Relationship Between Fat, Cholesterol and Coronary Heart Disease

Donald J. McNamara*

Coronary Heart Disease

Heart Disease Mortality

In order to evaluate the relationship between dietary fats and cholesterol with the incidence of heart disease and the potential for heart disease risk reduction, one must recognize the enormous impact of cardiovascular disease on the health of the population. In the United States, cardiovascular disease afflicts over 65 million individuals and accounts for almost one million deaths each year. Diseases of the heart and blood vessels are the single largest cause of mortality in this country, a finding also true for almost every industrialized country in the world. It has been estimated that in this country there is one death from cardiovascular diseases every 32 seconds. The estimated cost of this epidemic is roughly 83 billion dollars each year in medical costs and lost productivity. Obviously, as with any epidemic of such magnitude, it is essential that the medical community define the risk factors involved in cardiovascular disease incidence and initiate prevention programs to reduce disease incidence.

Heart Disease Risk Factors

Numerous epidemiology studies, both international and within populations, have consistently shown that cardiovascular disease arises from multiple risk factors (Keys et al. 1986; Anderson et al. 1987). Three major life-style factors which increase risk are high blood pressure, cigarette smoking and elevated plasma cholesterol levels. In addition, it is now clear that obesity, with its associated high blood pressure, elevated blood lipids and sedentary life style, also represents an independent risk factor for coronary heart disease (Hubert et al. 1983). Risk factors which cannot be altered include male sex, increased age and genetics. Clinical research is only beginning to define the very significant role genetics plays in determining coronary heart disease incidence in the population and the ways in which genetic predispositions for the disease can be altered by either life style changes or drug interventions.

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Plasma Cholesterol Levels and Heart Disease Risk

This presentation will concentrate on the role of dietary interventions in reducing plasma cholesterol levels and, in theory, cardiovascular disease risk. Over the past 15 years, there has been increasing attention paid to the importance of lowering the high plasma cholesterol levels found in our population and the National Cholesterol Education Program was initiated by the National Institutes of Health to specifically address this issue. Based on their recommendations, the risk of cardiovascular disease has been defined as average for individuals with plasma cholesterol levels of less than 200 mg/dl, borderline-high for cholesterol levels between 200 and 240 mg/dl, and high when cholesterol values are greater than 240 mg/dl. The National Cholesterol Education Program (1988) has also formulated dietary guidelines which they have recommended to every man and woman over two years of age. These dietary recommendations are based on both epidemiological data from international studies and clinical studies of the plasma cholesterol responses of patients to dietary modifications.

Dietary Fat Saturation and Heart Disease

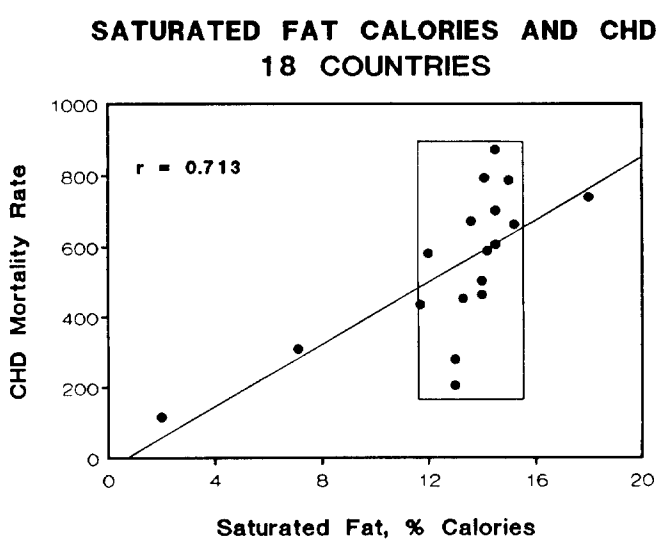
Epidemiologic data demonstrate a positive correlation between coronary heart disease mortality rates and the percentage of total calories derived from saturated fatty acids (Keys et al. 1986; Hegsted and Ausman, 1988). While this relationship is statistically significant (Figure 1), it should be noted that between the range of 12% to 16% of calories from saturated fat, the rate of coronary heart disease mortality varies from 200 to 800 per 10,000 per year. Clearly, interpretation of these epidemiological data is skewed by the low saturated fat intakes and low heart disease death rates of a few populations and differences in dietary saturated fat fails to explain the large differences between different populations. Intake of polyunsaturated fat has been shown to have a modest negative correlation with coronary heart disease mortality, but this relationship rarely reaches statistical significance.

