AHA Medical/Scientific Statement

Special Report

Rationale of the Diet-Heart Statement of the American Heart Association

Report of the Nutrition Committee

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A fundamental goal of the American Heart Association is to prevent and reduce the incidence of cardiovascular disease. Of long-standing concern to the AHA has been whether diet is a substantial factor in the genesis of atherosclerosis and, if so, how the American diet can be modified to reduce or delay the onset of atherosclerotic complications. Two of the major functions of the AHA's Nutrition Committee have been to integrate the continuously emerging scientific evidence on the relation between diet and cardiovascular disease and to regularly update recommendations based on that evidence.

Evolution of AHA Diet Statements

In 1957 a group chaired by Dr. Irvine H. Page prepared a report that summarized the evidence on the relation between diet and atherosclerosis.[1] A review of the data led that group to conclude that (1) diet is important in the pathogenesis of atherosclerosis, (2) the fat and total caloric content of the diet are the dominant contributing factors, and (3) the type of fat, or the balance between saturated and certain unsaturated fats, may also be important. In 1961 an updated report was prepared on the possible relation of dietary fat to heart attacks and strokes.[2] This report recommended that (1) overweight persons should decrease their caloric intake and attempt to achieve desirable body weight; (2) weight reduction should be facilitated by regular, moderate exercise; (3) the diet should be altered by reducing intake of total fats, saturated fats, and cholesterol and by increasing intake of polyunsaturated fats; (4) particular attention should be given to dietary alteration by men at increased risk for coronary heart disease (CHD) (eg, those with a previous atherosclerotic event, a strong family history of CHD, elevated plasma cholesterol, or hypertension); and (5) dietary changes for those at high risk should be medically supervised.

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The 1968 AHA diet statement provided more precise information about desirable intakes of different nutrients.[3] The desirable intake of fat for the general population was set at 30% to 35% of total calories, of which one third was to be saturated, one third monounsaturated, and one third polyunsaturated fatty acids. A reduction of cholesterol intake to less than 300 mg/day was also recommended. In subsequent statements the AHA recommended that the intake of saturated fatty acids, the major dietary influence on serum cholesterol levels, be decreased to less than 10% of total calories, that polyunsaturated fatty acids supply up to 10% of total calories, and that the remainder of the ingested fat be monounsaturated fatty acids.[4,5] Relatively low sodium intake was suggested because of evidence that excessive sodium intake may raise blood pressure in many people. The AHA later recommended that caloric intake from fats be reduced to less than 30%. The AHA continued to recommend a reduction of saturated fat intake to less than 10% of total calories and that polyunsaturated or monounsaturated fatty acids or carbohydrates be substituted for saturated fatty acids.[6] Quantitative upper limits were made for sodium intake (not to exceed 3 g/d) and for ethanol consumption (not to exceed 1 to 2 oz/d).[7,8]

Since the original recommendations were published, average fat consumption in the United States has fallen from 40% to 42% of calories in the 1960s to approximately 36% to 37% of calories, largely because of a substantial reduction in saturated fat to approximately 13% to 14% of calories.[9,10] There has been a simultaneous increase in adults' consumption of polyunsaturated fatty acids from about 4% to 7% of calories. Dietary cholesterol consumption has decreased from about 700 mg/d to approximately 220 to 260 mg/d for women and 360 mg/d for men.[11] These dietary changes have been temporally associated with a substantial reduction in CHD mortality,[12,13] although a causal relation cannot be proven.

Current Dietary Recommendations

The AHA's current dietary recommendations continue to be based on the belief that modification of risk

factors will decrease risk of CHD. These modifiable risk factors include elevated levels of plasma cholesterol, particularly low-density lipoprotein (LDL) cholesterol; decreased plasma levels of high-density lipoprotein (HDL) cholesterol; increased blood pressure; cigarette smoking; diabetes mellitus; obesity, especially central (visceral) adiposity; and physical inactivity. All of these factors except smoking can be modified by diet.

For the purpose of modifying these risk factors, especially high plasma and LDL cholesterol, the AHA recommends that less than 30% of calories be consumed as total fat, with less than 10% of total calories from saturated fat; that polyunsaturated fats provide up to 10% of calories; and that cholesterol consumption be restricted to no more than 300 mg/d. Furthermore, an attempt should be made to achieve and maintain desirable body weight. Sodium chloride consumption should not exceed 7.5 g/d (3 g/d of sodium) and ethanol intake should not exceed 2 drinks or 1 oz of ethanol per day.

Reduce Intake of Saturated Fatty Acids, Total Calories From Fat, and Dietary Cholesterol

Restriction of fat intake is the cornerstone of these dietary recommendations. Primary emphasis is on reducing consumption of saturated fatty acids, because they are the predominant dietary determinant of plasma and LDL cholesterol levels, and hence of CHD risk. A decrease in the proportion of calories from all types of fat will facilitate a reduction of saturated fatty acid intake. Low-fat diets may also reduce the risk of certain cancers and be of value in weight control.

Polyunsaturated and monounsaturated fatty acids cause a decrease in LDL cholesterol level beyond that due to reduction of saturated fatty acid consumption. Because no free-living populations chronically consume more than 10% of caloric intake as polyunsaturated fatty acids, consumption of these fatty acids in excess of 10% of calories is not recommended. The remainder of the fatty acids consumed should be monounsaturated. Polyunsaturated fatty acids are categorized as omega-6, derived from vegetable oils, and omega-3, derived from fish oils. There is not sufficient research for recommending the intake of large amounts of omega-3 fatty acids, especially as fish oil supplements.

Dietary cholesterol restriction is also important, because it can independently increase plasma and LDL cholesterol levels.[14] The AHA recommends that dietary cholesterol intake be less than 300 mg/day.

Reduction in the intake of saturated fatty acids and cholesterol can be achieved by the use of low-fat dairy products and skim milk, substitution of vegetable oil margarines for butter, and replacement of fatty meats with reasonable portions of fish, poultry, and lean meats. Restricting the use of eggs will further reduce intake of dietary cholesterol.

Increase Intake of Carbohydrates

If caloric intake is kept constant, reducing the intake of fats to less than 30% of calories generally will require that dietary carbohydrate intake increase from 45% to 55% of total calories. This increase should be in the intake of complex carbohydrates, the long-chain carbohydrates present in beans and peas, grain products (breads, cereals, pasta, and rice), and fruits and vegetables, all of which are low in fat. Complex carbohydrates provide dietary fiber as well. However, there is no sound basis for recommending the intake of large amounts of dietary fiber (such as in supplements) as a means of achieving optimal levels of plasma lipids or preventing CHD.[15]

Achieve and Maintain Desirable Weight

Diet-related cardiovascular risk factors usually are accentuated by obesity. The excess body fat is frequently distributed centrally. Central obesity in middle-aged adults is associated with insulin resistance, hypertension, glucose intolerance, and lipid abnormalities (dyslipidemia), and an increased risk of CHD.[16] Weight loss can reduce blood pressure, improve glucose tolerance and insulin resistance, and correct dyslipidemia. Moderate aerobic exercise should be used as an adjunct for weight control.[17] High-carbohydrate diets also are less calorically dense than high-fat diets and may play a role in preventing and treating obesity.[15] Unfortunately, maintenance of weight loss is difficult to achieve.

Reduce Salt Intake

Many hypertensive people are salt sensitive with respect to blood pressure. Although some normotensive people may also be salt sensitive, practical methods to reliably determine who these people are are not available. Because there is no reliable way to predict who will benefit from reducing salt intake, and because Americans consume considerably more salt and sodium than is required, the AHA considers it prudent for most people to restrict their intake of salt in case they are salt-sensitive. Therefore the AHA recommends that salt intake be restricted to no more than 7.5 g/d, the equivalent of 3 g of sodium.

For Those Who Drink, Alcohol Intake Should Not Exceed Two Drinks Per Day

Chronic heavy alcohol use can cause hypertension and cardiomyopathy in addition to its many other harmful effects. However, people who consume less than two drinks per day have a reduced risk of coronary artery disease compared with the risk for nondrinkers.[18] Therefore, for those who consume alcoholic beverages, the AHA recommends that consumption not exceed two drinks (1 oz alcohol) per day. (For this guideline a drink is considered to contain approximately 14 g of ethanol and is defined as 12 oz of beer, 6 oz of wine, or 1.5 oz of 80 proof liquor.)

Rationale and Documentation of AHA Position on Diet

Modifiable Risk Factors

The interrelations among diet-related risk factors and CHD, particularly that between diet and plasma lipoproteins, must be reviewed briefly to clarify the rationale behind the dietary recommendations.

Cholesterol is transported in plasma in macromolecular particles called *lipoproteins.* The majority of plasma cholesterol is in low density lipoproteins (LDL); hence elevations in total cholesterol reflect elevations in LDL. LDL appear to be atherogenic, because a high level of this lipoprotein is a significant risk factor for CHD.[19] A smaller fraction of the plasma cholesterol is present in the very-low-density lipoproteins (VLDL), and their

remnants occur predominantly in the intermediate-density lipoprotein density range. Levels of these predominantly triglyceride-rich lipoproteins are increased in patients with hypertriglyceridemia. The relation between triglyceride level and CHD is less clear. Although a univariate relation between triglyceride level and CHD is consistently observed, it is often lost in multivariate analyses after controlling for high-density lipoprotein level. The remaining cholesterol in plasma in the fasting state is present in HDL. There is a clear inverse relation between HDL concentration and risk for CHD, such that HDL appears to be antiatherogenic.[20] Dietary cholesterol and fat are transported in plasma in chylomicrons, which are rapidly cleared from the blood and are usually not present in blood samples obtained after an overnight fast. There is little conclusive evidence about the potential atherogenicity of chylomicrons and their remnants.

Thus, high levels of total, and particularly LDL, cholesterol increase CHD risk; low levels of HDL may do so further. Evidence for the potential atherogenicity of VLDL, chylomicrons, and their remnants is incomplete. Reduction of LDL level is associated with reduced CHD risk,[21] slowing of atherosclerotic progression,[22-25] and even, in some recent coronary angiographic studies, regression of established atherosclerotic lesions.[24,25] Increases in HDL level may also be associated with reduced CHD risk.[26]

Plasma lipid and lipoprotein levels are affected by nutritional and genetic factors (Table 1). The relative contribution of these factors differs from person to person so that, although plasma lipid and lipoprotein levels can be influenced by diet, the effect will be greater in some than in others.

