oesophageal pH monitoring data. *Eur J Pediatr* 1990; 149: 598-602.

- 9 Vandenplas Y, Lepoudre R, Helven R. Dependability of esophageal pH monitoring data in infants on cut-off limits: the oscillatory index. *J Pediatr Gastroenterol Nutr* (in press).

Elimination of high titre HIV from fibreoptic endoscopes

SIR,—I would like to congratulate Dr Hanson and his colleagues on their encouraging paper concerning the elimination of high titre HIV from fibreoptic endoscopes.¹ It confirms that thorough cleaning and removal of all organic material is the most important step in the decontamination process and necessary for disinfectants to be fully effective.² Unfortunately, the last sentence of Dr Hanson's excellent article, which advocates the use of machines to ensure good cleaning, may be misunderstood in three ways:

- (1) That trained and experienced endoscopy staff need not be employed or existing staff can be replaced by a machine;
- (2) That equipment does not need manual cleaning before being put into automated systems;
- (3) That even in the absence of predisinfection manual cleaning, equipment has been decontaminated effectively because it has been put through an automated 'cleaning' and disinfection cycle.

There are at present no automated disinfection machines available which can replace manual cleaning with brushes before disinfection.² Trained and experienced staff are required² because endoscopes and their accessories need to be dismantled according to manufacturers' instructions so that all contaminated areas can be cleaned and disinfected appropriately. In inexperienced hands contaminated instruments may be left to be cleaned at a more convenient time, allowing organic material to dry in the channels. Disinfection machines, which are often claimed to be effective cleaners, cannot carry out proper disinfection unless equipment has been cleaned manually beforehand and all organic material has been removed. The presence of any organic material will prevent adequate penetration of disinfectants.² This has been shown in a case report where an endoscope, which was later found to be contaminated with *Salmonella typhimurium*, was put into an automated cleaning/disinfection machine without prior manual cleaning.³ Nine days after the presumed contamination, *S typhimurium* could still be recovered from the endoscope despite it having gone through several automated cleaning/disinfection cycles during that time. Another efficacy failure of an automated machine has been reported from the United States, where, after adopting an automated method of cleaning endoscopes, a hospital noted a dramatic increase in the prevalence of bile cultures positive for *Pseudomonas aeruginosa*.⁴ They traced the organism to a single endoscope contaminated with *P aeruginosa*. Although the instrument had been cleaned and disinfected repeatedly with an automated system, several channels were not adequately cleaned or dried by the washer/disinfector.

Despite rejecting the use of automated cleaning/disinfection machines without prior manual cleaning I do advocate their appropriate use for consistent disinfection. Moreover, they reduce staff contact exposure to glutaraldehyde liquid and to vapour during the disinfection cycles, though they may increase vapour exposure during the filling and emptying of machines

(J R Babb, personal communication). Automated machines are complementary to manual cleaning and to trained and experienced staff, but cannot replace them.

CHRISTIANE S NEUMANN
Gastroenterology Unit,
Dudley Road Hospital,
Birmingham B18 7QH

- 1 Hanson PJV, Gor D, Jeffries DJ, Collins JV. Elimination of high titre HIV from fibreoptic endoscopes. *Gut* 1990; 31: 657-9.
- 2 British Society of Gastroenterology. Cleaning and disinfection of equipment for gastrointestinal flexible endoscopy: interim recommendations of a Working Party. *Gut* 1988; 29: 1134-51.
- 3 Hawkey PM, Davies AJ, Viant AC, et al. Contamination of endoscopes by *Salmonella* species. *J Hosp Infect* 1981; 2: 373-6.
- 4 Allen JJ, O'Connor-Alten M, Olsen MM et al. *Pseudomonas* infection of the biliary system resulting from use of a contaminated endoscope. *Gastroenterology* 1987; 92: 759-63.

Reply

SIR,—We agree entirely with the points raised by Ms Neumann. It is only through misinterpretation of the last sentence of our paper that our views differ. Our intended emphasis was on the first part of the sentence that the large reductions in HIV achieved in our study were the result of manual cleaning. It has been suggested that endoscopes contaminated with

HIV must be cleaned in an automated machine and our findings do not support this view. I welcome Ms Neumann's reminder that there is no substitute for trained endoscopy personnel and that endoscopes must be precleaned before being placed in any of the currently available 'automatic' machines.

P J V HANSON
Guy's Hospital,
St Thomas Street,
London SE1

Systemic chemotherapy for *Helicobacter pylori* eradication?

