A Family’s Four-Year Search for a Diagnosis

A teen’s lungs fail and a race to Duke begins

Research is driving new therapies for seizures

stories
A newsletter for friends of Duke Children’s
Dear Friend of Duke Children’s,

When I was in medical school, I decided to specialize in pediatric immunology and rheumatology – perhaps because it was a field of mystery. Every patient was different, and making a diagnosis was always a challenge.

Many things have changed since then, but autoimmune diseases — when the body’s own immune system turns on itself — continue to be challenging and often heartbreaking for families.

To understand what I mean, read Lucas’s story in this issue. This remarkable family searched for four years before discovering the cause of their son’s violent episodes.

Also in this issue, read about some amazing research involving a brand new use for an old drug. Quinidine has been used for decades to treat irregular heart rhythms. Could it help children with unexplained seizures?

Finally, don’t miss Lindsey’s story. This brave girl beat the odds after her lungs were attacked by a devastating combination of infections.

I continue to be so proud of the courage of all our patient families, our care providers, and our researchers. These are the people who make Duke Children’s the extraordinary place it is.

Because nothing matters more,

ANN REED, MD
Chair, Department of Pediatrics

HOW YOU CAN HELP

You can support lifesaving research and patient care at Duke Children’s.

Make a gift any of these ways:
1. Use the envelope bound into this newsletter
2. Use the secure online form at gifts.duke.edu/dch
3. Call us at 919-385-3137
The March of Dimes has designated Duke Medicine, in collaboration with the University of Chicago and Northwestern University, as its fifth Prematurity Research Center. Over the next five years, the March of Dimes will invest $10 million in the Center, which is solely dedicated to solving the public health challenge of premature birth. The United States still has one of the highest prematurity rates among developed nations of the world. A total of 11.4 percent of children are born before full term.

Leaders of the center at Duke are Greg Crawford, PhD, assistant professor in the Department of Pediatrics; Amy Murtha, MD, professor and vice chair for research in the Department of Obstetrics and Gynecology and an associate professor in the Department of Pediatrics; and Haywood Brown, MD, chair of Obstetrics and Gynecology.

MARCH OF DIMES COMMITS $10 MILLION

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Conjoined twins separated at Duke

Duke Children’s surgeons separated conjoined twins during a nine-hour operation that took place in June 2015. Eight-month-old twins, Josiah and Aryan Covington, were attached at the hip and shared a liver. The two boys recovered rapidly and are expected to lead healthy lives.

Pediatric surgeon, Henry Rice, MD, (left) holds Josiah while mom Vanessa Covington cradles Aryan.
DEANNA ADKINS, MD

TRANSGENDER CLINIC LAUNCHED

Duke Children’s has launched a new center for gender-related disorders. The Center for Child and Adolescent Gender Care opened in July 2015 and is the first of its kind in North Carolina and one of only a handful in the Southeast. **Deanna Adkins, MD**, a pediatric endocrinologist who founded the center, says it provides support and medical care to transgender children and help to those with problems developing gender due to chromosomal problems or other issues. 📺

$20 million grant received for HIV vaccine development

Two research teams at Duke have received $20 million in grants from the National Institutes of Health for their projects to develop an HIV vaccine. **Sallie Permar, MD, PhD**, of the Department of Pediatrics, received an $11 million grant. **Mary Klotman, MD**, chair of the Department of Medicine, received $9 million. Both are five-year grants.

Permar was one of 102 researchers honored by President Obama with a Presidential Early Career Award for Scientists and Engineers, the highest honor bestowed by the U.S. government to outstanding scientists and engineers beginning their independent careers.

She was the senior author on a paper published in the *Proceedings of the National Academy of Sciences*, describing a newly-isolated substance in breast milk that inhibits HIV replication and may protect infants from acquiring the virus from mothers who carry the infection. In 2012, she received a New Innovator Award from the National Institutes of Health. 📺

DUKE CHILDREN’S IS NATION’S NINTH CERTIFIED DUCHENNE CARE CENTER

Duke Children’s has been named a Certified Duchenne Care Center by Parent Project Muscular Dystrophy (PPMD), a nonprofit organization leading the fight to end Duchenne muscular dystrophy (Duchenne).

