CENTER FOR
HUMAN NUTRITION
NEWSLETTER

UT SOUTHWESTERN MEDICAL CENTER

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American Heart Association honors two UT Southwestern doctors

Dr. Scott Grundy, director of the Center for Human Nutrition and chairman of clinical nutrition, and Dr. Ronald Victor, chief of hypertension, have received two of the top awards presented by the American Heart Association.

Dr. Grundy was honored with the Gold Heart Award, an annual award and the highest honor the association gives to volunteers who have provided continued distinguished service.

Dr. Victor received the association's Louis B. Russell Jr. Memorial Award for outstanding service to minority and underserved populations. In 2003, Dr. Victor initiated a program at two Dallas-area barbershops to improve the awareness, treatment and control of high blood pressure among African-American men by having the barbers measure their customers' blood pressures when they came in for a haircut.

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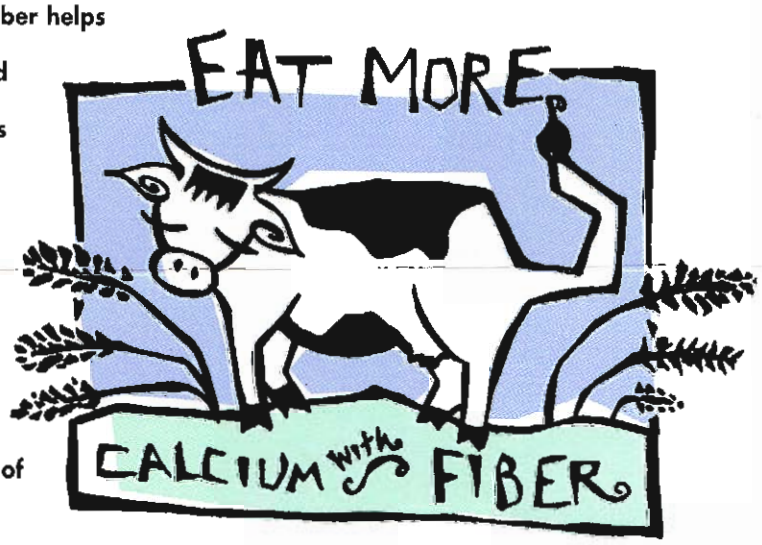
Against the grain

Diabetics on high-fiber diets might need extra calcium, study finds

The amount of calcium your body absorbs might depend, in part, on the amount of dietary fiber you consume.

Researchers at UT Southwestern report that patients with noninsulin-dependent (type 2) diabetes absorbed less calcium when they consumed 50 grams of fiber a day than when they ate 24 grams a day.

"We already know that fiber helps improve your cholesterol and glucose control and improves your bowel regularity. Our new findings suggest that dietary fiber reduces the body's capacity to absorb calcium," said Dr. Abhimanyu Garg, professor of internal medicine and an investigator in the Center for Human Nutrition. He is senior author of a study appearing online in Diabetes Care.



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FIBER FINDINGS

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"Because more calcium equals better bone health, we recommend that people on high-fiber diets talk to their physician about increasing their dietary calcium as well, in order to get the most benefit from both."

Dr. Garg said it's important to speak with a physician or a registered dietitian before increasing your calcium intake because excessive levels may cause kidney stones.

The American Diabetes Association (ADA) recommends a daily intake of 24 grams of dietary fiber, but the average American consumes about 14 to 15 grams a day.

Sometimes called "roughage," dietary fiber is the indigestible portion of plant foods that pushes food through the digestive system, absorbing water and easing defecation. Calcium is a nutrient found in food that is absorbed by the body and then excreted in urine, feces or sweat. It is the most abundant mineral in the human body.

Prior research at UT Southwestern has shown that a high intake of dietary fiber, mostly from fruits and vegetables, lowers blood glucose levels and leads to decreased insulin levels in the blood, as well as lowering blood lipid concentrations in patients with type 2 diabetes, the most prevalent type of diabetes.

For the current study, 13 patients with type 2 diabetes ate either a high-fiber diet (50 grams per day) or the moderate-fiber diet (24 grams per day) recommended by the ADA for six weeks, then switched to the other diet for six weeks. All participants stayed at UT Southwestern's Clinical and Translational Research Center (CTRC) for the final week of each six-week period.

