Transient Sucrase and Starch Intolerance

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Before 1964, when Shmerling et al demonstrated that sucrase-isomaltase (SI) is decreased in children with active celiac disease (1), Herter (1908), Heubner (1909), Howland (1921), Fanconi (1938), and Andersen (1947) already had shown that patients with celiac disease (CD) did not tolerate sucrase or starch (2–6). By means of continuous perfusion of the small intestine with monosaccharides and disaccharides, Beyreiss and Hoepffner demonstrated a clinically relevant loss of lactose digestion and a less pronounced but still significant decrease in sucrase digestion associated with villous atrophy, which is present in several intestinal diseases in addition to CD such as inflammatory bowel disease, food allergy, infectious diseases, protein-energy malabsorption, and immunodeficiencies (7). The decrease can be reversed by successful treatment of the underlying disease. In the case of CD, the digestion of disaccharides is significantly improved after several weeks on a gluten-free diet. Reexposure to gliadin, however, results in renewed reduction of lactose and sucrase digestion (8). Studies have shown that sucrase activity, which is reduced in active CD, increases during remission when a gluten-free diet is prescribed. After 2 years, however, recovery of sucrase activity in the distal duodenum does not reach that of controls, although the clinical effect is observed much sooner (9,10). Villous atrophy in CD occurs within 4 hours of exposure to gliadin (13). During this time, alterations can be noted in villous height-to-crypt depth ratio, enterocyte height, and intraepithelial lymphocyte count (14). In CD, secondary disaccharidase deficiency correlates with low-grade mucosal lesions (15,16). Sucrase activity also is suppressed by gliadin in the organ culture of biopsies from patients with CD (17).

In addition to the loss of enterocytes in villous atrophy, proinflammatory cytokines from the epithelium and dendritic cells and lymphocytes of the lamina propria contribute to the suppression of some disaccharidases. Interleukin-6 and interferon-γ decrease SI synthesis in Caco2 cells, in contrast to tumor necrosis factor-α, which increases its synthesis; such an effect could not be demonstrated for lactase (18). Expression and activity of SI also is decreased in the small intestine of the 2,4,6-trinitrobenzene sulfonic acid–induced colitis model (19). There is evidence that SI can be localized in the cytosol of a significant part of enterocytes under inflammatory (dysplastic) conditions (20). This is evident in cells characterized by rapid uptake of antigen into the cytosol of enterocytes (21). The labeling density of SI on the apical membrane, or rapid uptake of antigen into the cytosol of enterocytes cells, is decreased strongly. The cytoskeleton, which consists of actin and the actin-associated protein, villin, is severely altered in these cells. Gliadin but not ovalbumin binds to actin, affecting the cytoskeleton and SI biosynthetic transport to the apical membrane (22,23). SI also was found in the cytosol of Caco2 cells after disruption of the brush border assembly, induced by inhibition of villin expression using antisense RNA (24). The mechanism of the cytosolic localization of SI is still obscure.

The phenotypic heterogeneity of secondary (transient) sucrase intolerance is widespread and characterized by normal morphology of the mucosa. Besides perfusion studies, several diagnostic tools are available. A 13C-bread test after a 13C-sucrose load is a noninvasive approach to measure sucrase digestion (25). Genotyping allows the determination of mutations, including compound heterozygosity, which have effects on folding and function of SI as demonstrated in expression studies (26). Frozen intestinal biopsies can be assayed for in vivo enzyme activity (27), mosaic expression pattern (28,29), and subcellular localization of SI. Such diagnostic tests may help differentiate secondary from primary sucrase intolerance.

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The term recurrent abdominal pain (RAP), based on the pioneering work of Apley and Naish, describes children who have chronic abdominal pain without an identifiable organic basis.