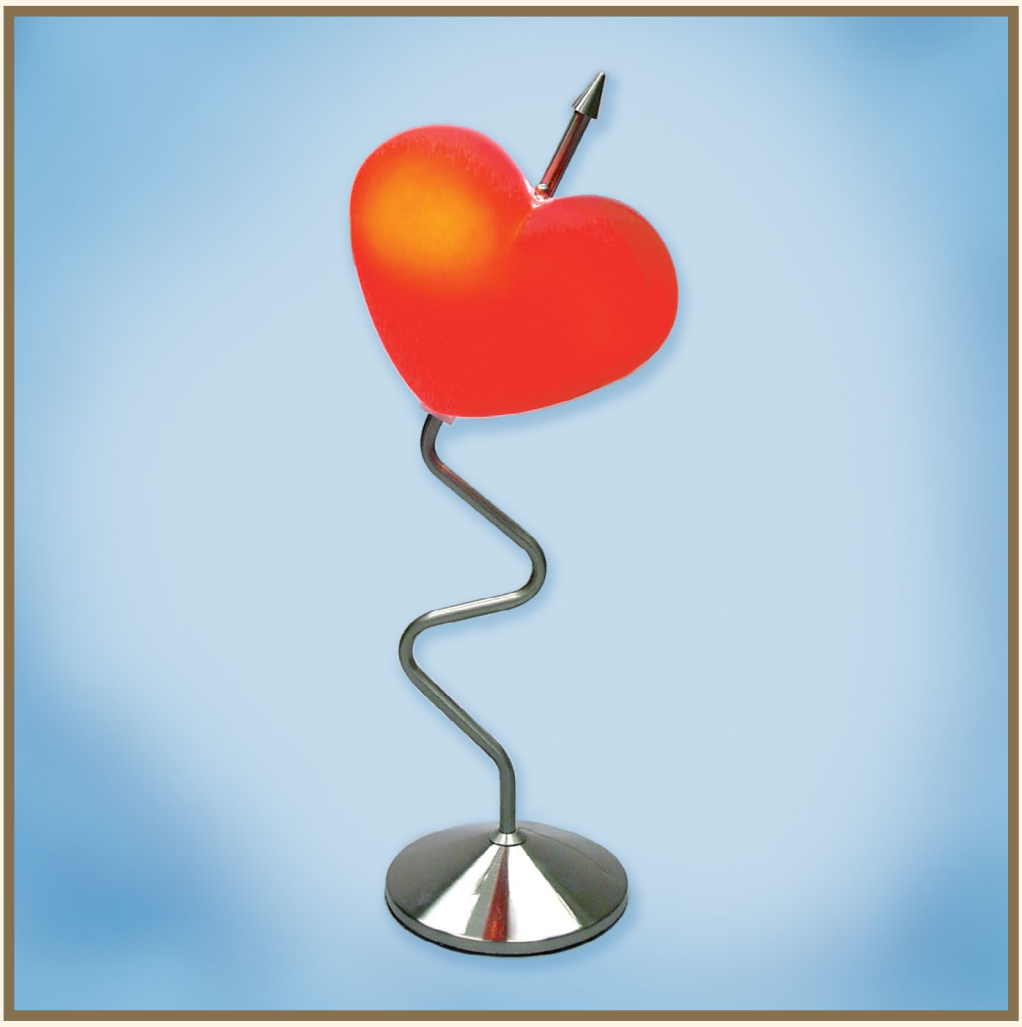
HeartWATCH

SPRING 2012

A Physician Newsletter Produced by the Texas Heart Institute



Texas Heart® Institute

at St. Luke's Episcopal Hospital

Texas Heart Institute Continues to Lead the Way in Heart Transplantation and Mechanical Circulatory Support

Abstract: Since the late 1960s, heart transplantation and mechanical circulatory support have been important focuses for Texas Heart Institute researchers and surgeons.

For more than 40 years, the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) has been a leader in heart transplantation and mechanical circulatory support. Although initial experience with heart transplantation in the late 1960s proved disappointing, interest in this procedure was renewed in 1982 with the advent of improved immunosuppressants that could effectively combat tissue rejection. Since then, the THI team, led by O. H. Frazier, MD, Chief of the Center for Cardiac Support, has performed 1233 heart transplants.