CTRC staff prepared both diets so that they contained the same number and proportion of calories from carbohydrates, fats and proteins, as well as an equal amount of minerals such as calcium, phosphorous, magnesium, sodium and potassium. The high-fiber diet included numerous fiber-rich foods including cantaloupe, grapefruit, papaya, okra, winter and zucchini squash, granola and oatmeal. No supplements were used.

"We should encourage people to try food sources rich in fiber and calcium such as spinach, broccoli, figs, papaya, artichoke, okra, beans, mustard and turnip greens, and cactus pads."

—Dr. Abhimanyu Garg

Patients eating the higher-fiber diet excreted less calcium through their urine than they did when eating the moderate-fiber diet.

"The reduction of urinary calcium excretion on high-fiber diets tells us that the amount of dietary fiber has a direct impact on calcium absorption," Dr. Garg said. "In other words, the participants excreted less calcium on the high-fiber diet because the additional fiber caused their bodies to absorb less calcium."

Though most of the additional fiber in the high-fiber diet was soluble fiber, Dr. Garg said he cannot say for sure whether soluble or insoluble fiber affects calcium absorption.

"Generally, more fiber of either type is beneficial," he said. "We should encourage people to try food sources rich in fiber and calcium such as spinach, broccoli, figs, papaya, artichoke, okra, beans, mustard and turnip greens, and cactus pads."

Other UT Southwestern researchers involved in the study were Dr. Meena Shah, lead author and clinical associate professor of clinical nutrition; Dr. Manisha Chandalia, clinical associate professor of internal medicine with the Center for Human Nutrition; Beverley Adams-Huet, assistant professor of clinical sciences; Linda Brinkley, former research dietitian; Dr. Khashayar Sakhaee, chief of mineral metabolism; and Dr. Scott Grundy, director of the Center for Human Nutrition.

The work was funded by the National Institutes of Health and Southwestern Medical Foundation.

Panel at Friends' annual meeting tackles weighty issue of obesity

THE CLICHÉ THAT EVERYTHING IS BIGGER IN TEXAS unfortunately plays out in our bulging waistlines - more than two-thirds of the population is overweight or obese. While Texans aren't alone in facing the battle of the bulge, it's clear that much could be done to reduce obesity in the Lone Star State. Curbing this epidemic is at the heart of much of the nutrition, metabolism and obesity research currently under way at UT Southwestern Medical Center.

"Four years ago, Texans spent more than $10 billion a year on obesity-related medical care," Dr. Jay Horton, professor of internal medicine and molecular genetics, said at the recent Friends of the Center for Human Nutrition's annual meeting. "That number has already increased and is only going to continue to increase if we don't do something to address the problem now."

Dr. Horton served as moderator of a panel discussion on nutrition, metabolism and obesity research at the May 7 meeting. The other panelists were Nobel laureates Dr. Joseph Goldstein, chairman of molecular genetics, and Dr. Michael Brown, director of the Erik Jonsson Center for Research in Molecular Genetics and Human Disease; Dr. Abhimanyu Garg, professor of internal medicine; and Dr. David Mangelsdorf, chairman of pharmacology.

Dr. Brown, co-director with Dr. Goldstein of the W.M. Keck Foundation Gene Manipulation Laboratories, called obesity a social problem.

"People with means can afford to eat a proper diet, pay a fitness trainer and exercise," he said during the meeting on the 14th floor of the T. Boone Pickens Biomedical Building and Conference Center. "Obesity is a problem among the poor."

Drs. Brown and Goldstein shared the 1985 Nobel Prize in physiology or medicine for their discovery of the basic mechanism of cholesterol metabolism. Their groundbreaking research led to the development of statins to treat high cholesterol.

More recently, Dr. Brown said, they have identified an enzyme that works with the hormone ghrelin – sometimes called the hunger hormone – to stop hunger, as well as a protein that tells the body whether it's time to make or burn fat. "We can solve the world's energy crisis right here at UT Southwestern," Dr. Brown joked.

Dr. Mangelsdorf explained how several hormones his lab has identified help the body regulate itself when and after eating.

"We first identified a hormone called FGF19, which tells your liver and organs when the meal is over and that it's time to reset your digestive processes," said Dr. Mangelsdorf.

"We then identified a second hormone, a liver-produced starvation hormone called FGF21 that tells the body to start using and burning stored fat when it has been in a fasting state."

