Optimal Nutrition for the Prevention of Coronary Heart Disease: A Worldwide Challenge

The worldwide spread of the coronary heart disease (CHD) epidemic is, in part, related to unfavorable changes in dietary patterns in the developing world. Much has been learned about optimal nutrition for the prevention of CHD. These lessons can, and should, be applied to countries where the burden of CHD is rapidly increasing, in order to help slow the progression of the CHD epidemic, to save many lives, and to prevent considerable disability worldwide. (*Ethn Dis.* 2003;13[suppl2]: S2-91–S2-96)

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Introduction

Coronary heart disease (CHD) remains the leading cause of death in the United States, despite dramatic improvements in the prevalence of risk factors and care for the disease. Projections suggest that this epidemic is spreading, rather than receding, worldwide. By 2020, CHD is predicted to be the leading cause of death and disability, not only in the developed world, but also in the developing world ("emerging market economies").[1] One of the principal reasons for the spread of this epidemic is changing dietary patterns in developing countries. It is widely accepted that lifestyle modification represents the cornerstone of CHD prevention, through control of tobacco addiction, consumption of optimal diets, and increased physical activity. Pharmacological control of lipid abnormalities and elevated blood pressure is not economically viable in much of the developing world. Accordingly, it is reasonable to review contemporary information on optimization of diet for control and prevention of CHD in populations at risk.

For almost a century, the relationship between diet and CHD has been the subject of intensive study. In Russian studies, atherosclerosis was produced in rabbits fed a diet high in cholesterol and saturated fat.[2] In the following decades, animal studies using different models conclusively demonstrated a relationship between dietary intake of cholesterol and fat, and the production of atherosclerosis. Epidemiologic studies have also suggested a strong relationship between a population's consumption of fat, and its prevalence of atherosclerotic vascular disease. Contemporary basic clinical and epidemiologic research now suggests a wide array of biological inter-mediaries, which are influenced by diet, and are capable of increasing CHD risk (Table 1). Clearly, the role of diet is far more complex than that suggested by the original diet/heart hypothesis. As recently reviewed by Hu and Willett,[3] multiple dietary pathways are involved in the promotion of cardiac health and illness, with many different nutrients implicated in the process by epidemiologic and clinical investigations. What has been learned about the role of these nutrients in cardiovascular disease in Western populations can, and should, be applied to our understanding of the emerging CHD epidemic in non-Western societies. By applying the dietary knowledge gained over the last several decades, we now have the opportunity to slow the advancing burden of CHD worldwide, and, indeed, to prevent considerable death and disability. Therefore, it is appropriate to review our understanding of diet's potential role in CHD prevention, specifically focusing on diet interventions that are likely to be applicable in the developing world.

Population Studies

The 7-country study directed by Ancel Keys, and begun in the early 1950s, is the landmark epidemiologic study associating diet with cardiovascular outcomes.[4] The findings of the 7-country study demonstrated that populations differing in dietary fat consumption also differed in concentrations of blood cholesterol and in CHD rates. Sixteen different cohorts were studied from 7 different countries around the world, and the 10-year CHD death rate (among individuals free of disease at the time the study was initiated) was found to be highly correlated with the total cholesterol values of the cohorts themselves. These cholesterol levels were, in turn,
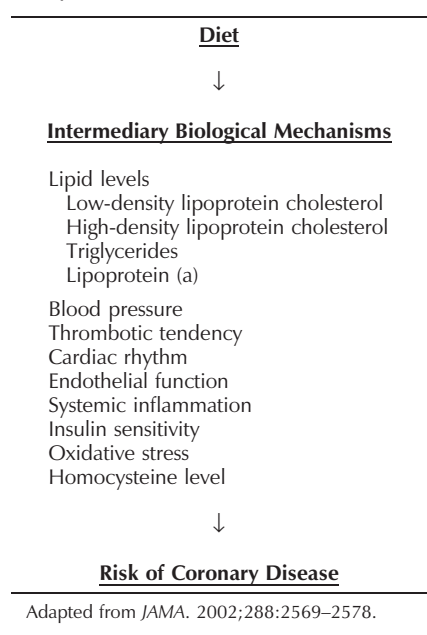
One of the principal reasons for the spread of this epidemic is changing dietary patterns in developing countries.

highly correlated with the dietary fat and cholesterol consumption of the populations studied. More than any previous work, this landmark series of studies verified conclusions from prior smaller studies that diet, blood cholesterol levels, and CHD mortality were critically linked.

