

Publicity for Ambilhar

SIR,—With reference to your comments on Ambilhar (29 January, p. 249), a separate letter on the technical aspects of the matter is being sent to you by the head of our Medical Division here. There are, however, three points to which I feel your attention should be drawn.

First, Ciba being an international company, the announcement of the launching of a new drug is always made simultaneously in the major countries of the world, whether or not the drug is going to be marketed in these countries.

Secondly, Ambilhar is not going to be made available to the medical profession in Britain except in special circumstances—and then only with Dunlop approval.

Thirdly, the reason for the press conference was not in connexion with the availability of Ambilhar as a treatment in Britain, but was concerned mainly with the fact that the chemical itself is intended to be produced in large quantities at our factory at Grimsby. The whole object of the conference was to give this information as wide publicity as possible and to indicate that foreign-based pharmaceutical companies sometimes do specifically manufacture certain products in the United Kingdom, thereby assisting British exports.

This, Sir, was the theme of the press conference, and the fact that other interesting aspects of the new drug and bilharziasis were highlighted by both the scientific and the popular press must be taken as normal when public announcements like this are made.

Finally, I would draw your attention to the fact that almost simultaneously with the above conference in December we sent out from Horsham to a number of scientific journals and to all daily papers a press release of the first total synthesis of cephalosporin in Basle by Professor Woodward, the Nobel prize winner. This has received mention in only two British chemical journals so far; and since the implications of this scientific achievement in this part of the antibiotic field, particularly in Britain, are considerable, you will no doubt agree that a press conference might have been a better way of ensuring greater publicity for such an achievement. For your information, the first detailed chemical report of this synthesis will be appearing in the *Journal of the American Chemical Society* next month.—I am, etc.,

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** What we criticized was "the recent publicizing of Ambilhar in the lay press despite a lack of reports in scientific periodicals of its effectiveness." Professor A. W. Woodruff also drew attention in our correspondence columns (29 January, p. 291) to the embarrassment publicity of this kind can cause to a clinician such as himself.—Ed., *B.M.J.*

Treatment of Hypertension with Methyldopa

SIR,—We were interested to read the favourable report by Dr. R. W. D. Turner and his colleagues (15 January, p. 133) on

the treatment of hypertension with methyldopa. We have recently completed a long-term follow-up of 60 patients with severe hypertension (mean basal diastolic pressure 134 mm. Hg) treated with hypotensive drugs for a mean period of three years. A satisfactory fall in blood-pressure (standing diastolic blood-pressure consistently less than 110 mm. Hg) was obtained in 80% of subjects treated either with guanethidine or methyldopa, but 56% of those on guanethidine had major side-effects, compared with only 12% of those on methyldopa (although a third on this drug experienced initial lassitude). No difference was found in the response to therapy in renal or essential hypertension, nor was methyldopa less effective in the most severe cases. Because of its effectiveness in blood-pressure reduction and the low incidence of side-effects we now regard methyldopa as first choice in the treatment of severe hypertension.—We are, etc.,

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Severe Hypothermia due to Combination of Psychotropic Drugs and Alcohol

SIR,—The following case is reported since it records complete recovery from severe hypothermic coma and emphasizes once more the dangers of combinations of various psychotropic drugs, especially when taken with alcohol.

A 43-year-old woman was admitted on 13 October 1965, after being found unconscious at home, where she lived alone. The alarm was raised after no signs of activity had been noticed in the house for 48 hours. It was later established that she had been depressed for some years and had attempted suicide with sodium amylal in 1959. In June of last year she had in-patient treatment at another hospital and was discharged on sodium amylal, 60 mg. t.d.s., isocarboxazid (Marplan) 10 mg. t.d.s., and perphenazine (Fentazin) 4 mg. t.d.s. She continued this treatment together with an unspecified amount of alcohol in the form of wine and spirits. Ten days before admission she discontinued Marplan and three days later started amitriptyline (Tryptizol) 25 mg. t.d.s., increasing to 25 mg. q.d.s. She also drank large quantities of red wine and had no subsequent recollection of the events which led up to her losing consciousness.

