DISORDERS OF FAT ABSORPTION

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Increased understanding of the basic physiological principles involved in the digestion and absorption of fat has greatly facilitated understanding and management of the various "malabsorption" states that occur in clinical medicine.

The major portion of ingested fat is in the form of triglycerides, which consist of glycerol combined in low energy ester linkages with three fatty acids. They are insoluble in water and extensive emulsification and hydrolysis must occur before absorption is possible.

In the presence of bile salts, the churning movements of the intestine produce a coarse, turbid and unstable emulsion which is attacked by water-soluble pancreatic lipase, resulting in hydrolysis of the triglycerides to glycerol, free fatty acids and monoglycerides. The lipase only acts in an alkaline pH which is readily provided during digestion, by the simultaneous secretion of bicarbonate from the pancreas.

The end products of pancreatic digestion are now prepared for absorption by the formation of a micelle, which is a physicochemical state produced by the admixture of conjugated bile salts, free fatty acids and monoglycerides. The resulting solution is optically clear, stable and has a particle diameter of less than 200 A. This greatly increases the surface diameter of this mass, and thus facilitates the absorptive process. The bile salts are not absorbed with fat in the proximal small bowel but are released from the micelle complex, absorbed from the terminal ileum and returned via the mesenteric blood to the liver for re-excretion into the duodenum.

The exact **mechanism** of fat absorption is unknown. Pinocytosis, the process of "phagocytosis" of fat by the mucosal cell does not adequately explain the ability of the intestine to selectively absorb hundreds of grams of fat daily. The alternative explanation of active transport of fat is more widely accepted. Fat is actively absorbed in the form of free fatty acids and monoglycerides, the energy for this reaction being supplied by adenosine triphospate produced by intracellular glycolysis or oxidative phosphorylation. Inside the intestinal mucosal cell, fatty acids are converted to fatty acyl Co A and then reesterified to triglyceride. The latter then obtains a phospholipid-protein coating and is delivered into the mesenteric lacteals as fat droplets or chylomicrons $\frac{1}{2}$ - 1 micron in diameter. The chylomicrons are then transported to the vascular system by way of the thoracic duct. (Table I)

Absorption of glycerol and short chain fatty acids of less than 10 carbon atoms is quite different from the above mechanism. They are transported across the mucosal cell without reesterification and appear in the mesenteric capillary blood in loose association with albumin. They are then transported directly to the liver by the portal venous system. This difference in the mode of transportation of fatty acids of varying chain length is of more than academic interest, because the malabsorption of long chain fatty acids produced by obstruction of the mesenteric lymphatics can be corrected by the administration of a diet which contains short chain fatty acids which are transported via the portal venous system. (Table II)

Having received the basic concepts of fat absorption we are now in a position to appreciate the disordered function that occurs in the various malabsorption states.

Clinical malabsorption is present when greater than 7% of dietary fat is excreted in the stool. There are numerous causes of malabsorption, but for practical purposes

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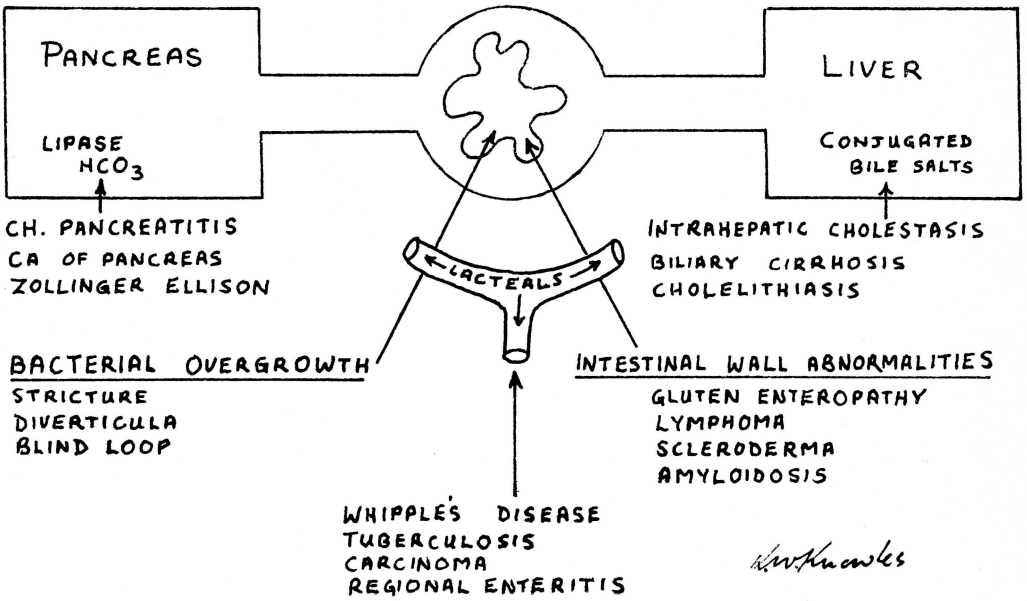

