Fats, Cholesterol, and Coronary Heart Disease  
A Review of Recent Progress 

By Norman Jolliffe, M.D.

WHAT dietary advice can the medical profession now give to patients who ask, "What can I do to help avoid coronary heart disease?" Agreed to by almost all medical authorities is, "Never become overweight, and if overweight reduce and stay reduced."1 Also agreed to, but less unanimously2 is the additional admonition "If the family history includes early deaths from atherosclerosis or, if the blood cholesterol is above average, the patient would also be well advised to restrict his fat intake to not more than 25 or 30 per cent of the total calories." To this medical consensus, I have additionally recommended that a significant portion of this dietary fat be derived from the predominantly unsaturated fats and oils, and extend the coverage to all men of voting age and to all women after their 40's.3

What findings within recent years have been so significant as to change our thinking on atherosclerosis from "one of hopelessness to one of hopefulness," from "Does diet have anything to do with atherosclerosis?" or, more specifically, "Does fat have anything to do with atherosclerosis?" to "What type of fat is involved?" "How great is the effect?" and "What is the mechanism of their action?" Finally, "How can these factors be applied in practical dietetics and to public health practices?"

Although all major discoveries have their foundations in the more distant past, (and this one is not an exception), the immediate break-through was started by Kinsell et al.4 in 1952, who showed that the ingestion of certain different vegetable oils under the rigidly controlled conditions of a metabolism ward was followed by a major fall in plasma cholesterol and phospholipid levels. This finding was soon confirmed by several laboratories5-10 but not all vegetable oils possessed this cholesterol-lowering property and not all animal fats and oils raised cholesterol. At this point Bronte-Stewart, Antonis, Eales, and Brock11 clearly showed that certain marine and vegetable oils which, in their natural state, lowered the elevated serum cholesterol level in man, after hydrogenation acted to elevate it just as do certain naturally occurring highly saturated fats, e.g., those derived from coconuts and cow's milk. This discovery, now confirmed in other laboratories11,12 has clearly proved to be of fundamental importance, like the finding of an important piece in a complicated jigsaw puzzle. The entire puzzle in all its details is not yet clear because many pieces have not yet been found, but the broad outline and framework are now evident and are of firmness sufficient to base broad dietetic recommendations. In this respect it is of utmost importance to determine whether or not people in their usual environment can be induced by public health methods to modify their diet over a long period of time so that their blood lipids, as measured by the cholesterol-lipoprotein system, will be favorably influenced. Then, and possibly only then, can one obtain sufficiently large groups of test subjects to determine directly whether or not this dietary change is followed by a favorable...
Table 1.—Prevalence of Aortic Arteriosclerosis in the Bantu (After Laurie and Woods)\(^{15}\)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Sex</th>
<th>Per cent stage 1</th>
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<th>Per cent stage 3</th>
<th>Per cent stage 4</th>
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<tbody>
<tr>
<td>20-29</td>
<td>M</td>
<td>26</td>
<td>35</td>
<td>26</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>28</td>
<td>50</td>
<td>22</td>
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<td>18</td>
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<tr>
<td>30-39</td>
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<td>25</td>
<td>46</td>
<td>8</td>
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<td>17</td>
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<tr>
<td></td>
<td>F</td>
<td>32</td>
<td>32</td>
<td>30</td>
<td>—</td>
<td>6</td>
</tr>
<tr>
<td>40-49</td>
<td>M</td>
<td>19</td>
<td>25</td>
<td>17</td>
<td>6</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>15</td>
<td>25</td>
<td>30</td>
<td>—</td>
<td>20</td>
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<td>50-59</td>
<td>M</td>
<td>14</td>
<td>41</td>
<td>8</td>
<td>16</td>
<td>37</td>
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<tr>
<td></td>
<td>F</td>
<td>5</td>
<td>16</td>
<td>52</td>
<td>16</td>
<td>19</td>
</tr>
<tr>
<td>60-69</td>
<td>M</td>
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<td>18</td>
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<tr>
<td></td>
<td>F</td>
<td>—</td>
<td>11</td>
<td>31</td>
<td>37</td>
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<tr>
<td>70 plus</td>
<td>M</td>
<td>—</td>
<td>—</td>
<td>53</td>
<td>29</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>—</td>
<td>—</td>
<td>77</td>
<td>23</td>
<td>13</td>
</tr>
<tr>
<td>Number of subjects</td>
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<td>80</td>
<td>73</td>
<td>56</td>
<td>47</td>
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<tr>
<td>Per cent of subjects</td>
<td></td>
<td>14.7</td>
<td>26.6</td>
<td>24.3</td>
<td>18.7</td>
<td>15.7</td>
</tr>
</tbody>
</table>

influence on deaths from atherosclerosis, particularly in men under age 65.

**Prevalence of Coronary Heart Disease**

To appreciate fully the significance of the recent developments in our basic knowledge of fat metabolism, it is necessary to review briefly the background information regarding fats, cholesterol, and atherosclerosis. Coronary atherosclerosis is recognized by most investigators as the keystone of the problem of coronary heart disease.\(^{13}\) It is also true, but not so well recognized, that the differences in prevalence of coronary heart disease in various populations do not exactly parallel the degree or extent of atherosclerosis. For example Becker\(^{14}\) did find aortic atherosclerosis at autopsy common among the Bantu, a finding concurred in by Laurie and Woods.\(^{15}\) Their over-all findings are shown in table 1. However, it is important to note that although aortic atherosclerosis is common in the Bantu, coronary heart disease as a cause of death is a rarity while cerebral vascular complications are not much different from those in European populations. Some other factor, or factors must also be present to determine which of several individuals with approximately equal amounts of coronary atherosclerosis are going to develop clinical coronary heart disease. Among the additional factors thought to play a role are the chance strategic location of the atherosclerosis plaques, anatomic variations of the coronary artery vessels, and abnormal intravascular clotting. This last item includes increased blood coagulability and "shudging," decreased fibrinolysis, and changes in such other factors as lipid clearing and capillary fragility. Nevertheless, when coronary atherosclerosis can be largely prevented, delayed, or postponed, or when these additional factors have been largely controlled, life expectancy at age 50 may be significantly lengthened.

