LETTERS TO THE EDITOR

Strongyloidiasis

EDITOR,—We were delighted to read Dr Grove's leading article on the protean manifestations of strongyloidiasis (*Gut* 1994; **35:** 437–40) and the case report by Dr Delarocque Astagneau *et al* of a case presenting with biliary obstruction (*Gut* 1994; **35:** 705–6), particularly with the reported increase in the incidence among migrant workers and holiday travellers to endemic areas. We recently submitted a case report of a West Indian man living in the United Kingdom since 1965 with disseminated strongyloidiasis who, similar to the patient in the case report, was also seropositive for human T lymphotropic virus (HTLV)-1.[1] These cases highlight the well recognised association between HTLV-1 infection and disseminated strongyloidiasis, particularly in areas of high prevalence in the West Indies and southwest Japan.

Thirty eight to 47·8% of patients from a Japanese series with disseminated strongyloidiasis were HTLV-1 positive.[2–4] Infection with HTLV-1, commonly associated with the adult T cell leukaemia/lymphoma syndrome in Japan and HTLV-1 associated myelopathy/tropical spastic paraparesis in the West Indies, causes impaired cell mediated immunity without reducing T cell helper/suppressor ratios, and may cause a predisposition to disseminated helminthic infections by reducing serum concentrations of IgE and IgE binding factors.[5] Relapse rates after treatment for disseminated strongyloidiasis with a single agent are higher in HTLV-1 positive patients. Patients from the West Indies or Japan with disseminated strongyloidiasis should therefore be screened for HTLV-1 infection. Treatment with at least two agents is recommended with closer follow up for symptoms and signs of recrudescence or re-infection.[6 7]

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Pancreas in end stage renal disease

EDITOR,—I read with interest the article by Lerch and colleagues (*Gut* 1994; **35:** 401–7) describing the development of pancreatic insufficiency in experimental renal failure. I, however, was very surprised to see one of my papers[1] given as a reference for statements in the introduction and discussion of their manuscript to support claims that exocrine pancreatic insufficiency occurs in renal failure. In contrast, we showed increased trypsin and normal lipase secretion in patients with renal failure undergoing dialysis.[1] Confusion may have arisen because we reviewed the data of others published before our article and gave a number of references that reported normal or decreased pancreatic secretion in renal insufficiency.[2–6]

Of possible interest, we also found that patients with renal insufficiency had raised plasma concentrations of hormones that affect pancreatic secretion, which led us to hypothesise that the raised hormone concentrations may cause morphological changes of the pancreas.[1 7] One of the important problems of the rat model of renal failure discussed by Lerch and colleagues is that severe renal insufficiency is only transient; serum creatinine decreased to almost normal values by 56 days. It is entirely possible that severe renal insufficiency was not present long enough to cause prolonged physiological changes such as constantly increased hormonal concentrations to cause morphological abnormalities.

Another possible problem with the study of Lerch *et al* was use of questionable controls; comparisons were made to caerulein pancreatitis which, according to the authors, causes acute pancreatitis whereas the aim of their study was to determine if renal insufficiency causes chronic pancreatitis.

These problems raise the question of whether the study of Lerch *et al* provides much useful information to resolve the question of pancreatic functional and morphological abnormalities in human renal failure.

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Reply

EDITOR,—Dr DiMagno raises some important questions regarding our study and the participation of the exocrine pancreas in chronic renal disease. The data in his earlier report[1] indeed show that the exocrine pancreas responds with increased digestive enzyme secretion (trypsin) to cholecystokinin (CCK) or meal stimulation in vivo and this finding is in accordance with the increased secretory response (amylase and lipase), which we found in vitro at the time interval where renal insufficiency was most severe in our animals (*Gut* 1994; **35:** 401–7). His work was meant to be referenced at a different place in our paper and we apologise for this error.

