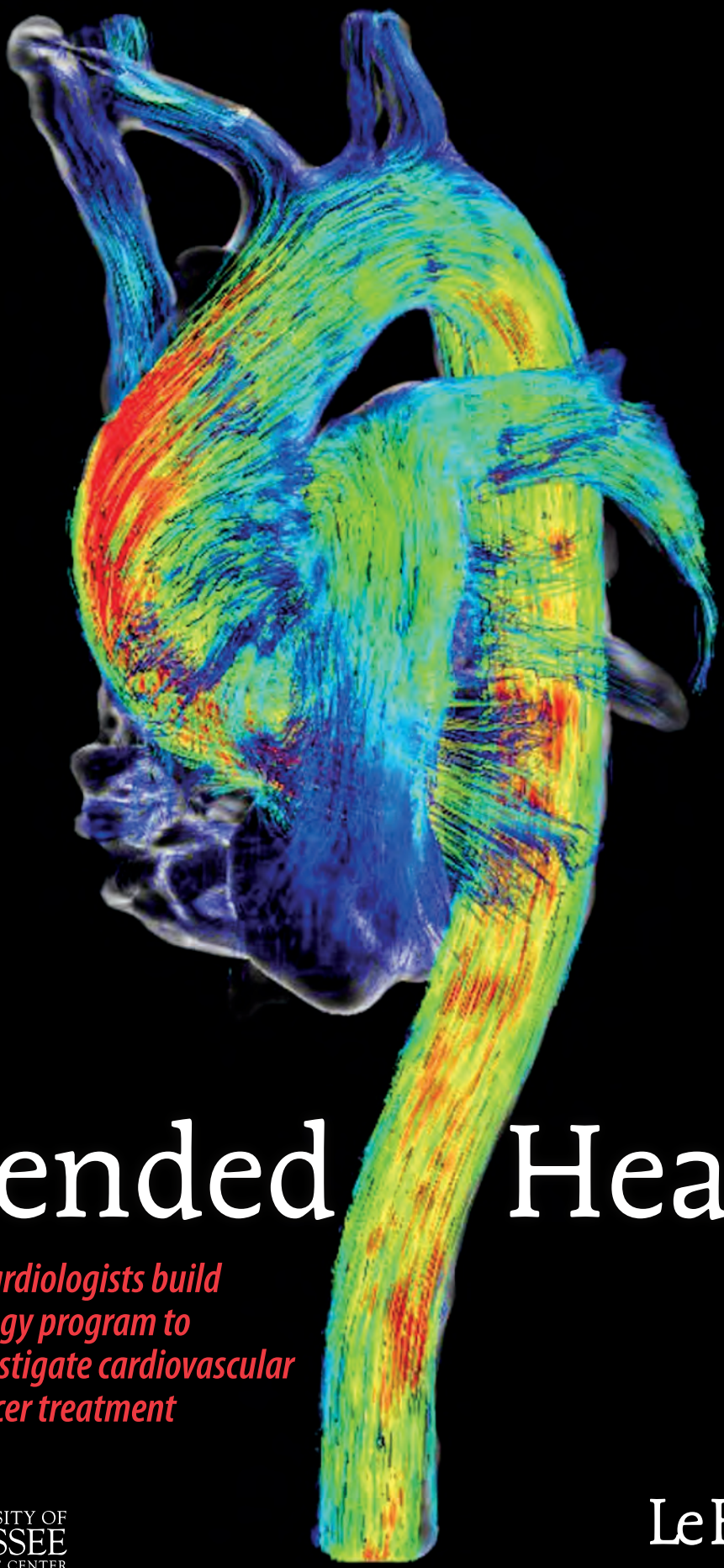
SPRING 2020

DELIVERING ON A PROMISE



Mended Hearts

Le Bonheur cardiologists build cardio-oncology program to manage, investigate cardiovascular effects of cancer treatment

THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

Le Bonheur Children's Hospital

Research: Allergic asthma protects from H1N1 influenza virus and Streptococcus pneumoniae

Pre-existing allergic asthma protects from severe morbidity from influenza A virus (IAV) and *Streptococcus pneumoniae* (Spn) co-infection because of extensive alterations in the respiratory tract including immunological and microbiological differences. This Le Bonheur research, published in *Scientific Reports*, was prompted by the results from the 2009 swine flu pandemic during which asthmatics had less severe outcomes of influenza including reduced bacterial pneumonia and ICU admittance as compared to non-asthmatics.

