Summary of the Third Report of the National Cholesterol Education Program Adult Treatment Panel III

[*Rev Cardiovasc Med.* 2001;2(3):160–165]

Key words: Coronary heart disease prevention • Cholesterol • Triglycerides • Hypercholesterolemia

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines represent the latest evolution of expert opinion on the evaluation and management of cholesterol. The new guidelines focus on primary prevention in high-risk patients. The primary goal of therapy remains low-density lipoprotein (LDL) reduction. The new features of ATP III include recommendations that:

Summary by Norman E. Lepor, MD, Cedars-Sinai Medical Center, Los Angeles, CA, and Robert E. Vogel, MD, University of Maryland School of Medicine, Baltimore, MD

- Diabetic persons without overt coronary heart disease (CHD) should receive the same aggressive cholesterol therapy as CHD patients;
- Under a Framingham-based global risk assessment for primary prevention, persons with a 10-year risk of a coronary event greater than 20% require the same aggressive cholesterol therapy as CHD patients (coronary disease–equivalent risk);
- Patients with the metabolic syndrome require the most aggressive cholesterol therapy;
- LDL cholesterol below 100 mg/dL is the ideal level;
- Abnormal high-density lipoprotein (HDL) cholesterol is defined as below 40 mg/dL versus the previous definition of below 35 mg/dL;
- Normal triglycerides are less than 150 mg/dL and borderline high triglyceride levels are between 150 and 199 mg/dL;
- A complete lipoprotein profile should be the initial screening test for adults 20 years of age and older and should be obtained every 5 years;
- Stanol/sterol ester margarines and soluble fiber should be part of dietary management;
- Treatment should be continued beyond LDL cholesterol for those with fasting triglycerides above 200 mg/dL.

Table 1
ATP III Classification of LDL, Total Cholesterol, and HDL Cholesterol (mg/dL)

LDL Cholesterol	
<100	Optimal
100–129	Near optimal/above optimal
130–159	Borderline high
160–189	High
>190	Very high
Total Cholesterol	
<200	Desirable
200–239	Borderline high
>240	High
HDL Cholesterol	
<40	Low
>60	High

Risk Assessment

All adults 20 years of age or over should have a complete fasting lipid profile (total cholesterol, LDL, HDL, and triglycerides) every 5 years. The new classifications for total LDL and HDL cholesterols are given in Table 1. Non-LDL coronary risk factors should then be used to modify the appropriate goals for LDL cholesterol in primary prevention patients. These risk factors include cigarette smoking, hypertension (blood pressure > 140/90 or currently on antihypertensive medication), HDL-C under 40 mg/dL, family history of premature coronary heart disease (CHD in first-degree relative: male < 55 years old or female < 65 years old), and age (men > 45 years, women > 55 years).

Those multiple-risk-factor primary prevention patients who have a coronary event risk over 20% (CHD-equivalent risk) per 10 years are considered high risk and require a treatment goal of LDL under 100 mg/dL. Other patients in this highest-risk/most aggressive treatment category include those with a history of CHD or other forms of atherosclerotic disease (peripheral vascular disease, abdominal aortic aneurysm and symptomatic carotid artery disease), and diabetes mellitus. Patients with more than two risk factors and an event risk of 20% or less per 10 years require an LDL-C goal of below 130 mg/dL. Those with one or no risk factors require an LDL goal of under 160 mg/dL.

The determination of CHD risk in patients without diabetes, CHD, or other atherosclerotic disease (primary prevention) is organized into a simple two-step process:

1. Count the number of risk factors (HDL > 60 mg/dL counts as a –1 risk);
2. For patients with more than two risk factors, a 10-year risk assessment is performed using the Framingham risk score for men and women (Figures 1 and 2). For patients with fewer than two risk factors, such scoring is not carried out.

Though life-habit risk factors, such as obesity and sedentary lifestyle, and emerging risk factors, including hs-C-reactive protein, homocysteine, lipoprotein(a), impaired glucose tolerance, and fibrinogen, are not part of this calculation process, their presence can be used in individual patients to assist with assessing the risk of CHD events and therefore the intensity of lipid therapy.

