MD

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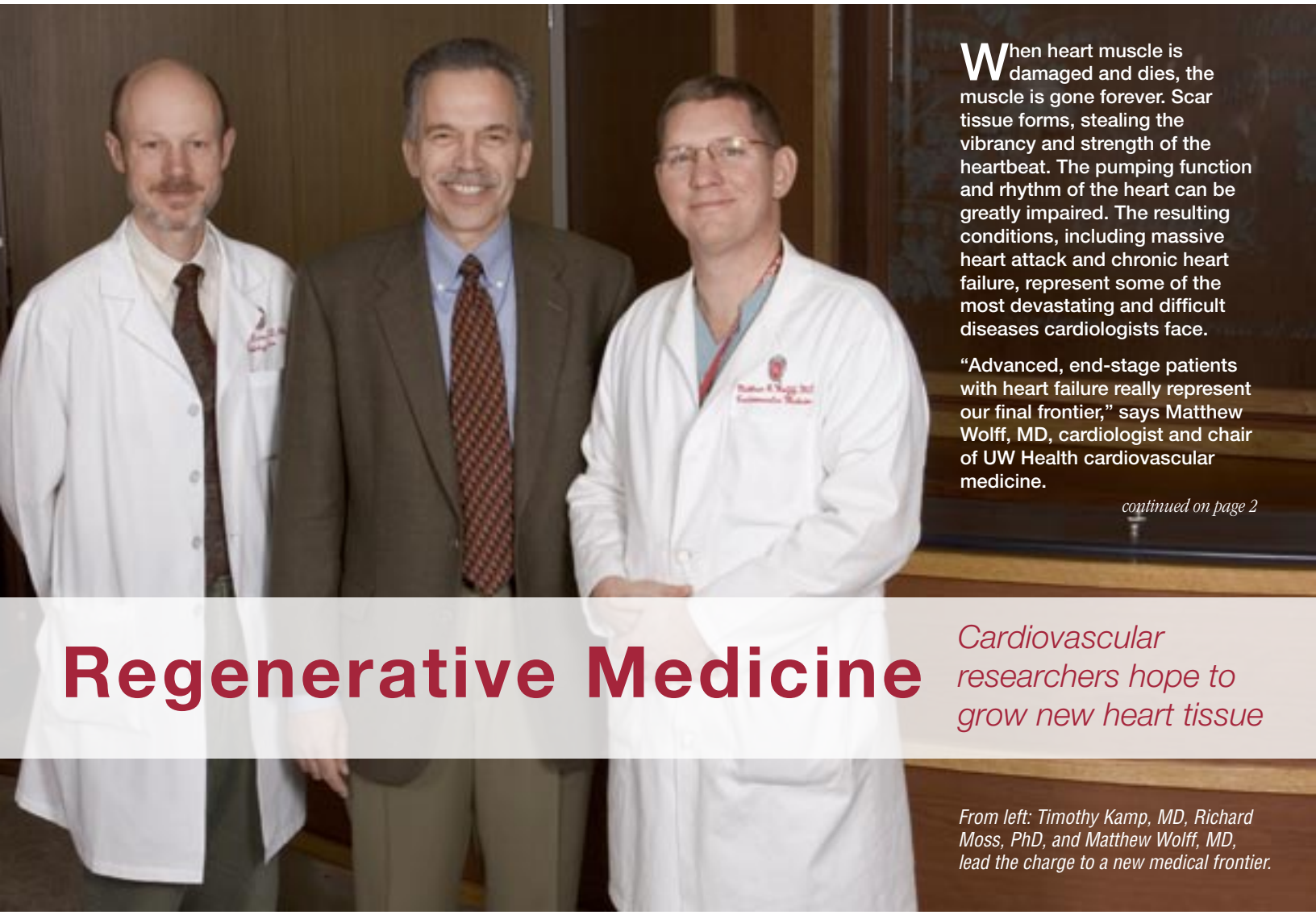

When heart muscle is damaged and dies, the muscle is gone forever. Scar tissue forms, stealing the vibrancy and strength of the heartbeat. The pumping function and rhythm of the heart can be greatly impaired. The resulting conditions, including massive heart attack and chronic heart failure, represent some of the most devastating and difficult diseases cardiologists face.

