News
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**Honored gastroenterologist researching cholesterol imbalances leading to atherosclerosis, gallstones.

DALLAS--Two major diseases, atherosclerosis and gallstone disease, occur when there is a tilt in the body's delicate cholesterol balance. In both, excessive levels of cholesterol prove unmanageable for body processes that normally monitor cholesterol, says Dr. John M. Dietschy, professor of Internal Medicine at The University of Texas Health Science Center at Dallas.

Dietschy was recently awarded Germany's Heinrich Weiland Prize for his work in cholesterol metabolism. The presentation marks the first time one university has received two Weiland prizes. The other award at UTHSCD went to Drs. Joseph Goldstein and Michael Brown for their work on low density lipoprotein (LDL) receptors. Named for a Nobel Prize winner who died in 1957, the prize is given annually for work in the chemistry, biochemistry and physiology of fats and lipids.

Dietschy's studies are directed at why atherosclerosis and gallstones occur. He is investigating which factors regulate cholesterol throughout the whole body--in particular, which organs are most responsible for manufacturing cholesterol and for taking up cholesterol from the bloodstream. His conclusions offer valuable information on cholesterol balance in citing why drugs for lowering cholesterol are sometimes ineffective.

To examine the roles of different organs in cholesterol balance, Dietschy is using a radio-isotope that rapidly penetrates all cell membranes in several species of laboratory animals. These radio-labeled markers are attached to cholesterol molecules, making it possible to measure rates at which organs clear cholesterol from the bloodstream.

"Then we measure how much isotope is synthesized into new cholesterol. There is a whole animal synthesis rate and an organ synthesis rate. We want to know what factors regulate cholesterol in each organ. All have different rates," says Dietschy.

Every tissue needs cholesterol for making cell membranes. Most tissues synthesize the majority of this necessary cholesterol themselves, taking up only small amounts of cholesterol from the bloodstream.

Serious problems occur when the body synthesizes too much cholesterol and can't rid itself of the excess. In the liver is a cholesterol pool that must be removed, either by circulating it throughout the bloodstream to feed cells or by excreting it into bile. Problems relate to circulating cholesterol that cells don't need and bile cholesterol, which can't be dissolved adequately.

"It is very difficult to treat high levels of cholesterol in the body. You give a drug to limit cholesterol absorption and the body makes more. You drain cholesterol and the body makes more. As long as the body can adapt by changing cholesterol synthesis levels, the circulating cholesterol in the blood remains essentially constant," he says.

Atherosclerosis develops when blood cholesterol levels become elevated. Cells in artery walls get force-fed the fatty substance. Bloated cells, described as "foam cells," gradually replace normal tissue. Scar tissue eventually forms, hardening and narrowing the vessels with connective tissue and calcium. Blood flow to heart and brain is then reduced with devastating results--heart attack or stroke.

Gallstones result when bile becomes supersaturated with

cholesterol. Cholesterol turns to crystal and stones form.

"All populations with a high incidence of gallstones, such as American and European, secrete too much cholesterol into the bile relative to our ability to take it out," says Dietschy, a gastroenterologist. "When it's put into bile, there is a secretion of detergents in the liver to take it out by dissolving it. But for reasons we don't understand, the body sometimes synthesizes more cholesterol than bile salts can dissolve," Dietschy says.

Gallbladder stones, one of the most common maladies of Western society, has an incidence approaching one million new cases in the U.S. each year, and 500,000 gallstone operations are performed yearly. Five thousand to 8,000 die each year when gallstones perforate the gallbladder. In all, gallstones affect about 20 million Americans, and the cost of treatment is more than the amount spent on all types of cancer. Women are three times more likely to develop stones than men, especially if they are overweight.

Gallstones are of two types. Eighty percent are made up entirely or partially of cholesterol while the other 20 percent is made up of pigment stones of bilirubin.

The liver's role is to orchestrate the delivering of cholesterol into the bloodstream and into bile. Cholesterol is carried out into the bloodstream in water-soluble molecules called low density lipoprotein or LDL. LDL transports cholesterol to all tissues of the body and cells draw in the LDL-cholesterol through LDL receptors on the cell surface.

Since cells make most of their own cholesterol, it is believed that 75 percent of the cholesterol sent out into the bloodstream by the liver comes back to the liver.

The liver must deal with cholesterol coming from several sources. First, dietary cholesterol is absorbed in the intestines and then carried to the liver. Circulating cholesterol returns to the liver. Also, the liver makes a certain amount of cholesterol itself.

Through a finely tuned regulatory system, large amounts of dietary cholesterol can turn off the liver's normal synthesis of cholesterol in order to keep the rate of accumulation constant. However, obesity tends to increase plasma cholesterol levels anyway and puts a person at risk for the development of cholesterol gallstones. Weight loss, on the other hand, can be beneficial in lowering plasma cholesterol levels.

Cholesterol regulation outside the liver seems dictated by how active the tissue is. The more metabolically active organs require more cholesterol. The brain requires little cholesterol, while tissues like the intestines, lungs and kidneys, where new cell growth is occurring, have a large need for cholesterol.

"Ideally, with the new information we have on the regulation of cholesterol metabolism in animals and man, it would be possible to design better drugs for controlling both atherosclerosis and gallstone formation," Dietschy says.

Dietschy is director of the Gastroenterology Unit at UT Southwestern Medical School, a component of the health science center. He is a member of the Clinical Sciences Study Section at the National Institutes of Health. The researcher has been on the editorial board of many scientific publications, is a member of many associations and has authored numerous papers, book chapters and books. Last year he was president of the Southern Society for Clinical Investigation. He received an M.D. in 1958 from Washington University School of Medicine in St. Louis and came to Southwestern in 1963. He has been professor of Internal Medicine since 1971.

In 1978 Dietschy won the Distinguished Achievement Award of the American Gastroenterological Association for his contribution to better understanding the body's absorption processes.

Part of Dietschy's research has been supported by the Moss Heart Fund.

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