comparable to the inpatients. This point is clearly made in the article. Secondly, we were unable to find subjects over the age of 40 whom we could call "normal." A large proportion of the middle-aged population have extensive but occult vascular disease. It could be argued that the changes claimed by Dr Meade to be related to age are just as likely to be caused by occult atherosclerosis, especially as they are not seen in the women, who are known to be much less afflicted by atheroma. The fact that the fibrinolytic activity falls and then rises may also indicate the prevalence of occult disease in the population being surveyed, particularly as the fibrinogen does not fluctuate but shows a steady rise in both sexes.

The above comments are presented to show how difficult it is to study a disease which is common in what we thought to be normal subjects as well as those with clinical manifestations. Large numbers are unlikely to solve this problem. Exact quantification of the disease, occult and overt, will but is not yet possible.

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Effects of adrenaline during treatment with propranolol and metoprolol

SIR—Adrenaline causes vasodilatation in muscle by activation of β_2 -adrenergic receptors. After a single intravenous dose of the non-selective β -blocking agent propranolol this vasodilating action is lost: adrenaline induces a vasoconstriction with a resulting increase of the peripheral vascular resistance and a rise in blood pressure, presumably by stimulation of α -receptors. After a single intravenous dose of the selective β_1 -blocking agent metoprolol, however, the vasodilating action of adrenaline is largely preserved.¹

These observations could be of interest in the choice of a β -blocking drug in the treatment of hypertension if the difference between the effects of the two drugs were still present after a longer therapeutic use in hypertensive patients. Therefore, we compared the effects of propranolol (80 mg thrice daily) and metoprolol (100 mg thrice daily) in eight patients with essential hypertension (diastolic blood pressure between 100 and 120 mm Hg) in a double-blind crossover trial. There were four periods of four weeks' duration each: placebo—drug—placebo—drug. The active drugs were given in randomised order. At the end of each period we studied the effects of an infusion of adrenaline (8 μ g/min for 6 min) on the blood pressure and the blood flow in the forearm by means of mercury strain-gauge plethysmography.

The results, as changes arising during

adrenaline infusion, are shown in the accompanying table. Apparently the vasodilating action of adrenaline is still present after treatment with the β_1 -selective blocker for four weeks. It should be noted that on metoprolol this effect is not entirely normal: the decrease in vascular resistance is smaller than during placebo treatment. There is, however, no significant rise in mean arterial pressure. During propranolol treatment on the other hand the rise in blood pressure induced by adrenaline is considerable and significant. At the same time there is an important decrease in the blood flow in the forearm and a clear increase in the vascular resistance.

These results may be of clinical significance. During emotional stress endogenous adrenaline release increases,² while the blood flow through muscle rises.³ It is conceivable that adrenaline release caused by such stresses as emotion, anginal attacks, or hypoglycaemia is comparable with these adrenaline infusions. Then, during treatment with propranolol, considerable rises in blood pressure would result. This would not be the case during metoprolol treatment. Our results therefore seem to favour a selective β_1 -blocker over a non-selective one in the treatment of hypertension.

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¹ Johnsson, G, *Acta Pharmacologica et Toxicologica*, 1975, **36**, suppl 5, p 59.

² Levi, L, *Stress and Distress in Response to Psychosocial Stimuli*. Oxford, Pergamon Press, 1972.

³ Brod, J, et al, *Australian and New Zealand Journal of Medicine*, 1976, **6**, suppl 2, p 19.

Dangers of dextropropoxyphene

SIR—I read with interest your leading article on the "Dangers of dextropropoxyphene" (12 March, p 668) and would like to make the following observations.

(1) I think it is true to say that any pharmaceutical preparation of any clinical use is bound to have one side effect or another, and if side effects are not present it is highly likely that the preparation does not have any great effect.

(2) You discuss the problem of drug dependency and addiction but quote only one case where any possibility of addiction is present, and this due to evidence of the drug being found in the cord blood of a baby shortly after birth; this surely is not statistically significant. I also note with interest that there are no English references on the problem of drug dependency.

