

Bile salts and fat absorption

There has been a recent resurgence of interest in bile salt metabolism. Normally the body contains about 3 g. of bile salts. These comprise conjugates of cholic acid and chenodesoxycholic acid. The free acids are derived from the oxidation of cholesterol in the liver and once formed are conjugated with either taurine or glycine, after which they are secreted into the bile and so enter the small bowel.¹ They pass down the gut and are mainly reabsorbed by the ileum. This early observation² has recently been confirmed³ and an active transport system confined to the ileum has been demonstrated.⁴ This is teleologically satisfactory for it allows a high concentration of bile salts to be maintained in the lumen of the jejunum and yet prevents too great a loss of the total bile salt pool from the body; normally this is 0.8 g. a day¹. Once passed the ileocaecal valve the conjugated salts are both deconjugated and degraded. Many metabolites are formed, one of which is desoxycholic acid. Some of these are partially absorbed from the caecum, pass up the portal vein, are then conjugated and excreted in the bile. Thus, in man conjugates of desoxycholic acid represent previous bacterial degradation of cholic acid.¹

Various functions have been attributed to bile salts. They are extremely active surface agents and they probably facilitate emulsification of the long-chain fatty acid triglycerides and so aid the action of pancreatic lipase, which to be effective has to work on an emulsion at an oil/water interface,⁵ but their precise effect on pancreatic lipolysis is still open to question. Even so, it is doubtful if impaired digestion of triglyceride as the rate-limiting step in fat absorption in the absence of bile, for under these circumstances triglycerides are absorbed as fast as free fatty acids.^{6, 7}

Another property is to disperse fat into a water-soluble form.⁸ Verzár⁹ showed that oleic acid dissolved in a bile salt solution could pass through a membrane and suggested that bile might pass through the mucosa in this form. This property has been studied and its relation to fat absorption explored by Hofman and Borgström using techniques developed by detergent chemists.^{10, 11, 12} Bile salts after reaching a critical concentration form aggregates rather than precipitate out of solution and so they behave like long-chain paraffin soaps. The micro aggregates of detergents are called micelles and may entrap lipid soluble compounds. The concentration at which this aggregation occurs is called the critical micellar concentration and is normally exceeded in the small bowel lumen. Hofman and Borgström have shown that intestinal contents subjected to high speed centrifugation separate into an upper creamy layer and lower water clear phase and that this water clear solution is rich in fat, comprising mainly fatty acid and monoglyceride.¹¹ It may be shown *in vitro* that these two compounds are the most soluble in micellar solutions as compared with triglyceride and diglyceride.

The idea that bile salts may stimulate the mucosal phase of fat absorption⁹ has been revived.^{7, 13} It has been suggested that bile salts may stimulate the esterification of absorbed fatty acids,^{13, 14, 15} and also that in the absence of bile a large proportion of long chain fatty acids once absorbed pass into the systemic circulation via the portal vein rather than via the lymph. One problem of accepting a possible mucosal role of bile salts is that bile salts are not absorbed by the jejunum. However, some observations have suggested that, although there is little net transport of bile salts from the jejunal lumen into the extracellular fluid, bile salts can shuttle back and forth between the lumen and the jejunal cell.¹⁶

What of the effect of bile salt deficiency? As previously stated, it is of interest that fatty acid absorption is depressed to the same extent as that of triglyceride but even so up to 50% of fat can be absorbed in the absence of bile. On the other hand, other lipid-soluble substances, such as cholesterol, vitamin D, vitamin K, and carotene, are nearly completely dependent on the action of bile to facilitate their absorption.^{17, 18, 19} It seems probable therefore that micellar dispersion of steroids is

obligatory for their absorption while, although the absorption of digestion products of triglycerides is facilitated, it is not obligatory. This may explain the impaired absorption of vitamins D and K in obstructive jaundice which is often quite out of proportion to the degree of steatorrhoea, whereas in pancreatic disease, although steatorrhoea may be gross, osteomalacia and a bleeding tendency are extremely rare. It should be noted that intraluminal bile salt deficiency may occur not only in biliary obstruction and with biliary fistulae but also after excision of the ileum and caecum.²⁰

A disorder in bile salt function has been suggested as an explanation of the mechanism of malabsorption in the blind loop syndrome. In this condition the small bowel, normally sterile, is invaded by colonic bacteria. These are known to split conjugated bile salts and also form desoxycholate.¹ Free desoxycholate has been demonstrated in the luminal fluid of such patients^{21, 22, 23} and experimental animals with a stagnant loop and might theoretically inhibit fat absorption in two ways. The first is by desoxycholate inhibiting the small bowel mucosa's ability to esterify long-chain fatty acid *in vitro*.^{13, 21} It should be pointed out, however, that feeding desoxycholate has not produced steatorrhoea in rats and, indeed, there is no evidence that *in vivo* mucosal glyceride biosynthesis is depressed; in fact, it possibly stimulates that of the bile fistula rat.²⁴ The other alternative is that desoxycholate is very poor at forming micelles. Indeed, in dogs with an experimental blind loop syndrome the proportion of the luminal lipid in the micellar phase was much smaller than in control dogs, while the steatorrhoea in these dogs was overcome by feeding taurocholate.²² It should be pointed out that neither of these suggestions has been proven and certainly at the moment the disordered bile salt metabolism does not explain the disturbance in absorption of other nutrients, especially B₁₂.

One further word of caution: there will no doubt be a large number of investigations published on the micellar phase in the intestinal contents of man. It should be pointed out that this will only give an estimate of the steady state that may be obtained rather than give an estimate of what actually is happening, for pancreatic lipolysis is an explosive process and one may well expect extensive hydrolysis to take place during aspiration of intestinal contents and during the centrifugation to form a separated micellar phase.

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