

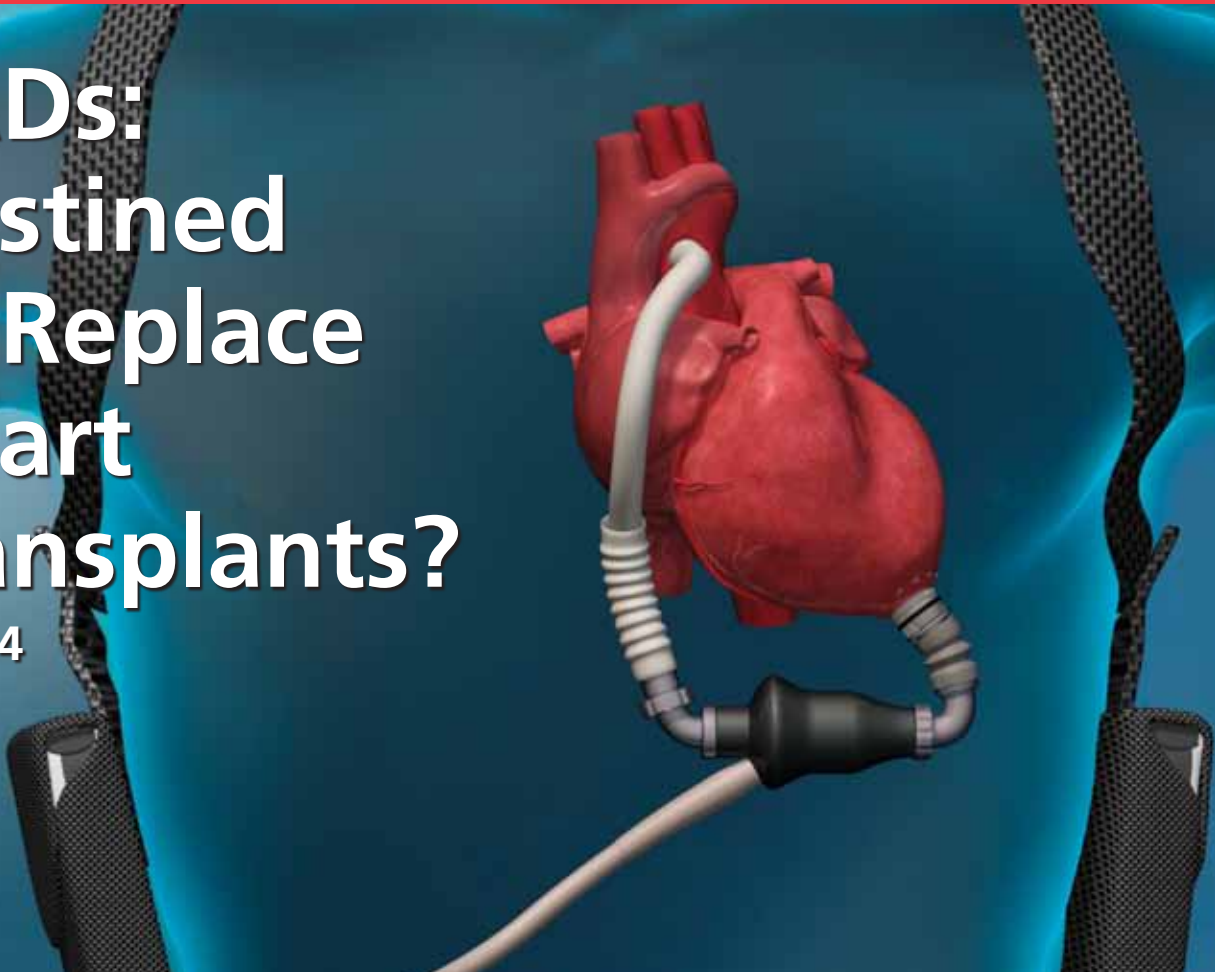
**UH**

# Heart & Vascular **Innovations**

University Hospitals Harrington-McLaughlin Heart & Vascular Institute

## VADs: Destined to Replace Heart Transplants?

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# Leading the Revolution



We are in the midst of many exciting developments that we are proud to report in this issue of *UH Heart & Vascular Innovations*. Regenerative medicine, mechanical hearts, antithrombotic therapies, and wound healing are all undergoing revolutionary changes. And University Hospitals Harrington-McLaughlin Heart & Vascular Institute is at the forefront of these advancements.

