

FINDINGS

Winter/Spring 2020 • omrf.org

A MYSTERIOUS ILLNESS STOLE LEAH CAMPBELL'S ABILITY TO SEE AND MOVE. WOULD IT TAKE HER LIFE, TOO?

HER BODY,
HER PRISON

Please help us
help Sydney!



Your gift will support medical projects like the search for new therapies for Sydney Rutz, who suffers from a unique skeletal disorder.

FEATURES



HER BODY, HER PRISON

8

Leah Campbell lost her sight to an unknown illness. Then it stole her ability to move. Could doctors stop the mystery disease before it took her life?



TRIAL RUN

14

Adam Cohen decided to learn about clinical research by volunteering as a study participant. There was only one, small problem.

ALSO IN THIS ISSUE



Chartered in 1946, OMRF is an independent, nonprofit biomedical research institute dedicated to understanding and developing more effective treatments for human disease. Its scientists focus on such critical research areas as cancer, diseases of aging, lupus and cardiovascular disease.

CHAIRMAN OF THE BOARD Len Cason, Esq.
PRESIDENT Stephen Prescott, M.D.
EDITOR-IN-CHIEF Adam Cohen
MANAGING EDITOR Shari Hawkins
ART DIRECTOR Jenny Lee
GRAPHIC ASSISTANT Rachel Smith
WRITER Ryan Stewart
PHOTOGRAPHER Brett Deering

405-271-8537 • 800-522-0211
findings@omrf.org

© 2020 Oklahoma Medical Research Foundation.
All rights reserved. Reproduction in whole or in part
without permission is prohibited.

SICKLE CELL MILESTONE

4

Work that began at OMRF in the 1980s gives birth to a life-changing medication

THE GIVERS

5

For Regena and Brownie Browne, philanthropy is a joint venture

ASK DR. P

6

What's the difference between Alzheimer's and dementia?

VOICES

7

For Catherine Tatum, "If I can wake up or get up, it's a good day."

RETURN OF THE NATIVE

22

Heather Rice left Watonga for Harvard, but now she's back in Oklahoma



A Sickle Cell Milestone

Work that began at OMRF in the 1980s gives birth to a life-changing medication

When Novartis announced in November that the U.S. Food and Drug Administration had approved the company's new drug to treat sickle cell anemia, the press release didn't mention Oklahoma. But it should have. The drug, known as Adakveo, is based on discoveries made by OMRF physician-scientist Dr. Rodger McEver.

The FDA's decision came following a 52-week clinical trial showing treatment with the drug led to a significant reduction in pain crises for sickle cell patients. Adakveo is now available in hospitals and clinics in the U.S., with European approval currently pending.

"I've treated sickle cell patients, and their suffering is extreme," says McEver, a hematologist and OMRF's Vice President of Research. "It's the dream of every physician, and certainly every scientist, to do something that can make a difference with patients."

In sickle cell disease, red blood cells change from their customary round or oval shapes to form a crescent or "sickle." The cells stack up in vessels, causing inflammation and excruciating pain. In some cases, the condition leads to organ damage, stroke and even death.

While the condition affects people of all races, it's most prevalent in those of African heritage, who make up 90 percent of the sickle cell population. Health authorities estimate that 100,000 people in the U.S. and more than 1 million worldwide suffer from the disease.

In the lab, McEver developed an antibody that blocks the effects of P-selectin, a protein thought to be a driver in the development of pain crises for sickle cell patients. To explore clinical applications in humans, McEver helped create an

Oklahoma-based biotechnology company, Selexys. The company fine-tuned the antibody, making an experimental drug that bound to human P-selectin and blocked the protein's function.

The medication showed a 45 percent reduction in pain crises when administered intravenously every 4 weeks in a clinical trial involving 198 sickle cell patients. Based on those results, Novartis purchased Selexys and its experimental drug, now known as Adakveo.

"We know this drug can decrease the frequency of sickle cell pain crises in a significant and clinically

meaningful way," says Dr. Kenneth Ataga, who led the trial and serves as director of the Center for Sickle Cell Disease at the University of Tennessee Health Science Center at Memphis. The drug's approval, he says, "is an important advancement for people living with this very difficult condition."

For McEver, the drug represents the culmination of research that began in his lab more than three decades ago. "Pushing forward the body of knowledge is important," he says. "I hope this drug will help a lot of patients."



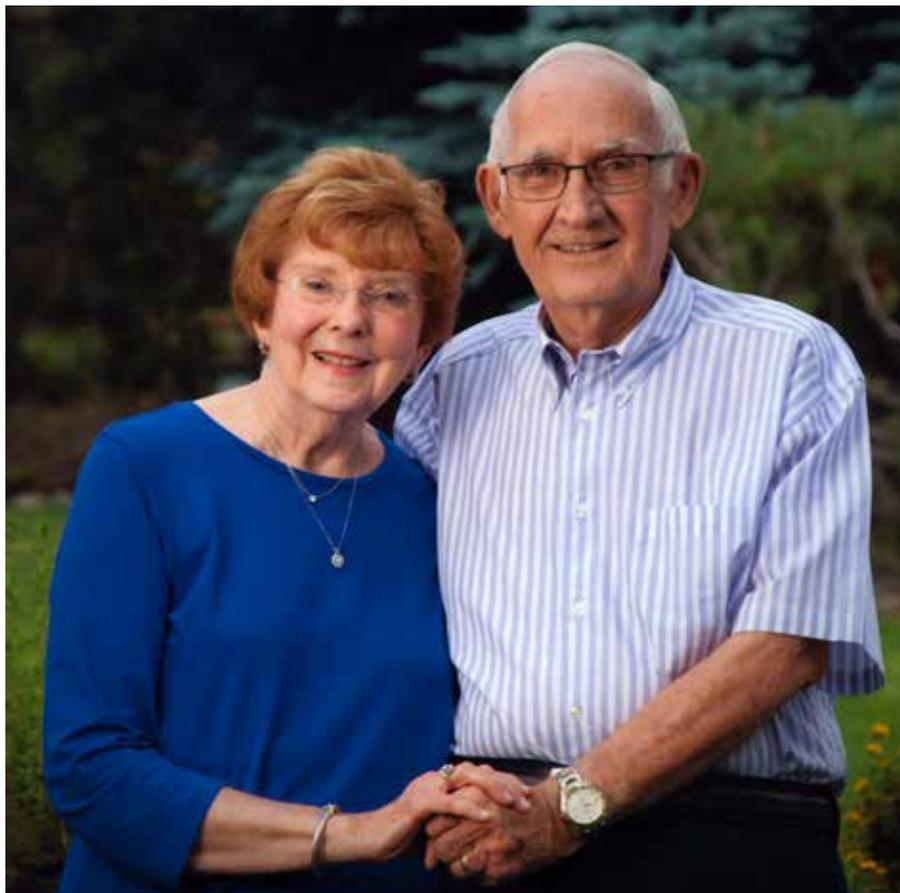
Dr. Rodger McEver

Three's Company

Adakveo is the third drug now available that's based on OMRF discoveries. The others are:

- **Soliris**, a medication for patients with certain rare blood disorders
- **Ceprotrin**, a therapy for protein C deficiency, a life-threatening congenital disease

For Regena and Brownie Browne, philanthropy is a joint venture



The Givers

They make their home in Oklahoma City now. But Regena and Brownie Browne often make the hour-plus drive west on Interstate 40 to their native Clinton. There, they visit their families' farms, each established before Oklahoma became a state in 1907.