Hypertension is a well established risk factor for cardiovascular disease.[27] Blood pressure can be influenced by body weight, alcohol consumption, and dietary sodium (especially sodium chloride). Diabetes mellitus also markedly increases CHD risk, especially in populations in whom plasma cholesterol levels are high[28] and in women, who have rates of CHD similar to those of diabetic men.[29] The expression of non–insulin-dependent diabetes is increased by obesity, which occurs when energy intake exceeds energy expenditure. Obesity has reemerged as a potentially important cardiovascular risk factor with the demonstration that central (visceral) obesity is often associated with dyslipidemia, hypertension, insulin resistance, and glucose intolerance.[30-32]

Plasma Cholesterol, Lipoproteins, and CHD

Epidemiological Studies

Epidemiological studies have shown a consistent and strongly significant correlation between total plasma cholesterol level and incidence of CHD.[33] Both CHD incidence and extent of atherosclerosis at autopsy can be explained to a large extent by variations in mean total cholesterol levels between populations. Among individuals within diverse populations, prospective studies of middle-aged men have shown a positive relation between CHD risk and total cholesterol levels above 200 to 220 mg/dl.[27] This association may be weak or absent in some populations with low mean total cholesterol levels or CHD risk.[34]

One of the studies particularly relevant to the US population is the Multiple Risk Factor Intervention Trial, in which 356 222 men aged 35 to 57 were screened. Age-standardized 6-year CHD mortality rates increased progressively over a broad range of total plasma cholesterol levels above 150 mg/dl. The relation between CHD and plasma cholesterol level is not linear, with the increase in CHD death rates being more evident at total cholesterol levels above 200 mg/dl and most marked at levels above 240 mg/dl. The 6-year mortality rate increased from 3.16 to 6.94 per 1000 between 153 and 226 mg/dl and increased further to 13.05 per 1000 as plasma cholesterol rose from 226 to 290 mg/dl.[35] A similar curvilinear relation appears to hold for the 23 490 black men included in this part of the study. Thus, total cholesterol level appears to be associated with CHD mortality in US men in a continuous but nonlinear fashion, with a stronger relation at levels above 200 mg/dl. Unfortunately, there is a paucity of comparable data for women.

Total cholesterol concentration generally reflects LDL cholesterol level. Epidemiological studies between and within populations also show a strong relation between CHD risk and LDL cholesterol levels. A direct relation between LDL concentration and extent of coronary atherosclerosis has also been shown in several angiographic studies. Furthermore, clinical trials and

TABLE 1. Effect of Nutritional Factors on Risk for Coronary Heart Disease

Lipoprotein/lipid	Variable	Effect on lipoproteins/lipid
LDL, total cholesterol	Saturated fat	Increased
	Monounsaturated fat	Lowered if substituted for saturated fat
	Polyunsaturated fat	Lowered if substituted for saturated fat
	Dietary cholesterol	Increased, but considerable variability seen
	Obesity	Increased
VLDL, triglyceride	Obesity	Increased
	Weight gain	Increased
	Fish oil	Decreased
HDL	Obesity	Decreased
	Total fat	Increased
	Carbohydrate	Decreased

LDL, low-density lipoprotein; VLDL, very–low-density lipoprotein; HDL, high-density lipoprotein.

angiographic studies provide good evidence that reductions in LDL cholesterol are associated with reduced incidence of CHD events and slowed progression of atherosclerotic lesions.

Intervention Trials

The relation between HDL cholesterol level and atherosclerosis is less clear. Some epidemiological studies show an inverse relation between CHD rates and HDL levels, especially in populations with relatively high levels of total cholesterol and high CHD rates.[36] HDL levels were inversely associated with CHD risk in the Framingham and Multiple Risk Factor Intervention Trial studies[35] and in studies in Israel and Norway. In addition, increase in HDL level in association with lowering of LDL level was associated with reduced incidence of CHD in the Lipid Research Clinics Coronary Primary Prevention Trial,[37] the Helsinki Heart Study,[38] and the Coronary Drug Project.[39] Recent intervention studies using quantitative coronary angiography have also suggested that progression may be further slowed and that lesions may even regress when increases in HDL occur concurrently with reductions in LDL cholesterol.[24,40] On the other hand, several studies have failed to show a relation between CHD mortality rates and HDL cholesterol.[41-43] Also, the association between CHD rates and HDL cholesterol levels between populations is less strong than that between CHD rates and LDL cholesterol levels. Furthermore, some populations (eg, African populations[44] and the Tarahumara Indians[45]) have both very low HDL levels and low CHD rates. However, these populations also have very low LDL cholesterol levels.

Most epidemiological studies have found a stronger correlation of CHD with plasma cholesterol than with plasma triglyceride. Plasma triglyceride levels have consistently been associated with CHD by univariate analysis, but the correlation often loses significance when levels of lipoprotein cholesterol, especially those of HDL cholesterol, are considered in multivariate analysis. Therefore, it is possible that plasma triglycerides may be a marker for some other CHD risk factors, such as decreased HDL cholesterol level, or the dyslipidemia (a combination of atherogenic lipoprotein compositional abnormalities) that frequently occurs in association with elevated levels of apolipoprotein B, the major structural apolipoprotein of VLDL and LDL. Little information is available about the influence on CHD risk of strategies specifically designed to lower plasma triglyceride levels.

Thus, LDL cholesterol level appears to be strongly associated with atherosclerosis and CHD risk. Variations in LDL cholesterol level explain much of the difference in CHD rates between populations and a large part of individual risk within populations at high risk of CHD. Furthermore, variations in HDL cholesterol level are inversely related to CHD risk, especially in populations prone to atherosclerotic complications by virtue of high total and LDL cholesterol levels.

The positive association of LDL cholesterol level and inverse association of HDL cholesterol level with CHD are strongest in men during middle age. In women the rise of cholesterol level with age is delayed, which may partly explain the lower rate of CHD among middle-aged women. However, most studies have excluded women, and additional data are urgently needed. There also is uncertainty about the relation between LDL cholesterol level and CHD risk in elderly men. Most studies show weaker or absent correlations between serum cholesterol or LDL cholesterol level and CHD risk in men over 65,[46] suggesting that the predictive effect of cholesterol for CHD decreases with age. However, some studies have shown a significant relation between LDL cholesterol and CHD risk even in older men.[19,47,48] Even if relative risk of high cholesterol level, as determined by risk ratios, declines with age, attributable risk rises because of the high rate of CHD events in the elderly. Data on the impact of cholesterol lowering on CHD in elderly men is also lacking. Although older subjects in the Los Angeles Veterans Administration Trial[49] and the Lipid Research Clinics Primary Prevention Trial[50] experienced risk reductions similar to those of younger subjects, the decline in CHD mortality in the US population has been less in older than in younger age groups. Additional information about women and the elderly clearly is needed.

Desirable plasma cholesterol level. Results of the Multiple Risk Factor Intervention Trial follow-up study indicated that the association of plasma cholesterol levels and CHD is a continuous variable throughout the range of cholesterol levels commonly seen in the US population. The relation becomes much stronger at plasma cholesterol levels above 200 mg/dl; therefore, the Adult Treatment Panel of the National Cholesterol Education Program on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults classified levels of blood cholesterol less than 200 mg/dl as desirable.[51] Levels above 240 mg/dl were classified as high, the risk of CHD at this level approximately twice that at 200 mg/dl. Intermediate levels (200 to 239 mg/dl) were classified as borderline.

The National Cholesterol Education Program Adult Treatment Panel also emphasized the concept of interaction among risk factors. The risk attributable to plasma cholesterol level is greater in the presence of other cardiovascular risk factors such as positive family history of cardiovascular disease, hypertension, cigarette smoking, diabetes mellitus, HDL cholesterol level less than 35 mg/dl, and obesity. In men the presence of one or more of these risk factors, and in women the presence of two or more, results in stratification into a different category for follow-up and treatment. The NCEP report thus provided convenient cutoff points for stratification of patients on the basis of total and LDL cholesterol levels and other cardiovascular risk factors. By National Cholesterol Education Program criteria, approximately 49% of the US population has desirable cholesterol levels. Forty percent of adults 20 years old and older would require fasting lipoprotein analysis; 29% of adults would be candidates for dietary therapy, and as many as 7% of adult Americans have high levels that warrant further intervention.[52] Since there is a relation between plasma cholesterol and CHD even at levels less than 200 mg/dl, it is possible that lower levels may be beneficial, especially in the presence of other CHD risk factors such as a family history of CHD, low HDL cholesterol level, and established CHD.

Genetic Hyperlipidemia

Although dietary factors undoubtedly affect plasma cholesterol level, they do so against a background of

genetic determinants. Genetic factors are likely to predominate in people with plasma LDL levels above the 90th to 95th percentile. Some patients with these high levels have monogenic forms of hypercholesterolemia. Approximately one in 500 has familial hypercholesterolemia, a disorder in which impaired clearance of LDL cholesterol due to defective LDL receptors is associated with marked elevations of plasma LDL cholesterol level and premature CHD. Others may have polygenic forms of hypercholesterolemia. Another genetic form of hyperlipidemia also associated with premature CHD is familial combined hyperlipidemia, which is characterized by increases in LDL cholesterol level, VLDL cholesterol level, or both. Up to 15% of patients with premature CHD may have this disorder.[53] Another genetic, albeit rare, disease is familial dysbetalipoproteinemia, which is characterized by high levels of remnant lipoproteins and β-VLDL, abnormalities of apolipoprotein E, and premature atherosclerotic disease. Familial defective apolipoprotein B is a recently described genetic disorder in which a defect in the structure of apo B impairs binding of LDL to its receptor,[54] leading to increased LDL cholesterol levels. Its incidence is not yet known. Another familial lipoprotein disorder associated with premature CHD is familial hypertriglyceridemia, in which plasma triglyceride levels are elevated and HDL cholesterol levels are low. These genetic forms of hyperlipoproteinemia provide strong support for the concept that elevated levels of plasma lipoproteins can accelerate development of atherosclerosis. They also indicate that not all hyperlipidemias are dietary in origin. For these genetic disorders, dietary modification alone is unlikely to normalize plasma lipid levels, and drug therapy is usually also required.

Most of the remainder of patients with cholesterol levels in the 75th to 95th percentile probably also have genetic forms of hypercholesterolemia. Dietary factors may affect plasma cholesterol in these patients, even though the dominant cause of their hypercholesterolemia seemingly is the interaction of multiple genetic factors with environmental factors such as diet. Thus, drug therapy in addition to dietary modification may be needed to reduce cholesterol levels in these patients to the desirable range if diet alone fails.

Finally, the role of heredity should be considered in the segment of the US population with plasma cholesterol levels in the 50th to 75th percentile, above the desirable range. Genetic factors probably affect plasma lipoprotein levels in these people as well, but diet may be the major factor. In this range, plasma cholesterol levels are probably determined by the interaction of diet with genetics, but despite hereditary influences dietary change alone may be sufficient to reduce plasma cholesterol to desirable levels.

Diet and CHD

Several lines of evidence have converged to underscore the key role of both composition and quantity of dietary constituents in atherogenesis and risk of CHD. One such line includes investigation of the relation between diet and atherosclerosis in laboratory animals, clinical investigation, and epidemiological and intervention studies.

Diet and Atherosclerosis in Laboratory Animals

Both dietary cholesterol and saturated fatty acids have been shown to increase atherosclerosis in susceptible animal species. The atherogenic effect of dietary cholesterol was first demonstrated in rabbits,[55] but has also been observed in several other animals, including pigs, guinea pigs, hamsters, some avian species, and some species of monkey. Other species of monkey, dogs, mice, and particularly rats are resistant to the atherogenic effect of diet.[55] In general, dietary cholesterol appears to be more atherogenic than saturated fatty acids in animals.

