death reported by Lim² is unlikely to have been due to flumazenil,⁴ while the mechanism of action in the death reported by Burr *et al* was a withdrawal of the protective action of benzodiazepines in a patient who had taken a multiple drug overdose.³ The same mechanism also explains the precipitation of ventricular arrhythmias in the report that Katz and colleagues quote in support of their own case.⁵

Benzodiazepines have a dampening effect on sympathetic nervous system activity,⁶ and animal studies suggest that they can increase the electrical stability of the heart in patients with acute myocardial infarction.⁷ There is little doubt that sympathetic activity in restless, waking, intubated patients is increased. This is primarily the result of irritation due to the endotracheal tube, a response that is augmented in the presence of hypoxia or pain, or both. In this setting reversing sedation with flumazenil unmasks increased sympathetic drive and cardiac electrical instability, thereby precipitating ventricular arrhythmias in an already severely damaged myocardium with compromised left ventricular function.

The conclusion can be only that the fatal drug actions in this case are similar to those reported elsewhere.^{3,5} There is no evidence for any direct cardiac effect of flumazenil.

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Preschool screening for cryptorchidism

EDITOR,—In describing the epidemiology of testicular cancer G M Mead relates 10% of testicular cancers to histories of unilateral or bilateral testicular maldescent.¹ In addition to cancer, testicular maldescent carries risks of infertility, torsion, and psychological effects. This highlights the need for effective screening programmes among preschool children to detect cryptorchidism and to provide appropriate treatment before 6 years of age.²

A quick analysis of hospital activity data in Wales for the six years 1985-90 (table) shows that in 1990 only 39% of all children were operated on before the recommended age of 6 (range 24.5-54.4% in 1985 and 26.2-46.5% in 1990). Although the numbers operated on before the age of 6 increased slightly during the period studied, the progress was deplorably slow—just 7.6% in six years.

In Wales local strategies for health gain are being

Age of children at orchidopexy in Wales, 1985-90. Figures are numbers (percentages) of children

Year	Age at orchidopexy (years)		
	<6	6-10	10-14
1985	151 (31.5)	228	101
1986	230 (34.2)	337	106
1987	206 (33.7)	304	101
1988	176 (35.2)	238	86
1989	197 (36.7)	238	102
1990	173 (39.1)	184	85

developed in 10 areas.³ Minimum datasets are provided to the directors of public health medicine from the Health Intelligence Unit (a central data collection and information unit for Wales) with the intention that the districts will use this information in developing local strategies and prioritising issues of greater need. Data on the treatment of undescended testis have been provided for the first time to all districts in the hope that their regular review will provide treatment to those children requiring orchidopexy within the first six years of life. Surely orchidopexy is far easier and simpler than the treatment of testicular cancer, infertility, or emotional problems associated with this condition. Community paediatricians and paediatric surgeons, along with public health physicians, have an important role in preventing complications of this condition later in life.

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Lung cancer and radon

EDITOR,—Stephen J Wozniak doubts the economic benefit of lowering radon levels in buildings on a mass scale to reduce the incidence of lung cancer.¹ He is right to say this, particularly as there is as yet no proof that radon in dwellings causes lung cancer.^{2,3}

Cornwall has been designated a high risk area by the National Radiological Protection Board, and many people are having their properties tested. When a high level is found (over 200 Bq/m³) householders are tempted to install ventilation systems to reduce the level. The standardised mortality ratio for lung cancer in the county for 1986-90, however, is 79, which scarcely suggests that radon is having a major effect.

An important study by the Imperial Cancer Research Fund is under way in Cornwall to test the hypothesis linking radon with lung cancer.⁴ Until this has reported, my advice to any inquirers is to delay a decision on remedial action in any domestic property.

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Symptoms after accelerated immunisation

EDITOR,—Mary E B Ramsay and colleagues conclude that local and systemic reactions occurred less commonly after accelerated immunisation schedules than after the standard schedule.¹ They found that redness and swelling at the injection site were significantly reduced in those children who received the accelerated schedule. The two groups, however, were immunised at different sites: 89%

of the control group were immunised in the thigh, and 89% of those given the accelerated schedule were immunised in the buttock.

