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 (amitryptyline) 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 amitryptyline 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 overdosage 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.
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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 backache. 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

The Oxford series suggests strongly that this excess is largely concentrated in the first two years of the disease, but this is not supported by the Christie data. Effusions arising from haematogenous spread should arise equally often on either side, so that the excess of ipsilateral effusions suggests another mode of spread. This other mode of spread is presumably permeation of the chest-wall, the tumour invading inwards towards the pleura rather than outwards towards the skin. Prompt and energetic treatment of the chest-wall after mastectomy, especially in stage II, may be worth while, even at the risk of a minor degree of lung fibrosis.—I am, etc.,

Radiotherapy Department, Churchill Hospital, Oxford. E. H. PORTER.

Hospital Infection with Pseudomonas pyocyanea

SIR,—The leading article on hospital infection with *Pseudomonas pyocyanea* (24 October, p. 1019) prompts me to call attention to an outbreak of meningitis caused by that micro-organism which occurred in one of the hospitals in our county several years ago.

At the request of the hospital administrator, an investigation was made of four cases of meningitis due to *Ps. aeruginosa* (the American equivalent of *Ps. pyocyanea*). Two of the patients died while the search for the cause was in progress.

The patients were of various ages (3½, 6, 7, and 35 years), resided in various parts of the county, and had no direct contact with one another neither before nor after admission to the hospital. They were admitted to three different wards for diagnosis and treatment for different illnesses (suspected poliomyelitis, suspected brain tumour, and acute glomerular nephritis). Each of the four patients had a diagnostic lumbar puncture performed on or soon after admission. The punctures were made by three different medical interns in the three wards. Normal spinal fluid was obtained in all four instances. On culture, two of the fluids were found to be sterile, the other two contained contaminants, *Ps. aeruginosa* and *C. diphtheroid*, respectively. As there was no evidence of cellular reaction at that time, these micro-organisms presumably were not present in the spinal meningeal space previous to the withdrawal of the spinal fluid.

Signs of meningitis appeared from 4 to 12 days following the initial lumbar punctures. On subsequent spinal taps, definite cellular response was evident in the spinal fluid (turbidity and marked increase in the number of leucocytes with a predominance of polymorphonuclear cells), and *Ps. aeruginosa* was isolated on culture of the spinal fluid of each of the four patients. The micro-organism was also isolated from the brain of the fatal cases on post-mortem examination.

In view of the history and distribution of the cases the only common-source factor appeared to be the central supply of the hospital where the lumbar puncture kits originated and were supposedly sterilized. Investigation revealed that the man who usually carried out the autoclaving had been on vacation during the period of the time the kits used on the four patients were autoclaved. During his absence an orderly unfamiliar and inexperienced with the procedures, and apparently indifferent to careful technique, operated the autoclaves.

An analysis of the records of 271 autoclaving procedures carried out by the substitute, and a study of the "ATI Steam-Clox" used with each pack, revealed that 43, or 16% of them, indicated undertiming, and 14% overtiming, of autoclaving, thus suggesting considerable laxity in this procedure. It was also found that only 15 out of 602 packs sterilized, or 2.5%, were undertimed for a comparable period by the regular staff. When these ratios are put to the chi-square test, an answer of 54 is obtained, indicating that their difference is definitely significant and it is most improbable that chance alone could have been responsible for it.

Study of other admissions to the hospital disclosed the presence of an infected burn case from which *Ps. aeruginosa* had been cultured, and a ruptured appendix showing the same organism. Review of the hospital procedures suggested that rubber gloves might have served to disseminate infection. Gloves were used in the dressing of the infected wounds, as well as in the performance of the spinal punctures. The soiled gloves were washed in a Westinghouse washing machine with added disinfectant and detergent, dried in a mechanical dryer, blown up, inserted into envelopes, and then subsequently, presumably, inadequately autoclaved. Bacteriologic study of limited available unused material "sterilized" during the critical period, and a search for missed cases among hospital patients who received lumbar punctures at that time, proved unrevealing.

Control measures were recommended to the hospital administrator and no additional case has occurred.

