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

Sir,

As Dr Cripps and his colleagues note (and as we emphasised in our article) the results of our study are applicable only to clinically stable patients with uncomplicated myocardial infarctions and the finding ought not be extrapolated to patients with complicated infarctions where the risk of future arrhythmic events is higher and the predictive accuracy of programmed ventricular stimulation may be better. Their study¹ and others including our own,²⁻⁴ support the clinical use of programmed ventricular stimulation in such patients.

Until recently there were few data on the clinical significance of inducible ventricular fibrillation in survivors of acute myocardial infarction. The results of our study and those of Denniss *et al*³ clearly show that inducible ventricular fibrillation is a non-specific response of little clinical significance in these patients. Therefore we agree that this arrhythmia should not be included as a positive end point in existing or future prospective trials of programmed

stimulation in survivors of recent myocardial infarction.

In our article we commented on the limitations imposed by the empirical antiarrhythmic treatment started in our first 10 patients with inducible sustained ventricular arrhythmias. The minimum length of follow up was at least 12 months in all but five patients, who were lost to follow up between four and eight months after the index infarction.

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Timing of treatment with oxygen radical scavengers and its influence on reperfusion injury

Sir,

In their editorial on oxygen radicals and myocardial damage (1989;61:4-8), Burrell and Blake pointed out that proof that there is specific, reperfusion-mediated damage depends on the administration of oxygen radical scavengers at the moment of reperfusion rather than before the onset of ischaemia. This is a valid point, but the reader may be left with the impression that the hypothesis of a specific reflow

injury remains to be tested because the editorial does not refer to the results of several pertinent published reports.

In the classic study by Jolly *et al*, administration of superoxide dismutase and catalase towards the end of the ischaemic period proved as effective in reducing infarct size as pretreatment.¹ Furthermore, in other studies administration of "anti-free radical" agents at the moment of reflow, *after* the ischaemic episode,

considerably reduced the myocardial concentration of oxygen radicals,² improved recovery of energy metabolism^{3,4} and of contractile function in isolated hearts^{3,4} and in anaesthetised dogs,⁵ and reduced infarct size in a long term canine model of coronary artery occlusion and reperfusion.⁶

Thus although the issue is not yet settled,⁷⁻⁹ there seems to be substantial evidence to indicate that, under certain circumstances, oxygen radicals can induce specific myocardial damage, which is separate from ischaemic damage, in various experimental models of post-ischaemic reperfusion. The studies that I draw attention to go some way to proving that scavengers of oxygen radicals given at the moment of reperfusion are effective in countering this specific myocardial damage.

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

Sir,

The results of many studies confirm the occurrence of a reperfusion event associated with the formation of oxygen free radicals in animals.¹ There is similarly convincing evidence that in the animal heart this event is associated with myocardial injury and that the extent of this injury may be modified by agents altering free radical mechanisms.² The optimal timing for such therapeutic intervention remains open to debate, but certainly some benefit may be achieved from treatment given after the ischaemic period.

However, small animals may be particularly susceptible to oxidative stress,^{3,4} and therefore more likely to benefit from antioxidant treatment, and the applicability of animal studies to patients with acute myocardial infarction is in some doubt.

From a practical point of view, long term prophylactic treatment for patients at risk of infarction with agents such as allopurinol seems unlikely to become widely established even if a small benefit were shown, and the potential beneficial effects of free radicals⁵ may be jeopardised by such treatment. An "anti-free radical" cocktail administered at the same time as a thrombolytic agent (that is after the ischaemic period, immediately before reperfusion) is the most promising starting point, and we agree with Ambrosio that any evidence that this may be beneficial in animals^{6,7} is encouraging. However, this does not alter our conclusion that therapeutic trials are not justified without further elucidation of free radical interactions in humans (1989;61:4-8).

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