Can lipoprotein(a) foretell heart trouble?

A new study casts doubt on a cholesterol carrier's ability to predict the future risk of a heart attack—at least for middle-aged white men. However, many researchers believe the carrier, lipoprotein(a), remains a potent independent risk factor for cardiovascular disease in certain groups. Indeed, a second new study suggests that this carrier can identify children at high risk of developing heart disease later in life.

Lipoprotein(a) belongs to a class of cholesterol-carrying molecules that circulate in the bloodstream. This lipid-protein conjugate, whose function remains mysterious, was discovered in 1963. Since then, study after study has shown that people with high concentrations of the substance in their blood have a heightened risk of heart attack and stroke. However, most of those reports were conducted retrospectively.

Now, cardiologist Paul M. Ridker of Harvard Medical School in Boston and his colleagues have conducted a prospective study of Lp(a)'s connection to risk of cardiovascular disease. The team studied 14,916 male physicians between the ages of 40 and 84 who had no history of heart attack or stroke and were part of a larger research effort known as the Physicians' Health Study.

The investigators measured the concentrations of Lp(a) and other lipids in blood samples that had been frozen at the start of the study. The team then kept track of the participants for an average of five years. During that time, they recorded the number of heart attacks suffered by the physicians.

When Ridker and his co-workers compared the men who remained healthy during the study period to those who developed a heart attack, they found no difference in the concentrations of Lp(a) in their blood. Even when the team took into account other risk factors, such as age and smoking, Lp(a) failed to emerge as an independent risk factor. The researchers detailed their findings in the Nov. 10 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. They also presented their data this week at the 66th Scientific Sessions of the American Heart Association (AHA), held in Atlanta.

Ridker was surprised that the team found no relationship between Lp(a) concentrations measured at the start of the study and the appearance of cardiovascular problems later in the study. They had expected their findings to back up previous reports of a link between this cholesterol carrier and the risk of heart attack.

However, the study doesn't rule out the possibility that Lp(a) will prove a predictor of heart disease risk for people in certain groups. The Physicians' Health Study analyzed data that came mostly from middle-aged white men, notes Elliot S. Barnathan of the University of Pennsylvania School of Medicine in Philadelphia in an accompanying editorial. It may be that Lp(a) readings can foretell heart disease risk for people under age 40, he says.

Another research effort, this one led by Charles J. Glueck of Jewish Hospital in Cincinnati, reveals that Lp(a) does indeed predict the likelihood of cardiovascular disease for young, high-risk individuals.

Glueck's team studied 49 children age 10 to 14 from families in which one parent had suffered a heart attack before age 45. They measured the concentrations of Lp(a) in the children's bloodstreams and compared those values to Lp(a) concentrations recorded in 49 children in the same age range whose parents reported no heart disease. All the children in this study were evaluated at the University of the Andes in Mérida, Venezuela.

The team discovered that the Lp(a) concentrations of children with a family history of heart problems were nearly twice as high as those of children from families without such a history. Glueck also reported his data at the AHA meeting. —*K.A. Fackelmann*

Food cravings tied to brain chemicals

Frustrated by your inability to resist snacking on potato chips or grabbing an extra cookie or two . . . or three? Blame your brain, suggest neuroscientists.

At least two chemicals in the brain convey very precise — and compelling — commands to the body about ingesting food, says Sarah F. Leibowitz of Rockefeller University in New York City. Her studies in rats indicate that one of these chemicals, called neuropeptide Y, causes carbohydrate cravings, while the other, called galanin, seems to underlie a yen for fat.

The more of each the body produces, the stronger the drive to eat those particular food groups, she says.

Now, scientists can slow production of these messengers by suppressing the genes that control output, she and her colleagues report this week in Washington, D.C., at the annual meeting of the Society for Neuroscience.

"There are clearly specific chemicals for specific appetites," she says. Because of parallels between what happens in rats and what is known about cravings and these chemicals in people, she predicts that her studies will lead to new ways to treat eating disorders in humans.

Leibowitz' group gave rats small pieces of a specific "antisense" genetic material (SN: 6/5/93, p.366) each day for four days. This synthetic DNA interfered with brain cells' ability to make neuropeptide Y, reducing stores by about 35 percent. As a result, the animals ate only about one-third their normal carbohydrate and fat calories, the team reports.

Other factors — such as hormones or the amount of glucose the cells are using — also modulate neuropeptide Y production, Leibowitz says. She and her colleagues observed that when they gave the rats a chemical that blocked glucose use, two areas of the brain's hypothalamus — the arcuate nucleus and the suprachiasmatic nucleus — produced more neuropeptide Y. Adding chemicals that may enhance sugar use by cells tended to result in decreased neuropeptide Y, the group notes.

Leibowitz reports that, particularly in female rats, the "eat fat" message can increase over time. Her group raised 41 females, feeding them a mixture of fat, protein, and carbohydrate. After 65 days, the researchers could distinguish the rats that preferred fats — fat made up 38 percent of their food intake, compared to the 13 percent consumed by so-called low-fat rats, she says.

The group could trace that preference back to when the rats were 21 days old, possibly even 10 days old. "There's a critical period [near weaning] that is strongly predictive for their [adult] appetite for fat," Leibowitz adds. Fat preference increases sharply when the rats enter puberty. Those choosing high-fat diets had more galanin in their brains than the other rats, she notes.

These results indicate that changes in cravings for sugar and fat are linked to changes in the amounts of neuropeptide Y and galanin. "To show that they are so tightly linked is giving me hope that there is some definable simplicity [to food preferences]," says Leibowitz.

Other researchers are not so sure, especially about the control of fat urges. "In other people's hands, [galanin] is marginally specific for fat," comments David A. York of Louisiana State University in Baton Rouge.

Once researchers understand the neurochemical and endocrine signals that guide appetites for fat and sugar, "we can work out ways nutritionally and pharmacologically for dealing with that," Leibowitz asserts.

But controlling these two messengers may not be part of the solution. "The real problem with neuropeptide Y and galanin is that they occur all over the brain and they regulate multiple systems [such as water intake and sexual behavior]," York says.

Also, "there must be at least 25 neuropeptides that affect food intake," he notes. "Undoubtedly, it's going to turn out to be a complex system." —*E. Pennisi*

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