exposures are measured imprecisely. *J Clin Epidemiol* 1991;**44**:1223-31.
8 Barker DJP, Osmond C. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. *Lancet* 1986;i:1077-81.
9 Ben-Shlomo Y, Davey Smith G. Deprivation in infancy or adult life: which is more important for mortality risk? *Lancet* 1991;**337**:530-4.
10 Davey Smith G, Shipley MJ, Rose G. The magnitude and causes of socio-economic differentials in mortality: further evidence from the Whitehall study. *J Epidemiol Community Health* 1990;**44**:265-70.

Treatment of hypertension in older adults

SIR,—The recent report on the principal results of the Medical Research Council trial of treatment of hypertension in older adults will provoke considerable interest and discussion. One conclusion was that the trial "found no primary cardioprotective effect of β blockers." I suggest that a more precise conclusion would be that the trial found that atenolol did not show a cardioprotective effect and that it confirms the lack of data on cardioprotection derived from studies on the hydrophilic β blockers. This group includes atenolol, nadolol, and sotalol. This should not detract from reports suggesting that lipophilic β blockers—that is, drugs like metoprolol, propranolol, and timolol—do have cardioprotective actions. The relevance of intrinsic sympathomimetic activity is not certain; some consider it a disadvantage.

The heart attack primary prevention in hypertension (HAPPHY) trial did not find that β blockers have a primary prevention role,[2] but this result was the overall conclusion derived from a beneficial effect of metoprolol and a slightly adverse effect of atenolol.[1] The Medical Research Council trial of 1985[4] is usually regarded as a negative study, but it included a large number of patients with very mild hypertension; about half the patients were female and at very low risk of having a coronary event; and it did not include data on silent infarcts.[5] When the data for non-smoking men are considered[4] and those with silent ischaemic episodes are included, the potential benefits of propranolol are revealed.[5]

The literature on β blockers in secondary prevention is extensive and includes a number of positive results from trials in which lipophilic β blockers were used. The best known are the Norwegian timolol trial,[6] the Gothenburg metoprolol trial,[7] and the β blocker heart attack trial of propranolol.[8] In each of these investigations the β blocker had a significant impact on sudden death, a major cause of death in post-infarct patients, but also the way in which one third of coronary events present in people with hypertension.

For the patient with angina and hypertension the most common major complication and the most common cause of death is coronary artery disease. The drug treatment most likely to reduce the risk of death, particularly sudden death, is a lipophilic β blocker. It would be a tragedy if conclusions based on studies in which hydrophilic β blockers have been used were to cast doubts about the potential value of the other β blockers.

MARTIN J KENDALL

Department of Medicine,
Queen Elizabeth Hospital,
Birmingham B15 2TH

1 MRC Working Party. Medical Research Council trial of treatment of hypertension in older adults: principal results. *BMJ* 1992;**304**:405-12. (15 February.)
2 Wilhelmsen L, Berglund G, Elmfeldt D, Fitzsimons T, Holzgreve H, Hosie J, *et al*. Beta-blockers versus diuretics in hypertensive men: main results from the HAPPHY trial. *J Hypertens* 1987;5:561-72.
3 Steering Committee of the HAPPHY Trial. MAPHY and the two arms of HAPPHY. *JAMA* 1989;**262**:3273-4.
4 Medical Research Council Working Party. MRC trial of treatment of mild hypertension: principal results. *BMJ* 1985;**291**: 97-104.
5 Green KG. British MRC trial of treatment for mild hypertension—a more favourable interpretation. *Am J Hypertens* 1991;**4**: 723-4.
6 Norwegian Multicentre Study Group. Timolol-induced reduction in mortality and reinfarction in patients surviving acute myocardial infarction. *N Engl J Med* 1981;**304**:801-7.
7 Hjalmarson A, Elmfeldt D, Herlitz J, Holmberg S, Málek I, Nyberg G, *et al*. Effect on mortality of metoprolol in acute myocardial infarction. *Lancet* 1981;ii:823-7.
8 Beta Blocker Heart Attack Trial Research Group. A randomised trial of propranolol in patients with acute myocardial infarction. *JAMA* 1982;**247**:1707-24.

SIR,—As one who took part in both of the Medical Research Council's trials of hypertension[1,2] I have some observations regarding K Beard and colleagues' study of managing sustained hypertension in elderly patients.[3]

Epidemiologically there seems to be good evidence for treating hypertension in elderly patients.[3] From general practitioners' point of view, this would generate an enormous amount of hard work, which should not be underestimated. Some of the advice given by Beard and colleagues on the practicalities of assessment, treatment, and follow up represent consultants' points of view and may not be feasible let alone cost effective in the community.

What of the patients' point of view? According to the worst profile in table IX of the Medical Research Council's report of its trial in older patients, I can expect a one in 11 chance of benefit if I take a diuretic for five years.[2] Against that, there is a one in six chance of getting an important side effect over five years with the same treatment, and the odds substantially worsen if I am one of the 50% who require additional treatment. If my general practitioner was good enough to explain these facts to me I might well be prepared to take a gamble and not take any tablets at all.[4] Furthermore, as the chances of a longer life seem improbable I would want some kind of guarantee that my life would be improved.

Until intervention trials take note of the participants' quality of life,[5] the costs may well outweigh the benefits.[6,7] I probably won't live the 200 or so years that are necessary to reap the benefits that the trials have to offer, but it may just feel like it.

So what does a general practitioner do now? I for one will continue to inform my patients to the best of my ability and allow them to make up their own minds.[8] At least that way I can give back to patients the freedom that they deserve.

