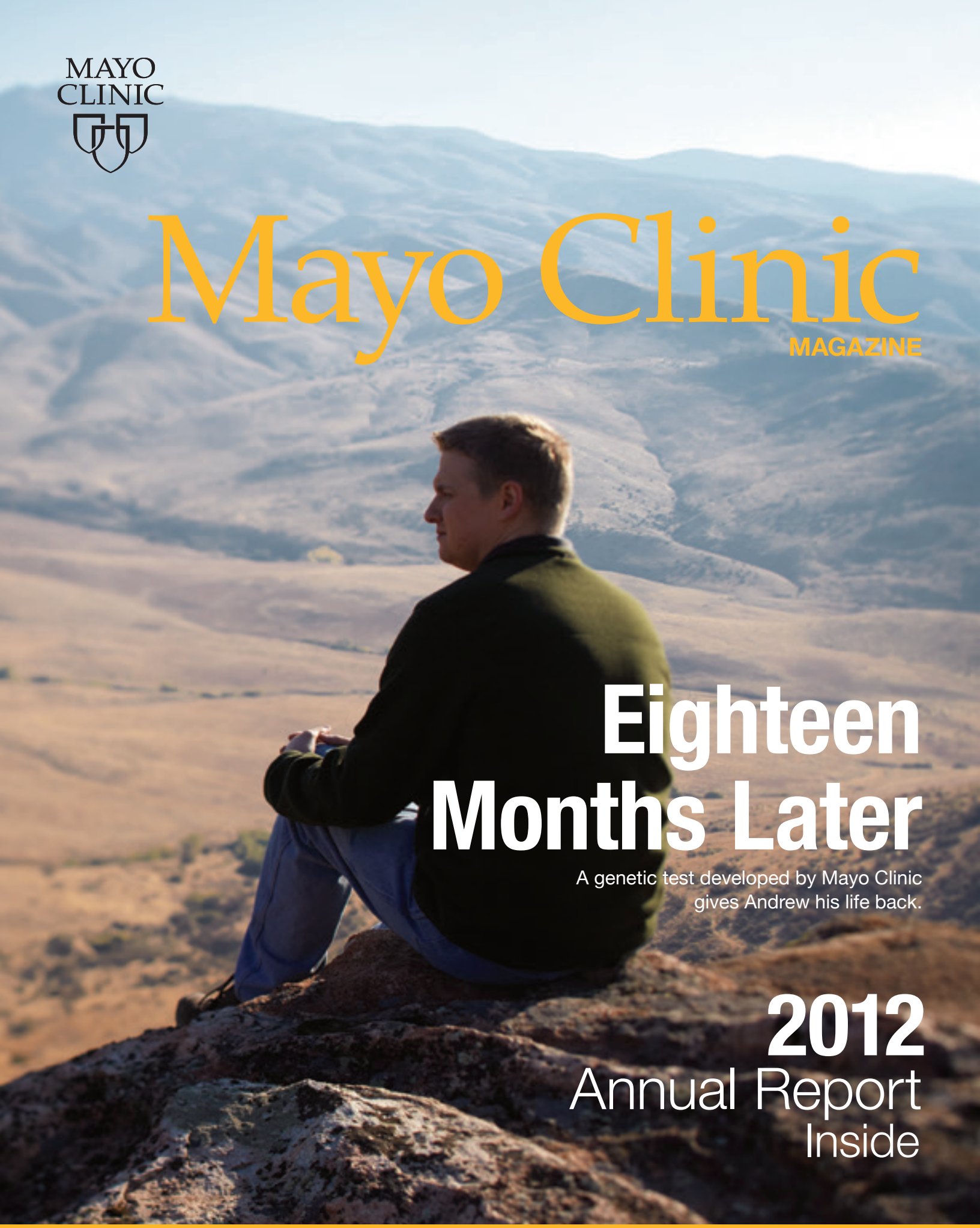

MAYO CLINIC

Mayo Clinic MAGAZINE

Eighteen Months Later

A genetic test developed by Mayo Clinic gives Andrew his life back.

2012 Annual Report Inside

2013 ISSUE 1

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In this issue: Making Connections to Save Lives

Mayo Clinic was founded on connections. It was the world's first multispecialty group practice, which connected many medical disciplines to focus on the needs of a single patient. It was the first to centralize patient medical records, which allowed caregivers to coordinate care quickly and efficiently.

That same pioneering tradition drives our care today, as you will find throughout this issue of *Mayo Clinic Magazine*.

You will see it in a mother's story about her son, who kept getting sicker and sicker until she brought him to Mayo, where doctors and researchers came together to administer a new genetic test developed by Mayo Clinic. It showed Andrew's medicines were making him sick.

You will see it in our drive to cure diabetes, which more and more researchers are saying is possible. Our effort unites physicians, institutions and a number of strategies, from mechanical implantation to bioengineered stem cells.

And you will certainly see it in our benefactors, like Lawrence and Marilyn Matteson, who focused their lives on ensuring children with cancer have a better future, and Jack Long, a 14-year-old who connected his New Jersey community to raise more than $10,000 for congenital heart research.

These are only a few of the countless stories about researchers, doctors, nurses, patients and benefactors allying to save lives. Thank you for being part of this special community, and enjoy this issue of *Mayo Clinic Magazine*.

Michael Camilleri, M.D.
Executive Dean for Development
Atherton and Winifred W. Bean Professor
Professor of Medicine, Pharmacology and Physiology, College of Medicine
Mayo Clinic Distinguished Investigator

Teenage Philanthropist

Determined to Make a Difference

Jack Long's goals for 8th grade:

Get New Jersey Gov. Chris Christie to declare a "Congenital Heart Defect Awareness Week"

Raise $10,000 for congenital heart research at Mayo Clinic

Undergo open-heart surgery to fix an anomaly

Check, Check and Check

> “Jack is just inspiring. He understands the importance and power of giving. We should all try to be more like this kid.”

Mayo Clinic President and CEO John Noseworthy, M.D., thanks Jack’s parents, Michael and Karen, for their son’s work.

For 14 years, Jack Long lived with Ebstein’s Anomaly, a rare congenital heart defect that carries a one-two punch. His right valve was out of position, and its leaflets were abnormally formed. Blood leaked through the valve, and now that Jack was a teenager, it was time to fix it before serious complications arose.

His family brought him from his hometown of Manasquan, N.J., to Mayo Clinic, which has more surgical experience fixing the anomaly than any institution in the world. It has performed more than 1,000 procedures over the last 40 years. The surgeon for most of them was Joseph Dearani, M.D. — Jack’s doctor.

“Results with surgery have steadily improved over the last two decades, so Jack’s quality of life and future outlook should be excellent,” Dr. Dearani says. “Jack is just inspiring. He understands the importance and power of giving. We should all try to be more like this kid.”

Jack initially came to Mayo for a consultation in the fall of 2012. When he got back to New Jersey, he explored with classmates and a teacher the idea of raising both awareness and funds for congenital heart defects. They came up with a slogan, “Live LONG, Beat STRONG,” and within days were sending


Dr. Noseworthy shows off his Live LONG, Beat STRONG bracelet.

letters to elected officials. Jack ordered bracelets and T-shirts and sold them out of his locker. His brother built a web page, livelongbeatstrong.com, that features ways to donate along with a video of Dr. Dearani explaining the condition.

Jack’s goal was to raise $1,000. He has exceeded it 10 times over and is still going. And the Monday he went into surgery, Gov. Christie signed the proclamation making the next seven days “Congenital Heart Defect Awareness Week” in New Jersey. ■

Our Symbiotic Selves

Harnessing the Power of Our Microbial Companions

As much as we would like to think so, our body is not our own. We are covered in microbes. They live on and even *in* us. In fact, for every human cell in our body, there are 10 microbial cells, covering our skin, informing our immune system and helping us turn food into nutrients.

These cells form their own microscopic communities, or microbiomes, which are ecosystems that live in symbiosis with our cells. Unfortunately, these ecosystems can fall out of balance when certain microbes grow out of control, causing illness and disease. For instance, one microbe in the intestine, *Clostridium difficile*, can cause dangerous colon inflammation, and even death if it grows unchecked.

The standard protocol is to give antibiotics that kill broad populations of bacteria, including the ones making people sick. The Center for Individualized Medicine is finding better solutions in certain cases. To treat serious intestinal infections, Mayo Clinic researchers are exploring ways to harvest the healthy and balanced microbiome of a donor and use it to restore the microbiome in sick patients.

With benefactor support, researchers are sequencing the genetic code of the entire microbiome of 100 patients who have suffered *Clostridium difficile* infection. The researchers are comparing it with the microbiome of healthy people. This will help determine whether an individual has a healthy community of intestinal bacteria or one that puts them at an increased risk for getting *Clostridium difficile*. This kind of information could help get the right treatment to the patient early and spare serious life-threatening complications.

"We have a dense population of bacteria in all parts of our body, with the largest majority being in our intestines and on our skin," says Heidi Nelson, M.D., the Fred C. Anderson Professor and director of the Center for Individualized Medicine's Microbiome Program. "Sequencing opens the door to a whole new horizon of understanding what bacteria are there and what they're doing there."

This knowledge will improve both diagnostic tests and treatment options. And it promises to lead to specific probiotics — delivered through pill or suppository — that will return a patient's microbiome to a healthy, vibrant state. ■

Making Regenerative Medicine a Reality

> “Patients responded favorably both in terms of their cardiac function and structure as well as in terms of their overall fitness.” — Andre Terzic, M.D., Ph.D

Once a heart attack damages tissue, there’s no way to heal the injury. This problem has vexed cardiologists for generations.

They are left treating symptoms — medicines to reduce built-up fluid, implanted stents to increase blood flow, pacemakers to control beat rhythm.

Many times the treatments work fine, and the patients go on to live normal lives. Other times, the damage is too great. The heart can’t make up for the loss of functioning tissue and steadily declines. The only option for these patients is a heart transplant, which carries its own risks and drawbacks, including a shortage of donor organs and a lifetime of immunosuppressive drugs to keep the body from rejecting the new organ.

One recent regenerative medicine study, C-CURE, is providing new hope for patients.

A collaboration spanning two continents and five countries showed stem cell treatment helped improve heart function following a heart attack. The Michael S. and Mary Sue Shannon Family Director of Mayo Clinic’s Center for Regenerative Medicine, Andre Terzic, M.D., Ph.D., co-led the study, which starts the healing process by harvesting a patient’s bone marrow in the hip and extracting its stem cells. The stem cells are then treated with growth factors to orient them to become heartlike cells and injected directly into the diseased heart.

Every patient in the study showed improvement. It was the first successful demonstration of the feasibility and safety of transforming adult stem cells into cardiac cells in humans.

“Patients responded favorably both in terms of their cardiac function and structure as well as in terms of their overall fitness,” says Dr. Terzic, who is also the Marriott Family Professor of Cardiovascular Research.

