736 EFFECT OF EXTRACELLULAR COPPER (Cu) ON METALLOTHIONEIN METABOLISM IN NORMAL AND MENKES FIBROBLASTS. Gundula U. LaBadie, Kurt Hirschhorn, Nicholas G. Beratis. Mt. Sinai Sch. of Med., Dept. of Peds., New York, NY.

Previously, we demonstrated that the abnormal accumulation of Cu in Menkes disease (MD) fibroblasts (Fb) is associated with an increased amount of metallothionein (MT) (2-3 times normal) (Pediat. Res., in press). To define the basic defect in MD, we investigated the effect of varying concentrations of extracellular Cu (exCu) on the regulation of CuMT metabolism in normal (N) and MD Fb. Relative levels of MT were measured by ^{35}S-cysteine incorporation into the 10,000 MW Cu-binding cytosolic protein. Total intracellular Cu was measured by atomic absorption spectrometry. After exposure of N and MD Fb to 2 ug/ml Cu (as $CuCl_2$) maximal levels of MT synthesis were attained within 8 h and remained elevated for at least 56 h. Additional Cu (up to 20 ug/ml) did not increase the rate of MT synthesis above that observed with 2 ug/ml. Pulse-chase experiments demonstrated no difference in the half-life ($T_{1/2}$=48-60 h) of MTs in N or MD Fb in the presence or absence of exCu. These results demonstrated that MT was an inducible protein in both N and MD Fb. Also, the rate of degradation of the MTs was the same in both the N and MD Fb. Although the mechanism of MT induction by exCu appears normal in MD Fb, the suppression of MT synthesis in the absence of excess Cu may be defective. This regulatory defect results in abnormally high constitutive levels of MT in MD Fb. Whether this defect in regulation of MT synthesis is transcriptional or translational is currently under investigation.

737 DITHIOTHREITOL (DTT) PROTECTS CYSTINOTIC FIBROBLASTS IN CYSTINE-FREE MEDIUM. Gerald Lancaster and Charles R. Scriver. MRC Genetics Group, McGill University-Montreal Children's Hosp. Res. Inst., Montreal, Quebec, Canada.

Nephropathic cystinosis is associated with extreme intracellular (lysosomal) storage of cystine (CySS). Reduced dithiothreitol (DTTSH) and cysteamine both decrease cellular CySS in cystinosis patients in vivo and may ameliorate the natural course of the disease. The mutant cellular function remains undefined. We studied survival of normal (n=4) and cystinotic (n=3) fibroblast lines in selective medium (CySS-free) with or without DTTSS or DTTSH in the medium. Control and cystinotic cells were matched for site of biopsy, age of donor, and passage number in culture. Cells plated at low density were washed and refed at 24 h with either control or selective media. Cell density was measured after further incubation (24 h). CySS-free medium was selective and caused detachment (>90%) of cystinotic and control cells; DTTSS (1-8 mM) and DTTSH (0.5-2 mM) both protected cystinotic cells but not control cells in the selective medium. Cystinotic cells preincubated with cysteamine (1 mM x 4 h) were not protected by DTT in CySS-free medium. These findings imply that cystinotic cells have the capability (presumably cytoplasmic in origin) to reduce DTTSS and use it to liberate CySS from their expanded intracellular pools to support growth. If CySS accumulation, or other events related to abnormal -SH metabolism are important facets of the cystinosis phenotype, there is a rationale for treatment with DTT, and like agents, in vivo.

738 PARENT-CHILD CORONARY HEART DISEASE RISK FACTOR ASSOCIATIONS. P.M.Laskarzewski,J.A.Morrison,P.Khoury, M.J.Mellies,C.J.Glueck. Univ. Cincinnati, College of Med., Cinti. General Hosp., LRC, GCRC, Cincinnati, Ohio.

Parent-child (P-C) coronary heart disease (CHD) risk factor (RF) associations were assessed in 430 P-C pairs in the Princeton School Study. P-C correlations of Quetelet index (Q), systolic and diastolic blood pressure (SBP,DBP), plasma total cholesterol (TC), triglyceride (TG), low, high, and very low density lipoprotein cholesterol (C-LDL, C-HDL, C-VLDL) were [Pearson's(PE), Spearman's(S) r, *p<.05,**<.02,***<.01,+<.001]

r	Q	SBP	DBP	TC	TG	C-HDL	C-LDL	C-VLDL
PE	.218+	.160+	.142***	.340+	.106*	.292+	.316+	.030
S	.186+	.143***	167+	.313+	.139***	.297+	.269+	.059

P-C RF relationships were most marked for TC, C-LDL, C-HDL,and Q. P-C associations for C-HDL,C-LDL, and Q were also examined by covariance analysis. C-HDL in P and C were positively related; the following interactions were significant:holding P C-HDL constant, P TG was inversely related to C C-HDL; holding C age constant, P Q was inversely related to C C-HDL; by race group, P SBP related inversely with C C-HDL. C C-LDL positively related to P Q, and inversely with P SBP. Holding P TC constant, P C-HDL was inversely related to C C-LDL. P Q and TG were positively related to C Q. Holding P C-HDL constant, P TC was positively related to C Q. Holding P age constant, P C-HDL was inversely related to C Q. Aggregation of P-C RF may account, in part, for the familial clustering of CHD. Knowledge of parental CHD RF should facilitate early identification of CHD RF in their progeny.