"Asthma is a complicated syndrome that develops through intricate gene and environment interaction," said Le Bonheur Researcher Amali Samarasinghe, PhD. "Our study aimed to understand the possible mechanisms at play in asthmatics during respiratory infections to determine how each asthmatic may respond."

Researchers developed a mouse model of asthma, influenza and pneumococcal pneumonia in order to study host-pathogen interactions in live tissue, which is unable to be observed in humans.

The results of the study revealed several ways in which allergic airways differ from non-allergic during co-infection of IAV and Spn including:

1. **The inflammation of allergic airways delayed or protected against severe disease from co-infection.**
2. **Allergic airways had a more diverse immune cell signature during co-infection.**
3. **Antibiotic treatment impeded protection from infection-induced morbidity in allergic mice.**
4. **Lung mucosal microbiome was more diverse in allergic airways, and antibiotic-induced dysbiosis rendered the allergic mice susceptible to severe disease associated with co-infection.**

"Underlying conditions present unique challenges and opportunities for invading pathogens," said Samarasinghe. "The extensive alterations in the respiratory tract during allergic asthma encompass both immunological and microbiological differences that can have a profound impact on susceptibility to infection."

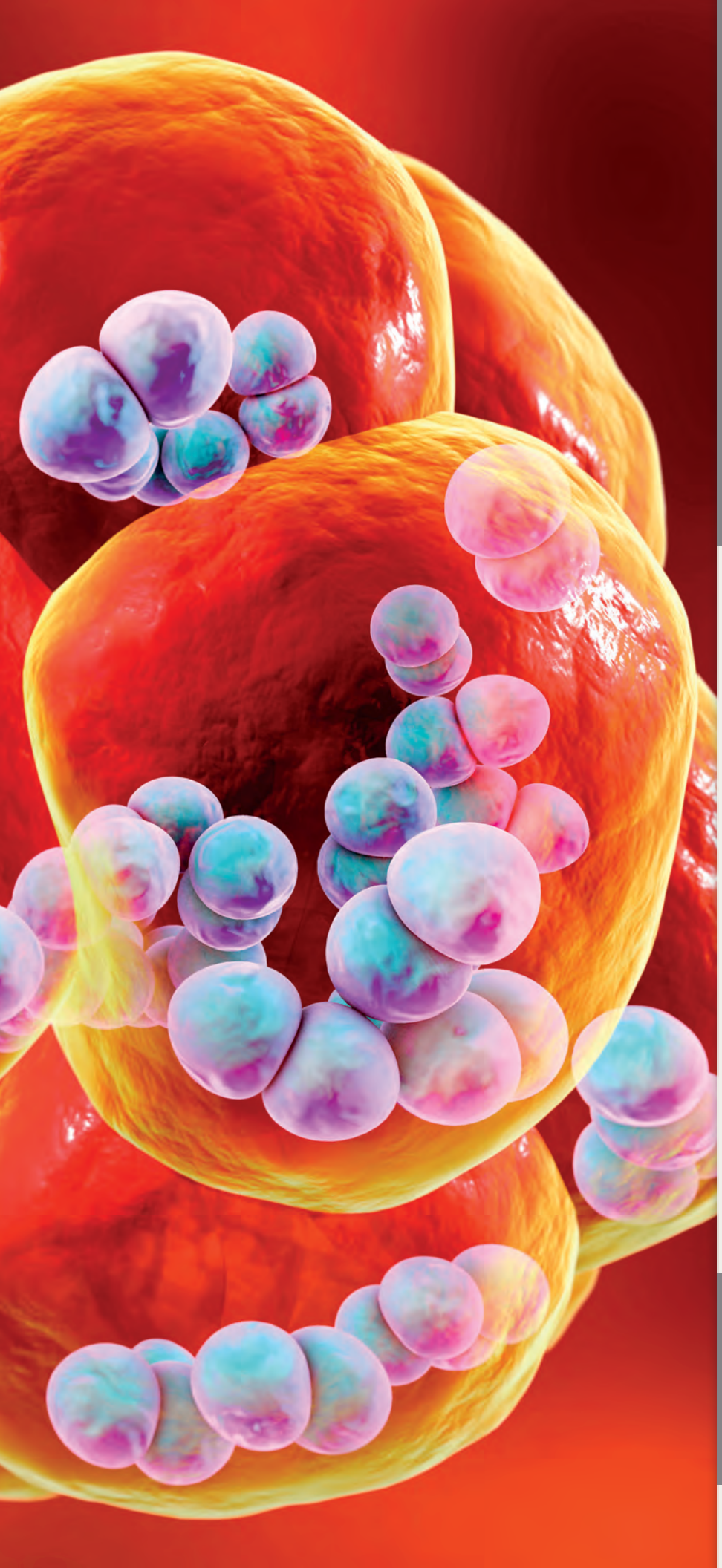
The results show that asthmatics have a distinct microbial signature that may contribute to the protective capacity of asthma during IAV and Spn co-infection. Any antibiotics should be prescribed with caution especially in patients with underlying chronic conditions.

