

Heart WATCH W I N T E R 2 0 0 6

A NEWSLETTER PRODUCED BY THE TEXAS HEART INSTITUTE



 TEXAS HEART[®] INSTITUTE

at St. Luke's Episcopal Hospital

High-Intensity Ultrasound Expands Options for Epicardial Ablation of Atrial Fibrillation

Abstract: A recently approved high-intensity focused ultrasound energy source is now being used to treat atrial fibrillation.

Atrial fibrillation (AF)

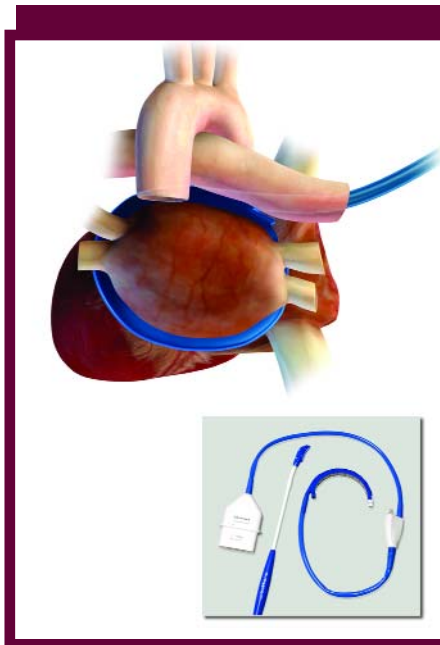
affects more than 2 million Americans, especially the elderly, and its incidence will increase as the average American grows older and lives longer.

For persons of any age, AF can cause disabling dyspnea, lethargy, palpitations, atrial blood flow stagnation, and other problems associated with reduced cardiac output. Thromboembolism, with the attendant risk of stroke or sudden death, is the most serious threat.

Historically, medical therapy, electrical cardioversion, pacemaker implantation, and technically difficult AF ablation procedures have been the mainstays of AF treatment. Now, AF ablation with precisely targeted high-intensity focused ultrasound (HIFU) has been added to this arsenal.

The most effective curative treatment for AF is the surgical Maze procedure, which was first used clinically by Cox in 1987. The original procedure involved creating a maze of transmural lesions on the atria to disrupt aberrant conduction pathways and channel the heart's native electrical impulses along a single pathway, thus restoring cardiac rhythm and dramatically reducing the risk of thromboembolism. Today, various energy sources, including radiofrequency, microwaves, lasers, and cryotherapy, are used instead of incisions to create transmural atrial lesions. These energy sources are used to perform a modified Maze procedure, which has become a clinical standard. In addition, the growing knowledge that not all lesions made in the original Maze technique are essential for cure has led to further modifications of the procedure, including highly selected blocking lesions to encircle the pulmonary veins, isolate the left atrial isthmus and its attendant coronary sinus, and isolate the right atrial isthmus.

"At present, no pattern of lesions is universally accepted, so it is difficult to interpret outcomes data from Maze studies," says Ross M. Reul, MD, director of Surgical Innovation at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH). "The HIFU



The high-intensity focused ultrasound delivery tool encircles the left atrium, where atrial fibrillation generally occurs.

technology could dramatically simplify the procedure by allowing standardized, reproducible ablation on the beating heart. Newer generations of the delivery system are being designed to make the procedure minimally invasive."

A HIFU-based system for epicardial ablation (Epicor; St. Jude Medical, St. Paul, MN) was approved by the US Food and Drug Administration in June 2004 and has been used by surgeons at THI/SLEH since June 2005. Our institution is one of only 15 centers in the United States currently using this technology.

In brief, the ultrasound delivery tool is wrapped around the left atrium anterior to the pulmonary veins, and probes are used to create additional lesions to complete the Maze procedure.

A recent European study found that the Epicor HIFU system could rapidly and reproducibly

create continuous, transmural lesions around the left atrium, producing 6-month cure rates of 80% in patients with continuous AF and a 100% cure rate in patients with intermittent AF (*J Thorac Cardiovasc Surg* 2005;130:803). The authors of that study suggest that the safety and success of the HIFU technique may be due to the weak interaction between acoustic energy and blood. Because ultrasound energy is more readily absorbed in soft tissues, high blood flow through the coronary arteries may protectively cool the endothelial lining during the procedure.

