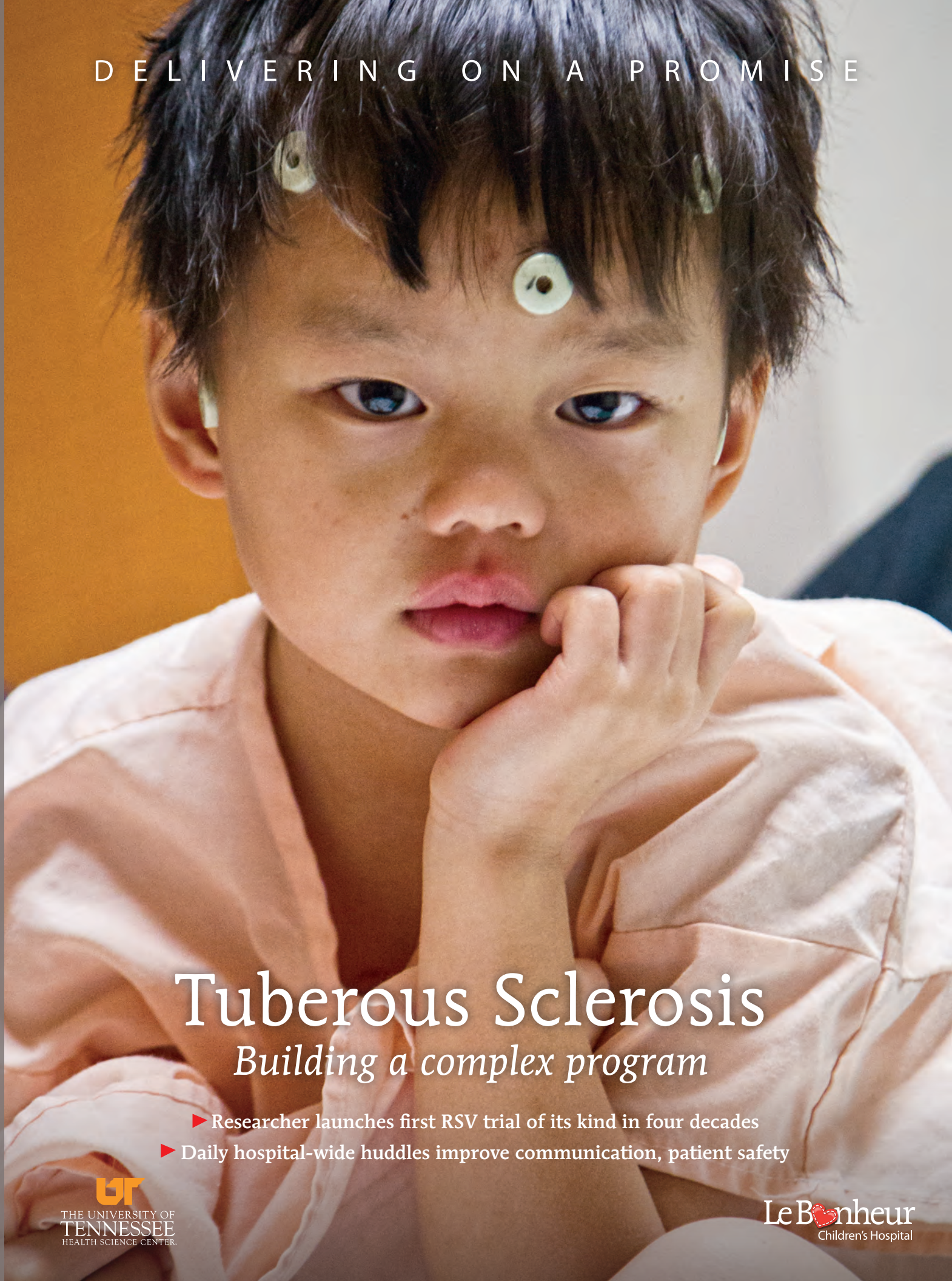
SPRING 2016

DELIVERING ON A PROMISE



Tuberous Sclerosis

Building a complex program

- Researcher launches first RSV trial of its kind in four decades
- Daily hospital-wide huddles improve communication, patient safety

THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

Le Bonheur Children's Hospital

LE BONHEUR EARNS TOP STS RATING

Heart Institute one of 10 programs to receive highest quality rating

Le Bonheur's Heart Institute recently received the highest possible rating, three stars, from The Society of Thoracic Surgeons (STS). Only 10 of the STS's 117 participating programs received three-stars in the Fall 2015 STS Congenital Heart Surgery Database Feedback Report. The three-star rating is awarded for excellence in cardiac surgery outcomes in a four-year period from 2011-2014.

The STS Congenital Heart Surgery Database compiles data from pediatric heart programs across the country and publishes surgical outcome information twice a year. Participating programs receive a one- to three-star rating semi-annually. The ratings are based on STS's mortality risk model, which takes into account the hospital's number of actual mortalities versus expected mortalities for a certain illness or condition.

The average survival rates for the majority of heart surgeries at Le Bonheur are considerably higher than the national average – especially in the most complex like the Norwood procedure – according to the STS report.

Le Bonheur publishes heart surgical outcome information on its website for families to see at www.lebonheur.org/heartoutcomes.

From left, Heart Institute executive co-directors Jeffrey Towbin, MD, chief of Pediatric Cardiology, and Christopher Knott-Craig, MD, chief of Pediatric Cardiovascular Surgery

Le Bonheur Children's Hospital

BEST CHILDREN'S HOSPITALS U.S. News & World Report RANKED IN 5 SPECIALTIES 2015-16

Le Bonheur Children's Hospital in Memphis, Tenn., treats more than 250,000 children each year in regional clinics and a 255-bed hospital that features state-of-the-art technology and family-friendly resources. Our medical staff of more than 240 physicians provide care in 40 subspecialties.

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

LE BONHEUR LEADERSHIP

Meri Armour – *President and CEO*
Jon McCullers, MD – *Pediatrician-in-Chief*
James "Trey" Eubanks, MD – *Surgeon-in-Chief*
Harris Cohen, MD – *Radiologist-in-Chief*

THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER.

The primary pediatric teaching affiliate of the University of Tennessee Health Science Center, College of Medicine

In this issue:

THE COVER:
Rinnie Pegg, 5, is a patient of Le Bonheur's Tuberous Sclerosis Center of Excellence. *Read her story on page 9.*

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TUBEROUS SCLEROSIS

Building a complex program

For Maddie Lens, it started with a slight jerk of the head, as she threw her hands up.

