Review of Serum Lipids and Apolipoproteins in Risk-assessment of Coronary Heart Disease

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ABSTRACT

Coronary heart disease (CHD), the leading cause of death in the western world, is multifactorial in nature. Abnormal lipoprotein levels are among the risk factors that cause atherosclerosis and, therefore, have been used as biochemical markers in assessing risk of developing CHD. The measurement of serum cholesterol, lipoprotein cholesterol, and apolipoproteins accurately and reliably has been hampered with technical difficulties. In addition, the interpretation of these tests and the determination of their clinical values have been challenging for both physicians and laboratory scientists. This article addresses and reviews the major current analytical and clinical concerns in the testing of lipids as well as the prevention and treatment of CHD.

Introduction

Coronary heart disease (CHD) is responsible for more than 550,000 deaths in the United States each year. It has been estimated that the direct and indirect costs of this disease surpass $60 billion a year. Atherosclerosis, the major cause of angina pectoris, stroke, and myocardial infarction, begins early in life and progresses silently for decades. By the time most individuals develop clinical manifestations of CHD, the atherogenic process is far advanced and markedly diminishes arterial blood flow.

Since sudden death can be the first manifestation of atherosclerosis and coronary artery bypass surgery does not prolong survival in patients with advanced disease, prevention of atherosclerosis is essential. Thus, investigators have been trying to identify risk factors and determine their usefulness in predicting the likelihood of an individual developing CHD. “Determinant” risk factors known to cause CHD include

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high blood pressure, cigarette smoking and elevated low density lipoprotein cholesterol (LDL) level. Other risk factors associated with but not yet shown to cause CHD include low high density lipoprotein cholesterol (HDL) level, obesity, diabetes mellitus, familial history of early CHD, physical inactivity, male gender, and behavioral pattern.

The levels of various lipoproteins and apolipoproteins are altered in patients with CHD. Epidemiologic findings such as those from the Framingham study have established an association between lipids, lipoproteins, and CHD and shown the usefulness of these biochemical parameters in predicting CHD risk. The present article will discuss the correlation of serum total cholesterol, lipoprotein cholesterol, and apolipoprotein concentrations with CHD, the methodologies used in assessing these parameters, and some recommendations for lowering CHD risk.

Total Cholesterol and Coronary Heart Disease

Cholesterol is an important element in the etiology of coronary artery diseases. As early as 1910, Windaus described the presence of cholesterol in the lesions of diseased arteries. Since then many studies have confirmed that free and esterified cholesterol accumulate in the aorta, coronary arteries, and cerebral vessels and that the rate of accumulation varies among individuals. The association between serum cholesterol and atherosclerosis in humans was first suggested in 1938 when Thanhauser and Muller each demonstrated familial aggregation of hypercholesterolemia and coronary artery disease. Further studies have shown that whenever the total cholesterol level is high, the incidence and prevalence of CHD are also high.

The Multiple Risk Factor Intervention Trial (MRFIT) demonstrated that the relationship between serum cholesterol and coronary death rates is positive and curvilinear. According to this study, if a risk ratio of 1.0 is assigned to a cholesterol level of 200 mg per dL (5.17 mmol per L), at 150 mg per dL (3.88 mmol per L) the ratio is 0.7. At 250 mg per dL (6.47 mmol per L) the risk ratio is 2.0, and at 300 mg per dL (7.76 mmol per L) it is 4.0. Pathological studies have helped to explain this curvilinear relationship by indicating that when 60 percent of the surface of coronary arteries is covered with raised plaque, critical phase is entered in which an increased serum cholesterol level will increase markedly the CHD risk.

In the past, “hypercholesterolemia” was defined as a cholesterol level above the 95th percentile for the non-diseased population. However, the results of the Lipid Research Clinics (LRC) Coronary Primary Prevention Trial (CPPT) have shown that the use of such a criterion to define “normal” values for serum cholesterol in the United States is misleading. The data available from this study suggest that levels between 200 and 240 mg per dL (5.17 and 6.21 mmol per L) are associated with an increased risk of developing premature CHD. The National Institutes of Health Adult Treatment Panel of the National Cholesterol Education Program (NIH-NCEP) has recently reported that total cholesterol level below 200 mg per dL (5.17 mmol per L) is considered desirable. Individuals with cholesterol levels between 200 and 239 mg per dL (5.17 to 6.19 mmol per L) are considered at moderate risk and those above 240 mg per dL (6.21 mmol per L) are at high risk. It is important to realize that this represents over 50 percent of the American adult population.

