HeartWATCH

SPRING 2003

A NEWSLETTER PRODUCED BY THE TEXAS HEART INSTITUTE

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

T-Wave Alternans Testing: A New Noninvasive Means of Preventing Sudden Cardiac Death

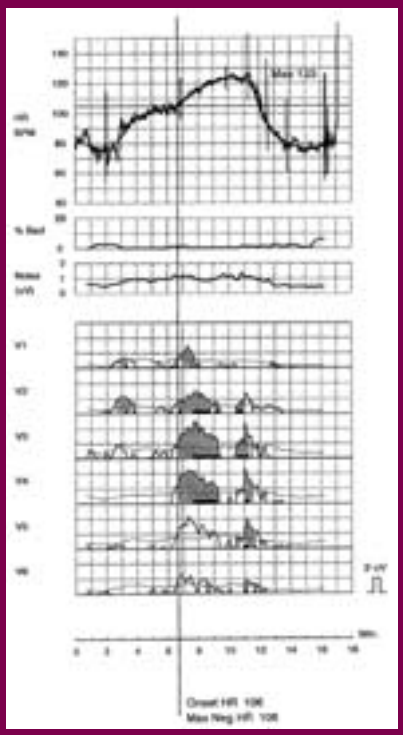
Abstract: A sensitive new noninvasive stress test is allowing cardiologists to detect T-wave alternans, a subtle electrophysiologic abnormality that predicts an increased risk of sudden cardiac death.

At least 300,000 Americans per year succumb to sudden cardiac death (SCD). Some of these individuals, who occasionally include well-known athletes, are young and apparently healthy at the time of their death. Usually, however, they have a history of myocardial infarction, congestive heart failure, cardiomyopathy, or syncope.

During the past 2 decades, implantable cardioverter-defibrillators (ICDs) have improved the treatment of patients at risk for SCD; but no noninvasive, cost-effective diagnostic test has been available for identifying these patients. Conventional noninvasive procedures, such as exercise stress testing and echocardiography, lack the specificity and predictive ability necessary for fulfilling this goal. In contrast, electrophysiologic testing can provide a definitive diagnosis but is too invasive, expensive, and time-consuming for widespread use. Recently, however, investigators have shown that a subtle electrocardiographic abnormality known as T-wave alternans (TWA) can identify patients with arrhythmias that might lead to SCD.

"In TWA, the morphology of the T wave alternates with every other heartbeat," says Arthur J. Springer, M.D., a cardiologist in the Texas Heart Institute's Department of Adult Cardiology. "Originally described in 1909, this abnormal pattern was widely regarded as an electrocardiographic oddity that had no particular clinical importance. In the 1980s, however, computer simulations suggested that TWA provides the electrical milieu that can lead to ventricular tachycardia (VT) and ventricular fibrillation (VF), the most common precipitating causes of SCD."

On the basis of this finding, a sensitive, noninvasive method for diagnosing TWA has been introduced. This approach, developed at Harvard University and the Massachusetts Institute of Technology, uses the fast Fourier transform spectral method in combination with special electrodes and noise-reduction software (Cambridge Heart, Inc., Bedford, MA) to measure microvolt-level TWA during exercise.



T-wave alternans in precordial region.

"The test is used for risk stratification of patients with a history of myocardial infarction and/or left ventricular dysfunction, for evaluation of syncope, and for identification of apparently healthy athletes who may be at risk for SCD," says Dr. Springer. "Nevertheless, it is not yet clear whether this approach can predict SCD in patients with right ventricular arrhythmias, such as those with right ventricular dysplasia or congenital heart disease."

During the test, 7 standard electrodes are placed on the patient's chest in the conventional 12-lead configuration, and 7 special electrodes are positioned in the Frank orthogonal configuration. The patient then undergoes exercise or pharmacologic stress to elevate the heart rate to 90–110 beats per minute, thereby increasing the sensitivity of the test. (Alternatively, atrial pacing may be used for this purpose, but then the test is no longer totally noninvasive.) Once the desired heart rate has been reached, exercise is continued for at least 3 minutes, after which electrocardiography is performed with the patient seated for another 3 minutes.

