into its performance are the criteria laid down in Section 1(1) of the Act and the ethical views of the patient, who would presumably not request the treatment if she had any ethical objections to it. The ethical principles of the doctors are involved only when the decision whether to terminate or not has been made.

As I have read some of the letters on this subject I have wondered how many of those who admit to a complete opposition to abortion would in fact be prepared to approach the problem of the individual patient in this objective way. If they are not prepared to do so they are not only failing in their duty to the patient as laid down in the NHS Regulations and by the accepted practice of giving the best possible advice to their patients, but they are guilty of trampling upon the ethical beliefs of their patients. Some people, both lay and medical, actually believe that in certain cases the termination of pregnancy is ethically desirable and that to allow it to continue would be unethical. The anti-abortionists do not seem able to grasp this and they write as if they have the monopoly of truth and virtue.

Let us hope that minorities, whether political or ethical, will always be protected from coercion, but that does not mean that the leaders of the majority must expose their own adherents to coercion in the opposite direction.

HERBERT H PILLING

Coroner's Court,
Sheffield

SIR,—Shorn of legal niceties the position is that since the passage of the Abortion Act a restricted abortion service has been provided in this country under the NHS. In my previous letter (26 June, p 1593) I was not concerned with the rights and wrongs of abortions; the point I made was that if an individual, or a minority group, contracted out of this service the burden on the remaining consultants (gynaecologists and anaesthetists) would be correspondingly increased and that it is understandable that employing authorities will tend to avoid creating a situation which is fraught with friction and dissatisfaction. I would agree that it is a further illustration of the potential dangers of an inflexible monopoly employer.

R SALM

Falmouth,
Cornwall

*.*This correspondence is now closed.—
Ed, *BMJ*.

Once-daily treatment of hypertension

SIR,—I have read with interest the paper by Drs A P Douglas-Jones and J M Cruickshank (24 April, p 990), and the letters from Dr E M M Besterman (5 June, p 1403) and Drs M J Kendall and R A Yates (5 June, p 1404). In a recent study¹ we showed that propranolol and pindolol given once daily gave control of blood pressure equivalent to that achieved with therapy three times a day. In this study we also observed the blood pressure at hourly intervals during the day and could find no difference in lying, standing, or exercise blood pressure. The mean daily dose of propranolol was 300 mg and of pindolol 30 mg. In a separate study we were also able to treat a larger number of hypertensive

patients with timolol given once daily. Once again control was achieved throughout the 24 hours.

These studies indicate to us that a once-daily dose of timolol, pindolol, propranolol, and, we suspect, most β -adrenoreceptor blocking drugs are as effective as the same dose given in three divided doses. The half lives of these drugs are, in the main, short and this indicates that effectiveness does not correlate directly with the plasma levels.

TREFOR MORGAN

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Heidelberg,
West Victoria,
Australia

¹Wilson, M, Morgan, G, and Morgan, T, *British Journal of Clinical Pharmacology*. In press.

SIR,—We read with interest the letters from Dr E M M Besterman (5 June, p 1403) and Drs M J Kendall and R A Yates (p 1404) comparing their experience in hypertension of once-daily dosing using metoprolol with once-daily administration of atenolol as reported by Drs A P Douglas-Jones and J M Cruickshank (24 April p 990). Dr Besterman indicates that with once-daily administration of metoprolol at a dose of 100-200 mg, but not at higher doses, control of the exercise blood pressure was sometimes lost at 24 hours. He wonders if the same might not also apply to atenolol. Drs Kendall and Yates describe the effect upon blood pressure of a single oral dose (200 mg) of metoprolol. They state that although a fall in blood pressure was present throughout the 24 hours, it achieved statistical significance only at 12 hours after the dose had been given.