"Advanced, end-stage patients with heart failure really represent our final frontier," says Matthew Wolff, MD, cardiologist and chair of UW Health cardiovascular medicine.

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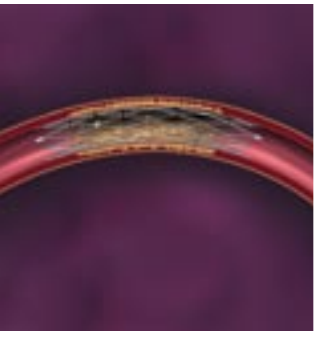
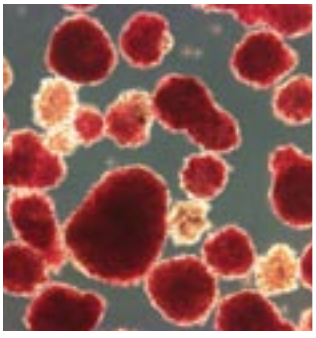
Regenerative Medicine

Cardiovascular researchers hope to grow new heart tissue

From left: Timothy Kamp, MD, Richard Moss, PhD, and Matthew Wolff, MD, lead the charge to a new medical frontier.





Regenerative Medicine *from page 1*

"Using statins and implantable defibrillators, we've made remarkable progress in the treatment and prevention of coronary artery disease and arrhythmias. But we still end up with patients who have failing hearts, where the only option is heart transplantation."

The need to discover less invasive therapies for these end-stage heart patients, more than 700,000 of whom die each year from heart-related issues, is the primary reason that UW researchers led by Timothy Kamp, MD, a professor of medicine and physiology in the UW School of Medicine and Public Health, are exploring an exciting possibility: Using all-purpose embryonic human stem cells to regenerate heart tissue.

"We're hoping we can find a strategy that will result in significant, if not complete improvement in the function of scarred areas of the heart over relatively short time frames," explains Wolff.

Kamp's early work seems promising. By transplanting all-purpose embryonic stem cells into mouse hearts damaged by induced heart attacks, Kamp's team was able to show that the cells morphed into cardio-myocytes (heart muscle); vascular smooth muscle, the muscle that forms the bulk of the walls of blood vessels; and endothelial cells, the flat cells that line the interior surfaces of blood vessels in the heart and throughout the body's circulatory system.

"The cell transplant didn't completely repair the heart, but it was encouraging," explains Kamp. "The heart ballooned out less and its ability to contract improved. The cells seemed to respond well to the area of active damage. There is something about the injury that favors engraftment and incorporation of those cells."

Kamp's research is housed in the UW Health's Cardiovascular Research Center, co-directed by Wolff and Richard Moss, PhD. The study appeared in a recent edition of the *Journal of Molecular and Cellular Cardiology*.

In addition to ethical questions surrounding the use of human embryonic stem cells, there are medical and biological issues to address before the therapy can be tested on humans. Human embryonic stem cells represent only one potential source of stem cell that can potentially be used for cardiac repair. Other sources include stem cells located in the bone marrow, in fat tissue, placental tissue or umbilical cords.

Delivery is another issue researchers must resolve. In the animal models, Kamp successfully injected the stem cells into the heart tissue through needles, resulting in a localized distribution. In theory, injecting the cells into coronary arteries could distribute the cells homogeneously to a larger area, but might also clog small branch vessels.

"Another outstanding question is, how are we going to guide these cells into becoming the cell type of choice?" asks Wolff. "It's not clear, for instance, that stem cells obtained form bone marrow have the potential to grow up to become heart muscles. They may only be able to become blood vessels, or even blood cells. If we're putting the stem cells into the heart, we want them to become heart-like tissue. We don't want them to become tumor tissue."