In “Research Connection,” **Marco Costa, MD, PhD**, reports how he and his colleagues – researchers at UH Harrington-McLaughlin Heart & Vascular Institute’s Research & Innovation Center – have developed a novel method to isolate autologous endothelial progenitor stem cells, adult stem cells that can be used to repair a patient’s damaged heart or non-healing lower extremity ulcer. This is an important advance because it eliminates the ethical questions that surround the use of stem cells from other sources, cell lines or individuals, and has the potential to minimize health complications.

Could it be true that, in the near future, heart transplants may no longer be necessary for patients with end-stage heart failure? **James C. Fang, MD**, and **Arie Blitz, MD**, provide an update on the newest developments in left-ventricular assist devices (VADs) in our cover story. It is anticipated that VADs may become so compact and comfortable, and their batteries so portable, that the standard heart transplant will be outdated for many patients.

Among its many services, UH Harrington-McLaughlin Heart & Vascular Institute offers specialized clinics for anticoagulation and antiplatelet monitoring. In “Preventing Stroke,” **Bruce Stambler, MD**, **Tom Lassar, MD**, and **Teresa Carman, MD**, provide an overview of new developments in antiplatelet and anticoagulation medications, including the possibility that we may finally have an efficacious and safe alternative to Coumadin/warfarin.

Lastly, in “Consultation,” Dr. Carman discusses the excellent physicians, surgeons, nursing staff and other specialists of the Center for Wound Care. Many options are available for treatment of non-healing wounds at our Center.

We are also pleased to announce the opening of a new site for UH Harrington-McLaughlin Heart & Vascular Institute at University Hospitals Ahuja Medical Center in Beachwood, Ohio. We will offer comprehensive cardiovascular services in this state-of-the-art facility, including diagnostic and interventional coronary and peripheral procedures, cardiac and vascular surgery, and pacemaker/ICD and ablation electrophysiology procedures.

To Heal. To Teach. To Discover.

Daniel I. Simon, MD, FACC, FAHA, FSCAI  
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Among the nation’s leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a nationally recognized leader in medical research and education.

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SCHOOL OF MEDICINE  
 CASE WESTERN RESERVE  
 UNIVERSITY

The commitment to exceptional patient care begins with revolutionary discovery. Faculty at the Case Western Reserve University School of Medicine, who also are physicians at UH Case Medical Center, are at the forefront of medical research and innovation. The School of Medicine is the largest medical research institution in Ohio and among the nation’s top medical schools for research funding from the National Institutes of Health.

# Research Promises Regenerative Potential

New heart or muscle cells may soon be derived from autologous endothelial progenitor stem cells



Marco Costa, MD, PhD, Director, Interventional Cardiovascular Center and Research & Innovation Center, University Hospitals Harrington-McLaughlin Heart & Vascular Institute

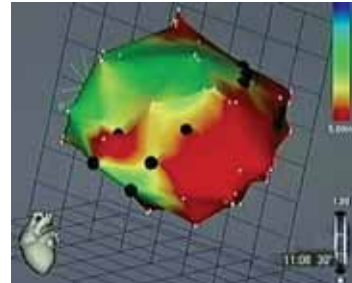
Recent advances in regenerative medicine show stem cell therapy may ultimately be used to create new blood vessels (angiogenesis), improve heart function, and reduce the risk of amputation in patients with peripheral vascular disease. And yet an obstacle stands in the way of realizing the promise of these breakthroughs: Autologous endothelial progenitor stem cells (i.e., adult “self” stem cells) compose a very small fraction of the cells in the blood (<0.002 percent), and it is difficult to obtain sufficient quantities of these cells to actually replace damaged cells in tissues such as the heart or muscle.