At first, Maddie's parents, Chris and Heather Lens, weren't overly concerned. But as the day went on, the spasms, later identified as seizures, grew in frequency. The first-time parents knew something was wrong.

Within 36 hours of her first seizure, and after a series of tests administered by doctors in Tulsa, Okla., Maddie was diagnosed with Tuberous Sclerosis Complex, or TSC. This genetic disorder causes tumors, or tubers, to form on a person's organs, primarily on the brain, eyes, heart, kidneys, skin and lungs. The tubers on Maddie's brain were causing seizures, but doctors also found them growing on her kidneys, heart and skin.

The news, Chris and Heather said, was crushing.

"When you have a child, you're excited about their future – is she going to be a cheerleader, what kind of car is she going to drive. When we got that diagnosis, it almost felt like those things were being ripped away from us," Heather said. "We had no clue what her future was going to look like."

Maddie is one of approximately 50,000 people in the United States living with TSC, according to the national Tuberous Sclerosis Alliance. On average, two newborns a day will be diagnosed with Tuberous Sclerosis Complex, or roughly one out of 6,000 births. Nearly 1 million people worldwide have been diagnosed with the condition.

When doctors in Oklahoma decided last fall surgery was necessary to control Maddie's seizures, the Lens family was referred to Le Bonheur. Under the care of the hospital's TSC specialists, Maddie underwent two

tumor

Neurologist James Wheless, MD, examines TS patient Maddie Lens. Wheless, co-director of Le Bonheur's Neuroscience Institute, also serves as co-director of the hospital's TS Center of Excellence.

surgeries in November to remove the tubers causing her seizures.

In the past decade, Le Bonheur has dedicated resources to expand its TSC research program, recruited targeted specialists, clinicians and researchers and adopted new technology that can be life-altering for patients like Maddie.

BUILDING A TUBEROUS SCLEROSIS COMPLEX PROGRAM

Because early diagnosis of Tuberous Sclerosis Complex is vital, Le Bonheur has recruited sought-after TSC experts, including neurologists, dermatologists, nephrologists and developmental pediatricians, each who specialize in treating the organs affected by the disease.

Building a comprehensive TSC program began, in part, with the recruitment of John Bissler, MD, co-director of Le Bonheur's Tuberous Sclerosis Center of Excellence. Le Bonheur leaders recruited Bissler more than two years ago from Cincinnati Children's Hospital Medical Center.

Leading the hospital's Pediatric Nephrology group, Bissler focuses on helping his patients manage the lesions growing on their kidneys and finding effective treatments that help slow tumor growth. Tuberous Sclerosis is a genetic disease that can be inherited from one parent with TSC or can result from a spontaneous genetic mutation. If a parent has TSC, the child has a 50 percent chance of inheriting the condition.

John Bissler, MD, co-director of Le Bonheur's Tuberous Sclerosis Center of Excellence, is intent on building a comprehensive program to tackle the disease.

> *"Tuberous Sclerosis is a disease that can affect every single organ in the body, and we really need to deliver care that is coordinated with every subspecialty. That is absolutely critical."*
>
> John Bissler, MD
> co-director of Le Bonheur's TS Center of Excellence

Researchers have found that two distinct genes cause TSC, and only one gene needs to be affected for the disease to be present. Both genes, when functioning normally, suppress tumor growth and carefully regulate cell growth through inhibition of the protein called mammalian

Watch Maddie Lens' story –
www.lebonheur.org/promise

Finding Support

TS mom forms Facebook support group to help other parents

When Brittany and Ryan Schwaigert's son, Greyson, was diagnosed with Tuberous Sclerosis Complex at 3 months old, the news was devastating.

The Schwaigerts first noticed Greyson's TS symptoms when he began having spasms. At first they thought it was nothing serious, but when the couple began talking with their parents and researching online, they learned he was suffering from infantile spasms. An MRI revealed tubers on Greyson's brain, and he was diagnosed with Tuberous Sclerosis. Greyson also has tumors on his eyes, skin lesions and suffers with polycystic kidney disease.

"It's like a Mack truck hitting you," Brittany said. "You Google it, and it's the scariest thing. We didn't know what to expect. We didn't know what would be in store for him."

But the Schwaigert family was determined to help their son live a normal and healthy life. It was a disease the Collierville, Tenn., family never heard of prior to their son being diagnosed more than seven years ago.

"We sat down and said, 'This isn't going to get the best of us. We're not going to let this win,'" Brittany said. "So we started getting really active with the Tuberous Sclerosis Alliance … we started educating ourselves as much as possible."

That education led Brittany to reach out on social media, connecting with other TS parents from around the world and listening to their stories and heartaches. Soon after, Brittany created the TS Mommies Facebook group, a place where TS moms can offer support, discuss medical questions and share their feelings.

In addition to information the Schwaigerts learned from other TS parents, the couple decided John Bissler, MD, and James Wheless, MD, who serve as co-directors of Le Bonheur's Tuberous Sclerosis Center of Excellence, should care for Greyson's TS. Under their watch, Greyson's epilepsy and polycystic kidney disease are kept under control via medication, and his angiofibroma are being treated with specially formulated cream created by Le Bonheur physicians.

"The doctors have been very progressive with his care," Brittany said. "They don't ever hesitate to change his medication if it isn't working."

"This isn't going to get the best of us. We're not going to let this win." Brittany Schwaigert

Greyson continues to visit his doctors twice a year for MRIs, EEGs and kidney ultrasounds. His brain tubers remain unchanged, and over the years the cysts on his kidneys have grown minimally.

Since starting TS Mommies three years ago, the group has grown from 20 mothers to nearly 1,200 members. The Schwaigert family said the group's success is due to mothers being able to speak freely about their child's disease without judgment.

"A lot of them are coming there for support because they have nowhere to go," Brittany said. "It is such an amazing place for mothers to talk with other mothers, and those other mothers can tell them that they are not crazy, and that's so important."

While the group is only open to TS mothers – no grandmothers, aunts or other female relatives – Brittany, who is Le Bonheur's Tuberous Sclerosis Alliance ambassador, said one day she may start a Le Bonheur-only TS Mommies group. A group for fathers with TS children also is a possibility. Because of the care the Schwaigert family received at Le Bonheur, both Ryan and Brittany now volunteer on the hospital's Family Partners Council.

TS Mommies, Brittany said, has helped countless families from around the world, including Heather and Chris Lens of Westville, Okla.

"The information we gained and the support we gained has been incredible," Heather Lens said. "Being able to meet people online and getting valuable information so quickly was a huge help. It was so nice knowing someone else had been there and done it and that we could get through it and be okay."

target of rapamycin (mTOR). Mutations in either gene can cause cells to divide excessively, which can lead to lesions throughout the body.

