Editorial

Nutrition, Atherosclerosis, and Infarction

One hears much these days about dietary fats as possible causative agents in atherosclerosis and, by implication, thrombosis and infarction, both coronary and cerebral. It may be well to remember that most experimental and clinical studies in this area relate to changes in the level of serum cholesterol or various lipid fractions. They do not relate directly to atherosclerosis, thrombosis, or infarction. True, in the last year or so some laboratories have included postmortem studies of actual atherosclerosis in addition to experimentally induced hypercholesteremia, and our laboratory has found a reasonable correlation between these two factors in early lesions produced in rats. One laboratory has reported the experimental production of coronary infarction in a sizable proportion of rats; nevertheless, the great mass of factual information is concerned only with changes of serum cholesterol, and these changes over a relatively short time.

Most epidemiologic studies in this area have dealt with crude death rates rather than age-specific death rates and with the information on death certificates as the cause of death. Both procedures may give erroneous results. A few epidemiologic studies have included levels of serum cholesterol, but seldom has the information on the causes of death been furnished by autopsy reports.

The level of serum cholesterol is certainly affected by the amount and kinds of fat in the diet, by a number of other components of nutrition, and by other metabolic activities such as change in body weight, relative concentration of certain hormones, exercise, and possibly by psychic stress. It is not possible to design an experiment in nutrition involving a major change in a source of calories and have only a single variable. Thus if fat is reduced in an isocaloric diet, either carbohydrate, protein, or both must increase. Defining with accuracy nutritional changes in the experimental manipulation of diets for man or changes in the usual diets of different groups of people becomes rather complicated.

Most experimental nutrition studies on raising the level of serum cholesterol and on the production of atherosclerosis involve the addition of cholesterol to the diet. At times the amount of cholesterol added to the diet has been large, as for example early studies from our laboratories where 5 per cent of the diet was cholesterol. Subsequent studies have shown that such large amounts are not necessary, and actually additions of the order of 1 mg of cholesterol per 3 to 5 calories of food consumed will result in a marked hypercholesterolemia and subsequent atherosclerosis. These studies have shown that there is both a time and an intensity factor in that the greater the level of dietary cholesterol, the shorter the time before positive results appear. Addition of cholesterol to experimental diets is a valid experimental procedure, for one is trying to produce a hypercholesteremia—and after all, man consumes a diet with a variable content of cholesterol.

With diets containing cholesterol, and more recently a small amount of cholic acid perhaps to favor absorption, it has been found that not only does the amount and type of dietary fat influence serum cholesterol (and atherosclerosis), but also the amount and type of dietary protein, carbohydrate, magnesium, and the additions of various uracil and pyrimidine compounds.

Nutrition is certainly involved (in experimental atherosclerosis), in a far more extensive and complicated way than simply through fatty acids, be they saturated, monounsaturated, or polyunsaturated. Thus, there is excellent evidence in the rat that a fat in which the predominant fatty acid is completely saturated (coconut-lauric acid) acts synergisti-

cally with a number of fats rich in the essential polyunsaturated fatty acids (linoleic and arachidonic) in providing a mixture of dietary fat that keeps serum cholesterol relatively low. Less extensive but similar data have been found also with the monkey and with man, but not with the chick.

The formula-feeding studies of a number of laboratories have shown strikingly that under the conditions of these studies fats rich in the polyunsaturated fatty acid linoleic acid, such as corn, cottonseed, or safflower oil, effect a decrease in serum cholesterol of the order of 10 to 30 per cent, depending on the initial level. These interesting studies are responsible for the wave of enthusiasm for the use of these oils in diets and emulsions of these oils as therapy. What is usually not appreciated is that these striking results were all obtained on formula diets, not on the addition of these oils to a "meat and potato" diet. On the latter there is much less evidence that a modest increase in the intake of these unsaturated oils has any effect other than to serve as an additional source of calories.

What relation does serum cholesterol have to atherosclerosis and infarction? Experimentally, the evidence is strong for atherosclerosis. The latter has now been produced in all species of animals studied when one has been able to produce a sustained elevation of serum cholesterol. It is unlikely that man would be different in this regard.

Experimentally, the evidence is weak for infarction, for only one laboratory has so far claimed to have produced infarction. It is necessary to mention that very drastic dietary conditions were necessary, and these occasionally resulted in an increase of serum cholesterol of the order of 40 times the normal. Further, infarction did not seem to be related to the level of cholesterol. Whether the milder hypercholesteremia seen in man is comparable in any way is problematical.

Evidence is also accumulating in man that an increase in serum cholesterol favors the development not only of atherosclerosis but also of infarction. However, it should be emphasized that atherosclerosis is undoubtedly a disease of multiple and additive etiology. Heredity, overweight, and hypertension are involved in addition to an increase in serum cholesterol. Further, the disease is more prevalent in smokers than in nonsmokers and in sedentary rather than physically active individuals. Since nutrition is concerned with many of these factors, it might well be a most significant factor in atherosclerosis. Its real promise would seem to lie in the area of prevention, for once one understands how nutrition is involved, opportunities for dietary changes should become available.

But it should be emphasized frequently that no discussion of nutrition and heart disease should be interpreted to mean that nutrition is the sole or perhaps even the major cause. It may be expected that the chronic diseases developing slowly over long periods will be influenced by multiple factors related to the genetic and environmental background of the patients. One of the major jobs of the researcher is to define the multiple factors involved and to determine their relative importance. The evidence today would indicate that nutrition is involved in various ways. Since the diet is subject to manipulation, there is real promise for prevention or treatment.

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