"In radiofrequency and cryosurgical epicardial AF ablation, the blood inside the heart chamber prevents the endocardial surfaces from reaching the temperature necessary for predictable ablation. In addition, the fat layer on the heart's surface acts as an insulator that may impede energy transmission to the target areas," Dr. Reul says. "HIFU waves, however, can travel for specified distances through the atrium without being affected by blood temperatures or insulating fat."

As the HIFU approach to AF ablation evolves, it may be especially attractive to younger AF patients seeking alternatives to a lifetime regimen of antiarrhythmic or anti-coagulant drugs.

"Newer, smaller, and better HIFU devices are already being developed," says Dr. Reul. "Thus, in the near future, HIFU-based ablation of AF promises to become even more standardized, more potentially curative, and more widely applicable across the whole spectrum of the disease." ●

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Periadventitial Fat and Atherosclerosis

Abstract: Ongoing research is elucidating the role of periadventitial fat in the development and progression of atherosclerosis.

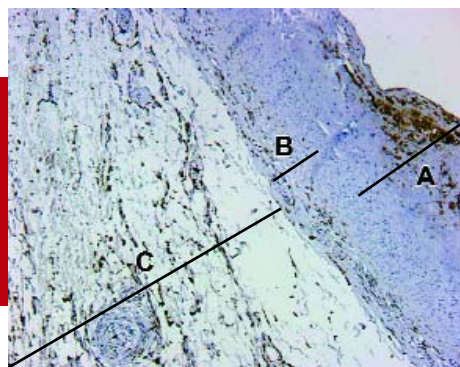
Traditionally, atherosclerosis has been deemed to be a gradual process of luminal narrowing that may eventually occlude an artery completely. The current belief is that inflammation within the artery causes vulnerable plaque to build up on the arterial walls until it ruptures, resulting in thrombotic occlusion of the artery. Emerging evi-

One study found that these inflammatory agents are expressed at significantly higher levels in perivascular fat than in subcutaneous fat (*Circulation* 2003;108:2460–6).

To determine the relationship between the inflammatory infiltrate of periadventitial fat and atherosclerotic plaque inflammation, the researchers at THI/SLEH analyzed the macro-

magnetic iron oxide (often used as a contrast agent for magnetic resonance imaging) is readily taken up by macrophages in the periadventitial fat and could conceivably be used to improve noninvasive imaging of inflamed arterial areas.

The involvement of periadventitial fat in atherosclerosis also has implications for therapeutic delivery methods. Because pericardial fluid



Human coronary artery stained for the macrophage marker CD68 shows macrophage infiltration in the atherosclerotic plaque, as well as in the adventitia and periadventitial fat. (A) atherosclerotic plaque; (B) adventitia; (C) periadventitial fat model.

dence now suggests that periadventitial fat may also play a role in atherogenesis.

Since 2000, this possibility has been the focus of investigations by researchers at the Texas Heart Institute at St. Luke’s Episcopal Hospital (THI/SLEH), including S. Ward Casscells, MD, director of the Vulnerable Plaque Research Laboratory; senior research scientist Deborah Vela, MD; and pathologist Silvio Litovsky, MD, formerly of THI/SLEH and now at the University of Alabama, Birmingham.

“The arteries most prone to serious atherosclerotic complications—the aorta, coronaries, and carotids—are coated with adipose tissue,” notes Dr. Casscells. “This periadventitial fat is particularly abundant around the coronary arteries, which suggests its involvement in atherosclerosis.”

Indeed, periadventitial fat is becoming recognized as an important source of inflammatory mediators, whose reaction with endothelial cells is considered a key step to atherogenesis. Adipose tissue secretes proinflammatory cytokines, such as interleukin-6 and tumor necrosis factor- α , which may be produced by macrophages within the adipose tissue.

phage content of the periadventitial fat of severely diseased coronary arteries.

“Macrophages were more numerous and densely packed in the periadventitial fat of atherosclerotic arteries containing large lipid cores than in that of fibrocalcific or nonatherosclerotic arteries,” explains Dr. Casscells. “The correlation between periadventitial fat inflammation and the inflammation that leads to vulnerable plaque suggests that some form of cross-talk goes on between the arteries and the periadventitial fat that surrounds them.”