The animals in which diets high in dietary cholesterol and saturated fat produce atherosclerosis also have an increase in serum cholesterol level in response to these diets. There is a strong positive correlation between changes in serum cholesterol level, especially LDL cholesterol level, and the development of atherosclerosis in these experimental models.[56-58] An inverse relation between HDL level and atherosclerosis has been demonstrated in animals[59] as well as in humans. In some species, such as rabbits, the diet-induced increase in serum cholesterol level is due mainly to an increase in remnant lipoproteins[55]; this increase is seen, but to a lesser extent, in humans consuming similar diets.[60] Animal studies have also demonstrated that regression of diet-induced atherosclerotic lesions can occur if the diet is changed to one that reverses the adverse effect on serum cholesterol.[61] In nonhuman primates, serum cholesterol levels must be reduced to less than 200 mg/dl for significant regression to occur.[62]

Although other dietary components, such as animal protein, trace metals, and vitamins, have been shown to alter serum cholesterol levels, the changes often are small, have not been consistent, and do not seem to occur in humans. For example, consumption of vegetable proteins leads to lower cholesterol levels than consumption of animal proteins in rabbits but not in humans.[63]

In most animal studies in which cholesterol has been added directly to the diet or omega-6 unsaturated fatty acids have been substituted for saturated fatty acids, the effect of the diet on atherosclerosis nearly always can be explained by its effect on serum cholesterol levels. However, several studies have shown an effect of omega-3 unsaturated fatty acids on atherosclerosis that may be more related to the effect of these fatty acids in inhibiting thrombosis or reducing the immune response than on lowering cholesterol levels.[64]

Interrelations between diet and genetic susceptibility to atherosclerosis have been demonstrated in some animal models, especially in some atherosclerosis-prone inbred strains of mice.[65] Studies in nonhuman primates have also demonstrated the phenomenon of dietary hyperresponsiveness and hyporesponsiveness, which has been more difficult to demonstrate in man.[66] However, the major contribution of animal studies is that they allow the relations among dietary components, serum cholesterol level, and atherosclerosis to be examined directly, which is difficult in humans.

Effect of Diet on Lipid and Lipoprotein Levels in Humans

Atherosclerotic lesions develop slowly in humans, and considerable time usually lapses between the develop-

ment of lesions and the onset of atherosclerotic complications. Diet studies in humans have therefore usually focused on serum lipid and lipoprotein levels and have not examined cardiovascular end points or atherosclerotic lesions directly. Although metabolic ward studies permit rigid control of the diet, many such studies have used liquid-formula diets, which potentially could affect lipids and lipoproteins in ways different from diets consumed by free-living subjects. Nonetheless, data from both metabolic ward and outpatient studies have provided consistent findings concerning the relation between individual dietary components and serum lipid and lipoprotein levels.

Fatty acids. For more than 30 years, studies have shown that dietary saturated fatty acids affect serum lipid and lipoprotein levels to the greatest extent. They raise serum total and LDL cholesterol levels, although the different saturated fatty acids have varying abilities to do so. Thus, short-chain (less than 10 carbon atoms) fatty acids and stearic acid (18 carbon atoms) do not raise serum cholesterol levels.[67] Stearic acid has recently been shown not to raise LDL cholesterol levels either, as it appears to be converted to oleic acid in the body.[68] Serum and LDL cholesterol levels are mainly affected by lauric (12 carbon atoms), myristic (14 carbon atoms), and palmitic (16 carbon atoms) acids.[67] Reduction in the intake of these cholesterol-raising saturated fatty acids results in a reduction in serum and LDL cholesterol levels both on metabolic ward diets and in well-controlled outpatient studies. Equations developed from carefully controlled clinical studies indicate that reducing saturated fat intake to less than 10% of calories can lead to a reduction of 4% to 5% in serum cholesterol levels for the population. For each 1% reduction in calories consumed as saturated fat, serum cholesterol level falls an average of 2.7 mg/dl,[67,68] although there is individual variability in response. Although these early regression equations did not take all these fatty acids into consideration, they nonetheless have been useful in predicting responses to dietary change.

The major sources of the cholesterol-raising saturated fatty acids are whole milk dairy products, fatty meats and poultry, and foods such as baked goods, predominantly those that contain dairy products, shortening, and the tropical oils—coconut, palm, and palm kernel (Table 2).

To reduce serum lipid and lipoprotein levels while keeping caloric intake constant, saturated fatty acids in the diet can be replaced by either polyunsaturated fatty acids, monounsaturated fatty acids, or carbohydrates, all of which have slightly different effects on serum lipids and lipoproteins. At one time there was considerable interest in the effects of omega-6 polyunsaturated fatty acids, especially linoleic acid (18 carbon atoms, two double bonds), because they were shown to lower cholesterol levels independent of a reduction in the saturated fatty acid content of the diet.[69] Previous AHA reports have therefore recommended that saturated fats be replaced as much as possible by polyunsaturated fats. There has been a gradual increase in polyunsaturated fat consumption in the United States, with polyunsaturated fatty acids, which are found primarily in vegetable oils such as corn, sunflower, and safflower oil, currently providing approximately 7% of total calories in the average American diet. However, when consumed in high quantities (in excess of 10% of calories) they have reduced both LDL and HDL levels in some[70] but not all[60] studies, although consumption of more modest amounts of polyunsaturated fatty acids usually has no effect on HDL level. There has also been the theoretical concern, based on animal studies, that high intakes of polyunsaturated fatty acids may promote cancer when consumed in very large amounts.[71] In addition, polyunsaturated fatty acids are susceptible to oxidation; their presence in large amounts in lipoprotein particles might therefore render the lipoproteins more susceptible to oxidative modification, which is believed to play a role in atherogenesis.[72] Because of these concerns and because no free-living population consumes more than 10% of calories as polyunsaturated fatty acids, interest has arisen in the use of other substitutes for saturated fatty acids so as to limit the intake of polyunsaturated fatty acids to no more than 10% of calories.

TABLE 2. Common Dietary Sources of Saturated Fatty Acids

	Lauric acid*	Myristic acid*	Palmitic acid*	Stearic acid*
Butterfat	3.1	17.7	26.2	12.5
Beef fat	0.1	3.3	25.5	21.6
Coconut oil	49.5	18.6	9.4	2.5
Palm oil	0.3	1.1	45.1	4.7
Palm kernel oil	49.6	17.0	8.0	2.4
Cocoa butter	0.0	0.0	26.0	34.0

*Percent of total fatty acids. Updated from Grundy and Denke, 1990.

Although the omega-3 polyunsaturated fatty acids eicosapentaenoic (20 carbon atoms, five double bonds) and docosahexaenoic acid (22 carbon atoms, six double bonds) have been reported to lower cholesterol levels,[73,74] they mainly reduce plasma triglyceride and cholesterol levels by reducing levels of VLDL and chylomicrons[75] and have only a minor and variable effect on LDL level.[76] HDL levels increase as triglyceride levels fall,[77] but LDL levels actually may increase with consumption of large amounts of the omega-3 fatty acids, especially in hypertriglyceridemic subjects.[78,79] These fatty acids may influence atherogenesis by mechanisms other than their effects on lipoproteins, most likely by altering thrombosis or reducing the immune response.[64] Fish are a rich source of omega-3 fatty acids and are also low in saturated fatty acids. Thus, consumption of fish in lieu of fatty meats can reduce saturated fat intake while providing potential benefit from omega-3 polyunsaturated fatty acids. However, the AHA does not recommend the use of omega-3 fatty acid supplements because their long-term benefits have not been demonstrated, and they can worsen glycemic control in non–insulin-dependent diabetics.[80]

Recently there has been a renewed interest in monounsaturated fatty acids as a replacement for saturated fatty acids. Although older studies[67] and some more recent investigations[69] have suggested that substitution of saturated fatty acids by polyunsaturated rather than by monounsaturated fatty acids leads to a slightly

greater reduction in serum and LDL cholesterol levels, other recent studies suggest that monounsaturated and polyunsaturated fatty acids reduce LDL to about the same extent.[60] When substituted for saturated fat in the diet,[60] the major benefit of monounsaturated fatty acids appears to result from the reduction in saturated fatty acid intake, and their net effect on serum lipids and lipoproteins is not much different from that of polyunsaturated fatty acids. Monounsaturated fatty acids may also have potential advantages. They do not lower HDL level[81-83] and are not susceptible to oxidative modification,[71] which plays a role in atherogenesis. In the Mediterranean region, large amounts of monounsaturated fatty acids are consumed as olive oil without evidence of adverse effects. Indeed, the prevalence of CHD in that region is relatively low,[83] although saturated fat intake is also very low in most of those countries. Monounsaturated fatty acids currently contribute 14% of calories to the average American diet; many of these are from animal products which are also rich in saturated fatty acids. Good vegetable sources of monounsaturated fatty acids are olive oil, canola oil, high oleic sunflower and safflower oil, and peanut oil. Because a major proportion of monounsaturated fatty acids in the average American diet are consumed with animal fats, a reduction of saturated fatty acids to less than 10% of caloric intake will actually produce a decrease in monounsaturated fatty acid intake. The AHA does not recommend a particular limit for monounsaturated fatty acid intake but rather recommends that total fat be less than 30% of calories, with saturated fatty acids constituting up to 10% of calories, polyunsaturated fatty acids up to 10% of calories, and monounsaturated fatty acids the remainder of fat calories (10% to 15% of total calories). Additional fat calories should be replaced with carbohydrates, especially complex carbohydrates.

Carbohydrates. Carbohydrates have also been used to replace saturated fatty acids eliminated from the diet. When carbohydrates are isocalorically substituted for saturated fatty acids, LDL cholesterol levels fall primarily as a result of the reduction in the intake of saturated fatty acids[84]; however, HDL cholesterol levels fall[85] and serum triglyceride levels increase[86,87] in many people with diabetes and people with preexisting hypertriglyceridemia, particularly if sucrose makes up a significant proportion of these calories.[88] Diets high in complex carbohydrates and very low in saturated fatty acids and cholesterol seldom raise plasma triglyceride concentrations in nondiabetics[89] and may even reduce levels in people with preexisting hypertriglyceridemia.[90] HDL cholesterol level also may fall because of consumption of a high-carbohydrate diet,[91,92] although this is not a universal finding.[90] However, there is no evidence that diets rich in complex carbohydrates, which lower both HDL cholesterol and LDL cholesterol levels, are associated with increased risk for CHD. Epidemiological studies have demonstrated an inverse relation between carbohydrate consumption and risk for CHD.[93] However, it is unclear whether this is an independent association because populations that consume diets high in carbohydrate tend to have a low intake of saturated fat.

Diets high in complex carbohydrate also tend to be high in both insoluble and soluble fiber. Certain types of soluble fibers (guar gum, pectin, oat bran), when consumed in very large amounts (more than 40 g/day), may reduce plasma total and LDL cholesterol levels.[15] Reductions in plasma lipid levels in response to ingestion of lesser amounts of fiber have been inconsistent and are affected by the baseline lipid level. Although populations consuming diets high in complex carbohydrates that contain increased quantities of fiber tend to have low rates of CHD, evidence for an independent effect of fiber on the incidence of CHD is not conclusive because such populations also consume diets low in saturated fatty acids.

