

# Role of Dietary Fat in Human Nutrition

## III—Diet and the Epidemiology of Coronary Heart Disease

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*The differential frequency of coronary heart disease has been noted among various populations in different parts of the world. Epidemiologic study of such groups, when taken together with other evidence, has tended to implicate the diet, especially the dietary fat, in these differences. The authors of this paper, the third in the series on dietary fat in human nutrition, present data supporting an association between the incidence of coronary artery disease, a high intake of total dietary fat, and the elevation of serum cholesterol.*

✚ Coronary heart disease is the end result of the interplay of several, perhaps many, factors and no single cause will explain the developments that lead to the final clinical picture. Serious ischemia of the myocardium and of the conduction system of the heart, which is the basic functional fault, can be produced by coronary atherosclerosis or thrombosis or, most commonly, by a combination of these obstructive processes. Atherosclerosis and thrombosis,

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NOTE: Please turn to page 1541 for additional information.

in turn, are each susceptible to more than one major influence.

Hereditary predisposition to atherosclerosis or thrombosis, or both, may operate through effects on the vessel wall, or through forces generated by the blood flow through a particular arrangement of the vascular architecture, or through peculiarities in the lipid cholesterol metabolism and such a genetic element may be critical in some individuals. But it is probable that genetic factors are not frequently dominant or that, at least, there is normally wide latitude for the operation of nongenetic influences in the eventual development of coronary heart disease. In other words, we can believe that environmental influences are of major importance for most people and that it is reasonable, therefore, to hope that research can show how the development of the disease may be prevented or so influenced that, in effect, it can be controlled.

Elsewhere, we (Keys, 1955) have discussed some of the reasons why genetic dominance may be discounted. Certainly the great differences in the incidence of coronary heart disease between different populations and within the same populations at different times are not explained by genetic factors.

The most recent evidence to this effect was obtained in our study during 1956 of Japanese men living in Japan, in Hawaii, and in Los Angeles. Coronary heart disease is rare in Japan, but it is fairly common among the Japanese in Hawaii and in Los Angeles the Japanese Nisei appear to suffer the same high frequency of the disease as do the local

**Table 1—Percentage Evidence of Severe (Grades 3 and 4) Coronary Atherosclerosis Found at Autopsy in Men Dying from All Causes, According to Age in Years. (Data for Minnesota from White, Edwards, and Dry, 1950)**

	30-39	40-49	50-59	60-69
Japanese in Kyushu	2	4	8	10
Japanese in Hawaii	8	10	30	33
Caucasians in Hawaii	18	38	64	78
Caucasians in Minnesota	20	40	73	70

Caucasians. It seems clear that men of the same genetic background differ markedly in regard to coronary heart disease when, as in the case of these Japanese, they change their mode of life toward the usual American pattern.

Table 1 summarizes the objective finding of severe (grades 3 and 4) coronary atherosclerosis found in recent large series of routine autopsies, death from all causes, among Japanese men in Japan (Kyushu) and in Hawaii as compared with white men in Minnesota and in Hawaii. The data from Japan were obtained by Noboru Kimura (see also Kimura, 1956), and their comparability was checked by a visit to Japan in 1956, as well as by Kimura's visit to Minnesota in 1954. The data from Hawaii were assembled by Nils P. Larsen and were reanalyzed by B. Bronte-Stewart. Comparable data are not available for Los Angeles, but both severe atherosclerosis and coronary heart disease are unquestionably very common there among the Japanese whose mode of life is indistinguishable from that of the local Caucasians in contrast to Hawaii, where the local Japanese mode of life is intermediate between the patterns of Japan and the continental United States, at least in regard to diet.

Such large series of autopsy studies are all too few and, in any case, it must be recognized that atherosclerosis is by no means synonymous with coronary heart disease, though the disease seldom appears in the absence of the underlying atherosclerosis. However, there

is little doubt that the frequency of coronary heart disease is closely correlated with the frequency of severe atherosclerosis and the indications are that differences of populations in atherosclerosis are reflected, in exaggerated form, in differences in incidence of and mortality from ischemic heart disease. Whereas Minnesotans and Caucasians in Hawaii appear to be some 10 times more prone to have severe atherosclerosis than do Japanese in Japan, the incidence of coronary occlusion and myocardial infarction seems to show even greater differences.