Under Dr. Frazier's leadership, THI also has amassed the world's largest and most varied experience in the development and clinical use of mechanical circulatory support systems. In 1986, Dr. Frazier initiated clinical trials of the HeartMate IP (implantable pneumatic) (Thoratec Corporation, Pleasanton, CA). It subsequently became the first implantable ventricular assist device (VAD) to be approved by the Food and Drug Administration (FDA) as a bridge to transplantation. Another version of this device, the HeartMate VE (vented electric), was initially implanted in patients in 1991 here at THI. One of these patients became the first to leave the hospital while supported by an implantable VAD. By early 2012, THI's heart failure surgeons had implanted more than 1500 circulatory support pumps, including VADs and TAHs (*Table*).

In 1988, Dr. Frazier and Dr. Richard Wampler performed the world's first clinical implant of a continuous-flow pump at THI. The Hemopump, about the size of a pencil eraser, rotated at 25,000 rpm yet did not injure the blood. It was safe and clinically effective for supporting patients with heart failure. The device's axial-flow technology had the advantage of preload sensitivity, which allows pump output to respond within a physiologic range to inflow pressure variations, although the number of rotations per minute remains constant.

The Hemopump (Medtronic Inc, Minneapolis, MN) showed that continuous-flow pumps could safely and effectively support the failing heart. The first implantable, long-term, continuous-flow pump, the Jarvik 2000 (Jarvik Heart, Inc., New York, NY), was first implanted clinically in April 2000 at THI after more than 10 years of in vivo and in vitro testing. Moreover, in November 2003, THI surgeons performed the first implant of the clinical HeartMate II (Thoratec), a device based on experience with the Hemopump. The HeartMate II was approved by the FDA for use as a bridge to transplantation in 2008 and as destination therapy in 2010. Since 2003, more than 10,000 HeartMate IIs have been implanted worldwide.

Texas Heart Institute Experience with Mechanical Circulatory Support, 1986–2011

Short-term support	Long-term support
BVS 5000	HeartMate IP
AB5000	HeartMate VE/XVE
TandemHeart	Thoratec VAD
Levitronix	HeartMate II
Hemopump	Jarvik 2000
Impella 5.0	MicroMed DeBakey
Impella 2.5	Jarvik 7
Orqis Cancion	DuraHeart
	HeartWare
	Novacor
	AbioCor
	SynCardia
728	**819**

Total = 1547

"Despite optimal medical or surgical management, the failing heart inevitably becomes unable to pump blood effectively without assistance," says Dr. Frazier. "Replacing failing hearts with transplanted ones is limited by donor heart availability—approximately 2000 hearts yearly in the United States—and the limited life of the donor organ. Therefore, there is an urgent need for pumps that can be left in place for long periods.

"Patients are benefiting from the extensive research and testing performed at our center," he continues. "We have bridged 568 patients to transplantation and have implanted pumps as destination therapy in 251 patients. A few of these patients recovered enough heart function while they were waiting for transplants to have their devices removed and to live normal lives without any additional support. I believe that the use of VADs as so-called bridges to recovery should be investigated further. Used in this manner, some selected patients might be spared both a transplant and a destination therapy device."

In addition, Dr. Frazier and his team hypothesized that 2 axial-flow pumps used together could autoregulate their outputs at a constant rotational speed, because the output pressure of 1 pump determines the input pressure of the other—a tandem arrangement potentially ideal for biventricular replacement. To test this hypothesis, THI surgeons have conducted research over the last 7 years under the auspices of a National Institutes of Health grant to study the effects of total heart replacement with dual continuous-flow VADs. The dual device has been tested for up to 3 months in more than 50 calves and has maintained normal end-organ function in the animals. Recently, 2 left ventricular assist devices were used successfully (off-label) here for a dying patient for whom no other treatment options were available.

"So far, the technical challenges inherent in developing a TAH have limited the application of these devices," says Dr. Frazier. "However, I am confident that with continuous-flow technology, we will be able to develop an artificial heart for effective long-term replacement of the failing human heart." ●

For more information:

Dr. O. H. Frazier

832.355.3000

Cell Therapy With Aldehyde Dehydrogenase Cells Shows Promise in Patients With Advanced Ischemic Heart Failure

Abstract: THI investigators have shown that cell therapy with autologous aldehyde dehydrogenase bright cells appears to be safe and feasible in patients with chronic heart failure.

