

Heart WATCH

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A NEWSLETTER PRODUCED BY THE TEXAS HEART INSTITUTE



TEXAS HEART INSTITUTE
at St. Luke's Episcopal Hospital

New Technique of Aortic Root Aneurysm Repair Spares the Aortic Valve

Abstract: Valve-sparing aortic root aneurysm repair prevents rupture and preserves the patient's natural valve, eliminating the need for lifelong anticoagulant treatment.

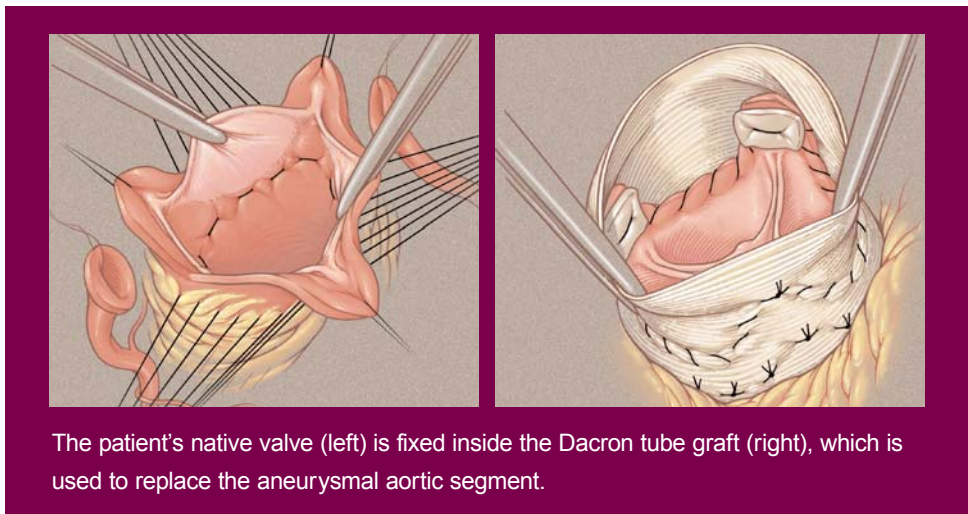
An aortic root aneurysm

is a dilatation of the ascending aorta where it exits the heart. Such aneurysms are usually asymptomatic unless they dissect or rupture—complications that are frequently fatal, even with emergency surgery. However, aortic root aneurysms may be detected early by routine x-ray imaging in patients with Marfan's syndrome, atherosclerotic vascular disease, hypertension, or other conditions associated with an increased risk of aortic aneurysm formation.

For these patients, prophylactic surgical intervention is frequently recommended when the aneurysm expands to 5–6 cm in diameter. Because the aneurysm (or its removal) could deform the aortic valve, causing it to leak, traditional repair involves replacing the entire aortic root and native valve with a composite valved graft. This graft consists of a bioprosthetic or mechanical valve incorporated into a Dacron tube. However, bioprosthetic valves eventually wear out, requiring replacement after 10–20 years. Being more durable, mechanical valves are more widely used, but they entail an increased risk of thrombosis; consequently, patients who receive them must take anticoagulant medications for the rest of their lives. Continuous use of these medications increases the risk of hemorrhage and related complications and does not entirely prevent thrombosis.

Recently, surgeons at the Texas Heart Institute (THI) and St. Luke's Episcopal Hospital (SLEH) began using a new technique to repair aortic root aneurysms while saving the natural valve. Like the traditional method, this procedure involves removing the entire aneurysmal segment, including the sinuses of Valsalva at the base of the aorta, and reconstructing the aorta with a Dacron graft. Surgeons then incorporate the native valve into the inner wall of the graft, where the valve can resume its normal function.

"In the past, surgeons believed that you couldn't take out the aneurysm without distorting the aortic valve so much that it



wouldn't work properly," says David A. Ott, M.D., a cardiovascular surgeon at THI/SLEH. "This new technique enables us to preserve the native valve and restore its physiologic shape."

First conceived by surgeons at the University of Toronto, the valve-sparing technique lowers the threat of thrombosis and, therefore, obviates the need for anticoagulant treatment after surgery. Avoiding anticoagulants is especially important for patients who have very active lifestyles or medical conditions in which hemorrhage is likely. Additionally, the native valve is inherently less likely to develop blood clots than is a mechanical valve, even without anticoagulants.

