Calendar of Events

**TEXAS HEART INSTITUTE CONTINUING MEDICAL EDUCATION SYMPOSIA 2002**

**Third Symposium on Congestive Heart Failure**
October 3–4, 2002
Texas Heart Institute—The Denton A. Cooley Building
Program Director: Sayed Feghali, M.D.

**Echocardiography in Congestive Heart Failure Patients**
October 4–5, 2002
Texas Heart Institute—The Denton A. Cooley Building
Program Director: Raymond Stainback, M.D.

**Controversies in Endovascular Treatment of Peripheral Vascular Disease**
November 16, 2002
Chicago, Illinois
Program Director: Zvonimir Krajcer, M.D.

**American Heart Association Satellite Symposium**
November 16, 2002
Chicago, Illinois
Program Director: James J. Ferguson III, M.D.; R. David Fish, M.D.; and James T. Willerson, M.D.

**SELECTED UPCOMING NATIONAL AND INTERNATIONAL MEETINGS**

**American Heart Association Scientific Sessions 2002**
November 17–20, 2002
Chicago, Illinois
Abstract deadline: Passed

**Society of Thoracic Surgeons 39th Annual Meeting**
January 31–February 2, 2003
San Diego, California
Abstract deadline: August 5, 2002

**American College of Cardiology 52nd Annual Scientific Session**
March 30–April 2, 2003
Chicago, Illinois
Abstract deadline: September 10, 2002

**International Society for Heart and Lung Transplantation 23rd Annual Meeting and Scientific Sessions**
April 9–12, 2003
Vienna, Austria
Abstract deadline: September 20, 2002

For information about any of the CME activities listed above, please contact cme@heart.thi.tmc.edu or call 832.355.2157.
One of every 2 women in the Western world will die of cardiovascular disease. Compared with men, women are typically shorter, weigh less, possess a smaller body surface area, and have smaller coronary arteries. “These factors alone are thought to increase the difficulty of coronary artery bypass grafting (CABG),” says Nancy A. Nussmeier, M.D., director of Cardiovascular Anesthesia Research at the Texas Heart Institute (THI). “Additionally, women develop angina or myocardial infarction later and tend to have more diffuse disease upon diagnosis, further increasing the risks and challenges of surgical intervention. Disconcertingly, cardiovascular disease–related mortality, while decreasing for men, is actually increasing for women.”

Disorder prevention messages are reaching men but seem to be too little, too late for women at risk for cardiovascular disease. To improve survival rates, cardiologists have progressively increased interventions for women in the last decade. Still, women tend to fare worse than men after cardiovascular surgery. “Women are rarely affected by coronary artery disease before menopause,” explains Dr. Nussmeier. “But women who do develop it are more likely to have diabetes, hypertension, congestive heart failure, obesity, and cerebrovascular or peripheral vascular disease. Postmenopausal women taking HRT and undergoing coronary artery bypass graft procedures had significantly improved in-hospital survival rates compared with women of the same age who had not been taking regular HRT. The effects may be most evident in cases of vascular injury,” Dr. Nussmeier emphasizes. “However, it is not yet clear whether survival is related to one or more specific cardiovascular benefits of estrogen or whether there is a selection or adherence bias at work, meaning that women who are willing to take a daily medication for prevention may have healthier lifestyles than women who don’t use hormones. While the findings are encouraging, more research is needed to clarify whether benefits of HRT are chronic or acute and how HRT can best be administered.”

Dr. Nussmeier plans to continue research designed to identify gender-based differences in the presentation and pathophysiology of cardiovascular disease and in interventional outcomes. Understanding specific risk factors and taking advantage of protective factors will help improve THI’s ability to care for patients of both sexes and may potentially save lives. “Women must be counseled as aggressively as men regarding their risk factors for cardiovascular disease,” Dr. Nussmeier says. “Primary care physicians who suspect coronary artery disease in their female patients should consider referring them to cardiologists early, when medication and lifestyle changes can yield positive results and surgical interventions are most likely to result in optimal outcomes.”

For more information: Dr. Nancy Nussmeier 832.355.2666

OPCABG + TMLR Performed Via a Left Thoracotomy

Abstract: In high-risk patients with coronary artery disease, OPCABG + TMLR, performed via a left thoracotomy, can relieve angina that is refractory to conventional medical and surgical therapy.

