Feature

Diet and heart disease: The role of cholesterol and fat

Despite its negative portrayal by the popular press, cholesterol is an essential part of human metabolism. Certainly, the role of cholesterol in health has been clouded by the public's confusion over serum versus dietary cholesterol and any relationship the two have to each other. The following article on the role of cholesterol and fat in diet and heart disease was prepared by Donald J. McNamara of the Department of Nutrition and Food Science, University of Arizona at Tucson.

There appears to be a great deal of confusion among the public concerning the term "cholesterol." This is understandable considering that there is "good" and "bad" cholesterol, dietary and plasma cholesterol, as well as average, moderate and high-risk plasma cholesterol levels. There also exists substantial confusion over the relationship between plasma cholesterol levels and intake of dietary cholesterol and fats, i.e., saturated fats, monounsaturated fats, polyunsaturated fats and the omega-3 fats found in fish oils. Added to all these issues is the quandary over what constitutes a high blood cholesterol level and what is an ideal level in terms of heart disease risk.

The "cholesterol phobia" established in the minds of the public not only creates a great deal of confusion and anxiety for the average person but also has significant repercussions on the overall nutritional balance and health of the American public. Internationally, the cholesterol scare already has altered the ways in which many individuals view the available food supply and has led many to stop eating some highly nutritious foods that are important components of a balanced diet.

Plasma cholesterol and cardiovascular disease

There is little debate that an elevated plasma cholesterol level is one of the three major risk factors for cardiovascular disease (CVD), the other two being hypertension and cigarette smoking. In addition to these, CVD risk increases with obesity, diabetes, glucose intolerance, a sedentary lifestyle and a Type-A personality. Heredity (or family history) also is an important risk factor.

It generally is agreed that a plasma cholesterol level greater than 240 milligrams (mg) per deciliter (dl) is related to increased risk for CVD and that a high plasma cholesterol level exacerbates the atherogenic effects of the other risk factors to increase substantially CVD risk. Recent evidence has shown that reducing elevated plasma cholesterol by hypocholesterolemic drug administration does reduce the incidence of fatal and non-fatal heart attacks (1) and actually can retard the progression of atherosclerotic plaques (2). The unresolved questions pertain to (a) the public health approach to take for individuals having plasma cholesterol levels of less than 240 mg/dl with a relatively lower risk for CVD and (b) the efficacy of low-fat, low-cholesterol diets in reducing plasma cholesterol levels and, in theory, CVD incidence.

Dietary versus plasma cholesterol

Over the past 25 years, numerous investigators have studied the relationship between changes in dietary cholesterol intake and related fluctuations in plasma cholesterol levels (3). Only a small number of these studies, however, were carried out using physiological ranges of dietary cholesterol intakes.

Most individuals undoubtedly will experience an increase in plasma cholesterol levels when challenged with a dietary cholesterol intake of more than 1500 mg/day. This is understood readily if one considers the physiology of cholesterol metabolism in humans. An average 70 kilogram (kg) adult produces 11 mg of cholesterol per kg body weight per day (770 mg) on a low cholesterol diet (i.e., less than 300 mg/day). When challenged with an intake of 1500 mg/day, the 60% absorption of dietary cholesterol will account for an input of 900 mg/day to the body. Under ideal metabolic balance, when the inputs from dietary sources and endogenous production are in perfect balance, such a challenge would require that synthesis be suppressed completely (which never happens) and even then, the excess input to the body would be 170 mg/day. Under these conditions, it is not surprising that plasma cholesterol levels increase in the majority of individuals fed a pharmacological dose of dietary cholesterol.

Rather than misinterpreting the reported responses to these extreme cholesterol challenge studies, we need to evaluate the potential effects of reducing dietary cholesterol intake from the current average of 450 mg/day to less than 300 mg/day. In terms of the overall difference in the amount of cholesterol absorbed by the body with these two intakes (assuming an average absorption of 60%), the 90 mg/day reduction would be expected to have a minimal influence on either whole body cholesterol metabolism or on plasma cholesterol levels. Changes in cholesterol intake of this magnitude are within a range that will be accommodated by the homeostatic mechanisms regulating endogenous cholesterol synthesis in most individuals (4). The available evidence indicates that when challenged with a modest increase in dietary cholesterol intake, most individuals (70%) are able to compensate for the increase by reducing endogenous cholesterol production coupled with other regulatory responses which maintain cholesterol balance in the body (4,5). These same studies show that for

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the remaining 30% of the population who lack precise feedback regulation of cholesterol metabolism, a modest reduction in dietary cholesterol intake does result in a reduction in plasma cholesterol levels (4,5).