Coronary artery disease was a rarity in mortality statistics prior to 1920. It has now become our no. 1 cause of death in middle age as well as after 65. Much of this reported increase unquestionably is factitious\(^{16, 17}\) resulting from increased medical awareness, fashions in medical diagnosis, better diagnostic methods and their wider use, as well as from changes in reporting. There remains, however, according to Lew, a 15 per cent increase between 1940 and 1955 that cannot be accounted for by these factitious factors. Although this increase seems to some to be insignificant, it amounts to 1 per cent per year since 1940, at which time much of the reported increase had already occurred. By 1940, both awareness and clinical diagnostic facilities had been largely developed and disseminated throughout the entire medical profession. This increase in reported death rates has been especially significant among younger and middle-age males. The *Lancet* editorially states . . . .\(^{14}\) All cardiologists whose experience goes back 30 years or more seem to agree with the vital statisticians that the higher mortality rates reflect a real increase in coronary artery disease, and also that young people . . . are now affected more often than formerly.\(^{18}\)

Important evidence that coronary heart disease has actually increased in middle age and after is the fact that life expectancy at
FATS, CHOLESTEROL, AND CORONARY HEART DISEASE

age 50 has not materially increased since 1900. For example, in 1900, life expectancy in the United States at age 50 was about 20.8 years while in 1950 it had increased but 2.2 years to about 23 years. This relatively small increase, 10.6 per cent, has occurred in spite of the conquering of pneumonia and many other acute infections during middle life, the saving of lives due to increased skill in surgery, the marked reduction in deaths from syphilitic heart disease, bacterial endocarditis, rheumatic heart disease, and tuberculosis.

The mortality from coronary heart disease is high in all the western industrialized countries of the world. But among them the ratio between the highest and the lowest may be as much as 4 to 1 and, between Japan and the United States, it is as high as 8 to 10 to 1 (table 2).

It is highest in the United States, Canada, Australia, New Zealand, and Finland but there are national, cultural, and ethnic groups in which such increases have not been observed and among whom the mortality from coronary heart disease is from one fourth to one tenth or even less of that in this country.

Examples are the Japanese, the Bantu in the Union of South Africa, Guatemalan Indians, Nigerians, Yemenite Jews in Israel, Italians and Sardinians in Italy, and low-income men in Madrid. These mortality rates must be critically examined, for there are differences in awareness, fashions in diagnosis, and differences in reporting, as well as true differences in the actual disease rate. Ordinarily, differences in reported rates of less than 1-fold between countries should, in most instances, be discounted, and in the absence of strong supporting data, be attributed to factitious differences. On the other hand, major differences of the order of 2, 4, or 10 to 1, or even greater cannot with prudence be ignored when there are means available for checking their rough accuracy. Ad hoc surveys have done much to support the rough accuracy of these statistical figures. These teams of competent observers failed to find a prevalence of coronary heart disease comparable in any way to that found in this country. As pointed out by Keys, it is not reasonable to suppose that in these places, only the patients with coronary heart disease stay away from doctors, hospital clinics, and the autopsy table, when patients with other diseases—cancer, cirrhosis of the liver, nephritis, cerebral vascular lesions, valvular heart disease, and so on—do appear and with a frequency approximately equal to that in the western civilized countries.

Vital statistics are often censured for their unreliability because of the considerable discrepancy in individual cases between the cause of death given on the death certificate and the actual one found at autopsy. This condition undoubtedly exists, but the final data based on the death certificates are approximately correct due to a balancing of errors. For

<table>
<thead>
<tr>
<th>Country</th>
<th>Death rate ISC category B-26</th>
<th>420</th>
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<tbody>
<tr>
<td>United States</td>
<td>704.7</td>
<td>660</td>
</tr>
<tr>
<td>Australia</td>
<td>577.4</td>
<td>516</td>
</tr>
<tr>
<td>Austria</td>
<td>293.9</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td>250.1</td>
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</tr>
<tr>
<td>Canada</td>
<td>588.3</td>
<td>550</td>
</tr>
<tr>
<td>Ceylon</td>
<td>103.4</td>
<td></td>
</tr>
<tr>
<td>Chile</td>
<td>267.3</td>
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</tr>
<tr>
<td>Denmark</td>
<td>294.8</td>
<td>260</td>
</tr>
<tr>
<td>Finland</td>
<td>621.7</td>
<td>483</td>
</tr>
<tr>
<td>France</td>
<td>109.9</td>
<td>106</td>
</tr>
<tr>
<td>German Fed.</td>
<td>313.7</td>
<td>194</td>
</tr>
<tr>
<td>Italy</td>
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<td>120</td>
</tr>
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<tr>
<td>New Zealand</td>
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<td>492</td>
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<tr>
<td>Norway</td>
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<td>210</td>
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<tr>
<td>Portugal</td>
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<td>Sweden</td>
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<td>Switzerland</td>
<td>273.0</td>
<td>173</td>
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<td>427.5</td>
<td>371</td>
</tr>
<tr>
<td>Yugoslavia</td>
<td>68.2</td>
<td></td>
</tr>
</tbody>
</table>

*ISC Category B-26 includes 420—arteriosclerotic heart disease, 421—chronic endocarditis, 422—other degeneration of the heart.
example, in a comparison of autopsy findings with the original death certificates in 1,889 subjects in 12 upper New York State hospitals in 1951 and 1952 there was full agreement in only 72.8 per cent of 276 deaths originally certified as due to "arteriosclerotic heart disease." This does not mean that the mortality rate from ischemic heart disease was overestimated by the original death certificates because autopsies disclosed 66 additional deaths from this disease that had been originally attributed to other causes in the death certificate; the final result was that the rate reported by the death certificates was 96.7 per cent correct.

In addition to the statistical data and the ad hoc field survey findings, other data support this contention that the prevalence of clinical coronary heart disease varies markedly in different groups. Clinicians with wide international and interracial experience long have held that at equal age, there are wide variations between countries, between races in the same countries, as well as between different socioeconomic groups in the same country. Necropsy studies support these differences. Thus it can be concluded that there are marked differences between countries and between communities in the age-specific mortality rates for coronary heart disease.

Environmental Factors

This increase in the prevalence of clinical coronary heart disease in some populations and the lack of observed changes in others in diet environment as a significant cause even though heredity and genetic factors may determine the degree of susceptibility. Among the environmental factors that have been considered are luxury living, stress, differences in physical activity, tobacco, and diet. Diet includes deficiencies, extra calories and the resulting obesity, protein intake, excess fat, and differences in fat quality. "Luxury living," "high standard of living," and "prosperity" are medically meaningless terms. One must find and designate more clearly the responsible factor or factors in these broad terms. Certainly, all aspects of "poverty," "low standard of living," and "depression" cannot be beneficial. Besides, who would be so naive as to recommend this as therapy for our coronary patients or as a public health measure to help prevent coronary heart disease!