Dietary Recommendations and Heart Disease Risk Reduction

Dietary Recommendations

Based on these epidemiological findings and a very significant volume of clinical trial data, it has been generally accepted that intake of saturated fat increases plasma cho-

Figure 1

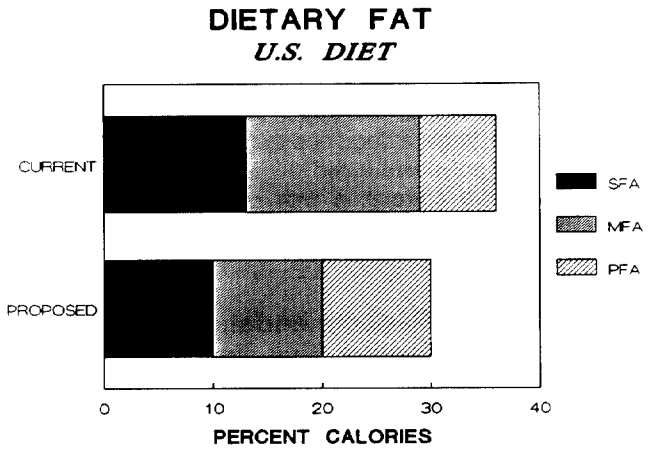


Relationship between coronary heart disease mortality and saturated fat calories in the 18 Countries Study. Data from Hegsted and Ausman (1988).

lesterol levels while polyunsaturated fat in the diet lowers cholesterol levels. It has also been widely assumed that dietary cholesterol makes a significant contribution to plasma cholesterol levels and that reducing cholesterol intake reduces plasma levels. Based on these considerations, the National Cholesterol Education Program (1988) has recommended that everyone over two years of age modify their diet to reduce total fat intake to less than 30% of calories, reduce saturated fat intake to 10% of calories, increase polyunsaturated fat to less than 10% of calories and reduce dietary cholesterol to less than 300 mg/day (Figure 2).

A number of assumptions are inherent in population-wide dietary recommendations. It is assumed that the recommended changes are effective in lowering plasma cholesterol levels and in lowering cardiovascular disease incidence and mortality. That the recommended changes have no long-term side effects. And that the recommended changes can readily be incorporated into a nutritionally sound dietary pattern. As will be seen, not all of these assumptions are necessarily valid.

Figure 2



Comparison of the dietary fat composition of the current American diet and recommended dietary pattern.

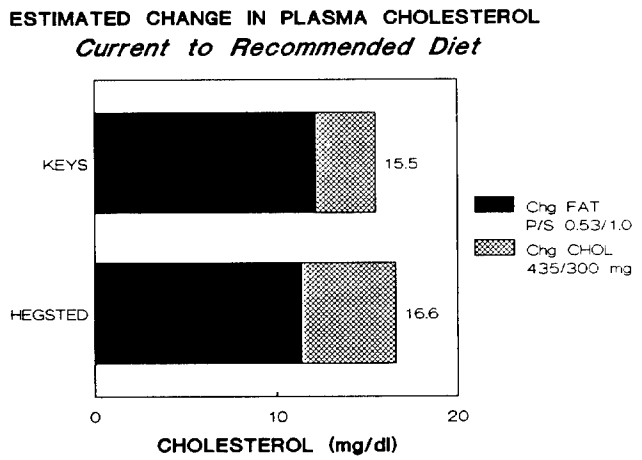
Plasma Cholesterol Response to Dietary Changes

