Effect of Cholesterol-Lowering Diet on Mortality from Coronary Heart Disease and Other Causes

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SUMMARY  International statistics indicate that there is a close correlation between the consumption of saturated fats (dairy fats and meat fats) and the mortality from coronary heart disease (CHD), and this conception has been confirmed by many epidemiological studies. Such studies alone, however, cannot prove the existence of a cause-and-effect relationship between these two variables; dietary intervention trials are needed.

The Finnish Mental Hospital Study was such a trial, conducted in two hospitals near Helsinki in 1959–1971. Practically total replacement of dairy fats by vegetable oils in the diets of these hospitals was followed by a substantial reduction in the mortality of men from CHD. Total mortality also appeared to be reduced. As to the causes of death other than CHD, none was significantly influenced by dietary change. This was also true for malignant neoplasms.

To alleviate the burden of CHD on public health, many investigators have recommended important changes in the quantity and quality of dietary fats.

THE IDEA THAT CORONARY HEART DISEASE (CHD) might, at least partly, be a nutritional disease, and hence, could be prevented by dietary means, deserves careful attention and consideration. A few investigators had expressed such views long ago, but this question remained largely neglected by the scientific community until World War II. This war was, among other things, a vast experiment in the sphere of foods, nutrition and disease. At that time, it was noted that the mortality from CHD decreased considerably in some countries. These were the countries which experienced the most severe food rationing measures and in which, particularly, the fat consumption drastically declined.

Norway and Finland were two such countries. In Norway during the war, there was a definite drop in the mortality from circulatory diseases and a concomitant drop in the consumption of fat in the form of milk, butter and eggs.\(^1\), \(^2\) When the normal food supply resumed after the war, the coronary mortality again rose and soon nearly matched the prewar statistics. Similar data are available from Finland.\(^2\), \(^3\)

In countries like the U.S., where the food supply remained practically normal in spite of the war, no appreciable changes in mortality were observed.\(^2\)

These wartime observations were instrumental in directing our attention to foods in relation to CHD and particularly to food fats.

It might be helpful to examine the more recent vital statistics released by the World Health Organization (WHO).\(^4\) The mortality from CHD (item A 83 of the International Classification of Diseases) among middle-aged men in a number of countries is shown in figure 1.

At the upper end of the scale are Finland and then Scotland, the U.S., Australia, England and Canada; at the lower end are Japan and the Mediterranean countries — Spain, Greece and Portugal. The difference between the first and the last countries is very large; the mortality in Finland is more than 10 times greater than in Japan. Most of the entries in the upper part of the list represent highly industrialized nations. Perhaps the modern way of life in the affluent societies has something which makes them unusually susceptible to CHD. Some researchers blame mental stress or lack of exercise, and others rich food or cigarettes.

The wartime observations tended to associate CHD with food fats. Figure 2 shows how the present fat consumption figures\(^5\) in countries show how they correlate with coronary mortality. In figure 2, the abscissa shows the total fat consumption, and the ordinate shows the coronary mortality. The consumption scale

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Figure 1. Mortality from coronary heart disease (CHD) among middle-aged men in certain countries. 

WHO = World Health Organization.

Figure 2. Correlation between total fat consumption and mortality from coronary heart disease (CHD).

Abbreviations: AL = Australia; AU = Austria; BE = Belgium; CA = Canada; DE = Denmark; FI = Finland; FR = France; GE = Germany (West); GR = Greece; IR = Ireland; IT = Italy; JA = Japan; NE = Netherlands; NO = Norway; NZ = New Zealand; PO = Portugal; SP = Spain; SWE = Sweden; SWI = Switzerland; UK = United Kingdom; US = United States; and YU = Yugoslavia.
is very wide, from some 170 g/day in Belgium, Germany and the U.S., to about 100 g in the Mediterranean countries, and finally to about 60 g/day in Japan. Still lower consumption figures (not shown in the figure) of about 20 g/day are found in some “developing” countries of Asia or Africa. There is a slight, but statistically significant correlation between total fat consumption and coronary mortality. But it is not sufficient to measure only the quantity of the fat consumed; the quality of that fat must also be considered.

**Categories of Food Fat**

The food fats may be divided into two categories: vegetable and animal, and the latter may further be divided into three subcategories: dairy fats, including the fats of milk and dairy products; meat fats, or more precisely, “land animal body fats;” and marine fats, consisting of fats of fish and of marine mammals, such as whales and seals. The properties and the fatty acid composition of these types of food fats are very different. Vegetable fats, such as soybean oil, corn oil, sunflower oil and, to a lesser degree, olive oil, are relatively unsaturated, as they contain substantial amounts of polyunsaturated fatty acids, mainly linoleic acid. Dairy fats and meat fats are much more saturated and contain only small quantities of linoleic acid. Marine fats are highly unsaturated and contain fatty acids with even five or six double bonds in their molecules.