"Tuberous Sclerosis is a disease that can affect every single organ in the body, and we really need to deliver care that is coordinated with every subspecialty. That is absolutely critical," Bissler said. "Having a place that is centrally located makes it easier for patients and their families who can come through Memphis."

Building a comprehensive TSC clinic was the goal for James Wheless, MD, Le Bonheur's chief of Neurology and co-director of Le Bonheur's Neuroscience Institute and TSC Center of Excellence. An expert in TSC himself, Wheless was instrumental in recruiting Bissler to join him. In the past five years, nearly a dozen faculty members have been recruited to Le Bonheur to focus on specific subspecialties that help manage a patient's TSC symptoms. By this summer, Wheless said he expects the medical staff to grow to 16, which will benefit the needs of all the patients who visit Le Bonheur's TSC clinic each year. The program is now attracting TSC patients from across the country and around the world.

Sarah Weatherspoon, MD, a Le Bonheur neurologist, was recruited in 2013 from Cincinnati Children's Hospital Medical Center, where she completed her residency and fellowship training. Weatherspoon, who specializes in TSC-related epilepsy, said she was excited to work at a "major center that attracts patients from all over the country."

"I wanted to be at an epilepsy center that provided

IDENTIFYING TUBEROUS SCLEROSIS COMPLEX

Symptoms of tuberous sclerosis include tumors or lesions that grow on parts of the body, most commonly on the skin, kidneys, brain, heart, eyes and lungs, according to the national Tuberous Sclerosis Alliance. The severity of TSC can range from mild skin abnormalities, and in severe cases, mental retardation or renal failure.

Skin abnormalities: Individuals with TSC often have skin growths on the face, body and nails. The growths, which can appear as patches of discolored skin or tumors on the face, are mostly harmless.

Brain: The most common affect is epilepsy or seizures. Seizures occur in approximately 85 percent of TSC patients. If a giant cell astrocytoma grows large enough, it can block the flow of fluid inside the ventricles of the brain, and the tumor will have to be removed or the ventricles shunted. Symptoms include vomiting, nausea and headaches as well as changes in appetite, behavior and mood.

Heart: Cardiac tumors are typically largest at birth and may shrink or disappear as the individuals grow older. Lungs: The three main pulmonary lesions found are lymphangioleiomyomatosis (LAM), multifocal micronodular pneumocyte hyperplasia and clear cell tumors. LAM is the most common. The average age of onset is 32–34 years old, and lung involvement is usually a manifestation of TSC in women. The first symptoms of lung involvement in an individual with TSC may be shortness of breath after mild exercise, spontaneous pneumothorax or coughing. Progression to pulmonary failure may develop, but not usually until the third or fourth decade of life. Some individuals will require a lung transplant.

Behavioral issues: Symptoms may include aggression, sudden rage, hyperactivity, attention deficit, acting out, obsessive-compulsive behavior, repetitive behaviors, being nonverbal and other autistic behaviors. Occasionally, individuals with TSC are also diagnosed with schizophrenia, bipolar disease, depression or other psychiatric disorders.

Eye abnormalities: The appearance of retinal lesions varies from mulberry lesions to plaque-like hamartoma. Retinal hamartoma, a defect in the pigment of the iris, has been observed in some. White depigmented patches also have been observed on the retina.

Other organs: Cysts and tumors sometimes appear in the liver, lung, pancreas and other organs.

*Tuberous Sclerosis Alliance

John Bissler, MD, has spent much of his career working to find treatment options for patients like Chloe Bredeson with tuberous sclerosis.

the latest treatments for patients, including clinical trials as well as procedures such as magnetoencephalography, transcranial magnetic stimulation and others as part of an epilepsy surgery evaluation," Weatherspoon said.

In addition to Weatherspoon, Wheless said recruiting additional talent, including Chief of Dermatology Teresa Wright, MD, Neurologist Stephen Fulton, MD, and Neuro-ophthalmologist Lauren Ditta, MD, helps create comprehensive care where TSC patients can visit multiple specialists in one visit.

"The program has expanded dramatically not only in scope of what we are able to offer but also in the recent number of kids in the area we are taking care of," Wheless said.

SEARCHING FOR A CURE

Although there is no known cure for TSC, specialized treatment can help manage specific signs and symptoms. At Le Bonheur, Bissler recently published a multi-center follow-up study on TS and lymphangioleiomyomatosis

There is no known cure for TSC. Individualized treatment can help manage specific symptoms of the disease.

(LAM) patients on mammalian target of rapamycin (mTOR) inhibitors for a renal angiomyolipomata. His findings: the drug is safe for patients and proved to be an effective way to decrease the amount of tumor growth.

Bissler began his tumor therapy work a decade ago with the discovery that mTOR helped reduce the size of renal angiomyolipoma, which is found in approximately 80 percent of TS patients. The original trial was published by Bissler in the *New England Journal of Medicine* in 2008 and followed patients on sirolimus. A follow-up *Lancet* study in 2013 showed more than 40 percent of patients on AFINTOR® (everolimus) had a 50 percent reduction in tumor size after a three-month period.

Bissler conducted another trial and examined long-term results, an average of 28.9 months, for 112 patients on everolimus for their angiomyolipomata, and nearly 82 percent of patients experienced a tumor shrinkage of 30 percent or more. Slightly more than 64 percent of patients experienced tumor shrinkage of half or more by week

Rinnie Pegg: TSC

By all accounts, Rinnie Pegg is your typical 5-year-old.

She likes to play video games – Nintendo's Smash Brothers is one of her favorites – with her older siblings, Bryson and Katie. She's talkative, likes arts and crafts projects and putting together puzzles. But when her parents, Elizabeth and Clark Pegg of Peachtree City, Ga., decided to adopt Rinnie more than two years ago, they knew she had serious medical conditions.

Prior to adopting Rinnie from the Jiangxi province in November 2013, her doctors diagnosed her with congenital heart disease. But when the Peggs brought their daughter to the United States, their cardiologist in Atlanta spotted tumors on her heart. Doctors also found tubers on her brain and kidneys and lesions on her skin. She was officially diagnosed with Tuberous Sclerosis Complex.

The tubers on her brain caused Rinnie to have up to 50 seizures a day, and cysts on her kidneys have led to early Stage 1 kidney failure, which, one day, may force the 5-year-old to undergo a kidney transplant.

In the beginning, the Peggs were able to control Rinnie's seizures with medication. But once the medications were no longer effective, the Peggs began researching and asking other TS parents for suggestions on the best TS doctors in the country. The family chose to send their daughter to Le Bonheur.