Based on data derived from studies by Keys et al. (1965) and Hegsted et al. (1965), predictive equations have been developed to estimate the plasma cholesterol changes which occur when intakes of saturated and polyunsaturated fats and cholesterol are modified. Based on these equations, it can be estimated that changing the American diet from its current pattern of fat and cholesterol intake to the recommended pattern, then plasma cholesterol levels will decrease on average 16 mg/dl. This represents a 7% decline with the majority of the decrease due to the drop in saturated fat calories and increase in dietary polyunsaturated fat. Decreasing dietary cholesterol from 450 mg/day to 300 mg/day has a very small effect, even though advertising and marketing attempts would have us believe that this is a major contributor.

Dietary Cholesterol and Plasma Cholesterol

The effect of dietary cholesterol on plasma cholesterol levels is actually very small. Analysis of 69 clinical studies indicates that on average, for every 100 mg/day change in dietary cholesterol intake, plasma cholesterol levels change 2.2 mg/dl or about 1% (McNamara, 1990). While there is some debate regarding the actual importance of dietary cholesterol in determining plasma cholesterol levels, the majority of data indicate that this is a very small determinant for most people. The public's confusion in associating dietary

Figure 3



Estimated changes in plasma total cholesterol levels changing from current to proposed dietary pattern. Estimates for plasma cholesterol changes due to changes in dietary fat composition (solid bars) and dietary cholesterol (hatched bars) based on equations of Keys et al. (1965) and Hegsted et al. (1965).

cholesterol with plasma cholesterol is one reason why it is so difficult to educate hypercholesterolemic patients who really need to make dietary changes in how to make effective changes in their eating patterns.

Heterogeneity of Responses to Dietary Interventions

It has often been assumed by the public that dietary interventions are universally effective and that reducing saturated fat in the diet will surely lower plasma cholesterol levels in everyone. It is now clear that the responses to dietary interventions are highly individualized with some patients being very sensitive to dietary fatty acids while others are relatively resistant to diet-mediated lowering of plasma cholesterol levels (McNamara et al. 1987). Studies by Wolf and Grundy (1983) have shown that when patients on a metabolic ward are switched from a typical American diet to the recommended diet, some patients have a significant cholesterol-lowering response, some have a modest response and others have either no change or a modest increase. Numerous studies have demonstrated similar heterogeneity of responses to dietary changes and these data raise the question of who will benefit from population-wide recommendations and who will change their diet without benefit (McNamara, 1987; Grundy and Denke, 1990).

Diet and the Ratio of Good Cholesterol to Bad Cholesterol

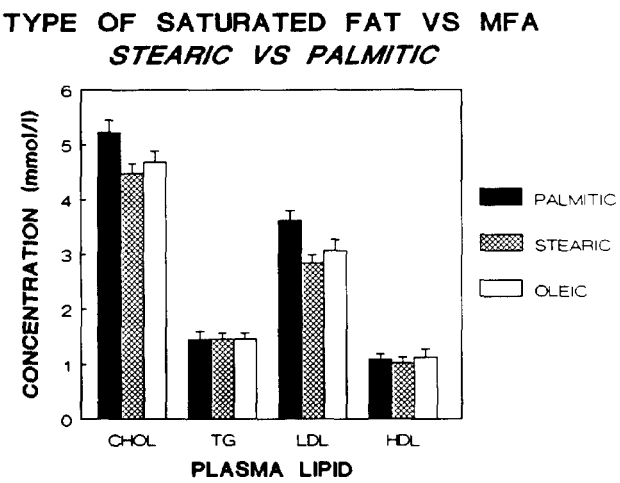
It is also clear from such studies that dietary changes have different effects on different lipoproteins, both low density lipoprotein cholesterol (LDL, the "bad cholesterol") and high density lipoprotein (HDL, the "good cholesterol") (Gordon et al. 1989). Ideally, a dietary change should lower the bad LDL cholesterol and increase levels of the good HDL; unfortunately, this is not always the case. Shifting patients from the current to the proposed diet lowers not only LDL cholesterol but also HDL; and in some cases, we see individual patients who lower the good cholesterol more than the bad cholesterol (Wolf and Grundy, 1983; Grundy, 1989; Mensink et al. 1989). Many investigators have voiced concerns over what the consequences of such changes mean in terms of cardiovascular disease risk since a major determinant of risk is the ratio of LDL to HDL cholesterol.