Dr. Springer emphasizes that "patients with TWA are at risk for SCD and should undergo invasive testing to further clarify their condition and determine whether they need drug therapy or an ICD. Conversely, patients without TWA are not at risk for SCD and need no further testing. This method has proved equal or superior to conventional electrophysiologic testing in predicting SCD. As the only procedure of its kind approved by the Food and Drug Administration, TWA testing is now covered by Medicare."

In addition, researchers are evaluating an even newer approach, based on ambulatory electrocardiographic monitoring, that uses a different algorithm. Because this method does not require special electrodes or attainment of a target heart rate, it would allow TWA to be detected while the patient goes about his or her daily activities. ●

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Clinical Trials Update

On February 24, 2003, surgeons at the Texas Heart Institute and St. Luke's Episcopal Hospital (THI/SLEH) performed the 10th implantation worldwide of an AbioCor® Implantable Replacement Heart (ABIOMED, Inc., Danvers, MA). It was the third such implantation performed at THI/SLEH as part of an ongoing, FDA-sponsored multicenter clinical trial that began in July 2001 and that will include a total of 15 patients. The longest-lived AbioCor recipient survived 512 days.

Autologous Bone Marrow Transplantation Shows Potential for Treating Severe Ischemic Heart Disease

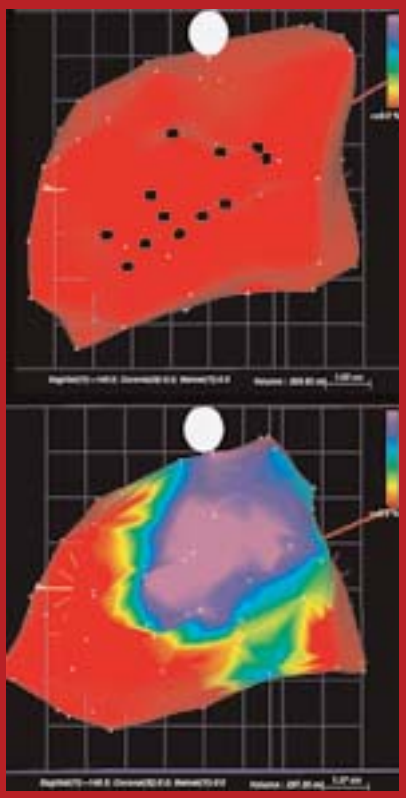
Abstract: In areas of hibernating myocardium, myocardial perfusion improved significantly after transendocardial injection of autologous bone marrow mononuclear cells.

Stem cell therapy has been proposed as a possible treatment for patients with ischemic heart failure. In the Summer 2002 issue of *Heart Watch* (www.texasheartinstitute.org/hwatch.html), we described the initial stages of a collaborative study between physicians at the Texas Heart Institute (THI) and physicians at Hospital Procardiaco in Brazil. These researchers hoped to learn whether transendocardial injection of autologous stem cells could promote the growth of new blood vessels and, thus, supply oxygen to damaged heart muscle.

"The initial results are in, and the outcome looks positive," says Emerson C. Perin, M.D., THI's director of New Cardiovascular Interventional Technology and lead investigator in the study.

The prospective, controlled study included 21 patients with severe ischemic heart failure who were ineligible for any other form of revascularization therapy; the first 14 patients were enrolled in the treatment group, and the last 7 patients were enrolled in the control group. All patients had to be receiving maximal medical therapy at the time of enrollment. Both groups underwent rigorous baseline evaluations including complete clinical and laboratory assessment, exercise stress testing, 2-D Doppler echocardiography, and dipyridamole SPECT perfusion scanning.

The methods used to prepare and inject the cells and to determine areas to be treated worked very well, according to Dr. Perin. About 4 hours before the cell-injection procedure, approximately 50 mL of bone marrow was aspirated from the posterior iliac crest. The bone marrow mononuclear cells were isolated, washed, and resuspended. About an hour before the cells were ready to be injected, patients underwent left heart catheterization with biplane left ventricular angiography for electromechanical mapping (EMM), which was used to determine the area to be treated. The general ischemic area identified by the SPECT study was matched with areas of viable myocardium, identified by EMM. Within this region, areas were considered viable for treatment if the unipolar voltage was >6.9 mV and local linear shortening was (preferably) less than 12%—an indication of hibernating myocardium.



