Lower patients' cholesterol now

Trial evidence shows clear benefits from secondary prevention

The first principle of the lipid hypothesis is that raised plasma cholesterol concentrations are associated with a high incidence of atherosclerosis and an increased risk of coronary heart disease. That assertion no longer stirs argument in medical circles. But the second principle—that both this risk and total mortality can be reduced by lowering plasma cholesterol concentrations—remains controversial. Polarisation of views has led over the past 20 years to the emergence of enthusiasts for whom cholesterol lowering and the prevention of coronary heart disease are almost synonymous and sceptics who attribute to lipid reduction more harm than good. This lack of consensus has been widely publicised by the media, and many people believe that the case for treating raised cholesterol concentrations is flawed and can be disregarded. The publication in 1994 of the results of several new trials has shown that this attitude is no longer tenable for one clearly defined category of patients—those who have already developed coronary heart disease.

Clinical decisions are rarely black or white. More often than not they are made with incomplete knowledge. This is certainly true in the prevention of cardiovascular disease. No one would challenge a policy aimed at reducing cigarette smoking, even in the absence of formal evidence from trials of a positive effect on the incidence of coronary heart disease. Consensus also exists that reducing the blood pressure decreases the frequency of cerebral vascular events. Cholesterol reduction is the one issue that has remained unresolved until now. The key questions are whether and when to treat raised cholesterol concentrations and to prescribe cholesterol lowering drugs—do the drawbacks of treatment outweigh its benefits? Faced with this dilemma—and mistakenly believing that the whole cholesterol lowering concept is still under debate—many practitioners choose to do nothing.

The new trial evidence has clarified the picture.[1-6] There is no longer any doubt about the benefit and safety of treating hypercholesterolaemia in patients who have had a myocardial infarction.[7] We shall summarise the recent data.

The largest secondary prevention trial, the Scandinavian simvastatin survival study, studied 4444 patients and showed that a 25% reduction in plasma cholesterol concentrations initially between 5·5 and 8·0 mmol/l (and a reduction in low density lipoprotein cholesterol by 35%) resulted after 5·4 years in 30% fewer deaths and 42% fewer coronary deaths.[1] No increase was seen in non-cardiovascular deaths. Two trials of the effects of a statin drug on coronary atheroma (considered together) showed that a decrease in cholesterol of 25-30% was associated with lessening of atheromatous obstruction. In one of these studies, the multicentre anti-atheroma study conducted over four years in patients with raised cholesterol concentrations, three serial coronary angiograms showed less progression of lesions, including fewer new lesions and total occlusions, and more regression in those treated with simvastatin than in controls.[2] Neither in this nor in the Canadian trial was any overall improvement seen in clinical events.[3] Neither, however, was designed to enable a change in such events to be appraised with confidence. The fourth study was a three year trial of lovastatin in asymptomatic hypercholesterolaemic men and women with early carotid atherosclerosis, who were followed with ultrasonography.[4] The results showed a favourable but not significant effect on the thickening of the intimal media and fewer major cardiovascular events compared with the placebo group. A further small three year trial of pravastatin was also associated with fewer coronary events.[5] Finally, a small double blind trial, the Harvard atherosclerosis regression project, added some additional perspective by suggesting that patients with more normal cholesterol concentrations (between 4·5 and 6·0 mmol/l) might not benefit (at least within three years) from statin treatment.

The favourable results of these secondary prevention trials go some way to resolve one of the central concerns of the cholesterol controversy. This is the suggestion—derived from earlier primary prevention trials—that lowering the cholesterol concentration might itself increase the risk of non-coronary death.[8] We can take some comfort from the Scandinavian simvastatin survival study, which showed that substantial reductions in circulating cholesterol—greater than those achieved in the earlier trials—were not associated with any evident increase in non-coronary mortality in patients known to have coronary heart disease, at least within five years of treatment. These results support the outcome of the longer program on the surgical control of the hyperlipidemias (POSCH) study, in which comparably large reductions in cholesterol were achieved by regional ileal bypass. The treated patients had no increase in non-coronary mortality after 12 years of follow up.[9] Any true adverse biological effect would be expected to be evident from these two trials.

