Implications of

Cheryl Moredich, RNC, MS, WHNP
Deborah Kark, MS, APRN, BC, ANP
Patricia Keresztes, RN, PhD

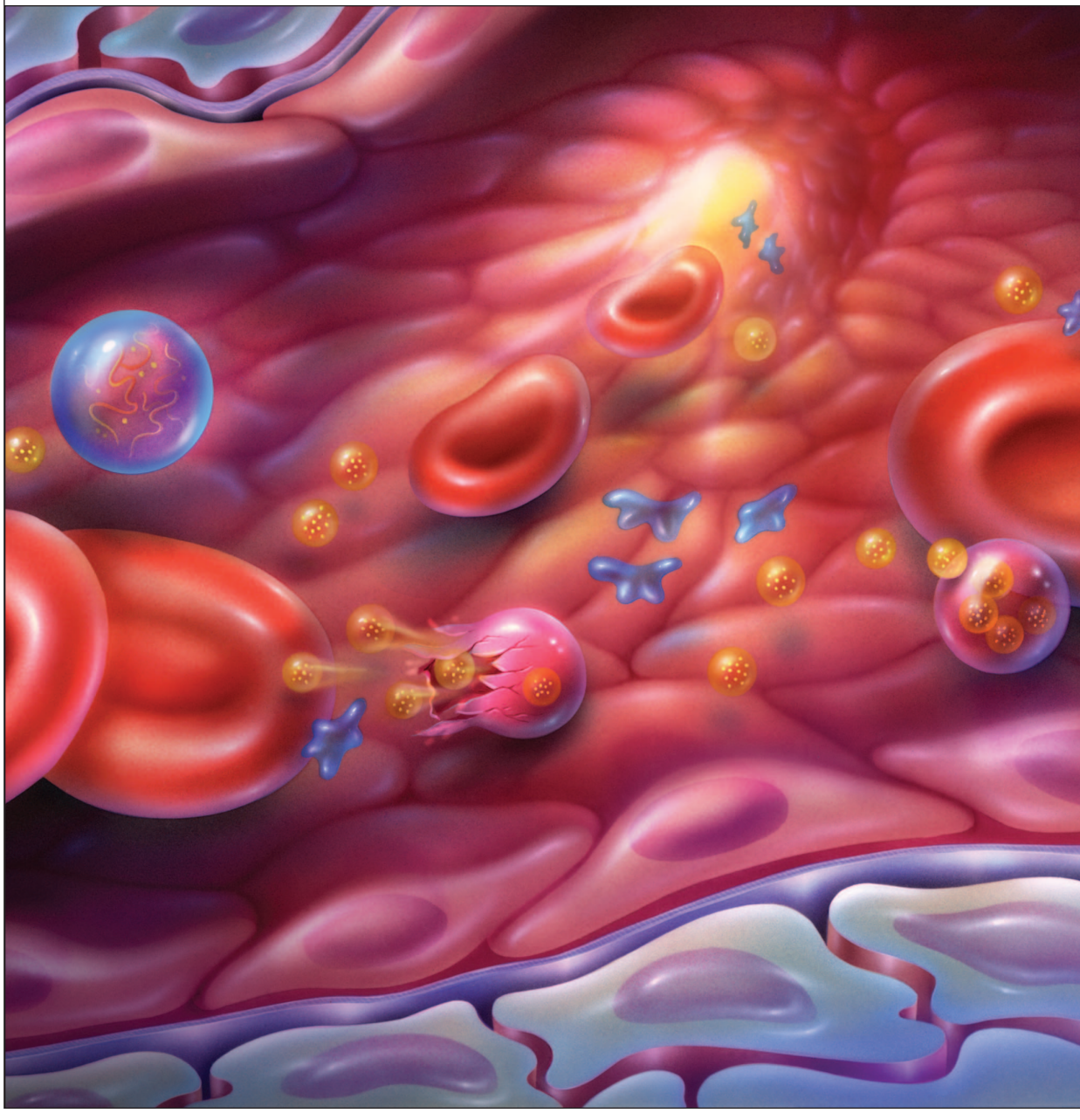


Illustration by Cynthia Turner

LDL Subclass B
in Patients at Cardiovascular Risk

Heart disease is the leading cause of death in the United States.[1] Unfortunately, many patients who had experienced a myocardial infarction (MI) were previously not considered at risk for heart disease. Although many clinicians use the Framingham Risk Profile[2] and standard lipid panels as screening tools, these may not be the best detectors when determining cardiovascular risk.

