Lifestyles, Major Risk Factors, Proof and Public Policy

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SUMMARY In this report major risk factors in coronary heart disease (CHD) are reviewed, with particular emphasis on the role of nutrition. International and national epidemiologic data indicate that reducing or eliminating certain risk factors (e.g., a diet high in cholesterol and saturated fats) may reduce the risk of premature CHD. Most trends indicate that many Americans are more concerned about diet for health reasons. Preventive measures for CHD are also discussed.

THIS IS A TIME of anniversaries. The first meeting of the Council on Arteriosclerosis — originally the American Society for the Study of Arteriosclerosis — took place in Chicago 30 years ago.

Next year will mark the 70th anniversary of the first successful production by Ignatowski of experimental atherosclerosis in rabbits, achieved by feeding them meat, milk and lipids.1 and it is 65 years since Anitschkow showed that the lesion resulted from the lipids — i.e., the cholesterol and fat — in the ingested animal products, and from the hypercholesterolemia they induced.1

It is also 20 years since the publication of the first prospective data on coronary risk factors from key U.S. epidemiologic studies — in Albany, Framingham and Los Angeles.2

In 1958, the first statement was disseminated to the public by the National Health Education Committee on the risk factors and their relevance to the massive coronary problem and its control.3 Shortly thereafter, the American Heart Association issued its first statements detailing the risks of cigarette smoking and a diet high in saturated fat and cholesterol.

This look backward is not just sentimental and nostalgic. In the words of Patrick Henry: "I have but one lamp by which my feet are guided, and that is the lamp of experience. I know no way of judging of the future but by the past."4

Anniversaries are proper times for taking stock, especially when feelings of doubt, skepticism, even nihilism are expressed — when such adjectives as "naive," "simplistic," "fragile," "dogmatic," and "premature" are used in describing scientific conclusions and public health recommendations widely accepted for years.

Are the doubting critics right? Have most of us — has the American Heart Association — erred over these years? This presentation explores these questions. The focus here is on the role of nutrition — particularly dietary lipid — in the etiology and pathogenesis of atherosclerotic disease, since this is a key question — allegedly the "most controversial" one.

I will first discuss the international epidemiologic data, beginning with the analyses based on data from the Food and Agriculture Organization (FAO) and the World Health Organization (WHO).

International Epidemiologic Data

Since the first study of this type, published in 1953 by Keys, at least eight additional reports have appeared.5-13 The report of Connor4 in 1961 demonstrated a significant relationship between average daily per capita cholesterol consumption and national coronary heart disease (CHD) mortality rates for middle-aged men.

In fact, all nine studies reported to date — and two additional ones recently completed in our Department — all show statistically significant associations between several dietary constituents and CHD mortality rates. In work with such data, our group — to avoid selection bias — took as its point of departure mortality data for 22 developed countries, published in a special WHO Report on the cardiovascular diseases.12 FAO national food balance data were available for 20 of these countries (table 1). The data show statistically significant correlations between several food groups and CHD mortality rates. Correspondingly, several nutrients — including saturated fat, cholesterol, calories — correlated positively and significantly with CHD mortality rates (table 2). Other variables related to lifestyle also showed significant associations, e.g., cigarette smoking per capita and automobiles per 1,000 population, the latter an index of sedentary lifestyle and of exposure to carbon monoxide (in addition to cigarettes).
These findings, indicating relationships between several aspects of life style and CHD mortality rates, are consistent with the concept of the multifactorial etiology of this disease, and specifically the role of modern living habits in industrialized society in its cause — i.e., "rich" diet, cigarette smoking, sedentary lifestyle.

Clearly, only tentative inferences are possible from such data considered in isolation. The problem is, how to arrive at sound inferences by determining which of the many statistically significant correlations are etiologically significant. The data alone cannot resolve this question. The task is to evaluate these data properly in the light of all other data sets, using well-established guidelines to weigh causative importance.

The following guidelines are based on criteria originally developed for the landmark Report to the Surgeon General on Smoking and Health,\textsuperscript{14} criteria for assessing whether epidemiologic associations are probably significant etiologically. They are:

1. Strength of the association.
2. Graded nature of the association.
3. Temporal sequence, i.e., does the presumed etiologic factor precede the disease?
4. Consistency of the finding, in study after study.
5. Independence of each of the associations.
6. Predictive capacity, i.e., ability based on the findings in one or more sets of populations to predict events in other different populations.

7. Coherence of the findings — in two senses, i.e., consistency of the epidemiological findings with those from other research methods (animal experimental, clinical and pathologic investigation), and coherence in that reasonable pathogenetic mechanisms are known, indicating the pathways whereby the etiologic agents act to produce the disease.

Over 25 years, the many studies using FAO-WHO data have repeatedly yielded results showing the strength of the association between several nutritional variables and CHD mortality rates, its graded nature, temporal sequence and consistency.

The second type of international epidemiologic research has involved comparison of postmortem findings. More than 20 years ago, Kimura analyzed 10,000 autopsy records from Kyushu, Japan, contrasted the rarity of severe coronary atherosclerosis in Japanese men and women aged 35–70 compared to Americans, and related the differences to the marked differences in habitual intake of saturated fat and cholesterol, and the associated marked differences in patterns of cholesterolemia (fig. 1).\textsuperscript{15, 16} Similar reports in the 1950s came from Africa and Latin America.\textsuperscript{17}

The most systematic and comprehensive study of this type has been the International Atherosclerosis Project (IAP).\textsuperscript{18} It quantitated the degree of atherosclerosis of the aorta and coronary arteries at autopsy in over 31,000 persons aged 10–69 who died during 1960–65 in 15 cities and countries — two of them highly industrialized populations (New Orleans and Oslo), the remaining largely non-industrialized, low-income populations of Latin America, Africa and the Far East. Marked differences among populations were recorded in the extent of severe atherosclerosis, both aortic and coronary. High-order significant correlations were noted both between percentage of calories from total dietary fat and occurrence of advanced atherosclerotic lesions, and between population mean level of serum cholesterol and occurrence of advanced atherosclerotic lesions. Data on saturated fat and dietary cholesterol were not reported. Level of animal

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### Table 1. Foodstuffs Per Capita, 1954-65 and Coronary Heart Disease Mortality Rate, Persons Age 35-74, 1971, 20 Country Study

<table>
<thead>
<tr>
<th>Food Group</th>
<th>CHD Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
</tr>
<tr>
<td>Eggs</td>
<td>0.524†</td>
</tr>
<tr>
<td>Dairy products and eggs</td>
<td>0.698‡</td>
</tr>
<tr>
<td>Meat, poultry, fish</td>
<td>0.563†</td>
</tr>
<tr>
<td>Meat, poultry, dairy, eggs</td>
<td>0.714‡</td>
</tr>
<tr>
<td>Meat, poultry, dairy, eggs, fish</td>
<td>0.713‡</td>
</tr>
<tr>
<td>Sugar</td>
<td>0.748‡</td>
</tr>
</tbody>
</table>

*P ≤ 0.05
†P ≤ 0.01
‡P ≤ 0.001

Units are calories/person/day.

The twenty countries include: Australia, Austria, Belgium, Canada, Denmark, Finland, France, German Fed. Rep., Ireland, Israel, Italy, Japan, Netherlands, New Zealand, Norway, Sweden, Switzerland, United Kingdom (England and Wales), United States, Venezuela.