Most recipients of the valve-sparing procedure at THI/SLEH have been men older than 60 years with aortic root aneurysms of various etiologies, including cystic medial degeneration, atherosclerosis, and trauma. However, the valve-sparing technique is not suitable for every patient with an aortic root aneurysm. In approximately half of all cases, the valve leaflets are calcified, torn, or infected, necessitating replacement of the valve and the aneurysmal segment of the aorta. But for a patient whose aortic valve is structurally normal or potentially repairable, the valve-sparing procedure is definitely an option.

"Because reconstruction or repair of the natural valve is generally preferable to lifelong anticoagulation, with its inherent problems," says Dr. Ott, "we believe that the valve-sparing method of aortic root aneurysm repair is worth considering for selected patients." ●

For more information:

Dr. David A. Ott
832.355.4917

CLINICAL TRIALS UPDATE

Two new multicenter trials of external cardiac assist devices will include THI/SLEH patients. One, a nonrandomized pilot study involving a total of 10 patients, will evaluate the safety of the CentriMag bearingless blood-pump system (Levitronix, Waltham, MA) as short-term treatment for postcardiotomy cardiogenic shock. The other, a randomized study involving up to 106 patients, will compare the safety and effectiveness of the TandemHeart percutaneous ventricular assist device (CardiacAssist, Inc., Pittsburgh, PA) with those of conventional treatments for cardiogenic shock.

C-Reactive Protein: A Powerful Predictor of Cardiovascular Events

Abstract: C-reactive protein, an inflammatory marker produced by the liver and by smooth muscle cells lining blood vessels, is not only a powerful predictor of cardiovascular events but also an atherogenic factor.

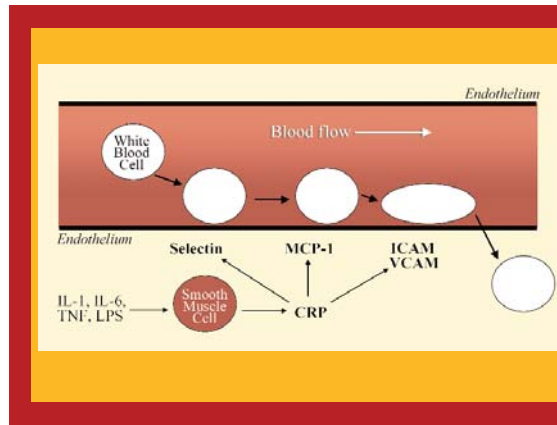
The recent medical news

has featured a number of stories about C-reactive protein (CRP), an inflammatory marker that is being increasingly recognized as a powerful, independent predictor of cardiovascular events. Produced by the liver and by smooth muscle cells that line the blood vessels, CRP is a nonspecific marker for various inflammatory conditions, including infections, autoimmune diseases, and cancer. Researchers have known about this acute-phase protein since 1930, but its importance to atherogenesis is only now becoming clear. The current interest in CRP reflects the belief that many cardiovascular diseases result from an inflammatory process.

At the Texas Heart Institute, James T. Willerson, M.D., medical director and director of Cardiology Research, and Edward T. H. Yeh, M.D., a research scientist and cardiologist, have been examining the role of CRP in diagnosing and treating cardiovascular disease. Dr. Willerson explains that CRP levels of less than 5 mg/L were formerly considered normal. "However, with today's more sensitive diagnostic methods," he says, "patients are deemed at high risk for cardiovascular events if their CRP level is greater than 3 mg/L and at low risk if this value is less than 1 mg/L."

In the ongoing 8-year Women's Health Study, which is being performed by Harvard researchers and includes 27,939 women, subjects with a CRP level of greater than 3 mg/L were 2.3 times more likely to have a cardiovascular event than those with a CRP level of less than 1 mg/L.

Despite the value of CRP testing, it should not replace older, well-established methods. "In fact, CRP and LDL cholesterol tests have a complementary function," says Dr. Willerson. "Together, the 2 tests can be expected to benefit millions of apparently healthy persons with otherwise undetected atherosclerosis. To minimize the influence of normal variations in any one patient, the physician should use the average of 2 CRP measurements, made 2 weeks apart."