TO ACHIEVE MORE COMPLETE coronary revascularization, surgeons at the Texas Heart Institute (THI) are combining off-pump coronary artery bypass grafting (OPCABG) with transmyocardial laser revascularization (TMLR), performed via a left thoracotomy, in selected high-risk patients. According to O. H. Frazier, M.D., chief of Cardiopulmonary Transplantation and director of the Cullen Cardiovascular Research Laboratory at THI, “Neither OPCABG, TMLR, nor the left thoracotomy approach is new in itself, but these techniques have only recently been combined. Because each one offers specific advantages, they complement each other.”

The off-pump technique avoids use of the cardiopulmonary bypass (CPB) machine, which has been standardly used for coronary bypass operations since 1968. Although CPB allows the heart to be stopped and provides a quiet, bloodless operative field, it can result in neurologic problems, renal insufficiency, a whole-body inflammatory response, and other postoperative complications. By avoiding CPB, OPCABG benefits patients who are at high operative risk because of multivessel stenosis, advanced age, severe systemic disease, atherosclerosis of the ascending aorta, or functional impairment of various organs. Intraoperatively, the heart continues to beat, while the bypass site alone is immobilized.

Although OPCABG offers many advantages, it may not always allow complete revascularization, especially of the circumflex and posterior descending arteries, which can be hard to reach and immobilize. Also, OPCABG is unsuitable for diseased vessels that are small, intramyocardial, diffusely atherosclerotic, or calcified. For these reasons, adjunctive TMLR can be advantageous. Introduced clinically in 1981, TMLR creates multiple laser channels in the ischemic myocardium to improve cardiac perfusion, including blood flow to areas unsuitable for bypass grafting. “Although its mechanism is not completely clear,” states Dr. Frazier, “TMLR often alleviates angina that is unresponsive to conventional treatment. By combining OPCABG and TMLR, surgeons can revascularize all diseased areas of the myocardium.”

For these combined procedures, a left thoracotomy (instead of a standard median sternotomy) can be used. The incision is larger than a mini-thoracotomy but smaller than a standard sternotomy. This approach is particularly advantageous in patients with poor skin and soft-tissue coverage resulting from previous sternotomies, sternal wound complications, mediastinal irradiation, or a radical mastectomy. According to Dr. Frazier, “In such cases, the previous sternotomy site would be both hard to reopen (because of dense adhesions requiring extensive dissection) and hard to reaccess (because of the lack of healthy wound margins). Furthermore, a left thoracotomy involves no aortic cross-clamping or lifting of the heart, so this approach may benefit patients whose ascending aorta is calcified.”

In addition, the left thoracotomy is compatible with full or partial CPB, should it become necessary, and with the following other methods: fibrillatory arrest, moderate hypothermia, femoral or descending thoracic aortic cannulation, and creation of proximal anastomoses in the descending thoracic aorta or subclavian artery. Between October 2000 and May 2001, THI surgeons performed OPCABG + TMLR via a left thoracotomy in 17 patients. One patient died of ventricular fibrillation 8 days postoperatively. Of the 16 survivors, none had angina at hospital discharge. At follow-up examination a mean of 6 months after surgery, 15 patients remained angiina-free, and 1 patient had mild angina. None had to be in their hospital. Therefore, concludes Dr. Frazier, “In these high-risk patients, OPCABG + TMLR significantly relieved angina, with an acceptable mortality and no major morbidity.”

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Assessing the Role of Gender and Hormone Replacement Therapy in Cardiovascular Disease

Abstract: A new THI study shows that hormone replacement therapy in postmenopausal women may dramatically improve survival rates after coronary bypass grafting.

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For more information: Dr. Nancy Nussmeier 832.355.2666


Operative Mortality (%) 5
Men
Women
1
2
3
Body Surface Area (m2)
In building up one of the world’s largest series of mitral valve repairs, surgeons at the Texas Heart Institute (THI) have developed simpler, more reliable techniques for treating mitral valve regurgitation. Since the 1960s, mitral valve replacement has been widely used to treat regurgitation. However, with the development of newly designed valvuloplasty rings, increasing surgical experience, and evidence of the durability of results, mitral valve repair has become the preferred method of treatment.

“In the early days of mitral valve surgery, repair wasn’t as simple as it is now,” continues Dr. Ott. “Useful surgical techniques had not yet been established.”

Experience here and elsewhere has shown that valve repairability greatly depends on pathology and on the surgeon’s familiarity with the repair technique. “Because mitral valve repair involves more ‘art’ than ‘science,’ experience counts for a great deal in obtaining good results,” explains Dr. Ott. Since 1980, THI surgeons have gained extensive experience in performing more than 3,000 mitral valve repairs.

