

FINDINGS

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My
mom
has
lupus.

She had me anyway.

Jack Friddle, born 6.29.2017



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You've Come a Long Way, Baby

Jack Friddle's mother suffers from lupus. But with the help of OMRF's Dr. Eliza Chakravarty, she had a healthy pregnancy—and a healthy baby boy.

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Alive

In 1968, doctors gave Greg Kindell six weeks to live. He's still here.

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.

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Pitch Perfect

A friendship born on the cricket pitch gives birth to a partnership at OMRF

On the street in front of the family home in southern India, Manu Nair's older brother would gather with neighborhood friends for impromptu cricket matches. Forced by his mother to include his younger sibling, the elder Nair would hand his 7-year-old brother a bat and pitch a hard, cork-cored ball at him at top speed. The idea was to scare the youngster off.

It didn't work.

Nair loved the excitement and competition. He developed some talent with the bat, learning to hit the fireballs the older children hurled at him. But, over time, his true cricket talent shone through. He was a bowler, the sport's equivalent of a baseball pitcher.

He joined his school team and bowled through high school. But he put aside his cricket whites in college, and he didn't don them again until more than a decade later, not long after he'd taken a job at OMRF as a licensing associate. "I was young and single and new to Oklahoma," recalls Nair. "So when a guy who worked in one of OMRF's labs asked me if I wanted to come out and play, I said, 'Sure!'"

Oklahoma City seems an improbable home for a cricket team. But twice each week from April until November, a group of enthusiastic local players—most, like Nair, expatriates from countries formerly part of the British empire—met up in south Oklahoma City to practice and compete against teams from around the state and region.

Known as the Strikers, they'd secured permission to build a pitch, a concrete rectangle covered with an Astroturf carpet that measures 66 feet by 10 feet, on a piece of city-owned land. On the pitch, a bowler hurls a red ball the size of an apple at a batsman. Fielders position themselves in a circle around the pitch, awaiting the chance to catch the ball if the batsman makes contact.

The Strikers were, says Nair, an enthusiastic lot. But they were disorganized. They also lost a lot.

Still, Nair enjoyed playing. And he made new friends. In particular, he grew close to a fellow Striker who also worked at OMRF.

Dr. Andrew Westmuckett had grown up playing cricket in East Sussex, England, and he'd continued to play collegiately at Greenwich University. Like Nair, he'd left the sport behind for a decade or so—during which time he'd earned his Ph.D. in biology—but picked it back up when he'd come to OMRF for a post-doctoral fellowship in the Cardiovascular Biology Research Program.

Over time, Westmuckett and Nair realized they shared a vision for improving the Strikers. With Westmuckett as president and Nair as treasurer, they wrote up a charter for the club and secured 501(c)(3) nonprofit status. They put

systems in place for selecting players and collecting dues. They introduced a strict "If you don't practice, you don't play" policy at matches. Probably not unrelatedly, says Westmuckett, "We started to play a lot better."

In 2008, the Strikers made it to the Oklahoma-Kansas championship for the first time. In the title game, they bested their long-time nemesis, a Tulsa-based club. "It was the culmination of a long process," says Westmuckett. "And it felt great."

The next year, Nair left Oklahoma to accept a job at the Mayo Clinic in Minnesota. Still, he and Westmuckett kept in touch. In 2014, Nair returned to OMRF to become the vice president of technology ventures. In that role, he'd lead the foundation's efforts to work with commercial partners to transform scientists' discoveries into therapies and other products that could improve patients' lives. To do that, he'd need the help of a scientist. In particular, Nair wanted someone he knew he could trust.

"I walked into Andrew's lab at OMRF and said, 'How would you like to come work for me?'" remembers Nair.

The proposal, while unexpected, intrigued the scientist. The job would tap many of the skills he'd developed working in OMRF's labs: scientific writing, project management, research oversight. Still, says Westmuckett, "If it had been anybody other than Manu, I would not have said yes."

That trust has paid off. In the four years since, the pair has patented numerous findings made in OMRF labs, then licensed those discoveries to biotechnology companies. They've also formed a series of research collaborations with industry partners that have advanced the work of OMRF researchers. Nair has taken the lead in working with the outside companies, while Westmuckett focuses on directing the projects within OMRF labs. "Our skillsets are complementary," says Nair. "We make a great team."

Westmuckett agrees. "I've enjoyed every moment of working with Manu."

Although knee replacement surgery this past spring has put Westmuckett's cricket career on ice, he's found his way back out to the pitch as an umpire. In spite of nearly two decades with the Strikers—he's the only person in club history to be honored with a lifetime membership—Westmuckett claims he can serve as an unbiased arbiter in matches against other squads. Even when his boss is bowling.

"Manu is still playing, and he's playing very well," says Westmuckett, sounding not particularly unbiased. "He's a very good bowler."

STRIKING OUT

Dr. Andrew Westmuckett (left) and Manu Nair at the Oklahoma City Strikers' pitch on July 12, 2018



Photo - Steve Sisney

Solving a Colon Cancer Mystery

For years, physicians have puzzled over why people with “clean” colonoscopies went on to develop colon cancer. With a new finding, OMRF’s Dr. David Jones may have solved this puzzle. The discovery could lead to a way to detect these cancers earlier and more effectively.

Trailing only lung cancer, colon cancer is the leading cause of cancer deaths for men and women, killing 65,000 Americans each year. Still, life expectancy improves considerably if the cancer is detected early: People whose colon cancer is discovered in the earliest stage have a 5-year survival rate of 90 percent, while those whose cancer is found in the latest stage have an 8 percent rate.

The most common method of screening is a colonoscopy, where doctors use a flexible scope to examine the colon. Yet physicians can miss certain cancer-causing polyps during these examinations.

“Some polyps are embedded in the surface of the colon, and they’re also flat and covered up,” says Jones, who holds the Jeannine Rainbolt Chair in Cancer Research at OMRF. “This makes them incredibly difficult for doctors to detect.”

For a long time, says Jones, it was thought colon cancers that developed in patients who had clean colonoscopies were coming about through some unknown mechanism that didn’t involve polyps. “Now it is clear these hidden polyps might be responsible for up to 30 to 40 percent of colon cancers that develop later,” he says.

Working with a team of researchers, Jones analyzed the genetic composition of the hidden polyps. “Most cancers—and most polyps—need more than one mutation to form. However, in these polyps, only one gene, called BRAF, was mutated,” he says.

Because of these telltale markers identifying the polyps, researchers could create a diagnostic test

DESPITE ROUTINE SCREENING, COLON CANCER KILLS 65,000 AMERICANS EACH YEAR.



