HeartWATCH

SPRING 2009

A Newsletter Produced by the Texas Heart Institute

Texas Heart® Institute

at St. Luke's Episcopal Hospital

The Texas Heart Institute at St. Luke's Episcopal Hospital Continues at the Forefront of Stem Cell Therapy

Abstract: Multiple trials are ongoing at THI at SLEH to develop the most effective stem cell regimens for the treatment of heart disease.

Phase I and II clinical trials have shown that autologous adult stem cell therapy is safe and holds promise as an effective treatment for cardiovascular disease. The preliminary success of stem cell therapy has led researchers to study how best to maximize its therapeutic efficacy. The Stem Cell Center at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) is leading the way by studying the issues involved in developing optimal stem cell regimens. In multiple trials at THI at SLEH, physicians and scientists are studying methods and timing of stem cell delivery, as well as the optimal dose and type of stem cell, for treating heart failure and acute myocardial infarction (AMI).

James T. Willerson, MD, President and Medical Director of THI at SLEH, and Emerson C. Perin, MD, PhD, Director of Research in Cardiovascular Medicine and Director of the Stem Cell Center at THI at SLEH, have extensive experience testing stem cells in experimental and clinical settings. In an early study in Brazil, these researchers were the first in the world to treat end-stage heart failure by performing direct transendocardial injection of patients' own stem cells. By showing that stem cell treatment was safe and effective, the results provided the first objective evidence of the benefits of this therapy. Later, the Brazilian study was continued at THI at SLEH in the first US Food and Drug Administration–approved trial designed to study the endocardial injection of autologous bone marrow–derived mononuclear cells (ABMMNCs) in patients with severe heart failure. The trial has just been completed, and early results are encouraging.

Two other FDA-approved trials of ABMMNCs to treat AMI patients are ongoing at THI at SLEH. Using 3-dimensional electromechanical mapping to guide injections, investigators are delivering ABMMNCs to viable tissue in the infarct border zones to prevent infarct expansion and limit deterioration of heart function.

"The studies are designed to evaluate the safety and timing of cell injection after AMI," says Dr. Perin. "The ability of stem cells to repair damaged heart muscle may be improved by delivering the cells during the critical period after inflammation subsides but before scar tissue develops."

In multiple trials at THI at SLEH, physicians and scientists are studying methods and timing of stem cell delivery, as well as the optimal dose and type of stem cell, for treating heart failure and acute myocardial infarction (AMI).

Another trial soon to be underway at THI at SLEH will examine the use of ABMMNCs in patients with chronic coronary heart disease, left ventricular dysfunction, and heart failure. Five centers will be participating in this study as part of the recently established Cardiac Cell Therapy Research Network sponsored by the National Institutes of Health.

ABMMNCs comprise a heterogeneous assortment of cells. A more homogeneous, selective population of stem cells may improve outcomes. Mesenchymal precursor cells (MPCs), derived from the bone marrow by using a highly specific selection procedure, have been safe and effective in preclinical studies. Because MPCs lack the cell surface markers that elicit immune responses, allogeneic MPCs can be used in clinical settings. The first patient ever to receive allogeneic MPCs was treated for an AMI at THI at SLEH in April 2008.

Allogeneic MPCs are being used in 2 FDA-approved phase II trials at THI at SLEH. The safety and feasibility of transendocardial delivery of allogeneic MPCs are being assessed in patients with AMI and in patients with heart failure. In these trials, called dose-escalation studies, 3 different cell doses are being studied to establish the optimal regimen. Allogeneic MPCs are obtained from a single donor rather than from the patient's own bone marrow, thus sparing patients the procedure otherwise necessary to collect bone marrow cells.

"We hope that stem cells will be used eventually to prevent the postinfarction cardiac remodeling that can lead to heart failure," states Dr. Willerson. "With the right stem cell regimen, we may be able to prevent, as well as treat, heart failure." ●

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Robert J. Schwartz, PhD, Brings His Expertise in Cardiac Regenerative Therapy to THI at SLEH

Robert J. Schwartz, PhD, has accepted the position of Director of Stem Cell Engineering and Co-Director of the Heart Failure and Stem Cell Research Laboratories at the Texas Heart Institute at St. Luke's Episcopal Hospital. He is also Professor and Director of the Center of Molecular Development and Disease, Institute of Biosciences and Technology at the Texas A&M Health Science Center; he will continue to hold that position. A leading expert in cardiac development and genetic regulation of cardiogenesis in congenital heart disease, Dr. Schwartz has received 11 US patents and many large grants, as well as awards from the American Heart Association. His interests include the roles that cardiac-enriched transcription factors and insulin-like growth factors play in stem cell/progenitor cell mobilization and engraftment in cardiac regenerative therapy.

