1117 DECREASED SENSITIVITY OF SERUM PARATHYROID HORMONE (PTH) TO HYPERCALCEMIA IN NEWBORNS M.Y. Dincsoy, R.C. Tsang, P. Laskarzewski, D. Dodson, I-W Chen, U. of Cincinnati Coll. Med., Cincinnati, Ohio

The supression of neonatal PTH by calcium has not been studied. Theoretically, decreased neonatal parathyroid glandular response to hypocalcemia may be associated with decreased PTH response to hypercalcemia. In 29 "exchange" transfusions (ET) with citrated blood in 25 neonates, we studied the supressibility of PTH from Ca bolus at the 100ml mark of ET. Infants had birth wt (mean±SD) 1732±656g, gestation 32± 4wks, postnatal age 5.2±3.8d and 5 min Apgar 6.8±2.6. There was a significant rise of serum PTH (ΔPTH_1) in response to decrease in ionized Ca of 1.4mg/dl during the first 100ml ET. At the 100ml mark of ET after Ca 9mg bolus, ionized Ca rose by 2.6mg/dl. Serum PTH (normal adults <180µl-Eq/ml) dropped from 218±16 SE to 184±16, 167± 13 and 169±11 at 1,2 and 3 min postCa respectively (paired t, p< .01). The nadir of PTH occured at 1 min in 20/29 occasions. Δ_2 PTH (postCa change of PTH from 0-min to nadir) was correlated with Δ_1-PTH, change of PTH in response to hypocalcemia (Spearman r=.47, p<.02). Lesser response of Δ_2-PTH occured with lower pre-exchange serum Ca (r=0.59, p<.01) and Mg (r=0.63, p< .01); no correlation of Δ_2PTH was obtained with postnatal age, gestational age and Apgars. Thus, infants with low serum Ca and Mg have lower PTH responsivity to hypercalcemia; infants with low PTH response to hypocalcemia also have low response to hypercalcemia; we speculate that the parathyroids of infants with hypocalcemia or hypomagnesemia are less responsive to changes in calcium.

1118 NORMAL OR ELEVATED SERUM 1,25 DIHYDROXYVITAMIN D_3 ($1,25(OH)_2D$) IN CHILDHOOD CHOLESTASIS (CC). Michael K. Farrell, James E. Heubi, Reginald C. Tsang, Donna Dodson, Mona Ho, Univ. Cinti. Coll. Med., Dept. Peds.

Cholestasis may lead to vitamin D deficiency and bone disease. We measured serum 25-OH vitamin D (25-OHD) (Haddad's assay, normal 20-40 ng/ml) and $1,25(OH)_2D$ (Eisman's assay, normal 17-44 pg/ml) in 13 CC patients ($\bar{x}$ age 6 yrs, range 0.5-17) and 6 age comparable controls. CC patients had steatorrhea (coefficient of fat excretion 27 ± 6%, normal < 5%). 25-OHD absorption, maximal increase in 25-OHD (Δ25-OHD), was measured after 10 µg/kg oral 25-OHD.

	n	Baseline 25-OHD (ng/ml)	Baseline $1,25(OH)_2D$(pg/ml)	Δ25-OHD
CC	13	13.5 ± 3.0*	77.5 ± 2.0	49.8 ± 13.8*
Controls	6	30.5 ± 8.3	49.3 ± 7.6	128.1 ± 32.6

($\bar{x}$ ± SEM; *p < 0.05 vs controls)

10 of 13 CC patients had 25-OHD < 20 ng/ml, yet 7 of 10 had 1,25 $(OH)_2D$ levels (range 47-250 pg/ml) above adult values; 3 of 10 were above pediatric control values (120,165,250 pg/ml). There was no correlation between baseline 25-OHD, Δ25-OHD and $1,25(OH)_2D$ levels (r = 0.18 and 0.06 respectively). No CC had active bone disease; serum calcium (9.8 ± 0.3 mg/dl) and phosphorus (5.5 ± 1.0 mg/dl) were normal in all. Parathyroid hormone was normal (< 180 µl-Eq/ml) in 10/11; in one infant it was 200 µl-Eq/ml. Conclusions: 1) Although serum 25-OHD and 25-OHD absorption are low in CC, serum $1,25(OH)_2D$ may be normal or elevated. 2) We speculate that maintenance of $1,25(OH)_2D$ levels is a response to calcium deficiency and compensatory mechanism to maintain calcium homeostasis.