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### Table 2. Nutrients Per Capita, 1954-65 and Coronary Heart Disease Mortality Rate, Persons Age 35-74, 1971, 20 Country Study

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>CHD Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total calories/day</td>
<td>0.635†</td>
</tr>
<tr>
<td>Cholesterol—mg/day</td>
<td>0.655‡</td>
</tr>
<tr>
<td>Total fat—g/day</td>
<td>0.588†</td>
</tr>
<tr>
<td>Saturated fat—g/day</td>
<td>0.676‡</td>
</tr>
<tr>
<td>Protein—g/day</td>
<td>0.674‡</td>
</tr>
</tbody>
</table>

*P ≤ 0.05
†P ≤ 0.01
‡P ≤ 0.001

See footnote, table 1, for list of countries.

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**Figure 1. High grade coronary sclerosis in consecutive autopsies, by age and sex. United States vs Japan.**\textsuperscript{15, 16}
protein consumption was also significantly related to severity of atherosclerosis. The authors of this project commented, "It was not considered etiologically important because of the strong supporting evidence for a primary role of fat, rather than protein, in determining... severity of atherosclerosis, and incidence of CHD."18 Other dietary variables, including sugar consumption and hardness of water, were not significantly related to severity of atherosclerosis.

These findings of the IAP are pertinent in regard to the strength of the association between dietary lipid and the underlying pathologic process, severe atherosclerosis, in regard to the graded nature of the association, and the consistency of the epidemiologic findings with various methods. As to the criterion of coherence, the data from the IAP and other studies on serum cholesterol and atherosclerosis were important steps beyond the FAO-WHO data in terms of mechanism, i.e., a pathogenetic pathway whereby diet operates long-term to produce severe lesions.

As to the third type of international study, comparisons of living population samples in different countries, several such investigations were reported in the decade immediately after World War II.17, 18 They recorded contrasting findings in the non-industrialized and industrialized sectors of the world. Consistently, groups of clinically normal people in the economically less-developed nations, ingesting predominantly vegetarian diets low in cholesterol, lipids and calories, had mean plasma cholesterol-lipid-betalipoprotein levels significantly lower than groups of clinically normal persons in the United States. Moreover, they exhibited a different pattern of change in plasma cholesterol level with age. Figure 2 gives an example of such contrasting patterns of serum cholesterol with age, for populations with markedly different patterns of habitual lipid ingestion, in this case data from industrialized countries.20 Note the much lower levels of mean serum cholesterol for the two Japanese populations at age 15 compared to Americans, Germans and New Zealanders, and the lower levels at all ages thereafter, well into middle age.

Thus, 20 years ago data were extant indicating that habitual diet was inducing a chronic hypercholesterolemia in tens of millions of Americans, contributing decisively to widespread severe atherosclerosis.

The Seven Country Study, carried out by Ancel Keys and his colleagues internationally, is the most comprehensive investigation so far undertaken in living population samples.21-22 This prospective international study of 18 cohorts deals with observations on approximately 12,000 men, originally aged 40-59. Marked differences were found in the prevalence and five-year incidence of CHD among the samples from the seven countries.

Amount and type of lipid habitually eaten — especially saturated fat, and inevitably cholesterol (not measured in the Seven Country Study) — varied markedly (fig. 3).22 Saturated fat intake and five-year CHD incidence rates showed a high-order positive correlation that
was statistically significant. Saturated fat intake and serum cholesterol levels of the populations were significantly correlated. In turn, serum cholesterol levels and CHD rates were significantly correlated.22

Baseline intakes of calories, poly-fat, mono-fat and protein were not related to CHD incidence rates, nor was sugar intake after controlling for saturated fat intake. Blood pressure and cigarette use were related to five-year CHD incidence rates.

In multivariate analyses, Keys and colleagues for the first time assessed the capacity of risk factor findings from an American study to predict CHD rates for European populations.23 With use of multiple logistic coefficients from the Framingham study, including coefficients for serum cholesterol, blood pressure, cigarette smoking, a high-order significant association was found between the five-year predicted and observed rates for the several populations.

In 1976, the first report of ten-year follow-up data from the Seven Country Study was published.24 As at five years, the essential interrelationships among dietary lipid, serum cholesterol and CHD rates remain manifest, at statistically significant levels.

Clearly, this key international living population study has contributed significant data to the association among lipid composition of the diet, serum cholesterol and CHD — in terms of the strength of the association, the graded nature of the association, its temporal sequence, its independence, capacity to predict by applying experience in one country to other populations, and in regard to coherence of the data (particularly the role of dietary lipid composition in influencing serum cholesterol, a key pathogenetic pathway).

A fourth type of international study has dealt with the effects of emigration. In the 1950s, several reports presented data indicating that changes in mode of life — particularly the shift to a “richer” diet as a result of emigration from less affluent parts of the world to a more affluent “Western” country — were associated with higher levels of serum cholesterol and higher CHD incidence and mortality rates — e.g., Yemenite Jews in Israel, compared to Ashkenazi and Sephardic Jews there; Neapolitans in Naples and Boston; Japanese compared to Japanese-Americans.17

Recently, findings have been forthcoming from the most comprehensive study of this kind, initiated in 1965 in middle-aged men of Japanese ancestry living in Hiroshima and Nagasaki, Japan; in Honolulu, Hawaii; and in the San Francisco Bay Area (the Ni-Hon-San Study). Nutritional studies at baseline showed striking differences between the Japanese and the two Japanese-American population samples.24-26 Mean intakes of total fat, saturated fat, cholesterol, unsaturated fat, total protein and animal protein and simple carbohydrate were lower in the Japanese than Japanese-American men. Mean relative weight and skinfold thickness of the Japanese were considerably less than those of the Japanese-Americans. Corresponding to these differences in nutritional patterns, mean serum cholesterol level of the Japanese men was 17% lower than for the Hawaiian men, and 21% lower than for the California men.

Clearly, these data lend further powerful support to the concept that diet plays a key role in the long-term determination of population serum cholesterol patterns.

The Ni-Hon-San Study has also reported substantially lower CHD prevalence, incidence and mortality rates for Japanese men compared to Japanese-Americans.27-30 The lower incidence rate in the Japanese compared to the Japanese-American men was decisively due to their lower mean serum cholesterol level and lower mean prevalence rate of hypercholesterolemia.30 Multivariate analysis further revealed that the relationship between serum cholesterol and risk was independent of other risk factors, with blood pressure also contributing significantly to risk in both populations.

**National Studies**

As to intra-national studies, particularly in the United States: Given the pervasive impact of norms of lifestyle on Americans, it is not surprising that studies
of adult samples have generally yielded similar mean serum cholesterol levels, reflecting similar group mean patterns of diet across the country.17, 31-33 Thus, in order to test whether within the U.S. population, differences in habitual diet pattern are associated with differences in group mean serum cholesterol and CHD incidence, special population groups have been identified for study, e.g., vegetarians. In 1954, Hardinge and Stare reported nutritional and serum cholesterol findings on groups of lacto-ovo-vegetarians and pure vegetarians, compared to groups eating the usual omnivorous American diet.24 The differences in serum cholesterol were sizable and clearcut — levels 15% lower for the lacto-ovo-vegetarians compared to the omnivores, and 29% lower for the pure vegetarians compared to the omnivores. These data demonstrated the capacity of Americans to have sizably lower serum cholesterol levels when ingesting diets lower in animal lipid than more usual American diets.

Recently, another set of data of this kind has become available from a study comparing residents of a Boston commune (where a so-called macrobiotic diet was eaten) and age-matched people from Framingham, ingesting usual American fare. The macrobiotic diet, relying principally on whole grains, beans and fresh vegetables as staples, resembled a Japanese diet. Compared to the group of controls, mean serum total cholesterol, low density lipoprotein (LDL) cholesterol and very low density lipoprotein (VLDL) cholesterol of the vegetarians were markedly and significantly lower (table 3).25 These large differences — ranging from 31-38% — could not be accounted for by the lower weights of the vegetarians.

