Can we reverse or retard an obstructive coronary lesion by risk factor intervention?

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There is general agreement that an association exists between certain risk factors and the occurrence of arteriosclerotic heart disease. Numerous intervention trials have been aimed at reducing these risks in the hope that if applied they will provide primary prevention or a secondary treatment which may retard or reverse obstructive lesions. However, recent reports cast doubt on possible benefits of such interventions except possibly in the case of treatment of florid lipid problems or abstinence from tobacco.[1–3] New critiques point out that previous clinical trials alleged to reverse the obstructive process suffer from poor design, lack of randomization, inadequate numbers, and have other serious methodologic shortcomings.[3]

In 1972 a Blue Ribbon Task Force of the National Heart and Lung Institute evaluated the currently available information on arteriosclerosis and formulated recommendations for long-range programs.[4] It implied that we do not understand the basic mechanisms or pathogenesis underlying development of the arteriosclerotic lesions, nor how various risk factors bring about development of clinical disease. It particularly noted that single risk factor interventions have failed, but it was hoped that because hy-

pertension, tobacco, and diet particularly stood out statistically as being associated with higher risk, control of all three at one time stood a better chance of affecting the arteriosclerotic process.

Lipids

In considering the effect of lower lipids, it appears that (1) dietary trials have failed to prove that low lipid diets, as a general health measure, can prevent arteriosclerotic heart disease in man; (2) although countless studies have proved the effectiveness of changing the diet in animals who have artificially produced arteriosclerotic obstructive lesions, species differences and the circumstances of creating the artificial obstructive lesions are dissimilar to those occurring in man and they cannot be transferred to clinical practice; (3) in order to prove the lipid hypothesis by an adequate test, such intervention would have to be applied in early childhood to prevent the onset of disease; (4) if the interventions were applied in early childhood, the results probably would not be known for 50 years; (5) patients who inherit lipid problems are those who are most likely to benefit from dietary change, but they represent only a minority of those suffering from obstructive vascular disease; and (6) lipid phenotyping might be indicated to search out the lipid victim for specific pharmaceutical or dietary therapy.

The failure of recent drug trials using lipid-lowering drugs to stop the progress and the eventual death of the patient with obstructive coronary lesions has caused the medical body to question whether the lipid hypothesis is correct.[5,6] A recent publication has questioned the veracity of numerous intervention trials of a dietary nature.[3] It now appears that no amount of public persuasion will succeed until the practitioners themselves become convinced on the basis of solid evidence.

Hypertension

Although most agree with the Veterans Administration study that antihypertensive therapy reduces the incidence of cerebral strokes, it is still not known whether the efficacy of antihypertensive therapy can be replicated in community programs for the purpose of primary prevention of coronary disease.[3] The ongoing national hypertension detection follow-up programs will provide answers to the question of whether mass community-based hypertension detection and treatment programs can accomplish the task of primary prevention of coronary heart disease and reduce mortality and morbidity associated with it.

Tobacco

It has been demonstrated that cigarette smoking increases the risk of coronary heart disease, but it is impossible to test these conclusions by formal double blind or randomized control clinical trials. Statistics indicate an excess mortality in patients with coronary disease who are smokers, but some investigators insist that this could be due to the behavioral abnormalities inherent in persons who smoke heavily.

Multiple risk factor trials

Multiple risk factor trials to test if control of diet, hypertension, and smoking will reduce cardiac mortality were implemented in 1972, but the

final results will not be forthcoming until 1982.

Exercise

The idea that regular physical exercise decreases the danger of death or disability from coronary atherosclerotic disease is based on a number of assumptions, some proven and some of questionable validity; but there are no convincing data to indicate that exercise will, in fact, decrease either the rate of development of atherosclerosis or prevent its complications.[4]

Obesity and diabetes

The arteriosclerotic lesions might not be due to obesity as such, but to two complications of obesity: diabetes and hypertension. Diabetes has been strongly incriminated as a risk factor, but it is difficult to implicate the associated hyperglycemia itself because the arteriosclerotic process may continue to advance, although blood sugar levels may be well controlled in the diabetic patient. Probably some undisclosed diabetic factor causes the premature atherosclerosis.

The role of the practitioner

Meanwhile the medical profession is frustrated because they do not have sufficient evidence to counsel the American public on primary prevention or secondary treatment that will be safe, effective, and economical. They have been stunned by failure of massive and expensive trials using lipid-lowering drugs. The practitioner cannot convince patients to change their life-style radically unless they are confident that it will provide positive results with a fair degree of certainty. With years of practice physicians have learned that, without solid proof, it is difficult to translate any measures in the form of treatment or change of life-style, for it will smack of propaganda. On the other hand, the most difficult thing they have to cope with is getting adequate scientific proof.

A public health approach depends so critically on having a convinced body of medical opinion to support such measures. It appears that medical body politic is not convinced today that lipid-lowering or other interventions are either feasible or effective in reducing the incidence of coronary heart disease in the general public.

We hope the answers will be forthcoming when the controlled clinical trial involving lipids, hypertension, and multiple risk factor interventions are completed. The cost of these national cooperative studies for the first 5 years was about $170 million, which is a small expenditure when compared to benefits of a possible reduction in health care costs, human suffering, and death.

What should the practitioner advise the patient until the answers are in? We agree with Kannel who stated, "Until more data on the efficacy of preventive measures become available, the practicing physician must decide for himself whether sufficient rationale for intervention exists. He must weigh the hazards against the potential benefits."[7]

Need for new directions in arteriosclerosis research

Coronary heart disease remains the number one health problem. Results of clinical pathologic laboratory and epidemiologic investigation of the past 200 years provide us with a wealth of knowledge on the natural history of the disease, but the etio-

logic mechanisms seem to elude us, emphasizing the need for new horizons in research. To achieve breakthroughs in the prevention, arrest, or reversal of obstructive vascular lesions, we need to supply priorities for:

1. Further basic research on the metabolism and physiologic function of the blood vessel wall.

2. Studies of the lining of the arterial wall, because recent investigations have indicated that an overgrowth of the smooth muscle lining of the arterial wall leads to accelerated atherosclerosis.

3. Application of interventions to human models where there appears to be an acceleration of the arteriosclerotic process, such as in the diabetic, the donor's heart after transplantation, those suffering from immunologic disease, such as lupus erythematosus, young patients treated with renal dialysis, patients with familial hyperlipidemia, and those whose families develop early arteriosclerosis without evidence of hyperlipidemia.

4. Endocrine studies to determine why women live 9 years longer than men and also do not develop clinical manifestations of arteriosclerosis until after menopause.

5. Study of environmental influences, such as those experienced by survivors of concentration camps who develop premature coronary or cerebrovascular disease.

6. Study of the relationship of genetics, genetic engineering, and heart disease.

We must complete the many intervention trials which could provide effective public health measures, but we also must provide a high priority for other new investigations which will explain the basic pathophysiologic processes. Unless a high priority of funding is provided for new directions of research to prevent, retard, or reverse the inevitable obstructive process, the eventual conquest of arteriosclerosis cannot be achieved.

References

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