CRP stimulates endothelial cells to express adhesion molecules, which attract circulating white blood cells into the arterial wall, setting up a local inflammatory reaction (i.e., atherogenesis). CRP, C-reactive protein; ICAM, intercellular adhesion molecule; MCP-1, monocyte chemoattractant protein-1; TNF, tumor necrosis factor; VCAM, vascular cell adhesion molecule.

Because CRP analysis requires only a simple blood test, it is an unusually economical diagnostic option. Moreover, the results are independent of age, sex, race, or the time of day when the test is done. At present, however, CRP testing is not being advocated for all patients. The American Heart Association and the Centers for Disease Control and Prevention state that the test is advisable (but not mandatory) for patients who, on the basis of traditional risk factors, are believed to have a 20% or greater risk of cardiovascular disease over the ensuing decade. In the United States, this group comprises about 40% of adults. Some experts would like to see CRP testing more widely performed, especially since at least 25% of heart attack victims have no known risk factors.

According to Drs. Willerson and Yeh, CRP may also be a direct participant in the atherogenic process. Dr. Yeh explains that this protein may help cause expression of vascular adhesion molecules on the arterial walls and may reduce production of nitric oxide, a substance that promotes vascular health.

Therefore, reduction of CRP levels may be beneficial. "In fact, it may accompany lifestyle changes such as smoking cessation, weight loss, exercise, and control of diabetes," Dr. Yeh says. "In addition, statin drugs have been shown to reduce CRP levels."

Drs. Willerson and Yeh are helping to design a long-term trial of statin therapy for

patients with a low LDL cholesterol level but a high CRP level. This trial, expected to start by spring 2004, will help determine the role of CRP reduction in cardiovascular disease prevention and treatment. ●

For more information:

Dr. James T. Willerson

832.355.3710

Dr. Edward T. H. Yeh

713.792.6242

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Anastomotic Connectors in Minimally Invasive Cardiac Surgery

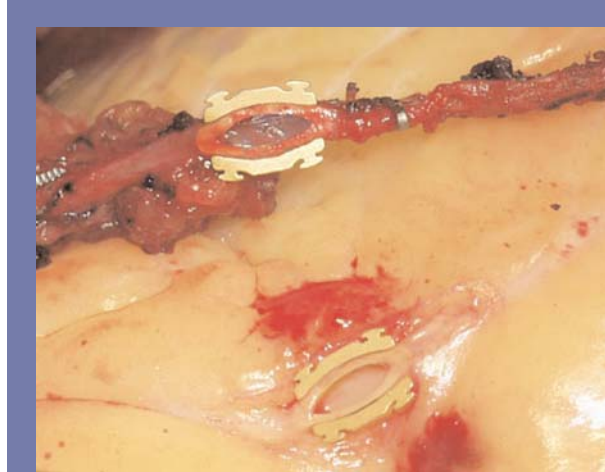
Abstract: Anastomotic connectors are being developed to make minimally invasive cardiac surgery simpler, safer, and more effective.

Minimally invasive technology allows surgeons to operate on the beating or non-beating heart in relatively small surgical fields. Coronary artery bypass grafting (CABG) and mitral valve repair (MVR) can be done through small incisions, or ports, without the need for a sternotomy. Using robotically assisted endoscopic systems, surgeons can achieve a level of precision and a range of motion comparable to that achieved during open heart surgery. Working in these confined surgical fields, however, necessitates new devices and techniques that will allow surgeons to work as quickly and dexterously, yet just as safely and effectively, as in wide surgical fields.

One particular area of development is anastomotic connectors. According to Ross M. Reul, M.D., director of Surgical Innovation at the Texas Heart Institute (THI), most connectors being developed for minimally invasive cardiac operations are intended for CABG. Proximal connectors have been relatively easy to develop because they generally involve a simple end-to-side anastomosis of bypass graft to aorta. Developing distal connectors has been more technically challenging because the graft and target coronary artery are smaller and the required angle of anastomosis is more oblique. Both mechanical and magnetic means of attachment are being investigated.

Currently, the only proximal connector clinically approved by the Food and Drug Administration is the mechanical Symmetry Bypass Aortic Connector (St. Jude Medical, St. Paul, MN). This device, made of the shape-memory metal nitinol, creates a stent-like anastomosis between a saphenous vein graft and the ascending aorta when struts on the connector snap into place inside and outside the aortic wall. The anastomosis, which takes about a minute to create, has proved reliable (*Ann Thorac Surg* 2003;75:1866–1870) but is vulnerable to thrombosis.

