MAYO CLINIC

Mayo Clinic

MAGAZINE

Celebrating 25 Years

Mayo celebrates a quarter century in Arizona

2012 ISSUE 1

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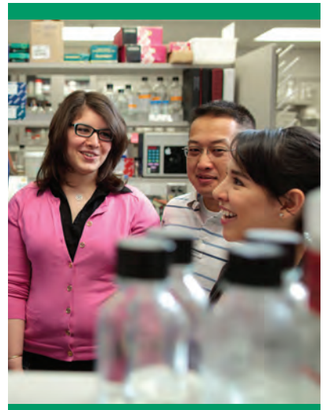

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In this issue: How Mayo gets people back to living their lives

Mayo has a long history of combat medicine. During World War I, the Mayo brothers helped establish Base Hospital No. 26, which deployed to France in December 1917. The base hospital received hundreds of wounded a day, and by the time it was demobilized a year later, the "Mayo Unit" had treated over 7,000 soldiers.

In this issue of *Mayo Clinic Magazine*, you'll read stories about how current advances in medical science are helping wounded troops get back to living their lives. Mayo's greatest contribution to military medicine may yet emerge in the field of regenerative medicine. One of its greatest potentials — that will benefit people injured on the battlefield or in civilian life — is regenerating nerves to a point where the patient regains feeling and function. You'll read about Mayo physicians and researchers searching for solutions to challenges that face service members, including biological threats, injury rehabilitation and psychiatric illness.

Helping people resume satisfying lives sometimes means reconstructive surgeries. In "Inspired to Save Lives," Samir Mardini, M.D., speaks about the new and fascinating field of hand and face transplantation and the research that bolsters it. You'll read about Tarek Obaid, a Mayo patient, who gave $10 million to Mayo Clinic to establish the Essam and Dalal Obaid Center for Reconstructive Transplant Surgery and how the gift reflects his own compassion for victims of war and trauma.

Other stories take you from transplantation to implantation — orthopedic style. In "Not All Knees Are Created Equal," Mayo patient Charlotte Chastain shares her story of life-interrupted and life-resumed. Mayo Clinic orthopedic surgeon Mary O'Connor, M.D., used new robotic technology in the knee replacement surgery to help Chastain get back on board the merchant marine ships she loves. In "A Thoroughly Modern Infection," you'll meet Elsie Discus Sexton, who credits Mayo with saving her leg. Sexton represents a growing number of people with disturbing stories about medical-device infections, including knee and hip implants. These patients are coming to Mayo Clinic for diagnosis and resolution — for hope and help getting back to the business of living.

After close to 150 years, Mayo Clinic's mission is still patient-centered; we help people resume satisfying lives by providing the best care to every patient every day through integrated clinical practice, education and research. True to our heritage, we recognize that all three aspects of our mission are intertwined. Without research, knowledge doesn't evolve. Without education — the sharing of that knowledge — patient care cannot advance.

We hope you enjoy this issue of *Mayo Clinic Magazine*. Each issue strives to bring you an inside look at Mayo Clinic, and each issue carries within its covers our thanks to you for the confidence you've placed in us.

Dr. Michael Camilleri
Executive Dean for Development

From Prison Chow to Lobster Bisque

A strong wind blows snow and shakes the bare trees as Greg Sands maneuvers up the long driveway of the country club. He pulls his hybrid Cadillac Escalade to the front door, gets out with a couple visitors in tow, smiles and asks the valet what he's been reading.

Moseying into the club's restaurant, Sands asks the host who's cooking today and teases the wait staff like nieces and nephews. "Are you my waiter today?" "No, Carley is taking care of you." "Oh, thank God." Everyone laughs as Sands and his guests take off their coats and sit down.

Greg Sands may not golf, but this is Greg Sands' turf.

> "Your choice to quit has been gone for a decade. It just controls your life. The drug is your higher power."

The dining room of this South Dakota country club is window-lined and empty except for a group of women playing bridge quietly in the far corner. It's late morning, too early for a lunch crowd. Sands samples the lobster bisque (today's special) and faces the golf course, which is covered in snow and swept by the wind and cold.

Before lunch, he and the visitors spend all morning talking. They continue to ask about Sands' past, about his present, about his future. He answers each question candidly and with humor. But each answer prompts more questions. Greg Sands has lived that kind of life.

"What was life like in prison?" asks one of the visitors. Sands laughs. "It was an uncomfortable environment."

The best thing that ever happened to Greg Sands — getting arrested

Less than 25 years ago, Sands lived a different life. A cocaine addiction drove everything he did — when he worked, when he got up, what he ate, what he thought.

And every day, his addiction got a little worse. He hit bottom several times, even checking into a rehab program once. But the addiction kept its hold on him.

"You're powerless over it," he says. "Stopping is not an option. Your choice to quit has been gone for a decade. It just controls your life. The drug is your higher power. It's your boss, your lover, your partner. It's everything in the world to you. There is nothing with greater strength over you than that substance."

In 1991, after serving two years in federal prison, Sands was released, landing in Sioux Falls with $50 and not much hope.

In his late 20s, Sands started dealing drugs to sustain his habit.

"I was my best customer and an extremely unsuccessful drug dealer," he says. But then the federal authorities intervened. On April 10, 1989, the FBI arrested Greg Sands for sending cocaine through the mail, and the federal government charged him with conspiracy to possess with intent to distribute.

It should have been his wake-up call, but Sands came to the pretrial hearing "a little intoxicated." So the judge sent him to Glory House, a halfway house for drug addicts, where director Dave Johnson twice caught him drinking.

Eventually Sands was found guilty of the drug charges, and the judge sentenced him to 36 months in federal prison. Greg Sands had finally hit his rock bottom.

"The first day in there, I cried," he remembers. "For a pack of cigarettes, someone will take out your kneecaps. And time goes painstakingly slow. That's the reality of prison."

About two years into his sentence, the Federal Bureau of Prisons was going to grant him supervised release under the condition that he live at Glory House, but director Johnson refused to accept him because of Sands' history of rule breaking. He was heartbroken. The fear of returning to prison would keep him clean, he knew, but the window of opportunity to get out had just slammed shut.

Miraculously, after four months, Johnson relented. Ten years later, Johnson admitted that he'd always planned to take Sands back, but he wanted Sands to fully understand the opportunity before him.

In 1991, after serving two years in federal prison, Sands was released, landing in Sioux Falls with $50 and not much hope.

"It's a tough road when you're an ex-con," Sands says. "But coming out and knowing what freedom is, well, it's a hell of a thing. I remember when I first sat in a good restaurant and I could actually order what I wanted. It was just unbelievable."

Sick and tired of being sick and tired — building a second chance

At 33, Sands wanted a new life. He was tired of living day to day, week to week. He was tired of uncertainty and chaos, tired of being an addict. So he turned to his pre-prison profession, drywalling, and worked every hour he could. He attended regular AA and NA meetings. And he met Pam.

The two worked hard, saved money, got married and started Sands Drywall in 1995 with Sands as its only employee. To grow the company, Sands talked the bank into giving him a loan, which leveraged everything he owned — the company, his tools, even his car. Only now he was building his own houses. He sold his first house within 92 days, paying the bank only $862 in interest.

"I could build houses the rest of my life and never have one go that good," Sands recalls with a smile.

> "It warms my heart because I know that facility helped save somebody's life."

Sands worked 40 hours a week to get his home building business off the ground, in addition to the 40 hours he put in drywalling. Soon he hired a guy to help. Then another guy. Then he saw an opportunity that no one had noticed before. Why not specialize, concentrating on drywall finishing work, taping and texturing?

Big contractors went for it. It meant quicker turnaround with one company's guys hanging the sheetrock and the other company's workers finishing the job right next to them. Before long, Sands employed a crew of 20. Then another 20. Seven years ago, Sands Drywall turned to steel stud framing and within 12 months was the largest steel stud framing company in South Dakota. Today the company employs about 200 workers.

When he was hungry, he was fed — repaying debts

Greg Sands remembers when he first tasted success. A financial adviser helped him understand what the business earned in a month. Sands' first thought was, 'How can I help people with this money, this blessing? What gifts can I give?' "I'm grateful for that thought," he says.

He makes sure his gifts have purpose — feeding people and fighting addiction. His first large donation built the Sands Freedom Center, a 24-bed halfway house for women with addiction. As an extension of Glory House, Sands Freedom Center also helps 250 to 300 men and women each year on an outpatient basis.

To further focus his philanthropy, Sands is establishing his own foundation. Last year, he served 3,000 Thanksgiving meals in Rapid City and Sioux Falls and aims to serve Thanksgiving dinner to every South Dakotan who needs it.

"I believe that will be achieved in short order," Sands says. "In two to three years, I'll see that done."

Every Christmas, through the foundation, he gives $50 to each resident of Sands Freedom Center and Glory House, the facility that helped turn his life around 20 years ago.

"It warms my heart because I know that facility helped save somebody's life," Sands says. "Though it may not seem like much, $50 can make a big difference to a person. When you have zero, $50 is a lot."

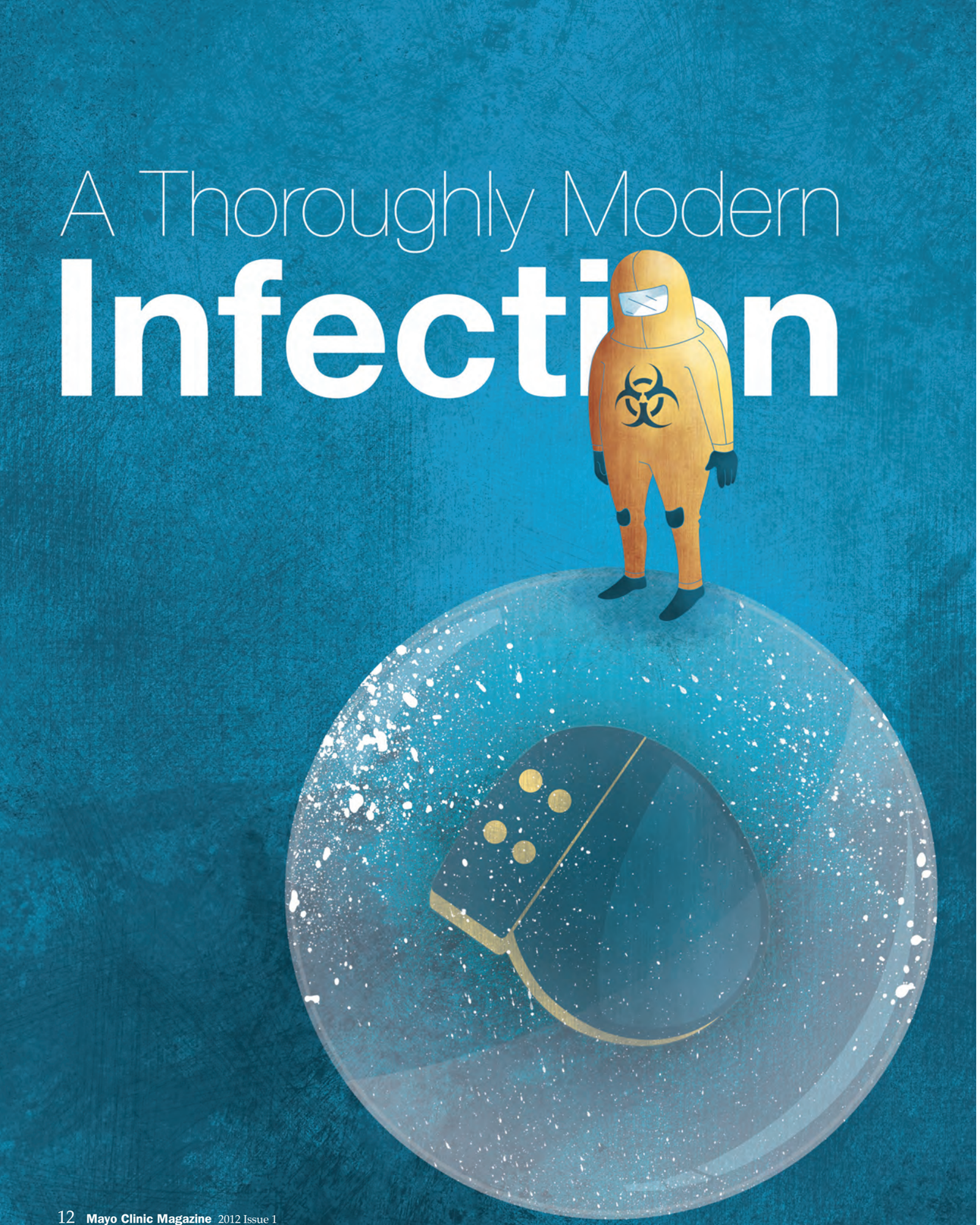
But Sands says his biggest gift will have the biggest impact — a major-level gift to the Mayo Clinic Samuel C. Johnson Genomics of Addiction Program.

