83 L.R.GARIBALDI*,P.DURAND, Dept. of Pediatrics 3, Istituto Gaslini, Genova, Italy. Soluble tyrosine-aminotransferase (STAT) deficiency tyrosinemia: four cases.

Type-2 tyrosinemia (T-2) is an inborn error of metabolism due to STAT deficiency resulting in high serum tyrosine (TYR) levels. Clinical features include palmoplantar hyperkeratosis, dendritic keratitis and mental retardation. We observed 4 patients (2 children, 2 adult women, serum TYR levels 16-35 mg/dl) from the same familiar group. Skin lesions were present in 3, corneal lesions in 2 and mental retardation in 3 of them. These findings compare to a prevalence of 76 % for skin lesions, 82 % for eye lesions and 53 % for mental retardation in the 17 cases (including our patients) reported up to now. Remarkably, the normotyrosinemic son of an affected mother from our group, born before maternal tyrosinemia was detected, presented with seizures and mental retardation early in life. Lowering of serum TYR by a semisynthetic diet (TYR 20 mg + PHEnylalanine 20 mg/Kg/day) in 2 patients was followed by clearing of eye and skin lesions in 1-2 months. This report confirms the phenotipic variability of T-2. If untreated, this disease may cause mental retardation in 50% or more of affected patients and/or in offsprings of affected mothers. Irreversible corneal clouding may follow longstanding keratitis. A diet of low TYR, low PHE content is recommended in infancy, childhood, during pregnancy and whenever corneal involvement is a prominent feature.

84 J. RAJANTIE[X], O. SIMELL[X] and J. PERHEENTUPA, Children's Hospital, University of Helsinki, Helsinki, Finland. Renal handling of citrulline in lysinuric protein intolerance (LPI): evidence for "metabolic run-out".

In patients with LPI, an autosomal recessive diamino acid transport disorder, plasma and urinary amino acids were measured basally, during i.v. infusion of citrulline at two rates (27 and 54 µmol/kg/30 min) and after an i.v. injection of citrulline (0.3 mmol/kg). The plasma concentrations and urinary losses of citrulline were higher than in controls. Plasma arginine and ornithine levels rose subnormally after the loads. In the patients, in contrast to the controls, the loads were followed by massive argininuria and moderate ornithinuria. The results suggest that 1) in human kidney reabsorption involves partial conversion of citrulline to arginine and ornithine ("metabolic run-out"), 2) in LPI, the diamino acid transport defect is located at the basolateral cell membrane of the renal tubule; this inhibits the efflux of arginine and ornithine, increasing their cellular concentration, which in turn inhibits the metabolic disposal of citrulline, and causes leakage of arginine, ornithine and citrulline into the tubule lumen.

85 P. GILLET*, N. PHILIPPE*, T. PHILIP*, Y. FROBERT* and R. FRANCOIS. Department of pediatrics, Hopital Edouard Herriot, Institut Pasteur and UER Alexis Carrel, Lyon, France. Failure of levamisole therapy in Buckley's syndrome.

A 6 year old boy presented from the age of 7 months a chronic eczema and recurrent cold staphylococcal abcesses, purulent otitis media and bacterial bronchopneumoniae. Laboratory investigations revealed a neutrophilic leukocytosis with moderate eosinophilia, a markedely increased serum Ig E concentration (constantly greater than 10.000 ui/ml), a diminished lymphocyte proliferation on exposure to non specific mitogens, and a deficient in vitro and in vivo chemotactic activity of polymorphonuclears. Delayed hypersensitivity was normal. Circulating B and T lymphocytes populations were normal. The phagocytic and bactericidal capacities of the polymorphonuclears were normal. There was no abnormality in humoral immunity : normal Ig G, Ig M and Ig A serum concentrations, normal specific viral and bacterial antibodies production. Complement activities were quantitatively and qualitatively normal. Serum histamine concentrations were normal. This child presents a disorder characterized by raised serum Ig E, recurrent staphylococcal infections and chronic eczema as first described by Buckley et al (Pediatrics 49, 59, 1972) and in which Hill et al (Lancet ii, 617, 1974) observed an isolated deficiency of polymorphonuclear chemotaxis. Levamisole, reported to be effective in this syndrome, was given during 9 months (3 mg/kg every other day) : there was a transient normalisation of the lymphocyte proliferative response to mitogens but no clinical improvment was observed.

