EDITORIAL

Secondary prevention of myocardial infarction: an uncertain feeling

IT is often said that in 10 years, half of what we know either becomes out of date or is discovered to be untrue—the uncertainty arises from not knowing which half. The management of myocardial infarction is one subject where we are particularly prone to feel that our seemingly secure base of knowledge is shifting under our feet: where are the six weeks' bedrest and anticoagulant régimes of yesteryear? We have further difficulty in applying the findings of epidemiological surveys, with all their statistical precision and apparent safety in numbers, to the patients we see, one at a time—individuals with their own quirks and modifying factors. Epidemiologists, we murmur to ourselves at the bedside, do not seem to include patients like ours in their surveys. What, then, are we to make of the advice coming out of the vast amount of research into the secondary prevention of myocardial infarction? How should we advise our patients whom we treat at home? What should we do if the policies at our local hospital seem to be at odds with the evidence and with our own, probably changing, inclinations?

Men aged 40–49 who have had a first myocardial infarct were found in a Swedish study (Wilhelmsson *et al.*, 1978a) to be 40 to 50 times more likely to die suddenly in the following year, and 10 times more likely in the second year, compared with healthy men of the same age. The older the patient at the time of the infarct, the smaller the difference, and with it the scope for intervention. The risk can be reduced in several ways: by taking drugs or by reducing risk factors like smoking and raised total cholesterol levels.

Drug treatment

Ever since the early trial by Snow (1965)—impossible to act upon because of its unsatisfactory design—there has been a feeling that in some way beta-blocking drugs ought to prevent heart attacks. There are now several trials—of practolol, propranolol, timolol and metoprolol—showing that they do (Wilhelmsson *et al.*, 1974; Norwegian Multicentre Study, 1981; Beta-blocker Group, 1982; Hansteen *et al.*, 1982), and several concluding that they do not (Reynolds and Whitlock, 1972; Barber *et al.*, 1975; Baber *et al.*, 1980; Wilcox *et al.*, 1980). Epidemiologists and pharmacologists continue to emphasize the comparatively small benefit in numbers, and the fact that it could be dangerous to extrapolate from trial populations to others (Rose, 1982). Thus Breckenridge (1982) calculates that the impressive 25 per cent decrease in mortality rate represents merely a change from eight patients in every 100 dying to six per 100. A further twist in the evidence is the lack of benefit after the first year. Nevertheless, this reduction is, according to Rose, a major therapeutic advance in controlling heart disease; it is a benefit not to be decried, since "few therapeutic advances in cardiology have been placed so clearly beyond argument".

It is therefore fair to conclude that, unless patients are in heart failure or have severe reversible airways obstruction, they should probably be maintained on a beta-blocker for at least a year. The choice of drug is probably not crucial, but many will prefer, like Hampton (1982), propranolol 80 mg b.d. or timolol 10 mg b.d. However, there is considerable doubt about whether the treatment benefits all survivors and for how long the drug should be continued.

Benefit from drugs affecting platelet aggregation is even more uncertain. The original North American trial of sulphinpyrazone (Anturane Group, 1980) showed a large reduction in deaths during the year following infarction, but it has been rightly criticized (Mitchell, 1980). However, a more recent Italian trial (Anturane Study, 1982), although achieving no significant effect on deaths, did show a 56 per cent reduction in myocardial reinfarction as well as the expected reduction in strokes (six strokes and two transient ischaemic attacks in the placebo group against one non-fatal stroke in the treated group). Treatment with sulphinpyrazone 400 mg b.d. was started between 15 and 25 days after the infarct and maintained for 20 months.

There have been six major controlled trials of aspirin after infarction, which taken together suggest a small (16 per cent) but significant reduction in deaths (*Lancet*, 1980). Dipyridamole alone has not been shown to affect outcome, but one very large trial of dipyridamole plus aspirin (Persantin/Aspirin Group, 1980) showed a small but significant reduction in deaths, slightly greater for dipyridamole plus aspirin than for aspirin alone.