This study was conducted in collaboration with St. Jude Children's Hospital Researchers Jason Rosch, PhD, Ti-Cheng Chang, PhD, and Peter Vogel, DVM, PhD.

View the full text article at **https://www.nature.com/articles/s41598-019-55712-8#Abs1**.

Research included in this report was funded by the Children's Foundation Research Institute.

Streptococcus pneumoniae



Le Bonheur Children's Hospital

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 45 subspecialties.

LE BONHEUR LEADERSHIP

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Jon McCullers, MD – *Pediatrician-in-Chief*
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In this issue:

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Aggressive chemotherapy that attacked Bailey Jessop's (above) osteosarcoma weakened his heart. Le Bonheur cardio-oncologists now have a mission to keep his heart healthy.

Mended Hearts

Le Bonheur cardiologists build cardio-oncology program to manage, investigate cardiovascular effects of cancer treatment

Middle school cross-country runner Bailey Jessop had complained of leg pain for weeks.

His mom, Le Bonheur physical therapist Kimberly Jessop, hoped it was growing pains. But Bailey had just signed up for a road race series with his dad, and Kimberly's gut told her to get it checked out just in case.

The verdict: osteosarcoma that required 40 weeks of aggressive chemotherapy, several surgeries to remove part of his femur and a new titanium prosthesis.

"The chemotherapy was so harsh on his body. He had an ECHO before every treatment," Kimberly said. "Toward the end of the treatment, we started to see signs of cardiomyopathy."

The chemotherapy that attacked Bailey's cancer eventually weakened his heart — presenting a new battle for Bailey. It's a reality that was not surprising to the Jessops, considering how cancer and its treatments can affect multiple systems.

It's also a reality that cardiologists at Le Bonheur Children's Hospital are working to change.

Today, more than 80% of children who are diagnosed with cancer will survive, thanks to advancements in cancer care. But that doesn't mean they all escape unscathed.

Long-term cardiovascular complications are now the leading cause of non-cancer morbidity and mortality in long-term childhood cancer survivors.

The growing population of childhood cancer survivors led Le Bonheur's Heart Institute to establish a formal cardio-oncology clinic at St. Jude Children's Research Hospital to care for those children. The challenge for them is clear: improve the quality of life for kids like Bailey and work to ensure that children with cancer don't also have to worry about weakened hearts.

Le Bonheur Heart Institute cardiologists specialize in chemotherapy-induced cardiovascular toxicity (including cardiomyopathy) in order to treat childhood cancer patients and survivors who now have weakened hearts.

NEW KNOWLEDGE IS NEEDED

Chemotherapy-induced cardiovascular toxicity is an emerging problem for pediatric cardiologists, as a new population of patients fight off the cancer that would have killed them more than a decade ago. Today, St. Jude estimates that there are more than 420,000 childhood cancer survivors in America.

Within Le Bonheur's cardio-oncology program, cardiologists provide heart care to St. Jude patients receiving treatment, as well as survivors who are experiencing late effects of cancer treatment.

Bailey Jessop underwent 40 weeks of aggressive chemotherapy to treat osteosarcoma. This treatment eventually weakened his heart.

420,000 childhood cancer survivors in U.S.

