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Gall stones in Crohn's disease: another hypothesis

EDITOR,—We read with interest the paper by Hutchinson *et al* (*Gut* 1994; 35: 94-7) suggesting that in Crohn's disease postoperative gall bladder hypomotility may be the main risk factor for the development of gall stones.

There are indeed several lines of evidence showing that decreased postprandial gall bladder motility participates in gall stone formation.¹ Recent data, however, show that filling and emptying of the gall bladder are complex processes. The gall bladder cyclically contracts during fasting to up to 40% of its maximal volume, just before the occurrence of phase III of the migrating motor complex (MMC) in the antroduodenal area.^{2,3} The mechanism of these cyclic contractions is not clear. Serum motilin peaks just before phase III of the MMC in the antroduodenal area.⁴ Moreover, exogenous motilin, producing premature MMCs in the gut, causes an increase in gall bladder motility similar to that seen during spontaneous gall bladder cyclic activity in dogs.^{3,5} It has therefore been suggested that the increment in plasma motilin concentrations may be responsible for the gall bladder contractions.⁵

We have recently studied 25 patients with uncomplicated, inactive Crohn's disease (mean Crohn's disease activity index 60.7). Gastrointestinal motility was studied during fasting (5 hours) and after a meal (1 hour) by standard perfusional manometry.⁶ Data obtained were compared with those of 33 healthy controls. The incidence of phase III of MMC was considerably reduced. In 13 of 25 patients phase III was absent (v 0 of 33 of healthy controls $p < 0.001$). In the other patients phase III was less frequent (one of 140 minutes v one of 99 minutes, $p < 0.05$), shorter in duration (4.6 (1) minutes v 6.9 (1), $p < 0.05$), and rarely starting from the stomach (four of 25 v 18 of 33, $p < 0.01$). Mean motilin values were in the normal range, but lacked a clear peaking during phase III of the MMC.

The high prevalence of gall stones in Crohn's disease is well established. The accepted mechanism of disturbed enterohepatic circulation of bile salts in these patients could perhaps be enhanced if a change in gall bladder motility also occurs. Hutchinson *et al* suggest that gall bladder sludge may occur because of prolonged fasting or parenteral nutrition in the post-operative period. They found a higher incidence of gall stones in patients with previous laparotomy compared with patients who had not had any abdominal surgery (32% v 13%, $p < 0.005$). They did not take into account, however, that the age of the patients, duration of the disease, and number of operations are dependent variables. The incidence of gall stones increases with age in Crohn's disease patients; but the incidence of surgery also increases in these patients with the duration of the disease.

We hypothesise that in some patients with Crohn's disease a reduction of cyclic phasic contractions of gall bladder occurs because of a decreased incidence of phases III of the

MMC in the antroduodenal area. The lack of periodic stirring and agitation of gall bladder bile may lead to supersaturation of bile and increase propensity for precipitation of salts and formation of gall stones in these patients.⁷

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Reply

Annese and Vantrappen state that the incidence of gall stones increases with age and duration of Crohn's disease. Our paper supports these statements (*Gut* 1994; 35: 94-7). The multivariate analysis of our data, however, showed that previous laparotomy also predisposed to gall stones, and that this was an important risk factor independent of age and duration of disease. Furthermore, the prevalence of gall stones was positively correlated with the number of previous operations. We found that the site of disease or intestinal resection did not seem to influence the risk of gall stones. These findings called into question the accepted explanation that changes in the enterohepatic circulation of bile salts predispose to gall stones in patients with Crohn's disease. Rather, we postulated that laparotomy may predispose to gall stones by inducing gall bladder hypomotility, and that the risk of gall stone formation increases with number of operations.

We did not study the mechanism of this phenomenon in our epidemiological study, but the interesting findings by Annese and Vantrappen on the migrating motor complex and motilin concentrations in patients with Crohn's disease may provide clues to the mechanism of gall bladder hypomotility in Crohn's disease.

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Value of granulocyte scintigraphy in inflammatory bowel disease

EDITOR,—We read with great interest the article by Sciarretta *et al* (*Gut* 1993; 34: 1364-9) on the value of technetium-99m

labelled granulocyte scintigraphy in Crohn's disease. Although we agree that technetium labelled granulocyte scintigraphy is of great value in the assessment of inflammatory activity in patients with inflammatory bowel disease (IBD), in providing information on the localisation, the extent, and the severity of the inflammation, we have some reservation concerning certain aspects of this study. The differentiation between ileal and ascending colon localisation is difficult. In a prospective study,¹ granulocyte scintigraphy was compared with operative and endoscopic findings. This study shows the unsuccessful anatomical differentiation with granulocyte scintigraphy in five of eight patients with a hot spot in the right lower abdomen. Therefore, we are curious to discover the criteria of the authors to differentiate between both of the localisations when there is a hot spot in the right lower abdomen.

We are surprised by the finding of a 100% sensitivity and specificity in the detection of intestinal fistula and abscesses. To our knowledge, this is the first study to claim a 100% accuracy with these diagnoses. From Figs 1 and 2 in the article, we cannot distinguish abscess or fistula from simple skipped lesions, which are quite common in Crohn's disease. Which criteria have the authors used in differentiating between skipped lesions and fistula? From the article it is not clear how many patients received the 24 hour scintigram, which was their main criterion for diagnosing an abscess. With which techniques have the abscesses and fistulas been subsequently confirmed? Is it possible that the choice of techniques, or procedures to confirm the diagnoses, have influenced the 100% specificity finding? Furthermore, because not all of the patients have been checked for fistulas and abscesses (only those with evidence on granulocyte scintigraphy) the sensitivity might be lower than the 100% mentioned in the article. In our prospective, blinded study,¹ the detection of abscesses and fistula with granulocyte scintigraphy was disappointing. The sensitivity and specificity for abscesses was 60% and 78%, and for fistulas 40% and 78%, respectively. For detection of fistulas and abscesses in the acute phase, computed tomography was more accurate in this and other studies.¹⁻⁴ Although the study by Sciarretta *et al* has confirmed the value of ^{99m}Tc-HMPAO granulocyte scintigraphy in assessment of activity and extent of IBD, the diagnostic accuracy of granulocyte scintigraphy might be less accurate than suggested. Therefore, despite the finding of Sciarretta *et al*, we would advise clinicians who see a patient with suspected abscess or fistula, to perform computed tomography before starting corticosteroid treatment.

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