(3) The problem most interesting to me is that of self-poisoning. The accident and emergency department of the Hull Royal Infirmary uses dextropropoxyphene-containing compounds in considerable quantity, and there is evidence (you quote 2.5 million NHS prescriptions in England

in 1970) to suggest that such compounds are perhaps the most commonly prescribed analgesic in the North Humberside area. I cannot, however, recollect having seen in the last year one overdose except in those cases where the overdose consisted of polypharmacy.

You conclude by asking the question, "How good is the case for using the drug at all?" The major problem stressed in your article is that of self-poisoning, and I think it would be fair to say that paracetamol, the preparation which causes us most concern, can be bought without restriction from any chemist in the country, and that any drug if taken in sufficient quantity will have overdosage side effects. I think we must also keep the problem of overdosage in perspective and note that, despite the massive usage of dextropropoxyphene over the past 12 years, it in no way compares with other preparations as far as the problem of overdose is concerned.

I suppose we must now look forward to a period where the drug firms will go into competition over the usage or non-usage of dextropropoxyphene, and will receive daily circulars extolling the virtues of their simpler, "less dangerous," but also less effective, products.

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Vitamin C and drug metabolism

SIR—Your leading article (19 March, p 735) on vitamin C deficiency in liver disease rightly points out the lack of information in man on the effect of such deficiency on drug metabolism by the liver. In guinea-pigs vitamin C deficiency results in decreased antipyrine metabolism¹ and reduced liver cytochrome P-450 levels.² Both these abnormalities are reversed by correcting the deficiency; indeed, there is some evidence that vitamin C supplementation in non-deficient animals might stimulate metabolism.³

However, in man administration of vitamin C to non-deficient volunteers does not appear to enhance the metabolism of antipyrine.⁴ In liver disease low concentrations of leucocyte ascorbic acid do seem to be associated with impaired antipyrine metabolism,⁵ although it is possible that both are reflecting the severity of the disease.

We have studied the effect of vitamin C deficiency on antipyrine metabolism in old age. The metabolic clearance rate (MCR) in 10 deficient people was 25.3 ± 8.8 ml/h/kg, compared with 33.5 ± 11.5 in 27 non-deficient old people. This difference is significant ($P < 0.05$). When eight of the deficient group were given vitamin C for two weeks the MCR improved from 26.1 ± 9.6 ml/h/kg to 36.5 ± 12.9 ml/h/kg. The difference was again significant ($P < 0.025$). No such improvement could be demonstrated in the non-deficient group.

It seems clear that vitamin C deficiency in man causes a small but demonstrable impairment in drug metabolism that can be reversed by correction of the deficiency. As vitamin C deficiency is known to occur in about half of the old people admitted to geriatric wards⁶ it could account for at least part of the reduction in drug metabolising ability found in the elderly.⁷

As vitamin supplementation in people with no demonstrable deficiencies does not alter drug metabolism, it can be concluded that no

Effects of adrenaline on mean arterial pressure (MAP), blood flow, and vascular resistance (MAP/flow) in forearm in eight hypertensive patients (mean $\pm$ SEM) and results of Student's *t* test for paired observations

	MAP		Blood flow		Vascular resistance	
	mm Hg	P	ml/100 ml tissue/min	P	MAP/flow	P
Placebo	0 $\pm$ 2		+ 2.6 $\pm$ 0.5	<0.001	- 22 $\pm$ 4	<0.01
Propranolol	+ 21 $\pm$ 3	<0.01	- 0.7 $\pm$ 0.4	>0.10	+ 21 $\pm$ 7	<0.01
Metoprolol	+ 5 $\pm$ 3	>0.10	+ 0.7 $\pm$ 0.3	<0.05	- 5 $\pm$ 2	<0.05
Placebo v propranolol	P < 0.001		P < 0.01		P < 0.01	
Placebo v metoprolol	P > 0.10		0.05 < P < 0.10		P < 0.05	
Propranolol v metoprolol	P < 0.01		P < 0.05		P < 0.01	

interaction between vitamin C and drugs is likely to occur at the level of hepatic metabolism in healthy people. This is not the case in the elderly and may not be the case for other groups known to have a high incidence of vitamin deficiencies.

