TABLE 349-5 PRIMARY LACTASE DEFICIENCY IN ADULT ETHNIC GROUPS

Ethnic Group	Prevalence of Lactase Deficiency, %
Northern European	5–15
Mediterranean	60–85
African black	85–100
American black	45–80
American white	10–25
Native American	50–95
Mexican American	40–75
Asian	90–100

Source: From FJ Simoons: Am J Dig Dis 23:963, 1978.

CARBOHYDRATES

Carbohydrates in the diet are present in the form of starch, disaccharides (sucrose and lactose), and glucose. Carbohydrates are absorbed only in the small intestine and only in the form of monosaccharides. Therefore, before their absorption, starch and disaccharides must first be digested by pancreatic amylase and intestinal brush border disaccharidases to monosaccharides. Monosaccharide absorption occurs by a Na-dependent process mediated by the brush border transport protein SGLT1.

Lactose malabsorption is the only clinically important disorder of carbohydrate absorption. Lactose, the disaccharide present in milk, requires digestion by brush border lactase to its two constituent monosaccharides, glucose and galactose. Lactase is present in almost all species in the postnatal period but then disappears throughout the animal kingdom, except in humans. Lactase activity persists in many individuals throughout life. Two different types of lactase deficiency exist—primary and secondary. In *primary lactase deficiency*, a genetically determined decrease or absence of lactase is noted, while all other aspects of both intestinal absorption and brush border enzymes are normal. In a number of nonwhite groups, primary lactase deficiency is common in adulthood. In fact, Northern European and North American whites are the only groups to maintain small-intestinal lactase activity throughout adult life. Table 349-5 presents the incidence of primary lactase deficiency in several ethnic groups. Lactase persistence in adults is an abnormality due to a defect in the regulation of its maturation. In contrast, *secondary lactase deficiency* occurs in association with small-intestinal mucosal disease, with abnormalities in both structure and function of other brush border enzymes and transport processes. Secondary lactase deficiency is often seen in celiac disease.

As lactose digestion is rate-limiting compared to glucose/galactose absorption, lactase deficiency is associated with significant lactose malabsorption. Some individuals with lactose malabsorption develop symptoms such as diarrhea, abdominal pain, cramps, and/or flatus. Most individuals with primary lactase deficiency do not have symptoms. Since lactose intolerance may be associated with symptoms suggestive of irritable bowel syndrome, persistence of such symptoms in an individual who exhibits lactose intolerance while on a strict lactose-free diet suggests that the person's symptoms were related to irritable bowel syndrome.

The development of symptoms of lactose intolerance is related to several factors:

1. *Amount of lactose in the diet.*
2. *Rate of gastric emptying.* Symptoms are more likely when gastric emptying is rapid than when it is slower. Therefore, skim milk is more likely to be associated with symptoms of lactose intolerance than whole milk, as the rate of gastric emptying after skim milk intake is more rapid. Similarly, diarrhea following subtotal gastrectomy is often a result of lactose intolerance, as gastric emptying is accelerated in patients with a gastrojejunostomy.
3. *Small-intestinal transit time.* Although the small and large intestines both contribute to the development of symptoms, many symptoms of lactase deficiency are related to the interaction of colonic bacteria and nonabsorbed lactose. More rapid small-intestinal transit makes symptoms more likely.
4. *Colonic compensation by production of SCFAs from nonabsorbed lactose.* Reduced levels of colonic microflora, which can follow antibiotic use, are associated with increased symptoms after lactose ingestion, especially in a lactase-deficient individual.

Glucose-galactose or monosaccharide malabsorption may also be associated with diarrhea and is due to a congenital absence of SGLT1. Diarrhea develops when individuals with this disorder ingest carbohydrates that contain actively transported monosaccharides (e.g., glucose, galactose) but not when they ingest monosaccharides that are not actively transported (e.g., fructose). Fructose is absorbed by the brush border transport protein GLUT 5, a facilitated diffusion process that is not Na-dependent and is distinct from SGLT1. In contrast, some individuals develop diarrhea as a result of the consumption of large quantities of sorbitol, a sugar used in diabetic candy; sorbitol is only minimally absorbed because of the absence of an intestinal absorptive transport mechanism for this sugar.

PROTEINS

Protein is present in food almost exclusively as polypeptides and requires extensive hydrolysis to di- and tripeptides and amino acids before absorption. Proteolysis occurs in both the stomach and the small intestine; it is mediated by pepsin, which is secreted as pepsinogen by gastric chief cells, and by trypsinogen and other peptidases from pancreatic acinar cells. The proenzymes pepsinogen and trypsinogen must be activated to pepsin (by pepsin at a pH <5) and to trypsin (by the intestinal brush border enzyme enterokinase and subsequently by trypsin), respectively. Proteins are absorbed by separate transport systems for di- and tripeptides and for different types of amino acids—e.g., neutral and dibasic. Alterations in either protein or amino acid digestion and absorption are rarely observed clinically, even in the presence of extensive small-intestinal mucosal inflammation. However, three rare genetic disorders involve protein digestion/absorption: (1) *Enterokinase deficiency* is due to an absence of the brush border enzyme that converts the proenzyme trypsinogen to trypsin and is associated with diarrhea, growth retardation, and hypoproteinemia. (2) *Hartnup's syndrome*, a defect in neutral amino acid transport, is characterized by a pellagra-like rash and neuropsychiatric symptoms. (3) *Cystinuria*, a defect in dibasic amino acid transport, is associated with renal calculi and chronic pancreatitis.

APPROACH TO THE PATIENT: Malabsorption

The clues provided by the history, symptoms, and initial preliminary observations will serve to limit extensive, ill-focused, and expensive laboratory and imaging studies. For example, a clinician evaluating a patient who has symptoms suggestive of malabsorption and who has recently undergone extensive small-intestinal resection for mesenteric ischemia should direct the initial assessment almost exclusively to defining whether a short-bowel syndrome might explain the entire clinical picture. Similarly, the development of a pattern of bowel movements suggestive of steatorrhea in a patient with long-standing alcohol abuse and chronic pancreatitis should prompt an assessment of pancreatic exocrine function.

The classic picture of malabsorption is rarely seen today in most parts of the United States. As a consequence, diseases with malabsorption must be suspected in individuals who have less severe symptoms and signs and subtle evidence of the altered absorption of only a *single* nutrient rather than obvious evidence of the malabsorption of multiple nutrients.

Although diarrhea can be caused by changes in fluid and electrolyte movement in either the small or the large intestine, dietary nutrients are absorbed almost exclusively in the small intestine.