Researchers at UH Harrington-McLaughlin Heart & Vascular Institute at University Hospitals Case Medical Center, however, have developed a novel method to isolate sufficient numbers of autologous endothelial progenitor stem cells (stem cells that express the CD34 receptor) that can be used to renew damaged heart or muscle tissue. Such stem cells have the advantage of being derived directly from the individual patient. This eliminates not only the ethical questions that surround the use of embryonic and non-autologous (i.e., non-self) stem cells but also the health-related complications that could arise by using stem cells from other sources, cell lines or individuals.

## ‘HEALTH SPA’ FOR CELLS

**Marco Costa, MD, PhD**, Director, Interventional Cardiovascular Center and Research & Innovation Center, UH Harrington-McLaughlin Heart & Vascular Institute; and Professor of Medicine, Case Western Reserve University School of Medicine, reports there are two methods for obtaining the stem cells. “One way is to give the patients granulocyte stimulating factor,” he explains. “This increases the number of stem cells in the blood, and then we can collect a large number of these cells by apheresis. The alternative, and the method we prefer, is to obtain a small number of cells from the patient’s blood and expand them for seven days in culture media, which is a kind of ‘health spa’ for the cells.”

The culturing procedure expands the cell population to obtain enough autologous endothelial progenitor stem cells to use for treatment. “Because of our ability to add cytokines and growth factors to control the growth environment,” Dr. Costa says, “these cells are healthier than those in the original cell population derived from patients with advanced diseases.”



3D electromechanical mapping of the heart showing areas of damage (red) and location of the sites of stem cell injection in a patient with previous heart attack

## UPCOMING CLINICAL TRIALS

Studies are in the research phase, but Dr. Costa’s group has shown the procedures to culture stem cells and inject them into target tissues for treatment are feasible in animal models. He and his group are participating in Phase I-III clinical trials of bone marrow-derived and peripheral blood-derived stem cells for the treatment of patients with ischemic and non-ischemic cardiomyopathy, advanced coronary artery disease, and recent myocardial infarction (3-21 days).

The patients who may ultimately benefit from this novel method to amplify and fortify autologous endothelial progenitor stem cells include those with advanced coronary artery disease, heart failure, acute myocardial infarction or peripheral arterial disease. Dr. Costa notes the physicians at UH Harrington-McLaughlin Heart & Vascular Institute are eager to evaluate individuals who might benefit from this procedure. “Patients who come to UH Harrington-McLaughlin Heart & Vascular Institute will find that they have many treatment options,” he says. “Some may benefit from other procedures that we already offer. If they meet inclusion criteria, however, some patients could be recruited to participate in stem cell trials that are actively enrolling patients or in exciting upcoming clinical trials.”

## For More Information

Learn about existing and novel treatment options offered by UH Harrington-McLaughlin Heart & Vascular Institute by contacting Stacey Mazzurco, RN, at **216-844-3130**.

# VADs Go Mainstream

Ultimately, will this technology prove superior to a heart transplant?



James C. Fang, MD, Director, Advanced Heart Failure & Transplant Center; Chief Medical Officer, University Hospitals Harrington-McLaughlin Heart & Vascular Institute

Until recently, patients with end-stage heart failure had no option but to await a heart transplant. The few donor hearts available, however, limit the number of heart transplant operations performed in the U.S. to about 2,200 per year. Therefore, while their medical condition continues to deteriorate, many potential transplant recipients will never receive a human heart.

