The Beat Goes On

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A Healing Bullet

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Welcome to the third edition of the Memorial Hermann Research Newsletter. This edition highlights clinical innovations and research in cardiology, reflecting the recent Houston Aortic Symposium: Frontiers in Cardiovascular Diseases, held April 4-6, 2008. This international conference was organized by Hazim J. Safi, M.D., and David D. McPherson, M.D., both affiliated with The University of Texas Medical School at Houston and the Memorial Hermann Heart & Vascular Institute-Texas Medical Center. Recognized by the World Health Organization in 2004 as an urgent threat to global health, cardiovascular diseases are a significant target not only of clinical care within Memorial Hermann but of research as well, and we are pleased to share some of our recent innovations and discoveries with you.

Sincerely,

Cheryl M. Chanaud, Ph.D., CCRP
Memorial Hermann Clinical Innovation & Research Institute

About Memorial Hermann Healthcare System
An integrated healthcare system, Memorial Hermann is known for world-class clinical expertise, patient-centered care, leading-edge technology and innovation. The system, with its exceptional medical staff and 19,000 employees, serves southeast Texas and the greater Houston community. To learn more, visit memorialhermann.org or call 713.222.CARE.
Cardiovascular medicine has seen great changes over the past 10 years, both in treatment and in diagnostic technology. All of these advances, which involve or depend on cardiac imaging, have a profound impact on patient outcomes.

Even so, vascular disease – particularly coronary artery disease – remains the greatest cause of death and disability in adults, despite the fact that it is also the most “detectable” and “curable” of all major life-threatening chronic illnesses.

K. Lance Gould, M.D., is the Martin Bucksbaum Distinguished University Chair in Cardiology, professor of cardiovascular medicine and executive director of the Weatherhead PET Center for Preventing and Reversing Atherosclerosis at The University of Texas Medical School at Houston. Since founding the Center in 1979, Dr. Gould has spearheaded research and development of cutting-edge cardiac imaging and treatment.

"Over those years, our efforts have distilled into a proven clinical service integrating the most advanced imaging and treatment program in the world," he says.

Studies have shown that noninvasive medical treatment, including intense drug management and the pursuit of a healthy lifestyle, can significantly decrease heart attack, death, stroke or the need for surgery.

Invasive revascularization procedures, or surgical treatments, may also provide benefit. These include the drug-coated stent – a small tube coated with medication to reduce possible blockages – that is permanently inserted into an artery to help hold it open, as well as bypass surgery.

But all of these technological advances raise the question: Which is the “ultimate” noninvasive imaging technique capable of guiding invasive procedures or noninvasive medical management of coronary artery disease?

ADVANCES IN NONINVASIVE HEART IMAGING: CARDIAC POSITRON EMISSION TOMOGRAPHY (PET) AND THE WEATHERHEAD PET CENTER

In a brief overview, here are a few of the latest cardiac imaging technologies found among the recent deluge of developments:

Heart scan – This computerized tomography or CT scan of the heart detects calcium, an important indicator of coronary atherosclerosis. Calcium, however, can be present without arterial narrowings or limited blood flow, therefore leaving the patient’s status uncertain.

Computerized tomography or CT coronary angiogram – This test is intended to assess the presence and severity of stenosis (narrowing) of the coronary arteries. However, even the most advanced scanner cannot differentiate varying degrees of stenosis.

Cardiac magnetic resonance imaging or MRI – The MRI provides a very good noninvasive image, but has not been proven clinically reliable for routine assessment of coronary artery disease or for measuring blood flow in the heart muscle, both necessary for diagnosing problems.

Standard heart imaging stress test – SPECT (single photon emission tomography) is the most common of noninvasive technologies. It is intended to assess coronary artery blood flow as affected by stenosis, but the results can be unreliable, yielding either a false positive leading to an unnecessary invasive procedure, or a false negative, missing the presence of significant coronary artery disease.

PROVEN PET

It is cardiac positron emission tomography, or cardiac PET imaging, that stands...
above the rest for detecting and evaluating severity of coronary artery disease.

PET imaging is the most accurate of all advanced technologies for identifying early or advanced blood flow abnormalities in the heart, even the mild changes caused by early coronary artery disease. It also assesses more advanced disease, serving as the basis for deciding on balloon dilation, stents or bypass surgery. PET also has the capacity to routinely measure the absolute blood flow in the heart muscle and determine absolute coronary flow reserve. This flow capacity may be reduced in early coronary atherosclerosis even before symptoms or before significant stenosis is seen on the invasive arteriogram.

The excitement surrounding the development of PET imaging is widespread, and for good reason. “It also shows whether an invasive procedure is necessary or not,” explains Dr. Gould. “If the maximum blood flow capacity in the heart muscle is adequate by PET imaging, then the coronary arteriogram or an invasive revascularization procedure is not needed and lifestyle/pharmacologic treatment is the best option,” he continues.

