Strip of nail removed (A) and flaps of nail wall (B) and nail fold (C) reflected to expose segment of germinal matrix (D) to be excised.

A simple and logical operation for unilateral embedded toenail was described by Heifetz in 1945.⁶ This consists of removal of a small segment of germinal matrix on the affected side of the nail. No sutures are required and healing occurs within a few days.

Mr Palmer and Mr Stevenson imply that their operation can be performed in the presence of sepsis, cutting through inflamed nail wall. A deliberate operation through inflamed tissues is bad surgical practice and sooner or later this will lead to severe exacerbations of infection. In infected cases it is safer to excise a small strip of embedded nail under local anaesthesia four weeks before surgery. This will enable an exact dissection of the portion of germinal matrix to be performed under ideal conditions.

A W FOWLER

Bridgend General Hospital,
Bridgend,
Mid-Glamorgan

¹ Watson-Cheyne, W, and Burghard, F F, *Manual of Surgical Treatment*, vol 2. London, Longmans, Green, 1912.

² O'Donoghue, D H, *American Journal of Surgery*, 1940, 50, 519.

³ Hyde, T L, *Northwest Medicine*, 1945, 44, 252.

⁴ Lake, N C, *The Foot*, 4th edn. London, Ballière, Tindall and Cox, 1952.

⁵ Fowler, A W, *British Journal of Surgery*, 1958, 45, 282.

⁶ Heifetz, C J, *Journal of the Missouri Medical Association*, 1945, 42, 213.

Rational dosage of non-cumulative drugs

SIR,—The vast majority of drugs prescribed have a half life in their persistence in the body and in their effect. Let us assume that the required effect is attained by 1 g of a certain drug and that it exerts half its effect after six hours. If 1 g is given every six hours the accumulated dosage will approach 2 g—that is, $1 + \frac{1}{2} + \frac{1}{4} + \frac{1}{8}$ etc. A simple rule for administration might well be to start with 1 g and to proceed by administering $\frac{1}{2}$ g every six hours of half the dosage every half life.

May we therefore in future be informed in the *British Pharmacopoeia* the average half life of every drug when that is practicable so that we can avoid the absurdities of prescribing drugs three times a day when the half life is a week.

D B JAMES

Marlow, Bucks

A prognostic sign in ECT

SIR,—Anaesthetists familiar with anaesthesia for electric convulsion therapy (ECT) must have observed, in a high proportion of cases, a phenomenon that could be of some prognostic value to the psychiatrist. I refer to a stage in the course of treatment when superficial arm and hand veins, previously contracted and almost invisible, making venepuncture excessively difficult, are found to be dilated and easily visualised or palpated, thus offering no difficulty in venepuncture. In my experience, shared with many psychiatrists with whom I work, this sign seems to mark the threshold of clinical improvement beyond which few further treatment sessions may be necessary.

I have been unable to discover any reference in the anaesthetic literature to this sign, but perhaps my psychiatric colleagues might be able to supply a convincing explanation of its aetiology. My uninformed guess is that it is (in part at least) a vasomotor effect in which skin temperature plays a major part. Cold, cyanosed extremities are commonly observed in severe depressive illness and, unless perpetuated by other causes, will give place to a normal skin temperature and relative vasodilatation as the clinical condition improves. Even with the onset of the generalised flush immediately following a single ECT venous dilatation may be briefly observed, especially on the dorsum of the hands.

HARRY L THORNTON

London NW8

Primum non nocere, or the pharmacological lucky dip

SIR,—A Bengali man was admitted with apparent digitalis intoxication. His electrocardiogram showed first-degree heart block, coupled ventricular ectopic beats, and S-T-segment changes consistent with digitalis effects, and his serum digoxin level was 4.9 nmol/l (3.8 ng/ml). It was not possible to relate this to dose times. There was no evidence of potassium depletion. He was in gross cardiac failure.