The Brownes met in 1962 through mutual friends and Regena's sisters. They dated for a while but ultimately pursued different paths. Brownie completed finance and marketing degrees at the University of Oklahoma and returned to Clinton, where he eventually became vice president of a local industrial company. After attending Oklahoma State University, Regena married and moved to Tulsa to teach elementary school music.

But Regena was left a young widow, and 20 years later, the pair reconnected. They wed and established a home in

Oklahoma City. "Everything has the right season in life," she says.

Now nearing their 28th wedding anniversary, the couple has retired. With no children, their pet, Chang, receives a disproportionate amount of attention. But in addition to their Siamese cat, the pair shares another mutual passion: philanthropy.

Together, they have a long history of supporting OMRF. For Brownie, it began with his mother, a registered nurse who started donating to the foundation in the 1970s. Soon after, he picked up the habit.

"I just followed her pattern of giving to OMRF all these years," Brownie says. When he wed Regena in 1992, supporting OMRF became a joint venture. "We're still giving," he says. In fact, he notes, "We sent in a gift just the other day."

They designate their gifts to fund projects in different disease areas.

But like many whose lives have been impacted by cancer, that disease ranks highest on their list: Brownie's mother developed breast cancer, Regena has survived three bouts with the disease, and prostate cancer struck Brownie (though he is, happily, now in remission).

The Brownes have decided to extend their philanthropic legacy by leaving their estates to charity. They've settled on their "three wishes" as recipients: the Clinton United Methodist Church, Clinton Public Schools and OMRF.

Thanks to careful investing, the Brownes have been lucky, says Brownie. "Between stocks and income from farming and the oil and gas industry, life's been awful good to us." By supporting OMRF, they want to pay that good fortune forward.

"We've had health issues going way back in both of our families, and that plays right into our reasons for giving to OMRF," Regena says. "You need money to keep the research going, and we're happy to do our part."



Paying It Forward

Planned giving represents a significant portion of OMRF's annual budget, funding key research projects in diseases ranging from cancer to Alzheimer's. In 2018, the foundation received 16 estate gifts totaling \$2.1 million. "We are extremely fortunate to have donors who understand the vital role that planned giving plays in transforming research today into new treatments tomorrow," says Sonny Wilkinson, OMRF Director of Development.

To learn more about planned giving at OMRF, please go to omrf.giftlegacy.com or contact sonny-wilkinson@omrf.org.

Alzheimer's or Dementia?

Dear Dr. Prescott,

You often hear about people who become forgetful as they age. But in some, the symptoms go far beyond losing their car keys or forgetting someone's name. How can you tell if it's Alzheimer's or dementia?

Ginger Coleman Kelso
Norman, OK



Dr. Prescott Prescribes

Dementia generally describes a group of symptoms that includes a decline in memory, cognitive skills and the ability to communicate. It most commonly strikes the elderly and was long referred to as “senility.” Alzheimer’s disease is actually a subset of dementia and its most common form, accounting for 60 to 80 percent of dementia cases.

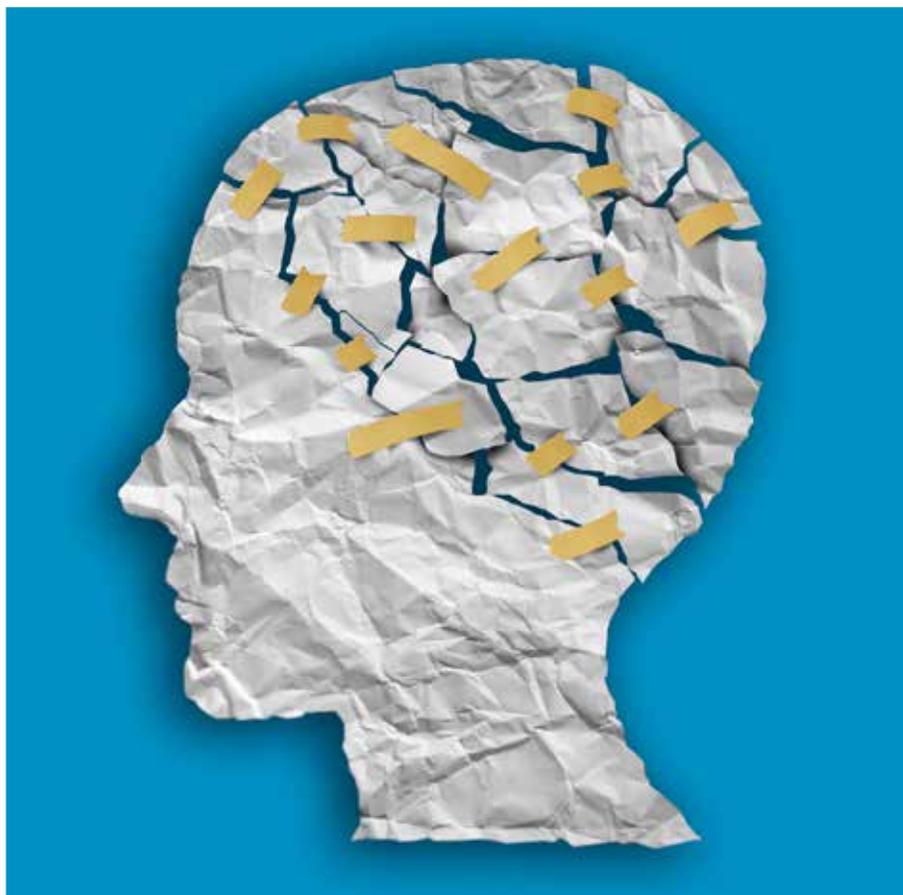
So, most people who have dementia also have Alzheimer’s. But, in the vast majority of cases, there’s no way to tell for sure.

Although researchers are working to develop a test for Alzheimer’s, we are not there yet. At present, the only way to diagnose the disease definitively is post mortem, by analyzing brain tissue following a person’s death.

One of the reasons diagnosis is important is that, while Alzheimer’s currently has no effective treatments, some other forms of dementia do. For example, vitamin deficiencies, thyroid problems, brain tumors, depression, excessive alcohol use, medication side effects and certain infectious diseases can all trigger dementia. However, each of these forms of the disease are potentially reversible with treatment.

Normal pressure hydrocephalus is another treatable type of dementia. Caused by a buildup of fluid in the brain, surgeons can relieve the condition by implanting a shunt to drain off excess fluid.

If you or a loved one show signs of dementia, seek medical treatment as soon as possible. An early evaluation by a physician offers the best opportunity to understand whether a particular case might be treatable—and, if so, to reverse it before that window shuts.



Dementia's Rising Tide

An estimated 5 million adults over age 65 had dementia in 2014. Experts predict that number will climb to as many as 14 million by 2060.