“The Symmetry connector is not used routinely here at THI and St. Luke’s, mainly



Magnetic device intended to create a sutureless anastomosis between a bypass graft (top) and coronary artery (bottom). (Reprinted with permission from Ventrica, Inc.)

because of the possible risk of thrombosis,” says James J. Livesay, M.D., a cardiovascular surgeon at THI. “However, it is used in selected cases in which aortic clamping or manipulation would greatly increase the risk of stroke, as for example in a patient with a calcified aorta.”

Distal connectors under development include the Magnetic Vascular Positioner (MVP) system (Ventrica, Inc., Fremont, CA) and a stent-like device from St. Jude Medical. The Ventrica MVP, which is used in Europe but not approved for clinical use in the United States, comprises 2 sets of magnets. Each set secures a surgically created elliptical opening in the graft and target vessel, respectively; when aligned, they create an instant anastomosis. The procedure, usually done in seconds, results in excellent short-term patency, as demonstrated in an ongoing European trial whose interim results were reported at this year’s meeting of the Society of Thoracic Surgeons.

Meanwhile, an interrupted sutureless device, the self-closing nitinol U-Clip (Coalescent Inc., Sunnyvale, CA), is being used in CABG (for anastomosis) and is under investigation for use in MVR (for annuloplasty).

“By eliminating knot-tying, the U-Clip can reduce the operative time by a third without

compromising subsequent hemodynamic flow,” says Dr. Livesay.

But sutureless connector technology is still viewed warily by some.

According to Dr. Reul, “Many surgeons are understandably hesitant to use sutureless connectors during CABG because of concerns about whether such devices can create functionally competent anastomoses with good long-term patency that generate little or no thrombus-promoting turbulence.”

“With time, the technical advantages of sutureless connectors should become clear,” says Dr. Reul. “Already, these devices appear to reduce operative and bypass times, avoid some problems inherent in inserting foreign materials into the vascular lumen, and promote excellent hemodynamics. Consequently, this technology promises to make minimally invasive surgery on the beating heart a safe, cost-efficient, and widely indicated alternative to open heart surgery.” ●

For more information:

Dr. Ross M. Reul
832.355.5884

Dr. James J. Livesay
832.355.4996

Search Continues for Ideal Immunosuppressive Regimens for Heart Transplant Recipients

Abstract: Researchers in transplant immunology are working toward the twin goals of patient-specific immunosuppressive regimens and antigen-specific allograft tolerance.

The goal of immunosuppressive therapy in cardiac transplantation is to prevent rejection of the allograft while maintaining sufficient resistance to infections and malignancy and minimizing the complications associated with long-term use of immunosuppressive agents. Although most early deaths (≤ 30 days after transplantation) are attributable to primary allograft failure or surgical complications, most late deaths (>30 days) are due to infection and neoplasia associated with long-term immunosuppression. Thus, there is a need for safe yet more potent and selective regimens and for ways to induce the immune system to establish antigen-specific allograft tolerance.

Early immunosuppressive regimens included azathioprine, high-dose corticosteroids, and antithymocyte globulin. In the early 1980s, the introduction of cyclosporine, in combination with low-dose corticosteroids and azathioprine, reduced the prevalence of acute rejection. Current triple-therapy regimens combine calcineurin inhibitors such as cyclosporine or tacrolimus, antiproliferative agents such as azathioprine or mycophenolate mofetil (MMF), and a corticosteroid. These regimens have drastically improved patient and graft survival, but the agents are nonspecific, and their continual administration increases the risk of infection, nephrotoxicity, diabetes mellitus, and neoplasia.

“We’ve improved the basic therapies and reduced the incidence of hyperacute and acute rejection, but chronic rejection remains the Achilles’ heel of long-term patient and graft survival,” says Frank Smart, M.D., medical director of Advanced Heart Failure and Cardiac Transplantation at the Texas Heart Institute at St. Luke’s Episcopal Hospital. “Although appropriate drug combinations are emerging, much work remains before we can effectively reduce chronic rejection.”

A current debate concerns the choice between cyclosporine and tacrolimus. Results of studies at the University of Pittsburgh and the University of Munich suggest that these 2

drugs are similarly effective and nephrotoxic, but that tacrolimus causes less hypercholesterolemia, hirsutism, gingival hyperplasia, and hypertension.

