HeartWATCH

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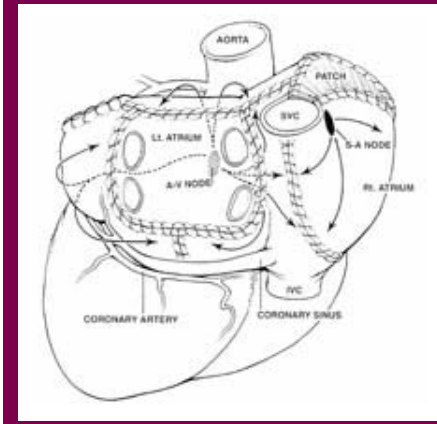
TEXAS HEART® INSTITUTE
at St. Luke's Episcopal Hospital

Maze Procedure Offers Highest Chance of Cure for Atrial Fibrillation

Abstract: For patients with atrial fibrillation, the Maze procedure offers the highest chance of a cure.

As the most common sustained arrhythmia, atrial fibrillation (AF) is a cardiac conduction disturbance in which the atria beat irregularly and rapidly, sometimes in excess of 400 beats per minute. AF has an overall prevalence of 0.5%, but the prevalence increases with advancing age, reaching 10% after the sixth decade. At any age, AF can be disabling, causing shortness of breath, lethargy, palpitations, stagnation of blood in the atria, and other problems associated with a reduced cardiac output. The most serious threat is thromboembolism, which may result in a stroke or sudden death. In elderly individuals with AF, the risk of stroke is nearly 5% per year, accounting for about 75,000 strokes annually in the United States alone. Because the Texas Heart Institute (THI) offers superior care for AF patients, many of them are referred here for treatment.

According to J. Michael Duncan, M.D., an associate surgeon at THI who has a special interest in arrhythmia surgery, "The heart's electrical impulse normally arises in the right atrium, in the sinoatrial node, and descends to the atrioventricular node via a single pathway. In AF, however, the electrical impulse breaks up into multiple re-entrant wavelets, which propagate simultaneously in the atria along aberrant pathways. As a result, atrioventricular synchrony is lost. The problem may be either paroxysmal or chronic. In chronic cases, the atria undergo remodeling, which increases the likelihood that AF will be perpetuated."



By making multiple incisions, the surgeon creates a "maze" on the atria, thus blocking aberrant pathways.

Treatment methods include medical therapy, electrical cardioversion, catheter ablation of the atrioventricular junction, implantation of a permanent pacemaker, and various surgical options. The only curative method is the Maze operation, introduced by Cox in 1987.

"This operation uses multiple incisions to create a 'maze' on the atria," Dr. Duncan explains. "The incisions block the atria's ability to create aberrant pathways. So the electrical impulse is channeled along a single pathway, which precludes creation of a re-entry circuit. Atrioventricular synchrony and atrial transport function are restored, eliminating the risk of thromboembolism."

The procedure has evolved through several modifications, the Maze III version having been the standard since 1992. It is a fairly complicated operation that usually necessitates cardiopulmonary bypass and may be combined with mitral valve repair or replacement or with coronary artery bypass grafting. The lesions may be created with cryosurgical or radiofrequency techniques rather than with a scalpel. Some surgeons place limited lesions around the pulmonary veins, in the left atrium alone; this approach may be quicker, but the results are less satisfactory. After the Maze III procedure, almost all patients have a significantly improved quality of life. Some patients have minor arrhythmias during the first 3 months after surgery. In addition, the disappearance of AF may unmask other arrhythmias that necessitate a permanent pacemaker.

"Between June 1992 and June 2002, my colleagues and I performed the Maze procedure in 54 patients with chronic or paroxysmal AF and in 1 patient with atrial flutter," says Dr. Duncan. "The patients had AF for 2 to 30 years. All of them were refractory to medical treatment or could not tolerate the necessary drug regimen. Most of the operations were performed for isolated AF. Fifteen patients had cryolesions instead of incisions. There were no operative deaths. At hospital discharge, 82% of the patients were in sinus rhythm. After a mean of 42 months, 94% were in sinus rhythm, and antiarrhythmic drugs were not generally needed. No strokes have occurred."

