53 I. REZVANI*, A.M. DIGEORGE*, L.R. GARIBALDI*, and M.SCHWARTZ* (Intr. by P. DURAND). Temple Univ. School of Med., Dept. of Ped., St. Christopher's Hospital for Children, Philadelphia, Pa., U.S.A. Serum concentrations of branched chained amino acids (BCAA) in neonates with classic maple syrup urine disease (MSUD) in the first 4 days of life.

Although serum levels of BCAA are elevated in MSUD at the time of diagnosis, data on serum levels of amino acids prior to development of symptoms are very limited. We have measured serum levels of BCAA during the first 4 days of life in 7 neonates from 3 families with affected offsprings. Three infants had MSUD and 4 were normal. All infants received 5% glucose in water for the first 12-24 hours and then were started on a formula devoid of BCAA. Valine and isoleucine were mildly elevated in cord sera of all 3 affected infants but leucine levels overlapped with those of normal siblings. Serum

	Affected (mean, µmole/l)			Nonaffected (mean, µmole/l)		
	Valine	Isoleu	Leucine	Valine	Isoleu	Leucine
Cord serum	284	84	155	205	60	127
4-8 hours	427	173	315	190	50	112
1 day	424	167	432	111	23	61
2 days	395	17	488	119	32	84
4 days	378	10	626	187	38	122

levels of all BCAA increased as early as 4 hours after birth while these levels decreased in normal infants during the same period. Isoleucine levels decreased below normal in affected infants at 2nd and 4th days of life while other BCAA continued to rise. These data indicate that diagnosis of MSUD can be made within a few hours of life even before feeding. (Supported by GCRC grant n. RR-75).

54 FIXED THORACIC KYPHOSIS IN JUVENILES AND YOUNG ADULTS: MASKED MUCOPOLYSACCHARIDOSIS (MPS) VII.

R. Gitzelmann & B. Steinmann
Dept. of Paediatrics, University of Zürich

We previously reported the chance finding of Alder type granulations in leukocytes of 19 and 16 year-old brothers (R. Gitzelmann et al., Helv.paediat.Acta *33*:413-428,1978). The only physical sign was a fixed kyphosis of the thoracic spine without discomfort. X-ray findings were modest, urinary acid mucopolysaccharides increased. Degradation of sulphated mucopolysaccharides by cultured skin fibroblasts was slowed, β-glucuronidase activity in serum, leukocytes and fibroblasts abnormally low thus documenting MPS VII. We speculated that this previously unknown late and mild form of MPS VII may exist undetected in the general population. We have now discovered a 15 1/2 year-old boy with a history of nervous dysfunction and pains who had Alder type granulations. From age 9 1/2 to 15 he suffered from back pain. He was minimally hunchbacked at 10 1/2 years. Today, he has a partially fixed thoracic kyphosis and complains of a tired back after heavy lifting. β-Glucuronidase was abnormally low in his serum and leukocytes. The parents' β-glucuronidase was normal in serum but intermediate in leukocytes. These observations document MPS VII as the first monogenic disorder of metabolism known to cause fixed thoracic kyphosis in seemingly healthy juveniles and young adults. As the course of this form of MPS VII is unknown, a search for further patients in young and older adults seems warranted.

55 R.J.WEST St.George's Hospital,London,SW17

FAMILIAL HYPERCHOLESTEROLAEMIA. FACTORS INFLUENCING DRUG COMPLIANCE

Thirty five children with FH, treated with cholestyramine, but without dietary restriction, have been followed for 6-8 years. For those remaining on treatment group mean plasma cholesterol was lowered by 30% in the first year, on a mean dose of 0.4g/Kg/day. In subsequent years group mean reduction varied between 26% and 44%.

Compliance with treatment declined with time; after 4 years only 68% remained on treatment, and only 48% by the end of 8 years.

An attempt to identify factors influencing compliance in this group shows:
Compliance was better in those starting the drug before the age of 10 ($p > 0.025$)
Compliance was not significantly better in those with a family history of premature IHD.
Compliance with cholestyramine was no worse than with a more palatable bile acid sequestrant (Secholex).
There was no sex difference in compliance rates.
Siblings all behaved concordantly.