Texas Heart Institute at St. Luke's Episcopal Hospital Is First in US to Use the 32-Channel Achieva 1.5T MR Scanner Clinically

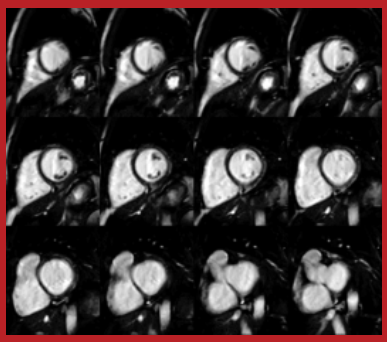
Abstract: The Achieva 1.5T MR scanner, which has a 32-channel coil, will enable physicians to speed image acquisition by up to 7 times.

Cardiac magnetic resonance imaging (CMRI) is used to assess cardiac morphology, function, and tissue characteristics. It produces images with exquisite soft-tissue contrast and high spatial resolution, poses a minimal risk to patients, and is accurate and reproducible. However, CMRI necessitates multiple breath-holds, which may result in blurry images in patients who cannot repeatedly hold their breath. Thus, a faster, more advanced MRI scanner is needed.

One such system, which has recently become available, is the 32-channel Achieva 1.5T scanner (Philips Healthcare; Andover, Massachusetts). The Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) has become the first institution in the United States to use this new scanner clinically.

According to Raja Muthupillai, PhD, an MR physicist and scientist in the Department of Diagnostic and Interventional Radiology at SLEH, most clinical MRI scanners have an array of 5 to 8 coils that receive MR signals. In contrast, the Achieva 1.5T scanner has 32 independent radiofrequency channels that can simultaneously acquire MR signals. This makes possible a variety of parallel imaging techniques that can speed up image acquisition. For example, clinicians can acquire 4-dimensional cine MR images of the heart during a single patient breath-hold (with standard scanners, every cine MR image requires a separate breath-hold). The new system also features multidirectional acceleration, a greater signal-to-noise ratio (SNR), and higher spatial and temporal resolution.

"With typical coil arrays, acceleration can be applied in only 1 direction," says Dr. Muthupillai. "By applying fast imaging techniques such as sensitivity encoding (SENSE) in multiple directions, physicians can speed image acquisition by up to 7 times. Therefore, the 32-channel coil permits clinicians to perform large-volume coronary magnetic resonance angiography (CMRA) in 2.5 minutes with the same resolution and coverage as in conventional CMRA, which takes 16 minutes per image."



Volumetric cardiac cine magnetic resonance images of the entire left ventricle at a temporal resolution of 50 ms, or 20 frames per second, obtained during a single patient breath-hold lasting 19 seconds. These 12 representative slices were extracted from the volumetric data acquired during diastole.

The old system is laborious and requires careful planning because only one 2-dimensional (2D) image can be acquired during an individual breath-hold. The 32-channel coil requires less advance planning because any 2D view can be generated at any time with multiplanar reformatting of the 3-dimensional data.

Moreover, the 32-channel coil provides large volumetric coverage, so the available SNR increases, making it possible to acquire images rapidly without compromising the spatial resolution. "This feature is critical for patients who have arrhythmias, especially arrhythmogenic right ventricular dysplasia," explains Dr. Benjamin Cheong, Director of Clinical Cardiovascular MRI. "For these patients, it is important to get images with a very high spatial resolution in a short time."

The new imaging system does not compromise temporal resolution. Images can be obtained with a temporal resolution of 6 ms (160 frames per second), facilitating assessment of diastolic dysfunction.