Research supporting the effectiveness of PET imaging has been conducted nationwide, but cutting-edge research is found at the Weatherhead PET Center in studies led by Dr. Gould and his team.

WEATHERHEAD PET CENTER FOR PREVENTING AND REVERSING ATHEROSCLEROSIS
The Weatherhead PET Center for Preventing and Reversing Atherosclerosis is a component of The University of Texas Medical School at Houston. The Center is physically located in Memorial Hermann-Texas Medical Center. This unique, integrated imaging-treatment management of coronary artery disease reflects the collaboration and commitment to excellence of both entities.

Dr. Lance Gould is a pioneer in cardiovascular medicine, and his work has now spanned the better part of the past four decades.

His discoveries extend from basic concepts of coronary blood flow, quantification of coronary artery stenosis and pharmacologic stress imaging, to the first demonstration of reversing coronary artery disease by intense combined lifestyle and pharmacologic treatment.

Dr. Gould developed the first, and currently the most advanced, program consisting of definitive noninvasive cardiac imaging as a guide to invasive procedures or vigorous lifestyle-pharmacologic treatment, reducing cardiovascular events by 80 percent to 90 percent compared to standard medical practice.

While not the only center to use cardiac PET imaging, the Weatherhead PET Center is a unique combination of extensive coronary expertise garnered since 1979, specialized cardiac software custom-developed at the Center and a significant number of publications regarding PET imaging and its use as a guide to managing coronary heart disease and invasive procedures.

The Center features of a complex integration of different areas of research, offering a comprehensive approach to diagnosis and treatment, with the main goal being to obtain the best possible outcome for patients. Research areas include:

Detection of early coronary atherosclerosis or coronary artery disease (CAD) – Dr. Gould first developed cardiac PET imaging for identifying early mild coronary artery disease. This won him the International vonHevesy Prize for research in Nuclear Medicine in 1978. That research continues with the
investigation of PET imaging technology, the physiology of stress imaging and the clinical applications of PET imaging.

Dr. Gould also developed the first concept of coronary flow reserve and pharmacologic stress for imaging blood flow in the heart muscle to detect and quantify coronary artery disease. His studies first showed that 50 percent of people with a parent or sibling with coronary heart disease have an abnormal cardiac PET scan indicating early silent coronary atherosclerosis.

**Preventing and reversing coronary artery disease by combined intense pharmacologic treatment and healthy lifestyle** – As PET imaging technology evolved, many patients were identified with silent or asymptomatic coronary artery disease that put them at high risk for future heart attacks. The condition of this group of patients had gone previously undetected by other imaging technologies.

The subsequent program Dr. Gould developed for this group, an intense program of cholesterol-lowering medications and lifestyle change, was found to reduce the risk of death or heart attacks and the need for bypass surgery or balloon angioplasty by 80 percent to 90 percent compared to patients undergoing usual care.

Using PET imaging, Dr. Gould and his team showed for the first time a regression of coronary artery disease and improved blood flow in the heart muscle in people undergoing the intense treatment program. The studies also proved stress PET imaging to be as accurate, or more so, than invasive coronary arteriography in following the progression or regression of coronary artery disease. Currently, PET imaging is a routine part of management for following change in the severity of CAD during treatment.

**Technology for imaging blood flow in heart muscle (myocardial perfusion)** – The very first PET scanner for imaging the entire heart at once was developed by Dr. Gould and the team he formed in 1979. His research has remained at the forefront of imaging technology.

Recent research by the team identified a major flaw in standard commercial PET-CT software and protocols that resulted in false positives. The defect was corrected by rewriting the software and revising...
the protocols. The resulting accuracy of quantitative measures of myocardial perfusion are imperative in identifying early coronary atherosclerosis, guiding lifelong preventive treatment, determining the severity of coronary artery disease and potentially eliminating unnecessary coronary arteriograms or surgical interventions.

Dr. Gould’s research in these separate areas also has an integrated focus, resulting in a powerful, rational, cohesive paradigm of cardiovascular medicine with better outcomes at a lower overall cost than any other standard of cardiovascular medicine.

FOR THE FUTURE
Dr. Gould’s concern over the limited recognition of cardiac PET imaging’s clinical value at this early stage compels him and his team to forge ahead in the research of this relatively new technological advancement, ultimately demonstrating the importance and effectiveness of cardiac PET imaging and bringing it into the realm of standard care.

Consequently, the future research of Dr. Gould and his team will address increasing the availability and decreasing the costs of the technology, as well as advancing the clinical application of this now-proven approach for treating coronary heart disease.

For information, call the Weatherhead PET Center for Preventing and Reversing Atherosclerosis at 713.500.6611. If our phone is busy, leave a message and we will return your call promptly.

IN MEMORIAM
This edition of the Memorial Hermann Clinical Innovation & Research Institute newsletter is dedicated to the memory of our friend and colleague Reshanda La Vet Robinson, who always brought a smile to us all.