The following secondary causes of hypercholesterolemia should be excluded:

- Diabetes mellitus
- Hypothyroidism
- Obstructive liver disease
- Chronic renal failure
- Anabolic steroids, progestins

Treatment Goals

All patients with elevated LDL-C should undergo lifestyle enhancements, including diet and exercise. These lifestyle changes are by far the most cost-efficient methods for cholesterol modification.

To lower LDL cholesterol, the NCEP recommends a diet containing:

- 25% to 35% of calories from fat;
- less than 7% of calories from saturated fat;
- less than 200 mg per day of cholesterol.

This recommendation differs from the American Heart Association (AHA) guideline of a low-fat (<30%) diet, which tends to increase triglycerides. Examples of

Age (y):	20–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79
Points:	-9	-4	0	3	6	8	10	11	12	13

	Points				
Total	**Age**				
Cholesterol	20–39y	40–49y	50–59y	60–69y	70–79y
< 160 (mg/dL)	0	0	0	0	0
160–199	4	3	2	1	0
200–239	7	5	3	1	0
240–279	9	6	4	2	1
≥ 280	11	8	5	3	1

HDL	
Cholesterol	Points
≥60 mg/dL	–1
50–59	0
40–49	1
<40	2

	Points				
	Age				
	20–39y	40–49y	50–59y	60–69y	70–70y
Nonsmoker:	0	0	0	0	0
Smoker:	8	5	3	1	1

	Points	
Systolic BP	**Untreated**	**Treated**
<120 mmHg	0	0
120–129	0	1
130–139	1	2
140–159	1	2
≥ 160	2	3

Point Total:	<0	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	>17
10-Year Risk (%):	<1	1	1	1	1	1	2	2	3	4	5	6	8	10	12	16	20	25	≥30

Figure 1. *NCEP/Framingham estimate of 10-year coronary heart disease risk in men.*

the cholesterol-lowering potential of foods are:

- 15% by stanol and sterol ester margarines (2 g per day);
- 10% by soy products containing 50 g isoflavones per day;
- 5% by oat bran 6 g per day.

The NCEP recommends the use of soluble fiber and stanol/sterol ester margarines to lower cholesterol.

Reduced physical activity is a major risk factor for cardiovascular disease. Myocardial infarction risk is reduced:

- 50% by walking 30 minutes (about 1.5 miles) daily;
- 80% by vigorous activity once or twice weekly;
- 90% by vigorous activity 3 or 4 times weekly; and
- 98% by vigorous activity 5 or more times weekly.

Physical activity provides a number of salutary effects on the cardiovascular system and coronary risk factors, including decreases in blood pressure and heart rate and increases in HDL cholesterol. The NCEP recommends at least 30 minutes of exercise daily.

Secondary prevention. In patients with CHD or CHD equivalents, the LDL-C goal remains less than 100 mg/dL. In patients admitted to the hospital for acute coronary syndromes or coronary procedures, a full lipid profile should be performed if the patient is not on lipid therapy.

In patients with LDL-C between 100 and 129 either at baseline or on lipid therapy, the following approaches are recommended:

Age (y):	20–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79
Points:	–7	–3	0	3	6	8	10	12	14	16

	Points				
Total	**Age**				
Cholesterol	20–39y	40–49y	50–59y	60–69y	70–79y
<160 (mg/dL)	0	0	0	0	0
160–199	4	3	2	1	1
200–239	8	6	4	2	1
240–279	11	8	5	3	2
≥280	13	10	7	4	2

HDL	
Cholesterol	Points
≥60 mg/dL	–1
50–59	0
40–49	1
<40	2

	Points				
	Age				
	20–39y	40–49y	50–59y	60–69y	70–70y
Nonsmoker:	0	0	0	0	0
Smoker:	9	7	4	2	1

	Points	
Systolic BP	**Untreated**	**Treated**
<120 mmHg	0	0
120–129	1	3
130–139	2	4
140–159	3	5
≥160	4	6

Point Total:	<9	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	>25
10-Year Risk (%):	<1	1	1	1	1	2	2	3	4	5	6	8	11	14	17	22	27	>30

Figure 2. *NCEP/Framingham estimate of 10-year coronary heart disease risk in women.*

- Initiate or intensify lifestyle and/or drug therapies to lower LDL-C;
- Emphasize weight reduction and increased physical activity in patients with the metabolic syndrome (abdominal obesity, atherogenic dyslipidemia–small LDL, hypertension, insulin resistance, and prothrombotic/proinflammatory states);
- Delay use or intensification of LDL-lowering therapies and consider the use of fibric acid derivatives or niacin if HDL-C is low or triglycerides are elevated.