Recent studies have linked increased cardiovascular disease with the presence of a small, low-density lipoprotein (LDL) subclass pattern.[3] An altered LDL subclass can identify cardiovascular risk and practitioners can help these high-risk patients by educating them about appropriate exercise and diet modification, and by prescribing appropriate medications.

Cholesterol Basics

Cholesterol is a naturally occurring waxy substance needed for the formation of hormones, bile, vitamin D, and cell wall membranes. With normal nutrition the body produces enough cholesterol to meet its metabolic demands. The liver makes cholesterol out of excess carbohydrates, first converting them into triglycerides, a lipid composed of fatty tissue and glycerol. Once absorbed into the bloodstream, the triglycerides are bound to circulating proteins forming lipoproteins that are transported throughout the body. Triglycerides help the body store fat.

There are five types of lipoproteins and each differs in its contents of cholesterol and triglycerides. The five lipoproteins are: chylomicrons, which carry dietary fat from the intestines to the liver, deliver triglycerides to muscle tissue, and deposit excessive triglycerides in fatty tissue; very low-density lipoproteins (VLDL), which distribute triglycerides to muscle cells, deposit excess triglycerides in fatty tissue, and can contribute to the buildup of cholesterol in the arteries; intermediate-density lipoproteins (IDL); LDL; and high-density lipoproteins (HDL).

High-density lipoprotein helps to remove LDL from the blood and is often referred to as the "good" cholesterol; it brings LDL back to the liver where it is broken down. Low-density lipoprotein is sometimes called the "bad" cholesterol because it transports cholesterol from the liver and deposits it on damaged artery walls causing fatty deposits to accumulate in the arteries. This can lead to reduced blood flow and the possibility of heart disease.

Measuring Lipid Levels

Lipid panel measurements include triglycerides, HDL, LDL, and total cholesterol, which is the sum of all the cholesterol present in the blood. The standard lipid panel provides the total levels of LDL and HDL; however, recent research suggests that measuring subclasses of LDL and HDL yields more information about a patient's overall risk of cardiovascular disease.[4-7]

Low-density lipoprotein contributes 60% to 70% of the total serum cholesterol. It can be separated into seven different kinds of particles, and based on the size of these particles, two LDL subclasses have been created: LDL subclass A and LDL subclass B. Although everyone possesses both subclass A and subclass B, the proportion of each determines an individual's cardiovascular risk. The particles in LDL subclass B are smaller and more dense than those found in LDL subclass A. These small particles infiltrate the arterial wall approximately 40% to 50% faster than the larger LDL subclass A particles do. An abundance of small LDL particles (measuring less than 257 angstroms) classifies a patient as LDL subclass B and serves as an independent marker for coronary artery disease.[8] Additionally, in patients with a LDL subclass B pattern, HDL is reduced, further increasing the risk of cardiovascular disease. A patient with the LDL subclass B pattern has a 300% greater risk for developing cardiovascular disease than the patient with LDL subclass A.[9]

Checking LDL Levels

Advanced lipid studies, which detect LDL subclass, are sel-

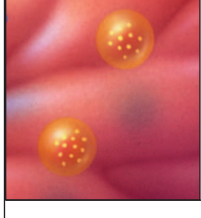
dom performed on patients with a LDL lower than 130 mg/dL. Relying solely on routine lipid profiles can exclude some high-risk patients from proper preventive treatment—it is imperative that practitioners order tests to determine LDL subclass.