—I am, etc.,

I. JACKSON TARTAKOW.
Nassau County Dept. of Health, Mineola, New York, U.S.A.

Diagnosis of Xanthelasma

SIR,—In their interesting paper describing the effects of the administration of Atromid to a small group of patients with high blood-cholesterol levels, xanthoma tuberosum, and xanthelasma palpebrarum, Dr. B. Mason and Professor C. Bruce Perry (9 January, p. 102) remark the absence of any effect on the lesions of two patients with xanthelasma palpebrarum in contrast with the disappearance of the lesions in four patients with xanthoma tuberosum.

Their findings might be illuminated and perhaps explained by surgical biopsy of the lid lesions that they accept as xanthelasma on presumably clinical grounds. I suspect they will discover, as I have done on several occasions, that these lesions are in fact simple miniature epidermoid cysts composed of keratin squames and not essentially lipid deposits at all.

Lentil-like yellowish nodules in the skin of the eyelids are often seen in adults of both sexes, but especially in the middle-aged and elderly—that is, the same patients in whom vascular disease and elevated blood cholesterol are not uncommon—but I think it is uncritical to call all such lesions xanthelasma palpebrarum without producing histological or chemical proof of the assumption.—I am, etc.,

London S.E.10. PETER J. E. WILSON.

Drugs for Algeria

SIR,—I have been interested in Algeria for many years now and am helping them all I can in their work of reconstruction. About a year ago I appealed for drugs to be supplied by way of doctors' samples. I have now heard again that they require vitamins and antihistamines. Dr. Marie-Jose Renard, of Tiza Rached (Grande Kabylie), and of the European Committee for Non-Governmental Aid has written me to make the appeal.

I would be very glad if you could appeal through your columns for such drugs. If they are left with me I will arrange for them to be sent on.—I am, etc.,

6a Belsize Park Gardens, London N.W.3. JOHN BAIRD.

Estimation of Haemoglobin

SIR,—In the article on haemoglobinometry in the series "To-day's Drugs" (2 January, p. 40) the comment is made that the M.R.C. grey-wedge is the "best available instrument for the enthusiastic practitioner." As one who has used this instrument for many years in general practice I am in complete agreement.

The price of the M.R.C. grey-wedge is, nevertheless, high. Without influencing its accuracy an attempt has been made—in collaboration with the manufacturers of the standard apparatus—to produce a simplified instrument at about half the price. This has been done by reducing the range. The M.R.C. photometer estimates haemoglobin from 4 g./100 ml. to 22 g./100 ml. In general practice a patient with a severe degree of anaemia or polycythaemia is best investigated by a competent haematologist. The modified grey-wedge photometer is only calibrated from 6 g./100 ml. to 16 g./100 ml. Thus by using a smaller grey-wedge a considerable reduction in costs has been achieved and accurate haemoglobinometry has been brought into the scope of even a single-handed general practitioner.

To make the instrument even more versatile it has been calibrated for use with either oxyhaemoglobin or cyanmethaemoglobin. There are two scales, one of which can be covered at a time. (A simple adjustment with two screws makes the selection easy.)

Field trials so far undertaken have shown the instrument to be satisfactory in use and accurate. The trials are not yet complete. Production should commence within a year. It will be manufactured by Messrs. Keeler, of Wigmore Street, London, who also make the M.R.C. grey-wedge photometer. They are calling the simplified photometer the "Haemoscope."—I am, etc.,

London W.12. STUART CARNE.

"Neo-Listerism"

SIR,—In the article on antiseptics (12 December, p. 1513) we are reminded that Lister was successful in reducing the number of wound infections by prophylactic application of an antiseptic (carbolic acid) to wounds and that antiseptics are still valuable in surgery for skin disinfection and to assist in the control of cross-infection. Implied in this statement is the idea that antiseptics are no longer suitable for application to wounds.

For ten years we have had at our disposal a non-toxic antiseptic suitable for direct application to tissues and not significantly inhibited by blood, serum, or pus. I refer, of course, to chlorhexidine (Hibitane). Yet this new antiseptic has received no universal recognition of its efficacy in sterilizing open wounds.

In 1965 we will celebrate the centenary of the first successful case treated antiseptically by Lister. Yet, ironically enough, a hundred years later in spite of having vastly superior antiseptics we have almost totally rejected Listerian principles. Lister's attitude can be