Duke Children’s is the ninth center to be certified by PPMD’s Certified Duchenne Care Center Program, which supports standardized, comprehensive care, and services for all people living with Duchenne. Duchenne muscular dystrophy is the most common fatal genetic disorder diagnosed in childhood, affecting approximately one in every 5,000 live male births. 📺
Katz honored

The National Foundation for Infectious Diseases (NFID) has honored Samuel L. Katz, MD, the Wilburt Cornell Davison Professor and chairman emeritus of pediatrics at Duke University, with the 2015 Maxwell Finland Award for Scientific Achievement.

Katz is an innovative physician-scientist whose pioneering work on the development and promotion of the Edmonston measles virus vaccine revolutionized children’s health and reduced childhood mortality worldwide. According to the NFID, “He has achieved what most investigators dream of: translation of his research into a global resource that has improved public health and the lives of many.”

Grants to help studies of malnourished children

Michael Freemark, MD, chief of pediatric endocrinology at Duke Children’s, and his collaborators have received grants from the European Commission and the Humanitarian Innovation Fund to test a novel technology to identify biomarkers that predict morbidity and mortality in malnourished children. The studies will be conducted in Indonesia, Bangladesh and Burkina Faso. Freemark is collaborating with the international aid agency Action Contre La Faim (Action Against Hunger) and Ashutosh Chilkoti, MD, chair of Duke’s Department of Biomedical Engineering.

The testing follows studies of malnourished children in Uganda, where the researchers identified two hormones (leptin and adiponectin) that predict the risk of death during inpatient hospitalization. The team developed a point-of-care assay for leptin and adiponectin, which will be used for studies in the developing world. This project is part of a new initiative designed to develop an integrated, multidisciplinary, institutional approach to child development and illness.

DUKE CHILDREN’S IN HONDURAS

Dennis Clements, MD

A team of Duke students and faculty traveled to Honduras in March, where they administered basic health care to nearly 453 local residents in four days. The trip was part of an ongoing effort to provide Duke nursing and medical students with hands-on experience in global health while improving access to health care in rural areas of Honduras. Duke Children’s Dennis Clements, MD, has led the annual trips for 15 years.
Retinal swelling in premature infants tied to poorer neurodevelopment

Using a portable, non-invasive imaging device, a team of Duke doctors has identified swelling in the back of the eyes of premature infants that correlates with poorer neurodevelopment as the babies grow.

The Duke team, which pioneered the use of the hand-held tool in infants, determined that almost half of the premature babies screened had swelling in the macula region of the retina, which is responsible for central vision.

After two years of follow-up study, the researchers found that the infants with retinal swelling shortly after birth later had significantly lower language and motor scores on a standard developmental test.

Cynthia Toth, MD, Duke pediatric retinal specialist, was senior author of the study.
Amid dreadful complications, including a snowstorm that halted emergency transport, a young girl fought for her life.

**ON THURSDAY, FEB. 12, 2015,** Lindsey Tew was having fun at the Midway Middle School Valentine’s Day Dance in Sampson County, North Carolina, when her throat started to feel scratchy. It didn’t seem like anything terribly serious; she was treated for strep the next day.

The following Monday morning, though, she was clearly ailing, with a fever, confusion, and severe chest congestion. Her mother, Kacey Register, drove Lindsey, still in her flannel pajamas and clutching her stuffed bear, to her pediatrician. “I remember stopping at a stop light on the way,” Lindsey says. “And that’s pretty much the last thing I remember.”
The race begins
Her lungs were full of fluid, her blood oxygen was critically low, and she was having serious trouble breathing. The pediatrician’s staff rushed her to nearby Betsy Johnson Hospital, where she was intubated to try to get air into her failing lungs and swiftly put into another ambulance—racing an approaching winter storm—to better-equipped Wake Med in Raleigh.

By late afternoon, Kacey and her husband Dax were listening in shock as doctors told them that their daughter—who just days before had been a perfectly healthy teenager, the “flyer” on her school’s cheerleading team—had been struck by a devastating combination of influenza, pneumonia, and a MRSA staph infection.