The current negative connotation given to cholesterol-containing foods in the diet has fostered advertising and promotion of cholesterol-free products, some that may have little value in a plasma cholesterol-reducing diet. Although many items claim to be cholesterol-free, some may contain saturated fats, thus having no plasma cholesterol-lowering benefit; if anything, they may raise the cholesterol level if they contain considerable saturated fatty acids. The confusion between dietary cholesterol and plasma cholesterol may lead some individuals, including those who are hypercholesterolemic and most needy of effective dietary interventions, to make ineffective dietary changes. These changes can negate important components of a balanced and nutritious diet without the plasma cholesterol-lowering benefit they seek, and in some circumstances, actually may tend to raise plasma cholesterol levels.

Aware of this confusion, the U.S. Food and Drug Administration (FDA) has proposed establishing standard definitions for labeling products as cholesterol-free, low cholesterol and reduced cholesterol. FDA published its proposed rule defining these terms in the Nov. 25, 1986, *Federal Register* and still is reviewing the comments it received.

Dietary fat and plasma cholesterol levels

Of all the various components of the diet, the most influential on plasma cholesterol levels is the quality of dietary fat. It is well-established that saturated fats increase plasma cholesterol levels while monounsaturated and polyunsaturated fats lower cholesterol levels (4). Unfortunately, it is neither as simple nor as straightforward a relationship as is often presented.

There still is considerable uncertainty as to the mechanisms of action of the different types of dietary fats on plasma cholesterol levels. For most individuals, an increased intake of saturated fats in the diet increases plasma cholesterol levels, especially the low density lipoprotein (LDL) cholesterol level that is related to increased risk for CVD. Studies suggest that in part this response may rely on the degree of saturation of the fat and on its chain length. Reiser et al. (6) reported that although a diet high in coconut oil resulted in a higher plasma cholesterol level than one high in safflower oil, there was little difference between the effects of dietary beef fat versus dietary safflower oil on plasma cholesterol levels.

A reduction in dietary saturated fat intake, whether by reducing total fat calories in the diet or by substituting monounsaturated or polyunsaturated fat, will result in a plasma cholesterol-lowering response in most individuals. However, the extent of the lowering varies substantially from person to person (5,7). In considering the available evidence relating the quality of dietary fat to plasma cholesterol levels, most studies have used excessively wide ranges of polyunsaturated to saturated (P/S) ratio of 0.45 to a ratio of 1.0 (4). Although the evidence is convincing that the quality of dietary fat plays a role in determining plasma cholesterol levels, the lowering of plasma cholesterol levels by this modest shift in fat quality is relatively small and highly variable.

The hypocholesterolemic effects of polyunsaturated fats have been recognized for almost 30 years yet only recently the potential cholesterol-lowering benefits of monounsaturates and omega-3 fish oils have been reported. Studies by Grundy and colleagues (8–10) have shown that substitution of monounsaturated fat for dietary saturated fat will lower plasma cholesterol levels without lowering the protective high density lipoprotein (HDL) cholesterol levels. This substitution also will maintain plasma triglyceride levels, which tend to be increased when fat calories are replaced by carbohydrates. As recently reviewed by Reaven (11), there are potential problems involved in attempting to treat elevated plasma cholesterol levels by replacing saturated fat calories with carbohydrates, especially simple carbohydrates, in terms of elevating plasma levels of triglycerides, insulin and glucose while decreasing HDL cholesterol levels. Substitution of monounsaturated fats for saturated fats in the diet may be a more reasonable replacement treatment for those who need intervention.

Contrary to the impression provided by the distributors of fish oil capsules, the cholesterol-lowering effects of the omega-3 fatty acids are relatively modest and some fish oil preparations, in fact, are high in cholesterol. The major benefits are in lowering elevated plasmatriglyceride levels and in reducing clotting tendency. The large amounts of omega-3 fatty acids required to achieve a minor cholesterol-lowering effect may present a different problem in that the increased caloric intake from fish oil capsules could exacerbate obesity, an existing health problem for many Americans. Although the epidemiological evidence suggests that whole fish consumption reduces CVD risk, the benefit of fish oil capsules as a plasma cholesterol-lowering agent has not been established clearly. Indeed, there is evidence to suggest that any CVD-risk reduction afforded by

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intake of omega-3 fatty acids may have less to do with changes in plasma lipid levels than to potential positive effects of omega-3 fatty acids on thrombosis (12).