Many cultures whose food supply is entirely, or largely, plant-based have low or absent rates of CHD.[5] For example, a great many rural Chinese have lived for many years without any recorded incidence of myocardial infarction.[6] Conversely, it has been recognized for some time now that individuals of Japanese ancestry developed progressively greater atherosclerotic burden as they moved eastward from Japan to Hawaii and to the West Coast of the United States.[7] While multiple factors are likely responsible for this increasing incidence of CHD, dietary change is surely a major cause.

In the United States, favorable dietary changes have occurred, likely as a result of combined cultural, economic, legislative, and educational forces. For example, 15-year trends (1980–1982 through 1995–1997) from the Minnesota Heart Survey[8] have demonstrated a nearly 10% decline in dietary fat, with associated decreases in total cholesterol levels and the incidence of hyperlipidemia.[8] Unfortunately, 3 worrisome factors accompany these favorable changes: 1) changes were less marked among women; 2) favorable trends established by the early 1990s have been partially reversed; and 3) the improvement in fat intake is paralleled by an actual increase

Table 1. Potential mechanisms by which diet might influence risk of coronary heart disease

Diet

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Intermediary Biological Mechanisms

Lipid levels
    Low-density lipoprotein cholesterol
    High-density lipoprotein cholesterol
    Triglycerides
    Lipoprotein (a)

Blood pressure
Thrombotic tendency
Cardiac rhythm
Endothelial function
Systemic inflammation
Insulin sensitivity
Oxidative stress
Homocysteine level

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Risk of Coronary Disease

Adapted from *JAMA.* 2002;288:2569–2578.

in total caloric intake.[8] These US observations have important implications for other countries in which the increasing epidemic of obesity is well documented. It has been suggested that the morbidity from obesity may be as great as that from poverty, smoking, or alcoholism.[9] The health risks established to be related to obesity are many, and encompass much more than the risk of CHD (Table 2). Broad constituencies have now come to recognize that the emerging worldwide problem of obesity must be aggressively managed. It is simultaneously tragic and remarkable that starvation and obesity are the greatest nutritional challenges that the world faces. Unfortunately, it appears that in many cultures, as economic conditions improve, the transition from starvation to obesity is abrupt. What can be done to alter this transition so that it leads to better nutrition and optimal weight? It is hoped that our understanding of the role of diet, dietary change, and nutritional components, can inform influential individuals in developing countries, including public officials, medical

Table 2. Obesity and Health Risks

Overweight and obesity are known risk factors for:
    diabetes
    heart disease
    stroke
    hypertension
    gallbladder disease
    osteoarthritis
    sleep apnea and other breathing problems
    some forms of cancer (uterine, breast, colorectal kidney, and gallbladder).

Obesity is associated with:
    high blood cholesterol
    complications of pregnancy
    menstrual irregularities
    hirsutism
    stress incontinence
    psychological disorders such as depression
    increased surgical risk.

Adapted from: www.niddk.nih.gov/health/nutrit/pubs/statobes.htm.

professionals, and educators, so that their populations are given opportunities for nutritional health.

DIET STUDIES

Since 1946, studies of dietary intervention in both the United States and elsewhere have consistently suggested, and, in some cases, clearly demonstrated, improvement in CHD outcomes. Most studies have focused on lower fat (usually lower saturated fat) diets, along with lower dietary cholesterol consumption.[10] Plagued by design, generalizability, and communication problems, the conclusions of these studies have never been widely adopted. Nevertheless, these findings provide lessons worthy of attention. An analysis of multiple dietary studies has focused on dietary shifts, such as those proposed by the National Cholesterol Education Program (NCEP) and the American Heart Association (AHA) over the past decade or two, emphasizing a reduction in dietary total and saturated fat.[10] Among free-living subjects, such dietary changes (adopting the diet suggested by NCEP and AHA) are associated with decreases of 10%–13% in total cholesterol, 12%–

16% in LDL cholesterol, and 8%–20% in triglycerides.[11] These changes could be assumed to result in at least a 10% decrease in CHD events over as short a period as 5 years.

