A 58-year-old postmenopausal Asian-Indian woman presented for a routine physical examination. She was 5’4” and weighed 150 lbs with a waist circumference of 36”. Upon examination, her blood pressure was 136/88 mm Hg. Her father died at age 56 years of a myocardial infarction and her mother died at age 70 years of complications of diabetes. Her siblings, aged 52, 50, and 78 years, are alive and healthy. She is a vegetarian and is relatively sedentary.

The patient showed clear evidence of the metabolic syndrome. Moreover, her ethnic origins contribute to the likelihood that she could have dyslipidemia, as Asian Indians that have migrated to western countries have been shown to have a higher prevalence of diabetes and elevated lipoprotein(a) [Lp(a)] than the Caucasian population.1 A lipid profile was ordered and the patient was instructed to return in 2 weeks to discuss the results. It was anticipated that the lab results would show elevated serum triglycerides, often observed in persons with the metabolic syndrome. Elevated triglycerides constitute an independent coronary heart disease risk factor.2

LABORATORY RESULTS AND DIAGNOSIS

The following lab values were reported for the patient:

- Total cholesterol: 274 mg/dL
- Triglycerides: 320 mg/dL
- HDL: 39 mg/dL
- LDL: 167 mg/dL
- Fasting glucose: 111 mg/dL
- Hs-CRP: 2.0 mg/L
- Homocysteine: 14 mg/dL

Both low-density lipoprotein cholesterol (LDL-C) and triglycerides were elevated, and high-density lipoprotein cholesterol (HDL-C) levels were significantly below the range considered to be acceptable for women according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines (ie, >50 mg/dL). Although this patient did not have a history of coronary heart disease, her age and family history contributes to her risk, as do her LDL-C and triglyceride levels. According to ATP III, LDL-C levels in the range of 160 to 189 mg/dL and triglyceride levels within the range of 200 to 499 mg/dL are categorized as high.

INTERVENTION

When triglycerides are borderline high (150-199 mg/dL), emphasis is placed on weight reduction and increased physical activity, but for high triglycerides (200-499 mg/dL) non–HDL-C becomes a secondary target of therapy. Aside from weight reduction and increased physical activity, drug therapy can be considered in high-risk persons to achieve the non–HDL-C goal.2 This particular patient was initiated on 10 mg of atorvastatin and counseled regarding the need for therapeutic lifestyle changes (TLC). Dietary intervention is the centerpiece of TLC, with ATP III recommending an intake of saturated fat of <7% of daily calories, and a total fat intake of 25% to 35% of total daily calories. The patient was advised that a nutritious diet with regular exercise will help to augment the effects of drug treatment by raising HDL levels. She was instructed to undergo additional lab tests in 3 months and to schedule a follow-up office visit 1 week later for additional evaluation.

FOLLOW-UP

Following 3 months of statin therapy, the patient’s lab results were as follows:

- Total cholesterol: 258 mg/dL
- Triglycerides: 200 mg/dL
- HDL: 45 mg/dL
- LDL: 140 mg/dL
- Fasting glucose: 108 mg/dL
- Hs-CRP: 1.5 mg/L
- Homocysteine: 12 mg/dL

Case Study

ASIAN-INDIAN WOMAN WITH DYSLIPIDEMIA AND THE METABOLIC SYNDROME

Michael H. Davidson, MD, FACC, FACP
Total cholesterol 215 mg/dL
Triglycerides 300 mg/dL
HDL 40 mg/dL
LDL 115 mg/dL
Glucose 107 mg/dL
Non-HDL-C 175 mg/dL

As a class, the statins are potent lipid-lowering drugs, achieving LDL-C reductions that range as high as 55% as well as reductions in triglycerides. They also modestly increase HDL-C at rates of 5% to 15%. While this patient has achieved positive results in terms of LDL-C reductions, based on ATP III guidelines, she is not yet at the non-HDL goal of <160 mg/dL.

INTERVENTION AND DISCUSSION
A number of therapeutic choices may now be considered:

1. Increasing the statin dose would likely result in modest decreases in LDL-C and triglycerides. However, combination therapy can achieve a greater lipid-lowering effect compared to increased dosing of monotherapy.

2. Adding a nonsystemic LDL-lowering medication to statin therapy. Bile acid sequestrants, such as colestipol, cholestyramine, and colesevelam, lower cholesterol levels by binding to intestinal bile acids and blocking their reabsorption, leading to increased fecal excretion and resulting in depletion of the hepatic bile acid pool. Hepatic cholesterol biosynthesis is stimulated, increasing expression of LDL-C receptors and enhancing LDL-C clearance. Bile acid sequestrants increase HDL-C by about 5% and usually have little or no effect on triglycerides, although colesevelam has been shown to raise HDL-C by as much as 11%. As elevated triglycerides remain a problem for this patient, bile acid sequestrants are not the agent of choice in this case. Adding ezetimibe (a cholesterol absorption inhibitor) 10 mg per day would result in similar reduction in LDL as a bile acid sequestrant, but it would also lower triglycerides an additional 5% to 10%.

3. Adding nicotinic acid to statin therapy is another option. These agents inhibit lipolysis in adipose tissue and reduce hepatic secretions of apolipoprotein B particles. Sustained treatment with 2 g of niacin can increase HDL-C by as much as 35% and decrease triglycerides by as much as 50%. However, these agents typically are not well tolerated by patients, who experience pronounced vasodilatory responses. A modified-release niacin reduces the flushing side effects and has a low rate of hepatotoxicity. There is also the potential for additional side effects, including hyperglycemia, hyperuricemia, gout, upper gastrointestinal distress, and hepatotoxicity.

4. Adding a fibric acid derivative to statin therapy will be most likely to achieve the non-HDL goal of <160 mg/dL in this patient. As a class, fibrates (gemfibrozil, fenofibrate, and clofibrate) affect lipoprotein levels by activating the signaling pathway of peroxisome proliferator activator receptor-alpha, altering cell metabolic activity. Whereas fibrate therapy reduces LDL-C only modestly, it increases HDL-C by 10% to 20% and lowers triglycerides by as much as 50%. Therefore, used in combination with statin therapy, this agent is most likely to achieve the patient's non-HDL goal of <160 mg/dL. She is advised to continue statin therapy and to add 160 mg of fenofibrate to drug therapy, as gemfibrozil has been associated with increased risks of myopathy.

FOLLOW-UP
Following 6 weeks of combination therapy, the patient was scheduled for another lipid profile, which showed significant improvement. Triglycerides dropped to 160 mg/dL and total cholesterol was 165 mg/dL. HDL-C approached optimal levels at 48 mg/dL, and non-HDL was 117 mg/dL. The patient was further encouraged to initiate lifestyle changes and was to be reevaluated in 6 months.

REFERENCES
CASE STUDY


3. Davidson MH. Combination therapy for dyslipidemia: safety and regulatory considerations. Am J Cardiol. 2002;90(suppl):50K-60K.