Although stem-cell therapy in humans is still several years away from approaching the realm of conventional therapy, Wolff and Kamp hope to begin human clinical trials using bone-marrow stem cells in heart-attack patients and patients suffering from peripheral artery disease within the next year.

"That latter group of patients may be very appropriate for bone marrow cells, because evidence shows that those type of cells preferentially grow up to become blood vessels, which is what people in that situation desperately need," says Wolff. "We're anxious to pursue that."

For more information regarding UW Health's clinical programs in advanced heart disease, call **1-800-438-3102 or (608) 263-7092.**

Safer by Design

New stent system opens up intracranial vessels, options

Intracranial blockages account for approximately 10 percent of ischemic strokes. Previously, patients at risk of stroke due to such blockages had limited options: pharmacological therapy, angioplasty with or without placement of a stent in the affected vessel, or extracranial-intracranial bypass surgery.

Each alternative has potential drawbacks. The risks of surgery in even the most accessible intracranial vessels are considerable. Medical therapy (primarily treatment with anticoagulant and/or antiplatelet medications) leaves many patients at considerable risk, as studies have shown that patients still carry a 12-22 percent risk of stroke within a year despite the medication. (In those having recurrent transient ischemic attacks, the risk can be as high as 40 percent.) And the earliest stents used, while effective in reducing stroke risk, were not designed for the specific anatomy of the small vessels in the brain.

That has changed. In November 2005, UW Health became one of the first four centers nationwide to offer the Wingspan stent system, following FDA approval in August. Specially designed for narrow and sometimes tortuous intracranial vessels, the stent system is designed to improve cerebral artery lumen diameter in patients with severe atherosclerotic disease that is refractory to medical therapy. "Severe" is defined as 50 percent or greater blockage in the vessel.

The Wingspan stent system is engineered to compress plaque and improve lumen diameter in intracranial vessels, which are smaller and more fragile than cardiac vessels. The system includes three components: a self-expanding stent, sheathed in a catheter that is guided into and through the femoral artery to the site of the blockage, and a balloon catheter that expands the blockage before the stent is placed in the vessel.

"The self-expansion feature of this system provides a more controlled operating environment and offers the patient a safer procedure," says Aquilla Turk, DO, of the neuro-endovascular team. "The system provides a safer option for high-risk patients who have not had effective treatment options thus far."

