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*****Research in progress to eliminate costly cholesterol gallstone treatment.

DALLAS--Cholesterol gallstones are rarely fatal. But they put an enormous drain on the nation's pocketbook.

An astounding $5 billion is spent annually for the removal of cholesterol gallstones. That's the same as the entire yearly budget for the National Institutes of Health. It's more than that spent each year for the treatment of all types of cancer combined.

"We need to understand how to prevent gallstones, not just treat them," says Dr. John Dietschy, chairman of the Division of Gastroenterology at The University of Texas Health Science Center at Dallas.

Researchers Dietschy and Dr. Lyman Bilhartz, assistant professor of internal medicine, agree that the key to prevention is cholesterol research. Currently they are searching through biological clues for ways to keep cholesterol gallstones from forming.

Their research is supported in part by the Southwestern Medical Foundation.

Hundreds of thousands of Americans develop gallstones each year, says Dietschy, and approximately 500,000 operations are performed every year for their removal. Today surgery, the primary mode of therapy for removal, costs about $5,000 to $10,000. The operation entails taking out the gallbladder containing the stones.

"We are hoping for a major expansion of research in this area at both the national and local levels," says Dietschy, who will soon attend an NIH conference in Bethesda, Md., where new initiatives in cholesterol gallstone research will be discussed. "Research is so important because gallstone disease is such a tremendous public health problem and such a large percent of the population is at risk. If gallstones could be prevented by dietary means or drugs, then we could save a great deal of patient discomfort and expense."

The problem, says Dietschy, is that the liver secretes too much cholesterol, which gets into bile and then precipitates out in the form of sand and grit. These small granules grow to form large stones. "In the face of certain hormonal and dietary factors, the liver cannot regulate cholesterol balance," explains Dietschy, "and there is an excess of cholesterol in bile."

Through basic research, Bilhartz and Dietschy have identified several major defects that cause cholesterol gallstones. They have developed animal models for cholesterol gallstone disease and have gained information about what regulates the output of cholesterol into bile. They also have defined the roles of hormones, dietary triglycerides and cholesterol in stimulating cholesterol gallstone formation.

Ten percent of all Americans will feel at some time the symptoms of cholesterol gallstones, says Dietschy. Another 15 percent of the population will develop stones without symptoms.

Gallstone symptoms include vomiting and severe, steady pain on the right side after a meal. Pain results when gallstones obstruct the bile ducts as they are trying to squeeze down to secrete bile. In about one percent of cases, cholesterol gallstone disease becomes fatal when stagnant bile becomes infected or stones perforate the gallbladder.

At highest risk of developing cholesterol gallstones are women over age 40, persons who are overweight and American Indians. Studies also show that those whose diets are high in polyunsaturated fats could be at greater risk, says Bilhartz, as

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are persons losing weight rapidly. Also, those taking drugs to prevent atherosclerosis may have an increased risk of gallstones, he says.

Once cholesterol stones form, the options for gallstone removal are limited, Dietschy says, with surgery as the preferred therapy. A second, less desirable, treatment is drug therapy with bile acids to dissolve cholesterol stones. Given as a pill, bile acids work only 10 or 12 percent of the time and have many accompanying side effects.

Other procedures, one involving the injection of ether to dissolve stones through a catheter in the gallbladder and another using shock waves to break up the stones, have their disadvantages. "Dissolving or breaking up gallstones does nothing to get rid of the defect that caused the stones in the first place," says Dietschy. "Patients immediately start to form new gallstones.

"Despite the therapies, the solution is not to treat gallstones but to prevent them," he says, "since hundreds of thousands of Americans develop gallstones each year."

Dietschy says the key to prevention is in knowing the basic cell biology of how and why excess cholesterol is secreted from liver cells.

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