Patients should have a thorough history taken, including family history and individual cardiovascular risk. The Framingham Profile may be used as a subjective risk assessment; however, a complete assessment requires an advanced lipid screen. Advanced lipid tests, such as the Vertical Auto Profile (VAP) test and the gradient gel electrophoresis test, check cholesterol parameters including total cholesterol, LDL, HDL, triglyceride, lipoprotein (a), IDL, VLDL, LDL subclass, HDL subclass, homocysteine, and C-reactive protein.[10] Results reveal any high-risk patterns and can help to identify patients who might otherwise remain untreated.

Plan of Treatment

If a practitioner knows a patient's LDL falls into subclass B, he or she can treat the patient preventatively. Patients presenting with an LDL subclass B pattern need holistic treatment through appropriate exercise, diet modification, and medications. As with other chronic conditions, the patient must be actively involved in his treatment, and the practitioner must diligently and persistently mold the three-part plan of care to best fit the patient's lifestyle and lipid disorder.

Goals of treatment for high cholesterol should be based on a patient's individual cardiovascular risk according to the ATP III guidelines (see Table: "ATP III LDL-C Treatment Goals"). Patients with diabetes and overt cardiovascular disease are considered to be at very high risk for future events and deserve intensive lipid-lowering therapy.[11] For these patients, it is recommended that LDL-C level be less than 70 mg/dL.[11] In patients with diabetes without overt CVD, LDL-C should be targeted to less than 100 mg/dL.[11]

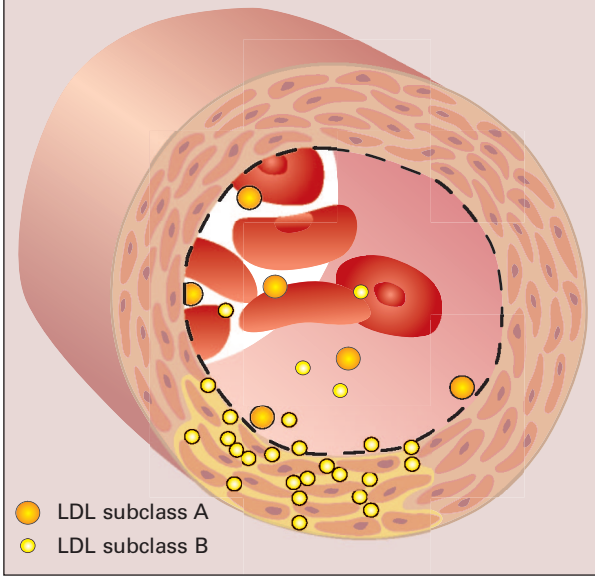


A patient with the LDL subclass B pattern has a 300% greater risk for developing cardiovascular disease than the patient with LDL subclass A.

Appropriate Exercise

Exercise is fundamental to achieve a desirable lipid profile and can help adjust the levels of subclasses of LDL. For patients in LDL subclass B, exercise increases the size of the LDL particle, bumping it into the healthier LDL subclass A pattern. This reduction in small particles helps to decrease the risk of cardiovascular disease. Exercise is also remarkably effective in increasing HDL levels.

Endothelial Wall Penetration by LDL Subclasses A and B



The American Heart Association (AHA) recommends moderate exercise most days of the week. For exercise to be effective for weight loss and cardiovascular risk reduction, the patient's heart rate should be between 70% and 85% of his calculated maximum heart rate.[12] The patient's maximum heart rate can be calculated via stress test or by subtracting the age of the patient from 220. Multiply the maximum heart rate by 70% and 85% to find the patient's target heart zone for exercise. For example, a 50-year-old patient's target heart zone would be between 119 bpm (220 – 50 x 0.70 = 119) and 146 bpm (220 – 50 x 0.85 = 144.5). Patients should slowly build up time and intensity of their workouts until they can work 30 minutes in this target zone daily, assuming this prescription fits their medical condition.