During this period, they have introduced several technical advances, including the use of cost-effective annuloplasty rings fashioned from Dacron tube grafts and a technique for repairing prolapsing valves that have ruptured or elongated chordae. This technique involves wedge resection of the posterior leaflet and continuous suturing of an annuloplasty ring in place. According to Dr. Ott, “Annuloplasty alone is enough in about 60% of cases, particularly when the mitral disorder is attributable to ischemic heart disease. However, in the rest of the cases, partial leaflet resection is also required. We have achieved excellent results with wedge resection of the posterior leaflet.”

“Though it’s more common elsewhere to use larger rings,” continues Dr. Ott, “we have noted that the smaller rings are highly effective in improving valve competency and do not result in valve stenosis. Our long-term success rate for valve repair is excellent, and exten-sive anticoagulation is seldom required.”

In patients undergoing valve repair alone, the mortality is low (less than 1% in some subgroups at THI). When mitral valve repair is combined with procedures such as coronary artery bypass grafting or the Maze procedure, the mortality increases according to the patient’s age and primary disease.

Many of these patients are gravely ill with combined valvular and coronary artery disease and may have a poorly functioning heart muscle. Under these circumstances, the combined procedures can be life-saving,” states Dr. Ott.

He believes that because of its simplicity and reproducibility, the continuous suture repair technique developed at THI will one day lend itself to robotic surgery because this technique would require fewer, less intricate knot-tying maneuvers on the part of the robot. In Dr. Ott’s opinion, “Mitral valve repair is well suited for robotic techniques, and the refinement of robotic devices and methods could revolutionize the surgical treatment of mitral valve disease.”

For more information:
Dr. David Ott
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Physicians and scientists at the Texas Heart Institute (THI) are extending stem cell research from the laboratory to the clinic in an ongoing effort to find effective treatments for heart failure and other forms of end-stage heart disease.

In a collaborative Brazilian study, 10 South American patients with congestive heart failure (CHF) have received a stem cell treatment utilizing their own bone marrow cells. Four of the patients received the treatment in December 2001; the others, in late April 2002. Their post-treatment course is being compared with the natural history of CHF in 5 control patients.

“Clearly this is a work in progress, and it’s still very early,” cautions James T. Willerson, M.D., medical director and director of Cardi- ology Research at THI. “We still need larger numbers of patients in the treatment and con-trol groups. Although we are encouraged and optimistic, we have no firm conclusions at this time.”

The clinical study in Brazil arose directly from laboratory research conducted at THI by Dr. Willerson, Yin J. Geng, M.D., Ph.D., di-rector of THI’s Atherosclerosis Research Lab- oratory; and Emerson C. Perin, M.D., director of New Intervventional Cardiovascular Tech-nology. After injecting fluorescently labeled canine embryonic stem cells into failing canine hearts and tracking the cells’ differ- entiation and disposition, the research team observed a 30% reduction in cardiac scar tissue within 2 weeks. In another study, stem cells injected into failing canine hearts improved heart function, as assessed by ultra- sound, within 1 month.

The immediate clinical goal is to replace dam-aged heart muscle cells and promote the growth of new blood vessels that will supply oxygen to damaged heart muscle. The long-term goal is to use stem cells as vectors for delivering genes into the failing heart in order to correct genetic abnormalities (e.g., defects in ion pumps, sarco-plasmic reticulum, and cardiac cell membrane receptors), promote blood vessel formation, and protect against oxidative injury.

The clinical treatment uses autologous stem cells harvested from the patient’s own bone marrow. These cells cost little to obtain, pose no threat of rejection, and keep the present work within the current regulatory boundaries of stem cell research in the United States.

“When we harvest the bone marrow, we can select the population of stem cells that we expect will develop into the physiological structures we want. We process the bone mar-row cells for about 3 hours and then inject them into the heart,” explains Dr. Perin, who is performing the clinical procedures in Brazil.

To inject the stem cells, the research team is currently using the NOGA electromagnetic mapping system (Cardios, Miami Lakes, FL). Purchased by THI 3 years ago for diagnostic purposes, this technology was considered too invasive for widespread use but has proved ideal for use in stem cell transplantation.