Dr. Muthupillai has finished preliminary testing of the 32-channel coil on a healthy volunteer, and the initial results are promising. "For example, it is now possible to obtain 24 cine MR slices of the left ventricle during a single patient breath-hold lasting 19 seconds. These images have a temporal resolution of 50 ms," he says (*see Figure*). Drs. Muthupillai and Cheong next plan to evaluate the clinical utility of the 32-channel coil in other volunteers and in patients. ●

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Contents

Alternative Anticoagulation Strategies Improve the Safety and Efficacy of Percutaneous Coronary Interventions

Abstract: Researchers are exploring newer, safer antithrombotic strategies that lessen bleeding and thrombotic events in patients undergoing percutaneous coronary interventions.

Although unfractionated heparin (UFH) is the standard for antithrombotic therapy during percutaneous coronary interventions (PCIs), it has a number of well-recognized limitations. Therefore, researchers are exploring newer, safer strategies designed to lessen bleeding and thrombotic events in patients undergoing PCIs. Investigators at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) are studying several new approaches, including the use of low-molecular-weight heparin (LMWH) instead of UFH, infusion of direct thrombin inhibitors, and varying infusion times for the direct thrombin inhibitor bivalirudin.

The limitations of UFH include difficulty in achieving reliable levels of anticoagulation because of this agent's relatively high degree of protein binding and its inactivation by platelet factor 4. Also, UFH tends to cause platelet activation and imposes a risk of heparin-induced thrombocytopenia. Unfractionated heparin also has a narrow therapeutic index, so in many patients the drug's concentration either does not reach therapeutic levels or does not remain within the therapeutic range at any given time. In contrast, LMWH provides a more reliable degree of anticoagulation and has a minimal effect on platelet activation.

"In particular, one LMWH, enoxaparin, has emerged as an important tool in the antithrombotic management of patients with acute coronary syndromes," says José G. Díez, MD, an interventional cardiologist in the Department of Medicine at THI at SLEH. "In the United States, the guidelines published by the American College of Cardiology and American Heart Association (ACC/AHA) give enoxaparin and UFH a Class IA recommendation for use in patients with non–ST-segment-elevation myocardial infarction (NSTEMI). Owing to this more widespread use of LMWH in patients with acute coronary syndromes, interventional cardiologists are more likely to encounter patients in the cardiac catheterization laboratory who have already received subcutaneous or intravenous LMWH."

Dosage Recommendations for the Use of Enoxaparin During Percutaneous Coronary Intervention

Patient Characteristics	Drug Regimen for PCI
No previous subcutaneous enoxaparin for <12 h before PCI	0.75 mg/kg IV enoxaparin with glycoprotein IIb/IIIa inhibitor
	1.0 mg/kg IV enoxaparin without glycoprotein IIb/IIIa inhibitor
Transitioning of patients receiving subcutaneous enoxaparin (1.0 mg/kg every 12 h):	
≥3 doses, last dose <8 h before PCI, or 30-mg IV bolus followed by a single subcutaneous dose <8 h before PCI	Proceed with PCI, no additional enoxaparin
<3 doses or ≥3 doses, last dose 8-12 h before PCI	0.3 mg/kg IV enoxaparin
Age >75 y, 0.75 mg/kg dose every 12 h before PCI	0.3 mg/kg IV enoxaparin

In a prospective study of the safety and efficacy of enoxaparin versus UFH by researchers at THI at SLEH, Baylor College of Medicine, and Tulane University Health Science Center, analysis showed that, compared with patients who received UFH for elective or emergency PCI, patients who received enoxaparin had a lower risk of bleeding and fewer ≥3-g/dL decreases in hemoglobin levels. Enoxaparin also produced a smaller decrease in the mean platelet count and in platelets >30% from baseline. After elective PCI, fewer enoxaparin recipients had cardiac troponin I (cTnI) levels ≥3 times the upper limit of normal.

Another approach to antithrombotic therapy is the use of direct thrombin inhibitors (DTIs), which are a class of anticoagulants that bind directly to thrombin and block its interaction with its substrates. Because DTIs act independently of antithrombin, they can inhibit thrombin bound to fibrin or fibrin degradation products. This makes DTIs more effective than heparin, because heparin appears to have a reduced capacity to inhibit fibrin-bound thrombin.