The LRC-CPPT findings, taken in conjunction with those of other cholesterol lowering trials, suggest that on the average each one percent, or two to
three mg per dL (0.05 to 0.08 mmol per L), reduction in cholesterol results in an approximate two percent reduction in CHD, a relationship of considerable clinical and public health significance. Moreover, the Cholesterol-Lowering Atherosclerosis Study (CLAS) demonstrated the benefit of cholesterol lowering in individuals with cholesterol levels between 185 to 240 mg per dL (4.79 to 6.21 mmol per L) and those with established disease.

The accuracy and precision of serum cholesterol measurements in clinical laboratories will determine the success of identifying hypercholesterolemia in a patient and monitoring his or her response to treatment. According to the 1986 College of American Pathologists (CAP) survey, more than half of all laboratories in the United States measure cholesterol with a bias of more than five percent from the "true value" (based on the Abel-Kendall method as the reference method) and with day-to-day imprecision higher than five percent. To utilize the data base generated by the LRC population prevalence studies in determining correctly someone's risk for CHD, the Laboratory Standardization Panel of the NIH-NCEP has set a goal to decrease the inaccuracy and imprecision in serum cholesterol determination to less than three percent, in all laboratories, over the next five years. Minimizing the inter- and intra-laboratory variations in cholesterol determination is essential for physicians to monitor reliably hypercholesterolemia and to assess CHD risk.

The Abel-Kendall assay is the recognized reference method for the determination of total cholesterol. However, according to the 1987 CAP survey, over 95 percent of all clinical laboratories in the United States determine serum cholesterol enzymatically. Numerous investigators have demonstrated an excellent correlation between the enzymatic and the reference method over a wide cholesterol concentration range.

**Lipoprotein Cholesterol and Coronary Heart Disease**

Plasma cholesterol does not exist free in solution. Together with triglyceride, phospholipids, and specific proteins, the apolipoproteins, cholesterol is transported through the bloodstream by the solubilizing carriers, the lipoproteins. These lipoproteins can be separated into five major classes according to their physical and chemical properties and are named according to their densities. In order of increasing density, the serum lipoproteins include (1) chylomicrons; (2) very low density lipoproteins (VLDL); (3) low density lipoprotein (LDL); (4) intermediate density lipoproteins (IDL); and (5) high density lipoprotein (HDL). The terms 'serum cholesterol' and 'total serum cholesterol' refer to the combined cholesterol components of these five lipoprotein classes. Cholesterol is not equally distributed among the lipoproteins. Seventy percent of serum cholesterol is present in LDL, while the rest is carried by HDL (20 percent) and the other lipoproteins. Since most serum cholesterol is present in LDL, a great deal of attention has been focused in the past decade on this lipoprotein in order to gain better understanding about its metabolic role and contribution to the premature development of the atherogenic process. The Nobel prize in medicine was awarded in 1985 to Drs. Joseph Goldstein and Michael Brown for their elucidation of the cellular LDL metabolism by receptor mediated endocytosis. Their findings are fundamental to our understanding of how plasma cholesterol levels are controlled.

Low density lipoproteins are the end products of VLDL catabolism. The liver synthesizes cholesterol and triglycerides
and secretes them into the bloodstream in the form of VLDL. These triglyceride-rich lipoproteins are degraded into IDL and then to LDL. Low density lipoproteins bind to high affinity receptors on plasma membrane and deliver cholesterol to extrahepatic cells and to the liver. Patients with familial monogenic hypercholesterolemia have defects in this pathway. The defects include reduced or absent LDL binding because of defective or absent LDL receptors, or defective internalization of the receptor-bound LDL particles. The consequence of the failure of LDL catabolism by receptor-mediated mechanism is the accumulation of LDL particles in serum. With the emergence of recombinant DNA technology and the availability of LDL receptor probes, prenatal diagnosis of homozygous familial hypercholesterolemics may be feasible. However, this technology is still in the developmental stage and is available only in research laboratories. Low density lipoproteins can also be degraded by scavenger cells or macrophages, a less efficient mechanism that requires high levels of plasma LDL to achieve a significant rate of removal. When scavenger cells are overloaded with cholesterol, they are converted to "foam cells", the early hallmark of atherosclerotic plaques.

