

UT SOUTHWESTERN

RESEARCHERS ARE

REACHING OUT TO

THE COMMUNITY IN

UNIQUE WAYS TO

STUDY AND PREVENT

HEART DISEASE.

COMMUNITY HEARTBEAT

BY BARBARA BEDRICK

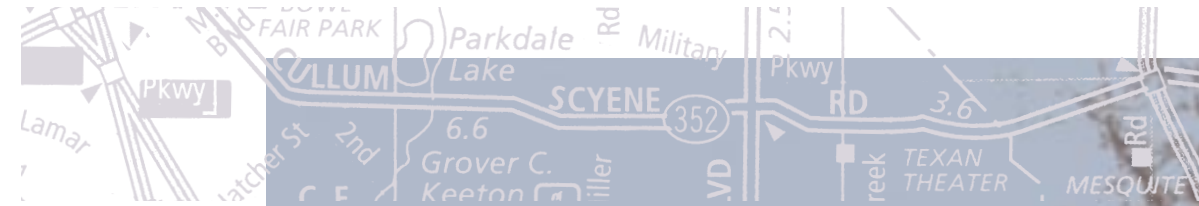
Since 1963, Carl Simon has managed Graham's Barbershop while handing out plenty of advice to his patrons. Snipping and shearing, Simon now also talks about cutting their blood pressure.

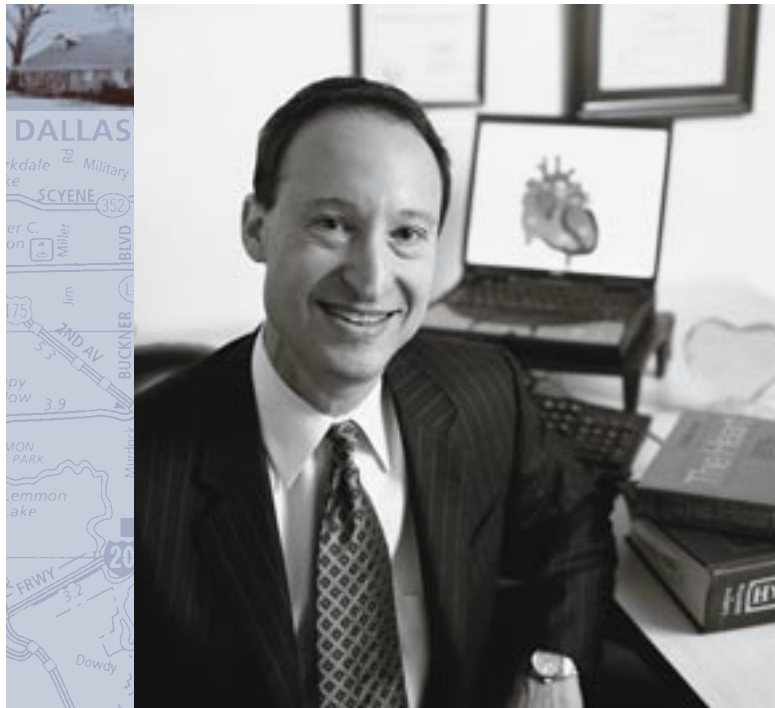
In the past six months, almost 2,000 clients have had their blood pressures measured in Graham's and two other Fair Park-neighborhood barbershops, and hundreds of African-American men with uncontrolled high blood pressure have been identified.

This neighborhood-based intervention study is an offshoot of the landmark Dallas Heart Disease Prevention Project — also known as the Dallas Heart Study — at The University of Texas Southwestern Medical Center at Dallas.

Heart disease, in particular high blood pressure, is highly prevalent in blacks, according to the Centers for Disease Control and Prevention.

“Despite impressive declines in the rate of heart disease among all Americans over the past 25 years, it is still the No. 1 killer of Americans, and African-Americans shoulder a greater burden than any other ethnic group,” said Dr. Ronald Victor, chief of hypertension at UT Southwestern.





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Hear disease kills more people every year in Dallas County than cancer, AIDS, motor vehicle accidents and violent crime combined, state health officials report.

Heart disease claims Dallas County residents at a higher rate than the nation's. On average, 14 people a day die of heart disease in Dallas County. To reduce that toll, researchers at UT Southwestern are forming collaborations between clinicians and basic scientists, with researchers nationwide and with Dallas community leaders, in a battle against cardiovascular disease.

INNOVATIVE CLINICAL RESEARCH

In 1998 the American Heart Association announced that the Donald W. Reynolds Foundation sought to establish a series of centers of excellence around the country to move toward cures for atherosclerotic heart disease, the most common cause of heart disease that leads to heart attacks. The foundation wished to fund cardiology centers to coordinate basic laboratory research with clinical studies involving patients with heart disease.