"The last two years it's just been going in and out of hospitals, traveling to multiple states, traveling everywhere trying to find her the best care," Elizabeth said. "Then we found Le Bonheur."

In January, Le Bonheur Chair of Pediatric Neuro surgery Frederick Boop, MD, performed a craniotomy to remove the tuber on Rinnie's right parietal lobe to control her seizures. After removing a quarter-sized piece of Rinnie's brain, she has been seizure free.

"Rinnie is just doing amazing," Elizabeth said. "She is consistently so much happier since the surgery."

TSC patient Rinnie Pegg underwent a right parietal craniotomy in January to remove a tuber and help control her seizures.

Learn more about Rinnie's story –
www.lebonheur.org/promise

Chair of Neurosurgery Frederick Boop, MD, checks in on Rinnie Pegg before she goes into surgery. In January, Rinnie had a small portion of her brain removed to help eliminate seizures caused by Tuberous Sclerosis.

Research has shown surgery sometimes helps control seizures caused by brain lesions that don't respond well to medication. Surgical procedures, such as laser treatment, may improve the appearance of skin lesions. With appropriate care, Bissler said many TS patients are able to enjoy a normal life expectancy, although careful monitoring and follow-ups are necessary.

Educational therapy is used to offset developmental delays or psychological therapy can help a person cope and adjust to living with the disease.

96. The drug also improved seizure activity and improve neurocognition for TS patients.

Aside from medications, surgery also can be an effective treatment for TS patients. Angiomyolipomata tumors can have their blood supplies interupted by a precedure called embolization. Bissler has the largest experience with this procedure in TSC patients.

USING TELEHEALTH

In addition to recruiting more specialists and clinicians, Bissler said telehealth, where Le Bonheur doctors can meet with their patients via a computer, smartphone or tablet, will be a key component for the program's future.

The goal is simple: reduce and limit travel time for patients and their families and give them the ability to speak with their doctors without having to leave their homes. With Le Bonheur's new telehealth program, patients can have digital, face-to-face consultations with their doctors, no matter where they are in the world.

"I want to build a personal relationship that doesn't create the unbelievable financial burden for the patients to travel, the loss of work or babysitters," Bissler said. "I've had patients tell me the bills they paid to come see me are 10 percent of their costs for the visit. The travel aspect is huge. I'd like to eliminate that. I'd like to eliminate that financial burden of the family too."

"We can help fill the gap for patients who cannot come to a (TS) center."

John Bissler, MD,
on using telemedicine in the TSC Center

Besides reducing the amount of travel for patients and their families, telemedicine helps facilitate better communication between physicians, Bissler said. No longer will doctors have to sift through or read through numerous emails, faxed documents or physician notes. Instead, the doctors can easily communicate with each other over the Internet.

In early January, Bissler conducted several

MEET THE TEAM

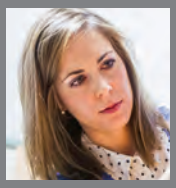
John Bissler, MD – FedEx Chair of Excellence Director, TS Center of Excellence Director, Division of Nephrology at St. Jude, Le Bonheur professor of pediatrics

James Wheless, MD – Professor and Chief of Pediatric Neurology, Le Bonheur Chair in Pediatric Neurology, University of Tennessee Health Science Center, Co- Director, Neuroscience Institute, Director, Le Bonheur Comprehensive Epilepsy Program, Co-Director, Tuberous Sclerosis Center of Excellence, Le Bonheur Children's Hospital

Frederick Boop, MD – Co-Director, Neuroscience Institute, Medical Director, Neurosurgical ICU, Le Bonheur Children's Hospital, Professor and Chairman, Department of Neurosurgery, University of Tennessee Health Science Center, Chief of the Division of Pediatric Neurosurgery, St. Jude Children's Research Hospital

Thomas Yohannan, MD – Pediatric Cardiology Assistant Professor, University of Tennessee Health Science Center

Ashley Pounders, RN, BSN, CCRN – TSC Clinical Coordinator, Le Bonheur Children's Hospital



Lauren Ditta, MD – Pediatric Neuro-Ophthalmology Assistant Professor, University of Tennessee Health Science Center

Teresa Wright, MD – Chief of Pediatric Dermatology, Le Bonheur Children's Hospital Associate Professor, University of Tennessee Health Science Center

Tonia Gardner, MD – Pediatric Pulmonology Assistant Professor, University of Tennessee Health Science Center

Stephen Fulton, MD – Pediatric Neurology Assistant Professor, University of Tennessee Health Science Center

Sarah Weatherspoon, MD – Pediatric Neurology Assistant Professor, University of Tennessee Health Science Center

Stephanie Einhaus, MD – Pediatric Neurosurgery Assistant Professor, University of Tennessee Health Science Center

consultations using telehealth technology. During one checkup, Bissler, who was broadcasting from his home office in the Memphis area, was able to speak with his patient in Hong Kong, along with the patient's doctor who lives in China. In another case, Bissler was able to visit with a patient who lives in Australia. With Le Bonheur's adoption of telehealth technology, doctors will have quick, global communication with their patients.

"I will be able to deliver care and communicate the issues with the patient and their physician simultaneously," Bissler said. "We can help fill the gap for patients who cannot come to a (TS) center."

Bissler believes telehealth technology will help create more advanced TS clinics, providing better care for everyone.

"Memphis is unique in that it has an extraordinary combined pediatrics residency program, and so I would like to dovetail off of that and develop clinics, and recruit physicians in different subspecialties that can care for the TS population," Bissler said. "If we develop training programs for TS specialists, they can go out and take better care of the community at large, globally."

Chris and Heather Lens say Le Bonheur has helped their 3-year-old, Maddie, achieve a better quality of life.

And building one of the country's best TSC clinics at Le Bonheur is what Chris and Heather Lens is hoping for. Both said Maddie's care at Le Bonheur has helped the 3-year-old achieve a better quality of life, and after two successful surgeries in November, it's been more than three months since her last seizure. Her communication abilities have doubled, Maddie's parents said.

"To be able to wake up in the morning and act like nothing is wrong, it's surreal because it took a few weeks to realize that this is our normal life," Chris said. "There are times now that I forget, until I see that scar, she had brain surgery, and she's just a normal little girl now."

ON TRIAL

Researcher launches first RSV trial of its kind in four decades

Scientists at Le Bonheur Children's are leading the first U.S. pediatric clinical trial of a new respiratory syncytial virus (RSV) antiviral in nearly 40 years, after demonstrating the new drug concept's success in fighting RSV in healthy adults.