In the search for the cause or causes of such differences one approach would be to examine all items of the mode of life that can be objectively evaluated. Thus, one might compare the populations of areas where coronary heart disease is exceedingly common, such as in the United States and Finland, with those in areas of intermediate frequency, such as the Netherlands and Northern Italy, and with populations that have a very low frequency, as in Japan, Southern Italy, and the Bantu of South Africa.

Among the endless list of items that

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might be studied at random, without regard to theoretical and mechanistic considerations, it is easy to rule out of primary consideration many factors that show no consistency with regard to the relative frequency of the disease. Climate, race, the use of alcohol and tobacco, degree of urbanization and industrialization, the stress forces of exposure to telephones, radios, street traffic hazards, personal cleanliness, indulgence in competitive business and sports, availability of doctors and hospitals seem to fall in this category; any or all of these may exert some influence but, if so, it would seem to be minor and secondary to other and more basic factors.

When we come to the diet, however, a relatively consistent pattern emerges and the suspicion arises that here is a primary factor. This suspicion is greatly enhanced by theoretical and experimental evidence that is lacking, so far, with regard to other items in the mode of life (Keys, 1956). As much of the evidence to be cited involves the serum cholesterol concentration the relevance of this factor must be considered.

### Serum Cholesterol Concentration

An important connection between the cholesterol-lipoprotein system in the blood and the production of atherosclerosis in man has long been recognized from innumerable demonstrations

of a tendency for the serum cholesterol level to be high in persons with recognized coronary heart disease and of the fact that persons suffering from other diseases characterized by elevated serum cholesterol values—myxedema, diabetes, nephrosis, xanthomatosis, familial hypercholesterolemia—are unusually prone to develop coronary heart disease. Recently, it has been shown that even single serum cholesterol measurements on American men who are apparently clinically "healthy," have prognostic value in regard to the subsequent development of unequivocal signs of coronary heart disease. Table 2 summarizes the relevant findings in this "forward" study.

A single measurement of serum cholesterol cannot be expected to predict the coronary future of individuals with high reliability. The serum cholesterol concentration shows much intraindividual variability and is responsive to changes in the diet within a few days so that it cannot be guaranteed that any single measurement is truly representative. Further, we note that atherosclerotic development usually extends over a very long time, often over many years, and that the final appearance of the clinical disease does not necessarily reflect a constant rate of progression of the atherosclerosis itself. The fact that, as shown in Table 2, a single measurement does have significant predictive

**Table 2—Numbers and Percentages of Men, Subsequently Developing Clinical Manifestations of Coronary Heart Disease, Whose Blood Analyses Showed Values Above the Median for the Sample of "Clinically Healthy" Men in Which They Were Studied. (Data from Circulation, Vol. 14, No. 4, Part 2, October, 1956)**

Item of Measurement	No. of Patients	Above the Median	
		No.	Per cent
S <sub>r</sub> 12-20	65	32	49
S <sub>r</sub> 20-100	65	42	65
Cholesterol	57*	41	72

\* Of these, 50 men, or 88 per cent, had cholesterol values over 200 mg per 100 ml.

value in spite of such severe limitations is most important. Further, we note that 88 per cent of the eventual "coronaries" had cholesterol values over 200 mg per 100 ml and that values as high as this are unusual in populations in which coronary heart disease is rare.

At best, the link from a single serum cholesterol measurement to the appearance of the disease must be through a series of very imperfect correlations—the correlation between the value in the particular blood sample to the serum or average of the concentrations in the past and in the future, the correlation between the habitual concentration and the actual development of atherosclerosis, past and future, and the correlation between degree of atherosclerosis and the production of the occlusion in a critical place, and so forth.

### Diet

For many years the experimental production of atherosclerosis in animals emphasized the diet, though we know that much of the evidence from animal studies does not apply directly to man. However, the major relevance of the animal experiments to the problem of atherogenesis in man is clear if we focus our attention on the cholesterol-lipoprotein system of the blood. The common feature in all atherosclerosis experimentally produced in animals is that it appears when an elevated serum cholesterol level is persistently maintained. And the work of recent years has increasingly shown the dominant influence of the diet of man as well as of animals on the cholesterol-lipoprotein system of the blood.

