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Fructose Metabolism

III. Enzyme Deficiencies[1]

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ENZYME DEFICIENCIES in various steps of the fructose metabolic pathways in different tissues result in biochemical abnormalities which may appear as clinical disease. There are four enzyme deficiencies of the fructose metabolic pathway presently known: sucrose-starch intolerance, essential fructosuria, fructose intolerance, and glycogen storage disease of muscle. Transient fructose malabsorption has been reported, but the nature of the abnormality is unknown.

Starch and sucrose intolerance is due to a deficiency of sucrase (1, 2). Since sucrase also acts on isomaltose (49), which is derived from the hydrolysis of dextrins and starch, probably in the form of an oligosaccharide (3–5), symptoms will occur not only with sucrose and isomaltose ingestion but also with dextrins and starch. The condition was first described in 1961 (6–8), when it was demonstrated that diarrhea occurred with dietary sucrose. It was then shown that isomaltose intolerance accompanied sucrose intolerance (9, 10). Direct determination of jejunal sucrase and isomaltase activity demonstrated the enzyme deficiency (1, 2). Separation of jejunal enzymes by acrylamide gel electrophoresis has shown one band with coexistent sucrase and isomaltase activity with half the maltase activity (11, 12). In patients, sucrase and isomaltase deficiency have not been dissociated by enzyme assay. Thus, it appears that only one enzyme abnormality accounts for sucrose-starch intolerance (13). Symptoms are not absolutely correlated with jejunal enzyme levels (9, 14–16). Infants develop a fermentative type of diarrhea with the stools containing lactic acid. If severe, dehydration and malnutrition may develop. Despite the diarrhea, anorexia does not occur. If the diarrhea is severe enough, secondary malabsorption may result. In older infants and children the symptoms may be less pronounced. The condition may be manifested by difficulty in toilet training (1). The combination of diarrhea, abdominal distention, and mild growth retardation may suggest the diagnosis of celiac disease (14, 17–19). Sucrase deficiency may be asymptomatic and be discovered only during a family survey because of clinical disease in other members of the family (6, 14).

Two species of sea lions are deficient in several intestinal enzymes including sucrase (20). Administration of sucrose to these animals produced severe fermentative diarrhea. Combined sucrase and lactase deficiency with sucrosuria and lactosuria has been reported, but enzyme assays were not done (21).

Because sucrase is located in the microvilli of the small intestinal mucosal cells

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(22–29), the effects of various gastrointestinal disorders on sucrase activity have been investigated. Low jejunal sucrase values occur in untreated celiac disease but appear to return to normal upon treatment with a gluten-free diet (17, 30–32). Decreased levels of sucrase have been reported in regional enteritis (32) and beta-lipoprotein deficiency (32). This latter patient also had decreased maltase and isomaltase activity and no detectable lactase activity. Electron microscopy showed intracellular fat accumulation but no abnormality of the microvilli. Combined sucrase and lactase deficiency has been described in a patient with steatorrhea and atrophic duodenal villi. Removal of dietary disaccharides resulted in clinical improvement and disappearance of the steatorrhea (33). Decreased sucrase activity has been reported also in cystic fibrosis (34, 35). The handling of disaccharide has been shown to be impaired after partial gastrectomy and gastrojejunostomy of the Billroth II type (36) and small bowel resection (37). Sucrosuria has been reported to occur in a number of diseases: regional enteritis, idiopathic steatorrhea, amyloidosis, mesenteric insufficiency, ulcerative colitis, duodenal ulcer, cirrhosis, Menetrier's disease, and in a wide variety of malignant diseases. In some of the neoplastic diseases, the sucrosuria decreased after therapy. The sucrosuria was not necessarily correlated with poor nutritional status (38).

Fructose malabsorption has been described in young infants in association with glucose and galactose malabsorption (39). Monosaccharide malabsorption occurred soon after birth, was severe and life-threatening, and survival was attained only by means of a sugar-free diet consisting of 3% butter fat, 3.5% casein, and 2% glycerol emulsified with deoxycholate. The sugar malabsorption was transient lasting 2 weeks to 5 months. Glucose-galactose malabsorption has been described by several authors (40–48) and in these cases fructose is the proper therapeutic agent.

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