“They gave her a 15 percent chance of survival,” Kacey recalls. “Her only real chance was to get to Duke. If they could get her to Duke and put her on ECMO, her odds would improve to 65 percent.”

A life-saving technology
ECMO is shorthand for the extracorporeal membrane oxygenation system, which essentially bypasses the lungs, allowing them to rest and recover; it draws blood, oxygenates it, and returns it to the body. Duke’s renowned ECMO program, now in its 25th year, treated its 1,000th patient in August 2015.

“ECMO does not fix anything,” says Ira Cheifetz, MD, chief of Duke Pediatric Critical Care, who directs the ECMO program. “It’s a ‘bridge’. Most of the time it is a bridge to recovery. This life-saving technology allows time for a patient’s lungs to recover.”

Lindsey needed Duke’s ECMO in a hurry, but by cruel coincidence, the snowstorm had brought Duke’s Life Flight medical transport unit to a halt. Cheifetz, by phone, talked Wake Med physicians through the process of maintaining a patient on ECMO support, and the Wake Med staff fought to keep her alive through the night.

“That,” says Kacey Register, “was the longest night of my life.”

A complication
Life Flight was cleared to go the next day, and Cheifetz joined the team making the trip to Raleigh to pick Lindsey up. He knew her chance of survival was slim without ECMO support.

The team hooked Lindsey up to their ECMO machine and rushed her back to Duke, but she was still far from out of the woods. Lindsey’s lungs were bleeding, making it too dangerous to administer the anticoagulant heparin, which is always given to ECMO patients to prevent dangerous blood clots.

Caroline Ozment, MD, pediatric critical care specialist at Duke, was part of the team caring for Lindsey. “A blood clot that traveled to the brain could have meant a stroke,” she says. “Because of this risk, I was very worried that she would have to come off ECMO before her lungs were ready.”

Lindsey, right, practices cheering with her junior varsity team at Midway High School.
Preparing for the worst

Lindsey’s doctors tried to help her parents prepare for what may lay ahead. “At one point Dr. Ira told us her lungs may be too badly damaged to heal,” recalls Dax Register. “He said, ‘We’re not giving up, but you should know we looking at a double lung transplant.’”

But after three and a half weeks, Lindsey turned the corner. Duke’s doctors eased her back toward health, and ECMO bought her the time she needed. On March 19, after four and a half weeks on ECMO, Lindsey was taken off the machine. It was the day before her 15th birthday.

She spent another two months in the hospital before she finally got to go home, but she got there in time to join her twin sister Haley at the school prom. She was able to start the fall semester at Midway High School, where she’s a freshman and a cheerleader. She can’t do quite everything she used to do—no flying, for example—and she has to be especially careful during flu season. But she’s back at home, sleeping in her own bed, although there’s not much room for her amid the pile of stuffed animals.

Inner strength

Lindsey’s family almost lost her last winter, but Duke Children’s and the ECMO program brought her back—and Lindsey’s own inner strength played an important role, too.

“At Lindsey’s last follow up at Duke they told her she was free to do anything! She could fly in an airplane, hold her breath under water, jump on a trampoline,” says Kacey. “When you consider everything—how sick she was, the snowstorm that kept us from getting to her, the fact that we couldn’t give her anticoagulants, and the length of time she had to stay on ECMO—it is remarkable that she has recovered so beautifully,” says Cheifetz. “She’s an amazing young woman.”

WANT TO HELP?

You can help more families like Lindsey’s by supporting research and patient care at Duke Children’s. Go to: gifts.duke.edu/dch
BRAIN UNDER ATTACK

BY CAROL HARBERS
A family endures a painful, four-year odyssey in search of a reason for their son’s violent behavior

Lucas had spent nearly half his life in an orphanage in Brazil, along with his sister. When he was 9, and his sister 11, the two of them got a second chance at life when they were adopted by Jack Reed and Ruben Quinones, now of South Florida. Reed and Quinones looked forward to helping to guide their son and daughter through all the joys and trials of life.

The first five years as a family were “normal,” says Reed. He describes Lucas at that time as a typical kid with boundless energy. But shortly after Lucas turned 14, life shifted in a way they never could have prepared for.

