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VARIANCE AND DISSENT
Presentation

The Questionable Role of Saturated and Polyunsaturated Fatty Acids in Cardiovascular Disease

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ABSTRACT. A fat diet, rich in saturated fatty acids (SFA) and low in polyunsaturated fatty acids (PUFA), is said to be an important cause of atherosclerosis and cardiovascular diseases (CVD). The evidence for this hypothesis was sought by reviewing studies of the direct link between dietary fats and atherosclerotic vascular disease in human beings. The review included ecological, dynamic population, cross-sectional, cohort, and case-control studies, as well as controlled, randomized trials of the effect of fat reduction alone. The positive ecological correlations between national intakes of total fat (TF) and SFA and cardiovascular mortality found in earlier studies were absent or negative in the larger, more recent studies. Secular trends of national fat consumption and mortality from coronary heart disease (CHD) in 18–35 countries (four studies) during different time periods diverged from each other as often as they coincided. In cross-sectional studies of CHD and atherosclerosis, one group of studies (Bantu people vs. Caucasians) were supportive; six groups of studies (West Indians vs. Americans, Japanese, and Japanese migrants vs. Americans, Yemenite Jews vs. Yemenite migrants; Seminole and Pima Indians vs. Americans, Seven Countries) gave partly supportive, partly contradictive results; in seven groups of studies (Navajo Indians vs. Americans; pure vegetarians vs. lacto-ovo-vegetarians and non-vegetarians, Masai people vs. Americans, Asiatic Indians vs. non-Indians, north vs. south Indians, Indian migrants vs. British residents, Geographic Study of Atherosclerosis) the findings were contradictory. Among 21 cohort studies of CHD including 28 cohorts, CHD patients had eaten significantly more SFA in three cohorts and significantly less in one cohort than had CHD-free individuals; in 22 cohorts no significant difference was noted. In three cohorts, CHD patients had eaten significantly more PUFA, in 24 cohorts no significant difference was noted. In three of four cohort studies of atherosclerosis, the vascular changes were unassociated with SFA or PUFA; in one study they were inversely related to TF. No significant differences in fat intake were noted in six case-control studies of CVD patients and CVD-free controls; and neither total or CHD mortality were lowered in a meta-analysis of nine controlled, randomized dietary trials with substantial reductions of dietary fats, in six trials combined with addition of PUFA. The harmful effect of dietary SFA and the protective effect of dietary PUFA on atherosclerosis and CVD are questioned. J CLIN EPIDEMIOL 51;6:443–460, 1998. © 1998 Elsevier Science Inc.

KEY WORDS. Atherosclerosis, cardiovascular disease, coronary heart disease, diet, polyunsaturated fatty acids, review, saturated fatty acids

INTRODUCTION

For many years, a fat-rich diet has been considered a major cause of atherosclerosis and cardiovascular diseases (CVD), in particular coronary heart disease (CHD). The nature of the so-called atherogenic diet has been disputed, but most health authorities consider saturated fatty acids (SFA) harmful and polyunsaturated fatty acids (PUFA) beneficial. The atherogenic diet is thought to operate by raising serum LDL-cholesterol, while a high LDL-cholesterol is thought to stimulate atherosclerosis and thus CVD [1–3].

Serum cholesterol can undoubtly be lowered by diet. However, this is surrogate evidence and is no proof that dietary fat is atherogenic, because a high serum cholesterol could be solely a risk marker that is secondary to the real cause(s). It is important to note, for instance, that several meta-analyses have shown diet and most cholesterol-lowering drugs to be ineffective as a means of preventing CVD. Moreover, the skeptic is not comforted by the positive effect on CVD achieved by the new cholesterol-lowering drugs, the statins, because this effect can be explained by other mechanisms than lowering cholesterol [4–6].

The dietary guidelines presented worldwide by national

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health authorities have had a great impact on food production and manufacturing and on the ordinary life of many people. With the aforementioned inconsistencies of the diet-heart idea in mind, I found it pertinent to examine the scientific evidence for these recommendations. If the diet influences blood cholesterol and if it is true that blood cholesterol is important for the development of atherosclerosis, then the diet must at least partly explain differences in the incidence and prevalence of atherosclerosis and CVD. Consequently I have concentrated on the studies that aimed to demonstrate a direct link between dietary fat, in particular its content of SFA and PUFA, and atherosclerotic disease.

MATERIALS AND METHODS

Observational studies, including ecological, dynamic population, cross-sectional, cohort, and case-control studies of the relationship between intake of total fat, SFA and PUFA, and atherosclerosis, CVD and CHD were sought by Medline and by references from reviews and papers. A similar search was made for controlled, randomized trials of the effect of dietary fat or SFA reduction alone, irrespective of whether or not mono- or polyunsaturates were added. Unpublished data from the trials were supplied by Dr. Fujian Song, NHS Centre for Reviews and Dissemination, University of York. The appropriate statistical yearbooks [7–9] were consulted in order to obtain national mortality rates from 1965–1969 and 1985–1989, and the latest ones, for CVD and CHD (groups 25–30, and 27, respectively, according to International Classification of Diseases (ICD), 9. revision); national food supply data 1961–1963 and 1983–1985; and gross national product (GNP) per capita.

The prevalence or incidence of CVD and CHD, and information about the intake of SFA, PUFA, and total fat were sought in the observational studies. In the trials, odds ratios (OR) with 95% confidence intervals were calculated for total and CHD mortality. Confidence intervals were derived by the logit method; significance for OR and mean, weighted OR for all trials were calculated as described elsewhere [10]. The latest national CHD and CVD mortality rates and changes of these rates between 1965–69 and 1985–1989 were correlated with fat supply data from 1983–85 and with their changes between 1961–1963 and 1983–1985, respectively. Associations were also analyzed by scatter diagrams to exclude evidence of non-linear relationships and false correlations due to outliers. Statistical significance was two-tailed.

RESULTS

Observational Studies

ECOLOGICAL STUDIES. Seven studies of the associations between fat consumption and CHD and/or CVD mortality in several countries were identified (Table 1) [11–17].

In a selection of six countries, Keys [11] found an almost perfect positive, curvilinear correlation between CHD mortality in middle-aged men, and the total intake of fat. However, using all available data from the same year (1948; 26 countries) Yerushalmy and Hilleboe found a much weaker association [12].

Previous ecological studies found that the consumption of SFA was associated with CHD mortality for men [12–17] (Table 1). In two studies this was valid for CHD mortality for women also [14,15], in one study no association was seen [16]. PUFA consumption was associated with CHD mortality for men in one study [14] and inversely associated in three studies [12,13,16], in one study no association was seen [17].

Food supply data matching the latest mortality figures were available from 38 countries on five continents [7–9]. SFA consumption was associated with CHD mortality in men, but the significance of the correlation coefficient depended on an outlier. Intake of total fat was inversely associated with CVD mortality in women (Figure 1) [7,8]. As seen from Figure 1, high intakes and low CVD rates were characteristic for countries with a high per capita GNP.

DYNAMIC POPULATION STUDIES. Numerous researchers have studied secular trends of fat consumption and CHD mortality in a single country. The scientific value of such studies is limited because trends may follow each other by chance. In the following I have therefore only reviewed studies that included four or more countries (Table 2) [15,18,19].