Mayo researchers are working to cure addiction at the molecular level by identifying specific genetic markers and developing therapies tailored to those addiction genes. Most conventional treatments focus only on changing behaviors through education and counseling and ignore underlying genetic factors.

Sands knows what that driving force feels like. For years he struggled to quit, but the addiction permeated every cell of his body, and it seemed like his very molecules pushed him on. It took years of failure and prison time for him to overcome his addiction. And by supporting the genomics of addiction program, he hopes to save others the same struggle.

"I have great belief in the genomics of addiction program to cure addiction," Sands says. "I believe that, someday, we will accomplish that. I have a mathematical mind, and as I studied what they're doing — it just adds up. It will be a reality." ■

A Thoroughly Modern Infection



An expanding roster of implanted medical devices has saved and improved countless lives, offering proof of tremendous strides to remedy aging or damaged human parts.

While new parts are replacing or repairing original equipment in a burgeoning number of patients, these foreign bodies also have introduced a new breed of highly fortified and potentially life-threatening infections.

Growing numbers of patients with tragic stories about medical-device infections flock to the Division of Infectious Diseases at Mayo Clinic in Rochester, Minn. They come to Mayo because of its worldwide reputation as a center of excellence for managing infections related to all kinds of devices. One team of Mayo specialists has the nation's largest practice in orthopedic device infections. A second team specializes in infections associated with cardiovascular implants, including electronic devices, vascular grafts, stents, assist devices and more.

Device-related infections are both hard to detect and hard to defeat. They infiltrate the body and attack from within, often growing for months before causing symptoms and then concealing their identity. Meanwhile, most of these infections build a fortress with multiple defenses against the body's immune system and antibiotics.

Instead of curing or relieving a condition, a device accompanied by infection can cause additional pain, additional time lost to disability, and additional recovery time. Studies indicate that each infection adds close to $60,000 to the cost of a prosthetic joint and $25,000 to $50,000 to the cost of an implanted cardiovascular device.

"Infection is one of the greatest fears of patients and surgeons among all medical-device complications because the patient could end up worse off than before," says Elie F. Berbari, M.D., a member of Mayo's Orthopedic Infectious Diseases service and education chair of the Division of Infectious Diseases. "If we can reduce the risk or the impact of infection, it's worth the effort in research."

In the United States, 1 million infections a year accompany a spectrum of indwelling medical devices — pacemakers, heart valves, prosthetic joints, penile implants, lenses, dental implants, shunts, stents and other artificial parts. The growing population of older Americans translates to a rising demand for implantable devices and proportionate increases in infections, which develop in about 4 percent of patients with a medical device.

"Many types of medical devices, or foreign bodies, are placed into patients as part of modern medical care. These interventions are huge success stories that have revolutionized care," says Robin Patel, M.D., director of the Infectious Diseases Research Laboratory at Mayo Clinic. "It's the intersection of modern medicine and basic biology that leads to new opportunities for infection. We didn't see this type of infection 50 years ago."

Microscopic defenses

The culprit behind most device-related infections is biofilm. Unlike free-floating bacteria, the traditional cause of infections, biofilm is a community of bacterial cells that adhere to a surface, construct a protective shell, and grow differently than mobile microbes. Biofilms regularly form on surfaces in nonsterile, damp environments, like shower floors and the inside of pipes. They also can grow on sterile implanted medical devices.

> "Infection is one of the greatest fears of patients and surgeons among all medical-device complications because the patient could end up worse off than before."

"A prosthetic joint is like a magnet for bacteria that evolves into biofilm, which is nothing more than a community of organisms that shelter themselves from threats," Berbari says. "Biofilms have developed elaborate mechanisms to survive."

Antibiotics used in clinical practice were not developed to act against biofilm, and most have little effect on bacteria in the biofilm state. Studies show that biofilm bacteria can be up to 1,000 times more resistant to antibiotics than mobile microbes.

Bacteria that don't cause illness while living on the patient's own skin can become toxic on an implant. These mild-mannered bugs, most often a form of Staphylococcus, or staph infection, likely enter the body during surgery. They adhere to the surface of the device and form a biofilm. The patient may not notice any signs of infection for months.

In most cases, an infected device requires one surgery to remove the device, antibiotics to clear up the infection, and a second surgery to implant a replacement device. If removal would endanger the patient, the infection may become a chronic condition, necessitating antibiotic treatment for life.

The infection specialists

Device infections are complex cases that involve multiple complications and require multiple specialists. For example, Infectious Diseases, Cardiology, Cardiovascular Surgery, Microbiology, Anatomic Pathology and other departments collaborate when a patient develops infective endocarditis, a life-threatening complication that results in inflammation of heart valves or the lining of the heart's chambers.

This collaboration carries over to research, where clinicians and investigators jointly pursue advances in the battle against biofilm. "We know quite a bit more now about these infections," Berbari says, "but we still don't know the whole story."

Larry M. Baddour, M.D., chair of the Division of Infectious Diseases, says Mayo teams learn from each other while pursuing answers in several areas.

Risk factors

Researchers have already shown that patients who are elderly, undergoing cancer treatment, have a chronic illness, or have a compromised immune system are most susceptible to device infections. Slow healing or developing an infection elsewhere also increases the risk.

Mayo's global registry on prosthetic-joint infections provides clues to uncover risk factors. Started in 1991 by Division of Infectious Diseases specialists Douglas R. Osmon, M.D., Arlen D. Hanssen, M.D., and James M. Steckelberg, M.D., the database documents the medical histories, symptoms, test results, treatments and outcomes for more than 5,000 patients who developed a prosthesis infection since 1969.

Similarly, nine Mayo studies since 2005 have analyzed risk factors for infection related to cardiovascular implantable electronic devices. These studies identified criteria to predict development of infective endocarditis.

Mechanisms

Understanding how biofilms form and grow will lead to better ways to prevent and treat device

infections. With funding from the National Institutes of Health (NIH), Patel and a University of Minnesota microbiologist are looking for the genes that give two bacteria their ability to form biofilm.

"If we can find the genes that impact biofilm formation in both these bacteria, chances are they are present in other bacteria as well," Patel says. "Then we can develop a drug to act against a number of bacteria. If we knock out those genes, they can't form biofilm." This type of drug might spare patients from surgery to remove an infected device or might prevent an infection altogether.

Diagnosis

Device infections are notoriously difficult to diagnose. Even when all signs suggest infection, biofilm's armor and fastidious growth may mask its identity on testing. If the type of pathogen remains a mystery, physicians don't know the best treatment.

Working with Mayo's Ultrasound Research Laboratory, Patel adapted the use of ultrasound technology to diagnose infections of artificial joints and other devices. When an infected device must be removed, Mayo places it in an ultrasound bath. The agitation of minute bubbles likely causes tiny tears in the biofilm, forcing bacteria out of their protective layer. Then researchers can identify the bacteria in the solution.

Patel and her colleagues also are working on multiple tools to pinpoint pathogens before removing the device. One strong possibility is a polymerase chain reaction (PCR) test of the surface of a prosthetic joint or fluid around it. This fast and powerfully sensitive technique could be used to "amplify" low counts of bacteria DNA sequences found in test samples. Other assays could test for inflammatory cells and other markers that indicate the presence of specific bacterial biofilms. In addition to differentiating between harmful and harmless microbes, diagnostic tests will need refining to determine whether the quantity of bacteria is enough to cause a problem.

"Our hope in the future is for a blood test for infection, so diagnosis would not be invasive to the patient," Patel says. "But that's still futuristic."

Treatment

Because most patients need a medical device to compensate for loss of function, removal of an infected device occurs as a last resort. The quest for better treatment aims to conquer biofilm without removing the device.

With funding from a five-year NIH grant, Patel is developing an electrical treatment of device infections.

"Testing a collection of bacteria in the lab, we can cure infections with a low amount of electrical current," Patel says. "It does work — with no antibiotic."

Further study of the "electricidal effect" on microbial biofilms will establish how little current and duration it takes to work. Patel foresees doses of electricity as a noninvasive tool to treat established infections and possibly prevent infections at the time of implant.

"We have a lot of work to do, but it's exciting to have a possible new way to treat device infections," Patel says.

> "Our hope in the future is for a blood test for infection, so diagnosis would not be invasive to the patient."

Prevention

The "best" infection to have is the one that never occurs. That's the one that costs nothing to treat and causes no harm to the patient. For that reason, Mayo researchers in the field of infectious diseases study prevention.

"We need new strategies to prevent infections and drive down the numbers of infections that occur," Patel says. "I suspect we'll need a

Focused on the Challenge

Facing endless unknowns on prosthetic-joint infections, Robin Patel, M.D., decided to give up patient care so she could devote more time to solving the mysteries of biofilms. Patel moved exclusively to laboratory work in 2007.

"We were seeing biofilm-associated infections in a huge number of patients referred here," Patel recalls of her 11 years as a clinician-researcher in the Division of Infectious Diseases. "I became really interested in understanding what goes on in bacterial biofilms with a view toward figuring out how to diagnose, treat and prevent biofilm infections."

Patel had completed her residency in internal medicine and a fellowship in infectious diseases through Mayo Graduate School of Medicine. Then she added a fellowship in clinical microbiology. Now a microbiologist, and primarily a bacteriologist, Patel has uncovered mechanisms and characteristics of bacterial biofilms, including Staphylococcus lugdunensis, a virulent, new staph species. She has championed numerous advances.