The fact that LDL particles carry most serum cholesterol and can be taken up by extrahepatic cells, particularly cells of the arterial wall, helps to explain the positive correlation between serum LDL cholesterol level and CHD risk observed in several epidemiologic studies. The NIH-NCEP recently issued guidelines for cholesterol screening. Patients with either total cholesterol concentration above 240 mg per dL (6.21 mmol per L) or cholesterol level of 200 to 239 mg per dL (5.17 to 6.19 mmol per L) and established CHD or at least two additional risk factors should be further evaluated by measuring their LDL cholesterol concentrations.

High density lipoproteins appear to have a protective role in CHD. Epidemiologically, increased levels of HDL cholesterol are associated with decreased risk of CHD. Although "immature HDL" is produced by the liver and intestine, some of its surface materials such as phospholipids and apolipoproteins, are obtained from IDL and chylomicron remnants, the breakdown product of chylomicrons. High density lipoproteins are said to mature as they accumulate cholesterol.

Currently, there is much controversy concerning the most effective use of HDL cholesterol values in estimating CHD risk. Some physicians employ a rule-of-thumb approach whereby the risk of CHD increases approximately 25 percent for each five mg per dL decrease in HDL cholesterol below the average value (45 mg per dL for males; 55 mg per dL for females). This concept has certain limitations in that misleading predictions of CHD risk can occur in persons with very low or very high total cholesterol values. Alternately, the HDL value can be interpreted in relation to the total cholesterol or LDL cholesterol value and expressed as a percentage, or ratio, which is then related to relative risk (table 1). Like the rule-of-thumb strategy, however, these combined value approaches possess certain limitations. For example, a man with a total cholesterol of 350 mg per dL and HDL cholesterol of 50 mg per dL can be interpreted as having the same level of risk as a man with a total cholesterol of 175 mg per dL and HDL cholesterol of 25 mg per dL if the total cholesterol/HDL cholesterol ratio is applied and interpreted without careful consideration of the magnitude of the total cholesterol (mostly LDL) value. In both cases the ratio obtained is seven, but most clinicians would agree that the risk of CHD is significantly lower in the
TABLE I
Relative Risk of Coronary Heart Disease as Suggested by Various Test Combinations for Males (M) and Females (F)*

<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>HDL†</th>
<th>Percent</th>
<th>T-Chol/HDL‡</th>
<th>LDL/HDL§</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>1/2</td>
<td>60</td>
<td>70</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Average</td>
<td>45</td>
<td>55</td>
<td>20</td>
<td>23</td>
</tr>
<tr>
<td>2x</td>
<td>25</td>
<td>35</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>3x</td>
<td>--</td>
<td>--</td>
<td>4</td>
<td>9</td>
</tr>
</tbody>
</table>

† HDL- High density lipoprotein cholesterol.
‡ T-Chol/HDL- Total cholesterol/high density lipoprotein cholesterol ratio.
§ LDL/HDL- Low density lipoprotein/high density lipoprotein cholesterol ratio

second case. It should be remembered that LDL and HDL cholesterol are independent risk factors having statistically different weighting factors for CHD risk.

High density lipoproteins can be divided into two density subpopulations, HDL 2 and HDL 3, that differ in their lipid and apolipoprotein compositions, metabolic roles and clinical significance. High density lipoprotein 2 can carry twice as many cholesterol molecules per unit of apolipoprotein as compared with HDL 3. Thus, HDL 2 can be viewed as a doubly efficient vehicle for the transfer of cholesterol from the peripheral tissues back to the liver. Clinical studies have demonstrated that the cholesterol content of the HDL 2 subfraction correlates better than that of total HDL or HDL 3 with increased risk of CHD.

Over the years, many systems have been developed for isolating, separating, and characterizing the lipoproteins. Most are based on the physicochemical properties of these complexes. Traditionally, lipoproteins are separated by sequential preparative ultracentrifugation and their lipid content quantified. This method is costly, technically demanding and time-consuming; therefore, it is primarily used in research laboratories.

