Calendar of Events

**Texas Heart Institute Continuing Medical Education Symposia**

Texas Heart Institute
Fourth Symposium on Cardiac Arrhythmias
February 8, 2003
Houston, Texas

Program Director: Ali Massumi, M.D.

**Selected Upcoming National and International Meetings**

- **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

- **American Heart Association Scientific Sessions 2003**
  November 9–12, 2003
  Orlando, Florida

Abstract submission begins: April 1, 2003
**Placements of leads for biventricular pacing (Reprinted with permission from Guidant Corporation.)**

**Abstract:** Biventricular pacing may be therapeutic for select patients with advanced congestive heart failure who do not respond to optimal medical therapies.

**Indications for the use of implantable cardiac pacemakers have expanded considerably in recent years. Traditionally used for treating bradycardia due to sinus node dysfunction or atioventricular (AV) node-His-Purkinje disease, pacemakers may soon be considered therapeutic for a variety of other conditions, including congestive heart failure (CHF).**

The modern pacemaker comprises 1 or 2 chambers, which are positioned in the right atrium and/or right ventricle via the subclavian or cephalic vein. The pulse generator is placed subcutaneously in the shoulder area. The pacing system, which delivers a weak current to the myocardium, initiates a propagating wave of depolarization. The pacemaker can also sense the presence or absence of intrinsic cardiac activity.

Patients with chronic systolic heart failure usually have interventricular conduction delays (e.g., left or right bundle branch block or non-specific conduction delays) that cause abnormal electrical depolarization. A prolonged QRS interval disrupts interventricular septal wall motion, decreases ventricular con-tractility, reduces diastolic filling time, increases mitral regurgitation, and generally impairs cardiac contraction. In CHF patients who have ventricular conduction delays, car- diac resynchronization therapy (CRT), by the simultaneous stimulation of both ventricles (i.e., biventricular [BiV] pacing), appears to improve systolic function.

“In patients with bradyarrhythmia or AV conduction abnormalities, a pacemaker serves as a backup, providing support in the absence of an intrinsic electrical impulse or conduction wave,” says John J. Seger, M.D., cardiologist and cardiac electrophysiologist at the Texas Heart Institute (THI) and St. Luke’s Episcopal Hospital. “Pacemakers implanted for CRT improve the overall efficiency of contraction. The aim is to pace the ventricles 100% of the time, thereby coordinating their contraction.” Historically, accessing the left ventricle for pacing was complicated and involved implanting epicardial pacing leads. Now, however, pacing systems have designed to allow access to the veins that drape the left ventricular myocardium. In addition to the right atrial and ventricular leads, another lead is advanced into the right atrium and the coro-nary sinus opening; it is then manipulated into the postero- lateral branch, which lies on the posterobasal region of the left ventricle. Simultaneous stimulation of the interventric- ular septum (via the right ventricular apical lead) and the postero- lateral wall of the left ventricle coordinates ventricular activation and improves ventricular mechanics. Moreover, by optimizing AV delay, it improves diastolic filling.

Several clinical trials have investigated CRT in patients with advanced CHF and irreversible, symptomatic heart failure due to ischemic or dilated cardiomyopathy, a prolonged QRS interval of >130 ms, a left ventricular end-diastolic dimension of >55 mm, and a left ventricular ejection fraction of <35%.

**For more information:**
Dr. John J. Seger
713.791.9444

**Placement of leads for biventricular pacing (Reprinted with permission from Guidant Corporation.)**

**Abstract:** A new computerized physician-order-entry system promises to improve the continuity of patient care while maximizing hospital resources.

**A new computerized physician-order-entry (POE) system, currently being implemented at St. Luke’s Episcopal Hospital (SLEH), is expected to streamline clinical care, improve hospital efficiency, and help busy physicians keep abreast of evolving guidelines in their field.**

“The system we are installing, Horizon Expert Orders™, made by McKesson Corporation, is based on a system developed at Vanderbilt University in Nashville,” says Patrick J. Hogan, M.D., an interventional cardiologist at SLEH and director of the Learning Resource Center of the Texas Heart Institute (THI). “As the first beta-testers, we have been evaluating the system for the past 12 months and plan to have it available hospital-wide within 2 years.”