Stress

Stress is a factor to be considered, particularly the type of stress related to western civilization, urbanization, and prosperity. Old-fashioned stress such as the stress of obtaining food to keep alive, the stress of "the jungle," the stress of mating or to obtain and keep a desirable mate, the frustrations of parenthood, and the noises of community living have certainly been with mankind ever since he developed a communal life. It is doubtful whether at any previous period of mankind these factors of old-fashioned stress have ever been less than at present. But the types of stress related to that of masses of people mobile upward economically with most persons feeling a bounden duty to elevate themselves and their children to a higher economic and social group, the stress of failing to escape from the boom, chatter, and jangle of television, radio, and the telephone—all may represent a newer type of stress to which mankind is making but poor adjustment. Studies showing differences between personality and emotional make-up of people having coronary heart disease and healthy controls have all been done retrospectively. No prospective study along this line has been reported. This type of study should be done.

Rosenman and Friedman have recently attempted to measure the effects of this type of stress on a group of 42 volunteer male accountants. This group was selected because of the unusual phasic variations of their work and its associated deadline. Serum cholesterol and blood clotting times were determined bimonthly and, in 83 per cent of the subjects, the maximum cholesterol concentrations occurred at the time of the maximum
stress as measured by nearness to income tax deadlines. Blood clotting time was shortened from an average of 9.4 minutes during minimal stress to 5 minutes at the time of maximum stress. The authors could not ascribe the changes in either cholesterol or blood clotting patterns to diet or to changes in weight. The subjects were free-living accountants noted for “snacks” at maximum work periods. These snacks, usually containing large amounts of saturated fats, could account for the failure to lose weight at maximum work periods, as well as the changes in blood cholesterol and clotting time. Also, all these subjects were on an ad libitum high-fat diet under which condition considerable fluctuations in blood cholesterol levels may occur. It remains to be proved whether or not this type of stress during a constant diet actually does influence the blood lipid levels.*

Old-fashioned stress and strain were certainly greater in England and Norway than in the United States during the World War of 1939-45. Yet, there is no sudden separation in the graphs of the mortality rates from coronary heart disease in England and in the United States during the war years to reflect the effect of stress and strain, particularly during the Battle of Britain. There is evidence that in Norway during the German occupation there was a significant decrease in mortality rates attributed to coronary heart disease.37 One can conclude from this data that stress is not a major factor in coronary heart disease.

Exercise

Regular physical activity undoubtedly plays an important role in maintaining cardiovascular efficiency, physical fitness, and a trim figure. But it cannot explain major differences in mortality statistics, otherwise the long-walking, bicycle-riding, exercise-loving Englishman should have a coronary heart disease rate more comparable to that of the Italian than to the little-walking, car-riding, physically indolent American. A cooperative study by physicians in Minnesota, Italy, Sweden, Spain, and South Africa38 finds that differences in serum cholesterol, and, by inference the coronary heart disease rate, were associated with different dietary fat intakes rather than differences in physical activity. However, as pointed out by Mann and his co-workers,39 physical activity can prevent the rise in blood cholesterol associated with an increased saturated fat intake provided the physical exertion is sufficient to prevent weight gain. At this point it is well to note that Gordon, Lewis, Eales, and Brock40 have demonstrated falling total blood cholesterol levels during periods of weight gain when the increase in calories was derived from sunflower seed oil.

It still remains problematic whether regular physical exertion produces its beneficial result by decreasing the blood cholesterol level or by increasing collateral circulation and circulatory efficiency. Both factors may play a role.

Tobacco

Excessive cigarette smoking has been indicated as a factor in coronary heart disease. According to Hammond,41 a high association exists between cigarette smoking and the incidence of coronary artery disease. The death rate from this cause was 75 per cent higher among cigarette smokers than for a comparable group of men who had never smoked. Moreover, death rates due to coronary artery disease increased with the amount of cigarette smoking. One may speculate that this could operate either through the vasoactive action of cigarette smoking on a previously damaged coronary vessel or it may well be associated with increased saturated fat consumption accompanying oral compulsion. Persons who smoke 2 or more packs of cigarettes a day.

*Since this paper was submitted for publication, Friedman and Rosenman have recently extended these observations by selecting their subjects according to degrees of stress and found higher serum cholesterol levels in the subjects most stressed as measured by their criteria. (Friedman, M., and Rosenman, R. H.: Association of specific overt behavior pattern with blood and cardiovascular findings. J.A.M.A. 169: 1286, 1959.)
may, in general, be those who also eat an unusual amount of saturated fat. This possible association may be a fruitful field for study.

**Climate**

There is no good evidence that climate is an important factor. The difficulty lies in that climate influences so many characteristics that even approximate comparability is almost impossible. However, some inference may be drawn from data for individual states in the United States. Florida and Maine have age-adjusted death rates of coronary heart disease in the same quartile (as well as other similar characteristics) and yet their climates are certainly different. On the other hand, adjoining states such as West Virginia and Maryland, or Mississippi and Louisiana, have essentially the same climate, yet the first of each pair has age-adjusted coronary heart disease rates in the lowest quartile whereas the second is in the highest quartile.

**Diet and Coronary Heart Disease**

Specific dietary deficiencies other than pyridoxine, certain amino acids, and essential fatty acids have not been related to coronary heart disease. As a matter of fact, differences in protein quantity varying from 11 to 20 per cent of total daily calories with calories and fat quality and quantity remaining constant has not resulted in significant alteration of the blood lipids. Olsen has demonstrated in 9 subjects that, with calories, fat quantity, and fat quality remaining constant, a reduction of protein from 100 Gm. daily to 25 Gm. daily resulted in a fall in blood cholesterol within 2 weeks. Twenty-five grams of total protein is within the range of protein inadequacy; this is not therefore within the range of either a practical or adequate human dietary regime. These observations do not prove that protein quantity or quality do not play a role in coronary heart disease. It is to be noted, however, that all other experimental factors producing atherosclerosis in the laboratory animal were always associated with changes in blood lipids. Protein per se, therefore, within the range of most adequate human dietaries holds little promise of being a significant factor in atherosclerosis.

Pyridoxine deficiency is now thought to operate through a disturbance in fat metabolism, resulting from failure to convert linoleic acid to arachidonic acid.

