concentration of the dialysate still gave a negative result.

This woman clearly had a massive overdose of tricyclic antidepressants and it was considered that her chances of survival were extremely poor. It seemed to us that haemodialysis was responsible for a dramatic clinical improvement. This does not seem to be supported by the analyses for the drug we were able to make. In fact the decrease in plasma imipramine level did not approach the half-time of $3\frac{1}{2}$ hours reported by Ciba-Geigy (N.Z.) Ltd. (personal communication). From our results no increase in the rate of fall of plasma imipramine occurred during dialysis. Unfortunately the lack of samples prior to dialysis leaves some doubt on this point. Our inability to locate any imipramine in the dialysate may be explained by the interesting comments of Drs. Asbach and Schüller (24 August, p. 524) who claim that imipramine is taken up by the polyvinyl chloride of the extracorporeal blood-line system. Our limited experience, that of Harthorne *et al.*³ and the recent letters from Drs. Asbach and Schüller have encouraged us to give early consideration to this form of treatment in patients with severe poisoning. However, the recovery of significant amounts of drug by forced diuresis may yet indicate that this method is the most suitable way of eliminating absorbed imipramine and other tricyclic antidepressants.—We are, etc.,

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¹ Grove, J., and Halliwell, J. V., in *Manual of Analytical Toxicology*, ed. I. Sunshine, p. 189, Cleveland, Chemical Rubber Company Press, 1969.

² Niyogi, S. K., *Forensic Science*, 1973, 2, 67.

³ Harthorne, J. W., Marcus, A. M., and Kaye, M., *New England Journal of Medicine*, 1963, 268, 33.

Poisoned Children

SIR,—I was interested to read Mr. M. Calnan's letter (28 September, p. 802). I believe that the distinction he draws between true poisoning and poisoning scares is not clinically useful. In practice parents are rarely certain exactly how much of a poisonous substance their children have taken. Sending children home who have probably taken only a negligible amount of a poisonous substance would be bound to lead to the occasional disaster. Mr. Calnan, in defining "true poisoning," says that the presence of a symptom or sign is necessary. However, it is the aim of treatment by rapid stomach emptying to prevent symptoms or signs occurring. I am in the process of examining prospectively cases of child poisoning admitted to hospitals in Cardiff under the age of 5 years. Of 85 cases so far studied, in only seven was the substance ingested innocuous. Indeed, it seems from Mr. Calnan's own figures that if only 44% of his cases were admitted overnight, the majority of children taking innocuous substances would be sent home and not figure in the 16,500 children admitted nationally each year for accidental poisoning.

Mr. Calnan mentions unnecessary procedures performed on children which may in fact do harm; by that I suspect he means gastric lavage. However, now the majority of paediatric departments are using ipecacuanha emesis, a procedure that is as effective as gastric lavage with minimal risk.¹ I cannot believe that the current debate on childhood poisoning is alarmist if 22 children died in 1972 from this cause.² Many more would certainly have died without therapy.

I am sure that Mr. Calnan is right that the health education campaign may not be as beneficial as it has been hoped. This is not only because of his evidence that 79% of medicines were in use within 24 hours of the accident. We have found that so far in our study in Cardiff serious stress is commonly found in the families of accidentally poisoned children, and at such times the parents are unlikely to remember health education propaganda.—I am, etc.,

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¹ Reid, D. H. S., *Archives of Disease in Childhood*, 1970, 45, 428.

² Registrar General's Statistical Review of England and Wales for 1972, Part 1, Tables, Medical, p. 176. London, H.M.S.O., 1974.

Liver Hamartomas in Patients on Oral Contraceptives

SIR,—The report by Dr. G. Vosnides and others (31 August, p. 580) of a case of liver hamartomas and its possible association with oral contraceptives merits comment in order to place this implied risk of adverse effects of oestrogen-progestogen preparations on the liver in perspective. Reports such as these might cause undue concern in women on the Pill.

The patient in question was receiving large doses of "oral contraceptives" and, in particular, was receiving doses of mestranol between 50 and 150 µg per day, well in excess of that recommended by the Committee on Safety of Medicines resulting from the findings of Inman *et al.*¹ We have shown² that in women taking this preparation there can be a high output of endogenous oestrogen at times. The significance of this remains to be clarified, but it does suggest that excessive ovarian activity can occur on occasion in women taking these preparations. In such a patient who is maintained on haemodialysis there is thus a possibility that large amounts of oestrogen, both exogenous and endogenous, might accumulate.

It would be preferable to use, and the menorrhagia is more likely to be kept in check by, an oestrogen-progestogen preparation which had a bias towards a major anti-oestrogenic effect on the genital tract such as the preparations containing larger amounts of norethisterone or its acetate with the oestrogen within the recommended dose rather than a low-dose combined preparation. If this proved to be inadequate to control the heavy bleeding the antioestrogenic effect could be augmented by adding extra norethisterone or its acetate as the case might be. This would obviate increasing the dose of both the oestrogen and progestogen as was done in the case reported. This would be particularly relevant

in the circumstances described and would minimize the risk of an accumulation of oestrogens within the body.—I am, etc.,

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¹ Elstein, M., *et al.*, *British Medical Journal*, 1974, 1, 11.

