LETTERS TO THE EDITOR

● *The British Heart Journal welcomes letters commenting on papers that it has published within the past six months.*

● *All letters must be typed with double spacing and signed by all authors.*

● *No letter should be more than 600 words.*

● *In general, no letter should contain more than six references (also typed with double spacing).*

Asymptomatic ischaemia during daily life in stable coronary artery disease: relevant or redundant

SIR,—In their interesting review on the prognostic implications of silent myocardial ischaemia¹ Mulcahy *et al*, referring to our paper on silent ischaemia after myocardial infarction,² wrote: "Solimene *et al* performed ambulatory ST segment monitoring in 40 patients eight weeks after a first myocardial infarction and followed them for two years. Six patients had asymptomatic ischaemia during ambulatory monitoring. No events occurred in them: there was one cardiac death in a patient without ischaemia." There was some misinterpretation of our data. In fact, our investigation showed that 11 (27.5%) out of 40 patients had silent ischaemia after infarction: five only on exercise testing, five on exercise testing and Holter monitoring, and one on Holter monitoring. Of those 11 patients, four (36%) had a non-fatal cardiac event whereas only one (3.6%) of 29 patients without silent ischaemia had a cardiac event (fatal reinfarction) during this two year follow up. Kaplan-Meier analysis showed that during this period patients without silent ischaemia were much less likely to experience a cardiac event (96.5%) than patients with ischaemia (62.3%) ($P < 0.007$). We concluded that silent myocardial ischaemia after myocardial infarction is of considerable prognostic significance—a somewhat different conclusion from that reached by Mulcahy *et al*.

MARIA CECÍLIA SOLIMENE
Instituto do Coração,
Av. Enéas de Carvalho Aguiar 44, 2o A,
050403-000 São Paulo, Brazil

1 Mulcahy D, Purcell H, Patel D, Fox K. Asymptomatic ischaemia during daily life in stable coronary disease: relevant or redundant? *Br Heart J* 1994;72:5-8.

2 Solimene MC, Ramires JAF, Gruppi CJ, *et al*. Prognostic significance of silent myocardial ischaemia after a first uncomplicated myocardial infarction. *Int J Cardiol* 1993;38:41-7.

This letter was shown to the authors, who reply as follows:

SIR—I thank Dr Solimene for her letter. Our review was about the prognostic significance of transient myocardial ischaemia detected on ambulatory ST segment moni-

toring and not exercise testing or any other investigation. In her letter Solimene confirms the figure we quoted of six patients with transient ischaemia on ambulatory monitoring after myocardial infarction.

In their study of 40 patients Solimene *et al* related silent ischaemia after myocardial infarction detected by any investigation (that is, exercise testing, $n = 10$; ambulatory monitoring, $n = 6$; one or the other, $n = 11$) to events, and not to a straight assessment of ambulatory ischaemia versus outcome. Only one "hard" coronary event (acute myocardial infarction or sudden coronary death) was reported by Solimene *et al* (cardiac death), and this occurred in a patient who did not have transient ischaemia on ST segment monitoring. We reported this in our review which focused on the relation between transient ischaemia and subsequent death or non-fatal myocardial infarction. Recurrence of angina (referred to as a non-fatal cardiac event by Solimene *et al*) was reported to occur in four patients with silent ischaemia on either exercise testing or ambulatory monitoring—Solimene *et al* do not state which. To reply to Solimene's letter in the context of our review, and to establish whether "soft" end points occurred in those with transient ischaemia during daily life, we would need to know how many of these four recurrences of angina occurred in those with only a positive exercise test, and whether anything further happened to them.

DAVID MULCAHY
Department of Health and Human Services,
Public Health Service,
National Institutes of Health,
National Heart, Lung, and Blood Institute,
Bethesda, Maryland 20892,
USA

Issues in cardiac pacing: can agism be justified?