TABLE I

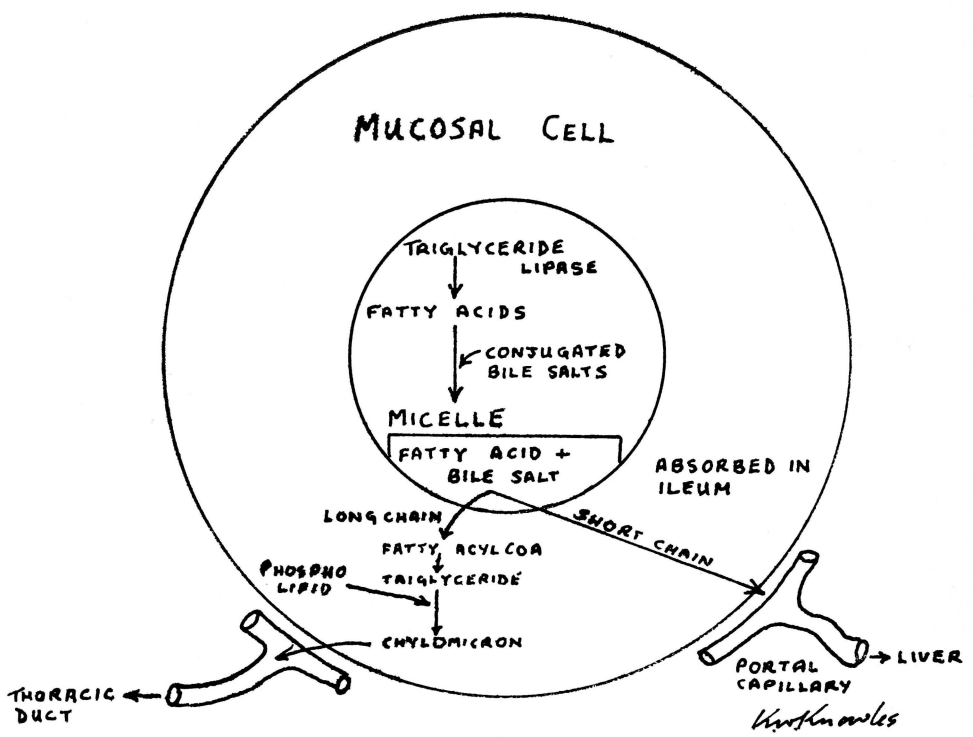

TABLE II

they can be divided into four general catagories: 1) Pancreatic Disfunction
2) Liver and Biliary Tract Disease
3) Disorders Within the Lumen or Intestinal Wall
4) Disease of the Mesenteric Lymphatics.

(1) PANCREATIC DISEASE:

Obstruction in the pancreatic duct or destruction of the pancreas by chronic pancreatitis or carcinoma will result in lipase deficiency and defective digestion of triglycerides. Diabetes and pancreatic calcification will suggest pancreatic disease but a firm diagnosis rests on the demonstration of a decreased concentration of bicarbonate in the intestinal juice following secretin stimulation. Pancreatic adenomas causing the Zollinger-Ellison syndrome are associated with malabsorption of fat because the excessive secretion of hydrochloric acid results in an acid duodenal pH which inactivates pancreatic lipase. A history of multiple refractory gastric ulcerations associated with electrolyte disturbances (hypokalemia) should raise the possibility of this condition. The demonstration of an excessive basal secretion of hydrochloric acid confirms the diagnosis.

(2) LIVER AND BILIARY TRACT DISEASE:

Intra-hepatic cholestasis, biliary cirrhosis and stone formation in the common bile duct will result in a diminished secretion into the duodenum of conjugated bile salts which are required for micelle formation and activation of pancreatic lipase. Such cases of malabsorption present no problem in diagnosis because they are invariably associated with clinical jaundice.

