Glucagon Therapy in Acute Pancreatitis

Sir,—Your leading article (1 December, p. 503) and the subsequent letter from Mr. C. W. Imrie and Professor L. H. Blumgart (5 January, p. 38) reflect a surge of interest in the treatment of acute pancreatitis. Though there are disagreements about many aspects of this condition, there is no dispute that its mortality rate is unacceptable high.

Unfortunately, very few trials of methods of treatment have been designed in ways which can lead to scientifically valid conclusions. As a consequence many misleading claims for different drugs have been made. It is for this reason that the Medical Research Council has set up a working party which is about to start a randomized, controlled clinical trial to compare glucagon, aprotinin (Trasylol), and a placebo in the treatment of acute pancreatitis.

One of the difficulties in assessing the treatment of acute pancreatitis in Britain is the fact that no single centre has the opportunity to treat sufficiently large numbers. Therefore our trial will be conducted on a multicentre basis and many colleagues have already indicated their willingness to participate. We know that when our findings are reported they will be subject to close scrutiny and that they may be criticized on the grounds of faulty dosage. We therefore wish to stipulate at this stage that the purpose of the trial is to test current claims for glucagon and aprotinin. If these prove to be wrong, it will be possible to test alternative dosages and alternative drugs.—We are, etc.,

ROSS FORGAN-SMITH
J. H. DARRELL
Department of Bacteriology, Royal Postgraduate Medical School, London W.12

Apomorphine Pharmacophobia and Renal Toxicity

Sir,—Professor W. St. C. Symmers (24 November, p. 460) has emphasized the need to treat systemic fungal infection with apomorphine B. He also quotes evidence that the drug is nephrotoxic and that this fact needs to be considered by prescribing physicians. Renal toxic manifestations of apomorphine B tend to return to normal on cessation of therapy, particularly if the total dose is less than 5 g.1 Winn has reported irreversible renal toxicity in patients who received total doses of 14 g, 16.7 g, and 21 g respectively of apomorphine. Reports of irreversible renal toxicity with total doses of less than 5 g are rare. There is evidence2,3 that a total dose of at least 2 g and preferably 3 g is necessary for cure of systemic fungal disease. Drutz et al.2 have criticized this recommendation and have successfully treated 13 patients with a variety of mycotic diseases using daily serum levels as a guide to therapy, adjusting dosage to achieve twice the minimum inhibitory concentration against the causative organism. Five of Drutz's patients, however, still received a total dose of at least 2 g of the drug. The rapid infusion4 of moderate doses (never more than 45 mg daily) of aprotinin over a prolonged period, to achieve a total dose of 2-5 g, is probably the best way to use this drug. Renal toxicity should not give cause for anxiety until the blood urea reaches 100 mg/100 ml and should not lead to premature cessation of treatment before this.—We are, etc.,

R. B. WELBOURN
Chairman of Working Party
Department of Surgery, Royal Postgraduate Medical School and Ham and Westminster Hospital, London W.12

ALAN G. COX
Co-ordinating Secretary
Clinical Research Centre and Northwick Park Hospital, Harrow, Middx.

High-dose Frusenide in Renal Failure

Sir,—We wish to make some comments about the paper of Dr. F. Cantarovich and his colleagues (24 November, p. 449) concerning the beneficial use of high-dose frusenide in established acute renal failure, since our own results appear different from those reported.

We conducted a single-blind randomized study on 66 patients with acute oliguric renal failure between 1971 and 1973. Criteria for retaining the patients in the study were as follows: recovery of established acute renal failure with initial urine output less than 500 ml/day and remaining less than 20 ml/hr after correction of shock and/or hypovolaemia when present; low urinary urea concentration; normal or high sodium concentration and/or urine:plasma osmolality ratio less than 1:1. (2) Absence of obstructive uropathy; absence of glomerulonephritis or systemic disease involving the kidney.

Plasma urea levels were maintained below 200 mg% using intravenous frusenide. To 33 of the patients a first dose of frusenide (3 mg/kg) was given intravenously and followed every four hours by doses ranging from 1 to 6 mg/kg, according to the diuretic response. The maximum daily dose was 1,200 mg. If no diuretic response was observed after three injections (doses of 15-20 ml/hr) frusenide was temporarily discontinued, but further treatment with the same protocol was attempted every five days until diuresis occurred. The remaining 33 patients did not receive frusenide, and an initial group of 15 patients did not differ significantly in respect of aetiology of acute renal failure, sex ratio, initial urine output, or mortality from the treated group. No significant difference in the results of treatment were seen between the two groups (see table).

The differences between the results obtained by Dr. Cantarovich and his colleagues and our own lead us to point out the salient