As the Maze procedure continues to evolve and be simplified, it should gain wider usage and benefit an increasing number of patients. Presently, it offers the highest chance of a cure for patients with AF. ●

Contents

For more information:

Dr. J. Michael Duncan

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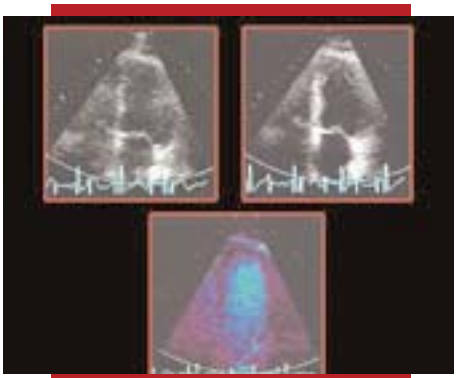
Imaging the Heart With Harmonics

Abstract: New ultrasound harmonic imaging techniques provide improved penetration and resolution and an improved signal-to-noise ratio for visualizing cardiac structure and function.

Cardiologists at the Texas Heart Institute at St. Luke's Episcopal Hospital (SLEH) routinely use a state-of-the-art ultrasound technique called harmonic imaging to visualize cardiac structure and function. Harmonic imaging goes beyond the limitations of conventional ultrasound by providing improved penetration and resolution and an improved signal-to-noise ratio. It is beneficial for hard-to-image patients, including those who are obese, are critically ill, are on ventilators, or have poor echocardiographic windows. Indeed, the main benefit of harmonic imaging is artifact reduction, because the echoes most likely to produce artifact are those least likely to produce harmonic waves.

Many people are familiar with harmonics because of their importance in music. Differences in harmonic frequencies are what give different types of musical instruments their characteristic tone color, or timbre. When a note is played, the fundamental frequency typically produces the predominant pitch. The variability of timbres among instruments (e.g., flutes vs. trombones), all playing the same note, results from a mixture of the fundamental frequency plus harmonic overtones that are multiples of the fundamental frequency.

Ultrasound waves work in a similar manner. In conventional imaging, when the tissue is evaluated with a band of frequencies centered at 4 MHz, the returning fundamental echo is also 4 MHz, and all secondary echoes are ignored. In harmonic imaging, however, transmitting a band of frequencies centered at 4 MHz will yield not only the fundamental echo but also harmonic frequency bands at 8 MHz, 12 MHz, and so on. Usually, the lowest secondary echo, called the "second harmonic," is used to generate an image of increased clarity.



Echoes of a hard-to-image left ventricle: conventional (top left), tissue harmonics (top right), contrast harmonics (bottom).

"The ribs and lungs have always made cardiac ultrasound difficult because ultrasound is not transmitted well through bone or air," says Raymond Stainback, M.D., medical director of Noninvasive Cardiac Imaging at SLEH. "Now echocardiography is able to provide improved hemodynamic and anatomic evaluation of the heart and great vessels. Newer harmonic-imaging modalities enable us to better distinguish true signals from noise, even in patients with hard-to-acquire images."

The improvement in imaging with harmonics is almost undisputed, which explains the method's rapid adoption. In the July 2001 issue of the *American Heart Journal*, researchers at the Erasmus Medical Center in The Netherlands reported on their use of both conventional and harmonic imaging to evaluate the sensitivity of dobutamine stress echocardiography for detection of coronary artery disease in 64 patients. With harmonic imaging, sensitivity was increased (94% vs. 78%) and specificity preserved. For diagnosing single-vessel disease, harmonic imaging was clearly superior (93% vs. 50%).

Use of contrast-specific imaging agents along with harmonic techniques provides enhanced evaluation of left ventricular function and cardiac structure. With this method, the harmonic signal is generated by a microbubble contrast agent, consisting either of albumin or of a phospholipid shell containing inert gas. These agents are displayed with optimal contrast and spatial resolution, and they light up intensely in the blood pool.

"With microbubbles, the returning signal can be louder than the traditional fundamental frequency reflection, thus greatly enhancing the image of the blood pool," says Dr. Stainback.

He explains that harmonic technology would not have been possible even a few years ago, because ultrasound computers could not have accurately processed the harmonic reflections returning from the body. Now, harmonic imaging is the standard method for assessing cardiac structure and function, especially in hard-to-image patients.

