TABLE 349-2 COMPARISON OF BILE ACID AND FATTY ACID DIARRHEA

	Bile Acid Diarrhea	Fatty Acid Diarrhea
Extent of ileal disease	Limited	Extensive
Ileal bile-acid absorption	Reduced	Reduced
Fecal bile-acid excretion	Increased	Increased
Fecal bile-acid loss compensated by hepatic synthesis	Yes	No
Bile-acid pool size	Normal	Reduced
Intraduodenal (bile acid)	Normal	Reduced
Steatorrhea	None or mild	>20 g
Response to cholestyramine	Yes	No
Response to low-fat diet	No	Yes

the rate of fecal bile-acid losses, resulting in maintenance of both the bile-acid pool size and the intraduodenal concentrations of bile acids. In contrast, patients with greater degrees of ileal disease and/or resection often have diarrhea and steatorrhea that do not respond to cholestyramine. In this situation, ileal disease is also associated with increased volumes of bile acids entering the colon; however, hepatic synthesis can no longer increase sufficiently to maintain the bile-acid pool size. As a consequence, the intraduodenal concentration of bile acids is reduced to less than the CMC, and the result is impaired micelle formation and steatorrhea. This second situation is often called *fatty acid diarrhea.* Cholestyramine may not be effective (and may even exacerbate the diarrhea by further depleting the intraduodenal bile-acid concentration); however, a low-fat diet to reduce fatty acid entry into the colon can be effective. Two clinical features—the length of the ileal section removed and the degree of steatorrhea—can predict whether an individual patient will respond to cholestyramine. Unfortunately, these predictors are imperfect, and a therapeutic trial of cholestyramine is often necessary to establish whether an individual patient will benefit from cholestyramine. Table 349-2 contrasts the characteristics of bile acid diarrhea (small ileal dysfunction) and fatty acid diarrhea (large ileal dysfunction).

Bile acid diarrhea can also occur in the absence of ileal inflammation and/or resection and is characterized by an abnormal ^{75}SeHCAT retention study and reduced ileal release of fibroblast growth factor 19, a negative regulator of bile acid synthesis, with a consequent increase in bile acid synthesis and secretion that exceeds ileal bile-acid absorption. The diarrhea in these patients also responds to cholestyramine.

LIPIDS

Steatorrhea is caused by one or more defects in the digestion and absorption of dietary fat. The average intake of dietary fat in the United States is ~120–150 g/d, and fat absorption is linear to dietary fat intake. The total load of fat presented to the small intestine is considerably greater, as substantial amounts of lipid are secreted in bile each day (see "Enterohepatic Circulation of Bile Acids," above). Three types of fatty acids compose fats: long-chain fatty acids (LCFAs), medium-chain fatty acids (MCFAs), and short-chain fatty acids (SCFAs) (Table 349-3). Dietary fat is exclusively composed of long-chain triglycerides (LCTs)—i.e., glycerol that is bound via ester linkages to three LCFAs. While the majority of dietary LCFAs have carbon chain lengths of 16 or 18, all fatty acids of carbon chain length >12 are metabolized in the same manner; saturated and unsaturated fatty acids are handled identically.

Assimilation of dietary lipid requires three integrated processes: (1) an intraluminal, or digestive, phase; (2) a mucosal, or absorptive, phase; and (3) a delivery, or postabsorptive, phase. An abnormality at any site involved in these processes can cause steatorrhea (Table 349-4). Therefore, it is essential that any patient with steatorrhea be evaluated to identify the specific physiologic defect in overall lipid digestion/absorption, as therapy will be determined by the specific etiology.

The digestive phase has two components, *lipolysis* and *micelle formation.* Although dietary lipid is in the form of LCTs, the intestinal mucosa does not absorb triglycerides; they must first be hydrolyzed

TABLE 349-3 COMPARISON OF DIFFERENT TYPES OF FATTY ACIDS

	Long-Chain	Medium-Chain	Short-Chain
Carbon chain length	>12	8–12	<8
Present in diet	In large amounts	In small amounts	No
Origin	In diet as triglycerides	Only in small amounts in diet as triglycerides	Bacterial degradation in colon of nonabsorbed carbohydrate to fatty acids
Primary site of absorption	Small intestine	Small intestine	Colon
Requires pancreatic lipolysis	Yes	No	No
Requires micelle formation	Yes	No	No
Present in stool	Minimal	No	Substantial

(Fig. 349-2). The initial step in lipid digestion is the formation of emulsions of finely dispersed lipid, which is accomplished by mastication and gastric contractions. Lipolysis, the hydrolysis of triglycerides to free fatty acids, monoglycerides, and glycerol by lipase, is initiated in the stomach by lingual and gastric lipases that have a pH optimum of 4.5–6.0. About 20–30% of total lipolysis occurs in the stomach. Lipolysis is completed in the duodenum and jejunum by pancreatic lipase, which is inactivated by a pH <7.0. Pancreatic lipolysis is greatly enhanced by the presence of a second pancreatic enzyme, colipase, which facilitates the movement of lipase to the triglyceride.

Impaired lipolysis can lead to steatorrhea and can occur in the presence of pancreatic insufficiency due to chronic pancreatitis in adults or cystic fibrosis in children and adolescents. Normal lipolysis can be maintained by ~5% of maximal pancreatic lipase secretion; thus, steatorrhea is a late manifestation of these disorders. A reduction in intraduodenal pH can also result in altered lipolysis, as pancreatic lipase is inactivated at pH <7. Thus, ~15% of patients who have gastrinoma (Chap. 348), with substantial increases in gastric acid secretion from ectopic production of gastrin (usually from an islet cell adenoma), have diarrhea, and some have steatorrhea believed to be secondary to acid inactivation of pancreatic lipase. Similarly, patients who have chronic pancreatitis (with reduced lipase secretion) often have a decrease in pancreatic bicarbonate secretion, which will also result in a lowering of intraduodenal pH and inactivation of endogenous pancreatic lipase or of therapeutically administered lipase.

Overlying the microvillus membrane of the small intestine is the so-called unstirred water layer, a relatively stagnant aqueous phase that must be traversed by the products of lipolysis that are primarily water insoluble. Water-soluble mixed micelles provide a mechanism

TABLE 349-4 DEFECTS IN LIPID DIGESTION AND ABSORPTION IN STEATORRHEA

Phase, Process	Pathophysiologic Defect	Disease Example
Digestive		
Lipolysis formation	Decreased lipase secretion	Chronic pancreatitis
Micelle formation	Decreased intraduodenal bile acids	See Table 349-1
Absorptive		
Mucosal uptake and re-esterification	Mucosal dysfunction	Celiac disease
Postabsorptive		
Chylomicron formation	Absent betalipoproteins	Abetalipoproteinemia
Delivery from intestine	Abnormal lymphatics	Intestinal lymphangiectasia