Cell therapy may offer an alternative therapeutic option for patients with chronic ischemic heart disease. However, the optimal type of stem cell to use in this patient population has not been determined, and novel cell types are being sought. A primitive population of bone marrow–derived cells has been isolated by using the cytosolic enzyme aldehyde dehydrogenase (ALDH), which is considered a marker for stem and progenitor cells. The novel population, called ALDH bright (ALDH^{br}) cells, comprises a multilineage mix of primitive cells, including those that express CD34, CD117, CD105, CD133, or CD166 markers. Thus, ALDH^{br} cell populations contain hematopoietic, endothelial, and mesenchymal progenitor cells—each of which contributes to repairing cardiac tissue damaged by ischemia. Furthermore, ALDH^{br} cells have been shown to promote angiogenesis and provide perfusion benefits in preclinical studies of ischemia.

These promising characteristics led investigators at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) to conduct the first randomized, controlled, double-blind study of the safety of autologous, bone marrow–derived ALDH^{br} cells in patients with advanced ischemic heart failure (*Am Heart J* 2012;163:415-421.e1). Headed by Emerson C. Perin, MD, PhD, Director of the Stem Cell Center at THI at St. Luke's, the researchers enrolled 20 patients with no options for revascularization who were randomly assigned to receive transendocardial injections of ALDH^{br} cells (n=10) or placebo solution (n=10).

"Our findings indicate that therapy with this novel cell population is safe and feasible in patients with ischemic heart failure who have no other revascularization options," says James T. Willerson, MD, President and Medical Director of THI at St. Luke's and a study investigator. "ALDH^{br} cells were prepared successfully from all patients in the treatment group. The cell-treated patients had no complications or adverse events during the periprocedural period (up to 1 month) and no deaths or exacerbation of heart failure during the 6-month follow-up period."

> *"We have shown that ALDH^{br} cell therapy appears to be safe and may yield perfusion and functional benefits in patients with chronic myocardial ischemia."*
>
> *—Emerson C. Perin, MD, PhD*
> *Director, Stem Cell Center*

Although the study's primary endpoint was safety, efficacy was assessed as a secondary objective 6 months after the injections. The investigators found that cell therapy had no effect on left ventricular ejection fraction or clinical status (New York Heart Association functional class or Canadian Cardiovascular Society angina class). However, left ventricular end-systolic volume decreased significantly from baseline to 6 months in the cell-treated patients (93.2 ± 46.1 to 85.9 ± 46.2 mL; P=0.04), whereas no change was seen in the control patients. Similar findings were noted with left ventricular end-diastolic volume, but the decrease in volume among the cell-treated patients was not large enough to reach statistical significance. In addition, maximal oxygen consumption increased over the 6-month period in the treated group (from 15.5 ± 6.3 to 17.7 ± 4.1 mL/kg/min; P=0.05) but did not change in the control patients (14.1 ± 4.8 to 14.6 ± 6.7 mL/kg/min). Furthermore, the investigators reported a trend toward a decrease in the reversible total perfusion severity score on single-photon emission computed tomography in the cell-treated patients; however, the perfusion defect severity (total severity score) did not change significantly in either group.

"This study lays the groundwork for determining the usefulness of ALDH^{br} cells in treating patients with chronic ischemic heart disease," says Dr. Perin. "Most studies of cell therapy in this patient group have examined the use of unselected bone marrow mononuclear cells or subpopulations of bone marrow mononuclear cells isolated on the basis of expression of cell surface markers. Here, we present the unique approach of using a functional marker [ALDH enzyme] to select a population of cells that may be particularly well suited for providing benefits in ischemic hearts. We have shown that ALDH^{br} cell therapy appears to be safe and may yield perfusion and functional benefits in patients with chronic myocardial ischemia." ●

For more information:

Dr. Emerson C. Perin

832.355.9405

Dr. James T. Willerson

832.355.6839

The study was funded by Aldagen, Inc., Durham, NC.

Contents

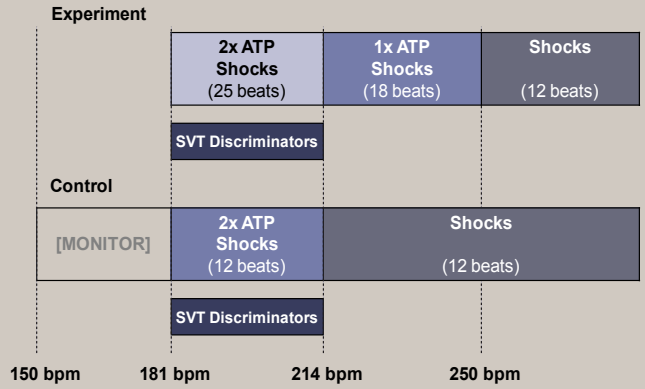
New Study Seeks Parameters for Prolonging the Time to First Shock in Patients With Implanted Defibrillators

Abstract: THI researchers have initiated a clinical trial to determine whether combining programming parameters reduces the shock burden in ICD and CRT-D patients.

Implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds) can be used to terminate ventricular tachycardia (VT) in patients with ventricular arrhythmias, coronary artery disease, or left ventricular dysfunction. Although shock therapy is an effective method of terminating VT, such therapy is painful, and repeated shocks can have negative psychological consequences for patients, impairing their quality of life. Avoiding inappropriate shocks for supraventricular tachycardia (SVT) and limiting the number of appropriate shocks to those necessary for converting ventricular arrhythmias could potentially reduce the number of painful shocks administered to patients with ICDs and CRT-Ds.

Researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) have initiated a randomized, multicenter trial to investigate which combination of parameters may increase the time to first shock in patients with these devices. Specifically, the researchers are aiming to determine whether higher detection rates, prolonged detection intervals, SVT discriminator parameters, and antitachycardia pacing (ATP) therapy will prolong the time to first shock without increasing the incidence of arrhythmia-related syncope in patients who have ICDs for primary prevention of sudden cardiac death.

The PROVIDE study (programming implantable cardioverter-defibrillators in patients with primary prevention indication to prolong time to first shock) (*Europace* 2011;13:1648–52) will enroll 1600 patients who receive St. Jude Medical (Sylmar, CA) ICDs and CRT-Ds for a primary prevention indication at up to 100 centers in the United States, including THI at St. Luke's. Follow-up evaluation will be conducted in a clinic or remotely, and patients will be enrolled until either 226 first shocks have been documented or the last of the 1600 patients has been enrolled and undergone evaluation for 1 year. The primary endpoint is the mean time to first shock; the safety endpoint is the rate of arrhythmic syncope.



Device programming for patients in the control and experimental groups of the PROVIDE trial. ATP = antitachycardia pacing, SVT = supraventricular tachycardia. (Reprinted from *Europace* 2011;13:1648–52 by permission of Oxford University Press.)

"Results from previous studies suggest that a combination of aggressive device parameter settings and ATP may help reduce the number of painful shocks in patients who receive devices for primary prevention," says Mohammad Saeed, MD, a staff cardiac electrophysiologist at THI at St. Luke's and principal investigator for the study. "The PROVE trial was the first large study to show the efficacy of using ATP in the primary prevention population."

For the experimental group, the parameters will include a slow VT zone (180-214 bpm, with 2 ATP attempts before high-output shock administration) and a fast VT zone (214-250 bpm, with 1 ATP attempt before high-output shock administration). A ventricular fibrillation therapy zone will be programmed for all rates greater than 250 bpm, resulting in a high-output shock. Parameters for the control group will be based on those from the PROVE trial (Programming Ventricular Tachycardia Therapy in Patients with a Primary Prevention ICD Indication) (*J Cardiovadsc Electrophysiol* 2010;21:1349-54 and *Heart Watch*, Spring 2011). Those settings were based on the ones from the PainFREE [Rx] II (Pacing Fast Ventricular Tachycardia Reduces Shock Therapies) trial and reflected empiric programming for a primary prevention indication.

"Avoiding unnecessary shocks is always the first consideration in programming these devices," says Mehdi Razavi, MD, Director of Clinical Arrhythmia Research at THI at St. Luke's and an investigator for the clinical trial. "Most efforts have focused on reducing inappropriate shocks for SVT, which is responsible for a large number of shocks. But we believe the problem could be further alleviated by preventing shocks for slower, hemodynamically stable ventricular arrhythmias and for those that might terminate on their own."

"Using the data we collect from PROVIDE, we hope to find the combination of programming parameters that will ultimately help us increase the time to first shock in these patients," adds Dr. Saeed. ●

For more information:

Dr. Mohammad Saeed
Dr. Mehdi Razavi
713.529.5530

Advances in Magnetic Resonance Imaging and Computed Tomography Allow Noninvasive Detection of Heart Disease

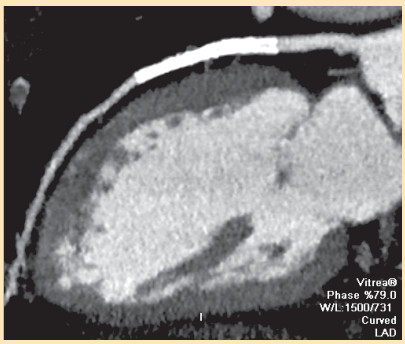
Abstract: Two noninvasive imaging methods—cardiac magnetic resonance imaging and coronary computed tomographic angiography—are benefiting patients at THI at St. Luke's.