An additional comparison has recently become available, with data on mortality, for three groups of California Seventh Day Adventists (non-vegetarian, lacto-ovo-vegetarian and pure vegetarian), compared to the general California population. Seventh Day Adventists have lower mean serum cholesterol levels than Americans generally.26 For 47,000 Seventh Day Adventist men age 35 and over, age-sex-standardized mortality rates were 34% lower for the non-vegetarians, 57% lower for the lacto-ovo-vegetarians, and 77% lower for the pure vegetarians compared to the general population.27 Seventh Day Adventists differ from the general population in other respects as well, e.g., abstinence from both alcohol and tobacco. It is reasonable to infer that the superior prognosis of the Seventh Day Adventist population for CHD is a result of multiple differences in lifestyle, including the differences in dietary lipid composition and diet-dependent differences in serum cholesterol levels.

Group vs Individual Measurement: A Paradox

Clearly, international and intra-national studies demonstrate a powerful relationship between habitual diet lipid composition and serum cholesterol in populations. This relationship is confirmed by intervention studies — demonstrating that change in lipid composition of the diet of groups yields change in mean serum cholesterol levels.17, 31, 38-46 Extensive animal-experimental work in several species, including non-human primates, is also confirmatory.17, 19, 31, 38, 46 Hence it has been a paradox that data from several U.S. epidemiologic studies yield only low-order or no correlations when the unit of measurement is the individual, i.e., when a test is made of the relationship between dietary lipid and serum cholesterol of individuals.31, 46-49

Dr. Kiang Liu40, 51 has set forth a set of factors which underlies this apparent paradox. One key factor is that in practically all studies on the relationship between dietary lipids and serum cholesterol of individuals, too few measurements have been made per person for accurate estimation of the true means of individuals. This is particularly a problem since intra-individual variation in dietary lipid intake of Americans is considerably greater than inter-individual variation. For example — given this problem — nine days of food records are needed to estimate the correlation between dietary lipid intake and serum cholesterol with reasonable precision, and to avoid marked underestimation due to intra-individual variability.

Failure to meet such requirements has been a key factor in the poor reported correlations between dietary lipid and serum cholesterol of individuals within the U.S. population. As comparisons of populations eating differently clearly indicate, and as nutritional experiments in man and animals confirm, dietary lipid is indeed an important factor influencing serum cholesterol levels.

One interesting aspect of human biology is that with the ingestion of more or less similar diets habitually, people differ widely in their serum cholesterol levels. It

| Table 3. Serum Cholesterol and Lipoprotein Levels in "Macrobiotic" Vegetarians and Controls in Boston |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Group                                           | Serum Cholesterol—mg/dl | 
|                                                 | Total           | LDL VLDL HDL   | Weight (kg)     |
| 115 Controls                                    | 184 ± 37        | 118 ± 34        | 17.2 ± 11.0     | 49 ± 12         | 73 ± 15         |
| 115 Vegetarians                                 | 126 ± 30        | 73 ± 24         | 11.8 ± 7.0      | 43 ± 11         | 58 ± 9          |
| Mean Difference                                 | 58 ± 48†        | 45 ± 44‡        | 5.4 ± 13.3‡     | 6 ± 15‡         | 15 ± 16‡        |
| % Difference                                    | -31.5%          | -38.1%          | -31.4%          | -12.2%          | -20.5%          |
| Mean Difference ∆                              | 55 ± 53‡        | 39 ± 46‡        | 4.6 ± 14.4*     | 9 ± 17†         | 0 ± 9           |

*P < 0.05  †P < 0.01  ‡P < 0.001  
Parallel matched pairs—N = 42. 
Abbreviations: LDL = low density lipoproteins; VLDL = very low density lipoproteins; HDL = high density lipoproteins.
therefore is possible to order people by serum cholesterol level and relate that variable to subsequent risk of developing atherosclerotic disease. Figure 4 displays representative findings of this kind from the national cooperative Pooling Project.39 62 In terms of the criteria of strength of the relationship, its graded nature and its temporal sequence, these data are clear.

This relationship is explored further in table 4 (from the Final Report of the Pooling Project), based on a unifactor logistic regression analysis.33 53 This set of data gives relative risks, i.e., the ratio of risk for men with higher serum cholesterol levels compared to those with lower levels. It also gives absolute excess risks, i.e., the difference in risk between those with higher levels compared to those with lower levels. It also estimates attributable risk in the population, the number of excess CHD cases attributable to hypercholesterolemia of varying degrees, i.e., number of cases that would have occurred if the entire population had levels of serum cholesterol like those of the two lowest quintiles. Of the 168 cases attributable to hypercholesterolemia, 74 — almost half — were due to "moderate" elevations of serum cholesterol in the range about 220–270 mg/dl. Thus, any tendency to focus exclusively on the clearly definable monogenetic

![Figure 4. National cooperative Pooling Project: serum cholesterol level at entry and ten-year age adjusted rates per 1,000 men for any major coronary event, which includes nonfatal M1, fatal M1 or sudden death due to CHD: U.S. white males age 30–59 at entry; all rates age-adjusted by ten-year age groups to the U.S. white male population.](http://circ.ahajournals.org/)

**TABLE 4. 8.6 Year Risk from Elevated Serum Cholesterol, Pooling Project, 5-Pool, 6,983 White Men Ages 40-59 at Entry, Data from Final Report, Age-Specific Univariate Logistic Analyses**

<table>
<thead>
<tr>
<th>Serum Cholesterol at Entry</th>
<th>Range (mg/dl)*</th>
<th>No. Men</th>
<th>First Major Coronary Events</th>
<th>No. Events</th>
<th>Unadj. &amp; Adj. Rate/1,000†</th>
<th>Relative Risk‡</th>
<th>Absolute Excess Risk per 1,000§</th>
<th>Excess Cases Attributable to Elevated Serum Cholesterol¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q-I + Q-II</td>
<td>86–222</td>
<td>2,794</td>
<td></td>
<td>182</td>
<td>65.2 (73.1)</td>
<td>1.00</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Q-I</td>
<td>86–199</td>
<td>1,397</td>
<td></td>
<td>96</td>
<td>68.7 (74.1)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Q-II</td>
<td>194–222</td>
<td>1,397</td>
<td></td>
<td>86</td>
<td>61.6 (72.3)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Q-III</td>
<td>218–243</td>
<td>1,397</td>
<td></td>
<td>108</td>
<td>77.3 (84.4)</td>
<td>1.15</td>
<td>11.3</td>
<td>16 9.5%</td>
</tr>
<tr>
<td>Q-IV</td>
<td>241–274</td>
<td>1,397</td>
<td></td>
<td>156</td>
<td>111.7 (114.5)</td>
<td>1.57</td>
<td>41.4</td>
<td>38 34.5%</td>
</tr>
<tr>
<td>Q-V</td>
<td>269–589</td>
<td>1,395</td>
<td></td>
<td>188</td>
<td>134.6 (140.1)</td>
<td>1.92</td>
<td>67.0</td>
<td>94 56.0%</td>
</tr>
<tr>
<td>All</td>
<td>86–589</td>
<td>6,938</td>
<td></td>
<td>634</td>
<td>90.8 (97.1)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

All Excess Events × 100 = 168/678 = 24.8%

The age-specific serum cholesterol ranges for the 5 age-specific quintiles:

<table>
<thead>
<tr>
<th>Serum Cholesterol Range—mg/dl</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–44</td>
<td>86–194</td>
</tr>
<tr>
<td>45–49</td>
<td>194–218</td>
</tr>
<tr>
<td>50–54</td>
<td>218–239</td>
</tr>
<tr>
<td>55–59</td>
<td>241–270</td>
</tr>
<tr>
<td>60–69</td>
<td>270–524</td>
</tr>
</tbody>
</table>

The overlap in the age-specific ranges is due to the fact that values of a given level (e.g., serum cholesterol 184 mg/dl, age group 40–44) were present in numbers exceeding the quintile count, and were therefore assigned randomly to the lower and higher quintile.

