UDCA + CDCA (both of which decrease the molar ratio of cholest erol in bile) increased from 41% before, to 50% and to 72% after 5 and 10 mg of UDCA day−1 kg−1 body weight respectively. There were concomitant decreases in the proportions of both cholic acid and its bacterial metabolite, deoxycholic acid but the proportion of lithocholate increased from 4-5% before to 9-0% during therapy. There were no changes in liver function or fasting serum lipids during treatment and no patient developed diarrhoea.

These results (i) show that treatment of non-obese gallstone patients with only 5 mg of UDCA day−1 kg−1 body weight consistently produces unsaturated bile and, (ii) confirm that, in the short term, UDCA causes neither diarrhoea nor hypertransaminasemia. UDCA continues to offer a promising alternative to CDCA for the medical treatment of gallstones.

109. JEJUNAL BACTERIAL OVERGROWTH WITH ABNORMAL INTESTINAL DECONJUGATION OF BILE SALTS AND INDICANURIA AFTER JEJUNO-ILEAL BYPASS SURGERY FOR OBESITY


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Hepatic steatosis and liver failure are the most serious complications reported after jejuno-ileal bypass. We could not relate adverse changes in liver function following intestinal bypass to halothane anesthesia, degree of weight loss after surgery, or hepatitis B infection (Maxwell et al., 1977, British Medical Journal, II, 726).

Intestinal bacteria may contribute to the pathogenesis of these complications, but experimental data are inconclusive. We have quantified proximal jejunal flora, and investigated intestinal bacterial metabolism of bile salts and tryptophan.

Elevated counts of both aerobic and anaerobic bacteria were obtained following culture in 11 of 13 patients, but deconjugated bile acids demonstrated in only two of them. However in the 10 patients studied with the [14C]glycocholate breath test, all showed enhanced bile acid deconjugation. Urinary indican excretion was significantly higher in a group of 15 bypass patients (766 ± 80/24 h) than in controls (127 ± 80/24 h; P < 0.001).

Abnormal bacterial colonization occurs in the proximal small bowel following bypass. However, as significant bile acid deconjugation is infrequent at this site, the abnormal intestinal bacterial metabolism demonstrated probably occurs more distally.

These results provide an explanation for the cholaemia noted by Sherr et al. (1974, American Journal of Clinical Nutrition, 27, 1369) after intestinal bypass. Abnormal intestinal bacterial metabolism of dietary constituents and bile acids may contribute to hepatic dysfunction after bypass surgery.

110. THE EFFECT OF LACTULOSE ON AMMONIA PRODUCTION IN A FAECAL INCUBATION SYSTEM

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Porto-systemic encephalopathy (PSE) is thought to be caused by raised blood levels of toxic bacterial metabolites, particularly ammonia, absorbed from the colon. Oral lactulose has been used in treatment of PSE, but its mode of action is uncertain, and none of the theories put forward (change in colonic flora, trapping ammonia in the colon by acidification of colonic contents, or reduced ammonia absorption as a result of osmotic catharsis) have been fully satisfactory.

The effect of lactulose has been examined in an in vitro faecal incubation system which normally generates large amounts of ammonia from nitrogen sources (Vince, Down, Murison, Twigg & Wrong, 1976, Clinical Science and Molecular Medicine, 51, 313). We have studied the separate effects of (1) lactulose and other fermentable substrate, (2) fall in pH, and (3) acetate and lactate, the normal metabolic products of lactulose fermentation.

Addition of lactulose, glucose, sorbitol, mannitol and tartrate to the incubation system caused a fall in ammonia concentration, e.g. 30 mmol/l lactulose reduced ammonia from 6-9 to 2-7 mmol/l in 3 h, whereas controls rose to 10-9 mmol/l. This decrease was independent of pH fall and was due to bacterial assimilation of ammonia. Reduction in pH to less than 5.0 reduced ammonia formation, but unlike substrate fermentation did not lower the existing ammonia concentration. Acetate and lactate did not reduce ammonia formation.

If it recurred in vivo, the lowering of ammonia concentration caused by fermentable substrate may be beneficial in PSE. The results explain the failure of others to observe an increase in faecal ammonia in subjects taking lactulose.

111. DOUBLE-ISOTOPE MEASUREMENTS IN ASSESSING EARLY AND LATE CHANGES IN VITAMIN B12 ABSORPTION DURING ANTIBIOTIC THERAPY IN TROPICAL MALABSORPTION

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Impaired absorption of vitamin B12 occurs in patients with non-parasitic tropical malabsorption developing in the Middle and Far East (Tomkins, James & Walters & Cole, 1974, British Medical Journal, III, 380). The infective agent responsible for the mucosal lesion has not been precisely identified but overgrowth by enterobacteria within the upper small intestine may be important as previous studies, using the Schilling test, showed improvement in vitamin B12 absorption only in patients who were cleared of jejunal enterobacteria (Tomkins, James & Drasar, 1975, Lancet, I, 59). However, morphological lesions of the ileum also occur making it difficult to differentiate the effect of mucosal atrophy from that of bacterial metabolism in the genesis of vitamin B12 malabsorption.

The CRC whole-body counter was used to measure vitamin B12 absorption. In 18 patients with tropical malabsorption there was a significant relationship between vitamin B12 absorption and xylose excretion (r = 0.49, P < 0.05). In nine patients with steatorrhoea, vitamin B12 absorption 21.7 ± 14.9 (SD) % of dose was significantly less than in control subjects (62.8 ± 10.16%) (P < 0.001). In nine patients without steatorrhoea, vitamin B12 malabsorption was less marked (40.5 ± 11.2%) but still significantly different from control values (P < 0.001).

Sequential absorption measurements were made using 33Co- and 34Co-labelled vitamin B12 administered before and 48 h after the start of tetracycline therapy. A significant early increase (on average 21.6% of dose) occurred in five out of seven patients with steatorrhoea. There was further improvement in five out of six patients followed after 4 weeks of tetracycline, including the two patients who failed to respond initially. The early changes after antibiotics are unlikely to be due to epithelial cell regeneration and probably indicate that bacterial metabolism is an important factor in the vitamin B12 malabsorption of these patients.

112. THE KINETICS OF ELIMINATION OF A SODIUM L-LACTATE LOAD IN MAN: THE EFFECT OF LIVER DISEASE