completely to ignore the diversity of conditions loosely termed depressive and the clear need for matching the pharmacotherapy to the case. We regard the suggestion that either of two drugs of which there is limited experience should be the "antidepressant of first choice" as ill-founded and irresponsible.

P DALLY
J GOMEZ

Psychiatric Department,
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SIR,—I found the views expressed by Dr C L Brewer (20 August, p 523) concerning antidepressant prescribing interesting and challenging, as no doubt they were to other doctors and the pharmaceutical companies. Dr Brewer expresses the view that either mianserin or flupenthixol should be the antidepressant drug of first choice in general practice, but he makes no mention of hospital prescribing.

Large numbers of patients receiving antidepressants from their GP have been started on them in hospital; surely these patients are also at risk from taking an overdose—indeed the risk is probably greater since their depression is likely to have been more severe, necessitating hospital referral in the first place. Dr Brewer should therefore have carried the logic of his argument through to hospital practice, and not limited his strictures to general practice alone.

CLIVE STUBBINGS

Exeter, Devon

Fatal agranulocytosis attributed to co-trimoxazole therapy

SIR,—Professor D H Lawson and Dr D A Henry (30 July, p 316) suggest that we could have expected a "major increase" in the frequency of fatal blood dyscrasias if, as I suggested (11 June, p 1500), a substantial proportion of deaths from agranulocytosis were causally related to the use of co-trimoxazole. They point, quite rightly, to the difficulty in distinguishing cause from effect in patients in whom a blood dyscrasia, particularly agranulocytosis, is so closely associated with infection and its treatment with anti-infective drugs. If such therapy was coincidental, however, one might expect antibiotics such as ampicillin or the tetracyclines, some of which are used even more frequently than co-trimoxazole, to have been noted more often in the "drug history".

It is true that the frequency of fatal agranulocytosis has not changed since co-trimoxazole was introduced in 1968, ranging from between 19 and 38 deaths in each year (from 1960 to 1974). If co-trimoxazole was not a cause of agranulocytosis one might have expected a reduction in frequency to have dated from about this time because of the diminished use of at least one other drug known to be a frequent cause of blood dyscrasias.

Although adverse reactions are seriously under-reported, deaths attributed to chloramphenicol were reported to the (then) Committee on Safety of Drugs at an average rate of one per month up to the time of their publication of a pamphlet reminding prescribers about the dangers of this antibiotic (Adverse Reactions Series No. 4, 1967). This had a profound effect on the use of systemic

chloramphenicol and, apart from isolated deaths of travellers returning to the United Kingdom after treatment abroad, deaths from chloramphenicol-induced dyscrasias have virtually ceased to occur. Other changes in the past 10 years include a reduction in the use of thiouracil and a trend towards the use of co-trimoxazole in place of other sulphonamides. Thus the fact that there has been no change in mortality since co-trimoxazole was introduced may simply reflect a change in pattern of use of drugs liable to cause blood dyscrasias rather than the absence of cause-effect relationship. It is perhaps reassuring that the total mortality among the many patients receiving this mixture of drugs appears to be so small.

W H W INMAN
Principal Medical Officer,
Committee on Safety of Medicines

London EC2

When do we stop vaccinating against smallpox?

SIR,—With reference to your leading article on vaccinating against smallpox (13 August, p 413) it is felt that you have been slightly unjust to the armed Forces. While not disputing in any way the tenor of the arguments against routine smallpox vaccination, it does seem that insufficient account has been taken of the special position of the armed Forces. In the Army we do train or have training teams in African countries adjacent to the last known smallpox area. We have military attachés in most foreign countries. The spearhead battalion stationed in the UK, a task which rotates between different infantry battalions, is ready to move at very short notice to any part of the world. The services are always ready to meet the call for assistance in a disaster situation in any area. The Royal Navy and the Royal Air Force have similar commitments. In order to meet these commitments there may not be "plenty of time to immunise them before departure."