The consumption of these food fats varies significantly among nations. The consumption patterns in some countries are shown in figure 3. In the countries with high coronary mortality (the upper part of the figure) meat fats are usually the predominant food fats; the consumption of dairy fats is also often remarkably high (particularly in Finland, New Zealand and Ireland). On the other hand, vegetable fats are consumed in modest quantities only (except in the U.S.).

In the countries with low coronary mortality (the lower part of the figure), the consumption patterns are very different. Vegetable fats are the predominant type of food fats; the consumption of meat fats is much smaller and that of dairy fats usually very small.

Is it particularly meat fats and dairy fats which are conducive to CHD? The correlation between these fats and CHD mortality \( r = 0.66 \) is far higher than between total fats and CHD mortality \( r = 0.47 \). However, a still closer correlation is found between dairy fats alone and CHD mortality \( r = 0.75 \). This is illustrated in figure 4. At the upper end of the regression line are New Zealand, Finland and Ireland, the great dairying countries, and at the lower end are the Mediterranean countries and Japan. There is a remarkably good and statistically highly significant correlation between the consumption of dairy fats and the mortality from CHD.

In this examination of consumption patterns, the fats have been classified according to origin — vegetable and animal fats. This is, of course, essentially only a practical classification; the nutritional properties of fats are not so much determined by their source as by their fatty acid composition. In general,
however, animal fats may be regarded as primarily saturated and vegetable fats as mostly mono- or polyunsaturated.

Most of the preceding information is based on statistics, food consumption and vital statistics released by international organizations. Unfortunately, we cannot know how accurate and how comparable the figures from different countries really are. Therefore, additional evidence of another type would be highly desirable. In this regard, it is pertinent to refer to the investigations of the international team headed by Keys and carried out in seven countries according to strictly defined and uniform experimental protocol. This is the "Seven Country Study," which started in 1957 and was carried out in five European countries — Italy, Yugoslavia, Greece, Netherlands and Finland, and, in addition, in the U.S. and Japan. The food intake was carefully measured and the incidence of CHD was assessed by electrocardiography and other means. The results of this study provide solid support to the conclusions based on international statistics. A close correlation was found between the nutritional intake of fats of the saturated type and the incidence of CHD (r = 0.84). As the serum cholesterol values were found to be highly correlated with the intake of saturated fats (r = 0.89) and with CHD (r = 0.81), it appeared possible that the effect of saturated fats on CHD could be mediated through serum cholesterol.

Such observations have led to what is often termed "the lipid hypothesis": saturated fats (and cholesterol) of the diet elevate serum cholesterol and this again — presumably through accelerating atherosclerosis and possibly also through thrombotic phenomena — leads to an increased incidence of CHD. The cause-and-effect nature of the first link in this chain of events has been proven beyond any reasonable doubt: dietary fatty acids and cholesterol definitely influence serum cholesterol. It has been much more difficult to ascertain the nature of the second link: whether this, too, is a cause-and-effect relationship or only an indirect association. This question cannot be resolved by usual epidemiological studies alone. For this purpose intervention studies are required in which the diet of a suitable population is deliberately changed and the development of manifestations of CHD is followed over a sufficiently long period.

Such studies are not easy to carry out. They are costly and time-consuming, as large numbers of subjects and long observation periods are required for reaching conclusive results. Because of these difficulties, only relatively few such studies have until now been conducted.

**Finnish Mental Hospital Study**

The Finnish Mental Hospital Study was a long-term dietary intervention trial carried out by our

![Figure 4](http://circ.ahajournals.org/)

**FIGURE 4.** Correlation between consumption of dairy fats and mortality from coronary heart disease (CHD). Abbreviations for the countries are the same as in figure 2.

<table>
<thead>
<tr>
<th>Table 1. Design of Experiment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospital N</strong></td>
</tr>
<tr>
<td>First period 1959-1965</td>
</tr>
<tr>
<td>Second period 1965-1971</td>
</tr>
</tbody>
</table>
Table 2. Composition of the Diets (Means of the Two Hospitals)

<table>
<thead>
<tr>
<th></th>
<th>Experimental</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food energy (kcal/day)</td>
<td>2,820</td>
<td>2,830</td>
</tr>
<tr>
<td>Fats (g/day)</td>
<td>110</td>
<td>107</td>
</tr>
<tr>
<td>Fat energy (% total)</td>
<td>35</td>
<td>34</td>
</tr>
<tr>
<td>Saturated fatty acids (% total fatty acids)</td>
<td>26</td>
<td>54</td>
</tr>
<tr>
<td>Polyunsaturated fatty acids (% total fatty acids)</td>
<td>39</td>
<td>13</td>
</tr>
<tr>
<td>P/S</td>
<td>1.48</td>
<td>0.25</td>
</tr>
<tr>
<td>Cholesterol (mg/day)</td>
<td>282</td>
<td>480</td>
</tr>
</tbody>
</table>