Through the Center for Regenerative Medicine, Mayo Clinic will apply the study’s lessons to reviving other tissues, such as the liver, lung, nerves, pancreas and skin. ■

Dedicated to the Primary Value

53 Years of Serving Mayo Clinic and Its Benefactors

Mayo Clinic's Board of Trustees doesn't have a secret handshake. No rites of passage. But, according to Robert Smoldt, emeritus chief administrative officer, "Three words have been passed from one member to another, across the decades: 'Call Dale Rustad.'"

Dale began working at Mayo Clinic the year John Kennedy was elected president. His first job was with General Service, the frontline ambassadors of the Mayo Clinic Model of Care. Then, after working as a respiratory therapist, he was recruited to a series of positions that he infused with what Robert Waller, M.D., president emeritus of Mayo Clinic, describes as "Dale's exceptional passion for service."

One was managing the Mayo Foundation House from 1968 to 1996. Dale gave a personal greeting and ensured white-glove service to Mayo Clinic staff, spouses and distinguished guests. His attentiveness earned him the extra responsibility of administrative assistant to the Board of Trustees, where he set a record that no one will likely match: the longest term of service — 40 years — all with perfect attendance.

In 1996 Dale transitioned to development officer and manager of Benefactor Services and Trustees in Rochester. In 2002, Dale relocated to Arizona.

Over his career his commitment has earned him many professional awards including recognition from the National Restaurant Association, specialty training at the Culinary Institute of America and commendation from the U.S. Secret Service for supporting their protection of first families, heads of state and other prominent visitors to Mayo Clinic.

"In his role Dale brought the same standard of excellence that our physician colleagues do in the medical setting," says James Hodge, vice chair of the Department of Development. "Benefactors made gifts in honor of Dale and said his dedication inspired their support."

Now, as he reflects on his retirement from Mayo Clinic — the people he has known and the values they represent — Dale Rustad says simply, "It's been an honor to serve." ■

Making Surgery Safer

One Study Mayo Clinic Collaborated in Prevented About 135 Infections

> “We have to be continuously aware and relentless.”
>
> — Lynn Quast, R.N.

Lynn Quast, R.N., has firsthand experience with colorectal surgery, both as a nurse and as a patient. Almost three years ago, she developed diverticulitis, a painful inflammation of the colon that, if left untreated, can cause serious damage.

The night before the surgery, she worried. She had seen the effects of cutting into the bowels. She knew if all went well she’d be working again in five weeks. If not, she could face a life-altering infection that might require additional surgeries.

And she knew the national average of ending up back in the hospital with a serious infection was nearly one in six.

Everything went fine. Today, as surgical nurse manager at Mayo Clinic, Quast is working with her team to reduce the odds of infection. Recently, she co-authored a study that evaluated each step of the colorectal surgery process, from the patient’s presurgical skin preparation through the complex surgery and postoperative wound dressing. The study developed a set of protocols that, when applied consistently, reduced infections and improved patient outcomes.

One key new step is called “Time Out,” when the surgeon is ready to close the wound. The surgical technologist and nurse count and remove all contaminated sponges and instruments and open a sterile set. If needed, everyone puts on fresh gloves and changes gowns.

Within a year, surgical site infection rates at Mayo Clinic dropped from 9.8 percent to 4 percent.

The study involved seven U.S. health care systems, with Mayo Clinic surgeon Robert Cima, M.D., leading Mayo’s participation. The collaboration estimates the project saved more than $3.7 million by preventing 135 colorectal surgical site infections.

“It’s not just about cutting costs and being more efficient, though those are important considerations,” Quast says. “It’s about the patient not having to go through the added risk, pain and cost of an infection. We have to be continuously aware and relentless.” ■

12 More Reasons

There are countless reasons to choose Mayo Clinic — world-class expertise, cutting-edge research, efficiency of appointments, multidisciplinary approach — you name it. Here are just a few more.

1 Deep brain stimulation

Many patients who suffer from Parkinson's disease, Tourette syndrome or persistent depression find relief from their symptoms at Mayo Clinic, where physicians stimulate neural activity through surgically implanted electrodes in the brain.

2 Pancreatic cancer surgery through a keyhole

Surgeons at Mayo Clinic have found that laparoscopic surgery is equally effective to conventional surgery for many patients with pancreatic cancer.

3 Minimally invasive cardiac surgery

Mayo Clinic is reducing the size and impact of incisions while maintaining high-quality outcomes. This allows patients to get back to their lives even more quickly.

4 Better diagnosis for women with dense breast tissue

Dense breast tissue can frequently hide cancer from mammogram screenings. Mayo clinicians are using a new technology, Molecular Breast Imaging, that makes cancer cells highly visible and permits the detection of small breast lesions.

5 BEAUTY Project

The Breast Cancer Genome Guided Therapy Study will help doctors tailor chemotherapy to breast cancer patients based on their individual genomes and the genomes of their tumors.

7

Revolutionary proton beam radiation therapy

The Mayo Clinic Proton Beam Therapy Program, available in 2015 in Minnesota and 2016 in Arizona, will employ pencil beam scanning to more precisely target tumors, reducing damage to surrounding tissues and vital organs. (See story on page 29.)

6

Breakthrough technology for detecting recurrent prostate cancer

Mayo Clinic is the first institution in North America approved to produce and administer Choline C-11 Injection, an imaging agent that can detect recurrent prostate cancer much earlier. (See story on Page 14.)

8

Knowing the electrical wiring of the heart

When cardiologists need to stop heart rhythm irregularities, they sometimes have to cut "wires" in the heart. To perfect our understanding of those wires, Mayo Clinic doctors studied 620 hearts.

9

Hub-and-spoke telestroke networks

Mayo Clinic physicians and researchers helped prove the cost effectiveness of Internet communications between "hub" hospitals and outlying "spoke" hospitals while improving outcomes for patients affected by acute ischemic stroke. Telecommunications enhanced evaluation and treatment — especially for patients in rural settings where there may be limited access to neurologists.

10

Fixing birth defects in the womb

Mayo Clinic pediatric neurosurgeons can operate on children with spina bifida in the mother's womb to correct a defect in the coverings of the spinal cord that would otherwise result in paralysis of the legs, bladder and bowel of the newborn child.

11

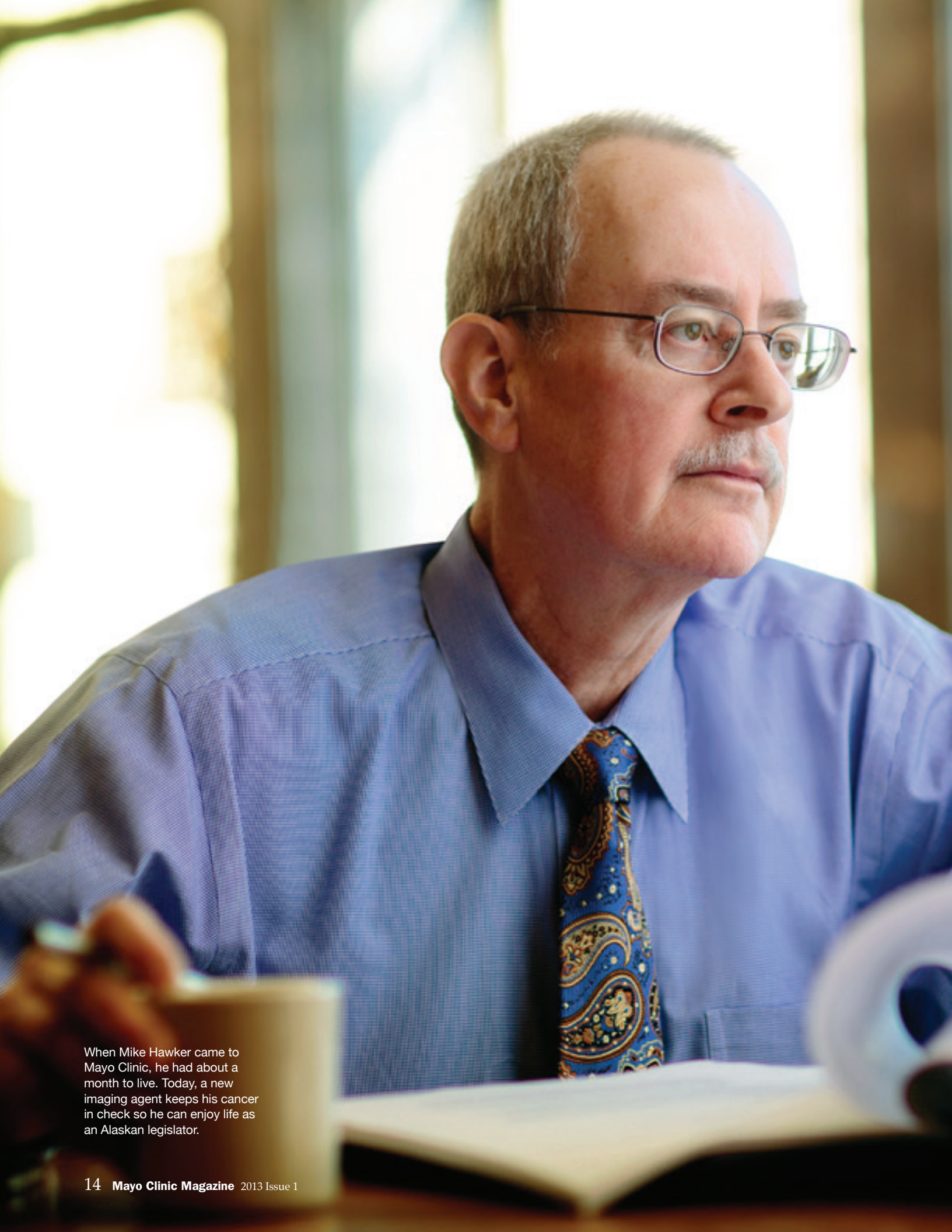
Prescriptions based on your genes

When we know the genes that influence the way a drug is handled in the body, we can select the right drug, at the right dose, such as for antidepressants and other drug classes. (See story on Page 34.)

12

Cutting-edge clinical trials

Mayo Clinic is conducting hundreds of cancer trials — often unavailable elsewhere — focusing on various methods to prevent, diagnose and treat the disease. Hundreds of other clinical trials are under way to better understand and treat conditions ranging from serious blood disorders to Alzheimer's disease to rheumatoid arthritis.



When Mike Hawker came to Mayo Clinic, he had about a month to live. Today, a new imaging agent keeps his cancer in check so he can enjoy life as an Alaskan legislator.

