Combining the Antidepressant Drugs

SIR,—Please forgive my returning to this topic, but constant and critical vigilance still seems to be necessary if psychiatrists are to continue to be able to use all their valuable new drugs without unnecessary anxiety being so constantly engendered, mainly by general physicians and pathologists.

A recent example is the reported death from hyperpyrexia supposedly due to combining both groups of antidepressant drugs in ordinary clinical dosage (5 December, p. 1465). This patient, fortunately, happens to have been an old one of mine whom I had twice treated in Belmont Hospital. Following her last discharge it was recommended that she stay on Nardil (phenelzine) alone, and not on Nardil and Pertofran (desipramine) combined, which was supposed to have contributed to her death. But it is most important to stress that she had actually been on combined phenelzine 45 mg. and Tryptizol (amitriptyline) 150 mg. a day for months on end during her two periods in hospital, and without any dangerous side-effects. This particular patient was depressed and guilty about certain past happenings. She was very unstable emotionally. Her future readmission to Belmont Hospital had again been suggested and refused shortly before she died.

No phenelzine at all, and only some desipramine, was found in the body at post mortem. But it was no doubt explained to the coroner that in theory a patient can collapse and die on ordinary therapeutic doses of Tofranil (imipramine) or amitriptyline for up to two weeks after the giving of the last dose of phenelzine.

At the inquest, however, the husband (despite no phenelzine being found in the body) said the patient had been taking one phenelzine tablet three times a day until the day before her death, and that she had not taken her desipramine 50 mg. three times a day at all regularly, and certainly not for 48 hours before her death. The only evidence that she had not taken an overdose of desipramine was the amount of tablets left in the bottles. But the coroner and his medical advisers must surely have forgotten that psychiatric patients very often hoard their drugs when they want to commit suicide. In fact, the whole case is full of doubts and uncertainties when the evidence is examined at all critically, especially as she had previously been on combined drugs for so long in hospital without harm and had also threatened suicide in the past.

This patient's symptoms of unconsciousness with hyperpyrexia, slow respiration, increasing cyanosis, rigid legs, and ankle clonus have, however, all been seen with suicidal overdoses of imipramine alone, and in cases of suicidal overdose with both groups of drugs combined. If the antidepressants had anything at all to do with it, the former is the most probable explanation of this patient's death, for she dreaded the threat of being sent back to the local mental hospital again.

Has anybody in this country really seen any of these supposed deaths from using both groups of antidepressants combined, *in properly adjusted dosages*, and when the intake of the drugs has been correctly known right up to the start of hyperpyrexia, collapse, and death? If so, will they report them immediately. Most cases, on critical examination, turn out to be due to something else or to drug overdosage.

As the fate of so many patients is at stake if we give up the use of combined antidepressant drugs; and as one psychiatric consultant in London is now being threatened with legal action for having prescribed both groups of drugs together, the report which you have just published could, Sir, help to put us all in further jeopardy. For some of us feel we must still go on prescribing these drugs in

combination, and risk the legal proceedings that are being made more certain as a result of the Witts Committee report and reports such as your recent one. For the combined use of these drugs is often the only way to help some patients, and to prevent suicides and prolonged suffering. And I personally still believe, as a result of five years' experience, that it is generally safe to give these drugs combined in proper dosages with great benefit to many patients.—I am, etc.,

WILLIAM SARGANT.

Department of Psychological Medicine,
St. Thomas's Hospital,
London S.E.1.

Ampicillin Intolerance

SIR,—I recently had occasion to treat a middle-aged woman for acute enteritis due to *Salmonella typhimurium*. The acute symptoms did not respond to cephaloridine but did so to oral chloramphenicol. Rectal swab cultures, however, remained positive. Accordingly she was started on a course of ampicillin, 1 g. q.i.d., each dose to be accompanied by 0.5 g. probenecid. The first dose was followed by a general panic reaction characterized particularly by severe claustrophobia. As she had a past history of several episodes of anxiety state with claustrophobia the drugs were not now blamed for her symptoms, in spite of her own accusations against them. She was sent home to continue with the course, but with the second dose exactly the same symptoms occurred. Unfortunately, with neither episode was there any objective data obtained and the patient is reluctant to undergo any experiment to determine which of the two drugs is responsible. She has, incidentally, no apparent defect in renal function, and no other organic disease.