Thus, despite small differences in serum levels of lipids and lipoproteins when saturated fatty acids are replaced by omega-6 polyunsaturated fatty acids, monounsaturated fatty acids, or carbohydrates, from a practical standpoint they all lead to similar changes because the major effect on serum and LDL cholesterol levels is due to the reduction in saturated fatty acid intake.

Cholesterol. Dietary cholesterol independently affects serum cholesterol and LDL levels.[60] In early animal studies atherosclerosis was induced by a diet consisting only of cholesterol, but it is apparent that dietary cholesterol has less of an effect on human serum cholesterol levels than in several animal species. Although some outpatient studies have failed to demonstrate an effect of dietary cholesterol on plasma cholesterol level,[94,95] most well-controlled studies, particularly those performed on metabolic wards, have demonstrated that dietary cholesterol has a plasma cholesterol–raising effect.[89] Regression equations developed to predict the effect of a reduction in dietary cholesterol on serum cholesterol levels showed an independent effect,[67] although the relation between cholesterol intake and serum cholesterol level is not linear. There is also considerable variability in response to dietary cholesterol between individuals,[96] which is not easy to reproduce. The effect of dietary cholesterol may also be modulated by the fatty acid content and composition of the diet.[97] In addition to increasing LDL levels by repressing LDL receptors, dietary cholesterol may also alter the composition of LDL and VLDL particles and may influence the composition of their apolipoproteins.[97] The impact of these changes is unclear at present.

In recent years the cholesterol intake of the US public has declined, mainly because of a decreased consumption of eggs, to an average intake of 220 to 260 mg/d by women and 360 mg/d by men.[11] Currently, egg yolks provide about one third of dietary cholesterol consumed, the remainder coming from dairy products, meat, poultry, fish, and baked goods. The AHA recommends consumption of no more than 300 mg of cholesterol per day. For each 100 mg/d decrease in dietary cholesterol, total plasma cholesterol level falls an average of about 7 mg/dl although as previously noted there is considerable individual variation.

Other components. Several other dietary components have been shown to affect serum and LDL cholesterol levels. These include trans fatty acids, soluble fiber, dietary proteins, and coffee. Although in a recent study consumption of large amounts of trans fatty acids, which result from partial hydrogenation of polyunsaturated fatty acids, raised LDL and reduced HDL levels,[98] these findings need to be confirmed in studies using

levels of these fatty acids that are likely to be consumed in the American diet. The amount consumed in the typical American diet is unlikely to have a major effect on these levels. The effects of soluble fiber, particularly oat bran, have received much recent attention. In people with normal plasma lipid levels, much of the cholesterol lowering associated with foods rich in soluble fiber is due to replacement of saturated fatty acids in the diet.[99] On the other hand, in those with borderline or elevated LDL cholesterol levels, oat bran can have a small, independent cholesterol-lowering effect.[100] As pointed out earlier, the hypocholesterolemic effect of vegetable protein observed in some laboratory animals is not seen in humans.[101] The hypercholesterolemic effect of coffee has been localized to an unidentified factor extracted from coffee during prolonged boiling.[102] This hypercholesterolemic effect is not seen when boiled coffee is filtered[103] and does not appear to cause a problem when common methods of coffee preparation in the United States are used.

Another potentially important but inadequately understood factor is the role of obesity in modulating the serum lipid and lipoprotein response to dietary saturated fat and cholesterol. Obesity appears to increase LDL levels,[104] probably by stimulating LDL production rates. Weight reduction by obese subjects has been associated with a lowering of LDL cholesterol levels in some studies. A more common effect of weight reduction is a reduction in triglyceride level and an increase in HDL cholesterol level.[17]

Epidemiological Studies

Evidence linking intake of saturated fatty acids with CHD morbidity and mortality is found in both cross-sectional and prospective epidemiological studies. In the cross-population and prospective cohort studies discussed below, lower intakes of saturated fatty acids were consistently associated with lower risk of CHD. These studies and others have been reviewed in detail in the Diet and Health report of the National Research Council,[15] the Surgeon General's Report on Nutrition and Health,[105] and the National Cholesterol Education Program Panel on Population report,[106] and readers are referred to these publications for a more complete discussion of the results and interpretation of these studies.

Cross-population studies. There is a consistent positive relation between saturated fat intake and CHD mortality in studies in which estimates of CHD mortality are obtained from national vital statistics and information on dietary intake is inferred from the national food balance (national estimates of food availability from which intake is usually inferred on a per capita basis). In most instances, low saturated fat intake is associated with low total fat intake. However, there is some evidence that populations that consume a diet high in total fat but low in saturated fat because of high monounsaturated fat levels have CHD mortality rates as low as in countries where low saturated fat intake is associated with low total fat intake.[107] As with all results from ecological studies, these data must be interpreted with caution because of the lack of comparability and completeness of mortality data between countries, as well as the lack of representativeness and specificity of these dietary data. The most important studies are as follows:

THE SEVEN COUNTRIES STUDY: In 1956 the Seven Countries Study began to investigate the epidemiology of coronary heart disease in 12 770 men, aged 40 to 59, from Finland, Greece, Italy, Japan, The Netherlands, the United States, and Yugoslavia. A strong correlation was found between the average percent intake of calories from saturated fatty acids and serum total cholesterol at 5, 10, and 15 years of follow-up.[108] These findings are consistent with the hypothesis that risk of early CHD death is increased by diets high in saturated fatty acids in populations in which coronary heart disease is a major cause of death.

JAPAN–HONOLULU–SAN FRANCISCO STUDY: In this cross-population study, investigators examined physical characteristics, dietary intake, and biochemical markers among three groups of Japanese men living in Japan, Hawaii, and California. Consumption of dietary saturated fat in the three populations was reported to be about 7%, 12%, and 14%, respectively. Differences in serum cholesterol levels and the rate of CHD mortality between the groups showed a trend similar to that seen for saturated fat intake. Japanese men in Japan had lower serum cholesterol and CHD mortality rates than those living in California, and serum cholesterol levels and CHD rates among Japanese men living in Hawaii were between those in Japan and California. Death rates from CHD were 1.7 times higher in Hawaii and 2.8 times greater in California than in Japan.[109]

Prospective cohort studies. Results from prospective cohort studies of the association between CHD and saturated fatty acid intake as a percentage of energy intake are inconsistent. In some studies no association has been shown between saturated fatty acid intake and CHD risk,[110] while in others only associations with polyunsaturated fatty acid intake, or with indexes that include intake of saturated and polyunsaturated fatty acids and cholesterol, have been shown. In some prospective epidemiological studies, notably the Western Electric Study,[13] the Ireland–Boston–Diet-Heart Study,[111] and the Honolulu Heart Program,[112] positive associations between dietary cholesterol intake and risk of CHD have been found.

WESTERN ELECTRIC STUDY: In 1957, 1900 participants in the Western Electric Study were randomly selected from a sample of 5397 middle-aged men employed by the Western Electric Company. Diet scores, which indicated dietary fat and cholesterol intake, were used to calculate predicted changes in serum cholesterol. Results showed a positive association prospectively between mean baseline diet score and the 19-year risk of death from CHD after adjusting for potentially confounding factors. There was also an independent effect of dietary cholesterol on CHD risk.[13]

THE IRELAND–BOSTON–DIET-HEART STUDY: The relation between dietary information collected 20 years before death from CHD was examined in three cohorts: men born and living in Ireland, men born in Ireland and living in the United States, and men born to Irish immigrants and living in the Boston area. Although there were no differences in mortality from CHD between the three cohorts, those who died of CHD had a higher intake of saturated fat and cholesterol and a lower intake of polyunsaturated fat than those who did

not. The results of this study also support the hypothesis that intake of saturated fat and cholesterol is related to the development of CHD.[111]

HONOLULU HEART PROGRAM: In 1965, as part of the Honolulu Heart Program, dietary intake and serum cholesterol measurements were collected from 7088 Japanese men living on the island of Oahu. Dietary intake was analyzed and related to the incidence of CHD during the next 10 years. The investigators found that men who developed CHD had a higher mean consumption of dietary cholesterol and a lower percentage of calories from carbohydrates than men who did not develop CHD.[112]

FRAMINGHAM STUDY: A positive association was shown between the proportion of calories from total fat, monounsaturated fat, and saturated fat and 16-year incidence of CHD morbidity and mortality among younger men aged 45-55 at baseline but not in older men aged 55-65 or in women. This association was seen after adjustment for other cardiovascular disease risk factors, including serum cholesterol, suggesting that there is an independent effect of dietary lipids on CHD incidence in men this age.[113]

It is important to note that correlations have not always been found between dietary fat intake, serum cholesterol concentration, and rate of CHD in US populations. This lack of an association is in all likelihood primarily because of a lack of wide variation of dietary fat intake among individuals in the United States.[11] Also, dietary intake has frequently been assessed with methods that do not accurately reflect intraindividual variation in dietary intake, tending to produce inconsistent associations of dietary fat intake with rates of CHD within populations. However, in the Western Electric Study, in which a method that provided adequate estimates of each man's usual dietary intake was used, an association was found between total dietary fatty acid intake and CHD rate in US men.

Intervention trials. Clinical trials to test whether dietary modification would change CHD risk prospectively were begun in the 1950s and 1960s. In two such studies, carried out in Chicago[114] and New York,[115] the subjects were free-living men following a prudent diet with restriction of saturated fat and cholesterol. These early trials suggested that lowering blood cholesterol levels with diet might reduce the risk of heart disease. However, because of small sample sizes and lack of subjects randomly assigned to a control group, the findings were not conclusive.

A controlled clinical dietary trial was carried out in 4178 male and 6434 female patients above age 15 in two mental hospitals in Helsinki, Finland. The study used a cross-over design with two periods of about 6 years each. A diet low in saturated fatty acids and cholesterol and high in polyunsaturated fatty acids produced a decrease in serum cholesterol and a decrease in CHD mortality rate.[116] A similar trial was carried out in a Minnesota mental hospital, in which a diet low in saturated fatty acids and cholesterol and high in polyunsaturated fatty acids was compared with a control diet high in saturated fatty acids. Rates of coronary events were lower in men on the cholesterol-lowering diets; however, this was true only for men who were younger than 40 at the start of the study.[117]

Another dietary trial was conducted at the Veterans Administration Domiciliary Facility in Los Angeles. A double-blind experimental design with a randomized control group was used for this study. Elderly male subjects aged 55 to 89 were randomly assigned to either a low–saturated fat, low-cholesterol diet high in polyunsaturated fatty acids or to a control diet, in which an average 15% of calories were consumed as saturated fatty acids and 650 mg of cholesterol were consumed each day. There were 424 men in the treatment group and 422 men in the control group. After 8 years there was a significant 23% reduction in CHD rates and cholesterol levels were 13% lower in the treatment group compared with the control group.[118]

In the London Medical Research Council Soybean Oil Study, approximately 400 middle-aged men were randomly selected to consume a control diet or a diet low in saturated fat and rich in soybean oil over a 4-year period. Mean cholesterol levels were 13% lower in the treatment group than in the control group, and CHD rate was 18% lower.[119]

The National Diet-Heart Study was conducted to determine the feasibility of conducting a dietary intervention study in the United States. This study demonstrated that a diet restricted in saturated fatty acids and cholesterol and rich in polyunsaturated fatty acids could produce reductions in serum cholesterol ranging between 20 and 30 mg/dl and that such reductions could be sustained over a 52-week period.[120] Reductions in cholesterol level were greater in men with higher initial levels and also in men who lost weight during dietary modification. This study also demonstrated that similar reductions could be achieved even if the diet was not rich in polyunsaturated fat but only restricted in saturated fat and cholesterol. However, the investigators concluded that it was not feasible to conduct a National Diet-Heart Study in the United States because of the very large number of subjects and the length of the study necessary for statistical significance. The National Heart, Lung, and Blood Institute used a cholesterol-lowering medicine, cholestyramine, in the Lipid Research Clinics Coronary Primary Prevention Trial to test the cholesterol–heart disease hypothesis rather than using dietary intervention.