SIR,—The continuing debate surrounding the cost effectiveness of rate adaptive pacing in the elderly remains handicapped by a lack of reliable data.¹ The antagonists would point to the absence of hard clinical evidence to support the use of sophisticated pacemaker technology in the elderly. Recent trials, however, which have specifically included elderly subjects, have confirmed the clinical impression that the elderly stand to gain as much from physiological pacing as younger patients.²⁻⁴ However, the biggest stick with which to beat the enthusiasts is that of cost. In a retrospective analysis, de Belder *et al* estimated that implantation of dual chamber pacemakers in all suitable patients (that is, those with advanced atrio-ventricular block and sinus rhythm) aged over 75 years would have added an extra £264 357 to the regional pacing budget (an increase of 57%).⁵ Given these figures it is little wonder that there is some reluctance to implement the BPEG guidelines in the elderly.⁶ It is important to realise, however, that these figures were based on the assumption that all electrophysiologically suitable patients aged over 75 would have been given DDD pacemakers.

Patients aged over 75 years may constitute a selected group in whom the presence of advanced conduction disease may be a marker of an advanced aging process. Limiting, non-cardiac disease or cognitive impairment—for example, previous stroke—is not uncommon in this

group and such patients would not normally be considered for a dual chamber system. We do not know what proportion of these patients are offered VVI systems on the grounds of limiting, non-cardiac disease or cognitive impairment. Nevertheless, it is clear that available estimates of the financial impact of the BPEG guidelines are likely to be exaggerated and serve only to foster inappropriate implantation policies.

In addition to further clinical trials, which are likely to confirm the overall benefits of physiological pacing in the elderly, we need reliable information on the costs of implementing these research findings.

M R HARGREAVES
O ORMEROD
Cardiac Department,
John Radcliffe Hospital,
Headington,
Oxford OX3 9DU

- 1 Payne GE, Skehan JD. Issues in cardiac pacing: can agism be justified? *Br Heart J* 1994;72:102-3.
- 2 Channon KM, Hargreaves MR, Cripps TR, Gardner M, Ormerod OJM. DDD vs VVI pacing in patients aged over 75 years with complete heart block: a double blind crossover comparison. *Q J Med* 1994;87:245-51.
- 3 Jordaens L, de Backer G, Clement DL. Physiologic pacing in the elderly. Effects on exercise capacity and exercise-induced arrhythmias. *Jap Heart J* 1988;29:35-44.
- 4 Avery PG, Banning AP, Lawson T, McGurk L, Buchalter MB. Age should not be a contraindication for physiological pacing [abstr]. *Br Heart J* 1994;71(suppl):P71.
- 5 de Belder MA, Linker NJ, Jones S, Camm AJ, Ward DE. Cost implications of the British Pacing and Electrophysiology Group's recommendations for pacing. *Br Heart J* 1992;305:861-5.
- 6 British Pacing and Electrophysiology Group. Recommendations for pacemaker prescription for symptomatic bradycardia. *Br Heart J* 1991;66:185-91.

The British Pacing and Electrophysiology Group Guidelines on pacemaker group prescription, published in 1991, have generated much controversy. It is clear that universal implementation of the BPEG guidelines will be very expensive. We need to know whether this expense is justified in terms of longevity, quality of life, reduction in strokes and effect on heart failure. We cannot know until we have the results of planned trials. Let us have a moratorium until then.—EDITOR

Detection of left ventricular dysfunction after myocardial infarction: comparison of clinical, echocardiographic, and neurohormonal methods.

SIR,—A major limitation of the Peel index, even in its modified form¹ is that it does not take into account the adverse prognostic significance of the association of myocardial infarction and ST segment depression. In thrombolytic trials such patients continue to have a high mortality despite treatment²⁻³—not only because ST segment depression is an independent predictor of poor prognosis⁴ but also because it sometimes signifies structural damage caused by previous myocardial infarction.⁵ Furthermore, even when patients with ST segment depression prove to have smaller infarcts than their counterparts with ST segment elevation, they still have more severe impairment of left ventricular systolic function.⁵ These patients should, therefore,

be targeted for interventions such as treatment with angiotensin converting enzyme inhibitors after myocardial infarction, perhaps even irrespective of criteria generally implemented in other post-myocardial infarction subgroups.