Although nicotinic acid has been shown to lower the blood cholesterol, the dose employed has been so large that the effects are pharmacologic rather than nutritive. Altschul and his colleagues reported that 1 to 4 Gm. of nicotinic acid ingested in a 24-hour period successfully reduced serum cholesterol levels in normal and hypercholesterolemic persons. Long-term effects of large daily doses of nicotinic acid in patients with hypercholesterolemia were subsequently observed by Parsons and others. They showed that significant reductions in the blood cholesterol and total lipids could be obtained in these persons with this therapy and maintained for periods up to 1½ years as long as therapy continued. Moreover, Parsons was able to show that this effect could not be obtained by the use of niacinamide, rather than nicotinic acid.

These studies were conducted with no change in the subjects’ previous diet. Presumably, then, all changes in cholesterol level could be attributed entirely to the use of nicotinic acid.

The exact mechanism that enables nicotinic acid to produce the observed changes in the blood lipids is not yet clear. However, the failure of niacinamide to produce similar results, and the large doses of niacin required, indicate that the effects of niacin are pharmacologic.

Obesity is also an important factor. It is associated, particularly in middle age with significantly higher mortality rates than in normal-weight subjects of comparable age and sex. Obesity possibly operates, in addition to a greater work load upon the circulatory system, by the obese subject’s consuming greater amounts of fat calories of the wrong quality and of saturated fat precursors than do their trim counterparts. But important as
obesity is, it has been pointed out by Keys that obesity in itself cannot explain differences of several-fold between countries, and he further observes that if obesity were eliminated in the United States, coronary heart disease would still be its no. 1 public health problem.

*Fat Consumption and Coronary Heart Disease Association*

The dietary factors that correlate best with reported international mortality rates of coronary heart disease are those associated with the fat and protein available for human consumption in national diets. These latter figures measure the food that enters into retail outlets. Much has been made of the fact that food balance figures are not a good index of actual fat consumption because of the considerable waste that exists between receipt by the retail store and disappearance from the plate. Indeed, there is much waste between the retail store and the mouth but that waste is not confined to one class of foods. As a matter of fact, there is even a possible higher waste at the retail stores of fresh fruits and vegetables than of fat, proportionately little of which is wasted at the retail level. From the market basket to the plate, the trimming and discarding of fats and the peeling, waste and spoilage of fruits, vegetables, and breads are proportionately not far different. The same is probably true for plate waste. Therefore, the 148 Gm. of fat that entered into retail sales in 1956 include much fat that is wasted; likewise there was an equal or greater waste of bread, fruits, and vegetables. Thus, the percentage composition of our calories derived from fat, carbohydrate, and protein at the retail level probably reasonably approximates that actually consumed. Support for this conclusion is the fact that dietary surveys indicate, almost without exception, that the approximate percentage composition of the diet as eaten agrees with the percentage contribution of food disappearance. Great significance can therefore be given to the figures on table 3 showing the percentage increase in fat calories in our national food supply since 1910. It has increased from 32.2 per cent in 1910 to over 41 per cent in 1955.

The first correlation between fat consumption and international death rates of coronary heart disease was made by Keys and his associates. As expressed in Keys and White this relationship between the total fat intake and coronary heart disease rates for males below 65 may be expressed as follows: Populations with fat intakes approximating 40 per cent of the total calories have high death rates; populations with total fat intakes below 20 per cent of total calories have low death rates; populations with intermediate fat intakes have intermediate death rates. This correlation between total fat and death rates of coronary heart disease was soon challenged by the National Dairy Council and later, among others, by Yerushalmy and Hilleboe, Page, Pollack et al., Yudkin, and Mann.

It was pointed out by the National Dairy Council Digest that, in Norway, Sweden, and Denmark, the percentage of total calories derived from either total fat or from animal fat is comparable with that of the United States or the United Kingdom, while death rates from heart disease at all ages or in the age groups of 50 to 54 years are only about one third of those in the United States. The National Dairy Council, however, did not distinguish between fats derived from marine animals, which are of the unsaturated type, and from land animals, which are predominantly saturated. At that time, however, the differences in quality of these fats were not generally appreciated. In the low coronary death rate-high fat intake countries (Sweden

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**Table 3.**—Fat Calories as a Percentage of the Total Calories Per Capita Available for Consumption in the United States in Selected Years. (After USDA)

<table>
<thead>
<tr>
<th>Year</th>
<th>Per cent</th>
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<tbody>
<tr>
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<td>33.5</td>
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<td>1930</td>
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<td>1940</td>
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<td>1950</td>
<td>40.1</td>
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<tr>
<td>1955</td>
<td>41.4</td>
</tr>
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</table>
Norway, Denmark) the consumption of both fish and marine oils is large—several times that of the United States. In addition, the consumption of unhydrogenated vegetable fats is larger.

Following the National Dairy Council, Yerushalmy and Hilleboe were the next to question seriously the total fat concept. They considered that “the dietary fat-heart disease association is not unique or specific since the association between fat and heart disease mortality is not so strong as that between animal protein and heart disease.” Yerushalmy and Hilleboe additionally criticized certain previous work on the association between dietary fat and mortality rates as failing “to probe further, to go beyond the simple, apparent association and to investigate related variables.” However, like the National Dairy Council, Yerushalmy and Hilleboe considered all fat as equal in quality and developed their paper only on the information available in November 1955. They made correlations between several dietary constituents and death rates from coronary heart disease (B-26) and found even better rank correlations (table 4) with total calories, animal fat, and animal protein than with total fat. Yerushalmy and Hilleboe did not point out that in low-calorie countries (less than 2,700 calories) the total fat consumption was generally low and usually paralleled or varied with the total calories. Where consumption of animal protein is high (more than 5 per cent of calories), the total fat intake was also high (more than 30 per cent of calories). In both instances, as pointed out by Jolliffe and Archer, the dietary fat accompanying these 2 factors accounted for practically all of their associations. Thus, according to Yerushalmy and Hilleboe’s criterion of “valid” association, the saturated-type fat-coronary heart disease association is valid and accounts for almost 70 per cent of the variation in B-26 death rates in the 20 countries examined (table 5). When international food consumption figures are tabulated so as to obtain more accurate data of fat quality, a more definite answer may be obtained.

