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Changes in ATP III focus on diabetes and the metabolic syndrome

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The third Adult Treatment Panel (ATP III) of the National Cholesterol Education Program highlights the importance of hypertriglyceridemia and low levels of high-density lipoprotein (HDL) cholesterol in determining risk of coronary heart disease (CHD), according to H. Bryan Brewer, Jr., MD. In his presentation, he summarized the primary goal of ATP III of optimizing low-density lipoprotein (LDL) cholesterol levels and the major changes from previous reports, representing updated guidelines for clinicians.

"Previously, the guidelines had focused only on LDL cholesterol, which was clearly a limitation," said Dr. Brewer. "It wasn't until ATP III that hypertriglyceridemia and low HDL were addressed. Patients with diabetes and those with metabolic syndrome are the ones most affected by these dyslipoproteinemias." ATP III has also introduced the concept of non-HDL cholesterol as a secondary target of therapy, he added.

An HDL cholesterol level of <40 mg/dL is now considered low, in contrast to the 35-mg/dL cut point in the past. Triglyceride classifications have also been altered, he noted. Triglyceride level of <150 mg/dL is now considered normal; borderline-high is 150 to 199 mg/dL; high is 200 to 499 mg/dL; and very high is >500 mg/dL.

The ATP III has also introduced the Framingham risk score, to be used in calculating 10-year risk in patients with two or more CHD risk factors and in defining LDL goals for therapy. The result is a determination of global risk status based on lipid and nonlipid risk factors.

CHD risk equivalent

Of particular importance is the new designation of CHD risk equivalent, which carries the risk potential for major coronary events equal to that of established CHD. The CHD risk equivalence includes clinical manifestations of cardiovascular disease (peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease), diabetes, and a Framingham 10-year risk score >20%. "There's a growing body of data that clearly illustrates the marked increased risk for cardiovascular disease in the diabetic patient," he said. In the East-West Study, patients with diabetes were found to have the same risk of cardiovascular events as patients without diabetes who had already had a myocardial infarction (MI). Patients with diabetes and a history of MI were at markedly higher risk for future events.

The LDL cholesterol goal in patients with CHD or CHD risk equivalent is now <100 mg/dL. For persons with a 10-year risk for car-

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diac events of 10% to 20%, the LDL cholesterol goal is <130 mg/dL, and for persons with 0 or 1 CHD risk factor, the LDL goal is <160 mg/dL.

Other forms of dyslipoproteinemia

Patients with dyslipoproteinemias other than elevated LDL cholesterol may also be at increased risk for cardiovascular events. "A large number of patients have hypertriglyceridemia and low levels of HDL as their risk factor for CHD," said Dr. Brewer. Among them are patients with diabetes and those with the metabolic syndrome. In ATP III, a diagnosis of metabolic syndrome requires three of five of the following conditions—abdominal obesity, triglycerides ≥150 mg/dL, low HDL (<40 mg/dL men; <50 mg/dL women), blood pressure ≥135/85 mm Hg, and blood glucose ≥110 mg/dL.

Identifying patients who are at increased risk for CHD based on their triglyceride level is more difficult than with LDL cholesterol level, according to Dr. Brewer. Also, a subset of persons with familial hypertriglyceridemia have high levels of triglycerides that are not associated with a markedly increased risk of CHD. In contrast, patients with familial combined hypercholesterolemia, hypertriglyceridemia–low-HDL syndrome, type 2 diabetes, or with metabolic syndrome have hypertriglyceridemia that is associated with an increased risk of CHD.

The difference in risk patterns lies in the difference in the type of lipoprotein particles in the plasma. "Those who have triglyceride-rich remnants tend not to have a markedly increased risk for CHD, whereas those who have cholesterol-rich remnant particles are at risk for CHD," he said.

Patients with hypertriglyceridemia who are at increased risk for CHD have atherogenic, cholesterol-rich remnant particles that are taken up directly by macrophages, resulting in increased cholesterol concentration, formation of foam cells, and the development of atherosclerotic plaque.

These patients also tend to have dense LDL; such lipoproteins are susceptible to oxidation and are more atherogenic than normal LDL. Dense LDL has a decreased affinity for the LDL receptor and penetrates more easily into the vessel wall. Finally, HDL cholesterol is rapidly metabolized in at-risk individuals, causing a reduction in the HDL cholesterol level.

Assessing non-HDL cholesterol

Non-HDL cholesterol was introduced by the ATP III to facilitate treatment paradigms for patients with increased triglycerides and low HDL.

"Non-HDL cholesterol goals become important in patients with triglyceride levels greater than 200 mg/dL and low HDL," said Dr. Brewer. "When LDL is reduced below 100 mg/dL, you need to assess the non-HDL cholesterol. The primary target of therapy is still the LDL cholesterol goal before treating non-HDL cholesterol. If you don't achieve sufficient lowering of non-HDL cholesterol, you can either use higher doses of statins or add niacin or a fibrate," he said. ■