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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,¹ but this result was the overall conclusion derived from a beneficial effect of metoprolol and a slightly adverse effect of atenolol.² The Medical Research Council trial of 1985³ 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.⁴ When the data for non-smoking men are considered⁴ 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.

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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.

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SIR,—It was ironic that in the issue of the *BMJ* detailing the cardioprotective value of diuretics in elderly hypertensive patients¹ and the doubtful value of lowering serum cholesterol¹ and triglycerides² 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.”³ 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^{4,5} and no evidence whatsoever that these supposed changes have any detrimental effects on cardiovascular mortality.”^{6,7,8,9}

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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 one³ 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 shown⁶ in patients undergoing endourological manipulation of urinary calculi, in whom the incidence of