Beta-adrenergic Blocking Agents in Patients with Renal Failure

SIR,—Drs. Priscilla Kincaid-Smith and A. S. P. Hua are disturbed (24 August, p. 520) by our suggestion that beta-adrenergic blocking agents should not be used in patients with moderately severe renal failure (27 April, p. 193). They refer to a previous publication¹ to show that temporary deterioration in renal function in such patients may occur with the introduction of any hypotensive drug. Their evidence appears to be based on experience with one patient with malignant hypertension who was given 6 different drugs, and is not relevant to the cases described by us. We refer Drs. Kincaid-Smith and Hua to our paper, where they will find that the maximum change in diastolic blood pressure in any of the three cases was 10 mm Hg during the period that renal function deteriorated. Their comments do not shed any light on the mechanism of the events we described.

Drs. Kincaid-Smith and Hua will no doubt agree that renal function should be monitored during the course of therapy with hypotensive drugs in patients with renal failure. Our experience leads us to suggest that this may be especially important when beta-blocking drugs are prescribed and needs to be emphasized now that these agents are being so forcefully promoted in general practice.—We are, etc.,

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¹ Kincaid-Smith, P., Fang, P., and Laver, M. C., *Clinical Science and Molecular Medicine*, 1973.

Malabsorption in Overland Travellers to India

SIR,—Dr. S. Margaret Farquharson's interesting observations (24 August, p. 519) on the frequency of episodic diarrhoea and the use of sulphonamides, tetracyclines, and metronidazole in overland travellers are in general similar to our own (10 August, p. 380). A characteristic of treatment in our subjects was the repeated use of very short courses of therapy, which varied from one to a maximum of seven days on antibiotics. A number of patients did take metronidazole for varying periods, but this did not cure their symptoms.

We agree that amoebiasis should be excluded and that particular care is needed. The technique described by Alen and Ridley¹ at the Hospital for Tropical Diseases ensures a high diagnostic rate by concentrating the amoebae in a faecal extract by 10% formalin and ether. None of our patients had the cystic forms of entamoeba in their stools: these may, of course, be present in asymptomatic subjects who had had amoebiasis in the past. The vegetative forms of amoebae are usually associated with colonic and rectal invasion with symptomatic disease but no fat or xylose malabsorption. Coexisting amoebiasis was not considered a problem in our subjects since they had a normal mucosa on sigmoidoscopy as well as repeatedly negative examinations of the stool.

We are more concerned with the diagnostic problem of giardiasis than amoebiasis and now include microscopic examination of

a smear from a jejunal biopsy² as well as screening of jejunal aspirate and stool specimens before excluding giardiasis. We do not believe a clinical response to metronidazole can be used to infer either giardia or entamoeba infestation since metronidazole also has antibacterial properties.³ Furthermore, we are finding a considerable number of patients with giardiasis who prove resistant to metronidazole treatment.

Dr. Farquharson's suggestion that metronidazole may be a non-specific agent of benefit in the treatment of the cases of malabsorption has been considered, but our preliminary information does not support this suggestion.

We thank Dr. Farquharson for re-emphasizing the importance of achieving a complete diagnosis in this type of patient, who is often reluctant to be investigated fully.—We are, etc.,

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¹ Allen, A. V., and Ridley, D. S., *Journal of Clinical Pathology*, 1970, 23, 545.

² Kamath, K. R., and Murugasu, R., *Gastroenterology*, 1974, 66, 16.

³ Prince, H. N., et al., *Applied Microbiology*, 1969, 18, 728.

Wartime Penicillin

SIR,—I feel one statement in the Personal View of an "angry young man" (10 August, p. 407) requires a rebuttal. Dr. Terry Hamlin in an interesting article among other things says that he is reminded "of the wartime doctor forced to watch children dying of pneumonia, while the penicillin to save them went to cure the troops' gonorrhoea." As this statement has been repeated in other places I might perhaps be allowed to put the true facts on paper.