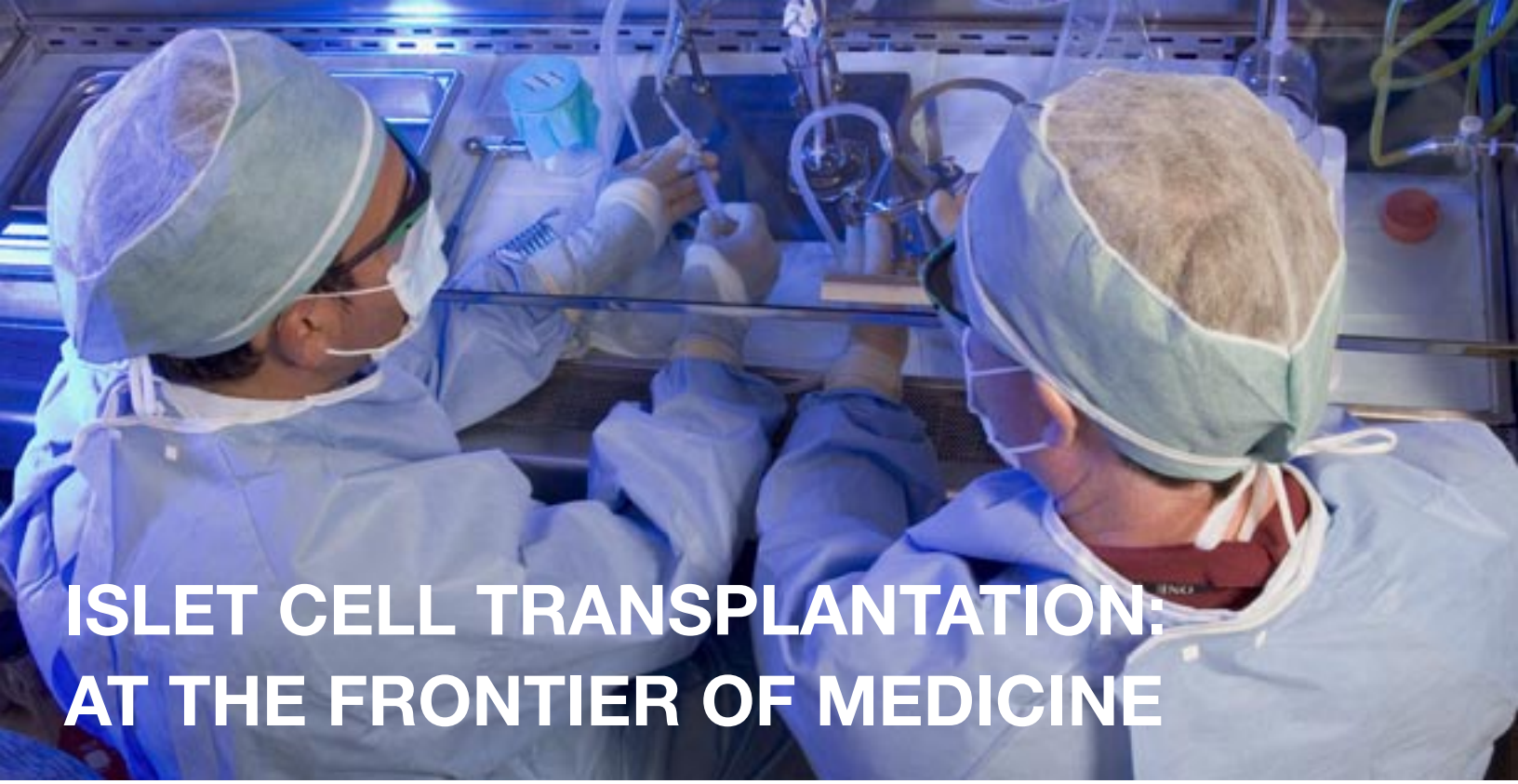
The new system was approved by the FDA under a "humanitarian device exemption," which acknowledges that the device has been shown to be safe and has probable benefit for patients who do not have other effective treatment alternatives. As of early January, the UW Health neuro-endovascular team had deployed approximately 25 of these newer stents in patients at high risk of stroke. Turk, along with Beverly Aagaard Kienitz, MD, of interventional neuroradiology, and David Niemann, MD, of neurosurgery, form the UW Health team.

Stent placements are performed in the XMR suite at UW Hospital, which includes both angiographic and MRI capabilities. Most patients spend one to three days at the hospital and typically can return to normal activities within a week.

The stents, constructed of nitinol, are compatible with MRI systems operating at field strengths of 3.0 Tesla or less. Patients with implanted stents must continue to use anti-platelet medications.

"The best candidates for an intracranial stent include those who have had multiple TIAs, who have significant blockages that can be accessed, and who are not well-controlled by current medical therapy," says Aagaard-Kienitz. "It is not indicated for patients who cannot take anti-platelet or anti-coagulation therapy ."

For more information on the Wingspan stent, contact **(608) 263-4730** or visit **uwhealth.org.**



ISLET CELL TRANSPLANTATION: AT THE FRONTIER OF MEDICINE

Surgeons with UW Health's transplant program have a stellar reputation for treating diabetes with pancreas and simultaneous kidney-pancreas transplant surgery. Since 1982, they've performed more than 1,000 pancreas transplants. Building upon this experience and success, the program now offers pancreatic islet cell transplantation for patients with Type I diabetes.