"Everything my research team does helps us to learn more about these biofilms and the next step in combatting medical-device infections," she says. "Ultimately, we want to provide better care for all patients with device infections."

multipronged approach. It won't be one approach because these infections are multifaceted."

"We're trying to understand the factors that can lead to a device infection and optimal ways we can control or modify these factors," Berbari says. "We still don't understand where all infections come from. There are still a lot of factors we need to identify to help reduce the chance of infection."

To make device surfaces less inviting to biofilms, manufacturers have tried coating devices with antiseptics or antibiotics and switching to materials that offer pathogens less grip. Meanwhile, Mayo investigators look closely at best practices — the optimal strategies for prevention of infections.

Studies using the Mayo registry on prosthetic-joint infections have shown that the infection rate drops when antibiotics clear up staph infections carried by the patient before surgery; the patient bathes with antiseptic solution before surgery; the patient receives antibiotics during surgery; and the fixation cement around the prosthesis contains antibiotics. Additional studies will establish precise recommendations and evaluate other strategies, such as the use of special barriers, ultra-filtered air or ultraviolet germicidal air purifiers during surgery.

"We know what works to prevent device-associated infections, but we also need to research the optimal strategies to implement those interventions universally," Berbari says.

Going forward, Mayo Clinic remains at the forefront of improving management of medical-device infections.

"We will follow a structured format for every patient with certain types of device infections," Baddour says. "We plan to collect data to identify what is helpful and what we can do better. Our hope is for improved care and reduced cost."

Spreading the Knowledge

To help address the growing number of prosthetic-joint infections, Mayo Clinic created a specialized fellowship program in orthopedic infectious diseases in 2008. Since then, two fellows have completed the one-year program. Graduates are proficient in the diagnosis, management and prevention of all types of musculoskeletal infections.

EXPERTISE HELPS

Save a Leg

Energetic and active at age 77, Elsie Dicus Sexton of Fayetteville, Ark., wasn't about to let osteoarthritis slow her down. Bone-on-bone knee pain intruded on her treadmill workouts and woke her at night, so in March 2008 she had total knee replacement on both legs. She was home in four days, back to work in one week, and driving within two weeks.

All was well until her right knee started swelling and feeling hot — signs of infection that baffled doctors for close to two years.

"I still work every day," says Sexton, who runs her own property management company. "I had to be at the office, but I couldn't just get up and go with my leg hurting."

Doctors took a fluid sample from one side of her knee, then the other side. They performed surgery for possible removal of the prosthetic joint, but opted instead for six weeks of intravenous antibiotics. Physicians referred her to a dermatologist, then to an oncologist who surgically extracted tissue samples that tested negative for malignancy.

"The doctor went deep for the tissue specimens," Sexton recalls. "The incision never healed. It kept draining and draining."

The knee opened up, leaking synovial fluid, in January 2010. Her local doctor suggested getting to a major medical center. For Sexton, that meant Mayo Clinic in Rochester, Minn.

"We've always gone to Mayo for everything," Sexton says. She is a former registered nurse, and her husband, Giles A. Sexton, M.D., is a retired physician. "We've been going there since the 1960s. Since the '90s, we've been back every year for physicals."

Mayo's team approach brought together orthopedic surgeon Arlen D. Hanssen, M.D., an international leader and researcher in the field of bone and joint infection, and the Orthopedic Infectious Diseases service. Based on criteria developed at Mayo, testing of fluid from Sexton's knee confirmed the diagnosis of an infection. Hanssen surgically removed the prosthetic knee joint, inserted a temporary, antibiotic-loaded block, and put her leg in a cast. Novel technology invented at Mayo Clinic dissolved a biofilm on the prosthesis. Testing identified the pathogen as Staphylococcus lugdunensis, which has been studied extensively by Mayo's Infectious Diseases Research Lab. For six weeks Sexton used a wheelchair and received optimal intravenous antibiotics to cure the infection. The team then implanted a new prosthetic knee.

"If the infection had kept on, I probably would have lost my leg," Sexton says. "The knees are great now. I'm walking and going to the gym to exercise every day."

How to **Squash a Superbug**

As the head of a Mayo Clinic lab that engineers vaccines, Michael A. Barry, Ph.D., tries to protect people from the diseases they fear most. "That motivates me — what frightens people," Barry says. "One thing that scares me is MRSA."

Methicillin-Resistant Staphylococcus aureus (MRSA), the so-called superbug, has developed resistance to many antibiotics. It primarily affects people in health care settings, including those who have had an implanted medical device.

Barry is leading a novel effort to develop a vaccine against MRSA, which typically originates on the patient's own skin.

"Normally, you go after the pathogen, but we're trying something different," says Barry, who has joint appointments in the Division of Infectious Diseases and the Department of Immunology. "We're trying to vaccinate against the proteins that destroy the antibiotic."

Using a Cold War analogy, Barry explains that antibiotics triggered an arms race with S. aureus, a common microbe that rarely causes an active infection in healthy people. Following its development in the 1940s, physicians used penicillin to treat boils, impetigo and other painful skin conditions caused by S. aureus. They cured the infection, but spurred the microbes to evolve and become resistant. Researchers countered with methicillin. Since then, new strains have developed resistance to methicillin and other antibiotics.

Instead of trying to develop another antibiotic that could lead to further resistance, Barry's team chose to target the pathogen's resistance. Ideally, a vaccine will knock out the proteins behind resistance, leaving the bacteria vulnerable to a simple antibiotic like penicillin.

"We're trying to devolve it," Barry says. "Over time, the bacteria have acquired genes to produce proteins that protect against antibiotics. Since it became resistant by acquiring a protein, maybe we can use that protein against the bacteria."

Barry and Reeti Khare, then a grad student in the lab, devised the idea about three years ago. Khare, now working on her doctorate, has been testing vaccines against two proteins. In mice, the vaccine generates immune responses to release antibodies against the proteins.

"I am optimistic," says Barry, who is also collaborating with Robin Patel, M.D., of the Infectious Diseases Research Laboratory. MRSA is an increasingly complex bug, with up to 1,700 proteins. Barry sees potential to add target proteins to the vaccine to neutralize other toxic functions, such as the pathogen's ability to hide or its ability to create a biofilm.

"Normally, you go after the pathogen, but we're tryng something different. We're trying to vaccinate against the proteins that destroy the antibiotic."

Michael A. Barry, Ph.D.

"There are no vaccines against most medical-device infections," Barry says.

A vaccine could be administered in advance to disinfect a patient before surgery, or it could be used to treat an established infection. If the resistance-fighting strategy proves effective, physicians could apply the same technique to other infections, such as drug-resistant tuberculosis.

"Vaccine is the least expensive medical intervention we have," he says. ■

Inspired to Change Lives

Sometimes people are wounded as deeply by the way others react to their injury as they are by the injury itself. This is particularly true when that injury happens to a person's face or hands.

Tarek Obaid, of Riyadh, Saudi Arabia, recognized the anguish that accompanies extreme facial injury, and he wanted to help. At 35 years old, he became one of the youngest Mayo Clinic benefactors to reach Philanthropic Partner level, Mayo's highest level of recognition, with a $10 million gift to support reconstructive transplantation. Reconstructive transplantation at Mayo Clinic includes hand and, in the future, face transplant for patients who require complex reconstruction that conventional methods cannot address.

To understand what led someone this young to give a gift of this magnitude, is to recognize the relationships that have influenced Tarek Obaid.

"My parents have been the most important people in my life," he says. "My late father gave his guidance and strong support in my upbringing, in university and in the business world. And my mother? She's the one who's always been there for me, the one I could talk to."

"Growing up, our family always believed that it's important to give. And if we found ourselves in a position to give, we wanted to give to a place that could save lives, or change the meaning of life for people."

> "Growing up, our family always believed that it's important to give."

Those values influenced Obaid's long-held interest in the latest medical treatments, which he followed by reading scientific reports and staying current on emerging medical technologies. When his father became ill, Obaid became even more involved.

"My father died of cancer," he says. "Unfortunately we weren't able to help him. So now I want to know about everything that's new in medicine. I'm driven to do this."

In 2009, Obaid made his first trip to Mayo Clinic, where his visit was coordinated by a childhood friend, Samir. In fact, Samir Mardini, M.D., is a professor of surgery and a facial reconstructive surgeon at Mayo Clinic.

"Samir and I became friends when I was less than a year old," says Obaid. "Samir's father was the physician who gave my brother and me our first vaccinations when we were just kids."

Eventually, the friends grew up and pursued different careers. Obaid left for Geneva, Switzerland, to attend school; and later he went on to Georgetown University. Following college he worked in investment banking and real estate before founding his own company, PetroSaudi, in 1995. Mardini also attended Georgetown University. He continued on to become a surgeon, joining Mayo Clinic's Department of Surgery in 2006.

Inspired by his father's illness and his own experience as a Mayo Clinic patient, not to mention his respect for the work of his friend Samir, Obaid's ideas about medical care and his interest in new discoveries and treatments took shape.

"Traumatic injury, for instance, changes the way people live their lives," says Obaid. "If people have a disability that everyone sees when they go outside, eventually they stop wanting to leave their home. And that's horrible. I wanted to do what I could to help these people in despair."

Knowing that Mayo is the place that can make a difference, he decided to support reconstructive transplantation at Mayo Clinic in honor of his parents, Essam and Dalal Obaid. His gift establishes the Essam and Dalal Obaid Center for Reconstructive Transplant Surgery. It includes an honored scholar position named after his grandfather Ahmad Obaid, as well as an endowed program fund and an operating fund, also named in honor of the Obaid family.

"With severe facial deformity, people can live, but not be 'alive,'" says Mardini. "This gift changes that by helping people gain or regain their quality of life."

Obaid's mother, Dalal says, "We're so proud of this gift. As a mother, it sickens me to read in the papers about the sons and daughters disfigured from tragic accidents and injuries. But now, seeing my son has done this — it's a blessing and I feel I extend this blessing to other mothers."

"We make this gift in honor of the Obaid family values, particularly hope," says her son. "My family considers hope the most powerful emotion. It's hope that provides the fortitude to persevere, and it's hope that gives people strength.

Tarek Obaid and Samir Mardini, M.D.

Eat. Smile. Live.

For six weeks in 2011, Samir Mardini, M.D., traveled to reconstructive microsurgical centers in Taiwan, France and Slovenia plus Cleveland and Boston to learn all he could about face transplants.

The opportunity to learn from pioneers in face transplantation and meet face transplant recipients was his reward for being named 2011 Godina Traveling Fellow by the American Society for Reconstructive Microsurgery, and it was an important step in Mayo Clinic's move into reconstructive transplantation.

"The point of talking to those who've been working in this field is to avoid the same steep learning curve," says Mardini.

It's just a matter of time before Mayo Clinic performs its first face transplant — a vision brought closer to reality by Obaid's gift, which will cover part of the cost of face and hand transplants for those who cannot afford care. The gift also provides perpetual funding for transplant research.

