The Alabama Center for Childhood Cancer and Blood Disorders

2022 IMPACT REPORT

Children's of Alabama®

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT CANCER 2022-23

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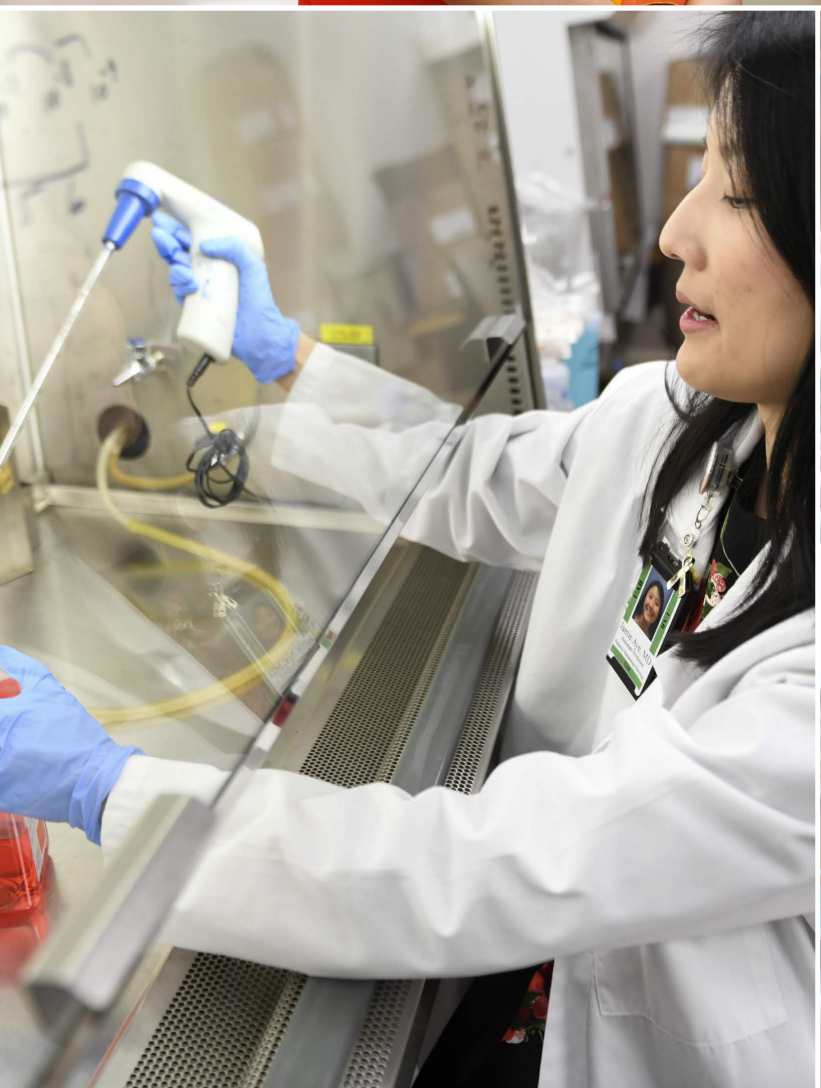

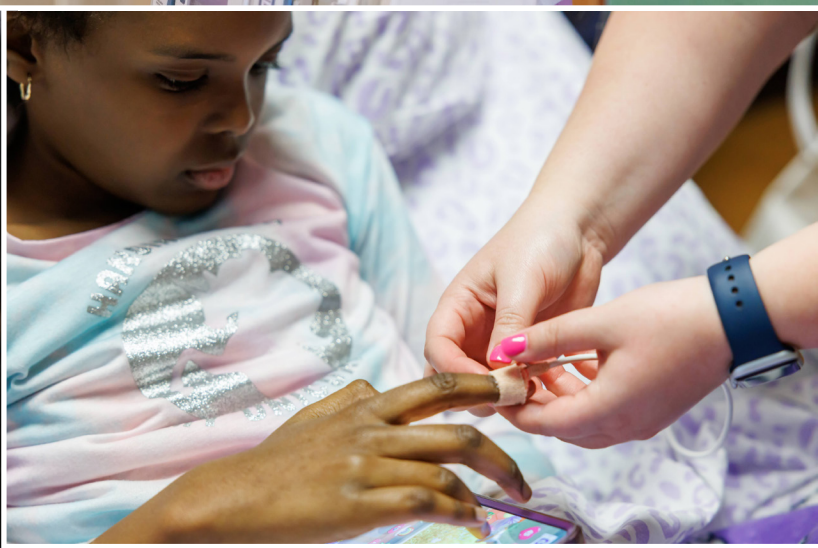

WE CARED FOR MORE THAN **2,000** PATIENTS WITH SERIOUS & LIFE-THREATENING CANCER & BLOOD DISORDERS

DIVISION DIRECTOR NOTE

As I reflect on my first three years at Children's of Alabama and the ways our team has shifted to meet the greatest needs of our patients and to advance research for more effective treatments, I am proud of what we continue to achieve together. At the heart of everything we do is providing the best care possible for our patients.

