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.

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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.

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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.

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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.

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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

the drugs should be administered optimally in the way we suggest and that no compromises should be made which lead to a reduction in the response rate or the safety of the treatment.

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J H GOLDIE

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¹ Edelsteyne, G A, *et al*, *Lancet*, 1975, 2, 209.

² Hart, J, personal communication.

Shadow over Maltese medicine

SIR,—In your leading article (19 November, p 1304) you describe the Maltese Government as totalitarian. I am curious to know how you came about this conclusion. The Labour Government in Malta is in power following wins in general elections in 1971 and 1976. You also omit to mention in your resumé of the situation why the doctors were sacked from Government employment. The Maltese Legislative Assembly passed a law that 60 posts in medical service (less than one-third of the total) should form part of essential services and that anyone holding one of these senior posts who absented himself from work without reason would be dismissed. The doctors' failure to provide such services required by Maltese law led to their dismissal. The Australian Parliament has passed some rigid legislation, yet I never read any *BMJ* editorial about Australia.

Your allegation that Malta is in the queue for membership of the EEC baffles me. Malta has repeatedly said in world forums that she wants to be a political bridge between southern Europe and the Arab world. We refuse membership both of the EEC and the Arab League.

You claim to be supporting Maltese students to come to England. I claim and will provide proof if necessary that the aid you mention goes only to students who take an anti-Maltese Government stand. Since when has the BMA become a political organisation? Your attempts to stifle Malta's tourist industry will surely impress Maltese readers of the love you claim to have for an island which for her bravery in defence of freedom was awarded the George Cross.

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Final-year medical student

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Plight of Maltese medical students

SIR,—Mr Toni Pellegrini (12 November, p 1285) in reply to Scrutator's comments (15 October, p 1036) on the plight of Maltese medical students attempts without justification to shift the responsibility for these students' predicament on to the shoulders of the Medical Association of Malta (MAM).

The untimely interruption of the final-year students' qualifying examinations was not due to any directive to this effect by the MAM. It was the direct result of the Government's police-enforced lock-out of local as well as external examiners from the teaching hospital in retaliation to the association's limited industrial action. This action was limited to "cold" surgical operations and non-urgent outpatient clinics and, contrary to what was

stated by the Maltese Director of Information, did not affect the treatment of emergencies. The imposition of the lock-out becomes all the more illogical when one considers that only a few days earlier the Government had resorted to legislation ostensibly to ensure the provision of an adequate supply of sorely needed housemen.

Confronted with this unexpected situation, the MAM, with the assistance of the BMA, took the initiative to help air-lift the students concerned to the United Kingdom to enable them to sit for the London Conjoint Board examinations.

The plight of Maltese medical students has since been further aggravated by the Government's decision, without prior consultation with the university authorities and the medical faculty, to restructure the medical course. This, coupled with the ruthless decimation of the teaching staff through dismissals and suspensions, has left the medical school a mere shadow of its former self and of doubtful viability. Under such circumstances can one blame the students now in their fourth year for deciding to leave Malta to resume their medical training overseas, where they can look forward to achieving a recognised medical qualification?

There is one further point in Mr Pellegrini's letter which concerns present medical standards in Government hospitals and which requires rebuttal. This association is in possession of a fully documented dossier of cases treated by foreign specialists. Available information leads us to the conclusion that medical standards have deteriorated abysmally since the start of the present dispute. This runs counter to the interests of the Maltese patients, who, in their large majority, prefer to be treated by their compatriots rather than by a motley crew of imported doctors whose presence is delaying rather than facilitating an equitable solution to the present impasse.

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Glucagon and secretin in aspirin-induced erosive gastritis

SIR,—Glucagon has been reported as being of value in preventing aspirin-induced gastric mucosal damage in dogs¹ and cold-restraint gastric mucosal damage in rats.² Secretin has been observed to reduce duodenal ulcer pain in man³ and to prevent peptic ulceration induced by pentagastrin in cats.⁴

We have investigated the effect of glucagon and secretin on aspirin-induced gastric erosions in the rat, using a method previously described to study the effects of aspirin on rat stomach.^{5,6} The rats were fasted for 24 h and then given a subcutaneous injection of either glucagon (50 µg/kg), secretin (10 U/kg), or saline. Thirty minutes later each rat received an oral dose either of a glucose saline solution containing 53 mmol aspirin/l to a dose of 128 mg/kg suspended in 0.5% carboxymethylcellulose or a control solution consisting of glucose saline and 0.5% carboxymethylcellulose. The animals were killed 4 h later with ether and the stomachs examined for erosions. The results were recorded in two ways: firstly, if any rat had more than one erosion greater than 1 mm it was termed positive; secondly, a grading system for the

erosions was used, each erosion being allocated a score from 1 to 4 depending on its size and these scores being added to give the total score for each rat. The incidence of erosions (percentage of rats graded positive) and the mean score for each group were then calculated.

In 23 control rats not given aspirin the incidence of erosions was 4.3% and mean score 0.9. In 71 rats receiving saline subcutaneously the aspirin significantly increased the incidence of erosions to 64.8% and the mean score to 13.5. In 34 rats given glucagon before aspirin the incidence of erosions was 67.7% and the mean score 16.1, while in 36 given secretin the incidence was 86% and the mean score 19.4. The incidence of gastric bleeding in those animals receiving glucagon or secretin before aspirin administration was therefore not significantly less than in those animals receiving only saline.

The results do not confirm the protective effect previously reported of glucagon in aspirin-induced erosive gastritis and fail to show a protective effect of secretin under these circumstances.

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¹ Lin, T M, and Warrick, M W, *Archives Internationales de Pharmacodynamie*, 1974, 210, 279.

² Guth, P H, *et al*, *Gastroenterology*, 1975, 69, 1048.

³ Holst, J J, Hof, L, and Rune, S J, in *Gastrointestinal Hormones and Other Subjects*, ed E H Layren, p 116. Munksgaard, Copenhagen, 1971.

⁴ Konturek, S J, *American Journal of Digestive Diseases*, 1968, 13, 874.

⁵ Semple, P F, and Russell, R I, *Gastroenterology*, 1975, 68, 67.

⁶ Carmichael, H A, *et al*, *Gut*, 1976, 17, 33.

Prolonged malaria prophylaxis

SIR,—My attention has been drawn to a letter from Professor L J Bruce-Chwatt (12 November, p 1287) concerning a note from your expert in relation to antimalarial drugs for airline pilots (17 September, p 757). Having read at the same time the editorial response to Professor Bruce-Chwatt's letter, I write to express grave concern with the possible consequences that could follow the literal acceptance of the advice now given by your expert—namely, that malaria prophylaxis is really necessary only in Africa. The expert notes a report by Mr J H Kelsey (26 November, p 1415) that several patients from West Africa have been showing visual impairment associated with the ingestion of chloroquine over several years. In most cases the dosage taken by these patients is not specified and it is by no means clear that chloroquine or its equivalent was taken in the standard recommended dosage of 300 mg base weekly. Like Professor Bruce-Chwatt, I know of no other evidence to suggest that the long-term consumption of chloroquine in this dosage has led to visual impairment. Alternative prophylactic drugs are, however, available, as has been pointed out by both your expert and others including myself.¹

The implication in your expert's original comment that aircrew may need to take additional chloroquine if they develop a fever, thereby increasing the risk of visual impairment, seems to me most unrealistic. I cannot imagine any intelligent airline pilot dosing himself at frequent intervals with chloroquine in this manner. If by chance such an individual