Two major CHD prevention diet trials were carried out in Oslo, Norway, by the Oslo Heart Study group. In the first study, the subjects, 412 men who had had a myocardial infarction, were randomly assigned in equal numbers to a control diet containing approximately 16% of calories as saturated fat and 550 mg of cholesterol per day or to an intervention diet in which the saturated fatty acid content was 8.5% of calories, the polyunsaturated fatty acid content was 20.7% of calories, and the cholesterol content was 264 mg/d. At the end of the study, mean cholesterol levels were 15.5% lower in the treatment group than in the control group. Over a 5-year period there was a 35% lower incidence of CHD in the treatment group than in the control group.[121]

A second Oslo Diet Heart study was conducted with 1232 asymptomatic hypercholesterolemic men. The interventions included instruction on a low–saturated fat, low-cholesterol diet (mean intakes: 8.2% of calories as saturated fat, 7.2% of calories as polyunsaturated fat, and 289 mg of cholesterol per day) by a dietitian as well as the physician, and also advice to reduce or stop

smoking cigarettes. The control group's diet was estimated to include 18.3% of calories as saturated fat, 7.1% of calories as polyunsaturated fat, and 527 mg of cholesterol per day. Unlike many of the previously described dietary intervention studies, the intervention diet was not enriched in polyunsaturated fatty acids. Over the course of this study, the mean serum cholesterol level in the treatment group was 13% lower than in the control group. In addition, cigarette smoking was about 40% less in the treatment group. Over the 5-year course of this study, a 47% reduction in prospective CHD incidence was observed.[122] The success of the two Oslo studies has been attributed in part to the fact that subjects were seen regularly and given dietary instruction by the dietitian and strong encouragement by the physician. These data indicate that mean reductions in serum or plasma cholesterol of about 13% can be achieved with dietary instruction if repeated reinforcement is provided by the dietitian as well as the physician.

The effect of dietary modification on progression or regression of coronary atherosclerosis has been assessed by serial angiography. In the Leiden Intervention Trial, 53 patients with established coronary artery disease were placed on a strict vegetarian diet, containing 6.6% of calories as saturated fat, 16.8% of calories as polyunsaturated fat, and approximately 60 mg of cholesterol per day, for a 2-year period. Cholesterol levels were reduced by 10% from baseline with no change in HDL cholesterol levels.[123] In this study coronary lesion growth was strongly correlated with the total/HDL cholesterol ratio but not with other parameters. Disease progression was significant in patients whose total/HDL cholesterol ratios were greater than 6.9. In contrast, no coronary lesion growth was observed in patients who had lower values for total/HDL cholesterol ratio throughout the trial.

The Multiple Risk Factor Intervention Trial, a multicenter clinical trial that began in 1973, was designed to evaluate the effect on CHD of dietary intervention with simultaneous reduction of other risk factors. From a cohort of 361 662 middle-aged men at high risk, 12 866 were randomly assigned to either a special intervention or a usual care group. Participants in the special intervention group reduced their serum cholesterol levels by 7.5% after 6 years. Men who lost weight in addition to modifying their diets had the greatest reduction in cholesterol levels. An inverse relation of high-density lipoprotein cholesterol with incidence of CHD was found.[124]

A number of large prospective trials have been conducted to test the concept that lowering cholesterol with drugs or surgery will reduce the risk of heart disease. The largest was the World Health Organization Study, in which more than 10 000 asymptomatic middle-aged hypercholesterolemic males were randomly assigned to receive either placebo or clofibrate treatment over a 5-year period.[125] There was a 20.9% lower incidence of CHD over a 5-year period in the treatment group compared with the placebo group, but excess mortality was noted in the drug therapy group.[121] In the Coronary Drug Project, no such excess mortality was noted at either 5 or 15 years in middle-aged men with prior myocardial infarction who were treated with clofibrate, but only a 9.5% reduction in CHD incidence was observed in this study.[39] In the niacin-treatment limb of the Coronary Drug Project, a 19.8% reduction in incidence of CHD events was observed in the treatment group. At 15 years, 9 years after the end of the study, a significant reduction of 11% in total mortality was noted.[125]

In the Lipid Research Clinics Coronary Primary Prevention Trial, which involved 3806 asymptomatic middle-aged hypercholesterolemic men, cholestyramine was used to achieve a 19% reduction in CHD incidence and an 11% reduction in LDL cholesterol levels. Subjects with the greatest reduction in LDL cholesterol level had the greatest reduction in CHD risk. It is of interest that subjects with normal or above-normal HDL cholesterol levels benefited to a greater extent from LDL cholesterol reduction than did those with low HDL cholesterol levels.[37]

In the Helsinki Heart Study, 4081 males with non-HDL cholesterol values greater than 200 mg/dl were randomly assigned to receive placebo or gemfibrozil. A 34% reduction in CHD incidence was noted in subjects taking gemfibrozil compared with those taking the placebo, and they had mean triglyceride reductions of 35%, LDL cholesterol reductions of 9%, and increases in HDL cholesterol of 10% compared with the placebo group. Multivariate statistical analysis revealed that the increases in HDL cholesterol level as well as the decreases in LDL cholesterol level were both associated with statistically significant benefit in terms of CHD risk reduction. No such benefit was associated with the marked decreases in triglyceride levels.[123]

In the Program on the Surgical Control of the Hyperlipidemias (POSCH), the effect of partial ileal bypass surgery on mortality and morbidity from CHD was assessed in 838 patients with hypercholesterolemia. After a mean follow-up period of nearly 10 years, total plasma cholesterol levels were 23% lower, LDL cholesterol levels were 38% lower, and HDL cholesterol levels were 4.3% higher in the surgery group than in control subjects. Although no significant overall effect on mortality was noted, mortality in the surgery subgroup with cardiac ejection fraction greater than 50% was 36% lower than in the control group. When the deaths due to CHD and nonfatal myocardial infarction were combined, the event rate was 35% lower in the surgery group than in the control group.[128] These results provide evidence for the beneficial effects of plasma lipid modification and the reduction of atherosclerosis progression.

The most positive effects on mortality reduction were observed in the Stockholm Ischemic Heart Disease Secondary Prevention Study, in which 550 male survivors of myocardial infarction were randomly assigned to usual care or usual care plus administration of clofibrate and niacin. At the end of 5 years, 30% of the control group and 22% of the treatment group had died ($P<0.05$, 27% reduction in all causes of mortality). Most of the difference was due to a significant 36% reduction in death from CHD.[129] These data indicate that lipid-lowering agents can have a positive effect on CHD mortality.

In all these studies, the effect on CHD rates was related with the change in cholesterol achieved by the intervention, whether by diet or drug treatment. Several recent studies using quantitative coronary angiography have provided further evidence that lowering cholesterol

with diet and drugs can reduce lesion progression and even lead to regression of some lesions. In the Cholesterol Lowering Atherosclerosis Study, 162 subjects with established CHD who previously had been treated with coronary bypass surgery were randomly assigned to either placebo or the combination of niacin and colestipol. The study was the first to demonstrate significant angiographic improvement in both vein grafts and native coronary arteries after 2 years of aggressive lipid-lowering therapy that reduced LDL cholesterol level and increased HDL cholesterol level. The improvement was seen over a range of baseline cholesterol values from normolipidemic to markedly hypercholesterolemic.[22]

In the Familial Atherosclerosis Treatment Study, serial quantitative angiography was performed on 120 men who had elevated plasma apolipoprotein B levels and documented CHD. The 2½-year double-blind study included coronary angiography at baseline and after treatment. Study subjects were randomly assigned to either a control group, a group treated with a combination of lovastatin and colestipol, or a group treated with niacin and colestipol. In the lovastatin and colestipol group LDL cholesterol level was decreased by 46% and HDL cholesterol level was increased by 15%, while in the niacin and colestipol group LDL cholesterol level was decreased by 32% and HDL cholesterol level was increased by 43%. In the conventional therapy group, 46% of patients had definite lesion progression while regression was the only change in 11%. Progression was less frequent among patients who received lovastatin and colestipol (21%) and those who received niacin and colestipol (25%), and regression was more frequent in the treatment groups: 32% in the lovastatin and colestipol group and 39% in the niacin and colestipol group. Clinical events, including death, myocardial infarction, or revascularization, occurred in 11 of 52 patients assigned to conventional therapy compared with 3 of 46 patients taking lovastatin and colestipol and 2 of 48 taking niacin and colestipol. This study indicates that intensive lipid-lowering therapy can reduce progression and increase regression of coronary lesions as well as reduce the incidence of cardiovascular events in men with established CHD.[24] In all of these drug studies, diet therapy was an important component for both the treatment and placebo groups, so it was not possible to examine the independent effects of diet.

In the University of California, San Francisco, Specialized Center of Research study, combined drug therapy was used to treat 72 men and women with familial hypercholesterolemia. Quantitative angiography before and after 26 months of therapy indicated net progression of lesions in control subjects and net regression in treated subjects. The change in percent area stenosis was correlated with LDL level.[25] Similar changes were noted in men and women, suggesting that the benefits of lipid lowering are independent of gender.