86 J.-M.MATTHIEU, J.REIGNER*, J.-M.BOURRE* and E.GAUTIER Service de Pédiatrie,CHUV,1011 Lausanne, Switzerland.

High cerebroside sulfotransferase activity in a hereditary demyelinating neuropathy.

'Trembler', a spontaneous, dominantly-inherited murine mutation causes spastic paralysis and an action tremor in mice. Peripheral nerves of Trembler mice show recurrent demyelination, remyelination and onion bulb formation resembling findings reported for onion bulb neuropathies in man. The metabolism of sulfatide, a lipid enriched in myelin, was investigated in this mutation. The sulfatide content of the nerve was decreased in Trembler mice but reflected the low myelin content. The specific activity of cerebroside sulfotransferase (CST), the enzyme responsible for the transfer of sulfate to cerebroside to form sulfatide, was increased by 257 percent in 15-day-old mutants. No activator or inhibitor effect and no lack of product inhibition could explain these results. In mutant PNS, Km, Vmax and heat sensitivity values for CST differed from controls In contrast, no abnormality could be demonstrated in mutant brain. These results suggest the presence of an abnormal enzyme, with a decreased affinity for its substrate but present in larger amounts. *In vivo* incorporation of radioactive sulfate into sulfatide and non-lipidic material was increased. The lack of accumulation of sulfatides could be explained by the low levels of substrate available and high arylsulfatase A activities. High arylsulfatase A activities with normal CST activities were observed in demyelinating diseases.

87 M. RENLUND[+], P. AULA[+], K.O. RAIVIO and A. LUNDBLAD[+] I Dept. of Pediatrics, University of Helsinki,Finland and Inst. Clin. Chem., University Hospital,Lund,Sweden

SALLA DISEASE - CLINICAL AND BIOCHEMICAL FINDINGS

Salla disease is a recently described autosomal recessive lysosomal storage disorder. So far, 31 patients aged 3-63 years have been identified in Finland and one probable case in Sweden. The main clinical symptoms are early onset (3-6 months) and slow progression of severe psychomotor retardation (IQ 20-30), moderate or severe ataxia, slightly coarse facial features and good-humoured nature. There is no hepatosplenomegaly and the eyes are normal except for a diverging squint (50 %). EEG shows slowly progressive low-voltage, and 1/3 of the patients have convulsive episodes. Lysosomal storage is seen in several types of cells by electronmicroscopy: fibroblasts, sweat gland cells, Schwann cells, hepatocytes, Kupffer cells and cultured fibroblasts. The patients have vacuolated lymphocytes (1-15 %). Urinary excretion of amino acids, organic acids, glycosaminoglycans, and oligosaccharides is normal. The excretion of free N-acetylneuraminic acid is 10-15 times higher than normal. Preliminary studies indicate storage of free N-acetylneuraminic acid. So far, no enzyme defect has been detected, although a number of lysosomal hydrolases, including neuraminidase, have been assayed.

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88 D.Rating*, E.Jäger-Roman* and H.Helge, Dept. of Pediatrics, Free University of Berlin, F.R.G.:

THE DEVELOPMENT OF N-DEMETHYLASE ACTIVITY MEASURED WITH ^{13}C-AMINOPYRINE BREATH TEST.

Measurement of specifically labelled CO_2 in exspired breath after aminopyrine (AP) demethylation by the hepatic mixed function oxidase system has been shown to be a reliable method for estimation of hepatocellular function. We used the ^{13}C-AP breath test to measure the normal development of the N-demethylase activity and started ^{13}C-methacetin breath test for investigation of O-dealkylation in children. 25 children with normal liver function, aged 2 days to 14 years, received 5 mg/kg body weight AP orally. $^{13}CO_2$ analysis in breath was performed with a mass spectrometer Varian MAT 230. Results were calculated as cumulative %-recovery of the administered dose. ^{13}C after 2 hours (%-dose), corrected for body weight and endogenous CO_2 production.

In neonates no ^{13}C excretion could be detected. N-demethylase activity then slowly increased and reached adult levels by 2 years of life (%-dose = 12.2 ± 2.1). Children with liver disease (%-dose = 4.0 ± 1.3) and treated with antiepileptic drugs (%-dose=16.7 ± 2.5) could be well discriminated. Neonates whose epileptic mother were treated with primidone during pregnancy showed a ^{13}C excretion similar or better than normal adults, thus demonstrating pre- or perinatal inducibility of the N-demethylase activity.