“The system will help physicians make deci-sions by presenting clinically relevant informa-tion about a specific patient’s condition, along with treatment protocols and evidence-based guidelines,” explains Dr. Hogan. “The POE system will automatically insert the correct spelling, dosage, and frequency into the prescription, along with the latest drug-infor-mation reminders,” says Dr. Hogan. Physi-cians can create their own templates for drugs they frequently prescribe. The system will notify the user of any omissions, drug-to-drug interactions, or drug allergies in the patient’s record, as well as any over-the-counter or alternative medications that might adversely interact with the prescription. A network of computer terminals will be strate-gically placed in intensive care units and else-where throughout the hospital to provide physicians with immediate access to magnet-ic resonance images, angiograms, laboratory data, and patient histories, in addition to POE order sets.

Although the system is designed to be user-friendly, intensive training will be provided when the system is implemented throughout the hospital, and ongoing support will be available.

“The use of a POE system like ours has been enthusiastically endorsed by The Leapfrog Group, a nationwide consortium of more than 100 leading health-care-benefit providers that works with medical experts to identify problems in hospital systems and propose solutions for improving them,” explains Dr. Hogan.

“The POE system will improve patient safety, protect patient privacy, and enhance the quality of our medical records,” con-cludes Dr. Hogan. “It will allow our house staff to provide the most up-to-date patient data and will offer precise data regarding the use of hospital resources.”

**For more information:**
Dr. Patrick J. Hogan
713.791.9400

**Abstract:** Computerized Physician-Order-Entry System Will Streamline Clinical Care

Physicians should consider the use of CRT in patients with New York Heart Association (NYHA) class III or IV function secondary to ischemic or dilated cardiomyopathy, a prolonged QRS interval of >130 ms, a left ventricular end-diastolic dimension of >55 mm, and a left ventricular ejection fraction of <35%.

“Current patient-selection guidelines for BiV pacing include medically refractory sympto-matic patients with NYHA class III or IV function secondary to ischemic or dilated cardiomyopathy, a prolonged QRS interval of >130 ms, a left ventricular end-diastolic dimension of >55 mm, and a left ventricular ejection fraction of <35%.”

“For our group has the largest experience in this region with the implantation of biven-tricular devices, and we work closely with the personnel in THI’s heart failure and trans-plant programs,” says Dr. Seger. “Although device implantation can be challenging, the clinical response in selected patients is remarkable.”

**For more information:**
Cardiologist Patrick J. Hogan, M.D., demonstrates computer-ized physician-order-entry system.
Cardiovascular Centers Are Feeling the Effects of America’s Worst-Ever Blood Shortage

Abstract: Because of new safety restrictions, imposed at a time when donations were already declining, an expanded blood donor pool is urgently needed.

Donation of white and red blood cell units in 2001 versus 2002. The sharp increase in donations during 2001 was a temporary phenomenon caused by the September 11th terrorist attacks.


Contents
Biventricular Pacing for CHF 2
Blood Shortages in Cardiovascular Care 3
CHF Management in a Heart Failure Center 4
Emerging Indications for the Jarvik 2000 LVAD 4
Gene Therapy for Atherosclerosis 6
Computerized Physician Order Entry 7
Calendar of Events 8

For more information:
Dr. Arthur W. Bracey 832.355.2782

Although hospital blood banks are seldom in the limelight, their services are essential to cardiovascular patients, particularly those undergoing complex surgical procedures. According to Arthur W. Bracey, M.D., medical director of the Transfusion Service at St. Luke’s Episcopal Hospital (SLEH) and a pathologist at the Texas Heart Institute (THI), cardiovascular patients use up to 24% of the blood transfused in the United States. Recently, however, many centers have felt the effects of a continuing blood shortage. “During the past 2 years,” says Dr. Bracey, “the nationwide demand for blood has risen by 11%, but donations have increased by only 8%. Concurrently, new screening restrictions, designed to ensure blood safety, have eliminated thousands of donors.”