Yudkin in an extensive analysis of environmental factors associated with death rates of coronary heart disease made the observation that “...one begins to have the uneasy feeling that both the proponents and the opponents of a dietary hypothesis are quoting only those which support their view.” He then correlated many environmental factors with the death rates of coronary heart disease. Like the National Dairy Council and Yerushalmy and Hilleboe, he showed that total fat-coronary heart disease association was not so high as that with calories and animal fats. He also showed that vegetable fats alone or hydrogenated fats alone did not correlate any better than total fat. He also observed that there seems to be a threshold level of total fats (about 30 to 35 per cent of calories or around 120 Gm. of fat) above which coronary heart disease was common, while below this level it was uncommon. Yudkin also made the observation that, over the years in the United Kingdom, the best correlation of all was with the number of registered radio and television sets, indicating that a non-sequitur must be validated by methods other than statistical association.

The paper by Page, Stare, Corcoran, Pol-

**Table 4.—Rank Correlation Coefficients* between Various Dietary Components and Death Rates from Arteriosclerotic and Degenerative Heart Disease (B-26) in 22 Countries†**

<table>
<thead>
<tr>
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</tr>
<tr>
<td>Calories from fat</td>
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<tr>
<td>Animal fat$</td>
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<td>0.677</td>
</tr>
<tr>
<td>Vegetable fat$</td>
<td>-0.236</td>
<td>-0.468</td>
</tr>
<tr>
<td>Calories from protein</td>
<td>0.709</td>
<td>0.172</td>
</tr>
<tr>
<td>Animal protein</td>
<td>0.756</td>
<td>0.643</td>
</tr>
<tr>
<td>Vegetable protein</td>
<td>-0.430</td>
<td>-0.651</td>
</tr>
</tbody>
</table>

*Critical values of $r$ for $\alpha = 0.05$ and $\alpha = 0.02$, when $N$ is 21, are $\pm 0.438$ and $\pm 0.531$; when $N$ is 22 they are $\pm 0.428$ and $\pm 0.508$.

†Above data taken from table 3 of Yerushalmy and Hilleboe.

‡For 21 countries, data not available for France.
lack, and Wilkinson is a report to the American Heart Association and to the American Society for the Study of Arteriosclerosis (rather than from either of these organizations). The body of the report is a critical and sobering review of the literature up to early 1957 on the epidemiologic factors of coronary heart disease. Their conclusions however, are as follows (italics mine):

Atherosclerosis, cerebral thrombosis, and myocardial infarction are diseases in which numerous factors are involved. Diet and nutrition are important factors in experimental atherosclerosis and, very probably, in the human disease. Thrombosis and infarction of the cerebral, cardiac, and renal vessels occur in severely sclerosed arteries, but so far neither has been clearly produced experimentally.

Evidence is presented to suggest a possible general association with high fat consumption, but it is difficult to disentangle this from calorie balance, exercise, changes in body weight, and other metabolic and dietary factors that may be involved. Thus the evidence at present does not convey any specific implications for drastic dietary changes, specifically in the quantity or type of fat in the diet of the general population, on the premise that such changes will definitely lessen the incidence of coronary or cerebral artery disease. On the other hand, the fact that obesity is a nutritional failure, that it is caused by consuming more energy than one expends, that the dietary fats are the most concentrated source of energy, providing some 40 to 45 per cent of the daily calorie intake, suggests that many should consume less calories. For most, this will mean eating less fat.

Prudence, as well as habit and taste will dictate the selection of a diet with some fat. Diets providing 25 to 30 per cent of the calories from fat, rather than the current 40 to 45 per cent in the American diet can still provide palatable meals for our accustomed tastes.

The key points of nutritional common sense for better health generally, and most likely in regard to atherosclerosis specifically, consist of a balanced, varied diet that adjusts total calories to reach or maintain a desirable weight. Such a diet should provide more protein from lean meat, fish, poultry and animal products, and a reasonable selection of fruits and vegetables. The fat content should be sufficient only to meet calorie and essential fatty acid demands.

These conclusions obviously apply to the general population, and not to patients, or to individuals with a strong family history of early deaths from cardiovascular disease, who are being observed with some regularity by their physicians. Here, the newer concepts of nutrition readily suggest various types of diet therapy that may prove useful in certain patients. Investigative procedures of this type, together with continued basic research, will, in time, provide the facts upon which sound dietary recommendations may be made to the public at large and which may help in lessening the prevalence of cerebral and coronary heart disease with consequent stroke and myocardial infarction.

It is recognized that this is a joint paper and that it was written to satisfy all 5 contributors. Nevertheless, it is difficult to reconcile the 3 recommendations in italicized type
above. The first recommends no drastic change, which, in many instances, has been interpreted as no change at all, the second a moderate decrease in fat from 40-45 per cent to 25-30 per cent of the calories, while the third suggests only enough fat to meet essential fatty acid and calorie needs.

Mann\textsuperscript{58} in his review of the epidemiologic data, along with Yerushalmy and Hilleboe and Page et al., questions the validity of these data. This point has been dealt with at length previously by Keys\textsuperscript{61} and reviewed by Jolliffe.\textsuperscript{3} As previously mentioned it is recognized by all that methods of recording, reporting, and degrees of medical sophistication may well account for differences of 100 per cent between countries of similar technologic development. But differences in age-specific coronary heart disease rates between countries and communities of 200 to 1,000 per cent, when other methods such as the ad hoc surveys of Keys and his associates exist to check the rough accuracy of these vital statistics, cannot with prudence be ignored.

Examination of some of Yu\textsuperscript{2}kin's tables yields some information on this point. For example, in the United Kingdom, Denmark, Sweden, and Norway, where technologic development and medical sophistication are high and approximately similar, the reported death rates in 1952 from coronary heart disease for men aged 55 to 64 varies from 239 in Norway to 470 in the United Kingdom. Certainly no prudent individual would consider that the physicians in Norway are assigning some other causes of death to more than half of their cases of coronary heart disease, or, as an alternative, that physicians in the United Kingdom are labeling with coronary disease more than half of the patients who do not have it at all.

In addition to the statistical data noted above, other supporting evidence is the experience of clinicians that the prevalence of coronary heart disease does, in fact, vary markedly in different groups.

Changes in Fat Quality

In addition to a 29-per cent increase (9 percentile points) in the past 45 years in the percentage of total calories derived from fat available in our national food supply (table 3), the accompanying change in fat quality may be of even greater significance. Historically, a nation's increased prosperity is quite regularly accompanied by an increased consumption of fats of the saturated type (meat, milk, and eggs) at the expense of fats from unsaturated sources (from fish, grain, nuts, and vegetables) and of carbohydrates from grain and tubers. This change in fat quality regularly accompanies an increase in the Western standard of living. In addition, the greater the marbling of the meat and the richer the milk, the greater is their prestige value. Meat, milk, and dairy products have become prestige foods largely because: (1) they are universally liked and easy to prepare; (2) they are more expensive, therefore desirable, when compared to the leaner products; and finally (3) through clever advertising and promotion operating in a milieu of regulatory legislation favoring these products the modern housewife is made to feel guilty unless she serves her family more marbled meat and fat dairy products than are called for by a nutritious and well-balanced diet. For example, the 31 ounces of milk products, in terms of fluid whole milk, consumed per capita daily in the United States\textsuperscript{52} is almost double the desirable goal of 16 ounces recommended for most countries.