² Inman, W. H. W., *et al.*, *British Medical Journal*, 1970, 2, 203.

Cardiovascular Disease and Peptic Ulcer

SIR,—In your leading article (28 September, p. 760) you describe the problems in determining whether the association between cardiovascular disease and peptic ulcer is real. In two recent articles my colleagues and I discussed aspects of this association. In the first article¹ we reported 51 patients who underwent surgery for their abdominal aortic aneurysms. Twelve of these 51 patients were found to have an associated peptic ulcer at operation. Seven of these 12 patients developed complications following the resection of their abdominal aneurysm which were due to the associated peptic ulcer—namely, to haemorrhage or to perforation of the ulcer. On the basis of these findings we felt that this association was not only real but should influence the management of patients with abdominal aortic aneurysms.

In our second article² we analysed the amputation rates in 300 patients who underwent arterial reconstructive surgery for severe ischaemia of the leg. Seventy-one of these 300 patients also had an associated ulcer. In those with an ulcer the chances of losing a leg were from two to three times as high as in those without, and the chances of losing both legs were four times as high. In every other respect—sex, age, pattern of disease, and type of surgical treatment—the two groups (those with and those without an associated ulcer) were comparable.—I am, etc.,

A. P. BARABAS

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¹ Bouhoutsos, J., Barabas, A., and Martin, P., *British Journal of Surgery*, 1973, 60, 302.

² Bouhoutsos, J., Barabas, A., and Martin, P., *Postgraduate Medical Journal*, 1972, 48, 671.

Understanding Blindness

SIR,—Dr. J. A. Shaw in his Personal View (21 September, p. 738) does a great service not only in publicizing the difficulties of his unseeing fellows, but also in helping those of us who work with the visually handicapped by improving our insight into a situation which a sighted person can never fully appreciate.

I have always found personal accounts of illness written by medical men particularly helpful in my attempts to understand a patient's point of view. I believe we could learn a great deal if more doctors with impaired vision would put their thoughts on paper. I do not believe that doctors' awkwardness with the blind is simply a result of their frustration at not being able to cure blindness. Indeed, I think Dr. Shaw's suspicion that doctors' attitudes are no different from those of laymen is correct. Blindness is, after all, a state entirely beyond

the experience of a sighted person. Blind-folding will give some idea of the physical disabilities of the blind but no idea of the heightening of his other senses which he may eventually employ. It cannot reproduce the emotional background. We are so used to "eye to eye" relationships with our fellows that we inevitably feel insecure at our first meeting with someone with whom this is impossible.

As for teaching, I do not foresee any improvement in the situation as less and less time becomes available for specialized teaching of this sort. The task of equipping the family doctor to anticipate the odd ophthalmic disaster is bound to take precedence over training him for all but the most rudimentary aspects of care and rehabilitation of the blind and partially-sighted. Nevertheless, the family practitioner must have confident recourse to others who can supply this expertise, and such others will be grateful to Dr. Shaw for helping their understanding.—I am, etc.,

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Vitamin D and Myocardial Infarction

SIR,—It was most interesting to read in Professor V. Lindén's article (14 September, p. 647) that according to his investigations the consumption of vitamin D was significantly higher in infarction patients than in control subjects.

As Professor Lindén points out, fish liver is the natural source of vitamin D in Norway. In Britain the main source is egg yolk, one of the few natural foods in the diet containing vitamin D in quantity. My research on the intake of eggs in the United Kingdom¹ shows a rapid rise in consumption since 1920, apart from short periods of relative deprivation during the 1939-45 war. I have demonstrated that the rise in egg consumption closely follows the rise in mortality from coronary heart disease, and though egg yolk is also a rich source of cholesterol it may be that the presence of vitamin D in the yolk is an added potent factor associated with coronary heart disease as highlighted by my investigations.

While the aetiology of coronary heart disease is considered to be multifactorial, the potential danger of consuming eggs in quantity should not be overlooked.—I am, etc.,

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¹ Eskin, F., *Community Health*, 1971, 2, 179.

Glucagon in Management of Perforated Oesophagus

SIR,—I read with interest the paper by Mr. O. Daniel and his colleagues (21 September, p. 720) on the use of glucagon in the treatment of acute diverticulitis. I have used it in the management of iatrogenic rupture of the oesophagus in elderly, bad risk patients. Many of these patients are unacceptable candidates for major surgery and any agent that may assist in the conservative management of the case is of interest.

Glucagon is a potent suppressor of gastric secretion.¹ Since the initial mediastinitis after

perforation of the gullet must be largely due to chemical irritation, any agent that reduces both the quantity and acidity of gastric secretion might be expected to be of benefit. Furthermore, there is evidence that glucagon diminishes gastric motility and also has an antispasmodic effect on the lower oesophageal sphincter.² Reducing motility in the upper gastrointestinal tract should diminish the amount of gastro-oesophageal contents expelled through a perforation.