These restrictions were implemented because of concern about bovine spongiform encephalopathy (“mad cow disease”). Its human form, variant Creutzfeldt-Jakob disease (vCJD), has caused at least 90 deaths in Europe but has not been contracted in the United States. In 1999, per Food and Drug Administration (FDA) guidelines, American blood banks stopped accepting donations from persons who have spent at least 6 months in the United Kingdom since 1980. In addition to protecting injured arteries and laying the groundwork for future clinical trials.

In this changing landscape, basic scientists in the Wafic Said Laboratory for Gene Therapy Research at the Texas Heart Institute (THI) are developing gene therapies for atherosclerosis and thrombosis and laying the groundwork for future clinical trials. These researchers, led by the laboratory’s director, Pierre Zoldhelyi, M.D., are testing therapies for enhancing the cellular expression of factors that oppose neointimal proliferation and thrombosis in pigs and atherosclerotic Watanabe rabbits. The pig is an excellent model because of its large size and propensity for blood clotting and thrombus formation, and the Watanabe rabbit is an established model of human familial hypercholesterolemia. In both models, balloon angioplasty is used to injure arteries and initiate vascular responses associated with atherosclerosis and restenosis (e.g., inflammation, thrombosis, and stenosis).

“In the atherosclerotic Watanabe rabbit,” says Dr. Zoldhelyi, “we can restore function of the vasodilator and antiplatelet agent prostacyclin and inhibit tissue and smooth muscle cell accumulation. Unlike drug therapy, gene therapy achieves this by introducing genes for COX-1 and TFPI directly into balloon-injured arteries, thus reducing neointimal formation and thrombosis and improving vessel dilation.”

In pigs and Watanabe rabbits, the laboratory’s researchers have successfully inhibited thrombosis and restenosis by delivering the TFPI gene locally to balloon-injured vessels. Also, by incubating vein grafts with the COX-1 gene before implantation, they have succeeded in preserving and maintaining normal blood flow through the treated grafts for up to 4 weeks after implantation in cholesterol-fed rabbits.

In addition to protecting injured arteries against atherosclerosis, the THI researchers are introducing genes encoding antithrombotic and anti-inflammatory proteins into the endothelial cells of vein grafts in order to create thromboreistant vein grafts, thereby inhibiting vein graft bypass deterioration and the potentially lethal thrombosis that follows atherosclerotic plaque rupture.

To deliver therapeutic genes directly into target cells, Dr. Zoldhelyi and his colleagues have relied mainly on vehicles, or gene vectors, called adenoviruses. The “recombinant” (or genetically altered) adenovirus is the most widely used vector in cardiovascular gene therapy. Although it naturally causes self-limiting infections in the human respiratory tract, it also efficiently infects endothelial cells and cardiomyocytes. To deter unwanted immune reactions and gene delivery to unintended cellular targets, the adenovirus is stripped of as much of its pathogenic machinery as possible before therapeutic genes are inserted. Nevertheless, the search is under way at THI and elsewhere for less pathogenic vectors, both viral and nonviral.

One promising vector now being used in the gene therapy laboratory is the adenovirus-associated virus (AAV), which normally is nonpathogenic in humans, infects a wide variety of cells, and can be prepared in high titer. “Once incorporated into some cardiovascular cells, AAV’s may be able to continue expressing their therapeutic genetic cargo for years,” says Dr. Zoldhelyi. “So one aim of ours is to use AAV where we once used adenovirus to see if this is an alternative therapeutic safety and efficacy.” Dr. Zoldhelyi and his group have recently secured grants from the National Institutes of Health and the American Heart Association for preclinical investigations of AAV-based gene therapies.

For more information:
Dr. Pierre Zoldhelyi 832.355.3187

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In 2002, the Centers for Disease Control found increasing evidence that another infectious agent, West Nile virus (WNV), is a blood-borne pathogen. Researchers at THI, the Wafic Said Laboratory for Gene Therapy Research at the Texas Heart Institute (THI), and the Jarvik 2000 LVAD are developing gene therapies for atherosclerosis and thrombosis and laying the groundwork for future clinical trials.