A much-used argument for the diet-heart idea is the concurrent decline of animal fat consumption and CVD mortality in Finland, Norway, Sweden, and Great Britain during World War II [20]. However, the mortality curves turned upward again in Finland in 1943, two years before the end of the war, and in 1945 in England-Wales, when the consumption of animal fat still was low [21,22].

Masironi [15] found that changes of CHD mortality, and changes of total fat and SFA intake in 23 countries were unrelated or inversely related (both sexes, total fat: $r = 0.18$; NS; SFA: -0.27; NS). In a study of 18 countries, Marmot *et al.* [18] found no correlation between changes of SFA intake between 1955 and 1965 and changes of CHD mortality 10 years later. In the MONICA project, intake of animal fat increased by 10–136% in 18 of 27 countries. In three of these 18 countries, CHD mortality was unchanged ($\pm 5\%$), while in eight of them it decreased by 6 to 27% [19].

Trend data for mortality from CHD and CVD between 1965–1969 and 1985–1989, and for food supply during 1961–1963 to 1983–1985 were available from 33 countries. In 13 of these countries, mortality from CVD had changed in the opposite direction to the consumption of animal fat, and in 17 countries to total fat. In 15 countries mortality from CHD had changed in the opposite direction to the supply of animal fat, and in 19 countries to total fat.

TABLE 1. Ecological correlations between intake of fats and cardiovascular mortality 0–9 years later in eight studies

Author(s) [reference]	Intake year(s)	Mortality year(s)	Countries (*n*)	Cause of death	Correlation coefficients: Total fat[a] Men	Total fat[a] Women	SF or SFA[a] Men	SF or SFA[a] Women	PF or PUFA[a] Men	PF or PUFA[a] Women	Hypothesis[b]
Keys 1953 [11]	1949	1948–1949	6	AHD-1	[c]						
Yerushalmy and Hilleboe [12]	1949	1948–1949	22	AHD-2	+0.59		+0.68		−0.47		Supported
Jolliffe and Archer [13]	1952–1955	1954–1955	20	AHD-2	+0.73		+0.83		−0.32		Supported
Lopez-S *et al.* [14]	1948–1959	1957–1960	15	AHD-1	+0.71	+0.65	+0.80	+0.71	+0.52	+0.46	Contradicted
Masironi [15]	1947–1949	1955	25	AHD-2	+0.63	(+0.70)[d]	+0.73	(+0.70)[d]			Supported
Jacobs *et al.* [16]	1979–1981	1987	31	CVD			−0.02	−0.31	−0.31	−0.28	Contradicted
	1979–1981	1987	31	IHD			+0.25	−0.02	−0.49	−0.27	Contradicted
Artaud-Wild *et al.* [17]	1975–1977	1977	40	IHD	+0.62		+0.77		−0.03		Supported
This study	1983–1985	1989–1992	38	CVD	−0.21	−0.40	−0.01	−0.23			Contradicted
	1983–1985	1989–1992	38	IHD	+0.13	−0.13	+0.33	+0.07			Contradicted

Abbreviations: AHD-1: B26, group 420 (arteriosclerotic heart disease, including coronary heart disease)+422 (other myocardial degeneration) according to the International Classification of Diseases (ICD) seventh revision; AHD-2: B26, group 420, 421 (chronic endocarditis) and 422 according to ICD-7; IHD: A83 (ischemic heart disease) according to ICD-9; CVD: group 390–459 according to ICD-9.

[a]Per capita food disappearance rates according to Food and Agriculture Organization of the United Nations (FAO), e.g., the quantities of food produced in a country adjusted by imports, exports, and changes in stocks excluding non-food uses and deducted wastage up to the retail stage, divided by the number of population [12].

[b]The terms supported and contradicted in this and the following tables indicate whether saturated fat is associated with increased and polyunsaturated fat is associated with decreased atherosclerotic disease. The terms are used to quantify the number of supportive and contradictive studies; they do not imply that the individual study proves or disproves the diet-heart idea; other, more powerful factors may have confounded the result.

[c]Strong, curvilinear correlation.

[d]Values in parentheses both sexes.

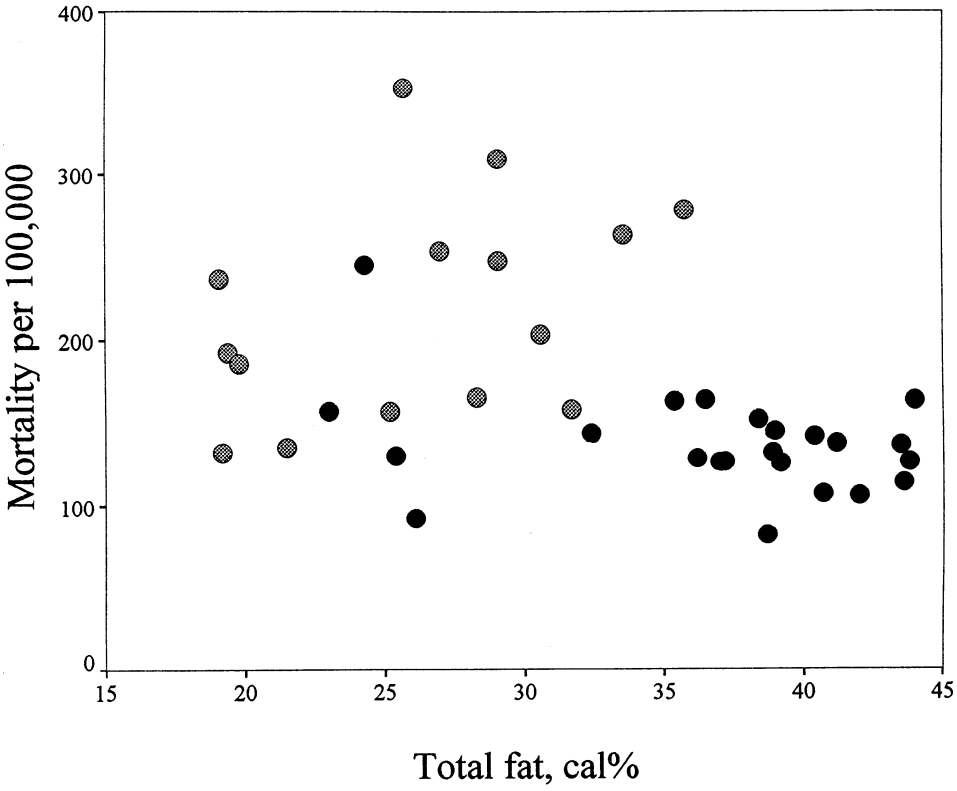

FIGURE 1. Age-standardized death rate from cardiovascular diseases (ICD 9, B25–30; based on new world standard) for women 1985–1989 according to WHO [8] by per capita total fat consumption 1983–1985 according to FAO [7]. Solid circles: Countries with a per capita BNP above 2000 $ [9]. Correlation coefficient $r = 0.40$; $P = 0.013$.

Table 2 gives a summary of the results for trends in CHD mortality and animal fat consumption.

CROSS-SECTIONAL STUDIES. The rareness of atherosclerosis and/or CVD among Bantu people, Pima Indians, West Indians, Yemenite Jews, and the Japanese has been ascribed to their low intake of fat. As will be shown in the following, these relationships were not clearcut, however. Moreover, there were many more populations who consumed little fat, but had a relatively high degree of atherosclerosis and/or CVD, while others who consumed large amounts of fat, especially animal fat, had relatively little atherosclerosis and/or CVD.