**Baffling symptoms**

Lucas started showing symptoms of anxiety, which escalated into something else. “He began having violent episodes,” says Reed. “He destroyed the house. He jumped out of moving cars and broke ribs. When he would start walking in circles around the house, we knew we were in for a rough night. Even the dog sensed something and would become very scared,” says Reed.

Reed, who has an advanced degree in psychology, didn’t know what was causing these episodes, but he knew what it looked like. “It looked like psychosis,” he says.

In the spring of Lucas’s eighth-grade year, the family was sitting in church when Lucas began trembling and drooling. His body became stiff, and he couldn’t talk.

Lucas’s parents took him to children’s hospitals near their home in South Florida. Thus began an incomprehensible, four-year journey from hospital to hospital in several East Coast states. The family moved to be closer to hospitals they hoped would help. More often than not, Lucas ended up as an inpatient in the hospitals’ psychiatric wards.

Luca’s family, left to right: Ruben Quinones, Jack Reed, and Suellen Quinones-Reed.
A desperate search
Reed’s background and instincts told him his son’s issues were neurological, not psychological. “We begged, ‘Please test him, my kid is having seizures’ ” says Reed. Tests were either not performed, or inconclusive.

In one year, Lucas had placements in nine psychiatric wards. One particular long-term placement in Florida lasted only a week. “He was kicked out because he destroyed the camp during a violent episode,” says Reed.

He also spent time in the intensive care unit, and for nine days, on a ventilator for a collapsed lung.

“He had so many clots in his lung that when the scan was read, we were told it looked like lung cancer,” he says. It was not lung cancer, but there still was no definitive diagnosis for Lucas’s worsening state.

To North Carolina
Lucas had trouble speaking, walking, and reading. Testing showed his IQ had plummeted. He couldn’t figure out how to close the pizza box. This, after being named Student of the Year in his first year at his first U.S. school.

“We were seeing doctors in Washington, D.C., and they told us we were going to lose him, but that they couldn’t help.” says Reed. “They said, ‘Go to Duke.’” They did, immediately.

Lucas had been sick for four years at this point.

Lucas and his family arrived at Duke Children’s and went to the Emergency Department. There, they met Egla Rabinovich, MD, a pediatric rheumatology specialist, who ordered testing. A few days later, Lucas’s care was handed over to Heather Van Mater, MD, another specialist in rheumatology and autoimmune diseases.

Reed, Quinones, and Lucas met with Van Mater and William Gallentine, DO, a pediatric neurologist. “They came in with an office box full of medical records,” says Van Mater. Immediately, she saw red flags — including the seizures and the sudden drop in IQ — that didn’t fit with a psychiatric diagnosis.

After test results were reviewed, the diagnosis was confirmed: Lucas had something called Hashimoto encephalopathy, an autoimmune disorder that causes brain inflammation. It is rare and often misdiagnosed.
“The psychological symptoms with this disorder can be so prominent that it is hard to see beyond that,” says Van Mater. “Some patients don’t have the classic signs of brain inflammation, so it is difficult to diagnose.” Even when imaging of the brain is performed, the inflammation doesn’t always show up.

As for the blood clots in Lucas’s lungs, there has never been a good explanation, although it could have been related to medication he had been treated with.

**The power of caring**

For more than two years, Duke Children’s has had a clinic especially for patients like Lucas. It is multidisciplinary, with specialists in autoimmune disorders and neurology working side-by-side with psychiatrists. Van Mater calls it an “all-in approach.”

When patients come to the clinic, all three specialists meet with them at the same time. “It is traumatic for the family to re-tell the story of what they’ve been through, so we want them to only have to tell it once,” explains Van Mater.

Lucas was treated with a protocol of steroids, plasmapheresis to remove antibodies, and an immunosuppressant to “reset” his immune system. He stayed at Duke as an inpatient for six weeks.

“They saved his life,” says Reed.

Lucas agrees, but thinks credit goes to his father first. “If it weren’t for him, I wouldn’t be alive. He kept questioning, he kept researching.”

**Finding meaning**

Today, Lucas is 19 years old, a high school graduate, and making his way through his new life with the support of a loving, devoted family. Looking back on all he went through, he says the hardest moment came when he was leaving for a hospital in Virginia and dad Ruben suffered a stroke. “I wanted to be there to help him, but I couldn’t,” says Lucas.

