

# Lab Focus

January 2002—periodic insert to 'Scope from Fairview Clinical Laboratories

## New NCEP Cholesterol Practice Guidelines

New clinical practice guidelines on the prevention and management of high cholesterol in adults were issued by the National Cholesterol Education Program (NCEP), National Heart, Lung, and Blood Institute, National Institutes of Health in May 2001. The guidelines, the "Third Report of the NCEP Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults," also referred to as Adult Treatment Panel (ATP) III, represent a major update from NCEP.

Features of the new guidelines:

### Focus on Multiple Risk Factors

- Raises persons with diabetes without coronary heart disease (CHD) to CHD risk equivalent level.
- Uses Framingham projections of ten-year absolute CHD risk to identify certain patients with multiple (two or more) risk factors for more intensive treatment.
- Identifies persons with multiple metabolic risk factors as candidates for intensified therapeutic lifestyle changes.

### Modifications of Lipid and Lipoprotein Classification

- Identifies LDL cholesterol less than 100 mg/dL as optimal.
- Raises category for low HDL cholesterol from less than 35 mg/dL to less than 40 mg/dL.
- Lowers the triglyceride classification cutpoints to give more attention to moderate elevations.

### Support for Implementation

- Recommends a complete lipid profile (total, LDL, and HDL cholesterol and triglycerides) as the preferred initial test.
- Encourages use of plant stanols/sterols and viscous (soluble) fiber as therapeutic dietary options to enhance lowering of LDL cholesterol.
- Presents strategies for promoting adherence to therapeutic lifestyle changes and drug therapies.
- Recommends treatment beyond LDL lowering for persons with triglycerides greater or equal to 200 mg/dL.

The ATP full report, executive summary, and quick desk reference are available on the internet at [www.nhlbi.nih.gov/guidelines/cholesterol/index.htm](http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm). The NCEP ATP III Quick Desk Reference and Framingham point scores for estimation of ten-year risk are attached.

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## Heparin Induced Thrombocytopenia (HIT)

To follow common practice in the medical community for detecting platelet heparin antibodies in patients with HIT, we are changing our testing algorithm.

Beginning on January 1, 2002, patients with HIT will be routinely screened by an Elisa Platelet Factor 4 (PF4) assay at Fairview-University Medical Center (F-UMC).

If the Elisa test is negative or strongly positive, the results will be reported out and no further testing will be recommended.

If the Elisa test is indeterminate or weakly positive, Dr. Aysola will contact the referring physician for clinical information and to discuss whether further testing is needed. If confirmatory testing is indicated, the currently used platelet aggregation test will be recommended.

After receiving a negative Elisa result, clinicians can request a platelet aggregation test in cases where the clinical picture is highly suggestive of HIT by calling the special coagulation lab at 612-273-4797.

Currently we use the heparin-induced platelet aggregation test for the diagnosis of HIT. This test has a low sensitivity and high specificity, so it is not ideal for screening. The PF4 ELISA-based assay has a better sensitivity but is less specific. This test can be falsely positive in heparin-treated patients who do not have thrombocytopenia, most frequently in patients undergoing cardiac surgery.

Since the diagnosis of HIT is best established by evaluating the clinical events and the test results together, we think this change in testing will enhance our ability to diagnose or rule out HIT in the future.

The test can be ordered on the F-UMC Coagulation request form by checking the Platelet Heparin Antibody (PHA) test, or by writing in HIT.

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# ATPIII Guidelines At-A-Glance

## Quick Desk Reference

### Step 1 Determine lipoprotein levels-obtain complete lipoprotein profile after 9 to 12 hour fast.

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

##### LDL Cholesterol-Primary Target of Therapy

<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

### Step 2 Identify presence of clinical atherosclerotic disease that confers high risk for coronary heart disease (CHD) events (CHD risk equivalent):

- ◆ Clinical CHD
- ◆ Symptomatic carotid artery disease
- ◆ Peripheral arterial disease
- ◆ Abdominal aortic aneurysm

### Step 3 Determine presence of major risk factors (other than LDL):

#### Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals

- ◆ Cigarette smoking
- ◆ Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)
- ◆ Low HDL cholesterol (<40 mg/dL)\*
- ◆ Family history of premature CHD (CHD in male first degree relative <55 years; CHD in female first degree relative <65 years)
- ◆ Age (men ≥45 years; women ≥55 years)

\*HDL cholesterol ≥60 mg/dL counts as a "negative" risk factor; its presence removes one risk factor from the total count.

