● 1189

USE OF BIOSTATOR GLUCOSE CONTROLLER (CLOSED-LOOP) TO ESTIMATE INSULIN NEEDS ON A PORTABLE PUMP (OPEN-LOOP): EFFECT OF PREVIOUS METABOLIC CONTROL. Hulda J. Wohltmann, Ronald K. Mayfield, Francis M. Sullivan, Sharon A. McCoy, John A. Colwell, Medical Un. S.C., Depts Ped & Med., Charleston.

Fourteen insulinopenic diabetics were treated with a closed-loop Biostator Glucose Controller for 24-48 hours followed by 7-10 days of continuous subcutaneous insulin infusion (CSII) in 12 patients. Percent distribution of pre-meal insulin during optimal control with CSII was predicted by the Biostator (r=0.66, slope = 0.89 x intercept=0.24, P<.001). Control during closed-loop feedback, expressed as mean of pre-meal, peak and two hour post meal blood glucose was correlated with HbA_1C prior to control (r=0.67, P<.01).

During CSII insulin requirements decreased significantly 19± 4.4% M±SE, (P<.025). The decrease in insulin was accompanied by good glucose control: 111±6.9 vs 100±4.3 mg/dl. In the 3 patients displaying the largest decrease in insulin requirements (25-44%) during CSII, initial HbA_1C (13.5±1.3%) was greater than in patients whose requirement decreased less (HbA_1C 10±.86%, P<.05).

Conclusions 1) Distribution of insulin for programming of CSII can be established with a closed-loop insulin delivery system and may shorten the time required to achieve optimal metabolic control. 2) Metabolic control during closed-loop insulin delivery is influenced by the previous state of control as assessed by HbA_1C levels. 3) Over 7-10 days of tight metabolic control with CSII, insulin requirements decreased, with the greatest decrease occurring in patients who have been in poor control.

1190

EFFECT OF HUMAN GROWTH HORMONE (hGH) TREATMENT ON FAT METABOLISM. Joseph I. Wolfsdorf, Abdollah Sadeghi-Nejad, and Boris Senior. Tufts University School of Medicine, New England Medical Center, Boston.

Administration of pharmacological quantities of hGH to humans and animals causes a brisk rise in serum free fatty acids (FFA). Studies in fasting GH-deficient humans have yielded divergent results. Adults show unimpaired lipolysis or even increased lipolysis and ketogenesis; hypopituitary children had normal beta-hydroxybutyrate (BOHB) levels which decreased with hGH treatment.

To resolve this issue we measured fat-derived fuels in 14 GH-deficient children (11.3±5.3 years, mean±S.D.) fasted for 24 hours, before and after three months of treatment with conventional doses of hGH, and 18 normal fasting children (9.1±4.5 yrs).

	SURFACE AREA M^2 (mean±S.D)*	FFA* mM	GLYCEROL* mM	BOHB* mM	INSULIN* μU/ml
GH DEFICIENT	0.97±0.55	1.86±0.55	0.18±0.10	1.55±1.31	10.3±7.8
TREATED		1.98±0.83	0.18±0.11	1.94±1.71	6.5±7.3
NORMAL	1.06±0.40	2.24±0.47	0.18±0.08	2.53±1.25	7.6±6.0

In all three groups BOHB levels correlated inversely with age and with glucose concentrations. On fasting, FFA ($p < 0.025$) and BOHB ($p < 0.025$) were lower in GH-deficient than in normal children. Although hGH treatment caused only a small increase in FFA ($p < 0.25$), BOHB increased significantly ($p < 0.05$).

Although lipolysis and ketogenesis increase in fasting GH-deficient children, growth hormone is required for these processes to occur optimally.

● 1191

FAT-DERIVED FUELS DURING 24-HOUR STARVATION IN CHILDREN. Joseph I. Wolfsdorf, Abdollah Sadeghi-Nejad, and Boris Senior. Tufts University School of Medicine, New England Medical Center, Boston.

During prolonged fasting, adults show a gradual rise in the blood levels of free fatty acids (FFA) and betahydroxybutyrate (BOHB). In children, by contrast, ketonuria is frequently present after a relatively short fast and is often viewed as an indication of a pathological process. Despite the importance of fat-derived fuels, there is a surprising scarcity of information concerning blood levels of FFA and ketones in fasting children of various ages. We studied the metabolic response to a 24-hour fast in 23 normal children (mean age=8.3, range 1.9-16.7 years).

TIME hrs	FFA* mM	BOHB* mM	GLUCOSE* mM	*mean±S.D.
Post-prandial	0.401±0.276	0.21±0.13	5.53±0.96	
16	1.742±0.626	1.22±1.15	3.98±0.88	
20	2.146±0.729	1.79±1.19	3.57±0.70	
24	2.461±0.685	2.83±1.30	3.27±0.70	

There was a rapid and progressive rise in FFA and BOHB concomitant with a fall in glucose. The concentrations achieved at 24 hours were comparable to those seen in fasting adults after about one week. There was an inverse correlation (r=0.701; $p < 0.001$) between fasting BOHB levels and age.