Through an incision in the femoral artery, doctors can thread a catheter into the left ven-tricle, measure the electrical and kinetic capa-bilities of the heart, and pinpoint damaged or weakened areas of the heart muscle. The same catheter can then be used to deliver millions of stem cells to damaged areas.

“The process is somewhat like a video game. The NOGA system gives us a real-time, 3-dimensional, color-coded image, so we can target the treatment sites within a millimeter of precision,” says Dr. Perin. THI’s stem cell researchers are now seeking U.S. Food and Drug Administration approval for clinical use of this therapy here in the United States.

We expect to publish the initial results of the experimental therapy in the next 6 months,” says Dr. Perin, “and we hope to make the treat-ment available to patients here at the Texas Heart Institute by the end of 2002.”

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Dr. James Willerson
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Insights Into Vulnerable Plaque Are Changing How Physicians Detect and Treat Heart Disease

Physicians have long believed that atherosclerosis gradually and progressively leads to complete arterial occlusion and, consequently, to myocardial infarction (MI). However, they now realize that angiographically moderate lesions are more likely to lead to acute coronary syndromes. As a result, researchers have a new scenario for the occurrence of MI: rupture of the thin, fibrous cap that covers a vulnerable atherosclerotic plaque.

Studies have established the role of inflammation in the initiation, progression, and rupture of vulnerable plaque. Absorption of circulating lipids or acute arterial wall changes abnormal endothelial behavior and cytokine release. Cytokines attract inflammatory monocytes that penetrate the arterial walls and absorb lipids, eventually coalescing to form a soft, inflammatory lesion with a thin, fibrous cap. Smooth muscle cells then decrease the synthesis of new collagen fibers. The macrophage activity increases the synthesis of proteases, which break down the collagen and elastin in the plaque’s extracellular matrix, weakening the fibrous cap and predisposing it to rupture. Upon rupture, the thrombogenic contents of the plaque join with circulating clotting agents in the bloodstream, creating a potentially fatal clot.

The focus is now on detecting such plaque, minimizing inflammation, and thereby preventing MI. These plaque lesions are usually moderate in size and buried inside the arterial wall, they are hard to detect, and their composition cannot be easily characterized. Researchers are experimenting with intravascular ultrasound, angiography, and magnetic resonance imaging to detect vulnerable plaques and to identify those most likely to rupture.

“Surprisingly, the tests rely on to gauge the severity and risk of coronary disease—stress tests and angiography—are not very useful as predictors of MI,” says James M. Wilson, M.D., assistant chief of Cardiology and co-director of Cardiology Education for St. Luke’s Episcopal Hospital. They give an accurate estimate of an individual’s chances of dying of MI but not of where or when that infarction may occur.

Having discovered temperature variations in plaques surgically removed from excised carotid arteries of rabbits, researchers at the Texas Heart Institute (THI) are testing infrared technology as a way to detect these “hot” plaques.

“Atherosclerotic plaques at risk of rupture are inflated and, therefore, show a slight increase in temperature,” says James T. Willerson, M.D., medical director and director of Cardiology Research at THI and a co-investigator in the project. “If these plaques can be identified, we can treat them, thereby preventing heart attack and stroke.”

In addition, two large studies have proved that low-grade, chronic inflammation indicated by elevated levels of the inflammatory marker C-reactive protein (CRP) is another effective way to predict the risk of atherosclerotic complications and may be useful as an added screening tool.

“Case-control studies from the Physician’s Health Study have provided evidence that optimal screening for occult coronary atherosclerosis and increased risk of MI should combine lipid studies, clinical history, and an inflammatory marker such as CRP,” says Dr. Wilson.

Meanwhile, the goal of therapy is to stabilize vulnerable plaque. CRP levels can be lowered through diet, exercise, and smoking cessation. Preliminary studies show that statins can also lower CRP levels, possibly because these agents have anti-inflammatory effects on nonatherosclerotic vulnerable plaque. In addition, statins appear to reduce the thrombogenicity of ruptured plaques by decreasing expression of the tissue factor that initiates clotting.

“Our medical armamentarium includes aspirin, clopidogrel, statins, and ACE inhibitors,” says Dr. Wilson. “Three of these four drugs should probably be given to any patient with atherosclerosis, regardless of whether the patient has yet had a true clinical event. However, intensive medical therapy is costly and not without risk, which underscores how important accurate identification of subclinical disease is for assessing the near-term risk of MI.”

