155 HUMAN LYMPHOCYTES AS AN INVESTIGATIVE TOOL OF SULFUR-CONTAINING AMINO ACID METABOLISM.

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The activities of five enzymes involved in methionine metabolism were determined in human lymphocytes at their resting phase and during blastogenesis in vitro. Blastogenesis was induced by purified phytohemagglutinin. Enzymes assayed were: 1) methionine adenosyltransferase (MAE) (EC 2.5.1.6); 2) cystathionine synthase (CS) (EC 4.2.1.22); 3) 5-methyltetrahydrofolate homocysteine-methyltransferase (MTHF) (EC 2.1.1.13); 4) cystathionase (EC 4.4.1.1.); 5) N5,N10-methylene-tetrahydrofolate reductase (CH2-THF) (EC 1.1.1.68). The results were as follows: The specific activity of MAE and MTHF increased two- to fivefold in human lymphocytes after 72 h in culture; thereafter a slight decrease in their specific activity was observed. The specific activity of CS was maximal in unstimulated human lymphocytes and slightly decreased during stimulation. Cystathionase and CH2-THF activities were present in human lymphocytes 96 h after stimulation. Their activity was not measured in the resting lymphocyte. These data suggest that cultured human lymphocytes may serve as a tool for studying inborn genetic errors involving methionine metabolism.

156 ACROFACIAL DYSPLASIA (A.D.) : DECREASED ACTIVITY OF ACID SIALIDASE IN FIBROBLASTS.

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In three unrelated children with slow growth and shortness of stature, lumbar hyperlordosis, flexion contractures at the hips, short hands and feet and with restricted interphalangeal joint mobility, the diagnosis of acrofacial dysplasia was proposed. Skeletal changes were minimal, except for those in the hands. The two older patients had heart valve abnormalities, one of them mild hepatomegaly. These children cannot be distinguished from patients with geleophysic dysplasia, a probably genetically heterogeneous disorder of connective tissue with as yet unknown enzyme defect. In the fibroblast strains from two of the patients, a reduced activity of acid sialidase was observed (see table) but no increase of either total or free sialic acid. No other storage compounds were detected. The other lysosomal acid hydrolases tested in the fibroblasts were normal.

Patient	Clinical features	Statistics	Sialidase*
N=15	controls	$\bar{x}$ range	26 12-47
C.S.	A.D.	$\bar{x}$ of 3 assays	5.2
K.B.	A.D.	$\bar{x}$ of 2 assays	7.4
X.Y.	sialidosis	-	0.2

*expressed as nM of 4MU/mg prot./hr/at 37°C

157 MICROCEPHALY WITH IMMUNO-DEFICIENCY AND CHROMOSOME INSTABILITY.

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In 1981 Weemaes et al.(Acta Paediatr.Scand.70:557-564 1981) reported on two Dutch children with microcephaly, stunted growth immunodeficiency and chromosome instability.
Recently Seemanova et al.(Am J.Med Genetics 20:639-648 1985)described 9 patients from 6 families with microcephaly, immunodeficiency and increased risk for lymphoreticular malignancy.
Both humoral and cellular immunity were disturbed in the patients. Cytogenetic studies in our Dutch patient and three Csechoslovak patients, still alive, revealed multiple rearrangements of chromosomes 7 and 14. There was also an increased sensitivity of the chromosomes to X-rays and abnormal DNArepair synthesis after irradiation of the cells. The laboratory findings of these patients are identical with those in ataxia telangiectasia. The clinical symptons are different, however, because all patients have microcephaly but neither ataxia nor telangiectasia.