The overlap in the quintile levels for the overall age 40–59 cohort reflects the small differences in quintile cut points for the age-specific strata.

†Relative risk is the ratio of the age-adjusted rates for men in the specified quintile compared to the age-adjusted rate for Q-I + Q-II.

‡Absolute excess risk per 1,000 is the difference between the age-adjusted rate for the specified quintile and the rate for Q-I + Q-II.

§Based on the estimated (expected) number of men in the specified quintile who would have experienced a major coronary event if the rate for this quintile had been the age-adjusted rate for Q-I + Q-II (73.1 per 1,000 per 8.6 years), rather than the observed age-adjusted rate.

¶Adjusted rate per 1,000; mean of age-specific rates for age groups 40-44, 45-49, 50-54, 55-59 (see tables 22A-22D, Pooling Project Final Report).

Number of excess events.

Percent of all excess events.
TABLE 5. Serum Cholesterol and 10-Year Risk of Myocardial Infarction and Coronary Heart Disease Death, Univariate Analysis—Pooling Project Men 40-54

<table>
<thead>
<tr>
<th>Study</th>
<th>Coefficient</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albany</td>
<td>0.008</td>
<td>4.53</td>
</tr>
<tr>
<td>Chicago Gas Co</td>
<td>0.006</td>
<td>2.60</td>
</tr>
<tr>
<td>Chicago W Elec Co</td>
<td>0.006</td>
<td>4.03</td>
</tr>
<tr>
<td>Framingham</td>
<td>0.008</td>
<td>3.03</td>
</tr>
<tr>
<td>Tecumseh</td>
<td>0.019</td>
<td>4.75</td>
</tr>
</tbody>
</table>

From Table 16, Sec. 31, Framingham Reports.

abnormalities (e.g., primary familial hyperbetalipoproteinemia, occurring about once in every 500 live births), or on the 2.5% represented by the two standard deviation cut-off, or on the 95th percentile, clearly means neglect of the mass problem of hypercholesterolemia and the associated mass problem of CHD attributable to it.

**Serum Cholesterol and CHD Risk**

This significant relationship between serum cholesterol and CHD risk prevailed in the Pooling Project for the 30-54 age group, but not for the 55-59 group. The recent report in the *Journal of the American Medical Association* from the Framingham study has clarified this anomaly: When the analysis was taken beyond total serum cholesterol, to evaluate the contribution of LDL, VLDL and high density lipoprotein (HDL) cholesterol separately, it became clear that LDL cholesterol was significantly and independently related to risk for both men and women at least into the seventh and eighth decades of life. The data also indicate that HDL cholesterol was inversely related to risk, a finding that in no way invalidates the extensive evidence on the critical role of LDL in human atherogenesis, and the significant relationship of LDL level to risk for both younger and older persons, male and female.

The relationship of serum total cholesterol to risk has been consistently shown in study after study. Table 5 presents representative data on this matter for the five cohorts of the Pooling Project individually. In these univariate logistic analyses, any t value of 2.0 or greater is statistically significant. Clearly, for each of these studies — as for many others — serum cholesterol is related to risk.

When the relationship of serum cholesterol to risk is considered while controlling simultaneously for blood pressure and cigarette smoking status (table 6), it is shown consistently to be an independent significant relationship. Table 6 further documents that both blood pressure and cigarette smoking also relate consistently and independently to risk. As to these other two major risk factors, their measurement in teenagers, the middle-aged and the elderly has shown them to be significantly and independently related to CHD risk in populations with the nutritional-metabolic prerequisites for atherosclerotic disease.

With the multiple logistic regression model it is possible to classify individuals simultaneously by their status with respect to these three major risk factors, and to order them from low to high into expected quintiles of CHD risk. Briefly, relative risk was over five times higher for men of the fifth quintile compared to men of the first (table 7). The age-adjusted rate for men of the first quintile was only 34/1,000 in almost ten years, i.e., a rate similar to that of the Japanese in Japan. Absolute excess risk ranged up to 147/1,000 for men of the fifth quintile. If the rate for the first quintile is regarded as the standard, then altogether there were 426 excess cases attributable to sub-optimal status with respect to these three major risk factors. These 426 excess cases represented almost two-thirds of all cases — a measure of the potential for prevention of premature CHD in the United States.

In the last several years, a number of studies have reported on predictive capacity when one such data set on a group of Americans is applied to another U.S. population. Figure 5, from the work of Keys and colleagues, is representative of the results of such analyses. In this case, coefficients from the northwest railroad study were applied to predict risk for men from four other Pooling Project studies, the men were ordered into deciles of predicted risk, and the observed and predicted rates were compared. There was good agreement.

The final criterion for assessing the etiologic significance of epidemiologically demonstrated associations is the criterion of coherence. In its first sense, are the epidemiologic data consistent with findings from other research methods? A few examples: Of critical importance are the metabolic ward studies, demonstrating the effects of dietary lipid composition on serum cholesterol levels — 63 experiments by Keys, Anderson and Grande; 36 by Hegsted and colleagues; several by Mattson et al.; by Ahrens et al., and by many colleagues. Table 8 illustrates one of these from Connor et al., showing with use of diets of mixed ordinary foodstuffs that dietary cholesterol from eggs and beef significantly influences serum cholesterol, irrespective of neutral fat composition of the diet. The effect is significant and consistent with findings from the epidemiologic studies, i.e., these data meet this aspect of the criterion of coherence.

Table 6. Major Risk Factors and 10-Year Myocardial Infarction and Coronary Heart Disease Death, Multiple Logistic Analysis—Pooling Project Men 40-54

<table>
<thead>
<tr>
<th>Study</th>
<th>Serum Cholesterol</th>
<th>Diastolic BP</th>
<th>Cigarette Use</th>
<th>t Value for Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albany</td>
<td>4.16</td>
<td>3.41</td>
<td>4.51</td>
<td></td>
</tr>
<tr>
<td>Chicago Gas Co</td>
<td>2.06</td>
<td>3.56</td>
<td>4.98</td>
<td></td>
</tr>
<tr>
<td>Chicago W Elec Co</td>
<td>3.56</td>
<td>3.15</td>
<td>2.97</td>
<td></td>
</tr>
<tr>
<td>Framingham</td>
<td>3.22</td>
<td>3.30</td>
<td>3.19</td>
<td></td>
</tr>
<tr>
<td>Tecumseh</td>
<td>4.67</td>
<td>3.23</td>
<td>2.62</td>
<td></td>
</tr>
</tbody>
</table>

From Table 20, Sec. 31, Framingham Reports.
Table 7. 8.6 Year Risk from Three Major Risk Factors (Sodium Cholesterol, Diastolic Blood Pressure, Cigarette Smoking), Pooling Project, 5-Pool, 6,875 White Men Ages 40-59 at Entry, Data from Final Report, Age-Specific Multivariate Logistic Analyses