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- ¹ Axelrod, J, *et al*, *Journal of Pharmacology and Experimental Therapeutics*, 1954, **111**, 176.
² Zannoni, V G, and Sato, P H, *Annals of the New York Academy of Sciences*, 1975, **258**, 119.
³ Sato, P H, and Zannoni, V G, *Biochemical Pharmacology*, 1974, **23**, 3121.
⁴ Wilson, J T, *et al*, *Journal of Clinical Pharmacology*, 1976, **16**, 265.
⁵ Beattie, A D, and Sherlock, S, *Gut*, 1976, **17**, 571.
⁶ Griffiths, L L, *et al*, *Gerontologia Clinica*, 1967, **9**, 1.
⁷ O'Malley, K, *et al*, *British Medical Journal*, 1971, **3**, 607.

Day treatment for the elderly mentally infirm

SIR,—In the last decade there has been an emphasis on providing long-term day hospital treatment for the elderly mentally infirm. We would like to report the outcome of 23 women and six men with senile dementia who were admitted to the Glenside Psychogeriatric Day Hospital in 1970, 1971, and 1972.

The patients' average age on admission to the day hospital was 75 years and the average period of attendance was one year for men and 18 months for women. Twenty patients eventually stopped day treatment because of admission to hospital for inpatient care; another five were admitted to Part III accommodation, and the remaining four died suddenly at home. It is probably worth noting that of the 20 patients admitted to hospital 17 died within four months. Two of the remaining three are still alive, but in fact one of these, though technically an inpatient, spends most of the time living at home with her family. The five patients admitted to Part III accommodation lived on average for another 20 months, but they are now all dead.

One cannot possibly arrive at definite conclusions with such small numbers. However, the figures indicate that day hospital treatment might be as effective as inpatient care in supporting people with senile dementia in the remaining years of their lives. Certainly of our 29 patients only three eventually required longer term inpatient hospital treatment, although another five did need to be admitted to residential accommodation for the elderly mentally infirm.

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Levamisole treatment

SIR,—When an unexpected event occurs during the treatment with a new drug, the medicine is commonly suspected of being involved in the genesis of the phenomenon. Obviously if this is a single observation it ought to be interpreted cautiously, as more data are needed before the possible role of the drug can be settled. This attitude was apparently also adopted by Dr A F El-Ghobarey and co-workers, who reported the recurrence of a varicose ulcer in a rheumatoid arthritis patient treated with levamisole (5 March, p 616).

In contrast to this observation levamisole

may speed up the healing of chronic leg ulcers as well. In a multicentre double-blind study performed by Belgian dermatologists¹ 59 patients with chronic leg ulcers were randomly assigned to a 20-week treatment with either levamisole (2.5 mg/kg for two consecutive days every week) or a placebo as a supplement to previously ineffective local therapy. At the end of the 20-week observation period no healing of the leg ulcers was observed in some of the placebo-treated patients, whereas by that time the cure rate had risen to 100% in the levamisole group. This difference resulted in a levamisole-associated shortening of the median healing time.

It follows that delayed healing of leg ulcers is certainly not a consistent observation with levamisole treatment, and that, if the reported recurrence of a leg ulcer was truly levamisole-related, this observation was in all probability due to an additional factor such as a drug-induced allergic reaction. The concomitant occurrence of mouth ulcers in this patient might indeed point to such a reaction. On the other hand it is clear that the causes of leg ulcerations are so numerous and that their clinical course is often so unpredictable that the explanation may well be found elsewhere. In this context it may be worth recalling that levamisole was stopped in June 1976. As one of the brightest summers within living memory started in Scotland around that time as well, one may wonder whether the rheumatic complaints were perhaps beneficially affected by the climatological changes. A greater mobility of the patient may indeed have facilitated venous circulation in her legs, creating better opportunities for healing of the ulcer.

