Dietary Factors in Arteriosclerosis: Sucrose

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ABSTRACT

Epidemiological studies show that coronary heart disease is more common in wealthier countries than in poorer. Such studies cannot, however, isolate which of the dietary or nondietary characteristics of affluence help to cause the disease; they provide only clues that need to be subjected to experimental study. Experiments should be designed on the basis of their ability to produce the multiple abnormalities associated with coronary heart disease (CHD) and not only hypercholesterolemia. They should also explain the association of CHD with obesity, diabetes mellitus, cigarette smoking, and physical inactivity. These considerations suggest that the underlying abnormality that produces CHD is a disturbed hormonal balance. Experiments have shown that a high consumption of sucrose produces not only the wide range of abnormalities seen in CHD but also an increased blood concentration of insulin and cortisol. Since a low intake of sucrose confers many other health benefits, it is a more logical dietary recommendation than that of substituting polyunsaturated fat for saturated fat.

The earliest suggestion about the role of diet in coronary heart disease (CHD) was derived largely from epidemiology. Different populations with widely different prevalences of CHD were compared and were found to have differences in fat consumption that roughly paralleled the prevalence of the disease. Similarly, as one population became more and more affluent, there was an increase in both fat intake and coronary disease. These relationships are not only with fat intake but with any measure of affluence. Twenty years ago the best correlation with the increased prevalence of CHD in Britain, even better than that with any dietary constituent, was found to be with the increase in the number of people having radio and television (1). Any one of the characteristics of affluence, dietary and nondietary, could, on the basis of population comparisons, be indicted as producing CHD.

A second difficulty arises because CHD is caused not by just one factor but by several, a statement with which virtually all observers now agree. One cannot then expect to isolate any one factor by comparing populations that differ in several ways and in varying degree. A population in which many people smoke cigarettes but who are extremely active might have no more CHD than a population in which the people do not smoke but are very sedentary.

This last statement assumes that there really is evidence that both cigarette smoking and sedentariness increase the likelihood of people developing the disease. The evidence comes from the next stage in epidemiology, which moves from a study of populations to a study of individuals. This shows that, within one population, the man who does not smoke is less likely to develop the disease than the man who does smoke, who in turn is the more likely to develop CHD the more he smokes.

As regards diet, the search in individuals for a relationship between fat intake and heart disease has been unsuccessful (2). Two separate studies have shown that men with a first known coronary attack had been taking more sugar than had control subjects (3,4). The inability of other workers to confirm this observation may be due to faults in the design of their studies (5).

LIMITATIONS OF EPIDEMIOLOGY

Whatever the reason for the negative results with fat intake, and of some of the negative results with sucrose intake, epidemiological studies should be taken only as clues that determine the direction for experimental investigation. This is clearly necessary for epidemiological studies that yield contradictory, confusing, or unconvincing results, as do all the studies that have sought to identify dietary components in the etiology of CHD.

There is one epidemiological fact, however, that presents the most promising clue, but which has been entirely or largely ignored as a basis for experiments designed to discover the causes of CHD. Women before the menopause have a relative immunity to CHD, which is largely lost after the menopause, which strongly suggests the possibility that the basis for the development of the disease is an abnormality in hormone activity. This seems to be much more plausible than the commonly held view that CHD is based on a simple disturbance of some biochemical transformation, such as the synthesis of cholesterol from saturated fat.

In addition to the differences in prevalence of CHD between men and women, other features support the idea that experimental studies
should be based on the hypothesis that the disease is determined by a disturbed hormone balance. Firstly, CHD is commonly associated with an abnormally high concentration of insulin and cortisol in the blood. A very recent study has shown that the degree of coronary atherosclerosis, as revealed by angiography, is related to the concentration of cortisol in these patients (6). Secondly, in addition to the increased concentration of these hormones, and the increased blood cholesterol concentration that occurs commonly though not universally, there are increased blood concentrations of triglycerides, uric acid, and blood glucose, a diminished glucose tolerance, an increased platelet adhesiveness, and an abnormal platelet behavior in electrophoresis. It is difficult to explain this wide range of apparently unrelated abnormalities other than by a disturbance in hormone activity.

**RELEVANT EXPERIMENTS**

Ideally, an experimental search for a cause of coronary heart disease would be to see whether the suspected factor actually produces the disease. But none of the ordinary laboratory animals can be made to develop CHD as seen in man, and it is of course out of the question that one should attempt to do so in man. One is left then with short or long term experiments in animals, and with short term experiments in man, in which to attempt to reproduce some of the characteristics of CHD such as the changes in the blood described above. Experiments should be designed with three objectives in mind:

1. to see whether the suspected agent produces not simply an increase in the concentration of cholesterol but as many as possible of the abnormalities that are associated with CHD;
2. to discover whether the agent produces features that are also produced by other, and recognized, etiological agents — for example, cigarette smoking and physical inactivity; and
3. to see whether the results help to explain the clinical link between CHD and other conditions such as obesity and diabetes mellitus.

It is along these lines that the hypothesis that a high intake of sucrose is one of the causes of CHD has been tested. Since the increase in sucrose intake that has taken place in Western countries, especially in the past century or two, has been accompanied by a fall in the starch intake of about the same magnitude (7), these experiments have compared diets that are identical in all respects except in the nature of the carbohydrate, permitting comparison of the effects of sucrose with those of starch.

**EFFECTS OF DIETARY SUCROSE**

In experiments of this kind, carried out with several species including rats, spiny mice, pigs, and man, diets with sucrose produced an increase in the concentrations of plasma cholesterol, triglyceride, and uric acid; a diminution in glucose tolerance; an increased platelet adhesiveness; and a change in electrophoretic behavior of the platelets (8). There is also an increase in the plasma concentration of insulin and of cortisol. All these features are found in patients with coronary disease.

Cigarette smoking also causes an increase in plasma insulin, whereas physical activity causes a fall, thus bringing sucrose into line with these two agents as suggested causes. Both obesity and maturity onset diabetes are frequently associated with an increase in the concentration of plasma insulin. There is also a tissue insensitivity to the action of insulin, which is another effect of dietary sucrose (9). Moreover, the diminished glucose tolerance, on which the diagnosis of diabetes rests, is a feature both of obesity and of coronary heart disease.

On quite different grounds, we suggest a more serious approach by clinicians and health educators in general to the promotion of a reduction of sucrose intake as an important health measure. In comparison to the current widespread and drastic dietary recommendations that saturated fat be reduced and that polyunsaturated fat be increased, we recommend simply a reduction of sucrose. The relative merits of these recommendations can be assessed by seeking answers to the following three questions:

1. Will it reduce the risk of developing coronary heart disease?
2. Will it have any other benefits?
3. Does it present any possible hazard?

In our view, there is a stronger case for implicating sucrose in causing CHD than for implicating fat. For example, there is no way of linking diabetes mellitus and obesity with CHD through the known effects of substituting polyunsaturated fatty acids (PUFA) for saturated fatty acids. But for the purposes of this discussion, it will suffice to say that there is equal though incomplete evidence for the fat hypothesis and the sucrose hypothesis.

**BENEFITS AND HAZARDS OF DIETARY CHANGE**

What are other benefits that would accrue