In patients with LDL-C above 130 mg/dL, intensive lifestyle modifications should be initiated. Because most patients will require medication to achieve the goal of LDL-C under 100 mg/dL, medical therapy can also be initiated at this time.

In patients with LDL-C below 100 mg/dL, further LDL-C lowering is not required. Emphasis should be placed on controlling other lipid (low HDL, elevated triglycerides) and nonlipid risk factors and on the treatment of the metabolic syndrome.

Primary prevention. Patients with diabetes or with more than two risk factors and a 10-year risk of CHD of above 20% should be treated according to the secondary prevention goals outlined above.

In patients with ≥2 risk factors and 10-year risk of 10% to 20%, the intensity of treatment is adjusted according to LDL-C levels and level of risk. The goal for LDL-C is less than 130 mg/dL.

In patients with a CHD 10-year risk of 10% to 20%, lifestyle modifications should be initiated and maintained for three months. If the resulting LDL-C does not meet the goal, drug therapy should be initiated. For lower-risk patients (10-year risk under 10%), the LDL-C goal remains less than 130 mg/dL. Lifestyle modification is recommended, and only if LDL-C is over 160 mg/dL should drug therapy be considered.

For patients with one or no risk factors, the goal for LDL-C is under 160 mg/dL. First-line therapy is lifestyle modification. If LDL-C is 160 to 189 mg/dL, an adequate trial of diet and exercise should be initiated; drug therapy is optional. Factors that could favor drug treatment include strong single-risk factors (heavy smoking, poorly controlled hypertension, strong family history of premature CHD or a very low HDL-C), multiple life-habit risk factors and emerging risk factors, and those who's 10-year risk approaches 10%. If LDL-C is above 190 mg/dL, drug therapy can be considered.

Drug Therapy

General considerations. The drugs most useful in managing dyslipidemias include reductase inhibitors, bile acid sequestrants, fibric acids, and nicotinic acid. When drug therapy is indicated for reducing LDL cholesterol, reductase inhibitors are generally initiated as first-line therapy. Exceptions include pregnancy, hepatic disease, or a history of myositis while taking these agents. Bile acid sequestrants or nicotinic acid can be added if LDL cholesterol is not reduced to goal levels. Increased triglycerides and/or reduced HDL cholesterol with LDL cholesterol under 130 mg/dL respond best to fibric acids and nicotinic acid, respectively. In mixed dyslipidemia, with LDL above 130 mg/dL, a reductase inhibitor should be initiated, with addition of a fibric acid or nicotinic acid if goals are not achieved. A non-HDL (LDL+VLDL) cholesterol under 130 mg/dL is a useful goal in patients with coronary heart disease or with coronary heart disease–equivalent risk. With combined therapy, symptoms of myositis and liver function should be monitored closely. In severe cases, three agents may be used.

Secondary prevention. Consideration should be given to initiating or enhancing drug therapy in patients during hospitalization for a major coronary event. This avoids the treatment gap that occurs after patients are discharged from the hospital and before their outpatient follow-up. Most patients with CHD or CHD-equivalent risk will need LDL-lowering drug therapy.

Drug therapy should be initiated if lifestyle modifications do not result in meeting the LDL-C goals.