56 H. Siemes+, M. SIEGERT+ and F. HANEFELD+, Dept. of Pediatrics, Free University of Berlin, Berlin-West, F.R.G. THE CSF-PROTEIN PATTERNS IN CHILDREN WITH ACUTE CEREBELLAR ATAXIA AND WITH MEDULLOBLASTOMAS

CSF-protein profiles of 25 children with acute cerebellar ataxia and of 14 patients with a medulloblastoma at diagnosis were examined by quantitative zone electrophoresis in agarose gel. The profiles were compared with those obtained from a control group of 86 children and those from 61 patients with acute aseptic meningitis. The data from the latter group demonstrated the CSF-protein pattern of partial blood-CSF barrier (B-CSF-B) breakdown. The children with acute cerebellar ataxia showed no or only minor signs of a B-CSF-B impairment. However, CSF changes indicative of a severe lesion of B-CSF-B occurred in 9 out of 14 children with a medulloblastoma. A striking finding was that 12 patients revealed a marked increase of CSF-gammaglobulin. In 5 children this finding was associated with only a slight disturbance of B-CSF-B. Moreover, in 5 of the children with medulloblastoma oligoclonal CSF gammaglobulins could be detected clearly indicating local immunoglobulin synthesis within the CNS. Acute cerebellar ataxia can be differentiated from medulloblastoma by means of CSF-protein electrophoresis. The occurrence of oligoclonal gammaglobulins in medulloblastomas could mean synthesis of antibodies against tumour tissue.

57 I.SIPILÄ[X], O.SIMELL[X], J.RAPOLA[X] and A.VANNAS[X] (Introduced by J.Perheentupa). Children's Hospital, University of Helsinki, Helsinki, Finland. Treatment of patients with gyrate atrophy of the choroid and retina with hyperornithinemia (GA) with creatine, a clinical trial.

GA is an autosomal recessive disease involving the eyes and type II muscle fibers. In the eyes, progressive atrophy of the choroid and retina starts by age 5-9 years and leads to virtual blindness in 20-40 years. Muscular involvement is clinically mild. The patients have 10-20-fold increased plasma ornithine concentrations, caused by lack of ornithine amino-transferase. Elevation of ornithine strongly inhibits arginine-glycine amidinotransferase, and decreases subsequently production of guanidinoacetic acid and creatine. We gave to 6 GA patients per os creatine 0.75-1.5 g divided in 3 daily doses. Muscle biopsies before treatment showed tubular aggregates and atrophy of type II muscle fibers in all but one subject. In control biopsies after 1 year of treatment, the atrophy was almost absent and very few cells contained tubular aggregates. The changes in cell size were highly significant. There was some progression in the choroidoretinal atrophies justified by photographs, but the Goldman visual fields showed some improvement. The treatment caused no side effects in the patients.

58 L.MORPHIS*,A.CONSTANTOPOULOS and N.MATSANIOTIS. First Department of Pediatrics of Athens University. The effect of bilirubin and aminophylline on protein kinase activity in rabbit brain.

Cyclic AMP dependent protein kinase activity expressed as pMoles of labelled Pi (from γ^{32}P-ATP) incorporated into histone (the substrate) per mg of protein,per min,following intravenous injection of bilirubin and/or aminophylline was studied in rabbits. It was found that: 1)bilirubin reduces protein kinase activity from 2429±253 (controls) to 1270±198 pMoles (bilirubin-treated animals),whereas aminophylline promotes it from 2589±296 (controls) to 3588±393 (aminophylline-treated animals).Both reduction and promotion of this enzyme activity caused by bilirubin and aminophylline respectively are statistically highly significant ($p < 0.001$), 2) cAMP in vitro and aminophylline in vivo restore the inhibition of the enzyme caused by bilirubin (cAMP:from 1270±198 to 1595±221, aminophylline: from 1270±198 to 2164±265) to a statistically significant degree ($p < 0.001$). These data are in agreement with our previous in vitro findings in the literature (Cytobios, 17:19,1976),in which bilirubin inhibits protein kinase activity by way of competition with cAMP.