“The most potent combination is tacrolimus, MMF, and steroids,” says Dr. Smart. “The major downside is increased diabetes and infection rates if patients become ‘over’ suppressed. Regardless, this drug combination has nearly eliminated hemodynamically significant rejection.”

Researchers are also comparing the antiproliferative agents azathioprine, MMF, and rapamycin. Most data suggest that MMF is superior to azathioprine in preventing or alleviating allograft rejection and causes no additional adverse effects. Rapamycin appears to be especially effective in combination with a calcineurin inhibitor, and a recent study (*N Engl J Med* 2003;349:847–858) showed the rapamycin analogue everolimus to be more efficacious than azathioprine.

One advantage of rapamycin is that its enhanced potency may allow marked reductions in cyclosporine doses and early withdrawal of corticosteroids. Although few programs use a completely corticosteroid-free

“We’ve improved the basic therapies, . . . but chronic rejection remains the Achilles’ heel of long-term patient and graft survival.”

protocol, most attempt to wean patients from corticosteroids during the first 4–12 months after transplantation.

“Patients weaned from steroids do not have the associated problems of obesity and osteoporosis, and their quality of life improves,” says Dr. Smart. “We have begun to attempt prednisone weaning aggressively in certain patients—particularly elderly men because they have fewer episodes of rejection.”

The ultimate goal of immunosuppression is allograft tolerance. Current strategies include co-stimulatory blockade, cytokine modulation, clonal deletion, chimerism, peptide-based therapies, and use of molecularly engineered cells. However, the human immune system’s redundancy makes tolerance elusive. Although reports of allograft tolerance continue to emerge, researchers still cannot predict which patients will become tolerant and by what mechanism. According to Dr. Smart, the goal continues to be a balance of immune suppression and immune competence, resulting in some degree of microchimerism and tolerance.

“Future immunosuppressive therapy will be more patient-specific. Patients with more powerful immune responses, such as young patients, African Americans, and women, will be treated more aggressively,” says Dr. Smart. “Improved monitoring will mean lower drug doses. And, as we elucidate the role of cytokines in the immune response, we will develop agents that are more specific. Allograft tolerance will come as our understanding of the genetic manipulation of the antigen response matures.” ●

For more information:

Dr. Frank Smart
832.355.3977

Addressing Depression in Patients with Coronary Heart Disease

Abstract: Depression is common in patients with coronary heart disease, but a variety of effective treatment approaches are available.

Symptomatic coronary

heart disease (CHD) affects approximately 6 million people in the United States. A leading cause of death, CHD is also associated with a variety of medical and psychiatric morbidities, including depression. A recent *JAMA* article states that 39% of patients who have a myocardial infarction become clinically depressed within 4 weeks after that event (*JAMA* 2003;289:3106–3116). In patients who subsequently develop CHD, depression often persists; in fact, the prevalence of depression is at least 13% among CHD patients and possibly as high as 78% among patients hospitalized for CHD (*AACN Clin Issues* 2003;14:3–12).

“In cardiac patients, depression is not much different than in depressed patients who are otherwise healthy,” says Priscilla Ray, M.D., a psychiatrist at the Texas Heart Institute (THI) and St. Luke’s Episcopal Hospital (SLEH) who specializes in treating depression. “Both groups have a consistently depressed mood and no longer enjoy their favorite activities. The only difference is that depressed CHD patients begin with a focus on their physical health that can progress to a serious preoccupation. For example, if their doctor tells them to reduce the fat in their diet, they may cut out fat completely and start living on rice and seaweed.”

Depression in cardiac patients can be difficult to diagnose. Because approximately half of depressed CHD patients have no previous history of depression, they may not recognize the illness for what it is. They may also try to downplay the severity of their mood change.

“These patients may not realize that they are depressed,” says Paula Waller, L.M.S.W.-A.C.P., a medical social worker at SLEH who works with heart failure patients. “Often it is a family member, not the patient, who first mentions the depression to a doctor or social worker.”