Research at THI/SLEH has also revealed macrophage-like activity in the periarterial fat of atherosclerotic laboratory mice, but it is not yet clear whether this activity begins before endothelial dysfunction appears.

“However, it is possible,” says Dr. Casscells, “that large numbers of monocytes or macrophages could enter a plaque through the adventitia or the periadventitial fat, even in the early stages of atherosclerosis.”

Although the effects of the role of periadventitial fat in atherosclerosis are not yet clear, this new paradigm may someday change the diagnosis and treatment of atherosclerosis. Superpara-

directly contacts the entire coronary network and its surrounding fat, bathing the pericardium with a delivery vehicle containing, for example, therapeutic angiogenic factors may be an effective way to treat the entire coronary tree.

“Further study of the role of periadventitial fat in atherosclerosis will continue to inspire the development of more effective diagnostic and therapeutic techniques,” says Dr. Casscells. ●

For more information:

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Mechanical Complications Sometimes Necessitate Pump Exchange in Left Ventricular Assist Device Patients

Abstract: Although accepted as therapy for end-stage heart failure, left ventricular assist devices remain vulnerable to mechanical complications that may necessitate pump exchange.

As more patients receive

long-term mechanical circulatory support, device-related complications are becoming more frequent. Thromboembolic events, infection, and mechanical failure still occur despite improvements in left ventricular assist device (LVAD) technology, implantation techniques, and patient management. In the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial, LVAD malfunctions necessitated pump replacement in almost 15% of patients (*N Engl J Med* 2001;345:1435–43).

In a phase II pivotal study, 4 patients at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH) who were initially supported with pulsatile HeartMate XVE pumps (Thoratec, Pleasanton, CA) have had them replaced with smaller, continuous flow HeartMate II pumps.

All of these patients received their pumps as destination therapy and were enrolled in the HeartMate II trial in a special cohort whose HeartMate XVEs had failed. Although the HeartMate XVE's predicted mechanical durability is approximately 2 years, the mean pump durability in the THI/SLEH experience is 17 months. In a recent retrospective analysis of the HeartMate XVE experience, serious mechanical pump failures occurred in 3% of supported patients by 6 months and in 18% by 1 year (*Eur J Cardiothorac Surg* 2004;25:958–63).

Pump malfunctions, however, are not the only possible cause of mechanical complications necessitating pump replacement. Intra-abdominal pump placement has been associated with bowel perforation or obstruction, as well as diaphragmatic hernia and wound dehiscence after device explantation. Although preperitoneal placement is thought to reduce the incidence of these complications, the inflow conduit of pumps in this position may kink, leading to thrombosis.

"Originally, the pulsatile HeartMate was implanted preperitoneally," says O.H. Frazier, MD, chief of Cardiopulmonary Transplantation and director of the Cullen Cardiovascular



The HeartMate II (left) and HeartMate XVE (right).

Research Laboratories at THI. "The first recipients developed hematomas in the closed space around the device, leading to pump-pocket infection, sepsis, multiorgan failure, and death. So surgeons began placing pumps intraperitoneally. However, abdominal complications led some groups to return to preperitoneal placement. Nonetheless, in our experience, intraperitoneal placement is well tolerated. It remains our preferred technique, provided the patient's body habitus permits it."

In 1 of the pump-exchange patients at THI/SLEH, a preperitoneally implanted HeartMate XVE was successfully exchanged for a HeartMate II after the patient had a device-related stroke that was apparently caused by inflow-conduit kinking due to the preperitoneal placement.

"This case showed that a pulsatile LVAD may be safely exchanged for a continuous flow pump when necessitated by device-related thrombogenesis," says Dr. Frazier. "It also highlights the importance of monitoring the inflow-conduit position, especially in thin patients."

Of the other 3 HeartMate XVE patients who underwent pump exchange, 2 had a pump malfunction related to bearing wear (the primary reported cause of LVAD failure), and 1 had a driveline infection and an apparent pump stoppage 14 months after HeartMate XVE implantation. Although complete LVAD removal was considered in these patients, all 3 still required mechanical circulatory support and, therefore, underwent pump exchange.

There has been 1 other pump-exchange procedure at THI that involved the exchange of 1 continuous flow HeartMate II for another. In that case, a sudden fall damaged the external drive, stopping the pump.