Led by Jon Odorico, MD, and Luis Fernandez, MD, both UW transplant surgeons, UW Health has joined the ranks of only a handful of medical centers in the world to offer this particular therapy through selective clinical trials. Currently, islet transplants are experimental and done only as clinical research.

Islet cell transplantation involves removing islet cells from a donor pancreas through a refined extraction process in a laboratory and transplanting them into the body of the recipient. The islets are infused into the main portal vein in either of two ways: percutaneous transhepatic portal vein cannulation or minimally invasive surgery. The goal of this type of transplant is to inject enough islet cells into the patient so that they begin to produce a sufficient amount of insulin to maintain normal blood sugar without the need for insulin injections or an insulin pump. Patients sometimes need multiple islet cell transplants to achieve this objective.

Because the entire pancreas must be used to obtain enough islet cells for the transplant to be effective, all pancreases used for islet cell transplantation are recovered from deceased organ donors.

The benefits associated with the procedure appear promising. Approximately 75-80 percent of patients who receive an islet cell transplant have been able to stop taking insulin injections completely. Islet cell transplantation is still investigational: Neither the precise benefit to patients nor the duration of insulin independence after islet transplant is known. Still, for patients unable to completely stop insulin injections, many are expected to benefit from improved glucose control and may regain their ability to sense low blood sugar levels. Indeed, the majority of patients are able to eliminate their dangerous unanticipated hypoglycemic episodes.

As with all transplants, there is a risk of rejection. Islet cell transplants require patients to take immuno-suppressive medications that inhibit the immune system's ability to destroy the transplanted islet cells. These medications expose the body to some risks such as increased risk of infection and certain types of cancer, and can also be associated with unpleasant or medically important side effects.

Risks associated with the procedure itself are minimal, but may include minor bleeding or, in rare cases, portal vein thrombosis. Subjects may have to receive more than one (and up to three) islet transplant procedures that may require subsequent hospitalization.

Before islet cell transplantation was an option, patients suffering from diabetes faced three transplant treatment options. Because kidney failure may occur in certain cases, the first and most common is simultaneous kidney and pancreas transplant. The second alternative is to receive a kidney transplant first, usually from a live donor, then receive a pancreas transplant from a cadaver donor at a later date. Third, in a few cases, patients may receive a pancreas transplant alone, without a previous or simultaneous kidney transplant.

There are two groups of patients who should consider islet cell transplantation:

- Patients with Type 1 diabetes who are considered "brittle" diabetics and have poor sugar control despite a course of intensive insulin therapy, or are unaware of the onset of low blood sugar levels.
- Patients with Type 1 diabetes who have a functioning kidney transplant and are already taking immunosuppressive medications.

Enrollment for clinical trials at UW Hospital and Clinics is open for both patient groups. For more information about islet cell transplantation at UW Health, contact **(608) 262-7159** or visit **uwhealth.org/transplant.**

Cardiac Surgery and the Older Patient

It's an option—often a successful one

With increases in life expectancy and a growing elderly population, demand for geriatric cardiac surgery has increased.

Older patients are often characterized as risky or ill-suited candidates for cardiac surgery and transplants. Research and procedures at UW Hospitals and Clinics, however, suggest these patients will not only survive surgery; they will also have an improved quality of life.

Heart surgeon Niloo Edwards, MD, author of "Aging Heart Disease and its Management: Facts and Controversies" and the head of the UW Health's cardiothoracic surgery program, says that while cardiothoracic surgery poses risks for any patient, young or old, often the benefits outweigh the risks.

"The most important thing older patients should know is that surgery is not only feasible but successful," says Edwards. "People underestimate how the ability to care for older patients has progressed. Older patients are physiologically different, but there are many things we can do to improve their quality of life and help them live longer."

At UW Health, an expert team of cardiologists and cardiothoracic surgeons evaluates each patient and designs a specific treatment plan tailored to the patient's needs. Careful, individualized management translates into better care and outcomes, one of many reasons Solucient named UW Hospital and Clinics one of the nation's top cardiovascular hospitals.