<table>
<thead>
<tr>
<th>Quintile of Risk, Based on Entry Values for 3 Factors</th>
<th>First Major Coronary Events</th>
<th>Relative Risk*</th>
<th>Excess Risk per 1,000†</th>
<th>Excess Cases Attributable to the Three Major Risk Factors‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Men</td>
<td>No. Events</td>
<td>Unadj. &amp; Adj. Rate/1,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q-I</td>
<td>1,375</td>
<td>42</td>
<td>30.5 (34.2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Q-II</td>
<td>1,375</td>
<td>72</td>
<td>52.4 (58.3)</td>
<td>1.70</td>
</tr>
<tr>
<td>Q-III</td>
<td>1,375</td>
<td>109</td>
<td>79.3 (79.3)</td>
<td>2.32</td>
</tr>
<tr>
<td>Q-IV</td>
<td>1,375</td>
<td>160</td>
<td>116.4 (127.9)</td>
<td>3.74</td>
</tr>
<tr>
<td>Q-V</td>
<td>1,375</td>
<td>238</td>
<td>173.1 (180.9)</td>
<td>5.29</td>
</tr>
<tr>
<td>All</td>
<td>6,875</td>
<td>621</td>
<td>90.3 (96.3)</td>
<td>-</td>
</tr>
</tbody>
</table>

All Excess Events $\times 100 = 426$
All Expected Events $\times \frac{662}{62} = 64.4\%$

*Relative risk is the ratio of the age-adjusted rates for men in the specified quintile compared to the age-adjusted rate for Q-I.
†Absolute excess risk/1,000 is the difference between the age-adjusted rate for the specified quintile and the age-adjusted rate (34.2/1,000) for Q-I.
‡Based on the estimated (expected) number of men in the specified quintile who would have experienced a major coronary event if the rate for the quintile had been the age-adjusted rate for Q-I (34.2/1,000/8.6 years), rather than the observed age-adjusted rate. Number and percent of all excess events shown, respectively.
§Adjusted rate/1,000; mean of age-specific rates for age groups 40-44, 45-49, 50-54, 55-59 (see tables 37A-37D, Pooling Project Final Report).

Animal-Experimental Findings

As to the vast array of animal-experimental findings, only one major development of recent years is noted: the extensive research on diet-induced atherosclerosis in non-human primates. Among the many important studies, Wissler and colleagues noted the ability to induce atherosclerosis in rhesus monkeys by feeding usual American diets.\(^{59}\) When a “prudent” diet lower in saturated fat, cholesterol and calories was fed, hypercholesterolemia and atherogenesis were much less marked.

All levels of severity of the atherosclerotic lesion can be reproduced in experimental animals, including non-human primates. In cholesterol-fat-fed monkeys, peripheral gangrene and massive myocardial infarction have occurred.\(^{46,60}\)

The interplay among dietary lipid, diet-induced hypercholesterolemia and other factors has also been shown in primates, e.g., the work of Ruth Pick on the aggravating effects of hypertension in cholesterol-fat-fed monkeys, and the benefits of discontinuation of the atherogenic diet for the hypertensive animal.\(^{61}\)

Regression of lesions has also been repeatedly demonstrated in monkeys — by Armstrong, Connor and colleagues, by Wissler and Vessilinovitch and others.\(^{38,60,62,63}\)

Life Styles and Risk Factors:
Their Etiologic Significance

As to the other aspects of coherence, reasonable pathogenic mechanisms, recent work has further elucidated mechanisms whereby the major lifestyle and risk factor traits operate at the arterial wall cellular and subcellular level to induce the severe lesions necessary for clinical atherosclerotic disease.

From the evidence summarized here, there is every reason to conclude — based on all seven criteria set forth — that the epidemiological associations between the major lifestyle and risk factor traits, first and foremost diet high in cholesterol and saturated fat, are etiologically significant. In the multifactorial causation of this disease, all four traits are operative — diet high in cholesterol and saturated fat, diet-dependent hypercholesterolemia, hypertension and cigarette smoking. Since the data from both animal and human studies — e.g., the Japanese experience\(^{12,15,17,20,22,24-30}\) — indicate that high blood...
pressure and cigarette smoking are minimally significant for atherogenesis in the absence of the nutritional-metabolic prerequisites, it is further reasonable and sound to designate "rich" diet as a primary, essential, necessary cause of the current epidemic of premature atherosclerotic disease raging in the western industrialized countries. Cigarette smoking and hypertension are important secondary or complementary causes.

In any sound formulation of this general conclusion, it is further important to note that the chain of causation from dietary lipid composition to serum cholesterol to atherosclerosis is not the sole nutritional pathway. In terms of diet composition, factors in addition to dietary cholesterol and saturated fat contribute to atherosclerosis. Thus, habitual high salt intake apparently serves to set the stage for hypertension in the genetically susceptible. High alcohol intake probably has a similar influence. Low intake of complex carbohydrates, particularly pectins, may also have a negative influence by contributing indirectly to hypercholesterolemia. And imbalance between energy consumption and expenditure resulting in obesity also contributes to risk, both by increasing proneness to hypertension and hypercholesterolemia, and as an independent risk factor, at least for persons during young adulthood and early middle age.

While these conclusions with respect to causation do indeed rest on an extensive foundation of fact, nonetheless it would be good to have data from direct controlled experiments on man to support them further. What, then, is the status of studies of this type? For optimal understanding, it is appropriate to set down the hypotheses that might theoretically be tested: The "ideal" experiment would be a direct test of etiology, i.e., an induction experiment. Joseph Goldberger tested his inference about pellagra as a deficiency disease by exposing volunteer prisoners to the diet of the "3 Ms" to produce the disease. (This protocol would not pass a Human Experimentation Committee today.)

Such a direct test of the role of "rich" diet in the etiology of atherosclerotic disease would involve randomizing hundreds of thousands of newly-weaned infants to two groups, one to subsist for decades on a diet high in cholesterol and saturated fat, the other on a diet low in these constituents, e.g., a Mediterranean or Far Eastern diet — with all other aspects of life style held constant for the two groups. The endpoint would be incidence and mortality from atherosclerotic disease in the two groups over the several decades necessary for definitive assessment. Clearly, this direct test of etiology is not feasible, either practically or ethically. Therefore, actual trials — undertaken or proposed — test hypotheses in the area of disease prevention, rather than disease induction. For example, in the years from 1959–1971 many of us worked hard to bring a large-scale single-factor diet-heart primary prevention trial into being. After completion of the National Diet-Heart Feasibility Study, and years of discussion, the NHLI Task Force on Atherosclerosis in 1970–71 recommended that it not be undertaken. And in fact no effort of this kind is in progress in this or any other country, nor is there any sign that any such effort will be mounted in the foreseeable future.

Instead, the Task Force recommended — and the NHLBI implemented — a multifactorial intervention trial, the Multiple Risk Factor Intervention Trial (MRFIT).44-46 Here a clear understanding of what is and what is not being tested is crucial: After decades of exposure to environmental and physiological factors associated with proneness to atherosclerotic disease, is it possible to reduce its incidence and mortality in men in the upper 10% of risk by multifactorial lifestyle and drug intervention to lower serum cholesterol, blood pressure and cigarette smoking (drug intervention solely for control of hypertension)? This is the "primary" prevention hypothesis being tested by MRFIT. It is far removed from a direct test of the etiologic question, i.e., the induction trial beginning in infancy. Should its result be positive, it will have great practical significance as a direct demonstration of ability to influence the course of the disease even when the individuals are very high risk and the limited intervention efforts are begun only in middle age. Such results would also in a general way confirm the conclusions that lifestyle and risk factors are important in producing the disease. However, it will be difficult to separate the contributions of each of the three interventions to disease prevention. Hence, a positive result will make only a limited contribution to the further elucidation of disease etiology; and a negative outcome will not represent a decisive test of the role of lifestyle in general, and "rich" diet in particular, in the etiology of the disease, since it is entirely possible that such a result would be a consequence of "too little and too late." To make this clear is in no sense to
denigrate this major undertaking, since it is indeed very valuable and important.