Electromechanical maps (posterolateral view) of the same patient at baseline and 4 months' follow-up after injections (sites in black) in areas of poor contractility. The follow-up map shows marked improvement in contractile function in the areas of injection (purple, blue, and green areas). (From *Circulation* 2003; 107:935-938; with permission from the American Heart Association.)

About 1 mL of cells was loaded into the needle of a NOGA injection catheter. "Although we have not yet determined the ideal dosage, we used about 25 million cells per patient, divided into 15 injections," says Dr. Perin. None of the 14 treated patients had major periprocedural complications, and all of the patients were discharged, per protocol, on the third postprocedural day.

The study is nearing its 6-month follow-up point, and the results remain good. The most recent official follow-up evaluation was at 4 months. At that time, according to Dr. Perin, "both cardiac function and cardiac geometry had improved. There was a 31% relative increase in the ejection fraction, a significant decrease in the end-systolic volume, and a 73% reduction in the total reversible defect."

On the basis of their early results, Dr. Perin and his colleagues believe that transendocardial injection of autologous bone marrow mononuclear cells holds great promise for patients with severe ischemic heart disease who have areas of viable myocardium.

"Our work shows that stem cells can enhance perfusion in areas where the myocardium is hibernating but capable of recovering once perfusion is restored. As yet, we aren't positive how this happens, but we speculate that a complicated sequence of events, including cell-to-cell interactions, ultimately results in angiogenesis. We saw increased contractility at the injection sites, which was likely due to the improved perfusion in these areas." ●

For more information:

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Contents

Algorithm for Managing Perioperative Bleeding in Clopidogrel Recipients Undergoing CABG

Abstract: THI researchers have developed an algorithm for managing perioperative bleeding and platelet therapy in clopidogrel recipients undergoing elective coronary artery bypass procedures.

Because of its established ability to protect against ischemic events, the platelet-aggregation inhibitor clopidogrel (Plavix®) is now commonly used in the management of cardiovascular disease. However, because of the long time to platelet recovery after this agent is stopped (3–5 days), clopidogrel recipients scheduled for coronary artery bypass grafting (CABG) are at increased risk of excessive perioperative bleeding. With few historical clinical data to guide them, physicians have not been sure when to discontinue clopidogrel before operation or whether the risk of bleeding with clopidogrel outweighs the risk of an ischemic event without it. In addressing the problem, clinicians at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH) have developed an algorithm that improves the management of perioperative bleeding and platelet therapy in such patients.

"Despite the risks of excessive postoperative bleeding and the general consensus that clopidogrel be stopped 7 to 10 days before operation," says Nancy A. Nussmeier, M.D., director of Cardiovascular Anesthesia Research at THI, "many patients continue taking clopidogrel up to the day of surgery, even if the procedure is completely elective. Consequently, more of them require transfusion, straining already low blood supplies and increasing their hospital stay."

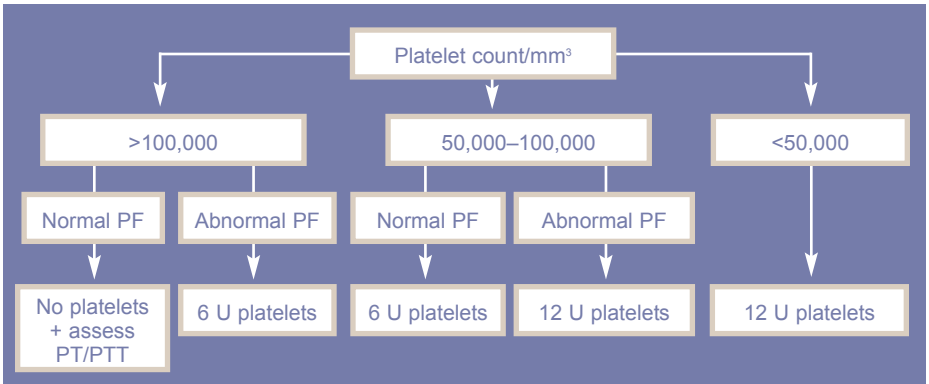
To improve perioperative transfusion support for these patients, Dr. Nussmeier and THI cardiovascular anesthesiologist LiQian Chen, M.D., Ph.D., recently led a prospective study of 90 patients who underwent elective CABG at THI/SLEH. Half of the patients had received clopidogrel within 7 days before operation. Previous studies showed that use of clopidogrel within that period increased the number of transfusions and the volume of chest-tube drainage. However, in those studies, says Dr. Nussmeier, the need for transfusion was determined empirically rather than by any uniform laboratory or clinical criteria.