Dr DiMagno further suggests that renal failure was only severe during the initial phase of our observation period, while, at the stage of developing glomerulosclerosis[2] uraemia was much milder. We agree that an animal model entailing total (in contrast with subtotal) nephrectomy combined with longterm haemodialysis would have more adequately reflected the situation in human end stage renal disease. Such an animal model, however, would be extremely challenging to establish in the laboratory and the course of uraemia in our setting was clearly severe enough to significantly affect pancreatic exocrine function, morphology, DNA, protein synthesis, cellular turnover, and regeneration. We therefore maintain that subtotal nephrectomy, although not truly reflecting end stage renal disease in humans, is a valuable tool to study the effects of renal insufficiency on the exocrine pancreas.

Dr DiMagno reminds us that the pathophysiology as well as the sequelae of uraemic pancreaopathy are still a matter of controversy and ongoing study.[3] As indicated in the abstract of our report it was previously unclear whether uraemic pancreaopathy 'should be regarded as a manifestation of chronic pancreatitis, arising from recurrent attacks of acute pancreatitis, or represents a distinct entity'. To consider these questions we have used for comparison a standard rat model of pancreatitis that combines most of the biochemical and cell biological characteristics reported in other existing animal models of pancreatitis. The changes affecting the pancreas in renal failure bear no resemblance with any of the different features of pancreatitis we investigated. They did, however, resemble toxic damage of the pancreas and we therefore concluded that uraemic pancreaopathy is distinct from pancreatitis and probably does not result from recurrent attacks of pancreatitis. The initial hypothesis that recurrent attacks of acute pancreatitis might participate in the changes of the uraemic pancreas is not as improbable as Dr DiMagno suggests because the incidence of acute pancreatitis is significantly increased in patients with end stage renal disease.[4] We agree that it would have been very interesting to include an additional non-invasive control model to represent chronic pancreatitis in our study (compared with the acute changes associated with the caerulein model we used). Unfortunately no such animal model exists.

The hypothesis proposed by Dr DiMagno that a chronic increase of circulating CCK[1 5] is responsible for the changes associated with uraemic pancreaopathy is intriguing, and, although we have not measured CCK in our rat model, is not excluded by our data. The same increase in

serum CCK, however, is found in patients with chronic alcoholic pancreatitis[6] and regarded as a consequence rather than the cause of the disease.

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Imaging of the common bile duct

EDITOR,—The finding by Hainsworth *et al*, that the combination of clinical history, liver function tests, and ultrasonography generated a negative predictive value of 91% in the age range 21–88 (unit A) (*Gut* 1994; **35:** 991–5), implies that, in subgroups such as the elderly, characterised by a high degree of prior probability of cholelithiasis,[1] and, hence, choledocholithiasis,[2] the negative predictive value of these diagnostic criteria might well be lower, because the negative predictive power is inversely correlated with the prevalence of the condition under diagnostic consideration.[3 4] With increasing age, therefore, there should be greater justification for routine imaging of the common bile duct either by ERCP or by cystic duct cholangiography, in prospective candidates for laparoscopic cholecystectomy.

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EDITOR,—We have read with great interest the study by Hainsworth *et al* (*Gut* 1994; **35:** 991–5) regarding the options for managing the common bile duct in patients undergoing laparoscopic cholecystectomy. However, there are several points that need further discussion.

Firstly, the criteria for selecting patients with high risk of common bile duct stones are vaguely described. There is no precise description of what they have considered a dilated or non-dilated common bile duct on ultrasound scan. Besides, isolated increases in serum alkaline phosphatase or serum bilirubin, or both are poor indicators of common bile duct obstruction (as described by themselves). Liver function tests, however, have a high specificity and negative predictive value, especially if γ glutamyltransferase and aminotransferases are also raised.[1 2]

Secondly, it is surprising that 12 patients were found to have a positive cholangiogram in unit A, but only four patients had common bile duct stones after ERCP. To assume that stones had passed spontaneously is rather speculative. Thus, eight of 12 patients should be considered to have had an unnecessary exploration of the common bile duct. Moreover, we cannot find any explanation why ERCP was delayed up to 96 days after laparoscopic cholecystectomy.