The multinational study will recruit patients at medical centers around the world and will be led by Le Bonheur's John DeVincenzo, MD, medical director of Le Bonheur's Molecular Diagnostics and Virology Laboratories, and internationally recognized respiratory virus researcher in Le Bonheur's Children's Foundation Research Institute.

DeVincenzo published his findings on the study of antiviral therapy ALS-008176 in the November edition of

(above) Three-month-old Taylor Gresham was the first patient enrolled in a clinical trial of the RSV antiviral ALS-008176. The study is the first pediatric trial of its kind in the United States in nearly 40 years.

the *New England Journal of Medicine*. Findings showed that the drug safely and very rapidly stopped viral replication, reduced viral load, and reduced the symptoms of the infection in adults experimentally infected with an infant's RSV virus. Reducing the viral load likely will reduce the disease severity in children, said DeVincenzo, who also serves as professor of Pediatrics, and professor of Microbiology, Immunology and Biochemistry at the University of Tennessee Health Science Center (UTHSC).

> *"Findings showed that the drug safely and very rapidly stopped viral replication, reduced viral load, and reduced the symptoms of the infection."*
>
> John DeVincenzo, MD
> director of Molecular Diagnostics
> and Virology Laboratories

Steven and Masey Gresham's 3-month-old son, Taylor, was the first Le Bonheur patient to receive the ALS-008176 drug in early February.

Taylor's symptoms: severe cough, difficulty breathing and the inability to to keep his eyes open for long periods or get enough oxygen from his lungs. When Le Bonheur doctors suggested treating Taylor's RSV with the new antiviral drug, the Holly Springs, Miss., residents agreed.

Masey Gresham says her son, Taylor, quickly improved after he received the RSV antiviral study drug.

"Seeing him lying in bed with eight tubes coming out of him, opening his eyes just a few times a day because he was so weak was heartbreaking," Steven said. "We felt it was the right thing to do. If we could save countless other children from having to suffer, or even possibly future brothers and sisters from having to endure this, it would be worth it."

In the last 15 years, Le Bonheur has been part of numerous experimental therapeutic advancements, developmental pathways and antiviral therapies to find a cure for RSV.

The medicine, ALS-008176, was developed by Alios Biopharma Inc., in collaboration with laboratories at Le Bonheur Children's Hospital and physicians from UTHSC and may lead to more effective methods for doctors to treat RSV.

"ALS-008176 can inhibit the replication of RSV even if the cells of the respiratory tract have already been infected with the virus," DeVincenzo said. "As a result, this treatment has a very profound antiviral effect, which is likely to be effective even if started at a later stage of RSV infection."

RSV is the most common cause of lower respiratory tract infections in young children worldwide, and there's currently no vaccine or effective treatment available. Almost every child will get the virus by his or her second birthday, and RSV will cause 25-40 percent of children to develop bronchiolitis or pneumonia. Infants who are hospitalized due to RSV often develop asthma that persists into

John DeVincenzo, MD, administers ALS-008176 to 3-month-old Taylor Gresham. DeVincenzo has spent his career studying RSV and currently has four antiviral programs in development.

adulthood. Each year, approximately 125,000 children are hospitalized in the United States, according to the Centers for Disease Control and Prevention (CDC). In 2013, the virus caused 1.5 million pediatric outpatient visits.

With Le Bonheur leading the way to finding more effective treatments for RSV, the Greshams are hopeful that ALS-008176 will one day lead to a cure. Although Taylor may have received a placebo medicine or the real drug, when Le Bonheur physicians began administering the experimental medicine to him, his health quickly improved.

"He's doing great," Steven said. "One of the nurses is convinced because she's never seen such a quick turnaround in a baby his age."

Learn more about Dr. DeVincenzo's RSV work –
www.lebonheur.org/promise

Endocrinology chief aims to build top diabetes program

When pediatric endocrinologist Ramin Alemzadeh, MD, joined Le Bonheur in summer 2015, he envisioned creating a team-based program to help children living with diabetes.

Teamwork, Alemzadeh explained, is a key factor to building one of the country's best pediatric diabetes programs.

Alemzadeh, who last July was named chief of Pediatric Endocrinology at Le Bonheur, specializes in management of type 1 and 2 diabetes, lipid disorders, metabolic bone disorders, polycystic ovary syndrome, disorders of growth and puberty and adrenal disorders. He comes to Memphis from the University of Illinois-Chicago where he was chief of the Division of Pediatric Endocrinology and Diabetes.

Division Chief of Pediatric Endocrinology, Le Bonheur Children's Hospital

Professor, Department of Pediatrics,
The University of Tennessee Health Science Center

Creating one of the nation's best diabetes centers and expanding Le Bonheur's educational programs for families motivates Alemzadeh. He was drawn to diabetes care since its etiology is not clearly understood and hopes to help his patients better manage the disease.

"I have great regard for families who manage the day-to-day challenges with children who have type 1 diabetes," he said. "It's really about taking care of these families and providing a lot of support so they can navigate through the challenges of diabetes and make them successful adults. Our challenge is to provide the best care and also provide the tools and skill sets so they can become independent and are able to manage their diabetes as young adults and later."

Endocrinology fellow Nader Kasim, MD, joined Le Bonheur in 2014 and has been on board with Alemzadeh's priorities, which include streamlining patient care for newly diagnosed children with outpatient treatment. Previously, all new onset diabetics were admitted for an overnight stay in the hospital. But reducing or eliminating the need for an overnight stay helps relieve the burdens on families and also creates a "stress-free and reassuring environment."

Alemzadeh also pioneered a team-based, multi-

disciplinary approach where nurses, dietitians, psychologists and physicians provide diabetes education and support for children and their families.

"He is striving toward integrating the multi-disciplinary teams that are a necessity for diabetes care," Kasim said. "He is attempting to streamline the care for patients such that most of their needs can be addressed within one visit."

The program is also training nurses to be diabetes educators.

"A clinic visit by a child and their family consists of initial evaluation by a nurse, followed by a dietitian and then by a physician or nurse practitioner," Alemzadeh said. "When you are dealing with a chronic disease like diabetes, it's not just a physician, but a team that can provide a lot of input and also strategically provide education."

"Our challenge is to provide the best care and also provide the tools and skill sets so they can become independent and are able to manage their diabetes as young adults and later."

Ramin Alemzadeh, MD
chief of Pediatric Endocrinology

That education, Alemzadeh hopes, will lead to a healthier community and better preventative care of type 1 and 2 diabetes.

"He is unifying the division by creating protocols such that care can be seamless and unified among providers," Kasim said. "His multi-disciplinary approach is also bringing improved diabetes care."