Dietary Fatty Acids and Plasma Cholesterol Levels

Stearic Acid

Conventional wisdom held that all saturated fatty acids raised plasma cholesterol levels while all polyunsaturated fats lowered plasma cholesterol and that monounsaturated fatty acids and carbohydrates had a neutral effect on plasma lipids. It is now clear from a variety of studies that not all saturated fats are hypercholesterolemic and that monounsaturated fats are not neutral. Clinical studies have shown that intake of stearic acid, a fatty acid found in meats and cocoa butter, actually lowers plasma cholesterol levels when compared to palmitic acid (Figure 4) (Bonanome and Grundy, 1988). Based on these findings, it can be concluded that there are in fact only two major fatty acids in the American diet which raise plasma cholesterol levels, myristic and palmitic acids. Obviously, we do not as yet understand the full impact of saturated fatty acid chain length on plasma cholesterol levels (Reiser et al, 1985).

Figure 4

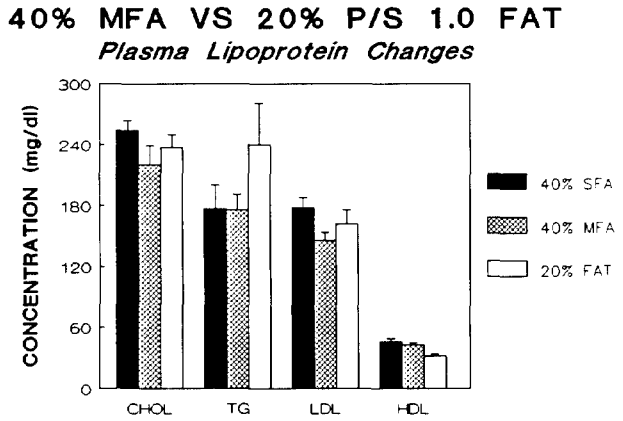


Effects of saturated fat versus monounsaturated fat (MFA) on plasma lipids and lipoproteins. Clinical data of study comparing effects of dietary intakes of palmitic, stearic and oleic acid rich diets (40% of calories) on plasma cholesterol (chol), triacylglycerol (TG), LDL and HDL levels (Bonanome and Grundy, 1988).

Monounsaturated Fatty Acids

One finding from epidemiology studies is that in countries with a high intake of monounsaturated olive oil, there is a relatively low incidence of coronary artery disease (Keys et al. 1986). These findings do not fit with the concept that intake of monounsaturated fatty acids had a neutral effect on plasma cholesterol and the findings were reinvestigated. Clinical studies have now shown that when saturated fat in the diet is substituted with monounsaturated fat, plasma cholesterol levels are lowered (Mattson and Grundy, 1985; Grundy, 1989; Mensink et al. 1990). What makes these studies so important is the finding that the primary lowering effect was on the atherogenic LDL cholesterol and that the protective HDL cholesterol levels remain unchanged (Figure 5). These data suggest that monounsaturated fatty acids may actually be a better substitute for saturated fat than polyunsaturated fat. There is also some debate regarding the relative benefits of a 30% low-fat diet versus a more modest fat diet rich in monounsaturated fatty acids. This question is raised because low-fat, high-carbohydrate diets have been shown to lower HDL cholesterol levels; a finding not observed with moderate fat diets rich in the monounsaturated fat oleic acid (Grundy, 1989; Mensink et al. 1990).