Fortunately, recent technological advances have allowed development of left-ventricular assist devices (VADs), mechanical hearts that offer a way to maintain survival until a heart transplant becomes an option. Thus, the VAD is often used as a “bridge” to a heart transplant, and about one-third of heart transplants are performed in patients who had a VAD placed originally.

## HAVING OPTIONS

Now, researchers at UH Harrington-McLaughlin Heart & Vascular Institute at University Hospitals Case Medical Center have shown technology has improved to the point where in the near future VADs may eliminate the need for heart transplants. “The public and the medical community need to know that end-stage heart failure patients have options,” says **James C. Fang, MD**, Director, Advanced Heart Failure & Transplant Center; Chief Medical Officer, UH Harrington-McLaughlin Heart & Vascular Institute; and Professor, Case Western Reserve University School of Medicine. “The outstanding team at UH Harrington-McLaughlin Heart & Vascular Institute offers phenomenal expertise and an individualized approach to treatment that includes VAD placement as one possibility.”

As an example, Dr. Fang highlights a female patient with a history of smoking, vascular disease, poor circulation and lung disease. “Because she was a smoker and had additional medical complications, she was not a candidate for a heart transplant. Nevertheless, she was dying from heart failure and actually had suffered a massive heart attack a few months earlier.” In the past, a woman in this situation would have had no option but to accept palliative care and hospice, where she would die within several months. The new generation of VADs has dramatically changed this. “We were able to offer her VAD therapy and she has been completely resuscitated,” Dr. Fang says. “Her quality of life is about as normal as you can get, except that she is wearing a battery-operated device.”

## THE EVOLUTION OF VADS

The landmark REMATCH trial compared VAD therapy with medical therapy alone in patients who had end-stage heart failure but were not heart transplant candidates because of coexisting medical conditions, drug abuse or other factors. The study showed patients who underwent placement of the first-generation VADs (for example, HeartMate) displayed a marked improvement in survival and quality of life as compared with patients on continued medical therapy, explains **Arie Blitz, MD**, Director, Heart Transplantation and Mechanical Circulatory Assistance, University Hospitals Case Medical Center; and Assistant Professor, Case Western Reserve University School of Medicine. These devices, however, had limited mechanical durability and patients experienced a high rate of medical complications. In addition, the first-generation VADs were bulky, noisy and noticeable to the patient and those in close proximity to the patient. “On average,” Dr. Blitz says, “patients with the original HeartMate device had to undergo VAD replacement about 16 months after the first implantation.”

As technology and techniques have improved, VADs have evolved into a good option for many patients. Second-generation VADs (for example, HeartMate II) utilize a different technology. In ancient times, the Archimedes Screw was used to pump water for irrigation from low-lying land to higher ground. Now, miniaturized VADs propel blood in an analogous manner by way of a spinning device and are used to (1) salvage patients in acute cardiogenic shock, (2) facilitate myocardial recovery in individuals with dilated cardiomyopathy, (3) “bridge” appropriate patients to heart transplantation, and (4) serve as a permanent therapy (i.e., destination therapy) in those individuals who are not candidates for heart transplantation, such as the elderly or those with other medical conditions or complicating factors.

## A SECOND-GENERATION DEVICE

“As device therapy continues to evolve, the hope is that ‘destination therapy’ will become a viable alternative to heart transplantation,” Dr. Blitz notes. Continued technological innovation will result in the widespread use of VADs in the coming years. “With the recent FDA



Arie Blitz, MD, Director, Heart Transplantation and Mechanical Circulatory Assistance, University Hospitals Case Medical Center



The complete HeartMate II assembly, including implanted pump, controller, batteries and holster



Implantable portion of the HeartMate II device

approval of the HeartMate II both as a 'bridge' to heart transplantation and for 'destination therapy,' we now have a second-generation device that yields superior results as compared to the first-generation devices. The durability of the HeartMate II is expected to be in excess of five years, it is nearly silent, and it infringes less on the patient's quality of life."

