Coronary heart disease (CHD) remains the leading cause of death in the United States with more than 40% of all deaths each year directly attributed to the disease. Current evidence suggests that early identification and aggressive modification of risk factors offer the most promising approach to reducing the burden of CHD. Dyslipidemia has been identified as the primary risk factor leading to the development of CHD. It is estimated that nearly 65 million Americans require some form of lipid-modification therapy.

The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) set of guidelines released in May 2001 provides physicians with evidence-based recommendations on the classification, diagnosis, and treatment of lipid disorders. New features of the guidelines include a scoring system for calculating CHD risk, as well as the identification of CHD risk equivalents, lower treatment target goals, and an emphasis on conditions conferring a higher risk for CHD, such as the metabolic syndrome. The ATP III emphasis on risk assessment substantially increases the number of patients considered at risk for CHD and will expand the number eligible for lifestyle and drug interventions.

This article highlights the new recommendations and reviews the impact of ATP III on osteopathic physicians.

(Key words: atherosclerosis, cholesterol, coronary heart disease, dyslipidemia, low-density lipoprotein cholesterol [LDL-C])
modifications and pharmacologic therapy. In May 2001, the Adult Treatment Panel (ATP) of the National Cholesterol Education Program (NCEP) issued its third set of guidelines (NCEP ATP III) for the identification and management of dyslipidemia. Building on ATP I (1988) and ATP II (1993), ATP III pays increased attention to the identification and quantification of risk factors for CHD and therefore vastly expands the number of Americans eligible for lipid-lowering therapy.

With these changes, ATP III presents a challenge to physicians and the healthcare system to identify at-risk patients, implement effective therapy, and ensure that patients meet target goals (Figure 1). Osteopathic physicians, many of whom focus on primary care with an emphasis on treating the entire patient, are in the vanguard for the reduction of CHD risk. Therefore, osteopathic physicians are uniquely positioned to have an impact on the implementation of the new guidelines.

New features of the ATP III guidelines

Consistent with previous editions, the new ATP guidelines provide an evidence-based approach for the detection and treatment of lipid disorders. Adult Treatment Panel III follows ATP II by continuing to focus on reduction of low-density lipoprotein cholesterol (LDL-C) as the primary goal of therapy and advocates that the intensity of therapy be adjusted to the degree of risk. The ATP III set of guidelines also reiterates the importance of lifestyle changes such as weight loss, dietary modifications, and increased physical activity in reducing CHD risk (Figure 1).

New features of the guidelines include the use of a risk assessment tool based on data derived from the Framingham Heart Study, the identification of diabetes (with or without clinically evident CHD) as a CHD risk equivalent, more aggressive lipid target levels, and the recognition that patients with the metabolic syndrome should be provided intensified lipid-modification therapy (Figure 1).

Adult Treatment Panel III places patients into one of three categories of CHD risk (high, moderate, low) and identifies specific LDL-C treatment goals for each (Figure 2). The LDL-C target levels for patients with CHD and CHD risk equivalents (highest risk) are now less than 100 mg/dL. For patients with two or more risk factors (moderate risk), the target level is less than 130 mg/dL, and for patients with zero or one risk factor (low risk), the goal is less than 160 mg/dL.

Adult Treatment Panel III also recognizes the role high-density lipoprotein cholesterol (HDL-C) and triglycerides play in modifying CHD risk and therefore raised the target level for HDL-C from less than 35 mg/dL to less than 40 mg/dL and lowered target goals for triglycerides to less than or equal to 200 mg/dL.

Further, ATP III recognizes that the heightened emphasis on risk assessment, the inclusion of CHD risk equivalents, and the more aggressive treatment goals will significantly increase the number of patients eligible for therapy and challenge physicians and the healthcare delivery system to implement the guidelines. Therefore, ATP III also presents strategies for promoting adherence to therapeutic lifestyle changes (TLC) and drug therapy.

Assessment of risk for coronary heart disease

The Framingham risk scoring system incorporated into ATP III quantifies the 10-year risk for a coronary event. Point scores are calculated according to the presence of five major CHD risk factors (age and gender, total cholesterol, systolic blood pressure, HDL-C level, and smoking status), with each risk factor worth a certain number of points. When added together, the sum yields an estimate of the risk for having a coronary event in 10 years. A properly conducted assessment places patients into one of the three risk categories and forms the basis for all subsequent treatment decisions.

Patients with documented CHD and CHD risk equivalents are automatically placed in the highest risk category. The CHD risk equivalents carry a risk for a major coronary event equal to that of established CHD and include diabetes, peripheral vascular disease, symptomatic carotid artery disease, and abdominal aortic aneurysm. The new set of guidelines places patients with these conditions in the same risk category as those with clinically evident CHD (eg, >20% 10-year risk of CHD). The LDL-C treatment goal for patients in this high-risk category is less than 100 mg/dL.