Alemzadeh also has co-authored more than 60 publications in various medical journals, is the former the director of the children's hospital diabetes program at Medical College of Wisconsin and the former director of pediatric endocrine and diabetes with the University of Tennessee Health Science Center in the 90s. At Le Bonheur, he also plans to recruit more faculty and staff to help develop research and programs. Expanding the program also includes the hiring of Christy Foster, MD, a current fellow who will officially join in July.

"We hope that we are providing diabetes control for children in this area because while everybody is waiting for a cure of diabetes, we cannot afford having kids in poor control," Alemzadeh said. "We've shown through studies that when you are able to control children's blood sugar levels you can actually prevent complications of diabetes. It shows conclusively that you can prevent it."

Ramin Alemzadeh, MD

Education and Training

- North Shore University Hospital/Cornell University Medical College, fellowship in pediatric endocrinology, metabolism and nutrition
- Newark Beth Israel Medical Center, pediatrics
- North Middlesex Hospital, internship in surgery and medicine
- St. George's University School of Medicine, medicine

Recent Experience

- Professor and chief, division of pediatric endocrinology and diabetes University of Illinois at Chicago (2011-2015)
- Director, children's hospital diabetes program Medical College of Wisconsin (1999-2011)
- Director, pediatric endocrine and diabetes University of Tennessee Health Science Center (1991-1999)

Clinical Focus

- management of type 1 and 2 diabetes
- lipid disorders
- metabolic bone disorders
- polycystic ovary syndrome
- disorders of growth and puberty
- adrenal disorders

TIME OUT

Daily hospital-wide huddles improve communication, patient safety

The concept is simple. Every weekday at 9:05 a.m., leaders from each Le Bonheur Children's Hospital department gather in a conference room to discuss current issues related to patient safety.

The issues vary each day. The pharmacy has issued a drug shortage for PCA vials. The C-arm X-ray machine is inoperable. Isolation gowns are on backorder.

The daily 15-minute huddle, called a Daily Safety Brief, has improved interdepartmental communication and reduced the time it takes to resolve safety-related issues since it was implemented in April 2015.

The idea is quickly becoming a best practice for children's hospitals nationwide.

"It's about bringing the right people together for a focused, deliberate report about safety events and risks," said Donna Vickery, director of Quality and Performance Improvement at Le Bonheur Children's.

A look back, a look ahead

For each brief, one leader from every department comes prepared to report on any significant safety or quality issues that have occurred in the last 24 hours – and any issues expected to occur within the next 24 hours. Issues might include critical drug shortages, missing or inoperative equipment or personnel shortages.

At one of the first Daily Safety Briefs at Le Bonheur, a representative from radiology reported that a piece of

Members of each Le Bonheur department gather every morning at 9:05 a.m. to discuss patient safety-related issues.

diagnostic equipment had been inoperative for two months. The equipment was repaired that very day after being brought to the group's attention, said Vickery.

Departments say the daily briefings help staff to plan their day, knowing what issues — like product shortages or staffing problems — are happening throughout the hospital.

The group also discusses any "watchers" – patients deemed to be at highest risk and in need of special interdisciplinary communication and planning.

"The discussions give anyone a structured way to escalate care as needed," said Vickery. "It helps departments better plan their day."

Reported issues are prioritized and categorized as green, yellow or red. Red issues are most critical to patient safety. Problems are assigned owners with timeframe for resolution.

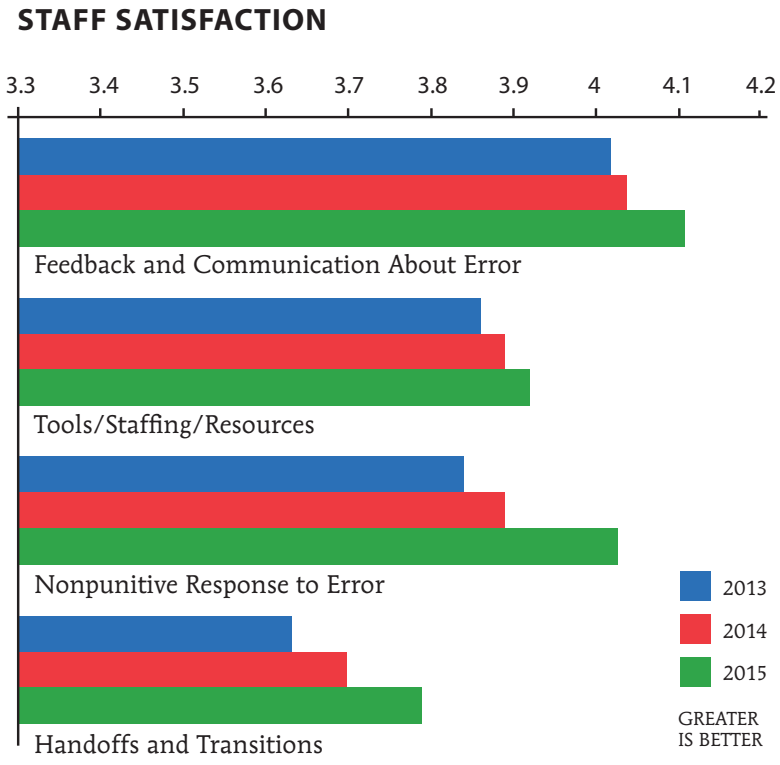
Eight months after implementing Daily Safety Briefs more than 70 reported safety-related issues had been resolved.

Situational awareness

The daily briefings are part of a larger focus of becoming a high reliability organization – a safe hospital with zero patient harm events. And part of high reliability means

Daily Safety Briefs at a glance

- Monday through Friday, 9:05 a.m.; 15 minutes
- One leader from each department attends
- Led by Administrator on Call
- Look back, look ahead: Discuss issues from last 24 hours and anticipated issues in the next 24 hours
- Problems are assigned owners with timeframe for resolution
- Purpose: early identification and resolution of problems and shared situational awareness



Le Bonheur Children's 2015 Associate Feedback Survey showed improved responses in 2015 to questions about feedback and communication, non-punitive response to error and handoffs and transitions. Daily Safety Briefs were implemented to focus on immediate needs and provide rapid response time.

improving staff's situational awareness, said Bill May, MD, Le Bonheur's chief medical officer.

A concept initially formalized by the United States Air Force decades ago, situational awareness is now used in numerous other high-risk industries. In health care, the idea is that situational awareness – or knowing what's going on within your environment – helps clinicians make better decisions and deliver safe patient care.