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Surgical or Endovascular Repair of Abdominal Aortic Aneurysms at Risk of Rupture

Even though patients with abdominal aortic aneurysms (AAAs) can live for years without intervention, in many cases their aneurysms will continue to expand until the risk of rupture exceeds the risk of repair. At that point, intervention is needed. Ruptured AAAs cause an estimated 15,000 deaths each year, and up to 9% of people over 65 years old may have asymptomatic AAAs. According to the surgical literature, the typical AAA expands in diameter an average of 0.6 cm a year and should be repaired when it reaches 5 cm in diameter. In a recent editorial (May 9, 2002), the New England Journal of Medicine agreed that this limit might even be reasonably extended to 5.5 cm.

“Based on our own clinical experience, surveillance with imaging of abdominal aortic aneurysms less than 4.5 cm in diameter is a wise course to follow in most cases,” says George J. Reul, M.D., associate chief of Cardiovascular Surgery at THI. “When the time comes for intervention, patients will have an excellent chance of a successful repair by either surgical or endovascular means and a return to a normal lifestyle.”

Open surgical repair is well established as the standard of care for AAAs, but the endovascular alternative is fast gaining in attention and popularity. Physicians at THI are experienced in both approaches.

“Surgical repair of the aorta is always a challenge, especially now as patients are coming to us older and sicker and often with coexisting vascular disease and other morbidities,” says Dr. Reul. “We have found, however, that most complications are preventable. The overall operative mortality, as shown in a recent series of 716 surgical patients at THI, remains relatively low at 2.3%; when ruptured aneurysms and complex suprarenal aneurysms are excluded, the mortality dips to 1.4%. Endovascular repair of an AAA is a relatively new technique, having been first performed in 1991 by Parodi and associates in Argentina. Since then, this minimally invasive approach has slowly gained acceptance, mainly because of its potential for avoiding the morbidity and mortality associated with surgery and anesthesia. Cardiologists at THI have been intimately involved in the clinical testing of several endoluminal stent grafts for the repair of AAAs (including Medtronic’s AneurX and Guidant’s Ancure).”

“These clinical trials have shown that endovascular repair can shorten the surgery and anesthesia time, lessen operative blood loss, reduce serious adverse side effects by 50%, and hasten the patient’s return to a normal lifestyle,” says Zvonimir Krajcer, M.D., co-director of the Peripheral Vascular Disease Service at THI. Dr. Krajcer and his team have performed endovascular repairs with various stent grafts in 442 patients, achieving a technical success rate of 99%. They are now trying to minimize the procedure’s invasiveness and to expand its applications by pioneering the percutaneous repair of AAAs.”

“The best of our knowledge,” says Dr. Krajcer, “THI is the only institution in the United States that is repairing these aneurysms with stent grafts percutaneously under local anesthesia.”

Despite its promise and applicability to high-risk patients, endovascular repair has some limitations. Stent grafts cannot be used in patients with narrow, tortuous arteries or aneurysms that originate too close to the renal arteries. An endoleak (i.e., blood flow into the aneurysm sac after repair) occurs in roughly 20% of cases. In most instances, the endoleak is due to branch flow or collateral flow and does not cause the AAA to expand; if an endoleak does cause expansion, though, it can often be repaired without surgery.

Surgical or Endovascular Repair of Abdominal Aortic Aneurysms

Abstract: Many cardiovascular specialists are now focused on detecting vulnerable plaque, minimizing inflammation, and thereby preventing myocardial infarction.

Abstract: Abdominal aortic aneurysms at risk of rupture can be repaired by surgical or endovascular means.

For more information:
Dr. Zvonimir Krajcer
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Dr. George Reul
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Abstract:

Many cardiovascular specialists are now focused on detecting vulnerable plaque, minimizing inflammation, and thereby preventing myocardial infarction.

Insights Into Vulnerable Plaque Are Changing How Physicians Detect and Treat Heart Disease

Surgical or Endovascular Repair of Abdominal Aortic Aneurysms at Risk of Rupture

Abstract:

Abdominal aortic aneurysms at risk of rupture can be repaired by surgical or endovascular means.

Even though patients with abdominal aortic aneurysms (AAAs) can live for years without intervention, in many cases their aneurysms will continue to expand until the risk of rupture exceeds the risk of repair. At that point, intervention is needed. Ruptured AAAs cause an estimated 15,000 deaths each year, and up to 9% of people over 65 years old may have asymptomatic AAAs. According to the surgical literature, the typical AAA expands in diameter an average of 0.6 cm a year and should be repaired when it reaches 5 cm in diameter. In a recent editorial (May 9, 2002, the New England Journal of Medicine), the authors opined that this limit might even be reasonably extended to 5.5 cm.