HIDE AND SEEK

Dr. David Jones has found a clue to detecting hidden, cancer-causing polyps.

to analyze fecal samples to look for these changes prior to a colonoscopy. “If changes are present, it would be a way for the doctors to know to look for a hiding polyp,” says Jones.

Further analysis by the researchers also showed the mutation caused a wave of alterations in the DNA. “It’s probably the change in BRAF combined with these other changes that leads to polyps forming.”

The work was published in the scientific journal *PLOS One*. According to Jones, “It’s a huge step in the right direction that could have clinical relevance for patients in a meaningful way.” Next up, he says, are studies of how these genetic changes cause the cascade that ultimately leads to cancer.



Illustration: Doug Chayka

Veg Out, See Better?

We all know regular servings of food from our gardens are important for good health. Now, a new research project at OMRF aims to show how a chemical found in a host of vegetables could help prevent vision loss.

With a four-year grant from the National Eye Institute, Dr. Scott Plafker will study whether a compound that's naturally produced in broccoli, cabbage, cauliflower and Brussels sprouts can protect eyes as they age. Called sulforaphane, it's previously been shown to guard cells from stress and to have anti-cancer effects.

"The positive effects of sulforaphane are so widespread that it is in about 30 clinical trials at this very moment," says Plafker, a scientist in OMRF's Aging and Metabolism Research Program. Researchers are currently testing its effects on conditions ranging from autism to epilepsy. "With this grant, we're going to look at its protective effects specifically in age-related macular degeneration."

Age-related macular degeneration is a leading cause of irreversible blindness among the elderly in the U.S. The

disease is characterized by death of the light-sensing photoreceptor cells in the macula region near the center of the retina. As a consequence, patients progressively lose their central vision.

With the new grant, Plafker and his OMRF research team will study whether sulforaphane can preserve vision by maintaining and protecting the layer of cells in the retina that supports the function of light-sensing photoreceptors. Dr. Michael Boulton from the University of Alabama at Birmingham School of Medicine and Dr. Raju Rajala from the Dean McGee Eye Institute will also collaborate on the project.

"I'm very excited about this, because sulforaphane is readily available in vegetables," says Plafker, who joined OMRF in 2011. "People can get it with ease, and they can get it without prescriptions or high costs. That's the best kind of treatment."



Vaccine Reality Check



Dear Dr. Prescott,

In this age of anti-vaccine believers, how do we convince parents that vaccinating their children is a responsible action, not only for their children, but for the health of all children? JOHN PRESCOTT, AUSTIN, TX

Thanks for the question, son.

We all look for cause-and-effect explanations when something goes wrong. So, when a young child gets vaccinated and a few months later is diagnosed with a condition like autism, it's human nature to assume the two are linked.

But they're not.

In 1998, a gastroenterologist named Andrew Wakefield published a paper falsely claiming he'd found a link between vaccines and autism. The work has since been retracted, and Wakefield was stripped of his medical license. Subsequent studies have demonstrated there's no link between autism and any vaccine or vaccine ingredients. Still, Wakefield's fake science has taken on a life of its own.

The best defense against such misinformation

BIG SHOT
Immunizations prevent 2 to 3 million deaths each year, according to the World Health Organization.

is, of course, truth. However, as Mark Twain wrote more than a century ago, "A lie can travel halfway around the world while the truth is putting on its shoes." And that was pre-Internet.

In this country, measles was declared eliminated in 2000. Fueled by anti-vaccine beliefs, the disease has since experienced a resurgence, with more than 2,000 new cases in the U.S. Outbreaks like the one at Disneyland in California in 2014-15 that infected more than 130 people are becoming more common.

A recent report found many cities fall below the 90 to 95 percent threshold for childhood mumps, measles and rubella vaccination needed for so-called herd immunity (which protects everyone, not just those who've been vaccinated). In some rural areas, the figure is now below 80 percent. With such numbers, the question is not if there will be a new outbreak; it's when.

There is, of course, no way to cleanse the Internet of anti-vax sentiment. But the messenger can be more important than the message, so it's up to trusted sources to act as voices of reason. That means physicians and medical researchers writing open letters like this one. It also means parents like you discussing these issues with friends and peers in your community.

Trust can be rebuilt over time. In Great Britain, where vaccination rates fell precipitously following Wakefield's fraudulent study, public health authorities waged a sustained, concerted campaign for childhood vaccinations. As a result, rates have climbed back up to 95 percent.

Finally, let your legislators know how you feel. Three states—Alabama, California and West Virginia—have now banned non-medical exemptions to childhood vaccines. That trio now shows both the highest vaccination rates and the lowest incidence of vaccine-preventable disease. Coincidence? I don't think so.