For decades, cardiac catheterization with angiography has been the standard technique for imaging the heart and detecting cardiovascular disease. More recently, catheterization has been used with echocardiography for this purpose. However, catheterization is invasive, and echocardiography does not work well from all angles of view or in patients of all body types. To enhance patient safety and improve image quality, new noninvasive imaging techniques have been introduced. Together, 2 such techniques—cardiac magnetic resonance imaging (CMRI) and coronary computed tomography angiography (CCTA)—now rival cardiac catheter angiography and echocardiography for diagnosing heart disease. Whereas CMRI has become a standard method of evaluating both ischemic and nonischemic cardiomyopathy, CCTA is emerging as the preferred noninvasive modality for imaging the coronary arteries in selected patients.

Benjamin Cheong, MD, Clinical Director of Advanced Cardiac Imaging in the Department of Diagnostic and Interventional Radiology and Cardiology at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's), discussed these 2 technologies at the 11th Annual Texas Update in Cardiovascular Advancements held on December 10, 2011, at THI at St. Luke's.

"Compared with other imaging techniques, CMRI has superior temporal and contrast resolution, a high signal-to-noise ratio, and relatively high spatial resolution," states Dr. Cheong. "Additionally, CMRI does not require ionizing radiation, and gadolinium—the contrast reagent injected intravenously during this procedure—is non-nephrotoxic at the approved dose."

Not only does CMRI provide morphologic, functional, and perfusion information, it also provides tissue characterization, which cardiac catheterization and angiography cannot do and which echocardiography can do only to a certain extent. Delayed-enhancement MRI (DE-MRI) can be used to assess the viability of myocardial tissue because DE indicates necrosis. Another technique, T2-weighted MRI, can be used to detect myocardial edema, which can occur almost immediately after plaque rupture. Detecting edema early may enable clinicians to treat patients before their heart tissue is irreversibly damaged. Furthermore, both DE-MRI and T2-weighted MRI can help establish prognosis—patients with myocardial necrosis or edema have worse outcomes than those without these indicators.



Coronary computed tomography (CT) angiogram of the left anterior descending (LAD) artery imaged by the new 256-slice CT scanner. This curved multiplanar reformation of the LAD shows a long intravascular stent in the proximal to mid LAD. Narrow vascular stents are normally difficult to image, but the new "iterative reconstruction" algorithm significantly reduces image noise and, therefore, improves image clarity.

Although CMRI comes close to being a "one-stop service," it does not replace all other cardiac imaging techniques. "Patients with certain kinds of medical devices, such as pacemakers, implantable defibrillators, and older types of cerebral aneurysm clips, may not be able to undergo an MRI scan safely," explains Dr. Cheong. "Also, it is difficult to monitor patients while they are in the scanner because the electrocardiogram becomes distorted; therefore, this technique may not be an option for critically ill patients. Moreover, CMRI will never replace echocardiography, which is still the first-line approach for evaluating heart disease."

Angiography may be performed with CMRI, but CCTA is a better method for imaging the coronary arteries. Because it has higher spatial resolution, CCTA provides clearer images of the small, high-flow coronary vessels, including their distal branches, than does CMRI. Also, the imaging time is shorter for CCTA than for CMRI. Unlike CMRI, however, CCTA requires an iodinated contrast agent and ionizing radiation.

In addition, CCTA can be used to evaluate coronary artery calcification, which indicates atherosclerosis. Therefore, this approach can be used to rule out obstructive heart disease. "Patients who come to the emergency department and have no obstructive disease on CCTA can be safely discharged, avoiding hospitalization and reducing costs," says Dr. Cheong. "Coronary artery calcification can also indicate an increased risk of cardiovascular events; however, the presence of even a large amount of calcification does not necessarily indicate significant obstructive lesions."

Other applications of CCTA include evaluating atherosclerotic plaques and, possibly, assessing myocardial perfusion.

Recently, St. Luke's acquired a 256-slice CT scanner that can image the entire heart in only 3 seconds (about 3 heartbeats). This faster acquisition time greatly reduces motion artifacts and radiation exposure during CCTA and permits a significantly shorter breath-hold than standard 64-detector CT requires.