He said that he took two tablets regularly each day but later revised this to five. Someone brought a plastic carrier bag to the ward containing his tablets. These are recorded in the accompanying table. The five daily tablets were, he said, two Slow-K, one ampicillin capsule ("very good, doctor, very good"), and two white tablets. He drew the last items from

the phial (No 12) marked "Valium" which contained three populations of tablets—prochlorperazine, frusemide, and Buscopan (hyoscine butylbromide). Each evening must therefore have afforded him a new therapeutic surprise—tranquillity, profound diuresis, or little detectable effect. His wife, who would certainly have noticed, could not help, being in Bangladesh. His general practitioner also shared his nationality, so presumably language had not been a problem. He agreed that while he had taken digoxin, it was not part of the "regular five." Compliance with a schedule of five daily doses would be likely to be less than 25%.¹

A drug cupboard audit should be a regular part of the treatment history and examination in every case. We have encountered many who keep a pharmacological bran tub or lucky dip, but this patient is so far the most unusual. We are trying the effect of giving him a little diagram with coloured tablet symbols set against meal times, but do not yet know whether we have communicated better than anyone else.

DUNCAN VERE

Department of Pharmacology
and Therapeutics,
London Hospital Medical College,
London E1

¹ Galtey, M S, *Journal of the Royal College of General Practitioners*, 1968, 16, 39.

Breast-feeding and the BBC

SIR,—Apropos the recent correspondence on breast-feeding it might amuse your readers to know that when I wrote to the BBC suggesting that one way in which they could help to promote breast-feeding was to show it as a natural activity on the screen this was described as "eccentric" by their director of programmes. O tempora! O mores!

JOHN DAVIS

University Department of
Child Health,
St Mary's Hospital,
Manchester

Conception and congenital abnormalities after chemotherapy for leukaemia

SIR,—We read with much interest the report by Dr J A Russell and others (19 June, p 1508) of two men who fathered children with congenital abnormalities after they had received chemotherapy for acute myelogenous leukaemia. This prompts us to report a patient

Drug name on container	Instructions on label	Actual contents of container	State of contents
(1) Slow-K	One, 3 × daily	42 Slow-K	Moist, frosted, and sticky
(2) "	(Bengali writing)	7 Slow-K	
(3) "	"The tablets/capsules"	95 Slow-K	
(4) Penbritin	500 mg 4 × daily	nil	Heavily worn symbols
(5) "	500 mg 6-hourly	nil	
(6) "	250 mg 4-hourly	17 ampicillin capsules	
(7) "	250 mg 6-hourly	13 ampicillin capsules	
(8) Digoxin	0.25 mg (Bengali)	28 digoxin tablets	
(9) "	0.25 mg daily	18 digoxin tablets	
(10) "	0.25 mg, two daily	64 digoxin tablets	
(11) Valium	5 mg 3 × daily	2 diazepam tablets	
(12) "	5 mg, one at night	245-mg prochlorperazine tablets	
(13) "	One at night	24 40-mg frusemide tablets	
(14) Stemetil	5 mg, "one to be taken twice times a day"	20 Buscopan tablets	Worn symbols
(15) Aldactide	3 × daily	15 10-mg diazepam tablets	
(16) Buscopan	2 × daily	nil	
(17) Lasix	40 mg daily	nil	
(18) "	40 mg "The tablets/capsules"	2 frusemide tablets	
(19) "	40 mg, one to be taken a day	29 " "	

of ours who is in long-term remission after chemotherapy of acute myeloblastic leukaemia in childhood. He is now married and has two normal children.

In September 1963, when aged 9 years, he was found to have acute myeloblastic leukaemia, was treated with prednisone and 6-mercaptopurine, and went into remission. He relapsed in January 1965 and was then treated with prednisone and methotrexate, achieving a further but short remission and relapsing in July 1965. This second relapse was treated with prednisolone and cyclophosphamide and was followed by complete clinical and haematological remission which has been maintained ever since. Treatment was stopped at the end of 1967.