"In the few hours when the HeartMate II was not functioning, the patient remained asymptomatic," says Dr. Frazier. "Any regurgitant flow there was, was not significant enough to cause heart failure symptoms. Echocardiography also confirmed that some cardiac recovery had occurred, but not enough to warrant device removal."

To exchange that pump, surgeons were able to unscrew the connectors via an abdominal incision without reentering the chest. Of the other 4 pump-exchange patients, 3 underwent a redo sternotomy, and 1 had a chevron bilateral subcostal incision.

"These patients received the HeartMate XVE initially because the HeartMate II would probably have been unsuitable at that time," says Dr. Frazier. "However, by the time the pulsatile pump failed (18–24 months post-implantation), right ventricular function had improved and pulmonary resistance decreased. Thus, the smaller, better-tolerated, continuous flow HeartMate II could meet their circulatory demands." ●

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Simultaneous Endovascular Repair of Descending Thoracic and Abdominal Aortic Aneurysms Now Possible

Abstract: New technology is making the endovascular repair of complex aortic aneurysms safer and more effective than ever before.

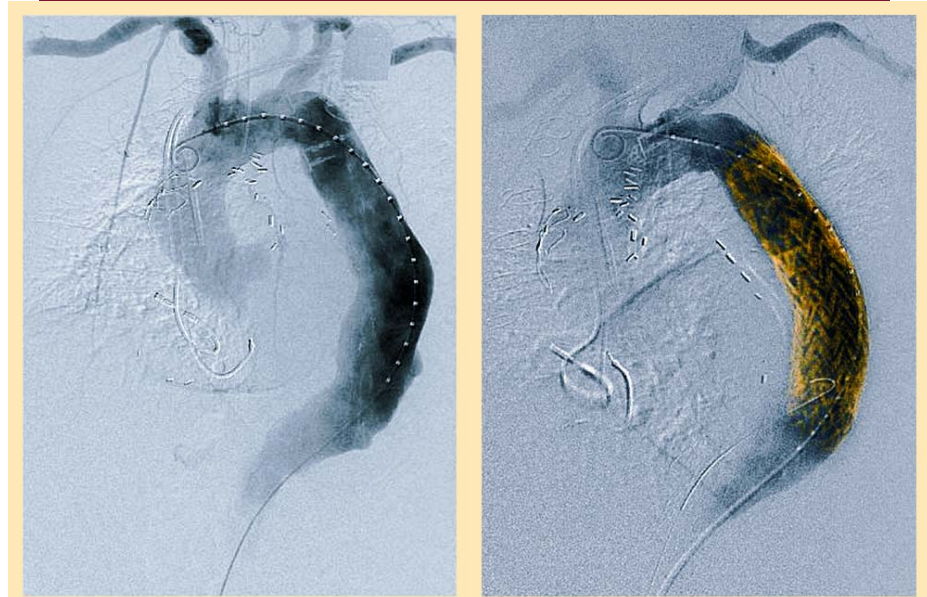
Aneurysms of the thoracic and abdominal aorta can be caused by a variety of processes that weaken the aorta over time, as well as by aortic dissection, the Marfan and Ehlers-Danlos syndromes, and mycotic infection. These aneurysms may remain asymptomatic for years, but they will usually begin to produce symptoms before growing large enough to rupture.

The traditional treatment for aortic aneurysms is open surgical repair, but such procedures, when conducted in the thoracic aorta, tend to be complex and highly invasive. They are especially risky for patients who are elderly or have multiple comorbidities. As a result, open surgical repair of descending thoracic aortic aneurysms (DTAAs) carries a significant risk of paraplegia, paraparesis, renal failure, and death. Thus, endovascular stent-grafting may offer a better alternative for DTAA repair in high-risk patients.

“Endovascular stent-grafting of the descending thoracic aorta is accomplished by deploying a cloth-lined metallic stent inside the aorta,” says Joseph S. Coselli, MD, chief of Adult Cardiac Surgery at the Texas Heart Institute at St. Luke’s Episcopal Hospital (THI/SLEH) and professor and chief of Cardiothoracic Surgery at Baylor College of Medicine. “The stent-graft is positioned and secured in the segments of the normal aorta above and below the aneurysm, providing a conduit for blood flow while effectively excluding the pathological portion of the aorta. This significantly reduces the risk of rupture and death over time.”