In patients without documented CHD or CHD equivalents, assessment of CHD risk using the Framingham risk quantification system is essential to determine the most appropriate course of therapy. Patients with two or more major risk factors are considered to be at a moderately increased risk for CHD, with a 10-year risk of less than 20%. Therapy for the patients in this category should be

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**Figure 1. Challenges, emphasis, and new features of the Adult Treatment Panel III guidelines.**

- **Challenges**
  - Identify patients at risk for CHD
  - Implement effective therapy
  - Ensure that patients meet target goals

- **Emphasis**
  - Risk assessment
  - Reduction of low-density lipoprotein cholesterol (LDL-C) as primary goal of therapy
  - Adjustment of intensity of therapy to degree of risk
  - Importance of lifestyle changes to include:
    - weight loss
    - dietary modifications
    - increased physical activity

- **New features**
  - Use of a risk assessment tool based on data derived from the Framingham Heart Study
  - Identification of diabetes as a coronary heart disease (CHD) risk equivalent
  - More aggressive lipid target goals
  - Intensified lipid-modification therapy for patients with the metabolic syndrome
  - Raising target for high-density lipoprotein cholesterol level (to < 40 mg/dL)
  - Lowering target for triglyceride concentration (to < 200 mg/dL)
  - Strategies for promoting adherence to treatment regimens
Current treatment trends

With the increased emphasis on risk assessment and aggressive new treatment goals, it is estimated that the number of patients eligible for CHD risk reduction through lipid-modification therapy in the United States is currently at 65 million. The type and extent of therapy is dependent on the patient’s CHD risk. Two primary modalities advocated by ATP III for lowering LDL-C, and therefore CHD risk, are ATP TLC and drug therapy.

Therapeutic lifestyle changes

First-line therapy for all patients is TLC and may be substantial enough in groups at lower risk to reach their LDL-C goals. Components of TLC that have demonstrated effectiveness in lowering LDL-C include eating a healthy diet, regular physical activity, smoking cessation, and weight loss. Dietary changes should include a reduction of saturated fats to less than 7% of total calories, reduction of intake of dietary cholesterol to less than 200 mg/d, addition of plant sterols and stanols at a level of 2 g/d (commercially available in special margarines), and incorporating viscous fiber into the diet at a level of 10 g/d to 25 g/d. Weight reduction can reduce LDL-C levels and ameliorate the risk factors associated with the metabolic syndrome by improving insulin sensitivity and serum glucose uptake. Physical activity raises HDL-C levels and decreases the concentration of very low-density lipoprotein cholesterol and triglycerides. Smoking cessation also results in a reduction of CHD risk.

Pharmacologic therapy

Although ATP III emphasizes the importance of nonpharmacologic therapy, it recognizes limitations of such therapy and encourages the addition of drug therapy if TLC fails to move a patient to goal after 3 months. High-risk patients will most likely require drug therapy along with TLC from the onset of treatment. As stated earlier, treatment goals and lipid thresholds for initiating drug therapy are based on the patient’s degree of risk.

For patients with the highest risk for coronary events, the LDL-C threshold for initiation of therapy is greater than or equal to 130 mg/dL (after a 3-month trial of TLC) and the goal is less than 100 mg/dL. For patients with LDL-C between 100 mg/dL and 129 mg/dL, drug therapy is optional and physicians are encouraged to use their professional clinical judgment to determine the nature of therapy required to reduce CHD risk.

For patients with moderate risk without definite CHD or CHD risk equivalents but with more than two major risk factors and a 10-year risk of 10% to 20%, the threshold is greater than or equal to 130 mg/dL and the target is also less than 130 mg/dL.

For patients at moderate risk but with a 10-year risk of less than 10%, the threshold for LDL-C is greater than or equal to 160 mg/dL and the target is less than 130 mg/dL.

Currently available lipid-modifying drugs

Four classes of lipid-modifying drugs are currently available in prescription form, including bile acid sequestrants, nicotinic acids, fibrin acid derivatives, and bile acid sequestrants.
and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins). Statins, the most widely used lipid-modifying agent, decrease LDL-C by inhibiting cholesterol synthesis and reduce LDL-C by 25% to 50% in a dose-dependent manner.

The currently available statins are differentiated by the LDL-C lowering elicited at a given dose. Several large clinical outcomes trials have demonstrated that statin use reduces the incidence of CHD events, including myocardial infarction, coronary death, stroke, and total mortality. Bile acid sequestrants are another commonly used agent.

Bile acid sequestrants can be used as monotherapy when moderate reductions in LDL-C are required to achieve goal or as add-on therapy to statins, particularly in patients with severe dyslipidemia.

A third class of agents is nicotinic acid, or niacin. Nicotinic acids provide a moderate LDL-C-lowering action, but the primary utility of these agents is in combination with statins for patients who have elevated triglyceride concentrations or low HDL-C levels or both.

Fibrates, or fibrates, are a fourth class of lipid-modifying agents that possess minimal LDL-C-reducing capacity, but these agents are useful in patients with combined forms of hyperlipidemia. Fibrates are especially effective in patients who have severe hypertriglyceridemia.