In this changing landscape, basic scientists in the Wafic Said Laboratory for Gene Therapy Research at the Texas Heart Institute (THI) are developing gene therapies for atherosclerosis and thrombosis and laying the groundwork for future clinical trials. These researchers, led by the laboratory’s director, Pierre Zoldhelyi, M.D., are testing therapies for enhancing the cellular expression of factors that oppose neointimal proliferation and thrombosis in pigs and atherosclerotic Watanabe rabbits. The pig is an excellent model because of its large size and propensity for blood clotting and thrombus formation, and the Watanabe rabbit is an established model of human familial hypercholesterolemia. In both models, balloon angioplasty is used to injure arteries and initiate vascular responses associated with atherosclerosis and restenosis (e.g., inflammation, thrombosis, and stenosis).

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For patients with suspected or confirmed congestive heart failure or cardiomyopathy, the Heart Failure Center of the Texas Heart Institute and St. Luke’s Episcopal Hospital (THI/SLEH) provides multiple levels of medical management, which range from patient education to identification of optimal candidates for cutting-edge interventions and clinical trials.

“The Heart Failure Center is a unique resource for patients from around the world,” says THI/SLEH cardiologist and heart failure specialist Reynolds M. Delgado III, M.D. “We can assess their need for advanced new therapies and can optimize their medical regimens to improve symptoms and minimize the risk of death.”

The center offers dietary and pharmacologic counseling for patients and their families; it also offers active support groups and access to the latest treatments through clinical trials.

Two of the newest intravenous medicines that have shown promise in THI/SLEH studies are milrinone (Primacor®), which boosts the heart’s pumping power, and nesiritide (Natrecor®), which simultaneously improves cardiovascular and renal function in heart failure patients.

“The physicians at our institution have unparalleled experience in treating heart failure. In addition to being renowned for heart transplantation, we offer advanced therapies such as left ventricular assist devices and biventricular pacing,” says Dr. Delgado. “We have implanted more Jarvik 2000 ventricular assist devices than any other center in the world.”

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According to the American Heart Association, nearly 5 million Americans are currently living with heart failure, and 550,000 new cases are diagnosed each year. Fortunately, survival has dramatically improved in the past 50 years because of modern medical and surgical treatments.

“For building strong relationships with our patients and teaching them how to recognize symptoms and avoid fluid overload, we can intervene earlier and improve lives,” Dr. Delgado emphasizes. “Our data show that the Heart Failure Center has reduced hospital admissions by 30% and lengths of stay by 4 days.”

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For more information:
Heart Failure Center 832.355.3961
Dr. Reynolds M. Delgado III 713.383.9500

Abstract: The Heart Failure Center at THI/SLEH improves patient outcomes by offering specialized case management.

### Clinical Trials Update

In an ongoing collaborative Brazilian trial (see Summer 2002 issue of Heart Watch), 14 heart failure patients have now been treated with a form of cell therapy developed at THI. The therapy utilizes a patient’s own bone marrow cells. The outcomes of study patients are being followed up and compared with those of 16 control patients. According to Emerson C. Petis, M.D., director of New Interventional Cardiogenic Technology at THI, who performed the clinical procedures in Brazil, the therapy has led to symptomatic and functional improvement in treated patients. THI/SLEH is seeking approval from the Food and Drug Administration to begin a similar study here in the coming year.

The Jarvik 2000 LV AD is a relatively new device that offers several advantages over other pumps for treating chronic heart failure.

Because the pump is positioned intravenously, surgical implantation is markedly simplified. Experience at the Texas Heart Institute and St. Luke’s Episcopal Hospital (THI/SLEH) has shown that the Jarvik 2000 is associated with fewer intraoperative complications and less blood loss than larger, pulsatile LVADs. According to O.H. Frazier, M.D., chief of Cardiopulmonary Transplantation and director of Cardiovascular Research at THI/SLEH, “Keeping the pump inside the heart prevents inlet graft kinking, decreases the incidence of thrombosis and pannus formation in the inlet graft, and avoids inlet obstruction by the septum or lateral wall of the heart.”