Lipoprotein electrophoresis, which separates these complexes according to their charges, has been useful in the visual qualitative evaluation of lipoprotein patterns in patients with hypercholesterolemia. However, this technique has some serious limitations. Lipoprotein electrophoretic patterns alone do not differentiate normal from abnormal lipid transport because only the ester bonds of triglyceride and cholesterol ester are stained; free cholesterol and phospholipids remain unstained. Therefore, a patient with biliary cirrhosis could have an electrophoretic pattern that appears normal in spite of the presence of a free cholesterol concentration well over 1000 to 2000 mg per dL, a tremendous increase in phospholipid levels, and an abnormal lipoprotein form (lipoprotein X). Lipoprotein electrophoresis should therefore be coupled with a quantitative method, such as the determination of total cholesterol.

Poly-cation precipitation is the most commonly used technique for the separation of HDL and its two subfractions in clinical laboratories. Selected combinations of polyanions and divalent cations, such as heparin-Mn ++, phosphotungstate-Mg ++ and dextran sulfate-Mg ++, have been used to precipitate VLDL and LDL, leaving HDL in the supernatant fluid. The cholesterol content of HDL is subsequently measured.

A double precipitation procedure is usually used for the separation of HDL 2 and HDL 3 fractions (21). Precipitation solutions, similar to those used for the separation of HDL from the other lipoproteins except for a higher salt concentration, are added to the HDL supernatant to precipitate the HDL 2 fraction and leave HDL 3 in the supernatant. The cholesterol content of HDL 3 is then measured directly in the supernatant while that of HDL 2 is estimated by subtracting HDL 2 cholesterol from total HDL cholesterol.
LDL cholesterol is not currently measured in most clinical laboratories. However, it can be estimated using the equation of Friedewald:

\[
LDL \text{ cholesterol} = total \text{ cholesterol} - (HDL \text{ cholesterol} + \text{triglyceride} \times 0.20)
\]

This method of estimation is reasonably accurate when the plasma triglyceride level is below 400 mg per dL. However, the reliability of such an estimation is dependent on the accurate determinations of total cholesterol, triglyceride, and HDL cholesterol. The LRC reference values of LDL cholesterol at the 75th and 90th percentile are reported in table II. It has been suggested that the LDL/HDL cholesterol ratio is a useful predictor of CHD risk only when the LDL cholesterol values are between 100 and 200 mg per dL. Below 100 mg per dL and above 200 mg per dL, the LDL cholesterol value itself may be the best predictor of CHD risk. If the LDL cholesterol is below 100 mg per dL, then the risk is so low that the ratio calculation is not useful. Above 200 mg per dL, aggressive management may be indicated irrespective of the HDL level.

The NIH-NCEP current recommendations for the diagnosis and treatment of hypercholesterolemia are represented in figure 1. Individuals who are considered at high risk should have their LDL cholesterol levels estimated before implementing therapy.

### Apolipoproteins and Coronary Heart Disease

In the early 1970s, Alaupovic suggested that apolipoproteins should also be considered when evaluating the contribution of lipids and lipoproteins to the development of CHD. Since apolipoprotein A (apo A) and apo B are the major proteins in HDL and LDL, respectively, they received special attention.

Apolipoprotein A consists of two major proteins, apo AI and apo AII, that constitute about 90 percent of total HDL protein. Apolipoprotein AI activates lecithin cholesterol acyl transferase, a plasma enzyme that specifically acts on circulating HDL to form cholesteryl ester and lysophosphatidyl-choline, while apo AII appears to play a structural role in HDL.

There are two major forms of apolipoprotein B, apo B-48 and apo B-100, which are synthesized by the intestine and liver, respectively. Apolipoprotein B-48 is present in chylomicrons, while apo B-100 is present in VLDL, LDL, and HDL. Both apo B-100 and B-48 play an important role in regulating cholesterol synthesis and degradation. The B apoproteins control the interaction of LDL and chylomicron remnants with specific receptors of liver and extrahepatic cells. Since the clinical significance and serum concentration of apo B-100 have been determined and those of apo B-48 remain unknown, the term serum apo B usually refers to apo B-100.