(3) DEFECTS WITHIN THE INTESTINAL TRACT:

Abnormal anatomical arrangements occurring as the result of partial gastrectomy, by-pass or extensive resection, cause malabsorption through a loss of absorptive surface, rapid intestinal transit and inefficient mixing of fat with pancreatic lipase and bile salts.

More difficult to explain is the steatorrhea which occurs with partial obstruction, diverticula or blind loops in the small bowel. Bacterial overgrowth, and the conversion of conjugated to unconjugated bile salts by bacteria is the most attractive explanation, for it has been demonstrated that unconjugated bile salts will inhibit the uptake of fatty acid by the intestinal mucosal cell. Treatment may be the surgical correction of obstruction and blind loops or the prolonged administration of appropriate antibiotics.

Intestinal malabsorption can also occur without an anatomical abnormality of the small bowel. The defect may be a loss of intestinal villi as the result of gluten enteropathy or an actual infiltration of the intestinal wall in such systemic disorders as lymphoma, amyloidosis or scleroderma. It is especially important to recognize the presence of gluten enteropathy for it is known that the toxic property of wheat in susceptible individuals is due to peptides containing proline and glutamine. The institution of a rigid free diet results in a clinical remission and a return of normal intestinal villi.

(4) OBSTRUCTION OF MESENTERIC LYMPHATICS:

Malabsorption will occur in the presence of a normal intestinal mucosa and adequate amounts of digestive enzymes if the draining lymphatics are blocked. Congenital defects, carcinoma, tuberculosis, reginal enteritis and Whipple's disease cause such an obstruction. The latter disease is diagnosed by the presence of P.A.S. positive particles and dilated lymphatics in per oral intestinal biopsy material. Clinical remission in this disease can be obtained with prolonged tetracycline therapy. It is also important to remember in this group of diseases that symptomatic improvement of the steatorrhea will occur, with the institution of a diet containing short chain fatty acids which are transported via the portal blood rather than the lymphatic system.

It is beneficial at this point to review and evaluate the more common diagnostic procedures used in the investigation of the malabsorption syndrome.

Malabsorption of fat is suggested by the gross appearance of the stool **and the** microscopic demonstration of fat droplets using a sudan III stain. However, definitive diagnosis requires a quantitative chemical determination of a 72 hour stool collection. If excretion is greater than 7% of ingested fat, steatorrhea is present. Radiological

examination of the upper gastrointestinal tract should be performed in all cases. The demonstration of flocculation of barium in the small bowel is present in most cases and special attention should be directed toward the detection of duodenal loop abnormalities and pancreatic calcification.

I^{131} labeled triolein and oleic acid have been used in the differentiation of pancreatic from primary intestinal lesions. It was suggested that, whereas triglycerides; (I^{131} triolein) were absorbed poorly, fatty acids (I^{131} oleic acid) might be absorbed normally by patients with pancreatic disease. The failure to obtain a chemically pure form of I^{131} triolein has decreased the validity of this test.

Similarly the decreased absorption of radioisotopes of vitamin B 12 was thought to be specific for primary intestinal lesions, especially those involving the ileum. However, more recent evidence indicates there is also deficient absorption of vitamin B 12 in pancreatic insufficiency which returns to normal with the administration of pancreatic extract and bicarbonate.

Glucose tolerance tests are frequently used in diagnosis. A diabetic curve occurs in pancreatic disease and a flat curve in primary intestinal malabsorption. The absorption of D-xylose is abnormal in gut lesions and frequently normal in pancreatic disease. However, results are not reliable in the presence of thyroid, liver and renal disease.

The increased urinary excretion of 5-hydroxyindolacetic acid which occurs in gluten enteropathy and Whipple's disease is of limited diagnostic importance, but, nevertheless, is of interest because of the implication that a disorder of serotonin metabolism occurs in some malabsorption states.

The most valuable procedures in the investigation of the malabsorption syndrome are the secretin stimulation test and a per oral small bowel biopsy. The demonstration of a decreased concentration of bicarbonate in the duodenum following secretin stimulation, establishes the presence of pancreatic insufficiency.

A small bowel biopsy with blunting and atrophy of the intestinal villi is characteristic of gluten enteropathy and the presence of granulomas suggests regional enteritis. Special staining procedures are required to demonstrate amyloidosis or Whipple's Disease.

This has been a review of the normal and altered physiology of fat absorption. A clear understanding of physiological principles and the application of suitable laboratory techniques will often enable one to make an exact etiological diagnosis and institute specific therapy.