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Evidence refutes link between iron and CHD

Autopsy results on patients with iron-overload syndromes have added more evidence against the hypothesis that high serum ferritin levels can increase the risk of heart disease.

Michael Miller, M.D., director of preventive cardiology at the University of Maryland, used computerized autopsy records from the Johns Hopkins Hospital in Baltimore, dating back to 1889 to examine whether patients who had died of either hemochromatosis or multiorgan hemosiderosis had evidence of coronary artery disease.

He found the opposite to be true. Among the 41 people who had died of iron-overload diseases, only 12% had been described at their autopsy as having advanced or severe coronary artery disease, compared to 38% of the 82 people who had died of other causes, he reported in the *Journal of the American Medical Association* (1994;272:231-233).

"I think this study really refutes the hypothesis," Dr. Miller said.

The report brings to four the number of U.S. studies that have found no support for the iron-heart disease hypothesis, first put forward a decade ago by a South Car-

olina physician and backed by Finnish data published in 1992.

"There might still be something related to iron stores, but at this point the bulk of the evidence does not support the hypothesis," said Meir J. Stampfer, M.D., professor of epidemiology and nutrition at

support the idea that excess iron raises the risk of heart disease, and published a recent study in the *American Journal of Epidemiology* showing that iron levels can be lowered by vigorous exercise (1994;140:148-160).

That study, involving 1,743

Only 12% who had iron overload died of severe coronary artery disease

Harvard University School of Public Health in Boston.

Dr. Stampfer presented a study last year at a meeting of the American Heart Association measuring levels of stored ferritin in men who had suffered heart attacks and healthy men. He found no increased risk of myocardial infarction associated with high ferritin levels.

Another study published earlier this year by researchers at the National Center for Health Statistics, showed that among 4,518 men and women, those with the highest levels of serum ferritin actually had slightly lower risks of death.

Yet the Finnish team, led by Jukka T. Salonen, M.D., of the University of Kuopio, continues to

Finnish men between the ages of 42 and 60, found that men who exercised vigorously for over two-and-a-half hours a week had 16.8% less iron in their blood than those who exercised less than 15 minutes a week.

Dr. Salonen's team caused a stir in 1992 when they first reported that the higher the level of stored iron, the greater the risk of having a myocardial infarction.

But given the growing number of studies refuting those results, Dr. Stampfer said that the new study on stored ferritin and exercise probably has no public-health implications.

"I think it's a great idea for people to exercise vigorously and on a reg-

ular basis," Dr. Stampfer said. "If the iron thing turns out to be true, that's another reason to exercise, but we already have plenty of reasons."

One remaining possibility that the Baltimore study could not test is that high serum ferritin increases the risk of coronary heart disease only when a patient also has high levels of low-density lipoproteins.

"Our results do not rule out the possibility that elevated levels of LDLs combined with iron stores may be important in promoting atherosclerosis," Dr. Miller wrote. "In cultured endothelial cells, iron enhances oxidation of LDL, and oxidative modification of LDL appears to be the critical element in the development of atherosclerosis."

The Finnish study had found that the highest risk of heart disease was in those who had elevated levels of both LDL and iron, suggesting that the iron was causing the oxidation of the LDL.

But because iron overloads lower the production of cholesterol, few patients in the Baltimore study had high LDL levels.

"One possibility is that we narrowed the focus to patients who have both high iron and high LDL," Dr. Miller said. —D.H.