A similar analysis can be made with studies currently in progress here and abroad using unifactor drug intervention to control risk factors, e.g., antihyperlipidemic or antihypertensive drugs; but any extrapolation of negative results from a drug trial to the diet issue is scientifically invalid.

The “First Generation” Diet Trials

With this brief review of the issues involved in the randomized controlled trials, let us summarize the findings of the four “first generation” diet trials begun in the 1950s. All of these studies, undertaken with limited resources, dealt “only” with hundreds of participants, rather than the thousands — or more properly the tens of thousands — needed for an adequate sample size to assess the primary prevention potential. Two of them, carried out with free-living men in Chicago and New York, demonstrated an ability to recruit large numbers of such persons into such studies, to keep them active and to influence dietary habits and serum cholesterol levels to a significant degree over months and years. Thus, they clarified important matters that were totally unclear in the late 1950s. However, both their small sample sizes and their lack of randomized control groups precluded their ability to produce a definitive result in terms of the CHD disease endpoint — despite their favorable trends in this regard as well.

The third study of the first generation diet trials, the Finnish mental hospital study, did not produce negative results, as is occasionally misrepresented, at least for the male patients; on the contrary, they were decidedly positive and significantly so with respect to the coronary and cardiovascular endpoints.

Among these early studies, the Los Angeles Veterans Administration domiciliary facility investigation was the only one with a double blind randomized controlled design. It, too, was handicapped by inadequate sample size, as well as by the fact that the median age of its participants was 65.5 years, with a large proportion of the men manifesting atherosclerotic disease at entry, so that it was a mix of a primary and secondary prevention study. The diet in this study, too, was low in saturated and cholesterol, and high in polyunsaturated fat. Thus, it was confounded by whatever problems exist from ingestion of diets high in polyunsaturated fat, an unresolved issue — witness the excess of cholelithiasis in the Los Angeles study. The diet effected and maintained a 12.7% net reduction in serum cholesterol over the more than eight years of the study. Cumulative incidence of “hard” atherosclerotic disease endpoints was significantly less in the men of the experimental group, compared to the controls, particularly for the subgroup free of atherosclerotic disease at entry (fig. 6), and for the men less than age 65 and hypercholesterolemic at entry. However, no significant difference in mortality rates for all causes was recorded between the two groups, due to an excess of accidental and neoplastic deaths in the experimental group, which negated the positive effect on atherosclerotic disease mortality. Thus, this study also failed to yield a definitive and unequivocal answer.

A fifth study, in Minnesota mental hospitals, has presented an oral report indicating a significantly favorable effect on the disease endpoint for men under 40 given a serum cholesterol lowering diet low in saturated fat and cholesterol and high in polyunsaturated fat, compared to a control group eating a usual American diet. However, negative results were reported for older men and for women. The results have not yet been published.

Thus, trials have shown some encouraging results, but not clearcut, consistent and unequivocal ones. And, given the nature of the studies in progress, this problem probably will not be much further along in several years.

Theory from Data

Everyone in the field, therefore, is once again left with the task of arriving at best judgment concerning the etiological issues based on the available data, which clearly do not include unequivocal findings from randomized controlled trials. My positive estimate is based on the stipulated criteria. In relying on these criteria, one other question of scientific methodology must be considered. It has been argued that the total body of “indirect” evidence — epidemiologic, clinical, pathologic animal experimental — permit only the formulation of hypotheses concerning man. Only “direct” experiments, i.e., randomized controlled trials, permit the decisive testing of hypotheses and therefore the arrival at sound scientific conclusions concerning etiology. Based on this approach to the methodology of science, allusions are made, for example, to the diet-heart “hypothesis,” thereby indicating that any concept of the etiologic role of diet in the causation of the disease is completely conjectural and tentative at this time.

**Figure 6. Los Angeles Veterans Administration Domiciliary Study; cumulative incidence for all “hard” end points (definite myocardial infarction, sudden death due to CHD, definite cerebral infarction, ruptured aneurysm, amputation), 590 men free at entry of definite or possible atherosclerotic disease, 1959-1967.**
TABLE 9. Per Capita Annual Consumption U.S.A., 1940-1974

<table>
<thead>
<tr>
<th>Commodity</th>
<th>1940</th>
<th>1950</th>
<th>1974</th>
<th>Percent Change 1940-1974</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eggs—no.</td>
<td>319</td>
<td>389</td>
<td>287</td>
<td>-10.0 -26.2*</td>
</tr>
<tr>
<td>Total milk fat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>solids—lbs</td>
<td>33</td>
<td>29</td>
<td>20</td>
<td>-39.4</td>
</tr>
<tr>
<td>Lard—lbs</td>
<td>14</td>
<td>13</td>
<td>3</td>
<td>-78.6</td>
</tr>
<tr>
<td>Shortening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>margarine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>other edible</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fats and oils—lbs</td>
<td>18</td>
<td>26</td>
<td>50</td>
<td>+177.8</td>
</tr>
<tr>
<td>Poultry—lbs</td>
<td>17</td>
<td>25</td>
<td>51</td>
<td>+200.0</td>
</tr>
<tr>
<td>Beef—lbs</td>
<td>55</td>
<td>63</td>
<td>117</td>
<td>+112.7</td>
</tr>
</tbody>
</table>


This reflects a basic misunderstanding of the methodology of science. Were it to prevail, the entire bodies of knowledge acquired in modern times by geology, astronomy and evolutionary biology would have to be classified as hypothesis rather than theory, since they rest almost exclusively on observational, rather than experimental, data. It would have to be the hypothesis of gravitation, not the theory of gravitation; the hypothesis of relativity, not the theory of relativity; the hypothesis of evolution, not the theory of evolution. In fact, sound methodology throughout the sciences recognizes the ability to arrive at valid conclusions concerning etiological relationships based on proper assessment of observational data.

The terms hypothesis and theory both have precise meanings in the language of science. The Random House unabridged dictionary states “A hypothesis is a conjecture put forth as a possible explanation of certain phenomena or relations, which serves as a basis of argument or experimentation by which to reach the truth”; and “A theory properly is a more or less verified or established explanation accounting for a known fact or phenomenon.”

Given the vast body of consistent information from many research methodologies on the relationship between lifestyle and atherosclerotic disease, particularly diet and atherosclerotic disease, it is inappropriate to use the term hypothesis in speaking about this general area of knowledge.

Conclusions with respect to these matters have profound implications, for medical care and public health — and for public policy. As noted at the beginning of this presentation, over the last two decades repeated statements by expert groups have advised health professionals and the public on life styles and risks factors — and on improving habits of eating, smoking, exercise — for preventing premature CHD.58 66 And the American people have to a degree heard and acted on the recommendations, by reducing intake of total fat, saturated fat and cholesterol, and by partially substituting unsaturated fat, mono and poly, for saturated fat. Overall trend data, available from the U.S. Department of Agriculture, are summarized in table 9.53 71

Trends in Risk Factors

Note the trend for eggs — since 1950, a decline of 26%.