The procedure is performed through a single groin incision with the aid of general or local anesthesia. Patients usually spend a night in the recovery room and 1 to 2 days in the hospital after the procedure.

The 2 hybrid suites at THI/SLEH (see *Heart Watch, Fall 2005, texasheart.org*) provide an environment where complex aortic aneurysms and other cardiovascular lesions can be repaired with open surgery, endovascular aortic stenting, or both.



Angiograms show an aneurysm of the descending thoracic aorta before (left) and after (right) endovascular exclusion with a stent-graft (superimposed image).

Recently, Dr. Coselli and colleagues used the hybrid suites to perform a rare simultaneous endovascular repair of an abdominal aortic aneurysm (AAA) and a DTAA in a single patient. The AAA was repaired first, with a Gore Excluder endograft (W.L. Gore & Associates, Flagstaff, AZ). The DTAA was then repaired with a Gore TAG thoracic endoprosthesis (W.L. Gore), which was approved by the US Food and Drug Administration earlier this year. The Gore TAG is currently the only stent-graft approved for DTAA repair.

Although the procedure was wholly endovascular, Dr. Coselli considered the hybrid suites the best place to perform it.

“The hybrid suites offer 2 important advantages for complex endovascular procedures,” says Dr. Coselli. “First, the suites have the best imaging capabilities available anywhere. Second, they are equipped for both endovascular and open surgical procedures, so we can im-

mediately switch from one approach to the other if necessary.”

This kind of flexibility, Dr. Coselli says, enables THI/SLEH to provide a comprehensive approach to all thoracic aortic pathology.

“It allows us to select the best treatment for every patient with aortic disease, including those for whom open repair is inadvisable. Our surgeons can carry out open procedures, perform concomitant open and minimally invasive procedures, and convert immediately from endovascular to open repair on the rare occasions when this is necessary. The natural consequence of this flexibility is reduced morbidity and postoperative complications.” ●

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Sudden Cardiac Death in Young Athletes

Abstract: With new insights and improved technology, sudden cardiac death due to undiagnosed coronary artery anomalies in young athletes should become more preventable.

In October 2005, Jason Collier, a 28-year-old center for the Atlanta Hawks basketball team, died suddenly at home after experiencing shortness of breath. The 7-foot, 250-pound Collier had seemed in excellent health. However, an autopsy revealed that he had hypertrophic cardiomyopathy, which caused a sudden fatal arrhythmia.

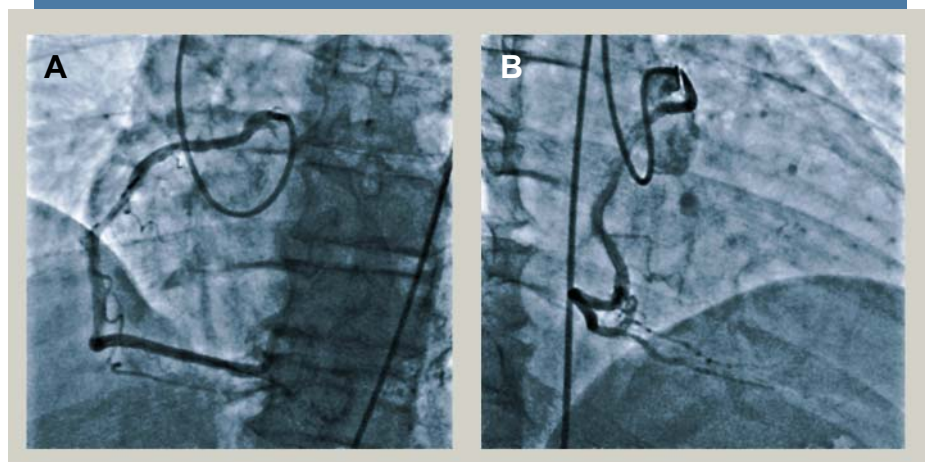
Collier is only the latest in a series of high-profile young athletes to succumb to sudden cardiac death (SCD) during or shortly after vigorous exercise. Other victims—about 100 annually in the United States—never make national headlines.