3x↑ *chance of a cardiac event, compared to cancer-free peers*

10x↑ *chance of heart failure, compared to cancer-free peers*

Jeffrey A. Towbin, MD, serves as chief of Cardiology at both Le Bonheur and St. Jude and established the clinical and research facets of the program after he was recruited to Memphis five years ago. Under his leadership, Le Bonheur has since recruited four cardiologists to focus on chemotherapy-induced cardiovascular toxicity.

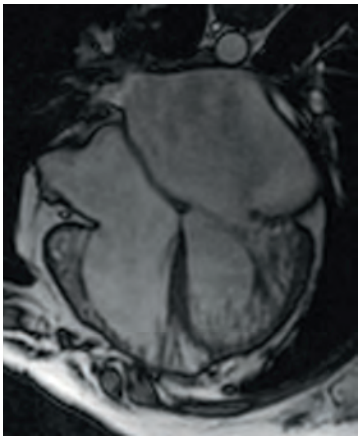
"The field must train cardiologists with expertise in cardio-oncology," said Towbin, who also serves as executive co-director of Le Bonheur's Heart Institute and St. Jude Chair of Excellence in Pediatric Cardiology. "We are seeing large numbers of patients who have received cancer chemotherapy and may have developed cardiovascular abnormalities or will develop cardiovascular dysfunction in the future."

Towbin says he believes more research is needed to understand the basic mechanisms that cause certain children to be at higher risk than others — and that research would facilitate the development of preventative measures, as well as targeted treatment for affected individuals.

For example, literature suggests that the anthracyclines class of cancer drugs can

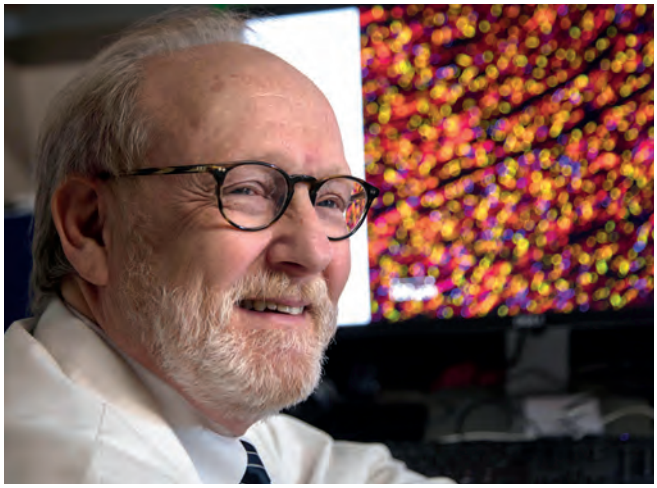
cause dilated cardiomyopathy, where the heart becomes enlarged and squeezes poorly. In Memphis, though, cardiologists have found that, in addition to dilated cardiomyopathy, many children at St. Jude develop a problem with heart relaxation, called restrictive cardiomyopathy or restrictive physiology. Therapies are different between dilated and restrictive cardiomyopathy.

"In addition, newer agents being used now have significant potential for affecting cardiovascular function and, in fact, may have even more significant impact. New knowledge is needed," Towbin said.



Cardiac MR with restrictive physiology

Pediatric Cardiologist Jason Goldberg, MD, was recruited to Memphis after his fellowship at Texas Children's Hospital — a heart failure and transplant center where he saw an increasingly high number of children and young adults who had developed heart failure after undergoing cancer therapy.



Chief of Cardiology Jeffrey A. Towbin, MD, is working on research that could facilitate the development of preventative measures and targeted treatments for chemotherapy-induced cardiovascular toxicity.

"Specialists at St. Jude had similarly found accelerated rates of heart attacks and cardiac death among young adults who had received chemotherapy," Goldberg said. "While specific chemotherapies, such as high-dose anthracyclines, have known cardiotoxic

Le Bonheur's team of pediatric cardio-oncologists study and treat cardiovascular toxicity in patients who have undergone chemotherapy at St. Jude Children's Research Hospital.

profiles, I observed significant cardiomyopathy and heart failure among children who had not received high doses of anthracyclines."

Additionally, many children who have undergone chemotherapy have heart rates and blood pressures that are higher than normal, Goldberg said.

"I believe that identifying and treating these early subtle signs of heart disease in children undergoing cancer therapy can prevent future heart disease and heart failure," he said. "This work is most salient at St. Jude, where more children have had successful cancer treatment than anywhere else."