Numerous investigators have studied the potential interplay between fat quality and cholesterol quantity in determining plasma cholesterol levels. Because these data are contradictory, the majority of the available evidence does not support the hypothesis that an increased dietary cholesterol intake has a greater plasma cholesterol-elevating effect if consumed with a saturated fat diet than with polyunsaturated fat intake (4,5). It has been shown that the precision of the feedback regulatory responses to an increased dietary cholesterol intake is not altered by the quality of the dietary fat (5). These two dietary components appear to exert their respective effects on plasma cholesterol levels by independent mechanisms.

Modification of plasma cholesterol and CVD risk

Two important considerations in any evaluation of a public health approach for reducing the incidence of CVD in the population must address the questions of what level of plasma cholesterol constitutes risk and what potential benefits will be gained by dietary intervention.

The level of plasma cholesterol constituting increased risk for CVD continues to be debated. However, most authorities agree that a cholesterol level greater than 240 mg/dl clearly is associated with increased CVD risk. Approximately 25% of the population falls into this group. The obvious question then is whether this constitutes a large enough percentage of the population to warrant mass intervention to reduce plasma cholesterol levels by dietary alterations. To answer that question, one must evaluate the plasma cholesterol-lowering efficacy of a fat-modified diet and the potential for reducing CVD incidence.

Mean changes in blood cholesterol often are discussed in the diet-heart disease debate. However, the efficacy of a fat-modified diet on the extent of cholesterol lowering varies substantially from patient to patient. As the dietary intervention concept addresses mass intervention, one can assume that an average of 6.7% reduction in plasma cholesterol levels can be obtained by modification of fat in the diet (the actual changes being higher for some and lower for others). Given this reduction, what decrease in CVD would be predicted? According to the model developed by Taylor et al. (13), lifelong adherence to the "prudent diet" with a 6.7% plasma cholesterol-lowering effect will extend life expectancy by three days to two months for low-risk

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individuals and 18 days to 12 months for those at high risk. Using the same epidemiologically based model, these investigators found that lowering blood pressure would extend life expectancy by 24 months and stopping cigarette smoking would result in an increased life expectancy of 23 to 63 months (13). Based on this model, cholesterol levels have the least impact on life expectancy. Therefore, the most logical approach would be to reduce all CVD risk factors that are modifiable. An important component of this approach is that individuals must know their plasma cholesterol levels and act accordingly if CVD risk exists. One objective of the recently established National Cholesterol Education Program (NCEP) is to encourage people to learn their blood cholesterol levels.

Epidemiology and the diet: heart disease relationship

Epidemiologic studies relating dietary factors and CVD risk come from studies of various cultures with differing rates of mortality and studies within our own society. The data, however, do not consistently support the concept that dietary interventions to lower plasma cholesterol levels will reduce CVD incidence. For example, studies within the U.S. show that dietary changes do not relate to reductions in plasma cholesterol levels or CVD mortality (14). No correlation between dietary changes and CVD mortality is observed when one considers international data (15). Thus at this time, epidemiologists are not able to explain the patterns of changes in lifestyle to changes in CVD deaths (15).

One of the most baffling epidemiological anomalies is that Japan, a country with one-sixth the heart disease mortality rate of the U.S., has had a significant increase in the average plasma cholesterol level (16) without a corresponding increase in heart disease mortality. In fact, the heart disease mortality rate in Japan has

Cholesterol guidelines

The National Heart, Lung and Blood Institute's (NHLBI) recently released report, "Cholesterol Treatment Recommendations for Adults," suggests that "diet is the cornerstone of treatment of high-risk cholesterol levels." According to the Oct. 10, 1987, issue of *Food Institute Report*, the report is an updated supplement to previous expert committee studies such as the 1984 National Institutes of Health Concensus Panel on Lowering Blood Cholesterol to Prevent Heart Disease.

The report, written chiefly for physicians, notes, "The view that diet modification is impractical or doomed to failure for most patients is not justified. Many individuals have successfully modified their diets and have obtained a reduction in cholesterol levels. Much of the problem of high cholesterol levels among Americans is due to dietary excesses, and diet modification is the rational approach to this problem for most people." The guidelines suggest that people with high cholesterol levels be treated with a general cholesterol-lowering diet for three months, followed by a more stringent diet, if necessary, for another three months.

As outlined in the report, the Step-One Diet calls for the reduction of major and obvious sources of saturated fatty acids and cholesterol; the Step-Two Diet suggests that saturated fatty acids and cholesterol be reduced to a minimum level. Both diets recommend eating a varity of foods.