Paolo Angelini, MD, a cardiologist at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH), has long had a special interest in coronary artery anomalies, an important cause of SCD.

"In athletes less than 35 years old," Dr. Angelini explains, "sudden death is most often due to hypertrophic cardiomyopathy, as in Mr. Collier's case. The next most common cause is a coronary anomaly—usually anomalous origination of a coronary artery from the opposite side of the aorta with respect to normal."

These anomalies entail a narrow coronary ostium caused by a newly discovered mechanism that Dr. Angelini's group recently characterized with intravascular ultrasonography. What was once regarded as an anomalous course between the aorta and pulmonary artery has actually been found to be a passage inside the aortic wall; at this level, the coronary artery cannot grow with the patient, so it becomes severely compressed. During exertion, the pressure inside the aorta further compromises blood flow in the anomalous artery.

Dr. Angelini recently treated an 18-year-old football player who developed progressive shortness of breath and effort-related palpitations with near syncope. Nuclear magnetic resonance imaging confirmed the existence of a coronary anomaly. Stress testing elicited ischemia, and catheterization revealed an anomalous right coronary artery (RCA) arising from



Angiograms of a right coronary artery (RCA) that originates anomalously from the left sinus of Valsalva. (A) Left anterior oblique view of the RCA. The proximal portion of the artery appears unobstructed. (B) Right anterior oblique image of the RCA, showing critical ostial obstruction (intramural, at the aortic wall). An intravascular ultrasonography catheter is in place and helped to confirm the severe stenosis.

the left sinus of Valsalva. The patient underwent stenting of the RCA and was discharged on a 6-month regimen of aspirin and clopidogrel. He will limit his physical activities for 3 months, then be reevaluated. Without this treatment, his life might have ended suddenly and tragically.

"This case emphasizes the improved opportunities that newer technologies, especially noninvasive nuclear magnetic resonance and computed tomographic angiography, offer for identifying high-risk individuals before SCD occurs," says Dr. Angelini.

In his native Italy, annual screening of all athletes is mandatory and includes electrocardiography and echocardiography. In the United States, however, screening of high-school and college players is limited to history-taking and a physical examination. Because of the large population involved, mass screening of all athletes with specialized consultations and tests would be impractical and prohibitively expensive.

"Instead," says Dr. Angelini, "the goal should probably be to identify athletes with

a history of angina, exertional dyspnea, lightheadedness, syncope, and other suspicious symptoms or a family history of SCD. These athletes should undergo electrocardiography, echocardiography, and other diagnostic procedures as indicated by a specialist. In most cases, the underlying abnormality can be successfully treated."

"By establishing a systematic national registry of coronary and myocardial anomalies," he adds, "physicians could clarify the natural history of these anomalies in young athletes and formulate a widely accepted, evidence-based approach for preventing SCD." Dr. Angelini has instituted a database for coronary anomalies, available through the THI website at <http://texasheart.org/Education/Resources/caac.cfm>. ●

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Posttraumatic Stress in the Wake of Disasters May Affect Cardiovascular Health

Abstract: Traumatic stress related to natural and man-made disasters may have both acute and chronic effects on cardiovascular health.

Natural and man-made

disasters cause not only deaths, injuries, and property damage but also many sources of stress for survivors and their loved ones. Situated on the Gulf Coast, an area prone to floods, hurricanes, and industrial accidents, Houston—home of the Texas Heart Institute at St. Luke’s Episcopal Hospital (THI/SLEH)—has felt the fallout from such disasters, most recently hurricanes Katrina and Rita.

“Katrina evacuees had many sources of intense stress,” says Evangelina Hammonds, LCSW, CTS, a clinical social worker and certified trauma specialist in SLEH’s department of Non-Invasive Cardiology and Cardiac Rehabilitation. “For many evacuees, the main stressor was uncertainty—not knowing the location or condition of family members or the state of their homes, and not being able to find out.”

Many evacuees are still dealing with post-traumatic stress.

“Although not everyone who experiences posttraumatic stress will develop posttraumatic stress disorder (PTSD),” Ms. Hammonds explains, “many have ongoing distress and anxiety that interfere with their daily activities. Those with PTSD have usually experienced or witnessed a life-threatening or otherwise highly distressful event that is outside the range of normal human experience. Depending on their personal coping skills and social support system, affected individuals may become chronically hypervigilant and overwhelmed with intrusive thoughts.”

