reported a rise of 22 beats/min after a similar dose in acute asthma, while we have shown a rise of 28 beats/min one minute after salbutamol 200 µg injected over a one-minute period to convalescent asthmatics.⁵ Indeed, Mr Neville and his colleagues reported a rise of 31 beats/min on completion of their intravenous injection. It would seem likely that had Professor Femi-Pearse measured the pulse rate sooner after completion of the bolus injection of salbutamol a greater tachycardia would have been apparent. In view of these other reports we feel that salbutamol should be administered intravenously *slowly* (over at least five minutes) and that, with time, cardiotoxic effects or deaths will be observed if this effective bronchodilator is given rapidly as suggested.

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¹ Tickner, T R, *et al*, *Thorax*, 1976, 2, 240.

² Taylor, M W, *et al*, *British Medical Journal*, 1976, 1, 22.

³ Goldberg, R, *et al*, *Postgraduate Medical Journal*, 1975, 51, 53.

⁴ Fitchett, D H, McNichol, M W, and Riordan, J F, *British Medical Journal*, 1975, 1, 53.

⁵ Spiro, S G, *et al*, *British Journal of Clinical Pharmacology*, 1975, 2, 495.

Obstetric flying squads and mobile resuscitation units

SIR,—You published a letter from us last year (13 March 1976, p 650) in which we supported the use of mobile resuscitation units (MRUs) for the early management of patients with myocardial infarction. We went on, however, to stress our conviction that measures for resuscitation and immediate care are similar irrespective of the nature of the emergency. We suggested that there was no need to restrict the use of MRUs to one type of emergency and that immediate care teams could provide skilled aid to patients whether for a myocardial infarction, road accident, or some other medical emergency.

We were therefore especially interested to read two recent articles on obstetric flying squads. While Mr I L C Fergusson and Miss J M Watson (21 February, 1976, p 446) concluded that "few if any circumstances in modern obstetric practice merit continuing the flying squad in the urban area," they reported that in three of the 25 calls in their series the patients were clinically shocked. Dr D K James (22 January 1977, p 217) reported a series of 81 calls, of which 36 were made to general practitioner units and 45 to patients' homes. He concluded that the service was still of great value and "represents a much safer method [than an emergency ambulance call] of transporting an obstetric patient in an emergency" (our italics). It was notable that in all the calls to patients' homes the patients were brought back to the base hospital after being treated by intravenous infusion with or without sedation.

We would like to reiterate our belief that all medical emergencies can be effectively handled in the first instance by a general purpose MRU. Immediate care teams who staff these MRUs can be trained in basic methods of resuscitation and such teams would be effective in handling obstetric emergencies since the objective is the same—safe transport to hospital. Obstetric help to general practitioner units would seem to be in a somewhat different

category since such units should be adequately equipped and only require specialist staff. The basis of an MRU is that it can convey both skilled help and equipment to the seriously and suddenly ill from whatever cause. Only by adhering to this principle will the widespread development of MRUs become economically possible.

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SIR,—While we do not wish to be critical of Dr D K James's excellent article (22 January, p 217) we do feel that some different conclusions may be drawn from his figures. We do agree with him that in assessing the value of a flying squad service certain facts concerning time and manpower are quantifiable but personal judgments are not. In assessing the whole future of the flying squad service we feel that it is these judgments that need reconsideration and that they should not be too greatly preconditioned by old obstetric ideology.

With reference to his figures for the West Berkshire area, we would accept that in general terms the calls to the GP maternity units were justifiable on the grounds that 40% of these patients subsequently required transfer to hospital and that 60% actually had an obstetric procedure carried out in the unit. In this sense time and hospital accommodation were saved in these cases. However, we would take issue as to the efficacy of the flying squad when called to the patient's home. All these patients required subsequent transfer to hospital and no obstetric procedures were carried out in the home. Indeed, the only treatment given before arrival at hospital was an intravenous infusion for some patients. It is clear to us that in view of the times quoted in Dr James's article these patients could have received their infusion earlier had they been taken directly to hospital by the ambulance service. The question that remains to be answered is whether any of them benefited by being assessed before transfer. Here the facts seem to speak for themselves in that, since transport was inevitable in every case, any assessment would be confined to whether an infusion was required, and since an infusion would have been effected more quickly had the patient gone straight to hospital we can only conclude that the expense and manpower involved in supplying a flying squad are not justified in calls to the patient's home.

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Allergy to diazepam—or vehicle?

SIR,—Dr Louis Milner's report (15 January, p 144) concerning a case of allergy to diazepam describes a local reaction in the buttock after an injection of Stesolid 10 mg. Diazepam is very slightly soluble in water and all injection formulations of this drug contain solubilisers such as propylene glycol, phenylcarbinol, or macrogoliricinoleas, which in their turn are known to cause allergic side effects.