- ◆ Note: in ATP III, diabetes is regarded as a CHD risk equivalent.

### Step 4 If 2+ risk factors (other than LDL) are present without CHD or CHD risk equivalent, assess 10-year (short term) CHD risk (See Framingham tables).

#### Three levels of 10-year risk:

- ◆ >20% - CHD risk equivalent
- ◆ 10-20%
- ◆ <10%

### Step 5 Determine risk category:

- ◆ Establish LDL goal of therapy
- ◆ Determine need for therapeutic lifestyle changes (TLC)
- ◆ Determine level for drug consideration

#### LDL Cholesterol Goals and Cutpoints for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories

Risk Category	LDL Goal	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)	LDL Level at Which to Consider Drug Therapy
CHD or CHD Risk Equivalents (10-year risk >20%)	<100 mg/dL	≥100 mg/dL	≥130 mg/dL (100-129 mg/dL; drug optional*)
2+ Risk Factors (10-year risk ≤20%)	<130 mg/dL	≥130 mg/dL	10-year risk 10-20%: ≥130 mg/dL
			10-year risk <10%: ≥160 mg/dL
0-1 Risk Factor <sup>^</sup>	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160-189 mg/dL; LDL-lowering drug optional)

\* Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol <100 mg/dL cannot be achieved by therapeutic lifestyle changes. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g. nicotinic acid or fibrate. Clinical judgment also may call for deferring drug therapy in this subcategory.

<sup>^</sup> Almost all people with 0-1 risk factor have a 10-year risk <10%, thus 10-year risk assessment in people with 0-1 risk factor is not necessary.

### Step 6 Initiate therapeutic lifestyle changes (TLC) if LDL is above goal.

#### TLC Features

- TLC Diet:
  - Saturated fat <7% of calories, cholesterol <200 mg/day
  - Consider increased viscous (soluble) fiber (10-25 g/day) and plant stanols/sterols (2 g/day) as therapeutic options to enhance LDL lowering
- Weight management
- Increased physical activity

Source:

National Institutes of Health  
National Heart, Lung, and Blood Institute

## Step 7 Consider adding drug therapy if LDL exceeds levels shown in Step 5 table:

- ◆ Consider drug simultaneously with TLC for CHD and CHD equivalents.
- ◆ Consider adding drug to TLC after 3 months for other risk categories.

### Drugs Affecting Lipoprotein Metabolism

Drug Class	Agents and Daily Doses	Lipid/Lipoprotein Effects	Side Effects	Contraindications
HMG CoA reductase inhibitors (statins)	Lovastatin (20-80 mg) Pravastatin (20-40 mg) Simvastatin (20-80 mg) Fluvastatin (20-80 mg) Atorvastatin (10-80 mg) Cerivastatin (0.4-0.8 mg)	LDL ↓18-55% HDL ↑5-15% TG ↓7-30%	Myopathy Increased liver enzymes	Absolute: ◆ Active or chronic liver disease Relative: ◆ Concomitant use of certain drugs*
Bile acid sequestrants	Cholestyramine (4-16 g) Colestipol (5-20 g) Colesevelam (2.6-3.8 g)	LDL ↓15-30% HDL ↑3-5% TG No change or increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute: ◆ Dysbeta-lipoproteinemia ◆ TG >400 mg/dL Relative: ◆ TG >200 mg/dL
Nicotinic acid	Immediate release (crystalline) nicotinic acid (1.5-3 gm), extended release nicotinic acid (Niaspan®) (1-2 g), sustained release nicotinic acid (1-2 g)	LDL ↓5-25% HDL ↑15-35% TG ↓20-50%	Flushing Hyperglycemia Hyperuricemia (or gout) Upper GI distress Hepatotoxicity	Absolute: ◆ Chronic liver disease ◆ Severe gout Relative: ◆ Diabetes ◆ Hyperuricemia ◆ Peptic ulcer disease
Fibric acids	Gemfibrozil (600 mg BID) Fenofibrate (200mg) Clofibrate (1000 mg BID)	LDL ↓5-20% (may be increased in patients with high TG) HDL ↑10-20% TG ↓20-50%	Dyspepsia Gallstones Myopathy	Absolute: ◆ Severe renal disease ◆ Severe hepatic disease