"Interpretation of the echocardiogram may be affected as much by what is not seen as by what is seen," says Dr. Stainback. "Harmonic imaging reduces diagnostic uncertainty, particularly in ill patients for whom the result could influence medical and surgical decisions. For this reason, harmonics will undoubtedly lead to improved patient care." ●

For more information:

Dr. Raymond Stainback

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Clinical Trials Update

THI is participating in a clinical trial of intravenous *o*-raffinose cross-linked human hemoglobin (hemoglobin raffimer) in patients undergoing coronary artery bypass grafting (CABG). Hemoglobin raffimer belongs to a new class of investigational drugs called "oxygen therapeutics," which are designed to deliver oxygen to bodily tissues. The drug will be evaluated for its ability to safely and effectively avoid or reduce the need for donor blood transfusions during surgery while preventing the clinical consequences of acute anemia due to intraoperative blood loss. The study, being performed here and at other centers in the United States, Canada, and the United Kingdom, will enroll 180 patients aged 18–80 years. Nancy A. Nussmeier, M.D., director of Cardiovascular Anesthesia Research, will lead THI's efforts in the trial.

Angiotensin Receptor Blockers Find Place in Heart Failure Therapy

Abstract: Angiotensin receptor blockers are being investigated as an alternative or adjunct to standard therapy for heart failure.

In the 2 decades since vasodilation was first proposed as a means to treat hypertension and heart failure, the combination of an angiotensin-converting enzyme (ACE) inhibitor and a β-blocker to induce neurohormonal blockade has become the standard of care for many patients with congestive heart failure (CHF). However, to help achieve maximal ACE inhibition, new therapies involving angiotensin receptor blockers (ARBs) have come under investigation.

ACE inhibitors affect a variety of neurohormonal and biologic pathways. They block the conversion of angiotensin I to angiotensin II and hinder the breakdown of bradykinin, resulting in vasodilation, reduction in aldosterone synthesis and release, lessened activation of the sympathetic nervous system, and decreased expression of vascular growth factors.

"From the beginning, cardiologists everywhere were quick to recognize the benefits of the ACE inhibitors," says Edward K. Massin, M.D., a staff cardiologist at the Texas Heart Institute. "When the toxic effects of angiotensin on the myocardium were later delineated, the rationale for the use of ACE inhibitors became even clearer."

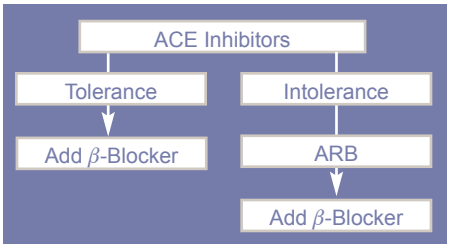
ACE inhibitors mainly work by antagonizing the renin-angiotensin-aldosterone system. In patients with hypertension and heart failure, this system is activated by reductions in renal blood flow and in sodium delivery to the distal tubules, which stimulate release of the catalytic enzyme renin. Renin converts the precursor angiotensinogen into angiotensin I, which ACE then converts into angiotensin II. In patients with heart failure, this cascade of events is intensified by the response of the sympathetic nervous system. ACE inhibitors work by breaking this cycle. Clinical studies have shown that ACE inhibitors improve the prognosis and reduce the mortality and hospitalization rates for patients with CHF.

Unfortunately, 2 shortcomings have been exposed. First, some patients cannot tolerate ACE inhibitors because of deleterious side effects, including severe cough, rash, hypotension, hyperkalemia, and renal dysfunction. Second, ACE inhibitors cannot completely block the production of angiotensin II.

"Soon after the clinical introduction of ACE inhibitors," Dr. Massin notes, "it was observed that in many patients the angiotensin II levels first dipped and then began to climb. Investigations into this phenomenon revealed biologic pathways leading to angiotensin II that do not necessarily involve ACE."

This discovery led to the development of ARBs, which block the effects of angiotensin II at its target. The ARBs produce fewer and less severe side effects than do ACE inhibitors and improve exercise tolerance and symptoms of heart failure. At present, ARBs are approved for use as second-line therapy for hypertension and CHF in patients who cannot tolerate ACE inhibitors. Meanwhile, investigations continue into the use of ARBs alone or combined with standard heart failure therapy.