In the St. Thomas' Atherosclerosis Regression Study, 90 hypercholesterolemic men with coronary artery disease were assigned to groups receiving no intensive lipid-lowering therapy, diet intervention, or diet intervention plus cholestyramine. The proportion of patients with overall disease progression was significantly reduced in both intervention groups, and the proportion with an increase in luminal diameter was higher in both treatment groups. The change in mean absolute width of the coronary arteries correlated with the LDL cholesterol levels and the LDL/HDL cholesterol ratio. Diet therapy alone slowed disease progression and increased regression; diet plus cholestyramine had additional beneficial effects.[40]

Data from these intervention trials support the concept that aggressive lipid-lowering therapy with either diet intervention or drug therapy is beneficial in reducing CHD lesions and events. Results from animal studies, epidemiological surveys, and clinical trials all provide highly consistent evidence that intake of saturated fatty acids and cholesterol directly raises serum total and LDL cholesterol levels. Also, there is consistent and convincing evidence that high serum levels of total and LDL cholesterol contribute directly to atherosclerosis and CHD. Although this does not prove a direct link between diet and CHD, the conclusion that such a link exists is almost inescapable. The combined data from animal, clinical, and epidemiological studies strongly implicate the US diet as being in part responsible for the high incidence of CHD in our society and present a strong challenge to most Americans to improve their dietary habits. Because of this challenge, the AHA has made dietary recommendations for the American public. Failure to make such recommendations would condone consumption of the current American diet, which on average is too high in total calories, saturated fats, and cholesterol. The AHA recommendations are supported by and are consistent with the recommendations of other expert groups and panels as published in the Surgeon General's Report on Nutrition and Health,[105] the Diet and Health Report of the National Research Council,[15] and the National Cholesterol Education Program Panel on Population report.[106]

Diet and Blood Pressure

In addition to serum cholesterol, the other major CHD risk factor that can be affected by dietary factors is hypertension. An association between obesity and hypertension has been amply documented. Higher levels of blood pressure have also been associated with a number of nutrients, including high intakes of sodium chloride, alcohol, saturated fats, and sucrose and low intakes of calcium, magnesium, and potassium.[130-135] However, of all the specific nutrients that may affect blood pressure, the two most convincingly related to hypertension are sodium chloride and alcohol. Based on current knowledge about the impact of obesity and sodium chloride and alcohol intake on blood pressure, the AHA believes it is appropriate to make recommendations concerning these factors for the general population. However, for the individual, the relative importance of each of these recommendations should be prioritized, depending on current nutritional status, family history of hypertension, race, and other factors.

Obesity

Within populations, blood pressure is correlated with body weight, and change in body weight over time is associated with change in blood pressure. Centrally located body fat appears to be a more important determinant of blood pressure elevation than peripherally located body fat, although not exclusively so. It has been estimated that 60% of hypertensive people are more than 20% overweight.[136] In overweight hypertensive

people, blood pressure may be reduced by weight loss even when sodium chloride intake is not reduced. For example, in one study in which dietary salt was not restricted, blood pressure decreased to normotensive levels in 75% of obese hypertensive patients after an average weight reduction of 10 kg.[137] Based on pooled results of controlled dietary intervention trials, it has been estimated that a mean change in body weight of 9.2 kg is associated with a decrease of 6.3 mm Hg in systolic blood pressure and a decrease of 3.1 mm Hg in diastolic blood pressure.[138] Moreover, a significant fall in blood pressure will frequently occur even with only modest weight loss.

Obesity-related hypertension is often associated with insulin resistance and hyperinsulinemia. Indeed, recent preliminary evidence suggests that some nonobese patients with essential hypertension are insulin resistant and hyperinsulinemic.[139] Obesity, especially central obesity, is also associated with other cardiovascular disease risk factors, including dyslipidemia, low HDL levels, and diabetes.[140] Thus, weight reduction is an important recommendation for overweight hypertensive people. Furthermore, avoidance of obesity beginning early in life, or supervised weight reduction for those above their desirable weight, is strongly recommended. Moderate exercise is a useful adjunct to caloric restriction in a weight control program.

Sodium Chloride

Evidence for an association between sodium chloride intake and blood pressure is based on both epidemiological observations and clinical trials of sodium chloride restriction. Within populations, correlations of blood pressure with intake of sodium chloride are modest or nonexistent. However, evidence for a relation between sodium chloride intake and blood pressure is more convincing in studies across populations. A recent study, Intersalt, described the relation between standardized measurements of blood pressure and 24-hour urinary sodium and potassium excretion in more than 10 000 people at 52 centers around the world. Two principal findings of Intersalt were (1) a decrease of 100 mEq/d (2.4 g sodium chloride/d) in sodium intake is associated with a 2.2-mm Hg decrease of systolic blood pressure, and (2) a 100-mEq/d lower sodium intake is associated with attenuation of the rise of systolic blood pressure that occurs between the ages of 25 and 55 by 9 mm Hg.[141] Although these modest differences in blood pressure may not appear to have much consequence in an individual, when extrapolated to the general population these small changes have potentially important public health consequences for the prevention of cardiovascular disease.

Results of therapeutic trials of sodium chloride restriction document a modest but significant reduction of blood pressure. In a review of 23 randomized trials including a total of more than 1500 subjects, salt restriction in hypertensive people reduced systolic blood pressure by an average of 4.9 mm Hg and diastolic blood pressure by 2.6 mm Hg; in normotensive people the reductions were 1.7 mm Hg and 1.0 mm Hg, respectively.[142] In trials lasting 5 weeks or longer involving people aged 50 to 59, a 50 mEq/d reduction of sodium intake was associated with a reduction in systolic blood pressure by an average 5 mm Hg and with a reduction of 7 mm Hg in those with high blood pressure; diastolic pressure was lowered by about half as much.[142]

Interactions of sodium with other ions. Dietary intake of other ions may modify the blood pressure response to sodium. In both animal models of salt-sensitive hypertension and in humans it appears that blood pressure is not increased by a high intake of sodium when it is provided with anions other than chloride.[143,144] Although most dietary sodium is consumed as sodium chloride, it is possible to consume relatively large amounts of sodium without chloride, for example in sodium bicarbonate and monosodium glutamate. Consequently, recommendations for sodium intake should specifically refer to sodium chloride. High dietary intakes of calcium and potassium may each attenuate the sodium chloride–induced rise of blood pressure in humans,[145-148] although there is insufficient data to recommend consumption of calcium or potassium in excess of the Recommended Daily Allowance to lower blood pressure.

Individual response to sodium chloride. Within populations, individuals vary in their response to dietary sodium chloride. Genetic, demographic, and physiological markers of salt sensitivity are being investigated. The most convincing evidence for genetic susceptibility to sodium chloride is derived from animal studies.[144] In humans, there also may be a familial predisposition to salt sensitivity, although reliable genetic markers are not yet available. A higher prevalence of salt sensitivity is seen in blacks, obese people, older people, and people with higher levels of blood pressure.[146,147]

Opinion is divided concerning the recommendation that the entire population avoid excess consumption of sodium chloride. Arguments for this recommendation are that current intake far exceeds physiological needs; the tendency for blood pressure to increase with a high sodium chloride intake occurs over the entire population; and identification of salt-sensitive people is neither practical nor economically feasible at present. Arguments against this recommendation are that there is limited or no proven benefit of such restriction for a large segment of the population; potential benefit is restricted to salt-sensitive hypertensive people; and there are potential (although undocumented) adverse health consequences of sodium chloride restriction to people who sweat excessively from exercise or salt-losing diseases.

The AHA recommends that the general public, especially blacks and those with a family history of hypertension, limit intake of sodium chloride and specifically that intake not exceed 7.5 g/d. This amount contains 3.0 g sodium or 127 mEq sodium. However, a more liberal sodium chloride intake is advised during conditions of excessive sodium chloride loss, for example diarrhea, vigorous exercise in a hot environment, high fever, and rare salt-losing conditions. A therapeutic trial of more rigorous salt restriction is advised for hypertensive people who are most likely to be salt sensitive.

Alcohol

In recent years alcohol intake has been recognized as an important, independent correlate of blood pressure. A number of cross-sectional studies have documented a small but significant elevation of blood pressure, compared with nondrinkers, in people consuming three or more drinks per day. Consumption of more than two

drinks per day has been estimated to account for 5% to 7% of cases of hypertension; the effect in men is greater than in women.[150] Several short-term studies suggest a therapeutic benefit of decreasing alcohol consumption in hypertensive people. In controlled studies, reduction of alcohol consumption has been associated with a reduction of 4 to 8 mm Hg in systolic blood pressure and a lesser reduction of diastolic pressure.[151] The blood pressure of normotensive people may also decrease in response to a reduction of alcohol consumption.[152] Because of the effect of alcohol on blood pressure, intake should not exceed two drinks per day.

Other Important Concerns

The above comments underlie the rationale for making diet recommendations for the prevention of cardiovascular diseases. These recommendations are the result of years of deliberations within the AHA, and there is not universal agreement on every aspect of the final statement. Areas of controversy and concern about the AHA's recommendations are addressed below.

Is the AHA diet nutritionally adequate?

In some underdeveloped, nonindustrialized parts of the world where a low-fat, high-carbohydrate diet is consumed, malnutrition is common. This finding has led to questions about the nutritional adequacy of the modified-fat diet recommended by the AHA. The AHA recommendations have always stressed the importance of a well-balanced, nutritionally adequate diet. Extensive analysis of possible menus has shown that the diet recommended by the AHA can easily be made adequate in protein, vitamins, and minerals and need not be deficient in any required nutrient. A diet with 25% to 30% of calories consumed as fat has more fat than the Japanese diet, in which only 20% to 25% of calories are consumed as fat, and life expectancy in Japan exceeds that in the United States at every age.[109] Italians, who eat less saturated fat than recommended in the AHA diet, also have somewhat better life expectancy.[153] Consumption of a wide variety of foods should ensure adequate intake of all macronutrients and micronutrients.

Is the AHA diet appropriate for growing children and adolescents?

The AHA, the National Cholesterol Education Program Panel on Population Strategies, and recently the National Cholesterol Education Program Pediatric Panel have recommended that all Americans older than 2 years reduce their intake of fat, saturated fat, and dietary cholesterol to levels recommended by the AHA. Questions have arisen about the safety of restricting fat and cholesterol intake by children and adolescents. Infants (under 2 years old) are excluded from the recommendation because there are no data on the safety of low-fat diets in infancy and a higher percentage of calories from fat may be needed during this period of rapid growth. Children between the ages of 2 and 4 can gradually adopt the diet habits of the family. The Recommended Daily Allowances for zinc, iron, and calcium are relatively high for toddlers and adolescents, so they should consume adequate amounts of foods providing these nutrients, especially lean red meat, low-fat dairy products, cereal products, and legumes. The primary emphasis of diets for children is on providing adequate calories and nutrients for normal physical activity, growth, and development. This recommendation can easily be achieved while following the AHA dietary recommendations. The recommended diet is reasonable, emphasizing a variety of foods and adequate calories that meet the Recommended Daily Allowances and provide for optimal growth and development. Several studies of American children have demonstrated the safety of the diet for those over 2 years old.[154] In addition, in some countries, such as Israel, where children eat diets similar to the AHA diet, children are in good health and attain the same body size as Americans.[155]

Is the AHA diet effective in reducing plasma lipid levels and risk of CHD?

The effects of dietary change on blood cholesterol levels, and especially on LDL cholesterol level, have been evaluated in controlled metabolic studies,[156] clinical trials,[157,158] and community programs.[22,157,158] In community studies, when there is no intensive nutritional program the decrease in serum cholesterol levels has generally been about a third of this estimated decrease because of incomplete adherence to dietary recommendations.[159] More intense dietary intervention programs have resulted in much greater decreases in serum cholesterol and LDL cholesterol levels.[40] A greater reduction in plasma cholesterol level may be obtained by concomitant weight reduction in overweight people. Calculations suggest that reduction of the intake by the US population of saturated fatty acids from 13% to 14% to 10% of calories and of cholesterol to less than 300 mg/d will result in a reduction of 5% to 10% in mean serum cholesterol level from the previous level of approximately 210 mg/dl.