Primary prevention. Drug therapy should be initiated if lifestyle modifications do not result in meeting the LDL-C goals. Continuation of lifestyle modifications, including exercise, reduced intake of saturated fats (to below 7% of total calories, with cholesterol under 200 mg/day), and weight reduction, are mandatory, along with concomitant drug therapy. Focus on LDL reduction remains primary, therefore LDL-C lowering agents, including statins,

Main Points

- The National Cholesterol Education Program Adult Treatment Panel III guidelines for primary prevention have LDL-C goals of <100 mg/dL in diabetics and those patients with at least two CAD risk factors and > 20% risk of coronary event over ten years as defined by the Framingham risk model.
- All adults 20 years of age or over should have a complete fasting lipid profile (total cholesterol, LDL, HDL, and triglycerides) every 5 years.
- Non-LDL coronary risk factors should be used to modify the appropriate goals for LDL cholesterol in primary prevention patients.
- All patients with elevated LDL-C should undergo lifestyle enhancements, including diet and exercise. Statins remain the mainstay for LDL reduction therapy with the use of niacin and binding resins also considered.
- Recommends treatment beyond LDL for patients with fasting triglycerides > 200 mg/dL including by using fibric acid derivatives and niacin carefully added to LDL reducing agents.

bile acid sequestrants or nicotinic acid, can be used. The patient's response should be monitored 6 weeks after initiating therapy, with intensification of therapy with either higher doses or combinations of therapy for suboptimal results. LDL-C should be reassessed 6 weeks later. Once goal LDL-C levels are attained, attention can turn to non-LDL-C lipid and non-lipid risk factors.

Increasing evidence suggests that hypertriglyceridemia is an independent risk factor for coronary heart disease.

Special issues. *Elevated serum triglycerides.* Increasing evidence suggests that hypertriglyceridemia is an independent risk factor for CHD. A variety of conditions contribute to hypertriglyceridemia, including obesity, smoking, excess alcohol use, high-carbohydrate diet, diabetes, nephrotic syndrome, chronic renal failure, and certain drugs such as corticosteroids, retinoids, and higher doses of beta blockers. Hypertriglyceridemia is frequently seen in patients with the metabolic syndrome (truncal obesity, insulin resistance, hypertension, small-dense LDL, low HDL-C, elevated triglycerides, and hypercoagulability). Normal triglyceride levels are now defined as under 150 mg/dL; borderline levels, between 150 and 199 mg/dL; high triglycerides, between 200 and 499 mg/dL; and very high triglycerides, above 500 mg/dL. The atherogenic triglyceride-rich particles are called remnant lipoproteins, which are partially broken down VLDL particles. In clinical practice, VLDL-C is the best estimate of the level of this atherogenic triglyceride-rich particle, making VLDL-C levels a target for intervention. The ATP III guidelines identify the sum of LDL-C and VLDL-C cholesterol levels, or "non-HDL cholesterol," as a secondary target in patients with triglyceride levels above 200 mg/dL. The goal for non-HDL cholesterol in these patients is 30 mg/dL greater than the LDL-C level. This assumes that a normal VLDL level is ≤30 mg/dL, which corresponds to a triglyceride level of about 150 mg/dL. The Friedewald equation is: total cholesterol equals LDL-C plus HDL-C plus triglycerides divided by 5. In patients with borderline triglycerides (150 to 199 mg/dL), emphasis should be placed on weight reduction and increased physical activity.

In patients with elevated triglycerides, the careful addition of niacin or fibric acid derivatives to statin therapy can be considered. In situations where triglyceride levels are above 500 mg/dL, the focus of therapy should be the reduction of levels to less than 500 mg/dL to avoid complications such as pancreatitis. Once this level has been achieved, the focus returns to LDL reduction.

Low HDL cholesterol. ATP III guidelines have changed the definition of low HDL-C from 35 mg/dL to 40 mg/dL, a level which is strongly associated with CHD, particularly in women. In these patients, LDL-C remains the primary focus of treatment. When low HDL-C is associated with high triglycerides (200 to 499 mg/dL), achieving goal levels of non-HDL cholesterol can be a secondary priority. Treating isolated low HDL-C with fibric acid derivatives or niacin is usually reserved for patients with CHD and CHD-equivalent risk.

ATP III guidelines have changed the definition of low HDL-C from 35 mg/dL to 40 mg/dL.

Diabetic dyslipidemia. LDL-C modification is the primary focus in patients with diabetic dyslipidemia to achieve levels above 100 mg/dL. When triglyceride levels are greater than 200 mg/dL, non-HDL cholesterol becomes a secondary target of therapy. ■