After an intense nationwide competition, the first Donald W. Reynolds Cardiovascular Clinical Research Center was established at UT Southwestern in October 1999 with a \$24 million grant, the largest single grant to one medical center for heart-disease research.

Dr. Helen Hobbs, director of the Eugene McDermott Center for Human Growth and Development at UT Southwestern, directs the Reynolds Center.

“What captured the imagination of the review group was that we proposed bringing together the best of population science and laboratory science to focus on disparities in heart health,” said Victor, principal researcher for the Dallas Heart Study and for center projects studying high blood pressure.

Hobbs and Dr. Scott Grundy, director of the Center for Human Nutrition at UT Southwestern, are the principal researchers for the projects studying cholesterol.

“Most heart-disease studies are multicenter studies and include populations from different regions of the country,” Hobbs said. “We designed the Dallas Heart Study to be performed solely in the community in which we work and provide health care.

“In the first phase of the study we will learn a great deal about heart disease in Dallas County, including its geographic and demographic distribution. We will learn about the risk-factor profile of our own population. If the participants in the study agree by signing a consent form, we can recontact them to take part in future studies, which may include more detailed testing to probe the underlying mechanisms that cause heart disease. We can also perform family studies to explore the genetic underpinning of the disease.

“In the second phase of the study, we will take what we have learned about heart disease in our own community to design educational and therapeutic interventions with the goal of reducing heart disease in Dallas County.”

Dr. Eric Olson, chairman of molecular biology at UT Southwestern, also is a principal researcher in the Reynolds Center. His focus is on defining the pathways involved in enlargement of the heart and the use of stem cells to potentially repair a damaged heart.

To ensure success, a team of individuals with diverse talents was required. Dr. Ronald Peshock, assistant dean for informatics at UT Southwestern, oversees the heart imaging studies performed at the Mary Nell and Ralph B. Rogers Magnetic Resonance Center. Drs. DuWayne Willett, associate professor of internal medicine, and Patrice Vaeth, assistant professor of internal medicine, are the project

managers for the Dallas Heart Study. Dr. Ivor Benjamin, professor of internal medicine, leads the education of cardiology trainees and junior faculty in patient-oriented research.

The four goals of the Reynolds Center are to:

- Enhance the prevention of atherosclerotic heart disease;
- Reduce premature death and disability from heart disease throughout Dallas County;
- Close the ethnic gap in heart disease in Dallas County;
- Create a large group of study participants from the community to participate in future studies of heart disease.

“Our goal is to learn why more people are not being treated to avoid the development of heart disease,” said Hobbs, holder of the Eugene McDermott Distinguished Chair for the Study of Human Growth and Development and the Dallas Heart Ball Chair in Cardiology Research. “What are the barriers to treatment in our community? We are hoping to use this information we gather to design intervention studies that will be tailored to the particular problems of the people we serve as physicians.”

BUILDING A COMMUNITY PARTNERSHIP

Nine months before recruitment began in the Dallas Heart Study, the research team formed a community advisory board, led by the Rev. Zan Holmes, Rodger Meier and Liz Flores-Velasquez, and recruited Myra Hollins as director of community outreach.

“We have excellent relationships with the community due to the hard work of our Community Advisory Board,” Hobbs said. “We are learning a tremendous amount about our community, its neighborhoods, its attitudes and the distribution of disease.”

The Dallas Heart Study randomly surveyed about 15,000 Dallas County residents of all social classes and geographical locations. By design, half of the study participants are female and half are minorities, to ensure adequate representation of heart disease in women and ethnic groups.

“We exceeded our study goals, recruiting more than 6,000 Dallas County residents, ranging in age from 18 to 65, to participate in the Dallas Heart Study,” Victor said. “Because participants could not volunteer but were selected at random, each one represents hundreds of people like themselves with the same socio-demographic background and the same characteristics. This gives us a more accurate view of heart disease and its risk factors throughout Dallas County.”

Three phases made up the Dallas Heart Study's initial project. The first phase included a 60-minute in-home questionnaire surveying not only medical

and family history of heart disease but also personal knowledge, attitudes, and beliefs about its prevention and treatment. In Phase 2, blood and urine specimens were collected; these will be used to discover new early markers of heart disease, including genetic profiles. In Phase 3, participants came to the Rogers Center to obtain electrocardiograms to chart the heart's electrical activity as well as a series of imaging studies of the heart and body.