"We are evaluating the recombinant DTI bivalirudin and the effectiveness of varying its infusion times," says Dr. Díez. "Along with Dr. R. David Fish and Dr. James M. Wilson, both of whom are cardiologists at THI at SLEH, we are exploring new infusion protocols in combination with dual antiplatelet therapies in hopes of minimizing ischemic events while preserving the lower incidence of bleeding complications that bivalirudin provides."

Current ACC/AHA guidelines give bivalirudin a Class I recommendation for use in NSTEMI and STEMI patients and in patients undergoing PCI. ●

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Additional Grafts Within Arterial Territories Do Not Improve Outcomes in Coronary Artery Bypass Patients

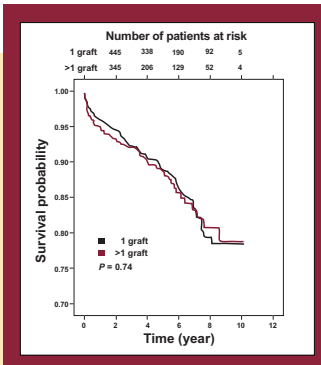
Abstract: A study recently published by surgeons at THI at SLEH suggests that CABG patients who receive more than 1 graft per arterial territory do not benefit from the extra grafts.

In patients who undergo coronary artery bypass grafting (CABG) operations, complete revascularization (placement of a graft to each of the patient's diseased major artery systems) improves short- and long-term survival rates. Knowing this, surgeons at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) and the Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC) wondered: If complete revascularization improves a patient's likelihood of survival, could additional revascularization improve it further?

To address this question, Joseph S. Coselli, MD, Chief of Adult Cardiac Surgery at THI at SLEH and Professor and Chief of Cardiothoracic Surgery at Baylor College of Medicine; Danny Chu, MD, Assistant Professor of Surgery at Baylor College of Medicine and a cardiovascular surgical staff member at both THI at SLEH and the MEDVAMC; and their colleagues retrospectively examined the outcomes of 1129 consecutive CABG procedures performed at the MEDVAMC. For each patient in the series, CABG was indicated because there was greater than 50% stenosis in at least 1 of 3 coronary artery territories: the left anterior descending/diagonal, circumflex/ramus, or right coronary artery. During the CABG procedure, 580 patients received only 1 graft to each diseased territory, whereas 549 patients received more than 1 graft to each territory.

Data regarding these patients were obtained from the MEDVAMC's Continuous Improvement in Cardiac Surgery Program database and from the patients' computerized medical records. In analyzing the patients' postoperative survival, the investigators adjusted for many potential confounding factors, including patient age, concomitant diseases, New York Heart Association functional class, preoperative albumin and creatinine levels, and cardiopulmonary bypass and aortic cross-clamp times. The results were recently published in the *Journal of Thoracic and Cardiovascular Surgery* (2009;137:60-4).

"There were some differences between the 2 groups," says Dr. Coselli. "The patients who received only 1 graft per territory tended to be sicker preoperatively, having a greater prevalence of left main coronary artery disease, triple-vessel disease, peripheral vascular disease, angina, and chronic obstructive pulmonary disease. The patients who received more than 1 graft per territory had longer cardiopulmonary bypass times and aortic cross-clamp times because of the extra time required to place the additional grafts."



A graph showing the similarity between the Kaplan-Meier survival curves for CABG patients with 1 graft per territory and CABG patients with multiple grafts per territory.

However, both before and after adjusting for potential confounders, the investigators found that patients who received multiple grafts per territory fared no better or worse than patients who received only 1 graft per territory.

"Both groups of patients had similar mortality rates, both in the first 30 days after surgery and during the mean follow-up period of 5.3 years," Dr. Chu says. "Intergroup rates of postoperative adverse events, including stroke and renal failure, were also similar, both in the short term and the long term."

The investigators concede that their study had at least 1 important methodologic drawback: the decision of whether a patient should receive single or multiple grafts per territory was in the hands of the operating surgeon and was not determined randomly. However, the many potential confounders adjusted for in the analysis included risk factors that indicate more severe or diffuse coronary artery disease—presumably the main reasons why a surgeon might choose to revascularize multiple vessels within the same territory.