OMP JOLOBE
Department of Medicine for the Elderly,
Tameside General Hospital,
Fountain Street,
Ashton-under-Lyme, Lancashire OL6 9RW

- 1 Choy AM, Darbar D, Lang CC, *et al.* Detection of left ventricular dysfunction after acute myocardial infarction: comparison of clinical, echocardiographic, and neurohormonal methods. *Br Heart J* 1994;72:16-22.
- 2 Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. *Lancet* 1986;ii:397-402.
- 3 ISIS-(Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected myocardial infarction. *Lancet* 1988;ii:349-60.
- 4 Schechtman KB, Capone RJ, Kleiger RE, *et al.* Risk stratification of patients with non-Q wave myocardial infarction: The critical role of ST segment depression. *Circulation* 1989;80:1148-58.
- 5 Willich SA, Store PH, Muller JE, *et al.* High-risk subgroups of patients with non-Q wave myocardial infarction based on direction and severity of ST segment deviation. *Am Heart J* 1987;114:1110-19.

This letter was shown to the authors, who reply as follows:

SIR,—As Dr Jolobe states in his letter, the adverse prognostic significance of ST segment depression in patients with non-Q wave myocardial infarction is well recognised. In our study, however, the patient group was representative of all patients admitted with myocardial infarction (MI). Of 57 patients whose admission and follow up electrocardiograms were available for analysis 13 (23%) had a non-Q wave MI and of these six presented with ST segment depression. The mean left ventricular ejection fraction (LVEF) in those patients with non-Q wave MI and ST depression was 37.5% compared with 45.7% in those who presented with non-Q wave MI and ST elevation. It is notable that the mean modified Peel index, which includes a score for post-infarction angina, was 10.7 in the ST depression group and 7.3 in ST elevation group. In the patients who had a Q-wave MI, 17 patients had no ST depression on the admission electrocardiogram, 20 had reciprocal ST depression, and 2 had ST depression alone. The mean LVEF in those with no ST depression was 42.5% compared with 40.5% in the group with reciprocal ST depression.

In the light of current evidence, the decision on whether to start an ACE inhibitor after MI should be based on clinical and/or echocardiographic evidence of left ventricular dysfunction.^{1,2} Although our findings are consistent with previous reports of the association between ST depression and left ventricular dysfunction in non-Q wave MI, this association does not seem to apply in most patients with Q wave MI. Thus it does not seem that the addition of ST segment analysis to sorting methods such as the modified Peel index would significantly improve their sensitivity in the detection of

left ventricular dysfunction, except possibly in the subgroup of patients with non-Q wave MI.

DARWOOD DARBAR
NEIL C DAVIDSON
ANNA-MARIA J CHOY
CHIM C LANG
TERENCE H PRINGLE
GRAEME P MCNEILL
NORMAN SJ KENNEDY
ALLAN D STRUTHERS
Ninewells Hospital and Medical School,
Dundee DD1 9SY.

- 1 Pfeffer NA, Braunwald, LA, *et al.* Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 1992;327:669-77.
- 2 The AIRE Study investigators. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. *Lancet* 1993;342:821-8.

Will serum enzymes and other proteins find a clinical application in the early diagnosis of myocardial infarction?

SIR,—Dr Timmis discussed the limitation of early biochemical diagnosis of acute myocardial infarction in guiding thrombolytic therapy.¹