C H HAND

Bungay,
Suffolk NR35 1TD

1 Medical Research Council Working Party. MRC trial of treatment of mild hypertension: principal results. *BMJ* 1985;**291**: 97-104.
2 Medical Research Council Working Party. MRC trial of treatment of hypertension in older adults: principal results. *BMJ* 1992;**304**:405-12. (15 February.)
3 Beard K, Bulpitt C, Mascie-Taylor H, O'Malley K, Sever P, Webb S. Management of elderly patients with sustained hypertension. *BMJ* 1992;**304**:412-6. (15 February.)
4 Bursztajn HJ, Feinbloom RI, Hamm RM, Brodsky A. *Medical choices, medical chances: how patients, families, and physicians can cope with uncertainty*. New York: Routledge, 1990.
5 Bowling A. *Measuring health: a review of quality of life measurement scales*. Buckingham: Open University Press, 1991.
6 Stoate HG. Can health screening damage your health? *Br J Gen Pract* 1989;**39**:193-5.
7 Marteau TM. Psychological costs of screening. *BMJ* 1989;**299**: 527.
8 Tuckett D, Boulton M, Olson C, Williams A. *Meetings between experts: an approach to sharing ideas in medical consultations*. London: Tavistock, 1985.

SIR,—It was ironic that in the issue of the *BMJ* detailing the cardioprotective value of diuretics in elderly hypertensive patients[1,2] and the doubtful value of lowering serum cholesterol[3,4] and triglycerides[5] a statement should appear in the paper by Keith Beard and colleagues that "adverse lipid changes induced by thiazides may be important in younger [hypertensive] patients."[2] The reasons for this conclusion, the vagueness of the statement, and the fact that it was not referenced are puzzling. Given the available evidence in this issue of the journal and information published over the past 15 years might I suggest the following revision: "There is little or no evidence that thiazide diuretics have long term adverse effects on plasma lipids[6-9] and no evidence whatsoever that these supposed changes have any detrimental effects on cardiovascular mortality."[1,2,10,11]

G D JOHNSTON

Department of Therapeutics and Pharmacology,
The Queen's University of Belfast,
Belfast BT9 7BL

1 Medical Research Council Working Party. Medical Research Council trial of treatment of hypertension in older adults: principal results. *BMJ* 1992;**304**:405-12. (15 February.)
2 Beard K, Bulpitt C, Mascie-Taylor H, O'Malley K, Sever P, Webb S. Management of elderly patients with sustained hypertension. *BMJ* 1992;**304**:405-12. (15 February.)
3 Oliver MF. Doubts about preventing coronary heart disease. *BMJ* 1992;**304**:393-4. (15 February.)
4 Hulley SB, Avins AL. Asymptomatic hypertriglyceridaemia. *BMJ* 1992;**304**:394-6. (15 February.)
5 Smith GD, Pekkanen J. Should there be a moratorium on the use of cholesterol lowering drugs? *BMJ* 1992;**304**:431-6. (15 February.)
6 Williams WR, Borhani NO, Schnaper HW. The relationship between diuretics and serum cholesterol in HDFP participants. *J Am Coll Cardiol* 1983;**1**:623.
7 Veterans Administration Co-operative Study Group on Antihypertensive Agents. Comparison of propranolol and hydrochlorothiazide for initial treatment of hypertension. Result of short-term titration with emphasis on racial differences in response. II. Results of long term treatment. *JAMA* 1982;**248**:2004-11.
8 Multiple Risk Factor Intervention Trial Research Group. Mortality after 10½ years of hypertensive participants in the multiple risk factor intervention trial. *Circulation* 1990;**82**:1616-28.
9 Johnston GD, Wilson R, McDermott BJ, McVeigh GE, Duffin D, Logan J. Low dose cyclopenthiazide in the treatment of hypertension: a one-year community based study. *Quart J Med* 1991;**78**:135-43.
10 Collins R, Peto R, MacMahon S, Herbert P, Fieback NH, Eberlein KA, *et al*. Blood pressure, stroke and coronary heart disease. Part 2. Short-term reduction in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990;**335**:827-38.
11 New trials in older hypertensives [editorial]. *Lancet* 1991;**338**: 1299-300.

Monoclonal antibodies in sepsis and septic shock

SIR,—C J Hinds's editorial discusses the use of monoclonal antibodies in sepsis and septic shock.[1] Though the relative merits of different antibodies to endotoxin will no doubt continue to be debated, we think that, in addition to the cost, there are other issues that should be considered.

By giving antiendotoxin only after admission to the intensive care unit, we may miss the "therapeutic window" when it can be of most benefit. The onset of signs of sepsis seems to coincide with the release of cytokines such as tumour necrosis factor, which occurs 90 minutes after the administration of endotoxin.[2] So a delay has already been established before clinical signs appear. Giving antiendotoxin after the cascade has started may not halt its progress. This partly explains the inconsistencies in the studies Hinds mentions.

In the two main trials quoted treatment with antiendotoxin was delayed further: by a mean of 14·3 hours from diagnosis in one[3] and within eight hours in the other.[4] By this time about half of those without shock who are likely to develop this complication will already have done so.[5] This seemingly excessive delay probably reflects the ordinary clinical situation, considering possible hold ups in transfer to, and initial treatment in, the intensive care unit. If good haemodynamic control is obtained the temptation will be to avoid using an expensive and controversial drug; if not, the prognosis may already be poor.

We are not suggesting that antiendotoxin should be given indiscriminately as patients enter hospital. What is necessary is the ability to predict who is likely to develop sepsis, as we have recently shown in patients undergoing endourological manipulation of urinary calculi, in whom the incidence of