Dr. Mangelsdorf said his lab's findings on FGF21 help explain why the popular Atkins diet – which is based around a low-carbohydrate dietary regimen – helps many people slim down. "People on the Atkins diet generally eat fewer calories, so their body basically enters a fasting state, causing FGF21 levels to rise until the body begins using stored fat as fuel."

Dr. Garg said his research efforts continue to focus on lipodystrophy, a paradoxical disease in which patients with no body fat develop many of the health complications usually found in obese people.

NUTRITION PANEL (FROM LEFT) DR. ABHIMANYU GARG holds the Endowed Chair in Human Nutrition.
DR. MICHAEL BROWN, professor of molecular genetics and human disease, holds the W.A. (Monty) Moncrief Distinguished Chair in Cholesterol and Arteriosclerosis Research and the Paul J. Thomas Chair in Medicine.
DR. DAVID MANGELSDORF, professor of biochemistry, holds the Beatrice and Miguel Elias Distinguished Chair in Biomedical Science and is a Howard Hughes Medical Institute investigator.
DR. JOSEPH GOLDSTEIN holds the Julie and Louis A. Beecherl Jr. Distinguished Chair in Biomedical Science and the Paul J. Thomas Chair in Medicine.
DR. JAY HORTON holds the Dr. Robert C. and Veronica Atkins Chair in Obesity & Diabetes Research and is the coordinating investigator for a $22 million National Institutes of Health grant awarded to UT Southwestern's Task Force for Obesity Research in 2007.

For more than 20 years, he and his colleagues at UT Southwestern have led the way in identifying mutations in genes responsible for several forms of lipodystrophy and in identifying novel therapeutic approaches for these patients.

Some of Dr. Garg's most recent findings, in mice, have led to the initiation of a National Institutes of Health-funded clinical trial to determine whether eating an extremely low-fat diet could prevent many of the metabolic complications brought on by lipodystrophy.

"These patients are one in a million, but hopefully, our findings will lead to the development of new therapies for the metabolic complications of lipodystrophy, such as diabetes, fatty liver and high triglycerides," he said.

Laboratory is this former Army officer's new battlefield

The Meal, Ready-to-Eat, or MRE, may not be the pinnacle of gastronomical fare, but it serves a purpose. A single package provides at least 1,200 calories – about 35 percent of a typical male service member's daily caloric requirement – and has a shelf life of up to three years.

Dr. Deborah Clegg, assistant professor of internal medicine at UT Southwestern, had a hand in the development of MREs in the early 1990s.

"We were really focused on making sure that we met the nutritional requirements of the soldiers," said Dr. Clegg, a registered dietitian and former Army nutritionist who joined the faculty in April 2008. "We had to take into account the stress that's induced by fighting and whether the meals needed to be extra-fortified in certain nutrients to help offset the stress."

Dr. Clegg said she worked on the MREs as a dietetic intern at Brooke Army Medical Center in San Antonio. She later worked at Walter Reed Army Medical Center in Washington, D.C., as well as Fort Lee in Virginia and in Germany during the first Gulf War.

Though Dr. Clegg has since resigned her military officer commission, she said she enjoyed her time in the armed forces. "I'm an expert shot using an M16 rifle," she said. "I never would have had the opportunity to do that if not for the military."

Since leaving the military in 1993, Dr. Clegg has earned a master's degree in business administration from Boston University and a doctorate in nutrition from the University of Georgia. She was an assistant professor of psychiatry in the Obesity Research Center at the University of Cincinnati before coming to UT Southwestern.

Dr. Clegg admitted that her career has shifted since she graduated from Oregon State University with a bachelor's degree in nutrition in 1986.

"I was all human-focused and talking to people about weight loss and diets," she said. "Now, I am focusing on the molecular mechanisms by which nutrients influence food intake, body weight and energy homeostasis using a basic science approach."

"I WAS ALL HUMAN-FOCUSED AND TALKING TO PEOPLE ABOUT WEIGHT LOSS AND DIETS. NOW, I AM FOCUSING ON THE MOLECULAR MECHANISMS BY WHICH NUTRIENTS INFLUENCE FOOD INTAKE, BODY WEIGHT AND ENERGY HOMEOSTASIS USING A BASIC SCIENCE APPROACH."

— Dr. Deborah Clegg

She said her current research interests fall primarily into three areas. The first focuses on how estrogen is critical to body weight regulation.