Reconstructive transplants represent a natural progression for Mayo Clinic. The Mayo Clinic Transplant Center, already recognized as a national leader in organ transplants, provides the necessary infrastructure with an integrated team of physicians and other staff trained in transplantation, microsurgery, neurology, immunology, infectious diseases, psychology, psychiatry and rehabilitation. Mayo surgeons have developed and refined microsurgery techniques to reattach severed limbs

and reconstruct facial features. Meanwhile, Mayo's Center for Regenerative Medicine aims to expand transplants by finding ways to overcome the need for immunosuppressant drugs and challenges with organ rejection.

Also known as composite tissue transplants, reconstructive transplants are highly complex procedures that involve transferring skin, muscles, tendons, nerves, bone and blood vessels from a deceased donor. Mayo launched the first clinically approved hand transplant program in the United States in September 2010 and continues to screen for its first patient, likely someone who has lost the dominant hand or both hands.

The first successful hand transplant was performed in France in 1998. About 60 patients worldwide have received hand transplants, including bilateral transplants in the United States and Germany. For a hand transplant, which includes at least part of the forearm, surgeons typically connect three major nerves, two major arteries, nine muscles, 24 tendons, several veins and soft tissue. Encouraging results led to the first face transplant in France in 2005. About 20 face transplants have been performed in total.

Reconstructive transplantation offers the potential to significantly improve the lives of patients by restoring natural function, such as the ability to breathe, speak, swallow, smile and show emotion. In addition, creating a near-normal facial appearance can produce numerous psychological benefits for the patient, from rebuilding confidence to encouraging the patient to rejoin society.

Mardini and his colleagues can reconstruct an esophagus from a section of colon, a voice box from an appendix, a jawbone from a fibula, or a nose from rib cartilage and forehead skin. But they cannot recreate a mouth or the area surrounding the eye, where intricate nerve branches control muscles that pull in multiple directions beneath specialized tissue types. And, despite requiring several surgeries to transfer skin and other tissue from other parts of the patient's body, conventional methods provide less than optimal results for patients with extensive facial deformities.

In contrast, a face transplant can replace all that's damaged or missing — nose, lips, cheeks, chin, even teeth — in one large procedure.

"You want to restore the patient's appearance and function to as close to normal as possible. Face transplants give you that leap forward," says Mardini, who practiced the procedure on cadavers during two trips to France. "For some patients with congenital diseases or severe facial trauma, they have no other option."

Reconstructive transplantation offers the potential to significantly improve the lives of patients by restoring natural function, such as the ability to breathe, speak, swallow, smile and show other emotions.

While reconstructive transplants may not be life-saving, the procedures are considered life-giving. Our faces are inseparable from our sense of identity as well as our ability to interact and express emotions. People disfigured by trauma or disease may hide their faces behind a veil and withdraw from society. They may have difficulty speaking, breathing, chewing, swallowing or closing their eyes.

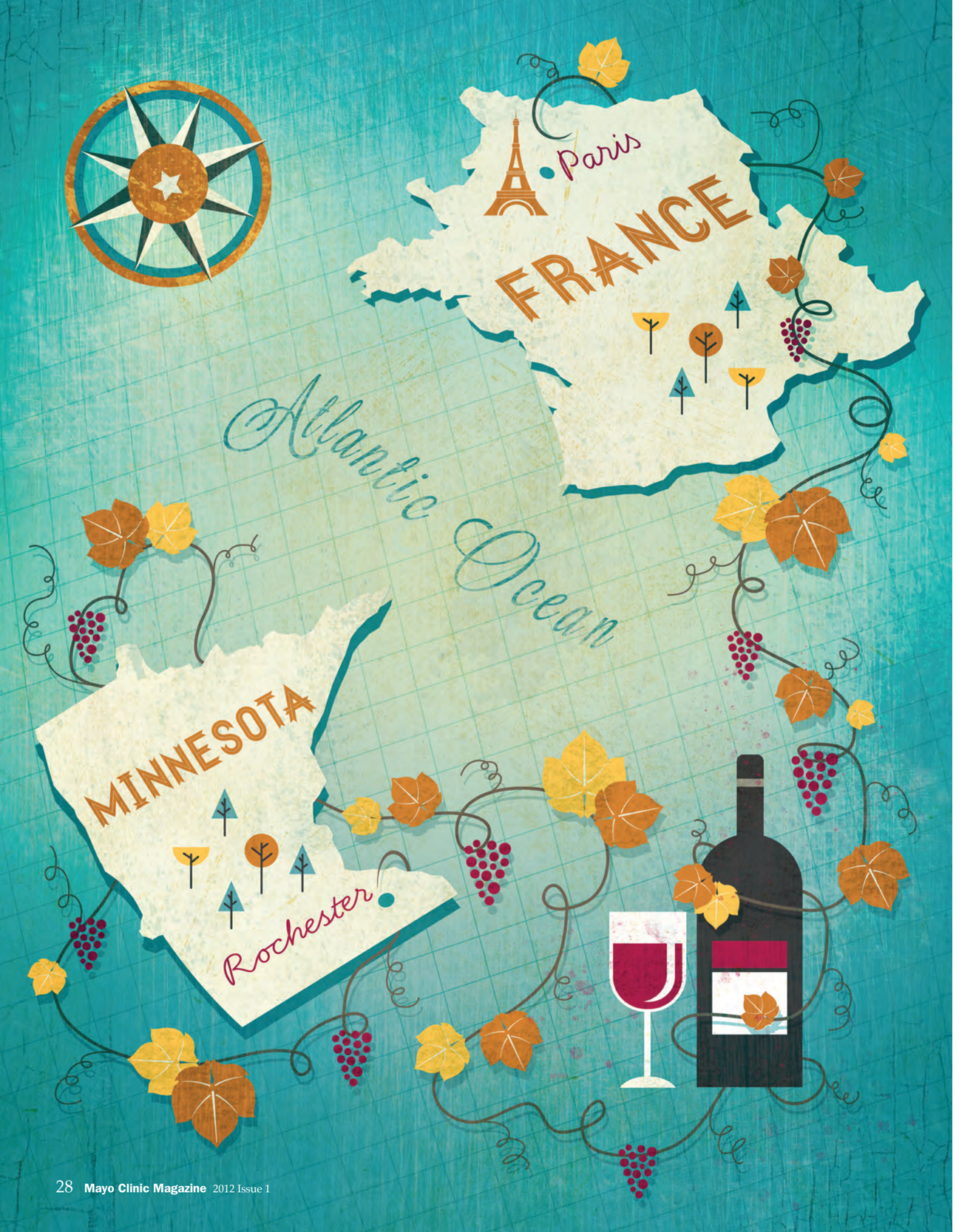
"Some of these people don't have a life. I know patients who don't leave the house and can't interact socially," Mardini says.

Transplant recipients typically have immense gratitude for the donor family's kindness and generosity. "It brought me back to life," a face transplant recipient told Mardini.

Whether face or hand, a reconstructive transplant involves years of rehabilitation, a lifetime of taking medications that suppress the body's immune system and management of assorted risks. Mardini views the high stakes of these procedures and the prospect of lifelong doctor-patient relationships as a major commitment and responsibility, which is why he insists on full disclosure of the risks and benefits before patients make a decision.

Mardini and his colleagues are working to improve and refine the procedure before Mayo's first face transplant. They have tackled research topics that include standardized psychological assessment of transplant candidates, stem-cell repopulation of damaged tissue, immunosuppression's effects on nerve regeneration in transplanted tissue, nerve reconstruction, artificial skin, targeted muscle reinnervation and functional muscle transfers. A key component of the long-term success of reconstructive face and hand transplant surgery will be research that advances the science behind immunosuppression, surgical techniques and psychological and neurological adaptation.

"The Obaid gift will propel our transplant program to the next level," Mardini says. "This is a new frontier in medicine, one that can offer patients results that are impossible to achieve with conventional techniques." ■



The Perpetual Philanthropist

Madame Sylviane Leducq, president of the Leducq Foundation's Board of Directors, shares her love for Paris, thoughts of marriage to husband, Jean, her relationship with Mayo Clinic and her foundation's cardiovascular research efforts on the world stage.

Bubbling and effervescent, Sylviane Leducq greets us in her elegant home overlooking the Arc de Triomphe and the Place de l'Étoile. For the next several hours, we find ourselves falling under her spell for, indeed, the French, especially the Parisians, are adept at conversation. When they do it as well as Sylviane Leducq, they are superbly entertaining.

Regaling us with reminiscences, Sylviane explains how she first came to know Mayo Clinic. "I sought treatment 40 years ago for allergies that were never cured. Yet, if it wasn't for my Mayo Clinic doctor, I would not have this life!"

Sylviane was born into a family of means. Her father worked as a chemist in a pharmacy in Provence near the Maritime Alps. Her mother was ambitious and encouraged Sylviane's father to focus on something useful, so he developed a medication that became a popular remedy for indigestion. Proving both effective and profitable, it allowed her parents to move to Paris.

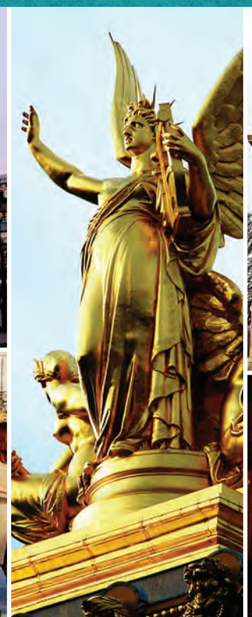
"I was born in my parents' home on Avenue Foch," she adds as she points out the window to a prominent building across a sprawling promenade. "My late husband, Jean Leducq, was born into privilege, too. He was a good friend of my brother's, and that is how we came to meet when I was 14 years old. Jean was seven years older.

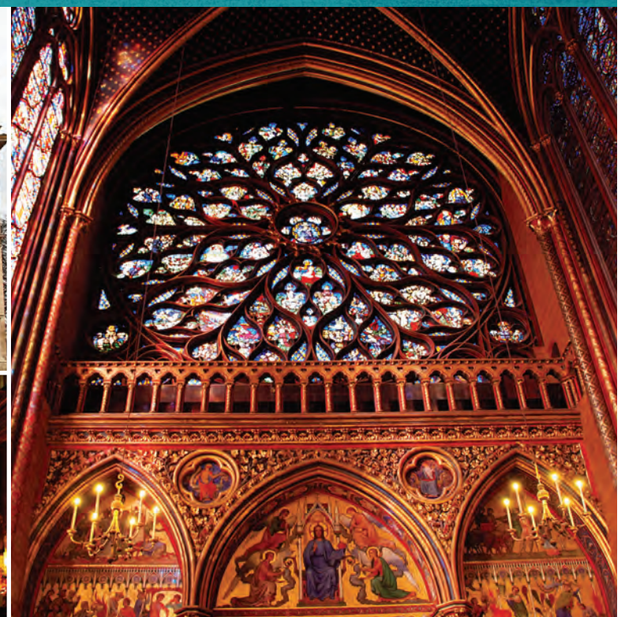
"Jean proposed marriage to me when I was 18 years old, but my parents made us wait until I was 20. We were married in La Madeleine." Remembering those years, Sylviane looks away and nods. "No two days were alike during our decades of marriage," she says. "Every day, Jean would summon me with the words, 'I have another idea.'"