Exercise prescriptions should include intensity, frequency, type of exercise, and duration; each component produces mechanical benefits or metabolic benefits. The mechanical benefits result from exercise performed at a higher level of intensity in a shorter duration. This can change the size and density of muscles, which enriches blood flow and enhances muscle contractions. Stronger muscle contractions can lower heart rate and blood pressure as well as lower the workload of the heart and its sus-

continued on p. 23

continued from p. 18

ATP III LDL-C Treatment Goals

Risk Category	LDL-C Goal	Initiate TLC	Consider Drug Therapy**
High risk CHD* or CHD risk equivalents† (10-year risk > 20%)	< 100 mg/dL (optional goal: < 70 mg/dL)||	≥ 100 mg/dL#	≥ 100 mg/dL†† (< 100 mg/dL: consider drug options)**
Moderately high risk 2+ risk factors‡ (10-year risk 10% to 20%)§§	< 130 mg/dL¶	≥ 130 mg/dL#	≥ 130 mg/dL (100-129 mg/dL: consider drug options)‡‡
Moderate risk 2+ risk factors‡ (10-year risk < 10)§§	< 130 mg/dL	≥ 130 mg/dL	≥ 160 mg/dL
Lower risk: 0-1 risk factor§	< 160 mg/dL	≥ 160 mg/dL	≥ 190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)

* CHD includes history of myocardial infarction, unstable angina, coronary artery procedures (angioplasty or bypass surgery), or evidence of clinically significant myocardial ischemia.

† CHD risk equivalents include clinical manifestations of noncoronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease [transient ischemic attacks or stroke of carotid origin or > 50% obstruction of a carotid artery]), diabetes, and 2+ risk factors with 10-year risk for hard CHD > 20%.

‡ Risk factors include cigarette smoking, hypertension (BP ≥ 140/90 mm Hg or on antihypertensive medication), low HDL cholesterol (< 40 mg/dL), family history of premature CHD (CHD in male first-degree relative < 55 years of age; CHD in female first-degree relative < 65 years of age), and age (men ≥ 45 years; women ≥ 55 years).

§§ Electronic 10-year risk calculators are available at http://www.nhlbi.nih.gov/guidelines/cholesterol

§ Almost all people with zero or one risk factor have a 10-year risk < 10%, and 10-year risk assessment in people with zero or one risk factor is thus not necessary.

|| Very high risk favors the optional LDL-C goal of < 70 mg/dL, and in patients with high triglycerides, non-HDL-C < 100 mg/dL.

¶ Optional LDL-C goal < 100 mg/dL.

Any person at high risk or moderately high risk who has lifestyle-related risk factors (e.g., obesity, physical inactivity, elevated triglyceride, low HDL-C, or metabolic syndrome) is a candidate for therapeutic lifestyle changes to modify these risk factors regardless of LDL-C level.

** When LDL-lowering drug therapy is employed, it is advised that intensity of therapy be sufficient to achieve at least a 30% to 40% reduction in LDL-C levels.

†† If baseline LDL-C is < 100 mg/dL, institution of an LDL-lowering drug is a therapeutic option on the basis of available clinical trial results. If a high-risk person has high triglycerides or low HDL-C, combining a fibrate or nicotinic acid with an LDL-lowering drug can be considered.

‡‡ For moderately high-risk persons, when LDL-C level is 100 to 129 mg/dL, at baseline or on lifestyle therapy, initiation of an LDL-lowering drug to achieve an LDL-C level < 100 mg/dL is a therapeutic option on the basis of available clinical trial results.

Adapted with permission from Grundy SM, Cleeman JI, Merz CNB, et al: Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. Circulation 2004; 110:227-39.

ceptibility to heart arrhythmias. It can also improve coronary circulation. Metabolic benefits are gained from exercise performed at a lower level of intensity for a longer duration with increased frequency. They change how the muscles process fuel, which changes the blood chemistry, including lowering LDL cholesterol levels, increasing LDL particle size, lowering triglyceride levels, raising HDL and HDL2 levels, lowering insulin levels, and increasing insulin sensitivity.[13] These changes result in increased protection against cardiovascular disease.