UW Health surgeons offer an array of advanced procedures—including coronary artery bypass grafts, mitral valve repair, minimally invasive surgery and ventricular assist device implants—to treat heart disorders ranging from valve complications to end-stage heart failure.

While more surgeries for older patients are performed off-pump, the biggest distinction is not the type of procedure, Edwards says.

"The difference between operating on a younger patient versus an older

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EXIT Strategy

Ex utero treatment saves newborn lives

Despite advances in medical expertise and technology, childbirth remains a risky procedure, particularly in cases in which the fetus develops airway problems caused by tumors in the chest or mouth.

Surgeons at UW Health are prepared to handle such a challenge, thanks to EXIT—ex utero intra-partum treatment, a surgical procedure used when there is a diagnosed abnormality that could threaten the baby during or shortly after delivery.

"EXIT is not something we use often, but it's very effective when needed," says Aimen Shaaban. MD, a UW Health pediatric surgeon who performed more than 100 EXIT procedures while at the Children's Hospital in Philadelphia, one of the centers that helped develop and perfect the technique. "The primary goal is to make the transition from in utero to birth safe."

In December, a team of physicians led by Shabaan performed the first EXIT procedure in Wisconsin on Madison Schmitz, a baby girl from La Crosse, Wis.. Shabaan estimates that UW Health surgeons will perform 6-8 EXIT procedures each year.

In the Schmitz case, the family's pediatricians had identified a cyst underneath the fetus's tongue. Physicans were concerned that the cyst could block the baby's airway during a normal birth, making it difficult or impossible for the baby to breathe. A rush to open the child's airway after birth would have been risky and could have taken several, critical minutes. Delays in providing oxygen could have resulted in irreversible brain damage or possibly death to the baby.

To avoid this scenario, members of the UW Health fetal treatment center, comprised of a multidisciplinary team of physicians and staff from UW Hospital and Clinics, UW School of Medicine and Public Health and Meriter Hospital in Madison, successfully performed an EXIT procedure on Madison Schmitz.

Physicians first administered general anesthesia to the baby's mother to relax the uterus and prevent contractions. During this time, the placenta continued to deliver oxygen and anesthesia to the baby.

Next, physicians delivered the baby through a modified C-section and inserted a breathing tube beyond the cyst and into her windpipe. At this point, she was fully delivered, and they cut the umbilical cord. Immediately following the procedure, staff took the baby to another room where they removed the cyst.

"The threshold for this procedure is a little lower," explains Shaaban. "The risk is to the mother, but the benefit is to the baby."

For more information on the EXIT procedure and the fetal treatment center, contact **(608) 263-9419** or visit **uwhealth.org**.

BALANCE IN THE KEY OF "D"

Can vitamin D help improve balance, prevent falls?

With treacherous ice and snow currently coating sidewalks and driveways, many older Wisconsinites live in fear of falls—and the broken bones that often result from them.

What if a simple dose of vitamin D could help reduce the risk of falling? Researchers with UW Health's Osteoporosis Clinical Research Center are currently recruiting patients for a study that aims to answer that question.

"We've recognized that vitamin D inadequacy causes osteoporosis," explains Neil Binkley, MD, UW Health osteoporosis specialist and lead researcher on the study. "There's also data that indicates that vitamin D is important in muscle function, and a lack of it causes muscle weakness, leading to an increased risk of falling."

Previous studies have noted that increasing vitamin D has a positive effect on muscle strength and balance in the very old and frail. The new study will focus on less older individuals who live in the community and remain active and mobile.

Participants will receive either a 8,400 IU of vitamin D once per week or placebo for the duration of the 16-week research study. At several points during the study, researchers will measure participants' body sway by asking them to stand on a balance platform. Participants will also undergo a formal gait assessment at UW Health's Rehabilitation Clinic. In particular, researchers will be measuring speed of gait and the amount of time an individual stands in what's called "double-stance" gait—both feet on the ground.