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Endovascular repair, which has slowly gained acceptance, mainly because of its potential for avoiding the morbidity and mortality associated with surgery and anesthesia. Cardiologists at THI have been intimately involved in the clinical testing of several endoluminal stent grafts for the repair of AAAs (including Medtronic’s AneuRx® and Guidant’s Ancure®). Their collective experience provides evidence that such treatments are safe, effective, and have been widely adopted in Europe.

For more information:

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Mitral Valve Repair at THI Has Been Made Simpler and More Reliable

Abstract: In building up a large experience with mitral valve repair, THI surgeons have developed simple, reliable techniques for treating mitral valve regurgitation.

In building up one of the world’s largest series of mitral valve repairs, surgeons at the Texas Heart Institute (THI) have developed simpler, more reliable techniques for treating mitral valve regurgitation. Since the 1960s, mitral valve replacement has been widely used to treat regurgitation. However, with the development of newly designed valvuloplasty rings, increasing surgical experience, and evidence of the durability of results, mitral valve repair has become the preferred method of treatment. In the early days of mitral valve surgery, repair wasn’t the default: “Bicuspid mitral valve surgery had not yet been established,” says Dr. Ott. “However, as it became clear that prosthetic valves weren’t perfect and often created circulatory and mechanical complications of their own, we and others began to look for dependable ways to repair diseased valves, especially those that were leaking and nonfunctional. It also became clear that repair was better than replacement at preserving left ventricular function after surgery.”

Experience here and elsewhere has shown that valve reparability greatly depends on pathology and on the surgeon’s familiarity with the repair technique. “Because mitral valve repair involves more ‘art’ than ‘science,’ experience counts for a great deal in obtaining good results,” explains Dr. Ott. Since 1980, THI surgeons have gained extensive experience in performing more than 3,000 mitral valve repairs.

During this period, they have introduced several technical advances, including the use of cost-effective annuloplasty rings fashioned from Dacron tub grafts and a technique for repairing prolapsing valves that have ruptured or elongated chordae. This technique involves wedge resection and pinpoint repair of the posterior leaflet, use of a smaller (25-28 mm) annuloplasty ring, and continuous suturing around the ring to secure it in place.

According to Dr. Ott, “Annuloplasty alone is enough in about 60% of cases, particularly when the mitral disorder is attributable to ischemic heart disease. However, in the rest of the cases, partial leaflet resection is also required. We have achieved excellent results with wedge resection of the posterior leaflet.”

“Though it’s more common elsewhere to use larger rings,” continues Dr. Ott, “we have noted that the smaller rings are highly effective in lessening valve competency and does result in valve stenosis. Our long-term success rate for valve repair is excellent, and exten- sive anticoagulation is seldom required.”

In patients undergoing valve repair alone, the mortality is low (less than 1% in some subgroups at THI). When mitral valve repair is combined with procedures such as coronary artery bypass grafting or the Maze procedure, the mortality increases according to the patient’s age and primary disease.

Many of these patients are greatly ill with combined valvular and coronary artery disease and may have a poorly functioning heart muscle. Under these circumstances, the combined procedures can be life-saving,” states Dr. Ott. He believes that because of its simplicity and reproducibility, the continuous suture repair technique developed at THI will one day lend itself to robotic surgery because this technique would require fewer, less intricate knot-tying maneuvers on the part of the robot. In Dr. Ott’s opinion, “Mitral valve repair is well suited for robotic techniques, and the refinement of robotic devices and methods could revolutionize the surgical treatment of mitral valve disease.”

For more information:

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Clinical Trials Update

Interventional cardiologists at THI are continuing research on drug-coated and drug-eluting stents, a new generation of devices that may significantly reduce the likelihood of restenosis after percutaneous coronary intervention. Following the encouraging SIRIUS trial of rapamycin (sirolimus)-coated stents (see Spring 2002 Interventional Cardiology), researchers here, led by Dr. David Fish, M.D., are now enrolling patients in the TAXUS IV-SR trial. This is a large randomized, controlled study of THI’s Atherosclerosis Research Laboratory and Emerson C. Perin, M.D., director of New Interventional Cardiovascular Technology. After injecting fluorescently labeled canine embryonic stem cells into failing canine hearts and tracking the cells’ differentiation and disposition, the research team observed a 30% reduction in cardiac scar tissue within 2 weeks. In another study, stem cells injected into failing canine hearts improved heart function, as assessed by ultrasound, within 1 month.