The patient married in 1972 and has a daughter aged 4 and a son aged 2 years, both clinically well. He was last seen (with his family) in June 1976 and found to be in continued haematological remission. Between her two normal pregnancies his wife had a miscarriage, but nothing is known about the condition of the fetus.

There are presumably other children who have achieved long-term remission after chemotherapy of acute leukaemia and have grown up to raise a family.

P BARKHAN
P R EVANS

Department of Haematology,
Guy's Hospital,
London SE1

The myth of phenelzine acetylation

SIR,—The assertion was made by Rawlins¹ and again in your leading article on monoamine oxidase inhibitors (10 July, p 69) that phenelzine is metabolised by acetylation. That this acetylation can be either fast or slow is the rationale behind the clinical studies with phenelzine in which patients are classified according to their acetylator phenotype. Evans *et al*² showed that slow acetylators complain of severe side effects but found no difference in improvement between fast and slow acetylators. On the other hand Johnstone and Marsh³ and Johnstone⁴ found that slow acetylators are more likely to improve but that there was no difference between the phenotypes in terms of side effects. The results from these studies are clearly conflicting.

In view of the possibility that acetylator phenotype is an important prognostic indicator for treatment with phenelzine perhaps it is time that the biochemical evidence for acetylation of phenelzine be considered.

A possible pattern for the metabolism of phenelzine (see figure) is based on the metabolism of isoniazid in man as outlined by Hughes⁵ and Peters *et al*.⁶ A necessary prerequisite for the polymorphic acetylation of phenelzine is the formation of acetylphenelzine, which has not been demonstrated in man or animals.

The pathway from phenelzine to phenylacetic acid has not been demonstrated in man although it is known to exist for mice.⁷ Whether metabolism proceeds by way of acetylphenelzine or directly to phenylacetic acid is still in question.

Clineschmidt and Horita⁸ have shown that in rat liver preparations phenelzine produces phenylacetic acid but suggest this to be by way of oxidative dehydrazination by monoamine oxidase (MAO), producing phenylacetaldehyde. The possibility exists that MAO activity has a bimodal distribution similar to slow and fast acetylation. Our studies in which pre-treatment MAO levels and acetylator phenotypes were measured in patients before treatment with phenelzine suggest that this possibility is unlikely.⁹

A third possible metabolic route has been described¹⁰ in which phenelzine is oxidised by MAO to a hydrazone, phenylethylidene hydrazine (PEH). This could, in fact, be the first step in the pathway suggested previously.⁸

Such studies with phenelzine on animal tissues may be criticised on the grounds of species difference, but claims that phenelzine is acetylated in man ought to be derived from evidence that acetylphenelzine exists and that it is synthesised polymorphically. The question remains not whether polymorphic acetylation exists but whether phenelzine is acetylated.

Meanwhile continued clinical investigation into the effectiveness of treatment with phenelzine based on acetylator phenotype must be considered only in the knowledge that the case for phenelzine acetylation is not yet proved.

ELIZABETH F MARSHALL

Research Unit in Psychological
Medicine,
University of Newcastle upon Tyne

- ¹ Rawlins, M D, *British Medical Journal*, 1974, **4**, 91.
- ² Evans, D A P, Davison, K, and Pratt, R T C, *Clinical Pharmacology and Therapeutics*, 1965, **6**, 430.
- ³ Johnstone, E C, and Marsh, W, *Lancet*, 1973, **1**, 567.
- ⁴ Johnstone, E C, *Psychopharmacology*, 1976, **46**, 289.
- ⁵ Hughes, H B, *Journal of Pharmacology and Experimental Therapeutics*, 1953, **109**, 444.
- ⁶ Peters, J H, Miller, K S, and Brown, P, *Journal of Pharmacology and Experimental Therapeutics*, 1965, **150**, 298.
- ⁷ Leverett, R, Leeson, G A, and Dubnick, B, *Abstracts of the American Chemical Society*, September, 1960, p 65C, quoted by Clineschmidt and Horita.¹¹
- ⁸ Clineschmidt, B V, and Horita, A, *Biochemical Pharmacology*, 1969, **18**, 1011.
- ⁹ Marshall, E F, and Campbell, I C. Unpublished observations.
- ¹⁰ Tipton, K F, and Spire, I P C, *Biochemical Pharmacology*, 1972, **21**, 268.
- ¹¹ Clineschmidt, B V, and Horita, A, *Biochemical Pharmacology*, 1969, **18**, 1021.