"If vitamin D inadequacy is contributing to unappreciated weakness and thereby increasing the risk for falling, then this study will show that we have a simple, cheap and nontoxic way to reduce falls," says Binkley. "That's obviously a good thing."

Binkley is among a growing number of physicians who believe the current recommended daily allowance for vitamin D (400 IU) is inadequate. He would like to see it raised to 1,000-1,200 IUs per day—about the equivalent of drinking three quarts of milk a day. Given that vitamin D is only available in a limited number of foods—fortified milk, egg yolks, certain types of fish—supplementation is often the only option.

"It's kind of counterintuitive that we have to supplement," he says. "You would expect our diet to take care of what we need, but that isn't the case."

To be eligible for the study, participants must be over the age of 70, low in vitamin D (taking 800 IU or less per day) and able to walk without assistance. For more information, call **(608) 263-BONE**.

Skin Deep

Non-invasive test reveals coronary artery disease in patients with no symptoms

A UW Hospital and Clinics study published in a recent edition of the *American Heart Journal* shows that a simple, non-invasive test to measure skin tissue cholesterol can detect early vascular disease.

The study used a PREVU Point of Care (POC) Skin Sterol Test, developed by PreMD Inc., a Toronto, Canada-based testing device manufacturer, to show that skin cholesterol levels have a significant association with increased carotid intima-media thickness (CIMT). CIMT uses ultrasound to scan the carotid arteries for evidence of atherosclerosis, and is an independent predictor of myocardial infarction and stroke.

"Just as many people who die suddenly from heart disease don't have prior symptoms, many patients who have high blood cholesterol never develop heart disease—while many patients with low blood cholesterol do," says James Stein, MD, a preventive cardiologist with UW Health, and principal investigator of the study.

The study, conducted at the UW School of Medicine and Public Health, included 81 patients without known vascular disease who were referred for determination of CIMT. Patients underwent B-mode ultrasonography of the carotid arteries and measurement of skin sterol using the POC test. CIMT was significantly higher among patients in the highest quartile of skin sterol ($p = 0.011$). Skin sterol was associated with increased CIMT even after adjusting for age, sex, glucose, systolic blood pressure, total high-density lipoprotein cholesterol ratio, and use of lipid-lowering therapy ($p = 0.031$).

While the skin-cholesterol test is not yet available for general clinical use, Stein is hopeful that studies like these will expedite wider use.

"There is considerable interest in non-invasive, simple and rapidly administered tests to better assess which patients are at increased risk," says Stein. "The significant association with increased CIMT suggests that skin sterol testing may help to identify asymptomatic patients who are at future risk of having a heart attack or stroke."

VEPTR

A new treatment for severe scoliosis

Pediatric patients with thoracic insufficiency syndrome (TIS), a rare congenital condition in which severe deformities of the chest, spine and ribs prevent normal lung development, often face daunting developmental hurdles as they grow.

Surgeons at UW Health now have another option to treat them—the Vertical Expandable Prosthetic Titanium Rib (VEPTR.)

Last year, Ken Noonan, MD, a UW Health pediatric orthopedic surgeon, and Aimen Shaaban, MD, a UW Health pediatric surgeon, recently became the first doctors in Wisconsin to use a VEPTR to treat a pediatric patient with TIS. The pair successfully implanted the device in a two-year-old patient with a 80-degree spine curvature.

"This procedure is not for run-of-the-mill scoliosis," says Noonan, who also tried body casting and a back brace to correct this patient's condition. "The VEPTR procedure is intended for patients under the age of four or five whose conditions are so severe that they would become life-threatening if left untreated as the child grew."

In the VEPTR procedure, surgeons implant an expandable metal rod that is curved to fit the back of the chest and spine, using hooks located at both ends of the device.