HAZIM J. SAFI, M.D.
PIONEER OF THE HEART

Hazim J. Safi, M.D., professor and chairman, Department of Cardiothoracic and Vascular Surgery, The University of Texas Medical School at Houston, has had a long career saving lives. Recently, together with David McPherson, M.D., he co-directed the first Houston Aortic Symposium. Dr. Safi credits the opening of the Memorial Hermann Heart & Vascular Institute-Texas Medical Center as the inspiration for the symposium. This one-stop-shop for heart patients opened on March 15, 2008, and is dedicated exclusively to heart and vascular surgeries, medicine and research. It joins the Memorial Hermann Heart & Vascular Institutes at Memorial City and Southwest, and Children’s Heart Institute.

“We have basically pulled all of our talented people in cardiovascular and aortic surgery and medicine to be in one place,” Dr. Safi says of the Institute. The Heart & Vascular Institute-Texas Medical Center, which has garnered architectural accolades and awards, boasts windows in all patient rooms.

“The building was designed so that all of the patient rooms have a window, to help prevent patients from developing postoperative delusion,” says Dr. Safi.

In addition to being heavily involved in the undertakings of the Institute, Dr. Safi has also developed an impressive collection of his published articles focused on an array of cardiovascular subjects, including prevention of stroke and complex operations.

In addition to his own work in cardiovascular and aortic surgery, Dr. Safi is currently collaborating with his colleague Dianna M. Milewicz, M.D., Ph.D., professor and director of the division of Medical Genetics at The University of Texas Medical School at Houston, in researching genetic variations that are linked to aneurysm development.
Panic is a common reaction to the mere suggestion that something threatens the health of a heart. But heart failure doesn’t have to be such a dire term, because the condition doesn’t necessarily mean the heart is about to give out, stop or “fail.” It just means the heart is having a hard time doing its job of pumping enough blood to meet the body’s needs.

Physicians and researchers at Memorial Hermann-Texas Medical Center would like to put the fear of the condition into perspective by ensuring that with early diagnosis and advances in its treatment, the condition can be seen as something to live with – even comfortably – rather than something to die from.

“People with heart failure can go on to live productive, happy lives, but they must strictly adhere to treatment and must be committed to taking a proactive role in the management of their own well-being,” says Deborah Meyers, M.D., visiting associate professor in the division of Cardiology at The University of Texas Medical School at Houston.

Heart failure is, however, a chronic progressive disease associated with substantial morbidity, especially in those patients who fail to take proper care. If allowed to progress without treatment, the condition can have a number of very negative effects on a patient’s life and longevity.

As the disease progresses, patients fail to respond as well to optimal medical management. Experts in heart failure are increasingly thinking of the disease progression within the context of the disease trajectories (Figure 1, page 9). As the disease progresses into the refractory (hard to manage) phase, patients experience symptoms at rest or with minimal exertion, have an increasingly restricted lifestyle and often require repeated or prolonged admission to the hospital to control symptoms related to congestion or hypoperfusion (decreased blood flow).

“Taking a proactive role in self-care, preservation and prevention is important to anyone afflicted with heart failure. So, early diagnosis and education about treatment are the keys to keeping the condition from progressing any faster than it has to, thus allowing a patient to live a longer, more productive and rewarding life,” adds Dr. Meyers.

**FIRST THINGS FIRST**

Most patients with heart failure due to systolic dysfunction – when the heart muscle is too weak to effectively pump blood throughout the body – respond well to medications and benefit from prescription drug therapy along with the varied treatments available in a multidisciplinary clinic, all with the important goal of improving symptoms, survival and quality of life.

ACE (angiotensin-converting enzyme) inhibitors and beta blockers are two of the most common medicines used to treat heart failure. Both are geared to blocking the harmful effects of stress

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hormones, which can worsen the condition. Other medications used to treat heart failure include angiotensin-receptor blockers (ARBs), aldosterone antagonists and diuretics used to reduce excess fluids in the body.

In addition to medication, visits to a multidisciplinary clinic can be very beneficial to effective treatment. Such a clinic offers care by a number of different individuals, including nurses specifically trained to treat heart failure patients, pharmacists, rehabilitation personnel and nutritionists, as well as physicians. Patients often see a number of care providers under the same roof and during the same visit to treat common modifiable factors that are known to hasten heart failure conditions, but that are usually overlooked in a routine hospital environment. All this allows patients to network within the healthcare system more effectively.

Patients wanting to keep their conditions at bay will follow the collective instructions of all multidisciplinary caregivers. This approach to treatment and therapy is ideal, as all possible elements of care and coaching can be found under one roof, optimizing the overall health of a patient and his or her quality of life.

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KEEPING PACE WITH THERAPY

Atrial synchronized biventricular pacemaker therapy or cardiac resynchronization therapy (CRT), which over the last decade has received increasing attention, offers another option for patients who find themselves with refractory heart failure, a progressed form of the disease.