Mina Acquaye
OMRF DONOR

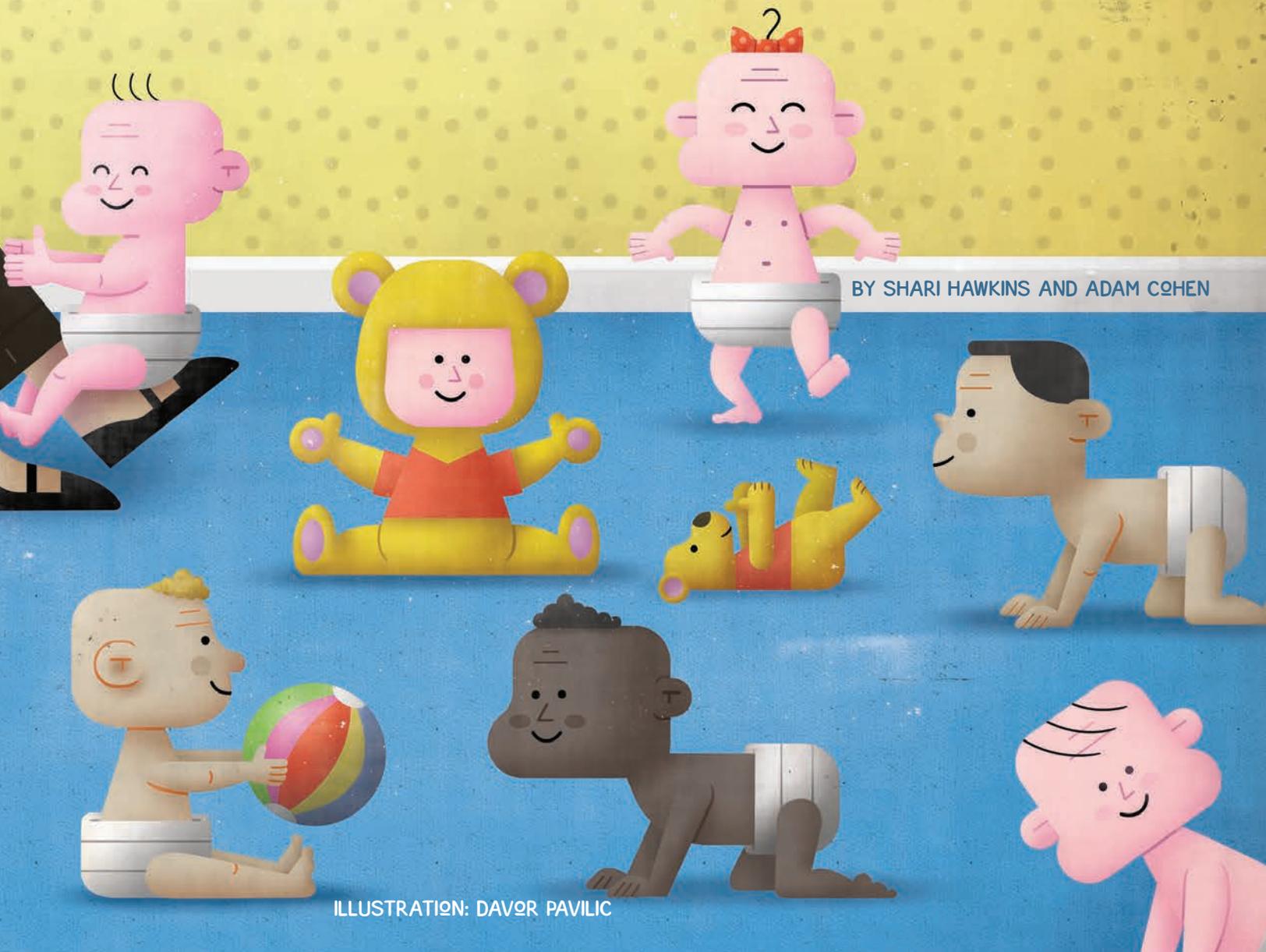
“I was excited to learn that OMRF is doing sickle cell research. I’d really like to see a massive effort put toward research for it all over the globe. Speed and magnitude are what’s lacking. Who’s going to solve problems like sickle cell? We are.”

Acquaye, a registered nurse, lost a sister and a child to sickle cell disease. She earmarks her gifts to this area of research at OMRF, where scientists have helped create an experimental drug to treat the illness.



Special Delivery

WHEN WOMEN WITH LUPUS WANT TO HAVE CHILDREN, THEY TURN TO DR. ELIZA CHAKRAVARTY



BY SHARI HAWKINS AND ADAM COHEN

ILLUSTRATION: DAVOR PAVLIC

It started with the bulletin board.

There, on a framed, cork rectangle that now hangs on the south wall of her office, Dr. Eliza Chakravarty began pinning up photos and cards featuring the children she calls “my babies.” And most were very young indeed. Swaddled in blankets or cradled in the arms of mothers and dads. One dressed as a mermaid. Another in a knit Winnie the Pooh costume. Many so new to the world their necks couldn’t yet support their oversized heads.

The board filled, but the photos and cards kept coming. Chakravarty couldn’t bear the thought of stowing even a single one in a drawer. So, on the wall behind her desk at the Oklahoma Medical Research Foundation, she continued the gallery.

But as the photo parade stretched out, a funny thing happened. The babies were joined by laughing toddlers. A young girl whitewater rafting. A pair of preschool-aged siblings doing their best Bruce Lee imitations.

“It’s hard to believe, but some of the kids are about to start first grade,” says Chakravarty.

While none are her biological children, Chakravarty tracks their progress almost as if they were. Really, it’s not a stretch to say she helped bring each one into the world.

In OMRF’s Rheumatology Research Clinic, where she’s been seeing patients since joining the foundation in 2011, the physician-scientist has developed a rare specialty: helping women with lupus have healthy pregnancies and healthy babies.

Although she’s not an obstetrician or a gynecologist, Chakravarty uses her training as an immunologist and a rheumatologist to guide women with lupus from conception to childbirth. She’s one of only a small cadre of physicians in the U.S. who focus on this area. But in a country with as many as 1.5 million lupus patients—overwhelmingly women, and many of child-bearing age—it’s an area of medicine that needs more attention, she says.

“Most American doctors have the philosophy of not giving any meds during pregnancy because of potential birth defects.” But, it turns out that “the underlying disease is actually the biggest risk to pregnancy.” For the best chances of a healthy pregnancy, she says, doctors should use the proper medications to keep the mother’s lupus in check.

It’s a fine line, but Chakravarty has made a career of walking it successfully. Still, it wasn’t long ago that her specialty was virtually unthinkable—right along with the idea of a woman with lupus wanting to have a child.

FOLLOWING MEDICAL SCHOOL and residency, Chakravarty began a fellowship in rheumatology and immunology at Stanford University in 2001, the year after she’d given birth to her daughter, Kiran. It had not been an



easy pregnancy. Infertility problems had made conception difficult. Then a viral infection landed Chakravarty in the hospital and ultimately led to pre-term labor.

“I definitely understand how terrifying it is to have an at-risk pregnancy,” she says. “But I also know the absolute joy of being a mother.” It was a joy she wanted to share with other women whose pregnancies faced significant obstacles.

At Stanford, she became involved with a clinical research study looking at the pregnancy outcomes for women with lupus. With her training in rheumatology (disorders that affect the joints) and immunology (the workings of the immune system), Chakravarty was a perfect fit for lupus.

In lupus, the immune system loses the ability to distinguish its own cells from foreign invaders. As a result, the body mistakenly turns its weapons on itself, launching attacks on a host of tissues and organs. Over time, these attacks, known as flares, can lead to debilitating arthritis, pain, exhaustion and, sometimes, organ failure.

Like many “autoimmune” diseases, lupus disproportionately strikes women. And it often does so at an early age. In the clinic at Stanford, Chakravarty worked with numerous lupus patients. She took a particular interest in those who wanted to become mothers.

“We were still in an era where doctors would often dismiss the idea out of hand,” says Chakravarty. “They’d say, ‘We just saved your kidneys’”—the organ most commonly affected by lupus flares—“‘why have a baby?’”

On the surface, their reluctance seemed to make sense. Lupus is a life-threatening condition caused by an out-of-balance immune system. And what swings the body more out of balance than pregnancy?

But Chakravarty understood that, for many women, the decision to have a child represented a life-defining moment. Not getting pregnant was simply not an option. At Stanford, she treated patients who ended up in kidney failure because they’d gone off all of their medications in pregnancy. “It was that important to them to be mothers.”