Researchers continue to explore whether CMRI or CCTA can predict cardiac outcomes and events. Ideally, both of these methods could help physicians identify higher-risk patients and choose the best treatment strategies. ●

For more information:

Dr. Benjamin Y. Cheong

832.355.8968

Texas Heart Institute Researchers Examine the Link Between Subarachnoid Hemorrhage and Neurogenic Stunned Myocardium

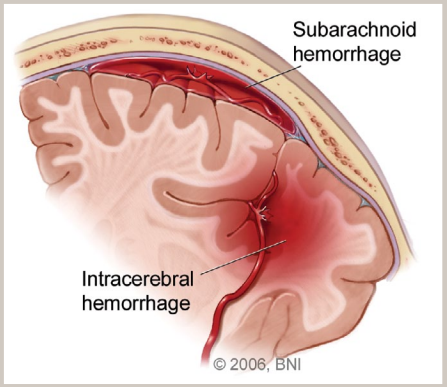
Abstract: Recent work at the Texas Heart Institute at St. Luke's Episcopal Hospital has shed light on cardiac dysfunction in patients with subarachnoid hemorrhage.

Subarachnoid hemorrhage—bleeding in the space between the arachnoid and pia mater membranes that surround the brain—is a life-threatening condition that typically results from a head injury or a ruptured cerebral aneurysm. A form of stroke, subarachnoid hemorrhage can cause significant damage to the brain, but it can also result in myocardial dysfunction. Clinically, this dysfunction can manifest as hemodynamic changes, electrocardiographic or echocardiographic abnormalities, and changes in the plasma levels of cardiac-specific biomarkers.

To better elucidate the nature of cardiac dysfunction in patients with subarachnoid hemorrhage, researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) and at 3 other institutions (Penn State University, Case Western Reserve University, and Johns Hopkins University) prospectively collected data from 26 patients with subarachnoid hemorrhage. The study was part of a project funded by the National Institutes of Health; José I. Suarez, MD, Professor of Neurology at Baylor College of Medicine, was the principal investigator.

The study's Cardiovascular Core Center was based at THI at St. Luke's. Here, the electrocardiographic, echocardiographic, and cardiac biomarker data were collected from all the patients and interpreted by cardiologists. Leading this group was José G. Díez, MD, a cardiologist and Senior Research Scientist at THI at St. Luke's, who designed the cardiology evaluation protocol for the study.

"We found both anatomical and functional cardiac abnormalities in a substantial fraction of the 26 patients with subarachnoid hemorrhage," Dr. Díez says. "For example, 37.5% of them had left ventricular hypertrophy, and 6.3% had wall-motion abnormalities. In addition, the electrocardiographic data showed that 31.6% of the patients had QT prolongation, 31.3% had abnormal repolarization, 6.3% had T-wave inversion, and 6.3% had ST-segment depression. Moreover, 27.2% of the patients had elevated cardiac biomarker levels. Overall, about a third of the patients had one or more of these indicators of cardiac injury.



Artist's rendition of a subarachnoid hemorrhage. (Used with permission from Barrow Neurological Institute.)

"Most of the patients were young and had previously been healthy," Dr. Díez adds, "so it is unlikely that these changes preceded the onset of subarachnoid hemorrhage. Also, some of the changes were temporary and resolved soon after they were detected."

In patients with subarachnoid hemorrhage, such findings are considered to indicate "neurogenic stunned myocardium." The exact mechanism by which this type of brain injury produces these cardiac effects is not clear, but it may involve excessive activation of the sympathetic nervous system, resulting in the production of large amounts of catecholamines that can affect the myocardium. This catecholamine release can increase the myocardial oxygen demand or cause coronary vasospasm, potentially leading to cardiac injury.

"Our findings suggest that clinicians need to familiarize themselves with neurogenic stunned myocardium," says Dr. Díez, "and they should test for it when patients present with subarachnoid hemorrhage. If signs of stunned myocardium are found, the treatment is similar to that recommended for acute coronary syndromes: beta-blocking agents, aspirin, and nitrates. Our results also support the concept of the neurocardiac axis—the interface between the central nervous system and the heart—which clearly warrants further investigation. In addition, as the study progresses, we may find that the cardiac changes related to subarachnoid hemorrhage are similar to those associated with takotsubo syndrome, also called broken heart syndrome." ●

For more information:

Dr. José G. Díez

281.599.6970

New Study at the Center for Women's Heart & Vascular Health

The Center for Women's Heart and Vascular Health at the Texas Heart Institute (THI) at St. Luke's Episcopal Hospital has initiated a study of risk factors for heart disease in underserved women of different ethnic groups. The study, Houston Heart Reach for Women, is designed to investigate racial disparities in the development of cardiovascular disease.