The Jarvik 2000 can also be implanted without cardiopulmonary bypass or with limited cardiopulmonary bypass (<10 min).

The Jarvik 2000 has other advantages. The pump speed can be easily regulated. With a simple dial mechanism, available to both patient and clinician, the speed can be increased from 8,000 to 12,000 rpm in response to increased patient activity. In addition, the pump is totally quiet. Like other continuous-flow devices, the Jarvik 2000 is small and can be implanted in small patients (those with a body surface area of <2 m²) who otherwise would not qualify for an LVAD.

Because the graft’s outlet cannula is placed in the descending aorta, the pump can be implanted less invasively through a left thoracotomy. Dr. Frazier adds that the graft can also be placed in the ascending aorta, which is usually done when concomitant cardiac procedures are performed (e.g., coronary bypass, valve surgery).

Clinical trials to evaluate the safety and efficacy of the Jarvik 2000 LVAD as a temporary bridge to heart transplantation began in April 2000 at THI/SLEH and include 22 patients thus far. Shortly thereafter, a clinical trial was begun in Oxford, United Kingdom. The Oxford protocol includes heart failure patients who are not transplant candidates and who will be supported long-term unless sufficient myocardial recovery occurs to allow the device to be removed. Other centers have also begun clinical trials. Thus far, the results have been encouraging, as the pump has led to the stabilization and recovery of critically ill patients.

“As a result of the clinical trials, we have already learned much about the best mode of operation and use of the Jarvik 2000,” says Dr. Frazier. “For example, we’ve learned that it’s preferable to allow the native heart to eject blood and the pump to assume the role of the heart’s pumping power, and nesiritide

### For more information:
Dr. O. H. Frazier 832.355.3000

Abstract: Much has already been learned about the use of the Jarvik 2000 left ventricular assist device, even though clinical trials began just 2 years ago.
For patients with suspected or confirmed congestive heart failure or cardiomyopathy, the Heart Failure Center of the Texas Heart Institute and St. Luke’s Episcopal Hospital (THI/SLEH) provides multiple levels of medical management, which range from patient education to identification of optimal candidates for cutting-edge interventions and clinical trials.

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The Heart Failure Center was established in late 1997 in recognition of compelling evidence that such centers improve outcomes, reduce costly hospital readmissions, and enhance the quality of life in chronically ill heart failure patients. Nurse-coordinator Cathy Eastwood, R.N., M.N., oversaw the founding of the center and now oversees its day-to-day operations.

“Our nursing staff provides personalized care for patients, including periodic follow-up calls, which can identify problems and prevent adverse events or unnecessary hospital admissions,” says Dr. Delgado. “Nurses ask the patients about their quality of life, weight, and overall mood, as well as medication side effects and symptoms, such as edema, dyspnea, or pain. We strongly encourage patients to participate in clinical trials, because even placebo recipients tend to respond well to the regimen of care offered by a heart failure study.”

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For more information:
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832.355.3961
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The pathophysiology of chronic heart failure is characterized by cardiac hypertrophy, which allows compensatory mechanisms to adjust to cardiac cellular impairment. As this compensation becomes inadequate for circulatory needs, symptoms of heart failure occur. As the heart increasingly dilates, medications become ineffective. In these cases, the best treatment is to unload the ventricle and augment the heart’s inadequate blood delivery with a left ventricular assist device (LVAD). The Jarvik 2000 intracavitary continuous-flow LVAD is a relatively new device that offers several advantages over pumps for treating chronic heart failure.

Because the pump is positioned intracavitarily, surgical implantation is markedly simplified. Experience at the Texas Heart Institute and St. Luke’s Episcopal Hospital (THI/SLEH) has shown that the Jarvik 2000 is associated with fewer intraoperative complications and less blood loss than larger, pulsatile LVADs. According to O. H. Frazier, M.D., chief of Cardiopulmonary Transplantation and director of Cardiovascular Research at THI/SLEH, “Keeping the pump inside the heart prevents inlet graft kinking, decreases the incidence of thrombosis and pannus formation in the inlet graft, and avoids inlet obstruction by the septum or lateral wall of the heart.”