> *"It's about bringing the right people together for a focused, deliberate report about safety events and risks."*
>
> Donna Vickery
> director of Quality and Performance Improvement

"It is important that we are all aware of the status of our facility and its capabilities to deliver efficient and safe care to our patients," said May. "The briefings align with our mission and purpose to take care of kids and not cause them harm."

May continues to receive positive feedback from staff about the Daily Safety Briefs. Clinicians appreciate that the discussions help break down silos, allowing them to pool ideas and resources to solve problems.

"Our safety team is multidisciplinary. These meetings allow us to know what our current challenges are and allow us to provide the safest care possible to our patients. The collaboration that occurs is outstanding," said Cynthia Cross, MD, medical director of the Hospitalist program at Le Bonheur.

The 2015 annual survey measuring staff satisfaction at Le Bonheur reported improved responses to questions about feedback and communication, non-punitive response to error and handoffs and transitions.

"We've created more transparency," said Vickery.

Number of patient safety-related issues discussed in Daily Safety Briefs
(issues by department)
April-November 2015

Radiology	**14**
OR/Periop	**13**
Med/surg floors	**8**
Pharmacy	**7**
Lab	**5**
NICU	**5**
SPD	**4**
CVICU	**3**
Peds chiefs	**3**
House	**2**
ED	**2**
Cath lab	**2**
RT	**2**
Rehab	**1**
Biomed	**1**
ECHO	**1**
EVS	**1**
PICU	**1**

Chief Medical Officer Bill May, MD, says he has seen improved communication among departments since the Daily Safety Briefs were implemented last spring. The discussions are helping break down silos, he says.

Finding the obesity gene

Study shows low levels of BDNF protein may cause growing weight problem

Joan Han, MD, (right) and her team of researchers are studying how a person's genetic makeup may predispose them to obesity.

A variation in the gene that produces brain-derived neurotropic factor (BDNF) may have an influence on obesity in both children and adults. The study, funded by the National Institutes of Health and led by Joan Han, MD, director of Le Bonheur's Pediatric Obesity Program, was published in the November issue of *Cell Reports*.

The study found that the less common version of the BDNF gene may predispose people to obesity due to it producing lower levels of BDNF protein, which helps the brain regulate a person's appetite. Han's study also suggests that boosting a person's BDNF protein levels may help someone with the genetic variation. Researchers also reported African Americans and Hispanics are more affected with the gene variation than non-Hispanic Caucasians.

"For people who have obesity, it's a struggle," Han said. "To have an explanation as to why it's so hard to control their body weight, this finding provides reassurance that it's not simply a matter of willpower. It gives them hope that doctors are really listening and

searching for specific treatments based on the cause of the problem. This is one more piece of the larger puzzle for understanding the causes of obesity and how we can address it."

Obesity is a problem particularly prevalent in Tennessee, which ranked 14th in the nation in self-reported obesity rates of 31.2 percent, according to a 2014 report by the Centers for Disease Control and Prevention (CDC), the latest figures. Neighboring states — Alabama, Arkansas, Kentucky and Mississippi — all reported higher obesity rates. Arkansas ranked No. 1 in the nation at 35.9 percent. Colorado had the lowest self-reported obesity rate at 21.3 percent.

In children between ages 2 and 19 years old, the national obesity rate is approximately 17 percent or 12.7 million children. High school obesity rates in Tennessee are higher than the national average of 13.7 percent. In 2013, the most recent numbers from the CDC, Tennessee reported an obesity rate among adolescents of 16.9 percent.

As juvenile obesity rates remain high, the wellbeing of children is at risk, Han says. Obesity can lead to life-long health problems, including high cholesterol, hypertension and diabetes.

Han and her team first analyzed the BDNF gene for naturally occurring genetic changes that alter levels of BDNF productions. After studying brain tissue samples, the team identified an area of the gene where a single change reduced BDNF levels in the hypothalamus, a portion of the brain that helps control body weight and eating. The team then examined the association of this gene variant with obesity in large groups of children and adults, completing analysis in January 2015 of information from more than 30,000 people.

After results were compiled, researchers found that the genetic change wasn't a rare mutation and the variation is common in the general population. Everyone has two copies of each gene, called alleles, and every person inherits a copy from each parent. The study marked

common alleles as "T" and the less common allele, which produces less BDNF protein, as "C."

> ***"We noticed people with the CC version of gene have a lower expression of the appetite suppressing protein BDNF and have a higher risk of being overweight."***
>
> Joan Han, MD
> Pediatric Obesity Program director

Researchers then studied the gene combinations, CC, CT and TT, and found people with the C allele — CT and CT — had a higher body mass index (BMI) than those with TT alleles. Results from the study concluded the C allele may be linked to obesity.

"We noticed people with the CC version of gene have a lower expression of the appetite-suppressing protein BDNF and have a higher risk of being overweight," said Han, who has spent her career studying genetic determinants of obesity in the general population and in patients with rare disorders associated with obesity.

Han and her team also discovered the C allele had trouble interacting with a protein called hnRNP D0B, which normally increases gene expression, so this disruption could explain the problem of lower BDNF production. After finding a possible genetic cause for obesity, Han said providing a scientific explanation for being overweight can be "comforting" for some.

Although genetics may play a role in childhood obesity, environmental factors also can contribute to the problem. Han said some environmental causes include children living a more sedentary lifestyle, increased portion sizes and higher sugar intake.

While Han and her research team may have found a scientific cause to being overweight, she and her fellow doctors at the Pediatric Obesity Program are still finding ways to help battle surging national obesity rates.

"We try to have precision medicine by developing individualized diet and exercise programs and finding specific drugs to treat specific genetic causes of obesity," Han said. "We need to see how each patient responds and learn from it to improve our approach to treating obesity."

Mapping brain function using a multi-modal approach

Researchers test less-invasive methods for pre-surgical brain mapping

Le Bonheur Children's Neuroscience Institute recently tested a multi-modal approach to pre-surgical brain mapping, comparing the combination's validity and precision to the traditional, but more invasive method of cortical stimulation mapping (CSM). Researchers, led by Abbas Babajani–Feremi, PhD, combined high gamma eletrocorticographic (hgECoG) recordings, functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS) to identify function-specific areas of the brain. The study made the cover of the March 2016 edition of *Clinical Neurophysiology*.

Results proved the combination is an effective way to determine which areas of the brain are responsible for specific functions prior to surgery. Finding an alternative to CSM is important, as CSM carries risk of electrically induced seizures and requires patient cooperation, which can be difficult in young or developmentally delayed patients.

