lowest saralasin infusion rate. At the higher infusion rates blood pressure decreased continuously to a minimum of 75/55 mm Hg at the end of the infusion period. At that moment the patient felt seriously ill, had a pale complexion, and vomited several times. After the infusion was stopped the blood pressure reached its preinfusion level within 30 min. Plasma renin activity (PRA) was measured at the beginning and the end of each infusion (see table).

	PRA (μg/l/3 h)	
	Before saralasin	After saralasin
Moderate sodium intake ..	10	6·3
After six days' chlorthalidone 100 mg/day	40	>125

The findings in this patient show firstly that saralasin infusion may lead to a potentially hazardous initial rise in blood pressure when PRA is low, as has been demonstrated by others,[2] and secondly that saralasin infused after severe sodium depletion with chlorthiazide diuretics and vigorously stimulated PRA may cause severe hypotension even at low-dose infusion rates.

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[1] Streeten, D H P, *et al*, *Circulation Research*, 1975, **36**, suppl I, p 125.
[2] Case, D B, *et al*, *American Journal of Medicine*, 1976, **60**, 825.

There's slow release and slow release

SIR,—In recent years several papers and letters have appeared in your columns[1-3] warning against the hazards of sustained-release oral preparations, the latest being that of Dr I P Carne-Ross (11 September, p 642). We are dismayed to see that the importance of the pharmaceutical formulation of such products is never stressed, and we feel that the time has come to draw attention to the matter.

To achieve controlled release, including slow release, of an orally administered drug at least two essentially different principles may be employed: the one-unit dose (for example, matrix tablets) and the multiple-units dose (for example, pellets or individually coated crystals distributed in capsules or tablets). The most importance distinction between these two principles lies in the fact that while a matrix tablet travels through the entire gastrointestinal tract remaining one non-disintegrated unit, the pellets or coated crystals are dispersed from the moment the capsule or tablet disintegrates, and *x*-ray studies[4 5] indicate that the spreading throughout the gastrointestinal tract is a function of time only.

Apart from carrying an almost negligible risk of the drug depot being trapped and causing local irritation and/or ulceration, the multiple-units dose possesses further advantages: the optimal absorption sites—generally localised in the small intestine—are reached earlier and better utilised because the emptying rate of the stomach is not a limiting factor for the onset of absorption from the small intestine, as in general is the case with a large compact unit, the effect of which must await its passage through the pylorus. Thus the importance of individual variations in stomach empyting rate and transit time as a whole is diminished and the predictability of the effect of a given dose is therefore increased.

In conclusion, we submit that when a controlled-release preparation of a drug is needed more care should be taken to secure that the formulation prescribed is in fact appropriate.

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[1] Spigelman, M, and McNabb, R W, *British Medical Journal*, 1971, **2**, 534.
[2] Alaily, A B, *British Medical Journal*, 1974, **1**, 103.
[3] Howie, A D, and Strachan, R W, *British Medical Journal*, 1975, **2**, 176.
[4] Green, M A, *Annals of Allergy*, 1954, **12**, 273.
[5] Feinblatt, T M, and Ferguson, E A, *New England Journal of Medicine*, 1956, **254**, 940.

Prematurity and neonatal death

SIR,—Mr R M Rush and his colleagues (23 October, p 965) have pointed out the relationship between preterm delivery and neonatal mortality. This is certainly in keeping with our experience. They state that prediction of preterm delivery is very difficult. Unfortunately, they have not reviewed previous obstetric history in their study.

During 1975 15 neonates died in this hospital, largely as a consequence of preterm delivery. Five of their mothers admitted to previous terminations; three were unmarried at the time of delivery; two were under the age of 16 and one over 40; two had had previous spontaneous abortions; three had a previous history of infant death; three were para 5 or more; one had had no antenatal care; two had had previous serious subfertility; two were delivered before arrival; two had had previous low-birth-weight preterm infants; one had had a previous infant with severe rhesus disease.

Only two of the 15 mothers had no adverse obstetric factors and were married girls in their early 20s. In contrast, preterm deliveries without these adverse factors (the vast majority) seem to have a good outcome in our experience.

Legal termination is followed by greatly increased fetal loss[1] from all causes, including neonatal death and preterm delivery, especially when cervical laceration has occurred.

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[1] Richardson, J A, and Dixon, G, *British Medical Journal*, 1976, **1**, 1303.

Palindromic rheumatism

SIR,—The short report by Dr E C Huskisson (23 October, p 979) is important for two main reasons. The first is that although palindromic rheumatism is a loose, ill-defined entity, in Britain it would appear to be often due to rheumatoid arthritis in episodic recurrent form, sometimes subsiding spontaneously, sometimes turning out to be a manifestation of some other disorder such as a reticulosis, but not infrequently gradually evolving into the clinical pattern of classical rheumatoid arthritis. In the past 30 years I have seen six such patients who in time became manifestly cases of rheumatoid arthritis, one remarkable in that for 20 years he suffered typical intermittent attacks of arthritis, with episodes of pain, stiffness, and swelling occurring for two or three days every few weeks or months and resolving completely each time until finally he was admitted to hospital with classical seropositive rheumatoid arthritis. What the original condition was that was described under the title of "palindromic rheumatism" by Hench and Rosenberg[1] is uncertain. Their cases were observed in military personnel in the USA during the last world war and do not seem to be the same disorders that we see in Britain today. Whatever palindromic rheumatism is will vary with the country from which it is described and the different infective and rheumatic processes prevalent at the time in that area. But the treatment of the different non-infective inflammatory arthropathies does not differ very greatly. In the absence of a known aetiology treatment is essentially symptomatic and palliative.

The second reason for emphasising the importance of palindromic rheumatism is that here we have an inflammatory polyarthritic process spontaneously switching on and off. Whatever factors or therapeutic agents will influence this disorder may well give us a lead to future therapeutic advances. In the past 30 years we have not infrequently seen the development of effective new drugs alter our ideas as to aetiology and pathological mechanisms in the arthritic disorders. Given a form of therapy which manifestly has positive action there will be no shortage of theories to explain that therapeutic effect. In medical therapeutics the cart has pulled the horse as often as not. So this small series of cases of a rare disorder and the effect on them of D-penicillamine described by Dr Huskisson is of particular interest and of some importance.

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Comparative diagnostic accuracy of barium meal and endoscopy

SIR,—In commenting on the study by Dr G W Stevenson and others (25 September, p 723), Dr M W Dronfield and his colleagues make some remarkable statements (23 October, p 1010). Surely a department of radiologists is entitled to be interested in diagnostic accuracy? The quality of their study adds considerable weight to the results of many others (including Dr Dronfield's) and to the increasing clinical consensus that endoscopy has greater potential than radiology in acute bleeding. In many hospitals the urgent barium meal has virtually been forgotten. Many comparative studies have been stopped, like that of Dr Stevenson and his colleagues, when "the physicians' preference for endoscopic demonstration of the bleeding site became too strong for random allocation to continue." Have not Dr Dronfield and his colleagues encountered similar problems in their randomised study? Are Nottingham physicians and surgeons really prepared to treat patients on the basis of an equivocal or negative barium meal when presumably expert endoscopy is available?

Dr Dronfield's letter suggests that Dr Stevenson's study was irrelevant. While I agree that the diagnostic argument can reasonably be closed, I believe that Dr Dronfield and his colleagues are also doing