Thirdly, we believe that the risk of a false-positive cholangiogram secondary to air bubbles in the common bile duct during laparoscopic cholecystectomy may be higher because the abdomen is insufflated with carbon dioxide and this gas could pass through the cystic duct during the insertion of the catheter.

Fourthly, Hainsworth *et al* state that 'selective cholangiography misses a proportion of common bile duct stones'. Prospective randomised studies have not proved this, however,[3 4] and suggest that cholangiography can be omitted in patients without indications of common bile duct disease.

Fifthly, no description of the treatment and follow up of patients in whom peroperative cholangiography failed is provided.

Sixthly, assuming that a false-positive result occurs in 0·4–6·5% of the cases when cholangiography is used on routine basis[1 4] common bile duct exploration in patients without choledocholithiasis would be increased. As common bile duct exploration, either supraduodenal or endoscopic, is associated to a higher risk of complications, the unsolved question is 'Does routine cholangiography really reduce morbidity and death rates in laparoscopic cholecystectomy?'

Finally, we believe that preoperative identification of patients with 'no/low' risk of choledocolithiasis in which peroperative cholangiography is not indicated[1 2] should be carried out by means of a clinical history, liver function tests, and ultrasonography. This policy will result in a lower incidence of false-positive cholangiograms without increasing the risk of retained common bile duct stones.

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1 Voyles CR, Sanders DL, Hogan R. Common bile duct evaluation in the era of laparoscopic cholecystectomy. *Ann Surg* 1994; **219:** 744–52.
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Reply

EDITOR,—We are glad that our paper has stimulated discussion and debate in this controversial field. Drs Mayol and Alvarez Fernandez-Represa seek clarification of the criteria used for categorising patients into 'low' and 'high' risk groups for bile duct stones. We relied on a combination of history, liver function tests, and bile duct diameter. In our paper, we set out individual features from the history, such as jaundice or pancreatitis, and showed their ability to predict the presence of duct stones.

The working definition of a dilated common bile duct used in the study was a diameter greater than 8 mm. While the probability of finding duct stones rises with increasing bile duct diameter,[1] interpretation of bile duct diameter is not a precise science. Bile duct diameter increases with advancing age, definitions of 'normality' vary between studies, and the overall sensitivity for detecting bile duct stones with ultrasonography ranges from 25–55%.[2 3]

Liver function tests are a very imprecise and non-specific way of detecting bile duct stones, which is the reason why most investigators have used a combination of factors to assign patients to 'high' and 'low' risk groups. We must take issue with our correspondents' interpretation of the large series reported by Voyles *et al.*[4] These authors do not cite any data on the sensitivity, specificity, and positive or negative predictive values of liver function tests in themselves. We await with interest full publication of the results from Mayol *et al.*

We were initially surprised too that, at the time of post-cholecystectomy ERCP, eight of 12 ducts had cleared. One of the eight had a complete block at the lower end of the common bile duct. The stone was sufficiently small to be removed at ERCP but, postoperatively, the patient developed pain and clearly passed the stone before ERCP was done. We believe that the other seven had stones in their bile ducts at the time of surgery for these reasons. Firstly, we used high quality C-arm image intensification, which is associated with a less than one per cent risk of false positivity.[5] This is dynamic and permits further flushing and assessment under vision where doubt exists. Secondly, the 16% detection rate for bile duct stones on unit A coheres with reported rates of 13–20% in patients undergoing open cholecystectomy.[6] Thirdly, spontaneous passage of duct stones is well reported in the context of acute pancreatitis and our paper suggests this is also true of patients undergoing laparoscopic cholecystectomy. Laparoscopic cholecystectomy may differ from conventional cholecystectomy in the degree of manipulation of the gall bladder before the cystic duct is ligated. It is certainly possible that some stones spill over during the procedure, only to subsequently pass spontaneously.

We know of no evidence that low pressure pneumoperitoneum encourages the formation of air bubbles in the biliary tree. First principles suggest that intra-abdominal pressure would equilibriate between the peritoneal cavity and bile duct lumen across the bile duct wall, in much the same way as