The new studies do not, however, resolve the possibility of an increase in non-cardiac mortality with cholesterol lowering in people without overt coronary heart disease. That question is unlikely to be settled finally until a trial with the statistical power to address this specific issue is completed.[10] If, as expected, the results of such megatrials show that lowering cholesterol reduces the incidence of coronary heart disease in those at high initial risk then the use of drugs to treat those at less high risk would still require the most careful appraisal.[11]

Jury still out on benefits in primary prevention

Conservatism in primary prevention is still justified. But it is no longer acceptable in the treatment of raised cholesterol concentrations in most patients with coronary heart disease after a myocardial infarction. The recently published joint guidelines of the European Atherosclerosis Society, the European Society of Cardiology, and the European Society of Hypertension reflect these findings by recommending treatment with cholesterol lowering drugs for patients with coronary heart disease and a plasma cholesterol concentration of over 6 mmol/l—but only if three to six months careful dietary counselling has failed.[12] To what extent these recommendations might apply to high risk healthy people without manifest coronary heart disease may become clearer with the publication within a year of the first long term primary prevention trial in which reduction of plasma cholesterol by 25-30% has been achieved by the use of a statin drug.[13]

The risks of continuing high cholesterol concentrations in patients after myocardial infarction are unequivocal, but they are still often ignored in several European countries, including Britain. The consequence is undertreatment. While treatment with the statin drugs is expensive, this cost should be set against the strength of evidence for and the magnitude of the benefit shown in the recently published clinical trials.

There is no longer any controversy about what to do for these patients and no justification for inertia.

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The importance of clinical skills

High technology investigations do not diminish the need for clinical skills

The advance of medicine depends on the union of clinical art with high technology science. Sophisticated investigative methods improve clinical awareness and ability, but doctors and nurses must know how to interpret the results produced by the instruments they use. They must be aware of the limitations and possibilities of error. Uncritical reliance on values obtained by machines can be dangerous.[1]

Over 100 hundred years ago Anstie commented on the value of the sphygmograph but warned that it should be "used in conjunction with the strictest and most diligent observance of other means of clinical research."[2] Thirty years ago Godber wrote, "Though mechanical aids and measuring devices extend the capacity of the doctors to serve the patient, they do not replace him. They are the adjuncts to the human relationship between doctor and nurse and patient; they cannot replace the art."[3]

A good example of the clinically inexperienced being dependent on high technology is provided by the Swan-Ganz catheter for measuring intracardiac pressures in critically ill patients. Certainly echocardiography gives more information about the mitral valve and ventricular function than examination alone, while coronary arteriography is essential to determine the detailed anatomy of coronary artery disease. But ultrasound cannot be used to refine the diagnosis of a silent abdominal aortic aneurysm unless it is first suspected on clinical examination. Furthermore, a history and clinical examination are needed to arouse the suspicion of infective endocarditis so that timely laboratory tests can lead to essential early treatment.

A clinical diagnosis can often be made after a careful history and a competent physical examination. Having made a diagnosis, the doctor must then ask: What more do I need to know? What is the most appropriate test? What will it tell me? Is it safe? Failure to proceed in this way leads to a burgeoning of investigations and tests, which take over from the bemused investigator.[4]

Although patients are delighted with the impressive equipment available for their treatment, they complain that doctors no longer listen to them: they can be too occupied with instruments and the results of complex tests. The more that doctors are obsessed with instrumental results the less likely they are to talk to patients. Yet patients talk more easily to doctors than to computers and are encouraged to do so by a good clinical approach. Also, good communication improves relations between doctor and patient and diminishes the risks of litigation. As far as treatment is concerned, it is the patient who must be treated, not merely the disease revealed by the result of the test. Algorithms, while valuable for guiding decisions, tend to trap the patient in a box, which if not designated for active intervention may result in isolation and failure of communication.

Recently, warnings for the future have been published in the United States. The following appeared in the house magazine of the American College of Physicians[5]: "an intern is working at a big city teaching hospital. He is called to see an elderly man with dyspnea. The patient begins to tell his story. At first, the intern appears to be taking notes; as we look more closely we see that he is entering key words into a portable computer. Instead of examining the old man, the intern touches various parts of the body with a probe and records physical data, an electrocardiogram, and a set of diagnostic images. Later, the intern loads the data into a computer terminal at the nursing station. Seconds later, the computer tells him that the patient has pneumonia." A professor of medical information was said to suggest that, this could be "the way for the future." But then what would happen when the computer breaks down?[6]

Later, St Clair *et al* evaluated the ability of house staff to diagnose the murmurs of mitral regurgitation, mitral stenosis, and aortic regurgitation produced on a patient simulator machine.[6] The correct diagnosis was made by only just over half the residents. Even worse was to follow. Noel *et al* produced videotapes scripted with deliberate obvious mistakes in history taking and examination, such as palpation of the thyroid gland in the wrong place and failure to ask a patient with diarrhoea about blood in the stools.[7] Many of the faculty teaching staff who critically evaluated the tapes missed the mistakes. In their excellent editorial the editors of the *Annals of Internal Medicine* asked, "Are clinicians replacing instead of augmenting their diagnostic armamentarium?"[8]

The young teachers and those they teach must be given the example of method by their senior colleagues. Clinical skills