Before prescribing an exercise plan, practitioners must evaluate the patient's age and overall fitness level in addition to risk factors and subclass values of LDL and HDL. This will ensure an appropriate individualized plan of exercise and determine whether a metabolic or mechanical exercise plan is needed. Treatment must be individualized to include lifestyle changes that are realistic and desirable.

A Healthier Diet

Diet therapy has a role in altering the LDL subclass. Patients should have body mass index (BMI) and waist circumference computed for assessment purposes. Target BMI is 18.9 to 24.9 and waist circumference should be less than 40 inches (102 cm) in men and less than 35 inches (88 cm) in women.

Patients with a BMI more than 25 or a waist circumference greater than the above measurements need weight-reduction counseling.

Dietary counseling should reflect current research and promote weight loss and optimal nutrition. Discuss weight and nutrition guidelines with patients in an unhurried manner. Patients will be more likely to follow a diet prescription if their healthcare practitioner emphasizes it as an essential part of their cardiovascular health plan and is specific about the plan. Careful patient

continued on p. 26

continued from p. 23

Lipid-Lowering Medications

Drug Class	Generic Name	Brand Name	Dose Range (mg/d)
Nicotinic acid (niacin)	Nicotinic acid	Niaspan	500-2,000
HMG-CoA reductase inhibitors (statins)	Atorvastatin	Lipitor	10-80
	Simvastatin	Zocor	5-80
	Lovastatin	Mevacor	10-80
	Pravastatin	Pravachol	10-80
	Fluvastatin	Lescol	20-80
	Rosuvastatin	Crestor	5-40
Bile acid sequestrants	Cholestyramine	Questran Questran Light	4-24 grams
	Colesevelam	WelChol	
	Colestipol	Colestid	2-16 grams in divided doses
Fibric acid derivatives	Gemfibrozil	Lopid	
	Fenofibrate	Tricor	1,200 in divided dose 54-145
Combination	Niacin (extended release)-lovastatin	Advicor	500/20
	Ezetimibe-simvastatin	Vytorin	10/10-10/80
Cholesterol absorption inhibitors	Ezetimibe	Zetia	10

Adapted from: Nurse Practitioner's Drug Handbook, 4th Ed. Philadelphia: Lippincott, Williams, & Wilkins, 2002.

follow-up is crucial, as is acknowledging efforts made by patients.

A 1999 study demonstrated that LDL and HDL subclasses could be improved by a low-calorie diet rich in olive oil.[14] This diet consists of complex carbohydrates, lean meat, generous helpings of fruits and vegetables, small portions of low-fat dairy, and monounsaturated fats such as olive oil. This hypocaloric diet encourages legumes, nuts, and oatmeal; it discourages sweets, refined carbohydrates, and fried foods.

Many experts recommend a Mediterranean diet with an emphasis on portion control. A Mediterranean diet emphasizes whole grains, colorful vegetables, fish, omega-3 fatty acids, and alpha-linoleic acid. This diet limits egg yolks, red meat, high-fat dairy products, and simple carbohydrates while reducing calorie intake; it helps reduce weight and cardiovascular risk. Patients who followed a Mediterranean diet were 50% to 70% less likely to suffer a repeat heart attack than those on a traditionally "American" diet.[15]

In September 2002, the National Institutes of Health published a report from the National Cholesterol Education Program (NCEP) Expert Panel on the detection, evaluation, and treatment of high blood cholesterol in adults.[11] The guidelines recommend the following: limiting total cholesterol intake to less than 200 mg/day; limiting saturated fat to less than 7% of total calories; limiting polyunsaturated fat to up to 10% of total calories; limiting monounsaturated fat to up to 20% of total calories; limiting total fat intake to 25% to 35% of total calories; limiting carbohydrates to 50% to 60% of total calories; increasing fiber to 20% to 30% of total calories; and limiting protein to 15% of total calories. Carbohydrate intake should be rich in whole grains, vegetables, and fruits; simple carbohydrates should be limited.[11,23]

Medications

Many individuals who have cardiovascular events have normal or near normal LDL-cholesterol levels. Metabolic situations, which ultimately injure the vessel's endothelial lining, play an important role in the development of atherosclerosis and subsequent coronary artery disease. Cigarette smoking, hypertension, obesity, insulin resistance, hypercholesterolemia, sedentary lifestyle, diabetes, and other factors are associated with endothelial injury. Even minimal injury can result in endothelial dysfunction, which is characterized by an increase in the vascular wall uptake of LDL. An abundance of small, dense, more atherogenic LDL, subclass B particles, promote faster infiltration of the lipid particles into the damaged arterial wall.