In this field both human and animal experiments have serious limitations which must be kept in mind. Different animal species show profound differences in the metabolism of cholesterol and lipoproteins, as well as in their responses to the diet. All animal species

so far studied differ sharply from man in quantitative details, which are all-important when we consider the practical problem of human diets. Further, the full development of atherosclerosis to the equivalent of coronary heart disease in man is only very rarely represented in these animals.

For obvious reasons controlled human dietary experiments are restricted to relatively short periods under artificial conditions that may have small relevance to normal life. Moreover, under the best of conditions the investigation is limited to such inferences as may be drawn from studies on the blood and its responses to dietary and other manipulations; neither atherosclerosis nor coronary heart disease is actually observed or studied in such experiments. However, recourse may be had to the study of the natural dietary experiments of human populations and the associated experiences of atherosclerosis and coronary heart disease. This is the epidemiologic approach which we wish to emphasize here.

### Magnitude of the Problem

An indication of the magnitude of the problem is given by the mortality figures. Examination of the causes of death in the United States vital statistics for 1953 clearly shows that coronary heart disease (International List No. 420) is our leading cause of death, accounting for nearly one-fourth of the total mortality. Moreover, most of the deaths listed under No. 422 classification are probably ascribable to the same basic cause. So, if deaths from violence and deaths under five years of age are subtracted, we have nearly 40 per cent of the total mortality produced by the results of inadequate blood flow through the coronaries. Most alarming is the frequency of coronary heart disease in relatively young men and the indication that this is rapidly increasing. The

mortality rate ascribed to coronary heart disease in men aged 45 through 49 increased by 24.9 per cent in the 12 years from 1940 to 1952 in the United States. It is unlikely that this increase is only the reflection of changing trends in diagnostic custom, though the latter probably plays some role.

The experience of life insurance companies gives a similar picture (Lew, 1953). While the total mortality rate (all causes) is decreasing in life insurance statistics, the mortality rate for the total of all heart diseases is increasing, and since coronary heart disease accounts for some three-fourths of all heart disease mortality, it seems evident that coronary heart disease has increased a great deal in the last 25 years. The probability that this is true is indicated by the disappointingly small improvement in the total mortality rate of middle-aged men in the past several decades, in spite of improvements in a number of causes of death that were formerly important, e.g., tuberculosis and rheumatic heart disease. An increase in mortality by coronary heart disease is observed in many other countries besides the United States. The total death rate in England and Wales between 1928 and 1953 shows a steady improvement among females, but not among males. Increases in coronary heart disease and in cancer of the respiratory system has apparently prevented any important net gain in the mortality rate of middle-aged men, in spite of the continuous reduction of other causes of death.

#### Epidemiologic Evidence of Countries with Lower Incidence of Coronary Heart Disease

The picture of very high mortality due to coronary heart disease which we observe in the United States and in some other countries is, however, not a universal finding. There are obvious difficulties in the comparison of the vital

**Table 3—Deaths Among White Men Aged 50–59 in the United States and the Corresponding Rates for Men in Italy**

	All Causes	Nos. 420, 422
Observed	108,630	38,039
Italian rate	87,795	12,869
Difference	20,835	25,173

statistics of different countries. The possibility of errors in the attribution of the cause of death and the use of different diagnostic criteria must be considered. But there is evidence that such factors cannot account for the different mortality rates reported. For some 15 or 20 countries in the world the vital statistics seem to be reasonably comparable. In a number of those countries independent clinical surveys have corroborated the general picture given by the vital statistics.

We are concerned with the causes of death listed under numbers 420 and 422 (arteriosclerotic heart disease, including coronary heart disease, angina pectoris, and myocardial degeneration). International List No. 421 (chronic endocarditis not specified as rheumatic) is not included because these cases of valvular heart disease cannot be considered as of arteriosclerotic origin merely because the physician does not certify that their origin was in rheumatic fever. A comparison of the mortality for men age 50–59 in the United States and in Italy is presented in Table 3.