In their discussion the authors argue that both a British study and an American study failed to show any difference in symptoms after immunisation at different sites.^{2,3} The results of these studies, however, are by no means conclusive: the British study compared types of vaccination rather than vaccination site, and the American study failed to control vaccine dose. Moreover, Ipp *et al* concluded that immunisations at different sites did have a significant bearing on the severity of local reactions, reactions in the thigh being more severe than those in the upper arm.⁴ We therefore believe that the site of immunisation may be a confounding variable when the results of this study are being interpreted.

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Monitoring ambulatory blood pressure in general practice

EDITOR,—We believe that some of David J Webb and colleagues' concerns about the widespread introduction of monitoring of ambulatory blood pressure in general practice are valid but that their conclusion, that the introduction of the technique in general practice should be postponed pending the outcome of clinical trials, is misguided.¹

That ambulatory blood pressure is superior in refining risk is not in dispute. The problem is that the criteria for treatment based on ambulatory readings are not well defined, and this is especially difficult in the care of patients with high clinic readings and low ambulatory readings. If ambulatory blood pressure is to be used for making decisions about hypertensive patients in the future then it is essential for research to include subjects in general practice.

In Oxfordshire the family health services authority has recently made ambulatory blood pressure units available to 50 general practices. Training in their use and appropriate support are being provided. Various collaborative research projects involving these general practices are being planned by the department of cardiovascular medicine and the department of public health and primary care in Oxford University.

In the meantime any implication that general practitioners will make wholesale changes to the treatment of hypertensive subjects by denying treatment to those with raised clinic pressures but normal ambulatory pressures (using similar criteria for intervention) is unfair. General practitioners are capable of interpreting the evidence as well as heeding the advice of specialist physicians. We believe that there is a strong place for moving monitoring of ambulatory blood pressure selectively into general practice provided its current limitations are emphasised, appropriate training and support are offered, and the monitoring units meet acceptable technical and performance standards.

Rather than agreeing with Webb and colleagues' suggestion to "await the outcome of definitive clinical trials," which may never take place, we would encourage greater use of ambulatory

blood pressure monitoring in general practice through collaborations such as those taking place in Oxfordshire.

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Multiple sclerosis: diagnostic optimism

EDITOR,—In his editorial on advances in diagnosing multiple sclerosis W I McDonald bases his optimistic conclusions on the contributions of magnetic resonance imaging.¹ As he states, this technique has helped not only in identifying the lesions in the central nervous system but by providing information on the stages of development (or recession) of the disease process.

Magnetic resonance imaging may, however, yield some other, disquieting findings. Apart from the surprising findings that this technique nearly always shows more lesions in a patient than are expected on the basis of the clinical picture and that lesions are often seen in areas remote from those under suspicion, it seems that similar findings may be observed in people who are entirely free of neurological symptoms. This has been emphasised in a recent report of a study examining use of the technique in migrainous patients²; to the authors' surprise, lesions were found on magnetic resonance imaging in seven of 32 healthy controls. Hyperintense lesions on T2 weighted sequences are well known in elderly subjects,³ but in this series the controls were aged 20-50 (mean 31). No mention is made of whether follow up studies were done in these subjects or whether gadolinium assisted repeat examination was performed.

Thus the finding of lesions on initial magnetic resonance imaging in people suspected of having multiple sclerosis, even in the usual age group, seems not to be sufficient evidence to clinch the diagnosis; repeated examinations, preferably with contrast media, should be done. A separate (and disturbing) question is whether multiple sclerosis, clinically silent, is far more ubiquitous than anyone has suspected.

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Pethidine in sickle cell crisis

EDITOR,—B J Pryle and colleagues confirm that the doses of pethidine commonly used to manage painful sickle cell crisis may lead to accumulation of its toxic neuroexcitatory metabolite, norpethidine.¹ We have also observed seizures in patients with sickle cell crisis receiving high dose intramuscular pethidine as analgesia. This can cause concern to the medical team as a fit may be the

presenting feature of a cerebrovascular event related to sickle cell disease, which would require urgent management including exchange transfusion.