An early example of a study focusing on saturated fat and cholesterol is the Oslo Diet-Heart Study, which randomized over 400 survivors of myocardial infarction to a diet low in saturated fat and dietary cholesterol, and high in polyunsaturated fat, and compared outcomes with those of a usual care group.[12] At the end of the follow-up period there were one-third fewer myocardial infarctions in the intervention group, and a non-significant, but highly suggestive, 26% decrease in CHD mortality. More recent diet intervention trials have focused beyond fat intake to include increases in fish intake, alpha-linolenic acid, and fiber consumption. In the Diet and Reinfarction Trial (DART), over 2,000 men who had suffered myocardial infarction were randomized to usual care, or to an intervention diet consisting of a reduction in fat, and increases in fish and fiber intake. At the end of 2 years, total mortality was reduced significantly by 29%.[13] Similarly, in the Lyon Diet Heart Study, post-MI survivors were randomized to a Mediterranean diet enriched with alpha linolenic acid, consumed partially through a supplement of canola oil-based margarine. The study demonstrated a very impressive 76% decrease in the risk of cardiac death (although the number of deaths were small).[14] Similarly, in the GISSI-Prevenzione Trial, post-MI patients given one gram/day of omega-3 polyunsaturated fatty acids by capsule demonstrated a significant reduction (15%) in the relative risk for cardiac events at 3½ years follow up. The benefit was primarily due to a decrease in death, particularly sudden cardiac death.[15]

Other secondary prevention trials have used coronary stenosis as a surrogate end point, and have demonstrated either regression of coronary artery lesions, or slowing of the progression of coronary atherosclerosis following dietary interventions. None of these studies, however, included dietary interventions alone. Different studies combined dietary interventions with physical activity, cholesterol-lowering medications, or multiple risk factor management strategies.[10] Although these regression trials cannot be cited as examples of direct improvement in atherosclerosis due to dietary interventions, they do, nevertheless, provide a supportive framework for understanding how diet is likely to improve atherosclerotic burden.

DIETARY COMPONENTS

It is reasonable to review the influence of specific, individual dietary components on cardiovascular health, as well as their potential to prevent CHD. More detailed reviews on the evidence base for these individual components have been published elsewhere.[3,16,17] More details on the statements below can be obtained from those references.

Saturated Fat

In populations whose diets are not primarily plant-based, saturated fatty acids are the principal dietary determinant of LDL cholesterol level. The relationship between saturated fatty acid intake and LDL cholesterol level appears to be relatively fixed, so that for every 1% increase in calories from saturated fats (as a percent of total caloric consumption), serum LDL cholesterol rises by about 2%. Similarly, a 1% reduction in saturated fat reduces LDL cholesterol by about 2%. The beneficial consequences of reducing intake of saturated fat has been demonstrated in a wide variety of observational and intervention studies. The relatively high saturated fat intake in Western diets is thought to be one of the major factors for the high population rates of CHD in Western countries. National recommendations for the United States suggest that the current mean saturated fat intake of about 11% of calories be decreased to <7%.[16,17]

Trans-fatty acids, in which double bonds are in the trans-configuration, occur with hydrogenation of vegetable oils, and are also found naturally in certain animal fats. Although the mechanism is incompletely described, prospective studies have strongly supported an association between higher intakes of trans-fatty acids and CHD incidence.[3] It is recommended that intake of trans-fatty acids be kept as low as possible. National regulatory policies, as well as local economic forces, often determine availability and use of substitutes for dairy (butter) spreads. Since margarine and other processed foods have been a major source of trans-fatty acids in Western countries, developing nations should observe this relationship, as similar products find their way to the market, and attempt to limit the trans-fatty content of such products.

Dietary Cholesterol

Although of a lesser impact than dietary saturated fat, dietary cholesterol can also be responsible for increasing LDL. The progressive decline in the intake of dietary cholesterol in the US population, resulting from decreased consumption of high fat meat, eggs, and other high fat dairy products, has contributed to the population's decreasing levels of total cholesterol. Consumption of <200 mg/day of cholesterol is considered optimal for LDL cholesterol control through dietary measures. While eggs remain a relatively inexpensive and reliable source of protein, particularly in poorer countries, strategies to prevent egg consumption from being excessive would likely be reasonable.

Mono- and Polyunsaturated Fat

Space does not permit a review of the detailed actions of dietary mono- and polyunsaturated fats. However, it is now clear that the previous focus on total fat, because of a desire to decrease saturated fat, has inadvertently led us

away from optimal consumption of mono- and polyunsaturated fats, both of which are associated with favorable lipid changes. Ideal sources of mono- and polyunsaturated fats include vegetables, plant oils, and nuts. Consumption of foods rich in these oils is usually possible, and associated with lower rates of CHD in populations where such consumption is relatively high (in the Mediterranean basin). Public policy focusing on the production of foods rich in "good" fats could represent economically, socially, and culturally wise strategies that would be easily supported by public institutions and officials in developing countries.