Source: U.S. Centers for Disease Control and Prevention



I'm 75, have MS and had a stroke 17 years ago. So, if I can wake up and get up, it's a good day. But we have to find cures for so many things, and I feel a real level of comfort giving to OMRF. Whenever I visit OMRF's MS Center, I have a 'grateful attack' for all you do for me and others with greater challenges than mine."



Catherine Tatum

Tulsa realtor Catherine Tatum, an OMRF patient and donor, volunteers with youth advocacy and education groups and just adopted her latest rescue dog, Chrissy.

GIRL, INTERRUPT

LEAH CAMPBELL LOST HER SIGHT TO AN UNKNOWN ILLNESS. THEN IT STOLE HER ABILITY TO MOVE. COULD DOCTORS STOP THE MYSTERY DISEASE BEFORE IT TOOK HER LIFE?

Leah Campbell's days begin about the time the sun rises. After waking and having breakfast, she answers dozens of emails. Often, she composes just as many new messages.

Throughout the day, Leah spends hours on the phone with fellow patients, helping them navigate the Medicare and Medicaid systems to ensure they don't miss out on the benefits they need. Earlier this year, she lobbied lawmakers on People with Disabilities Awareness Day at the state capitol. In August, she hosted a fundraising event for a favorite charity at a local restaurant.

Each week, she attends aquatic and equine therapy sessions and a Bible study class. She helps lead a support group and serves as Oklahoma's ambassador to a patient advocacy organization. This past summer, she started a new job with a company that provides voice-activated smart controls for operating lights, locks, thermostats and other systems around the house.

By the time everything winds down at the Campbell house, it's usually nearing midnight.

Days this packed would challenge almost anyone. But Leah manages this schedule despite obstacles most of us could not imagine. She is blind, and paralyzed from the chest down.

Leah spent her childhood in Altus, a town of 20,000 or so tucked into the southwest corner of Oklahoma. Her parents, Don and Theresa, taught at the local high school. Don, a biology teacher, brought home a microscope for Leah, as science—along with math—topped her list of favorite subjects.

In grade school, Leah would often set aside part of her lunch to entice animals to follow her home after school. Plied with bits of leftover sandwich, countless dogs and cats found their way to the Campbell house. On occasion, the would-be Doctor Doolittle brought home a snake, reptile or injured bird.

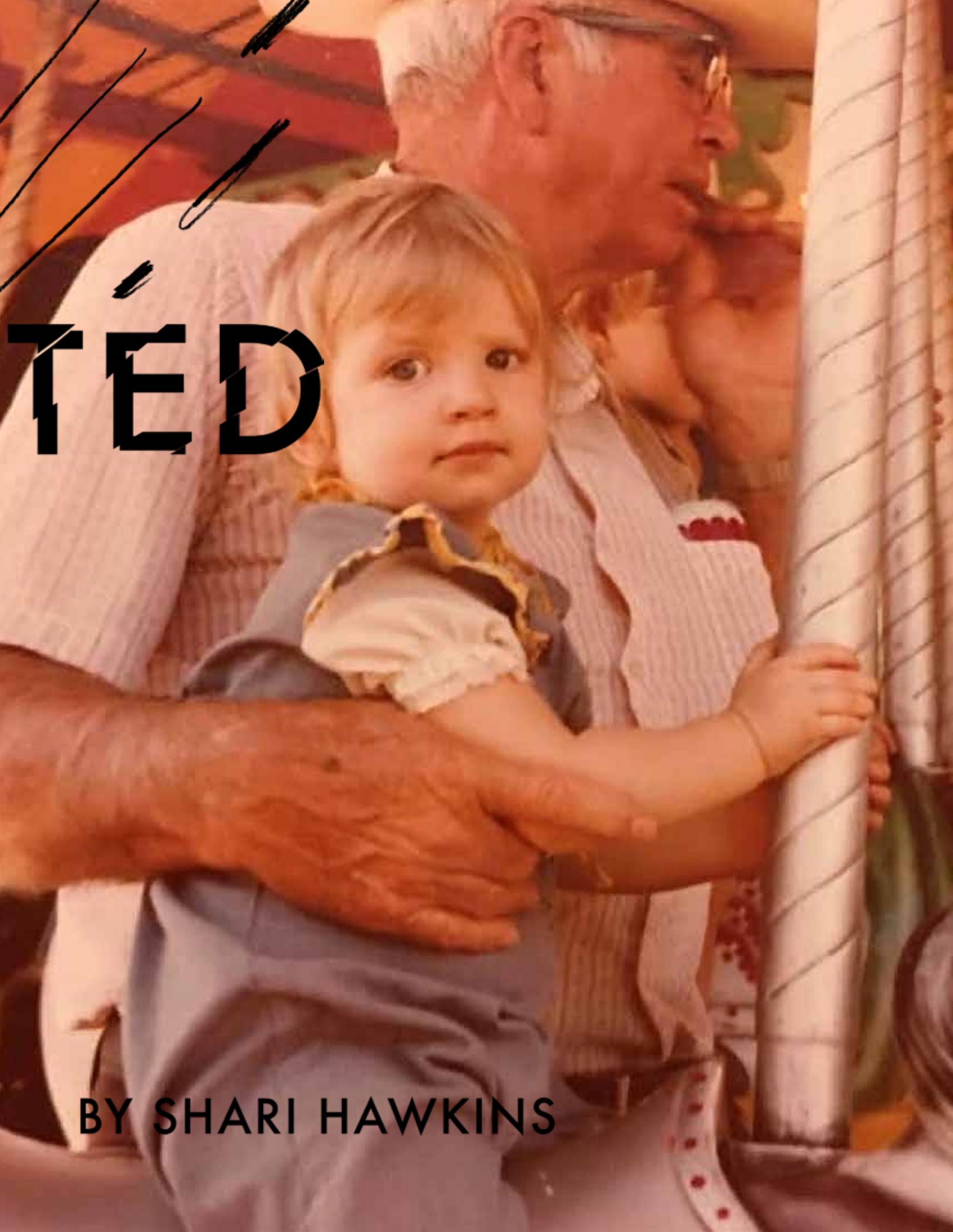
She played tennis, loved to swim and rode horses from the time she was a toddler. She excelled in her classes and hated to miss a day of school.

But on the last day of fifth grade, she was too sick to attend school. "It felt kind of like I had the flu or something," she remembers. "I just couldn't get up and go."

Her mother recalls that day as the start of a long cycle of antibiotics, nausea and doctor visits. Over the summer, Leah's weight plummeted; her eyesight began to deteriorate.

"We bombarded her with steroids, but she was unresponsive," says Dr. Bradley Farris, who treated her at the Dean McGee Eye Institute in Oklahoma City. "We had absolutely no idea what was triggering her immune system to do this. To say we were frustrated is an understatement."

That fall, Leah lost the ability even to see the chalkboard at the front of her classrooms. One morning, as Leah sat in her bedroom, she asked her mother to turn on the lights. They are on, Theresa told her. Leah



TED

BY SHARI HAWKINS

frantically waved her hand in front of her own face, unable to see it. "What's happening to me?!" she screamed. At 11, her world had gone dark.

Leah adjusted to her new life without vision. She learned Braille and devised ways to do her schoolwork with the help of other sounds. Her sense of hearing sharpened. Her parents even affixed a beeper to the basketball hoop in the driveway, and Leah could still make buckets.