The Italian death rate has been applied to a population of the same size as the population of United States. It is apparent that the higher total mortality of American men is amply accounted for by the higher mortality ascribed to coronary or ischemic heart disease. In fact, when this last cause of death is subtracted from the total mortality, the Italian figure is a little higher than the American mortality. The age- and sex-

specific mortality ascribed to coronary heart disease is also clearly much higher in the United States than in Italy according to life insurance experience in the two countries. Finally, surveys of the patient populations in hospitals and clinics are in full conformity (White, 1956).

Still more striking differences are observed when the vital statistics from the United States and Japan are compared as in Table 4. The mortality ascribed to coronary heart disease in Japanese males 50-54 years of age, is less than a tenth of the American mortality rate for this disease in the same age group. Moreover, the mortality among women of the same age in Japan is about one-fifth of the corresponding American mortality. It is significant to compare these data with those in Table 1 on the frequency of finding severe coronary atherosclerosis.

#### Incidence of Coronary Heart Disease in Hospital Populations

Information about the relative prevalence of coronary heart disease in different areas can be obtained by surveying the patients in the medical departments of the hospitals in the respective areas. This comparison has obvious

limitations, but is valuable if the hospitals are readily available to and are used by all the general population and all or nearly all of the patients in all of the hospitals are actually seen by experienced internists other than the doctors in charge of the patients in question. Further, the level of medical practice must be such that full histories, electrocardiograms, and so forth, are available. These criteria have been met in the surveys in three areas in the United States and in three areas in Italy summarized in Table 5.

The relative rarity of coronary heart disease in Italy compared with the United States is striking and it is interesting, too, that there are far more coronary patients in Bologna and Modena than in Sardinia and Naples. For the combined three United States areas 22 per cent of the medical patients are coronary heart disease cases, whereas in Italy the figure is 2.8 per cent. Perhaps more significant is the relative representation of coronary versus hypertensive heart disease in the United States and in the Italian regions. In the United States, the ratio of the former to the latter is 1.71; in Italy it is 0.39. Since these two diseases have similar age relationships and involve similar problems of medical care, their relative

**Table 4—Mortality Rates per 100,000, for United States Whites, 1953, and for all Japan, 1954, According to Official Vital Statistics, for Persons Aged 50-54**

No. Cause	Males		Females	
	United States	Japan	United States	Japan
(1) All causes	1,189	1,163	624	822
(2) All infective and parasitic diseases	39	177	11	88
(3) All violence	124	112	34	36
(4) = 1) - 2) - 3)	1,026	874	579	698
(5) All neoplasms	206	236	224	220
(6) Central N.S. lesions of vascular origin	69	239	67	195
(7) All diseases of the circulatory system	557	118	181	90
(8) Coronary heart disease (List No. 420)	426	20	89	13
(9) Myocardial degeneration (List No. 422)	19	13	19	9
(10) All hypertension (List Nos. 440-447)	46	12	38	9
(11) Ill-defined or not known	13	35	4	20

**Table 5—Summary of Findings in Surveys by Internists Independent of the Local Staff, on the Patient Populations of the Medical Departments in the General Hospitals of Minneapolis and St. Paul (Twin Cities), Boston, Albany (Veterans Hospital Only), Bologna and Modena (Emilia), Cagliari and Sassari (Sardinia), and Naples**

Item	"Twin Cities"	Boston	Albany	"Emilia"	"Sardinia"	Naples
Total medical patients	546	504	226	666	306	462
Rheumatic heart disease	36	26	5	59	20	41
Hypertensive heart disease	54	88	21	48	26	30
Coronary heart disease	141	77	61	29	6	5

representation in the patient populations is significant. It is interesting that in Italy, as in South Africa and Japan, hypertension is not uncommon and there is much reason to believe that in most cases the etiology of the two diseases is different and independent. Finally, we note it is agreed by all that our present high frequency of coronary heart disease affects men far more than women, but that in Italy and Japan, where the disease seems to be much less common, there is no great discrepancy between the figures reported for the two sexes.