"Our results are not conclusive, but they provide pilot data for a future randomized study of single versus multiple grafting," says Dr. Coselli. "These initial findings do suggest, however, that constructing multiple grafts to each diseased arterial territory takes up additional operating time without providing any particular benefit to CABG patients." ●

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Texas Heart Institute at St. Luke's Episcopal Hospital Is Honored for Clinical Excellence

For the third consecutive year, the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) was honored for clinical excellence in an independent study performed by Health Grades, a prominent healthcare ratings organization. The Institute was recognized for excellence in cardiac care, coronary intervention, stroke care, vascular surgery care, critical care, and women's stroke services. "Our unrivaled experience in the medical, interventional, and surgical treatment of heart disease has resulted in innovative care, better outcomes, and an improved quality of life for heart disease patients around the world," said James T. Willerson, MD, President and Medical Director of THI. "We are pleased to salute THI physicians, SLEH nurses, and support personnel for their roles in earning this important honor."

Researchers Further Knowledge of Cardiomyocyte Death and Renewal

Abstract: Cardiovascular pathologists at the Texas Heart Institute at St. Luke's Episcopal Hospital continue to study the self-renewing properties of the healthy and diseased human heart.

Mounting evidence in the medical literature supports the concept that the mature mammalian heart is not constrained by a fixed number of terminally differentiated myocytes. Rather, it appears that cardiac viability is maintained by a slow turnover of cardiomyocytes, which involves a balance of cardiomyocyte cell death and cardiac stem cell regeneration.

To gain a more complete understanding of this aspect of myocardial biology, cardiovascular pathologists at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) reviewed current knowledge about various forms of cell death and renewal and analyzed their importance in the pathobiologic processes involved in heart failure (*Cardiovasc Pathol* 2008;17:349-74).

"Cumulative evidence supports the notion that healthy hearts are subject to a low level of cardiomyocyte death and renewal," says Deborah Vela, MD, Senior Research Scientist in the Department of Cardiovascular Pathology at THI at SLEH. "Mitotic division of mature cardiomyocytes is rare, suggesting that cardiomyocyte renewal is likely to be mediated by an endogenous cardiac stem cell population and possibly by blood-borne stem cells—a biologic phenomenon limited in capacity. Consequently, persistent myocardial stress often leads to pathologic remodeling, in which the rate of cardiomyocyte death exceeds that of cardiomyocyte renewal, resulting in progressive heart failure."

The injured or stressed myocardium is subject to increased rates of cardiomyocyte death by 3 main modes: apoptosis, autophagy, and oncosis. Apoptosis and autophagy are forms of programmed cell death that involve self-activation of genetically regulated programs. Oncosis is a passive response to external stimuli such as hypoxia, ischemia, toxic chemicals and drugs, and cell-damaging inflammatory processes.

"The end result of this imbalanced cellular death and regeneration process is a structural cardiac dilatation that becomes increasingly difficult to stabilize or reverse by pharmacologic therapies or surgical intervention with ventricular assist devices," says L. Maximilian Buja, MD, Chief of Cardiovascular Pathology Research at THI at SLEH. "Therefore, a main focus of active research is to devise strategies that will enhance the stem cell response to chronic myocardial stress, leading to more effective myocardial remodeling."

Several therapeutic approaches are available for preserving cardiomyocyte viability in failing hearts, including inhibition of apoptosis with the use of broad-spectrum (ZVAD-fmk, YVAD-cmk) and selective (YVAD-aldehyde, AcYVAD-cmk, DEVD-aldehyde) caspase inhibitors and cardioactive drugs (beta blockers, angiotensin-converting enzyme [ACE] inhibitors, angiotensin II type 1 [AT1] receptor antagonists). Another approach is mitochondrial stabilization with the aid of nitric oxide, ATP-dependent potassium-channel openers, and ACE inhibitors and AT1 receptor antagonists.

With regard to myocardial regeneration, there is evidence that certain cardiomyocytes are capable of dividing in the healthy or diseased heart. Also, the myocardium is now known to contain an endogenous population of cardiac stem cells and bone marrow–derived stem cells; however, scar formation after cardiac injury often impedes cellular regeneration by either stem cell type. The limitations of this innate biologic response to cardiac injury have caused researchers to investigate other treatment approaches involving modulation of the inflammatory response and the use of exogenous stem cells and precursor cells.