The loss of her vision sometimes brought on feelings of self-consciousness. "When you're blind, you can't see how people are looking at you, so you worry about that," Leah says. Still, she took part in band, National Honor Society and FFA (previously known as Future Farmers of America), where she particularly excelled. She became an FFA officer, competed in public-speaking contests, qualified for the National FFA Band, and attended a leadership conference in Washington, D.C. She even showed lambs at livestock competitions.

"They wired a two-way radio under my jacket, and I had an earpiece in so the teachers could tell me which way to go when I entered the show ring," she recalls. "The biggest challenge came when I stepped into the arena, and the battery went dead. Luckily, the ring judge helped me finish."

Around that time, she was struck by sudden, violent attacks that doctors called paroxysmal spasms.

"It was like she was split in two," her mother says. "Her right side was fine, but on the left, she would sort of vibrate. Her foot would turn in, her leg would draw up tight, and her hand would clench. Her whole ribcage would spasm uncontrollably." She'd sometimes experience 40 to 50 of these episodes a day.

She saw pediatric neurologists and ophthalmologists, and endured test after test, but none could pinpoint what was happening. One suspected Lyme disease, while another tested for Rocky Mountain spotted fever. Suggestions ranged from consulting a psychiatrist to a brain biopsy.

The Campbells flew to a nationally renowned medical center, where

doctors ran more tests on Leah: a spinal tap, MRIs, blood work, X-rays. Many of their conclusions echoed the ones the family had heard many times before. But one radiologist said he'd only seen lesions in the brain like Leah's in patients with multiple sclerosis. He and his colleagues concluded she was suffering from relapsing remitting MS, where patients experience recurring disease symptoms over time.

"It was the happiest day of my life," Leah says, "because I finally had a diagnosis." Unfortunately, it turned out to be wrong.

After graduating second in her class from Altus High School, Leah attended Rhodes College in Memphis,

Tenn. Although she suffered with migraines and multiple relapses, with the help of her guide dog, Precious, she continued her studies. When she earned a degree in mathematics and a minor in business, she became the college's first blind graduate.

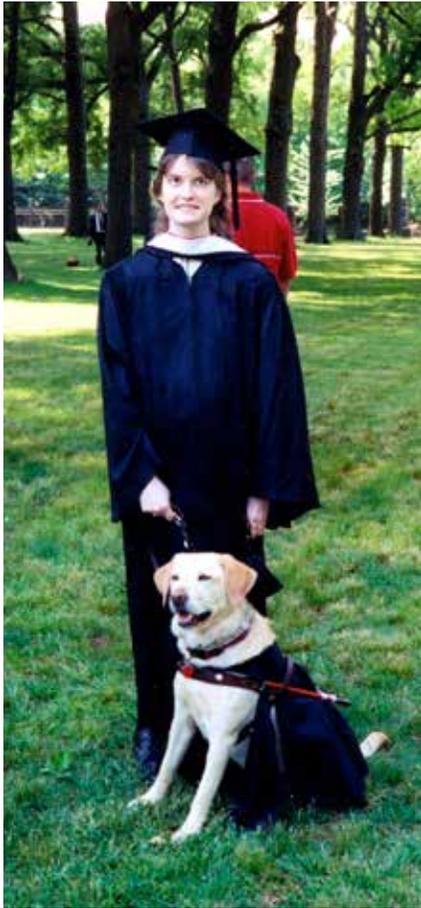
But before she could begin the next chapter of her life, her condition worsened. One Friday, she woke to find her body hypersensitive to touch and all sensation. The next day, she could hardly walk and had to use the wall to stay upright. By Sunday, she couldn't feel or move any part of her body below her chin.

"I couldn't even scratch my nose," she says.

A blur of visits to doctors and hospitals followed. One of those physicians was Dr. Gabriel Pardo.



Leah Campbell on her great uncle's horse at 13, just after she lost her sight, and (opposite page) at her Rhodes College graduation with her guide dog, Precious



Now the Director of OMRF's Multiple Sclerosis Center of Excellence, he took Leah under his care.

When Pardo did a comprehensive reassessment of Leah's case, what he found confused him. A spinal tap revealed large numbers of white blood cells in her spinal fluid, which is uncommon in MS. "That was a red flag," he says. Still, with no other plausible diagnosis, he continued to treat her with medications targeted at controlling MS.

Over the next three years, although she regained use of her arms, Leah's health otherwise continued to deteriorate. Whatever this disease was, its flares grew more frequent. The therapies Pardo relied on to tamp down MS seemed to have no effect.

Eventually, he decided to administer a newly developed blood test to Leah. When he did, Pardo finally arrived at a definitive diagnosis for his patient: neuromyelitis optica.

NMO occurs when the body's immune system launches an assault against its own healthy tissues as if they were harmful invaders. Those attacks primarily target the optic nerves and spinal cord, resulting in inflammation that can cause excruciating pain and vision loss. In some cases like Leah's, NMO, or Devic's disease, can invade regions of the brain or brain stem. The illness affects roughly 4,000 Americans, 80 percent of whom are women.

"NMO was initially considered a subset of multiple sclerosis and is so similar to MS that it often gets misdiagnosed," says Dr. Bob Axtell, an OMRF scientist who holds a pair of grants from the National Institutes of Health to study the disease. "This can be devastating for patients."

Indeed, that had been the case for Leah. For years, doctors had treated her with a common MS medication called interferon beta-1a, or Rebif. Not only does this medication fail

"What's happening to me?!" Leah screamed. At 11, her world had gone dark.

to help NMO patients; it actually worsens their condition.

Pardo immediately took Leah off the drug. Instead, he began treating her with rituximab, an immune-suppressing monoclonal antibody known to control NMO disease activity. And in the 13 years since he started her on that medication, she's had no relapses. "Her disease activity has been fully controlled," says Pardo.

Says Leah, "I owe Dr. Pardo my life."

Still, while regular doses of rituximab have kept NMO at bay, the disease had already run wild in her body for a full 17 years before Pardo

What's NMO?

Neuromyelitis optica, or NMO, is a rare autoimmune inflammatory disease of the nervous system. Like most autoimmune diseases, it overwhelmingly strikes women. While scientists don't know what triggers NMO, the disease occurs when the body's immune system attacks the spinal cord, optic nerves and, in severe cases, the brain. While certain medications can tamp down these attacks, there is no known cure. Over time, patients typically develop blindness, muscle weakness and paralysis.

Although NMO's symptoms are similar to multiple sclerosis, the two diseases require different treatments. In fact, MS drugs can worsen disease activity in NMO patients, sometimes with catastrophic consequences. "MS and NMO are almost like mirror images in certain ways," says Dr. Bob Axtell, who researches both diseases at OMRF. "But the biology of the conditions and treatment response are quite different."



Physical therapist Bobbette Miller treats Leah at OMRF while her parents, Don and Theresa, look on.

began treating her with the drug. “She has deficits that date to before she was a teenager,” he says. “The blindness, the paralysis—unfortunately, those are things we can’t reverse.”

In her bedroom at her home just outside of Oklahoma City, where she lives with her parents, Leah sits in her wheelchair. She’s positioned beside a hospital bed outfitted with a special alternating-pressure mattress that helps lessen incidence of bedsores. Still, she’s going to wound care for an especially severe one and recently underwent surgery for it.