Table 3. Contents of Adipose Tissue Linoleic Acid (18:2) and Myristic Acid (14:0) Near the End of the Dietary Periods (% Total Fatty Acids)—Males

<table>
<thead>
<tr>
<th></th>
<th>Hospital N</th>
<th>Hospital K</th>
</tr>
</thead>
<tbody>
<tr>
<td>18:2</td>
<td>14:0</td>
<td></td>
</tr>
<tr>
<td>First period (1964)</td>
<td>26.9</td>
<td>10.2</td>
</tr>
<tr>
<td>Second period (1970)</td>
<td>9.8</td>
<td>32.5</td>
</tr>
</tbody>
</table>

Table 4. Mean Serum Cholesterol Values (mg/100 ml)—Males

<table>
<thead>
<tr>
<th></th>
<th>Hospital N</th>
<th>Hospital K</th>
</tr>
</thead>
<tbody>
<tr>
<td>First period</td>
<td>216</td>
<td>268</td>
</tr>
<tr>
<td>Second period</td>
<td>267</td>
<td>236</td>
</tr>
<tr>
<td>Change</td>
<td>+51</td>
<td>-32</td>
</tr>
</tbody>
</table>

mining the fatty acid compositions of needle biopsy samples of adipose tissue taken from a large group of patients in each hospital. Table 3 shows the contents of two characteristic fatty acids near the end of the dietary periods: linoleic acid, derived mainly from soybean oil, and myristic acid, derived mainly from dairy fats. The fatty acid composition of the adipose tissue was closely associated with the diet. In each hospital toward the end of the experimental diet period (hospital N: the first period and hospital K: the second period) linoleic acid content was much higher and myristic acid content significantly lower than toward the end of the respective control period. These adipose tissue studies reveal that the diets consumed during the two periods had been very different in their fatty acid compositions and also that the adherence to the diets must have been good.

The dietary changes were followed by marked changes in the serum cholesterol levels (table 4). During the first period cholesterol was much lower in hospital N, which used the experimental diet. The reversal of the diets brought about a sharp reversal of the serum cholesterol values: a marked increase in hospital N, which was returned to the normal diet, and a somewhat smaller decrease in hospital K, in which the experimental diet was introduced. This diet thus proved to be definitely cholesterol-lowering, with mean reductions of 19% in hospital N and 12% in hospital K (mean value 15%).

The mortality studies comprised the total hospital populations, with more than 4000 male patients in all and nearly 11,000 person-years of observation. In about half of the cases necropsy was done, and the assignment of the cause of death was based on both clinical and postmortem evidence. All death certificates were reexamined by a member of our team, and, where necessary, brought into conformity with the rules established by WHO for selecting the cause of death. This was done “blindly,” i.e., without knowing from which hospital the certificate came. For calculating death rates the concept of person-years of risk was used.

Table 5 shows the results of the mortality study. Comparisons of the rates should be made primarily between the different periods of the same hospital, since there is less certainty about the mutual comparability of the populations of the two hospitals. Even in the same hospital the patient population changed through discharges and new admissions, but, as in mental hospitals generally, this turnover (12% per year) was low.

The most striking differences shown in the table were in coronary mortality. The differences were quite...
striking, with the experimental period mortality only about one-half of that of the control period mortality. Comparison of the mean values of the periods also indicated a much lower diet period mortality. Statistical testing showed that the differences for hospital N and also for the mean values were highly significant ($p < 0.002$). In hospital K, the difference, although of much the same magnitude, was on the borderline of statistical significance ($p < 0.06$). This was obviously due to the smaller size of the population in this hospital.

Table 5 also reveals notable differences in the mortality from all diseases. These differences were always in the same direction as those of coronary mortality, but were somewhat smaller and failed to reach the level required for statistical significance. About half the lives saved from coronary deaths by the use of the experimental diet may have been lost to deaths from other causes.

No consistent differences were observed in the other causes of death. This applies to cerebrovascular disease, other diseases of circulatory system and also to malignant neoplasms. The latter finding is noteworthy since some investigators have reported excess deaths from carcinoma among individuals assigned to a cholesterol-lowering diet. In our material the differences in the mortality from malignant neoplasms were small and showed no consistent pattern.

We feel that the findings of our study justify the conclusion that in men, a cholesterol-lowering diet, i.e., a diet low in saturated fats and relatively high in polyunsaturated fats, considerably reduced the mortality from CHD. They also indicate, though not conclusively, that total mortality was favorably affected by this diet.