If dietary modification fails to lower cholesterol level, the guidelines recommend that "first choice" and "second choice" drugs be prescribed. Lovastatin, a new drug approved by the U.S. Food and Drug Administration earlier this year, has been placed on the second-choice list.

Copies of the "Expert Panel Report on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults" (the complete report) or "Cholesterol Treatment Recommendations for Adults" (a summary) are available from the National Cholesterol Education Program, National Heart, Lung and Blood Institute, C-200, Bethesda, MD 20892.

Meanwhile, the National Cholesterol Education Program coordinating committee voted to approve guidelines for proposed mass cholesterol screenings in shopping malls, supermarkets and department stores. *Food Chemical News*, in its Oct. 14, 1987, issue, reported that the committee also plans a "know your number" advertising campaign based on its recommendations in the "Expert Panel Report on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults." The campaign urges that people learn their blood cholesterol "number" and what that number means to their health. Cholesterol levels under 200 mg/dl are classified as desirable; those between 200-239 mg/dl are rated as borderline-high risk and those over 240 mg/dl as high risk.

Claude Lenfant, head of NHLBI and committee chairman, said an expert panel on population education will be established. This panel will be asked to recommend specific dietary habits for all Americans and develop an educational system to "provide lay persons with vital information about cholesterol in their diet."

decreased at the same rate as the U.S. (17). Although it would be a gross misuse of the data to suggest that heart disease rates will decrease with increasing plasma cholesterol level, the data do suggest there is more to the low heart disease mortality in Japan than just dietary factors and a low average plasma cholesterol level. Such problems make a cause and effect interaction difficult to identify and impossible to prove.

"It can't do any harm"

One of the weakest arguments supporting the recommendation for general acceptance of the prudent diet is that "it can't do any harm." The American Academy of Peciatrics is not convinced that the prudent diet is harmless for young children (18), and many are equally unconvinced that the dietary recommendations will offer any benefit to the CVD risk relative to the nutritional health of the elderly and those existing below the poverty level. Some very high-quality nutritious foods, available at low cost, are excluded from a truly "prudent diet." With the public's current fear and misunderstanding of the diet-heart disease relationship, one must wonder how many have made nutritionally wasteful changes.

As eloquently commented on by Becker (19), the tyranny of health promotion, as he calls our present fixation, diverts our attention away from "...recognizing, and trying to modify, the social and economic determinants of health, disease and 'wellness'".

Population versus individual approaches to therapy

Most of us know our blood pressure, how many pounds overweight we are and whether we smoke. Very few of us know what our plasma cholesterol levels are and what the relationship between that cholesterol value and CVD risk may be. It is reasonable to recommend that everyone have their plasma cholesterol level determined and, if it is elevated, to initiate dietary changes to try reducing it (20).

To make effective dietary changes, a session or two with a registered dietitian who can recommend ways to modify the diet and still maintain nutritional quality is highly recommended. However, as dietary changes are not equally effective in all individuals, the follow-up measurement to determine any change in the cholesterol level is essential.

Two recent advances make this approach more simple than previously imagined. The new portable blood cholesterol analyzers, which only require a finger-stick blood sample, greatly have simplified screening procedures for large populations. A second major advancement has been in the area of drug therapy for those individuals with elevated plasma cholesterol levels who do not respond sufficiently to diet. Thus, it now is feasible to screen for the hypercholesterolemic individual at minimal cost, to initiate effective dietary intervention based on the lifestyle of the patient, and, if such interventions are not sufficient to reduce the elevated plasma cholesterol level to acceptable values, to prescribe effective cholesterol-lowering medication.

Lifestyle, diet and heart disease

Some of the risk factors for CVD such as genetics, secondary causes of hyperlipidemia, being male and aging simply cannot be changed. Other risk factors can be managed effectively and, generally, the public knows what risk factors they have. If overweight, diet; if a smoker, quit; if hypertensive, get therapy; if a couch-potato, get some exercise; and if hypercholesterolemic, make dietary changes. If those measures are ineffective, then discuss pharmacologic intervention with your physician. If none of the above apply, eat a balanced diet with a variety of foods consumed in moderation and enjoy good health.

In its 1980 report "Toward Healthful Diets" (21), the Food and Nutrition Board of the National Academy of Sciences stated, "Sound nutrition is not a panacea. Good food that provides appropriate proportions of nutrients should not be regarded as a poison, a medicine or a talisman. It should be eaten and enjoyed." The intrinsic value of such good advice should not be overlooked by the public nor by the biomedical community in its search for wellness.

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