Shelves line the perimeter of the room, stacked with boxes and papers, items of clothing and keepsakes. At one side of her bed sits a small table with a laptop computer, a long list of email messages apparent on the screen. On the other, a bedside table holds her Amazon Echo. “Alexa, what’s on my calendar for next Wednesday?” she calls out. “You have a doctor’s appointment at 9,” the robotic female voice answers.

Theresa enters the room and offers her daughter a glass of water. Leah receives it in her outstretched hands, takes a sip, then lowers the glass.



BRETT DEERING

It’s important for people to understand that she’s not a quadriplegic, Leah says. “I was once, but now I’m only paralyzed from here down”—she gestures to her upper chest. Still, though her hands work, she couldn’t feel the cup she held only moments ago. Heat, cold and even pain don’t register. Her father says he used to pray for Leah to be healed or

regain her vision or movement, but these days he just prays for God’s will.

Now retired, Don and Theresa remain Leah’s constant companions, helping her live as full a life as possible. But they’re both in their 70s, and they worry about the future. With knee and back problems, Theresa can’t lift her daughter as often as she once could. But her biggest concern is about what will happen when Don and she are gone. “I want her to be happy and safe and well-cared for, but no one else will take care of her the way we do,” Theresa says, wiping a tear from her cheek.

It’s expensive to live with physical infirmities like Leah’s. When they looked for their home, the Campbells needed a three-car garage to fit their specially equipped oversized van, which cost them \$56,000. They also had to remodel the house to accommodate Leah’s needs, adding things like a roll-in shower and an oversized saferoom with a door wide enough for a wheelchair.

Although Leah’s relapses are under control, she requires regular care at OMRF’s Multiple Sclerosis Center of Excellence, where she’s been a patient since Pardo joined the Center as its founding director in 2011. She’s at constant risk for fractures, skin ulcers,



BRETT DEERING

Leah spends a great deal of time in her room, so visits to aquatic therapy (opposite page) are a weekly highlight.

bladder and bowel dysfunction; Pardo and his team must remain vigilant to address issues that come along.

For one, rituximab, the drug that has successfully controlled Leah's relapses for more than a decade, isn't approved for the treatment of NMO (although another drug, Soliris, recently received approval as an NMO therapy). So, insurers consider rituximab's use for NMO patients off-label. Without coverage, the annual cost of infusions with the drug would run more than \$30,000.

"With Leah, we know insurance will deny it and say it's not indicated for NMO," says Pardo. "We have to enlist a case manager and a social worker to get her drugs every time she needs an infusion." But winning that "uphill battle," he says, is crucial, as any delay in treatment can cause significant harm to the patient. "So, we're like a dog on a bone, and we won't let go."

Theresa says it's this devotion to his patients that sets Pardo apart from other doctors. "He's caring and brilliant, funny and down-to-earth. He comes in, says hello to us and then turns 100 percent of his attention to her. He knows Leah's blind, but he looks right into her eyes. He treats her like a person, not a disabled person. That's how it should be."



The OMRF Multiple Sclerosis Center of Excellence

OMRF's MS Center provides comprehensive treatment and care for more than 3,000 patients in Oklahoma and surrounding states. As the Center's name suggests, most of those individuals have MS. But Dr. Gabriel Pardo and his team, which now includes Dr. Chelsea Berkley, a neurologist who joined OMRF in the fall of 2019, also treat patients with NMO.

"NMO is less common than MS, and our understanding of the disease is still evolving," Pardo says. With a simple blood test, his team can now distinguish between the two conditions. "We're finding more and more patients who at first didn't conform to the clinical diagnosis for NMO who actually have it."

For more information about the Center, go to omrf.org/mscenter



Dr. Gabriel Pardo

Despite the hurdles she faces, Leah remains optimistic about her future. "I'm just a positive thinker. My cup's always half full."

She enjoys her tailor-made job, which centers on improving the day-to-day lives of people with physical disabilities. In the spring, she's looking forward to attending a national patient day conference in Los Angeles. For her 42nd birthday in August, she plans to take a hot air balloon ride, just like the one she enjoyed last summer.

The Campbells are also training a new service dog for their daughter. A chocolate lab, Seaclaid (Gaelic for chocolate) will help Leah become more independent.

At each bend in the road, Leah says, her faith has helped sustain her. It has, she explains, provided

her with "resilience through life's interruptions." She continues to pray each day for independence.

If that doesn't come, though, she is at peace with her life. "Don't feel bad for me for where I am." There are even silver linings, she jokes. "Like I tell my nieces, I don't have to feel it when I get shots."

For OMRF's Dr. Bob Axtell, patients like Leah drive his search for answers in the laboratory. "The more we understand about NMO, the better the outlook will be for people struggling with this horrible condition."

Novel insights today, Axtell adds, could lead to new therapies for patients tomorrow. "People are working on those things. We're working on those things," he says. "Our greatest hope would be to reverse the damage that's been done. That's our holy grail." □

A person is sitting in a hospital bed, with their right arm extended on a table. A healthcare professional's hand is visible, holding a blood pressure cuff on the person's arm. The background is a clinical setting with a desk and some items on it.

THE AUTHOR
DECIDED TO
LEARN ABOUT
CLINICAL
RESEARCH BY
VOLUNTEERING
AS A STUDY
PARTICIPANT

THERE WAS
ONLY ONE,
SMALL
PROBLEM

TRIAL RUN

BY ADAM COHEN



I'VE NEVER BEEN A BIG FAN OF NEEDLES.

The very mention of the word takes me back to the allergy shots I received as a kid. Every spring and summer, ragweed and pollen reduced me to a sneezing, itchy, red-eyed mess. Still, if my mom had given me a choice, I would have opted to live with a perpetual case of hay fever, because the cure seemed so much worse.

Even now, just thinking about my weekly visits to Ms. DeSilets, a kindly nurse who lived around the corner, makes my heart quicken. And not in a good way.

The antiseptic tang that filled the air when she twisted the cap from the bottle of rubbing alcohol. The faint whoosh, whoosh, whoosh the cotton ball made while she wiped my skin clean. Then—don't look, don't look, why did I look?!—the grab of the needle as she plunged its slim shaft into my shoulder.