Sylviane complemented Jean's innovative restlessness with her resolute character and social acumen. As consummate entrepreneurs in ventures that ranged from uniforms and cleaning supplies to wine, caviar and a vineyard, Sylviane and Jean pursued each new challenge with gusto, enterprising spirit and meticulous attention to detail. No matter what the endeavor, neither would accept less than the highest quality.

Jean took over his grandfather's laundry and linen supply business in 1968 and grouped its activities into a new entity called Elis, an acronym for Europe Linge Service. Over the course of 50 years, the Leducqs built a successful international business involving the supply and care of linens and uniforms in Europe and North America.

Sylviane discusses the importance of building a sense of community and shared values within an organization. "Jean and I worked tirelessly on behalf of our employees. Jean provided an on-site employee banking facility to protect our staff from fraud. We hired people from many different countries, and many did not speak or read the native language. Others were far away from their families and friends. We made sure all employees had access to on-site legal and financial advisers, too. I arranged opportunities for women to learn about self-breast examination and to participate in other health classes. We sponsored programs where best employees were selected by the employees themselves. Winners received three-day vacations in London, Venice and other European getaways."





Off to America

In 1983 Jean pursued interests outside the laundry business in the United States. He and Sylviane moved to Culpeper, Va. Sylviane laughs. "I bought a map of the U.S. to learn where Culpeper was located after Jean made the decision to move there for our next venture. Living in a suburban neighborhood allowed me to meet people in a friendly, easy atmosphere. Other wives prepared meals and shopped for groceries, but I never learned how to cook. I remember the first time I used a blender. I filled it with all kinds of vegetables. I flipped the switch on, and it escaped down the block."

Turning to Mayo Clinic

During one of Sylviane's routine checkups at Mayo Clinic, she encouraged Jean to have a physical examination, too. Drs. Robert Frye and Robert Tancredi, cardiologists; Robert Wallace, a cardiovascular surgeon; and Sait Tarhan, an anesthesiologist, all recommended that Jean stay at Mayo to undergo a critical cardiovascular procedure. But Jean had important matters in France and opted to leave for Paris.

Not long after, in the midst of a major business deal, Jean fell seriously ill. He was admitted to a hospital in Nice, France, for a suspected heart attack. Concerned because his father and grandfather had died of heart disease in their 50s, Jean decided to return to Mayo Clinic for help.

With ties in both Europe and in North America, the Leducqs wanted Foundation Leducq to support collaborative work between researchers of the two continents. Two founding members of the foundation were Drs. Robert Wallace and Robert Frye, both of whom knew the Leducqs through Jean's experience at Mayo Clinic.

Since Jean Leducq's passing in 2002, Sylviane has assumed responsibilities for keeping their mutual visions alive. To support her in these endeavors, David Tancredi, M.D., Ph.D., the son of Robert Tancredi, M.D., Jean's cardiologist from Mayo Clinic, serves as the scientific director and member of the Board of Directors of the Foundation Leducq in Paris, France. Tancredi works with Martin Landaluce, also a member of the Foundation Leducq Board of Directors and the foundation's financial director.

Alarmed for her husband, Sylviane called Rollie Dickson, M.D., her point of contact at Mayo, who engineered a rescue flight from Nice to Rochester. The same Mayo physicians who had earlier recommended he stay in Minnesota for treatment flew to Nice to accompany Jean and Sylviane on an overseas flight for life back to Rochester, Minn.

She feared Jean would not live. In Saint Marys Hospital, Jean kept waking to find a priest at his side. Sylviane had been raising the small purple flag next to his hospital bed several times a day as a signal to call for a priest. He recovered and lived into his 80s.

Partners in health for life

Impressed with the quality of care he received, Jean and Sylviane continued to seek medical care at Mayo Clinic.

Sylviane exclaims, "Jean and I loved Mayo Clinic and were determined to fund a practice similar to it in a suburb of Paris. Political obstacles made it impossible to realize this aspiration."

But undaunted and unwilling to forego their vision, Jean and Sylviane began to think about creating a foundation to promote medical research. Shortly before the sale of their business, Jean and Sylviane created the Foundation Leducq, charging it with the mission of improving human health through international efforts to combat cardiovascular disease.

Roots in compassion and conscientious endeavors

Jean was anxious to plant the seeds of his next idea — a winery in California. He began acquiring small parcels of vineyard land in the highly regarded Napa Valley, including the historic Ehlers Estate vineyards, which he purchased in 2001. Located in St. Helena, the 42-acre property grows certified organic Bordeaux varieties with an emphasis on biodynamic farming practices.

In 2002, Ehlers Estate passed into the trust of Foundation Leducq. The visionary union of estate winery and philanthropic foundation has defined Ehlers Estate ever since, giving the winery a unique mission and sense of purpose that combines a pursuit of excellence with social responsibility. At Ehlers, an inspired and exceptional team of experienced professionals take pride in their work — making great wines while making a difference.

Farewells and new beginnings

It is now late afternoon and several glorious hours have passed since our arrival. We bid au revoir to Sylviane and her unforgettable hospitality. She has treated us like visiting gentry. Sylviane gently kisses us goodbye and reminds us as we wave farewell, "I can get good health care within a few minutes of my home. However, my close association with Mayo Clinic brings me back yearly to Rochester. I look forward to my next exam at Mayo Clinic. I will get to see my friends." ■

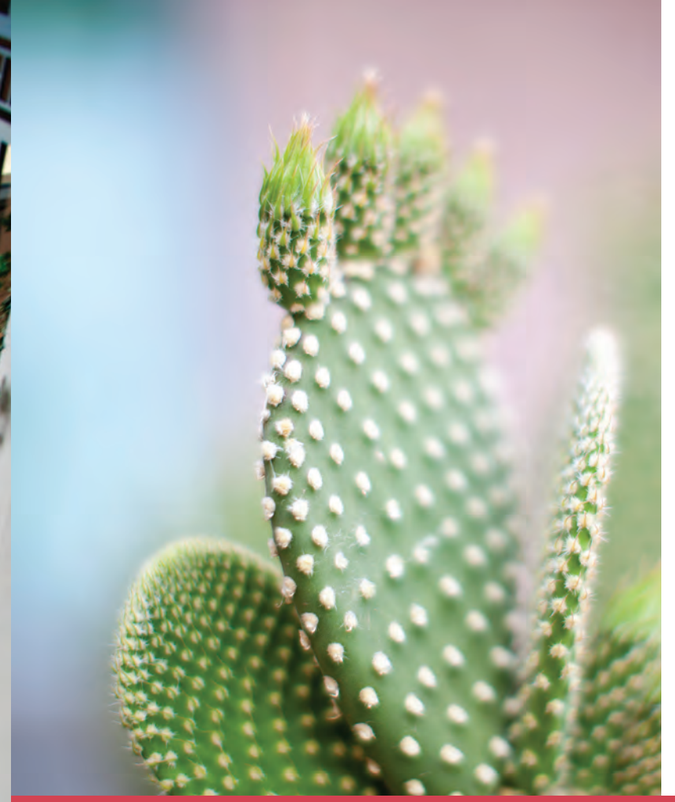
Mayo Clinic is proud to celebrate 25 Years

of providing care to patients in Arizona. The hard work and dedication of Mayo's staff, volunteers and benefactors have contributed to advances in patient care, education and research that will continue in the years ahead.

Scottsdale and Phoenix campuses offer a welcome sanctuary.

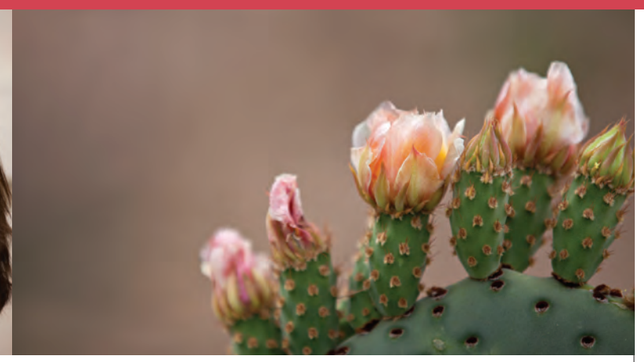
The sun sets against a mountain backdrop.


HONORING PHILANTHROPY



Mayo Clinic Hospital is a place of hope and healing.

Mayo Clinic staff remain committed to providing answers for patients.



Mayo Clinic is positioned to meet the growing needs of the Southwest and beyond.

Sustaining Our Wounded

Warriors

Mayo Clinic has a long tradition as a leader in military medicine. The clinic maintains a close relationship with the U.S. military and its active and former service members. "Many Mayo staff come from the military, and our institution shares with military medicine many of its core values," says Timothy Lineberry, M.D., a Mayo psychiatrist with longtime experience as a researcher and adviser on suicide prevention in the armed forces. "Those values include focusing on the patient, integrating the patient's care with what you see in the whole person and doing what's best for that patient."

Mayo's relationship with the military goes back to its earliest days. In 1864, President Abraham Lincoln appointed Dr. William Worrall Mayo as an enrollment surgeon for the U.S. Army draft board in Rochester, Minn., where the physician settled and eventually established the private practice that became Mayo Clinic. The Mayo sons, Drs. Will and Charlie Mayo, served in World War I, both achieving the rank of brigadier general. In the decades since, Mayo staff members served the military and its personnel with breakthroughs in medical preparedness and field practice that included:

- Setting up military laboratories and surgical suites.
- Teaching medical officers.
- Introducing the G-suit, parachute training and high-altitude oxygen equipment for aviators.
- Developing penicillin for field use.

Today Mayo Clinic continues its tradition of leadership and distinguished service with some 900 employees who serve or have served in the military.

Regenerating damaged bone and nerves

Troops serving in Iraq and Afghanistan have been particularly susceptible to arm and leg injuries. Although more than 90 percent of the wounded survive, many do so with serious life-altering injuries. “Battle armor is pretty good at protecting the abdomen and thorax and preventing blunt injury to the head,” says Michael Yaszemski, M.D., Ph.D., a Mayo orthopedic surgeon and biomedical engineer. The extremities of the body, however, are more exposed. “And because of the high incidence of these debilitating injuries, regenerating nerve and bone tissue is critical. All tissues are affected: bone, cartilage, muscles and nerves. Even if all the other tissues heal, nerves won’t repair on their own. Muscles won’t contract, there won’t be sensation, and there’s more risk for future injuries.”

Yaszemski, who is a brigadier general in the U.S. Air Force Reserve, and collaborator Anthony Windebank, M.D., a Mayo neurologist and molecular neuroscientist, are co-directors for nerve injury research in the Armed Forces Institute of Regenerative Medicine (AFIRM). Working together for the past seven years, the physicians have progressed from culturing nerve and bone cells in petri dishes to experimental work with animal models, in which they successfully regenerated peripheral nerves. And they are about to launch their first human regeneration study in humans.

The study targets patients who have a form of peripheral nerve damage that usually results in the loss of sensation around the ankle. In such patients, the team implants a tiny guidance channel made from a degradable polymer at the severed point of the nerve. Without the channel, the cut nerve ending would “grow, but without direction,” Yaszemski says. With the guiding structure of the channel, the sprouting nerve endings can “move along the channel and continue to the downstream cut end of the nerve and then on to the target muscle.” If the regenerative implant works, the patients regain sensation in their feet.