Pethidine analgesia in sickle cell crisis has other inadequacies: a study performed at this hospital in 10 patients admitted with painful sickle cell crisis showed that on 12 of 61 patient days norpethidine concentrations were greater than 500 µg/l while nine patients were receiving pethidine doses of 4.4-9.5 mg/kg/day and one patient was receiving 21 mg/kg/day.² At the same time visual analogue scales were used by the patients and nursing staff to assess the effectiveness of the analgesia. These showed that the patients were receiving suboptimal analgesia, had breakthrough pain while waiting for this controlled drug to be dispensed, and had depressed affect and discomfort at the site of the injection.

We now manage patients with sickle cell crisis by continuous subcutaneous infusion of morphine, the dose being based on body weight and the time to breakthrough pain after an initial injection of morphine given after assessment in the accident and emergency department. This has proved acceptable to most patients and provides smoother pain control: an added advantage is the boost facility, which gives the patients a measure of control over their analgesic requirements. Some patients, however, are unable to tolerate this regimen because of pruritis and, occasionally, bronchospasm.

As with all opiate regimens, the patient should be carefully observed for evidence of respiratory depression by regular measurement of the respiratory rate and continuous pulse oximetry. The infusion should be halted if this occurs. We recommend that other units evaluate this form of analgesia in their patients with sickle cell crisis.

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Maintenance treatment with methadone

EDITOR,—It is perhaps flattering that Colin Brewer and colleagues attribute "proprietary and parochial" powers to us when we merely wished to note the diversity of prescribing styles within Europe.¹ In our article we neither promoted nor opposed any single style; we merely reported on the diversity.²

The scope of the debate on drug treatment matters greatly, for it can easily create an artificial dichotomy that drives out the middle options. Brewer and colleagues imply that they have "exposed" our practice of prescribing injectable drugs. In fact, we have not only reported on this in passing³⁻⁵ but have also published an audit of injectable prescribing.⁶ This small aspect of practice, however, receives disproportionate attention: we doubt whether major gains in the provision of treatment will be made in this area.

There is indeed an increasing body of scientific evidence on the benefits of maintenance programmes using oral methadone,^{7,8} but Brewer and colleagues imply that the same quality data exist for prescribing injectable drugs. The gathering consensus on the benefits of methadone relates to oral methadone: the United Kingdom is probably (except for some small experimental projects⁹) the only country in the world to permit the prescribing

of injectable drugs to addicts. On any day nearly a quarter of a million addicts receive oral methadone worldwide, compared with probably fewer than 1000 who receive injectable methadone, morphine, or heroin. We would benefit from a clearer separation of the debates about maintenance treatment with oral and injectable methadone.

Maudsley Hospital has recently received funding to establish a new maintenance programme using oral methadone in south London, with which we plan to conduct the first controlled comparison of drug taking and risk behaviour for HIV infection. This form of treatment is expensive and must be delivered in a cost effective fashion that maximises the possible benefit to users. Careful scrutiny is needed to identify the key factors that enhance a positive outcome. There may be real benefit for some patients who receive maintenance treatment with injectable methadone, but if Brewer and colleagues are genuinely interested in delivering the best treatment to as many drug users as possible they should forgo the limelight of controversial minority approaches to treatment and look to a model of delivering maintenance with oral methadone which may benefit more than a handful of clients.

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Reformulated Omnopon

EDITOR,—We write to highlight several problems we have encountered recently with the reformulated Omnopon products. After the Committee on Safety of Medicines' *Current Problems* reported the genotoxicity of noscapine¹ we observed a considerable drop in the use of papaveretum to a low level. With the availability of the reformulated Omnopon, it was decided to buy this product in preference to the currently stocked generic papaveretum still containing noscapine despite the resultant increase in expenditure.

It is apparent, however, that the reformulated product cannot be easily substituted for the old product. Several potential problems have been identified if current prescribing practice continues. A common prescription is "papaveretum 20 mg," but the reformulated product is no longer papaveretum, and a dose of 20 mg is misleading. The "20" ampoules now contain 15.68 mg of the remaining constituents. This may cause errors of administration and confusion over records of controlled drugs.

The manufacturers recommend prescribing the reformulated products in millilitres of solution and stipulating the name of the product—either Omnopon or Omnopon Paediatric. This approach,