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THE NATION

UM traces genetic key to heart attacks

Mutation makes families prone to low levels of HDL, 'good cholesterol'

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Heart specialists at the University of Maryland Medical Center have identified the largest family known to carry a genetic mutation responsible for low levels of "good cholesterol." The defect predisposes relatives to heart attacks at an early age.

The mutation is so powerful that one family member, a woman in Circleville, Ohio, required quadruple bypass surgery at age 40. Her brother, a New Jersey welder, needed angioplasty at 35.

"I was extremely tired, and had a tightness and burning in the chest," Rebecca Amerine, a finisher in an Ohio plastics factory, said of the symptoms that alerted doctors to her problem. She is now 48.

The family — scattered in Texas, Oklahoma, Texas and New Jersey — consented to having their blood sent to the University of Maryland Medical Center.

Researchers there screened the samples for defects in a gene regulating HDL, a compound responsible for flushing fats from tissues and preventing the formation of clots in narrowed arteries.

Dr. Michael Miller, director of preventive cardiology, said the finding demonstrates the role that heredity can play in triggering biological processes that can clog arteries and lead to heart attacks.

He presents his findings today at the American Heart Association's annual conference in Anaheim, Calif.

Two years ago, Dr. Miller and his colleagues began their study by sending letters to 5,000 physicians across the country — asking them to identify families with extensive histories of heart disease and low HDL. Some of the doctors who knew of such families asked them to consent to offering blood samples for genetic analysis.

In Mrs. Amerine's family, the Maryland team identified a mutation of the "apo A-I" gene in 20 of 46 family members. The defect appears to accelerate the breakdown of HDL.

Fourteen of the 20 people who carry the mutation are still too young to experience symptoms of heart disease — even premature symptoms. They ranged in age from 6 to their early 30s.

Dr. Miller said he and his colleagues have notified their family physicians to watch for problems and to consider preventive therapies such as diet and medications.

Two of the other six family members — Mrs. Amerine and her brother, Thomas Lutz — have already experienced symptoms. The two compounded their risk by smoking.

"It appears this combination of smoking and low HDL is just devastating in accelerating the disease," he said. "Either one by itself increases the risk for heart disease, but the combination is just deadly."

While the defect alone gives someone a two- to fourfold increased risk of developing heart disease, smoking compounds the risk until it reaches 24 times that of a normal person.

Although "good cholesterol" levels vary greatly, the average for men is 45 to 50 milligrams per deciliter of blood. The average for women is 50 to 60.

Many people in Mrs. Amerine's family had measurements that were only a fraction of normal levels — including several with readings in the single digits.

Mrs. Amerine's was 12. Her teen-age son's was 4. Four brothers, including Mr. Lutz, had readings of less than 10. A sister measured 13.

HDL isn't important to everyone, Dr. Miller said. Vegetarians, for instance, can tolerate extremely low HDL because their eating habits tend to ensure low levels of total cholesterol in their tissues.