67

R.LODINOVÁ, V.JOUJA Institute for the Care of Mother and Child, Prague - Podolí, Czechoslovakia

The immunoglobulins and coproantibody formation in infants after artificial intestinal colonization with E. coli 083. Protective effect of orally administered antibody.

8 breast-fed and 9 bottle-fed infants were colonized after birth with a non-enteropathogenic E.coli strain.11 breast-fed and 10 bottle-fed infants were used as controls. In colonized infants the strain 083 was detected in the stool from the 2nd day and remained in predominance up to 16 weeks.The serum antibody against E. coli 083 increased between 4-16 weeks. The colonization did not influence significantly the serum immunoglobulin levels. In colonized bottle-fed infants the level of coproantibodies was significantly higher from 4 up to 16 weeks than in controls, in breast-fed colonized infants between 2-6 weeks. The colonization induced a formation of secretory IgA in bottle-fed infants from the 4th up to the 16th week. In breast-fed infants this effect was masked due to passive transfer of IgA via maternal milk. In 24 cases of diarrhoea caused by E. coli an antibody against E.coli 055,0111 and 026 was administered orally 7 times, 2ml/kg.In 19 infants the stools turned to normal.

68

F.A.Hommes,C.Bendien*,J.D.Elema*,Departments of Pediatrics and Pathology,School of Medicine, University of Groningen, The Netherlands.

Phosphoenolpyruvate carboxykinase deficiency. Inborn errors of 3 of the 4 enzymes specific for gluconeogenesis are known. The present report describes a deficiency of the 4th enzyme phosphoenolpyruvate carboxykinase (PEP-CK). characterized by severe hypoglycemia and extreme fatty changes of liver and kidney. A liver biopsy, taken immediately after death, demonstrated increased activities of glucose-6-phosphatase, fructose-1,6-diphosphatase and pyruvate carboxylase (40.6,15.9 and 3.3 µmoles per min. per g w.w. respectively) and a decreased activity of PEP-CK (0.7 µmoles per min. per g w.w.). The low activity of PEP-CK can explain the hypoglycemia. Light and electron microscopy showed extreme fatty changes of the liver and of the proximal tubuli of the kidney. The liver contained 55% (of wet weight) of chloroform-methanol extractable material. The fatty acid composition of these lipids showed an increased content of the C12 and C14 acids,pointing to an increased rate of fatty acid synthesis. These fatty changes may be explained by the specific localization of PEP-CK in man: for 80% in the mitochondria. In the absence of PEP-CK overproduction of citrate may occur, which will leave the mitochondria in exchange for malate, giving rise to the operation of a "citrate-malate" cycle. The net result of such a cycle will be the transfer of acetyl-CoA to the cytoplasm where it may serve as substrate for fatty acid synthetase.

69

R. GITZELMANN and B. STEINMANN*. Division of Metabolism, Department of Pediatrics, University of Zürich, Switzerland.

Antibody activation of mutant fructaldolase.

Antibodies that are specific for an enzyme may interfere with its catalytic activity: inhibition of the enzyme may occur but activation can also take place. Antibodies raised against certain wild type enzymes of bacteria and fungi have been found to activate some genetic mutants of the same enzymes. We would like to report the first antibody activation of a mutant human enzyme observed in vitro. Extracts of liver biopsy specimens from 5 children with hereditary fructose intolerance (HFI) were examined for fructaldolase activity. Typical reduction of the catalytic activity as well as reduced thermal stability of fructaldolase were demonstrated. When the extracts were reacted with antiserum against human liver fructaldolase B, up to three-fold activation of fructose-1-phosphate aldolase was observed in 3 out of 5 samples. This observation indicates genetic heterogeneity amongst HFI patients and perhaps more importantly, it lends support to the speculation that some day at least in some human mutants engineering of the mutant enzyme may become possible.

70

G. VAN DEN BERGHE, L. HUE* and H.G. HERS*, University of Louvain, Belgium.

Inhibition *in vivo* of the hyperglycemic action of glucagon. Study of the pathogeny of hereditary fructose intolerance.

The administration of fructose (F) to patients with hereditary fructose intolerance induces a profound hypoglycemia which is not relieved by glucagon. This lack of response was tentatively attributed to the partial (70 %) inhibition of phosphorylase *a* by F-1-P (Biochem. J.*134*,637,1973).

The administration of tagatose (T) to rats produces changes that are similar to those induced by F (accumulation of ketose 1-P, depletion of ATP and Pi), but last longer due to the slower metabolism of T. In controls, the SC administration of glucagon (0.1 mg/kg) provoked a 60 % rise of hepatic glucose and a 3-fold rise of glucose 6-P after 10 min. In rats treated with T (2 g/kg IP) 10 min before glucagon, both increases were completely abolished notwithstanding a normal activation of phosphorylase. This indicates a complete inhibition of phosphorylase *a in vivo*. The inhibitory effect of T-1-P on purified liver phosphorylase *a* was, however, not more pronounced than that of F-1-P.

Supported by the Fonds de la Recherche Scientifique Médicale and by the U.S. Public Health Service (grant AM 9235).