From spearheading a nationally shared registry of children with cancer and COVID that provides real-time information to pediatric oncologists, to increasing the number of clinical trials available at our hospital, to being recognized again as one of the top pediatric cancer programs in the country - this year has been full of notable highlights.

And, our reach is global. I recently visited Egypt with other members of the departments of pediatrics and surgery as part of our partnership with the Children's Cancer Hospital in Cairo, Egypt, which treats about 4,000 newly diagnosed cancer patients each year and is the largest specialized children's cancer hospital in the world. Through this relationship, we hope to train physicians from their hospital and from other parts of Egypt, Africa, and the Middle East, expanding the global outreach of Children's and fostering clinical research collaborations that not only benefit children in Alabama, but also impact patients across the globe.

It is my pleasure to share this report which highlights what your support makes possible. From innovative research to the family-centered care at the heart of our mission, we will continue to work toward a cure and provide the best care for children in Alabama and beyond. Your support is essential in fueling this progress. Thank you for being our dedicated partner.

Together, we are committed to a cure.

With gratitude,

Girish Dhall, M.D.
Benjamin Russell Endowed Chair in Pediatric Hematology & Oncology
Head, UAB Division of Pediatric Hematology, Oncology, and Blood & Marrow Transplantation
Director, The Alabama Center for Childhood Cancer and Blood Disorders at Children's of Alabama
Director, Neuro-oncology Program, Children's of Alabama
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Senior Scientist, O'Neal Comprehensive Cancer Center
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Girish Dhall, M.D.

NEW TREATMENT MAKES LIFE EASIER ON KIDS WITH SPECIFIC TYPE OF LEUKEMIA

ONLY **4%** OF GOVERNMENT FUNDED CANCER RESEARCH IS DEDICATED TO CHILDHOOD CANCER

It took just one weekend for life to change for Daniel Walker and his son Asher. In January 2016, Asher was diagnosed with leukemia. He had turned 5 years old just two weeks prior, and according to Daniel, he had been a "normal, regularly active child" up to that point.

The weather was freezing in central Alabama, and Asher was pale and seemed to have a cold. By Monday morning, his symptoms had worsened, so Daniel decided to keep him out of school. On the way to the bathroom that morning, Asher stumbled, fell on the floor and began vomiting.

Daniel knew something was wrong, so he set up an appointment with Asher's pediatrician. That doctor sent him to Children's of Alabama, where after a series of tests, physicians determined that Asher had leukemia. Initial results suggested he had acute myeloid leukemia (AML), a type of cancer that requires intensive chemotherapy treatments followed by months in the hospital recovering from each treatment cycle. He might even need a stem cell transplant—one of the most intensive types of leukemia treatments.

As Daniel was still processing the diagnosis, doctors at Children's were doing more genetic tests on Asher's leukemia cells. Two days later, they had more details. Asher had a specific subtype of AML called acute promyelocytic leukemia (APL). Historically, it has been extremely difficult to treat. Patients with APL need aggressive treatments, such as cytotoxic chemotherapy. They typically become very sick from both the disease and its treatments, and less than half are cured.

But in January 2016, when Asher was diagnosed, Dr. Matthew Kutny, a pediatric hematologist and oncologist at Children's of Alabama, was leading an early-stage clinical trial using a new APL treatment. If Asher joined the clinical trial, he could be treated for APL without needing chemotherapy. Asher would be exposed to far fewer toxins and spend less time in the hospital. "It was a no-brainer," Daniel said. He enrolled his son in the trial.

Initially, it wasn't easy. Daniel remembers nights during the first two weeks when Asher's oxygen levels would fall, and doctors would come into Asher's room with a portable X-ray machine to check him out.

Soon, Asher was able to leave the hospital and receive treatments in the outpatient clinic. He was even able to go to the grocery store with his dad on the way home from treatments and tag along while Daniel went to work, if needed.

"That was really a very positive aspect of this treatment: Asher could still be a kid, and he didn't have to worry about the struggles and the additional illnesses that come along with the more traditional chemotherapy treatment," Daniel said.

Asher's treatment lasted almost nine months. Aside from trips to Children's to be treated, his life was mostly normal, Daniel said. Eventually, he went into full

Matthew Kutny, M.D.

Matthew Kutny, M.D., served as the lead investigator on a national study that identified a new treatment option for children with a specific type of leukemia. The drug combination was found to be more effective with fewer side effects and reduces the need for chemotherapy; in some cases, it even eliminates it. The length of time of children undergoing treatment was reduced from more than two years to approximately nine months.

remission. Now, he returns to the hospital only once a year just to get bloodwork and is your typical 10-year-old. He has remained APL free for five years and enjoys playing frisbee, football and video games with his dad.