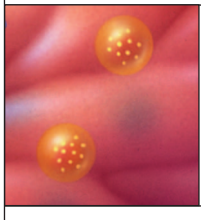
This endothelial injury makes the arterial walls more susceptible to oxidative damages and decreases the HDL-C levels while increasing the total LDL-C.[17] To treat this disorder and prevent atherogenic dyslipidemia, LDL subclass B patients may need a combination of medications (see Table: "Lipid-Lowering Medications").

Pharmacologic treatment, in conjunction with weight loss, proper nutrition, and exercise, can convert the smaller, dense LDL subclass B to the larger, buoyant LDL subclass A. When attempting to decrease cardiovascular risk factors, pharmacologic interventions should be added when indicated. Some medications have adverse effects, so patients should be routinely monitored. Periodic reevaluation of cholesterol test results will alert the practitioner to

changes in cardiovascular risk factors. Careful follow-up should include lipid profile, creatine kinase, and liver function at 12 weeks. Subsequent testing, based on these findings, should be given on an as-needed basis.

Niacin

Niacin, a B vitamin and mainstay of cholesterol treatment, lowers the distribution of the small, dense LDL subclass B particles and increases the number of the larger, more buoyant LDL subclass A particles, reducing atherogenicity.[18,19] Niacin also inhibits the liver's ability to produce VLDL and stimulates production of HDL. Adverse effects include vasomotor symptoms such as flushing, itching, and rash.



Patients receiving statins should have liver function tests drawn as a baseline and again after 12 weeks of treatment, then annually.

Niacin is available as a tablet (Niacor) and as an extended-release tablet (Niaspan). Regular tablets are taken two to three times a day and extended-release tablets should be taken at bedtime with a small, low-fat snack. To minimize flushing, the patient should predose with an aspirin 325 mg 30 minutes before taking Niaspan. Flushing may also decrease if patients avoid alcohol, hot spicy foods, and Chinese foods. Caution the patient about other factors that can cause vasodilation, which may promote adverse effects, such as caffeine intake and hot baths or showers. Niacin may increase blood glucose levels and warrants close monitoring in patients with diabetes.[20,21] Niacin is contraindicated in patients with peptic ulcer disease, hepatic dysfunction, and arterial bleeding; liver enzymes should also be monitored. Niacin can be administered with a statin—niacin can shift the LDL subclass B to LDL subclass A, while the statin lowers the concentration of LDL particles.[22] Patients need to be warned that prescribed niacin differs from supplemental niacin that can be purchased over the counter, and they should not attempt to self medicate.

Statins

HMG-CoA reductase inhibitors, or statins, are used to treat hypercholesterolemia, and their efficacy in lowering LDL has been documented in the literature.[23] Statins decrease cholesterol by inhibiting HMG-CoA reductase, an enzyme involved in cholesterol metabolism in the liver. Adverse effects of statins, which may be dose-dependent, are elevated liver enzymes, myopathy, and rhabdomyolysis. In severe myopathy and rhabdomyolysis, creatine kinase exceeds normal limits by 10 times or more, and patients report severe muscle aches and weakness.[24] Patients receiving statins should have liver function tests drawn as a baseline and again after 12 weeks of treatment, then annually. Any patient complaining of myopathy should have creatine kinase levels drawn. Liver disease is a contraindication for use of statins.

