Researchers find coronary artery calcification in obese youth

Obesity in adolescence has been associated with an increased risk for coronary heart disease in adulthood. Researchers at the USDA/ARS Children’s Nutrition Research Center at Baylor College of Medicine investigated if there were signs of coronary artery calcification (the buildup of calcium deposits in the coronary arteries) among adolescents. Such findings could indicate a greater risk of developing coronary artery disease in the future. Their results were recently published in the journal *Diabetes Care*.

Dr. Fida Bacha, associate professor of pediatrics at Baylor, and her colleagues recruited 90 obese adolescents for the study. Of these adolescents, 37 had normal glucose tolerance, 27 had pre-diabetes and 26 had type 2 diabetes. The adolescents underwent evaluation for coronary artery calcifications.

Researchers found that among overweight and obese adolescents, those who had coronary artery calcifications were more likely to have higher body mass index, fat mass and abdominal fat than those who did not. This was independent of other risk factors such as high cholesterol or blood pressure.

CONTINUED ON PAGE 4
Measuring how many calories people burn (energy expenditure) in everyday life is fundamental to many areas of nutrition research, and scientists have relied on several measurement methods in their studies. Many of these methods, however, interfere with usual behavior or have potential measurement errors, making the results difficult to interpret. One method—the doubly-labeled water method—has become increasingly important in nutrition research because of its noninvasiveness and accuracy.

“The doubly-labeled water method is noninvasive, and it measures total energy expenditure while patients and study participants are free living,” said Dr. Nancy Butte, professor of pediatrics at the USDA/ARS Children’s Nutrition Research Center at Baylor College of Medicine. “It’s been a really important tool for nutrition research across all stages of life, including infants, children and pregnant women.”

The ability to measure energy expenditure in a free-living environment is one of method’s key benefits because other important energy expenditure methods, such as room calorimeters, require that the subjects remain in a closed room over a 24-hour period while doing structured activities like sleeping, playing and exercising in an attempt to simulate their daily lives in the external, free-living environment.

The CNRC played a major role in the development of the doubly-labeled water method. It is a stable isotope method that tracks two end products of metabolism—carbon dioxide and water. Study participants drink a special type of water that is enriched with two non-radioactive isotopes. They then go about their normal daily routines for 5 to 14 days, collecting urine samples once a day. The urine is analyzed for the two isotopes from which measurements researchers can calculate carbon dioxide production and thereby estimate total energy expenditure (oxygen consumption) during the study period. Based on this information, researchers can determine how many calories the specific individual must eat to maintain a healthy body weight or to potentially reduce excess weight. Consequently, the doubly-labeled water method has been used to develop dietary reference intakes for energy intake (calorie consumption).

A recent study led by Dr. William Wong, professor of pediatrics at the CNRC, sought to verify the accuracy of the doubly-labeled water method over the decades since its first introduction. The study was published in the Journal of Nutrition.

The study showed that the outcome measures, such as energy expenditure or caloric intake, can be reproduced highly accurately over a long period of time, Wong said.

The instrumentation used to measure the isotopes in the doubly-labeled water method is known for its high accuracy and reproducibility. However, there was no scientific data in the literature until this publication to confirm that the measurements on the same samples over long periods of time can be reproduced accurately.

“These findings will allow anyone using the doubly-labeled water method to determine the long-term treatment effect, such as a reduction in energy intake on body weight, increase in physical activity on energy expenditure, or any other clinical treatment to combat obesity,” Wong said.

Others who took part in this research included Lucinda Clarke, USDA/ARS Children’s Nutrition Research Center; Susan Roberts and Sai Krupa Das, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston; Susan Racette, Washington University School of Medicine, St. Louis, Mo.; Leanne Redman, Pennington Biomedical Research Center, Baton Rouge, La.; James Rochon, Manjushri Bhapkar and William Kraus, Duke Clinical Research Institute, Duke University.

Research was funded by a National Institute on Aging grant with support from a USDA/ARS grant.
STUDY SHOWS EPIGENETIC CHANGES CAN DRIVE CANCER

In recent decades scientists have come to believe that epigenetic changes—which don’t change the DNA sequence but rather how it is “read”—play a role in cancer development. In particular DNA methylation, the addition of a methyl group (or molecule), is an epigenetic switch that can stably turn off genes, suggesting the potential to cause cancer just as a genetic mutation can. Until now, however, direct evidence that DNA methylation drives cancer formation was lacking.

Researchers at the USDA/ARS Children’s Nutrition Research Center at Baylor College of Medicine have now created a mouse model providing the first evidence that epigenetic alterations alone can cause cancer. Their report appears in the Journal of Clinical Investigation.

“We knew that epigenetic changes are associated with cancer, but didn’t know whether these were a cause or consequence of cancer. Developing this new approach for ‘epigenetic engineering’ allowed us to test whether DNA methylation changes alone can drive cancer,” said Dr. Robert Waterland, associate professor of pediatrics at Baylor and senior author of the study.

Shen and colleagues focused on p16, a gene that normally functions to prevent cancer but is commonly methylated in a broad spectrum of human cancers. They devised an approach to engineer DNA methylation specifically to the mouse p16 regulatory region (promoter). As intended, the engineered p16 promoter acted as a “methylation magnet.” As the mice reached adulthood, methylation at the p16 promoter gradually increased, leading to a higher incidence of spontaneous cancers, and reduced survival.

“This is not only the first in vivo evidence that epigenetic alteration alone can cause cancer,” said Shen, but this also has profound implications for future studies, because epigenetic changes are potentially reversible. Our findings therefore both provide hope for new epigenetic therapies and validate a novel approach for testing them.”

Shen, who is also with the National Cancer Institute-designated Dan L. Duncan Cancer Center at Baylor, predicts that this new approach will be widely useful because in addition to p16, there are many other genes and diseases other than cancer that are connected to epigenetics (such as neurodevelopmental diseases, obesity and diabetes).

“If we can identify epigenetic changes that predispose people to cancer, these may actually be treatable or preventable, so to me this fuels optimism regarding new ways to address cancer,” said Dr. Robert Waterland, associate professor of pediatrics at Baylor, who was also involved in the study.

Others who took part in the study include Da-Hai Yu, Pumin Zhang, Deborah Schady, Miao-Hsueh Chen, Yongtao Guan and Manasi Gadkari, all with Baylor. Funding for this study came from grants from the Sidney Kimmel Foundation, the U.S. Department of Agriculture-Agricultural Research Service, the March of Dimes and the National Institute of Diabetes and Digestive and Kidney Diseases (IK01DK081557), a part of the National Institutes of Health.
CALCIFICATION IN OBESE YOUTH
CONTINUED FROM PAGE 1

Researchers concluded that there is evidence of coronary artery calcification in obese adolescence.

“These findings are concerning,” said Bacha. “Early manifestations of atherosclerosis should not exist in adolescence.”

Bacha and researchers emphasize the increased risk of cardiovascular disease in obese adolescents and the need for early interventions to reverse obesity and the early signs of atherosclerosis.

Others who took part in the study include Daniel Edmundowicz from Temple University, and Silva Arslanian from the Children’s Hospital of Pittsburgh. This work was supported by the Thrasher Research Fund, University of Pittsburgh Ultrasound Research, U.S. Public Health Service grant K24-HD-01357, Richard L. Day Endowed Chair, Department of Defense grants FA7014-09-2-0008, MO1-RR-00084, UL1-RR-024153 and the U.S. Department of Agriculture/Agricultural Research Service.