"The combination of ARBs with ACE inhibitors and β-blockers is based on the same assumption originally used to justify the combination of β-blockers and ACE inhibitors, namely, the presumed additive blocking effect on neurohormonal activity. So far, the results have not completely confirmed an additive effect for ARBs," says Dr. Massin.



Algorithm for use of ACE inhibitors, β-blockers, and ARBs (assumes appropriate use of digitalis, loop diuretics, and spironolactone).

The Candesartan in Heart Failure–Assessment of Reduction in Mortality and Morbidity (CHARM) study, a large multicenter, randomized trial due to end next year, is examining whether candesartan is better used alone or with an ACE inhibitor in heart failure patients. The Evaluation of Losartan in the Elderly (ELITE) study and its ELITE II offshoot showed that the ARB losartan was better tolerated than the ACE inhibitor captopril but that it did not significantly improve outcome. The Valsartan Heart Failure Trial (Val-HeFT) found valsartan to be clinically efficacious as an alternative to ACE inhibitors in patients receiving the standard therapy for heart failure, significantly reducing mortality and morbidity and improving New York Heart Association functional class, ejection fraction, and quality of life.

As the evidence gathered in these and similar studies mounts, clearer indications should emerge for the use of ARBs in therapy for patients with heart failure. ●

Basic Science Report

Using a new technique, Yong-Jian Geng, M.D., Ph.D., and colleagues in THI's Heart Failure Research Laboratory have established an experimental cell culture system for inducing aggregates of mouse embryonic stem cells to differentiate into mature, functional cardiomyocytes. In culture, the stem cells aggregate, form embryoid bodies, and differentiate into clumps of rhythmically beating cardiomyocytes that can survive several weeks in vitro, even after several passages through culture. This new system will enable Dr. Geng's research team to explore the cellular and molecular mechanisms for early cardiac development and function and to devise basic strategies for stem cell therapies for cardiovascular disease.

For more information:

Dr. Edward K. Massin

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THI Mines Its Database to Improve Treatment for Cardiovascular Disease

Abstract: The Texas Heart Institute's comprehensive research database is being used to improve the safety and efficacy of surgical and interventional treatments for cardiovascular disease.

From its origin in the early 1960s, as notes jotted on index cards, the Texas Heart Institute (THI) research database has grown into a comprehensive electronic collection of data regarding more than 150,000 cardiovascular patients. This information is being used to improve the safety and efficacy of surgical and interventional treatments for cardiovascular disease.

With his departmental colleagues, William K. Vaughn, Ph.D., THI's vice president of Biostatistics and Epidemiology, maintains the database, a comprehensive, longitudinal clinical registry of all patients treated by THI staff at St. Luke's Episcopal Hospital. The secure electronic database stores information about patient demographics, risk factors, medical histories, physical findings, cardiac catheterization and angiographic procedures, operative anesthesia procedures, percutaneous catheter interventions, complications, and follow-up evaluations.

"As the U.S. population grows older, more people are requiring treatment for cardiovascular disease," says Dr. Vaughn. "It's increasingly important to ensure that such treatment remains safe, effective, accessible, and affordable. One way to meet this goal is to analyze and interpret as many data as we can gather about complications, risk factors, and post-treatment outcomes."

The roots of the database lie in the early 1960s, when Denton A. Cooley, M.D., began keeping a card catalog of all his surgical cases. For each patient, he documented the name, age, surgical procedure, postoperative results, and yearly follow-up results. In the early 1980s, an electronic surgical database was created to record similar data for all surgical procedures performed at THI; it coexisted with Dr. Cooley's card catalog until the late 1980s, when the two sources of information were finally combined.

"By the early 1990s," Dr. Vaughn points out, "it had become clear that our database was a gold mine of treatment information. Then we realized that it could be made even more useful and powerful by including risk factors, lab results, and medications, as well as data about newer interventions, such as coronary artery stenting, that were then entering clinical use."

"By creating a 'natural history' of each patient's cardiovascular disease and treatment, we made it easier for our clinicians to answer specific questions about treatments and their consequences," says MacArthur Elayda, M.D., Ph.D., cardiovascular epidemiologist and manager of Biostatistics and Epidemiology. "We also soon realized that, by placing the database at the disposal of THI's researchers, we could indirectly encourage research aimed at improving care for all of our cardiovascular patients."

