been interpreted as indicating that unknown intraluminal or mucus layer factor(s) might interfere with bacterial colonization. A recent report raises 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 substitute (CBS). As the bismuthic 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 very 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 CBS 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 inhabit the deeper part of the gastric mucosa and sequester themselves between the epithelial cells and sequestering themselves from gastric juice by sitting deep in the mucus layer. This intimate adherence of the bacteria to the gastric epithelial cells and its histological implications for disease production has been shown in a recent study. Systemic delivery only requires good contact with gastric secretion or intestinal fluid or diffusion into the gastro-intestinal lumen.

A potential weakness of this hypothesis is that antimicrobial therapy 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 of the gastric salt. It is of necessity, contact with H. pylori. Enterohelment of bacterial secretion of bismuth could be of benefit as it would effectively prolong the exposure time of the bacteria to the circulating drug. We believe this belief of luminal gastric drug delivery v systemic delivery of 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 gall stones and patients with gall stone disease. The association between diabetes and cholelithiasis has been defined also in the Italian population, but for this association it has not yet been 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 with the respective matched controls, the difference in lithogenicity was clearly seen. 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 an increased incidence of 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 non-insulin dependent diabetics nor 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.

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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 lipoprotein compositions. Moreover, it is now generally recognized that a simple concept of lithogenic bile is inadequate to account for cholesterol gall stone disease development.

We relate 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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Reply

Sir,—Pazzi et al have shown an association between high insulin concentration and cholesterol cholelithiasis in non-insulin dependent diabetics similar to what we have reported. In our study we also found a significant positive correlation between insulin concentration and very low density lipoprotein triglyceride concentration and a negative correlation between insulin concentration and high density lipoprotein cholesterol concentration. Pazzi et al did not find any association between lipid and lipoprotein concentrations and gall stone disease. They proposed that the effects of diet and oral hypoglycaemic agents could explain the association of a high insulin concentration and gall stone disease. While we have presented similar explanations for this association, we have also proposed that a high insulin concentration in patients with gall stone disease is related to insulin resistance. Indeed, our preliminary unpublished data show that...