disease that took place when the immigrant Indians from India were given large quantities of the refined product when working in the sugar plantations of Natal in Africa.

T L CLEAVE

Fareham, Hants

¹ Jennings, D, *Lancet*, 1968, 2, 1249.

Coronary heart disease and short stature

SIR,—Professor J N Morris and his colleagues in their article "Diet and heart: a postscript" (19 November, p 1307) state that short men are at greater risk of suffering coronary heart disease (CHD) than tall men.

A similar clinical impression¹ prompted me to record the heights of patients with confirmed CHD in my practice and to compare them with those of a random sample. It was found that of the 60 patients with CHD (43 men and 17 women), 44 were below average in height, their height being, on average, approximately 5 cm (2 in) below the mean height of the random sample.

One aspect of these findings is particularly interesting—the possible implication of a metabolic effect of growth hormone (GH) deficiency. Clearly, certain persons of short stature must have been deficient in GH before full growth was attained,² and it is reasonable to assume that GH deficiency continues into adult life in such persons. Although the exact function of GH in adults is not understood,² its metabolic functions are well established and if these are compared with the known facts concerning CHD we find: (1) GH stimulates triglyceride breakdown: established association between CHD and raised serum lipids; (2) GH plays a vital role in control of blood sugar: high incidence of CHD among diabetics; (3) GH deficient among persons of short stature: reported higher incidence of CHD in short persons; (4) GH injection reported to reduce serum cholesterol:³ hypercholesterolaemia long associated with CHD; (5) GH deficiency much more common among boys:² CHD much more common in men.

As the cause of CHD is still largely a mystery I submit that further study of the possible relationship between it and short stature, with particular reference to the effects of GH deficiency, may be fruitful.

L R JENKINS

Whitchurch, Cardiff

¹ Jenkins, L R, *British Medical Journal*, 1975, 1, 631.

² Tanner, J M, *Health Trends*, 1975, 7, 61.

³ Byers, S O, and Friedman, M, in *Advances in Growth Hormone Research*, ed S Raiti, p 843. Washington, DC, US Department of Health, Education and Welfare, 1974.

Incidence and mortality of acute pancreatitis

SIR,—I would disagree with Mr M J McMahon's belief that the incidence of acute pancreatitis does not vary between different regions in Britain (19 November, p 1350). In West Lothian, where alcoholism and cholelithiasis occur commonly, 64 patients were admitted with acute pancreatitis between January 1975 and November 1977. From a community population of 140 000 this represents an incidence of 238 cases per million of population per annum, more than double the incidence in Leeds. The diagnosis in each case

was based on clinical information and confirmed either by characteristic laparotomy findings or a serum amylase value greater than 2000 IU/l, the figure recommended by the recently published MRC study.¹ If one includes patients whose amylase values were greater than 1200 IU/l the incidence rises to 331 cases per million per annum. It would appear, therefore, that the incidence of acute pancreatitis varies on a regional basis and also according to the criteria of selection.

I would confirm, however, that in this hospital the mortality for acute pancreatitis is less than 10% and endorse the view that a 20% mortality rate is totally unacceptable.

DAVID F GRAHAM

Broxburn, W Lothian

¹ Cox, A G, et al, *Lancet*, 1977, 2, 632.

SIR,—I have read with interest the letters of Mr M J McMahon and Mr C W Imrie (19 November, p 1350). I would agree with both writers that the overall incidence of acute pancreatitis given in your leading article (22 October, p 1043) is too low by half. What concerns me more in their letters is that there still seems to be confusion over the interpretation of mortality rates for this condition. Surely this situation would be clarified once and for all if it were recognised that absolute death rate and percentage case mortality are separate entities and must therefore be used in different ways. The former did not change significantly over a 20-year period in Bristol,¹ though, as one would expect, there was some variation from year to year. Also on the published data there are still 3-5 deaths each year from acute pancreatitis in the Glasgow Royal Infirmary—a figure which has changed little over the past 17 years.^{2 4}