In preliminary studies, transplanted bone marrow mesenchymal cells (MSCs) have shown promise for use in cardiac repair. Results of a study by researchers at THI at SLEH suggest that MSCs improve healing of infarcted areas in dogs, primarily by producing a paracrine effect; the MSCs appear to alter the tissue environment and modulate angiogenesis, wound repair, and the inflammatory response (*J Histochem Cytochem* 2009;57:167-76).

"Achieving effective, tumor-free mammalian myocardial regeneration will require a more complete and sophisticated understanding of myocardial biology than is currently available. Although myocardial recovery and repair by stem cell or precursor cell therapy appear feasible, and although alteration of pathologic remodeling appears promising for preventing and treating heart failure, we must further our understanding of fundamental biologic processes before we can make any lasting advances in clinical treatment," says Dr. Buja. ●

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Low Body Temperature May Predict Congestive Heart Failure Complications

Hospitalization for congestive heart failure (CHF) is correlated with an increased risk of readmission and postdischarge death. Although many clinical parameters are associated with an increased risk of rehospitalization and mortality in CHF patients, no unique, simple variable definitively predicts these outcomes. In a recently published clinical study (*J Cardiac Fail* 2008;14:489-496), Amany Ahmed, MD, Ibrahim Aboshady, MD, and other researchers in the Advanced Physiologic Monitoring Laboratory at the Texas Heart Institute at St. Luke's Episcopal Hospital described how a low body temperature may predict CHF complications. Patients with low body temperatures at discharge and at the first follow-up visit were more than 5 times likelier to die than patients who were normothermic at discharge. A decreased body temperature after discharge was significantly correlated with early readmission (P=0.005) and death (P=0.01). These results concur with those from ongoing research studies (see *Heart Watch*, Spring 2008). By carefully monitoring the body temperature of CHF patients, physicians may readily be able to predict rehospitalization and death.

Heart Failure in Adults With Congenital Heart Disease Leads to New Challenges in a Special Population

Abstract: As children with congenital heart disease grow to adulthood, they are likely to develop other cardiovascular conditions, including congestive heart failure.

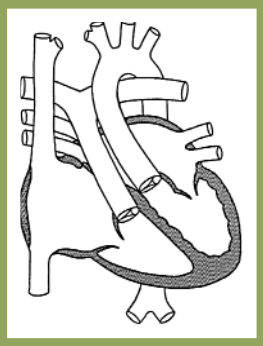
Most children born with congenital heart disease now live to adulthood—a circumstance that has created a new cardiovascular specialty for a growing population. In the United States, there are an estimated 1 million patients with adult congenital heart disease (ACHD), and congestive heart failure (CHF) will develop in many of these patients, sometimes resulting in death.

"When we care for patients with ACHD, we are racing against time, because their hearts function abnormally from birth," says Wayne J. Franklin, MD, Director of the Texas Adult Congenital Heart (TACH) Center and a cardiologist at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH). "We are now caring for a growing number of adults with repaired heart defects, and the resulting cardiac anatomy and physiology are often complex, leading to cyanosis, pulmonary hypertension, complex arrhythmias, and CHF."

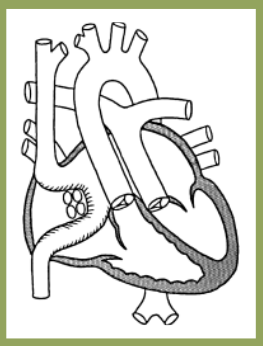
"It is difficult to determine exactly if or when CHF will begin in patients with ACHD," says Dhaval Parekh, MD, a cardiology fellow at Baylor College of Medicine and THI at SLEH. "The index event for many of these patients could, in fact, be birth."

However, the ACHD patients in whom CHF is most likely to develop are patients with a systemic right ventricle (those with corrected transposition of the great arteries); patients with a single ventricle (eg, hypoplastic left heart syndrome or congenital tricuspid atresia) who have undergone a Fontan procedure; patients with repaired tetralogy of Fallot who have pulmonary insufficiency; and patients with obstructive left-sided lesions (eg, mitral or aortic stenosis or coarctation of the aorta) (see *Figure*).