The potential effect of a change in serum cholesterol level and risk of CHD deaths has been estimated in several recent studies. The follow-up of the Multiple Risk Factor Intervention Trial 361 000 screenees suggests that a 1% reduction in serum cholesterol level will result in about a 2% reduction in CHD risk.[157] This may be an underestimation because of regression to the mean and the variability of a single cholesterol measurement; the reduction in CHD risk may be closer to 3% per 1% reduction in serum cholesterol level. Similar expectations (ie, a 2% reduction in risk for each 1% reduction in serum cholesterol level) have been estimated from clinical intervention trials such as the Lipid Research Clinics Primary Prevention Trial.[21]

Therefore, a 5% to 10% populationwide reduction in total plasma cholesterol levels might result in a 10% to 20% (or greater) reduction in the incidence of CHD. The risk of CHD death is curvilinearly related to blood cholesterol levels. Among the MRFIT screenees, the 10-year risk of CHD death increased from 1% for those with cholesterol levels of 180 to 189 mg/dl to 4.3% for those with cholesterol levels greater than 300 mg/dl. However, 20% of CHD deaths among men aged 35-57 at entry occurred in those with blood cholesterol levels less than 200 mg/dl, and about 60% were in those with cholesterol levels less than 240 mg/dl. Although the risk of coronary atherosclerosis is directly related to serum cholesterol level in both nonhuman primates[55] and humans,[160] there is substantial variation in the extent of atherosclerotic disease at any level of serum cholesterol

in a population. Therefore, even people with cholesterol levels of less than 200 mg/dl may have extensive atherosclerosis and be at risk of a heart attack. This increased risk may be related to other risk factors such as high blood pressure, cigarette smoking, and low HDL levels or to genetic susceptibility to atherosclerosis.[161-164] Therefore, a reduction in risk of CHD in most adults in the United States is likely to result if plasma cholesterol levels are lowered by further dietary modification.

The full effect of dietary change on serum cholesterol levels may not be predictable from equations derived from short-term diet studies conducted on the metabolic ward. Lifelong adherence to a diet low in total calories, saturated fats, and cholesterol and providing only calories sufficient for maintenance of desirable body weight may result in a greater lowering of cholesterol levels than that observed in short-term dietary studies. Evidence for a long-term effect of diet is found in special groups of people whose mean cholesterol levels are lower than would be predicted from equations developed on the metabolic ward. One such group is composed of vegetarians in a Boston commune who eat principally whole grains, beans, and fresh vegetables. Their total and LDL cholesterol levels were 31% and 38% lower, respectively, than age-matched controls.[165] In another report plasma total and LDL cholesterol were found to be 33% and 45% lower in male and female vegetarians.[166] The findings in these two groups of American vegetarians suggest that the relatively low mean cholesterol levels in these populations consuming very low intakes of saturated fats and cholesterol are due more to dietary effects than to racial or major genetic factors. The effect of diet on plasma cholesterol level and cardiovascular risk is also supported by the results of the Ni-Hon-San study, in which plasma cholesterol levels and cardiovascular disease risk in Japanese immigrants were progressively higher in Japan, Hawaii, and the West Coast of the United States.[109]

Another phenomenon possibly reflecting the long-term effect of diet is the increase in plasma cholesterol level that occurs with aging in the US population compared with populations in countries in which there is much less CHD. In US men the increase in serum cholesterol level is greatest in young adults until about age 45, while in US women the increase in total and LDL cholesterol levels is accentuated after menopause and probably continues to about age 65.[167] The mean serum cholesterol level of women increases from 195 mg/dl at age 35 to 44 to 217 mg/dl by age 45 to 54 to 237 mg/dl by age 55 to 64. Approximately 85% of 65- to 74-year-old women have serum cholesterol levels greater than 200 mg/dl, and 50% have cholesterol levels over 240 mg/dl. The increase in cholesterol level with age may be universal but appears to be less in other populations consuming diets with a lower content of saturated fatty acids, cholesterol, and calories than the typical US diet. High-cholesterol and saturated fatty acid–rich diets may suppress the LDL receptors. Dietary factors, especially saturated fat and cholesterol, as well as weight gain,[168] are important determinants of this increase in cholesterol level with age in both men and women. Prevention of atherosclerosis and heart attack should emphasize not only reducing the serum cholesterol level but also preventing the rise in serum, total, and LDL cholesterol levels that occurs in both sexes with increasing age. The first line of defense against high serum cholesterol level should therefore be a reduction in the intake of saturated fat and cholesterol and an attempt to prevent obesity.

Finally, the possibility must be considered that diet influences CHD by mechanisms other than plasma and LDL cholesterol levels. Perhaps other independent effects of diet are related to hypertension, interactions of lipoproteins and circulating blood cells with the artery wall, blood clotting, and susceptibility of lipoproteins to oxidative modification. For example, monounsaturated fatty acids in lipoproteins are resistant to oxidation, which may also be influenced by dietary antioxidants. However, there are insufficient data about the relationships among dietary antioxidants, oxidative modification of lipoproteins, and atherosclerosis for specific recommendations to be made at present. There also is the possibility that the link between diet and CHD may not be reflected entirely by fasting plasma lipid concentrations, particularly because postprandial lipoproteins may play a role in atherogenesis.[169]

Does the AHA diet overemphasize serum cholesterol and minimize other risk factors?

Because atherosclerosis is a multifactorial disease, the focus of the AHA dietary recommendations on factors that influence plasma total and LDL cholesterol levels has been questioned. However, the other major cardiovascular risk factors appear to play an atherogenic role against a background of high cholesterol levels. Their impact is markedly reduced in populations in whom plasma total and LDL cholesterol levels are low. For example, despite heavy cigarette smoking and a high incidence of hypertension, CHD incidence is much lower in Japan, where average cholesterol levels are low, than in the United States.[170] Although in Japan diabetes leads to accelerated development of atherosclerosis, the incidence of macrovascular complications in Japanese diabetics is considerably lower than in their American counterparts.[171] Therefore, if LDL cholesterol blood levels can be reduced by dietary means, the risks attributable to other factors may be lessened significantly. This is not to say that modification of other risk factors is not important, and from a practical point of view, such modification may profoundly influence cardiovascular risk in the US population. However, it is likely to yield the most benefit if plasma cholesterol levels are lowered simultaneously. Furthermore, the AHA diet is also designed to reduce blood pressure, and it stresses the importance of maintaining desirable weight.

Is the AHA diet practical for the US population?

The AHA diet is recommended for all healthy people over the age of 2. There is virtually unanimous agreement that saturated fatty acid intake should be reduced in the population. Most experts agree that a reduction in saturated fatty acid intake to less than 10% of calories should be the goal. Reduction in total fat intake to less than 30% of total calories is also recommended by many expert groups. According to the National Research Council, "[i]ntake of total fat per se, independent of the relative content of the different types of fatty acids, is not associated with high blood cholesterol levels and coronary heart disease."[15] A reduction in

saturated fatty acid consumption will lead to a lower fat intake, which is hypothesized to reduce the risk of certain cancers and possibly of obesity.

Only a small proportion of the US population, probably about 10% to 12%, meets the AHA recommendation for an intake of saturated fatty acids less than 10% of calories and of total fat less than 30% of calories. However, the intake of calories from both total and saturated fat is decreasing, so the AHA diet is an extension of ongoing dietary trends in the United States. With the availability of low-fat dairy products and low-fat meats, following the recommendations the AHA diet is feasible and does not require major changes in national eating patterns. Fast-food stores and restaurants frequently provide low-fat choices, and there should be a continued effort to reduce the relatively high fat content of the meals provided as part of the school lunch and breakfast program. From the standpoint of cost, most people can meet the AHA diet recommendations at no more expense than for the current typical US diet, which contains sizable quantities of relatively expensive animal products. There is a clear need for continued and expanded diet and health education.

Does weight reduction affect serum cholesterol and CHD independently of changes in diet composition?

The effect of obesity on cholesterol levels appears to vary substantially among individuals and has not been studied extensively as an independent contributor to hypercholesterolemia; neither has it been established whether the hypercholesterolemia induced by obesity is different in women than in men or even whether age modulates plasma lipid and lipoprotein response to obesity. Nonetheless, obesity is a contributing risk factor for CHD in men and women.[172] Achieving and maintaining desirable weight should be a goal for all people.

Weight loss is associated with a reduction in VLDL levels and an increase in HDL levels; the effect on LDL is variable and difficult to distinguish from changes in the fatty acid content of the diet. Weight loss can also reduce CHD risk factors such as blood pressure[17] and carbohydrate intolerance, but its independent effect in preventing CHD is unknown. Nonetheless, obesity is a risk factor for CHD, and because sustained weight loss can lead to an improvement in the risk factor profile, weight control, although difficult to achieve, is a potentially important component of cardiovascular risk reduction.

Is the AHA diet necessary for people at low cardiovascular risk?

The AHA diet is targeted mainly toward members of the population who are at increased risk for cardiovascular disease because of their serum lipid and lipoprotein levels, blood pressure, family history, or presence of other cardiovascular risk factors, all of which are prevalent in the United States. People with none of these risk factors may not benefit from the AHA diet because they are already at reduced risk. However, it is not always possible to accurately predict whether a person is at risk for cardiovascular disease, especially if risk factors have not been carefully assessed. Therefore, the AHA has adopted a population-based (public health) approach that targets the entire population. However, a person who has been determined to have desirable serum lipid and lipoprotein levels, no cardiovascular risk factors, no family history of cardiovascular disease, and is of optimal weight has less need for the AHA diet than a person with a higher serum cholesterol level or other evidence of increased cardiovascular risk. However, periodic reevaluation is advisable even for the person at low risk.

Is there a wide variability of response to the AHA diet?

There is considerable variability of response to reduction in intake of saturated fatty acids and especially of cholesterol. Furthermore, variability in laboratory results and biological variability in serum cholesterol levels have hampered evaluation of the response to dietary changes in individuals.[173,174] Nonetheless, some are likely to vary more in their response to dietary changes than are others.[65] Unfortunately, there are no simple ways of determining whether an individual is a hyperresponder, hyporesponder, or nonresponder to dietary change. In general, people with higher cholesterol levels are likely to benefit more from dietary measures than are those with low baseline levels.[175-177]

Is there a role for the AHA diet for people with genetic forms of hyperlipidemia?

Although many people with genetic forms of hyperlipidemia require drug treatment for management of the disorder, a low–saturated fat, low-cholesterol diet and maintenance of desirable body weight are important adjuncts to their management. Such people may require a greater reduction in saturated fatty acids (to 7% of calories or less) and cholesterol (to 200 mg/d or less) for optimal reduction in their serum cholesterol levels. The effects of diet and drug therapy on serum total and LDL cholesterol are independent and additive.[178] Consumption of a low–saturated fat, low-cholesterol diet may also help reduce the dose of drug required. Of the genetic forms of hyperlipidemia, only familial hypercholesterolemia is consistently expressed in childhood. Therefore, it is especially prudent for children and adolescents from high-risk families to restrict their intake of saturated fatty acids and cholesterol because of the possibility that they may develop manifestations of a genetic hyperlipidemia later in life.