Former Vice President Dick Cheney underwent placement of a HeartMate II in July 2010. "His announcement that he had undergone the procedure was a wonderful public service that illustrates how mainstream VAD therapy has become," Dr. Blitz notes.

It is anticipated that third-generation VADs may perform for 10 years or more, providing both longer life and an excellent quality of life. "Ultimately, we want to change the paradigm so that VAD placement is no longer an emergency procedure," Dr. Blitz says. "It is possible that it could become an elective procedure that is performed well before disaster strikes. We hope to prolong life rather than prolong death.

"In five years, heart transplantation could be an inferior choice for treatment of patients with end-stage heart failure. Patients with the VAD may have a superior quality of life. In my view, the perfect ventricular assist device will not require that the patient take blood thinners, and it will be quiet, durable and forgettable."

## Ask the Expert

Leading-edge treatment options for patients with advanced heart failure are available at UH Harrington-McLaughlin Heart & Vascular Institute. Contact James C. Fang, MD, **216-844-8242**, or Arie Blitz, MD, **216-844-4988**, for a consultation and evaluation.

# Preventing Stroke

The proper drug dosage helps to ensure fewer harmful effects



Tom Lassar, MD, Interventional Cardiologist, University Hospitals Harrington-McLaughlin Heart & Vascular Institute

Patients with coronary artery disease, peripheral vascular disease, cerebrovascular disease (stroke and transient ischemic attack), including those who receive stents and those with atrial fibrillation, are particularly vulnerable to the formation of blood clots. Two classes of drugs – antiplatelets and anticoagulants – are used to counteract this risk.

Antiplatelet medications are prescribed to prevent myocardial infarction and stroke. The first antiplatelet therapy was aspirin, but now some patients with coronary artery disease are treated with more potent antiplatelet agents such as clopidogrel. Recent clinical data, however, show some people do not respond well to these medications because of genetic factors and drug-drug interactions. Efforts to develop other, more effective drugs are under way, and University Hospitals Harrington-McLaughlin Heart & Vascular Institute researchers have participated in clinical trials of new antiplatelet agents including prasugrel (now FDA-approved) and ticagrelor (FDA approval pending), and will be involved in clinical trials of elinogrel.

Individualized point-of-care platelet testing services at UH Harrington-McLaughlin Heart & Vascular Institute are now available at UH Case Medical Center and UH Chagrin Highlands Health Center. It is now possible to measure the effect of antiplatelet agents on platelet function of the individual patient in order to maximize their effectiveness in preventing blood clot formation. “To tailor individual therapy, we will use platelet function testing,” says **Tom Lassar, MD**, Interventional Cardiologist, UH Harrington-McLaughlin Heart & Vascular Institute; and Associate Professor, Case Western Reserve University School of Medicine. “The Accumetrics VerifyNow point-of-care assay is easy to use and allows us to determine whether the individual patient is achieving the desired antiplatelet effect.”

## ANTICOAGULATION MONITORING SERVICES

Anticoagulants interfere with a different aspect of thrombosis than antiplatelet drugs. The most commonly used anticoagulant, warfarin, reduces stroke by about 60 to 70 percent in patients with atrial fibrillation. The potency of warfarin, however, is influenced by food and drug interactions, and patients must undergo regular blood testing to be certain they are receiving adequate doses of the drug. “Studies have demonstrated that less than 50 percent of patients receiving warfarin attained therapeutic levels of anticoagulation,” says **Bruce Stambler, MD**, Professor of Medicine, Case Western Reserve University School of Medicine. “Warfarin has a narrow therapeutic window; too much causes bleeding,

including in the brain, and too little can increase the risk for stroke.”