These observations stimulated us to study the results of an ongoing trial in moderately hypertensive patients treated with atenolol given once daily (dose 100 mg). In the first part of the study a six-week placebo run-in period was followed by a single oral dose of atenolol. The results were in agreement with those of Dr Besterman and Drs Kendall and Yates, the resting antihypertensive effect being present throughout the 24 hours but some escape occurring after exercise at 24 hours. The study was then repeated after a one-month period during which 100 mg of atenolol was given by mouth. In contrast to the acute study both resting and exercise blood pressures remained controlled throughout the whole 24 hours. The mean resting blood pressure after six weeks' placebo was 174/116 mm Hg; the mean resting blood pressure after one month's treatment (24 hours after the last tablet) was 154/94 mm Hg. After a further 100-mg tablet the mean resting blood pressure at 12 hours was 152/97 mm Hg and at 24 hours 142/92 mm Hg. The matching post-exercise mean blood pressures were 200/110 mm Hg after placebo, 171/87 mm Hg at the beginning of the 24-hour study, 168/95 mm Hg at 12 hours, and 171/92 mm Hg at 24 hours after the tablet.

It is therefore possible that atenolol in chronic administration does behave differently from metoprolol and that this difference might be a reflection of the longer plasma and biological half life of atenolol.

A M J WOOLFSON
M S KNAPP

City Hospital,
Nottingham

Toxicity of paracetamol in children

SIR,—I should like to draw attention to a case of accidental overdose of paracetamol in a 3-year-old child who was admitted to the paediatric unit of this hospital last month. She had ingested a full 100-ml bottle of the proprietary medicine Calpol, which contains 2.4 g of paracetamol. At no time during her stay in hospital did any untoward clinical features develop and plasma paracetamol levels estimated four and eight hours after ingestion were 0.28 and 0.15 mmol/l (45 and 25 μ g/ml) respectively. These levels were well within the safe range according to the graphs of Prescott *et al*,¹ which are designed to predict the likelihood of liver damage by plotting plasma paracetamol levels against time after ingestion. However, it is difficult to know how meaningful these results are as Prescott's work was restricted to adult patients. Indeed, there is very little information in the literature regarding paracetamol overdose in children and I should be very interested to hear from any workers on this subject, particularly in view of the fact that we now have an effective but potentially dangerous mode of treatment in the shape of cysteamine.

I am grateful to Dr Ralph Evans for his permission to write about the patient under his care.

S P GLASCOE

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¹ Prescott, L F, *et al*, *Lancet*, 1971, **1**, 1519.

Comparison of reflex effects of levodopa and bromocriptine in Parkinsonism

SIR,—Some of the effects of levodopa are counterproductive in Parkinsonism. For example, it increases the amplitude of the monosynaptic H response while at the same time it diminishes rigidity.¹ In the cat alpha motor neurones are facilitated by levodopa via a descending noradrenergic pathway.² Such a mechanism would explain the increase in H response amplitude in patients given levodopa and is consistent with the observation that the noradrenergic blocking drug phenoxylbenzamine potentiates the reduction in rigidity produced by levodopa.³

Bromocriptine has been shown to alleviate the symptoms of Parkinsonism,^{4,5} and pharmacological evidence suggests that it acts by stimulating dopamine receptor terminals in the brain. A previously tested dopamine-receptor stimulator, piribedil, was clinically disappointing despite a definite pharmacological action in the treated patients.⁶ On the basis of a comparison between levodopa and piribedil it was suggested that some of the benefit of levodopa could derive from the activation (directly or indirectly) of receptors other than dopamine receptors. Bromocriptine appears to be more useful than piribedil and possibly acts upon different subtypes of dopamine receptor. If a drug could be found that stimulated the nigrostriatal pathway without activating the noradrenergic spinal pathway it might surpass levodopa in relieving rigidity.

The effect of bromocriptine was therefore assessed in seven patients with Parkinsonism, selected because of an inadequate response to levodopa or Sinemet (carbidopa+levodopa). Four of the patients had postencephalitic Parkinsonism and the others had idiopathic Parkinsonism. Monosynaptic

reflexes and the tonic vibration reflex were measured by the methods previously described¹ while the patients were on their maximum therapeutic dose of levodopa. Bromocriptine was then substituted and the maximum therapeutic dose established (20-50 mg daily), the measurements being repeated after two weeks' treatment with this dose. Finally the original dose of levodopa was restored, bromocriptine withdrawn, and a third set of measurements made. No significant reflex changes occurred, suggesting that levodopa and bromocriptine share a similar spectrum of activity in this respect.