On this theoretical basis I gave glucagon to three elderly patients with perforated oesophagus. A subclavian central venous line was inserted immediately the diagnosis was made and oral fluids were withheld. Cephalothin was administered in bolus doses of 3 g every six hours and glucagon was given in an initial dose of 1 mg over five minutes and subsequently at a rate of 2 mg every six hours by continuous infusion. Glucagon was continued until a Gastrografin swallow indicated that the perforation was sealed off. This occurred within four days in one case and within five days in the other two cases. A noteworthy feature of these three cases was that at no time was it necessary to drain the chest. Only minimal amounts of fluid were detected in the pleural cavities.

In the light of these results I suggest that when it has been decided to treat a case of lower oesophageal perforation conservatively glucagon may well contribute to therapeutic success.—I am, etc.,

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¹ Dotevall, G., and Kock, N. G., *Gastroenterology*, 1963, 45, 364.

² Jaffer, S. S., et al., *Gastroenterology*, 1974, 67, 42.

Periodic Fever

SIR,—At what stage does one stop investigating a patient with recurring bouts of pyrexia and persuade him instead to accept a "diagnosis" of "Periodic Fever"?

A 65-year-old man has suffered from recurring bouts of fever for four years. The temperature rises to 38°-39°C for 24 hours every five days, with aching in the loins and varying degrees of prostration. All investigations have been negative and there has been no response to antibiotics or to steroids. A chance finding was that the expected spike of fever failed to appear on three occasions following administration of tetanus toxoid. Careful monitoring of temperature has shown accentuation of fever every 31 days, suggesting that the underlying rhythm is 124 hours, coinciding every 31 days with the normal circadian temperature rise. A pint (0.6 l.) of blood, removed at the height of the fever, produced a fever when retransfused on the third day, suggesting the presence of a circulating pyrogen.

Reimann and McCloskey,¹ in a recent report of a case of 23-day fever and mentioning a further instance of 14-day fever, make a plea for the recognition of periodic disorders due to unknown biorhythms and the avoidance thereby of the unnecessary expense and suffering of prolonged and fruitless investigation.

The purpose of this letter is twofold. Firstly, to seek help: I still feel the need to be aware of the possibility of a microbial cause for fever of five-day rhythm and, if there is one, it may be that some of your erudite readers have knowledge of it. Secondly, to bring to more general notice this extremely trying recurring disorder.

To give the term periodic fever a capital P and a capital F does not of course elevate

it to the status of a diagnosis. It may, however, draw attention to a problem still very much in need of elucidation.—I am, etc.,

T. H. BARRIE

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¹ Reimann, H. A., and McCloskey, R. V., *Journal of the American Medical Association*, 1974, 228, 1662.

Non-union of the Scaphoid

SIR,—Your leading article (5 October, p. 2) presents a well-balanced and thoughtful appraisal of the problems associated with non-union of the scaphoid. There are, however, two points which merit comment.

While grafting for non-union by the anterior approach has many adherents, it has the disadvantages of not achieving as rigid fixation as is possible by a carefully placed peg graft insertion via the posterolateral approach. This approach is objected to on the grounds of causing possible damage to the blood supply but is there any evidence to indicate that avascular necrosis or other complications have resulted from the use of this approach for the treatment of established non-union? The complication of avascular necrosis of the proximal fragment and semilunar, which is associated very particularly with varying degrees of perilunar transscaphoid dislocation, is not greater following open than closed reduction.

The second comment is that a careful excision of the whole scaphoid has proved a satisfactory procedure in the treatment of late un-united fractures, particularly those associated with osteoarthritic change. It should be emphasized, however, that if through some technical difficulty it is possible to remove only one fragment this should most certainly be the distal fragment, which is the portion affected by secondary arthritic change, the proximal fragment being in no danger in this respect. In all these operations it is certainly highly desirable to remove the distal $\frac{1}{2}$ in (8.5 mm) or so of the styloid process of the radius, but wide excision of the styloid process can affect stability.—I am, etc.,

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Management of Lithium Treatment

SIR,—I feel that in their paper on "Blood Levels and Management of Lithium Treatment" (4 September, p. 650) Dr. J. L. Crammer and his colleagues misrepresent the case as regards the diurnal variations in serum lithium levels. The evidence we have acquired from 23 experiments on patients stabilized for a minimum of 10 weeks on each of the three lithium carbonate preparations on the market is that following each dose as lithium is absorbed from the gastrointestinal tract there is a corresponding rise in the serum lithium level lasting for about two to four hours. Thereafter the level gradually declines over the interdose interval as lithium is eliminated through the kidneys. In the stabilized patient lithium equilibrium is maintained through the daily dose making good the renal lithium loss. The highest serum level found in 200 serum samples was 1.8 mmol/l. and in the vast majority of subjects the level did not fall outside the range 0.5-1.5 mmol/l. at any time during