Recent studies have shown that in CHD, changes in the serum levels of apo A and apo B are similar to those in the cholesterol levels of HDL and LDL, respectively. Apolipoprotein A levels are decreased and apo B levels are increased in individuals with CHD compared with those without disease. Many investigators have further demonstrated a specific

### Table II

<table>
<thead>
<tr>
<th>Low Density Lipoprotein Cholesterol mg/dL, (mmol/L)</th>
<th>75th Percentile</th>
<th>90th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>130 (3.36)</td>
<td>145 (3.75)</td>
</tr>
<tr>
<td>30-39</td>
<td>145 (3.75)</td>
<td>160 (4.14)</td>
</tr>
<tr>
<td>&gt; 40</td>
<td>160 (4.14)</td>
<td>180 (4.66)</td>
</tr>
</tbody>
</table>
**Figure 1.** Recommendations for diagnosis and treatment of hypercholesterolemia.

decrease in the level of apo AI in subjects with CHD. In contrast, the level of apo AII in these individuals was normal or slightly elevated. In light of these findings, apo AI may correlate better than apo A with increased risk of CHD.2

The clinical use of serum apolipoprotein determination for the assessment of CHD risk is relatively new but shows great promise. The plasma levels of apo AI and B discriminate better between individuals with angiographically documented CHD and normals than does the cholesterol level of the corresponding lipoproteins.16,23 Further studies have demonstrated that the apo AI/apo B ratio correlates very highly with the severity and extent of coronary artery stenosis.24 Compared to the LDL cholesterol/HDL cholesterol ratio, which is considered by many experts as the "best" marker for assessment of CHD, or the total cholesterol/HDL cholesterol ratio, the apo AI/apo B ratio was better correlated by severalfold.24 In addition, expressing the results as a ratio, apo AI/apo B, was shown to be far more effective than referring to the levels of apo AI and apo B alone. It also seems that apolipoproteins are more sensitive and specific than conventional lipid and lipoprotein profiling24 (table III).

The availability of specific antisera has led to the quantification of serum apo AI and apo B by a variety of immunochemi-
Radioimmunoassay, electroimmunoassay, radial immunodiffusion, immunonephelometry, and immunoturbidimetry have been used in both research and clinical laboratories. Most clinical laboratories, however, use either the immunoturbidimetric or immunonephelometric technique because they yield good precision and can be automated.

Accurate measurement of apolipoproteins has been hampered by technical problems because these proteins exist in complex mixtures with lipids, are relatively insoluble and cannot be assayed on the basis of their functions. In the past few years, some of these problems have been solved. Numerous techniques for delipidating apoproteins, in order to unmask their antigenic sites and provide a maximum antigen/antibody interaction, have been described.

Because of the instability and self-association of purified apolipoproteins, the use of serum as a secondary standard is recommended. The absolute values of secondary standards currently depend on the immunochemical method. Standardization of materials and methods will improve the comparability of normal values and help ensure that values obtained for abnormal populations are comparable among various methods and laboratories. The Center for Disease Control is currently conducting an international survey as a first attempt to standardize apo AI and apo B assays.

The other important issue in apolipoprotein measurement is the determination of appropriate reference ranges. Based on the new definition of "normal cholesterol value" 6 it is reasonable to expect that optimum ranges will be similarly set for apolipoproteins. Until the role of apolipoproteins in atherogenesis is understood and information such as reference ranges are determined, it will be difficult to develop dietary and drug treatment strategies on the basis of apolipoprotein values.

Prevention of Coronary Heart Disease

Because atherosclerosis is clinically silent throughout most of its course, cardiovascular epidemiologists have been focusing on the asymptomatic period in order to identify habits, traits, and other factors that can be used to identify individuals at increased risk of having a clinical coronary event. Some of the identified risk factors cannot be modified, such as male sex, age, and family history of early events. Factors that can be altered include cigarette smoking, blood pressure, and cholesterol concentration.