A New Hope

An Imaging Agent Available First at Mayo Clinic Detects Recurrent Prostate Cancer Earlier

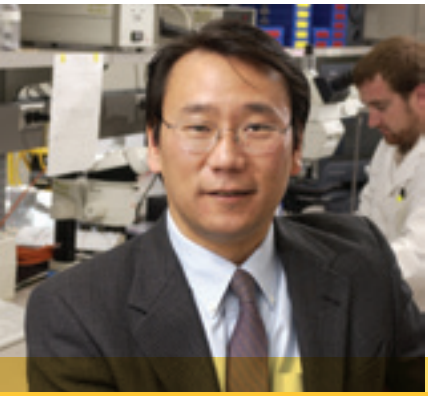
> I saw my death and accepted my mortality.

Huddled into a ball on his airplane seat, watching out the window as the Alaskan landscape slowly receded, Michael Hawker thought it was the last time he'd see the Land of the Midnight Sun.

Prostate cancer had so riddled his body — spreading to his spine, femur, lymph nodes, pelvis, bladder and eye sockets — that his life expectancy was less than a month. He was flying to Mayo Clinic, Rochester, Minn., looking for a miracle.

"I had come to the point where I saw my death and accepted my mortality," the Alaska state legislator says.

His wife, Carol, hadn't. Fighting to give her husband one last chance, she called Mayo Clinic to find a physician with experience in widely metastatic neuroendocrine prostate cancer. When she reached the urology appointment desk, Eugene Kwon, M.D., research co-director for the Department of Urology and the Cancer Immunology and Immunotherapy Program, happened to be walking by and overheard his name and a bit of the conversation.



Dr. Kwon asked to speak to the caller. Within days Michael and Carol were at Mayo Clinic.

Dr. Kwon asked to speak to the caller.

"That is remarkable in itself," Michael says. "I understand doctors just don't take cold calls."

Within days of that conversation, Michael and Carol boarded a plane headed to Rochester, Minn.

The Most Miserable Week of My Life

Despite four months of chemotherapy in Alaska, Michael's cancer grew unchecked. "My body was completely debilitated, and my wife had to do everything for me," he says. "I hardly remember the plane ride to Minnesota."

Upon Michael's arrival at Mayo Clinic on Dec. 1, 2010, Dr. Kwon ordered a back-to-back series of bone, pelvic, bladder and prostate biopsies and started Michael on hormone therapy to fight the cancer. "It was quite literally the most painful and worst week of my life," he says.

By Dec. 8, Michael's prostate-specific antigen (PSA) levels had dropped from 36 to six.

Michael had given up fighting his cancer, but his wife, Carol, hadn't. She called Mayo Clinic and immediately got an appointment with Eugene Kwon, M.D.

"We just couldn't believe it," Michael says. "This was the first time in six months we received news other than 'you're going to die.'"

And so began Michael's long-term relationship with Dr. Kwon and Mayo Clinic. Within a few months of receiving hormone treatment, Michael's PSAs were nearly undetectable and stayed that way until the fall of 2012.

Keeping Cancer at Bay

Dr. Kwon views Michael's cancer as a major offender on probation. To keep his cancer in line, Michael has his PSA levels checked regularly with doctors in Alaska, and every six months he returns to Mayo Clinic for a thorough once-over.

In Sept. 2012, Michael's PSA level increased from 0.1 to 0.2 ng/mL. For most men, such an infinitesimal increase wouldn't cause concern. But for Michael, who had cancer throughout his body, the slightest increment is a four-alarm call to action. As soon as his numbers started rising, Michael headed back to Mayo to

Michael pans for gold with his nephew Derek Bradish.

Choline C-11 injection can help locate cancer when PSA levels are at least half of what traditional imaging techniques can detect.

pinpoint where the cancer was hiding through a powerful new diagnostic tool: Choline C-11 Injection, which can help locate cancer when PSA levels are at least half of what traditional imaging techniques can detect.

Detecting and Defeating Recurrent Prostate Cancer

This new imaging technique uses a radioactive form of the vitamin choline, which cancer cells readily absorb. Clinicians inject a small amount of the agent into a patient's vein and then use a positron emission tomography (PET) scanner and computer to see where the agent collects. The result is a detailed map of a person's cancer.

The FDA approved Mayo Clinic as the first institution in the United States that can manufacture and administer Choline C-11 Injection. The technical name for the compound is 11C choline. The 11C denotes that a carbon atom has been made radioactive and has a half-life of 20 minutes, which means for every 20 ticks of the clock the agent loses 50 percent of its efficacy.

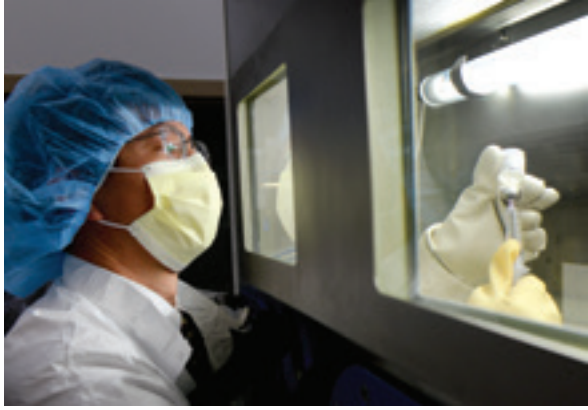
Its short lifespan means 11C choline needs to be made for each patient and administered within minutes of its creation. Michael's Choline C-11 Injection identified four spots of prostate cancer activity. After clinical confirmation of the imaging results, doctors quickly treated him with radiation therapy, and today Michael's cancer is once again in check.

A Game Changer

Until this technology became available, determining how to treat recurrent prostate cancer could be a guessing game as physicians couldn't tell where the cancer was. Even if a traditional PET scan revealed a mass that early, it was very difficult to tell what the mass might be — Scar tissue? Arthritis? An inflammation? Cancer? Choline C-11 Injections help change that dynamic so doctors can react more quickly and craft more targeted therapies.

Back in Alaska, Michael is healthy and feeling on top of the world. "I have been granted a second chance at life by the people who work at Mayo Clinic and the tools and technology they have. I recognize this and am grateful for it. Every day burns a little bit brighter. I only have so many days left on this planet, and I truly want to leave a legacy of something good. I cannot describe how happy I am to be alive." ■

Ping Fang prepares a dose of 11C choline for injection. Once ready, it has to be used within minutes.



The Right Thing to Do

Pharmaceutical companies have known of 11C choline's imaging power for some time, but none have spent precious development resources pursuing it. From a profit point of view, it has three strikes against it: it's not patentable; it's only good for a short amount of time (20-minute half-life); and it's virtually impossible to distribute in mass quantities.

But Mayo Clinic's Eugene Kwon, M.D., Val Lowe, M.D., and Joseph Hung, Ph.D., knew it had potential to impact the care of prostate cancer patients. So, with the help of colleagues Jeffrey Karnes, M.D., and Christopher Mitchell, M.D., they pursued, on their own time, Mayo Clinic's first New Drug Application (NDA) with the FDA.

They didn't have $4 billion, which *Forbes Magazine* reports is the average amount a pharmaceutical company spends for every drug approved. And they didn't want to wait patiently the typical 10-plus years it takes to put a drug through the usual approval process.

"We pursued this because it's the right thing to do," says Dr. Lowe, a specialist in nuclear medicine and PET imaging at Mayo Clinic. "We believe it will save more lives."

So, armed with years of research and published literature, the Mayo team met with the FDA to determine if Choline C-11 Injection qualified for a new drug application. The FDA gave the green light to the researchers and granted a priority review for the application. Within nine months of the researchers' application submission, the FDA approved Mayo Clinic as the first institution in the United States to manufacture and administer Choline C-11 Injection to help identify recurrent prostate cancer.

"The evidence is compelling," says Dr. Hung, director of the Mayo Clinic PET Radiochemistry Facility. "We were hoping the FDA would agree. And they did."

Mayo physicians want to use Choline C-11 Injection to investigate where prostate cancer manifests in the body and determine what treatments work best for which forms of prostate cancer. The team is also specifically interested in developing the next generation of other radioisotopes to pinpoint all types of cancer and other diseases, like Alzheimer's. ■

The Race Is On

How Mayo Clinic Is Using Cutting-Edge Regenerative Medicine Technology to Find a **Cure for Diabetes**

Caroline can never escape her diabetes. It was there on her first day of school, at her first communion. It's there every Halloween, every Christmas, every vacation. She's pricked her finger eight to ten times a day since she was 3 years old, including the six birthdays she's had since she was diagnosed.

She understands that it wasn't her fault that her body turned on itself, that her immune system attacked her insulin-producing islet cells. To quote Caroline, "Diabetes doesn't care how cute you are. Diabetes doesn't care how well you play soccer. Diabetes doesn't care who your friends are or how much your family loves you."

From the outside, her life looks perfectly normal. She plays soccer, swims with friends and goes to ball games with her family. But in the background is the relentless hum of type 1 diabetes, with vigilant blood sugar surveillance and insulin adjustments.

Her parents, Tom and Michelle Schlehuber, are thankful for the lifesaving medications and technologies that keep their daughter alive, but they pray for the day when Caroline isn't one missed reading away from the emergency room, when her life isn't dominated by glucose meters and insulin pumps.

That day may be closer than they imagined.

New Possibilities

The road to discovery is long and riddled with ideas proven wrong. Researchers repeatedly see the most promising ideas fail when subjected to rigorous scientific method. The experience leaves most of them hesitant to use a certain four-letter word — "cure." Instead they use euphemisms like "advancing care" and "better treatments."

But something seems to be stirring among diabetes researchers. One occasionally hears whispers of the word. Some are becoming even bolder with statements like, "It's no longer if we cure diabetes, but when."

The reason for the optimism is that one proven cure already exists. Patients with type 1 diabetes who have received pancreas transplants have seen their disease go away completely. Unfortunately, the transplant requires a lifetime of immunosuppressive drugs whose side effects can be more harmful than diabetes.

The success of transplants shows a cure is possible. But how do we get there without the full transplant? Without the drugs? Researchers are making extraordinary progress toward answering these questions. So much so that many believe the race is on to find a cure. And Mayo Clinic might have the edge.

> "It's no longer if we cure diabetes, but when."

Movement Sensors: Setting Mayo Apart

Delivering the right amount of insulin at the right time requires assessing factors such as blood glucose, ambient temperature, time of day and, crucially, activity levels.

On that front, Mayo Clinic's motion-sensing device sets its artificial pancreas apart. Developed by Mayo endocrinologist James Levine, M.D., Ph.D., Dr. Richard F. Emslander Professor in Endocrinology and Nutrition Research, the device feeds quantitative data derived from movement and exercise into the artificial pancreas system, increasing the real-time accuracy with which individualized insulin dosages are calculated.

"That's potentially a very important thing," says Yogish Kudva, M.B.B.S. "We are ahead of everyone else in terms of bringing this technology into this area of research."

"I genuinely believe that now is the time for diabetes, and there is a lot going on at Mayo that has major promise," says Stephen Russell, M.D., Ph.D., deputy director for Translation in Mayo Clinic's Center for Regenerative Medicine. "We know we can turn this new stuff into clinical reality."