Several recent THI studies have relied heavily on the database. Among them is a study, published last year in the *Journal of the American College of Cardiology*, that assessed the long-term outcomes of balloon angioplasty, repeat stenting, rotational atherectomy, and coronary artery bypass grafting (CABG) in diabetic and nondiabetic patients with in-stent restenosis. Another study, published this year in the *Annals of Vascular Surgery*, analyzed the THI experience with combined abdominal aortic aneurysm repair and CABG.

One very promising application of the database, according to Dr. Vaughn, is its use in linking genetic markers of cardiovascular disease with treatment outcomes. In a collaborative study, researchers at THI and Harvard Medical School are now accruing data about postoperative outcomes (*see story this issue*). Also, THI recently entered into a research partnership with The University of Texas (UT) Health Science Center at Houston, Baylor College of Medicine, and UT M. D. Anderson Cancer Center to build and maintain a secure database called TexGen, which will combine genetic and clinical information about patients undergoing cardiovascular procedures. The THI database provides the clinical data for TexGen.

"Our research database is unique," says Dr. Vaughn, "because it integrates data about every cardiovascular patient who comes through the doors of THI. It benefits our physicians, who can use the database to better manage the patient's condition; our researchers, who can more quickly and effectively evaluate and predict trends in care across large groups of patients; and the wider medical community, with whom our researchers will eventually share their findings." ●

Current Research Topics Involving THI's Research Database

- Clinical and genetic markers of restenosis
- Gamma brachytherapy for in-stent restenosis
- Aortic valve replacement in patients with poor ejection fraction (≤35%)
- Myocardial revascularization in young patients (≤40 years old)
- Percutaneous coronary intervention in the elderly
- Management of isolated left main lesions
- Atrial fibrillation after coronary revascularization
- Risk-adjusted survival after CABG versus survival after coronary stenting
- Angiographic morphology and survival after CABG versus coronary stenting in diabetic patients
- Coronary artery anomalies
- Ventricular septal rupture after acute myocardial infarction
- Cardiac tumors

CABG = coronary artery bypass grafting.

For more information:

Dr. William K. Vaughn

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New ACC/AHA Guidelines for Managing Patients with Acute Coronary Syndromes Reflect Recent Findings

Abstract: Recent changes to the ACC/AHA guidelines for management of patients with unstable angina and non–ST-segment elevation myocardial infarction primarily concern initial medical management.

Earlier this year, the American College of Cardiology and American Heart Association (ACC/AHA) announced changes in their jointly published guidelines for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction (available at www.acc.org or www.americanheart.org). The changes primarily concern the initial medical management of these acute coronary syndromes (ACS).

"Since the last version of the guidelines was published in September 2000, there have been several important trials in patients with acute coronary syndromes. By adjusting their recommendations for what constitutes the 'standard of care' for such patients, the ACC and AHA have answered the challenge of translating this new information into practice as quickly as possible," says James J. Ferguson III, M.D., associate director of Clinical Cardiology Research at the Texas Heart Institute (THI).

Largely on the basis of the CURE trial, which assessed the adjunctive use of clopidogrel with aspirin in conservatively managed patients with non–ST-segment elevation ACS, clopidogrel has now been assigned a more prominent role in the initial medical treatment of conservatively managed patients (class I, level B when used with aspirin) and patients in whom a percutaneous coronary intervention (PCI) is planned (class I, level B). The exact timing of clopidogrel initiation, however, has not been addressed. In patients taking clopidogrel for whom coronary artery bypass grafting (CABG) is planned, the drug should be withheld for 5–7 days (class I, level B).

The importance of glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors in patients with non–ST-segment elevation ACS has been modified. Their use is still strongly recommended (class I, level A) when catheterization and PCI are planned, although the new guidelines state that a GPIIb/IIIa inhibitor may be administered immediately before PCI. In high-risk patients with ongoing ischemia whose treatment plan will not include an early invasive procedure, the use of GPIIb/IIIa inhibitors has been downgraded. Eptifibatide and tirofiban now carry a class IIa, level A recommendation. In light of the GUSTO-IV trial, abciximab is no longer recommended (class III, level A). In patients without ongoing ischemia and other high-risk features, and for whom no PCI is planned, eptifibatide and tirofiban carry a class IIb, level A recommendation, whereas abciximab (again in light of the GUSTO IV trial) is not recommended (class III, level A).

