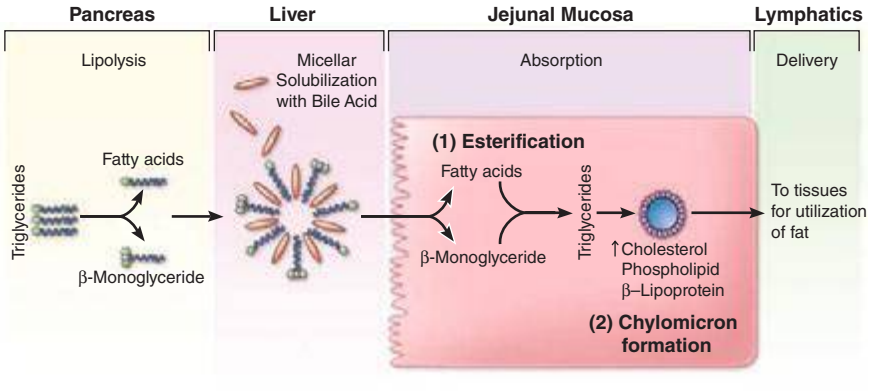

FIGURE 349-2 Schematic representation of lipid digestion and absorption. Dietary lipid is in the form of long-chain triglycerides. The overall process can be divided into (1) a digestive phase that includes both lipolysis and micelle formation requiring pancreatic lipase and conjugated bile acids, respectively, in the duodenum; (2) an absorptive phase for mucosal uptake and re-esterification; and (3) a postabsorptive phase that includes chylomicron formation and exit from the intestinal epithelial cell via lymphatics. *(Courtesy of John M. Dietschy, MD; with permission.)*

by which the water-insoluble products of lipolysis can reach the luminal plasma membrane of villous epithelial cells—the site for lipid absorption. Mixed micelles are molecular aggregates composed of fatty acids, monoglycerides, phospholipids, cholesterol, and conjugated bile acids. These mixed micelles are formed when the concentration of conjugated bile acids is greater than its CMC, which differs among the several bile acids present in the small-intestinal lumen. Conjugated bile acids, synthesized in the liver and excreted into the duodenum in bile, are regulated by the enterohepatic circulation (see above). Steatorrhea can result from impaired movement of fatty acids across the unstirred aqueous fluid layer in two situations: (1) an increase in the relative thickness of the unstirred water layer that occurs in bacterial overgrowth syndromes (see below) secondary to functional stasis (e.g., scleroderma); and (2) a decrease in the *duodenal* concentration of conjugated bile acids below the CMC, resulting in impaired micelle formation. Thus, steatorrhea can be caused by one or more defects in the enterohepatic circulation of bile acids.

Uptake and re-esterification constitute the *absorptive phase* of lipid digestion/absorption. Although passive diffusion has been thought to be responsible, a carrier-mediated process may mediate fatty acid and monoglyceride uptake. Regardless of the uptake process, fatty acids and monoglycerides are re-esterified by a series of enzymatic steps in the endoplasmic reticulum to form triglycerides, in which lipid exits from the intestinal epithelial cell. Impaired lipid absorption as a result of mucosal inflammation (e.g., celiac disease) and/or intestinal resection can also lead to steatorrhea.

The re-esterified triglycerides require the formation of *chylomicrons* to permit their exit from the small-intestinal epithelial cell and their delivery to the liver via the lymphatics. Chylomicrons are composed of β-lipoprotein and contain triglycerides, cholesterol, cholesterol esters, and phospholipids and enter the lymphatics, not the portal vein. Defects in the *postabsorptive phase* of lipid digestion/absorption can also result in steatorrhea, but these disorders are uncommon. Abetalipoproteinemia, or acanthocytosis, is a rare disorder of impaired synthesis of β-lipoprotein associated with abnormal erythrocytes (acanthocytes), neurologic problems, and steatorrhea (Chap. 421). Lipolysis, micelle formation, and lipid uptake are all normal in patients with abetalipoproteinemia, but the re-esterified triglyceride cannot exit the epithelial cell because of the failure to produce chylomicrons. Small-intestinal biopsy samples obtained from these rare patients in the postprandial state reveal lipid-laden small-intestinal epithelial cells that become perfectly normal in appearance after a 72- to 96-h fast. Similarly, abnormalities of intestinal lymphatics (e.g., intestinal lymphangiectasia) may also be associated with steatorrhea as well as protein loss (see below). Steatorrhea can result from defects at any of the several steps in lipid digestion/absorption.