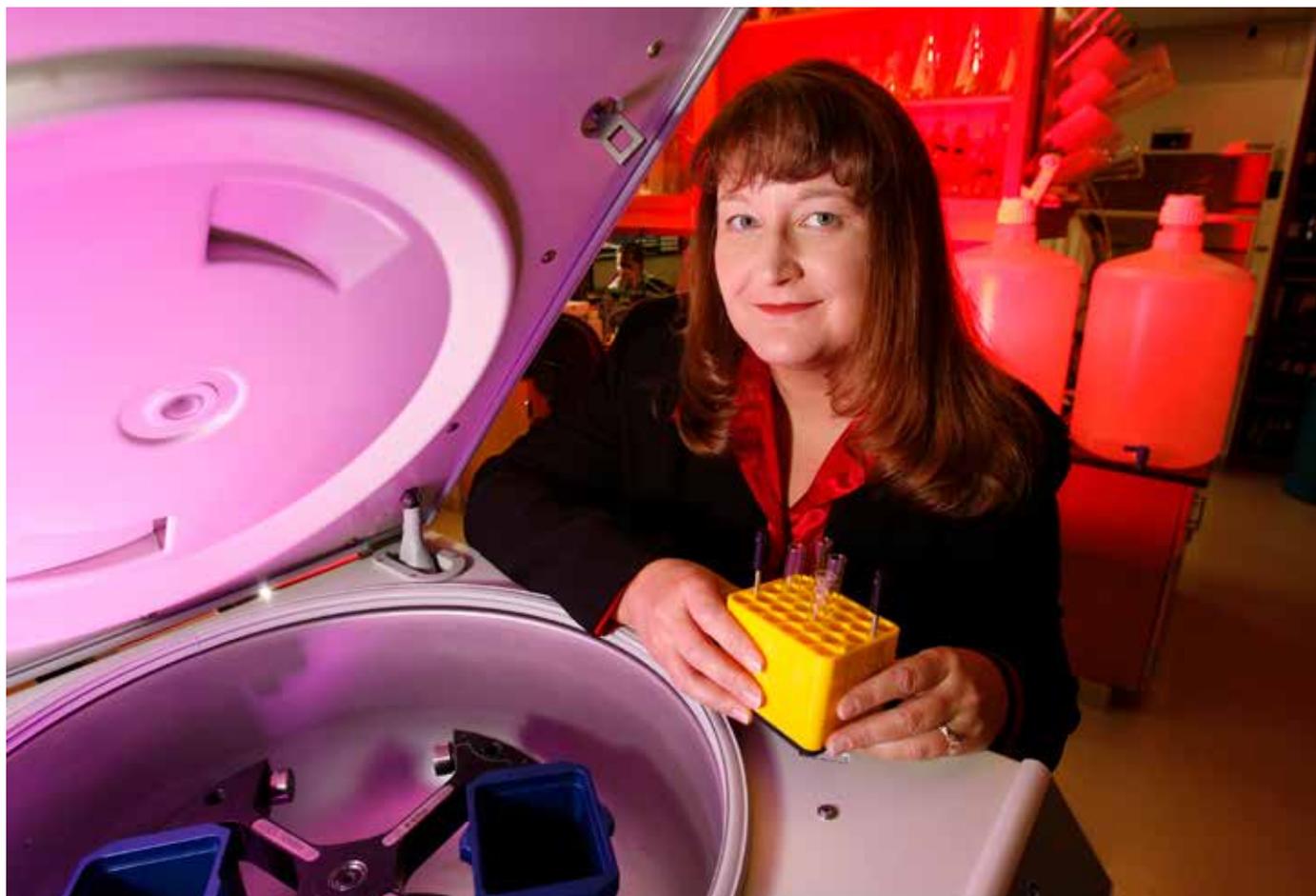
Still, like so many fears, I suspect this one originated from a deeper place. Something evolutionarily hardwired, like a primordial dread of snakes and high places.

My aversion to needles stops me from giving blood. It transforms my annual physical into the nadir of my year, a vein-pricking nightmare that marches inexorably toward me for 364 days. On numerous occasions, the mere sight of a needle buried in the skin, extracting or inserting vital fluids through an attached tube, has left me dizzy and drenched in sweat.

When a nurse ran an epidural into my then-wife's lower back in preparation for the birth of our first son, it was I who nearly passed out. "Hello!" I remembered Julie saying with—understandable—irritation as the nurse and her mother attended to me. "I'm the one with a needle in my spine about to have a baby."

So, it's hardly surprising that, in 17 years of working at OMRF, I've never volunteered as a clinical research subject. Until now.

Dr. Judith James leads a pair of research studies at OMRF aimed at preventing autoimmune diseases before they take hold.



STEVE SISNEY

In clinical research, scientists study health and illness in people. Simply put, this work involves human participants, and it offers researchers a way to probe the hypotheses they've developed in laboratories.

At OMRF, much of that clinical research centers on autoimmune disease. In these conditions, which include lupus, multiple sclerosis, type I diabetes and rheumatoid arthritis, the immune system becomes unbalanced and, as a result, turns its weapons on the body's own cells. To date, researchers have identified more than 80 different autoimmune illnesses. The National Institutes of Health estimates that, together, these disorders affect approximately 25 million Americans.

Dr. Judith James leads OMRF's research efforts in autoimmune disease. She heads the foundation's

Arthritis & Clinical Immunology Research Program, where more than a dozen different laboratories seek out more effective ways to treat and prevent autoimmune diseases. James also serves as OMRF's Vice President of Clinical Affairs, a position that marries laboratory investigation with clinical initiatives, a category that includes both patient care and human research studies.

An M.D. rheumatologist and Ph.D. immunologist, James has spent more than a quarter-century studying how autoimmune diseases begin. From the get-go, clinical research studies have served as a keystone for her work.

"We are focused on trying to understand the difference between human health and pathogenic conditions—disease," says James, who holds the Lou C. Kerr Endowed Chair in Biomedical Research. "To do that,

we need participants from a broad variety of different health statuses."

Like clinical studies done by most medical researchers, James' revolve around the collection of biological samples from human subjects. Volunteers fill out questionnaires about their medical histories, then donate blood (and, on occasion, saliva, hair and other biological materials). The volunteers typically fall into two, distinct groups: those with the condition that researchers wish to study, and healthy "controls."

"Healthy controls give us a way to compare the group we're looking at with a 'normal' population," says James. To the extent that researchers can control or match as many variables—things like age and gender—in the healthy participants with those of the study population, it allows them to tune out potentially

confounding factors and zero in on what might be causing different health outcomes in the two groups.

In autoimmune disease, though, there exist many shades of gray. Sometimes, individuals who think they are healthy may, in fact, be carrying certain proteins in their blood known to predict the onset of conditions like lupus and rheumatoid arthritis. These people may have some clue, like an affected relative or a stray symptom, that they could be teetering on the edge of autoimmune illnesses. Or they may have no idea at all. Either way, it's this group that plays a central role in James' research.

"Over the past decade, we've been trying to understand where autoimmune disease starts. We've learned that some is genetic risk, and some is the development of abnormal blood proteins," she says. "We also know that family members of patients sometimes have the same blood markers but never go on to get sick."

Separately, observational studies had found that when physicians treated autoimmune disease patients with a common anti-malarial medication, the patients showed improved mortality rates and lower incidence of heart disease, diabetes and other disease-related complications. Better still, the drug, Plaquenil (hydroxychloroquine), has been available to patients for many years and, says James, "has a very low side-effect profile."

Fitting these pieces together, James and her colleagues hypothesized that if they were able to identify individuals at risk for developing autoimmune illness—before they actually developed full-blown disease—giving them Plaquenil might slow disease onset. It might also lessen the symptoms when illness eventually took hold.

"Even when patients come to the doctor and get all the best medicines we currently have, the disease still

leads to deformities, shortened lifespans and things we just can't fix," James says. "Now, we might be able to dial this back and prevent people from moving into full-blown lupus."