Building a New Pancreas for Tight Glucose Control

Mayo Clinic's Yogish Kudva, M.B.B.S., and Ananda Basu, M.D., M.B.B.S., hope to transform life for people like Caroline with a hands-free device called the artificial pancreas.

Functioning just like a biological pancreas, the artificial pancreas uses an abdominal patch that continuously measures blood sugar. A pager-sized pump then delivers exactly the right amount of insulin at exactly the right time. Precision is critical because abnormal blood sugar levels can cause disabling and life-threatening complications such as heart attacks and strokes and damage the nerves, eyes and kidneys.

The artificial pancreas will free people with diabetes from daily preoccupations over finger pricks, blood reads and daily shots. Many diabetics have insulin pumps already, but the artificial pancreas represents a sea change because it minimizes patient decision making.

Looking to the future, Dr. Kudva says, "We're very excited."

Working in partnership with the University of Minnesota, Mayo investigators are developing a novel continuous blood sugar sensor to improve its performance and usability. Mayo investigators are also refining the algorithm that controls insulin delivery so it can be individualized for each patient.

In an upcoming clinical trial, Mayo researchers will use hard data from humans with type 1 diabetes to predict insulin needs, setting Mayo's efforts apart from other studies that have relied on computer simulations. By next year, Drs. Kudva and Basu hope to test the artificial pancreas

in the real world as patients use it for weeks at a time, integrating the device into their daily lives.

Replacing Damaged Cells

The immune system wages war on any virus, bacteria or fungus it considers an invader of the body. As with Caroline's type 1 diabetes, the immune system mistakenly targets the body's own islet cells, compromising the pancreas's ability to monitor blood sugar levels and release insulin.

Mayo Clinic investigator Yasuhiro Ikeda, D.V.M., Ph.D., is investigating a cutting-edge regenerative approach to replace these essential islet cells in the pancreas. Tapping the body's power to heal itself, Dr. Ikeda is working to generate new islets from the diabetic's own skin or blood.

The process extracts cells from the patient and converts them into stem cells. Dr. Ikeda has taken these bioengineered cells — known as induced pluripotent stem (iPS) cells — a step further by inducing them to grow into glucose-responsive, insulin-producing cells in the laboratory. The iPS technology and its promise for humankind have been recognized by the 2012 Nobel Prize in Physiology and Medicine.

"Our future goal is to make customized islets from iPS cells and then hopefully put them back into the patient," Dr. Ikeda said.

Dr. Ikeda has improved blood sugar levels in diabetic mice for short periods of time using this promising technology. His next steps are to improve the responsiveness of the bioengineered islets to blood sugar fluctuations and increase the amount of insulin they produce. Human trials could start in the next three years.

Stopping Diabetes in Its Tracks

A problem lingers even if lost islets can be replaced: The patient's body could reject them as the immune system attacks the newly transplanted islets.

In this regard, Dr. Ikeda believes that recent advances in gene therapy

A New Source of Insulin

Gene therapy promises to protect islets from the immune system, but it could also provide a source of insulin separate from the pancreas. In this approach, clinicians would inject insulin genes directly into muscle tissue.

"That gives you a source of insulin that's constantly coming into the bloodstream," says Stephen Russell, M.D., Ph.D., the Richard O. Jacobson Professor of Molecular Medicine.

This therapy likely won't be a good fit for type 1 diabetics because it could cause blood sugar levels to run dangerously low. But there are many Type 2 diabetics who require continuous, long-acting insulin for whom this type of gene therapy could have benefits.

"What this could do for type 2 is to improve the convenience of therapy," Dr. Russell says.

A Center Dedicated to Diabetes Research

Highlighting its leadership role in fighting diabetes, Mayo Clinic is home to a Diabetes Research Center.

Under the leadership of John Miles, M.D., the Earl and Annette R. McDonough Professor, the center focuses on translational research and facilitates the application of scientific discoveries for the ultimate purpose of preventing, treating and curing diabetes.

The Center is structured to promote interactions among investigators, collaboration between disciplines, and shared resources among all participants — individuals, departments and institutions.

hold great promise in preventing the autoimmune response to islets that mark the progression of diabetes.

"If we can suppress autoimmunity, we should be able to suppress the disease," he says.

To reach islets with tremendous precision, Dr. Ikeda uses a mild, non-disease-causing virus called adeno-associated virus (AAV), which travels through the bloodstream to deliver a gene that suppresses the immune system's attack in a localized area.

Dr. Ikeda has already used the gene, called Interleukin-10, to prevent the onset of diabetes in diabetes-prone mice. That success drove him to pursue an even more challenging discovery: How do you stop diabetes in its tracks once islet destruction begins?

"Once the immune response kicks in, it's very hard to reverse it," he says.

In pursuit of a landmark discovery, Dr. Ikeda is focused on stopping the progression of diabetes during its so-called "honeymoon" stage. This is the critical period — roughly two years in humans but much shorter in the lab mice Dr. Ikeda is testing — during which the immune system gradually decimates islets in the pancreas.

If diabetes can be stopped early enough, Dr. Ikeda believes a critical mass of islets will be preserved to maintain necessary insulin levels. He hopes clinical trials focused on this approach to gene therapy can start soon.

Rebooting the System

Another possible treatment for diabetes, called cell therapy, is also aimed at protecting islets from the immune system.

"My hope is we reset the system: that you prevent the cells from killing the islets, the islets repair, and you go on with your life," says Allan Dietz, Ph.D., an investigator in Mayo Clinic's Human Cellular Therapy Laboratory, which is integral to Mayo Clinic's regenerative medicine endeavors.

Cell therapy involves the use of mesenchymal stem cells, which can be produced in large quantities from a fat biopsy and implanted back into a patient.

"When you get wounded or have an injury, these are the cells that mediate repair," Dietz says.

> “If we can suppress the autoimmunity, we should be able to suppress the disease.”

There’s a good chance that mesenchymal stem cells can suppress the immune system safely in a targeted area to prevent the destruction of islets while helping islets repair themselves, Dietz said. He noted that new trials could start soon if funding were available.

Working Toward a Cure

Though Caroline’s family began praying for a cure the day they learned she had diabetes, they began working toward it almost as soon.

Within months of the diagnosis, the family formed Team Caroline and participated in Juvenile Diabetes Research Foundation’s Walk to Cure Diabetes in San Diego. About 15 friends and family members joined in. Over the past six years, their involvement has grown, and last year about 100 people donned bright green shirts and walked with them through Mall of America in Minnesota to raise awareness and funds to support research.

Their goal was $15,000. They exceeded it by more than 20 percent. ■

The Biotrust: Focusing the Power of Regenerative Medicine

The stem cell approach is the heart of regenerative medicine. In the past few years its promise has started to become reality with Mayo Clinic delivering regenerative treatments for osteonecrosis, tendonitis and reconstructive surgery. The mesenchymal stem cell strategy that holds so much hope for diabetes treatment is already being tested in many other diseases, including amyotrophic lateral sclerosis (ALS) and heart disease.

Two assets uniquely position Mayo Clinic to focus this momentum on diabetes — the best endocrinology and diabetes program in the country (as ranked by *U.S. News & World Report*) and the Center for Regenerative Medicine, a catalyst in advancing new knowledge into delivery of next-generation cures.

With the growing interest in regenerative medicine research and treatment, Mayo Clinic established the Regenerative Medicine Biotrust, which will help researchers more efficiently collect samples, process cells and share results.

“The process of harvesting a cell, differentiating it into specialized tissues, expanding it into big numbers, then using them for real applications in research, clinical applications, clinical trials, etc. – that’s complicated,” says Dennis Wigle, M.D., Ph.D., director of the Regenerative Medicine Biotrust. “You need an infrastructure to be able to do that.”

Building on Mayo Clinic’s expertise in biobanking, the Regenerative Medicine Biotrust will give researchers and clinicians access to living cells. The approach will fast-track discovery in areas like diabetes, accelerating the time-consuming processes of specimen collection and conversion. In this way, teams of scientists and clinicians will develop focused questions and go right to the prepared cells to find the answer.

And as soon as an answer is found, the Regenerative Medicine Biotrust will accelerate the translation to clinical application.

“The Biotrust puts Mayo at the cutting edge in investigating how fast we can make new technologies, apply new technologies and do it for real clinical care,” Dr. Wigle says. “This will advance regenerative solutions for our patients.” ■

Investing
IN THE FUTURE
Parents Inspired Him to Help Others

Gordon Gunnerson hated what his parents had to go through at the end of their lives. First his father fought heart disease, then developed dementia. It became so bad he eventually reverted back to childhood.

About four years later, when Gordon was succeeding in real estate in Lake City, Mich., his mother developed cancer. After watching his father's decline, he knew his mother needed him, so in 1996 he left behind a client list that took decades to build. Gordon took care of her, watching the cancer slowly take her body and eventually her mind.

"It really bothers me to see people forget, and they don't seem to know where they are," Gordon says. "It's a real shame."

The experience led Gordon to make a difference in the larger community. Shortly after his mother died, a social worker and a group of nurses showed him the need for an assisted living facility in Lake City. He saw it as a perfect opportunity to help people who have nowhere to turn when it isn't safe or feasible for them to live alone anymore.

"I traveled for a year studying facilities, talking with people, asking about costs," Gordon says. "And I hired someone to do a feasibility study on the idea."

He processed all that hard data, which showed his community could support a 90-bed facility, but it didn't show where the money would come from.

Gordon's mother had raised him to be pennywise, to not buy anything unless he had the cash. He had never borrowed money. Not for his first car, not for his house, not for anything. Ever. Getting past this point of pride was a very big step. Unfortunately, every local bank rejected him, citing his lack of experience in the assisted-care facility business. But in 2002, a new bank in Traverse City, Mich., opened. He presented his data and convinced them to give him a $5 million loan.

Gordon oversaw the construction of the high-quality assisted living facility and named it Belle Oakes in honor of his mother, Isabele. For the next six years, he ran it himself, making sure clients were surrounded by people who cared and understood the needs of older people with dementia.

Giving Back

In 2007, Gordon's blood pressure became worrisomely high. He sold Belle Oakes and slowed his pace of work, spending more time at his cabin on Round Lake, which he calls a bit of paradise. But he wanted to continue making a difference for people with dementia. So he turned to Mayo Clinic.

Gordon first came to Mayo Clinic as a young man seeking help for his blind brother. Gordon remembers teams of experts focusing on his brother, trying to help.

"They charged my brother $50 for the weeklong visit," Gordon recalls. "And because they knew he didn't have a job, they offered him the option of paying 50 cents a month, to our local bank, so he didn't even need to buy a stamp."

Over the years, Gordon turned to Mayo Clinic time and again. Each time, he came

> “The only thing I’m hoping for is a solution for Alzheimer’s.”

away grateful for the kindness and care shown to him and his family. He is especially thankful for Chris Batchelder, a development officer who became a close friend. At one point, Chris visited Gordon’s dad every day for weeks while he was hospitalized in Saint Marys.