Consequently, the THI researchers first established an algorithm to guide perioperative transfusion. The algorithm's laboratory criteria included the hemoglobin level and a complete coagulation profile (i.e., prothrombin time [PT], activated partial thromboplastin time [PTT], platelet count, and platelet function determined by techniques including adenosine diphosphate [ADP] aggregometry and automated Platelet Function Analyzer 100 [PFA-100] analysis). The coagulation profile was repeated serially in each patient. Red blood cells were transfused when the hemoglobin level dropped below 8 g/dL, fresh frozen plasma units when indicated by PT and PTT, and platelets according to the algorithm (see figure).

"In addition to the laboratory tests," says Dr. Chen, "the clinical criterion for transfusion was excessive microvascular bleeding in the operating room or chest-tube drainage of greater than 250 mL/hour after the first hour in the intensive care unit."

"The study," says Dr. Chen, "allowed us to demonstrate that half the patients in the clopidogrel group did not require platelet transfusions at all for adequate hemostasis, that measurements of platelet aggregation enabled us to predict which patients would require transfusion, and that patients with bleeding due to clopidogrel were successfully treated with blood products as directed by the algorithm. We also confirmed that postoperative bleeding was significantly greater in patients who had taken clopidogrel than in controls."

"Our algorithm allowed us to conserve scarce blood resources and manage bleeding promptly and consistently in clopidogrel recipients," says Dr. Nussmeier. "Consequently, we now use this algorithm in managing all bleeding in our cardiac surgery patients. However, we have yet to determine how early it is safe to discontinue clopidogrel before operation and how to prevent extensive bleeding in those patients who cannot discontinue the drug." ●



Bleeding management algorithm for platelet transfusion. PF, platelet function; PT, prothrombin time; PTT, partial thromboplastin time. Normal PF, >50% aggregation (ADP aggregometry) and <128-second closure time (PFA-100 analysis); abnormal PF, <50% aggregation and >128-second closure time.

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Assessing Revascularization Options for Patients With Diabetes

Abstract: For the growing diabetic population, percutaneous intervention and surgery continue to pose unique risks.

Diabetes is assuming epidemic proportions, necessitating increasingly complex management of adult patients with this disease, particularly those who require revascularization for atherosclerosis. Consequently, cardiovascular centers such as the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH) are providing highly specialized care for diabetic patients who require percutaneous or surgical interventions.

"Choosing the best treatment for patients with diabetes and atherosclerosis, particularly those who are insulin-dependent, is a constant challenge for cardiologists," says James M. Wilson, M.D., director of Cardiology Education at THI/SLEH and assistant chief of Cardiology at SLEH. "Although new modes of revascularization are constantly being explored, diabetic patients continue to fare worse than their nondiabetic counterparts."

Although percutaneous transluminal coronary angioplasty (PTCA) was rapidly adopted and popularized because it is less invasive than coronary artery bypass grafting (CABG), Dr. Wilson says that PTCA has not proved as effective as CABG in the long run.

"Diabetes not only fuels the progression of coronary atherosclerosis," notes Dr. Wilson, "but it is also closely associated with medium-term PTCA failure. In fact, restenosis is so prevalent among diabetic PTCA patients that many of them have occlusion of the treated vessel within 6 months. Two thirds of those with multivessel disease are eventually referred for CABG."

