in fact blocked this hypokalaemia to a much greater degree than practolol. This is further supported by the results of our recent study (PC O'Connor, *et al.* Presented at a meeting of the British Pharmaceutical Society, September 1982) with a selective beta₂-adrenoceptor antagonist, ICI 118551. Single oral doses of 20 mg in normal volunteers completely blocked the fall in serum potassium concentration during an adrenaline infusion (placebo: 4.08 ± 0.21 mmol/(mEq)/l to 3.32 ± 0.25 mmol/l, $p < 0.002$; ICI 118551: 3.82 ± 0.13 mmol/l to 4.03 ± 0.22 mmol/l, NS). The inhibitory effect of this selective beta₂-antagonist on adrenaline induced hypokalaemia was much greater than we have previously found for a selective beta₁-antagonist.³ It has also been shown in experiments on isolated skeletal muscle preparations that adrenaline stimulates potassium ion influx (and sodium ion efflux).⁵ These changes in transmembrane cation flux do not seem to be dependent on changes in circulating insulin.

Overall, therefore, we believe that salbutamol induced hypokalaemia is more likely to be due to stimulation of a beta₂-adrenoceptor linked Na⁺ K⁺ ATPase rather than secondary to changes in carbohydrate metabolism.

A D STRUTHERS
H L ELLIOTT
J L REID

University Department of
Materia Medica,
Stobhill General Hospital,
Glasgow G21 3UW

¹ Massara F, Tripolina A, Roturino M. *Eur J Pharmacol* 1970;10:404-7.

² Porte D, Graber AL, Kuzinya T, Williams RH. *J Clin Invest* 1966;45:228-35.

³ Struthers AD, Reid JL, McLean K, Rodger JC. *Clin Sci* 1982;62:1P.

⁴ Berend N, Marlin GE. *Br J Clin Pharmacol* 1978;5:207-11.

⁵ Clausen T, Flatman JA. *Br J Pharmacol* 1980;68:749-55.

SIR,—Dr A D Struthers and others quite correctly point out that administration of adrenaline is associated with transmembrane cation flux, and we agree that current evidence supports direct beta₂-adrenergic stimulation as the most likely mechanism for the observed hypokalaemia. This may not be directly relevant, however, to plasma potassium changes which occur after salbutamol, a drug with properties similar to but not identical with those of adrenaline. At therapeutic doses salbutamol is a relatively selective beta₂-agonist, but at higher plasma concentrations beta₁-agonist effects may become prominent.¹ Adrenaline has both alpha- and beta-adrenoceptor agonist properties.

Both salbutamol and adrenaline cause beta₂-receptor mediated glycogenolysis leading to a rise in plasma glucose concentration. As Dr Struthers and others state adrenaline inhibits insulin release, but this seems likely to be due to alpha-agonist action on the pancreatic B cell.² Salbutamol, on the other hand, leads to a prompt release of insulin mediated by beta-adrenoceptors which is unrelated to beta₁-mediated glycogenolysis.³ A rise in circulating insulin concentrations undoubtedly leads to a fall in extracellular potassium which is independent of catecholamine related transmembrane cation flux.⁴

We agree that propranolol may block the beta₁-effects on carbohydrate metabolism and the beta₂-effects on potassium influx following salbutamol poisoning leading to a fall in plasma glucose concentration and a rise in

plasma potassium concentration and this was of course the substance of the penultimate paragraph in our report. It remains possible, however, that glucose and insulin responses which differ from those which occur after adrenaline may be in part responsible for salbutamol induced hypokalaemia. Resolution of this controversy awaits the development of agonists and antagonists which are rather more selective than those currently available.

J M C CONNELL
G T MCINNES

Department of Medicine,
Western Infirmary,
Glasgow G11 6NT

¹ Marlin GE, Turner P. *Br Med J* 1975;ii:715-9.

² Cryer PE. *N Engl J Med* 1980;303:436-44.

³ Goldberg R, Joffe BI, Bersohn I, Van ASM, Krut L, Seftel MC. *Postgrad Med J* 1975;51:53-8.

⁴ De Fronzo RA, Feig A, Ferrannini E, Wahren J. *Am J Physiol* 1980;238:E421-7.