In an investigation¹ we have used a new type of vehicle for diazepam. The drug is dissolved in soybean oil, which is then

emulsified in water in the same way as is used for the intravenous administration of fat for parenteral nutrition (Intralipid). About 1500 patients have been treated intravenously so far and we have not seen any case of allergic manifestations except one in which the connection with diazepam was doubtful as the patient was concomitantly treated with co-trimoxazole. This diazepam emulsion preparation has been found to be markedly free from side effects, thus confirming the opinion that diazepam per se is very well tolerated even in parenteral use.

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¹ Dardel, O von, Mebius, C, and Mossberg, T, *Acta Anaesthesiologica Scandinavica*, 1976, 20, 221.

Growth in renal failure

SIR,—The interesting and valuable paper by Dr P R Betts and others (12 February, p 416) demonstrates the difficulty in assessing the importance of a single variable such as energy intake on growth in children with different degrees of renal insufficiency where other factors are involved. The majority of patients in their study were growing normally and did not have very marked impairment of renal function; thus any effect of energy supplementation could easily have been obscured. Of the 11 children who received supplements, only four had a height below the 3rd centile, and three a growth velocity below the 3rd centile. In addition, growth data were not available for one patient (an infant) and two children had entered puberty and therefore were not strictly comparable with the others.

The method of allocation of the children is unclear to us. If it was on the basis of one nutritional assessment at the start of the study, then analysis of the influence of diet on growth in the preceding year is precluded. On the other hand, if the dietary data refer to analyses during the preceding year rather than at the end it can be shown by a Wilcoxon rank sum test¹ that the five children (excluding the infant and pubertal children) who had energy intakes of less than 80% of recommended daily allowance (RDA) had significantly poorer growth velocities ($P > 0.02$). After energy supplementation when the energy intake improved in three of the five children, no difference in growth velocity is apparent. Only seven of the children (including the pubertal children) had a glomerular filtration rate (GFR) of less than 25 ml/min/1.73 m², which is the level the authors have previously reported to be associated with a reduction in growth velocity.² In the period before supplementation a significant correlation ($r = 0.82$, $P < 0.05$) exists between growth velocity and energy intake, whereas in the supplement period no significant correlation ($P > 0.1$) can be demonstrated.

The question is, do the authors provide enough data to suggest that the decreased energy intake of some children with chronic renal failure is not a causal as well as a related factor in the reduced growth velocity? Only three prepubertal children had both a low GFR (< 25 ml/min/1.73 m²) and a low energy intake ($< 80\%$ RDA) and growth velocity in all of them was greater when on supplements, although in one energy intake did not alter.

Poor energy intake is certainly not the only cause of growth retardation in chronic renal failure and may indeed not be the most important, for, while growth may improve with supplements, many children still grow poorly in spite of apparently adequate intakes.³ Provided the children accept them, feeding energy supplements would still seem to be justified. As the authors have demonstrated, they may have the advantage of limiting spontaneous intake of protein and other nutrients which may need to be reduced in renal failure.

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chronic renal insufficiency, suggesting that their reduced energy intake is a related but not necessarily causal factor. As we stressed in our last paragraph, we feel that if energy supplementation were to result in increased growth velocity, then this is more likely to occur when commenced in early childhood; indeed, the only child to show a significant increase in growth velocity with increased energy intake was aged 2.8 years when supplementation started.

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¹ Betts, P R, and Magrath, G, *British Medical Journal*, 1974, 2, 189.
² Chantler, C, et al, *Medizinische Mitteilungen*, 1976, 50, suppl 11, p 57.

¹ *Scientific Tables, Documenta Geigy*, ed K Diem, 6th edn, p 191. Manchester, Geigy Pharmaceutical Co Ltd.

² Betts, P R, and McGrath, G, *British Medical Journal*, 1974, 2, 189.

³ Chantler, C, et al, *Medizinische Mitteilungen*, 1976, 50, suppl 11, p 57.

*The authors sent a copy of this letter to Dr Betts and his colleagues, whose reply is printed below.—ED, *BMJ*.

SIR,—We thank Dr Chantler and his colleagues for their additional interpretation of our data (12 February, p 416). We agree that many of our children had only a moderate degree of renal insufficiency; nevertheless, nine of the 11 children who received energy supplementation were below the 50th centile for height and nine of 10 children had a height velocity below the 50th centile in the preceding year. Since growth velocity was determined over a 12-month period before the study this information was not available in case 7, who was only 0.6 years old on entry. We felt justified in including the two pubertal boys (cases 16 and 17) in our analysis since their energy intake and growth velocity did not parallel one another. Had they shown an increase in both these factors their data would have been difficult to interpret.

