1243 ULTRASTRUCTURE OF FREEZE SUBSTITUTED LIVER IN REYE'S SYNDROME (RS). Jacqueline S. Partin and John C. Partin. SUNY at Stony Brook, Dept. Pediatrics, Stony Brook, NY.

Rapid-frozen liver biopsy tissue and freeze-substitution (FS) or cryo-thinsectioning offer new methods of morphology, biochemistry, and x-ray microanalysis. Three liver biopsies from patients with RS and three from children with other diseases were studied by a new technique: rapid freezing and freeze substitution with osmium tetroxide-acetone. As previously described in muscle, mitochondrial (Mt) intracristal spaces are nonexistent and cristae appear as tight seven-layered structures in both RS and non-RS liver. Pleomorphism of RS Mt is striking; Mt enlargement is not watery expansion, but a non-aqueous milieu with no disruption of cristae and no ice artefact. In severely injured liver cells in RS, two populations of Mt are present. In contrast to Mt, peroxisomes contain large ice crystals, and their contents may be mainly aqueous. Large pools of smooth endoplasmic reticulum are discretely outlined, without ice artefact, as are Golgi lamellae. All hepatocyte organelles are easily recognizable by standard EM criteria, but membranes and spacial relationships differ from traditional EM processing. Thus, pleomorphism of Mt in RS is not an artefact of chemical fixation. The Mt matrix is not watery swelling: the matrix must contain material which prevents ice formation, probably protein.

1244 SIGNIFICANCE OF TRANSPORTED GLYCINE IN THE CONJUGATION OF BENZOATE IN SPARSE-FUR (spf) MUTANT MICE WITH ORNITHINE TRANSCARBAMYLASE DEFICIENCY. Ijaz Qureshi, Jacques Letarte, Thérèse Rouleau, and René Ouellet. Pediatric Research Center, Ste.Justine Hospital, Montreal, Que.

Sodium benzoate (SB) therapy in hyperammonemic children is based on the elimination of excess nitrogen as hippurate, but its mechanism is speculatory. We gave 2 % SB in drinking water to normal (+/Y) and spf/Y mice. After acclimatization for 48 h, i.p. ^{3}H-glycine and ^{14}C-serine were given as sources of transported and biosynthesized glycine respectively. 24 h urine was analyzed for total hippurate, free glycine and orotate. Hippurate spots were separated by TLC and counted for radioactivity. Output of hippurate and free glycine increased significantly in SB treated spf/Y and +/Y as compared to untreated mice, while orotate excretion decreased ($p < 0.013$). Specific activity of ^{3}H and ^{14}C (DPM/µmol hippurate) showed significant increases in treated groups, indicating utilization of transported and biosynthesized glycine. However, ^{3}H:^{14}C ratio showed predominant use of ^{3}H-glycine. The ratio was higher in treated spf mice as compared to untreated controls (3.1 ± 0.7 Vs 1.5 ± 0.04; $p < 0.02$); same increase was seen in +/Y (1.9 ± 0.2 Vs 1.0 ± 0.1; $p < 0.01$). The results indicate that transported glycine has a bigger contribution in the formation of hippurate *in vivo* than glycine synthesized from serine. Since glycine is highly ammoniagenic, we postulate that the conjugation of excess glycine transported from body pools would result in depletion of ammoniagenic potential. This would be supplemented by the effect of glycine biosynthesis through reactions requiring a metabolic input of NH_3.

1245 IDIOSYNCRATIC HEPATOTOXIC RESPONSE TO SODIUM VALPROATE (SV) IN A SUB-POPULATION OF SPARSE-FUR (spf) MUTANT MICE. Ijaz Qureshi, Jacques Letarte, Beatriz Tuchweber, Ibrahim Yousef and S.R. Qureshi*. Centre de Recherche pédiatrique, Hôpital Sainte-Justine, Montréal, Qué. Canada.

Groups of six normal +/Y and six spf/Y mice with X-linked ornithine transcarbamylase (OTC) deficiency were given SV in drinking water in increasing concentrations of 0, 0.05, 0.15 and 0.25 % for 3 days each. Two out of six spf/Y mice became symptomatic at low intakes (34-85 mg/kg/d). One of these died and the other was sacrificed. Its plasma NH_3 was 440 µM as compared to 255 ± 42 in other spf/Y. Four spf/Y and all +/Y survived the treatment (intake: 612-715 mg/kg/d). SV intake was similar in surviving animals. There were no significant changes in orotate excretion; α-amino N increased progressively. Liver carbamyl phosphate synthetase (CPS-I) increased significantly in treated mice, while no changes were seen in OTC activity.

Severely affected spf/Y mice showed centrilobular necrosis with cytoplasmic vacuolization and microvesicular steatosis, indicating an idiosyncratic/hepatotoxic response. All other treated mice showed random single cell necrosis. On electron microscopy, the severely affected spf/Y had swollen mitochondria, dilated RER and glycogen depletion. The results indicate the existence of a susceptible sub-population in spf/Y mice which develops SV toxicity at low doses, and can be differentiated from other spf/Y mice by a different histopathologic response.