Hypersensitivity after a sea urchin sting

SIR,—There may be another explanation for Dr H E Kane's miserable and protracted symptoms (2 October, p 950), which were only indirectly related to the sea urchin sting. Is it possible that he had ciguatera poisoning? His symptoms are very suggestive of that little known condition, which is becoming quite a serious problem world wide.^{1 2}

The fact that Dr Kane was stung by a sea urchin on the hand in Yugoslavia suggests that he is a traveller and possibly goes snorkeling or scuba diving. The less adventurous bather is likely to be stung by a sea urchin on the foot. The fact that Dr Kane was sunbathing some weeks after his holiday in July suggests that he may have taken another overseas holiday and on that occasion may have eaten a poisoned fish. The relation with the sea urchin sting might be no more than that Dr Kane is an adventurous swimmer and skin diver who some weeks after the sea urchin's sting went on another holiday to indulge his sport of spear fishing. On this second holiday he caught a large grouper, barracuda, or large snapper which he consumed with the results that he describes. The fact that friends may have shared his meal does not invalidate the possibility of ciguatera; evidently it does not always affect all who are exposed to the toxin. I would be most interested to know whether my hypothesis might be correct.

Sea urchin spines can remain in the body almost indefinitely. As I write this letter I can see under the skin of my fingers the black streaks of sea urchin spines acquired in the Caribbean 12 years ago; I was snorkeling.

G H VALENTINE

War Memorial Children's Hospital,
London,
Canada N6B 1BB

¹ Heimbecker RO. *Can Med Assoc J* 1979;120:638.

² Bagnis R, Kuberski T, Laugier S. *Am J Trop Med Hyg* 1979;28:1067.

Maintenance of remission in ulcerative colitis with oral preparation of 5-aminosalicylic acid

SIR,—In their evaluation of 5-aminosalicylic acid coated with an acrylic based resin (9 October, p 1012) Dr M J Dew and others have performed a study of considerable therapeutic interest, and it is therefore

important that correct conclusions be reached. They state that 5-aminosalicylic acid "was as effective as sulphasalazine in maintaining remission in ulcerative colitis," but we doubt whether this is reasonable.

The relapse rate on 5-aminosalicylic acid was, if anything, rather greater than that on sulphasalazine (9/34 (26%) versus 6/33 (18%) respectively), but the relatively small numbers included in the trial make a type II error (claiming no difference when one does in fact exist) possible. To have an 80% chance of detecting a real difference due to a doubling of relapse rate from 20% to 40% on 5-aminosalicylic acid compared with sulphasalazine with a p value of 0.05 would require 100 patients in each group, and to have only a 50% chance of doing so would require over 50 patients in each group.

On the other hand the trial was large enough to be able to detect a difference between relapse rates of 20% and 75% (the latter being what might have been expected with a placebo), so that 5-aminosalicylic acid coated with acrylic may have some effect. Dr Dew and others could still be right in their contentions, but their evidence is not strong enough to support them.

C J HAWKEY
M J S LANGMAN

Department of Therapeutics,
City Hospital,
Nottingham NG5 1PB

*. *We sent a copy of this letter to Dr Dew, who replies below.—Ed, BMJ.

SIR,—Thank you for allowing us the opportunity to reply to the letter from Dr C J Hawkey and Professor M J S Langman. We would accept their comments that our preliminary trial of acrylic coated 5-aminosalicylic acid for patients with ulcerative colitis indicated that it was therapeutically active but that it may either be as good as or slightly inferior to sulphasalazine. We must await results of further trials both by ourselves and by others, but there are considerable practical difficulties in achieving treatment groups containing 100 or more patients, which might be necessary to distinguish acrylic coated 5-aminosalicylic acid from sulphasalazine.

MICHAEL J DEW

Department of Gastroenterology,
University Hospital of Wales,
Cardiff CF4 4XW

Drivers, binge drinking, and gamma-glutamyltranspeptidase

SIR,—We read with interest the recent article by Dr J A Dunbar and others (16 October, p 1083) on the use of serum gamma-glutamyltranspeptidase activity to identify problem drinkers. We found a similar lack of response by this enzyme to an acute intake of alcohol.

A lower dose of alcohol than that used by Dr Dunbar and others (0.6 g/kg body weight) was given to eight healthy volunteers (seven men and one woman; age range 18-47 year) to mimic social drinking. A blood sample was taken before and 17 and 24 hours after alcohol ingestion. The serum activity of gamma-glutamyltranspeptidase was measured by the method of Szasz *et al*¹ (reference intervals: men 6-25 U/l; woman 4-18 U/l) on a Vitatron-Akes enzyme analyser (MSE Ltd, Crawley, Sussex, UK). Analysis of variance carried out by standard procedures² indicated that there were no significant changes in serum gamma-glutamyltranspepti-