158 TSH AND T_3 RESPONSES TO TRH IN CHILDREN WITH TYPE I INSULIN-DEPENDENT DIABETES MELLITUS (IDDM)

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TSH and T_3 responses to TRH (7mcg/kg i.v.) were evaluated in 28 diabetic children (9 males, 19 females; age range 3.5-18 yr) with stable HbA_1c range between 4.5 and 10.1% and in 16 non-diabetic controls (C) (5 males, 11 females; age range 5-17 yr). TRH test was performed at 8.00 a.m. before insulin therapy and serum samples were obtained at 0', 20', 30', 60' and 120' for TSH and at 0' and 120' for T_3 measurements (RIA). Basal TSH was lower in 8 ketotic children (KC) than in 20 hyperglycemic non-ketotic subjects (HNK) (1.5 ± 0.3 mIU/ml vs 2.7 ± 0.9; $p<0.01$), while no difference was found between HNK and C. TSH response in HNK was similar to C; it was lower in KC than in HNK ($\Delta 9.2\pm3.2$ mIU/ml vs 17.0 ± 5.4; $p<0.05$. Peak 10.9 ± 3.3 mIU/ml vs 20.2 ± 7.5; $p<0.01$. Area 743 ± 248 vs 1577 ± 987; $p<0.05$). Basal T_3 was lower in HNK than in C (1.33 ± 0.5 ng/ml vs 2.05 ± 0.31; $p<0.025$); no difference was found between HNK and KC. T_3 response was lower in HNK than in C (1.8 ± 0.5 ng/ml vs 2.9 ± 0.45; $p<0.001$); it was lower in KC than in HNK (1.27 ± 0.36 ng/ml vs 1.8 ± 0.5; $p<0.05$).
Our data show that diabetic ketoacidosis reduces TSH and, consequently, T_3 responses to TRH; besides, hyperglycemic non-ketotic subjects have normal TSH, but low T_3 response. These observations confirm that children with type I diabetes mellitus, as adults, present "low T_3 syndrome", both in ketotic and non-ketotic status. After releasing hormone stimulus there is low T_3 response in diabetic subjects, while in ketoacidosis this phenomenon could be due also to reduced TSH response. In hyperglycemic non-ketotic children a real depression of peripheral metabolism of T_3 is found, correlated with metabolic control.

159 EARLY SIGNS OF RENAL AND NEUROLOGICAL INVOLVEMENT IN CHILDREN WITH DIABETES MELLITUS

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Neuropathy and nephropathy are two secondary complications often seen in the IDDM patient. Aim of this study was to look for early signs of these complications in young diabetics and whether there was a correlation with age, duration and control of diabetes (HbA_1). Furthermore we investigated if there was a correlation between neurological and nephrological findings. So far 18 asymptomatic IDDM patients (age mean +/- SD: 12.4 +/- 2.5 years , 13 boys - 7 girls, duration of disease 0.4 - 9.2 years) and 11 controls (11.7 +/- 1,9 years, 7 girls - 4 boys) were neurophysiologically examined by means of EMG, nerve-conduction velocity studies and somato-sensory evoked-potentials (SSEP). 24-hour urine samples were collected and examined for microalbuminuria and b-glucosaminidase. Preliminary results show significant differences in nerve conduction velocities and indications suggesting early central nervous involvement in the patient-group. However no clear correlation between these findings and HbA_1, age and duration of disease was found although higher HbA_1 levels were found in those patients with greater number of nerves involved. We found no correlation between the neurophysiological findings and the degree of microalbuminuria and the urinary levels of b-glucosaminidase.

160 METABOLIC AND ENDOCRINE PROFILES IN A LOW BIRTH WEIGHT PREMATURE INFANT WITH PANCREAS APLASIA

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The significance of insulin and glucagon for the regulation of blood glucose as well as the importance of insulin and insulin-like growth factor (IGF I) for growth development in premature infants was studied in a rare case of total absence of the pancreas as part of a complex congenital malformation. Due to the total lack of insulin and glucagon the infant showed severe hyperglycemia soon after birth. Daily insulin requirement to achieve normoglycemia was striktly correlated to the amount of carbohydrate infusion and was only 1/10 of the dose given in premature low birthweight infants with neonatal transient diabetes mellitus. Over a life period of 6 month the child showed a progredient growth retardation besides an undisturbed mental development even in the case of insulin substitution and parenteral nutrition to overcome the exocrine pancreas dysfunction. The endocrine profile revealed normal TSH, T4, T3, glucocorticoids and STH, but surprisingly a total lack of IGF I. Summarizing, the metabolic and endocrine profile of this child demonstrates for the neonatal period of preterm infants the significance 1. of glucagon for insulin sensitivity and glucose balance and 2. of IGF I and insulin for growth development.