The recommendations for use of heparin and low–molecular-weight heparin (LMWH) have also been upgraded. Anticoagulation with subcutaneous LMWH or intravenous unfractionated heparin (UH) (in addition to aspirin and/or clopidogrel) carries a class I, level A recommendation. Enoxaparin specifically has been deemed preferable to UH, unless CABG is planned within 24 hours (class IIa, level A).

In light of the TACTICS-TIMI 18 trial, early invasive management is considered superior to conservative management for higher-risk patients, including those with ST-segment depression and/or positive biomarkers in addition to recurrent ischemia and other previously noted risk stratifiers. The recommendation for early invasive management has been upgraded to class I, level A.

With regard to longer-term therapy, clopidogrel (75 mg daily) has been upgraded as the preferred alternative for patients who do not tolerate aspirin (class I, level A). Combination therapy with aspirin and clopidogrel for 9 months is now recommended after an episode of ACS (class I, level B). A 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor is recommended for patients with low-density lipoprotein levels greater than 100 mg/dL, beginning 24–96 hours after admission and continuing up to and after hospital discharge (class IIa, level B).

These and other changes in the management of ACS will be discussed by Dr. Ferguson at a THI-sponsored symposium, *Advancing the Standard of Care: Putting Science into Practice*, on November 16, 2002, in Chicago, Illinois. ●

Classification of Recommendations and Level of Evidence for ACC/AHA Guidelines

Classification of Recommendations

Class I	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
	Class IIa. Weight of evidence/opinion is in favor of usefulness/efficacy
	Class IIb. Usefulness/efficacy is less well established by evidence/opinion
Class III	Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful

Level of Evidence

A	Data derived from multiple randomized clinical trials
B	Data derived from a single randomized trial, or non-randomized studies
C	Consensus opinion of experts

Source: Manual for ACC/AHA Guideline Writing Committees. Available at www.acc.org/clinical/manual. Accessed September 1, 2002.

For more information:

Dr. James J. Ferguson III

832.355.3710

Collaborative Study Explores Links Between Gene Expression and Postoperative Outcomes

Abstract: A cutting-edge study is exploring the role of genetic expression in cardiovascular surgical morbidity and mortality.

A novel collaboration

between functional-genomics researchers at Harvard Medical School and the Texas Heart Institute (THI) may lead to a revolutionary approach to reducing the morbidity and mortality of cardiovascular surgical procedures. The study, sponsored by the National Heart, Lung, and Blood Institute, is exploring the influence of genetic markers and their expression on surgical outcomes.

"Functional genomics involves using genetic information from clinical studies to examine the influence of genetic variability on disease characteristics and outcomes," says Charles D. Collard, M.D., a cardiovascular anesthesiologist at THI and an associate professor of anesthesia at The University of Texas Health Science Center at Houston and Baylor College of Medicine. "Recent data suggest that specific genotypes entail the risk of adverse perioperative clinical outcomes. Our joint study will look broadly at outcomes in the acute perioperative setting. Myocardial infarction, stroke, death, bleeding, thrombotic events, coronary bypass graft failure, need for prolonged ventilation, use of hospital resources, and quality of life are just some of the outcomes we'll explore."

Dr. Collard's research colleagues for this study are Simon C. Body, M.D., and Stanton K. Shernan, M.D., both anesthesiologists at Harvard; Paul Ridker, M.D., M.P.H., associate professor of medicine at Harvard and a nationally renowned cardiologist and researcher; and Nader Rifai, M.D., director of Laboratory Medicine at Children's Hospital at Harvard.

The study, which began in July 2001, will follow up selected cardiovascular surgical patients longitudinally to measure coagulation and inflammatory markers in their blood. Before surgery, samples are taken for genotyping. Before, during, and after surgery, additional samples are taken and used to determine the circulating levels of the proteins produced by the genes, such as coagulation factor V and interleukin 6. Researchers record each patient's complete history and postoperative morbidity in a comprehensive database.