Asher was one of 154 pediatric APL patients who participated in the national study, which was led by Dr. Kutny and coordinated by the National Cancer Institute. Between 2015 and 2019, more than 80 institutions across the Children's Oncology Group (COG) enrolled patients in the clinical trial. It found that the treatment of arsenic trioxide and all-trans retinoic acid (ATRA) without cytotoxic chemotherapy was just as effective as the traditional chemotherapy treatment while being far less challenging to the patient. It's now the new standard of care for these patients. The study was published in the Journal of the American Medical Association–Oncology in November.

"We're excited as a COG investigator to be in an era where we can offer patients a far more effective and less toxic approach to treating cancer," Kutny said. "This is what we hope represents the future for many childhood cancers, that we can move away from the more toxic and intense treatments toward a more targeted approach that really attacks specifically the genetic changes that occurred in the cell that turned it into a cancer cell," Kutny said.

Kutny hopes doctors will find ways to refine the treatment process even further in the future. Kutny says there are some encouraging early studies on converting the arsenic trioxide treatment to an oral form, which would prevent patients from missing school. That means the treatment that already has set a new standard of care still has room to get better.

Identifying New Treatments with Innovative Clinical Trials

New and innovative therapeutic strategies are critical to improving the cure rate of pediatric cancers and decreasing immediate and long-term side effects. Clinical trials play a key role in developing and identifying these new drugs and therapeutics, and philanthropy plays a key role in fueling this work.

Currently, Children's has 90 active hematology/oncology clinical trials available through the Clinical Trials Office, which was developed in 2019. This means our families to have access to the newest therapies via promising clinical trials right here in Alabama without having to travel out of state.

"As a pediatrician and an oncologist, I've had to have really difficult talks with families about what their child is facing and what type of therapy they're going to have to go through to be cured. So being able to offer a therapy that is less intense and has fewer side effects, but at the same time has amazingly high survival rates, is a really good feeling," Kutny, said.

Five years after participating in Dr. Kutny's study, Asher is your typical 10-year-old. He has remained APL free for five years and enjoys playing frisbee, football and video games with his dad, Daniel.

TRAINING FUTURE LEADERS IN CANCER CARE

Since 1992, our pediatric hematology/oncology fellowship program has trained 39 fellows who have become national and local leaders in the pediatric hematology/oncology field. Fellows work on innovative research and treat patients during their fellowship training, so the impact of their work has ripple effects throughout the entire cancer program.

"We send our fellows out to institutions all across the country," says Kimberly F. Whelan, M.D., who completed the fellowship herself and now directs the program. "And as that number has grown, it's been wonderful to see the opportunities for networking and collaboration and the impact our fellows are having on the field — not only here in Birmingham, but across the country."

Kimberly Whelan, M.D.

Recently, the program added two additional fellowships for hematology/oncology fellowship graduates who want additional training: one in bone marrow transplantation and one in neuro-oncology. As the field as a whole is moving away from general hematology/oncology and into more sub-specialty, disease-specific care, the need to have dedicated training in these fields is important.

Only a handful of programs in the country offer two sub-specialty fellowships. The addition of these training programs elevates Children's of Alabama on a national scale and keeps our cancer center competitive. It also directly impacts the level of care that children in Alabama receive—ensuring that they have access to exceptional sub-speciality care.

AT OUR CENTER, MORE THAN **300** DEDICATED PEDIATRIC HEALTHCARE PROFESSIONALS PROVIDE EXCEPTIONAL PATIENT CARE, EDUCATION & RESEARCH

NEW BMT PROGRAM DIRECTOR FOCUSED ON EXPANDING IMMUNOTHERAPY

As Joseph Chewning, MD, takes over as the clinical director of the Pediatric Blood and Marrow Transplantation (BMT) Program at Children's of Alabama, he has an eye toward the program's future, especially when it comes to immunotherapy.

It's a field that Chewning says is growing very quickly. CAR-T cell therapy, in particular, is changing the paradigm for blood cancer treatment. With CAR-T, the child's own immune cells are programmed to recognize and destroy a patient's cancerous cells. Children's became certified in 2018 to provide the therapy to children and young adults with recurrent acute lymphoblastic leukemia (ALL). As the new clinical director of the pediatric BMT program, Chewning wants to make sure Children's can use CAR-T and other immunotherapies to help as many patients as possible.

"That's really the goal for the program going forward—to continue to expand the novel treatments that we can provide for the children of Alabama, including cellular therapies," he said.

Joseph Chewning, M.D.

Chewning's focus on immunotherapies is one part of his overall goal of providing the best quality care for patients in the safest way possible.

"It's really important to me that we fulfill the responsibility we have to the children of our state," he said.