Despite the efficacy of statins in modifying lipid levels and reducing coronary events, alternative agents are needed. Some patients are unable to tolerate statins, or they are not candidates for use of these agents because of either or both tolerability and safety concerns. In these cases, physicians and patients are forced to use bile acid sequestrants, niacin, fibrates, or other less common modes of therapy. These agents, however, vary in their effectiveness in reducing LDL-C levels owing to low efficacy of the agent or poor compliance due to undesired side effects.

A promising new alternative mode of therapy was recently approved by the US Food and Drug Administration (FDA). Phase II data suggest that ezetimibe, the first selective inhibitor of intestinal cholesterol absorption, appears to have substantial potential for use as monotherapy in patients at low risk for CHD who require only a modest reduction in their LDL-C level or for those who do not tolerate statin therapy. In addition, ezetimibe, when used in combination with a low-dose statin in patients at moderate to high risk for CHD, can elicit a reduction in LDL-C comparable to reductions seen at the highest statin doses.

Implementation of the ATP III guidelines

The ATP III set of guidelines, with an emphasis on risk assessment and new treatment goals, presents an enormous challenge to physicians and the healthcare system in terms of implementation and patient compliance. Previous guideline adherence rates indicate that achieving the new goals will be difficult. The ATP II guidelines, although much less complex, were rarely followed in patients with CHD, let alone in patients with subclinical disease. Data from the Lipid Treatment Assessment Project (L-TAP) demonstrated that only 18% of those with CHD achieved ATP II goals and that less than 40% of all patients on lipid-modification therapy receive sufficient lipid lowering to reduce CHD risk. Because overall adherence and goal achievement was low with previous guidelines, the challenges inherent in achieving ATP III goals are clear.

The ATP III acknowledges that primary prevention of CHD offers the greatest opportunity for reducing the clinical and economic burden of CHD in the United States. The clinical approach to CHD prevention begins in the primary care office and requires an informed physician who does not focus solely on a specific symptom and who implements early risk screening that includes an assessment of the overall health of the patient. Because nearly 60% of all osteopathic physicians practice in primary care and account for more than 100 million primary care visits per year, they are uniquely positioned to influence the implementation of the ATP III guidelines. Thus, DOs can have a significant impact on the reduction of CHD risks in their patients.

Osteopathic physicians also treat a large number of patients who have limited access to healthcare. Consequently, DOs must educate their patients about the importance of taking responsibility for their own health through the incorporation of healthy lifestyle habits.

References


Large numbers of patients have undiagnosed dyslipidemia, and those who do receive a diagnosis are often given inadequate therapy. The American Heart Association estimates that more than 100 million adults in the United States have total cholesterol levels greater than 200 mg/dL and at least 40% of these individuals have cholesterol levels in excess of 240 mg/dL. The true number of dyslipidemic individuals in the United States may never be known because of the enormity of effort and magnitude of cost required for screening all at-risk individuals. Because more than 12.6 million Americans have coronary heart disease (CHD) and more than 500,000 deaths are attributed to this disease each year, physicians should be strongly encouraged to heed the advice of the National Cholesterol Education Program.

Despite increased attention placed on the identification and treatment of dyslipidemia, this condition remains undiagnosed and untreated in a significant number of patients. The recently released National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) set of cholesterol management guidelines increases to more than 65 million the number of Americans eligible for lipid-modifying therapy. Recent data, however, suggest that even with the availability of multiple regimens with proven efficacy, as many as 50% of all patients do not have their cholesterol assessed and less than 45% receive lipid-modifying therapy. In addition, less than 25% of patients are treated to their NCEP target low-density lipoprotein cholesterol (LDL-C) level. Persistence with therapy is another challenge, as more than 70% of patients fail to maintain their therapy beyond 12 months. If a realistic attempt is to be made to reduce the risk of coronary heart disease among Americans, diagnosis of dyslipidemia and treatment to therapeutic targets must be improved. This article discusses the underdiagnosis and undertreatment of lipid disorders and reviews the role of osteopathic physicians in strategies achieving ATP III LDL-C goals.

(Key words: Adult Treatment Panel III [ATP III], compliance, cholesterol, dyslipidemia)

Dr Clearfield is a professor of medicine and associate dean for clinical research at the University of North Texas Health Science Center at Fort Worth/Texas College of Osteopathic Medicine. Dr Clearfield represented the American Osteopathic Association, a member organization of the National Cholesterol Education Program Coordinating Committee, which approved the Third Report of the National Cholesterol Education Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Dr Clearfield is a member of the speakers bureau of AstraZeneca, Merck & Co, Pfizer Inc, and Sankyo Pharma Inc, and he has received grant/research support from AstraZeneca and Pfizer Inc.

Correspondence to Michael B. Clearfield, DO, Associate Dean for Clinical Research, Office of the Dean, Texas College of Osteopathic Medicine, University of North Texas Health Science Center at Fort Worth, 855 Montgomery St, Fort Worth, TX 76107-2699. E-mail: mclearfi@hsc.unt.edu