In both diabetic and nondiabetic patients, surgical risk is often the reason for choosing PTCA. When Dr. Wilson reviewed THI's surgical database to assess the risk of myocardial infarction and stroke associated with a single revascularization procedure, he found that CABG is indeed more hazardous. Because patients who received stents had a greater mortality and risk of myocardial infarction, however, the outcomes of CABG versus PTCA were equivalent at 2 years, and CABG was more effective beyond 5 years.

"Clinicians must weigh greater procedural risk against better long-term performance," says Dr. Wilson.

Recent developments in percutaneous interventions, such as concomitant use of glycoprotein (GP) IIb/IIIa inhibition or drug-eluting stent procedures, may improve the survival of diabetic patients with multivessel disease.

> *"Although new modes of revascularization are constantly being explored, diabetic patients continue to fare worse than their nondiabetic counterparts."*
>
> *— James M. Wilson, M.D.*
> *Assistant Chief*
> *Cardiology*

The SIRIUS trial showed that, compared with conventional stents, sirolimus-coated stents dramatically reduced restenosis in patients with high-risk blockages. In addition, such stents reduced target-vessel failure (defined as cardiac death, myocardial infarction, or the need for revascularization) from 21% to 6.6%. The Food and Drug Administration will soon approve the sirolimus-eluting stent for use in lesions similar to those studied in the SIRIUS trial.

Despite these promising results, Dr. Wilson urges a conservative approach to treating diabetic patients with atherosclerosis. He cites firm evidence from the Bypass Angioplasty Revascularization Investigation (BARI) trial (*N Engl J Med* 1996;335:217–225) that the mortality of diabetic patients taking insulin or oral hypoglycemic agents is markedly lower after CABG using an internal mammary graft than after PTCA.

"Stenting leaves us dependent upon a diseased, diabetic coronary bed that is vulnerable to rapid, thrombotic disease progression. Surgical therapy restores a multifocal coronary circulation that may be more capable of maintaining myocardial perfusion during disease progression. No revascularization method is more reliable than an internal mammary graft to the left anterior descending artery," says Dr. Wilson.

"Diabetes worsens the prognosis of patients with atherosclerosis whether they are treated medically or surgically," he adds. "A randomized trial comparing outcomes after drug-eluting stent implantation and CABG is in the planning stages. Meanwhile, the evidence strongly suggests that patients with diabetes and multivessel coronary disease amenable to an internal mammary graft should be referred for CABG, while those ineligible for surgery are best treated percutaneously. Physicians should consider each patient individually, assessing both coronary morphology and comorbid conditions before proceeding with a management plan." ●

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Gene Polymorphisms in Myocardial Infarction Come Under Increasing Scrutiny

Abstract: As the tools for genetics-based research become more refined, the search intensifies for genes associated with increased risk of myocardial infarction.

Myocardial infarction (MI) is a leading cause of death in the United States and a major hindrance to quality of life. Both MI and its principal cause, coronary artery disease, arise from a complex interplay between environmental and behavioral risk factors and genetic factors resulting in hemodynamically significant stenosis, altered vasomotor control, and the potentially deadly disruption and thrombosis of vulnerable plaques. Consequently, as the tools for genetics-based research become more refined, so does the search for genes associated with an increased risk of MI.

The sheer size of the human genome is daunting (approximately 3 billion base pairs and at least 30,000 genes), but the search is made more manageable because variations among individuals occur in only 0.1% of the human genome. This small fraction contains variant regions called polymorphisms, most consisting of single base-pair substitutions in stretches of DNA. Because these single nucleotide polymorphisms (SNPs) often occur in genomic regions not involved in encoding proteins, they usually remain functionally silent and harmless. When they do occur in a coding region, however, they may affect not only the function of the proteins directly encoded but also the phenotypes produced by adjacent genes. Therefore, by looking at genomic variation between patients with and without a history of MI (or significant CAD), researchers hope to identify polymorphisms associated with an increased risk.

"Genotype association studies are being widely applied to untangle the genetic basis of MI," says Pierre Zoldhelyi, M.D., director of the Wafic Said Molecular Cardiology and Gene Therapy Research Laboratory at the Texas Heart Institute (THI). "However, because of the disease's complexity, the multiplicity of its environmental modifiers, and the small phenotypic effect of certain allelic variants, results have been mixed and have not yet generated risk markers that can be used routinely in clinical evaluation."