In CHD patients, the causes of depression are varied and only partly understood. Anxiety about illness and death is a contributing

SYMPTOMS OF MAJOR DEPRESSION*

- Depressed mood
- Loss of interest in normal activities
- Significant weight loss/gain
- Insomnia/hypersomnia
- Psychomotor agitation/retardation
- Fatigue/loss of energy
- Feelings of worthlessness
- Impaired concentration or decisiveness
- Thoughts of death or suicide

*Diagnosis requires that ≥ 5 symptoms, including depressed mood and/or loss of interest in normal activities, be present most of the day, nearly every day for at least 2 weeks, and cause significant distress or impairment.

Source: American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, ed 4. Washington: American Psychiatric Association; 1994.

factor, but even more critical in many cases is the loss of function that accompanies CHD.

“Being unable to do the things they used to do not only interferes with the ability to enjoy life, but also prevents patients from fulfilling their roles as the breadwinner or caretaker for their families,” says Ms. Waller. “And because these patients often don’t look especially sick, others may not understand why they can’t play with the kids or carry in the groceries anymore.”

Biological disturbances may also cause or aggravate depression in CHD patients. β -blockers, steroids, and other medications can dramatically affect mood. In addition, tissue trauma caused by myocardial infarction or cardiac surgery can elevate a patient’s levels of pro-inflammatory cytokines such as interleukin-1 β and tumor necrosis factor- α , which are implicated in depression (*Neurosci Biobehav Rev* 2002;26:941–962).

To help depressed CHD patients, SLEH/THI staff members employ several forms of treatment. Most such patients are prescribed

supportive psychotherapy and antidepressant medications by staff psychiatrists, who must always be aware of potential interactions between antidepressants and the many other drugs CHD patients take. Patients may receive individual and family counseling or attend support groups like the one Ms. Waller runs for heart transplant candidates. Exercise and social interaction are also encouraged. The goal of these interventions is to support patients in their rehabilitation and to help family members or other caregivers do the same.

“Patients need someone who understands what they are going through and the limits imposed by their heart disease,” says Dr. Ray. “But patients also need encouragement to recover their ability to do things for themselves.” ●

For more information:

Dr. Priscilla Ray
713.797.0112

BASIC SCIENCE REPORT

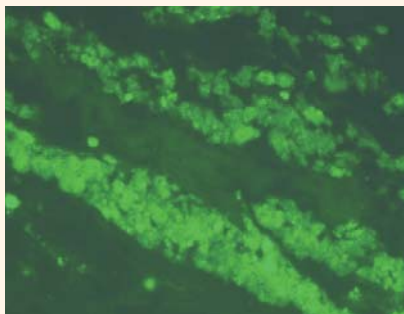
With an eye toward future clinical studies, THI researchers are exploring possible relationships between influenza, atherosclerosis, and vulnerable plaque in a mouse model of atherosclerosis. S. Ward Casscells, M.D., Mohammad Madjid, M.D., and colleagues are studying pathophysiologic (e.g., inflammatory and autoimmune) mechanisms by which influenza affects vessel walls and the ways in which these responses destabilize vulnerable plaques. They are also characterizing these effects immunologically and histopathologically and are evaluating the protective effects of influenza vaccination and new antiviral drugs such as neuraminidase inhibitors. Similar studies are planned in diabetic atherosclerotic mice.

Laboratory Research Supports Ongoing and Future Trials of Stem Cell Therapy

Abstract: Laboratory research at the Texas Heart Institute provides a basis for ongoing and future trials of stem cell therapy.

Stem cell therapy is slowly becoming a clinical reality. A recent review article (*N Engl J Med* 2003;349:570–582) describes a wide range of in vivo experiments and clinical trials that are using stem cells to treat numerous life-threatening diseases. Among these efforts is an ongoing collaborative trial being conducted in Brazil by researchers from the Texas Heart Institute (THI) in selected patients with congestive heart failure (*see box this page*). The success of this and other such trials depends on close collaboration between physicians at the bedside and researchers in the laboratory. At THI, physicians are working closely with scientists in the Heart Failure Research Laboratory, headed by Yong-Jian Geng, M.D., Ph.D.

“In the ongoing Brazilian trial and THI’s planned stem cell therapy trials in humans,” says Dr. Geng, “our role is to design, test, maintain, and fine-tune the stem cell techniques necessary for this therapy. We need to make sure the stem cells are optimal in both quality and quantity. We are also exploring novel methods for separating out stem cells and for increasing their therapeutic potency through gene manipulation.”



