attention to sodium. We suggest that the changes in blood pressure that they saw were due to changing the dietary sodium, and that 24-hour urine collections would have revealed this.

Dietary fibre may not be irrelevant. Varying fibre amount and type might have altered the availability of cations for absorption in the bowel. This, however, is speculation and could not be detected by comparing tables of dietary sodium content. In any event, there is no case for relating this study to Burstyn's experiments with fat-enriched diets for rabbits (references 6-9 in the paper) until the major confounding variable of effective cation intake has been taken into account in both species.

The report also omits any mention of a search for an effect of age on blood pressure in the subjects, and does not refer to the age distributions of the various experimental groups. It is clear that blood pressure was measured in many different ways (at home, at work, at a health centre; with a standard and a random zero instrument; thrice weekly and on a single occasion) but we are not told how the various methods were distributed between the groups and during the crossover experiment.

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¹ Anon. *Lancet* 1975;ii:1325-6.

² Biachi G, et al. *Clin Sci Mol Med* 1974;47:435-48.

³ Dahl LK, et al. *Circ Res* 1974;34:94.

⁴ Parisi J, et al. *Amer Heart J* 1973;85:22-34.

⁵ Morgan T, et al. *Lancet* 1978;ii:227-30.

⁶ Magnani B, et al. *Clin Sci Mol Med* 1976;51:625-6S.

⁷ Freis ED, *Circulation* 1976;53:589-95.

SIR,—Angela Wright and others (15 December, p 1541) recently reported that a high-fibre diet exerted a hypotensive effect on the blood pressure of normal volunteers, the mechanism of which is not known. The diet of primitive societies with a low prevalence of hypertension is not only high in fibre content but low in sodium and rich in potassium. Modest modification of sodium intake may be helpful in the treatment of mild hypertension¹ and potassium supplementation in the diet may exert an ameliorating effect on the development of hypertension and protect from hypertensive complications.² Wholemeal bread has double the potassium content of white bread and All Bran has a much higher potassium content than cornflakes.³ It is possible that alteration of sodium and potassium intake by the volunteers in this study could have caused the blood pressure changes observed. In addition to information concerning the electrolyte content of the diets prescribed, any information on the changes in weight in these volunteers would be of interest, especially as potassium may have a natriuretic effect.⁴

It is surprising to observe such low standard errors in blood pressure measurement as those quoted in this paper when one notes the age range (18-60 years) of the volunteers and the fact that exercise was undertaken between each inflation of the cuff. On a low-fibre control diet the systolic blood pressure of 17 of their volunteers was 121.2 ± 1.6 mm Hg and the diastolic blood pressure was 78.5 ± 1.7 mm Hg. Using a London School of Hygiene "blind" sphygmomanometer we found that the supine systolic blood pressure

of 19 male medical students, aged 20-22 years, was 123.4 ± 2.4 mm Hg and the supine diastolic blood pressure was 66.4 ± 2.3 mm Hg. Bigger standard errors are normally found in groups of subjects with the age range given in the paper.

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¹ Morgan T, Adam W, Gillies A, Wilson M, Morgan G, Carney S. *Lancet* 1978;ii:227-30.

² Meneely GR, Battarbee JD. *Am J Cardiol* 1976;38:768-85.

³ Paul AA, Southgate DAT. *McCance and Widdowson's the composition of foods*. 4th ed. London: HMSO, 1978.

⁴ Young DB, McCaa RE, Pan YJ. *Circ Res* 1976;38(6 suppl 2):84-9.

*We sent copies of these letters to Dr Burstyn, whose reply is printed below.—ED, BMJ.

SIR,—The letter of Dr Williams and his colleagues suggests that the effect we report (15 December, p 1541) may have been due to changes in the sodium intake of our subjects. Although we did not measure the sodium intake of the people participating in our study, we have no reason to suppose that they should synchronously change their food salting habits to confound our experiment. The high-fibre bread we gave our subjects would have supplied them with 31 mmol(mEq) sodium a day, while the low-fibre bread supplied 38 mmol/day (based on their mean intake of about 1 kg of bread a week). This difference of 7 mmol/day represents 8% of the rather low sodium intake recommended by the US Senate Select Committee on Nutrition¹ and less than 5% of the sodium intake typical of Western man, hardly sufficient to account for the effect we report.