The clinical effects of bromocriptine resembled those described in larger series.^{4,5} The three patients who had not responded at all to levodopa did not respond to bromocriptine. The three who had troublesome end-of-dose akinesia reported longer and more predictable release periods with bromocriptine, provided they took it every two to three hours; two took small doses of Sinemet twice daily in addition. One of these patients has subsequently developed postural hypotension, the symptoms of which are relieved by wearing elastic stockings. The seventh patient maintained a partial response with bromocriptine but experienced the same side effect, confusion, as with Sinemet and has preferred to stay on his former treatment.

These observations fail to support the hypothesis that bromocriptine has a more specific effect than levodopa in Parkinsonism. Nevertheless, bromocriptine is a useful addition to current remedies.

I thank The London Hospital and Ciba-Geigy Laboratories for financial support. Bromocriptine was supplied by Sandoz Products Ltd.

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¹ McLellan, D L, *Journal of Neurology, Neurosurgery and Psychiatry*, 1973, **36**, 342.

² Baker, R G, and Anderson, E G, *Journal of Pharmacology and Experimental Therapeutics*, 1970, **175**, 212 and 224.

³ Andrews, C J, *Australian and New Zealand Journal of Medicine*, 1971, **1**, suppl 1, p 24.

⁴ Calne, D B, *et al*, *British Medical Journal*, 1974, **4**, 442.

⁵ Parkes, J D, *et al*, *Journal of Neurology, Neurosurgery and Psychiatry*, 1976, **39**, 184.

⁶ McLellan, D L, *et al*, *Acta Neurologica Scandinavica*, 1975, **51**, 74.

Dietary fibre

SIR,—I would like to add some comments to the answer given by your expert to the question "What is the most effective source of fibre in the diet and how much should be taken?" (12 June, p 1461).

I agree with the comment that "fibre" is a mental shorthand for a mixture of components and that we do not know which of these is important. It is, however, possible to say a little more about the complex polysaccharides that can be regarded as "dietary fibre" in bran. Bran does not have a constant composition and the amounts of dietary fibre that it contains will depend on its method of production, and specifically on the amount of associated endosperm. The starch in this endosperm will dilute the dietary fibre, and a bran prepared by sieving wholemeal flour may contain more starch and less dietary fibre than a bran separated earlier in the milling process.

Subject to the above I think that better values for a typical bran are as follows: crude fibre (approximately equivalent to cellulose plus lignin), 9-12 g/100 g; and total dietary fibre, 36-46 g/100 g. Bran dietary fibre therefore contains 60-75% of the total as non-cellulosic polysaccharides (hemicelluloses, etc), of which arabinoxylans constitute a major pro-

portion. Brans of this type usually contain about 22-27 g/100 g of starch. Wholemeal breakfast cereals contain approximately 12 g/100 g total dietary fibre, and a preparation such as All-Bran about 27 g/100 g. Almost all breakfast cereals contain some maltose and in none of these are the amounts likely to have any laxative effect.

My colleagues and I have analysed a range of typical foodstuffs and have produced from this a guide to calculating dietary fibre that has recently been accepted for publication.²

D A T SOUTHGATE

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¹ Trowell, H, *et al*, *Lancet*, 1976, **1**, 967.

² Southgate, D A T, *et al*, *Journal of Human Nutrition*. In press.