Disasters can leave large numbers of people with posttraumatic stress. This may cause a sudden increase in the local incidence of various medical problems, including cardiac diseases.

“Posttraumatic stress can have acute effects on cardiovascular function,” says James M. Wilson, MD, a cardiologist and director of cardiology education at THI. “Stress increases heart rate and blood pressure and stimulates epinephrine and norepinephrine production; this may trigger arrhythmia, wall-motion ab-

normalities, and peripheral and coronary artery vasoconstriction, decreasing the ejection fraction and promoting cardiac ischemia. Also, evidence suggests that stress causes coagulation abnormalities in some individuals, predisposing them to thrombosis. These findings may explain the rise in sudden cardiac death rates often seen in areas affected by war or other major disasters.”

In the long term, stress may not only aggravate existing cardiovascular disease but also contribute to chronic heart conditions. Several studies have found high rates of myocardial infarction, ischemic heart disease, and other cardiovascular disorders among war veterans diagnosed with PTSD and among disaster survivors. These diseases usually manifest years after the traumatic event, suggesting that stress contributes to their initial development (*Ann NY Acad Sci* 2004;1032:141–53).

“Animal studies suggest that stress-induced epinephrine production and other neurohumoral activity may result in endothelial dysfunction in coronary arteries, fueling the advance of atherosclerotic lesions,” Dr. Wilson explains. “This may be why atherosclerosis appears to advance more quickly in animals and people who have stronger cardiovascular responses to mental stress in laboratory studies.”

Although there is debate about whether treating chronic stress can prevent heart disease, evidence suggests that stress management interventions can reduce the hemodynamic ef-

fects of stress. In a recent randomized trial, stress management training (which included coping skills, cognitive therapy, and relaxation) was compared with exercise and conventional care in patients with stable ischemic heart disease (*JAMA* 2005; 293:1626–34). Both stress management training and exercise reduced the cardiac effects of mental stress (ie, a low ejection fraction and wall-motion abnormalities) and improved vasodilation. Stress management also improved baroreflex sensitivity and heart rate variability, 2 known prognostic factors in ischemic heart disease.

“Physicians should be aware of the causal role of posttraumatic stress in cardiac disease,” says Ms. Hammonds. “When patients report stress-related symptoms, such as sleeplessness, fatigue, stomachache, back pain, headache, and nausea, the clinician should ask about significant stressors in the patient’s life.”

“Given the potentially far-reaching effects of posttraumatic stress,” adds Dr. Wilson, “such questions may help clinicians to accurately diagnose current cardiac problems and prevent future ones.” ●

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- **Clinical Use of Tissue Doppler Echocardiography and B-Type Natriuretic Peptide in Patients with Heart Failure** (from Cardiology Grand Rounds, September 30, 2005)
- **Early Recognition and Management of Peripheral Arterial Disease to Prevent Functional Impairment, Stroke, and Myocardial Infarction** (from Cardiology Grand Rounds, October 28, 2005)
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Calendar of Events

TEXAS HEART INSTITUTE CONTINUING MEDICAL EDUCATION SYMPOSIA

Texas Heart Institute 7th Symposium on Cardiac Arrhythmias

New Pharmacologic and Interventional Strategies

Program Director: Ali Massumi, MD
February 18, 2006 • Houston, Texas

American College of Cardiology Texas Heart Institute Satellite Symposia

Program Directors: James J. Ferguson III, MD;
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March 11, 2006 • Atlanta, Georgia

Texas Heart Institute 6th Texas Update in Cardiovascular Advancements

Program Director: James T. Willerson, MD
March 31–April 1, 2006 • Houston, Texas

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Society of Thoracic Surgeons 42nd Annual Meeting

January 30–February 1, 2006 • Chicago, Illinois

American College of Cardiology 55th Annual Scientific Session

March 12–15, 2006 • Atlanta, Georgia

International Society for Heart and Lung Transplantation 26th Annual Meeting and Scientific Sessions

April 5–8, 2006 • Madrid, Spain

American Heart Association Scientific Sessions 2006

November 12–15, 2006 • Chicago, Illinois
Abstract submission ends May 26, 2006

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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" for 15 consecutive years.