TABLE 2. Change of saturated fat consumption by change of CHD mortality for men (number of countries)[a]

Consumption of saturated fat	CHD mortality		
	Increased	Unchanged[b]	Decreased
Increased	30	10	23
Unchanged[b]	6	5	10
Decreased	5	3	11

[a]The data are from four sources: consumption changes in 23 countries between 1947 and 1962 versus mortality changes 1955 and 1965 [15]; consumption changes in 18 countries between 1954–56 and 1963–65 versus mortality changes between 1960–64 and 1970–74 [18]; consumption changes in 27 countries between 1961 to 1985 versus mortality changes between 1972 and 1984 [19], and consumption changes in 35 countries between 1961–63 and 1983–85 versus mortality changes between 1972 and 1984 (this study; see Methods).

[b]±5%.

In the following, I review the results from the studies which have been frequently used as an argument for the so-called prudent diet together with the most contradictory ones. Table 3 [23–61] provides a summary of the findings for studies that included a control group for both diet and CVD.

Bantu People. There is general agreement that coronary heart disease is extremely rare among Bantu people from the Cape province in South Africa [23]. Keys and his group [24] argued that the most important cause is their low intake of fat. As evidence they reported an intake of saturated fat of about 50% of the intake of white people [24].

Curiously, among Bantu people, other atherosclerotic diseases are just as frequent as among white people. Based on the heart dissections of 15 Bantu and 17 European control individuals, Elliott suggested that the rareness of CHD among Bantu people was not necessarily due to their diet, but may be due to anatomical peculiarities of their coronary vessels [23].

West Indians. The prevalence of anamnestic and electrocardiographic CHD among West Indians from St. Kitts was 2.3% in men aged 40–49. According to chemical analysis of the diet of a few families, the total intake of fat was only 17 cal% [62]. This study is often mentioned as being supportive to the diet-heart idea. However, no comparison group was presented.

In an autopsy study, blinded samples of black people from Haiti and South Carolina were compared in order to ascer-

TABLE 3. Summary of the cross-sectional studies that included a control group for diet and cardiovascular disease (for the Pima and Navajo Indian, and the Indian migrant studies, dietary and cardiovascular information are taken from different sources)

Index and comparison groups	Male (%)	Age (range or mean)	Sample size (*n*)	Diet information	Fat measure: index vs. comparison group		Atherosclerotic outcome measure: index vs. comparison group		Hypothesis[a]
Bantu vs. European [23,24]	100	40–58	132 vs. 114	E	SF PF	↓ S	CHD	↓↓	Supported
Black Haitians vs. black Americans [25]	59	20–99	128 vs. 139	A[b], D[b]	SF TF PUFA	↓↓↓ S ↑↑↑	CoScl AoScl	↓* S	Supported Contradicted
Japanese vs. Americans [26]	Not given	10–80+	260 vs. 1275	G	SF TF	↓↓ ↓↓	AoScl: 10–59y 60–80+y	↓ S	Supported Contradicted
Japanese vs. Americans [27]	61	0–80+	1408 vs. 5033	G	SF TF	↓↓ ↓↓	CeScl	↑	Contradicted
Japanese vs. US executives [28]	100	35–59	827 vs. 962	A[b]	SF PF	↓ ↑	CHD	↓↓	Supported
Japanese vs. Americans [29]	100	25–44	34 vs. 68	G	SF TF	↓↓ ↓↓	CoScl AoScl	↓** ↓**	Supported
Japanese vs. Japanese migrants in Honolulu [30,31]	100	30–69	3322 vs. 9878	A, C[b]	SFA TF PUFA	↓↓↓ ↓↓ ↑	CHD	S	Contradicted
Japanese vs. Japanese migrants in San Francisco [30,31]	100	30–69	3322 vs. 3809	A, C[b]	SF TF PF	↓↓↓ ↓↓ ↑	CHD	↓	Supported
Migrants living Japanese way with US diet vs. migrants living US way with Japanese diet [32]	100	30–54	663 vs. 489	A, B[b]	SF	↑↑	CHD	↓↓	Contradicted
Semirecent vs. early Yemenite migrants in Israel [33]	Not given	55–64	30 vs. 20 families	C[b]	SF PF	↓ S	CV; m w	↓↓ S	Partly supported
Yemenites vs. recent and early Yemenite migrants in Israel [34,35]	50	20–68+	36 vs. 23	C, D	TF SF	↓ ↑	AoScl CoScl	↓** ↓*	Contradicted
Seminole Indians vs. Caucasians [36]	38	25+	516 vs. 422	A[b]	SFA PUFA TF	S ↑ ↑	CHD	↓	Partly supported

continued

TABLE 3. *Continued*

Index and comparison groups	Male (%)	Age (range or mean)	Sample size (*n*)	Diet information	Fat measure: index vs. comparison group		Atherosclerotic outcome measure: index vs. comparison group		Hypothesis[a]
Navajo Indians vs. non-Indian Americans [37]	43	30–62	331[d]	A[b,c], L[b]	SF SFA PUFA	S S ↓	CHD	↓↓↓	
As above [38]	64	20–80+	81 vs. 5060				CoScl, AoScl	↓↓	
Navajo Indians vs. Americans [39]	50	15–65+	150,000[d]				CHD	↓↓↓	
As above [40]	0	20–90	107[d]	A	SF	S			All Navajo studies taken together: contradicted
Pima Indians vs. Americans [41]	50	40+	701 vs. 9500				CHD, m w	↓↓NS ↓NS	
Pima Indians [42]	?	?	51 vs. Framingham population [64]	B	SF TF	↓ ↓			
Diabetic Pima Indians vs. diabetic Americans [43]	41	50–79	1093[d]				CHD, m w	↓ ↓↓	
Pima Indians vs. Americans [44]	0	25–44	277[d]	A	SFA PUFA TF	S S S			
Pima Indians vs. Americans [45]	47	18–74	575[d]	A, B	SFA PUFA: m w	↓ S ↑			All Pima studies taken together, partly supported
Black vs. white Americans [46]	100	40–74	437 vs. 337	A, B[b]	SF PF	↑* ↓*	CHD	↓↓↓	Contradicted
Pure vegetarians vs. lacto- and non-vegetarians [47]	0	35+	293 vs. 14595	B	SF	↓↓[e]	CHD	↑↑	Contradicted
Masai people vs. Black Americans [48]	100	14–55+	391 vs. 410	H	SF	↑↑	CHD	↓	Contradicted
Masai people vs. Americans [49]	100	10–60+	50[d]	H	SF	↑↑	ASc1[b]	↓↓	Contradicted

Indians vs. Chinese and Malaysian [50]	50	All	Indian vs. non-Indians in Singapore	A[b]	TF PF	S S	CHD	↑↑↑	Contradicted
North vs. South Indians [51]	Similar	18–55	178,311 vs. 161,719	Various sources[b]	SF PF	↑↑↑ ↓	CHD	↓↓↓	Contradicted
Migrants from India vs. British caucasians [52]	91	49	34 vs. 68				CoScl	↑*	
As above [53]	50(?)	20–64	Indian residents in London vs. British population				CHD	↑*	
As above [54]		20–69	Indian migrants vs. British population				CHD	↑*	
As above [55]	?	?	184 Indian households vs. British population	C vs. National Food Survey	SF PF	↓ ↑↑			
As above [56]	100	45–54	20 vs. 20	B, D, L	TF P/S	S ↑↑***			Indian migrant studies taken together: contradicted
15 cohorts in 12 countries [57]	50	10–69	23207	K	SFA TF	Unrelated Related	AScl		Contradicted
13 cohorts in 7 countries [58]	100	40–59	12763; 5-year follow-up	C[b], D[b]	SFA PUFA	Related Unrelated	CHD		
As above [59]			11579; 15-year follow-up	C[b], D[b]	As above	As above	CHD		
As above [60]			12707; 25-year follow-up	C[b], D[b]	As above	As above	CHD		Seven countries: partly supported