Carbohydrates

While substitution of carbohydrates for saturated fat can lead to a decrease in LDL cholesterol, increased intake of carbohydrates (particularly in the absence of mono- or polyunsaturated fats) is associated with a decrease in HDL cholesterol, and, occasionally, a dramatic rise in triglycerides. Current national recommendations suggest limiting intake of carbohydrates to no more than 60% of total calories, with lower intake suggested for those with the metabolic syndrome, those with elevated triglycerides or low HDL cholesterol, and in diabetic individuals. Further, intake of carbohydrates should be derived from whole grain products, vegetables, and fruits, whenever possible.

Protein

While dietary protein has only a minimal effect on serum lipids, the specific use of soy proteins, particularly when substituted for animal proteins, appears to lower LDL cholesterol. If the population derives protein largely from animal sources, then egg whites, fish, skinless poultry, and lean meats represent optimal sources.

Fiber

Soluble forms of dietary fiber can reduce LDL cholesterol, probably by their binding actions in the intestines. Accordingly, sources of this type of fiber (eg, oats, guar, pectin, and psyllium), generally low in cost, should be encouraged.

Omega-3 fatty acids derived from marine sources (primarily eicosapentaenoic acid and docosahexaenoic acid), and from flax seeds, canola, or soybean oil (principally α-linolenic acid), appear to have a potential role in the prevention of CHD. Studied for many years in a variety of contexts, it is now clear that relatively high doses of these oils can be used to treat individuals with high levels of triglycerides. Of more practical import in the developing world, it is clear that even modest consumption of fish, or these vegetable oils, appears to be associated with a lower risk of fatal CHD. This effect appears to be due to their anti-arrhythmic potential, and perhaps to the associated decreasing thrombotic tendency, induced by even low-dose consumption of omega-3 fatty acids. This has led the AHA to recommend at least 2 servings of fish per week.[18] Depending on cultural, geographic, and economic circumstances, it is likely that plant sources of these oils will be more accessible in many countries. Populations with access to fresh fish can expect improved cardiac health through consumption of marine-based Omega-3 oils. In both cases, both public policy and business factors could favorably influence the availability of these protective substances.

Folate

Epidemiologic and clinical studies strongly support the role of folic acid in cardiovascular disease prevention.[19] Mechanisms for this association are becoming increasingly clear, and likely involve the metabolism of certain amino acids, particularly homocysteine, as well as effects on endothelial function. Improvement in folate status can be accomplished pharmacologically through vitamin supplementation, a strategy that is likely to be impractical in much of the world. However, nutritional changes which include dietary shifts to include foods rich in folate (citrus fruits and vegetables), or food that is "fortified," may well be more practical in the developing world. The latter strategy has been deployed in the United States, and its impact is evident from Framingham Heart Study data, which demonstrate a significant increase in folate levels among middle-aged and older adults, since this national fortification program was begun in 1998.[20]

Antioxidants and Vitamins

A considerable body of experimental evidence points to the role of oxidative stress in the development of atherosclerosis, with the oxidation of LDL being important in both the development and progression of CHD. Large observational studies have suggested that diets high in antioxidant-rich foods are associated with reduced risk of CHD. A controlled trial from China found a slight (nonsignificant) decrease in CVD mortality among individuals receiving beta carotene, Vitamin E, and selenium supplements.[21] However, a series of large-scale randomized trials have now demonstrated, at least in Western populations, that antioxidant supplements, particularly Vitamin E and beta carotene, do not reduce risk of CHD. Antioxidant supplements are, therefore, not recommended, although diets rich in antioxidants are recommended.

Alcohol

It is likely that alcohol has a dual impact on cardiovascular disease. Many observational studies have reported that moderate alcohol consumption (no more than 2 drinks/day for men, and one drink/day for women) is associated with reduced risk for CHD in middle-aged and older adults. Putative mechanisms include a favorable impact on HDL cholesterol and potential improvement in hemostatic factors. Greater than moderate levels of alcohol consumption, however, increase cardiovascular and

non-cardiovascular complications. High alcohol intake (typically ≥3 drinks/day) is associated with elevated blood pressure, which can be reversed by drinking less. Greater than moderate alcohol intake can also lead to caloric excess, with its additional impact on cardiovascular risk. The non-cardiac dangers of over-consumption of alcohol are well known. Accordingly, in cultures with generally low alcohol consumption, it would not be reasonable to institute policies or provide incentives to decrease alcohol consumption. In societies where alcohol consumption is ingrained in the culture, however, efforts to prevent excess alcohol consumption are strategically wise for a broad range of public health issues.