Cyclosporine, macrolide antibiotics, various antifungal agents, and cytochrome P-450 inhibitors (fibrates and niacin should be used with appropriate caution.)

## Step 8 Identify metabolic syndrome and treat, if present, after 3 months of TLC.

### Clinical Identification of the Metabolic Syndrome-Any 3 of the Following:

Risk Factor	Defining Level
Abdominal obesity*	Waist circumference^ Men >102 cm (>40 in) Women >88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	Men <40 mg/dL Women <50 mg/dL
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥110 mg/dL

\* Overweight and obesity are associated with insulin resistance and the metabolic syndrome. However, the presence of abdominal obesity is more highly correlated with the metabolic risk factors than is an elevated body mass index (BMI). Therefore, the simple measure of waist circumference is recommended to identify the body weight component of the metabolic syndrome.

^ Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased, e.g. 94-102 cm (37-39 in). Such patients may have a strong genetic contribution to insulin resistance. They should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.

### Treatment of the metabolic syndrome

- Treat underlying causes (overweight/obesity and physical inactivity):
  - Intensify weight management
  - Increase physical activity.
- Treat lipid and non-lipid risk factors if they persist despite these lifestyle therapies:
  - Treat hypertension
  - Use aspirin for CHD patients to reduce prothrombotic state
  - Treat elevated triglycerides and/or low HDL (as shown in Step 9)

## Step 9 Treat elevated triglycerides.

### ATP III Classification of Serum Triglycerides (mg/dL)

<150	Normal
150-99	Borderline high
200-499	High
≥500	Very high

### Treatment of elevated triglycerides (≥150 mg/dL)

- ◆ Primary aim of therapy is to reach LDL goal
- ◆ Intensify weight management
- ◆ Increase physical activity
- ◆ If triglycerides are ≥200 mg/dL after LDL goal is reached, set secondary goal for non-HDL cholesterol (total-HDL) 30 mg/dL higher than LDL goal.

### LDL vs. Non-HDL Cholesterol for Three Risk Categories

Risk Category	LDL Goal	Non-HDL Goal
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	<100 mg/dL	<130 mg/dL
Multiple (2+) Risk Factors and 10-year risk ≤20%	<130 mg/dL	<160 mg/dL
0-1 Risk Factor	<160 mg/dL	<190 mg/dL

### If triglycerides 200-499 mg/dL after LDL goal is reached, consider adding drug if needed to reach non-HDL goal:

- ◆ intensify therapy with LDL lowering drug, or
- ◆ add nicotinic acid or fibrate to further lower VLDL.

### If triglycerides ≥500 mg/dL, first lower triglycerides to prevent pancreatitis:

- ◆ very low fat diet (≤15% of calories from fat)
- ◆ weight management and physical activity
- ◆ fibrate or nicotinic acid
- ◆ when triglycerides <500 mg/dL, turn to LDL lowering therapy.

### Treatment of low HDL cholesterol (<40 mg/dL)

- ◆ First reach LDL goal, then:
- ◆ Intensify weight management and increase physical activity
- ◆ If triglycerides 200-499 mg/dL, achieve non-HDL goal
- ◆ If triglycerides <200 mg/dL (isolated low HDL) in CHD or CHD equivalent consider nicotinic acid or fibrate.