Research on data collected from more than 22,000 patients with symptomatic heart failure shows that CRT resulted in a 22 percent reduction in mortality and a 37 percent reduction in morbidity defined as hospitalization when combined with optimal pharmacotherapy. Implant success in this large series of patients was 93 percent with a relatively low rate of complications. Improvements in quality of life were noted in the CRT patients.

IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY

Implantable cardioverter defibrillator therapy (AICD) is another option for primary and secondary prevention therapy for ventricular arrhythmias. This therapy has been established in high risk patients to reduce sudden cardiac death by 57 percent and all-cause mortality by 26 percent.

Research from both randomized and observational trials, which include more than 18,000 patients, demonstrated a 20 percent mortality benefit of AICDs in patients with ejection fractions of less than 35 percent, the majority with NYHA (New York Heart Association) functional Class II-III symptoms, therefore a somewhat “less sick” population of patients.

The RAFT: Resynchronization/Defibrillation for Advanced Heart Failure trial is an ongoing study regarding the effectiveness of combined CRT/AICD devices. Given the results of the companion study, which demonstrates that there is an incremental benefit of adding AICD to CRT therapy, most patients believed to be CRT eligible should be considered at present for combined CRT/AICD therapy.

CARDIAC TRANSPLANTATION

Long considered the “gold standard” cure for advanced heart failure, cardiac transplantation, unfortunately, is severely limited by the low availability of donor hearts. Currently only 3,000-5,000 annual heart transplants are performed worldwide. When compared to the vast number of heart failure patients, these numbers render the therapy trivial in its availability.

“Patients are often referred for transplantation prematurely, without a complete
“Patients are often referred for transplantation prematurely, without a complete evaluation and trial of optimal medical management. In the presence of optimal medication and therapeutic care, many patients can defer transplantation for years, if not indefinitely,” says Dr. Meyers.

ELIGIBILITY
Only a select group of patients with refractory heart failure are considered to be “transplant eligible.” The general consensus among the transplant community is that the “ideal candidate” for transplantation is relatively free of physical, mental or psychosocial co-morbidity conditions, which can limit the success of the procedure or the survival of the patient after the transplantation.

It is important to note that the “gold-standard cure” is more realistically a trade of one chronic condition for another. The improved survival and quality of life that result from a successful transplantation come at the cost of needing long-term, complex monitoring and medical management of a myriad of effects, toxicities and complications arising from the use of required immunosuppressive medications.

The development of progressive transplant coronary disease in the transplanted heart is also a possibility and limits the survival of most patients to less than two decades. Re-transplantation can be considered, but the results are inferior to those achieved with a first transplant.

PALLIATIVE CARE
Palliative care, a focus on relieving symptoms rather than curing a condition, is an appropriate option for patients whose condition has entered the refractory stage, and who have exhausted all other available therapies, yet still suffer from severe symptoms of heart failure. Clinicians should be familiar with the indicators guiding the timing of referral to palliative care programs. (Table 1, page 10)

There are no easy answers surrounding the prospect of the end of life. Discussions pertaining to end-stage care must be carefully individualized.

“I would argue for an integrated model that provides multidisciplinary care including palliative care physicians, heart failure cardiologists, heart failure nurse specialists and the support of the full allied health team until the time of death,” says Dr. Meyers.

IN SUMMATION
There are many known causes for heart disease and just as many unknown ones,
but the fact remains that the condition is a chronic and progressive one that with time can reach a refractory state. When detected early, however, there are therapies, treatments and favorable multidisciplinary care that can delay or even halt the progression of the disease, giving patients who embrace treatment and throw themselves proactively into the maintenance of their personal health a chance at a flourishing and happy life.

“I agree we have to be honest about the fact that heart failure is a chronic progressive disease – the trajectory shows that. But if it is optimally treated, we can offer patients therapy that can delay or even halt the progression of the disease,” says Dr. Meyers.

CLINICAL IDENTIFIERS OF ADVANCED HEART FAILURE

DESPITE MAXIMAL medical management patient experiencing:

**NYHA* Class IV Heart Failure** ("Unable to carry on any physical activity without discomfort. Symptoms of CHF present at rest (severe CHF)"1).

**Consistent** clinical indicators of worsening failure including:
- Creatinine levels >2.3 mg/dL
- Hyponatremia (serum Na <130)
- Worsening renal function (from baseline)
- Tachycardia >100 b.p.m.
- Arrhythmias (specifically ventricular)
- Persistent hypotension (not related to hypovolemia)

**Refractory** symptoms including:
- Pain
- Orthopnea
- Fatigue
- Dyspnea
- Paroxysmal nocturnal dyspnea
- Nausea
- Edema / Abdominal distension
- Poor appetite /weight loss (>10% weight loss over 6 months or BMI <15% of normal weight)

**Withdrawal** of Angiotensin Converting Enzyme Inhibitors, Angiotensin Receptor II Antagonist and Beta-blockers due to symptomatic hypotension or worsening renal function.