SIR,—Recent studies indicate the involvement of *Helicobacter pylori* in several upper gastrointestinal disorders including antral type B gastritis, duodenal ulcers, and non-ulcer dyspepsia.¹⁻⁵ The approach to delivery of drug treatment for *H pylori* infection is currently based on the concept of therapeutic delivery from the gastric juice after drugs have been given orally. The aim of this is eradication. Ulcer relapse rate has been found to correlate with recurrence of infection.⁶ Success rates range from 33-100% for immediate eradication of *H pylori*, with many patients having a recurrence within one month of stopping treatment,⁷ often with the same bacteria.⁸ The fact that bacteria are sensitive in vitro but much less so in vivo to a number of antimicrobials has

Illustration of alternative concepts of delivery of xenobiotics to gastric *Helicobacter pylori*. (A) Presently accepted mechanism. (B) The alternative interpretation. (C) The rationale of intravenous treatment with antibiotics.

been interpreted as indicating that unknown intraluminal or mucus layer factor(s) might interfere with antimicrobial action. A recent report raises the possibility of antimicrobial resistance consequent on previous suboptimal exposure,⁹ which emphasises 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 subcitrate (CBS).¹⁰ 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 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.¹¹ 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* inhabit the deeper part of the gastric mucus film and often insinuate themselves between the epithelial cells¹² sequestering themselves from gastric juice by sitting deep to the mucus layer.¹ This intimate adherence of the bacteria to the gastric epithelial cells and its histopathological implications for disease production has been shown in a recent study.¹³ Systemic delivery only requires good contact with gastric secretion or interstitial fluid or diffusion into the gastroduodenal lumen.

A practical extension of this hypothesis is that antimicrobial treatment should be given systemically 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 at the gastric site^{11,14} hence, of necessity, contact with *H. pylori*. Enterohepatic circulation of bismuth^{15,16} could be of benefit as it would effectively prolong the exposure time of the bacteria to agents in the circulation.

We believe that this issue of luminal gastric drug delivery v systemic delivery is of critical importance for drug formulation and overall treatment strategy.

SHAMSUL ISLAM
ALLAN J McLEAN
Clinical Pharmacology Department,
Alfred Hospital,
Melbourne, Australia

- 1 Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* 1981; i: 1311–5.
- 2 Lambert JR, McLean AJ. Pathogenicity of *Campylobacter pylori* in the upper gastrointestinal tract – implications for modern therapy. *Med J Aust* 1989; 151: 120–2.
- 3 Peterson WL, Lee E, Skoglund M. The role of *Campylobacter pylori* in epidemic gastritis with hypochlorhydria. *Gastroenterology* 1987; 92: 1575.
- 4 Hazell WL, Hennessy WB, Borody TJ, et al. *Campylobacter pyloridis* gastritis II: distribution of bacteria and associated inflammation in the gastroduodenal environment. *Am J Gastroenterol* 1987; 82: 297–301.
- 5 McLean AJ, Harrison PM, Ioannides-Demos LL, Byrne AJ, McCarthy P, Dudley FJ. Microbes, peptic ulcer, and relapse rates with different drugs. *Lancet* 1984; ii: 525–6.
- 6 Marshall BJ, Warren JR, Blynco ED, et al. Prospective double-blind trial of duodenal ulcer relapse after eradication of *Campylobacter pylori*. *Lancet* 1988; ii: 1437–41.
- 7 Tytgat GNJ, Rauws EAJ, de Koster EH. *Campylobacter pylori*. Diagnosis and treatment. *J Clin Gastroenterol* 1989; 11 (suppl 1): 49–53.