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Clinical trials to evaluate the safety and efficacy of the Jarvik 2000 LVAD as a temporary bridge to heart transplantation began in April 2000 at THI/SLEH and include 22 patients thus far. Shortly thereafter, a clinical trial was begun in Oxford, United Kingdom. The Oxford protocol includes heart failure patients who are not transplant candidates and who will be supported long-term unless sufficient myocardial recovery occurs to allow the device to be removed. Other centers have also begun clinical trials. Thus far, the results have been encouraging, as the pump has led to the stabilization and recovery of critically ill patients.

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This use (i.e., to augment cardiac output rather than completely unload the heart) is what Dr. Frazier believes will become the Jarvik 2000’s niche. “I believe this LVAD will be an excellent choice for class III and IV patients who are homebound on medical therapy, but more experience is needed before we can definitively state its best use and mode of operation,” says Dr. Frazier.

For more information:
Dr. O. H. Frazier
832.355.3000

The FDA approved the HeartMate LVAD for permanent use on November 6, 2002, the Food and Drug Administration approved the HeartMate left ventricular assist device (Theratec Corporation, Pleasanton, CA) as destination therapy for the estimated 20,000 to 30,000 Americans with advanced congestive heart failure who are ineligible for a transplant. Previously, the battery-operated HeartMate was approved only as a bridge to transplantation. THI has been closely involved with the development of the HeartMate for 30 years.

Abstract: Much has already been learned about the use of the Jarvik 2000 left ventricular assist device, even though clinical trials began just 2 years ago.

Abstract: The Heart Failure Center at THI/SLEH improves patient outcomes by offering specialized case management.

The Jarvik 2000 continuous-flow left ventricular assist device.

Specialized Heart Failure Center Improves Survival and Quality of Life for Symptomatic Patients

For more information:
Heart Failure Center
832.355.3961
Dr. Reynolds M. Delgado III
713.383.9500

The Jarvik 2000 is small and can be implanted in small patients (those with a body surface area of <2 m²) who otherwise would not qualify for an LVAD. Because the graft’s outlet cannula is placed only a portion of the cardiac output. Ejection usually occurs at pump speeds below 10,000 rpm and results in a more normal physiologic condition. In this manner, the Jarvik 2000 works as a true assist device, enhancing the function of the failing heart.”

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Cardiovascular Centers Are Feeling the Effects of America’s Worst-Ever Blood Shortage

Abstract: Because of new safety restrictions, imposed at a time when donations were already declining, an expanded blood donor pool is urgently needed.

For more information:
Dr. Arthur W. Bracey
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Over the last 10 years, the molecular understanding of cardiovascular physiology and pathophysiology has improved immensely as a direct result of the cloning and study of key cardiovascular genes, including those for vascular endothelial growth factor, cyclooxygenase-1 (COX-1), and tissue factor pathway inhibitor (TFPI). This has led to the design of cardiovascular gene transfer strategies, the primary goal of which is to effect desired therapeutic effects by introducing appropriate genes into cardiovascular cells. Early clinical studies of cardiovascular gene therapy are now focusing on angiogenesis, and insights gained from them will probably be applied to the problems of restenosis and heart failure and to the prevention of vulnerable plaque rupture and graft atherosclerosis.