739 TRANSIENT BIOPTERIN SYNTHETASE DEFICIENCY IN A NEWBORN WITH PHENYLKETONURIA. Reuben Matalon, Kimberlee Michals, Ching-Lun Lee and Jon C. Nixon. Dept of Peds Univ. of Ill., Chicago, Ill., and Dept. of Medicinal Biochem., Wellcome Research Laboratories, Research Triangle Park, N.C.

Atypical forms of phenylketonuria (PKU) are associated with defects in the synthesis or regeneration of the biopterin cofactors. In order to prevent irreversible neurological damage, patients with hyperphenylalaninemia are being screened for biopterin. A newborn male was found to have 34.4 mg/dl of phenylalanine on the 7th day of life. Dietary therapy for PKU was begun and at the age of 19 days urine biopterin levels were analyzed by the method of Fukushima and Nixon (Anal.Bioch. 102, 177, 1980). Urine neopterin (N) was 879 ng/ml and biopterin (B) 142 ng/ml with an abnormal ratio of N/B of 6.2 (normal < 2).Urine biopterin determination was repeated on the 28th day of life and at this time N was 2155 ng/ml and B was 605 ng/ml, N/B 3.6. A week later the baby's urine was examined again and the ratio of N/B was 3.0. Because of the abnormal ratio of N/B, challenge with L-tetrahydrobiopterin, 2 mg/Kg, was given orally with no effect on blood phenylalanine which remained at 18 mg/dl after 4 and 6 hours. At 40 days of age urine biopterin approached normal values and N/B was 1.3. These findings suggest a transient form of biopterin synthetase deficiency not previously reported. In newborns with hyperphenylalaninemia where abnormal ratio of N/B is found, repeated determinations are needed in order to avoid a false diagnosis of atypical PKU.

740 NEWBORN SCREENING FOR PHENYLKETONURIA (PKU): WHEN SHOULD THE INFANT BE TESTED? Edward R.B. McCabe, Gayle A. Mosher, Linda McCabe, and Richard J. Allen, U. Col. Sch. of Med., Dept. Peds, U. Col. at Denver, Dept. Psychol., Denver; U. Mich. Med. Sch., Depts. Peds. and Neurol., Ann Arbor.

Changing nursery practices have raised the question of the diagnostic validity of newborn PKU screens drawn before the third day of life. To answer this question, a survey of PKU patients and unaffected siblings was conducted. The following phenylalanine blood levels (phe, mg/dl) were measured in these two groups:

	Normal			PKU			
	N	$\bar{X}$	SD	N	$\bar{X}$	SD	t
Cord Blood	21	2.3	1.3	14	3.2	1.3	0.52 (NS)
0 -12 hrs	12	2.6	0.7	12	5.2	1.9	2.18 (p<0.05)
12-24 hrs	33	1.9	0.6	20	6.4	2.8	3.69 (p<0.001)
24-48 hrs	31	1.7	0.5	30	10.6	4.0	5.86 (p<0.001)
48-72 hrs	33	1.8	0.7	31	16.9	7.8	7.29 (p<0.001)
72-96 hrs	8	1.8	0.4	23	22.0	8.8	7.86 (p<0.001)

When the initial classification (PKU if phe $\geq$4) was compared with the ultimate diagnosis, 6 of 22 patients with PKU had phe <4 in the first 24 hrs; these 6 patients did not differ from the others in feeding patterns. After 24 hrs all PKU patients had phe $\geq$4. Using the stated criterion, no patient in this population would have been misdiagnosed after the first day of life. However, $\bar{X}$-2SD $\geq$4 is not observed for the PKU group until after 72 hrs. Therefore, these data suggest, on statistical grounds, that PKU patients may be missed by a screening program even if tested on the third day of life.

741 A DEMOGRAPHIC STUDY OF TRISOMY 13. Patricia L. Monteleone, Ross Anderson, Su-chiung Chen, Soraya Nouri, James A. Monteleone, Kutay Taysi, St. Louis University School of Medicine and Washington University School of Medicine, Cardinal Glennon Memorial Hospital for Children and St. Louis Children's Hospital, Department of Pediatrics-Adolescent Medicine, St. Louis, MO.

Trisomy 13 occurs with an incidence of 1/8000 live births. Thirty-one patients with Trisomy 13 diagnosed over the past 19 years at our institutions were reviewed. Parameters evaluated were age of parents, sex, occupation, prenatal history, parity, family history, geographic area, clinical features, and birth month. 23/31 (74%) were male; three periods of the year with higher incidence (28/31) were found (March-April, July-August, and November-December); mean age of mother was 29.6 years (median 28 years). Trisomy 13 in our patients was associated with increased parity. Family history revealed 2 patients who had relatives with Trisomy 21; 2 patients had relatives with polydactyly; 2 patients had relatives with cleft lip/palate. These data refute previous data which indicate a sex ratio in Trisomy 13 of 1:1 and 2 maternal age peaks. In addition, the data support a higher incidence in males, 3 peak months of occurrence, an increased risk with increased parity. The occurrence in the family of cleft lip/palate and polydactyly, which are characteristic features of Trisomy 13 syndrome, as well as other trisomies suggests that there may be other genetic influences affecting nondisjunction in families.