We conclude that moderate ketonemia and ketonuria in children after a relatively brief period of food deprivation is a normal physiologic response. The assessment of ketonuria should depend on quantitative blood assays interpreted according to age.

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PRENATAL THERAPY OF HOLOCARBOXYLASE SYNTHETASE DEFICIENCY - William Yang, Lorraine Allan, Mary Saunders, Roy Gravel, Krishnamurti Dakshinamurti and Karl S. Roth, Univ. of Pa. and Univ. of Manitoba Sch Med., Toronto Hosp. for Sick Children.

A 25y.o. G_4P_3Ab. woman who had previously delivered at least one and possibly two infants affected with a holocarboxylase synthetase deficiency was given biotin, 10mg p.o. daily over the last 4 wks. of pregnancy. No attempt at amniocentesis was made because of the late gestational stage of presentation. Twin male infants were delivered by elective C-section at 40 wks. gestation. Fibroblast cultures were begun immediately after birth, assay of which subsequently showed one infant to be normal and the other affected. However, daily monitoring of organic acids in urine and plasma over the first week of life showed no abnormality in either infant, both of whom appeared phenotypically normal. The subsequent clinical course of the affected baby has been reported elsewhere and documented clear biotin-responsiveness of the defect in vivo. Biotin measurements provided evidence that biotin administration during late pregnancy was effective in raising cord blood biotin to 4-7 fold control levels (30-48ng/ml vs. 7.34±0.55ng/ml). We conclude that it is possible to safely and effectively raise fetal blood biotin to therapeutic levels by oral administration of 10mg daily to the mother, in this case obviating the need for prenatal diagnosis and its attendant risks.

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CHOLESTEROL EXCRETION STUDIES IN FAMILIAL HYPERCHOLESTEROLEMIC CHILDREN. James H. Zavoral, Dawn C. Laine, Linda K. Bale, Diane L. Wellik, Ralph A. Ellefson, Kanta Kuba, William Krivit, and Bruce A. Kottke. University of Minnesota, Minneapolis, Minnesota.

Normal (N) and familial hypercholesterolemic (FHC) siblings' excretion of fecal neutral sterols (FNS) and fecal bile acids (FBA) were compared as a possible mechanism to explain the hypercholesterolemia of FHC.

Fifteen children, 5 N and 10 FHC, age 7-16, were studied on two diets. Diet A contained 188 mg cholesterol per day and Diet B contained 30 mg cholesterol per day. Children were admitted for 14 days. Three pooled stool samples, three days each, were collected with two markers and analyzed for FNS and FBA by TLC and GLC techniques.

	Diet A		Diet B		
	N	FHC	N	FHC	
Cholesterol mg	199	178	32	29	
FBA mg/kg	4.2	3.9	5.6	5.4	*.005
FNS mg/kg	6.7	7.2	7.6	10.5	*.002

In Diet A there was no difference in FBA or FNS between N and FHC siblings. In the low cholesterol diet (Diet B), there was a significant increase in FBA and FNS excretion in FHC, but not in normals. The feedback mechanism for cholesterol production was intact in FHC children. Decreased FBA or FNS excretion does not explain the hypercholesterolemia in FHC children.

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MINOR HEMOGLOBINS IN DISORDERS OF CARBOHYDRATE METABOLISM. W. Patrick Zeller, Marvin Cornblath, Herbert C. Schwartz and Robert Schwartz; Depts. of Pediatrics, Brown and Stanford Univ., and Neonatal and Ped. Med. Branch, NICHD; Providence, R.I.

The minor hemoglobins, Hb A_{Ia+b}, are less well characterized than Hb A_{Ic} (the glucose adduct), but are probably adducts of phosphorylated hexoses. Hb A_{Ic} has been shown to reflect the integrated plasma glucose level over previous weeks. Minor hemoglobins, Hb A_{Ia+b} and Hb A_{Ic}, were measured by high-performance liquid chromatography (HPLC) in children and adults with insulin-dependent diabetes under variable control, glycogen storage diseases (I, IX) and fructose-1,6-diphosphatase deficiency.

(mean±SD) Subjects	N	Hb A_{Ia+b} (%)	Hb A_{Ic} (%)	Pl. Glucose (mM/L)
Adult Controls	22	1.86±0.17	5.46±0.41	4.89±0.60
Insulin-Dependent	33	2.68±0.52	11.5±3.15	14.6±11.7
GSD Type Ia,b	11	3.19±0.58	5.43±0.9	3.34±1.47
GSD Type IX	2	2.0 - 2.1	5.0 - 5.8	2.72 - 4.28
Fructose-1,6-D'Pase	1	3.6	6.0	5.0

Elevation of Hb A_{Ic}, which was lowered by dialysis, was only found in the diabetics ($p < .001$). In contrast, subjects with Type I GSD and Fructose-1,6-D'Pase deficiency had elevated Hb A_{Ia+b} ($p < 0.001$), which was not altered by dialysis. Since these latter disorders are often associated with lactic acidosis and hypoglycemia, glycolytic intermediates in the red blood cells are likely adducts. Analysis of the individual minor hemoglobins may serve in the screening and management of these disorders.