In this changing landscape, basic scientists in the Wafic Said Laboratory for Gene Therapy Research at the Texas Heart Institute (THI) are developing gene therapies for atherosclerosis and thrombosis and laying the groundwork for future clinical trials. Researchers, led by the laboratory’s director, cardiologist Dr. Pierre Zoldhelyi, M.D., are testing therapies for enhancing the cellular expression of factors that oppose neointimal proliferation and thrombosis in pigs and atherosclerotic Watanabe rabbits. The pig is an excellent model because of its large size and propensity for blood clotting and thrombus formation, and the Watanabe rabbit is an established model of human familial hypercholesterolemia. In both models, balloon angioplasty is used to induce arteries and initiate vascular responses associated with atherosclerosis and restenosis (e.g., inflammation, thrombosis, and stenosis). “In the atherosclerotic Watanabe rabbit,” says Dr. Zoldhelyi, “we can remove fraction of the vasodilator and antiplatelet agent prostacyclin and inhibit tissue factor, a pro- In pigs and Watanabe rabbits, the laboratory’s researchers have successfully inhibited thrombosis and restenosis by delivering the TFPI gene locally to balloon-injured vessels. Also, by incubating vein grafts with the COX-1 gene before implantation, they have succeeded in preserving and maintaining normal blood flow through the treated grafts for up to 4 weeks after implantation in cholesterol-fed rabbits.

In addition to protecting injured arteries against atherosclerosis, the THI researchers are introducing genes encoding antithrombotic and anti-inflammatory proteins into the endothelial cells of vein grafts in order to create thromboreistant vein grafts, thereby inhibiting vein graft bypass deterioration and the potentially lethal thrombosis that follows atherosclerotic plaque rupture.

To deliver therapeutic genes directly into target cells, Dr. Zoldhelyi and his colleagues have relied mainly on vehicles, or gene vectors, called adenoviruses. The “recombinant” (or genetically altered) adenovirus is the most widely used vector in cardiovascular gene therapy. Although it naturally causes self-limiting infections in the human respiratory tract, it also efficiently infects endothelial cells and cardiomyocytes. To deter unwanted immune reactions and gene delivery to unintended cellular targets, the adenovirus is stripped of as much of its pathogenic machinery as possible before therapeutic genes are inserted. Nevertheless, the search is under way at THI and elsewhere for less pathogenic vectors, both viral and nonviral.

One promising vector now being used in the gene therapy laboratory is the adenovirus-associated virus (AAV), which normally is nonpathogenic in humans, infects a wide variety of cells, and can be prepared in high titers. “Once incorporated into some cardiovascular cells, AAV’s may be able to continue expressing their therapeutic genetic cargo for years,” says Dr. Zoldhelyi. “So one aim of ours is to use AAV where we once used adenovirus to see if this improved therapeutic safety and efficacy.” Dr. Zoldhelyi and his group have recently secured grants from the National Institutes of Health and the American Heart Association for preclinical investigations of AAV-based gene therapies.

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**Abstract:** Biventricular pacing may be therapeutic for select patients with advanced congestive heart failure who do not respond to optimal medical therapies.

**Indications for the use of implantable cardiac pacemakers have expanded considerably in recent years. Traditionally, for treating bradycardia due to sinus node dysfunction or atrioventricular (AV) node-His-Purkinje disease, pacemakers may soon be considered therapeutic for a variety of other conditions, including congestive heart failure (CHF).**

The modern pacemaker comprises 1 or 2 leads, which are positioned in the right atrium and/or right ventricle via the subclavian or cephalic vein. The pulse generator is placed subcutaneously in the shoulder area. The pacemaker system, which delivers a weak current to the myocardium, initiates a propagating wave of depolarization. However, not all patients with chronic systolic heart failure usually have interventricular conduction delays (e.g., left or right bundle branch block or nonspecific conduction delays) that cause abnormal electrical depolarization. A prolonged QRS interval (QRS >130 ms) and interventricular septal wall motion, decreases ventricular contractility, reduces diastolic filling time, increases mitral regurgitation, and generally impairs cardiac contraction. In CHF patients who have ventricular conduction delays, cardiac resynchronization therapy (CRT), by the simultaneous stimulation of both ventricles (i.e., biventricular [BiV] pacing), appears to improve systolic function.

“In patients with bradycardia or AV conduction abnormalities, a pacemaker serves as a backup, providing support in the absence of an intrinsic electrical impulse or conduction wave,” says John J. Seger, M.D., cardiologist and cardiac electrophysiologist at the Texas Heart Institute (THI) and St. Luke’s Episcopal Hospital. “Pacemakers implanted for CRT improve the overall efficiency of contraction. The aim is to pace the ventricles 100% of the time, thereby coordinating their contraction.”