Figure 5



Effects of diets containing saturated (SFA) and monounsaturated (MFA) fat at 40% of calories to a low (20% of calories) polyunsaturated fat diet. Clinical data of study comparing effects of SFA and MFA high-fat diets and a low-fat on plasma cholesterol (chol), triacylglycerol (TG), LDL and HDL levels (Grundy, 1986).

Risk-Benefit Considerations

There have also been some concerns voiced regarding potential risks of increased intake of polyunsaturated fat diets. There is a history of the effects on intake of monounsaturated fat rich diets in a number of Mediterranean countries, whereas we have no information regarding the effects of intake of a diet containing 10% polyunsaturated fat. Concerns involve a number of health aspects including lowering of HDL levels, increased cancer risk, altered immune function, gallstone formation and lipid oxidation (Grundy, 1989). We are faced with a number of questions and uncertainties regarding what is the most effective, safest dietary change we can make to lower cardiovascular disease incidence in the population. Many investigators believe that the question is far from settled.

Cholesterol Lowering and Heart Disease Prevention

And how effective should we expect any intervention to be in lowering cardiovascular disease incidence and mortality in the population? Hopefully, any recommended dietary change will be effective in lowering plasma cholesterol levels and result in significant reductions in cardiovascular disease incidence. If we consider the relative efficacy of various plasma cholesterol-lowering drug trials, we see that lowering plasma cholesterol levels did achieve some degree of reduction in coronary heart disease mortality. Unfortunately, there is little evidence that such trials had any effect on total mortality; patients died of other causes and overall mortality rates remained relatively constant (Rossouw and Rifkind, 1990).

Another approach to evaluating the potential benefits of dietary interventions is to consider the magnitude of change in the distribution of plasma cholesterol in the population and how this change would affect coronary heart disease mortality. Based on the clinical data, we can predict that initiation of the recommended dietary changes will result in an average reduction in plasma cholesterol of 16 mg/dl. Considering 6-year rate per 10,000 of coronary heart disease mortality in the various risk classifications, we find that the dietary change has little effect on 50% of the population classified as average risk, a reduction in mortality of 4.7 deaths per 6 years per 10,000 in the borderline-high group, and a saving of 3.2 lives in the high-risk group. Overall, the reduction in mortality equals 8.5 per 10,000 per 6 years (D.J. McNamara, unpublished).

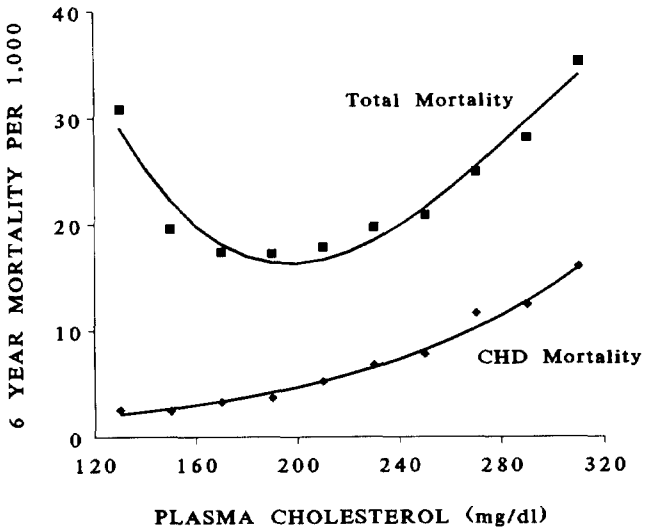
The risk reduction potential of a life-long adherence to the recommended dietary pattern can also be considered using data to evaluate increased life expectancy (Taylor et al. 1987). For a low-risk individual who is normotensive, does not smoke and has a high HDL level, the increased life expectancy is 3 days to 3 months. For the high-risk patient with hypertension, who smokes and has a low HDL cholesterol, the increase is 18 days to 12 months. On a relative basis, it has been estimated that with a 40-year old male who has high blood pressure, treatment of the hypertension will increase life expectancy by 36 months. If that same patient smokes and quits, the increase is 63 months. If that same patient has high blood cholesterol and changes his diet, the increase is 7 months. Obviously, intervention to treat the different risk factors results in differences in potential increases in life expectancy. Unfortunately, dietary changes have a relatively modest effect.

