

**Reply**

SIR.—We are grateful to Dr Arnold for raising the role of antibiotic prophylaxis in patients with common bile duct (CBD) stones requiring endoscopic sphincterotomy (ES).

The issue (prophylactic mezlocillin *versus* cephalozolin) is, however, not as clear cut as might at first appear. The following are important and interrelated points that have to be considered: (1) The Leicester and Manchester ES<sup>1</sup> series are based on different groups of patients. In the Leicester series referrals from outside of Leicester were deliberately excluded in order to reduce bias, allowing comparison with Leicester surgical patients; in other words restricting our study to a closely defined patient population. The Manchester ES series was based on patients referred from the North West of England and North Wales. If we were to include referrals from outside Leicester, we would have had to include more than 200 additional patients during the same study period. These overall results would then look more like the Manchester series. (2) The number of patients with one or more septic complications was 14 (13.2%) – this was not clear in our text. We used rigid criteria to determine this and this figure may not be directly comparable with other series, particularly those involving referrals from outside the local catchment area. (3) There has been no rigid policy about antibiotic prophylaxis and ES in Leicester, but there has been a major switch to iv cefuroxime in recent years. Patients with acute cholangitis were treated by combination therapy which usually included iv gentamicin.<sup>2</sup> Development of post-ES cholangitis ± septicaemia led to institution of combination chemotherapy. (4) Most organisms in the biliary tree will be covered by cefuroxime; the problem of pseudomonas spp<sup>3</sup> may have more to do with inadequate disinfection of the instruments. The important finding in this study was that ERCP/ES resulted in more patients with infected gall bladders; pseudomonas spp was just one component of this. (5) Post-ES complications have been found to be independently correlated with medical risk factors and the level of serum bilirubin (multivariate analysis).<sup>4</sup> Both these factors were significantly greater in the Leicester compared with the Manchester ES series. (6) Although there was no statistically significant difference in the incidence of acute cholangitis between the Leicester and Manchester ES series there were more in the former (29/106 cases *versus* 15/81 cases). The incidence of septic complications post-ES (cholangitis and empyema of the gall bladder) in Leicester was higher in those presenting with cholangitis.

For the above reasons we are not entirely convinced that mezlocillin should be used as the routine prophylactic agent. What is certain is that all patients

should be treated along 'surgical lines' before ES, including iv fluids and appropriate antibiotics. In the case of acute cholangitis being present before ES, or developing afterwards, broad spectrum iv antibiotic therapy should be used to include cover against pseudomonas spp. What seems crucial is that CBD clearance or drainage<sup>5</sup> should be achieved *ab initio*.

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**Mixed endocrine adrenal tumour causing steatorrhoea**

SIR.—Thesleff *et al* have recently described a mixed endocrine and renal tumour causing diarrhoea which was dramatically improved during  $\alpha$  adrenoreceptor blockade with phenoxybenzamine.<sup>1</sup> This was thought to be because of inhibition of catecholamines which had been suppressing exocrine pancreatic secretion.<sup>2</sup> We recently have seen a 42 year old man with a two year history of watery diarrhoea who was found to have an adrenal phaeochromocytoma secreting catecholamines and vasoactive intestinal peptide (VIP). Before surgery he was routinely given phenoxybenzamine and propranolol resulting in immediate cessation of his diarrhoea. In this case we believe the mechanism for his response may be due to the beta adrenoreceptor blockade and not alpha adrenoreceptor blockade.

For two years before diagnosis he had suffered increased bowel frequency ( $\times 10/\text{day}$ ) and the presence of undigested food in his stool. During this time he had remained well apart from a weight loss of 2 kg. Six months before diagnosis he was referred to one of us (MB) for further investigations. Clinical examination was normal, blood pressure 130/80 mm Hg, with no postural change. Urea and electrolytes, liver function tests were normal. Faecal fats were marginally raised at 24 mmol in 24 hours (normal  $<18$  mmol/24 hours). Xylose absorption and small bowel biopsy were normal. An abdominal computed tomography scan showed an 8 cm tumour between the right kidney and liver. Angiography showed this to be a suprarenal tumour typical of a pheochromocytoma. Subsequent urinary VMA levels were raised at 33  $\mu\text{mol}$  in 24 hours. A gut hormone profile showed a grossly raised VIP at 300 pmol/l (normal  $<30$  pmol/l) with raised calcitonin at 0.08 pmol/l (normal  $<0.03$ ), somatostatin was normal.

Before surgery he was given phenoxybenzamine 20 mg tds and propranolol 40 mg tds and the patient was delighted to report immediate cessation of his diarrhoea of two years standing. At operation a well encapsulated pheochromocytoma was removed and subsequently he has had no further diarrhoea. Vasoactive intestinal peptide calcitonin and urinary VMA concentrations have returned to normal.

VIP is a potent hormonal secretagogue stimulating adenylate cyclase activity in human small large bowel and leads to a rise in cyclic AMP.<sup>3</sup> This may lead to diarrhoea.<sup>4</sup> Adrenaline and noradrenaline via alpha adrenergic receptors lead to a decrease in fluid secretion.<sup>5</sup> Therefore, introduction of the alpha adrenergic receptor blocker should abate this effect and worsen diarrhoea. *In vitro* beta blockade has a direct inhibiting action on adenylate cyclase and may lead to a decrease in fluid secretion.<sup>6</sup> This is supported by *in vitro* studies in rats with propranolol.<sup>7</sup>

The abrupt cessation of diarrhoea in this case may have been caused by alpha adrenergic receptor blockade and improved pancreatic secretion, but this was unlikely as steatorrhoea was only mild. We believe that symptoms improved because of beta adrenoreceptor blockade causing an inhibitory effect on adenylate cyclase intestinal secretion.

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## Non-cirrhotic portal hypertension with hypoxaemia

SIR,—We read with interest the paper by Babbs *et al* (*Gut* 1988; **29**: 129–31) on a case of non-cirrhotic, portal hypertension associated with hypoxaemia. We would like to report an extensively studied hypoxaemia associated with a nodular regenerative hyperplasia of the liver (NRH).

A 20 years old Caucasian woman presented with rest dyspnoea and on examination was found to have hepatomegaly and splenomegaly. Laboratory investigation showed: haemoglobin, 10.5 g/dl; white cell count,  $5.8 \times 10^9/\text{l}$ , platelet count,  $94 \times 10^9/\text{l}$ , prothrombin time, 16 seconds (control, 14). Serum aspartate, alanine aminotransferase,  $\gamma$  glutamyl transferase and alkaline phosphatases were noted to be increased (twice the upper limit normal range). Immune circulating complexes were present, anti-nuclear antibody were positive to 1/500; HBsAg, IgM HBc, HBsAb, IgM HAV and HIV<sub>1</sub> (LAV/HTLV III) antibodies were absent from the serum. Endoscopy showed grade II oesophageal varices. Percutaneous liver biopsy with reticulin stain (Gordon-Sweet) permitted the diagnosis of NRH, showing regenerative nodules without hepatic fibrosis. Mesenteric angiography confirmed portal hypertension. Chest roentgenogram and pulmonary function tests (lung volumes and capacities) were normal. Arterial blood gas values on room air were as follows: pH, 7.46; PaO<sub>2</sub>, 46 mm Hg (supine position); PaCO<sub>2</sub>, 23 mm Hg. A right to left shunt, without abnormality of ventilation perfusion distribution, was evidenced by alveolar-arterial (A-a)