Ultimately, Chakravarty decided, her role was not to counsel patients about whether to become pregnant. “To me, if women want babies, they should be able to have them. It’s not for me to judge their decisions.” Instead, she’d build her specialty around what followed those decisions.

BABY BACKER Dr. Eliza Chakravarty is one of only a handful of physicians in the U.S. who specialize in helping women with lupus have children.



Photo: Steve Sisney



Photo: Brett Deering

FAMILY MATTERS With Chakravarty’s help, Katie Friddle gave birth to Eleanor (now 6) and Jack (1).

“Every time a woman comes to me and says, ‘I want to get pregnant,’ I’m in,” says Chakravarty. “We work hard to reduce risk factors for pregnancy complications as much as possible before conception, but we cannot take away all risks, which vary case by case.” Her aim is to give that pregnancy the best chance of success. It’s a lofty goal, and one that helps her build a deep and personal bond with each patient. “You’re helping to make a whole person. What could be cooler than that?”

IN HER PRACTICE, Chakravarty determined the prevailing wisdom—lupus patients need to get off their medications if they want to get pregnant—did not yield the best outcomes. She soon joined a small circle of physician-researchers who sought, through trial and observation, to map new paths to safer pregnancies.

“Instead of taking patients off their meds, we’d switch to ones not associated with increased risks of birth defects,” she says. The key, she found, “was to keep inflammation in the body in check.” The traditional approach of halting treatment during pregnancy did exactly the opposite.

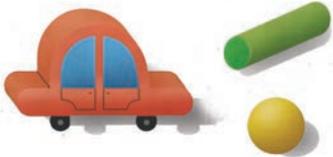
“One of the things we’ve learned is that having active disease while pregnant is not only dangerous for the mother, but it’s also a big risk factor for pregnancy complications,” says Chakravarty. In particular, disease activity during the first trimester carries the highest risk of causing miscarriage, birth defects, premature delivery and low-birthweight babies.

Consequently, Chakravarty and her colleagues treat the disease aggressively at the outset of pregnancy. That can mean, for example, resorting to steroids such as prednisone to counter flares. “Prednisone has a lot of side effects,” she says, “But it works fast.” While the mother’s placenta largely protects a fetus from the steroid’s effects, “you still want to use the lowest doses for the shortest period.”

Chakravarty typically works in tandem with an obstetrician/gynecologist. “They know pregnancy, but they may not be comfortable with treating lupus because they haven’t had enough training in that area.” The patient will keep her usual schedule of visits with the OB/GYN, and she’ll also see Chakravarty at regular intervals—generally once a trimester, unless there are problems. Chakravarty

also gives her sicker patients her cell number, which she answers anywhere, anytime. “I want to make sure the communication line is always open.”

This approach has served her patients well in the more than 200 lupus pregnancies Chakravarty has cared for. Every mother has survived, as have the overwhelming majority of babies. Unfortunately, though, there have been miscarriages. Each one, says Chakravarty, is “devastating.” Even with her many years of medical experience, “It never gets easier.”


CHAKRAVARTY DOESN'T IMPOSE many conditions on her patients. “Their goal is to live their lives; my job is to adjust their treatment to maximize their ability to do that.” But there is one rule that is non-negotiable: After a successful pregnancy, she gets to hold the baby.

Of course, she loves cradling the bundles of joy. But that post-delivery visit also ushers in a new, equally important phase of care: postpartum treatment.

The OMRF physician follows her patients closely after they give birth to ensure their disease remains stable. “I worry their lupus will flare postpartum,” as hormonal changes that occur with delivery, breastfeeding and stopping breastfeeding can act as triggers for lupus. “I don't want to see women who are trying to bond with their babies also have to deal with symptoms of the disease.”

However, that's precisely what happened to Katie Friddle.

Under Chakravarty's care, Friddle's pregnancy with her daughter, Eleanor, progressed normally. “I was stable, and my lupus symptoms were completely under control,” she says. “It was almost as if I didn't have lupus at all.” Eleanor was born healthy, and Friddle breastfed her daughter without a problem. But when her daughter began weaning, Friddle says, things began to “get screwy.”

Her days would begin with her hands feeling puffy and stiff. Sometimes, her ankles and knees would also swell. The pain and inflammation interfered with her ability to go about her normal activities—raising Eleanor, working as a historic preservation officer in the Oklahoma City Planning Department. But things really went off the rails when Friddle and her husband, Shane, took Eleanor to the zoo one spring day.

Despite applying sunscreen, Friddle suffered what she at first believed was a moderate sunburn. But lupus can cause extreme sensitivity to ultraviolet rays, and by the next morning, her skin had turned bright red. Her joints ached, and she was running a fever. She eventually “put two and two together” and realized her symptoms were likely related to her lupus. She called Chakravarty, who quickly admitted her to the hospital.

There, tests showed that Friddle's white blood cell count was plummeting. Something—sun exposure, the hormonal effects of halting breastfeeding, or, most likely,

a combination of both—had caused her body to turn on itself. Friddle was suffering a lupus flare, a serious and potentially life-threatening bout of disease activity.

For four days, her physicians treated her with massive doses of steroids. Over time, the drugs quelled the widespread inflammation that had sent her immune system into attack mode.

“I'd never had a flare that severe before,” says Friddle. But the episode served as a wake-up call of sorts. “I had to come to grips with the fact that this was going to be my reality, dealing with fatigue and joint inflammation.”

That autumn, she began experiencing soreness in her hip. An MRI revealed vascular necrosis; the bone in her hip was collapsing due to lack of blood supply. “The ball of my femur was basically flattened,” she says. Her doctors couldn't say for sure, but they suspected the long-term use of prednisone to control lupus flares had caused the condition.

Following months of mounting pain and immobility, Friddle opted to undergo hip replacement surgery. She was 31 years old.

AFTER A SUCCESSFUL recovery, Friddle continued to see Chakravarty regularly. Through a combination of careful monitoring and medication adjustments, the flares had subsided. When she nervously broached the idea of a second child, Chakravarty gave her the thumbs up. “As always, Eliza was supportive and encouraging,” says Friddle.

The OMRF physician worked closely with her patient to plan for the pregnancy. They tracked Friddle's symptoms, and Chakravarty changed her meds to “pregnancy safe” options. Once Friddle conceived, Chakravarty encouraged her to be vigilant and to keep in constant contact. “She helped me learn to listen to how I was feeling and to speak up—call, come in, get checked out—if something was off.”