Historically, accessing the left ventricle for pacing was complicated and involved implanting epicardial pacing leads. Now, however, pacing systems have been designed to allow access to the veins that drain the left ventricular myocardium. In addition to the right atrial and ventricular leads, another lead is advanced into the right atrium and the coronary sinus, and then it is manipulated into the posterolateral branch, which lies on the posterior basal region of the left ventricle.

Simultaneous stimulation of the interventricular septum (via the right ventricular apical lead) and the posterolateral wall of the left ventricle coordinates ventricular activation and improves ventricular mechanics. Moreover, by optimizing AV delay, it improves diastolic filling.

Several clinical trials have investigated CRT in patients with advanced congestive heart failure who are nonresponsive to medical therapies. The Multivit-Stimulation in Cardiomyopathy (MUSTIC) trial evaluated the effects of BiV pacing in patients with New York Heart Association (NYHA) class III CHF and interventricular conduction delay; BiV pacing was associated with an improved quality of life and a 20% greater 6-minute walk distance. In the Multi-site In-Sync Randomized Clinical Evaluation (MIRACLE) trial, which involved a similar patient population, BiV pacing improved NYHA functional class, quality of life, and left ventricular dimension and function. The Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) study is ongoing, and results are not yet available.

“Clinical biventricular pacing studies have uniformly shown an improved overall quality of life and functional status, without any increase in overall mortality,” says Dr. Seger. “Studies designed to assess whether such pacing offers an overall mortality benefit are still underway.”

Current patient-selection guidelines for BiV pacing include medically refractory symptomatic patients with NYHA class III or IV function secondary to ischemic or dilated cardiomyopathy, a prolonged QRS interval of >130 ms, a left ventricular end-diastolic dimension of >55 mm, and a left ventricular ejection fraction of <35%.

“Our group has the largest experience in this region with the implantation of biventricular devices, and we work closely with the personnel in THI’s heart failure and transplant programs,” says Dr. Seger. “Although device implantation can be challenging, the clinical response in selected patients is remarkable.”

**For more information:**

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**Cardiologist Patrick J. Hogan, M.D., demonstrates computerized physician-order-entry system.**

**A new computerized physician-order-entry (POE) system, currently being implemented at St. Luke’s Episcopal Hospital (SLEH), is expected to streamline clinical care, improve hospital efficiency, and help busy physicians keep abreast of evolving guidelines in their field.**

“The system we are installing, Horizon Expert Orders™, made by McKesson Corporation, is based on a system developed at Vanderbilt University in Nashville,” says Dr. Patrick J. Hogan, M.D., an interventional cardiologist at SLEH and director of the Learning Resource Center of the Texas Heart Institute (THI). “As the first beta-testers, we have been evaluating the system for the past 12 months and plan to have it available hospital-wide within 2 years.”

“The system will help physicians make decisions by presenting clinically relevant information about a specific patient’s condition, along with treatment protocols and evidence-based guidelines,” explains Dr. Hogan. “The POE system has been enthusiastically endorsed by The Leapfrog Group, a nationwide consortium of more than 100 leading health-care-benefit providers that works with medical experts to identify problems in hospital systems and propose solutions for improving them,” explains Dr. Hogan.

“The POE system will improve patient safety, protect patient privacy, and enhance the quality of our medical records,” concludes Dr. Hogan. “It will allow our house staff to provide the most up-to-date patient data and will offer precise data regarding the use of hospital resources.”

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**Computerized Physician-Order-Entry System Will Streamline Clinical Care**

**Abstract:** A new computerized physician-order-entry system promises to improve the continuity of patient care while maximizing hospital resources.
Calendar of Events

TEXAS HEART INSTITUTE CONTINUING MEDICAL EDUCATION SYMPOSIUM

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

SELECTED UPCOMING NATIONAL AND INTERNATIONAL MEETINGS

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

American Heart Association
Scientific Sessions 2003
November 9–12, 2003
Orlando, Florida
Abstract submission begins: April 1, 2003