When one turns to case mortality this is a different matter. In Bristol the incidence of diagnosed disease was at its highest in 1961-5, when there was a peak in interest and so percentage mortality fell relatively. In Glasgow there has been a 3- to 4-fold increase in 1971-6 as compared with 1960-70,^{2 4} but again as the absolute death rate has remained unchanged it seems reasonable to assume that this increase mainly represents a diagnostic explosion rather than a sudden epidemic of the disease. The decrease in case mortality from 18.9% in the 1960s to under 9% at the present time must therefore be largely relative. Mr Imrie has quoted the Medical Research Council study,⁵ with an overall mortality of 11%, in support of his argument that mortality rates in the region of 20% are not "part of acceptable clinical practice in this country." However, this was a multicentre trial and the various contributions were far from uniform. At one extreme one hospital contributed 40 patients with only one death (mortality 2.5%), while another centre provided 20 patients, six (30%) of whom died. From this brief discussion it must be concluded that case mortality should no longer be used as a clear measure of success or failure of a treatment except when it is applied within a controlled study. In particular, it does not provide a basis for comparison between one group of cases and another when these groups are separated either by time or by geography. If such comparisons are to be made these must be based on absolute death rates.

Mr McMahon states his belief that modern methods of treatment have achieved "a reduction in mortality" and similar claims

have been made by others.⁴ I too very much hope that we are treating acute pancreatitis better today than 10 years ago and certainly we have a much better understanding of the changes that occur in this disease. However, it must be stated that at the present time there are no hard data that a salvage is in fact occurring. Indeed, from published figures of absolute death rate already quoted there is regrettably no evidence of any such trend at all. Well-designed trials will be required if proof of benefit for any particular form of treatment is to be obtained. This will not come from arguments based on spurious statistics.

J E TRAPNELL

Royal Victoria Hospital,
Bournemouth, Dorset

¹ Trapnell, J E, and Duncan, E H L, *British Medical Journal*, 1975, 1, 176.

² Imrie, C W, *British Journal of Surgery*, 1974, 61, 539.

³ Imrie, C W, and Blumgart, L H, *Bulletin de la Société Internationale de Chirurgie*, 1975, 34, 601.

⁴ Imrie, C W, et al, *British Society of Gastroenterology Meeting*, York, 1977.

⁵ Cox, A L, et al, *Lancet*, 1977, 2, 632.

Outpatient chemotherapy for breast cancer

SIR,—We appreciate Mr B V Palmer's interest (19 November, p 1354) in our paper on safe and effective chemotherapy for breast cancer using a kinetically based approach (22 October, p 1064). However, we are a little concerned about the modifications that he proposes in the protocol in order to make it suitable for administration to outpatients.

The safety and effectiveness of our protocol depend on its being administered exactly as stated and with all the precautions rigorously observed. Mr Palmer's first suggestion that giving the methotrexate as a single intravenous injection instead of an infusion "is unlikely . . . [to] make a marked difference to the tumour response rate" is incorrect. Quite apart from any experimental considerations it has already been shown clinically that administering methotrexate as a single intravenous injection in this combination reduces the response rate from over 60% to approximately 40%.^{1 2} Although Mr Palmer's alternative suggestion of giving the methotrexate by mouth might more closely simulate an infusion pharmacologically, it would still mean that patients would have to take their entire leucovorin "rescue" at home.

In our view there are grave disadvantages to administering chemotherapy on an outpatient basis. Firstly, many patients do not actually take their drugs so that any assessment of their therapeutic value cannot accurately be made. Secondly, it is much more difficult to control side effects—for example, nausea and vomiting—which most patients experience during the 30 hours or so of their treatment. Thirdly, the potentially lethal bone marrow depression from the oral methotrexate may not always be avoided if the patient, either because of vomiting or human error, does not take his leucovorin.

One of the reasons that cancer chemotherapy is regarded as extremely toxic is often the somewhat casual way in which it is administered without regard for underlying scientific principles. The adoption of Mr Palmer's suggestions would not only reduce the response rate but might well bring chemotherapy once again into disrepute. We feel that if patients with breast cancer are going to be given chemotherapy at all, then