Jack Friddle was born in June 2017. The pregnancy was uneventful, and the healthy newborn tipped the scales at seven pounds.

Chakravarty adjusted her patient's treatment regimen following Jack's birth. These days, Friddle feels great. “My blood work has been very good and stable, and I really don't have any symptoms to report.”

She knows her bout with lupus is far from over. But with Chakravarty in her corner, she feels confident about managing her disease. “Eliza is so responsive and knowledgeable. She always helps me think through my options and my goals for my health.”

Chakravarty is only too happy to help her patients navigate the waters of pregnancy—and beyond. “I care about them. I care about their babies. My goal is for every one of them to live happy, healthy lives.”

Each year, come the holidays, there are few things Chakravarty enjoys more than receiving a fresh batch of cards. Her bulletin board may be full, but there's still plenty of space left on the walls for new photos of kids. No matter their age, they'll always be her babies. ■





Alive

IN 1968, DOCTORS GAVE GREG KINDELL
SIX WEEKS TO LIVE. HE'S STILL HERE.

BY ADAM COHEN AND SHARI HAWKINS

Like most organizations, OMRF maintains a general contact email address. It's a place where people—and businesses and spammers—send their inquiries when they don't know whom, exactly, at the foundation to ask.

A handful of new messages typically arrive each day. "You'll see lots of vendors trying to sell things," says Ryan Stewart, a public relations specialist at OMRF who helps monitor the account. "And there's a steady stream of requests from patients." Sometimes, they're people trying to make appointments in one of OMRF's clinics. "Or it can be someone suffering from a disease who's read an OMRF press release about their condition." Stewart does his best to separate wheat from chaff, referring earnest inquiries to the appropriate parties at OMRF—and ignoring junk.

One morning this past February, Stewart opened up the "Contact OMRF" mailbox and began scrolling through the messages. Amidst the LinkedIn requests to connect and canned sales pitches, he saw a subject line that caught his eye: "Cancer survivor story."

The message came from a friend of a man named Greg Kindell. The email explained that at age 17, Kindell was diagnosed with acute myeloid leukemia, an aggressive form of leukemia. At the time—1968—this was essentially a death sentence.

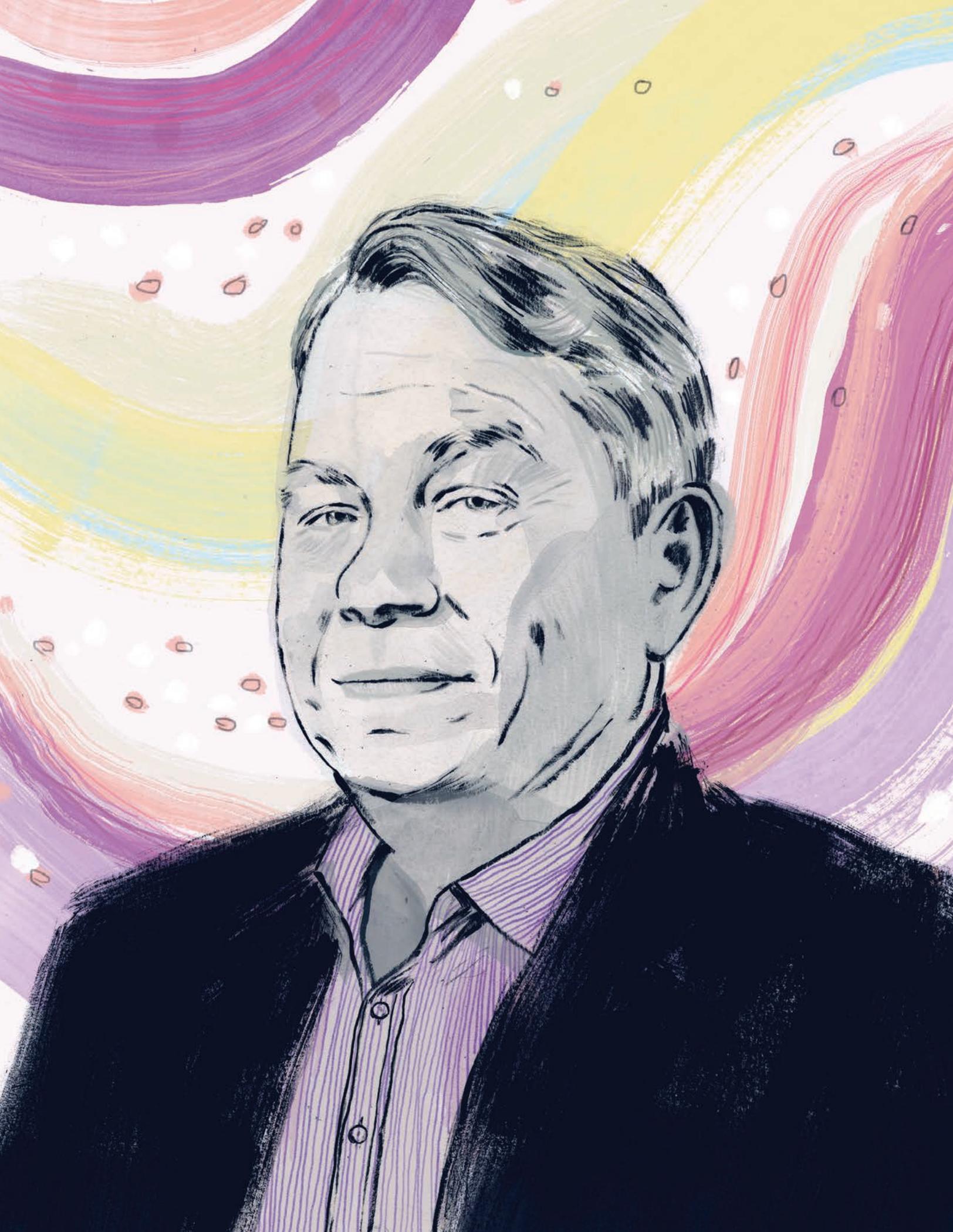
Kindell was referred to the OMRF research hospital. The facility was a sort of final option for people suffering from deadly diseases, primarily cancers. There, OMRF physicians tried experimental treatments in a last-ditch effort to save patients' lives.

Most of the time, it didn't work.

But, the email said, Kindell's story was different. Now almost 67, he was preparing to celebrate the 50th anniversary of the moment his doctors at OMRF had declared him cancer-free. In the five decades since, the disease had not returned.

"I was wondering if you ever do a celebration story on survivors," wrote Kindell's friend. "Please let me know if you are interested, and I can put you in contact with him."