* * * Our expert writes: "I was most interested to read Dr Southgate's letter and pleased that we shall at last have a table of foodstuffs with their calculated dietary fibre contents. His contribution to nutritional research is already outstanding. Inadvertently he has drawn a red herring across the original question, which was on the construction of high-residue diets. Specifically All-Bran is clearly not all bran and in the context in which it was being discussed it was not being used as a breakfast cereal but as a therapeutic addition to diet. Notwithstanding Dr Southgate's assurances, malt is an excellent laxative and All-Bran seems to produce more liquid stools than plain bran supplements."—ED, *BMJ*.

Cutaneous bullae and frusemide in chronic renal failure

SIR,—We read with great interest the article by Professor A C Kennedy and Dr A Lyell (19 June, p 1509) describing seven patients with cutaneous bullae and chronic renal failure. However, Gilchrist *et al*¹ from America, Korting,² from West Germany, and Burry and Lawrence³ from Australia have also described five, two, and four similar cases respectively. In addition, we have reported five other cases⁴ and agree that the cutaneous bullae appear to be associated with chronic renal failure, frusemide therapy, and exposure to sunlight but not with porphyria.

One of our five patients has again developed bullous lesions on her hands this summer during the recent sustained sunny weather. She has a year-old renal transplant with a creatinine clearance of 33 ml/min and is taking frusemide 40 mg daily, prednisolone 14 mg daily, and azathioprine 50 mg twice daily. It is possible that her extensive lesions are the result of a phototoxic reaction to frusemide and impaired renal function. To date one other patient has died and the recurrence of the lesions has not been recorded in the remaining three patients.

We are unaware of any report of seasonal recurrence of these cutaneous bullae.

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¹ Gilchrist, B, Rowe, J W, and Martin, C, *Annals of Internal Medicine*, 1975, **83**, 480.

² Korting, G W, *Dermatologica*, 1975, **150**, 58.

³ Burry, J N, and Lawrence, J R, *British Journal of Dermatology*, 1976, **94**, 495.

⁴ Keczkas, K, and Farr, M J, *British Journal of Dermatology*. In press.

Requests for references

SIR,—I wonder whether others besides myself are becoming concerned about the increasingly slack manner in which many health authorities in the United Kingdom are making requests for references for medical appointments at all levels.

There was a time when such a request took the form of a polite, individually prepared letter from a medical colleague in the specialist department concerned or one signed by a medical administrator. Nowadays, even for consultant appointments, they often arrive in the form of a scruffy circular over the indecipherable cyclostyled signature of someone described as "personnel officer," and I have even received one subscribed by the ultimate insult of an indecipherable cyclostyled "per pro" signature.

The security accorded to references is also often in grave doubt. It may be that the ethics of sending references about the work of a medical colleague to a non-medical administrator must be reluctantly accepted, but the propriety of despatching it in the envelope provided by some health authorities is palpably suspect; this may not be addressed to a named or designated officer and is frequently not even marked "in confidence." Sometimes, too, the request arrives at the last moment in a second class envelope and the referee is compelled to resort to the telephone if he has the interest of his candidate at heart.

There are still some health authorities which ask for references in a courteous and confidential manner. I am always happy to oblige them but, in general, requests for references from NHS authorities compare unfavourably with the increasing number received from medical institutions in North America, Australia, and elsewhere overseas.

T B BOULTON

Royal Berkshire Hospital,
Reading

Misleading statistics

SIR,—I have only belatedly received and read your leading article (7 February, p 303) on misleading statistics and would wholeheartedly agree with your emphasis on the dangers of highly significant statistical correlations that may erroneously point to causal relations.

However, you then suggest that environmental causes of disease may be determined by the demonstration of differences in incidence of disease and relating them to similar variations of the causal factors. This may also lead to false associations. Travelling in one of our high Himalayan valleys the other day one noticed the profusion of wild white roses. The villagers will tell you that these cause diarrhoea—not by taking them, but merely by their presence. The high incidence of diarrhoea at this time of year is a fact, as also the white roses, but there is no logical connection between the two.

This surely is the lesson from John Snow's classical epidemiological investigations, that it is not enough to find significant associations, but the hypothesis must include a logical connection between cause and effect.

J S BERKELEY

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Thimphu,
Bhutan