To test the theory, James and her fellow researchers organized a pair of clinical research studies. One (known as SMILE) examines people predisposed to lupus, while the other (StopRA) looks at those likely to develop rheumatoid arthritis. Both follow the same blueprint: identify at-risk individuals, split them into two groups—one treated with Plaquenil, the other with placebo—and see what happens next.

Recruiting volunteers who don't know they might develop lupus or RA seems like a metaphysical impossibility. Yet, it turns out, that's precisely where I come in.

•
OMRF's Rheumatology Center of Excellence is tucked into the first floor of the foundation. I walk by it



BRETT DEERING

Dr. Eliza Chakravarty (in black) leads OMRF's Institutional Review Board. "Our focus is on the person volunteering to participate in the research," she says.

MOST OF MY ANSWERS TO THE “HAVE YOU EVER HAD...?” QUERIES ARE NO. THIS BODES WELL FOR MY HEALTH, BUT NOT FOR MY ELIGIBILITY FOR THE TRIALS.

every day multiple times—on my way to the cafeteria, a conference room or one of many other destinations. Other than when I guide an occasional lost patient to its doors, the space rarely registers a blip on my consciousness. But on this day, it lights up all the synapses in my frontal lobe.

I sit in the Center’s infusion suite, in a chair designed to allow someone to draw blood from either of the occupant’s arms. But at this moment, I am otherwise occupied.

Terese Aberle, a physician assistant with more than a decade of experience working with lupus and RA patients at OMRF, is going over my screening questionnaire with me. I’ve filled out five pages detailing my general health history, plus another form devoted specifically to issues I might have with my connective tissue, a telltale signal of autoimmune disorders.

Most of my answers to the “Have you ever had...?” queries are no. This bodes well for my health, but not for my eligibility for the SMILE and StopRA trials. Still, one particular response has piqued Aberle’s interest.

“Tell me,” she says, “about your fingers changing color in the cold.”

Sometimes, I explain, my fingertips become white or purple after I’ve finished a long run on a winter day.

She palpates my fingers. “Any sores?” I shake my head no. “Any pain or numbness when they warm up?” Again, no.

“The color change could be a sign of Raynaud’s syndrome,” which can be linked to certain autoimmune diseases, she says. But because I have none of the secondary symptoms, she explains, “It’s probably nothing to worry about.”

Aberle proceeds to examine the joints in my fingers and toes, squeezing gently at each juncture. She shows particular interest in the joints that connect my fingers to my hands and my toes to my feet. “If you had rheumatoid arthritis, those would be swollen and sore,” she says. Happily, mine are neither.

By the end of our session, Aberle tells me she’s found no overt signs of autoimmune disease. Oddly, I feel somewhat deflated. “Does that mean I can’t be part of the study?”

“We’ll still go ahead and draw your blood,” Aberle tells me. “If you test positive for certain biomarkers, we could still enroll you.”

If not? “We’ll use your samples as healthy controls for the Oklahoma Immune Cohort,” a collection of other clinical research studies of autoimmune diseases.

Although I’m neither a Ph.D. nor an M.D., I’d wanted to contribute to the research that goes on at OMRF. And now, she’d assured me, I could. All that remains is to draw eight vials of blood from my arm.

Like all research involving human participants, studies at OMRF are overseen by an institutional review board, or IRB. Created when Congress signed the National Research Act into law in 1974, IRBs provide an independent review of studies that seek to use human subjects to answer a research question. Their charge is three-fold: ensuring that research is conducted in an ethical manner; verifying adherence to federal regulations and state laws; and protecting the rights and welfare of human subjects.

Lawmakers saw the need to create IRBs in the wake of World War II, where Nazi physicians and scientists conducted savage experiments on concentration camp prisoners. But ethically questionable research happened in the U.S., too. The notorious Tuskegee syphilis study denied treatment to hundreds of black men living with the disease for decades, even after penicillin became a known cure. And at Philadelphia’s Holmesburg Prison, researchers in the 1950s and 1960s exposed inmates to a variety of dangerous compounds, including the active ingredient in Agent Orange, the cancer-causing defoliant used by American forces in the Vietnam War.

IRBs introduced a novel concept. Rather than scientists operating autonomously, an independent committee would oversee their work. “The IRB’s focus is the person volunteering to participate in the research,” says Dr. Eliza Chakravarty, who chairs OMRF’s IRB. “Our goal is to ensure that the design of the study is as safe as it can be for the participant. And to guarantee that people are fully informed of the potential risks and benefits before they enroll in a study.”

IRBs consist of individuals from a wide range of backgrounds: people with scientific and medical training, legal experts, ethicists and members of the community at large. Like a jury, each member brings unique perspective and expertise. Together, the group possesses knowledge and insights greater than any of its individual members. This diversity of viewpoints and talents, along with the board’s independence, makes the IRB an ideal body for ensuring



BRETT DEERING

Thanks to her participation in a clinical trial of an experimental drug for multiple sclerosis, Oklahoma City's Tonja Martin has received almost seven years of free medication. "I don't know what I would have done without it," she says.

that every research project involving human participants is conducted in an ethical, safe and legal manner.

An attorney, I joined OMRF's IRB in 2004, as its legal expert. While I'd already spent a decade practicing law, this represented my first foray into the realm of human-subjects

research. In the 15 years since, what I've learned about this highly regulated area of the law could fill a textbook. Nevertheless, in a field as highly regulated, complicated and rapidly evolving as this, what I don't know would also fill a tome, and probably a thicker one at that.

While one of our charges is to review and approve each of the more than 100 protocols that are typically active at OMRF, the task that occupies the lion's share of our time is monitoring the 30 or so clinical trials underway in the foundation's clinics at any given time. Unlike a simple blood draw, where participants would expect neither considerable risk nor benefit from participation, clinical trials test experimental treatments on patients suffering from disease.

"In the development of new medications or other approaches to treat a disease, we need to go through a scientifically rigorous process that ultimately will tell us in an objective way if our approach is effective," says Dr. Gabriel Pardo, Director of OMRF's Multiple Sclerosis Center of Excellence. "We also look at whether the therapy is safe. Are we putting people at risk for other problems?"

Every drug available in the modern era has gone through this process, says Pardo, who currently oversees clinical trials for roughly two dozen multiple sclerosis medications at OMRF. And for patients with conditions like MS, trials offer direct benefits.

"First, they receive access to medication that is not otherwise available that might prove to be very effective or even revolutionary for their disease management, and this access usually comes years before the therapy would be approved by the FDA," Pardo says. Also, the study sponsors—usually, the pharmaceutical companies who've developed the new treatments—provide the treatment free of charge. "That means patients often don't have any out-of-pocket expenses."

For those affected by MS, a progressive condition that can rob its victims of mobility, balance and sight, a typical course of treatment involves regular infusions with biologic drugs. The annual cost of treatment with even one such medication can run \$40,000 or more. Patients without insurance, or those whose insurance won't pay for certain drugs or carries significant deductibles or copays, often face a terrible dilemma.

“My medication was \$3,400 a month, and my insurance didn’t want to pay,” says Tonja Martin of Oklahoma City, who was diagnosed with MS in 2010. “So, I had to start using my money I’d saved for retirement to pay for it.”