There has also been renewed interest in anticoagulants (Mitchell, 1981). After the excessive optimism of the 1950s was shot down by a number of trials, none of

them very well designed, the clinical consensus in Britain appeared to be that anticoagulants reduced the considerable risks of pulmonary embolism during the six weeks following myocardial infarction, but had no effect on reinfarctions. As this conclusion coincided with an end to prolonged bedrest as a method of treatment (and a cause of pulmonary embolism), anticoagulants almost disappeared, either as treatment or as secondary prevention. In 1981, however, the argument was effectively reopened by a rigorously designed and performed double-blind trial of long-term anticoagulants in elderly survivors of infarction in Holland (Sixty-plus Reinfarction Study, 1980). Unlike all previous trials, thrombotest activity was kept strictly within the range 5–10 per cent in over two thirds of the 12,785 participants throughout the two years of the trial. Incidence of reinfarction was reduced by two thirds, and total mortality was down by 44 per cent at two years. There was no increase in strokes in the anticoagulated groups, but there were 27 extracranial non-fatal bleeding episodes compared with only three in the placebo group. These results are more convincing than any of the trials of platelet-disaggregating drugs, and merit serious thought for our patients. If we do return to anticoagulants they must be strictly controlled, as they were in this trial.

Control of risk factors

After a first infarction, advanced atheroma must be assumed, and only those causal factors that operate independently of atheroma are worth controlling. Changes in dietary fat make little or no difference at this stage, a view endorsed by epidemiological studies. They show that, from the age of 50 onwards, there is little positive relation between total cholesterol and the incidence of myocardial infarction. The negative association with the amount of high density lipoprotein (HDL) cholesterol in the serum persists in older people (Gordon *et al.*, 1977), but this fraction is influenced more by smoking and exercise than by diet. Reduction of obesity after infarction is certainly beneficial, but, except in people under 50, more specific cholesterol-lowering diets are probably not effective.

In terms of proven effect, by far the most important step is to stop smoking, and this should be given priority over weight reduction if these aims conflict. In fact, stopping smoking is the only change in known risk factors which has been proved to cause a continuing decline in risk after a first infarction (Hammond, 1972; Gordon *et al.*, 1974). It is essential that action be taken during the episode of infarction itself, when the patient and relatives are most receptive to advice. In an excellent study in Göteborg following up 97 per cent of 528 men with first infarcts, 8 per cent were non-smokers, 15 per cent ex-smokers and 77 per cent current smokers at the time of the infarct. Over half the smokers, 57 per cent, stopped smoking while still in hospital, and fewer than 10 per cent of these resumed smoking during the two-year follow-up period. Of the 43 per cent who did not stop while in hospital, on the other hand, fewer than 10 per cent gave up later during the following two years. At the end of the two years, 6 per cent of those who stopped smoking had died compared with 13 per cent who did not stop (Wilhelmsson *et al.*, 1975, 1978a). All of these figures were replicated almost exactly by a similar study in Dublin, which followed 213 men over five years (Mulcahy *et al.*, 1975).

Although treating hypertension in survivors of myocardial infarction will prevent some strokes and heart failure, neither the Göteborg (Wilhelmsson *et al.*, 1978b) nor any other study has given good evidence that control of blood pressure at this stage reduces reinfarction. There is also not much evidence in favour of exercise programmes, although a study by Bethel and his colleagues, soon to be published in this journal, shows very promising results. In another controlled trial in survivors of both sexes aged under 57, there was no difference in survival after four years' follow-up, although fitness as measured by a bicycle ergometer had significantly improved in the trainees compared with random controls, and effort tolerance in those with angina had improved 100 per cent (Wilhelmsen *et al.*, 1975). Exercise training improves morale, return to work and the quality of life, and is justified on these grounds alone, but there is as yet no convincing evidence that it improves prognosis.

Conclusion

The conclusion must be that control of smoking is far more effective than any other intervention after infarction, and probably reduces risks by about 50 per cent. Firm advice on smoking should be given first priority by everyone concerned with the care of myocardial infarction patients, higher than any other technical, pharmaceutical or behavioural measures. Practical policies should be worked out to suit local circumstances (Buckley, 1982a, 1982b). Audit of these policies should be carried out, and several suggestions are contained in the College's report on the prevention of arterial disease (RCGP, 1981).

JULIAN TUDOR HART
General Practitioner, Glyncorrwg
S. L. BARLEY
Journal Editor

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