- 8 Langenberg W, Rauws EAJ, Widjokusomo A, Tytgat GNJ, Zanen HC. Identification of *Campylobacter pylori* isolates by restriction endonuclease DNA analysis. *J Clin Microbiol* 1986; 24: 414–7.
- 9 Becc MCJM, Janssen AJHM, Clasener HAL, De Koning RW. Metronidazole-resistant *Helicobacter pylori*. *Lancet* 1990; 335: 539–40.
- 10 Eberhardt R, Kasper G. Effect of oral bismuth subsalicylate on *Campylobacter pylori* and on healing and relapse rate of peptic ulcer. *Rev Infect Dis* 1990; 12: S 115–9.
- 11 Froome PA, Wan AT, Keech AC, McNeil JJ, McLean AJ. Absorption and elimination of bismuth from oral doses of tripotassium dicitrate bismuthate. *Eur J Clin Pharm* 1989; 37: 533–6.
- 12 Petros CW, Applesran MD, Cohen H, Valenzuela JE, Chandrasoma P, Laine LE. Prevention of *Campylobacter pylori* and association with antral mucosal histology in subjects with and without upper gastrointestinal symptoms. *Dig Dis Sci* 1989; 33: 649–53.
- 13 Hessey SJ, Spencer J, Wyatt JJ, et al. Bacterial adhesion and disease activity in *Helicobacter* associated chronic gastritis. *Gut* 1990; 31: 134–8.
- 14 Nwokolo CU, Gavey CJ, Smith JTL, Pounder RE. The absorption of bismuth from oral doses of tripotassium dicitrate bismuthate. *Aliment Pharmacol Therap* 1989; 3: 29–39.
- 15 McLean AJ, Froome PRA, Wan AT. Biliary handling of bismuth subcitrate in man. *Clin Pharmacol Ther* 1989; 44: 150.
- 16 Islam S, Cheung T, McLean AJ. Factors modulating the absorption of colloidal bismuth subcitrate in the rat. *Clin Exp Pharmacol Physiol* 1990; Suppl 16.

Diabetes and cholelithiasis

SIR,—We read with interest the study by Laakso *et al* on serum lipids and lipoprotein in patients with non-insulin diabetes and with gall stone disease.¹ The association between diabetes and cholelithiasis has been defined also in the Italian population,^{2,3} but the reason for this association has not yet been clarified. It is generally held that patients with diabetes secrete a more lithogenic bile than non-diabetics.⁴ In the few studies that have compared diabetics with age, sex, and weight matched controls, however, neither the insulin dependent diabetics nor the insulin independent diabetics had a bile cholesterol saturation index higher than that of control subjects.⁵ 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 reports⁶ on 120 patients affected by type II diabetes we too observed that in diabetics 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 HbA_{1c}, body mass index, and duration of diabetes between patients with gall stones and those without gall stones. In our study, in non-insulin dependent diabetes 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, however, that it is necessary to take into account the effects of diet and, above all, prolonged use of oral hypoglycaemic agents which may bias the interpretation of plasma lipid pattern and the level of insulinaemia. 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 being 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 lipoprotein 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 relation between plasma and biliary lipid compositions. Moreover, it is now generally recognised that a simple concept of lithogenic bile is inadequate to account for cholesterol gall stone development.

We agree with Laakso *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.⁴

P PAZZI
L TREVISANI
S SARTORI
1st Medical Department,
S Anna General Hospital
D SIGHINOLFI
V ALVISI
Institute of Internal Medicine,
University of Ferrara,
44100 Ferrara,
Italy

Correspondence to: Dr P Pazzi, 1st Medical Department, S Anna General Hospital, Corso Giovecca, 203, 44100 Ferrara, Italy.

- 1 Laakso M, Suhonen M, Julkunen R, Pyörälä K. Plasma insulin, serum lipids and lipoproteins in gall stone disease in non-insulin dependent diabetic subjects: a case control study. *Gut* 1990; 31: 344–8.
- 2 De Santis A, De Luca C, Cantagalli A, et al. The diabetes-cholelithiasis association in a case-control study. *Ital J Gastroenterol* 1988; 20: 158–9.
- 3 Pazzi P, Putinati S, Sighinolfi D, Trevisani L, Verdianelli G, Alvisi V. The diabetes-cholelithiasis association in a hospital-based case-control study. *Ital J Gastroenterol* 1989; 21: 313.
- 4 Ponz de Leon M, Ferendones R, Carulli N. Bile lipid composition and bile acid pool size in diabetes. *Dig Dis Sci* 1978; 23: 710–6.
- 5 Haber GB, Heaton KW. Lipid composition of bile in diabetics and obesity-matched controls. *Gut* 1979; 20: 518–22.
- 6 Greco A, Pazzi P, Galvani F, Putinati S, D'Ambrosi A, Alvisi V. Prevalence of gallstone disease and associated factors in diabetic patients. *International Meeting on Pathochemistry, Pathophysiology and Pathomechanics of the Biliary System, Bologna, 14–16 March 1988; A221.*

Reply

SIR,—Pazzi *et al* have shown an association between high insulin concentration and cholelithiasis in non-insulin dependent diabetes similar to what we have reported.¹ 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. In contrast, 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 prolonged use of 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.² Indeed, our preliminary unpublished data show that