### Pathogenesis of Atherosclerosis and Coronary Heart Disease

Since, experimentally, the closest connection exists between diet and atherogenesis, it is reasonable to examine the diets of populations differing in the frequency of atherosclerosis and coronary heart disease. And since a major connection between the diet and the disease seems to be through the serum cholesterol concentration, we must keep this variable in mind. It will be seen that the incidence of atherosclerosis and coronary heart disease seems to be related to the proportion of fat in the habitual diet, and this fact is in general agreement with the theory that atherosclerosis is usually primary in coronary heart disease and that atherosclerosis is promoted by the cholesterol-lipoprotein in the blood which, in turn, is strongly

influenced by the fat content of the habitual diet. This theory does not claim an exclusive role in the pathogenesis but admits the action of other influences. The most obvious of other influences must be factors, other than the atherosclerosis itself, that promote thrombosis. But here too, dietary fat may play a role by rendering the blood unduly coagulable, Buzina and Keys, 1956; Keys, Buzina, Grande, and Anderson, 1951, and by inhibiting fibrinolysis (Greig, 1956).

The evidence in support of this theory can be summarized as follows:

1. The atherosclerotic lesion primarily involves a deposit of cholesterol and this is mainly, if not entirely, derived from the blood.
2. Patients with atherosclerotic heart disease, as a group, tend to have higher serum cholesterol than normals or patients not exhibiting clinical signs of the disease.
3. Atherosclerosis can be produced in animals by dietary manipulations which increase the blood serum cholesterol concentration.
4. Patients having diseases characterized by elevated blood cholesterol values tend to develop early atherosclerosis.
5. Measurements of serum cholesterol concentration have predictive value in distinguishing the persons who will, in the future, develop coronary heart disease.
6. Elevation of the fat content of natural human diets tends to increase the serum cholesterol level and low-fat diets have the opposite effect.
7. Observations from different countries indicate that periods of food and particularly fat restriction are generally accompanied by a decrease in the incidence of atherosclerotic diseases and this change in disease is reversed when fat is restored to the diet.

8. Fatty meals shorten the coagulation time of the blood and, when the clot is formed, inhibit fibrinolysis.

The evidence obtained in epidemiologic studies indicates in fact that populations subsisting on high-fat diets do tend to have high cholesterol concentrations in their blood and a high incidence of atherosclerotic diseases. And it is significant that every low-fat diet population so far studied proves to have a low incidence of atherosclerosis and/or coronary heart disease.

**Fat Intake and Blood Serum Cholesterol in Different Populations**

During the last few years work done in countries in many parts of the world has provided considerable evidence which indicates a quantitative relationship between the proportion of fat cal-

ories in the diet and the blood cholesterol concentration. Values obtained in 21 groups of men aged 40-49 are assembled in Figure 1.

Since some of these observations have been obtained with individuals of different racial background the question can be raised as to whether an influence of race on the serum cholesterol is involved in the apparent relationship to diet fat. Yet Figure 1 shows that individuals of the same racial stock, but of different dietary habits, show large differences in the level of serum cholesterol as illustrated by the differences between the Italians in Naples, Sardinia, and Bologna. Similar observations have been obtained in Spain (Keys, et al., 1954). Low-income Spaniards, with low-fat intake, have much lower serum cholesterol than more prosperous Spaniards consuming diets richer in fat. The

