Azathioprine in Psoriasis

Sir,—Following the report of azathioprine in the treatment of psoriasis by Dr. A. du Vivier and others (12 January, p. 49) I thought it would be of interest to report the possible myopathic effect of azathioprine in this disease. Myopathy is not uncommon in renal transplant recipients on both azathioprine and prednisone but myopathy due to azathioprine alone has rarely been reported.

A 62-year-old man who had had psoriasis for 16 years developed exfoliative dermatitis three months before admission on azathioprine. Systemic methotrexate had been stopped because of haemorrhagic cysts. After a month on azathioprine 200 mg daily (2·4 mg/kg) he developed progressive weakness of the legs and difficulty in walking. The weakness of the deltoids and supraspinatus with absence of arm jerks and some weakness of the proximal leg muscles with depressed knee jerks, absent ankle jerks, and flexor plantar responses. The muscles were not tender and there was minimal wasting. There was no clinical evidence of peripheral neuropathy and the clinical impression of myopathy was confirmed on electromyography. At this time the patient was putting about 80 g of cholesterol per day on to his skin with exclusion. After stopping azathioprine and changing the cholesterol to betamethasone 17-valerate 0·1%, diluted 10 times, muscle strength returned to normal within three weeks.

Systemic absorption of local fluorinated steroids has not previously been reported to produce myopathy and it seems likely that in this patient azathioprine alone produced the myopathy.—I am, etc.,

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Coxsackie B Virus and Diabetes

Sir,—Dr. D. R. Gambale and others (3 November 1973, p. 260) recently reported the association of positive titre levels for Coxsackie B4 virus and diabetes mellitus, supporting their earlier findings.1 The significant association was in the 10–19 year-old subjects. The incidence of positive titres is high in the population they studied, and it is unexplained whether all cases but a small proportion of children have diabetes. The virus can be found in communities without prior exposure to the virus which suffered an epidemic, as Hadden and others suggested.3

We recently studied such a community on the Pribilof Islands in Alaska, U.S.A. In the winter of 1967–8 an epidemic caused by Coxsackie B4 occurred in a previously unexposed population, as determined by pre-epidemic sera. Of the 116 persons with diabetes and positive neutralizing antibody titres (1:4,
1-16). After the epidemic 89 (77%) had a four-fold titre rise, if those under 20 years of age 46 out of 50 had positive titres after the infection. Clinical illness occurred in over 50% of infected subjects.

Five years later a follow-up study was done using venereal disease research laboratory glucose tolerance test. Serum neutralizing antibody titres and two-hour plasma glucose levels were measured. Of the 136 persons under 25 years of age (M = 65, F = 71) the highest two-hour plasma glucose level was 133 mg/100 ml. Persistence of positive titre levels was also documented since 77% of these subjects had a positive neutralizing antibody titre level.

Even though it was in the young diabetic that Dr. Gamble and his colleagues were able to show the strongest association with positive Coxackie B4 titres we could not show that Coxackie B4 infection caused a single case of diabetes, though the attack rate in the 136 under 20 years of age at the time of the epidemic was extremely high. [We are, etc.]

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Serotonin and the Mesenteric Circulation

Sir,-Dr. I. M. Murray-Lyons and others (29 December, p. 770) reported some unusual cases of gangrene of the small intestine in patients with carcinoid tumours of the small bowel and with raised blood levels of 5-hydroxytryptamine (5-HT). They found proliferative changes in the elastic tissue in the wall of the mesenteric vessels. Anthony and Drury,1 reporting similar changes in the elastica in cases with small bowel carcinoid, postulated that some substance or substances produced by the carcinoid tumour caused the changes in the elastica, which in turn compromised blood flow and contributed to bowel necrosis in some cases. This hypothesis has not been proved directly. The elastica lesions have not been reproduced experimentally and the theory does not explain the presence of the elastica lesions almost exclusively in the mesenteric circulation.