When a person consumes any item of food in excess of energy and nutritional needs, he is faced with 2 possibilities: (1) continue the excess amount of that particular food but cut down on other foods, and thus risk a deficiency disease; or (2) continue to eat sufficient amounts of other food for nutritional need and thus become obese.

The other major factor contributing to the change in fat quality is "hydrogenation," a process by which oils such as cotton seed or soy bean are changed into solid fats. As commonly carried out in this country, hydrogena-
tion produces 4 types of chemical change, according to the Committee on Fats in Human Nutrition of the Food and Nutrition Board: 42

1. Hydrogen is added at double bonds, producing saturated from unsaturated fatty acids or step-wise decreasing the number of double bonds in polyunsaturated acids as indicated by a lowering of the iodine number. The melting point is raised.

2. The double bond may shift position along the carbon chain, producing iso-acid forms. These new unsaturated acids may have the same iodine number but may differ from the original in melting point.

3. The predominantly occurring cis configuration may change to the trans configuration. This isomerization also leaves the iodine number unchanged but leads to a significant rise in the melting point. For example, oleic acid melts at 13°C and is liquid; its trans isomer melts at 44°C and thus is solid at room temperature.

4. With linoleic, linolenic, or arachidonic acids there may be conjugation, in which system the double bonds are not separated by a methylene group. These conjugated systems are relatively rare in natural food fats.

The net result of all these changes is a fat solid at ordinary room temperature with an iodine value about that of olive oil. The linoleic acid content has been reduced from around 50 per cent originally to 3 to 8 per cent after hydrogenation.

Brown 63 has estimated that hydrogenation of cotton seed oil and soy bean oil alone destroys over 1 billion pounds of linoleic acid annually which, it may be calculated, amounts to about 8 Gm. per person per day. Since, according to McCann and Trulson, 64 our total daily intake of linoleic acid is 9.7 Gm. per person per day (2.7 per cent of the 3,220 calories per day total diet shown), these 8 grams destroyed, if added to the diet, would almost double the linoleic acid content and bring it up to almost 5 per cent. Thus, a significant loss of an essential nutrient has occurred, especially if the requirement for linoleic acid is proportional to the intake of saturated fat or if the minimum requirement is somewhere between 5 and 10 per cent of our calories.

As shown by Kinsell et al., 65 10 per cent of the diet as linoleic acid in short range, metabolic ward experiments will result in a fall in blood cholesterol and phospholipids in the majority of the age group of 20 to 29 years. This may indicate that the requirement for linoleic acid in this age is somewhat less than 10 per cent of the daily calories.

The nutritional effects of the isomers formed during hydrogenation have been extensively studied 66 and, in terms of growth, maturation, and reproduction, such fats are equivalent to their precursors. Since trans-acids do not replace cis-acids 67, 68 in remedying essential fatty acid deficiencies, it seems probable that some of these isomers formed by hydrogenation are metabolized through different pathways. 11 That this is true has been amply demonstrated in the experimental animals. 69, 70 More than an isomer's being non-equivalent and therefore a nonsubstitute, it may actually have a deleterious effect, e.g., certain isomers of thiamine act as antithiamine. In a similar manner, the isomers of the essential fatty acids may act as metabolic antagonists to the natural form. 67

Hydrogenation, as a practical commercial process, began about 1915 and its use increased steadily until at present most of the table spreads and cooking fats are highly saturated either naturally or by hydrogenation. Even peanut butter is often hydrogenated to prevent separation of oil from the peanut meat.

Other factors of significant but lesser importance in changing the quality of the fats we consume are the rising milk consumption, the increased marbling of our meats, and the increased availability of high-fat “heat and serve” prepared dishes. It is thus undeniable that coupled with a 29-per cent increase in total fat consumption, the quality of the fat also has changed.

Effect of Fat Quality on Blood Cholesterol
The importance of this change in fat quality lies in the fact that several groups of observers 4, 7, 21, 23, 71-73 have conclusively demonstrated that feeding diets consisting principally of highly saturated fat results in high levels of blood cholesterol and of certain lipid
fractions of the blood. By contrast, substitution or addition to the diet of certain oils, all of which are naturally rich in linoleic or certain other polyunsaturated acids, results in a statistically significant fall of total serum cholesterol. The effects of these dietary supplements of marine and vegetable oils containing the polyunsaturated fatty acids has been maintained by the Cape Town investigators for 6 months. This time is probably sufficient to indicate that this effect will continue in normal persons as long as adequate amounts of these oils rich in the polyunsaturated fatty acids are included in the diet. This evidence seems highly significant when coupled with the observation that the middle-aged males of populations habitually consuming a high proportion of these polyunsaturated acids have much lower average blood cholesterol levels than those who consume large amounts of the highly saturated fats in countries such as the United States. This statement as yet precludes independent diseases affecting cholesterol metabolism such as myxedema, nephrosis, or idiopathic hypercholesterolemia; many diabetic subjects, however do not seem to be exceptions since they usually respond like non-diabetic individuals.

Most significantly, whenever these oils, which produce a fall in blood cholesterol, or their polyunsaturated fatty acids are hydrogenated and then fed, the favorable effect on the cholesterol level is no longer obtained. This fact has been adequately confirmed. These fats now act to raise the cholesterol level just as do certain fats naturally highly saturated, such as butter and coconut oil.

This finding does not prove that saturation or unsaturation is the fundamental cause for changes in the cholesterol system. It may be a factor presently known, such as the amount of linoleic acid present in the metabolic mix-

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*Since this paper was submitted for publication, this observation has been further confirmed in 79 free-living normal weight men aged 50 to 59. (As reported by Jolliffe, N., Rinzler, S., and Archer, M., at the Annual Meeting of the National Vitamin Foundation, March 3, 1959.)

...ture; it may be the proportion of the polyunsaturated acids, chiefly linoleic, to the amount of saturated fats; or it may be a factor, as yet unknown, that is intimately associated in nature with these polyunsaturated fatty acids.