“I learned a lot from that man,” Gordon says. “He worked long hours and always put people first.”

Chris helped Gordon realize he could maintain financial stability while advancing his goal to help people fight dementia. The solution was a charitable gift annuity, which pays back in cash a percentage of a philanthropic gift. So with the proceeds from the sale of Belle Oaks, Gordon established a $1 million charitable gift annuity to advance Mayo Clinic’s Alzheimer’s disease research.

“I want Mayo Clinic to have money to do more experiments to solve more problems and help more people, especially people with Alzheimer’s,” Gordon says. “The only thing I’m hoping for is a solution for Alzheimer’s.” ■

A Win-Win-Win Gift

A CHARITABLE GIFT ANNUITY IS A TAX-DEDUCTIBLE GIFT THAT ALSO PRODUCES INCOME FOR THE GIVER.

Advantages for the benefactor:

- A steady income (an annuity) unaffected by market performance.
  - Income is determined by the percentage of the original gift. The percentage is set by age, with older individuals receiving higher percentages.
- A reduced tax burden.

Advantages for the institution:

- The ability to start work earlier.
- Long-term support.

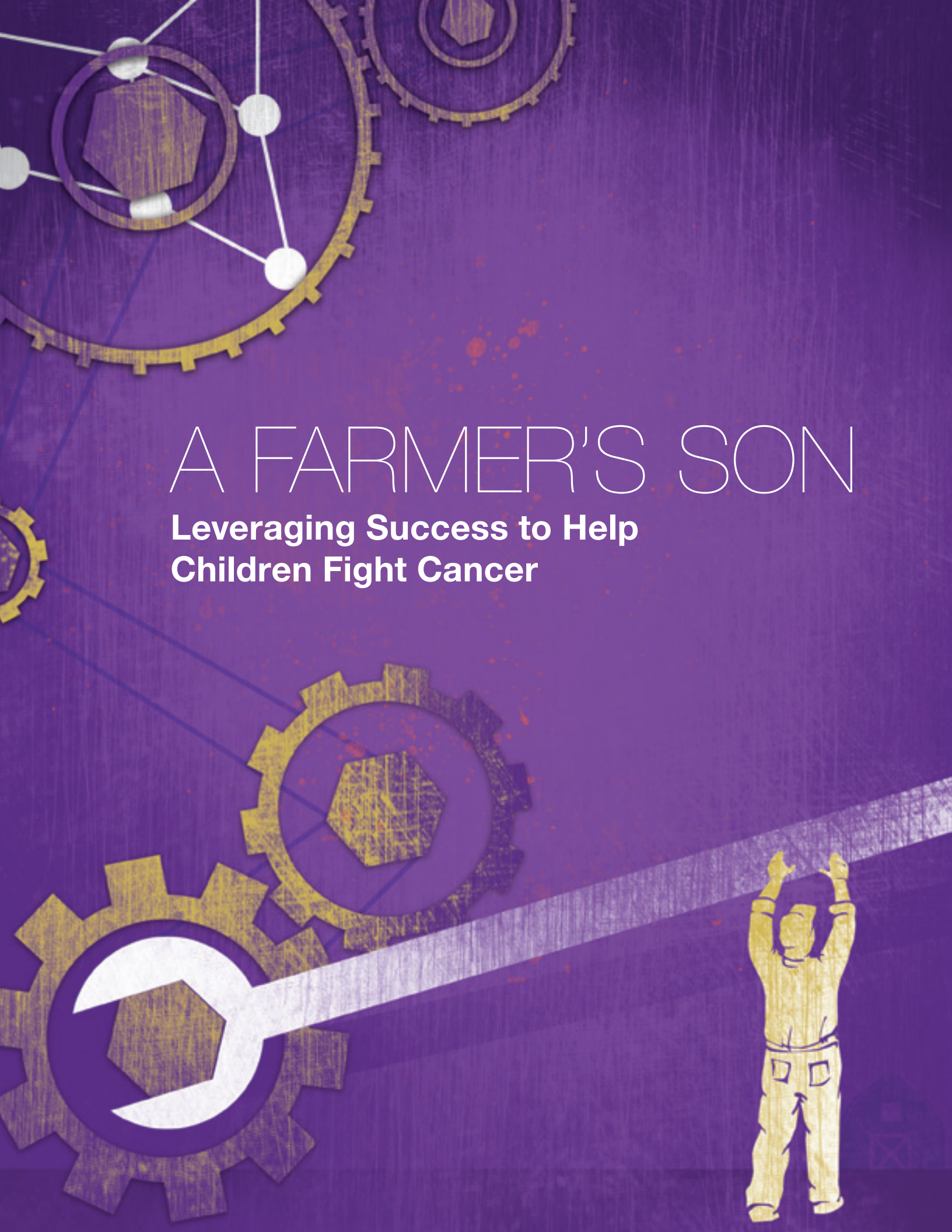
Advantages for both:

- A strong, lasting partnership.
- Advancing the goal to improve health care.

If you have questions, contact Mayo Clinic Office of Gift Planning at 1-800-297-1185 or GIFTPLANNING@mayo.edu. Or visit our new website: plannedgiving.mayoclinic.org.

A FARMER'S SON

Leveraging Success to Help Children Fight Cancer



Not many men know how to skin a skunk and sell the hide, overhaul a tractor, cut commercial timber, milk a cow, dredge a lake, build a winch and remember to call his wife every single day.

But Lawrence Matteson does.

He remembers walking trap lines along the Skunk River as a kid. Every morning he and his brother followed its winding banks, shooting and collecting game on the way. At the end of the line was their one-room schoolhouse, and each morning the boys' teacher gathered their guns and game to hold in the woodshed until the day's lessons were over.

Back then, Lawrence couldn't fathom his life's journey and how the skills he learned working the family farm played into his future. He was more focused on selling the hide that he skinned and the nightly dinner his mother made from her sons' hunting excursions.

"We ate a lot of blackbird pie," Lawrence reflects, his past glimmering in his now 83-year-old eyes. "My mother could cook just about anything we brought home. Squirrel. Rabbit. She was a remarkable woman."

Growing up in southern Iowa along a Mississippi tributary, exploring the countryside for hours on end, Lawrence and his brother Gene experienced freedom that few kids understand today.

"We entertained ourselves," Lawrence says, recalling that his mother always knew that her sons were by the tracks when she heard the blast from a train whistle blowing in the distance.

Hard Work Pays Off

And although Lawrence fondly recalls blue summer skies and roaming the land, he also remembers hard work and fickle machinery. In high school, the brothers took over the farm chores

when their father went to work for the railroad, and it was up to them to keep the equipment running smoothly. "We overhauled the tractors — removing pistons and rods — and completely rebuilt them from the ground up," Lawrence remembers.

Later, when the brothers took over the family farm, they built their own logging equipment and started a timber company in the off-season. Looking for a way to leave the farming business and capitalize on his mechanical abilities, Lawrence started working on heavy machinery at a local fertilizer plant. When the company suggested he buy a dredge and dig up the harbor, Lawrence did what he'd been doing all along, put new life into an old machine and went to work. Before long, he bought another dredge and expanded his business.

CONQUERING CANCER

We all know someone with cancer. Whether a father or a friend. A neighbor or coworker. Cancer has a devastating reach, indifferent to age, race or gender.

Banishing cancer from a body can be difficult, especially when it entrenches itself in or near organs where surgery, chemotherapy and radiation risk damaging vital tissue.

Mayo Clinic Cancer Center is fighting back with proton beam therapy.

Proton beam therapy using pencil beam scanning safely passes through sensitive organs and delivers concentrated radiation to a tumor. This keeps healthy tissue safe, reduces health care costs because it creates fewer side effects and lowers the incidence of recurrent cancer. Children — still growing and most vulnerable to the side effects of radiation — will benefit the most.

The Richard O. Jacobson Building on Mayo Clinic's campus in Rochester, Minn., will begin treating patients in mid-2015 and patients will receive treatment in the spring of 2016 on Mayo Clinic's Phoenix, Ariz., campus. The Rochester building is named in Mr. Jacobson's honor in recognition of his generous gift to Mayo Clinic and the Proton Beam Therapy Program.

Generous benefactors like Mr. Jacobson and Lawrence and Marilyn Matteson are allowing Mayo Clinic to offer proton beam therapy to patients, providing hope and healing to those with cancer. Currently we are 60 percent toward achieving our fundraising goal. ■

To learn more, please visit:
www.mayoclinic.org/proton-beam-therapy

"It just grew," Lawrence says. And grew. The L.W. Matteson Company became one of the largest freshwater dredging and marine construction companies in the United States. About 40 years after buying his first dredge, Lawrence, along with his son Larry, sold the company for $45 million.

Innovate and Work the Trenches

Looking back, Lawrence attributes much of his success to a combination of the skills and work ethic he gained on the farm and taking chances on high-risk jobs that many contractors avoided — like removing millions of cubic yards of sand and silt by pushing it through huge portable pipes over a mile long.

"My biggest asset in dredging was that I didn't know a thing about it," Lawrence says. "So I didn't have the limitations that others put on themselves when they think something can't be done."

"Fortunately," he adds grinning, "it worked out."

Often Lawrence worked on equipment shoulder to shoulder with the mechanics. "I had a lot of good people working with me," he says. "It helps a lot in business if the guys know I can do everything with the equipment that they can."

An innovator at heart, Lawrence often designed and built machinery to tackle monumental jobs and problems as they arose. He and his crew worked 12-hour days up and down the Mississippi. The long hours didn't leave a lot of time for family, though when counting his blessings, Lawrence always includes his wife of more than 30 years, Marilyn, their three children, seven grandchildren and seven great-grandchildren.

And Always Call Your Wife

Even though Lawrence sold his company, he remains involved as a consultant. Just like he's done for his entire career, Lawrence leaves for work every Monday morning and comes home Friday afternoon. "That's what keeps us married," Marilyn teases. Although distance may make the heart

grow fonder, a loving call from the husband every night doesn't hurt.

In 2009 Lawrence's work schedule came to a halt when he was diagnosed with prostate cancer. Longtime Mayo patients, the couple spent nine weeks in Rochester while Lawrence received treatment at Mayo Clinic Cancer Center.

Smiling, he says, "It's the most time we have spent together."

Placing her hand on his, Marilyn winks and says, "It even worked out, too." She adds, "One of the things that impressed me the most at Mayo was that Larry would have a test and results by the end of the day. We never had to wait for a specialist or an answer."

Taking Aim at Cancer

The Mattesons' experience at Mayo Clinic Cancer Center and Lawrence's innate understanding of powerful machinery and complex construction attracted the couple to Mayo Clinic's Proton Beam Therapy Program — which will house two particle accelerators on two campuses. The Rochester project alone uses enough structural steel to equal the weight of nearly 10 Statue of Liberty sculptures.