The mechanism of lipid digestion/absorption outlined above is limited to *dietary* lipid, which is almost exclusively in the form of LCTs (Table 349-3). Medium-chain triglycerides (MCTs), composed of fatty acids with carbon chain lengths of 8–12, are present in large amounts in coconut oil and are used as a nutritional supplement. MCTs can be digested and absorbed by a pathway different from that involved in LCT digestion and absorption; at one time, MCTs held promise as an important treatment for steatorrhea of almost all etiologies. Unfortunately, they have been less therapeutically effective than expected because, for reasons that are not completely understood, their use often is not associated with an increase in body weight.

In contrast to LCTs, MCTs do not require pancreatic lipolysis as they can be absorbed intact by the intestinal epithelial cell. Further, micelle formation is not necessary for the absorption of MCTs (or MCFAs, if hydrolyzed by pancreatic lipase). MCTs are absorbed more efficiently than LCTs for the following reasons: (1) The rate of absorption is greater for MCTs than for LCFAs. (2) After absorption, MCFAs are not re-esterified. (3) After absorption, MCTs are hydrolyzed to MCFAs. (4) MCTs do not require chylomicron formation to exit intestinal epithelial cells. (5) The route of MCT exit is via the portal vein and not via lymphatics. Thus, the absorption of MCTs is greater than that of LCTs in pancreatic insufficiency, conditions with reduced intraduodenal bile acid concentrations, small-intestinal mucosal disease, abetalipoproteinemia, and intestinal lymphangiectasia.

SCFAs are not dietary lipids but are synthesized by colonic bacterial enzymes from nonabsorbed carbohydrate and are the anions present at the highest concentration in stool (80–130 m*M*). The SCFAs in stool are primarily acetate, propionate, and butyrate, whose carbon chain lengths are 2, 3, and 4, respectively. Butyrate is the primary nutrient for colonic epithelial cells, and its deficiency can be associated with one or more colitides. SCFAs conserve calories and carbohydrate: carbohydrates that are not completely absorbed in the small intestine will not be absorbed in the large intestine because of the absence of both disaccharidases and SGLT1, the transport protein that mediates monosaccharide absorption. In contrast, SCFAs are rapidly absorbed and stimulate colonic NaCl and fluid absorption. Most antibiotic-associated diarrhea not caused by *Clostridium difficile* is due to antibiotic suppression of the colonic microbiota, with a resulting decrease in SCFA production. As *C. difficile* accounts for only ~15–20% of all antibiotic-associated diarrhea, a relative decrease in colonic production of SCFA is likely the cause of most antibiotic-associated diarrhea.

The clinical manifestations of steatorrhea are a consequence both of the underlying disorder responsible for its development and of steatorrhea per se. Depending on the degree of steatorrhea and the level of dietary intake, significant fat malabsorption may lead to weight loss. Steatorrhea per se can be responsible for diarrhea; if the primary cause of the steatorrhea has not been identified, a low-fat diet can often ameliorate the diarrhea by decreasing fecal fat excretion. Steatorrhea is commonly associated with fat-soluble vitamin deficiency, which requires replacement with water-soluble preparations of these vitamins.

Disorders of absorption may also be associated with malabsorption of other dietary nutrients— most often carbohydrates—with or without a decrease in dietary lipid digestion and absorption. Therefore, knowledge of the mechanisms of digestion and absorption of carbohydrates, proteins, and other minerals and vitamins is useful in the evaluation of patients with altered intestinal nutrient absorption.