By focusing mainly on single candidate genes, earlier studies identified many potential risk markers, such as the ApoE gene associated with lipoprotein metabolism and the methylene tetrahydrofolate (MTHFR) gene associated with homocysteine metabolism. Now, genetics research is being done on a much larger scale, utilizing constantly expanding genomic databases (including the human genome map), established polymerase chain reaction assays that allow amplification of very small DNA samples, and emerging automated DNA-chip microarray technology that provides exponentially higher data output.

For example, Yamada and colleagues identified genotypes for 112 polymorphisms of 71 candidate genes in more than 5,000 Japanese individuals with or without a history of MI (*N Engl J Med* 2002;347:1916–1923). Culled from public databases, all 71 candidate genes had been previously tied to coronary artery disease, hypertension, diabetes, or hyperlipidemia. Three genes in particular appeared to warrant further study: connexin 37, involved in communication between vascular endothelial cells; stromelysin-1, involved in matrix metabolism; and plasminogen-activator inhibitor type 1, involved in fibrinolysis.

"Of particular interest to us here at THI are polymorphisms involved in the inflammation associated with plaque rupture and arterial thrombosis," says Dr. Zoldhelyi. "These include genes that encode mediators of inflammation, cell signaling, and fibrous cap weakening such as endothelial adhesion molecules, cytokines, and extracellular matrix-degrading enzymes."

Examples of Gene Polymorphisms Linked to Myocardial Infarction

Gene	Polymorphism	Findings
ApoE	ε4	Association with CAD and cardiovascular death
Connexin 37	C1019T	Significant association with MI risk in men
ICAM-1	Lys469Glu	Possible association with MI and CAD
E-selectin	Ser128Arg	Association with CAD in younger patients (<50 years)
MTHFR	677 C→T	Association with CAD and acute MI in several studies
P-selectin	Pro715	Possible protective role in MI
PAI-1	-657 4G/5G, HindIII-RFLP, $(CA)_n$	Marginal association of 657 4G/5G with MI in women
Stromelysin (MMP-3)	5A-1171/6A promoter polymorphism	Possible association of 5A allele with MI risk and of 6A allele with CAD progression; genotype-specific associations with CAD risk and smoking
PCAM (CD31)	Val125Leu, Asn563Ser	Association with MI and early CAD in small studies

CAD= coronary artery disease; ICAM = intercellular adhesion molecule; MI = myocardial infarction; MTHFR = methylene tetrahydrofolate; PAI = plasminogen-activator inhibitor; PCAM = platelet endothelial cell adhesion molecule.

The future clinical usefulness of disease-susceptibility gene markers in preventing MI remains controversial. Different groups have generated conflicting data on the clinical significance of many of the candidate genes, and several studies have noted that the effects of certain polymorphisms vary by sex, genetic background, or environmental modifiers.

"Despite the uncertainty," Dr. Zoldhelyi says, "the search for genetic risk markers is contributing significantly to our understanding of the molecular pathways leading to acute MI and to our ability to prevent MI and other lethal cardiovascular diseases." ●

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Medical Web Sites Are Helpful Tools for Busy Physicians

Abstract: The World Wide Web provides important electronic services and resources for all physicians, whether they are novice or seasoned Internet users.

The Internet has changed the practice of medicine by providing access to virtual libraries of medical textbooks and journals, Web-based courses such as continuing medical education (CME) activities, and forums for communicating with colleagues; increasing the efficiency of patient care; and allowing worldwide collaborative research among investigators. Moreover, many journals now prefer or require electronic manuscript submission.

According to the *2002 AMA Study on Physicians' Use of the World Wide Web*, in which 977 physicians were interviewed, two thirds of those who use the Web are online daily, a 24% increase from 1997. Physicians are also online 7.1 hours per week, up from 4.3 in 1997. The trend of Web use among physicians 60 years or older has also increased—65% now use the Web, compared with 43% in 1997.