"I'm also interested in how nutrients, specifically different types of fatty acids, impair insulin signaling in the brain," she said. "The third area is sort of a conglomeration of the two, which is looking at how nutrients, again fatty acids, cause breast cancer."

While many researchers study body weight regulation, Dr. Clegg's research differs in that she studies the role of estrogen and specifically focuses on females in her research. She said the animals' menstrual cycles pose a challenge, but the potential discoveries are worth the extra effort.

Her prior research in mice has begun to elucidate the mechanistic role estrogen may have in modulating body weight after menopause and reductions in circulating estrogen. Specifically, she is looking at how this mechanism is associated with shifts in body fat distribution and changes in energy expenditure that often result in weight gain in older women.

"I'm trying to figure out whether there's a way we can shift body weight distribution – especially in postmenopausal women – to favor the subcutaneous depot to protect women from diseases associated with visceral (tummy) fat deposition. We recently found that a male fat cell is not like a female fat cell. There's so much we don't know."

UT Southwestern research may help target "bad" cholesterol

Researchers at UT Southwestern have found that a protein responsible for regulating "bad" cholesterol in the blood works almost exclusively outside cells, providing clues for the development of therapies to lower LDL.

"The fact that it works mostly extracellularly provides more opportunities to develop different kinds of therapies," said Dr. Jay Horton, professor of internal medicine and molecular genetics and co-author of the study, which is available online and in the *Journal of Biological Chemistry*.

The protein, called PCSK9, disrupts the activity of a key molecule called the low-density lipoprotein receptor, or LDLR. This molecule, which is made and secreted in the liver, latches onto the LDL receptor. This binding, however, triggers a chain of biochemical reactions that leads to the destruction of the LDL receptor.

"Approaches to block the protein's activity in the blood should be successful in reducing plasma cholesterol levels."

– Dr. Jay Horton

With fewer receptors available, more of the so-called "bad" cholesterol remains in the bloodstream.

Dr. Horton said these new findings show that PCSK9 principally acts as a secreted protein to cause the degradation of LDL receptors. "Therefore, approaches to block the protein's activity in the blood should be successful in reducing plasma cholesterol levels," he said.

Too much LDL cholesterol in the blood is a major risk factor for heart disease, heart attack and stroke because it contributes to the buildup of plaque that clogs the walls of arteries. Up to 30 million people worldwide take a class of drugs called statins to lower their cholesterol to within recommended healthy limits.

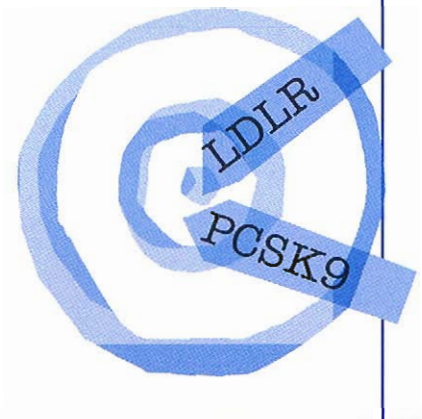
To determine whether PCSK9 works inside or outside the cell, the researchers designed peptides – the building blocks of proteins – to jam the interaction between PCSK9 and the LDL receptor. They then added the peptides to a cultured cell medium to see if they could block the activities of PCSK9. The peptides prevented the secreted PCSK9 from binding to the surface of the LDL receptors.

Dr. Horton said the fact that PCSK9 performs its destructive duties outside cells provides more opportunities for drug development.

"It's much easier to design inhibitors of PCSK9 function to work outside a cell than to develop a small molecule that works inside a cell," he said.

Dr. Horton's previous studies have shown that mice lacking PCSK9 have LDL cholesterol levels less than half those of normal mice.

Studies by other UT Southwestern researchers have found that people with mutations in the PCSK9 gene, which prevented them from making



normal levels of the PCSK9 protein, had LDL cholesterol levels 28 percent lower than individuals without the mutation and were protected from developing coronary heart disease. That research was led by Dr. Jonathan Cohen, professor of internal medicine, and Dr. Helen Hobbs, director of the Eugene McDermott Center for Human Growth and Development.

Dr. Horton said it's now up to pharmaceutical companies to develop drugs that will block these PCSK9 activities. "Our work paves the way for a more active pursuit of antibody and peptide approaches to block the destructive actions of PCSK9," he said.