ILLUSTRATION BY ANNA HEIGH



OMRF OPENED its research hospital in 1951. Funded by private gifts and a pair of federal grants, the idea was to provide patients with cutting-edge therapies when all other treatment options had failed. “Our hospital provided the most advanced kind of translational research we had then,” says OMRF President Dr. Stephen Prescott.

The lion’s share of patients were children suffering from cancer, a disease that befuddled researchers and physicians alike. “Was it caused by a virus? Environmental changes? We had no intellectual framework for knowing what was really going on with cancer back then. It was all very vague, with many more questions than answers,” says Prescott, who was a cancer researcher and served as executive director of the University of Utah’s Huntsman Cancer Institute before coming to OMRF.

Blood cancers like leukemia proved particularly challenging. “The standard treatment for cancer was surgery to excise tumors,” says Prescott. “But in leukemia, there are no tumors to remove.”

IN THE SPRING OF 1968, Greg Kindell was preparing for his junior track season at Pryor High School in northeast Oklahoma. Running up to 8 miles a day, the teen developed an infected toe. He also found himself more easily fatigued than usual. “I figured it was from running so much and wasn’t concerned,” he says. Eventually, the problems warranted a trip to his family physician, where the doctor prescribed a round of antibiotics.

Still, Greg grew weaker. When he experienced a prolonged bout of vomiting, his mother took him back to the doctor. There, he underwent blood work.

The results revealed sky-high levels of white cells, a signal that his body was fighting much more than a toe infection. At a hospital in Pryor, a subsequent test of his bone marrow confirmed what Greg’s physician feared: The 17-year-old was suffering from acute myeloid leukemia.

The most common form of cancer in children, AML floods the bone marrow and blood with abnormal white blood cells. These aberrant cells crowd out the normal white blood cells that act as the immune system’s primary defenders, leaving the body prone to infection and illness.

At the time, there was no treatment for AML. Greg’s physician told his mother the cancer was terminal. Your son has no more than six weeks to live, he said.

Still, the doctor offered one, faint ray of hope. In Oklahoma City, he knew OMRF was initiating a clinical study of people suffering from AML. Physicians at OMRF were seeking about 30 patients, all of whom would receive an experimental treatment for their leukemia.

The treatment, an aggressive form of chemotherapy, was unproven. But it was Greg’s only option. With his mother’s blessing, the doctor made arrangements to enroll Greg in the trial. After a hastily arranged family gathering—Greg didn’t realize it at the time, but it was his mother’s way of giving his relatives a chance to say good-bye to a young man they thought they’d never see again—mother and son made the 150-mile drive to OMRF.



Chemotherapy worked in 1968 the same way it does today. Doctors introduce powerful chemical agents to the bloodstream to kill off cancer cells. However, the chemicals are blunt instruments. Cells with naturally short lifespans that grow and turn over quickly, like those found in hair follicles and the lining of the mouth, die along with the cancer cells. Patients lose their hair, and many are plagued with painful sores in their mouths and elsewhere. Nausea, fatigue and fevers are commonplace.

The morning after beginning intravenous treatments at OMRF, Greg awoke to a wave of nausea that intensified as the day went on. The next round of chemotherapy left him vomiting uncontrollably.

“At that time, protocols were usually a combination of two or three different drugs,” says Dr. Richard Bottomley, who treated Greg at OMRF. In some patients, the drugs showed activity against AML. But physicians had no way of predicting who would respond—and who wouldn’t.

Treatment was further complicated by the fact that proper chemotherapy dosages were relatively unknown a half-century ago. How much was too much? How long should



SICK DAYS During his senior year at Pryor High School, Greg Kindell traveled to OMRF one week each month for chemotherapy—but told none of his classmates.

patients receive therapy? Over-suppression of bone marrow could leave patients anemic or dangerously immunocompromised. As a result, some ultimately died from the very medicines doctors hoped would save their lives.

“OMRF’s hospital did a good job with what we knew at the time,” says Bottomley. “But patients often were extremely sick before they arrived here, so they started treatment at a disadvantage.”

That was the case with Greg. Desperate to beat back his leukemia, doctors continued his high-dosage chemotherapy in spite of the side effects.

Greg’s hair fell out. At times, his skin grew too painful to touch. Nurses had to devise soft slings out of sheets to turn and maneuver him in his hospital bed. Night sweats left Greg’s bedding and pajamas wringing wet, requiring changes three to four times a night.

The nausea persisted, and Greg’s weight plummeted, eventually dropping from 142 to 95 pounds. He grew more frail each day. The infected toe flared again and became septic. Weakened by the daily rounds of chemotherapy,

he slipped in and out of consciousness. At the three-week mark, he recalls overhearing doctors tell his mother they were concerned he wouldn’t make it through the night.

THREE months after he was admitted to OMRF’s hospital, his doctors declared Greg in remission. His cancer was under control, at least for the time being. He could go home, but his treatments would continue. Greg would travel to OMRF one week each month for booster treatments to keep his illness at bay.

He told none of his friends in Pryor why he was gone so often. He wanted to live a normal life and put leukemia behind him. Still, the disease cast a shadow over everything. For example, he says, dating was out of the question. “I didn’t want any girls to get too close to somebody who was probably going to die. It was easier that way.”

Greg stuck with his monthly week-long visits through high school. After graduation, his ongoing treatment schedule seemed to preclude college. “I was going to miss one week a month, so it was basically impossible.”

Fortunately, his uncle, who was president of Murray State College in Tishomingo, understood Greg's situation and offered a solution. "He told me that as long as I got my work in, they wouldn't hold those absences for chemo against me."

Whether it was the treatments or something else, the leukemia showed no signs of coming back. Over time, Greg felt healthier and grew more confident about his future. And, as might be expected of a young person, he eventually grew impatient with his once-monthly stays at the foundation.

"I wanted in and out on time," he says. If there were any delays, he'd cause a stir. "I had things to do and wanted to be on the road as soon as I could."

Maxine Watson supervised the nursing staff in OMRF's research hospital and, even at a half-century's remove, remembers Greg well. "Greg was a sweetheart. He was so positive about his life." When he'd come for his booster treatments, she says, "He'd wait and wait for that last drip to come. As soon as it did, he'd call us and say, 'My bottle's empty! Let me go home now!'"

When Greg reached three years in remission, he made an appointment with the doctor who headed OMRF's cancer section. "I asked him how long I was going to need to keep taking chemo," Greg recalls. "He said, 'We don't know.'"

Of the 31 AML patients who'd enrolled in the OMRF study, only Greg and one other had survived. The doctor told Greg that no more than a few dozen AML patients worldwide had lived as long as Greg. "And he said that most of them were still taking the drugs."