On examination she was comatose and hypothermic (rectal temperature 82.5° F. (28° C.)). Her pupils were dilated but exhibited hippus. Muscle tone was flaccid except for the left leg, which was spastic. Tendon reflexes were all elicited, but delayed and prolonged, and plantar responses were flexor. Pulse 42, regular, poor volume. Systolic blood-pressure 70 mm. Hg. Curious large areas of hard swelling of the skin and subcutaneous tissue with superficial blistering were noted in the right thigh and shoulder regions and were attributed to cold injury.

Investigations.—Urine—protein, positive; sugar, negative. Deposit—occasional leucocytes, hyaline casts, and red blood cells. Haemoglobin 92%. White blood cells 5,400/c.mm. Urea 20 mg./100 ml. Gastric washing—tests for barbiturates and salicylates negative. Serum barbiturate (as di-ethyl-barbituric acid) 0.7 mg./100 ml. Electrocardiogram—sinus rhythm rate 60, low voltage, otherwise normal. Chest x-ray normal. Minute ventilation 5 l./minute. Arterial pH 7.2; Paco₂ 60 mm. Hg (eight hours later 54 mm. Hg).

Progress and Treatment.—She was intubated and given continuous oxygen, though not artificial

ventilation. Soluble penicillin was given intramuscularly, and intravenous therapy included hydrocortisone, mephentermine, 8.4% sodium bicarbonate, 25% mannitol, Rheomacrodex, 5% dextrose, and normal saline. During the first few hours 600 ml. urine was obtained by catheterization, but she then became oliguric, passing only 350 ml. slightly blood-stained urine over the remainder of the first 24 hours. During this period, however, her systolic blood-pressure was maintained at 90 mm. Hg, her temperature rose gradually to 97.6° F. (36.4° C.), and she became restless. The following day she recovered consciousness, and blood-pressure, urine output, and temperature returned to normal. There were no untoward sequelae. Steroids were tailed off, sedatives and tranquillizers were not required, her skin lesions gradually healed, and she was discharged from hospital on 28 October 1965.

It proved impossible to establish whether an overdose had been taken, even after discussion with the patient's relatives, doctor, and chemist, and inspection of her various bottles of tablets. She persistently denied that she had, at least deliberately, taken an overdose of any of her drugs, though too much reliance cannot be placed on this. If an overdose of isocarboxazid or amitriptyline had been taken, one might have expected hyperpyrexia rather than hypothermia, while a large amount of sodium amylal would have perhaps produced more severe respiratory depression and a higher serum barbiturate level. Nevertheless, hypothermia was a feature of the case of amitriptyline and amylal poisoning described by Stark and Bethune,¹ and Benaim² has also seen one case of severe hypothermia and hypotension due to amitriptyline overdose. The short period elapsing between discontinuing isocarboxazid and commencing amitriptyline and the ingestion of large amounts of red wine were in any case other important factors in the production of her illness.—I am, etc.,

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REFERENCES

- 1 Stark, J. E., and Bethune, D. W., *Lancet*, 1965, 2, 390.
- 2 Benaim, 1965, personal communication

Bleeding after Tonsillectomy

SIR,—The recent spate of articles and letters on this subject has a highlight thrown on it by a quotation in Sir Zachary Cope's review of a book on American surgery (1 January, p. 37).

A Civil War surgeon remarked that he had seen a casualty whose "arm had been torn entirely off, and three inches of the brachial artery was hanging out of the wound and pulsating to within an inch of its extremity." We all remember the picture of the "Miller of Thetford," whose right arm was torn off by his entanglement in his mill machinery and who made a complete recovery.

These incidents should give the clue to our successful prevention of bleeding after adenotonsillectomy operations, utilizing Nature's safe and certain elastic recoil of vessels.

By using blunt guillotines, adenotomes, and curettes we can wrench-enucleate tonsils, and remove adenoids, and never have a haemorrhage.

But the bad design of many guillotines, etc., has made them unpopular, and the