“Through my military service, I’ve developed a firsthand appreciation of the need for these therapies,” Yaszemski says. “In consideration of the dedication of the young women and men in the armed forces, we must do whatever we can to help. War is such a sad thing, but one good thing can come from it — innovations that benefit the civilian population.”

> “Through my military service, I’ve developed firsthand appreciation of the need for these therapies.”
>
> Michael Yaszemski, M.D.

Motion training for amputees

Two medical statistics concern Kenton Kaufman, Ph.D., the head of Mayo Clinic’s Motion Analysis Laboratory. The first is the rising incidence of multiple limb amputations among service members in Afghanistan, where rugged terrain often prevents use of armored vehicles. “In Iraq, soldiers traveled in armored vehicles, so when an IED exploded, they were somewhat protected,” he says. “Now in Afghanistan they are on foot patrol due to rugged environments. Since 2009, the number of amputees has almost doubled, and the number of individuals with multiple limb amputations has tripled.”

The second statistic is more surprising: Every year, 64 percent of those who experience above-knee leg amputations experience a fall. Falls are a well-recognized hazard for older adults. But people who have undergone a limb amputation, particularly an above-knee amputation, face an even greater challenge maintaining their balance.

Kaufman and his staff are finding new ways to keep the growing number of amputees upright and out of harm’s way while improving their gait and reducing the effects of arthritis, bone loss and other physical complications that often trouble them. He and his team use motion studies and the observation of amputees in virtual reality settings to examine the biomechanics of walking. They try to analyze exactly how people who have lost lower limbs fall. Their work is supported by a grant from the U.S. Department of Defense, and they collaborate with a national consortium of institutions focused on the rehabilitation of wounded veterans.

> “Since 2009, the number of amputees has almost doubled, and the number of individuals with multiple limb amputations has tripled.”

The key to improving the mobility of amputees, Kaufman believes, is to develop new training methods for rehabilitating them. “Surprisingly, old technologies devised after World War II are still prescribed for active amputees,” he says. New techniques involving microprocessor-equipped prosthetics and different training approaches give patients better gait and balance, increased confidence and the ability to live more actively.

“Once patients trade old prosthetics and training methods for new ones,” Kaufman says, “it takes about 18 weeks to adjust to the new way of walking, but it’s unquestionably better for them.”

Safer and more effective vaccines

In some parts of the world, anthrax vaccines are mandatory for U.S. military personnel. “Although the risk of anthrax at any one time for our service members is low, an outbreak would have extraordinary impact and would become a national security issue,” says Gregory Poland, M.D., who leads Mayo Clinic’s Vaccine Research Group and its Program in Translational Immunovirology and Biodefense.

Poland led a 10-year study of the anthrax vaccine at Mayo, which in the past was thought to require six doses to bring full immunity. “The research showed that we could eliminate one of the doses and that we could give it intramuscularly, instead of under the skin, which decreases troublesome side effects without affecting the levels of protection provided by the vaccine,” he says. These findings are valuable to the Department of Defense because improvement in the vaccine would simplify troop movements and increase survivability of service members in the event of exposure to the virus.

Many medical advances, like blood transfusion and dialysis, emerged first through wartime medicine. “It’s an important thing for Mayo to be doing,” says Poland. “It not only benefits our service members, but ultimately each of us. Take the smallpox vaccine, for example. This work was initiated by the military, but it benefited the entire population.”

Although the world celebrated the 30th anniversary of the eradication of smallpox in nature in May 2010, there are strains of the laboratory virus that could be stolen or synthesized by enemies. Currently, upwards of 30 percent of the U.S. population can’t tolerate the smallpox vaccine because of various medical conditions that would allow the live vaccine virus to propagate in the body and cause illness or death. “That’s why we need a safer vaccine,” says Poland. “We should never be without a vaccine against smallpox.”

Gregory Poland, M.D., leads Mayo’s Vaccine Research Group and its Program in Translational Immunovirology and Biodefense. Because of his particular expertise, he was appointed president of the Defense Health Board, which directly advises the Secretary of Defense on bioterrorism threats to troops. He chaired the committee that helped the Department of Defense prepare for an influenza pandemic and wrote the recommendations for biologic countermeasures to bioweapon threats.

Poland, who comes from a military family, was awarded the Secretary of Defense Medal for Outstanding Public Service for his medical work.

Better military medicine through simulation

The Mayo Clinic Simulation Center offers high-quality training facilities that help prepare medics for real-world situations. Mayo Clinic's Walter Franz, M.D., a 20-year U.S. Army reservist and colonel, remains convinced that bringing realism to the training of military medical personnel better prepares them for what they will encounter in combat zones. As commander of the 945th Forward Surgical Team, a group of medical specialists likely to ship out for Afghanistan next year, he has decided to train his team with high-fidelity mannequins, sound effects and other simulated sights and sounds from the battlefield. The simulation center is an excellent place for medics to rehearse, refine and practice some of their combat medical skills.

Franz joined Mayo Clinic's outreach program to Haiti after its 2010 earthquake and trained in the simulation center for that effort. "That experience made me wonder about getting our Army guys in here for training," he says. Now, participating reservists experience four levels of training at Mayo's simulation center. They begin practicing treatments on static mannequins with simulated wounds; next comes the use of live volunteers with simulated injuries who can respond to the trainee. Training then moves to high-fidelity mannequins that manifest vital signs and give computer-controlled responses to treatment decisions. Lastly, the training involves even more realistic mannequins, operated from a control booth, that bleed, have heartbeats, open their eyes and show wounds.

"We're doing now for combat medicine what we've been doing in mainstream medical training for some time. Using these mannequins we can create high-stress scenarios like those in Afghanistan, even adding audiovisual effects like helicopter noise and radio traffic," Franz says. "There's always some degree of uncertainty when you don't have practical experience. We're using simulation as a way to gradually increase the stress level of training so medics will feel more comfortable out in the field."

About 150 people have taken advantage of the simulation training at Mayo Clinic. "I'm proud that Mayo and the Army are working together to develop a new generation of medics who care for people in combat," Franz says. "It's a small but vital part of Mayo's mission."

A mission to understand suicide

The causes of suicide in military and civilian life are enormously complex — a difficulty that Mayo psychiatrist Tim Lineberry, M.D., well appreciates. "Military suicide rates are typically lower than among civilians because of medical, psychiatric and conduct screening before anyone joins the armed forces," he says. "But recently those rates have increased in the military. Clearly they are influenced by the decade we've spent at war and multiple other reasons. It's challenging to determine exactly what's responsible."

Lineberry works with the Department of Defense to identify suicide research priorities and coordinate studies. A former Air Force psychiatrist, he has spent many years working with the U.S. military on its suicide prevention programs. "Suicidal behavior is strongly associated with psychiatric illnesses like depression. But other factors play into it too," he says. "Substance abuse, various genetic factors, combat experiences, family and life stress, and differences between reservists and the regular military. Some who die by suicide in the military have never deployed to combat zones." In 2011, 288 active duty Army and reserve soldiers committed suicide. "And each suicide is tragic. Families, friends and military units are all affected."

Compared with combat injuries and deaths, military suicide remains a relatively rare event, which contributes to the challenge in identifying those at risk. Lineberry hopes to see the military develop evidence-based tools that will identify people at risk for suicide. "The idea is to conduct a long-term study that follows people to determine the actual risk factors of suicide, quantifies the exposure people have to those factors, then analyzes all the data," he says. "Suicide is a complex multifactor behavior, and we have to break things down to simple parts to understand what drives it." ■

Mayo Graduate School

Mayo Graduate School strengthens Mayo Clinic, a fact recognized in 1917 when Mayo began offering education programs.

Still, nearly 100 years later, many people underappreciate the intertwined nature of basic biology and medicine. Mayo Graduate School helps make that connection clear through a focus on understanding the language of cells and molecules. This is one way the school helps move new medical ideas safely and effectively into clinical practice.

"Having a program like Mayo Graduate School makes it possible for Mayo to do everything better — making some discoveries that help patients today and others that will help patients in a hundred years," says Mayo Graduate School Dean L. James (Jim) Maher III, Ph.D.

Maher came to Mayo Graduate School 16 years ago for the same reason physicians and scientists continue to come — Mayo's commitment to education along with its renowned scientific training program. Today, as Maher takes over leadership of the school, he also continues his research and mentoring students in his lab, which studies the nucleic acids, DNA and RNA to develop new approaches to artificial gene regulation in cancer and inflammatory diseases.

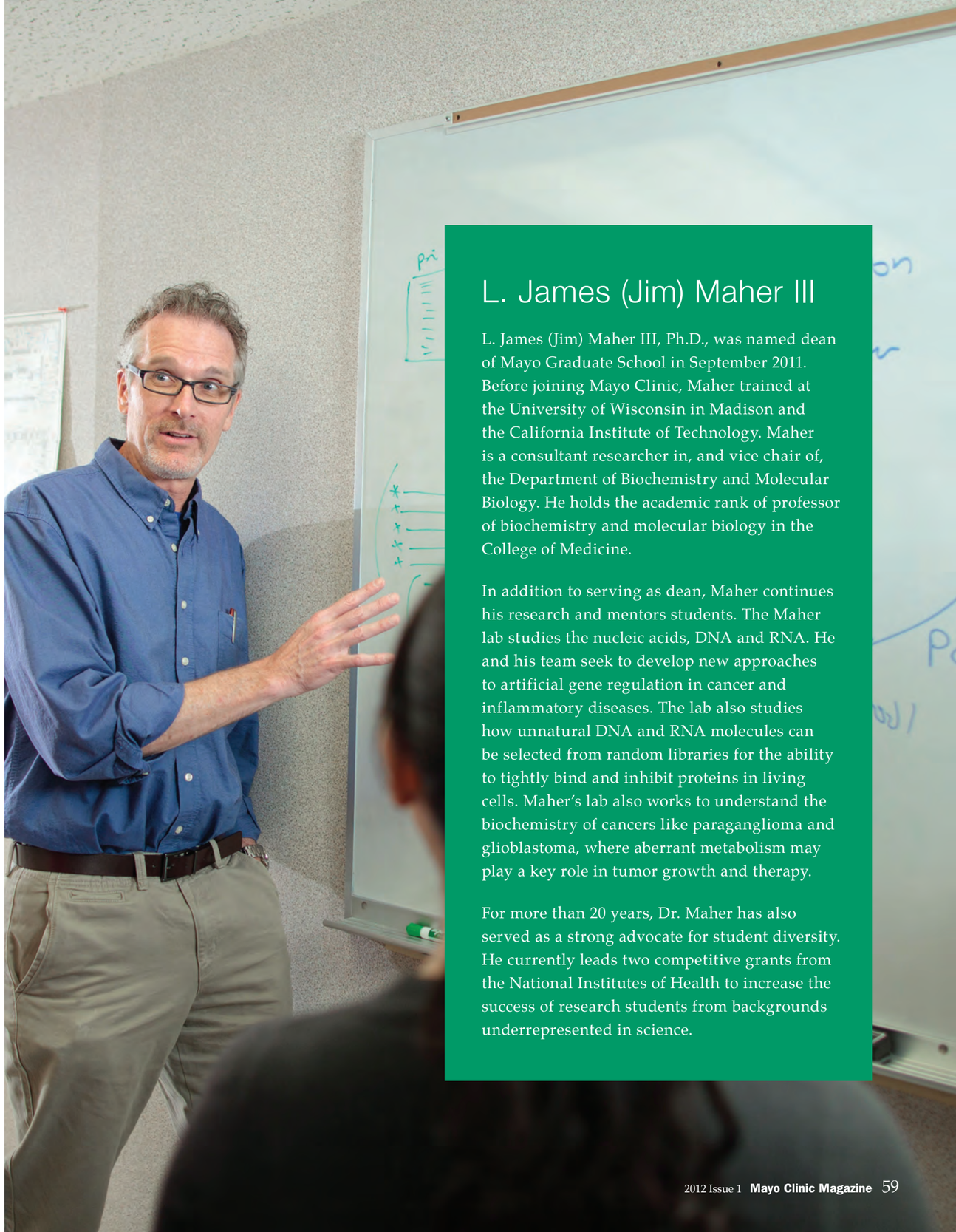
Preparing for the unexpected

"Many of our students are working on fundamental problems: *How do cells work in the first place? How does the body work? How do its systems function?* And in the process of learning," Maher says, "we often make discoveries that will help people in the long run."