Dr Williams and his colleagues are also dissatisfied with our blood pressure measurement techniques. All of the blood pressures apart from those of our 12 hypertensive patients were measured with Hawksley Random Zero sphygmomanometers in an office at the university. The two observers standardised their techniques carefully. Only one of these observers measured the blood pressures of the hypertensive patients at their own homes using an ordinary Accoson sphygmomanometer. We did not have large enough numbers of participants over the age of 30 to look for any effect of age on blood pressure. The average age of our subjects (with the exception of the hypertensive patients) was 26 and did not differ between experimental groups.

The letter of Dr Parfrey and his colleagues quite correctly asks how we managed to keep our standard errors small. The precision of our measurements was achieved by taking blood pressure readings three times weekly, each of which was itself the mean of three sphygmomanometer inflations. Between inflations subjects were asked to clench their fist sufficiently to prevent pooled blood from distorting subsequent diastolic pressure values. Furthermore, a group of 36 people whose systolic pressures were measured three times on a single occasion yielded the following result: first measurement— 128.7 ± 2.3 ; third measurement— 123.5 ± 2.2 . These were compared with the blood pressures of 36 of our experimental volunteers (who were age matched with the above group) towards the

end of their control periods (unfortunately, we had not preserved the three individual blood pressure values of our volunteers from the beginning of their control periods): first measurement— 117.8 ± 1.7 ; third measurement— 117.8 ± 1.6 . The systolic pressures of people who are unaccustomed to blood pressure measurements drops significantly ($p < 0.001$) in the four minutes between the first and third measurement. This is not the case with the "trained" volunteers who have had two weeks of blood pressure measurements. The systolic pressures of the "untrained" people were higher than those of the "trained" people (first measurement— $p < 0.001$; third measurement— $p < 0.05$), although the diastolic pressures of the two groups were very similar. Finally, the standard errors for the blood pressure readings are considerably larger for the "untrained" group (which are similar to those of Dr Parfrey and others) than the "trained" group. It appears that repeated blood pressure measurements over a period of days improve precision in two ways: (a) by allowing the observer to take mean values and (b) by accustoming the individual to the measurement and hence reducing the variability of this measurement (that is, producing lower systolic pressures in the third reading of "untrained" people and lower mean systolic pressures in "trained" people).

The suggestion by Angela Wright and her colleagues that potassium may have played a part in producing our results is an interesting one. Our bran-enriched wholemeal bread contained more potassium than our white bread and would have provided (with the 5 g bran a day given to the volunteers) 18 mmol(mEq)/day potassium, compared with 5 mmol/day provided by the low-fibre bread. This difference of 13 mmol/day amounts to 20% of the average daily potassium intake.² That this may have affected our results is undeniable, although it required 135 mmol/day potassium to reduce the blood pressure in the two cases of salt-induced hypertension cited by Meneely and Battarbee.³

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¹ Select Committee on Nutrition and Human Needs. *Dietary goals for the United States*. Washington: United States Senate, 1977.

² Davidson S, Passmore R, Brock JF, Truswell AS. *Human nutrition and dietetics*. 6th edn. Edinburgh: Churchill Livingstone, 1975.

³ Meneely GR, Battarbee JD. *Am J Cardiol* 1976; 38:768-85.

Sclerosant treatment for hydroceles and epididymal cysts

SIR,—My experience of sclerosant treatment in the management of hydroceles and epididymal cysts differs widely from that reported by Mr H Thomson and Mr M Odell (22 September, p 704).

As a result of Moloney's¹ enthusiastic article¹ I set up a prospective study and treated approximately 75 patients between 1 January 1976 and 31 December 1978. The results in the first 56 patients were reported in detail earlier this year.² In summary, assessment one to two years after treatment showed 95% cure for hydroceles and 100% for epididymal cysts. Side effects and complications were minimal, none requiring surgical intervention. The few complications

were in the larger hydroceles and I would certainly recommend that this form of treatment be reserved for hydroceles less than 500 ml unless the patient's general condition precludes surgery.