Other UT Southwestern researchers involved in the current study were senior author Dr. Thomas Lagace, former postdoctoral researcher in molecular genetics; lead author Markey McNutt, graduate student; Dr. Hyock Joo Kwon, assistant professor of biochemistry; Dr. Chiyuan Chen, postdoctoral researcher in molecular genetics; and Justin Chen, summer student research fellow.

The work was supported by the Perot Foundation, the National Institutes of Health, the UT Southwestern Medical Scientist Training Program and the Canadian Institutes of Health Research.

HONORS

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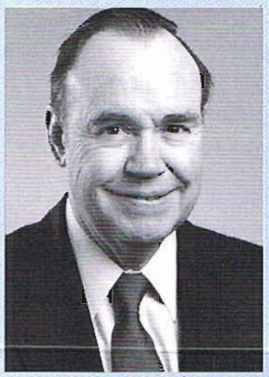
Dr. Victor, director of the Houston J. and Florence A. Doswell Center for the Development of New Approaches for the Treatment of Hypertension, holds the Norman and Audrey Kaplan Chair in Hypertension and the Dallas Heart Ball Chair in Hypertension and Heart Disease at UT Southwestern.



"This award represents recognition not only of my work, but also of the accomplishments of the American Heart Association in preventing heart disease in America."

— Dr. Scott Grundy

An American Heart Association volunteer since 1973, Dr. Grundy has played a pivotal role in the development of the AHA's recommended treatment guidelines for reducing risk factors associated with cardiovascular disease.

He has served on more than 20 of the organization's national committees and task forces, often as chair, and served as the association's first representative to the U.S. National Cholesterol Education Program (NCEP) when it was established in 1985.

In 1993 and 2001, Dr. Grundy headed the NCEP Adult Treatment Panels II and III, made up of the nation's top cholesterol experts. The group was charged with setting national guidelines for controlling cholesterol to prevent coronary heart disease.

"The NCEP has set the standard for treatment of high blood cholesterol in the United States, and I was privileged to be the chair of the treatment panel of the NCEP between 1991 and 2005," Dr. Grundy said. "The guidelines set by the NCEP not only have been accepted as the standard in this country, but they also have been influential worldwide"

More recently, Dr. Grundy chaired the AHA's Council on Arteriosclerosis, which he helped expand to include thrombosis and vascular biology, and helped form the Council on Nutrition, Physical Activity and Metabolism.

"I've worked with the American Heart Association for more than 30 years and have been involved in many of its prevention programs to reduce heart disease in the U.S.," Dr. Grundy said. "I feel great pride in what has been achieved. This award represents recognition not only of my work, but also of the accomplishments of the American Heart Association in preventing heart disease in America."

Dr. Grundy received the American Heart Association's Award of Merit in 1983 and its Distinguished Achievement Award in 1997, and he was one of six physicians selected by the organization as a Distinguished Scientist in 2005.

He has published more than 300 original papers and numerous solicited articles and book chapters. He also has served on the editorial boards of the American Heart Association journals *Circulation* and *Arteriosclerosis, Thrombosis, and Vascular Biology.*

Dr. Grundy received his undergraduate degree from Texas Technological College, now Texas Tech University; earned a combined medical and master's degree from Baylor College of Medicine in 1960; and was awarded an honorary degree in medicine from the University of Helsinki, Finland. He is a member of the Institute of Medicine, the American Society for Clinical Investigation, the Association of American Physicians, the American Society for Clinical Nutrition and the American Institute of Nutrition.

Ward off illness with exercise, foods that reduce stress

Keeping stress levels in check is important for overall health and wellness.

Numerous studies have shown that people who are constantly stressed are also more vulnerable to everything from colds to heart disease.

Bernadette Latson, assistant professor of clinical nutrition at UT Southwestern School of Health Professions, says the best way to address stress, particularly for office workers, is to get away from the computer monitor and take a brief walk or stretch break.

Incorporating stress-fighting foods into your daily diet also can help.

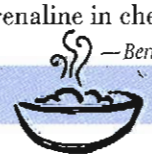
"A bowl of warm oatmeal will boost a calming brain chemical known as serotonin, while foods rich in omega-3 fatty acids will help keep the stress hormones cortisol and adrenaline in check," says Ms. Latson, a registered dietitian.

Other stress-fighting food suggestions from Ms. Latson include:

- A glass of skim or low-fat milk before bed can help reduce tension and anxiety and promote sleep.
- Oranges, rich in vitamin C, strengthen the immune system and reduce stress hormone levels.