The Matteson's gift to the program — launching in 2015 in Rochester and 2016 in Arizona — helps deliver the most precise form of radiation therapy. Unlike conventional radiation, proton beam spares healthy tissue from harm while safely treating cancer next to critical organs. It's especially beneficial to children, whose bones and tissues are still growing.

"This technology will greatly benefit children who are fighting terrible cancers," Marilyn says. "They won't have the residual effects that could affect them for the rest of their lives as they might with conventional radiation. That's something we want to support."

Thanks to generosity and donors like the Mattesons, benefactors are providing hope and healing. To learn more about the Mayo Clinic Proton Beam Therapy Program, please visit: **mayoclinic.org/proton-beam-therapy** ■

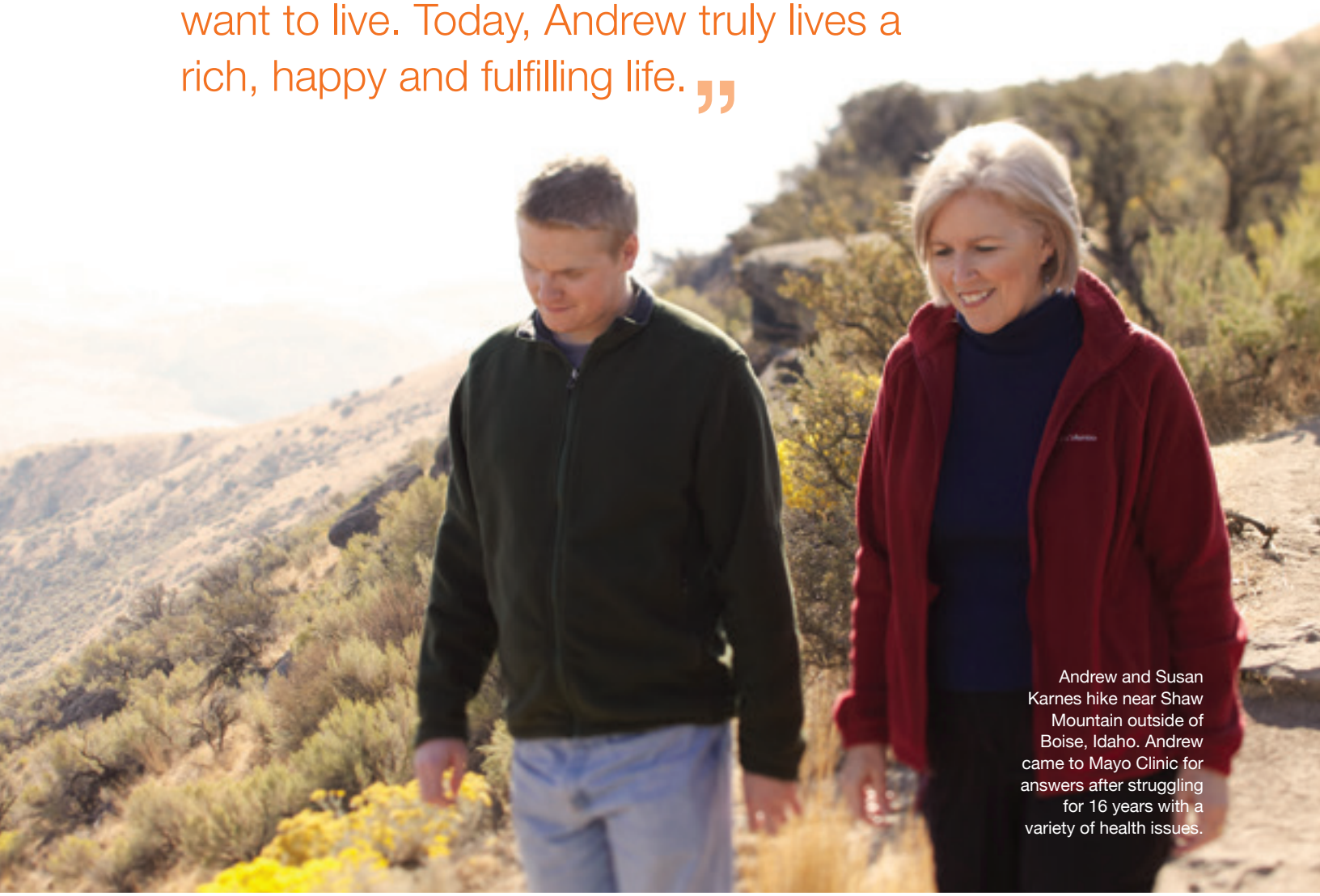
Eighteen MONTHS LATER

An Individualized Medicine Test Developed by Mayo Clinic Gives a Mother Her Son Back

Written by Susan McKeague Karnes

When my parents became Major Benefactors of Mayo Clinic, they did so selflessly. They aimed to help others, to support research, to fund efficacious medicine — and to save lives. I am certain that my father, who died a few weeks before my son Andrew went to Mayo, never dreamed that the generosity of Mayo benefactors, and a test developed by Mayo's scientists, would save one very precious life.

> “18 months ago, our youngest son did not want to live. Today, Andrew truly lives a rich, happy and fulfilling life.”



Andrew and Susan Karnes hike near Shaw Mountain outside of Boise, Idaho. Andrew came to Mayo Clinic for answers after struggling for 16 years with a variety of health issues.

On a brilliant autumn afternoon last October, my son sent a text message, a 17-second video taken atop a mountain that he had just climbed with his dad.

As the camera panned, I glimpsed my smiling husband and Idaho’s stunning Sawtooth Mountains. The final frames remain forever etched on my heart: my son Andrew’s steady hand emerged in the foreground and formed a “thumbs up.”

Ordinary moments like that one, a happy father-and-son hike in the wilderness, may be mundane for most families, but for ours it was nothing short of a miracle. A miracle created by Mayo Clinic.

Eighteen months ago, Andrew was a psychiatric patient in the death grip of suicidal depression, the frightening nadir of a 16-year struggle that began with a simple strep infection.

Our youngest child was a fairly typical 10-year-old Texan — happy and energetic. But then during the second week on a regimen of antibiotics, cough suppressants and

decongestants, Andrew exhibited a puzzling set of behaviors consistent with obsessive-compulsive disorder (OCD).

Within a year, his hands developed a mild tremor. A medication was prescribed. In junior high, he was diagnosed with anxiety; medications were adjusted. Two years later, he was diagnosed with depression. At 17, he began to battle poor sleep and fatigue.

For 16 years, medications were added, adjusted, changed. Andrew grew quieter and lost his characteristic optimism. My husband and I consulted with his specialists and expressed concern. Physicians cited studies and family members with benign tremor or mild anxiety, and convinced us to continue the course of treatment. I was admonished to accept my son's psychiatric diagnoses rather than question them.

In 2011, Andrew's condition deteriorated. His OCD, anxiety and depression grew severe — all exacerbated by profound fatigue and the tremor in his hands, now too debilitating for him to easily eat or use a cell phone. Traditional treatments were failing.

When hospital lab tests indicated abnormal thyroid function, Andrew's psychiatrist recommended we take him to Mayo Clinic. In fact, I had already begun arrangements. My parents had been benefactors and patients for years. Given Andrew's baffling array of symptoms, we urgently needed Mayo's interdisciplinary approach and exemplary level of care.

In early July, we traveled from our home in Texas and met Andrew's primary physician at Mayo, internist Dr. Kevin Fleming. My journal noted, "He is extremely thorough and seems to take us very seriously." I wrote those words as a sigh of relief as I felt the first delicate sprig of hope.

Dr. Fleming and his colleagues proved thorough indeed. Within weeks, they eliminated numerous conditions. Yet EEG, MRI and EMG results seemed to propel us toward serious treatments — deep brain stimulation for the tremor and electroconvulsive therapy for the OCD. Before implementing the therapies, we visited psychiatrist Dr. Shirlene Sampson for another consultation.

A Consultation Changes Everything

Listening to my concern about Andrew's numerous medications and noting my husband's sensitivity to certain drugs, Dr. Sampson suggested Andrew undergo a cytochrome P450 test that Mayo scientists developed. The results measured Andrew's ability to metabolize medications.

Days later, a smiling Dr. Sampson greeted us. Test results proved that Andrew poorly metabolized medications through two enzymes, 2D6 and 2C19, common pathways for many drugs — in Andrew's case, for the exact ones he took.

Intermediate metabolizers like Andrew do not process medications at the same rate as normal metabolizers. His symptoms, Dr. Sampson explained, were likely the result of toxicity. In other words, he had too much medicine built up in his system.

In mid-August, we returned home and, under medical supervision, began the slow and difficult process of weaning Andrew from his medications. Because of his metabolism

A Fairy-Tale Life

A wide smile crosses Marea McKeague's face as she sits in her daughter's home in Eagle, Idaho, and talks about her family — she's still smitten.

"Gordon was my best friend," she says. "Everything we did, we did together. It really has been a fairy-tale life."

Gordon and Marea attended the same high school (Hyde Park in Chicago) but never met. They certainly knew of each other in the neighborhood, and family members still recall Gordon's stories of Marea's red hair and wide smile, but it wasn't until after Gordon returned from World War II that they became friends. In 1948 they married and spent nearly 63 years together, raising three daughters and a son. Marea says they constantly challenged each other to learn, explore and achieve. Like many of his generation, Gordon served in the military before entering the private sector. During his 32-year career in the energy industry, he generously supported historical, environmental and educational organizations.

Over the years, the couple began receiving care at Mayo Clinic and came to trust its commitment to putting the needs of the patient first.

"Gordon loved Mayo Clinic," Marea says. "He just loved it. He was so amazed at everything they did. They were so thorough."

Gordon and Marea began contributing to Mayo Clinic in 1999, long before their grandson, Andrew Karnes, would eventually find lifesaving answers there.

"Andrew has become a whole new person," Marea says. "I'm so pleased — we're all so pleased — at the care he received from Mayo."

In 2005, the McKeagues were inspired to become Major Benefactors after quietly watching the interaction between Mayo staff and pediatric patients. Their gift created the Gordon and Marea McKeague Endowed Fund to Support Children's Cancer Research.

> "Gordon was my best friend. Everything we did, we did together. It really has been a fairy-tale life." — Marea McKeague

"It truly broke their hearts to see vulnerable children and their loving parents suffer through prolonged and often ineffectual treatments when they knew science could develop more effective protocols and eventually cure cancer if given sufficient funding," says daughter Susan McKeague Karnes. "Mom and Dad understood that every cent counted. They were proud to support Mayo's research."

Though Gordon passed away in 2011, the McKeagues' generosity continues with Marea's recent commitment to advance cardiovascular research. ■

Scan the QR code to view a video of Andrew's story and learn more about Individualized Medicine or visit http://mayoresearch.mayo.edu/center-for-individualized-medicine/

Susan Karnes, Andrew Karnes and Marea McKeague play with Baron in the Karnes' home in Eagle, Idaho. Susan wondered if Andrew would ever overcome his symptoms before his trip to Mayo Clinic.

profile, we reduced drugs in small increments over many days and weeks — at less than half the rate of a normal metabolizer.