Ahrens and his co-workers seem to be inclined to the total unsaturated theory, as expressed by the iodine number. Kinsell and Sinclair are more inclined to a concept of essential fatty acid deficiency; while Keys and his co-workers lean toward a balance between the saturated:polyunsaturated fatty acids with mono-unsaturated fatty acids playing a neutral role.

Keys et al. have developed a formula for predicting the change (\( \Delta \)) in blood cholesterol when persons under constant metabolic conditions are subjected to changes in dietary fat. The fats tested include coconut oil, olive oil, lard, corn oil, cottonseed oil, sunflower seed oil, butterfat, safflower seed oil, and sardine oil as well as the mixed fats of the usual American diet. The amounts of the fats tested range from about 8 per cent to slightly over 40 per cent of the total calories of the diet. The Keys' formula follows:

\[
\Delta \text{cholesterol} = 2.74 \Delta S - 1.31 \Delta P
\]

where \( \Delta \) cholesterol is the average change in mg. of total cholesterol per 100 ml. of serum, \( \Delta S \) is change in saturated fatty acid intake as per cent of total calories, \( \Delta P \) is change in polyethenoid fatty acid intake as per cent of total calories.

In practical terms this formula indicates that the cholesterol-raising effect of 1 Gm. of a saturated fat can be offset by 2 to 3 Gm. of a high-linoleic acid oil such as corn, cottonseed, or sunflower seed. Thus the removal of 1 Gm. of butterfat from the diet has about the same serum cholesterol-lowering effect as

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*Since this paper was submitted for publication, Ahrens et al. have published an interesting observation made on 2 subjects that menhaden oil, low in linoleic acid but high in certain other polyunsaturated fatty acids, lowers the blood cholesterol as effectively as corn oil. (Ahrens, E. H., et al.: The effect on human serum-lipids of a dietary fat, highly unsaturated but poor in essential fatty acids. Lancet 1: 115, 1959.)
the addition of 2 to 3 Gm. of one of the high linoleic acid oils. In practical dietetics it would seem that the simple addition of an oil high in linoleic acid to the presently high-fat diet (40-45 per cent) would require impractically large additions (3 oz. = 810 calories or more). The subject would be confronted with a choice of either cutting down iso-calorically on the protein and carbohydrate portions of the diet and risk deficiencies in proteins, minerals, and vitamins or of becoming obese. On the other hand, restricting the saturated fatty acids to about 10 per cent of the calories in the diet with 10 per cent or more from polyunsaturated fatty acids derived from vegetable seed oils, fish and other marine sources, and from grains, vegetables, and fruits permits a palatable gourmet-type diet, one that lowers the blood cholesterol in the majority of persons and which contains as much or more protein, minerals and vitamins than the present diet high in saturated fat and "empty calories" and low in polyunsaturated acids.

The previously noted discrepancies between the total fat-coronary heart disease association, particularly in certain high-fat, low-death rate countries such as Norway, Sweden, and Denmark, may now be explained by the high proportion of fat derived by the people of these countries from fish, marine, and vegetable oils containing relatively large amounts of the polyunsaturated fatty acids, a possibility suggested by J. M. Morris (1956) and recently elaborated by Jolliffe and Archer. In Norway, Sweden, and Denmark, these oils make a major contribution to the total fat consumption instead of their minor role in the American diet. Panel I of figure 1 shows the coronary heart disease-total fat association while Panel II shows the correlation when unhydrogenated fats derived from vegetables, fruit, nuts, grains, and marine sources are subtracted from the total fat. The latter association is very high and explains almost 70 per cent of the deviation from the straight line relationship. The countries appearing in the lower right hand quadrant of Panel I are no longer exceptions that tend to discount the fat-coronary heart disease postulate.

**Blood Cholesterol and Coronary Heart Disease**

It has been demonstrated without contradiction that populations with a high average total blood cholesterol in their middle-aged men (over 220 mg. per 100 ml.) have a high rate of coronary heart disease. Keys pointed out that 2 rules hold: First, "Whenever a population has a relatively high serum cholesterol average for its clinically healthy males—220 mg. per 100 ml. or more for middle-aged men—that population exhibits a relatively high incidence of coronary heart disease. Examples are men in many parts of the United States, in London, Malmo, Sweden, Netherlands, Western Germany, upper-class men in Madrid, and Europeans in Cape Town, South Africa." Second, "Populations with low serum cholesterol averages—less than 200 mg. per 100 ml. for middle-aged men—exhibit relatively little coronary heart disease. Examples are men in Southern Italy and Sardinia, poor men in Madrid, Bantu in Johannesburg and Cape Town, Guatemalan Indians, Natives in Nigeria, and Yemenite Jews. Cape Coloured men in South Africa and men in Bologna may be intermediate examples." Major exceptions to these generalizations have not yet been found in population studies.
In our country the report of the cooperative study of lipoproteins and atherosclerosis\textsuperscript{80} throws much light upon this subject, particularly from an epidemiologic point of view. In this study, a single blood cholesterol determination was made on 4,914 men who were then followed for "new events" over the next 1 to 2 years. The average blood cholesterol of this group of men, aged 40 to 59, was 240 mg. per 100 ml. As a group, over this short period of time, 2.58 times as many men who had blood cholesterol above 240 developed a definite "new event" as did those whose blood cholesterol were below 240. This study does not indicate that a single blood cholesterol determination has any considerable value in predicting a "new event" for an individual in a year or two. It is, however, of significant epidemiologic value. If an analysis of definite "new events" is made by tertile as in table 6, it becomes clear that the third of the American male population of this age group with the highest blood cholesterol has 3 times the probability of suffering such an event as those in the lowest tertile, where prudent men would prefer to be.

Population studies thus indicate a very definite relationship between (1) the amount and quality of the fat consumed, (2) the beta-lipoprotein fraction, and (3) the death rate from coronary heart disease in middle age.

With respect to the quality of the fatty acid involved, Rutstein et al.\textsuperscript{81} have shown in vitro, how a polyunsaturated fatty acid (linolenic) prevented the intracellular deposition of lipoid that had been caused by the addition of cholesterol to tissue cultures of human aortic cells. Rutstein et al. concluded that in these cultures in a medium containing human blood serum, deposition of lipoid can be (a) induced by adding cholesterol, (b) reversed by replacing the cholesterol-containing medium by normal medium, (c) prevented by adding linolenic acid (a polyunsaturated fatty acid), and (d) potentiated by adding stearic acid (a saturated fatty acid).