It is clearly important to have long-term follow up in this type of study and I plan to continue reviewing the patients I have treated.

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¹ Moloney GE. *Br Med J* 1975;iii:478-9.

² Nash JR. *Br J Surg* 1979;66:289-90.

Beta-blockade, myopathy, and thyrotoxicosis

SIR,—The report by Dr J C Forfar and others (24 November, p 1331) on proximal myopathy and myositis associated with the use of beta-blocking agents prompts us to call attention to another clinical situation leading to myopathy during beta-blockade.

We have recently treated three male patients, aged 36-57 years, who developed thyrotoxicosis during treatment with the beta-blocking drugs timolol, pindolol, and propranolol. All of them showed chronic thyrotoxic myopathy, and one was in addition suffering from chronic diarrhoea. On examination, two of them were considered clinically euthyroid. There was no nervousness, hyperkinesia, or tremor. The third patient had some thyrotoxic symptoms such as increased sweating and occasional palpitations. The pulse rate of the patients was 80-90 beats/min, and all showed regular sinus rhythm. The most prominent finding in all the patients was wasting of the proximal muscles of the extremities. The muscle power, however, was only slightly impaired.

Apparently, the diagnosis of thyrotoxicosis was delayed in two of the patients. The symptoms had lasted from one to six months, and the patients had lost 10-16 kg before their thyroid function was tested. One of the patients underwent extensive gastroenterological examinations because of chronic diarrhoea of six months' duration. In another patient the diagnosis of thyrotoxicosis first became evident when the drug treatment was interrupted because of a suspicion of an uncommon side effect of beta-blockade.

All the patients showed unequivocal biochemical hyperthyroidism, with serum total thyroxine concentrations of 296-323 nmol/l (23-25 mg/100 ml); the normal range is 60-160 nmol/l (4.7-12.4 mg/100 ml). The myopathy was corrected after the treatment of thyrotoxicosis in each patient despite continued treatment with the beta-blocking agents.

Electromyographic abnormalities of some degree have been found in 90% of thyrotoxic patients, but clinically evident myopathy is infrequent. Beta-blocking agents may improve the muscle power in thyrotoxic myopathy,² and indeed in our patients the muscle power was rather good in relation to the severe degree of muscle atrophy. However, in the report of Dr Forfar and his colleagues the myopathy and myositis were ascribed to treatment with the beta-blocking agents. It remains an assumption that there might be some additive effects of thyrotoxicosis and beta-blockade on the myopathy in our patients.

Little attention has been paid to the development of thyrotoxicosis during beta-blockade.³ This coincidence is probably rather common, because both treatment with beta-blocking agents and thyrotoxicosis are common clinical conditions. Beta-blocking

agents mask many of the most typical clinical signs of thyrotoxicosis, such as tachycardia, tremor, and nervousness, without affecting the underlying metabolic disorder, except the deiodination of thyroxine to triiodo-thyronine.^{4,5} On the other hand, the development of thyrotoxic myopathy is not prevented by beta-blockade. Thus thyrotoxicosis presenting with atypical clinical symptoms and signs is probably the most common aetiological factor to be considered in proximal myopathy developing during beta-blockade.

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¹ Ramsay ID. *Lancet* 1966;ii:931-4.

² Pimstone N, Marine N, Pimstone B. *Lancet* 1968; ii:1219-20.

³ Shenkman L, Podrid P, Lowenstein J. *JAMA* 1977; 238:237-9.

⁴ McDevitt D. *Postgrad Med J* 1976;52 suppl 4:157-61.

⁵ Anonymous. *Br Med J* 1977;ii:1039-40.

Combined antidepressant treatment

SIR,—Dr J P R Young and his colleagues (24 November, p 1315) are to be congratulated on having carried out the first controlled comparison of combined antidepressant therapy. Their results show clearly that trimipramine was superior to combined antidepressants and monoamine oxidase inhibitors alone.