There has also been a 39% decrease in milk fat solids available for consumption, an important source of saturated fat and cholesterol (table 9).53 71

Available lard (pork fat) has gone down sharply, while vegetable fats and oils have gone up almost threefold. The vegetable fats have become softer (less hydrogenated), i.e., soft margarine, liquid shortenings and non-hydrogenated oils low in saturated fats and high in unsaturated fats (table 9).53 71

All of these trends are favorable. They indicate decreased per capita consumption of saturated fat and cholesterol from the indicated sources. But that is not the whole story. Meat available for consumption rose 30% from 1950-1974, up to 188 pounds per person. Beef has accounted for the greatest increase, going from 55 pounds per person in 1940 to 117 pounds in 1974, a rise of 113% (table 9).53 71 And most of this beef is from the feedlots, i.e., from animals markedly fattened before slaughter, so that their flesh is "richly" marbled. A sizable proportion is consumed — either at home or at fast-service restaurants — as hamburger or cheeseburger, high in saturated fats and cholesterol.

The trend from the 1950s to the 1970s is a decline in mean dietary cholesterol available of about 8% and in saturated fat of about 3%, with an increase in polyunsaturated fat of about 49% to about 6% of total calories. Correspondingly, data from several studies indicate that a fall has occurred in mean serum cholesterol levels of adults. Data collected in Chicago, Minneapolis and Tecumseh, and from the MRFIT and Lipid Research Clinics (LRC) mass screening efforts, indicate that for some strata this fall has been significant. Table 10 presents findings of this kind for middle-aged, employed men, from surveys in Chicago in 1958 and 1967-1973. Data from the LRC indicate that the changes are related to social class: the higher the socioeconomic status, the lower the intakes of cholesterol and saturated fat, and the lower the serum cholesterol levels.

In keeping with these findings, about 45% of a random sample of Americans recently told Department of Agriculture surveyors that they have changed their diets for health reasons,72 and 88% told the Gallup Poll they wanted to know more about nutrition.73 Clearly, some progress has been made in improving norms of nutritional practice in the United States, at least in regard to cholesterol and saturated fat intake, but the progress has been limited.

TABLE 10. Serum Cholesterol Levels, 1958 and 1967-1973

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean serum cholesterol—mg/dl</td>
<td>239</td>
<td>248</td>
<td>214</td>
</tr>
<tr>
<td>Prevalence of serum cholesterol 260 or higher</td>
<td>29.2%</td>
<td>36.0%</td>
<td>10.0%</td>
</tr>
<tr>
<td>220 or lower</td>
<td>33.6%</td>
<td>30.5%</td>
<td>58.4%</td>
</tr>
</tbody>
</table>
Given this record of progress in nutrition, and continuing need, a brief comment is necessary on an aspect that has been addressed repeatedly since the first AHA Committee, under Dr. Irvine H. Page in 1961, prepared the first AHA statement on diet and CHD: Are nutritional recommendations for significant reduction in saturated fat and cholesterol intake — as well as avoidance of excessive calories, salt, alcohol — applicable for the whole population, or “only” for high risk people? In fact, the AHA statements since 1961 have repeatedly advised improved nutrition for all Americans, as did the Report of the Inter-Society Commission for Heart Disease Resources and other documents by expert groups. In part, this approach has reflected the fact that nutrition-related excess risk tends to be the norm rather than the exception among Americans, as noted earlier in presenting the unifactor and three-factor data from the Pooling Project. High risk is epidemic here, and rich experience of over a century with epidemic problems shows that a societal approach is necessary for their control, i.e., the one-to-one doctor-patient relationship does not suffice, especially when aspects of mode of life are involved in the chain of causation, and this chain must be broken at one or more links to achieve prevention. Even if one considers only the upper quintile of risk as the segment of the population for a strategic preventive focus, one is speaking of millions of people and — inevitably in any effort to improve eating habits — their families.

The Bureau of the Census reports that families numbered about 55 million in the United States in 1975; one-fifth means 11 million families, constituting over 37 million people. To reach these numbers effectively for purposes of improving nutrition requires sustained skillful use of all the channels of communication — TV, radio, other media, schools and work places, community organizations, the supermarkets, the physicians and other professionals who see these very high risk people and their families as patients. That is, a focus starting solely with the upper 20% at highest risk — if it is to be a serious public health endeavor, one aiming to achieve critical mass in terms of improved nutrition among millions — must “go public.” It must speak to everyone, via the many channels of communication. In that sense, the distinction between an approach to high risk people only vs one to the whole population is a schematic abstraction, without actual meaning in terms of a societal effort in the real world.

Moreover, as noted above in discussing the three-factor data from the Pooling Project, over 50% of excess risk among middle-aged American men is in quintiles 2–4, rather than in the highest quintile (Q-5). Many of these people may be only “mildly” hypercholesterolemic, even “normocholesterolemic” by standards still widely accepted, but they are nonetheless at high risk given their overall pattern of lifestyle and mix of major risk factors, including the pivotal one of “rich” diet. Moreover, as also noted earlier, nutrition-dependent risk is not only a matter of dietary lipid. It also encompasses calorie balance, salt, and alcohol. And all the long-term prospective data indicate that with the norms of human behavior that have been prevalent in the U.S. population — particularly the “rich” diet, almost universal among Americans until recently — no level of serum cholesterol has been found to be risk-free.

It is in the context of all of the foregoing that the clinician must approach the all-too-rare patient with a mean serum cholesterol in adulthood of 180 mg/dl, and advise him about diet. For him too, the data indicate that improved nutrition has meaning. And in terms of the population-at-large, and the strategic public policy approaches, there is no real issue: Either a population-wide sustained effective public health effort for better nutrition, or no real effort and no real progress.

As to the other key aspect of lifestyle, although per capita cigarette use in the U.S. remains the highest in the world, a downward trend has been recorded since the publication in 1964 of the landmark Report to the Surgeon General on Smoking and Health. For all adult men, the prevalence rate has declined about 25%. However, the major unsolved problem is smoking among teenagers, especially the recent precipitous increase among teenage girls.

For adult men and women, the data by socioeconomic strata are similar to those indicated for diet by the LRC findings: The percentage of continuing smokers was lowest among college graduates, highest for the least educated. “Rich” diets and cigarette smoking are becoming social diseases, more widely prevalent among the less educated, i.e., those with less ready access to modern scientific information.

The sharp downturn in per capita consumption of cigarettes in 1967–69 provides a vital lesson (fig. 7). During those years, “equal time” messages were presented on radio and television. With the 1970 Congressional legislation banning cigarette advertising on radio and TV, these messages all but disappeared, as the tobacco industry apparently recognized would happen. Since then cigarette advertising has been switched to magazines, newspapers and billboards, at a cost of about $400 million per year. By comparison, the health educational efforts stemming from the voluntary and official agencies have been modest.

As to the high blood pressure problem, the era of “judicious neglect” and “therapeutic nihilism” ended with the dramatic positive results of the VA randomized controlled trial of antihypertensive medication. While questions remain about the benefit-to-risk ratio of long-term pharmacological treatment of so-called “mild” hypertension, the overall positive results of the VA study properly alerted the health professions and policy-makers to do something about the unsolved public health problem of hypertension.

Efforts of recent years — the work of the National High Blood Pressure Education Program, the AHA, and many other professional and lay organizations — have increased the proportion of hypertensives detected, treated and controlled in the population from about 12% to three or more times that low per-
stroke; 177,400 additional deaths from all causes (table 12). The all causes data are especially encouraging, not only because they are the bottom line, but also because this concordance among the rates strongly supports the conclusion that the decreases in CHD rates are real, not spurious. Moreover, for a period during the late 1950s and early 1960s, all causes mortality rates for young adult and middle-aged American males (white and black) were on the rise. Hence the recent break in the curve is most welcome; and the latest data indicate that the downtrend continued in 1976 and 1977. But despite the recent progress, U.S. rates remain among the highest in the world.