Pardo, who was treating Martin, offered her the chance to participate in a clinical trial of an MS medication that had yet to reach the market. Like many such studies, this one was a “double-blind” trial, meaning that neither she nor Pardo would know if she was receiving the experimental drug or a placebo. Still, Martin jumped at the opportunity.

“I decided to try it, and the program had me go in for an infusion every six months,” she remembers. Like most new biologic treatments for MS and other autoimmune diseases, this one

benefit and side effects at no cost through 2021.

Not every clinical trial works out this way. Some drugs prove ineffective. Others carry side effects that end up outweighing their benefits. And, regardless, many patients receive doses of placebo rather than experimental therapies.

Still, for Martin, the process has been “miraculous. I had relapsing-remitting MS, and now I’m living symptom-free.” She’s received almost seven years of free medication, saving her hundreds of thousands of dollars in potential drug costs. “I don’t know what I would have done. Literally.”

Martin opted to take part in the trial because “whether it worked for me or not, at least I would have tried to help and would have been a part of

a moment before wrapping it with a bandage. “You did great.”

A week later, I’m sitting at my desk, when Keyser’s name pops up on my phone. When I answer, she tells me, “We have your test results.”

My complete blood count came back normal. The same was true for my anti-CCP antibody test, which indicates that I neither have nor am at risk for rheumatoid arthritis.

A test of my anti-nuclear antibodies (ANA), a possible signal for lupus, came back at slightly elevated levels. But, Keyser explains, “As we grow older, these tend to run a little bit higher.” So, as a 51-year-old, I had nothing to worry about.

I won’t, I realize, be needed for the StopRA or SMILE trials. My role in this process will end with this phone call.

READY TO ROLL UP YOUR SLEEVE?
IF YOU’D LIKE TO PARTICIPATE IN A CLINICAL RESEARCH STUDY AS A PATIENT OR HEALTHY CONTROL, PLEASE CALL JACKIE KEYSER AT (405) 271-7745 OR EMAIL CLINIC@OMRF.ORG. TO READ MORE ABOUT SPECIFIC DISEASE TOPICS AND ASSOCIATED PATIENT STUDIES, VISIT OMRF.ORG/PATIENTS.

was time-consuming; the infusion process took seven hours. Still, Martin quickly found that it paid dividends. “I knew after the second treatment something was different.”

Even though she couldn’t know for sure, she was convinced her I.V. treatments contained the medication, not placebo. “I went from dizzy and feeling like I was falling to having a more normal life—more energy and more confidence doing things. I felt like I used to feel.”

Martin continued on the trial until its conclusion. At that point the sponsor, a drug company, “unblinded” the trial and revealed that she had, in fact, been on the drug. The company then permitted her to continue receiving the medication as part of continued evaluation of the drug’s

helping others.” That desire, born of altruism, has now paid dividends she scarcely dared hope for. “OMRF,” she says, “has saved my life.”

As it turns out, my blood draw is no big deal. Jackie Keyser, a registered nurse with decades of experience, looks approvingly at my right arm as she ties a rubber band around my bicep. “You have good veins,” she says. “This should be easy.”

She gently slides a needle into the hollow of my elbow, makes a bit of small talk with me, and before I know it, she’s pulling the rubber band from my arm.

“All done?” I ask, finally mustering the courage to look.

“Yes,” she says, removing the needle and applying pressure to my vein for

Still, I confess, I’m a bit disappointed I can’t be of more help. I’ve only just gotten started, and already I’m done.

That’s not exactly true, she reminds me. Researchers will store my blood as part of the Oklahoma Immune Cohort. There, they’ll use it for years to come, comparing my immune system to those of patients with conditions like lupus, MS and RA.

Besides, Keyser reiterates, “This is very good news. You’re a perfect healthy control.” I hang up the phone, letting her words sink in.

After a moment, I make a promise to myself to volunteer for another research study. In the grand scheme of things, maybe needles aren’t so bad after all. 📍

Additional reporting by Ryan Stewart

Return of the Native

On her way from Watonga, Okla., to earning her doctorate at Harvard, **Heather Rice** got her first taste of working in a lab as an OMRF Sir Alexander Fleming Scholar. She liked it so much, she decided to make a career of it. Now, she's come back to her home state, as an assistant professor and Alzheimer's researcher at the University of Oklahoma Health Sciences Center.

What drew you to OMRF's Fleming Scholar program?

As a freshman at OU, I didn't fully understand what options were available in the biomedical field outside of careers in medicine. When my professors discussed the research they did in their labs, it sounded really exciting to me. I remembered my high school biology teacher talking about the Fleming program, and I thought that would be the perfect opportunity for me.

How did it compare to high school science classes?

My time at OMRF was unlike anything I had ever experienced in a classroom. The first time my mentor handed me a pipette, I had no idea what to do with it. I learned a lot that summer! It also taught me that to be successful, you had to be able to combine scientific knowledge and technical skills together with creative thinking.

Did it influence your career choice?

That summer solidified my decision to pursue a research career, and I haven't left the lab since. It also fueled my passion to obtain a Ph.D. and lead my own lab one day. Just as importantly, it gave me the confidence that I could do it.

Dr. Heather Rice

Assistant Professor of Biochemistry & Molecular Biology
University of Oklahoma Health Sciences Center

- OMRF Fleming Scholar
- Hometown: Watonga, Okla., pop. 5,000
- B.S. in zoology/biomedical sciences, University of Oklahoma
- Ph.D. in neurobiology, Harvard University
- Postdoctoral fellowship, VIB-KU Leuven Center for Brain and Disease Research, Leuven, Belgium
- Research focus: Alzheimer's disease



Rice with fellow Fleming Scholars in the summer of 2004 and, opposite page, today at the University of Oklahoma

How did OMRF prepare you for graduate school?

Because I was introduced to research so early in my undergraduate career at OMRF, I was able to gain even more research experience during my remaining three years at OU. That in-depth undergraduate research familiarity was absolutely critical for me in gaining acceptance to Harvard—and for me being successful once I was there.

Words of wisdom for students thinking about applying?

It's really the best way to become immersed in science and in research at such an early stage. You will grow so much as a person and a scientist. I grew more in those two months than I have at any point in my life.

What brought you back to Oklahoma?

When I thought about where to launch my own lab, I was passionate about contributing to the growth, training and mentoring of students in Oklahoma. In coming back, it is my goal to bring recognition and funding to my home state and to help expand Alzheimer's disease research in Oklahoma.

What have you missed most about your home state?

Certainly family and friends, but also how friendly everyone is, including strangers. OU football and Thunder basketball rank right up there, too. And I've enjoyed all the new areas that have popped up around Oklahoma City in the 12 years I've been gone.

“My time at
OMRF was unlike
anything I had ever
experienced in
a classroom.”





825 N.E. 13th Street
Oklahoma City, OK 73104



Non-Profit Org
U.S. Postage

PAID

Permit No 639
Oklahoma City, OK

Fifty Is Nifty

December marked a half-century since Chip Morgan joined OMRF. During that time, he rose from part-time accounting clerk to Executive Vice President and Chief Operating Officer; he's now stepping down to a part-time role. "As much as anyone in the institution's history, Chip has helped make OMRF what it is today," says OMRF President Dr. Steve Prescott.