Postoperative pain

SIR,—If the recommendations in your leading article on postoperative pain (18 September, p 664) were more widely implemented much suffering would be prevented. In this hospital a technique is being developed that may improve the comfort and convalescence of patients following major thoracic and abdominal operations.

When postoperative pain first requires relief papaveretum is injected in boluses of 2 mg each minute intravenously until adequate analgesia is produced. This is assessed by the patient saying that he is comfortable and confirmed by the ability to cough effectively without pain. An hour later double this dose is injected intravenously over 12 hours by a Handley clockwork pump or a Lund lymphangiogram pump.

Since the technique is at present confined to the intensive care unit no adequate comparisons can be made with patients treated with conventional analgesia routines. But it is hoped to extend the facility to general surgical wards in the near future. Observations indicate that the initial dose varies within wide limits and shows little correlation with age, weight,

or severity of pain. But once established, the initial dose provides a safe and reliable guide to subsequent continuous intravenous infusion during the next two days. After the first 24 hours the 12-hourly dose may be reduced by one-quarter each 12-hour period.

The patients are comfortable, alert except during periods of natural sleep, cough and move about the bed, and even out of bed, in comfort, suffer no respiratory depression and remarkably little nausea and vomiting, and in particular experience fewer and less severe spasms of the rectus muscles. On two occasions only out of more than 50 cases so treated analgesia has been insufficient during the maintenance period. In both relief was obtained by emptying a distended bladder. It is pleasant to be able to record that this work has received the enthusiastic support and encouragement of the surgeons and gynaecologists of this hospital.

E N S FRY

Department of Anaesthesia,
North Tees General Hospital,
Stockton-on-Tees,
Cleveland

Hysteria today

SIR,—In your leading article "The search for a psychiatric Esperanto" (11 September, p 600) there is the interesting comment that hysteria is "virtually a historical curiosity in Britain."

This kind of statement depends very much on what one means by hysteria. The notion of the disorder has changed in that now we believe there is usually some underlying nosological entity, but this new attitude cannot by itself imply that hysterical behaviour has subsided. Hysteria may be occurring less frequently in young women, but it appears perhaps even more often in older women, among whom in the last couple of years I have seen at least nine patients with hysterical ataxia, collapsing, pseudocyesis, and hemiparesis.

This change in distribution carries some interesting sociological connotations. Possibly younger women as they become more emancipated in progressive societies react to stress in ways other than hysterical, such as becoming depressed and behaving violently to themselves and others, not to mention losing their sexual drive, whereas their older sisters respond according to the mores of their upbringing.

Among males, those who are in some kind of submissive role and therefore like the young women of the last generation seem to be no less subject to hysteria.

Even in developed countries hysteria will, in the words of Sir Aubrey Lewis, outlive its obituarists.

G G WALLIS

High Royds Hospital,
Ilkley, W Yorks

Burning feet

SIR,—Professor G A Fitzgerald and his colleagues (8 May, p 1149) have provided a full and interesting case report of their patient with "burning feet" associated with polycythaemia rubra vera. They may not, however, be correct when they state that this condition has not been described before. Whitby and Britton¹ draw attention to erythromelalgia accompanying polycythaemia rubra vera. I have mentioned it also in my book *Arterial Surgery*.²

The condition may be combined with an ischaemic form of erythromelalgia, as in the