Other Medications

Other medications used to treat elevated cholesterol levels include fibrates and resins. Fibrates effectively lower triglyceride and raise HDL levels. Adverse effects include gastrointestinal symptoms, myopathy, elevated liver enzymes and creatinine, and cholithiasis. Fibrates may also be used to treat LDL subclass B in conjunction with niacin or added to a statin as a substitute for patients intolerant of niacin. Patients who are on combination therapy must be watched vigilantly for elevation of liver function tests and myopathy. Fibrates cannot be used in patients with hepatic or severe kidney dysfunction or in patients with preexisting gall bladder disease.

Resins, also known as bile-acid sequestrants, bind to cholesterol-rich bile acids in the intestine and promote excretion of cholesterol in the stool. Although resins can lower LDL, they have little effect on HDL and may increase triglycerides. Resins should be taken 30 minutes before dinner or the largest meal. Gastrointestinal adverse effects, such as constipation and bloating, may be too bothersome for some patients, making compliance difficult. Increasing fiber and water intake may help to prevent these adverse effects.

Conclusion

Patients with elevated levels of LDL subclass B have an increased risk of cardiovascular disease. Current screening methods for cardiovascular disease may not be sufficient to identify patients at risk; practitioners should use routine cholesterol panels, as well as appropriate diagnostic tests, such as advanced lipid profiles. When an advanced lipid profile identifies an at-risk patient, he can benefit from the management of a nurse practitioner through a regimen of exercise, diet modification, and medications—but the patient must be the center of the prescription and the practitioner must offer constant encouragement. This combination of treatment will often improve the patient's LDL subclass, thereby decreasing cardiovascular risk.

Heart disease in the United States has proven recalcitrant to decades of preventive attempts. However, as practitioners learn more about the fine-tuning of lipid testing, and about tailoring exercise, diet modification, and medication to each patient, it may be possible to change patients' lifestyles and extend their lives.

REFERENCES

1. The Centers for Disease Control and Prevention (CDC): The burden of chronic diseases and their risk factors: National and perspective studies 2002, United States. Available at: http://www.cdc.gov.
2. US Department of Health and Human Services: ATP III Guidelines. NIH publication No. 01-3305, May 2001.
3. Boizel R, Benhamou P, Lardy B, et al.: Ratio of triglycerides to HDL cholesterol is an indicator of LDL particle size in patients with type 2 diabetes and normal LDL levels. Diabetes Care 2000;23(11):1679-85.
4. Chapman M, Guerin M, Bruckert E.: Atherogenic dense low-density lipoproteins European Heart Journal 1998;19(Supplement A):A24-30.
5. Capell W, Zamboan A, Austin M, et a1.: Compositional differences of LDL particles in normal subjects with LDL subclass phenotype B. Arterioscler Thromb Vasc Biol 1996;16:1040-6.
6. Superko R.: Lipoprotein subclasses and atherosclerosis. Front Biosci 2001;6:355-65.
7. Kondo A, Muranaka Y, Ohta I, et al.: Relationship between triglyceride concentrations and LDL size evaluated by malondialdehyde-modified LDL. Clin Chem 2001;47(5):839-900.
8. Superko R, Tucker L.: Before the heart attacks. New York, NY: Rodale Inc., 2003;45-83.
9. Yannios, T.: Heart disease breakthrough: The 10-step program that can save your life. New York, NY: John Wiley & Sons, Inc., 1999;24-45.
10. Orso, R.: The role of expanded cholesterol testing. The Female Patient 2003;28:23-7.
11. Grundy SM, Cleeman JI, Merz CNB, et al: Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. Circulation 2004; 110:227-39.
12. Goldberg, N.: Women are not small men: Life-saving strategies for preventing and healing heart disease in women. New York, NY: Ballantine Publishing Group, 2001;257-301.
13. Yanios, T: Heart disease breakthrough: The 10-step program that can save your life. New York, NY: John Wiley & Sons, Inc., 1999;176-200.
14. Zambon A, Sartore G, Passera D.: Effects of hypocaloric dietary treatment enriched in oleic acid on LDL and HDL subclass distribution in mildly obese women. J Intern Med 1999;246:191-201.
15. Goldberg N.: Women are Not Small Men: Life-Saving Strategies for Preventing and Healing Heart Disease in Women. New York, NY: Ballantine Publishing Group, 2001.
16. O'Mara N.: The American Heart Association guideline for the prevention of cardiovascular disease in women. Prescriber's Letter 2003; Detail-Document #200315.
17. Superko H and Nejedly M.: Small LDL and its clinical importance as a new CAD risk factor: A female case study. Progress in Cardiovascular Nursing 2002;17(4):167-173.
18. Rosenson R.: Antithrombotic effects of nicotinic acid. Atherosclerosis 2003;171(1):87-96.
19. Yannios T.: Heart disease breakthrough: The 10-Step program that can save your life. New York, NY: John Wiley & Sons, Inc., 1999;176-200.
20. Miller M.: Why triglycerides need to be aggressively managed: A guide for physicians. Cardiovascular Reviews and Reports 2003;24(10):520-26.
21. Worz C and Bortoff M.: Treating dyslipidemic patients with lipid-modifying and combination therapies. Pharmacotherapy 2003;23(5):625-37.
22. McKenney J, McCormick L, Schafer E. et al.: Effect of niacin and atorvastatin on lipoprotein subclasses in patients with atherogenic dyslipidemia. Am J Cardiol 2001;August I;88(3):270-4.
23. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). JAMA 2001;285:2486-97.
24. Lenffant, C.: ACC/ANA/NHLBI Clinical advisory on the use and safety of statins. Cardiology Review 2003;(Supplement)20:9-11.