The immediate clinical goal is to replace damaged heart muscle cells and promote the growth of new blood vessels that will supply oxygen to damaged heart muscle. The long-term goal is to use stem cells as vectors for delivering genes into the failing heart in order to correct genetic abnormalities (e.g., defects in ion pumps, sarco- plasmic reticulum, and cardiac cell membrane receptors), promote blood vessel formation, and protect against oxidative injury. The clinical treatment uses autologous stem cells harvested from the patient’s own bone marrow. These cells cost little to obtain, pose no threat of rejection, and keep the present work within the current regulatory boundaries of stem cell research in the United States.

“We expect to publish the initial results of the experimental trials in the next 6 months,” says Dr. Perin, “and we hope to make the therapy available to patients here at the Texas Heart Institute by the end of 2002.”

For more information:

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Physicians and scientists at the Texas Heart Institute (THI) are extending stem cell research from the laboratory to the clinic in an ongoing effort to find effective treatments for heart failure and other forms of end-stage heart disease. In a collaborative Brazilian study, 10 South American patients with congestive heart failure (CHF) have received a stem cell treatment utilizing their own bone marrow cells. Four of the patients received the treatment in December 2000; the others, in late April 2002. Their post-treatment course is being compared with the natural history of CHF in 5 control patients. “Clearly this is a work in progress, and it’s still very early,” cautions James T. Willerson, M.D., medical director and director of Cardiology Research at THI. “We still need larger numbers of patients in the treatment and control groups. Although we are encouraged and optimistic, we have no firm conclusions at this time.”

The clinical study in Brazil arose directly from laboratory research conducted at THI by Dr. Willerson; Yong J. Geng, M.D., Ph.D., director of THI’s Atherosclerosis Research Laboratory; and Emerson C. Perin, M.D., director of THI’s Atherosclerosis Research Laboratory. Through basic research at THI and collaborative clinical studies in Brazil, researchers are exploring stem cell therapy as a treatment for heart failure.

Abstract: Through basic research at THI and collaborative clinical studies in Brazil, researchers are exploring stem cell therapy as a treatment for heart failure.

Mitral valve repair involving wedge resection of the posterior leaflet and continuous suturing of an annuloplasty ring in place.

Canine stem cells before injection into the canine heart. Blue stain, stem cell nuclei; red stain, stem cell membranes.

Moving From Bench to Bedside

Mitral Valve Repair at THI Has Been Made Simpler and More Reliable

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**Abstract:** In high-risk patients with coronary artery disease, OPCABG + TMLR, performed via a left thoracotomy, can relieve angina that is refractory to conventional medical and surgical therapy.

**OPCABG + TMLR Performed Via a Left Thoracotomy**

Although OPCABG offers many advantages, it may not always allow complete revascularization, especially of the circumflex and posterior descending arteries, which can be hard to reach and immobilize. Also, OPCABG is unsuitable for diseased vessels that are small, intramyocardial, diffuse, athereosclerotic, or calcified. For these reasons, adjunctive TMLR can be advantageous. Introduced clinically in 1981, TMLR creates multiple laser channels in the ischemic myocardium to improve cardiac perfusion, including blood flow to areas unsuitable for bypass grafting. “Although its mechanism is not completely clear,” states Dr. Frazier, “TMLR often alleviates angina that is unresponsive to conventional treatment. By combining OPCABG and TMLR, surgeons can revascularize all diseased areas of the myocardium.”

For these combined procedures, a left thoracotomy (instead of a standard median sternotomy) can be used. The incision is larger than a mini-thoracotomy but smaller than a full median sternotomy. This approach is particularly advantageous in patients with poor skin and soft-tissue coverage resulting from previous sternotomies, sternal wound complications, mediastinal irradiation, or a radical mastectomy. According to Dr. Frazier, “In such cases, the previous sternotomy site would be both hard to reopen (because of dense adhesions requiring extensive dissection) and hard to reclose (because of the lack of healthy wound margins).” Furthermore, a left thoracotomy involves no aortic cross-clamping or lifting of the heart, so this approach may benefit patients whose ascending aorta is calcified.” In addition, the left thoracotomy is compatible with full or partial CPB, should it become necessary, and with the following other methods: fibrillatory arrest, moderate hypothermia, femoral or descending thoracic aortic cannulation, and creation of proximal anastomoses in the descending thoracic aorta or subclavian artery. Between October 2000 and May 2001, THI surgeons performed OPCABG + TMLR via a left thoracotomy in 17 patients. One patient died of ventricular fibrillation 8 days postoperatively. Of the 16 survivors, none had angina at hospital discharge. At follow-up examination a mean of 6 months after surgery, 15 patients remained angina-free, and 1 patient had mild angina. None had to be rehospitalized. Therefore, concludes Dr. Frazier, “in these high-risk patients, OPCABG + TMLR significantly relieved angina, with an acceptable mortality and no major morbidity.”