**Dependence** on inotropes.

**Repeated** admissions to acute care setting (>3 admissions in 6 – 10 months).

Department of Health and Aged Care, “Palliating the Symptoms of Advanced Heart Failure Project,” Palliative Care Working Committee, Queensland Health 2007.

*New York Heart Association

**TABLE 1**
A Triple-A Threat
SILENT AND SWIFT: PROTECT YOURSELF AGAINST AAA, A POTENTIALLY FATAL CONDITION

Nothing is more challenging than preparing for the unknown. But when it comes to the heart and blood vessels, “better safe than sorry” can take on a whole new meaning: the difference between life and death.

Abdominal aortic aneurysm (AAA) is a silent predator. The condition occurs when the abdominal aorta – a large blood vessel in the abdomen that flows to the pelvis and legs – swells and balloons outward. As the aneurysm grows, so does the chance that it will rupture.

When an AAA ruptures, a patient can bleed to death within hours or minutes. Roughly half of all patients with a ruptured aneurysm die. This is why screening is so important.

“People should know that detecting an aneurysm is easy to do with a simple, noninvasive screening test called an ultrasound. In less than an hour, patients can determine if they have one,” says Sheila Coogan, M.D., assistant professor in the department of Cardiothoracic and Vascular Surgery at The University of Texas Medical School at Houston.

CHECK PLEASE
Over 15,000 people annually succumb to what should easily be a preventable death. But most individuals aren’t even aware that they have an AAA until it is too late.

An abdominal aortic aneurysm often displays no particular symptoms until the time of rupture. Small aneurysms can rupture, but are generally deferred from treatment until the size is greater than 5 centimeters, when the risk of rupture outweighs the risk of surgery.

“Nothing is more frustrating than knowing that you could have helped a patient with an easily treatable problem had he or she presented for treatment in time,” says Dr. Coogan.

Studies show that ultrasound screening followed by surgical repair of any aneurysm found saves lives. Finding an AAA in time, however, is the biggest problem. This is why the first step to detecting one is an ultrasound screening.

An abdominal aortic aneurysm can develop in anyone, but people who smoke, are 65 or older or have a family history of aneurysm are at

“Nothing is more frustrating than knowing that you could have helped a patient with an easily treatable problem had he or she presented for treatment in time.”

CONTINUED ON PAGE 11
greater risk. AAA, however, is four times more common in men than women.

Recent federal guidelines recommend ultrasound screening for abdominal aortic aneurysm in men age 65 or older who have smoked a minimum of 100 cigarettes in their lifetime. Additionally, screening should be performed on anyone with a family history of aneurysms. Medicare has covered screenings with no deductible since January 2007. Those wanting to take advantage of the service must meet one or more of the risk criteria.

**THE FUTURE OF DRUG THERAPY**

The matrix metalloprotease-9 (MMP-9) enzyme – believed to break down connective tissue in the aorta – is released by inflammatory cells in the body. High levels of MMP-9 and related enzymes are believed to be contributors to the formation of aneurysms by altering the structure of the aortic wall. A change in the structure of an enzyme called elastin, which provides strength and elasticity to the wall of the aorta, may contribute to the initial enlargement of the artery that ultimately results in an aneurysm.

A better understanding of what causes an aneurysm and triggers its growth could potentially pave the way for the development of effective drug therapy, medication geared to slow or completely prevent the swelling, rupture and/or size of an aneurysm.

“Most of my patients would love to take a pill to avoid future surgery,” says Dr. Coogan, regarding the welcomed idea of drug therapy.

While there is currently no proven form of medical therapy for AAA, studies on Doxycycline have shown favorable results in mice. The drug has reduced the growth rate of AAA by effectively taming the aortal activity of MMP-9, thus reducing its effect on the artery.

**SURGICAL OPTIONS/MINIMALLY INVASIVE ENDOVASCULAR STENT GRAFT REPAIR**

Once an abdominal aortic aneurysm has surpassed 2 inches or 5 to 5.5 centimeters in diameter, surgical treatment is recommended. Open aneurysm repair and endovascular stent graft repair (EVAR) remain the two most effective surgical treatments for the condition to date. Aneurysm morphology dictates whether open or endovascular AAA repair is best for an individual patient.

“People should know that detecting an aneurysm is easy to do with a simple, non-invasive screening test called an ultrasound. In less than an hour, patients can determine if they have one.”

A stent used in the reinforcement of an artery.
During an open aneurysm repair, also known as surgical aneurysm repair, the damaged part of the aorta is replaced by way of an abdominal incision with an aortic graft constructed of a durable nylon material. The graft, which is shaped like the patient’s healthy aorta, allows blood to flow readily through it again, usually for the long term – 90 percent of open repairs are successful for the duration of a patient’s life. Most patients are discharged within a week after open surgery; however, it may take six weeks to three months before they feel like their energy level has returned to normal.