Salt (sodium chloride) Intake

A preponderance of evidence indicates that a high intake of salt adversely affects blood pressure, and, therefore, cardiovascular risk. Reducing sodium intake can both prevent hypertension in persons at risk, and can improve control of hypertension for those with elevated blood pressure. While the desire for highly salted food is likely an acquired cultural phenomenon, it is not one that is easy to reverse. Optimal population strategies to control salt intake would involve policy and business incentives to reduce the large amount of non-discretionary salt added during the course of food processing; in addition, legislative and policy forces can pressure food manufacturers to reduce the amount of salt present. Racial differences in hypertension are well known, and populations with higher incidence rates of hypertension would be well served by increased public focus on salt consumption. In addition, controlled trial evidence (the DASH trial) has demonstrated that dietary patterns high in fruits, vegetables, low fat dairy products, whole grains, poultry, fish, and nuts—all good sources of potassium, calcium, and magnesium—can favorably influence blood pressure, independent of sodium levels.[22] This represents yet another powerful reason to encourage greater consumption of these healthy foods.

Nuts

Although relatively high in fat, and previously proscribed by many dietary recommendations, nuts are known to contain predominantly mono- and polyunsaturated fats, which, as noted above, have favorable effects on HDL and LDL cholesterol. A number of prospective observational studies have suggested a strong favorable association between nut consumption and lower risk of CHD and CHD events.

DIETARY COMPONENTS VS DIETARY PATTERNS

Recommendations for "heart healthy" diets clearly need to focus on overall dietary patterns, rather than on individual components. The individual component approach, while easy to base on expanding scientific knowledge, is often impractical to achieve. Observational studies and controlled trials have, therefore, increasingly focused on optimal diets and dietary patterns. Such diets must be culturally appropriate to successfully encourage adherence, a principle likely to be at least partly responsible for the success of the Lyon Diet Heart Study, with its specific enriched Mediterranean diet tailored to the study population. Similarly, in the Indian Heart Study,[23] a semi-vegetarian diet was introduced (rich in fruits, vegetables, grains, and nuts), resulting in a highly significant reduction in coronary death rate and non-fatal MI. With the increasing prevalence of obesity throughout the world, and with the importance of obesity as an "avenue by which diet can influence risk of CHD,"[3] it seems clear that cardiovascular health through dietary intervention can be achieved only through broad population strategies encompassing public policy, public health, education, and business interests.

Preliminary evidence from a South African cost-effectiveness analysis suggests that hypertension treatment based on risk-based guidelines is both plausible and cost-effective on the African continent.[24] Favorable dietary patterns, and their influence on a broad range of risk factors, would integrate well with

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Table 3. American Heart Association Dietary Guidelines*

A Healthy Eating Pattern Including Foods From All Major Food Groups
Major guidelines:
- Consume a variety of fruits and vegetables and grain products, including whole grains.
- Include fat-free and low-fat dairy products, fish, legumes, poultry, and lean meats.

A Healthy Body Weight
Major guidelines:
- Match intake of energy (calories) to overall energy needs; limit consumption of foods with a high caloric density and/or low nutritional quality, including those with a high content of sugars.
- Maintain a level of physical activity that achieves fitness and balances energy expenditure with energy intake; for weight reduction, expenditures should exceed intake.

A Desirable Blood Cholesterol and Lipoprotein Profile
Major guidelines:
- Limit intake of foods with a high content of saturated fatty acids and cholesterol.
- Substitute grains and unsaturated fatty acids from vegetables, fish, legumes, and nuts.

A Desirable Blood Pressure
Major guidelines:
- Limit the intake of salt (sodium chloride) to <6 g per day.
- Limit alcohol consumption (no more than 1 drink per day for women and 2 drinks per day for men).
- Maintain a healthy body weight and a dietary pattern that emphasizes vegetables, fruits, and low-fat or fat-free dairy products.

*Adapted from: *Circulation.* 2000;102:2284–2299 (reference 16).

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such a concept. Accordingly, it would seem wise to test the application of guidelines based on risk assessment, with treatment recommendations focusing on lifestyle changes, particularly dietary ones, that can be influenced broadly, and potentially cost-effectively, in developing countries.

The compelling evidence gathered for many decades in Western countries provides a robust evidence base on which to make recommendations (Table 3) to populations not yet overburdened with CHD—a situation likely to change if we do not act soon. This epidemic has burdened the developed world for nearly half a century; our goal should be to prevent it from afflicting the developing world for the next half century.

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