Abbreviations: S = similar (±10%); ↓ = 50 to 90% of the comparison group; ↓↓ = 25 to 50% of the comparison group; ↓↓↓ = Less than 25% of the comparison group; ↑ = 1.1 to 2 times the comparison group; ↑↑ = 2–3 times the comparison group; ↑↑↑ = more than 3 times the comparison group; A = 24-hour recall; B = "usual long-term intake" according to Burke [61], or similar; C = 7-day record; D = food analysis; E = not specified; F = follow-up questionnaires; G = national per capita disappearance rate; H = authors' interviews and observations; K = collected from the literature; L = serum or adipose tissue analysis for fatty acids; SF = animal or saturated fat; SFA = saturated fatty acids; PF = vegetable or polyunsaturated fat; PUFA = polyunsaturated fatty acids; TF = total fat; Ascl = arteriosclerosis; AoScl = aortic sclerosis; CoScl = coronary sclerosis; CeScl = cerebral sclerosis; m = men; w = women.

[a] Explained in legend to Table 1.
[b] diet was studied in a subsample only.
[c] Absolute figures were not given.
[d] Size of comparison group was not given.
[e] Assumed.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

tain degree of atherosclerosis [25]. For each age group, coronary atherosclerosis was more pronounced among the Americans. However, the degree of aortic atherosclerosis was similar although the Americans ate five times more animal fat.

Japanese and Japanese Immigrants. Autopsy studies of Japanese and American adults were available from 1959 and 1969, respectively [26,27]. At that time the per capita consumption of total fat was about 40 cal% in the United States and 10–15 cal% in Japan; while saturated fat was 28 cal% and 5–10 cal%, respectively [7]. In the study of Gore *et al.* [26] Americans below 60 had slightly more atherosclerosis in the aorta than Japanese. However, after that age no differences were seen. In the study by Resch *et al.* [27], cerebral atherosclerosis was more pronounced among Japanese of all age groups. In a more recent study [29] more raised lesions were found among black and white New Orleans men below the age 45 compared with Japanese men of the same age, in accordance with the findings by Gore *et al.*

In a study of Japanese and American telephone executives [28], the latter showed more often signs and symptoms of CHD (except for mild effort pain) although hypertension, diabetes, cigarette smoking, and lack of exercise was much more prevalent among the Japanese executives.

The Ni-Hon-San study of Japanese men in Japan, and Japanese migrants in Honolulu and San Francisco, is commonly used to support the diet-heart idea because fat intake and CHD mortality were highest in San Francisco, where the food was fat-rich, and lowest in Japan where the food was lean [30]. The data from Honolulu disagree, however, because the consumption of SFA was almost four times higher than in Japan [30], but the prevalence of CHD was the same [31].

The best predictor of CHD mortality in the Ni-Hon-San study was cultural upbringing. Those who adhered to the Japanese way of life had much lower mortality than those who were brought up in the American way. This association was maintained after adjustment for the major risk factors. Nor was it due to diet, since those who were brought up in a non-traditional fashion but preferred the lean Japanese food had almost twice as much CHD than those who were brought up traditionally but preferred American food [32].

Yemenite Jews. All studies of Jews from Yemen have shown that those who had resided in Israel for more than 10 years had more aortic and coronary atherosclerosis than recent emigrants [33,34]. This finding has often been explained by an increasing amount of fat in their diet based on questions to early and recent migrants. Cohen *et al.* [35] were alone in also studying the diet in Yemen and confirmed that the total fat intake increased in relation to the length of the period after emigration. However, this increase included only vegetable fat; cal% from animal fat was highest in Yemen, intermediate in recent settlers, and lowest in early settlers.

American Indians. CHD is rare among American Indians. However, the number of Indians in each study was small (see Table 3). Nevertheless, all studies pointed in the same direction. Thus, in 147 Apache Indians above 40 not one ECG recording characteristic of CHD was obtained; using the Framingham data as a standard measure, the expected number was 17 in men and 3 in women [63]. The number of CHD deaths in Seminole Indians above age 25 was only 50% of that of Caucasians from the same district [36]. Over a 6-year period, only one Indian from an isolated Navajo tribe died from CHD [37]; the predicted number based on the Framingham data should have been about 12. In autopsies, moderate or marked atherosclerosis was seen in 14% of Navajo Indians compared with 37% in non-Indians of the same age [38], and their discharge rate for acute myocardial infarction was only 1/5 to 1/10 of the general population's [39]. Pathologic Q-waves were rare in Pima Indians as were myocardial infarctions in autopsies [41]. Between 1958 and 1982, the mortality from CHD for American Indians in New Mexico was only about 1/5 of the mortality for US whites [64].

These findings were not associated with a low intake of SFA. In a few studies, Indians ate a meagre diet, but most studies found that the consumption of animal fat was at least as high as for other Americans (Table 3). Unfortunately, the meticulous study of the Navajo diet by Darby *et al.* [65] did not give quantitative data, but it is obvious from their report that the Navajo diet was rich in animal fat.

The Pima diet is often claimed to be meagre and accordingly is in agreement with the diet-heart idea. This may have been true previously, but as early as in 1959 Hesse [42] found that Pima Indians ate 24 cal% fat, most of which was SFA; in 1971 Reid *et al.* [44] reported a total fat intake of 44.1 cal%, with 15.9 cal% from SFA. In 1996 total fat was 36.2 cal% and SFA 13.3 cal% [45]. These figures are similar with those reported for Americans in Framingham [66,81] and in the Telecom study [28].

Black Americans. A large study of non-fatal CHD in black and white Americans in Evans County [46] showed that high social class white males ate a more "prudent" diet than black males, but had a much higher CHD death rate and a much higher prevalence of CHD, adjusted for age, serum cholesterol, and blood pressure.

Vegetarians. In a follow-up study of American Seventh-Day Adventists [47] 18 of 293 pure vegetarian women, 131 of 6462 lacto-ovo-vegetarian women and 134 of 8133 non-vegetarian women died from CHD, corresponding to standard mortality ratios (SMR) of 94, 42, and 49, respectively, calculated from the death rates in the general California population. SMR for pure vegetarian men was lower than for lacto-ovo- and non-vegetarian men, but this group was small and SMR was based on only two deaths.

Masai People. Masai warriors are known for their excessive intake of animal fat [48]. In spite of that EEC abnormal-

ities were less frequent than in Americans and complicated, atherosclerotic lesions were rare [48,49].

South Asian Indians. In a study from Singapore, Indians ate about 8% less fat than Chinese, but their CHD mortality was about four times higher [50].

CHD mortality in 1.15 million Indian railway workers was seven times higher in South India than in Punjab, and mean age at death from CHD was 44 in South India and 52 in Punjab [51]. The difference in mortality could not be explained by smoking habits, physical activity, or socioeconomic factors, and workers from Punjab ate 19 times more fat, mostly animal fat, than workers from the south.