Are there potential dangers in increasing polyunsaturated fatty acid intake as part of the AHA diet?

The cornerstone of the AHA diet is a reduction in the intake of saturated fatty acids. Limiting saturated fatty acids to less than 10% of calories and total fat to less than 30% of calories requires partial substitution with polyunsaturated fatty acids, monounsaturated fatty acids, and carbohydrates. Although polyunsaturated fatty acids appear to have an independent cholesterol-lowering effect,[179] the AHA recommends that polyunsaturated fatty acids (both omega-6 and omega-3) be limited to no more than 10% of calories, especially because no free-living population consumes more than this amount. There are theoretical concerns that excessive intake of polyunsaturated fatty acids might increase the risk of cancer, accelerate the aging process, or even

accelerate atherogenesis because these fatty acids are susceptible to lipid peroxidation.[69] However, there is no evidence that any of these consequences occur in humans at the levels of polyunsaturated fatty acid intake recommended by the AHA.

Does the AHA diet not go far enough? Should the AHA recommend very low-fat diets?

Countries in which the population consumes diets very low in fat, such as Japan, have much lower rates of CHD than does the United States.[180,181] These differences are confounded by other variables such as differences in weight and alcohol consumption. Recently, very low-fat diets have been advocated for the treatment of patients with established coronary artery disease.[182] Although preliminary results look promising, interpretation is difficult because of the very high dropout rate during randomization, the small number of people in the studies, and the many other changes, such as in body weight, exercise, cigarette smoking, and stress management, that take place concurrently.

There is little information about the potential value of such diets for the US population. Low-fat vegetarian diets are associated with low serum lipid and lipoprotein levels, and communities that habitually consume such diets have strikingly low CHD rates, but consumption of very low-fat diets requires major lifestyle changes. Such changes cannot be made without major commitment and extensive education to ensure adequacy of nutrient intake. The positive effect of these very low-fat diets may be due to the fact that they are very low in saturated fat. Although such diets may be beneficial for some patients with established CHD, and nutritionally sound low-fat vegetarian diets are generally associated with low serum cholesterol levels and CHD rates, the AHA believes that there is insufficient justification to recommend widespread consumption of very low-fat diets by the entire US population.

Are low cholesterol levels, such as may result from following the AHA diet, associated with an increased risk of cancer, suicide, homicide, or accidents?

A major concern is whether low cholesterol level or decreases in cholesterol level by diet or drug therapy increases other risks, especially those for cancer, suicide, homicide, and accidents. The association between low serum cholesterol level and some diseases has been noted in several large cohort studies that have followed up subjects for many years. In the 10-year follow-up of the Multiple Risk Factor Intervention Trial screenees, the total mortality rate was 5.4% in those with a serum cholesterol level less than 140 mg/dl, declined to 3.8% for those with a serum cholesterol level of 170 to 179 mg/dl, and then increased to 9.1% for those with a serum cholesterol level greater than 300 mg/dl. An increase in non-CHD mortality has also been reported for people with cholesterol levels less than 160 mg/dl in other studies. The reason for the small increase in total mortality in people with very low cholesterol levels has generated a great deal of interest. Factors that may account for a low serum cholesterol level in some people consuming a typical American diet include, first, genetic variations in lipoprotein metabolism. It is possible that genetic factors that contribute to low serum cholesterol levels may also be related to increased risks for other diseases. A second and more likely reason for the relation between very low cholesterol and increased morbidity and mortality is that certain diseases or environmental factors contribute to both a low cholesterol level and an increase in risk for mortality. These diseases include cancer and certain infectious diseases that often result in a substantial decrease in cholesterol level long before there are clinical manifestations of the disease. Also, people with liver disease or excessive intake of alcohol have lower-than-average cholesterol levels.

There is no evidence of any excess mortality among populations such as vegetarians who normally consume a very low-fat, low-cholesterol diet and have low serum cholesterol levels or in international populations with low serum cholesterol levels compared with those with higher serum cholesterol levels. There is also no clear evidence in these populations that low serum cholesterol levels are causally related to suicide, homicide, cancer, or other adverse events.

It is important to evaluate the potential ill effects of any new drug therapy that lowers serum cholesterol level. To date, however, there is little evidence of any relation between cholesterol-lowering drugs and increased risk for cancer and other diseases, although an increase in homicides and suicides has been reported in some studies.[183]

Research is needed to determine the reasons for low cholesterol levels of some people consuming a typical American diet, the possible mechanisms for these low levels, and their relation, if any, to other diseases. Nevertheless, the benefits of reducing risk for heart attack by lowering serum cholesterol levels clearly outweigh even a potential small risk for other diseases.

How does the AHA diet affect serum HDL level?

A high serum HDL level is associated with a lower risk of CHD, but there is little evidence that serum HDL level can be raised by dietary changes. Nonsmokers who are lean and physically active tend to have higher serum HDL levels than smokers who are overweight and sedentary. Polyunsaturated fatty acids and monounsaturated fatty acids both have a neutral effect on HDL levels in the long term.[81,184] There is some evidence that high intake of carbohydrates may be associated with lower serum levels of HDL.[83] This effect may be transient in some people. However, if the increase in carbohydrate intake is accompanied by a substantial reduction in intake of saturated fatty acids, then the serum LDL level is reduced concurrently, with a net reduction in the LDL/HDL ratio. There is no evidence that the reduction in serum HDL level associated with a low-fat, high-carbohydrate diet has any adverse effect on risk for CHD. Furthermore, populations who consume low-calorie, low-fat, high-carbohydrate diets have low CHD incident rates compared with rates in the United States.[34]

The risk of lowering serum HDL level may be different for women than for men. For example, in women, serum HDL level is a stronger CHD risk predictor than is serum LDL level.[185] Therefore, further studies are required to determine the significance for women of consuming diets that may potentially reduce HDL levels. However, the AHA diet, which emphasizes a mod-

est restriction in fat intake, does not appear to reduce serum HDL level.

What is the rationale for recommending the AHA diet to children?

The AHA recommends that a diet low in saturated fat should be started after a child reaches the age of 2, with a gradual reduction of fat intake as the child begins to eat with the family. As discussed earlier, consumption of a wide variety of foods should ensure nutritional adequacy of the diet. No studies provide proof that lowering blood cholesterol levels in children by decreasing the saturated fatty acid and cholesterol content of the diet will reduce the risk for CHD in adulthood. However, evidence is accruing that atherogenesis may be influenced by diet, even in children. Both animal and human studies have shown that preatherosclerotic and atherosclerotic lesions can occur during childhood, and the extent of lesions is directly related to blood cholesterol level.[186] Lipid levels tend to cluster in children and adults in families with a high prevalence of premature CHD.[187] Children from these families are likely to be at risk for atherosclerotic complications. Blood cholesterol levels are high in children in countries in which there is a higher intake of fat (especially of saturated fat) and in which the incidence of CHD in the adult population is high. Several studies have shown that serum cholesterol levels tend to track from childhood into the young-adult years. Therefore, many children with high blood cholesterol levels will have high levels as adults.[188]

The evidence suggests that high serum cholesterol levels in childhood can be associated with high cholesterol levels and CHD in later years and supports the desirability of lowering blood cholesterol levels in children. Although benefit to children might not be immediately apparent, good dietary habits and lower serum cholesterol levels carried into adulthood could contribute significantly to the prevention of CHD. Furthermore, healthy eating patterns established in childhood are likely to be easier to continue during adult life.

Are specific recommendations to reduce blood pressure necessary for the entire population?

As discussed earlier, the AHA's recommendation to limit salt intake has general but not universal agreement. It is clear that nutritional factors other than salt, especially obesity and ethanol consumption, also play important roles in determination of blood pressure and therefore need to be included in recommendations aimed at reducing blood pressure. It is also acknowledged that reduction in blood pressure as a result of control of salt intake may be modest or even nonexistent in many people who are not salt sensitive. However, because methods for readily detecting salt sensitivity are not available, the AHA has recommended that the US population limit its intake of salt to help reduce blood pressure in members of the population who are salt sensitive. Furthermore, because the estimated benefits of a population's controlling salt intake in reducing cardiovascular events are substantial, and since the population is consuming salt far in excess of biological need, the AHA considers its recommendation to limit intake of sodium chloride good public health policy.

Summary of AHA Strategy for Dietary Modification of CVD Risk

The AHA believes that the most reasonable strategy for the prevention of cardiovascular disease should include both a population-based public health approach that recommends a generalized diet change for all healthy Americans and a high-risk approach that identifies and treats individual patients who have unusually high serum lipid levels or other risk factors.

It should be stressed that the generalized diet change recommended for the healthy US population is a moderate eating pattern, that it is a continuation of ongoing national trends, and that it is nutritionally adequate. A diet containing less total fat, saturated fatty acids, cholesterol, sodium chloride, and alcohol is likely to lessen CHD risk; therefore, a continued change toward such a diet seems prudent. There is almost uniform agreement that controlling intake of calories to achieve desirable weight is likely to have significant health benefits. However, maintenance of weight loss is often difficult and will require increased levels of physical activity for the population at large.

With the high-risk approach, people with modifiable risk factors are identified and treated. The guidelines of the National Cholesterol Education Program and the Joint National Committee on High Blood Pressure Control provide simple, practical approaches to the detection, evaluation, and treatment of patients at increased cardiovascular disease risk. Goals of this high-risk approach include educating the public about cardiovascular disease risk factors, urging people to have their cholesterol levels and blood pressure checked, and educating physicians about the detection, evaluation, and management of high blood cholesterol levels and hypertension. The National Cholesterol Education Program recommendations enable physicians to detect those who are at high risk because of their blood cholesterol levels. The AHA diet for the general population should then be followed by the patient, with the physician giving close attention to counseling, monitoring, and follow-up. When used therapeutically, the diet is referred to as the Step I diet. If the Step I diet alone fails to reduce LDL cholesterol to the target level, more stringent dietary therapy should be prescribed (Step II diet) to further reduce saturated fatty acids and cholesterol. For patients with genetic forms of hyperlipidemia, the Step I diet will usually result in only a modest reduction in plasma and LDL cholesterol levels. Dietary change alone is unlikely to be sufficient to bring plasma lipid levels into the desirable range. Often, the Step II diet combined with drug therapy, as outlined in the National Cholesterol Education Program Adult Treatment Panel guidelines, will be required to lower LDL cholesterol to target levels. Similarly, blood pressure may be controlled by weight control and diet alone in some patients with hypertension, although many will also require drug treatment. However, diet should be considered an important adjunct for the treatment of both hypercholesterolemia and hypertension, because it may lessen the dosage for patients who require drug therapy.

In summary, simultaneous education of the general public about hygienic measures to reduce cardiovascular disease risk (ie, a population-based approach) and of

physicians about detection and modification of risk factors (ie, the high-risk approach) is the most appropriate approach to the prevention of cardiovascular disease.

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