An endovascular stent graft procedure is a newer and less invasive treatment than open repair. It is performed inside of the artery by way of catheters introduced into the body through small incisions in the groin and then guided to the affected area through blood vessels.

The endovascular stent graft, or endograft – a tube constructed of fabric and metal – is then guided over wires and secured at the site of the aneurysm, where it will serve as reinforcement to the aorta.

Because of the smaller incisions and overall reduced physical trauma of this procedure, recovery is usually easier for the patient and requires less time.

While endograft repair of AAA may have lower short-term complications, the stent requires more maintenance and follow-up to ensure it continues to work properly, and its long-term durability falls short when compared to that of the open repair alternative.

**JUST WHAT THE DOCTOR ORDERED**

While many physicians believe that an open aneurysm repair is still the best way to correct the problem, all aneurysms are different, as are all patients. So what may work for one patient may not be the best option for another.

Consulting with a vascular surgeon remains the best way of getting information on the options for screening, prevention and/or treatment.

The nationally renowned team of aortic specialists at Memorial Hermann-Texas Medical Center, led by pioneer cardiothoracic and vascular surgeon Hazim Safi, M.D., includes dedicated surgeons, anesthetists and nurses with extensive experience in both types of surgical management, offering patients the best of care.

For information regarding AAA screening or repair, please contact Sheila M. Coogan, M.D., at Sheila.M.Coogan@uth.tmc.edu or 713.500.5304.

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Dr. Coogan visits with Jack Morgan, one of her patients.

The large black bulb between the arrows in the center of the image is an abdominal aortic aneurysm. Please note that it is 2 to 3 times larger than the rest of the artery.

After the stent, this image shows how we can bring the aneurysm back to normal size (again between the arrows), avoiding rupture.

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A Healing Bullet

Injecting a miniature doctor into the human body to roam around and search for maladies and diseases to fix is an impossibility, but the idea is materializing in another way, at least in the world of cardiology.

According to researchers in the division of Cardiology at The University of Texas Medical School at Houston, affiliated with Memorial Hermann-Texas Medical Center, this revolutionary science consists of a liposome. Once injected into the body, this miniature spherical vesicle, which carries proteins or other healing agents, is geared to identify and combat targeted objects while releasing its medical load.

“This has been the dream of doctors and scientists for 100 years,” says Melvin Klegerman, Ph.D., associate professor of cardiology. “This magic-bullet technology will widen the therapeutic window by delivering maximum efficacy and minimum toxicity.”

These smart vesicles are currently limited to testing with animals, but show exceptional promise for use in humans, in applications including diagnostics and targeted drug therapy.

**VULNERABLE PLAQUE LEADS TO A VULNERABLE PATIENT**

Until recently, it was believed that the narrowing of an artery due to the accumulation of fatty plaque was the main culprit of heart attack or stroke. Research now shows that these blockage types are responsible for only a small percentage of these cases.

“People think that it is the narrowing of the arteries due to buildup that is causing the trouble, but it is the composition of plaque, not the severity of the clogged arteries, that is the real danger,” explains Susan Laing, M.D., associate professor of cardiology.

The real culprit is vulnerable plaque – a soft, fatty plaque located within the arteries – that, when it ruptures through its thin wall coating, spills into the artery and clumps with various components excreted due to inflammation, forming a clot large enough to block the artery and kill by causing a stroke or heart attack.
With no efficient way available today to detect vulnerable plaque, doctors must rely on gauging the presence of significantly narrowed coronary arteries in a patient by way of conventional methods, such as CT or MRI imaging tools, and some emerging blood tests. Intravascular ultrasound, usually performed during an angioplasty, has the ability to measure plaque burden but it is invasive and not routinely provided to otherwise asymptomatic patients.

With 70 percent of heart attacks starting at less than a 50 percent stenosis (narrowing of the artery), and vulnerable plaque causing a vast majority of heart attacks and strokes – it is believed to be up to 85 percent – detecting and ultimately treating vulnerable plaque as early as possible is of major importance in fighting the No. 1 killer of Americans: heart disease.

Enter the liposome. With its ability to be easily injected intravenously into the human body, its effectiveness in detecting and ultimately treating patients with vulnerable plaque would win hands-down over any potential advantages of a diagnostic test alone.

“We’re using liposomes as a smart tracer to diagnose disease and highlight vulnerable plaque as a beacon,” explains Patrick Kee, M.D., assistant professor of cardiology.

“The artery walls remodel, so you can’t really see a narrowing of the artery. That’s why using liposome technology has been a major cardiovascular focus, targeting to markers in association with vulnerable plaques and loading them with different drugs,” adds Dr. Klegerman.