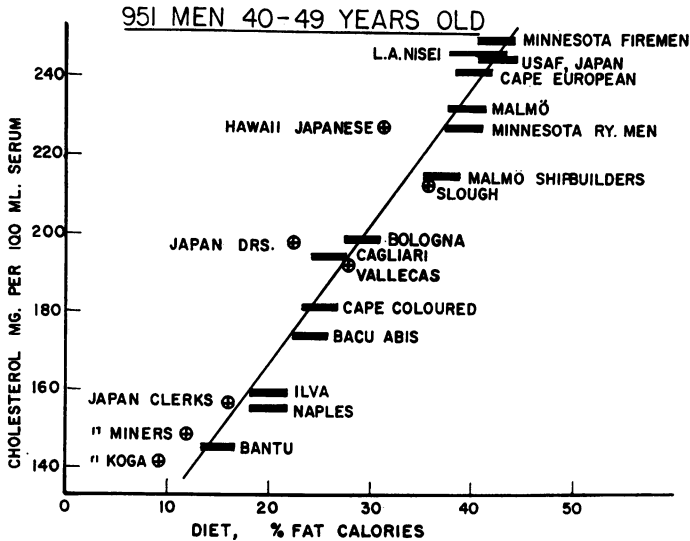


Figure 1—Average Diet and Serum Total Cholesterol Concentration in Clinically Healthy Men Selected as Representative of 21 Population Groups. Heavy Manual Labor is Represented by Japanese Farmers at Koga and Coal Miners, Italian Steel Workers at Ilva (outside Naples), Italian Coal Miners at Bacu Abis (in Sardinia) and Shipbuilders at Malmö, Sweden. All Other Men Were Engaged in Sedentary or Moderately Light Work. "USAF Japan" refers to U. S. Air Force Personnel Stationed in Japan. L. A. Nisei Are Second Generation Japanese in Los Angeles



lack of racial effect is most clear in the recent studies on Japanese men in Japan, in Hawaii and Los Angeles (A. Keys; N. Kimura; A. Kusukawa; B. Bronte-Stewart; N. P. Larsen; and M. H. Keys, to be published). The Nisei in Los Angeles, whose diet proved to average about 39 per cent fat calories, had serum cholesterol values indistinguishable from those of the Los Angeles Caucasians and almost 100 mg per cent higher than the Japanese in Japan subsisting on diets providing from 9 to 14 per cent fat calories.

Populations subsisting on diets of different fat content not only show different blood serum cholesterol for individuals at a given age, but also a different pattern of change of serum cholesterol with age. Minnesotans subsisting on a high-fat diet show a sharp increase of blood serum cholesterol between 35 and 50 years of age, while the Neapolitans, Spaniards, Bantu, and Japanese, subsisting on diets poor in fat, show only a small increase of the blood serum cholesterol as age increases. Again, the observations in Spain indicated that while the poor population shows only a small age trend in serum cholesterol, the rich Spaniards with higher fat consumption have serum cholesterol concentrations and age trends comparable to those found in United States. Furthermore, it is interesting that coronary heart disease is rarely found among these poor Spaniards, but is quite common among the rich.

Much the same situation in regard to the age-cholesterol trend is observed in South Africa where three different groups of population of different economic level and dietary habits coexist. The European consuming the diet highest in fat shows also the highest serum cholesterol values, the lowest values are found among the Bantu eating the diet of lowest fat content, and the Cape Coloured people are intermediate. Again, coronary heart disease is very frequent

among the Europeans, not common among the Cape Coloured people, and remarkably infrequent among the Bantu.

### Discussion

It has been possible here to discuss only very briefly the problem of the relationship between the diet, atherogenesis, thrombogenesis, and the development of coronary heart disease. While a great deal more evidence could be cited in support of the general theory outlined previously, it is more useful to devote some of the limited space here to questions that may be asked in criticism of it.

Questions that have been raised about the Eskimo are most easily answered. There are only a few thousand Eskimos in the world and most of them now live, and have for many years, on diets much lower in fats than the American average. The few primitive Eskimos do, however, eat a diet which is as fat as, and possibly on occasion even fatter than, that of the U. S. Armed Forces. This is interesting but is completely non-informative with regard to coronary heart disease. The primitive Eskimo does not know his own age, but it is known that anything beyond the age of 30 years is considered "old" and that only very few primitive Eskimos ever reach age 50. Obviously, exceedingly few of the primitive, high-fat diet Eskimos attain an age when they would be susceptible to coronary heart disease; perhaps, there are a total of 100 such men in the world Eskimo population and even this may be an overestimate. In any case, there is no evidence at all as to frequency of atherosclerosis among Eskimos, let alone among the primitive Eskimos.

The case of the Navajo is somewhat similar but it has been complicated by erroneous statements. Page, Lewis and Gilbert (1956) stated that "Navajos usually eat a typically American diet.

...” and that there is “striking lack of coronary disease among the Navajo people while consuming the average American diet.” This claim about the Navajo diet is startling to persons who know anything about the Navajos and is, as a matter of fact, completely contrary to the very limited amount of dietary information available to Page, et al.