Within a month, Andrew's OCD dissipated. His psychiatrist in Texas said he no longer met the clinical criteria for the diagnosis. A month later, his doctor scratched the diagnosis of depression. Andrew also has learned new skills — including how to avoid moderate anxiety through tapping and using a light to help regulate his sleep cycle. My husband and I marveled at the change in our son. His mood and tremor improved on a daily basis.

Today, life is redefined. In early 2012, my husband and I moved to Idaho. Andrew opted to move, too, and start life over with his clean bill of health.

Eighteen months ago, Andrew was on medical leave. Today, he enjoys a job with a national company and volunteers at Zoo Boise. Eighteen months ago, Andrew napped frequently throughout the day, awoke 38 times an hour and never felt rested. Today, he sleeps well, wakes refreshed and enjoys hiking and mountain biking. Eighteen months ago, our youngest son did not want to live. Today, Andrew truly lives a rich, happy and fulfilling life.

Talk about a "thumbs up." The vista for Andrew is limitless, as is our gratitude for Mayo Clinic's benefactors, scientists and physicians. ■

Finding the Right Drug

AT THE RIGHT DOSE AT THE RIGHT TIME FOR EVERY PATIENT

Mayo Clinic's Richard Weinshilboum, M.D., is often called the father of pharmacogenomics.

It's a question that has troubled physicians since the invention of medicine: Why does a drug work for one patient but not for another?

The answer lies in our genetic makeup, and pharmacogenomics helps uncover those answers. It's a complicated word with an easily understood premise — finding you the right drug at the right dose every time. It allows physicians to determine your response to specific drugs and drug interactions before it occurs.

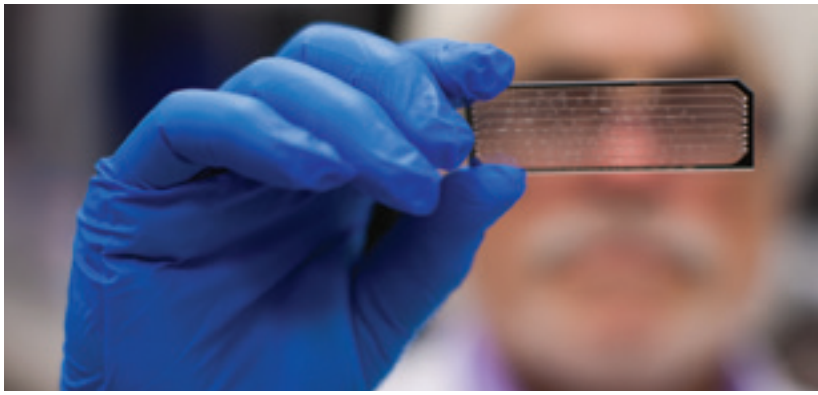
"Modern drugs are very powerful agents that can do great good but also great harm," says Richard Weinshilboum, M.D., director of the Center for Individualized Medicine's Pharmacogenomics Program and the Mary Lou and John H. Dasburg Professor of Cancer Genomics. Dr. Weinshilboum is often called "the father of pharmacogenomics," though the scientist demurs: "The only thing that I'm father of is my two children."

Supported by benefactors, his efforts laid the groundwork for three decades of Mayo Clinic's leadership in the field. His research set the stage for applying genetic variation to individualized drug treatment, and his mentorship has built one of the best pharmacogenomics teams in the world.

"Mayo is perceived as a leader because of a group of talented people here," says Dr. Weinshilboum. "Our collaborations include an entire network across the United States, including most of the National Institutes of Health, as well as international collaborations with Canada, Germany and Japan."

With continued support,

> “Modern drugs are very powerful agents that can do great good but also great harm.”
>
> — Richard Weinshilboum, M.D., Director of the Center for Individualized Medicine’s Pharmacogenomics Program



Dr. Weinshilboum and the team are taking pharmacogenomics to the next stage — developing studies in areas of breast cancer (BEAUTY), prostate cancer (PROMOTE) and cardiovascular disease (TAILOR-PCI). The studies are using genotyping and Whole Genome Sequencing to determine treatment options both before care starts and after, tailoring the process to each individual.

And it’s just the start. Recently, the Center for Individualized Medicine launched a pilot program placing genetic information in a limited number of patients’ electronic medical records. The data will give physicians a deeper understanding of the patient to ensure the best possible clinical decisions.

“Eventually, every patient at Mayo will have this information embedded in their medical record,” says Gianrico Farrugia, M.D., director of the Center for Individualized Medicine. “It’s the intersection of genomics, computerized learning and physicians. It means even more individualized care for every Mayo Clinic patient.” ■

Gene Gumshoe

“Pharmacogenomics has great potential,” says John Black, M.D., a psychiatrist and lab director whose team in the Department of Laboratory Medicine and Pathology developed the genotype test that identified Andrew as a poor metabolizer of his medication.

“These types of tests are helping physicians individualize drug treatment for many people with a broad array of illnesses. We already have 22 tests available with many, many more in the pipeline.”

With benefactor support, his team is making a foray into next-generation sequencing, which will add another 65 to 70 genes that clinicians can use in tailoring treatment once they have been shown to be clinically relevant.

“Mayo does a lot of gene testing for patients, about 300 samples per week,” Dr. Black says. “That’s more than 15,000 results a year to help patients with their medications.” ■

When Mistakes **Are Okay**

Mayo Clinic's Simulation Centers Replicate Reality to Prepare Caregivers for Any Situation

Code Blue is as serious as it gets in a hospital. A patient is in cardiac or respiratory arrest and needs immediate, lifesaving care.

The team of doctors, nurses and other personnel must make split-second decisions while racing to perform CPR, start IVs and hooking up monitors.

Despite what we see on television, Code Blue is fairly uncommon, with most hospitals averaging one a month. Yet, when only 15 percent of patients survive a cardiac Code Blue nationwide, practice can mean the difference between life and death.

"You can read that stuff all day in a book, but until you have to do it in the moment, you don't really know it," says internal medicine resident William Palmer, M.D., who knew his skills were up to snuff during one harrowing night in the hospital at Mayo Clinic in Florida.

He and his team faced four cardiac arrest Code Blues with three patients. They administered nearly 15,000 chest compressions, three airway intubations and 14 heart shock treatments.

The team saved every patient. He credits the success to simulation training.

"The mock code simulation courses have made our codes drastically more efficient and organized," Dr. Palmer says.

> "The mock code simulation courses have made our codes drastically more efficient and organized."

Safe to Make Mistakes

Today's simulation education is stunningly realistic.

Mayo Clinic's simulation centers are filled with rooms that are exact replicas of clinical spaces — operating rooms, intensive care units, emergency departments, and even patient rooms.

Some "patients" are advanced mannequins that talk, sweat, bleed, change pupil size and exhibit medical symptoms that may occur with a variety of conditions, from heart trouble to dehydration. Other patients are trained actors who work with staff to accurately portray scenarios. State-of-the-art technology simulates robotic surgery, colonoscopy, complex laparoscopic surgery, ultrasound, fluoroscopy and other imaging techniques.

The lifelike environment allows staff members to rehearse again and again, to make mistakes in a safe environment. Without ever talking with a patient, they can

gain experience with the most complicated scenarios, such as four Code Blues in one night.

"In our simulation center, we can replicate any scenario or situation you can imagine," says David Thiel, M.D., medical director of Florida's new J. Wayne and Delores Barr Weaver Simulation Center. The facility can link with Mayo's other two simulation training centers in Minnesota and Arizona to efficiently run drills that impact all three sites.

However, despite medical simulation's ability to help surgeons, nurses and housekeepers become better and faster, no grants or industry sources of funding are available. Mayo Clinic partners with generous benefactors to integrate simulation into its medical education.

"Simulation provides an environment where we can push ourselves in complicated cases and practice so we minimize risk for the patient," Dr. Palmer says. ■

A Wider **Impact**

J. Wayne and Delores Barr Weaver's Gift to Mayo Clinic Advances Their Community

On a bright Saturday afternoon, about 50 students from northeast Florida high schools cluster around IV drips, heart monitors and tracheal tubes. There's no need to grab the teens' attention. They are eager to try their hand at performing complex heart procedures, gastrointestinal surgeries and more.

Luckily the patients aren't real, though they breathe, sweat, talk and even die. They're mechanical mannequins in Mayo Clinic's J. Wayne and Delores Barr Weaver Simulation Center in Florida. The students are here as part of a free, daylong medical "boot camp" provided by the Mayo School of Health Sciences.

"It's very cool because you get to see all the different things that go on in a hospital," said Alexandria Sample, a 9th grader at Bishop Kenny High School in Jacksonville. "I wanted to go into a neonatal care unit, but now I really like the cardiology unit."

Arianna Cotton, 10th grader at Orange Park High School in Orange Park, Fla., surveys the world of medical options at the semiannual boot camp, which has a waiting list to participate. "There's a lot you could do," she says. "There's so much they have to teach you."

The experiences of these students meet at least one goal set by the Weavers when they provided $7 million to help construct the new 9,600-square-foot facility. The former owners of the Jacksonville Jaguars wanted to advance health care beyond Mayo's walls by improving collaboration and access to advanced training throughout the Jacksonville area.

"Delores and I believe simulation training will have a tremendous impact on improving the quality of health care in Jacksonville," J. Wayne Weaver says.

The Weavers understand that their gift will not only help Mayo become better by enabling its staff to rigorously train in a safe environment, but it will help caregivers throughout the area become better as they train in Mayo's Model of Care.

Bobbi Logsdon, an advanced registered nurse practitioner and assistant professor at Jacksonville University, teaches her nursing students basic and advanced skills in the simulation center. Like many colleges and universities, Jacksonville University doesn't have a teaching resource like this.