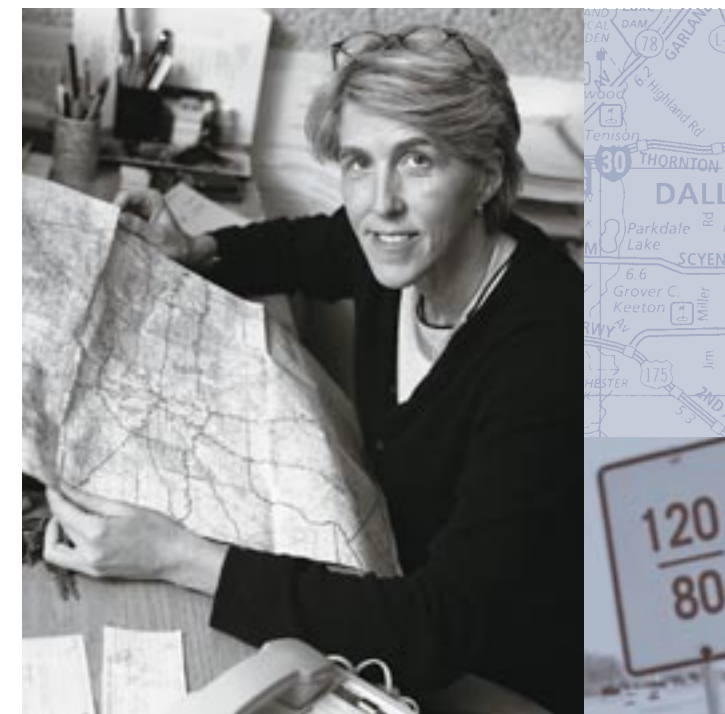
The imaging tests included electron-beam computed tomography to measure calcium deposits in the heart and magnetic resonance imaging to produce three-dimensional images of the heart. Doctors, using a DEXA scan, also measured fat distribution throughout each participant's body. Blood pressure was taken at all three visits.

“Entering our fourth year of the Dallas Heart Study, we had more than 1 million MRI images to evaluate and review,” said Willett.

Kevin Burns, an African-American participant who coaches youth softball in DeSoto, expressed relief after hearing his test results. “I didn't have a family history, but I worried I had high blood pressure or an even bigger problem,” he said.

But for many, the Dallas Heart Study was an urgent wake-up call.

“Already, the study has helped save many lives in Dallas County,” Victor said. “We have identified more than 500 people with high blood pressure who did not know they had it until they participated in the Dallas Heart Study. We urged each of them to go to community-based or Parkland Memorial Hospital physicians to get it under control.”



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— DR. HELEN HOBBS





High blood pressure, or hypertension, which affects 50 million Americans, is often referred to as the silent killer because its symptoms often go unnoticed until complications occur.

Many in the Dallas Heart Study learned they had high levels of glucose, including diabetes, or had high cholesterol. Diabetes affects more than 16 million Americans and, like high cholesterol, is a risk factor for coronary heart disease.

"The tremendous community participation in this study is important," Victor said. "Most of what we know about risk factors for heart disease was derived from the Framingham Heart Study, in which 99 percent of the participants were Caucasian. The Dallas population is much more representative of the entire United States."

What Hobbs, Victor and their colleagues discover may help determine how doctors treat heart disease in women and minority groups, including blacks and Hispanics, where health problems have historically received less focus than they have in white men. Understanding behaviors and beliefs, Hobbs said, may be key to assembling a comprehensive health-care strategy that employs the most effective courses of action in medications, treatments and therapies to improve the control rates and reduce deaths from heart disease in men and women of all races.

"We are learning that there are significant differences in the attitudes and beliefs about heart disease in different ethnic communities," Hobbs said. "We cannot use the same messages and approaches when we design interventions to increase the awareness and treatment of heart disease."

While unraveling the mysteries of heart disease and intervention, UT Southwestern researchers also face a shift in the nation's "stroke belt." The Southeastern seaboard, once considered to hold that dubious title because of its high rates of strokes, hypertension and heart disease, has nearly surrendered the distinction to the Southwest.

"The 'stroke belt' is moving to Texas, and the rates of heart disease and stroke are becoming higher in Texas than in many other states," Victor said. "Whether it's lifestyle or diet, we're not certain."

GENETICS OF THE HEART

After more than three years of research, Hobbs can appreciate how far the study has come, and how much remains to be done. The DNA of each participant has been banked for genotyping.

"We will be analyzing more than 1,000 sequence variations in the human genome and determining how they relate to heart disease or to risk factors for the development of heart disease," Hobbs said.

Study researchers will define genetic factors contributing to hypercholesterolemia, an inherited inability to metabolize cholesterol, and will study the genetic determinants that control plasma levels of cholesterol-rich lipoproteins, which in high concentrations are associated with coronary atherosclerosis.