The principal investigator for Houston Heart Reach for Women is Stephanie Coulter, MD, Director of the Center for Women's Heart & Vascular Health. She and her team will work with local community service groups to screen uninsured or underinsured women in the Harris County area. The researchers will screen non-pregnant women 30 years or older. The screening will include a full lipid panel, fasting blood glucose levels, blood pressure, and other indicators of cardiovascular disease risk. Screening will be done free of charge to the participants, who will receive a written record of their results, as well as health recommendations from THI cardiologists. Screening and data collection will continue in the same population each year. By focusing on low-income women, mostly from minority racial groups, Houston Heart Reach for Women will serve several subpopulations that are underrepresented in cardiovascular research.

Highly Electronegative Very-Low-Density Lipoprotein Causes Endothelial Cell Damage

Abstract: Patients with metabolic syndrome have increased levels of a highly electronegative very-low-density lipoprotein that is toxic to vascular endothelial cells.

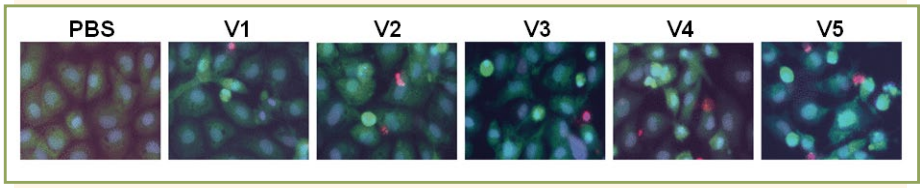
Very-low-density lipoproteins (VLDL) comprise a class of heterogeneous lipoproteins that are derived from triglycerides. Patients with metabolic syndrome (MetS)—a group of metabolic risk factors related to the development of diabetes mellitus and cardiovascular disease—often have increased plasma levels of triglycerides and triglyceride-derived VLDL. However, little is known about how VLDL may directly affect the vascular endothelium or how VLDL may be altered in patients with MetS.

Researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) recently characterized the VLDL of patients with MetS and examined whether varying degrees of electronegativity contribute to changes in VLDL functionality. Chu-Huang (Mendel) Chen, MD, PhD, Director of Vascular and Medicinal Research at THI at St. Luke's, and his colleagues found that patients with MetS have increased levels of a highly electronegative VLDL that is toxic to vascular endothelial cells (*Diabetes Care* 2012;35:648-53).

"We have called the most electronegative VLDL 'V5' because it is the 5th and last subfraction of VLDL yielded by anion-exchange chromatography," says Dr. Chen. His research team isolated VLDL from plasma samples of asymptomatic individuals who did or did not meet the criteria for MetS according to the National Cholesterol Education Program–Adult Treatment Panel III guidelines (study group, n=13; control group, n=13). The researchers chromatographically resolved the VLDL into 5 subfractions (V1-V5) with increasing electronegativity.

"First, we examined the distribution of V1 to V5 in MetS and control patients," states Dr. Chen, "and we found that the percentage of V5 VLDL was significantly higher in MetS patients than in control individuals [$P<0.05$]. Furthermore, we found that the plasma concentration of V5 was almost 3-fold higher in MetS patients than in control individuals [$P<0.001$]."

When the researchers attempted to determine whether the VLDL subfractions varied in protein content, they found that apolipoprotein (apo) B100 levels decreased and apoC levels increased from V1 to V5, indicating that V5 is an apoC-rich VLDL. The high electronegativity of V5 may be related to the enrichment of apoC lipoprotein, but this and the role of these lipoproteins in V5 bioactivities require further investigation.



Epifluorescence photomicrographs showing nuclear staining of human aortic endothelial cells exposed to equal concentrations of very-low-density lipoprotein subfractions V1 to V5. Condensed or fragmented nuclei indicate cells that are undergoing apoptosis. Nuclei, cytoplasm, and dead cells are stained blue, green, and red, respectively. PBS = phosphate-buffered saline.

