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NON-KETOTIC HYPERGLYCINEMIA (NKH) TREATED WITH STRYCHNINE. Jose M. Garcia-Castro, Harvey L. Levy, Vivian E. Shih, C.R. Lao-Velez and P. Flores-Garcia. Univ. of Puerto Rico Sch. Med., Dept. of Pediatrics, Harvard Med. Sch., Dept. of Neuro., and Mass. Gen. Hosp., Neuro.Service, San Juan and Boston.

Strychnine has been reported to be effective in the treatment of NKH (Pediat.Res. 11: 1016,1977). We have also had some success in similarly treating an infant with NKH. This infant is the offspring of a consanguneous marriage and was born after an uneventful fullterm pregnancy. Within the first 48 hours of life he developed lethargy, poor cry, poor suck and hypotonia. At one week of age he became apneic but was resuscitated. Laboratory studies revealed hyperglycinemia with plasma glycine 148 µmoles/dl (nl 32±9), CSF glycine 21.7 µmoles/dl (nl 0.7±0.2) and plasma/CSF glycine 6.8 (nl 30-35). Blood gases, blood ammonia, serum short-chain fatty acids and urine organic acids were normal. Treatment was begun with strychnine sulfate 0.04mg/kg/day. Improvement in tone and activity was noted within 2 days. The dosage of strychnine sulfate was gradually increased to a maintenance of 0.2 mg/kg/day. Subsequent myoclonic seizures and increased tone necessitated reduction in the dosage. Following strychnine treatment plasma and CSF glycine concentrations were lowered to 77.8 µmoles/dl and 12.9 µmoles/dl respectively with continuation of the plasma/CSF glycine at 6.0. It would appear that strychnine may be at least somewhat effective in treating the neonatal form of NKH. The mechanism for this effectiveness could be in a lowering of the glycine accumulation.

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STIMULATED NEPHROGENOUS CYCLIC AMP AS A PARATHYROID (PT) FUNCTION TEST IN THALASSEMIA MAJOR. J.M.Gertner, A.E.Broadus, M.Grey, M.Genel and H.A.Pearson, Depts. of Pediat. & Med., Yale Univ. Sch. of Med., New Haven.

As the detection of subclinical hypoparathyroidism in transfused thalassemic patients is hampered by assay insensitivity at low PTH levels, we used a provocation test as a dynamic measure of PT reserve. PTH response was assessed by using urinary cyclic AMP (cAMP) as a function of response. cAMP excretion correlates well with PTH activity, particularly when combined with plasma cAMP to calculate nephrogenous cAMP excretion.

Eight patients aged 9-26 with thalassemia major and iron overload (ferritin 2-6 µg/ml vs normal <0.15),all with normal baseline serum calcium and phosphorus, and 4 young adult controls received 50 mg/kg disodium EDTA IV over 3 hours. Ionized calcium fell by 0.64 ± .33 mg% (controls 0.87 ± .33). Urinary cAMP rose by 1-5.2 nmol/100 ml glomerular filtrate (GF); control 1.2-5.1. In 4 patients nephrogenous cAMP rose 1.3-2.8 fold (controls 2.0-10.2 fold). The oldest patient showed the lowest rise in urinary cAMP (1.0 nmol/100 ml GF) and in nephrogenous cAMP (1.3 fold rise).

We conclude that the response of the nephrogenous component of urinary cAMP to PT provocation with EDTA is a reliable, generally applicable test of PT reserve. The finding of well preserved PT function in at least 7 of our 8 patients is consistent with the clinical observation that overt hypoparathyroidism is a late and uncommon complication of thalassemia major. (Supported by Grant RR-125, GCRC Branch, NIH.)

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COPPER, ZINC, MANGANESE, VANADIUM AND IODINE CONCENTRATIONS IN THE HAIR OF CANADIAN LOW-BIRTHWEIGHT NEONATES - R.S.Gibson, M.S.DeWolfe, Dalhousie University Dept. Pediatrics, Halifax, Canada (Spon. by R.B.Goldbloom)

The copper, zinc, manganese, vanadium and iodine status of low-birthweight Canadian neonates has been evaluated using the hair concentrations of these elements as an index. Hair samples from 37 pre-term (26 - 36 weeks gestation), 24 full term low birthweight (FTLBW) and 38 full term normal birthweight (FTNBW) infants were analyzed using neutron activation analysis.

The hair concentrations of copper, zinc, manganese and vanadium did not differ significantly in the FTLBW and FTNBW groups suggesting that status of these metals at birth is independent of birth weight. A significant negative correlation of hair zinc with gestational age both within the pre-term group and within the three groups as a whole exists and is perhaps associated with a reported fall in the foetal serum zinc level towards term. In contrast, hair vanadium concentrations in the pre-term group were found to be significantly lower. The median hair iodine concentration of low birthweight infants was significantly higher (115 ppm) than that of the FTNBW group (14.5 ppm p = 0.001).

No correlations of the copper, zinc, manganese and vanadium hair concentrations with the variables sex, parity and socio-economic status of the mother were found.

Although prematurity and intrauterine malnutrition are associated with low trace metal body stores, the results suggest that hair concentrations at birth do not reflect the body stores of the infant but perhaps the current trace metal intake.