When it was decided that all the available penicillin should be allotted to the army it was handed over to a small research team. This was a combined R.A.M.C. and M.R.C. project and as I was in charge of this team I remember well the specific and rigid instructions that I received. There were three conditions in which penicillin was not allowed, and one of these was gonorrhoea, and this rule was firmly adhered to. Later of course when penicillin became freshly available from American sources I am not in a position to say how it was used.

One of the reasons it was not used for venereal disease was the obvious one of it being in short supply and the other more scientific one was that a full evaluation of it had already been carried out by Florey in Oxford. I know of no child dying of pneumonia while penicillin was being given to troops to cure their gonorrhoea. I feel it is necessary to state this as the article in question has been given rather unfortunate publicity.—I am, etc.,

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74a Tapeworms and Isolation

SIR,—The article on an isolation system for general hospitals (6 April, p. 41) lists tapeworm among the infecting agents which do not require any isolation. This is true for *Taenia saginata* (beef tapeworm), the only

tapeworm of human importance endemic in Britain. Cysticercosis, including cerebral cysticercosis, results from the ingestion of ova liberated from segments of *Taenia solium* (pork tapeworm). Segments escape from the anus and may lie in bedclothing, so it would be well for nurses to exercise a degree of isolation similar to that for amoebic dysentery, where cysts convey the infection.—I am, etc.,

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Hypertension and Myocardial Infarction

SIR,—I was most interested to read Dr. I. McD. G. Stewart's letter (27 July, p. 251) in reply to your leading article (5 January, p. 1). I have recently concluded a three-year study of 365 patients in general practice, all suffering ischaemic heart disease, which concerns principally the infarction rate and death rate in these patients in relation to their treatment. The results confirm my original observations¹ on the beneficial effects of beta-block treatment.

I have also analysed the same group of patients relating history of raised blood pressure to infarction rate and death rate from infarction. Taking an arbitrary blood pressure of 140/90, those with pressures above that level suffer nearly 50% more infarctions, 50% more fatal infarctions, and more than double the number of sudden deaths than do those with blood pressures below that level—whatever their treatment may be. If one classifies by treatment and blood pressure, then those *not* on beta-block treatment and having a blood pressure above the arbitrary level of 140/90 have nearly double the infarction rate, double the fatal infarction rate, and nearly three times the number of sudden deaths than those in the group with blood pressures below this level. It is interesting to record that the rates for both these groups—above or below 140/90—on beta-block treatment are virtually the same but only half that of the low blood pressure group not on beta-blockers. Sudden death numbers in these last two groups vary little from those in the low blood pressure group not on beta-block treatment.

So if the two groups with blood pressures above 140/90 are compared we find that those not on beta-block treatment have an infarction rate nearly four times that of those on beta-block treatment, more than four times the fatal attack rate, and more than three times the number of sudden deaths. If those with previous infarctions are excluded the differences are even more marked.

My conclusions so far, then, are that whether or not there are any aetiological relationships there is a definite increased risk of infarction and death in those with raised blood pressures compared with a similar group with "normal" blood pressures. Secondly, there is a very significant beneficial effect on the infarction rate when beta-blocking drugs are used in treatment. As Dr. Stewart says, the beneficial effects of the treatment of hypertension have been proved—apart from the effects on myocardial infarction. But we now have an accepted treatment for hypertension—the beta-blocking drugs—which I contend also reduce the infarction rate.

Evidence from the Framingham survey²

suggests that the risk of every clinical manifestation of ischaemic heart disease is increased in hypertension. So it would seem to me that by including a beta-blocker in the treatment of hypertension the benefit to the patient will also include a lesser risk of infarction and not a greater risk.—I am, etc.,

D. M. D. LAMBERT

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- ¹ Lambert, D. M. D., *Lancet*, 1972, 1, 793.
² Kannel, W. B., and Dawber, T. R., *British Journal of Hospital Medicine*, 1974, 11, 508.

Chickenpox from Herpes Zoster

SIR,—The report (8 June, p. 568) of two hospital outbreaks of chickenpox originating from herpes zoster was of great interest, particularly as importance is attached to the fact that the majority of staff affected were from overseas and so might have been expected not to have had the same levels of immunity as a corresponding group of native British adults.