● 1119 THYROID HORMONE REGULATION OF HUMAN MONONUCLEAR LEUKOCYTE ACID LIPASE ACTIVITY. David N. Finegold, George M. Hoffman and Paul M. Coates. Jos. Stokes, Jr. Res. Institute, Children's Hosp. of Philadelphia, Phila., PA

Low density lipoprotein (LDL) metabolism is sensitive to thyroid (T) hormone status. Receptor-mediated LDL degradation is increased in human skin fibroblasts by triiodothyronine (T_3). Acid lipase (AL), the lysosomal enzyme which hydrolyzes cholesteryl esters (CE) in a number of tissues, is similarly regulated by T hormones: liver AL activity is reduced in hypothyroid rats and increased by T_3 or thyroxine (T_4). The relationship between AL activity and T status in man is not known but reduced AL activity is associated with hypercholesterolemia and T status is known to influence cholesterol levels in man. Eight hypothyroid and 14 hyperthyroid children at various stages of treatment had mononuclear leukocyte AL activity measured. T status was determined by measuring serum T_3, T_4, thyroid-stimulating hormone and thyroid-binding globulin. AL activity was positively correlated with serum T_3 (AL = 2.48 log T_3 + 2.45, r = 0.54, p <0.01). In a second study, five adult euthyroid male volunteers were treated for 4 days with 50µg T_3 t.i.d. All showed decreased serum cholesterol (mean reduction 14%, p <0.05) and increased AL activity (mean increase 22%, p <0.05). These data suggest that AL activity in man is modulated by T_3 levels. In addition to genetic control of AL activity, hormonal control of AL expression may be important in regulation of human cholesterol metabolism. (Supported in part by HL-18723).

1120 IN VITRO INHIBITION OF HUMAN PLACENTAL AMINO ACID (A-A) UPTAKE: SYNERGISM BETWEEN NICOTINE (Nic) AND ACETALDEHYDE (AcH). Stanley E. Fisher, Mark Atkinson, Ian Holzman, David H. Van Thiel, (Spon. T. K. Oliver). Univ. of Pitt. Sch. of Med., Pittsburgh.

A recurrent problem in understanding the pathophysiology of the fetal alcohol syndrome (FAS) is separation of the effects of alcohol drinking habits from other social habits (e.g. smoking). Work in this laboratory has suggested that in vivo ethanol (EtOH) and in vitro AcH inhibit A-A transport across the placenta, thereby contributing to the etiology of the FAS. Furthermore, it is known that pharmacologic concentrations of Nic inhibit A-A uptake by human placental villi. Therefore, we investigated the effect of physiologic concentrations of EtOH, AcH and Nic upon in vitro uptake of ^{14}C-α-amino isobutyric acid (AIB) by human placental villi. In 4 experiments with EtOH (200 mg/dl) and Nic (0.2 uM), there was no difference ($p > 0.2$) (matched pair analysis) in 90 minute uptake of AIB between control (C) and EtOH, Nic or EtOH plus Nic exposed tissue. In 8 additional experiments, there was no difference ($p > 0.2$) between C and Nic (0.2 uM). AcH (2.0 uM) showed a trend for lowered uptake (% inhibition 11.1 ± 3.7, mean ± SEM) ($p < 0.1$). However, AcH plus Nic resulted in a significant ($p < 0.03$) reduction in AIB uptake (% inhibition 22.8 ± 4.9) when compared to C or AcH alone. CONCLUSION: (1) Nic alone, at a concentration found in smokers' sera, does not impair placental uptake of A-A. (2) AcH, at the very low concentration of 2.0 uM, causes slight inhibition of uptake. (3) Nic plus AcH appear to be synergistic, significantly inhibiting placental A-A uptake. Therefore, we speculate that cigarette smoking may potentiate placental insufficiency associated with EtOH ingestion.