The history of health care is peppered with stories about scientists looking into nonmedical questions but "accidentally" making discoveries that revolutionize patient care. "My favorite example is warfarin, which today we use as a blood thinner," says Maher.

It was discovered by accident at the University of Wisconsin in the 1930s. A disgruntled farmer needed to understand why his cows were dying. The farmer brought a dead cow and about 100 pounds of sweet clover to the veterinary pathologist, a biochemist at the university, who was so curious that he began studying the problem. He soon realized that something in the hay was blocking the cows' blood clotting systems — a fungus or mold was producing a chemical during the fermenting process, which happened because the hay hadn't been allowed to dry thoroughly. He identified this something as a tiny molecule that blocks proper blood clotting. That solved the problem for cows. Eventually, however, he wondered whether preventing blood from clotting could be useful in clinical practice. His curiosity led to the discovery of warfarin, an anticoagulant used to prevent heart attacks, strokes and blood clots.

Mayo Graduate School provides advanced scientific training toward Ph.D. degrees in biomedical research and has become a national destination for biomedical training of diverse research scientists.



L. James (Jim) Maher III

L. James (Jim) Maher III, Ph.D., was named dean of Mayo Graduate School in September 2011. Before joining Mayo Clinic, Maher trained at the University of Wisconsin in Madison and the California Institute of Technology. Maher is a consultant researcher in, and vice chair of, the Department of Biochemistry and Molecular Biology. He holds the academic rank of professor of biochemistry and molecular biology in the College of Medicine.

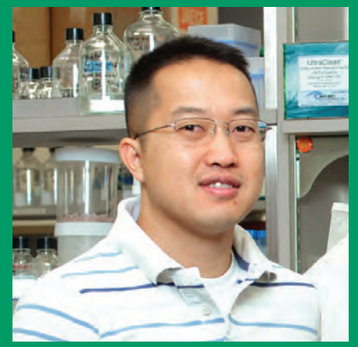
In addition to serving as dean, Maher continues his research and mentors students. The Maher lab studies the nucleic acids, DNA and RNA. He and his team seek to develop new approaches to artificial gene regulation in cancer and inflammatory diseases. The lab also studies how unnatural DNA and RNA molecules can be selected from random libraries for the ability to tightly bind and inhibit proteins in living cells. Maher's lab also works to understand the biochemistry of cancers like paraganglioma and glioblastoma, where aberrant metabolism may play a key role in tumor growth and therapy.

For more than 20 years, Dr. Maher has also served as a strong advocate for student diversity. He currently leads two competitive grants from the National Institutes of Health to increase the success of research students from backgrounds underrepresented in science.

Meet the students in Maher's lab

Estefania Mondragon
A native of Oaxaca, Mexico, Estefania Mondragon takes on the challenge of finding new short RNA and DNA molecules that fold into exotic shapes. The purpose of her work is to create new research tools, maybe even new drugs.

Justin Peters
A graduate of Wartburg College in Waverly, Iowa, Justin Peters gets back to the basics of the DNA molecule by probing its essential features, particularly what makes the DNA molecule stiff.



Yeng Her
Born in Cambodia, Yeng Her was accepted into Mayo's M.D./Ph.D. Medical Scientist Training Program. For the Ph.D. portion of his work, Yeng studies a rare form of cancer, familial paraganglioma, which is intriguing because it can run in families.

According to Maher, most discoveries important to health care have a story such as this. "These discoveries were made by curious people. They were trying to understand why an animal gets sick under certain circumstances, or how bacteria work, and in solving the problem, they uncovered something that became extremely useful in the hospital and clinic," says Maher. "The point is that it's impossible to predict which research areas will have clinical impact."

That's why it's crucial for Mayo to maintain a balanced portfolio of research projects and to train a diverse range of scientists who are prepared for the unexpected. "To hold that medical research is about fixing human problems by studying humans is not what history teaches," says Maher. "In fact, the best place to study a human problem may not be with a human at all. It might be with a zebrafish or an insect, in a fungus or a mouse. Graduate school trains scientists to ask the question: How might we study this problem?"

Committing to curiosity

"We can't know which will become the most pressing future problems, so it's curiosity that we want to reward," Maher says. "Curious people are the ones who will solve the problems that have real

> "Investing in bright, curious scientists remains one of the best investments anyone can make."

patient care implications for the future. We choose students who are curious, so curious they'll keep working even when they encounter failure after failure. We want people who are so curious they'll say, 'I don't care. I'm going to try this again.' Why? Because that's a realistic view of what five years of graduate school and a life in science looks like. The scientist's life is full of frustrations and uncertainties. So, the kinds of people who thrive in science are particularly driven, bright, energetic people. They're people who generate their energy from curiosity, because the research system is not always rewarding."

Once Mayo Graduate School accepts a student, it promises to pay a stipend for five years, covering their cost of living. Students are free to follow their passion and choose a lab that matches their interest. This practice sets apart Mayo Graduate School from most graduate programs where students are dependent on the funding of the investigator for their learning experience. "The student is the center of what we do here. The program piques students' natural curiosity by empowering them to choose their own paths," says Maher.

Preparing for choice

Traditional graduate programs assume biomedical scientists are headed to grant-funded laboratories in academic medical centers and universities. Mayo Graduate School takes a different view. It recognizes that today's biomedical scientists have many career options, and it will go further by giving students firsthand exposure to novel career opportunities like patent adviser, device designer, health care delivery engineer, science administrator and science policy expert.

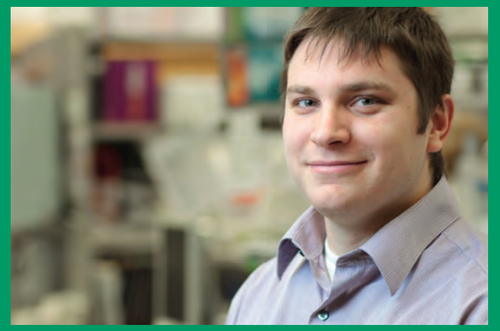
Shaking up the science world

By design, few Mayo Graduate School degree recipients stay at Mayo Clinic after graduation. It's an aspect of Mayo's scientific thinking that differs from its medical thinking.

"The medical education system at Mayo likes to identify the best people, groom them and hold them," says Maher. "In science, that's not our philosophy. We look for the best people, train them, and then make sure they go out to shake up the scientific world with their contributions to health care at major universities and companies across the world."

"Graduate school is an investment in long-term thinking. That investment isn't something that goes away when the student graduates," says Maher. "We're talking about investing in the student, an investment that extends to a person's lifetime career with decades of future research potential — including the training of dozens of other scientists and sharing findings through publications and presentations. A gift to Mayo Graduate School is a gift to the world. With a relatively small investment, you're touching hundreds of future researchers. Investing in bright, curious scientists has got to be one of the best investments anyone can make."

Folding RNA molecules inside a computer



John Paul Bida

Proteins, DNA and RNA all begin as unfolded chains that must fold properly inside cells. Biochemists have long been stumped by the question of how these long molecules fold into their functional forms. And that question has been a focus of the molecular biology lab of Jim Maher III, Ph.D., dean of Mayo Graduate School. His lab explores the creation of drugs to control which genes are "on" and "off" within living cells. Although both healthy and diseased cells constantly control their own genetic recipes, scientists have yet to devise drugs that can do this artificially.

"In our approach we use tiny folded threadlike RNA molecules as molecular decoys to block the transcription factor proteins we choose to target." (A transcription factor is a protein that binds DNA at specific sites where it can then regulate the flow of genetic information.) Maher's lab has published research papers discussing how the selected RNA decoys fold up to fool their target transcription factors. The RNAs fold into shapes that imitate DNA. By imitating DNA, the decoy RNAs entice transcription factors to bind, preventing them from controlling genes normally. In fact, says Maher, "The ability of short RNA chains to fold up in ways that imitate the structure of DNA is surprising and unexpectedly elegant."

Even after decades of collaboration with computer scientists, however, the ability to predict how molecules fold remained elusive. That is, until student John Paul Bida came to Mayo Graduate School with his impressive background in mathematics and a passionate interest in studying the use of ultrafast computing to predict how short RNA strands would fold. If he could predict how RNA strands would fold, he could help Maher's lab accomplish what was needed — to design folded RNAs that imitate the shape of DNA.

Thousands of hours of computer programming and hundreds of pages of computer code later, Bida successfully harnessed Mayo Clinic's banks of advanced parallel computers to perform calculations in seconds that would otherwise take days or weeks. Sitting in his research office overlooking Rochester, Bida built the necessary new approaches, sending commands from his Mac laptop to direct the herd of clustered computers in a building several blocks away.

The result is a new computer program that Bida and Maher call RSIM. They describe RSIM in an issue of *RNA Journal*, a publication read by molecular biologists worldwide. They present the advances in predicting RNA folding and offer at no charge a location on the Internet where other scientists can copy and test Bida's new tools.

"We're excited to use RSIM for our own goals, but just as excited to share the software with other scientists," says Bida. "That's how science works."

After recently completing his Ph.D. from Mayo Graduate School, Bida has begun his postdoctoral fellowship training at Stanford University. ■

Computer predictions of folded RNA molecules

Not All Knees are **Created Equal**

Charlotte Chastain beat the odds when she graduated from her seafaring apprenticeship program in 2009 and joined the U.S. Merchant Marines. Chastain was 55 at the time and two decades older than anyone else in her class, which started with 31 trainees and graduated only 11 of that group. And though she is an avid walker and swimmer, the program's rigorous physical training punished her knees.

"I've always told my children to never quit what they start," says Chastain, an artist and mother of two who joined the U.S. Merchant Marines after her apprenticeship. "I thought about that many times during training, especially at night when I was icing and elevating my knees to relieve the pain."