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1246 IDDM AND CONGENITAL HYPOGAMMAGLOBULINEMIA (CHGG). Nezam Radfar, Gilbert A. Friday, Ramamurti Chandra, David P. Skoner, Paul K. Stillwagon, Philip Fireman, Dept. of Ped., Mercy Hospital and Children's Hospital of Pgh, PA.

Viral and immunologic factors are believed to contribute to the development of IDDM. It is not clear if subclinical pancreatitis without islet-cell antibodies (ICA) will manifest IDDM. A 19 year old white male receiving γglobulin since infancy for CHGG developed IDDM (BG, 690 mg/dl; serum insulin <3.0 uu/ml; HbA1, 15.6%). Clinical course included recurrent infections since infancy, recurrent diarrhea and chronic lung disease. He had normal sweat Na. Fecal fat, 8.9 gm/24h (NL: <7.0). Low urinary PABA (48%), after bentiromide ingestion and improvement of diarrhea with pancreatic enzyme therapy were suggestive of pancreatic exocrine deficiency. Serum IgG, 159 mg%; IgM, 12 mg%; undetectable IgA and IgE; poor antibody responses to influenza and pneumococcal vaccine; absent B cells, but normal lymphocytes, 1095 (15%); T cells, 887 (81%), and suppressor cells, 504 (46%); deficient helper cells, 285 (26%) with reversed H:S ratio, 0.56. Normal lymphocyte PHA stimulation and negative delayed hypersensitivity skin tests. Antibody titers were low to CMV and EBV and absent to Coxsackie B 1 to B 6. ICA and immune responses to insulin were negative. His non-diabetic brother with common variable HGG had similar immune status except for 3% B cells; normal suppressor cells, 256 (27%); helper cells, 348 (42%) and H:S ratio, 1.36. Defective immune regulation in this patient may have facilitated the development of subclinical pancreatitis with resulting exocrine deficiency and IDDM without ICA. To our knowledge this is the first report of association of IDDM and CHGG.

1247 HYPONATREMIA AND ADH SECRETION IN TUBERCULOUS MENINGITIS IN CHILDREN. Madu Rao, Lew Herod, Phillip Steiner, and Laurence Finberg. State University of New York, Downstate Medical Center, Department of Pediatrics, Brooklyn, New York.

The following report is to provide evidence that ADH hypersecretion is not a part of the causation of hyponatremia in TBC meningitis. Over a 13 month period at Downstate Medical Center, there have been 3 children admitted with hyponatremia in conjunction with TBC meningitis. In all the 3 children we measured the plasma ADH levels by using a radio immune assay. The significant findings in the patients at the time of admission are as shown in the table.

Patient	B.P.	Urine sp. gr.	serum Na^+	Plasma ADH (mU/ml)
J.J.	110/70	1010	126	1.3
C.R.	98/70	1014	129	3.0
L.S.	125/75	1018	130	2.6

The above findings clearly show no increased ADH response in children with TBC meningitis presenting with hyponatremia. In 1952 we (J.C.I. 31:300) showed that in TBC meningitis there is a disturbance of mechanism governing ionic equilibrium between cells and extracellular fluid resulting in hyponatremia. This study supports the concept that ADH hypersecretion is not ongoing in these patients and that ADH may well be unrelated to the hyponatremic state in TBC meningitis.

1248 LONG-TERM ZINC PROTAMINE GLUCAGON AND ORAL STARCH IN THE MANAGEMENT OF FAMILIAL NESIDIOBLASTOSIS. Susan R. Rose, George P. Chrousos, Penelope Feuillan, Marvin Cornblath and James B. Sidbury. National Institute of Child Health and Human Development, NIH, Bethesda, Maryland 20205 and Department of Pediatrics, University of Maryland, Baltimore, Maryland.

Chronic or prolonged hypoglycemia can have devastating effects on a child's neurologic function. Support of normoglycemia is thus pivotal. We report the management of a child with familial nesidioblastosis who had failed to tolerate and respond to diazoxide therapy following a subtotal pancreatectomy at the third week of life. Long acting intramuscular zinc protamine glucagon was given with some success twice daily for 3 1/2 years along with frequent oral dextrose supplements. However, early morning hypoglycemia persisted, and wide fluctuations in plasma glucose levels occurred during 48 hours of frequent sampling (coefficient of variation 56.8%). At the fourth year of treatment circulating anti-insulin antibodies were found in our patient interfering with the plasma insulin determinations. Subsequently, we showed presence of trace amounts of insulin in the zinc-glucagon preparation Oral starch granules (1.25 tbsp/10 lb of body weight) were substituted for dextrose supplements and glucagon was discontinued. Over the subsequent months, plasma glucose concentrations have been more stable (coefficient of variation 23.6%) and within the normal range (70-120 mg/dl). We conclude that oral starch may be an effective treatment or therapeutic supplement in states of hyperinsulinism.