He will soon start classes at Broward College in Fort Lauderdale. “I want to be a firefighter, or a therapist, or maybe a researcher,” he says. “I believe that everything happens for a reason. I haven’t figured out all the reasons for what I went through, but I know that I want to help people.”

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**HOW TO MAKE A GIFT TO DUKE CHILDREN’S**

Your gift can support the compassionate care and cutting edge research Duke Children’s is known for. Go to: gifts.duke.edu/dch or use the envelope bound into this newsletter. Thank you!
THE BODY ELECTRIC

CAN A DRUG THAT AFFECTS ELECTRICAL ACTIVITY IN THE HEART HELP CHILDREN WITH UNEXPLAINED SEIZURES? by Angela Spivey

Photo: Oocytes of the African clawed frog in a Petri dish. Duke researchers used these eggs to study genetic mutations.

RESEARCH DRIVES NEW THERAPIES

New and better treatments require research. You can support Duke Children’s researchers! Use the envelope in this newsletter, or go to gifts.duke.edu/dch. We are grateful for your support!
**QUINIDINE** is a medication used to treat irregular heart rhythms (arrhythmia). A research collaboration at Duke Children’s suggests that it—or similar drugs—also have potential in treating certain types of drug-resistant seizures.

For some patients, none of the known anti-seizure medications—a dozen or more—will help, says Mohamad Mikati, MD, chief of the Duke Division of Pediatric Neurology. At Duke, he can offer to enroll these patients in a research study of precision medicine, which uses genetic testing to find the exact cause of a problem and prescribe a personalized treatment.

Working with Duke geneticists Yong-hui Jiang, MD, PhD, and Vandana Shashi MD, and David Goldstein, PhD, former director of the Duke Center for Human Genome Variation, the research team will conduct a type of genome sequencing called whole exome sequencing. This testing is much more extensive than would normally be offered to patients in a clinic.

In two recent patients with severe drug-resistant seizures, this testing identified a genetic mutation that causes increased activity in potassium channels in brain cells. “Every cell in the brain is like a battery, and the cells have channels,” Mikati explains. “The balance between potassium and other ions inside and outside the cell determines how it functions. The neurons discharge when they need to discharge and stay quiet when they don’t. It’s like a computer that has to have the right amount of electricity in every chip in order for it to function correctly.”

The mutation that the Duke researchers identified causes the potassium channel in brain cells to “leak,” Mikati says. “The cells are much more excitable, and every now and then it becomes too much, and the patient gets a seizure.” Such patients can have many seizures a day.

Once a suspected problem mutation is found, scientists in a basic neuroscience lab can try to recreate it, so they can figure out how to correct it. For these two recent patients, collaborators in Australia did this using immature eggs from an African clawed frog; because these eggs are large and easy to handle, they’re often used for experiments that involve testing electro-physical activity. After inserting the suspect genetic mutation into the eggs, the researchers tried different treatments to correct the resulting abnormality.

The researchers tried quinidine because it’s known to reduce activity in the potassium channel in the heart. And in the frog eggs, it worked—it calmed the increased electrical activity caused by the mutation.

So Mikati turned to Duke pediatric cardiologist Michael Carboni, MD, to help him devise a safe treatment protocol using quinidine for children with seizures. After the patients were treated, the results were reported in the journal Annals of Neurology.

In one case, the treatment has greatly reduced the frequency of seizures. “Quinidine is something that should be tried in patients with these kinds of mutations, but it must be used judiciously while observing the heart. One cannot use it willy-nilly, so to speak,” Mikati says.

In another case, the patient did not respond. “We think the reason is that maybe quinidine does not cross to the brain as much as you would like,” Mikati says. “But development of other drugs that are similar to it would hopefully help such patients. Personalized medicine can help guide not just therapy, but also drug development.”

> “Development of other drugs that are similar to [quinidine] would hopefully help such patients. Personalized medicine can help guide not just therapy, but also drug development.” — Mohamad Mikati, MD
BOUNCING ALONG

1. Give ’em a hand
   *Hyundai Hope on Wheels*
   Launched Childhood Cancer Awareness Month at Duke Children’s at the annual handprint ceremony. Duke Children’s patient Ady Brickhouse, 4, adds her handprint to the many others on the coat of her doctor, Dan Wechsler, MD, chief of pediatric hematology-oncology.