Another team of scientists led by Olson, director of the Nancy B. and Jake L. Hamon Center for Basic Research in Cancer and the Nearburg Family Center for Basic Research in Pediatric Oncology, is working to solve the puzzle of cardiovascular disease at the genetic level.

"My lab is working at the most fundamental level to understand how the heart works, and we're continually discovering new genes and new mechanisms for how the heart functions," Olson said. "Understanding the heart is like putting together a jigsaw puzzle. You can't put the puzzle together until you have all the pieces."

Olson's team has identified a new gene, called *HOP*, which regulates the number of heart muscle cells during development. The findings were published in the September 2002 issue of *Cell*.

"The *HOP* protein could be a really important piece of the puzzle for how the heart forms," said Olson, holder of the Robert A. Welch Distinguished Chair in Science. "Heart cells lose their ability to divide after birth, and that's the biggest hurdle in cardiovascular medicine because that means when the adult heart gets injured from a heart attack, it has no way to repair itself. So if one could develop strategies that could induce heart cells to divide, it would have very important implications."

The DNA of Dallas Heart Study participants with congenital or acquired heart disease will be studied and also will be screened for mutations in the *HOP* gene.

The identification of another heart gene regulator, *HDAC9*, is another primary focus of Olson's heart study projects. In a study published in the August 2002 issue of *Cell*, Olson described the mechanism by which *HDAC9* regulates cardiac hypertrophy, or enlarged hearts.

"Our goal at the Dallas Heart Study is to be able to explain heart failure in the context of a pathway from A to Z – all the steps involved," Olson said. "Once you know all the steps, then you can develop drugs or at least rationally think about how to develop drugs to target various steps in the pathway."

Olson's second study project involves angiogenesis, the development of new blood vessels, and gene transfer research. There are two approaches, each with different hurdles, but Olson believes both are possible.



FROM LEFT TO RIGHT: GRAHAM'S BARBERSHOP; CARL SIMON AT WORK; AND FELTON STEVENS JR., RESEARCH ASSISTANT, TAKES CHESTER SMITH'S BLOOD PRESSURE.

BARBERSHOPS ARE IDEAL SETTINGS FOR ONE-ON-ONE EDUCATION IN A FAMILIAR ENVIRONMENT, PROVIDING A UNIQUE OPPORTUNITY TO SEE IF THE CONTROL OF HYPERTENSION IN BLACK MEN CAN BE IMPROVED. "GETTING ONE'S BLOOD PRESSURE MEASURED IN THE BARBER'S CHAIR COULD BECOME AS INGRAINED AS GETTING ONE'S HAIR CUT." — DR. RONALD VICTOR

One approach is to convert nonheart cells into heart cells by transferring in the master genes for heart formation — using either any nonheart cell or a stem cell. The other approach, Olson said, is to find the undiscovered signal that enables heart muscle cells to divide.

"I think it's going to be possible to regenerate the heart. I really do," said Olson. "I think there is going to be a way to unlock the ability in the heart to repair itself, and that's going to be a revolutionary therapy. No one yet has done effective gene therapy in humans."

"The heart has a very precise electrical activity that sustains its rhythmic contractions one time per second. If you disturb the architecture of the heart, it can mean electrical disturbances that can cause sudden death."

To restore function to the damaged heart, some very precise remodeling will be required.

"What is so unique about the Dallas Heart Study is that there are so many people across the country studying just one facet of heart disease, either just basic science or just epidemiology," Olson said. "There are few, if any, other examples where the entire research effort is brought together under one umbrella in an interlocking way so that the ideas and the technologies freely flow between the groups, and I believe that has made this a very special project."

SNIPPING A DEADLY DISEASE

UT Southwestern researchers are beginning to use the wealth of information about heart disease in Dallas County to devise and test new interventional programs to improve early detection and prevention of heart disease and its risk factors.

The pilot study spin-off involving Graham's and the other barbershops is called "Cut Your Pressure." The goal of the project is to determine if barbershops are effective places to improve the early detection and treatment of high blood pressure in black men, the group identified by the Dallas Heart Study as having the highest rates of untreated high blood pressure.

"We chose the neighborhood barbershop because it casts a wide net," Victor said. "Our pilot data indicated that African-American men are loyal customers of their chosen barbershop and average several haircut visits per month."

Barbershops are ideal settings for one-on-one education in a familiar environment, providing a unique opportunity to see if the control of hypertension in black men can be improved, Victor said.

"Getting one's blood pressure measured in the barber's chair," Victor said, "could become as ingrained as getting one's hair cut." ❁



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— DR. RONALD VICTOR