"A bowl of warm oatmeal will boost a calming brain chemical known as serotonin, while foods rich in omega-3 fatty acids will help keep the stress hormones cortisol and adrenaline in check."

— Bernadette Latson



A Question of Nutrition? ..... Ask Dr. Carson

Q: What are omega-3 fatty acids? Why are they important?

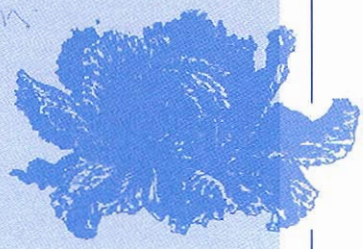
A: Omega-3 fatty acids are one of several types of fat in our diet. Whether we are eating steak, salmon, ice cream or salad dressing, we eat fat in the form of triglyceride. Within the triglyceride there are fatty acids. Some are saturated fatty acids that raise our blood cholesterol. Others are unsaturated fatty acids, which can be omega-3, omega-6 or omega-9 fatty acids. Omega-3 fatty acids are perhaps the healthiest of the unsaturated fats because they can reduce inflammation, as well as slow blood clot formation. Omega-3 fatty acids are found in fatty fish and in some plant foods, such as flaxseed and soybean oil. Eating fatty fish (such as salmon, albacore tuna or sardines) twice weekly is beneficial. Other fish provide smaller amounts of omega-3 fatty acids. Plant sources of omega-3 fatty acids are less powerful in promoting health than the omega-3 from fish.

Q: Are high-protein diets bad for the heart?

A: Following a high-protein diet to lose weight can be good for the heart. However, a return to previous eating habits that results in weight regain is bad for the heart. For those who need to lose weight, the real trick is to find a program that promotes weight loss and then to use the same program or another strategy to keep from regaining the weight.
Research says that whether you reduce carbohydrates, keep protein high or limit fat, you can lose weight. However, once you are at a healthy weight, if you eat a high-protein diet that is also high in animal fat (saturated fat), your LDL cholesterol will climb along with your risk for heart disease. The bottom line is to eat only the number of calories you need to maintain a healthy weight. Regular physical activity makes it easier to keep the energy equation in balance.

Q: There seems to be an endless list of B vitamins. What do they do for me? Are any of them crucial to my overall health and wellness?

A: Yes, there are at least eight different B vitamins. As vitamins they are important to our overall health. A vitamin is an organic substance the body cannot make and is vital for life. B vitamins all help in their own ways to foster metabolic reactions in our body. We should pay particular attention to the ones most likely to be inadequate in our diet. In the United States, it is easy to get enough thiamin, riboflavin and niacin when we eat whole grains and enriched grain products. We must try harder to get enough folate and vitamin B12. Together with vitamin B6, they help maintain normal blood levels of the amino acid homocysteine. Getting adequate folate is especially important around the time of conception to reduce the chances of a birth defect, such as spina bifida. Great sources of folate include orange juice, dark green leafy vegetables and dried beans. Getting adequate B12 is important later in life; aging reduces the ability to absorb B12. After the age of 50, we should get B12 in a fortified food (i.e. cereal) and/or a multivitamin to ensure optimum absorption. Vitamin B12 is present only in animal products, so strict vegetarians should get it in fortified foods or a supplement.



DR. JO ANN CARSON

If you have "A Question of Nutrition" for the "Ask Dr. Carson" column, please mail to:
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Make the Friends of the Center for Human Nutrition a part of your balanced information diet

Joining the Friends makes you part of the effort to improve the quality of life today and for the future. As heart disease, obesity and diabetes become almost daily headline issues, the Center's work becomes increasingly more important. Your membership will support the research of promising young scientists and ensure that excellent nutrition research continues well into the future. Your membership also entitles you to receive the Center for Human Nutrition Newsletter and the Fresh News postcard four times a year, to attend regular meetings with other members and distinguished nutrition scientists, and to receive letters from Dr. Scott Grundy clarifying and updating current nutrition issues.

Annual membership in the Friends is a tax-deductible contribution of $1,000 per individual or couple. Membership in the Younger Friends, which has activities oriented toward those 40 or younger, is $250. A category has been added to the Younger Friends for those who are 41 to 45 years of age and that fee is $500 per year. To join the Friends of the Center for Human Nutrition, call 214-648-2344 or access our Web site at www.utsouthwestern.edu/donatenow.

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