Southmead Hospital experienced a similar outbreak in March 1974 in which, in contrast to the above reports, all affected staff members were native to the British Isles. The source was an immunosuppressed patient with Waldenström's macroglobulinaemia and facial herpes zoster. The latter diagnosis was confirmed by electron microscopical examination of the vesicular fluid, and the rash was treated topically with 25% idoxuridine in dimethyl sulphoxide. The staff members affected were the house officer, ward sister, a male night nurse, a nursing auxiliary, and a student nurse. All had been in close contact with the patient shortly after his admission, and had developed chickenpox 14-17 days later. The wife of the night nurse also developed chickenpox 14 days after her husband. No patient was involved. The source patient died of intercurrent *Escherichia coli* septicaemia two days before the first case was diagnosed. Measures introduced when the outbreak became apparent were effective in its control.

This outbreak shows that native British adults may be as much at risk of developing chickenpox as those who spent their childhood overseas. It also illustrates the high infectivity of herpes zoster in the immunosuppressed patient. We thank Dr. S. K. R. Clarke, Public Health Laboratory, Bristol, for the examination of the vesicle fluid by electron microscopy.—We are, etc.,

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Alkaline Phosphatase Levels in Epileptic Subjects

SIR,—In reply to Drs. P. Rødbro and C. Christiansen (22 June, p. 667) I should like to say that neither my methods nor my opinions have changed during the past three years. We have now carried out two separate surveys of the patients at the Chalfont Centre for Epilepsy^{1,2} and some of these results may help to clarify the apparent existing controversy.

In the first survey 48 out of 160 epileptic patients had raised plasma total alkaline phosphatase levels (defined as >10 and >12 King-Armstrong units (K.A.U.)/100 ml in females and males respectively). Of these 48, 18 (37.5%) had raised levels of bone isoenzyme (>5 K.A.U./100 ml). In the second survey 88 out of 310 epileptics had raised total alkaline phosphatase levels; 32 (36.4%) of the 88 had bone isoenzyme levels above 5 K.A.U./100 ml. Of the total number of 50 epileptics with raised bone alkaline phosphatase levels, 23 (46%) were aged between 16 and 20 years compared with only 16% of the total population. As can be seen from fig. 1, bone alkaline phosphatase levels are higher in epileptics aged 16-20 years than in

similarly aged normals, but the epileptic values decrease to normal levels between 21 and 25 years of age.

The histogram (fig. 2) shows that though 5-6% of adult epileptics (perhaps those most at risk of developing clinical osteomalacia) have raised plasma bone alkaline phosphatase levels, 14% of the population have bone alkaline phosphatase levels of less than 0.5 K.A.U./100 ml. Only one normal subject (1.6% of the population) had a similarly low level of bone alkaline phosphatase. The difference between the two groups was significant ($P < 0.005$). Mean plasma levels of bone alkaline phosphatase are thus no higher in adult epileptics than in adult normals.

Having described the syndrome of "anti-convulsant osteomalacia" in some detail,^{3,4} we have no reason now to deny its existence. What we are suggesting is that there may be a second anticonvulsant-drug-mediated bone effect possibly showing up in those epileptics with low bone alkaline phosphatase levels, many of whom also have a degree of hypocalcaemia.—I am, etc.,

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- ¹ Richens, A., and Rowe, D. J. F., *British Medical Journal*, 1970, 4, 73.
² Rowe, D. J. F., 1973, Ph.D. Thesis, University of London.
³ Dent, C. E., et al., *British Medical Journal*, 1970, 4, 69.
⁴ Stamp, T. C. B., et al., *British Medical Journal*, 1972, 4, 9.

Larrey and Débridement

SIR,—The review of Robert G. Richardson's recent book *Larrey: Surgeon to Napoleon's Imperial Guard* (24 August, p. 527) mentions Larrey's use of "débridement" in the

Fig. 1 Fall in level of plasma bone alkaline phosphatase with age in normal and epileptic subjects.

Fig. 2 Plasma bone and liver alkaline phosphatase isoenzyme levels in adult normal and epileptic subjects.