The authors express surprise at these results because they do not accord with their clinical experience that combined antidepressant therapy is effective in depressive disorders. This might be because the patients in the study differed from those normally treated by combined antidepressant therapy in clinical practice in that they suffered from mild and moderate depression only. Combined antidepressant drugs are normally reserved for patients who have failed to respond to other forms of treatment. While this should not be regarded as a prerequisite for starting combined antidepressant therapy, such patients usually suffer few unwanted effects while on combined therapy because of tolerance to previous and often prolonged single-antidepressant medication. Marked unwanted effects during combined antidepressant therapy was noted in Dr Young's study and this is likely to hinder drug compliance and clinical response.

The tendency for unwanted effects to be experienced more with monoamine oxidase inhibitors and combined antidepressant therapy may have been responsible for the relatively low mean dosage of monoamine oxidase inhibitors taken in the study. There is now good evidence that clinical response to phenelzine is greater in a daily dose of 60-90 mg,¹⁻³ whereas the average dosage in Dr Young's study was 44-45 mg daily.

Although combined antidepressant therapy should not be used for mild and moderate depression as first-choice treatment this does not mean that it has no place in other depressive and associated disorders.

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¹ Ravaris CL. *Arch Gen Psychiatry* 1976;33:347-50.

² Quitkin F, Rifkin A, Klein DF. *Arch Gen Psychiatry* 1979;36:749-60.

³ Tyrer P, et al. *Br J Psychiatry* (in press).

Aggressive patients—what is the answer?

SIR,—I read Dr A Bailey's comments (8 December, p 1509) on Dr K Raghus's letter (3 November, p 1147) with respect to aggressive patients with increasing unease and incredulity.

If I have grasped the meaning of Dr Bailey's comments correctly, do I now have to make meaningful inquiries as to the psychological status of the person demanding a visit for another person, accepting that this is an "indication of the intermediary's agitation"—however rude, objectionable, or threatening that "agitated intermediary" may be?

Let me ask this. If you had a burst pipe, your house was rapidly filling with water, and in your "state of agitation" you asked your neighbour to send for the plumber, whereupon he rang the aforesaid person at, perhaps, 2 am with the request "Send the bloody plumber," would you really expect him to come?

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Mebendazole and hydatid disease

SIR,—I have followed with great interest the recent reports of pyrexia following mebendazole therapy for hydatid disease. We have recently excised a 2-litre hydatid cyst of the liver in a young woman. Full-dose mebendazole therapy was started five days preoperatively and samples of venous blood and intact daughter cysts were collected at operation for mebendazole levels, which we have been unable to measure. In the postoperative period a swinging pyrexia developed, which we attributed to infection in the residual cavity. However, fluid from the closed suction drain was sterile on aerobic and anaerobic culture.

The hypothesis of Mr I M Lyon and Mr K W Reynolds (3 November, p 1111) that the pyrexia is due to drug-induced cyst necrosis is difficult to accept. There is no good evidence in man that mebendazole penetrates intact, established cysts in sufficient levels to produce destruction. Heath¹ had great difficulty in destroying experimental cysts in mice and Reisin's experiments² showing that mebendazole entered cysts by simple perfusion were conducted in vitro.

A full course of mebendazole costs the NHS £185. Unless the drug can be shown to penetrate cyst fluid in therapeutic doses sufficient to destroy viable daughter cysts its use in established hydatid disease must be open to question—especially as Benex³ showed that only a small amount of living germinal tissue is required to produce a new *Echinococcus granulosus* cyst.

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¹ Heath DD, et al. *Parasitology* 1975;70:273.

² Reisin IL, et al. *Int J Parasitol* 1977;7:189.

³ Benex J, *Ann Parasitol (Paris)* 1968;43:573-82.

Snail-eating mummy?

SIR,—As a parasitologist I was most interested in the review "Buried treasure" by Dr John Cole (1 December, p 1412), which mentioned the finding of a calcified worm of *Dracunculus* (guinea-worm) in the abdominal wall of a mummy. However, without wishing to appear