After finding that V5 was significantly increased in patients with MetS, Dr. Chen and his team examined the effects of V5 on endothelial cells. They found that V5 induced significant apoptosis in cultured human aortic endothelial cells ($P<0.001$). Apoptosis was progressively decreased in cells treated with subfractions V4 to V1, V1 having a negligible effect. Similarly, V5 but not V1 induced oxidative stress, as indicated by the production of reactive oxygen species. Importantly, unfractionated VLDL from MetS patients, but not from control individuals, induced oxidative stress and apoptosis in endothelial cells—a finding that may have significant clinical implications.

"The results of our in vitro studies suggest that V5-enriched VLDL is directly harmful to the vascular endothelium and may add to the overall lipoprotein-associated atherogenicity in patients with cardiometabolic disorders," says Dr. Chen. "The fact that the least electronegative VLDL subfraction, V1, failed to induce oxidative stress further indicates the importance of minimizing the concentration of V5 in the plasma. In future studies, we plan to investigate the mechanisms of V5's bioactivities and the potential clinical benefits of reducing plasma V5 levels." ●

For more information:

Dr. Mendel Chen

832.355.9026

James F. Martin, MD, PhD, Has Joined THI

James F. Martin, MD, PhD, formerly of the Texas A&M Health Science Center, has joined the Texas Heart Institute at St. Luke's Episcopal Hospital as Director of the Cardiomyocyte Renewal Laboratory and Senior Research Scientist. A developmental biologist, Dr. Martin has identified genes in newborn laboratory mice that prevent their hearts from generating new muscle cells. Determining the molecular mechanisms that control cardiac muscle cell growth could lead to the development of new therapies that promote cardiac cell proliferation after a myocardial infarction. Specifically, on the basis of Dr. Martin's work, researchers may be able to develop a drug to temporarily disrupt genetic pathways in the heart that repress cell growth, enabling cardiac cells to regenerate more efficiently after a heart attack. Dr. Martin is also collaborating on projects with Texas Children's Hospital and Baylor College of Medicine.

HeartWATCH
SPRING 2012

Non-Profit
Organization
U.S. Postage
PAID
Houston, Texas
Permit No. 7249

Texas Heart® Institute
Scientific Publications
Mail Code 1-194
P.O. Box 20345
Houston, TX 77225-0345
texasheart.org

Cover: Item donated by Madeleine McDermott Hamm for the Celebration of Hearts display in the Wallace D. Wilson Museum of the Texas Heart Institute at St. Luke's Episcopal Hospital—The Denton A. Cooley Building.

Receive all the latest news and information
www.texasheart.org E-NEWS

Calendar of Events

Texas Heart Institute Continuing Medical Education Symposia

Fourth Annual Denton A. Cooley Lectureship
Texas Heart Institute
April 27, 2012 • Houston, Texas
Program Co-Directors: Denton A. Cooley, MD, and James J. Livesay, MD

Joint Session
Denton A. Cooley Cardiovascular Surgical Society 18th Symposium
Michael E. DeBakey International Surgical Society 19th Congress
Barton Creek Resort and Spa
June 21–24, 2012 • Austin, Texas
Program Co-Directors: Joseph S. Coselli, MD, and Robert J. Salem, MD

For information about Texas Heart Institute CME activities, please e-mail cme@texasheart.org or call 713-218-2200. To view or complete selected online CME courses (certificates are available online), please visit www.cme.texasheart.org. New courses are added regularly.

Selected Upcoming Local, National, and International Meetings

International Society for Heart and Lung Transplantation 32nd Annual Meeting and Scientific Sessions
April 18–21, 2012 • Prague, Czech Republic
www.ishlt.org/meetings/annualmeeting.asp

American Surgical Association 132nd Annual Meeting
April 26–28, 2012 • San Francisco, California
meeting.americansurgical.info

American Association for Thoracic Surgery 92nd Annual Meeting
April 28–May 2, 2012 • San Francisco, California
www.aats.org/annualmeeting/

Society of Cardiovascular Anesthesiologists 34th Annual Meeting and Workshops
April 28–May 2, 2012 • Boston, Massachusetts
www.scahq.org/sca3/events/2012/annual/

Heart Rhythm Society 33rd Annual Scientific Sessions
May 9–12, 2012 • Boston, Massachusetts
www.hrsonline.org/sessions/

BEST HOSPITALS U.S.News NATIONAL CARDIOLOGY & HEART SURGERY 2011-12

For 21 consecutive years, the Texas Heart Institute at St. Luke's Episcopal Hospital has been ranked among the top 10 heart centers in the United States by *U.S. News & World Report*'s annual guide to "America's Best Hospitals."