Accumulation of fluorescently labeled bone marrow stem cells (green) injected into an ischemic animal heart in which a myocardial infarction had been induced experimentally.

Current projects in the Heart Failure Research Laboratory involve both adult and embryonic stem cells. Adult stem cells can be derived easily and inexpensively from a patient’s bone marrow and can be transplanted back into that patient without risk of rejection. Embryonic stem cells are derived from embryos left over from in vitro fertilizations and fetal tissue, so use of these cells is controversial. Because embryonic stem cells are not yet approved for human use and because U.S. law severely restricts stem cell research, embryonic stem cells are studied mainly in the laboratory setting.

“In supporting the ongoing Brazilian trial, we’ve learned how ‘plastic’ adult bone marrow stem cells can be,” says Dr. Geng. “They may become both heart and blood vessel cells. This challenges the established notion that adult stem cells from a specific tissue are fated to become cells of that particular tissue type. We’re also learning about the limitations of adult stem cells as compared with embryonic stem cells, namely, that adult stem cells have built-in ‘clocks,’ such as progressive shortening of telomeres with each cell division, that shorten cell life spans and weaken the cells’ differentiating potential.”

The Heart Failure Research Laboratory has also been conducting experiments with stem cells in vitro and in animal models. A principal aim is to identify early markers and regulatory factors involved in stem cell differentiation. Dr. Geng and colleagues recently showed that the cytokine leukocyte-inhibiting factor (LIF), an established experimental inhibitor of stem cell differentiation, greatly hinders the ability of mouse embryonic stem cells to become beating cardiomyocytes in culture, whereas the widely used solvent dimethyl sulfoxide (DMSO) promotes that ability. In other studies using mouse embryonic stem cells, the researchers examined the regulatory role of calcium and potassium channels in stem cell maturation and differentiation. They discovered that ion-channel activity is important for the stem cells’ ability to clump together, adhere to culture dishes,

and eventually transform into beating cardiomyocytes. The researchers also discovered that at least one type of voltage-gated potassium channel, which plays a major role in cardiac excitability, is important for early clumping and adhesion.

“Through basic research, we continue to improve our protocols for autologous adult stem cell therapy in patients with congestive heart failure and to better understand how stem cells differentiate,” says Dr. Geng. “Soon, we will focus more on teasing out the genetic components of embryonic stem cell proliferation and differentiation and applying what we learn to correcting genetic abnormalities of the heart.” ●

For more information:

Dr. Yong-Jian Geng
832.355.9160

BRAZILIAN STEM CELL TRIAL FOLLOW-UP CONTINUES

In a collaborative Brazilian trial, researchers continue their follow-up of 14 heart failure patients who have undergone a stem cell therapy developed at THI. The treatment entails injecting a patient’s own bone marrow stem cells into the left ventricle. “The follow-up period has passed 1 year, and most patients continue to show symptomatic and functional improvement, including better myocardial oxygen consumption,” says Emerson C. Perin, M.D., the trial’s principal investigator and director of New Interventional Cardiovascular Technology at THI. Five patients have been removed from the heart transplant waiting list. THI and SLEH are still seeking approval from the Food and Drug Administration to begin a similar trial here.

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Editorial Office 832.355.6630
jrichard@heart.thi.tmc.edu

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call 1.800.872.9355

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Calendar of Events

TEXAS HEART INSTITUTE CONTINUING MEDICAL EDUCATION SYMPOSIA

Texas Heart Institute New Modalities for Treating Heart Failure

October 24–25, 2003

Brownsville, Texas

Program Director: Reynolds M. Delgado III, MD

Texas Heart Institute Congestive Heart Failure Summit

November 6, 2003

Houston, Texas

Program Directors: James T. Willerson, M.D.;
O. H. Frazier, M.D.

American Heart Association Satellite Symposium

Advancing the Standard of Care:
Exploring New Frontiers

November 8, 2003

Orlando, Florida

Program Directors: James J. Ferguson III, M.D.;
James T. Willerson, M.D.; R. David Fish, M.D.

SELECTED UPCOMING NATIONAL AND INTERNATIONAL MEETINGS

American Heart Association Scientific Sessions 2003

November 9–12, 2003

Orlando, Florida

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

International Society for Heart and Lung Transplantation 24th Annual Meeting and Scientific Sessions

April 21–24, 2004

San Francisco, California

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