

tion of emetine, especially in view of its known myocardial toxicity.

Having thus dismissed emetine as a potential treatment for bronchopulmonary aspergillosis, we would confirm the views expressed in your article that amphotericin B is currently the most effective treatment available. Similarly, 5-fluorocytosine is effective against sensitive yeasts (provided they remain so), but we would like to point out that while clotrimazole does cause gastrointestinal side effects, it has also been shown to have no detectable effect against bronchopulmonary aspergillosis using clinical and mycological criteria.²—We are, etc.,

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- ¹ Jesiotr, M., *Scandinavian Journal of Respiratory Diseases*, 1973, **54**, 326.
² Crompton, G. K., and Milne, L. J. R., *British Journal of Diseases of the Chest*, 1973, **67**, 301.

New Curriculum

SIR,—I was fascinated to read the letter from Dr. M. F. Green (31 August, p. 578) describing the new curriculum at the Royal Free Hospital. The preclinical course concerning "Man and his Environment" is of great interest. It is, however, surprising that he does not mention any contribution to this course from general practitioners—who are daily concerned with treating man in his environment. It is equally surprising that the teaching in sexual matters is to be covered by preclinical staff, obstetricians, and a specialist in community medicine, while the management of most of the sexual problems which present in the National Health Service is conducted by general practitioners.

It would seem that the Royal Free Hospital could only improve their course by obtaining assistance from those doing the bulk of the clinical work in these fields. Some of the London schools and all the medical schools in the provinces have found that using the resources provided by patients in general practice and their doctors for teaching about subjects rarely encountered in the teaching hospital is remarkably successful.—I am, etc.,

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Complications of Carbenoxolone Therapy

SIR,—The letter from Dr. A. N. Kingsnorth (31 August, p. 579) stimulated by the recent article by Dr. G. J. Davies and others (10 August, p. 400) tends to cloud the issue. The presentation of carbenoxolone side effects is not invariably congestive cardiac failure, and this is clearly demonstrated in the original paper. In the absence of ileus the oral administration of potassium supplements is equally effective as, and less hazardous than, their intravenous infusion: to overcome the cumulative deficit of hundreds of milliequivalents of potassium will in any case require days rather than hours. Most serious of all, there is no "good case" for the use of an "aldosterone-antagonist-like diuretic agent." Quite the reverse, since it

has been shown¹ and is accepted in undergraduate textbooks² that spironolactone will actually prevent the effect of carbenoxolone in healing gastric ulcers. Thiazide diuretics¹ will prevent the fluid retention without altering the healing, but will certainly further exacerbate potassium loss. The only way to combat this is to administer large quantities of potassium-containing drugs.³

The best current policy is to use carbenoxolone only in patients with normal serum potassium and blood urea and without signs or history of heart failure or hypertension. The course of treatment should be carefully monitored to ensure prompt detection of weight gain or hypokalaemia. If it is desired to reverse or prevent the fluid retention or potassium loss, then thiazides plus substantial amounts of potassium chloride are indicated on present information. The aldosterone antagonist spironolactone is definitely contraindicated.

In the situation where the patient is committed to three different drugs totalling maybe more than a dozen tablets daily a single potassium-retaining diuretic tablet might well be preferable. Criteria for the ideal diuretic are adequate prevention of sodium and water retention, prevention of potassium loss, and freedom from antagonism of the healing action of carbenoxolone. The possibly useful agents available are triamterene and amiloride, which have both been proposed.⁴ Our search of the literature has not found any work establishing the value of either of these agents with carbenoxolone therapy and we are at present engaged in a trial to evaluate amiloride.—We are, etc.,

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- ¹ Doll, R., Langman, M. J. S., and Shawdon, H. H., *Gut*, 1968, **9**, 42.
² Laurence, D. R., *Clinical Pharmacology*, 4th edn., p. 215. Edinburgh, Churchill-Livingstone, 1973.
³ Bateson, M. C., *American Heart Journal*, 1974, **88**, 124.
⁴ Cranston, W. I., in *Modern Diuretic Therapy*, ed. A. F. Lant and G. M. Wilson, p. 175. Amsterdam, Excerpta Medica, 1973.

SIR,—The article by Dr. G. J. Davies and others (10 August, p. 400) raises certain questions and requires clarification.

Carbenoxolone has been in clinical use for over a decade and over 400 papers relating to it have now been published. Thus the incidence and nature of any side effects have been carefully and widely documented in the world literature, as have all those cited by the authors. That some of these complications can be quite severe has long been recognized and this information widely disseminated to the medical profession by the pharmaceutical firm marketing it. The data sheets on Biogastrone¹ (used in the treatment of gastric ulcer) and Duogastrone² (duodenal ulcer), which have been sent to every practising doctor in the United Kingdom, carry very clear warnings regarding their use, including any contraindications, and the message is quite clear. Carbenoxolone sodium treatment has to be regularly and medically supervised. However, this in no way compromises either the efficacy or the indications for such treatment, as has also been borne out by a recent critical review of carbenoxolone in the treatment of peptic ulcer.³

An analysis of the case histories cited by Dr. Davies and his colleagues would indicate that the severity of the complications was avoidable in cases 1, 3, 4, 6, and 8; case 2 was treated with the inappropriate preparation of carbenoxolone in too large a dose and for too long, while the remaining two patients should not have been treated with it at all. As Dr. Davies and his colleagues themselves admit, a proper awareness of the usage of carbenoxolone would have avoided most of the complications which they describe.

It would also be of great interest to know over what period of time these cases were assembled and the actual incidence of complications they represent. Finally, until further properly controlled clinical trials have clearly disproved the value of carbenoxolone in other gastrointestinal conditions then it is misleading to conclude that the only indication for its use is in proven benign gastric ulcer.—I am, etc.,

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- ¹ *A.B.P.I. Data Sheet Compendium 1974*, p. 88. London, A.B.P.I., 1974.
² *A.B.P.I. Data Sheet Compendium 1974*, p. 91. London, A.B.P.I., 1974.
³ Lewis, J. R., *Journal of the American Medical Association*, 1974, **229**, 460.

Channel Tunnel

SIR,—Dr. J. B. Kelynack (7 September, p. 631) makes a good point about noise and the channel tunnel rail link, but might I draw attention to another and potentially far more serious hazard associated with the tunnel itself?

The tunnel will be the first land link between Britain and the Continent and we will thus lose our physical isolation. Wild animals must inevitably get through to make a mockery of our quarantine regulations. With rabies spreading steadily westwards across Europe and with the fox an increasingly important carrier, I trust someone can give us reliable assurance of our continued protection from this disease.—I am, etc.,

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Prazosin and Hydrallazine in the Treatment of Hypertension

SIR,—We noted with interest the preliminary report by Drs. G. S. Stokes and M. A. Weber (11 May, p. 298) on the anti-hypertensive effects of prazosin. We have conducted a double-blind crossover trial comparing the antihypertensive effects of prazosin and hydrallazine in combination with a beta-blocking agent and a thiazide diuretic, the results of which will shortly be published.

The double-blind addition of capsules containing either 1 mg of prazosin or 25 mg of hydrallazine produced a significant fall in the blood pressure in this study. We had assumed from open studies that 25 mg of hydrallazine was equivalent to approximately 1 mg of prazosin, but the results of the controlled trial suggest that the hypotensive effects of 25 mg of hydrallazine may be rather greater than those of 1 mg of prazosin.