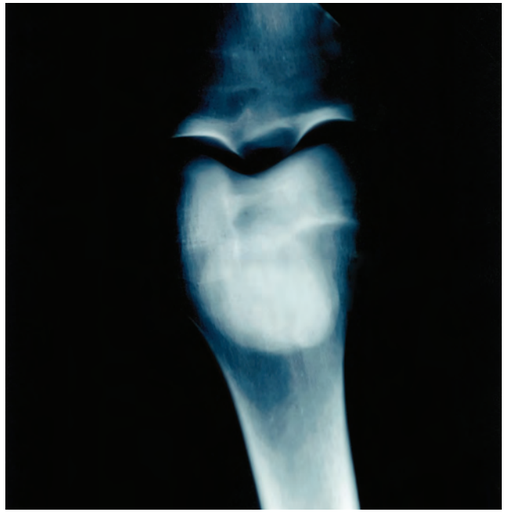
After a few trips at sea, Chastain realized that she needed more than willpower to continue serving in the merchant marine, which transports cargo and other goods on international waters. Her knees rebelled against life on board, which meant standing for up to 14 hours a day during voyages that often last four months. "I'd never experienced that kind of pain before, especially when the ocean was rocking the ship," she says. "I knew I had to see a doctor." Her first experiences with orthopedic specialists were far from encouraging. They tried cortisone shots but those didn't work for long. She asked about surgery, but was told she was too young for total knee replacement. Another surgeon described a different procedure, but it sounded "too horrible to even consider," she says. No one mentioned partial-knee replacement.

Then, on the advice of a friend, Chastain went to Mayo Clinic to see Mary O'Connor, M.D., chair of orthopedics at the Florida campus. Not only was she a candidate for partial-knee replacement, O'Connor told her, but also for a new procedure using robotic technology. The technology helps surgeons preserve more bone and place the knee implant more precisely compared with other techniques. "The procedure is so new that we have no long-term data on it yet, but its advantages should translate into better-aligned, longer-lasting partial-knee replacements," O'Connor says.

Chastain opted for the procedure. And it's working. She lives a pain-free, active life on her two partially replaced knees. "Life at sea is tiring, but that's all," she says. "I'm so thankful for my mobility. I can't say enough about Dr. O'Connor and Mayo Clinic. She was the first physician who offered a solution."

O'Connor says Chastain's outcome from the surgery isn't unusual. And the same is true of the thorny path that Chastain endured to get to her. "A lot of female patients have similar stories," O'Connor says. "Surgery is not discussed with them, and they feel like no one takes them seriously. Charlotte's case was especially clear. She had a lot of pain and arthritis. She needed surgery, plain and simple, and a partial-knee replacement was a great option for her. I was concerned that there had been some subtle bias against her; that as a woman she was perceived to be exaggerating her symptoms."

Research supports O'Connor's contention of bias. A recent Canadian study compared the treatment of male and female patients with the same degree of moderate knee osteoarthritis. The study discovered



alarming discrepancies. Family-practice physicians were twice as likely to recommend knee-replacement surgery to male patients. Orthopedic surgeons were 22 times more likely to recommend surgery to the male patients.

That finding becomes more striking when fitted into the overall picture of knee osteoarthritis. The disease is more common in women than in men. And when knee-replacement is recommended to female patients, they typically wait longer, compared with men, to opt for the procedure. As a result, compared with men, by the time they are treated women typically have more advanced disease and less quality-of-life improvement after surgery.

O'Connor says this treatment gap isn't easy to solve, but she's starting with the basics — biology. She has a research grant from the Society for Women's Health Research, a nonprofit agency in Washington, D.C., to lead a U.S.-Canadian study that is searching for differences in knee tissue in male and female knee-replacement patients.

"Women report more pain after surgery, the pain persists longer and they have less gain in function," O'Connor says. "We know that every cell in our bodies has a sex. Every one of those cells is influenced by the fact that, for instance, I'm female, and I have more estrogen than a male. But we don't have a good understanding of how the biology of sex influences pain, postoperative rehabilitation and other fundamental aspects of patient care. If we can identify differences in pain fibers, for example, we might then identify different strategies for women."

The eye of the beholder

O'Connor also hopes to close the gender gap within the orthopedics field itself. Only 5 percent of board-certified orthopedists are female. Orthopedics is one of the least diverse specialties in medicine;

Dr. O'Connor hopes to close the gender gap within the orthopedics field. Only 5 percent of board-certified orthopedists are female.

the American Academy of Orthopedic Surgeons has made diversity a priority. O'Connor is doing her part, serving as a board member of the Perry Initiative, a national organization that promotes orthopedics and engineering professions to women.

"We need this kind of outreach," O'Connor says. "We hosted a local workshop, here in Jacksonville, for high school girls, to show them what these careers are like. The excitement on their faces was amazing. They learned they can use power tools. They can suture and apply bone clamps. It was great fun."

Mayo Clinic places increasing emphasis on diversity and health disparities research. In 2010, the clinic launched the Office of Diversity and Inclusion. Its director, Sharonne Hayes, M.D., a cardiologist, says diversity is simply a fact in today's society — one that Mayo Clinic must address to provide the best care.

"Diversity is here," Hayes says. "We see it every day, even here, in the cornfields of Rochester, Minnesota, where we have 62 languages spoken at home among students in our public schools. If we're going to meet the demands of our population and stay relevant, we need to be able to care for all types of patients and in a culturally and gender-sensitive way."

To meet those goals, Hayes' office has outlined six priorities aimed at providing the best care to every Mayo Clinic patient in a culturally appropriate manner, leading health care disparities research and creating a diverse Mayo Clinic workforce. But with changes in health care delivery and the promise of individualized medicine before us, a natural question arises: How do diversity and inclusion fit into the mix? Seamlessly, Hayes answers.

"It's really the simplest form of individualized medicine there is," she says. "And studies like Dr. O'Connor's have the potential to branch into other directions, too, and across all of our priorities. For me, our priorities start with diversity and inclusion. Both are essential for us to do the best for every patient every day." ■

From Discovery **to Practice**

In the field of translational research, clinicians and scientists seek to apply the discoveries generated through basic scientific inquiry to the treatment or prevention of disease. Yet the therapies, diagnostic tools and patient care practices that could help patients live longer and healthier lives often encounter tough terrain during early stages of development.

A well-recognized bottleneck occurs when clinicians, scientists and product developers make a discovery but haven't advanced it enough to entice commercial interests to support its development. That's the difficulty. In taking scientific discovery to the clinical world, the major challenge is ensuring financial support for the early phases of development.

The program receives about 70 applications per year; each application involves on average three to five investigators. Of those applications, between 10 and 15 make the second round, and about half of those are funded.

Mayo Clinic's President's Discovery Translation Program was created to help solve that problem by marrying principles from the investment world with the clinic's world renowned science, all in an effort to speed research and development to patient application.

"The primary intent of this program is to realize value through the transfer of intellectual property to the clinical practice and society at large," says John Noseworthy, M.D., Mayo Clinic president and CEO. "Expediting scientific discovery toward advanced treatment options for patients remains the overriding priority, and it also serves to enhance the national and international competitiveness of Mayo Clinic as a global destination in health care."

Since its inception, the program has benefited from continuous support from grateful patients. Indeed, over half of the investment in the fund has come from philanthropy. The remainder has come from return on investments from prior successes. What started as conversation among Mayo Clinic clinicians, scientists and philanthropists has grown to a structured program under the auspices of the president and CEO and a designated leadership oversight group. This group is supported by a scientific advisory group that competitively evaluates requests for funding from Mayo Clinic investigative teams.

Twice per year, in January and June, the program invites proposals from clinicians and scientists in all fields of medicine and surgery across the enterprise. A first round of evaluation reviews short "Letters of Intent" that give advisory group members enough information for an initial assessment of clinical and commercial relevance. Those making it to the second round are asked to submit a full application, which the 25-member advisory group evaluates. The advisory group then recommends a number of these applications to the leadership oversight group — chaired by Dr. Noseworthy — for one to two years of funding for up to $300,000.

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The funding structure proves innovative and successful. Twenty-three of the projects have yielded a commercial event, including licenses and start-ups.

Most notable projects have advanced to the stage of clinical testing. One project, involving a peptide intended to treat congestive heart failure, is currently in mid-stage clinical trials. Another is a device that physicians may use to repair damaged heart valves. That device is in clinical trials in Europe.

The industry calls the trek from discovery to patient application "bench to bedside." And the ability to fund further developments of bench discoveries plays strongly into successful commercialization efforts. "Moving a new discovery from the bench to early clinical studies has allowed us to find commercial partners. Together with these partners, we're able to fund further clinical development and eventually move the discovery to quality clinical care, the ultimate mission of Mayo Clinic," says Andrew Danielsen, a member of the Mayo Clinic Ventures technology transfer office. Another important feature of the program, Danielsen adds, is that proceeds from its commercial successes are plowed back into the program to fund further research and development.

Even in an ideal environment, it is a challenge to bring discoveries to the bedside.

"This program provides targeted resources at a critical stage of product development, and that helps drive the discovery-translation-clinical application process," says Andre Terzic, M.D., Ph.D., chair of the program's scientific advisory group.

The key to the Discovery Translation Program, adds Michael Pfenning, the program's administrator, is to promote outstanding science that, whether laboratory-based or clinical, carries significant promise for patients. Clearly, finding the right industry partner also is a critical factor in the work of the Discovery Translation Program.

"We need good science plus good business," says Pfenning. Terzic agrees. "If you have good science, but you don't have an equal amount of good business, you won't make it to the bedside." ■

"If you have good science, but you don't have an equal amount of good business, you won't make it to the bedside."

If These Walls Could Talk

Honoring Our Benefactors

Philanthropy at Mayo Clinic began with its founders, and the tradition of giving continues to be a hallmark of Mayo's practice today.

Mayo benefactors are people from around the world and all walks of life. Their generosity supports Mayo's belief that health care is for the good of all people and the needs of the patient come first.

Philanthropic recognition levels honor benefactors who offer their partnership and support to Mayo Clinic.

This outpouring of generosity strengthens Mayo's accomplishments in research, education and patient care. Without philanthropy, Mayo's mission could not be sustained.

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Mayo honors benefactors throughout its campuses in a variety of ways. Each name displayed represents a unique person or organization and their story of giving.

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Featured in the Halls of Benefactors located at all campuses in Minnesota, Florida and Arizona are the names of those whose giving totals more than $100,000. Each name is hand-engraved on quarried slate from Vermont and Pennsylvania — each slate piece is different in its veining, which represents the uniqueness of the individuals and organizations represented.

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Patients, families and visitors see marble from around the world — different colors, textures and reflections impart a sense of security and well-being.

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A green marble wall in Rochester honors the foremost benefactors of Mayo Clinic. The individuals and organizations named here represent many generations, many places and many walks of life. They share a commitment to helping achieve a healthier future by investing their gifts in the facilities and programs of Mayo Clinic.

Mayo recognizes that each benefactor brings a story with their gift. To capture some of the stories and honor Philanthropic Partners, customized storyboards are located in prominent locations throughout the Mayo campuses.

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Electronic recognition kiosks are located in high-traffic areas on the Mayo Clinic campuses. These "electronic family albums" honor members of recognition groups and alumni societies.

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For all levels of gifts, Mayo expresses its gratitude. ■

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