Symposium

Inflammatory Disease of the Bowel:
Treatable Physiologic Disorders Following Surgical Treatment

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I would like to discuss with you today the pathophysiologic and clinical sequelae of ileal resection, many of which are treatable. I will review choleraheic enteropathy or bile-salt diarrhea, post-ileectomy steatorrhea, and hydroxy-fatty acid diarrhea.

The ileum has two major functions, active absorption of vitamin B$_{12}$ (deficiency of which will eventually lead to macrocytic anemia), and active absorption of bile salts, which return to the liver via the “enterohepatic circulation” or re-excretion in bile.

I would like to pose a therapeutic challenge to emphasize the clinical problems under consideration. A 62-year-old woman underwent resection of 80 cm of distal ileum and ileo-ascending colonic anastomosis in 1970, for Crohn’s disease with obstruction. Postoperatively, for the first time, she had severe watery diarrhea associated with severe pruritus ani, which led to maceration of the perianal area. In 1971, sigmoidal colostomy was performed because of the severity of the perianal problem. The patient continued to discharge as much as 20 bags full of diarrheic feces a day, and was socially incapacitated. She was readmitted in 1972 for evaluation of this problem and was found to excrete normal quantities of fecal fat. The object of treatment of this patient was to restore normal bowel function, with formed stools evacuated per rectum.

In order to understand the pathophysiology in this patient and its treatment, I would like to review briefly the biochemistry of digestion and absorption of fat. Virtually all the fat ingested is long-chain triglyceride, each molecule consisting of a glycerol base with three long-chain (C-16 to C-18) fatty-acid molecules esterified in the alpha, beta and alpha-prime positions on the glycerol molecule. Triglyceride is water-insoluble and cannot be absorbed; the object of the digestive process is to convert this large unabsorbable molecule to a tiny water-soluble absorbable form.

The stomach appears to play a very small role in digestion of fat. Its propulsion—retropulsion kneading action emulsifies fat, breaking it up into smaller particles and thus exposing more surfaces to subsequent digestion by pancreatic enzymes. Fat leaving the stomach is still unabsorbable triglyceride.

In the duodenum the undigested, insoluble triglyceride is acted upon by pancreatic lipase, an esterase that breaks off the fatty-acid molecules from the alpha and alpha-prime positions of the glycerol moiety, releasing two free fatty-acid molecules and leaving one fatty-acid molecule esterified...
in the beta position - a beta monoglyceride. These products of pancreatic lipolysis, free fatty acids and beta monoglycerides, are also water-insoluble and unabsorbable.

We now come to a crucial step in absorption of fat, the role of bile salts. Bile salts are synthesized by the liver from cholesterol, conjugated with taurine and glycine and excreted through the common duct into the duodenum. In order for normal absorption of fat to occur, conjugated bile salts must be present in the duodenum at or above a critical concentration, the “critical micellar concentration” (CMC). At or above that concentration, bile acids are capable of altering the physical state of insoluble fatty-acid molecules into a water-soluble form, in the physical structure known as a micelle. Fatty acids in micellar solution are absorbable.

We thus find, following the digestion of triglyceride by pancreatic lipase, the formation of mixed micelles (bile salts above CMC, fatty acids, beta monoglyceride, lecithin and cholesterol) in the duodenum. From this micellar solution, via poorly understood mechanisms, the lipid materials are absorbed.

Crucial to this discussion is the fact that in normal man fat is absorbed proximally so that virtually all absorption of fat occurs in the proximal jejunum. However, bile acids are not absorbed significantly in the jejunum, but remain in the gut lumen until they reach the site of their active absorption in the distal ileum. The distal ileal reabsorption site is about 95 per cent efficient, so that a total of approximately 24 g a day of bile acid that circulates through the bowel through the course of three meals daily (4 g body pool circulating twice each meal), 23.4 g recirculate to the liver via the enteropathic circulation and only 600 mg per day are lost into the colon. This loss is replaced by hepatic synthesis each day of an equivalent 600 mg. This recirculation of bile acid is thus crucial to normal absorption of fat.

Now let us apply these principles to a patient who has had an ileal resection. There are two groups of such patients one will have to deal with, first, those who have had “short ileal resection,” and second, those who have had “long ileal resection.” Let us look at the short ileal resection group.

Loss of ileal absorptive surface results in decreased absorption of bile acids from the terminal ileum. There will thus be a decreased amount returning to the liver. The liver, via a biofeedback mechanism, detects the reduced enterohepatic circulation and increases its synthesis. The amount of bile salt entering the jejunum is thus maintained at a normal level. Effective micellar solubilization of fat continues, and one has normal absorption of fat. Therefore, although the patient with a “short" ileal resection will lose more bile acids than normal into the colon, the liver will make up for that loss. The unabsorbed bile acids enter the colon. It has been well demonstrated by Phillips and others that in the colon bile acids block the absorption of sodium, and thus the absorption of water. This leads to a net secretion of water by the colon, producing watery diarrhea. Therefore, the effect of a short ileal resection is bile acid-induced stimulation of watery diarrhea. The pruritus ani that also occurs is due to the excess bile acids trapped in the skin area of the mucocutaneous anal junction. This is the syndrome of cholerheic enteropathy-pruritus ani with watery diarrhea, without steatorrhea, following ileal resection.

The “long ileal resection” patient undergoes more serious pathophysiologic changes. The liver of the long-resection patient is unable to compensate for the severe loss of bile salts. Here we have again decreased bile-acid absorption from the ileum. The hepatic synthesis increases maximally but is unable to keep up with the loss, resulting in a decrease in the bile salt concentration in the jejunum. When this concentration falls below the CMC, malabsorption of fat and