   Hyundai awarded Duke Children’s a $250,000 grant for pediatric cancer research. The grant funds will support the research of Michael Armstrong, MD, in neuroblastoma.

2. Duke Children’s Gala raises a smile
   *The Duke Children’s Gala*
   Brought together over 350 friends, supporters, and faculty at the Washington Duke Inn on March 24. With the theme “Raise a Smile,” the event was a tremendous success.

3. Healthy lifestyles
   *Durham kids and their parents learned about wellness and healthy eating, just in time for back to school.*
   At an event hosted by *Duke Children’s Healthy Lifestyles and Kohl’s Bull City Fit* on August 18, roughly 80 participants learned tips for packing healthy school lunches and staying fit. In this photo, Lili Andade-Hernandez and her father Cesar Izaguirre (background) learn a new exercise.

4. Thanks for your call
   *Hosted by MIX 101.5, Radiothon for Duke Children’s* was held in April 2015. Several patients and hosts from the “Gene & Julie Show” presented a check for more than $563,508—the total amount raised during the live two-day broadcast. Funds raised each year through the radiothon support medical specialties, clinical research, and patient and family services and programs.

5. We all scream for ice cream
   *Duke Children’s patients and their families were among the millions who participated in Dairy Queen Miracle Treat Day on July 30.*
   In addition to donating the proceeds from every blizzard sold that day, Triangle Dairy Queen owner Andrew Valkanoff also brought 400 ice cream treats to the hospital to share with the kids, families, nurses, doctors, and staff.
BOUNCING ALONG

6 $1 million and counting
Associates from 112 Walmart and Sam’s Club stores in the Triangle, Triad, and Wilmington areas gathered on April 22, 2015, to kick off Walmart and Sam’s Club Day, an annual miracle balloon fundraising campaign that takes place each spring.

This year’s kickoff event focused on cardiac care and research, care, and education. Walmart and Sam’s Club stores in the Duke area are on target to exceed their fundraising results from 2014 with more than $1.25 million raised in 2015 to date.

7 They braved the shave
Jacob Goeders, 13, and his dad Todd celebrate one year of Jacob being off treatments for leukemia by getting their heads shaved. Jacob wanted to raise $1,206 to match the days he was on treatment, but ended up with twice that amount.

8 For the kids!
The Dance Marathon programs at Elon University and N.C. State University soared to new heights this year, raising $180,086 and $67,001, respectively, in support of Duke Children’s. Elon’s program, Elonthon, is entering its 13th year, and N.C. State’s program is entering its fourth year. Duke University hosted its third Dance Marathon event on November 7, 2015.

9 A very happy reunion
Families of former Duke Intensive Care Nursery patients came together on Saturday, May 30, at the Museum of Life + Science. Over 350 families attended the free event to reunite with the ICN staff who cared for their babies and to connect with other families they met in the hospital.

10 Tee-time traditions
In July 2015 over 300 people celebrated the 30th anniversary of the Jim Valvano Kids Klassic at the Washington Duke Inn & Golf Club. This annual event raises money and awareness for pediatric cancer programs at Duke Children’s. Weekend activities included a silent auction and dinner on Friday night, and golf, a cocktail party, and dancing with the Band of Oz on Saturday. This year’s program paid tribute to the late Don Shea, a dedicated volunteer and founder and co-chair of the Jim Valvano Kids Klassic.
YOUR LEGACY CAN HELP SICK CHILDREN

You can make a gift that benefits children in the future and provides income to you now. An irrevocable gift of $10,000 or more to Duke Children’s will give you fixed lifetime income and an income tax charitable deduction.

It’s easy to establish a charitable gift annuity. We will do all the paperwork for you and manage the funds. Duke agrees to pay you a fixed amount each year for the rest of your life.

Sample payment rates

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Sample payment rates based on a donation of $20,000. Rates do not change once the annuity is established.

TO LEARN MORE, CONTACT US AT 919-385-3114 OR JOSEPH.TYNAN@DUKE.EDU.