The limitations of existing anticoagulant therapies have led to the investigation of other options, including a new class of oral anticlotting medications called direct thrombin inhibitors (for example, dabigatran). “At low doses (110 mg twice daily), dabigatran is as effective as warfarin for stroke prevention and is safer with less bleeding,” Dr. Stambler says. “At high doses (150 mg twice daily), it is superior to warfarin in stroke prevention with a similar incidence of bleeding. A major advantage of this agent is that it does not require regular blood testing to assess its therapeutic effect. Individuals on these drugs do not have to be seen regularly to monitor their blood coagulation system. Although dabigatran is approved for use in other countries to prevent blood clots after elective hip and knee replacement surgery, it is approved in the U.S. only for non-valvular atrial fibrillation.” Approval of new anticoagulant drugs like dabigatran and oral factor Xa inhibitors may improve the utilization of anticoagulants for prevention of thromboembolism in patients with atrial fibrillation. “The ultimate consequences of this effort,” says Dr. Stambler, “will likely be fewer strokes.”

The UH Harrington-McLaughlin Heart & Vascular Institute Anticoagulation Monitoring Service accepts new patients and ensures they receive the proper dose of their anticoagulant medications. With on-site blood testing, dosing adjustments, patient and family education, screening for potential food and drug interactions, home monitoring, and reports to the patient’s physician, the service is provided at UH Case Medical Center (Mather Pavilion) and at seven other University Hospitals health centers.

## Enrollment Information

“Education is key to successful anticoagulation therapy. We use point-of-care testing as an opportunity to monitor the effectiveness of antiplatelet or anticoagulation therapy, and also to provide patient education about food and drug interactions that may affect their care,” says **Teresa Carman, MD**, Director, Vascular Medicine, University Hospitals Case Medical Center; and Assistant Professor of Medicine, Case Western Reserve University School of Medicine.

For more information about the anticipated UH Harrington-McLaughlin Heart & Vascular Institute Antiplatelet Monitoring Clinic, call Tom Lassar, MD, at **216-844-7848**. To enroll in the UH Harrington-McLaughlin Heart & Vascular Institute Anticoagulation Monitoring Service, patients need a referral and the active participation of their physician. To schedule a patient appointment, a referring physician’s office should call **216-844-3800**.



Bruce Stambler, MD, Professor of Medicine, Case Western Reserve University School of Medicine

# When Wounds Won't Heal

UH experts apply a team approach to solve a common complication

Every year nearly 6 million Americans experience problem wounds that result from any number of clinical conditions, and healing can prove frustratingly difficult. "We commonly see patients with venous disease, diabetes, arterial disease and nutritional disorders who are at increased risk for developing non-healing wounds or have already developed these wounds," says **Teresa Carman, MD**, Director, Vascular Medicine, University Hospitals Case Medical Center; Medical Director, Center for Wound Care at UH Case Medical Center; Medical Director, Anticoagulation Monitoring Service, UH Harrington-McLaughlin Heart & Vascular Institute; and Assistant Professor of Medicine, Case Western Reserve University School of Medicine.

Non-healing wounds should be treated promptly to prevent additional complications and to minimize the pain and suffering experienced by the patient. The Center for Wound Care at UH Case Medical Center was established in 2008 to assist patients in managing wounds that require special expertise. "We are dedicated to providing our patients with state-of-the-art, outpatient clinical wound care," says Dr. Carman. "The Center for Wound Care offers a comprehensive, team approach that is designed to facilitate wound healing and minimize the risk of complications."

The Center is staffed by vascular medicine and vascular surgery physicians, and has excellent nursing support. When necessary, consultation services are available from UH specialists in plastic, orthopaedic and general surgery, dermatology, infectious disease, endocrinology, radiology, physical therapy, nutrition and pain management.

