been interpreted as indicating that unknown intraluminal or mucus layer factor(s) might interfere with the antibacterial action. A recent report posits the possibility of antimicrobial resistance consequent on previous suboptimal exposure, which emphasizes the need for an effective treatment regimen with a lower relapse rate.

Administration of bismuth subsalicylate (BSS) results in a high rate of _H. pylori_ eradication (75% eradication after four weeks), comparable to that of bismuth substrate (CBS). As the subsalicylate salt is insoluble in the stomach and peak plasma concentration does not occur until 1–2 hours after ingestion, absorption must occur in the duodenum or jejunum. In contrast, CBS is a soluble salt and is rapidly absorbed from the stomach, and the peak plasma bismuth concentrations occur 0.25 to 0.5 hour after the dose. The significant eradication of _H. pylori_ by BSS tends to suggest that the anti-_H. pylori_ effects are due to absorption of bismuth from the duodenum and subsequent exposure by way of systemic delivery. This is logically consistent with histological evidence which indicates that _H. pylori_ inhabits the deeper part of the gastric mucosal film and thus insinuates itself between the epithelial cells, sequestering themselves from gastric juice by sitting deep to the mucus layer. This intimate adherence of the bacteria to the gastric epithelial cells and its histological implications for disease progression has been shown in a recent study. Systemic delivery only requires good contact with gastric secretion or intraluminal fluid or diffusion into the gastroduodenal lumen. As such, this hypothesis is that antimicrobial treatment should be given systematically to yield improved results (Figure). Currently effective treatments (amoxicillin, erythromycin, tetracycline, or metronidazole) might be given intravenously initially for several days before continuing with oral treatment. CBS can be given orally since a high initial postabsorptive plasma peak occurs particularly with the tablets, indicating rapid absorption. The gastric site is the site of necessity, contact with _H. pylori_. Enterohelical circulation of bismuth could be of benefit as it would effectively prolong the exposure time of the bacteria to the agents in the circulation. We believe that the belief of luminal gastric drug delivery systemic delivery is of critical importance for drug formulation and overall treatment strategy.

**Letters**

**Diabetes and cholelithiasis**

_SIR,-_ We read with interest the study by Laasko _et al._ on serum lipids and lipoprotein in patients with diabetes and with gallstone disease. The association between diabetes and cholelithiasis has been described also in the Italian population, but the role of this association is not yet clarified. It is generally held that patients with diabetes secrete a more lithogenic bile than non-diabetics. In the few studies that have compared diabetics with age, sex, and weight matched controls were performed. For the insulin dependent diabetics or the insulin independent diabetics had a bile cholesterol saturation index higher than that of control subjects. Therefore, the secretion of a lithogenic bile by diabetics does not satisfactorily explain the observed frequency of gall stones in the diabetic population.

In one of our previous reports on 120 patients affected by type II diabetes we too observed that in diabetes with gall bladder disease fasting plasma insulin concentrations and daily average plasma insulin concentrations were appreciably higher than in diabetics without gall bladder disease. But we failed to show any differences in serum total and high density lipoprotein cholesterol, triglycerides, glycated haemoglobin HbA1c, body mass index, and duration of diabetes between patients with gall stones and those without gall stones. In our study, in insulin dependent diabetics, increased plasma insulin concentrations seemed to be associated with an increased risk of gall stones regardless of plasma triglycerides, plasma cholesterol, and obesity.

We believe that it is necessary to take into account the effects of diet and, above all, prolonged use of oral hypoglycaemic agents which might bias the interpretation of plasma lipid pattern and the level of insulinemia. Furthermore, it is likely that the patient's awareness of his gall stone condition (particularly if it is symptomatic) may cause pronounced changes in eating habits. In our study, in fact, all the patients were treated with oral hypoglycaemic agents in addition to a restricted diet.

Because cholesterol gall stones are generally thought to be the result of an altered lipid metabolism, information about the role of blood lipids in gall stone disease may provide indirect clues about the changes in lipid metabolism that are associated with their formation. But considerable controversy exists about the relationship between plasma lipid and bile composition. Moreover, it is now generally recognized that a simple concept of lithogenic bile is inadequate to account for cholesterol gall stone development.

We agree with Laasko _et al._ that changes in plasma insulin and serum lipid concentrations do not account for increased prevalence of gall stone disease in non-insulin diabetes. Abnormal gall bladder motility may play an important part in the pathogenesis of gall stone disease in these patients. Recently, impaired emptying of the gall bladder in diabetics was shown and the presence of an autonomic neuropathy seems to be a risk factor for such an impairment.

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Diabetes and cholelithiasis.

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*Gut* 1990 31: 1422-1423
doi: 10.1136/gut.31.12.1422

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