For the moment we tend to side with Espmark's view, but we are flexible and certainly we have no intention of continuing routine smallpox vaccination any longer than we consider to be necessary. Junior soldiers and apprentices are no longer vaccinated against smallpox until they reach man's service. Dependents are vaccinated only if it is required by the country to which they are proceeding.

The present policy may, if you like, be described as an insurance policy. In your leading article you agree that the country needs an insurance policy. At present the services prefer to be "paid-up members," already immunised, rather than depend on the stockpile principle.

WILLIAM S MILLAR
Director of Army Health
and Research

Ministry of Defence,
London SW1

Arc flash and the contact lens wearer

SIR,—There has been considerable correspondence between individuals, company management, and union officials on the one hand and general practitioners, ophthalmologists, and the optical profession on the other asking if a person's eyes are at risk if, while wearing contact lenses, he is subjected to an arc flash,

the normal precautions of wearing protective glasses being taken.

It is amazing that such a simple question should be asked so frequently when an ophthalmic surgeon¹ involved in this problem has gone on record as saying, "It is extremely likely that the contact lens, whether it be made of glass, plastic, or soft lens, would reduce the penetration of ultraviolet light, if not eliminate it completely, so that a person wearing contact lenses might be regarded as more protected than one not doing so. If he was wearing micro lenses the sclera and conjunctiva would not be covered, but even so protection would be given. On the other hand there is no doubt that if a micro contact lens wearer did sustain a flash burn he would have some degree of ultraviolet keratoconjunctivitis and this might be further irritated by the lens. I certainly do not regard this as a serious problem and would not dream of suggesting that anyone should stop wearing his contact lenses if he were likely to have an arc-welding flash. Now, on balance, I would be rather in favour of them."

A second statement has been made in an open letter from another ophthalmic surgeon²: "We have had advice and conclude that heat from an arc weld flash likely to affect the plastic of the contact lens would have the same effect on the plastic used in the protective goggle. There is no evidence that the goggle is affected by this degree of heat and therefore the plastic of the contact lens would likewise be unaffected. Furthermore the power correction in the contact lens will not concentrate the radiations more than the normal eye. Therefore the safety goggle, when worn, gives adequate protection to the contact lens wearer exposed to flash."

The question of the safety of the contact lens wearer exposed to arc flash continues to be asked because of statements published over the past 10 years. These statements, believe it or not, generated from a single incident misquoted and requoted since 1967. Such emotive statements as "When he later tried to take out his contact lens large areas of dried cornea came off his eyes with them. . . doctors were unable to save his sight"³ and "Contact lens hazard—contact lenses should not be worn even under spectacles in any area where an arc flash could occur"⁴ have been made.

The real story, as given by the Medical Director of the Bethlehem Steel Corporation in July 1972, is as follows. The injured employee was a welder, an employee of the Bethlehem Steel Corporation, working in a shipyard in Baltimore. On 26 July 1967, while he was plugging welding units into a 440-V service line, the electrical switch box "exploded." Witnesses describe "brilliant lights" accompanying the blow-up. The injured man was wearing contact lenses at the time and industrial safety glasses. He had no complaints following the incident and did not report any injury until the following day, at which time he reported the above facts and admitted that he had not removed his contact lenses for at least 12 h after the incident. He had large corneal ulcerations and was referred to an ophthalmologist as an emergency consultation. The two ophthalmologists who carried out the examination and treatment advised that in retrospect they believed that the electric flash had no part in the causation of the corneal injuries but that these resulted from neglect by the patient, absence of elementary precautions, and over-wear of the contact lenses. Within a few days his vision had returned to normal.

So we have one story, wildly reported, and by appearing in print gaining the substance of fact. What is a fact is that all the frequent discussion of this case has not resulted in the publication of one other case. It is important, therefore, that everyone should know the story so that inaccuracies can be refuted as soon as they are uttered, not after they have been published.

My thanks go to Mr Philip Cordrey, Contact Lenses Manufacturing Ltd, for supplying me with the correspondence which is the substance of this letter.