The mortality of infarct patients in Newham General Hospital who present without ST elevation is only a third that of those with ST elevation, none the less about one in 20 of such patients died. In addition, in infarct patients who present with predominant ST depression one year mortality is high (31%).² De Wood *et al.*'s angiographic study of non-Q wave infarction was performed up to 24 hours after acute myocardial infarction³ and the patency rate caused by spontaneous coronary re-canalisation would be expected to be higher than in the first 12 hours, the time window when thrombolytic therapy is believed to be effective.⁴ Even so, 26% of these patients had occluded coronary arteries and might have benefited from re-vascularisation treatment. The result of the ISIS-2 trial suggests that patients without ST elevation (except bundle branch block) would not benefit from thrombolytic therapy.⁵ However, the inclusion criteria of ISIS-2 raise the possibility that an appreciable number of these patients may not have had a myocardial infarction at all. No definitive data are currently available to guide treatment in patients with early biochemical confirmation of acute myocardial infarction, though the LATE study⁴ did include patients with old or equivocal electrocardiographic changes and raised concentrations of cardiac enzymes. The LATE study showed a significant reduction in mortality in patients treated with alteplase when thrombolysis was started 6-12 hours after onset of symptoms. Other treatments such as β blockers, ACE inhibition, and aspirin have been shown to be useful in the early management of acute myocardial infarction.^{5,6} Early biochemical diagnosis may be useful in guiding this treatment.

Furthermore the use of rapid assays may offer advantages in terms of efficiency; patients with atypical chest pain may be discharged earlier after negative results. None the less, to exclude acute myocardial infarction, myoglobin should be measured 4-6

hours after the onset of chest pain and creatine kinase MB 6-8 hours after the onset of chest pain.⁷

Rapid biochemical diagnosis of acute myocardial infarction may be useful in guiding treatment and the more efficient management in coronary care units of patients who present with chest pain.

H S LEE
Department of Cardiology, Killingbeck Hospital,
Leeds LS14 6UQ
S J CROSS
K JENNINGS
Department of Cardiology, Aberdeen Royal Infirmary,
Aberdeen AB9 2ZB

- 1 Timmis AD. Will serum enzymes find a clinical application in the early diagnosis of myocardial infarction? *Br Heart J* 1994;71:309-10.
- 2 Lee HS, Cross SJ, Rawles J, Jennings K. Patients with suspected myocardial infarction who present with ST depression. *Lancet* 1993;342:1204-7.
- 3 De Wood MA, Stiffer WF, Simpson CS, *et al.* Coronary arteriographic findings soon after non-Q wave myocardial infarction. *N Engl J Med* 1986;315:417-23.
- 4 LATE Study Group. Late assessment of thrombolytic efficacy (LATE) study with alteplase 6-24 hours after onset of acute myocardial infarction. *Lancet* 1993;342:759-66.
- 5 ISIS-2 (Second international Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988;ii:349-60.
- 6 Woods KL, Fletcher S. Long-term outcome after intravenous magnesium sulphate in suspected acute myocardial infarction: the second Leicester intravenous magnesium intervention trial (LIMIT-2). *Lancet* 1994;343:816-9.
- 7 Lee HS, Cross SJ, Garthwaite P, Jennings K. Rapid exclusion of acute myocardial infarction in patients without ST elevation using serial cardiac enzyme analysis with novel analyzers—myoglobin, creatine kinase and creatine kinase-MB enzymes [abstr]. *Br Heart J* 1992;68:107.

SIR,—Dr Timmis states correctly that there is doubt about whether the use of serum markers of myocardial damage to confirm myocardial infarction in patients with chest pain but without ST elevation in the electrocardiogram will lead to lives being saved by the use of thrombolytic therapy.¹ However, he overstates the case against the use of serum markers with a misleading discussion of the evidence. The fact is that no large study has yet been published to compare the vascular mortality of thrombolysis and placebo in the subgroup of patients who have a non-diagnostic electrocardiogram (ECG) on admission to hospital, but a confirmed diagnosis of infarction on discharge. The GISSI study enrolled 451 patients with ST depression on the ECG; the mortality in this whole group was 18.4%, and did not differ significantly whether streptokinase or placebo was used.² ISIS-2 enrolled 1137 such patients, and again the mortality rate of 18.6% was not improved by streptokinase.³ The ASSET study distinguished only between normal and abnormal ECGs without distinguishing specific ECG abnormalities.⁴ GISSI-2 enrolled patients with ST segment elevation only.⁵ In the LATE study, 93% of patients had a discharge diagnosis of definite or possible infarction.⁶ In the group of 2544 patients without ST elevation on the ECG, the 35 day mortality was 7.5% in the placebo group and 6.4% in the group treated with alteplase.