A mission sent in 1956 to check the Navajos at Fort Defiance, whence came the data used by Page, et al., found, as expected, that the Navajos eat far less meat and other fatty foods than the average American. Butter and milk are rarely used except for trifling amounts of canned milk in coffee. The only fat they consume in significant amount is lard used for frying bread. Perhaps a rough estimate for the average Navajo diet would be around 25 per cent of calories from fats (vs. United States average of 40+ per cent); this would correspond to the over-all food sales through the local trading post. Furthermore, coronary heart disease may be less common among the Navajo than among Minnesotans but it is certainly not vanishingly rare. Among a very small population with average age much less than in other areas of the United States, the Navajos in 1955–1956 still manage to exhibit an appreciable frequency of ischemic heart disease; among male patients admitted to the Medical Service of the Health Center, some 5 to 10 per cent are brought in because of atherosclerotic heart disease. In terms of frequency seen at Fort Defiance, the picture seems to be similar to Sardinia and the dietary fat level, likewise, seems to be similar.

More important than Navajos and Eskimos by far is the question as to why the vital statistics for the Netherlands, Norway, Sweden, and Denmark indicate a much lower mortality from coronary heart disease than our rate in the United States, though their diets are moderately high in fats. We observe

that the fat content of their diets is significantly lower than in the American diet; nevertheless, the difference in the frequency of coronary heart disease seems unduly great.

We observe, first, that the total mortality rates of middle-aged persons in these countries are generally remarkably low, not only from coronary disease but from the total of all other causes of death. We cannot help but wonder whether there is not some general factor at work—greater general vitality, better medical care, or something which affects many causes of death in middle age. In any case, there are no prevalence or morbidity data to show that either atherosclerosis or coronary heart disease are particularly low in those countries. A study on the incidence of severe coronary atherosclerosis seen at autopsy in Denmark showed a frequency not far from that observed in Minnesota at the same ages (Wanscher, et al., 1951). Hospital surveys in Lund and Malmö, Sweden, showed a patient burden of coronary heart disease lower than in Minnesota, but certainly very heavy (myocardial infarcts are far more common in Southern Sweden than in Italy). Obviously, comparative studies involving these countries are needed.

### Summary

The high frequency of coronary heart disease among American men, especially in middle age, is not found among many other populations, notably among Japanese in Japan and Bantu in South Africa. Experimental, theoretical, and epidemiologic evidence implicates the diet, and especially the fats in the diet, in these differences. The search for other factors so far has been unsuccessful.

It seems probable that the more common fats of the American diet, when eaten in large amounts as is often the case in the United States, may contribute to the production of relative hyper-

cholesterolemia and so to atherogenesis. Further, there is suggestive evidence that fatty meals may induce hypercoagulability of the blood and inhibition of fibrinolysis.

While dietary fat cannot be the sole responsible agent, the weight of accumulating evidence is such that the most extensive research on the question of the role of dietary fat in atherogenesis and thrombogenesis is warranted.

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## IV—Experimental and Clinical Evidence Relating to the Effect of Dietary Fat Upon Health in Man

THEODORE B. VAN ITALLIE, M.D.

*It has been suggested that hypercholesteremia in adult human beings results from a chronic deficiency of essential fatty acids. But while this hypothesis is attractive, there still are many questions that remain unanswered. In particular, the reciprocal roles of saturated and unsaturated fats in metabolism must be more specifically delineated. Furthermore, the author points out that a concern about the possible deleterious effects of dietary fat should not lead us to overlook the need for this nutritional component in the diet. This is the fourth contribution in the series on the role of dietary fat in human nutrition.*

\* In terms of health fat has been downgraded within the last few years, both as a constituent of the diet and of the

body. On the whole, the epidemiologic, clinical, and experimental evidence responsible for this disenchantment with fat has been well founded; yet, without prejudice to the excellent work that has led to disclosure of a relationship between diets high in saturated fats and hypercholesteremia, we can afford to be reminded that fat is still an important and valuable part of the diet. And, without in any way condoning gross obesity, we can still bear in mind that current standards for desirable weight are formulated primarily in terms of statistical longevity.<sup>1</sup> While, in principle, longevity might seem to be a highly laudable goal, other considerations may be of more immediate importance and these must be taken into account when we are sitting in judgment upon the