H J KERSLEY
President-Elect,
British Contact Lens Association

London

¹ Report to the Royal Society for the Prevention of Accidents from the Consultant Ophthalmic Surgeon to the Department of Employment, November 1973.

² Ruben, M, open letter on behalf of the Contact Lens Society, February 1976.

³ Circular to employees of Thames Valley Water Authority from the Senior Resident Engineer, 16 July 1975.

⁴ *Journal of Occupational Safety and Health*, October 1973.

Barbiturates and fractures

SIR,—Drs J B and E T Macdonald (20 August, p 483) have shown a highly significant correlation between the ingestion of barbiturate hypnotics and nocturnal fractures of the femur. It is curious that none of the patients sustaining fractures in the afternoon were on barbiturates; it would be expected that fractures would occur with an equal incidence in patients on barbiturates and those on non-barbiturate hypnotics if neither drug affected the likelihood of fractures occurring at this time. Either barbiturates protect against afternoon fractures (which seems unlikely) or other hypnotics predispose to fractures occurring in the morning and afternoon. Unfortunately there is no comparison of the temporal incidence of fractures in patients not taking hypnotics (a reflection, perhaps, of the overuse of these drugs in the elderly), so that neither intriguing possibility can be explored. It would also be interesting to know if there was a significant correlation between non-barbiturate hypnotic use and frequent falls, as there was with barbiturate use.

There is a high incidence of osteomalacia in elderly patients with fractures of the femur¹; and osteomalacia is a recognised complication of the chronic ingestion of long-acting anti-convulsant barbiturates² (for example, phenobarbitone), which reduce the level of circulating 25-hydroxycholecalciferol³ by inducing hepatic microsomal enzymes. This effect is likely to be of particular significance in the elderly, whose nutritional status with respect to vitamin D may already be less than ideal. That this may occur with other barbiturates (those with shorter plasma half lives, used as hypnotics) is suggested by the results of a recent survey in which patients taking these drugs were found to have lower serum calcium concentrations than controls.⁴ Though there was no significant increase in serum alkaline phosphatase activity in these patients and only 26.4% of the patients with fractures in the Macdonalds' survey were taking barbiturates in comparison with from 41% to 51% of newly referred outpatients (the increase between 1973 and 1976 is itself a worrying trend), the possibility of an increased incidence of osteo-

malacia is another reason for not prescribing barbiturate hypnotics in the elderly.

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¹ Jenkins, D H R, *et al*, *Journal of Bone and Joint Surgery*, 1973, **55B**, 575.

² Dent, C E, *et al*, *British Medical Journal*, 1970, **4**, 69.

³ Hahn, T J, *et al*, *New England Journal of Medicine*, 1972, **287**, 900.

⁴ Young, R E, *et al*, *Postgraduate Medical Journal*, 1977, **53**, 212.

SIR,—Drs J B and E T Macdonald (20 August, p 483) are to be congratulated on their excellent article. Should one prescribe barbiturates other than for epilepsy, then we initiate the hazard of addiction and poisoning. So often it is thought that our patient is the exception to the rule. It is highly dangerous to imagine any exceptions to this rule. Confusion, even dementia and terminal illness, are not always recognised as being related to chronic barbiturate administration.

Alas, I doubt whether this informative article will affect our prescribing. Fortunately a summary appeared in *The Times* of 19 August and this may be more effective. An American lawyer pointed the article out to me and the sooner relatives query every barbiturate prescription the sooner this problem will decrease.

ANTHONY CHURCHER

Eastbourne, Sussex

Superior vena caval obstruction complicating fiberoptic gastroscopy

SIR,—The case reported by Dr J Dawson (6 August, p 368) raises several interesting points.