Indian Migrants. Several studies showed that age-standardized CHD mortality in Indian migrants in Great Britain was about 1.5 times higher than that of the general population [50,51,53,54]. Coronary vessels were also more atherosclerotic [52]. However, the diet of these migrants had 20% less SFA and the P/S ratio was significantly higher than in the diet of the general population [55,56].

Comparisons between Several Populations. In the International Atherosclerosis Project, 15 populations were ranked by raised atherosclerosis and by selected diet components [57]. Correlation coefficients between rankings were significant for cal% from fat ($r = 0.67$), but not for cal% from fat of animal origin ($r = 0.07$).

In the Seven Countries study [58], the prevalence and incidence for CHD and major ECG findings were compared with diet in 13 of 16 cohorts. The intake of SFA correlated positively with prevalence and 5-year incidence of CHD mortality, but not with major ECG findings at entry (Fig. 2) [58]. No findings correlated with intake of PUFA or total fat. CHD mortality varied widely within some of the countries; despite similar risk factors and diet, the 5-year incidence of fatal CHD in Crevalcore, Italy, was more than twice that in Montegiorgio, while in Karelia it was five times higher than in West Finland; and on Corfu, 6–7 times higher than on Crete.

Similar figures were noted in the 15-year [59] and 25-year [60] follow-up studies, although the mortality differences within each country had diminished. However, in the 25-year follow-up, CHD mortality was still twice as high on Corfu as on Crete although they consumed more SFA and less PUFA on Crete than on Corfu.

COHORT STUDIES

CHD. In 21 studies, 28 cohorts of healthy people were followed for 4–23 years [66–86]. After adjustments for various risk factors, those who had CHD at follow-up were found to have eaten significantly more SFA than had CHD-free individuals in three cohorts [74,76,84] and significantly less in one cohort [86]; in 22 cohorts no significant differences were found. Significantly more PUFA had been eaten by CHD patients in three cohorts [72,86]; in one cohort [73] patients had eaten less PUFA, but the significance in that study was one-tailed only; in 23 cohorts no difference was found (Table 4) [66–86].

In a follow-up study of the control group in The Multiple

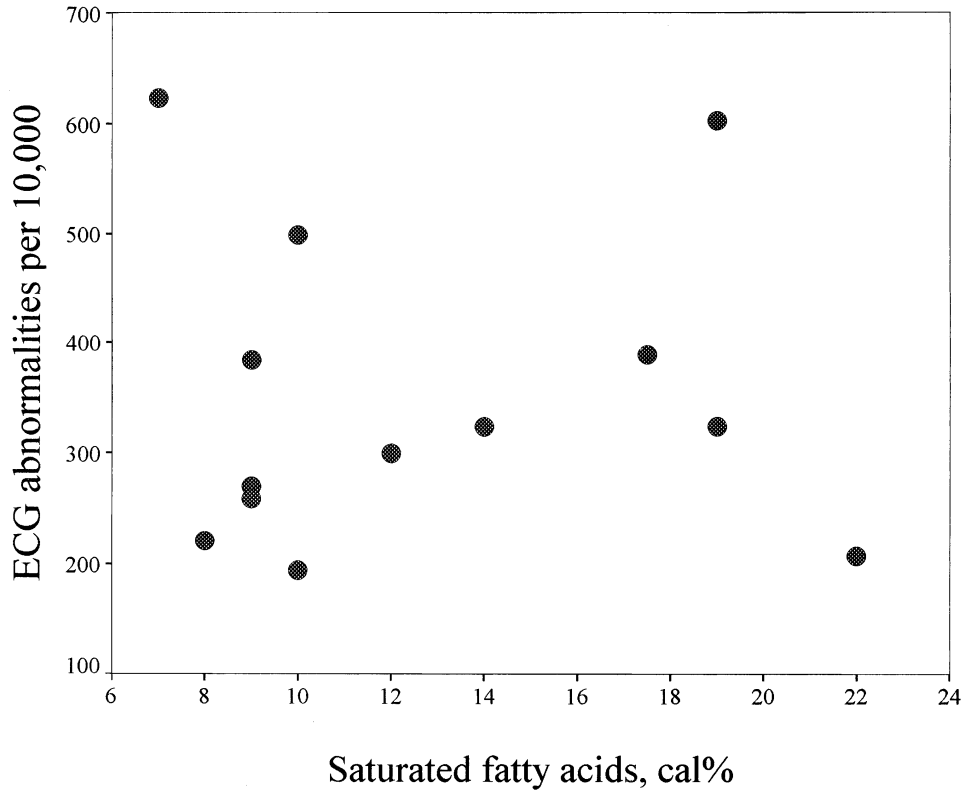

FIGURE 2. Major ECG abnormalities at entry in Seven Countries [58] by consumption of saturated fatty acids.

TABLE 4. Daily average intake of saturated and polyunsaturated fatty acids or animal and vegetable fat, total fat, and energy in CHD patients and CHD-free (none) individuals in 21 cohort studies of 151,097 individuals free of CHD at baseline.

Authors	Observation time (years)	Male (%)	Age	Sample size (CHD/none)	Diet information	SFA (cal%) (CHD/none)	PUFA (cal%) (CHD/none)	Total fat (cal%) (CHD/none)	Energy (kcal) (CHD/none)	Adjustments in separate regression models, or similar	Hypothesis[a]
Framingham 1970 [66]	16	100	37–69	32/380	B	28.9[b]/27.9[b]	10.8[c]/10.6[c]	39.8/38.9	3144/3127	a	Contradicted
	16	0	37–69	15/419	B	29.2[b]/27.2[b]	9.5[c]/9.4[c]	40.6/39.3	2163/2088	a	Contradicted
Paul *et al.* [67]	4	100	40–55	88/1797	G	17.2/16.7	3.9/4.0	43.2/43.1	3082/3174	bp, bw, pr	Contradicted
Medalie *et al.* [68]	5	100	45–64	431/9764	B	NS	NS	NS	NS	?	Contradicted
Morris *et al.* [69]	20	100	40–69	45/292	C	NS	NS	—	↓[***]	a, bw, f, pr, sm	Contradicted
Yano *et al.* [70]	6	100	45–68	179/7411	A	13/12[d,*]	7/6[d,*]	35/33[d,**]	2125/2290	a, al, bp, bw c, sm	Contradicted
Garcia-Palmieri *et al.* [71]											
Urban	6	100	45–64	213/5585	A	13.6/13.5	6.7/5.9[d,**]	38.0/36.6[*]	2305/2413	a	Contradicted
Rural	6	100	45–64	73/2347	A	13.1/12.6	3.9/3.9	32.3/32.2	2241/2353	a	Contradicted
Gordon *et al.* [72]											
Framingham	4	100	45–64	79/780	A,B	15.3/14.9	5.8/5.4	40.2/38.8	2488/2622	a	Contradicted
Puerto Rico	6	100	45–64	286/7932	A	13.5/13.3	6.0/5.3[**]	36.6/35.3[**]	2289/2395[*]	a	Contradicted
Honolulu	6	100	45–64	264/7008	A	12.7/12.3[d,*]	6.7/6.0[**]	34.9/33.4[*]	2210/2319[*]	a	Contradicted
Shekelle *et al.* [73]	20	100	40–55	215/1900	B	NS	↓([**])	—	—	a, al, bw, c, e, sm	Contradicted
McGee *et al.* [74]	10	100	45–68	456/6632	A	12.7/12.3[*]	6.3/6.0[d,*]	34.7/33.3[*]	2229/2309[*]	a, bp, bw, c, p, sm	Supported
Kromhout and Coulander [75]	10	100	40–59	30/827	B	17.7/17.6	5.9/5.9	41.8/41.7	531/3055[d,*]	a, bw, c	Contradicted
Kushi *et al.* [76]	20	100	30–69	110/891	B	17.4/16.9[e]	2.6/2.7	39.4/38.5	3208/3355	a, al, bp, c, e, sm	Supported
Lapidus *et al.* [77]	12	0	38–60	28/1424	A	—	—	NS	↓[***]	a, bp, bw, c, d, p, sm	Contradicted

