J. Donnelly. University of Florida Coll of Med, Depts of Pediatrics and Pathology, Gainesville, and University of Chicago, Dept of Medicine.

Dominantly transmitted asymptomatic HPI was discovered in 4 generations of a family by Gabbay *et al.* We add 2 instances of a white newborn girl and a black 11-month-old boy with profound HG. The girl developed HG (<5mg/dl) at 30 hrs with hypothermia and seizures; she was poorly controlled with cortisol and IV glucose (G), very sensitive to glucagon at 2 wks (from 19 to 70 mg/dl) and rapidly responsive to oral diazoxide (DZX). DZX suppressed insulin (I) levels from max 100μU/ml at 19mg/dl G to 7 at 142mg/dl. 80% pancreatectomy was done at age 10 wks; nesidioblastosis was found. Remission lasted 2 mos. DZX was again effective; the most recent effort to stop DZX, at age 5, failed after 10 days without drug when G was 17-40mg/dl, I 20μU/ml and PI 54% (nl 5-22). Parents, 2 sibs, maternal aunt and paternal grandmother had nl % PI; mat. grandmother had increase (44%). The boy had fasting seizure with G 32mg/dl, glucagon response (26-134), inappropriate I/G (13μU/ml / 19mg/dl, 16/16, 27/36) and HPI (75%). He responded to DZX after 5 days (G 69-107). 80% pancreatectomy was done at age 20 months; histology was normal. Recurrence was complete 4 mos later and DZX effective. Father, young and lean, had fasting hyperI (53μU/ml) and HPI (31%) with normal G tolerance. Mother and sister had normal % PI. HPI is not diagnostic of adenoma in infants with HG, but may indicate a familial abnormality. Good response to DZX may be a contraindication to surgery despite hyperI and/or HPI.

900 FRUCTOSE 1, 6-DIPHOSPHATASE AND GLUCOSE 6-PHOSPHATASE IN NEWBORN RATS WITH INTRAUTERINE GROWTH RETARDATION. Sharon R. Siegel, William Oh, and Delbert A. Fisher, UCLA-Harbor General Hosp., Department of Pediatrics, Torrance, CA

The intrauterine growth retarded (IUGR) newborn has impaired glycogen stores and is subject to hypoglycemia during the first few days of life. To assess the function of gluconeogenesis in newborn hypoglycemia, hepatic glucose 6-phosphatase (G6P) and fructose diphosphatase (FDP) enzyme activities were measured in 70 normal and 60 experimental IUGR rats during the first 5 days of life. IUGR was produced in the fetal rat by uterine artery ligation. Blood glucose concentrations at birth were 117±11 mg/dl (M±SEM) in control rats and 73±11 mg/dl in the IUGR rats (p<.01). Respective values dropped to 74±6 and 54±5 mg/dl on day 1 of the neonatal period, then increased in both groups; but the IUGR rats remained relatively hypoglycemic through day 4 (p<.01). The weight of the IUGR rats was lower through the third postnatal day, reaching control levels on days 4 and 5. G6P activities increased similarly in both groups during the neonatal period. The similar FDP activities at birth (1.54±.10 and 1.47±.20 μM/min/g liver) in control and IUGR rats increased in both groups during the newborn period. However, activities remained significantly lower in the IUGR rats through day 4 (3.09±0.2 vs. 4.53±0.6 μM/min/g liver in control rats, p<.01). Thus, low body weight, blood glucose, and hepatic FDP levels normalized by day 5 in newborn IUGR rats. These results suggest that hypoglycemia in the newborn IUGR rat is due to a combination of impaired glycogen stores and inadequate gluconeogenic enzyme activity.