The triangular relationship just noted between fat quantity and quality, coronary heart disease, and cholesterol level does not prove that a high blood level of cholesterol is the cause of atherosclerosis or of intra-arterial thrombosis. It does, however, demonstrate an uncomfortably close association which is further supported by the higher prevalence of coronary heart disease in individuals with diabetes, myxedema, nephrosis, and lipo-dystrophies in which hypercholesterolemia is a common factor. It is still further supported by the fact that the occurrence of myocardial infarction in patients with active hyperthyroidism is almost unknown, an association not generally appreciated and called to our attention by Littman, Jeffers, and Rose.\textsuperscript{82} It also correlates well with the fact that male castrates not only have a low blood cholesterol but seldom have coronary thrombosis and, with the corollary observation that in female castrates, high blood cholesterol levels are found along with frequent coronary heart disease.

**Speculation on the Role of Fat Quality in the Pathogenesis of Coronary Heart Disease**

Upon recognizing that there are degrees of susceptibility mediated by such unalterable factors as sex, race, heredity, and body constitution, and that such other environmental factors as physical activity, obesity, and excess tobacco play a role, it is apparent that the amount and type of fat intake are a major etiologic factor. Major differences of the order of 4:1 or more in death rates between countries reasonably can be explained only this way. One may even go so far as to state that without a high intake of saturated and hydrogenated fats, other factors such as stress and strain, physical indolence, obesity, luxury

<table>
<thead>
<tr>
<th>Tertile</th>
<th>Per cent of new events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17.5</td>
</tr>
<tr>
<td>2</td>
<td>29.8</td>
</tr>
<tr>
<td>3</td>
<td>52.7</td>
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living, or tobacco probably play only a minor role in producing a high rate of coronary heart disease in persons under 65 years of age. One may even reverse this statement and state that with an adequate intake of the polyunsaturated fatty acids these factors play a minor role. It is also equally evident that there are nonsusceptible persons who can tolerate, over a long lifetime, large amounts of naturally saturated fats. Unfortunately, there is no method presently available by which such persons can be recognized with certainty in advance. One may briefly speculate, as did Sinclair that the greater the saturated fat intake, the greater is the requirement for polyunsaturated fatty acids.

One can also follow with considerable confidence the cautious provisional judgment of Kinsell et al. that linoleic acid is a dietary “essential” for adults and that an early manifestation of its deficiency is an elevated plasma cholesterol. It is not clear whether atherosclerosis results from elevated cholesterol levels per se or as separate manifestations of certain polyunsaturated fatty acid deficiency. Still unknown is the relative importance of the role played by fats in intravascular clotting directly vs. atherogenesis. Information is now sufficient to develop provisional schema of possible roles of fat in the development of coronary heart disease. The schema given in figure 2 was that developed by Ahrens et al. As pointed out by Ahrens, the relationship between abnormal serum lipids and atherosclerosis may not be one of cause and effect. "Hypercholesterolemia and arteriosclerosis may both be genetically determined and the two manifestations of the disease need not be causally related." Wilkinson studied many members of a familial group with hypercholesterolemia and found no greater incidence of coronary disease in the members who had hypercholesterolemia than in those whose serum cholesterol was "normal."

The next schema was that of O'Brien (fig. 3) who brought into the picture blood clotting and fibrinolysis, but left with a large question mark the effects of dietary fats on the blood lipid levels. It seems that there is now sufficient evidence to extend O'Brien's schema further and derive one that can serve as a basis for further discussion (fig. 4). This schema includes the 3 possible pathways that "bad" dietary fats (which is equivalent to absolute or relative polyunsaturated fatty acid deficiency) may lead to coronary heart disease. The direct line through the center is essentially the Ahrens' schema. The line between "bad" dietary fat and abnormal blood lipids is solid to indicate its firmness. The accentuating and retarding factors recognize the modifications introduced by gonadotropic and thyroid hormones, conditional factors, and such disease factors as diabetes, nephrosis, and idiopathic lipodystrophies. The line between abnormal blood lipids and atherosclerosis is broken as this is not yet proved to the complete satisfaction of many people. The double-shafted arrow at "abnormal blood
Highly probable to proved; . . . > possible to probable; . . . > theoretical; AF > accentuating factors, e.g., genetics, hormones, diabetes, nephrosis, maleness; RF > retarding factors, e.g., genetics, hormones, femaleness; OF > other factors outside schema unrelated to dietary fats.

These 2 factors, increased coagulability and decreased fibrinolysis, account for the presence or absence of clinical coronary heart disease in persons with relatively equal amounts of coronary atherosclerosis. The double arrow pointing to "coronary heart disease" recognizes the other etiologic factors producing coronary heart disease such as aneurysms, embolizations, etc.

This schema is attractive for it affords a reasonable explanation of certain apparent contradictions in our knowledge of coronary heart disease, such as the relative immunity of women prior to the menopause. At this time their requirements for fatty acids are presumably much lower than those of men. The low incidence of coronary artery disease among certain high-fat-consuming groups may be attributed to their high intakes of polyunsaturated fatty acid. This theory also explains why the most affluent and the most advanced countries industrially, where the economy permits most people sufficient income for a luxury diet high in saturated fat, are the ones in which coronary heart disease has increased and is still increasing the most. It is also in these countries with high fat consumption that the most fat is hydrogenated, and the formation of isomers of the essential fatty acids may act physiologically as anti-essential fatty acid, like the isomers of thiamine, which act as antithiamine. It helps explain why coronary heart disease during World War II decreased in Norway when the occupying Germans commandeered the butterfat while their hydrogenation plants were destroyed by air action.

The next steps in transferring these results from metabolism ward and formula diets to public health practice are as follows:

1. Develop practical diets to replace metabolism ward and formula diets for the general public. These diets must be of nutritionally balanced, palatable and acceptable American foods which are available in every grocery store.

2. Demonstrate by public health methods that, if persons in their usual environment
can be induced to modify their diets over a long period of time, their blood lipids, as measured by the cholesterol-lipoprotein system, will be favorably influenced.

It remains to be proved, however, that a significant number of persons free-living and consuming common American foods can be so induced. This is in reality a clear challenge to our ability to motivate and educate so that a change in the diet of free-living persons will result.

3. Demonstrate whether a favorable change in the cholesterol-lipoprotein system produced and maintained by diet is associated in fact with a favorable change in morbidity and mortality from coronary heart disease, particularly in men under 65 years of age. From the evidence presently known it seems not too optimistic to predict that an answer to this can be given within a few years.

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