## ADVANCED TREATMENTS, EFFECTIVE OUTCOMES

The Center's physicians, surgeons and nurses have vast experience treating many kinds of non-healing wounds. Wounds that can be treated effectively include venous stasis ulcers, traumatic injuries, diabetic wounds, vascular ischemic wounds, burns, abscesses and postoperative wounds. To assess the nature of the wound and determine treatment options, a wound care specialist consults with each patient, performs an examination, reviews the medical history and provides a diagnosis. The team then works to develop an appropriate treatment plan that might include noninvasive vascular assessment, wound debridement, wound dressings and bioengineered skin grafting to aid wound healing. Orthotic and prosthetic support is provided to patients to facilitate offloading pressure and protection of the wounds. The patient's primary care physician is kept informed of the patient's progress and any other medical concerns that may arise during treatment.



Left leg wound before and after skin grafting and conservative wound care

Other personalized services include management of edema, pain, infectious diseases and nutrition. After the wound is healed, supportive care such as diabetes education classes are provided to the patient in an effort to prevent future injuries.

Within the UH system, Centers for Wound Care are located at UH Case Medical Center, UH Westlake Health Center, UH Richmond Medical Center and UH Bedford Medical Center.



Teresa Carman, MD, Director, Vascular Medicine, University Hospitals Case Medical Center

## Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy is available only at the Center for Wound Care at UH Bedford Medical Center. "Hyperbaric oxygen therapy is one of the many advanced treatments used in wound care," says Teresa Carman, MD. "In this procedure, concentrated oxygen is given to patients to promote wound healing." The air pressure inside a hyperbaric chamber is about two and a half times greater than its pressure in the atmosphere. This helps the blood carry more oxygen to be delivered to organs and tissues. In addition to wounds, hyperbaric oxygen therapy can be used to treat carbon monoxide poisoning, gangrene and numerous other conditions.

For more information about the Center for Wound Care at UH Case Medical Center and referral of patients, call Dr. Carman at **216-844-3800**. For information regarding the Wound Care Center at UH Richmond Medical Center, call **440-585-6101**. Information regarding hyperbaric oxygen therapy and consultation at UH Bedford Medical Center may be obtained by calling **440-735-4755**.



## NEWS & CME

# Honors and Recognition



Our clinical excellence is the result of a comprehensive, multidisciplinary team approach that not only involves our leading specialists and skilled surgeons but also a dedicated and caring nursing staff. Our Cardiac Intensive Care Unit has earned the prestigious Beacon Award for Critical Care Excellence, a top honor from the American Association of Critical-Care Nurses recognizing nursing excellence. Four other intensive care units at University Hospitals Case Medical Center have been recognized with Beacon Awards: Medical Intensive Care Unit, Reinberger Neuroscience Intensive Care Unit, Surgical Intensive Care Unit, and Rainbow Babies & Children's Hospital's Pediatric Intensive Care Unit. University Hospitals Case Medical Center is the only hospital in the state of Ohio and one of only two nationally with five or more Beacon Award-winning intensive care units.

## Save the Date

**UPDATE ON VASCULAR DISEASE: VENOUS THROMBOEMBOLISM IN 2011**

**Date:** Saturday, March 19, 2011

**Time:** 8:30 a.m. – 2:15 p.m.

**Location:** TBA

For more information, or to register for this event, please call **1-800-274-8263**. This activity has been approved for *AMA PRA Category 1 Credit™*

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## Rapid Referral

UH Rapid Referral is the fast and convenient way to get connected with UH Harrington-McLaughlin Heart & Vascular Institute specialists. Our doctors are here when you need us. Your patient will be scheduled and seen by one of our experts within 24 hours when you call the UH Rapid Referral line. It's that easy. Call **1-866-UH4-CARE (1-866-844-2273)**.



Image Courtesy of Apple

## Your Feedback Is Important

As a medical professional, your input is invaluable in helping us shape future issues of *UH Heart & Vascular Innovations*. We want to know what's important to you. Do you want to read about cutting-edge research, learn about the latest technology, or hear firsthand case studies of how others in your specialty are improving and saving lives? Tell us what you want to read about and your name will be entered to **win one of two Apple iPads!** Simply visit **[UHhospitals.org/innovations](http://UHhospitals.org/innovations)**.