The Role of Copper in Metabolizing Cholesterol

Copper doesn’t just belong in pennies. The human body needs it too, but only in small amounts. By studying the effect of this single nutrient on blood lipids, David Lei hopes to learn more about cardiovascular health.

Lei, a professor in the Department of Nutritional Sciences at the University of Arizona, is examining the mechanism responsible for hypercholesterolemia, or elevated blood cholesterol, induced by copper deficiency. Since the late 1970s Lei has been researching the influence of micronutrients on lipid (a fat component) metabolism, and has determined that copper is the most influential trace mineral in hypercholesterolemia.

“Severe copper deficiency is not common in the United States, but it has been observed in developing countries,” Lei said. “It occurs in malnourished populations in isolated areas — the Andes, for example.”

“It has also been found in infants fed solely on powdered milk. In Japan, milk powder is not supplemented, so marginal copper deficiency develops because straight cow’s milk is very low in copper.”

Lei also said copper is so essential that it is included in intravenous feedings in hospital patients needing long-term total supplemental feeding.

“The recommended safe and adequate range of dietary copper is 1.5 to 3.0 milligrams per day;” Lei said, “but in many institutional diets, the level can drop to one milligram per day or less.”

Natural sources of copper include liver, whole grains, nuts and legumes. Copper pipes can leach the element into the water supply, but it is important not to develop a toxicity from consuming too much copper.

A severe copper deficiency is characterized by anemia, abnormalities in white blood cells and in collagen metabolism, and elevated blood cholesterol. Because the link between copper and cholesterol levels has not been well-understood, Lei is conducting laboratory studies to find out how copper affects lipoproteins.

Lipoproteins carry lipids from the liver to the tissues in the body for either oxidation or storage. Blood cholesterol is mainly carried by two well-known lipoproteins: low density lipoproteins (LDL) and high density lipoproteins (HDL). High concentrations of LDL are associated with an increased incidence of coronary atherosclerosis, while greater amounts of HDL seem to have the opposite effect.

“HDL is thought to be involved in reverse cholesterol transport by taking cholesterol from peripheral tissues, including deposits in major arteries, back to the liver for excretion,” Lei said. “It is thought to be involved in cleaning out the arteries and in maintaining vascular health.”

Within each lipoprotein, the protein components are called apolipoproteins. In HDL, apolipoprotein A-1, also called Apo A-1, is the major component. Apo A-1 activates a plasma enzyme that affects cholesterol deposition and directs HDL to cells for uptake. In LDL, Apo B is the major apolipoprotein, and is involved in receptor-mediated uptake of LDL by liver and peripheral tissues.

What does all of this have to do with copper? Without copper, not only is more Apo B formed, but Apo A-1 production is also markedly increased, resulting in hyperapolipoproteinemia, or elevated apolipoproteins in the blood.

“Thus, we are only studying copper to understand how this mechanism is initiated,” Lei said.

Through observing the development of apolipoproteins A-1 and B in laboratory rats fed a copper-deficient diet, Lei is learning more about how copper turns on the gene expression of these proteins. Inducing copper deficiency in humans takes many months; in rats, hyperapolipoproteinemia will develop from a copper-deficient diet in three to five weeks. Although the mechanisms for Apo A-1 and Apo B synthesis operate slightly differently in humans, Lei’s work will provide basic knowledge regarding the process.

“By understanding how the Apo A-1 gene is turned on, we may one day be able to manipulate the mechanism of the cell to produce more HDL,” Lei said. “We may eventually be able to help a patient with low HDL level to raise it by stimulating the production of more Apo A-1.”

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