Still, Greg was ready to move on with his life. He decided to stop his treatments.

FOR THE NEXT TWO YEARS, Greg visited OMRF regularly for follow-up testing. When he and the other patient both reached the five-year survival mark, the news made the *Daily Oklahoman*. The *Tulsa World* ran the story on the front page.

By then, Greg was 22. Once he'd ended chemotherapy, he'd transferred to Oklahoma State University, where he'd soon earn a degree in forestry and conservation. He'd also gotten married.

Although his fellow survivor would later suffer a recurrence that proved fatal, Greg remained cancer-free. He enjoyed a long career as a conservationist for the U.S. Department of Agriculture. That work took him to every corner of Oklahoma and as far away as Iraq. He earned an award from the U.S. State Department for helping organize farm cooperatives as part of the reconstruction effort in that war-torn country.

After a year of retirement in Owasso, where he now lives, he decided he missed his work. So now he's back at it, splitting his time between jobs for the State of Oklahoma and the USDA.

OMRF CLOSED the research hospital in 1976. The reason, as with so many decisions organizations make, was money.

The hospital initially operated on a free care model, with OMRF obtaining grants from the National Institutes of Health to pay for patient expenses. But the NIH grants didn't keep up with the ballooning costs of cancer care. OMRF started billing patients, but those fees—which began at \$5 a day and only covered a portion of the costs—proved too little, too late.

Still, OMRF maintained its tradition of clinical research and patient care by opening a research clinic. As an outpatient clinic, it no longer maintained beds. That meant there were no more overnight stays or long-term residents like Greg. In the increasingly expensive and competitive market for healthcare, large hospitals would meet those needs.

Instead, OMRF's physicians would see patients who suffered from illnesses for which specialized care was not widely available and that were also being studied by OMRF researchers. This led to the creation of research clinics to treat Oklahomans suffering from autoimmune diseases like lupus, rheumatoid arthritis and multiple sclerosis.

STUDIES LIKE THE ONE GREG TOOK PART IN AT OMRF HELPED IMPROVE SURVIVAL RATES FOR TODAY'S LEUKEMIA PATIENTS.

Today, OMRF's Multiple Sclerosis Center of Excellence and Rheumatology Research Clinic care for thousands of patients. Like Greg, many participate in clinical trials of experimental medications, gaining access to cutting-edge therapies before they've become available in hospitals and doctors' offices. The information OMRF physicians gather from these and other studies, in turn, paves the way for better patient outcomes.

Indeed, this is what's happened in AML.

Early studies like the one Greg was a part of saved only a precious few lives. Nevertheless, the findings from those clinical trials enabled researchers to develop a deeper understanding of the condition. That feedback loop steadily improved the quality of care and survival rate for patients suffering from leukemia.

Even now, chemotherapy remains the backbone of AML treatment regimens. Decades of experience have enabled physicians to refine their approaches, with better understood and more precisely refined dosing regimens. Also, since Greg's diagnosis, researchers have figured out that AML is not a single disease but, rather, an umbrella that encompasses a group of sub-conditions. Depending on the specific subtype of a patient's AML, doctors often supplement chemotherapy with other treatments, including radiation, a class of drugs known as targeted therapies, and stem-cell transplants.

Using these approaches, the prognosis for AML patients has improved. The five-year survival rate is now 27.4



Photo: John Jernigam

TOGETHER AGAIN When Greg (left) visited OMRF in July, he was reunited with Dr. Richard Bottomley, one of the physicians who'd successfully treated him for leukemia a half-century before.

percent for all patients, according to the American Cancer Society. While still low compared to many other cancers, it's roughly ten-fold higher than it was 50 years ago, when Greg was diagnosed.

Young patients have seen the greatest leap forward. A 2015 study found a five-year survival rate of 36 percent for AML when first diagnosed between the ages of 19 and 30. In those, like Greg, where the disease was found at age 18 or younger, nearly half were alive a half-decade later.

WHILE NO ONE KNOWS why Greg responded to and survived chemotherapy at OMRF when no one else in the study did, Prescott suspects his youth may have played a role. "Younger people do better with leukemia," says OMRF's president.

Researchers have identified a number of changes in the DNA and chromosomes commonly found in people suffering from leukemias. Some of these changes, or mutations, happen over a person's lifetime as a sort of flaw in the aging process or due to exposure to radiation or cancer-causing chemicals. But in childhood leukemias, the mutations are often inherited from a parent.

"For young patients with a certain type of leukemia, the hypothesis is that the disease comes from a birth defect, a specific cancer stem cell or cells," says Prescott. "That cell

or group of cells is always there, and it keeps making new cancerous cells unless you kill it."

Chemotherapy sometimes can do just that. "Destroy the cancer factory, and the disease stops." Then, he says, "You can live your life."

THIS PAST SPRING, Greg's friends held a small party to mark his 50 years of living cancer-free. For Greg, the occasion brought back all sorts of memories. He recalled the arts and crafts area at OMRF, where a volunteer helped him make pots in between I.V. doses of chemotherapy. He remembered how his mother would cook him whatever meal he wanted when he finished a course of treatment. And he thought about the many other patients with leukemia he'd gotten to know during his years at OMRF. None had survived.

Yet Greg had enjoyed a full life. Like most, it had come with its share of peaks and valleys: marriage, fatherhood, divorce. He's endured the pain of losing a son. He cherishes the joy his daughter and grandchildren have brought him.

He knew that every person in that long-ago clinical trial would have valued the chance to live as he had. To grow up. To have a family. To turn 67 and think, okay, what will tomorrow bring?

In a way, he realized, he was living for each of them. ◼

Remembering Dr. William Thurman

When Dr. William Thurman joined OMRF as the foundation's seventh president in 1979, he brought the lab coat he'd worn since his days training as a pediatric oncologist. That powder-blue garment, along with the bow ties he favored, would become synonymous with OMRF. And while memorable, Thurman's sartorial flourishes would prove to be the least of his many legacies at OMRF.

He immediately set to work building the foundation's scientific programs. His first focus was cancer research, a rapidly emerging field in which OMRF's presence had diminished. Making use of an extensive Rolodex developed while chairing the pediatrics departments at the Memorial Sloan-Kettering Cancer Center and the University of Virginia, serving on the faculty at three other institutions, and a stint as provost at the University of Oklahoma Health Sciences Center, Thurman successfully recruited several nationally prominent cancer researchers to OMRF.