In a recent laboratory investigation in dogs, blood flow was measured with an electromagnetic flow meter simultaneously in the thoracic aorta, in the superior mesenteric artery (S.M.A.), and in the renal artery. An intravenous injection of 5-HT (0.03 mg/kg) caused a marked drop in flow which was most marked in the S.M.A. (fig.). The reason for this specific sensitivity of the mesenteric vascular bed to 5-HT is not known. Nor can it be stated with certainty that the human mesenteric circulation responds to 5-HT in a similar manner. However, this observation does suggest an alternative hypothesis for the aetiology of the elastica changes in the mesenteric vessels—that a decreased formation of 5-HT in the blood may lead to a chronic increase in resistance in the mesenteric circulation. The sustained increased resistance causes the degenerative changes in the elastica in the branches of the S.M.A. that in turn contribute to ischaemic necrosis in some cases of small bowel carcinoid.—We are, etc.,

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Serotonin Metabolism in Hepatic Encephalopathy

Sir,—We read with great interest the paper by Dr. A. J. Knell and others (23 March, p. 549) on serotonin metabolism in hepatic encephalopathy. Our interest in the metabolism of serotonin (5-HT) was aroused by a patient with cirrhosis of the liver who excreted large amounts of 5-HT and its precursor 5-hydroxytryptophan (5-HTP) in urine.1 The hepatic metabolism of 5-HT in experimental cirrhosis was characterized by decreased formation of sulphate conjugates, increased synthesis of glucuronide and conjugates,2 increased uptake of 5-HT by the liver,1 and deranged entero-hepatic circulation of metabolites of 5-HT.3, 4 Metabolism of 5-HT in the mucosa of the small intestine was disturbed only in the advanced stage of the cirrhosis, when the mucosa lost its ability both to store and metabolize 5-HT.2

A raised concentration of 5-hydroxyindole acetic acid (5-HIAA) in cerebrospinal fluid might well be related to increased excretion of 5-HT and 5-HTP in urine. According to our preliminary observations the storage and metabolism of 5-HTP in the small intestine mucosa of cirrhotic rats is disturbed like the intestinal metabolism of 5-HT. Thus an increased efflux of 5-HTP into the portal circulation may result in an increased transfer of 5-HTP to the central nervous system, where it is metabolized through 5-HT to 5-HIAA. This mechanism might be involved in the pathogenesis of the observed increase of 5-HIAA concentration in cerebrospinal fluid in patients with hepatic encephalopathy.—We are, etc.,

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British Medical Journal 25 May 1974

Laparoscopic Tubal Ligation

Sir,—I was extremely interested in the letter by Dr. K. R. Greene and others (6 April, p. 54). Only three days before that date and quite independently I did my first laparoscopic Pomeroy sterilization by virtually the same method as they described. I would confirm that it seems simple and safe and that a search of the literature suggests that it has not been tried previously. In this patient with a mobile uterus there would seem to be no need for two lower quadrant incisions because a single midline stab 2-3 cm above the symphysis pubis suffices. It would seem that the main hazards of the procedure are likely to be haemorrhage due to tearing of the mesentery of the Fallopian tube and, if one uses two stab incisions, accidental puncture of the inferior epigastric vessels by the operating team—[that] complication which should be avoidable if one remembers the surface markings of these vessels. Both complications should be excluded before withdrawing the laparoscope. Neither would be as serious as bowel burns and either would be an indication for laparotomy, for which consent should always have been obtained.

In due course I too hope to report a large series of patients having a laparoscopic Pomeroy sterilization. It would seem important to make an early and full assessment of a technique which requires only ordinary laparoscopy equipment, permits tubal ligation and transection, avoids the hazards of diathermy, and is surprisingly easy.—I am, etc.,

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Death during Dental Anaesthesia

Sir,—I have read with interest Dr. J. G. Bourne's letter on this subject (16 March, p. 516), but I do not feel that he has adequately emphasized the fact that a young, healthy person died needlessly. The patient had an unrecognized faint during the intravenous induction of anaesthesia in spite of the presence of the cardiac sign of pallor. In spite of this pallor and while in the sitting position the chair pure of nitrous oxide was given. The anaesthetic was administered by an operator anaesthetist, a practice which is not supported by the Society for the Advancement of Anaesthesia in Dentistry.1

While tragic errors of judgement have been made by most of us in the course of our professional careers we must realize that the very nature of liberty is that one be routinely anaesthetized the dental patient in the supine position, but this is purely because of the trend in dental ergonomics. I have never shared Dr. Bourne's anxiety about the sitting position and I never hesitate to use this position if the patient has, for example, a hiatus hernia or an abdominal