"Physicians look for credible sites with evidence-based material and source identification," says Marjorie Jackson, manager of the Library and Learning Resource Center at the Texas Heart Institute (THI). "Physicians who were originally skeptical now find Web-based information useful."

The main obstacle to widespread physician use of the Web is that most physicians do not have time to search thousands of sites. Ms. Jackson has found trends among the sites that THI physicians find helpful.

"Surgeons-in-training appreciate sites with multimedia and Webcasts for viewing operative techniques and live operations," she says. "Others like interactive e-learning with real-time e-mail or CME test sites with instant results."

Following are some sites that might be of interest to physicians.

The Clinical Statements/Guidelines pages of the American College of Cardiology (ACC) and the National Guideline Clearinghouse (NGC) provide databases of evidence-based clinical practice statements and guidelines. The ACC site provides free access to, and downloading of, guidelines; the NGC site allows users to link to structured abstracts, compare 2 or more guidelines side-by-side, and participate in electronic forums.

For cardiothoracic surgeons, the nonprofit CTSNet (Cardiothoracic Surgery Network) has more than 40 participating organizations. Surgeons can research cases, access online journals, communicate with colleagues, submit manuscripts electronically to CTSNet-affiliated journals, and conduct private electronic meetings. CTSNet is open to all cardiothoracic surgeons, including those in training.

MDConsult charges users on a per-month or per-use basis but offers full-text reference books and journal articles, daily compilations of articles from more than 100 publications, synopses of medical news stories, and a comprehensive drug database. According to MDConsult, its users view 7 million pages of clinical content each month. Medical Matrix, a fee-based medical search engine and directory, provides access to peer-reviewed sites. A team of physicians and medical librarians rates all the sites within Medical Matrix. When the user enters a search term, more than 1.5 million linked pages are searched, and Medical Matrix guarantees that the results will be relevant.

"Fee-based sites provide good navigational tools, peer-reviewed content, and current, original information," says Ms. Jackson. "However, if users do not wish to pay and have time to search, they will often find equally impressive resources available for free."

Other sites that deserve mention are Angioplasty, a site about interventional cardiology; the National Heart, Lung, and Blood Institute's Cardiovascular Information for Health Care Professionals; the National Library of Medicine's PubMed; The Heart, which provides users with weekly e-mail updates and a conference center schedule; and Query Server, a time-saving Metasearch tool. ●

For more information:

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Helpful Web Sites for Physicians

Name	URL	Fee
ACC Clinical Statements/Guidelines	www.acc.org/clinical/statements.htm	Free online viewing; $5/reprint
Angioplasty	www.ptca.org	Free; registration required for mailing list
CTSNet	www.ctsnet.org	Free; subscription needed to access online journals
MDConsult	www.mdconsult.com	$349.95/year for core and cardiology sections; free trial available
Medical Matrix	www.medmatrix.org	$79/year; free 24-hour trial available
National Guideline Clearinghouse	www.guideline.gov	Free
NHLBI Cardiovascular Information for Health Care Professionals	www.nhlbi.nih.gov/health/prof/heart/index.htm	Free
Open Text Corporation's Query Server	www.queryserver.com/health.htm	Free demonstration site; fee-based institutional subscriptions available
NLM PubMed	www.ncbi.nlm.nih.gov/pubmed	Free
The Heart	www.theheart.org	Free; registration required for full site access

ACC, American College of Cardiology; CTSNet, Cardiothoracic Surgery Network; NHLBI, National Heart, Lung, and Blood Institute; NLM, National Library of Medicine; URL, universal resource locator.

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Cover: Fabergé egg donated by Fayez Sarofim 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 Symposium

Texas Heart Institute Influenza Infection and Excess Cardiovascular Mortality:
A Call for Clinical Trials
April 26, 2003
Houston, Texas
Program Director: S. Ward Casscells, M.D.

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

Selected Upcoming National and International Meetings

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

Society of Thoracic Surgeons 40th Annual Meeting
January 26–28, 2004
San Antonio, Texas

American College of Cardiology 53rd Annual Scientific Session
March 7–10, 2004
New Orleans, Louisiana
Abstract submission begins: August 1, 2003

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