Cholesterol: The good, the bad, the unknown

February 21 2011, By Anya Martin

Two people are diagnosed with high cholesterol, one of the leading risk factors for heart disease, and follow similar therapies. One ends up with improved cholesterol levels, but the other doesn't.

The answer about whether either has a greater chance of heart attack or stroke may not be as simple as counting cholesterol levels in the bloodstream, at least when it comes to high-density lipoprotein, better known as HDL or the so-called "good" cholesterol, a new study indicates.

Doctors have long agreed that large levels of low-density lipoprotein - also known as LDL or "bad" cholesterol - can cause blockages in arteries, or blood clots, which can trigger a heart attack or stroke. However, greater levels of the other so-called "good" cholesterol - high-density lipoprotein or HDL - may be less important than how well your particular HDL removes the bad cholesterol from arteries and carries it back to the liver to ultimately pass out of your body.

These new findings won't have an immediate effect on your doctor's recommendations because no easy-to-perform clinical test for HDL efficiency is available now, but down the line, understanding more about how good, not just bad, cholesterol works can help researchers develop better treatments for heart disease, experts say.

"The evidence for lowering LDL is substantial, but the evidence for raising HDL is not as convincing," said Dr. Robert Eckel, director of the University of Colorado Hospital's lipid clinic, which specializes in the

treatment of cholesterol problems. "It's an important study because it opens new doors and may help explain some of the discrepancies out there in terms of patient outcomes."

In practical terms, a patient with high levels of good cholesterol may not be receiving as much protection as hoped for, but also a person with low levels that are very efficient may be better off than previously thought, said Dr. Daniel J. Rader, a cardiologist at the University of Pennsylvania who was the study's lead researcher.

"It's our first hint that the good cholesterol story is more complicated, that you can't just increase the level and expect it to work properly," said Dr. Christopher Cannon, a cardiologist at Brigham and Women's Hospital in Boston.

In other words, when developing and testing new medications to improve HDL levels, another question needs to be asked: "What kind of good cholesterol does it produce?" he added. Cannon just completed a clinical trial last fall, which found that an experimental drug called anacetrapib upped HDL levels by 138 percent in six months and maintained that rise over 18 months without the negative side effects shown by other medicines in the same class.

The oral medication being developed by Merck also reduced LDL levels by 40 percent among patients also taking a statin drug, the most popular medication class for lowering bad cholesterol. Anacetrapib will now proceed to a four-year global clinical trial involving 30,000 patients, which could lead to a submission for approval by the Food and Drug Administration sometime around 2015 to 2016, Cannon said.

Currently some other FDA-approved drugs are thought to raise good cholesterol, but niacin is the only one to do so by any significant level (25 percent), he added. Its clinical benefit has not yet been proven, and

many patients who take it experience uncomfortable side effects such as flushing and body aches, Cannon said.

A separate study found signs that HDL ability to remove bad cholesterol may be better in patients treated with anacetrapib than those who received niacin or no HDL-promoting medication.

About a third of all Americans, or 100 million, have high bad-cholesterol levels, one of the top risk factors, along with high blood pressure, for heart disease, attack or stroke, according to the Centers for Disease Control. Two-thirds don't have it under control.

Those numbers are sobering considering that heart disease also is the nation's biggest killer, with 800,000 deaths annually. It's also expensive, costing the country nearly $300 billion a year in direct medical costs alone, a number that is expected to triple in the next 20 years.

Marci Williams didn't worry much about being over 330 pounds, until she received the news at age 45 that she now had high LDL and blood pressure, as well as sleep apnea and Type 2 diabetes. Add in a family history of heart disease, and her cardiologist said she wouldn't make it to 50 unless she made major lifestyle changes.

"It was a very somber moment; it was a real 'whoa,'" said Williams, a financial analyst with a global shipping company who lives in Greensboro, N.C.

She started walking and biking regularly and eating healthier and also took a statin drug and niacin.

"I turned into this uber-compliant patient who was exercising like clockwork, counting carbohydrates, and taking my medicine exactly as prescribed," Williams said.

Within 16 months, she lost 180 pounds, and at age 49, she now has heart-healthy cholesterol levels, no sleep apnea and her diabetes under control, she added.

At age 34, Lisa Lee-Ranson also was overweight and had a family history of heart disease, but her wake-up call came when she felt a burning sensation while walking or climbing stairs. Doctors diagnosed blockages of more than 90 percent in two coronary arteries and soon she was undergoing double bypass surgery, she said.

Since then Ranson, who is now 47 and lives in Dunbar, W. Va., has shed 35 pounds, embraced a heart-healthy diet, and exercises three to four times by running the steps at her church or laps in its gym. She also has taken Lipitor, a statin drug; Zetia, one of a new class of LDL-lowering medications; and niacin.

However, unlike Williams, Ranson's levels have not improved to heart-healthy levels, and while she has not had another cardiovascular incident, the numbers worry her, she said.

"I'm probably exercising more now that I have more free time and am not working full time, and it's still not doing the job," Williams added.

A key next research step is to understand what characteristics of HDL make it function more or less efficiently, said Rader, who plans, with his team, to explore that question next.

"A related issue is whether HDL function, like height or hair color, is genetically determined," he added. "So the second goal is to hunt for genes in the genome in which variation determines HDL function."

Identifying an HDL function gene can be significant for developing new drug therapies that target specific genes to improve that function, Rader

said.

For now, though, anyone concerned about their heart health, especially if you have a family history of an early-onset heart attack, should continue to do the things that numerous studies have found reduce bad cholesterol levels, Eckel said.

In other words, have your cholesterol levels tested regularly, don't smoke, lose weight if you're overweight, be physically active and take any drugs prescribed by your doctor to reduce your bad cholesterol, he added.

"I have to emphasize that a healthy lifestyle is the number one step to reducing your risk of heart disease," Eckel said.