The results of prospective and retrospective studies have shown that the risk of heart disease from smoking is decreased by 90 percent after only one year of nonsmoking. The benefits of detection and control by hypertension are even more impressive. The Veterans Administration trials of the 1960s and 1970s have shown that treatment of moderate and severe hypertension can actually prevent stroke and heart attacks. The LRC-CPPPT, and more recently the Helsinki Heart Trial, have demonstrated that lowering the serum cholesterol level reduces the incidence of angina pectoris, heart attack and sudden death. Moreover, the CLAS study has shown morphologic improvement in established coronary lesions as a result of cholesterol lowering. In the latter two studies, the treatment used not only lowered LDL but also increased HDL. The contribution of increasing HDL to diminished risk is uncertain but suggestive.

The idea of altering diet to lower serum cholesterol is not novel. In 1961 the American Heart Association recommended a dietary strategy for preventing this disease. Improving dietary habits can be used to lower serum cholesterol for the whole population as well as individuals. Drug therapy should be reserved for individuals at particularly high risk. Public awareness of cholesterol as a risk factor has resulted in
noticeable behavioral changes over the last 20 years. Americans have decreased their consumption of milk and cream by 24 percent, of butter by 33 percent, of eggs by 12 percent, and of animal fat by 40 percent. The average consumption of cholesterol has dropped from 800 mg per day to less than 500 mg per day. However, the American Heart Association current recommendation for cholesterol consumption is 300 mg per day for men and 225 mg per day for women.¹⁸

Patients whose cholesterol levels are not reduced by diet may benefit from medication. Although five classes of drugs are available, no single ideal drug exists. Each drug has its distinctive advantages and side effects. The available hypocholesterolemic drugs include: (1) bile acid binding resin (cholestyramine and colestipol), (2) probucol, (3) nicotinic acid, and (4) fibric acid derivatives (gemfibrozil, clofibrate, fenofibrate, and bezafibrate), and competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase (lovastatin, mevastatin, and mevinolin). Bile acid sequestrants and niacin are proven to be effective and safe; therefore, they are usually the drugs of first choice in the treatment of hypercholesterolemia. The bile acids action is to enhance hepatic degradation of cholesterol into bile acids while niacin appears to suppress the hepatic synthesis of lipoprotein. Both drugs lower serum cholesterol by 15 to 30 percent. Fibric acids are the most widely used hypolipidemic drugs throughout the world. Their exact mechanisms of action still unclear. These drugs are well tolerated but can reduce cholesterol level only moderately, i.e., 10 to 20 percent. Probucol enhances the clearance of serum LDL but also reduces HDL. It is a well tolerated drug and decreases serum cholesterol moderately, like the fibric acids. In 1987 the Food and Drug Administration approved lovastatin, a HMG-CoA reductase inhibitor, for the treatment of hypercholesterolemia. Low doses of HMG-CoA reductase inhibitors are able to reduce serum cholesterol levels markedly without serious side effects. These drugs are analogous in structure to HMG-CoA and converted to mevalonic acid under the influence of HMG-CoA reductase, the rate limiting enzyme in the synthesis of cholesterol. Competitive inhibition of this enzyme almost blocks the formation of the metabolic products of mevalonic acid, such as cholesterol, dolicholubiquinone, and isopentyl adenine. If the long-term use of reductase inhibitors are shown to be free of serious side effects, HMG-CoA reductase inhibitors will be the drugs of choice in the treatment of hypercholesterolemia.¹³ Neomycin has also been used by some for cholesterol lowering.

Surveys conducted in 1983 indicated that many physicians reserved treatment for high cholesterol levels for those with levels in the top 1% to 10% of the population distribution.²⁹ In light of the MRFIT, LRC-CPPT, CLAS, Helsinki Heart Study findings, a much larger number of patients actually require treatment for hypercholesterolemia.¹⁰,¹²,¹³,¹⁴ Increased physical activity has been shown to be associated with a reduced risk of cardiovascular disease. In addition to its direct effect on the myocardium, exercise decreases total and LDL cholesterol and apo B and increases HDL cholesterol and apo AI.¹⁴ Although there is no epidemiologic support for the association of CHD and exercise, physicians are encouraged to recommend exercise to their patients to decrease CHD risk.

In summary, aggressive public education, alterations in dietary and smoking habits, successful therapies, and increased control of blood pressure are current recommendations to reduce coronary morbidity and mortality. Accurate and precise laboratory determination for serum lipids are an essential component of this effort.
References


