Cardiac Failure and Folate Deficiency

SIR,—Your interesting leading article on cardiac failure and folate deficiency (24 January, p. 188) commented on the possible causes of this association, and factors like impaired dietary intake and gastrointestinal malabsorption were mentioned. A contributory cause could well be excessive folate loss in the urine. Urinary folate excretion has been poorly studied, but we recently reported an unexpected increase of urinary folate in association with congestive cardiac failure.¹ As much as 61.6 µg. folate was lost per day, while normal controls excreted 0.1–18.0 µg. folate per day.

Urinary folate loss is unlikely to be the sole cause of folate deficiency in these patients, but could well be an important contributory factor in a patient with prolonged anorexia. One could speculate that excessive urinary folate results from abnormal folate liberation secondary to the liver damage of chronic congestive failure. Urinary folate excretion is increased in cirrhosis and acute hepatitis¹ and also after surgical trauma.²—I am, etc.,

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Computers for Transplantation

SIR,—It might be inferred from one of the signatories of the letter from Mr. J. P. Blandy and colleagues (31 January, p. 298) that the transplantation unit at St. James's Hospital, Leeds, participates in the scheme based on the London Hospital. This is, in fact, incorrect, since we are linked up with the scheme based on Newcastle, in which multiple centres from the north of England and southern Scotland participate, using sera provided from the National Tissue Typing Reference Laboratory at Bristol.

This decision provides the best solution for our transplantation service.—We are, etc.,

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Sickle Cell Trait and Leg Ulceration

SIR,—After the early confusion surrounding the various genotypes containing Hb S, the sickle cell trait emerged as a benign condition compatible with a long healthy life.

The frequency of leg ulcers in sickle cell trait remains unclear. Diggs, Ahmann, and Bibb¹ found no increase in the trait in 46 negroes with previous leg ulceration. A case of recurrent leg ulceration in a negro girl with the sickle cell trait has been described² and Wolfort and Krizek³ reported healed ulcers in 6 of 232 negro patients with sickle cell trait admitted to John Hopkins Hospital,

but no control figures were available.

In the ulcer clinic of the University Hospital of the West Indies haemoglobin electrophoresis has been performed routinely. Patients are referred to this clinic on the basis of leg ulceration alone and not selected on any other criteria. The sickle cell trait was present in 49 out of 250 patients with leg ulcers compared with estimates of 10.8% in the negro population.^{4,5} The likelihood of such a result occurring by chance is extremely low ($p < 0.001$) and there would appear to be a definite relationship between leg ulceration and the sickle cell trait.—We are, etc.,

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"Contributory Causes" of Death

SIR,—May I beg a small space in your columns to mention an aspect of death certification? I run an "Over 60's" club in this village, and from time to time assist bereaved members with the necessary formalities following death. Twice in the last year extra distress has been caused to two of our members by the entries on the certificate.

Both patients had died from carcinoma, but in one case a fractured femur occurred some eight weeks before death and this was given as a contributory cause. The sister of the deceased was greatly shocked when she was collected by the police and taken to the public mortuary to identify the body, and was told that a post-mortem examination and inquest would take place. In the second case cirrhosis of the liver was given as a contributory cause, and although the deceased was 82 a necropsy was essential in order to ascertain the extent of alcoholism—if any. In both these cases the funerals, previously arranged, had to be postponed. Could practitioners please warn relatives of the possible outcome of the causes of death entered on the certificate?—I am, etc.,

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Designated Areas Allowance

SIR,—This university is currently engaged on a research project on the geographical distribution of general practitioners in England and on the effect of the "designated areas" allowance. The project is supported by the Department of Health and Social Security, and we have received valuable help and co-operation at all stages of the research from the B.M.A.

One part of the project has involved a postal survey of about one in ten of all

general practitioners in England, and we are now in the concluding phases of the survey. More than four out of every five general practitioners who were approached have co-operated in the study, and this at a time when work-loads are in any case heavy and have been increased as a result of the influenza outbreak. May we through your columns express our sincere gratitude to all those doctors who have helped us? We are very conscious of the ever-increasing number of forms and questionnaires which general practitioners are asked to complete, and it was with some trepidation that we embarked upon this necessary part of the project. We hope that the very high response rate is a measure of the importance which doctors attach to the subject of the research, but we are in any case very appreciative of the interest which has been shown in our work.

Publication plans include a paper in one of the medical journals, and in addition a summary of the principal findings and conclusions will be made available to all the doctors who have participated.—We are, etc.,

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Proteins and Insulin Release

SIR,—Drs. J. Dupré and D. J. Chisholm (14 February, p. 434), in commenting upon our article (6 December, p. 598), state that "the experiments show that exogenous secretin or pancreozymin enhances [*sic*] the increase in blood insulin in response to intravenous infusion of amino-acids in man, an effect which has already been amply demonstrated." I doubt whether this effect is yet amply demonstrated. The experiments to which we are referred¹ used a *single* amino-acid, arginine, which is very much a special case in relation to both insulin and growth hormone secretion. Also, it is arguable that Dr. Dupré and his colleagues demonstrated no more than a simply additive effect in the case of arginine plus secretin, the absence of the figures for appropriate control experiments making this point uncertain.

Regarding the role of secretin in the insulin response to oral glucose, I accept the demonstration by Dr. Chisholm and his colleagues² that levels of secretin, as measured by their immunoassay, rise following oral glucose, but regard the relevance of this as debatable. Thus, in their study, the mean peak level of secretin (12.5 µg./ml.) was reached five minutes after drinking the glucose, and by fifteen minutes the mean level had almost returned to the fasting value. The corresponding insulin levels, however, showed no rise until ten minutes after the glucose, by which time the blood sugar was also significantly elevated. Furthermore, this peak level of secretin reached after glucose contrasts with sustained levels of >20 µg./ml. during the infusions of exogenous secretin in amounts (1 unit/minute) which are modest when compared with those used in most studies of the effects of secretin in man. On the other hand, in the