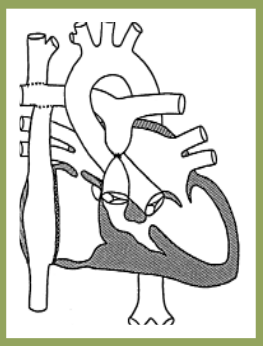
According to Drs. Franklin and Parekh, CHF develops in patients with ACHD for many of the same reasons that it develops in patients without congenital defects. Patients with ACHD often have a prolonged pressure overload, a sustained volume overload, and cyanosis leading to increased wall stress with episodic subendocardial hypoperfusion and adverse neurohormonal activation—all of which can lead to CHF.



Corrected transposition of the great arteries (unrepaired).



Transposition of the great arteries after a Mustard procedure.



Tricuspid atresia after a Fontan procedure.

"There is increasing evidence of ventricular interdependence, in which dysfunction of either ventricle negatively affects the other. For example, pressure or volume loading of the right ventricle can lead to alteration of the septal contour and left ventricular geometry, causing left ventricular dysfunction," says Dr. Parekh.

Physicians trained in ACHD are now addressing ACHD patients' problems from a scientific standpoint. Heart failure specialists have determined that plasma biomarker levels of norepinephrine, renin, angiotensin I and II, aldosterone, and vasopressin are usually abnormal in CHF patients. The same may be said for ACHD patients, and these abnormal levels can correlate with CHF severity and mortality. Dr. Franklin and his colleagues are also looking at other biomarkers, such as endothelin, B-type natriuretic peptide, matrix metalloproteinases, lipoprotein-associated phospholipase A2, cytokines, nitric oxide, and myeloperoxidase.

"There are no established guidelines for medical therapy in ACHD patients with CHF, so we are studying a number of therapies," says Dr. Franklin. "Angiotensin II receptor blockers and aldosterone antagonists have proved effective for treating acquired heart disease, but we should remain cautious about extrapolating their effectiveness to ACHD patients. Newer agents, such as phosphodiesterase type 5 inhibitors and endothelin receptor antagonists, should also be considered."

As for surgical treatment in ACHD patients, transplantation is an option, but only about 2% of heart transplants are performed for congenital disease. Experience is limited in the use of ventricular assist devices in these patients.

"Patients with ACHD do not easily fit in the worlds of pediatric or adult cardiology," says Dr. Franklin. "They have special problems that only physicians trained in ACHD can address. As more of the congenital heart disease population grows to adulthood, our challenges in dealing with ACHD patients will only increase." ●

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Calendar of Events

Texas Heart Institute Continuing Medical Education Symposia

Denton A. Cooley Cardiovascular Surgical Society 16th International Symposium: Surgical Mentors: Trusted Teachers

Moody Gardens Hotel and Conference Center
June 4–7, 2009 • Galveston, Texas
Program Directors: O. H. Frazier, MD, Igor Gregoric, MD, and Scott A. LeMaire, MD

23rd Practicum in Cardiovascular Magnetic Resonance Imaging

John S. Dunn and Jerome L. Howard Learning Resource Center at St. Luke's Episcopal Hospital
May 25–28, 2009 • Houston, Texas
Program Directors: Benjamin Cheong, MD, and Raja Muthupillai, PhD
For more information, please contact Teresa Rose at trose@sleh.com.

Selected Upcoming Local, National, and International Meetings

Society of Cardiovascular Anesthesiologists 31st Annual Meeting and Workshops

April 18–22, 2009 • San Antonio, Texas
www.scahq.org

International Society for Heart and Lung Transplantation 29th Annual Meeting and Scientific Sessions

April 22–25, 2009 • Paris, France
www.ishlt.org

Heart Rhythm Society 30th Annual Scientific Sessions

May 13–16, 2009 • Boston, Massachusetts
www.hrsonline.org

American Society of Echocardiography 20th Annual Scientific Sessions

June 6–10, 2009 • Washington, DC
www.asecho.org

Western Thoracic Surgical Association 35th Annual Meeting

June 24–27, 2009 • Banff, Alberta, Canada
www.westernthoracic.org

For information about Texas Heart Institute CME activities, please e-mail cme@heart.thi.tmc.edu or call 832.355.2157. To view or complete selected CME presentations (certificates are available online), please visit www.texasheart.org/Education/Resources/index.cfm. New courses are added regularly.

For 18 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."