1121 ECHOCARDIOGRAPHIC EVIDENCE FOR IMPAIRED MYOCARDIAL PERFORMANCE IN CHILDREN WITH TYPE I DIABETES MELLITUS. Nancy E. Friedman, Lynne L. Levitsky, Deborah V. Edidin, Dolores A. Vitullo, Samuel J. Lacina, Pipit Chiemmongkoltip. Pritzker School of Medicine, Univ. of Chicago, Michael Reese Hospital, Dept. of Pediatrics, Chicago.

Myocardial performance was assessed by M-mode echocardiography in 33 children (6 8/12-19 3/12 yr) with Type I diabetes mellitus and in 51 normal children (6 2/12-18 8/12). Left ventricular end systolic dimension (LVESD), and left ventricular end systolic volume/M^2 (LVESV/M^2) were greater in diabetics than controls. Left ventricular ejection fraction (LVEF), minor axis shortening (MAS), and velocity of circumferential fiber shortening (VCF) were less in diabetics than controls.

	LVESD (cm)	LVESV/M^2 (ml/m^2)	LVEF (%)	MAS (%)	VCF (circ/sec)
Diabetic	3.1±.1	28.1±1.3	59.2±1.2	26.2±1.0	0.96±.05
Control	2.8±.1	24.5±1.0	64.7±1.0	31.3±1.0	1.14±.04
	(p<.025)	(p<.05)	(p<.001)	(p<.001)	(p<.02)

Hgb A_1 levels in children with diabetes (15.5±0.6%, range 10.1-22.2%, normal 5.9-8.7%) correlated with clinical assessment of control (p<.01). Age, Hgb A_1, duration of diabetes, and clinical assessment did not predict myocardial function. We conclude that there is impaired myocardial contractility in some children with insulin-dependent diabetes not correlated with duration of diabetes, age, clinical assessment of control, or Hgb A_1. The long-term significance of this finding and the effect of improved control remain to be assessed.

1122 COPPER-BINDING (CuB) BY PROTEINS FROM KIDNEYS AND LIVERS OF BRINDLED HETEROZYGOTES (BrH). A. Garnica, S.M.T. Chang, Dept. of Pediatrics, U. of Fla. College of Medicine, Gainesville, Fla.

The Br (CeH/MoBrJ) mouse is a model for Menkes Kinky Hair Synd., a Cu metabolic disease. Extracts of Cu-binding protein (CuBP) were prepared from livers(Li) and kidneys(Ki) of adult Cu-loaded(CuL) and non Cu-loaded(NCuL) nl(CeH/HeJ) and BrH mice. S.C. $CuSO_4$ soln., 35µg/kg Cu/dx20d was given. Extracts were applied to Sephadex G-75-120; profiles were monitored by absorbance at 215, 250, 280 nm, [Cu], and [Cd]. Eight protein peaks (PP) were obtained, 6 Cu-containing. PP A, m.w. 37,000D, was present in Li only after CuL. Thus, PP A in Li may be Cu-induced. CuL seems to induce Cd-binding to PP A, except in Ki of BrH. PP B, m.w. 29,000D, is found only in Ki of NCuL BrH. PP C, m.w. 15,700D, is present in all extracts. A major PP in Li, the [Cu]:A215 is low in Li and Ki of nl and Li of CuL nl. PP D, est. m.w. 5,250D, is absent in Ki: in NCuL it is present only in Li of BrH. PP E from Li of nl is P-rich with minor CuB; it appears to bind Cd in Li of nl and BrH after CuL. PP F was observed only in Li of nl.

We cannot say whether P induction has taken place. The increase in CuB relative to PP suggests that excess Cu is bound to existing P. Our CuL data suggest that CuB in Li and Ki of BrH is similar to Br hemizygotes; these data indicate CuB among soluble P of nl and BrH is different. Question remains whether abnormal Cu content at tissue level in BrH can be explained only on the basis of soluble PBCu at a cellular level.