The smart liposome, loaded with plaque-fighting drugs, makes its way to vulnerable plaque by way of its special formulation: it’s echogenic. That is to say, it reacts to ultrasound, and in its presence releases its medical load.

“These liposomes are very efficient when exposed to ultrasound and are using ultrasound as a therapeutic agent not just a diagnostic agent as they are releasing their compounds when exposed to ultrasound, which acts as a therapeutic agent by causing them to release their compounds,” Dr. Klegerman explains.

According to Dr. Laing, the ultimate goal is to facilitate the diagnosis and treatment of vulnerable plaque by providing patients with liposome technology and transvascular ultrasound at any cath or imaging lab.

SPEARHEADING THE RESEARCH

Liposome therapy’s potential for lowering the mortality rate of heart attack and stroke patients is staggering, not to mention the potential rate of prevention for those at high risk. The technology’s promise has since spurred testing of its effectiveness in the treatment and diagnosis of cancer, too.

The University of Texas Medical School at Houston division of Cardiology – comprised of Patrick Kee, M.D., Ph.D.; Shaoling Huang, Ph.D.; Melvin Klegerman, Ph.D.; Hyunggun Kim, Ph.D.; Yong-Jian Geng, M.D., Ph.D.; Susan Laing, M.D.; and David McPherson, M.D. – is an active research group in Memorial Hermann-Texas Medical Center. It currently has two major grants to further this liposome research from the National Institutes of Health – one in the diagnostic area and one for gene and drug delivery.

Funded through the American Heart Association, the division of Cardiology has additional grants and is dedicated to the further expansion of this innovative line of research by way of shifting this technological study trial from animals to people in the near future.

“This technology is at least five years out,” Dr. Laing says. “We have a niche in this field of using liposomes as a delivery agent for drugs, and we’ve only begun to explore their potential as therapeutics.”
The fluttering of a heart is familiar to everyone, as it is associated with many human emotions, from love in all of its forms to the least desirable emotions of all: panic and grief. When heart flutters become too frequent or occur for no apparent reason, heart arrhythmia may be the underlying reason. The side effects that come along with it can be bothersome at best and, if left untreated, can even be fatal.

Memorial Hermann-Texas Medical Center has over 25 years of experience in cardiac electrophysiology, the treatment of heart arrhythmia, when the heart beat is either too fast or too slow. Patients benefit from this expertise and experience in diagnosis and treatment, including some of the most advanced technology to treat arrhythmias.

WHAT IS ARRHYTHMIA?

“Heart arrhythmias occur when the heart beats too quickly, too slowly or irregularly, and is caused by a malfunction in the electrical impulses which coordinate how the heart beats,” says Anne Hamilton Dougherty, M.D., F.A.C.C., F.H.R.S., F.A.H.A., professor of medicine and director of cardiac electrophysiology at The University of Texas Medical School at Houston.

Most people have experienced occasional, brief, usually harmless arrhythmias, such as feeling a skipped, fluttering or racing heartbeat. However, more than 4 million Americans, most over age 60, experience heart arrhythmias that may cause bothersome – sometimes even dangerous – signs or symptoms. These may include shortness of breath, fainting or even sudden cardiac death – an unexpected loss of heart function, breathing and consciousness that leads to death within minutes unless the person receives emergency medical treatment to restart the heart.

DIAGNOSIS

The medical team for heart arrhythmia patients at Memorial Hermann-Texas Medical Center is led by electrophysiologists. These are cardiologists, medical experts in heart care with specialized training in the diagnosis and treatment of heart rhythm disorders.

Diagnosis usually begins with electrocardiogram (EKG) recordings, but since many arrhythmias are intermittent and occur at unpredictable intervals, capturing a symptomatic event may require specialized EKG monitors. Additional facilities, useful for noninvasive risk stratification, include T-wave alternans testing and averaged EKGs. Tilt-table testing is useful in the evaluation of patients with unexplained syncope (fainting).
Invasive diagnostic procedures are also available. Implantable loop recorders may be surgically implanted to facilitate the diagnosis of rare arrhythmia events. Invasive electrophysiologic testing is also helpful in clarifying the nature of the problem. This procedure is performed in the cardiac catheterization laboratories and employs flexible catheters to record, map and stimulate cardiac rhythms to gather data about the patient’s condition.

**TREATMENT OPTIONS**

Medical treatment for heart arrhythmia is critical, but the method selection can only be made after a comprehensive diagnosis and consultation, which will determine the appropriate options available for individual patients.

“Medical treatment is usually required if the arrhythmia is causing significant symptoms or if it is putting the patient at risk of more serious complications,” says Dr. Dougherty. Some non-serious types of arrhythmia do not require medical treatment, in which case regular medical check-ups will be recommended. Depending on the cause of the irregular heartbeat, arrhythmias can be treated with:

- **Medications**
- **Catheter-based interventional procedures**
- **Medical devices, such as pacemakers**

Experimental treatments not available at other medical centers are conducted at Memorial Hermann-TMC, offering some eligible patients cutting-edge treatment through clinical research trials.