Khaw and Barrett Connor [78]	12	100	50–79	42/314	A	13.6/13.7	6.7/6.6	37.2/37.2	1997/2076	a, bp, bw, c, d, sm	Contradicted
		0	50–79	23/480		13.1/13.8	7.2/6.9	36.2/37.7	1479/1589	a, bp, bw, c, d, o, sm	Contradicted
Farchi *et al.* [79]	15	100	45–64	58/1536	C	8.0/9.0[d,*]	3.2/3.7	26.0/28.5[d,*]	2697/2900[d,*]	a	Contradicted
Caerphilly [80]	10	100	45–59	137/2197	C, D	29.7[b]/29.5[b]	—	40.9/40.1	2179/2313[**]	a, bw, s	Contradicted
Framingham 1991 [81]	16	100	45–55	99/321	A	NS	NS	↑[**]	NS	a, bp, bw, c, d, e, p sm	Contradicted
	16	100	56–65	114/279		NS	NS	NS	NS	a, bp, bw, c, d, e, p sm	Contradicted
Dolecek *et al.* [82]	10.5	100	35–57	175/5728	A	—	NS	—	—	a, al, bp, c, r, sm	Contradicted
Goldbourt *et al.* [83]	23	100	40+	1098/8961	B	NS	NS	NS	—	a, bp, c, d, sm	Contradicted
Esrey *et al.* [84]	12	53	30–59	52/3873	A	16.8/15.1[**]	6.0/6.5	42.5/39.8[d,*]	2162/2199	a, bp, bw, c, d, sm	Supported
	12	45	60–79	40/581		13.8/14.3	6.4/6.2	38.0/38.0	2051/1850	a, bp, bw, c, d, sm	Contradicted
Ascherio *et al.* [85]	6	100	40–75	734/43757	B, F	NS	NS	NS	—	a, al, bp, bw, c, f, fa, p, pr, sm	Contradicted
Pietinen *et al.* [86]	6.1	100	50–69	635/21930	B, D	↓[*]	↑[*]	—	—	bp, bw, c, f, p, pr sm	Contradicted
Total				5751/145,346							

Abbreviations: A, B, C, D, F, G: See legend to Table 3; a = age; al = alcohol; bp = systolic blood pressure; bw = body weight or other indices of obesity; c = blood cholesterol and/or other blood lipids; d = diabetes; e = ECG abnormalities; f = fiber intake; fa = family history; o = oestrogen use; p = physical activity; pr = profession; r = race; sm = smoking; NS = not significant. Symbols: ↑ CHD patients ate significantly more; ↓ CHD patients ate significantly less.

[a] See explanation in legend to Table 1.

[b] Animal fat.

[c] Vegetable fat.

[d] Statistical significance disappeared after adjustment for other risk factors.

[e] Significant after adjustment for other risk factors.

[*] $P < 0.05$.

[**] $P < 0.01$.

[***] $P < 0.001$. One-tailed test in brackets.

Risk Factor Intervention Trial, the crude intake of PUFA was inversely correlated with CHD mortality [82]. The relationship was marginally significant and disappeared after adjustment for the major CHD risk factors. It should also be mentioned that in the treatment group of the same trial, a 27% decrease of SFA and a 33% increase of dietary PUFA during six years [87] did not change CHD or total mortality significantly [88].

Large variations in fat intakes were reported from most of the cohort studies. In the first one from Framingham [66], the range of animal fat intake for men was 25–200 grams per day, for women 10–130 grams per day. In the study of McGee *et al*. [74] intake of SFA varied between 10 and 50+ grams per day. Khaw *et al*. [78] reported a mean SFA intake of 31.7 and 30.2 gram per day for men and women, respectively with standard deviations of ±12.9 and ±16.6. Similar variations were noted in other cohort studies [72,78, 80,81,84]. Ascherio *et al*. [85] found the median intake in the first quintile of SFA intake to be 17 grams per day, in the fifth quintile 33 grams per day, implying an even larger range individually.

Atherosclerosis. In four cohort studies [89–92], the degree of atherosclerosis was compared with dietary fats according to interviews performed 1–17 years previously. In one of these studies, TF was associated with atherosclerosis; in two of them, TF was inversely associated; in none of them atherosclerosis was associated with SFA, PUFA or the P/S ratio (Table 5) [89–92].

CASE-CONTROL STUDIES. Five studies (six cohorts) [93–97] of CHD including 478 cases and 698 control individuals, and one study of peripheral atherosclerosis including 208 cases and control individuals [98] were identified. In six of the seven cohorts, the control individuals had consumed more TF than had the CHD patients, as well as more calories. However, the differences were not statistically significant (Table 6) [93–98].

Experimental Studies

I found two primary-preventive and seven secondary-preventive controlled and randomized, unifactorial, dietary trials including 7088 individuals in the treatment groups and 7048 in the control groups [99–107]. Two studies were double-blind [102,106], one was single-blind [107], the others were open. Substantial reductions of animal or total fat intake were achieved in most studies. However, with the exception of one study [107], neither total or CHD mortality was lowered significantly, and mean, weighted odds ratios for both were close to unity (Table 7) [99–107].

DISCUSSION

Considering the emphasis with which the "prudent" diet has been promoted by health authorities all over the West-

TABLE 5. Correlation between fat consumption and degree of atherosclerosis at post-mortem in four cohort studies

Population	Male (%)	Age (Years)	Sample size (*n*)	Follow-up period (Years)	Diet information	Fat measure and atherosclerotic outcome	Adjustments in separate regression models, or similar	Hypothesis[a]
Residents of New Orleans [89]	100	20–60	253	1	[b]	TF related, SF, SFA and PF unrelated to raised coronary lesions	[c]	Contradicted
Residents of Puerto Rico [90]	100	45–64	120	12	A	TF inversely related to aortic and coronary sclerosis	a, al, bp, bw, c, d, p, pr, s	Contradicted
Japanese migrants in Honolulu [91]	100	45–68	258	17	A	TF, SF and P/S unrelated to aortic and coronary sclerosis	a, al, bp, bw, c, d, p, pr, s	Contradicted
Japanese migrants in Honolulu [92]	100	45–68	198	17	A	TF inversely related, SFA, PUFA and P/S ratio unrelated to cerebral sclerosis	a, al, bp, bw, c, d, p, pr, s	Contradicted

Abbreviations: See legends to Table 3 and 4.
[a]Explained in legend to Table 1.
[b]28-day recall by surviving spouse.
[c]Age distribution did not differ significantly in nutrient tertile groupings.