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CORD BLOOD HIGH DENSITY LIPOPROTEINS: LENINGRAD AND CINCINNATI. C.J.Glueck, A.N.Klimov, E.Ja.Magracheva, D.B.Shestov, D.W.Anderson, R.C.Tsang, E.A.Stein, P.M. Steiner. The Lipid Research Clinic of Cincinnati, Ohio, and Leningrad, U.S.S.R.

Cord blood total cholesterol (TC), triglyceride (TG), low and high density lipoprotein cholesterol (C-LDL, C-HDL)were studied in 423 and 500 Russian (R) and American (A) neonates to determine if previously reported higher C-HDL in R adult males (10 mg/dl > A males) would also be observed at birth. Consecutive live births in R and A were studied by a common protocol, using standardized Lipid Research Clinics laboratories. C-HDL percentile distributions were:

City	n	Min.	1	5	10	25	50	75	90	95	99	Max	X̄ ± SE
Leningrad	423	14	15	18	21	25	29	36	44	51	72	80	31±.5
Cincinnati	500	15	18	21	24	28	34	42	51	58	65	75	36±.5

Mean lipid and lipoprotein levels for male and female subsets from R and A neonate cohorts were as follows:

Males	R(n=86)	A(n=127)	Females	R(n=88)	A(n=133)
TC	65	70		70	74
TG	33	44		40	45
C-HDL	29	32		32	35
C-LDL	29	28		30	31
C-HDL/TC	.45	.47		.47	.49
C-HDL/C-LDL	1.1	1.3		1.3	1.36

C-HDL in A neonates was slightly higher than in R, as was TG and TC; the ratios of C-HDL/TC and C-HDL/C-LDL were similar. Within limits of genicity as expressed by cord blood, R and A C-HDL did not parallel adult C-HDL, suggesting adult environmental effects.

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CORD BLOOD HIGH AND LOW DENSITY LIPOPROTEINS:MALE-FEMALE DIFFERENCES. C.J. Glueck, R.C. Tsang, J.A. Morrison, P.M.Steiner. Lipid Research Clinic and Gen. Clin. Res. Center, U. Cincinnati, Coll. Med.

Since high density lipoprotein cholesterol (C-HDL) levels in adults are inversely related to risk of coronary heart disease, male(M): female(F) C-HDL differences may be important. Cord blood total cholesterol(TC), triglyceride(TG), and low density lipoprotein cholesterol(C-LDL) were studied in 464 live births (248 M, 216 F) to determine whether M:F differences in adults an in later childhood were also expressed in cord blood. In 873 schoolchildren (ages 6-17) from the Lipid Research Clinic prevalence study, F had higher TC and TG than M, slightly higher C-LDL, and ,at the end of adolescence, higher C-HDL. Mean ± SD TC, TG, C-HDL, C-LDL, and the ratio of C-HDL to C-LDL for the neonates were:

	TC	TG	C-HDL	C-LDL	C-HDL/C-LDL
F(n=216)	73±17	44±23	34 ± 10	32±12	1.24 ± .68
M(n=248)	68±15	42±30	31 ± 9	28±17	1.26 ± .62

At birth, F had higher TC(p<.001), C-HDL(p<.01), and C-LDL(p<.02). F TG levels did not differ from M, p>.1, and C-HDL/C-LDL ratios in F and M did not differ, p>.1. Lipid and lipoprotein levels are under combined genetic and environmental control. M:F differences in C-HDL in adults and adolescents are manifested in cord blood, as are the higher schoolchild F levels of TC and C-LDL. C-HDL levels are higher in adult blacks (vs. whites), and in Russian vs. American males, but do not differ in cord blood. M:F C-HDL differences may be "genetic" while racial and cross-cultural differences may in part, reflect environmental effects.

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INITIATION OF GLUCONEOGENESIS DURING FETAL DEVELOPMENT, Robert E. Greenberg and William Howell, Dept. of Ped., Univ. of New Mexico School of Medicine, Albuquerque.

Synthesis of glucose from non-carbohydrate precursors has been considered to be absent in fetal liver of many mammals, with post-natal appearance of gluconeogenesis subject to hormonal regulation. Using a new method for perfusion of fetal liver and isolation of hepatocytes, the development of gluconeogenesis in the rat fetus was investigated.

Fetal hepatocytes, isolated following in situ perfusion with collagenase, actively converted both alanine and pyruvate to glucose during the day prior to normal delivery. Glucose production in isolated hepatocytes was linear for at least two hours and was proportional to substrate concentration. Both glucagon (.014 to 1.4 uM) and oleic acid (.0064 to .64 uM) markedly enhanced conversion of both alanine and pyruvate to glucose; the effect of both was directly proportional to the basal rate of gluconeogenesis. Neither insulin nor b-OH butyrate inhibited glucagon or oleic acid enhancement of glucose production. Preincubation of fetal hepatocytes (21 day fetus) with glucagon effected a maximal increase in gluconeogenic rates.

These studies indicate that gluconeogenesis is initiated in isolated hepatocytes derived from the rat fetus just prior to term. Regulation of gluconeogenesis by hormones or fatty acids is proportional to basal rates of glucose production. Assuming no marked changes in endogenous glucagon or insulin secretion, initiation of gluconeogenesis during fetal development does not appear to be hormonally determined.