**Medications**

Many drugs are available to treat irregular or fast heart rates. In some cases, the drugs have to be taken for the rest of the patient’s life. Some may need to be taken for only a short period of time or until the heart improves. The following list includes most of the drugs commonly used for treatment of arrhythmias:

- Beta-blockers
- Calcium channel blockers
- Specific antiarrhythmic agents (quinidine, procainamide, disopyramide, flecainide, propafenone, sotalol, dofetilide and amiodarone)
- Anticoagulants

**Catheter-based Interventional Procedures**

- **Advanced 3-dimensional electro-anatomical mapping:** This computer-aided arrhythmia mapping is an aid to the diagnosis of complex arrhythmias and is particularly useful in precisely targeting therapeutic ablation. Memorial Hermann-TMC provides two different systems (CARTO and ESI) for this procedure.

- **Catheter radiofrequency ablation:** For arrhythmias caused by abnormal heart tissue, catheter radiofrequency ablation (heat) can be used to destroy the abnormal tissue. Catheters are threaded through the patient’s blood vessels to target the abnormal heart tissue. Intracardiac echocardiography may be used in conjunction with these procedures.
with the procedure to correlate anatomic details with electrical events or to assist in transseptal catheterization. Radiofrequency energy is then delivered by a cardiologist through the catheter to quiet the abnormal tissue. Alternative energy sources for ablation, including cryotheraphy (catheter freezing) are also used in the Memorial Hermann-TMC electrophysiology labs. Arrhythmias that are commonly ablated include:

- Supraventricular tachycardias
- Wolff-Parkinson-White syndrome
- Atrial tachycardia
- Atrial flutter
- Atrial fibrillation
- Ventricular tachycardia

Cardioversion: A procedure used to correct an ongoing episode of arrhythmia by resetting the heart to its regular rhythm (sinus rhythm). This can be done in two ways: with medication or electrically. On rare occasions, invasive cardioversion using intracardiac catheters is required.

Medical devices
Used to help correct some arrhythmias, these battery-powered devices are implanted to send electrical pulses into the heart tissue to regulate the heart rate. Most of these implants are performed in the Memorial Hermann-TMC cardiac catheterization suite. The devices may include:

- **Pacemaker:** If the heart beats too slowly (bradycardia), an electronic pacemaker can be implanted to speed up the heart rate.
- **Internal cardioverter defibrillator (ICD):** For arrhythmias in which the heart beats too rapidly (tachycardia) or quivers (fibrillates) instead of contracting normally, ICDs can be surgically implanted. The ICD sends electronic signals to the heart whenever the heart rate reaches a specified limit or goes very high. These signals automatically shock the heart internally into beating more slowly and pumping more effectively, just as a paramedic might apply external shock therapy.
- **Cardiac resynchronization therapy (CRT):** A special type of pacemaker designed to help relieve heart failure symptoms improves the coordination of the heart’s contraction. Both ventricles are paced in synchrony to correct electrical conduction delays. CRT is frequently combined with ICD therapy for patients with weak hearts.
- **Device lead extraction:** On rare occasions, implanted devices require specialized extraction procedures to remove problematic intracardiac hardware.

The medical team for heart arrhythmia at Memorial Hermann-TMC is dedicated to providing the latest in diagnosis and treatment of heart rhythm disorders and continues to pioneer research, paving the way for the best in future treatments and technology.

For additional information, contact the UT Medical School at 713.500.6590 or The University of Texas Cardiovascular Medicine Practice, 832.325.7211.
A MESSAGE FROM DR. MCPHERSON

As course co-directors, I and my colleague Hazim Safi, M.D., appreciate this acknowledgement by the Memorial Hermann Clinical Innovation & Research Institute of the significance of cardiovascular disease and research leading to improved patient care and outcomes. The international course conducted in April, 2008, Houston Aortic Symposium: Frontiers in Cardiovascular Diseases, was inspired by the opening of the Memorial Hermann Heart & Vascular Institute-Texas Medical Center, which joins the Institutes located at Memorial Hermann Southwest Hospital and Memorial Hermann Memorial City Medical Center, and Children’s Heart Institute. The conference sought to provide state-of-the-art research and treatment options to healthcare providers in various professions involved with these patients, with topics ranging from the pathophysiologic processes of aortic disease to evaluation techniques, surgical alternatives of aortic root replacement, and treatment of aortic aneurysms. This edition of the Memorial Hermann Clinical Innovation & Research Institute newsletter focuses on various aspects of the cardiovascular disease research and clinical care being conducted by the faculty of The University of Texas Medical School at Houston, in conjunction with Memorial Hermann-Texas Medical Center, and provides a glimpse into the extensive topics covered in the symposium.

Thanks to the Memorial Hermann Clinical Innovation & Research Institute for spotlighting a major health concern for the country and the world.

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