The questions we asked were whether an increased energy intake would result in (1) increased growth velocity and catch-up growth in children growing steadily along a given centile and (2) restoration of normal growth velocity in those in whom this was previously suboptimal. Dietary assessments were not made over a full year before the study as we had previously shown a relationship between energy intake and growth velocity.¹ Following supplementation it proved possible to increase the energy intake of four out of six children in whom this was previously suboptimal, yet only one of these four (case 8) showed significantly increased growth velocity. None of the five children with intakes greater than 80% of the recommended dietary allowance showed a significant increase or even reached the mean expected for their age. One of the six children (case 2) not receiving energy supplementation also significantly increased his growth velocity.

In answering the question whether the reduced energy intake of children with renal insufficiency is a causal or merely a related factor in their reduced growth velocity Dr Chantler and his colleagues have themselves shown that the provision of extra energy for children with terminal renal failure "did not ensure good growth."² We have shown similar results in children with milder degrees of

Timing of cervical smears

SIR,—I am most interested that Professor H C McLaren and Dr A J Lucas have found (12 February, p 445) that in some places in the USA it is obligatory to offer Papanicolaou tests to women under medical care in all hospital specialties. In this region, where screening for uterine cervical cancer is very comprehensive, cases of overt clinical cervical cancer still occur in the unscreened population and 75% of these women have previous hospital records. The taking of cervical smears should be part of routine hospital care.¹

I agree that carcinoma-in-situ is being diagnosed at an earlier age than it was 10 years ago, but this is relevant to the increase in the number of women under 25 years who are having smears taken. In this region, where 150 000 women have been screened, the detection rate is very low in women below 20 years of age. Very few cases occur at this age possibly because biopsy is seldom done as these young women can be followed with further smears. Only one case of microinvasive cancer has been found below 25 years of age, but four overt clinical cases have presented in women under 25 years who have never been screened. The detection rate of preclinical cancer is found to be 0.18% between 20 and 30 years, but rises steeply to 0.9% between 30 and 40 years, stays high, at 1.1%, between 40 and 50 years, and then begins to fall.

In addition to financial considerations, the frequency of repeating cervical smears must depend on the length of time, usually assumed to be about 10 years, that this disease remains at the in-situ stage, the efficiency of smear collection, and the reliability of the smear interpretation.

From 1968 to 1974 there were no deaths (Registrar General's figures) from cervical cancer in Scotland in women under 25 years.

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¹ *British Medical Journal*, 1976, 2, 659.

Vital follow-up of atypical cervical smears

SIR,—I should like to emphasise the importance of referring patients who have had two successive cervical smears showing abnormal cells for a gynaecological opinion.

I say this for the following reasons. Patients may have cervical smears taken by any or all of the following: their general practitioner, a family planning clinic, or at a routine gynaecological or postnatal clinic. Most of the laboratories associated with these clinics will suggest a six-month delay in repeating smears with "atypical or dyskariotic cells." It is easy to see that the cumulative effect of all these delays may add up to several years, sometimes with disastrous results for the patients. On the other hand it is often possible to pick up a carcinoma-in-situ from the second abnormal smear onwards.

It is therefore vital that the space on the smear form asking for the patient's general practitioner should be completed, together with the latter's correct address, even when the patient might not want to have her GP contacted. Ultimately it will be the GPs responsibility to be aware of this second abnormal report and to arrange appropriate and rapid referral.

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Voluntary Service Overseas

SIR,—Dr D C Morley and his colleagues (26 February, p 572) have eloquently put forward the case for the priority of socioeconomic development and preventive medicine in developing countries. No one would disagree with this, but their statement also actively discourages doctors trained in curative medicine from contributing. I believe that this is wrong.

At this moment people are dying in pain and misery from strangulated hernias, pneumococcal pneumonia, obstructed labour—the list is interminable. A health care system must be capable of relieving this suffering, not all of which is preventable. Western aid can help here, not just as a "pair of hands" but in training health workers, whether as doctors or as medical auxiliaries.

Let us encourage as many medical volunteers as possible to go to as many countries as possible. Even if some set out with the "wrong" motives and orientation I am certain that within a very few months they will appreciate the "real issues confronting those seeking to combat disease" and begin to tackle them, to the benefit of the communities they serve.

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Methadone: evidence of accumulation

SIR,—We are writing in consequence of the letter from Mr S T Leslie and others (5 February, p 375). From the results presented readers might have been confused into thinking that the accumulation of methadone in plasma is a continuous and indefinitely progressive process. However, this is not so, since the rate of accumulation decreases with each dose until a steady-state concentration is reached, after which no further accumulation occurs. The amount of drug that accumulates following multiple dosing can be calculated readily from a knowledge of both the drug half life and the dosing interval.¹