"The VEPTR device allows us to indirectly correct the spine by stretching on the ribs," explains Noonan. "We can expand it every six months or so to allow the child to grow before we consider a more permanent procedure like spinal fusion."

Unlike more standard surgeries to treat congenital scoliosis, like spinal fusion, the VEPTR device is designed to give the rib cage room to grow in children who suffer from chest wall or spine defects. While helping to straighten the spine, the VEPTR device separates the ribs to allow the child's lungs to develop.

"A fusion procedure stops the spine from getting worse but essentially stops it from growing," says Noonan. "It isn't a huge deal when you're 14 and done growing, but it is when you're two and need a lot of remaining spine growth."

Within six months of the surgery, patients can expect to see a dramatic improvement in their posture, says Noonan. "They will also have improved lung function as well as an increased energy level and ability to perform activities," he adds.

VEPTR was developed in 1987 by Drs. Robert Campbell and Melvin Smith of CHRISTUS Santa Rosa Children's Hospital in San Antonio, Texas. With great success, the surgeons implanted the first VEPTR-like device to stabilize and enlarge the thorax of a child who was missing ribs on one side of the thorax. Prior to the development of the UW VEPTR team, only seven centers in the United States were performing this procedure.

For more information about this procedure or to schedule an appointment, call **(608) 263-1344** or visit **uwchildrenshospital.org.**

Cardiac Surgery *from page 5*

one is how you manage the patient both pre- and post-operatively. It's not that a bypass is much different in an older patient; it's how you manage that patient to produce the best outcome."

When managed properly, recovery for older patients is similar to their younger cohorts. The risk of complications, such as stroke, is slightly higher for older patients; nevertheless, the majority of these patients have an improved quality of life and survival compared to peers who did not have surgery.

According to research by Edwards and others, there is no difference in long-term survival rates between younger and older patients. Research shows that elective surgery yields the best outcomes for both younger and older groups. "For older patients, if you can do the surgery electively, the outcome is the same and sometimes better than in the younger age group," says Edwards.

Postponing surgery until a crisis, such as acute myocardial infarction, causes some patients to select emergency surgery. Emergency procedures are two to ten times more risky than elective procedures.

Ultimately, the patient makes the final decision regarding his or her treatment.

For more information, please contact **(608) 263-0439**, or visit **www.uwhealth.org/heartandvascular.**

The **UW Health Cardiothoracic Transplant Program** recently celebrated another major milestone, becoming just the tenth hospital in the nation to perform its 1,000th heart/lung transplant. The accomplishment arrives in a year during which UW Health transplant surgeons also set a program record, performing 26 heart transplants and 43 lung transplants. The program performed its first heart transplant in 1973.

Dr. David Jarrard, MD

David Jarrard, MD, has been named the first John Livesey chair of urologic oncology.

University of Wisconsin
SCHOOL OF MEDICINE AND PUBLIC HEALTH

The UW School of Medicine has formally changed its name to the **UW School of Medicine and Public Health**, a title that betters reflect the new approach to addressing the most challenging health care problems in Wisconsin.

UW Health's Integrative Medicine Center has become one of 29 academic medical centers to join the national Consortium of Academic Health Centers for Integrative Medicine (CAHCIM), an organization charged with exploring methods of transforming how health care is delivered to patients and taught to medical students.

Center director David Rakel, MD, says one focus will be the challenges posed by the increaisng need for medical management of chronic diseases such as diabetes and asthma.

"We're going to have to understand the dynamic influences of what it means to facilitate healing," says Rakel.

Lucille Marchand, MD, has formally introduced integrative medicine into the UW Comprehensive Cancer Center and its affiliated clinics.

Lucille Marchand, MD

Marchand's is also involved in research on how integrative medicine can assist patients dealing with cancer achieve higher levels of wellness in their journey with cancer.

In addition, massage therapy and acupuncture services are now being be provided in UW Health cancer clinics on Wednesday and Thursday afternoons. A physician authorization is required for patients to receive these services.

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