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One of every two women in the Western world will die of cardiovascular disease. Compared with men, women are typically shorter, weigh less, possess a smaller body surface area, and have smaller coronary arteries. “These factors alone are thought to increase the difficulty of coronary artery bypass grafting (CABG),” says Nancy A. Nussmeier, M.D., director of Cardiovascular Anesthesia Research at the Texas Heart Institute (THI). “Additionally, women develop angina or myocardial infarction later and tend to have more diffuse disease upon diagnosis, further increasing the risks and challenges of surgical intervention. Disconcertingly, cardiovascular disease–related mortality, while decreasing for men, is actually increasing for women.”

Disease prevention messages are reaching men but seem to be too little, too late for women at risk for cardiovascular disease. To improve survival rates, cardiologists have progressively increased interventions for women in the last decade. Still, women tend to fare worse than men after cardiovascular surgery. “Women are rarely affected by coronary artery disease before menopause,” explains Dr. Nussmeier. “But women who do develop it are more likely to have diabetes, hypertension, congestive heart failure, obesity, and cerebral or peripheral vascular disease. Postmenopausal women may dramatically improve survival rates after coronary bypass grafting.

**Assessing the Role of Gender and Hormone Replacement Therapy in Cardiovascular Disease**

**Abstract:** A new THI study shows that hormone replacement therapy in postmenopausal women may dramatically improve survival rates after coronary bypass grafting.

Dr. Nussmeier emphasizes. “However, it is not yet clear whether survival is related to one or more specific cardiovascular benefits of estrogen or whether there is a selection or adherence bias at work, meaning that women who are willing to take a daily medication for prevention may have healthier lifestyles than women who don’t use hormones. While the findings are encouraging, more research is needed to clarify whether benefits of HRT are chronic or acute and how HRT can best be administered.”

Dr. Nussmeier plans to continue research designed to identify gender-based differences in the presentation and pathophysiology of cardiovascular disease and in interventional outcomes. Understanding specific risk factors and taking advantage of protective factors will help improve THI’s ability to care for patients of both sexes and may potentially save lives.

“Women must be counseled as aggressively as men regarding their risk factors for cardiovascular disease,” Dr. Nussmeier says. “Primary care physicians who suspect coronary artery disease in the female patient should consider referring them to cardiologists early, when medication and lifestyle changes can yield positive results and surgical interventions are most likely to result in optimal outcomes.”

**For more information:**
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Calendar of Events

**TEXAS HEART INSTITUTE CONTINUING MEDICAL EDUCATION SYMPOSIA 2002**

Third Symposium on Congestive Heart Failure
October 3–4, 2002
Texas Heart Institute—The Denton A. Cooley Building
Program Director: Sayed Feghali, M.D.

Echocardiography in Congestive Heart Failure Patients
October 4–5, 2002
Texas Heart Institute—The Denton A. Cooley Building
Program Director: Raymond Stainback, M.D.

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

American Heart Association Satellite Symposium
November 16, 2002
Chicago, Illinois
Program Directors: James J. Ferguson III, M.D.; R. David Fish, M.D.; and James T. Willerson, M.D.

**SELECTED UPCOMING NATIONAL AND INTERNATIONAL MEETINGS**

American Heart Association Scientific Sessions 2002
November 17–20, 2002
Chicago, Illinois
Abstract deadline: Passed

Society of Thoracic Surgeons 39th Annual Meeting
January 31–February 2, 2003
San Diego, California
Abstract deadline: August 5, 2002

American College of Cardiology 52nd Annual Scientific Session
March 30–April 2, 2003
Chicago, Illinois
Abstract deadline: September 10, 2002

International Society for Heart and Lung Transplantation 23rd Annual Meeting and Scientific Sessions
April 9–12, 2003
Vienna, Austria
Abstract deadline: September 20, 2002

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