TABLE 6. Daily average intake of saturated and polyunsaturated fatty acids or animal and vegetable fat, total fat and energy in six case-control studies of CHD patients and CHD-free control individuals (none) [93–97], and in patients with and without symptoms of peripheral atherosclerosis [98] Abbreviations: See legends to Table 5.

Authors	Sample size (CHD or peripheral atherosclerosis/none)	Age (range or mean)	Male (%)	Diet information	SFA (cal%) (CHD/none)	PUFA (cal%) (CHD/none)	Total Fat (cal%) (CHD/none)	Energy (kcal) (CHD/none)	Adjustments in separate regression models, or similar	Hypothesis[a]
Zukel *et al.* [93]	162/324	>35	100	B	18.7/18.9	3.6/3.6	44.8/45.3	2831/2782	a	Contradicted
Papp *et al.* [94]	20/20	42–65	100	C	—	—	39.4/39.5	3014/3074	a, bw	Contradicted
Little *et al.* [95]	86/84	30–80	100	C	—	—	36.3/37.9	1968/2179	a	Contradicted
Finegan *et al.* [96]	100/50	<60	100	B	19/18	4/4	41/39	3555/3591	a, bw	Contradicted
Bassett *et al.* [97]										
Hawaiian	42/84	49.7	100	C,D	13.3/13.2	5.4/5.9	34.4/35.7	1931/2497	a, bw, p, r, sm	Contradicted
Japanese	68/136	53.3	100	C,D	10.7/11.1	6.3/6.3	30.6/31.1	1838/2380	a, bw, p, r, sm	Contradicted
Sirtori *et al.* [98]	208/208	<30–69	96	F	—	—	25/30	—	a, s	Contradicted
Total	686/906									

Abbreviations: s = sex; other abbreviations, see legends to Table 3 and 4.
[a]Explained in legend to Table 1.

TABLE 7. Intake of total fat and SFA in nine controlled, randomized, unifactorial, dietary trials and their outcome

	Trial category		Sample			Diet				Total deaths			CHD deaths		
						Total fat		SFA							
Trial	Length (years)	Type	Size (T/C)	Mean age (years)	Male (%)	T/C (cal%)	δ (%)	T/C (cal%)	δ (%)	T/C (*n*)	Odds ratio	Confidence interval	T/C (*n*)	Odds ratio	Confidence interval
Low fat [99]	3	S	123/129		100	20.4/43.2	−53	—	—	20/24	0.85	0.44–1.63	17/20	0.87	0.43–1.76
Rose *et al.* [100]	2	S	54/26	55	100	28.8/32.6	−4[a]	—	—	8/1	4.35	0.51–36.8	8/1	4.35	0.51–36.8
Soya-bean [101]	4	S	199/194	?	100	46/42.3	+9[a]	—	—	28/31	0.86	0.49–1.50	25/25	0.97	0.55–1.79
Dayton *et al.* [102]	7	P	424/422	65.5	100	38.9/40.1	−3[a]	10/17	−53	174/177	0.96	0.73–1.27	41/50	0.80	0.51–1.23
Leren [103]	5	S	206/206	56.2	100	39/40[b]	−3[a]	8.5/—	—	41/56	0.67	0.42–1.05	37/50	0.68	0.42–1.10
Woodhill *et al.* [104]	5	S	221/237	48.9	100	38.3/38.1	+1[a]	9.8/13.5	−27	39/28	1.60	0.95–2.71	35/26	1.53	0.89–2.63
DART [105]	2	S	1018/1015	56.6	100	32.3/35.0	−8	—	—	111/113	0.98	0.74–1.29	97/97	1.00	0.74–1.34
Frantz *et al.* [106]	1.1	P	2197/2196	?	100	37.8/39.1	−3	9.2/18.3	−55	158/153	1.03	0.82–1.30	39/34	1.15	0.72–1.83
	1.1	P	2344/2320	?	0	37.8/39.1	−3	9.2/18.3	−55	111/95	1.16	0.88–1.54	22/20	1.09	0.60–1.97
Lorgeril *et al.* [107]	5	S	302/303	53.5	100	30.5/32.7	−7[a]	8.3/11.7	−29	8/20	0.39	0.17–0.89	3/16	0.18	0.05–0.62
Total			7088/7048							698/698			324/339		
Weighted mean											0.99	0.86–1.11		0.94	0.80–1.10

Abbreviations: T = treatment group; C = control group: P = primary prevention; S = secondary prevention; δ = difference between treatment and control diet.
[a]After addition of vegetable oil to the diet.
[b]Estimated from a population survey by the trial director.

ern world and the impact that this advice has had, it was a great surprise to discover the almost total lack of scientific evidence for that diet. In fact, support was mainly found in studies of the lowest scientific validity, the early ecological studies whose findings could be explained in another way.

Thus, the ecological correlation found by Keys between total fat consumption and heart disease [11] was most likely due to selection bias; it was not confirmed by his later study, Seven Countries [58], nor by the most recent ecological studies (Table 1). Another argument against causality was that the relationship was neither specific in terms of dietary fat or SFA, nor for CHD mortality [12,13,15]. As stressed by others as well and as seen from Figure 1, the intake of fats may instead be an index of a country's wealth. It should be recalled that the per capita disappearance rate represents the amounts of food available to the consumer and not necessarily those actually consumed. In the rich, westernized countries, where CVD was more common in the past, more fat, in particular animal fat, undoubtedly disappears during preparation and cooking and more is left on the plate than in poor countries. This leads to a falsely-high intake and a falsely-positive correlation. Accordingly, the positive correlations between total and animal fat and CVD mortality have disappeared or have even become negative with the decline of CVD and CHD mortality in the rich countries and with the inclusion of more data from the eastern European countries where fat consumption is low and CVD frequent (Figure 1). For the same reason, the negative correlation in Figure 1 does not imply that fat food protects against CVD in women; rather that women for unknown reasons more often die from CVD in poor countries where dietary fat is more effectively utilized, inducing a falsely-negative correlation.

It is unlikely that the ecological correlations between animal fat intake and CVD mortality reflect causality because there is no correspondence between their secular trends. In some countries, the increase or decrease were parallel to each other. However, it was more often the case that an increase or decrease of fat consumption either did not influence mortality, or it was followed by a change of mortality in the opposite direction (Table 2). It is obvious, for instance, that the decline of CVD mortality during World War II cannot be explained by a reduction of animal fat because CVD mortality increased again long before the increase of SFA consumption took place. Other factors may explain the wartime decline of CVD mortality, for instance the concurrent decline of body weight and blood pressure [21,22].

In the United States CHD mortality increased approximately ten-fold between 1930 and 1960, levelled off during the 1960s, and has subsequently decreased slowly [108]. During this decline the consumption of animal fat also has decreased. However, total fat consumption increased, and during the 30 years of sharply rising CHD, the consumption of animal fat decreased [108,109]. Similar discrepancies were noted in the United Kingdom [110].

Except in eastern Europe, mortality from CVD and CHD has decreased in most countries for many years. Better treatment may be another explanation than better prevention, because the 40% decrease of CVD mortality seen in Framingham between 1950 and 1970 was followed by a 40% increase in its prevalence [111].