Our results are in fair agreement with those of some other preventive trials, which have measured the incidence of CHD by the use of various "softer" end points. They also agree with the vast amount of epidemiological evidence on CHD gathered mainly during the last 2 or 3 decades and with the results of animal experiments in many species, including primates.

### Measures for Prevention

It is difficult to evade the conclusion that CHD is at least partly preventable by dietary means, but this is not to say that the problem of prevention could be completely and ultimately solved by dietary means. However, our knowledge is sufficiently extensive for its application to promote public health. It is not always judicious to wait for the final results and the irrefutable proof before taking action. Many lives could be saved and much good done by starting a little earlier. Although we do not yet have an absolute proof for dietary prevention of CHD, there is strong evidence for its effectiveness, and its safety.

Obviously, we should aim at lowering the high serum cholesterol values so prevalent among many populations. It is well-known how different dietary components affect serum cholesterol. Saturated fatty acids, mainly myristic and palmitic acids, as well as dietary cholesterol, tend to increase serum cholesterol, whereas polyunsaturated acids, mainly linoleic, tend to depress it. The effect of dietary changes can even be predicted semiquantitatively by means of equations, as shown below:

$$\Delta \text{Chol.} = 1.2(2 \Delta S' - \Delta P) + 1.5 \Delta Z$$

This equation was developed by Keys and co-workers. $\Delta \text{Chol.}$ is the change in serum cholesterol, $S'$ is saturated fatty acids minus stearic acid, $P$ is polyunsaturated fatty acids and $Z$ is a term dependent on dietary cholesterol. While such an equation is valid only for the population from which it was experimentally derived, it can, with certain reservations, be used more generally. This equation shows that decreasing dietary saturated fatty acids is twice as effective as increasing polyunsaturated acids. Hence the saturated fatty acids of the diet should be the prime target in our attempts at prevention.

The main sources of saturated fatty acids are dairy fats, derived from milk, cream, butter, and ice cream, and meat fats. Among meat fats there are considerable differences in the degree of saturation. Most saturated are ruminant fats — beef and mutton. Pork fat is less so, and poultry fat the least.

An increase of polyunsaturated fats of the diet would be the second point in prevention. This can be done by increasing the consumption of vegetable oils high in linoleic acid, such as corn oil, soybean oil and sunflower oil. These oils can be used as such, or they can be incorporated into foods such as margarine, milk in the form of "filled milk," cheese, ice cream, sausages and even meat. Most fish fats are good sources of highly unsaturated fatty acids.

The third point in prevention would be the reduction of the cholesterol of the diet. This could be achieved best by reducing the intake of high-cholesterol foods such as egg yolks, liver and kidney.

How much can be accomplished by these dietary changes in serum cholesterol? There is fairly extensive experience about the attempts to lower serum cholesterol values of populations. The observed reductions in the mean serum cholesterol have been some 10–15% among free-living populations and somewhat greater, 15–20%, among captive populations.

These reductions may seem relatively modest, and we may justifiably ask whether they possibly could accomplish much in the way of prevention. However, the situation is not so discouraging. Prospective studies
have shown that the interrelation between serum cholesterol and CHD is not linear, but represented by a power function \( y = a + bx^k \), in which the value of the exponent \( k \) is somewhere between 2–3. Thus, a small change in serum cholesterol would bring about a far larger change in the CHD incidence. According to the equation, a 15% reduction in serum cholesterol, which is attainable even among free-living populations, could be followed by a reduction of 30–40% in CHD.

Considering the momentous public health aspects of the diet-CHD relationships, it is not surprising that numerous organizations, official and semiofficial, have examined the available evidence and issued statements about measures to be taken. More than 15 such reports have been published.\(^{20}\)

One of the earliest, issued in 1968, was a joint statement by the Medical Boards of Norway, Sweden and Finland dealing with the desirable changes of diet.\(^{21}\) Of the more recent statements the three following are perhaps the most noteworthy: one published in Australia,\(^{22}\) the second in Britain,\(^{23}\) and the third and latest one in the U.S.\(^{20}\) The dietary recommendations made in these reports are to a large extent concordant. The total fat consumption should be reduced from the present high levels of 40–45% of total food energy to 35%\(^{23}\) or 30%,\(^{20,\, 22}\) or even to 25%\(^{25}\) of total food energy. This reduction should, above all, concern saturated fats, while the consumption of polyunsaturated fats should be increased. The desirable P/S ratio would be 1.0,\(^{20}\) or even 1.5.\(^{22}\) The dietary cholesterol intake should also be substantially diminished; from the present levels of about 600 mg daily to less than 300 mg daily.\(^{20,\, 22}\)

The recommendations made by these committees are consistent, clear-cut and well-founded. Their implementation, however, will obviously call for great changes in the prevailing consumption patterns; in many countries this may have significant economic and agricultural repercussions. Therefore, in spite of the potential great gains in public health, the implementation of these recommendations may be difficult.

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