Chewning wants to bring cutting-edge therapies to Children's so families in Alabama won't have to travel to get them.

"I've got four kids of my own," he said. "I can't imagine having a sick child who needs life-saving therapies and then having to separate from the rest of my family and go four or five states away."

INSPIRATION HAPPENS HERE – SYDNEY'S STORY

Sydney Sheppard knew she had a hard road in front of her when she was diagnosed with osteosarcoma. What she didn't quite know is that the journey would lead her to a lifelong decision to help others.

It all began when Sydney was 13 years old, and she started experiencing arm pain. She dismissed the pain for a while, but when her mom noticed one day how red and swollen her arm was, she knew they needed to see a doctor. The pediatrician called back almost immediately after an x-ray. "They thought they saw a tumor on my arm, and they thought it was cancerous," she says. "She was urging us to go on to Children's to get it checked out."

Sydney did go to Children's of Alabama, where a biopsy revealed osteosarcoma, a cancerous tumor in a bone. Doctors suggested a treatment plan of high dose chemotherapy to start right away and last for a year. After a few months of chemotherapy, Sydney proceeded with the other requirement on the treatment plan: limb salvage surgery. The surgery was successful, and she soon began physical therapy.

But, the very next summer, Sydney was struggling to bend her arm. She was back once again at Children's to examine what was going on. Doctors discovered that she had relapsed. "We found out that I couldn't bend my arm because there was a tumor there," she recalls. "It explained a lot, but it also led to a big decision of what to do."

After great consideration and consultation with other specialists, Sydney's oncologist felt that another limb salvage surgery would lead to a relapse or spreading of the cancer. At the time, the cancer was isolated to her arm, so amputation was the recommended course of action.

"I was devastated with that recommendation because I knew I wanted to become a physician before all of this happened, and I didn't know any doctors with just one arm," Sydney says. "A Child Life Specialist came and talked with me and shared a story with me about a surgeon she knew that lost a limb and that he was still working just fine. That opened my eyes a little bit."

Sydney decided to go with the recommendation of amputation. "It was a really tough decision," she says. "What made it even harder was that it was my right arm, my dominant hand, and I was at a rigorous magnet high school at the time. It was a lot to handle."

Though it was tough, Sydney shined. She went on to graduate from high school, then UAB and UAB's Heersink School of Medicine. She's currently a pediatric resident at Lurie Children's Hospital of Chicago. She ultimately hopes to pursue a fellowship in pediatric hematology/oncology and help other children on a journey she once walked herself.

"The doctors and nurses at Children's helped prepare me for this more than they know," Sydney says. "When I was in the hospital, those doctors and nurses became like family to me. They were there with me through everything. I'm excited to help other children when they are going through the scary situations like I once did while also showing that people with physical challenges CAN and SHOULD pursue medicine, too."

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BENCH-TO-BEDSIDE RESEARCH MEANS SICKLE CELL DISCOVERIES GET TO PATIENTS FASTER

Basic research is conducted in the laboratory, and clinical research is conducted studying patient data in the clinical setting. Traditionally, the two don't mix, with the basic happening before the clinical. Translational research, or 'bench-to-bedside research,' is a mix of the two designed to get new discoveries and treatments to patients faster.

Jeffrey D. Lebensburger, D.O., who directs the pediatric hematology section of Children's of Alabama's Department of Hematology and Oncology is using the translational research approach to find better ways to prevent early kidney disease in children with sickle cell disease.

Jeffrey D. Lebensburger, D.O.

Between 20 and 30% of children with sickle cell already demonstrate kidney injury before they hit their teens, and up to 70% will develop chronic kidney disease by the time they're middle-aged. Many will require dialysis or transplantation, often beginning in their 20s. However, the most commonly used test for kidney problems rarely identifies early signs.

Tracking the progression from childhood through adulthood, however, would take too long and cost too much. Yet mice genetically engineered to have sickle cell disease fully mature in just a few months, making them a perfect model for exploring kidney disease progression.

Dr. Lebensburger and his research partner, UAB assistant professor Malgorzata Kasztan, Ph.D. recently identified high levels of the protein endothelin-1 (ET), which binds to two receptors, ETA and ETB, as a key contributor to early kidney damage. Blocking the ETA receptors with an already FDA-approved drug, however, protected the mouse kidneys.

"That allows us to bring back to the patient what we're seeing in the mouse model and understand if it will continue into adulthood," Kasztan said. "Then we could potentially intervene earlier." At the same time, biomarkers of early damage they find in patient samples can be "mirrored" in the mouse model to confirm the results. Then interventions that work in the animal model can be tested in patients.

Not only do these discoveries mean better clinical care for current patients, but this type of research provides the foundation for clinical trials in humans. "That's an example of this bench-to-bedside approach: it works in the mouse model of sickle cell, so we can lobby the FDA to start a clinical trial in humans."