Dr. Paul Kincade, who then ran a thriving cancer research laboratory at Memorial Sloan-Kettering, was one of Thurman's first targets. "After a single visit to OMRF and Dr. Thurman, my lab staff was ready to leave New York and move to Oklahoma. And that's what we did," says Kincade, who would go on to spend more than three decades as a scientist at OMRF.

Thurman's bushy eyebrows, deep voice and soft, Southern accent—along with the bedside manner of a seasoned physician—bespoke trust. That impression, says Kincade, was spot-on. "He told me he could provide for my needs in the lab, and he was true to his word. He really took care of his people."

Although trained as a physician, not a laboratory scientist, Thurman had a keen eye for talent and trends in research. Sensing that immunology and autoimmune diseases were another area of increasing need, he recruited Dr. Morris Reichlin from the State University of New York at Buffalo to start a new research program in 1981. Today, that program, now known as the Arthritis and Clinical Immunology Research Program, is one of the nation's leaders in the field, earning recognition from the National Institutes of Health as one of only 10

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Autoimmunity Centers of Excellence. It employs more than 150 OMRF staff members, who study diseases that include lupus, rheumatoid arthritis and multiple sclerosis.

Thurman's ability to identify and foster scientific talent paid similar dividends in cardiovascular biology, where he brought in Drs. Charles Esmon, Fletcher Taylor and Rod McEver. Each would go on to make watershed contributions to the field, and their discoveries have led to lifesaving drugs—and another is poised to reach hospitals and clinics in the coming years.

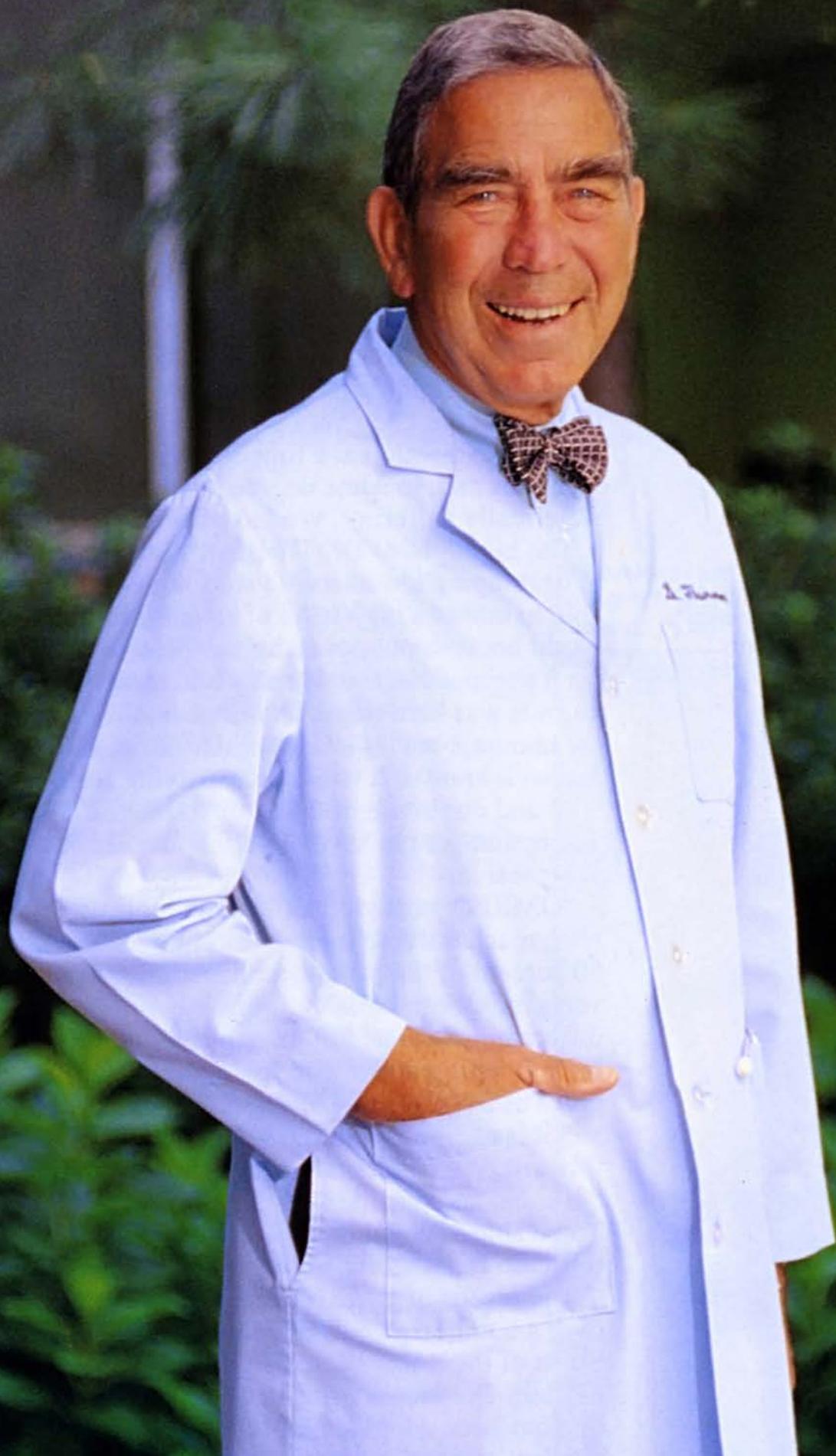
Thurman's ability to cultivate research success was no accident, says Kincade. "With Bill at the helm, we always had complete independence and the resources we needed to succeed."

As OMRF's research thrived under Thurman, the foundation expanded markedly. During his 18 years as president, the foundation's budget quadrupled, and it added hundreds of thousands of square feet of laboratory space with a trio of new research buildings.

"I think one of the things I've liked best about this job has been the opportunity to see OMRF grow from relative infancy to become a mature center of research excellence," Thurman told *The Oklahoman* upon his retirement in 1997. "It's also been a real pleasure to see research translated from our laboratories and become actual treatments for human disease."

Following his retirement, Thurman and his wife, Gabrielle, moved to the Seattle area. Still, they remained involved in the Oklahoma City community, staying in close touch with many friends (a group that included a multitude of present and former OMRF scientists). They also continued their long-time work with the Children's Center in Bethany.

In February, Thurman died at the age of 89. He is survived by Gabrielle, three daughters, eight grandchildren and a research foundation where his contributions live on.





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Bedlam Buddies

When heart disease was the opponent, even long-time rivals like the University of Oklahoma and Oklahoma State University could team up. In 1951, legendary Sooner head coach Bud Wilkinson (third from right) and his OSU counterpart, Jim Lookabaugh (second from right), helped kick off an American Heart Association campaign to benefit cardiovascular research at OMRF.