"Our specific aims are to establish a robust perioperative blood-sample repository for patients undergoing primary coronary artery bypass graft surgery requiring cardiopulmonary bypass," says Dr. Collard. "We also want to determine the relationship between the patient's genotype and certain phenotypes, such as inflammatory and coagulation expression. Moreover, we seek to identify genetic factors that predict adverse perioperative events and to define their impact on short-term and long-term outcomes and quality of life."

The team plans to recruit about 1500 patients over 5 years and then analyze the data. "We've collected data on several hundred participants. A large-scale study will yield measurable statistics that may lead to novel treatments for patients predisposed to certain adverse events as a result of cardiovascular surgery."

From each patient, researchers obtain written consent before blood samples are drawn. To ensure total patient confidentiality, the team employs a bar-code system that prevents anyone involved, including those who handle blood samples, from identifying study participants. "Many layers of security are built into the study design, which conforms to the guidelines of the National Institutes of Health and of the Institutional Review Boards of Brigham and Women's Hospital and THI. Furthermore, the information gathered in our study is not released to anyone outside the project, including the patients and their families," Dr. Collard emphasizes.

The collaboration between THI and Harvard will maximize the use of these institutions' leading research facilities and will bring a diverse patient population into the study, furthering research that could save thousands of lives.

"This study may give us insight into the molecular mechanisms that lead to complications during otherwise routine procedures," Dr. Collard explains. "More important, identifying specific genotypes may not only provide insight into why the response to surgery varies among individuals, but it may also decrease surgical morbidity and mortality through preoperative surgical risk assessment and the administration of prophylactic therapy." ●

For more information:

Dr. Charles D. Collard
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Examples of Genotypes Linked to Adverse Postoperative Outcomes

Gene	Gene symbol	Phenotype	Linked postoperative outcome
Apolipoprotein E	*APOE*	↑ TNF-α and IL-8; ↓ IL-1ra	Neurocognitive dysfunction
Chymase A	*CMA1*	↑ Conversion of angiotensin I to angiotensin II?	CABG restenosis
Coagulation factor V	*F5*	Activated protein C resistance	CABG restenosis; thromboembolism; renal allograft thrombosis
Endothelial nitric oxide synthase	*NOS3*	↓ Nitric oxide	↑ Vascular reactivity
Integrin β-3 (glycoprotein IIIa)	*ITGB3*	↓ Platelet activation threshold	CABG thrombosis, MI, neurocognitive dysfunction and death after cardiac surgery
Interleukin-10	*IL-10*	↓ IL-10	Renal transplant rejection
Tumor necrosis factor-α	*TNF*	↑ TNF-α	Need for prolonged mechanical ventilation; transplant rejection; sepsis

CABG = coronary artery bypass grafting; MI = myocardial infarction.

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Cover: Statue donated by former Secretary of State Alexander Haig 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.

Calendar of Events

Texas Heart Institute Continuing Medical Education Symposia

American Heart Association Satellite Symposium
Advancing the Standard of Care: Putting Science into Practice
November 16, 2002
Chicago, Illinois
Program Directors: James J. Ferguson III, M.D.; R. David Fish, M.D.; and James T. Willerson, M.D.

American Heart Association Satellite Symposium
Controversies in Endovascular Treatment of Peripheral Vascular Disease
November 16, 2002
Chicago, Illinois
Program Director: Zvonimir Krajcer, M.D.

Texas Heart Institute Fourth Symposium on Cardiac Arrhythmias
February 8, 2003
Houston, Texas
Program Director: Ali Massumi, M.D.

For information about any of the CME activities listed above, please contact cme@heart.thi.tmc.edu or call 832.355.2157.

Selected Upcoming National and International Meetings

American Heart Association Scientific Sessions 2002
November 17–20, 2002
Chicago, Illinois

Society of Thoracic Surgeons 39th Annual Meeting
January 31–February 2, 2003
San Diego, California

American College of Cardiology 52nd Annual Scientific Session
March 30–April 2, 2003
Chicago, Illinois

International Society for Heart and Lung Transplantation 23rd Annual Meeting and Scientific Sessions
April 9–12, 2003
Vienna, Austria

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