Clearly, several trends have been proceeding in parallel over these years: positive developments in emergency, acute and long-term care for patients with CHD, as well as the progress noted in controlling major risk factors. When such multiple socio-medical trends evolve over the years, it is virtually impossible to make a definitive scientific assessment as to the role of each of them singly, and all of them together in causing the decline in mortality rates. Nevertheless, these declines can be reasonably interpreted as indications of the preventive approaches recommended to the American people repeatedly over the last 20 years, recommendations that have been heeded and acted on to a significant degree by the health professions and the citizenry. Certainly it seems reasonable and sound to recommend — and to strive vigorously to achieve — continuation and expansion of these efforts, and effective resistance to self-serving interests seeking to turn the clock backwards, be they from the tobacco, meat, dairy, egg or other industries.

The Preventive Effort

The preventive effort must go on to achieve much greater critical mass. For this, a much broader societal effort must be mounted. Its main features are spelled out in the American Heart Association Public Policy Reference Paper, in the 1971 Report of the NHLI Task Force on Arteriosclerosis, in the Dietary Goals for the United States recently published by the Senate Select Committee on Nutrition and Human Needs, in the recommendations of the 1970 Inter-Society Commission Report on the Primary Prevention of the Atherosclerotic Diseases. This last report recommends: "... a strategy of primary prevention of premature atherosclerotic diseases ... as long-term national policy for the United States ... to implement this strategy, (commitment of) adequate resources of money and manpower to accomplish:

"Changes in diet to prevent or control hyperlipidemia, obesity, hypertension and diabetes; "Elimination of cigarette smoking; "Pharmacologic control of elevated blood pressure."38

To date, the strategic commitment has not been made, and the necessary bold multifaceted approaches have not been implemented. Despite the opposition of
powerful special interests, a general basis for such advances exists — in the policy statements of key professional, voluntary and semi-official organizations; in the concerns for prevention articulated by Senate and House Committees and by the Department of Health, Education, and Welfare; and in the expressed desires of the American people for effective leadership on these matters.

The post-World War II era has been productive in research on the role of lifestyles — "rich" diet first and foremost — in the etiology of the coronary epidemic. Based on the leadership initiatives of the AHA, it has also been the era witnessing the birth of a positive public policy to apply the research knowledge for the control of this epidemic — and the era witnessing the beginning of success in this effort.

Acknowledgments

It is a pleasure to acknowledge the cooperation of the author's senior colleagues in the long-term investigations presented here: es-

Table 11. Percent Change in Coronary Heart Disease Mortality 1940-1975, Ages 35-74

<table>
<thead>
<tr>
<th>Sex-Race</th>
<th>1940 to 1948</th>
<th>1949 to 1957</th>
<th>1958 to 1967</th>
<th>1968 to 1975</th>
</tr>
</thead>
<tbody>
<tr>
<td>White males</td>
<td>+14.9</td>
<td>+8.0</td>
<td>+2.3</td>
<td>-18.6</td>
</tr>
<tr>
<td>White females</td>
<td>-3.3</td>
<td>+0.5</td>
<td>-7.3</td>
<td>-23.6</td>
</tr>
<tr>
<td>Nonwhite males</td>
<td>+20.6</td>
<td>+18.7</td>
<td>+13.0</td>
<td>-29.2</td>
</tr>
<tr>
<td>Nonwhite females</td>
<td>+15.7</td>
<td>+10.6</td>
<td>+3.8</td>
<td>-34.9</td>
</tr>
</tbody>
</table>

Table 12. Lives Saved in 1975 by Decline in Mortality (1968 vs 1975) Ages 35-74

<table>
<thead>
<tr>
<th>Sex-Race</th>
<th>CHD</th>
<th>Stroke</th>
<th>All Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>White males</td>
<td>44,900</td>
<td>10,100</td>
<td>80,300</td>
</tr>
<tr>
<td>White females</td>
<td>25,300</td>
<td>9,000</td>
<td>51,300</td>
</tr>
<tr>
<td>Nonwhite males</td>
<td>8,200</td>
<td>4,600</td>
<td>22,600</td>
</tr>
<tr>
<td>Nonwhite females</td>
<td>7,900</td>
<td>5,000</td>
<td>23,200</td>
</tr>
<tr>
<td>All</td>
<td>86,300</td>
<td>28,700</td>
<td>177,400</td>
</tr>
</tbody>
</table>
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especially Howard Adler, Ph.D., David M. Berkson, M.D., Patricia Collette, M.A., Alan Dyer, Ph.D., Morton B. Epstein, Ph.D., Yolanda Hall, M.S., Mark H. Lepper, M.D., Howard A. Lindberg, M.D., Harley McKean, Ph.D., Louise Momjian, Ph.D., Dorothy Moss, M.S., Oglesby Paul, M.D., James A. Schoenberger, M.D., Richard B. Shekelle, Ph.D., Rose Stamler, M.A., and also Winston Batambara, M.D., Leonard Braude, M.D., Donald B. Cohen, M.D., Richard Cooper, M.D., George Farah, M.D., Eduardo Farinato, M.D., Jerome Frankel, M.D., Steven Gruijic, M.D., Virginia Jauch, M.S., Louis Kolokoff, M.D., Monte Levinson, M.D., Kiang Liu, Ph.D., Roger Nosal, M.D., C. R. Paynter, M.D., Peter Rhomborg, M.D., Ira T. Whipple, M.S. and Quentin D. Young, M.D. The author is also most grateful to the nurses, nutritionists, programmers, technicians, clerks and secretaries who contributed so well to this research — particularly Mary Blackshear, Roberta Crawford, Nancy Dalton, Helen Dean, Wanda Drake, Celene Epstein, Elizabeth Frazier, Elise Fuente, Dan Gar- side, Fran Hart, Eleanor W. Hicks, Ron Hoeksema, Betty Humbert, Dana King, Annyc Lev, William H. McAttee, Joy Nelson, Frances Petersen, Peggy Powell, Susan Shekelle, Margie Shores, Wesley Sime, Adele Stamler, Elizabeth Stevens, Tom Tokich, Ika Tomaszewsky, June Wallace, Julia Wannamaker, Carol Zehnde, and the entire staffs of the Chicago Health Research Foundation, the Chicago Heart Association Detection Project in Industry and the Heart Disease Control Program, Department of Adult Health and Aging, Chicago Health Department.

It is also a pleasure to express appreciation to the many Chicago organizations giving invaluable cooperation in the cited research efforts, particularly the Chicago Heart Health, Chicago Health Research Foundation, Chicago Heart Association, Peoples Gas Light and Coke Company, Newspaper Division of the Field Enterprises, American Oil Company, Armour and Company, Illinois Bell Telephone Company, Internal Revenue Service, International Harvester Company, Arthur Andersen and Company and the Western Electric Company.

It is also a pleasure to pay tribute to colleagues in the national cooperative Pooling Project: Drs. Henry Blackburn, John Chapman, Roy Dawber, Joseph T. Doyle, Frederick H. Epstein, Professor Felix Moore, Drs. William B. Kannel, Ancel Keys, Oglesby Paul and Henry L. Taylor.


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George Lyman Duff Memorial Lecture. Lifestyles, major risk factors, proof and public policy.
J Stamler

Circulation. 1978;58:3-19
doi: 10.1161/01.CIR.58.1.3
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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