Although the complication was unavoidable in his patient, its occurrence emphasises the need to avoid immediate endoscopy in patients with mediastinal obstruction and to wait until radiotherapy has reduced the obstruction. There is little urgency for a tissue diagnosis, as almost all these patients have carcinoma of the bronchus, though 2-3% have other tumours, and benign causes of superior vena caval obstruction are now very rare.¹

The second point is his comment that superior vena caval obstruction is an uncommon complication of carcinoma of the bronchus. In fact it occurs in 10-15% of these patients—that is, 3000-4500 patients every year in Britain. Its incidence is comparable to that of carcinoma of the bladder or of the oesophagus.

Lastly, although pain is often a feature of carcinoma of the bronchus, it is not a specific feature of superior vena caval obstruction.

N HOWARD

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¹ Howard, N, *Mediastinal Obstruction in Lung Cancer*. London and Edinburgh, Livingstone, 1967.

Nocturnal infusions

SIR,—I was pleased to see the paper by Mr I H Frazer and others (23 July, p 232) confirming that the incidence of infusion phlebitis is directly related to the duration of infusion. However, as pointed out previously,¹ the pre-

vention of thrombophlebitis is not the only reason for taking down infusions at night. Keeping infusions going overnight is rarely necessary as well as being unphysiological and potentially dangerous. At night fewer nurses are on duty and the darkness makes it difficult to keep an accurate check on infusions. With no nocturnal infusion the patient sleeps better—fewer checks by the nurses are required and the need to pass urine is reduced—and there is less chance of overloading the patient with fluid. In addition other patients in the ward have a more peaceful night and the nurses are free to attend to other duties.

The disadvantages of such a policy are the cost of extra infusion sets and the fact that housemen will have to put up infusions more frequently. However, as the infusions have to run for only 12-18 hours, smaller needles, which are easier to insert, can be used. Surely more peaceful nights for all patients in the ward and fewer complications more than compensate for these minor disadvantages. An added bonus for the houseman is that he is not disturbed at night because of trouble with his infusions.

In short, I maintain that except for intensive care and for the first postoperative night nocturnal infusions are rarely indicated, are potentially dangerous, and are unfair to our patients and our nurses.

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¹ Sturzaker, H G, *British Medical Journal*, 1975, **4**, 163.

Zinc again

SIR,—Your leading article (11 June, p 1493) comments on two papers which describe the apparent beneficial effects of oral zinc sulphate on acne vulgaris.^{1,2} Although "it is far too early to assess the full meaning of the findings," you hint that this work should be expanded and confirmed. However, we feel that the following comments are warranted before large-scale trials using oral zinc sulphate are started.

In their clinical study Michaëlsson *et al*¹ included a placebo group of 14 patients but "for ethical reasons" added oral zinc sulphate to their treatment after only four weeks of the 12-week study. With a placebo effect of between 19 and 56% improvement in acne vulgaris we feel it would not have been unethical to continue placebo until 12 weeks and provide data for meaningful analysis.

Our second point concerns the dosage of oral zinc sulphate. In Michaëlsson's studies each patient received a total daily dose of 600 mg effervescent zinc sulphate, equivalent to 135 mg of ionic zinc, which is many times the US National Research Committee's recommended dietary allowance of 15 mg ionic zinc per day. Although toxic side effects from oral zinc sulphate are said to be rare,³⁻⁵ acute zinc toxicity, manifest as nausea, vomiting, diarrhoea, and haemolytic anaemia, has been documented as occurring in patients with chronic renal failure receiving intermittent haemodialysis.^{6,7} Acute toxicity occurred with venous plasma levels of 45 $\mu\text{mol/l}$ (294 $\mu\text{g}/100\text{ ml}$). Unpublished work by Glover has shown that one 220-mg capsule of zinc sulphate causes the venous plasma zinc concentration to rise from a normal fasting value of 15.3 $\mu\text{mol/l}$ (100 $\mu\text{g}/100\text{ ml}$) to an average value of 40.1 $\mu\text{mol/l}$ (262 $\mu\text{g}/100\text{ ml}$) at 1½-3 hours. Several of the volunteers in this study became