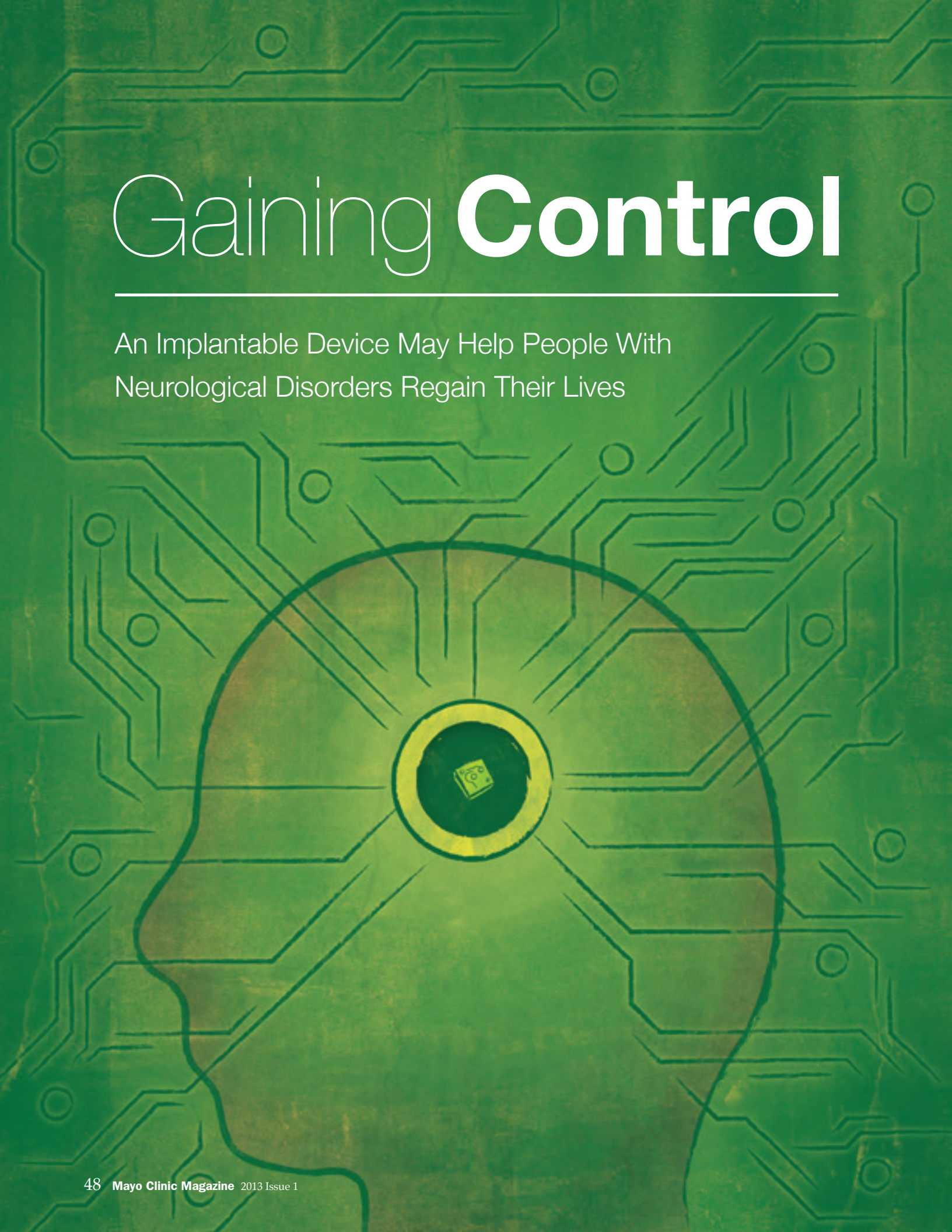
"Simulation compresses the learning curve, so students can become proficient and efficient at skills like setting up an IV pump," Logsdon says. "Students can learn sterile technique without breaking it in the actual operating room."

By opening their simulation center to others who train caregivers, the Weavers know that their gift will have the widest impact possible.

"We look forward to seeing organizations in the community sharing this resource and benefiting from Mayo Clinic's expertise," Delores Barr Weaver says. ■

Gaining **Control**

An Implantable Device May Help People With Neurological Disorders Regain Their Lives



"Can I show you something?" the researcher asks. Before anyone responds, his fingers quickly tap away at the computer. On his screen, a video frame paused on a lab rat appears.

"It's been paralyzed for weeks," explains Kendall Lee, M.D., Ph.D., a Mayo Clinic neurosurgeon. He clicks the play button, and the rat's right leg jolts to life. He plays more clips. In one, a leg slowly rises and falls. In another, both legs alternate movement, mimicking a swimmer's kick.

"It's not just twitch," he says. "We're controlling this wirelessly."

Resuming Communication

Imagine losing control of your body. Your limbs twitch. Your face contorts. You pick up a glass of water for a drink, but your hand shakes it empty. Unfortunately, for people with neurological disorders and psychiatric disorders, lack of control is central to their everyday lives.

One treatment strategy to help people with neurological-based movement disorders, such as Parkinson's disease, regain control over their bodies is "deep brain stimulation" (DBS). Electrodes implanted deep within the brain deliver mild pulses that stimulate the release of neurotransmitters, or chemicals, that activate neurons, the brain's message carriers.

"It's as if DBS is controlling the brain's pharmacology, the neurotransmitters in your brain that you're already making," explains Dr. Lee, a specialist in DBS. After DBS helps neurons resume normal communication with each other, disease symptoms subside.

Though often successful, the therapy has some drawbacks. During the surgical procedure, for instance, the patient must remain awake, and many patients are understandably hesitant to undergo brain surgery while conscious. But current DBS systems are an open loop, meaning that during surgery and follow-up recalibration sessions, physicians must rely on visible symptoms and the patient's subjective feedback — when I apply this stimulation, does speech improve? Do tremors lessen? No? Then let's try this…

This inexactness and inefficiency stand between DBS and its use for other neurological and psychiatric disorders, especially those that cause pain, mental and emotional distress, and other nonvisible conditions that are difficult to measure.

Dr. Lee and his colleagues in Mayo Clinic's Neural Engineering Lab think they have found a better answer. The team is developing a "smart" DBS system that wirelessly

monitors and measures neurotransmitters and uses concrete biological feedback to deliver precise stimulation.

"We're now combining the technology with our knowledge of biology, and making the biology better," Dr. Lee says.

Stimulus, Response

The challenge is building implantable wireless circuitry advanced enough to match the brain's sophistication. But Mayo's interdisciplinary approach is uniquely poised to succeed. It combines the neurosurgery team's medical skill with Mayo's expertise in engineering and microchips. Not many people realize that Mayo Clinic has its own Division of Engineering, chaired by Kevin Bennet, whose job is to design devices, systems and instruments that aren't available commercially. In other words, they custom-make tools to help patients. Working with Dr. Lee and his group, the engineers are developing wireless sensor and neurostimulator prototypes, which will use integrated circuitry custom-designed by Mayo's Special Purpose Processor Development Group, led by Barry Gilbert, Ph.D., the Rose M. and Morris Eisenberg Professor.

The collaboration already reached a significant clinical milestone last year with its Wireless Instantaneous Neurotransmitter Concentration Sensing (WINCS) system, a device that tracks real-time neurostransmitter changes in the brain. In an early phase clinical trial, it successfully recorded, wirelessly, the release of neurotransmitters in 15 Parkinson's and essential tremor patients undergoing DBS surgery.

"With WINCS, we're now seeing for the first time what is changing in the brain," Dr. Lee says. "It's really exciting, because now imagine — if we could take advantage of that knowledge — the type of things we can do with deep brain stimulation."

Dr. Lee's group is already finding out with the Mayo Investigational Neuromodulation Control System (MINCS), a wirelessly controlled neurostimulation device optically linked to WINCS. Researchers are using the implantable device in animal models to

The challenge is building implantable wireless circuitry advanced enough to match the brain's sophistication.

deliver precise brain stimulation wirelessly. It was the MINCS device that moved the leg of Dr. Lee's paralyzed rat.

The Next Generation

"Isn't that gorgeous?" Dr. Lee asks, admiring a picture of WINCS Harmoni.

It's the observation of a true scientist. To the untrained eye, WINCS Harmoni resembles a small circuit board pulled from a cell phone, but Dr. Lee sees its limitless possibilities — a smart, self-contained, implantable DBS system. Now in prototyping stage, WINCS Harmoni combines WINCS, MINCS and a complex algorithm that translates the biological feedback from WINCS into precise stimulation patterns delivered by MINCS.

As Dr. Lee describes the relationship between sensors, circuitry and science, he oddly passes on describing their interplay as "harmonious," an expected riff on the system's name. Realizing this, he pauses.

"By the way," he says, "Harmoni is not for 'harmonious.' It's the Korean word for grandmother, my way of honoring someone who's caring."

It's an apt distinction. Technological wizardry aside, WINCS Harmoni is meant to treat people and in many cases provide relief to families. Through smart DBS therapy, people with complex psychiatric disorders, unmanageable pain, spinal cord injuries, memory loss and a host of other difficult-to-treat disorders have hope — all because, as Dr. Lee puts it, Mayo has the tools to understand and control what's happening in the brain and spinal cord.

"My hope," he says, "is that this will open up a new era in medicine. If you look at all the medications we use that somehow affect the chemistry in the brain, we are now in an era where we can control the systems even better. So rather than going the shotgun approach of medicine, we can go with the smart systems of DBS."

Mayo's Neural Engineering Lab hopes to test WINCS Harmoni in patients this year. ■

Helping Mayo
GET CLOSER TO THE ULTIMATE GOAL

"This was one of the easiest commitments that we have had to make in our lives. Mayo Clinic gave David a chance in 1998 to get his life back. Since then we have felt the need to do what we can to donate to such a special place and great hospital.

"Our goals, by working with Mayo to start the Mayo Clinic Advanced Epilepsy Imaging project, are to have a future where people with epilepsy have a cure available to them, a cure that results in a life free of seizures and side effects. We feel Mayo's greatest resource in its epilepsy department is the commitment and experience of its physicians and its wonderful approach to the care of patients with seizures.

"It will bring us great satisfaction over the next years watching Mayo get closer to our ultimate goal: no seizures, no side effects."

David and Megan Hawk
Omaha, Nebraska

Thank You

Gifts of all sizes strengthen health care for people everywhere. Mayo Clinic is deeply grateful for each one and finds inspiration in such personal demonstrations of support.

Making an Impact

CUMULATIVE PHILANTHROPY

Each benefactor is recognized for philanthropic giving of $100,000 to $10 million or more in the Hall of Benefactors at Mayo Clinic in Rochester, Minn. Those who support our work in Florida and Arizona are also recognized in the Hall of Benefactors on the respective campus.

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Leaving the World a Better Place

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Committed benefactors who want to make a difference beyond their lives can do so through planned gifts. Benefactors who support Mayo Clinic through a bequest in their will or another type of planned gift become members of **The Mayo Legacy** and are recognized in electronic recognition kiosks in the Halls of Benefactors at all Mayo sites.

ALUMNI PHILANTHROPY

Having seen and felt the direct impact of philanthropy, Mayo Clinic alumni know the difference it makes better than anyone. Many become benefactors of Mayo to help maintain the highest quality of patient care, research and education. Their generosity is recognized in electronic recognition kiosks in the Halls of Benefactors at all Mayo sites.

Mayo Alumni Laureates	$100,000 or more
Doctors Mayo Society	$10,000 or more; bequest of $25,000 or more
Edith Graham Mayo Society (Mayo School of Health Sciences)	$1,000

Giving Back

ANNUAL GIVING

Some benefactors choose to support Mayo Clinic's work with yearly gifts and are recognized in electronic displays at Mayo Clinic in Rochester, Florida and Arizona. Six levels honor benefactors for annual philanthropy of $1,000 to $99,999.

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