There is one other fact that makes population-based dietary recommendations a concern to some investigators. Data from the Multiple Risk Factor Intervention trial indicates that the relationship between plasma cholesterol levels and total mortality is a J-shaped curve with total mortality increasing at cholesterol levels less than 160 mg/dl (Figure 6) (Stamler et al. 1986). When dietary interventions are recommended to the entire population, obviously some individuals with low plasma cholesterol levels will experience additional lowering and the effects of such changes remain unclear. There is some evidence suggesting increased colon cancer risk in men when cholesterol levels are very low; and the question that needs to be addressed is: What effect diet-induced lowering of plasma cholesterol below 160 mg/dl will have on the incidence of other diseases.

Trends in Coronary Heart Disease Mortality

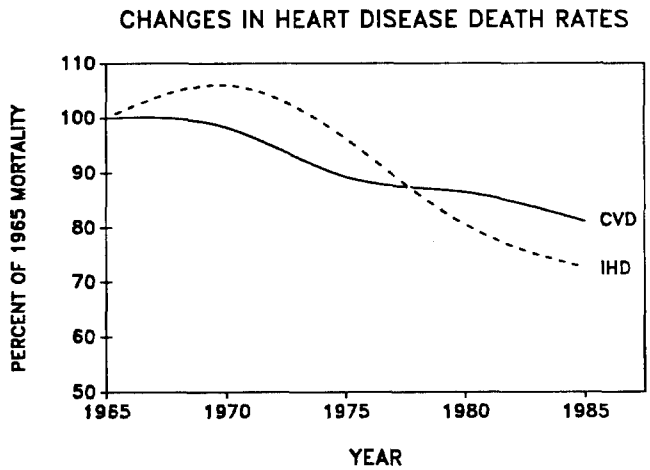
There is good news regarding the incidence of heart disease deaths in the population in that the rate of fatal heart attacks has been declining at a relatively constant rate since 1968 (Figure 7). The United States has experienced a significant reduction in heart disease mortality over this time period and this trend appears to be continuing. There has been substantial success in detecting and treating high blood pressure, in convincing people of the hazard of cigarette smoking, and in drug treatment of high plasma cholesterol levels. In addition, progress in surgical and pharmacological treatments for existing coronary artery disease have made substantial contributions to the decline in heart disease mortality.

Figure 6



Relationship between plasma cholesterol levels, coronary heart disease (CHD) mortality and total mortality. Data from Stamler et al. (1986).

Figure 7



Pattern of mortality rates from cardiovascular disease (CVD) and ischemic heart disease in the United States between 1965 and 1985.

Dietary Recommendations: Quality or Quantity

I would propose that there is an effective dietary approach to the prevention of cardiovascular disease in the population; one entailing getting Americans off their "fatty acids." Obesity is an independent risk factor for cardiovascular disease in addition to its contributions to high blood pressure, high blood lipids, adult onset diabetes and lack of exercise. When dietary changes to reduce the input of calories are coupled with efforts to increase caloric output through exercise, the overall cardiovascular disease risk profile can be substantially improved for the patient. This can be done without labeling highly nutritious foods as good or bad; without excluding red meat, eggs and dairy products from the diet; and without unwarranted concerns of what are the fat and cholesterol content of every item in the supermarket. Success in altering this risk profile involves eating a balanced, nutritious diet composed of a variety of foods consumed in moderation; only eating less of it.

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