The diet of the human race differs immensely around the world as do our ailments. If diet and disease were unrelated, any combination of them should be found in a population. This is in fact what was found. The low intake of animal fat in a few ethnic groups in the cross-sectional studies cannot explain their lack of atherosclerosis and CVD because other groups such as the Asian Indians and the vegetarian Seventh-Day Adventists also consume little fat but have a relatively high rate of CVD, while others, such as the people on Crete and in western Finland, the Navajo and Seminole Indians, the Masai warriors, some of the Japanese emigrants, not to mention the Punjabi, the most striking example, consume a lot of animal fat but have relatively little CVD.

Furthermore, the studies of the Japanese migrants, the Yemenite Jews, the American Indians, and the Bantu people, cross-sectional studies which have been used most frequently to support the prudent diet were either contradictory, or the findings could be explained in another way.

For decades, the most-cited study in this field is Seven Countries [58]. This study has generated many papers, but in principle nothing new (regarding the diet) has been added to the first observation, that the intake of SFA in 13 cohorts predicted future coronary mortality. This observation has been the main argument for the prudent diet. However, the evidence from Seven Countries is fairly weak. By now, the populations have been followed for 30 years. Nevertheless, Seven Countries remains a cross-sectional study because all the figures on CVD are related to the initial exposure data, the dietary information achieved from small subsamples of the populations at baseline. Seven Countries therefore has the same weaknesses that are connected with other cross-sectional studies. Most importantly, differences in CHD mortality between populations that have such large socioeconomic and cultural differences as in Seven Countries is confounded by large variations in other risk factors for CHD, known or unknown. More attention should be drawn to the great variations in CHD prevalence and incidence between cohorts within the same country that have a similar diet and similar genetic, cultural, and environmental backgrounds such as those in Finland, Greece, and in rural Italy, because such variations carry more weight than variations between populations that vary in almost all other aspects as well.

It should also be noted that no associations were found with the intake of PUFA and that the only cohort study (regarding the diet) based on the populations in Seven Countries, showed that individuals who had not had CHD at follow-up had consumed more SFA than had those who had CHD [79] (Table 4). Furthermore, intake of SFA was unrelated to major ECG abnormalities at entry. This finding

bears a stronger scientific weight, because the number of ECG abnormalities was much larger than the number of CHD events (in six districts, only five or fewer CHD deaths were noted after 5 years). Moreover, the ECG findings seem more reliable as evidence of CHD because all of them were classified in the American coordination center, whereas the clinical diagnosis of CHD was settled by local doctors with varying competence and diagnostic habits.

It may be objected that data from ecological and cross-sectional studies are inappropriate to disprove causality. However, if the diet was important, there should be no major disagreement with international food and vital statistics or with cross-sectional studies, and at least a majority should point in the expected direction. If the intake of animal fat in a district is 19 times higher than in another district of a country, but the CHD mortality, independently of other major risk factors, is only one seventh of that district [51], any possible effect of animal fat must be trivial and cannot justify a worldwide warfare against such products.

Furthermore, there was no support from the cohort or case-control studies either. After adjustment for other risk factors, a difference between the intake of SFA in CHD patients and CHD-free individuals was found in only four of 30 cohorts, and in one of these four the difference went in the wrong direction. No protective effect from an increased intake of PUFA was noted; CHD patients ate significantly more PUFA in three cohorts and no difference was seen in the others. Even more contradictory, no cohort study of atherosclerosis in post-mortems showed any association with dietary SFA or PUFA. These findings were the result of 31 cohort and case-control studies comprising the incredible number of more than 150,000 individuals. The lack of association was not due to individual differences being too small, as has been argued in the past. In the studies where the range of intake was reported, these varied with a factor of five up to a factor of ten between the lowest and the highest intakes.

It is often claimed that vegetarians are protected against CHD. However, vegetarians and other idealistic groups have other habits that are beneficial to the heart. As shown by the Seventh-Day Adventists study [47], a reduced fat intake is not the most important factor because non-vegetarian and lacto-ovo-vegetarian female adventists had a much lower CHD mortality than had pure vegetarians.

As the effect of dietary SFA on CVD is thought to be an enhancement of atheroma growth, the intake of SFA should be more strongly associated with atherosclerosis than with CVD. However, most studies showed no or even an inverse relationship. Moreover, atherosclerosis in the Geographic Study [57] should have been more closely associated with the intake of animal fat than with the intake of total fat, but there was no association with animal fat at all. The correlation with total fat was most likely due to a falsely-high intake in the rich countries, or to selection bias, because no specific pattern was seen when fat intake and degree of atherosclerosis were compared in seven cross-sectional studies of populations not included in the Geographic Study [25–27,34,38,49,52]; and no correlation, or a negative one, was seen between individual fat intake and atherosclerosis in autopsies [89,90,92]. It should also be noted that in the only trial which included a post-mortem evaluation of the vessels, aortic atherosclerosis was most pronounced in the treatment group [102].

The crucial test for causality is the randomized, controlled, clinical trial. In view of the conflicting results from the epidemiological studies, it was no surprise that the outcome was unchanged after dietary fat reduction in almost all trials, even in trials where dietary fat was lowered much more than recommended by any national health committee. Admittedly, the number of CHD deaths was a little lower in the treatment groups, but as the total number of deaths was identical in both groups and considering that most of the trials were open or single-blind, the aforementioned difference was most probably due to diagnostic error. In any case, the difference was far from statistically significant.

A recent trial, which included the addition of alfa-linolenic acid to the diet in the treatment group, was successful [107]. The result is interesting and should be tested by others, but it is not easily explained because the serum cholesterol was not affected by the diet.

The results presented here may surprise many readers. This is understandable since many reviews written by consensus committees and other expert groups have concentrated on the supportive or the allegedly supportive findings. Instead of exploring the numerous contradictory studies, they have ignored or misquoted them [112]. Obviously, readers may suspect me for having ignored supportive findings. The present review is far from complete. I have excluded many studies because of incompleteness or inferior quality and as the literature on diet and cardiovascular diseases is enormous, I may also have overlooked relevant papers. However, the reviews and papers written by those who have most eagerly argued for dietary changes, have been read with extra care. I am therefore confident that I have not ignored any major supportive study because such a study would with all certainty have been mentioned in these papers. And even if I had done, not even a dozen supportive epidemiologic studies can counterbalance the numerous contradictions.

CONCLUSIONS

Many of the contradictory studies mentioned above are open to criticism. Information about people's diet may be unreliable and even if correct it may not reflect past or future intake; diagnoses on death certificates are highly inaccurate; the classification of CHD and CVD varies with time and between countries; incidence and prevalence data are imprecise, especially in small population groups and in poor countries. As many of the data had been adjusted for sex and age alone, the imbalance of other risk factors may have

confounded the results. It may seem unjustified to refute the diet-heart idea with the aid of such studies. The point is that the few supportive studies were just as imperfect, if not more so, compared to the numerous unsupportive ones. It is elementary that a study which supports one's theory cannot be taken as a proof when a large majority of other studies of a similar nature and quality show the opposite. In this case, one cross-sectional study, three cohort studies, and one trial were unequivocally supportive, whereas all studies of the secular trends, more than 50 cross-sectional and cohort studies, and eight trials were contradictory.

A good theory makes a number of predictions that may be falsified by observation; if the observations disagree with the theory,it should be modified or abandoned. Few observations agree with the diet-heart idea, but a large number have falsified it most effectively. Man's diet possibly includes factors of importance to the vessels or the heart, but there is little evidence that SFA as a group are harmful or that PUFA as a group are beneficial.

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