"The main aim of our research is to introduce ways of preforming pre-surgical mapping of the brain functions with non-invasive methods," said Andrew C. Papanicolaou, PhD, co-director of the Neuroscience Institute. "We were able to specify the high degree of agreement of the results of the non-invasive method to those of the invasive methods, bringing us closer to the ultimate goal of substituting the methods without any loss in precision."

Babajani-Feremi A1, Narayana S2, Rezaie R3, Choudhri AF4, Fulton SP5, Boop FA6, Wheless JW5, Papanicolaou AC2. Language mapping using high gamma electrocorticography, fMRI, and TMS versus electrocortical stimulation. Clin Neurophysiol. 2016 Mar;127(3):1822-36. doi: 10.1016/j.clinph.2015.11.017. Epub 2015 Nov 26.

Stewardship program uses treatment guidelines, education to cut down on antimicrobial use

Implementation of an Antimicrobial Stewardship Program (ASP) at Le Bonheur Children's Hospital has resulted in a reduction of broad-spectrum antimicrobial use, according to a study published in the March 2016 issue of *Pediatric Critical Care Medicine*.

Infectious Disease Specialists Sandra Arnold, MD, (left) and Bindiya Bagga, MD, (center) helped develop unit-specific guidelines on antimicrobial use.

Strategies recommended for ASPs, including formulary restriction with preauthorization and prospective audit and feedback, can be difficult to implement with limited resources. The ASP team at Le Bonheur Children's developed unit-specific guidelines for treating common infections and used education to reduce overall antibiotic use and unwarranted use of broad-spectrum antimicrobials.

The program, which was implemented in June 2011, focused on Le Bonheur's pediatric, neonatal and cardiac intensive care units, where a baseline review found excessive use of broad-spectrum antibiotics and inconsistency in managing common pediatric infections.

"Antibiotics are a limited, precious resource – it's everyone's responsibility to be good stewards of their use," said Kelley Lee, PharmD, a lead investigator of the study and head of the ASP at Le Bonheur. Results of the program included:

- Reduction of hospital-wide targeted broad-spectrum antibiotic days of therapy (per 1,000 patient days) from 105 per month to 70 per month (33 percent reduction) in the post-implementation year.
- Reduction of targeted broad-spectrum antibiotic days of therapy by 99 percent, 75 percent and 61 percent in the cardiac, pediatric and neonatal ICUs, respectively, after guideline implementation.
- Decrease in annual purchases of most common broad-spectrum antibiotics from $230,059 to $86,887 (62 percent reduction) after guideline implementation.
- Median monthly purchases of most common broad-spectrum antibiotics decreased from $19,398 to $11,043 after implementation.

Le Bonheur launches CMV screening program

The spring, Le Bonheur began its CMV testing program for all newborns. Le Bonheur's parent system, Methodist Le Bonheur Healthcare, is also conducting the screenings.

CMV is a common virus that infects people of all ages, and many who are infected show no symptoms. About one in 150 children is born with congenital CMV. Most babies, 80 percent, with congenital CMV infection appear normal; however, 15 out of 100 babies without symptoms may develop hearing loss by the time they turn 3 years old. Without treatment or monitoring, the child can develop an intellectual disability.

Maria Carrillo-Marquez, MD

Le Bonheur Pediatric Infectious Disease Specialist Maria Carrillo-Marquez, MD, recommends testing children within the first seven days of life and testing involves collecting a saliva sample.

"Identifying babies with congenital infection who are at risk for developmental problems as soon as possible will allow us to provide early interventions for children to reach their maximum potential and to succeed," Carrillo-Marquez said.

Babies with abnormal test results will benefit from a thorough exam and additional testing to check for problems caused by the virus, including microcephaly, eye problems, hearing loss, liver inflammation and low platelets in the blood, among others.

Ongoing hearing damage and problems with development have been shown to improve with treatment using an antiviral medication in some patients. For babies without symptoms or who do not need antiviral treatment, follow-up hearing evaluations will be done until the baby is older.

Hains launches R01 NIH pyelonephritis study

Nephrologist David Hains, MD, is the co-principal investigator on the R01 National Institutes of Health-funded study, "The interface between critical acid-base mediator and the renal bacterial defense."

David Hains, MD

The four-year project will study the kidney's role in the innate defense of the kidney and urinary tract.

Hains and his lab members study antimicrobials within the urinary tract, specifically those that occur in multiple copies. His work founded the Innate Immunity Translational Research Center at Le Bonheur's Children's Foundation Research Institute. Hains and his co-investigator, Andrew Schwaderer, previously identified the murine model of intercalated cell deficiency that is susceptible to pyelonephritis. They have also demonstrated that intercalculated cells are involved in antimicrobial peptide production and secretion.

Hains is also a co-investigator on another NIH-funded grant, "The Impact of Diabetes Mellitus on Antimicrobial Peptide Production and Renal Bacterial Defense."

The study started in October 2015.

Early Success Coalition recognized for 'Community Excellence'

The Shelby County Early Success Coalition (ESC), led by Le Bonheur Children's Hospital, recently received a Governor's Award for Excellence in Early Foundations from the Tennessee Governor's Children's Cabinet.

More than 40 nominations were submitted for the awards, and winners were selected by teams of state employees and community partners based on criteria including family involvement, engagement of community leaders and collaboration across partners and systems. The ESC received the award program's Community Excellence Award.

EARLY SUCCESS COALITION

Le Bonheur Children's Hospital

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Le Bonheur achieves Magnet designation

Hospital receives ultimate nursing credential

Le Bonheur Children's Hospital has received Magnet designation by the American Nurses Credentialing Center (ANCC). Le Bonheur is among only 7 percent of hospitals in the country to have earned the distinction of Magnet status.

"This achievement is a testament to the exceptional care we provide to patients and families every day," said Nikki Polis, chief nursing officer of Le Bonheur Children's Hospital. "We are incredibly proud of our Le Bonheur family for achieving this momentous goal. Magnet is evidence that each and every one of us is committed to providing a higher standard of care for all children in need."

Directed by the ANCC, Magnet recognizes health care organizations for quality patient care, nursing excellence and innovations in professional nursing practice. Consumers rely on the designation as the ultimate credential for high quality patient care.

"Our Magnet journey will continue as we improve upon the care and devotion we show to patients, to families, and to one another," Polis said.

The ANCC Magnet Recognition Program designates health care organizations that demonstrate excellence in nursing practice, adherence to national standards for improving patient care, leadership and sensitivity to cultural and ethnic diversity. Hospitals undergo a rigorous evaluation that includes a document submission and an onsite evaluation of patient care and outcomes. Magnet hospitals must provide an annual status report on their progress and must undergo re-evaluation every four years to retain the designation.