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¹ Morias, J, *et al*, in preparation.

Future of child health services

SIR,—I write as a member of the Court Committee to comment on some of the proposals for primary health care for children. One purpose of the report is to stimulate constructive criticism and debate. There is apparently widespread misunderstanding of the key role suggested for general practitioners, indicating that the report has failed in some respects to put across the committee's conviction that it is in the best interest of child and family health to draw together all aspects of primary health care responsibility for children in the primary health care team based (wherever feasible) on group general practice. One reason for this failure may be the length of the report. Perusal of the summary recommendations is unfortunately no substitute for reading the report itself, so that the recommendations are considered in wider context and supported by the committee's reasoned arguments for the proposals. The importance of context is well illustrated by Dr D G E Alldridge's remarks (5 March, p 641); may I suggest that he reads the report? He will find no support for his apparently overriding concern to maintain "the authority of the doctor," but he will find reasoned arguments for all recommendations even though I imagine he will agree with few of them.

The considered opinion of general practice, as a key professional group within medicine, is obviously of the utmost importance. The report is first and foremost concerned with children and their health needs and is in no way a charter for any professional group however "generalist" or "specialist." There are no grounds for complacency about children's health, and the whole issue is of such importance that I hope the debate will reach greater heights and depths than the "most family doctors would oppose strongly . . ." objections voiced by Dr K J Bolden (29 January, p 292).

The report makes clear that for many reasons the present situation is inherently unstable; it is no basis on which to build and we must move forward. The committee's proposals are, in the considered judgment of its members, the best way to reconcile the special health needs of children with the need to keep primary child health care family-orientated. However, the "general practitioner paediatrician" concept is wide open to, and certainly needs, serious debate, and the fears of its fragmenting effect upon general practice expressed by Dr R H Westcott and others (26 February, p 577) should be groundless.

May I briefly emphasise some relevant points about the report's proposals?

(1) The level of training of *all* health personnel concerned with children needs to be raised if the special needs of this age group are to be met adequately. The committee welcomes unreservedly in this context the implications of vocational training in child health for all future GPs.

(2) All GPs would in future continue to be concerned directly with children, particularly so far as episodic illness is concerned. This is essential for various excellent reasons and will contribute to the maintenance of a family practice orientation.

(3) GPPs would continue to be involved with patients other than children. This is no mere lip service paid to the generalist tradition in family medicine, but is related to the major concern (which critics seem to be overlooking) to balance a child-centred emphasis and a family context for primary care.

(4) Suggestions such as "70%" of a GPP's time will be spent on children" are clearly not rigid, and should not be allowed to obscure the wider issues. Nevertheless, the committee saw the concept of a considerable degree of "special interest" in child health within group practice as the only effective and realistic way to ensure that health surveillance, school health, and a more meaningful preventive emphasis are incorporated into family practice. The training implications alone, which the report makes clear must go far beyond the envisaged scope of "generalist" vocational training, seemed to make this essential.

(5) The committee has described its proposals within the framework of group general practice, which appears in many ways (not just related to child health) to be the desirable model for the future. It is, however, at least implicit that, even when group practice has been developed as far as is feasible, there will remain large areas where the practical problems make such a pattern impossible; obvious examples are very rural general practice and the problems associated with urban areas. Clearly the model will have to be modified to meet the problems and needs of particular areas.

The terms "generalist" and "specialist" are already causing confusion. Dr Westcott and colleagues, for example, talk about the "specialty of general practice," and their penultimate sentence is rather silly; the fact that the committee was chaired by Professor Court does not make its proposals "his" or "specialist." It is worth pointing out that paediatrics and geriatrics are specialties in an age rather than system sense, and exist to meet the special needs of the respective extremes of the mortal age span. The special needs of children in this sense are what the Court report is all about,