Such a reaction to ampicillin or probenecid is quite unique in my experience, and I have used both drugs widely. The cause-and-effect relationship would seem clear in this patient, but I am not fully convinced. Perhaps other readers have encountered such cases.—I am, etc.,

Gateside Hospital,
Greenock.

J. H. MITCHELL.

The Solihull Stretcher

SIR,—I was interested in the ingenious modification of the corrugated rubber mattress described by Drs. H. B. Watson and P. H. Dennison (2 January, p. 61).

I note, however, that the three movable cushions have apparently been discarded. While the cervical support may be redundant, the other two have important functions apart from increasing skin friction. A correctly placed lumbar support of the right size prevents the flattening of the spine which otherwise occurs in a relaxed patient placed supine on a flat surface, and I am sure that this reduces the incidence of post-operative back-ache. The tendo Achillis's support takes the weight off the calf muscles and minimizes flattening of the veins, with consequent venous stasis. Although I cannot support the results by statistics, my impression is that venous thrombosis and pulmonary embolism are less common if this device is used. There would seem to be no reason why these accessories

should not be used with the modified mattress.—I am, etc.,

London N.6.

C. LANGTON HEWER.

Unusual Object

SIR,—Dr. P. N. Stanbury's experience (26 December, p. 1660) with intestinal obstruction from a clotted-milk mass is not exceptional and I have heard of several similar cases, including one of my own when engaged in diagnostic radiology. A colleague's wife had complained of upper abdominal pain and vomited a banana-like hard mass of clotted milk with relief. When I x-rayed her I saw that the barium collected in a pool the exact shape and size of this mass in the distal part of the duodenum, being held up by kinking at the duodenal-jejunal flexure when standing erect, but this was relieved when lying. At one time there was believed to be a sphincter at this site, but I think the more modern view is that kinking can occur in asthenic states about the relatively fixed flexure which is supported by the ligament of Treitz.—I am, etc.,

Hove 3, Sussex.

ESMOND MILLINGTON.

Pleural Effusion and Breast Cancer

SIR,—A review of the records of this department revealed 79 patients with pleural effusions secondary to carcinoma of the breast. In three cases bilateral effusions developed simultaneously, leaving 76 in which the side of the effusion can be compared to that of the primary tumour.

In 49 cases the effusion was ipsilateral, and in 27 contralateral, a just significant excess of ipsilateral effusions. There is no significant association between the laterality of the effusion and the original clinical stage of the disease, but both laterality and stage appear to be related to the time of appearance of the effusion. In the Table the two figures quoted in each group are the effusions occurring within two years of the first treatment, and those appearing later than this. The excess of ipsilateral effusions is concentrated in the first two years; this tendency is notable in all stages except stage I, and is statistically significant.

Some figures from the Christie Hospital, Manchester, provide a slightly different picture. They were provided by Professor Ralston Paterson and Miss M. Russell, and are quoted by their kind permission. The Christie figures show a significant excess of ipsilateral effusions (43 to 27), but this excess is not concentrated in the first two years, but spread evenly over the five-year period reviewed. The staging of the Christie series took account of pathological data, and so cannot usefully be compared with the purely clinical staging used in this series.

There appears to be a definite excess of ipsilateral effusions in cancer of the breast.

Stage	Ipsilateral	Contralateral
I	0+12	0+7
II	9+7	1+10
III	5+4	0+1
IV	10+0	4+3
Not known ..	1+1	0+1
Totals	25+24	5+22