AUTHOR DISCLOSURE

The authors have disclosed that they have no significant relationship or financial relationship with any commercial companies mentioned in this continuing education activity.

ABOUT THE AUTHORS

Cheryl Moredich is an Assistant Professor of Nursing at the School of Nursing, Purdue University Calumet, Hammond, Ind. **Deborah Kark** is an Associate Professor of Nursing at the School of Nursing, Purdue University Calumet. **Patricia Keresztes** is an Assistant Professor of Nursing at the School of Nursing, Purdue University Calumet.

CE **Earn CE credit online:**
Go to http://www.nursingcenter.com/CE/NP and receive a certificate *within minutes*.

INSTRUCTIONS

Implications of LDL Subclass B in Patients at Cardiovascular Risk

TEST INSTRUCTIONS

- To take the test online, go to our secure Web site at **http://www.nursingcenter.com/ce/NP**.
- On the print form, record your answers in the test answer section of the CE enrollment form on page 30. Each question has only one correct answer. You may make copies of these forms.
- Complete the registration information and course evaluation. Mail the completed form and registration fee of $19.95 to: **Lippincott Williams & Wilkins, CE Group**, 2710 Yorktowne Blvd., Brick, NJ 08723. We will mail your certificate in 4 to 6 weeks. For faster service, include a fax number and we will fax your certificate within 2 business days of receiving your enrollment form.
- You will receive your CE certificate of earned contact hours and an answer key to review your results. There is no minimum passing grade.
- Registration deadline is July 31, 2007.

DISCOUNTS and CUSTOMER SERVICE

- Send two or more tests in any nursing journal published by LWW together and deduct $0.95 from the price of each test.
- We also offer CE accounts for hospitals and other health care facilities on nursingcenter.com. Call **1-800-787-8985** for details.

PROVIDER ACCREDITATION:

This Continuing Nursing Education (CNE) activity for 3.0 contact hours is provided by Lippincott Williams & Wilkins (LWW), which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation and by the American Association of Critical-Care Nurses (AACN 00012278, CERP Category A). This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 3.0 contact hours. LWW is also an approved provider of CNE in Alabama, Florida, and Iowa, and holds the following provider numbers: AL #ABNP0114, FL #FBN2454, IA #75. All of its home study activities are classified for Texas nursing continuing education requirements as Type 1. This activity has been assigned 1.0 pharmacology credit. *Your certificate is valid in all states. This means that your certificate of earned contact hours is valid no matter where you live.*