"It's an emerging field where two complex disciplines cross."

Gary Beasley, MD, Le Bonheur Pediatric Cardiologist

Goldberg believes the collaboration with St. Jude, Le Bonheur and the University of Tennessee Health Science Center (UTHSC) will allow his team to better treat heart disease among survivors and comprehensively examine the long-term cardiovascular effects of cancer therapy.

"Children suffering from cancer shouldn't have to also worry about their hearts," said Pediatric Cardiologist Gary Beasley, MD. "We have an opportunity to work together between oncology and cardiology to develop strategies to treat cancer while minimizing the cardiovascular effects. It's an emerging field where two complex disciplines cross."

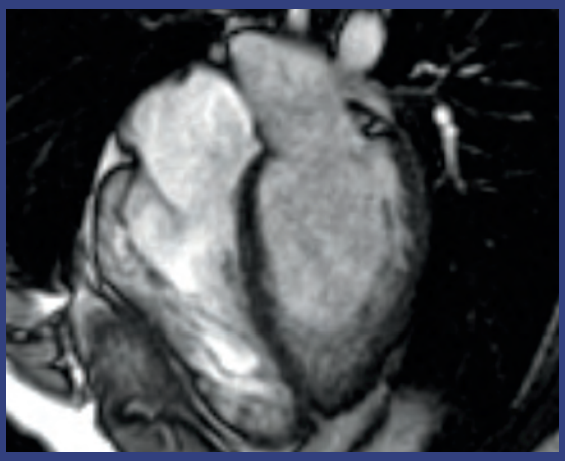
FINDING ANSWERS

The Le Bonheur Heart team — along with their colleagues at St. Jude — launched four active studies and have others awaiting IRB approval. The studies consider anthracycline-induced cardiotoxicity and other trends they've noticed in their patients.

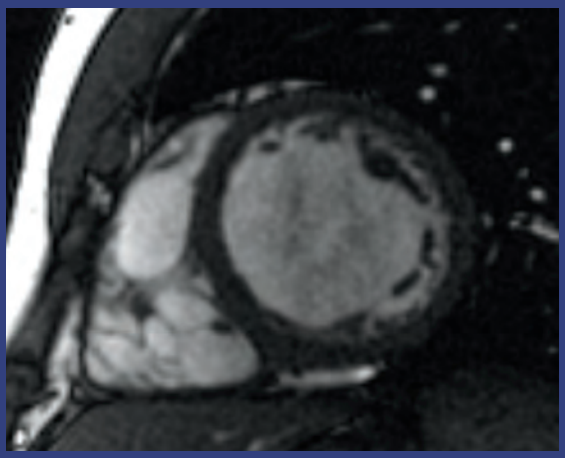
One of those studies, "Acute Hemodynamic Effects of Pediatric Hematopoietic Cell Transplantation," examines the cardiovascular risks of childhood hematopoietic cell transplantation — particularly less-studied conditions like hypertension, tachycardia and cardiac dysfunction. After finding a high prevalence of these conditions in a study group of 150 transplantation patients, the group presented initial work at the 2019 American Society of Bone Marrow Transplantation Meeting. Le Bonheur scientists are working alongside UTHSC and St. Jude researchers in this work.

Teams of Le Bonheur and St. Jude investigators have started to present very early work to groups studying pediatric hematology and transplantation and cellular therapies.

Chemotherapy-Induced Cardiomyopathy



Chemotherapy-induced cardiomyopathy will decrease function and cause a dilated ventricle. Above is a four-chamber cardiac MRI, and below is a short-axis cardiac MRI from a patient with chemotherapy-induced cardiomyopathy.



MEET THE TEAM
Cardio-Oncology

Jeffrey A. Towbin, MD
Chief of Pediatric Cardiology
Le Bonheur Children's Hospital
Chair of Excellence in Pediatric Cardiology
St. Jude Children's Research Hospital

Mohammed Absi, MD
Pediatric Cardiologist

Gary Beasley, MD
Pediatric Cardiologist

Jason Goldberg, MD
Pediatric Cardiologist

Hugo Martinez, MD
Pediatric Cardiologist

Kaitlin Ryan, MD
Pediatric Cardiologist

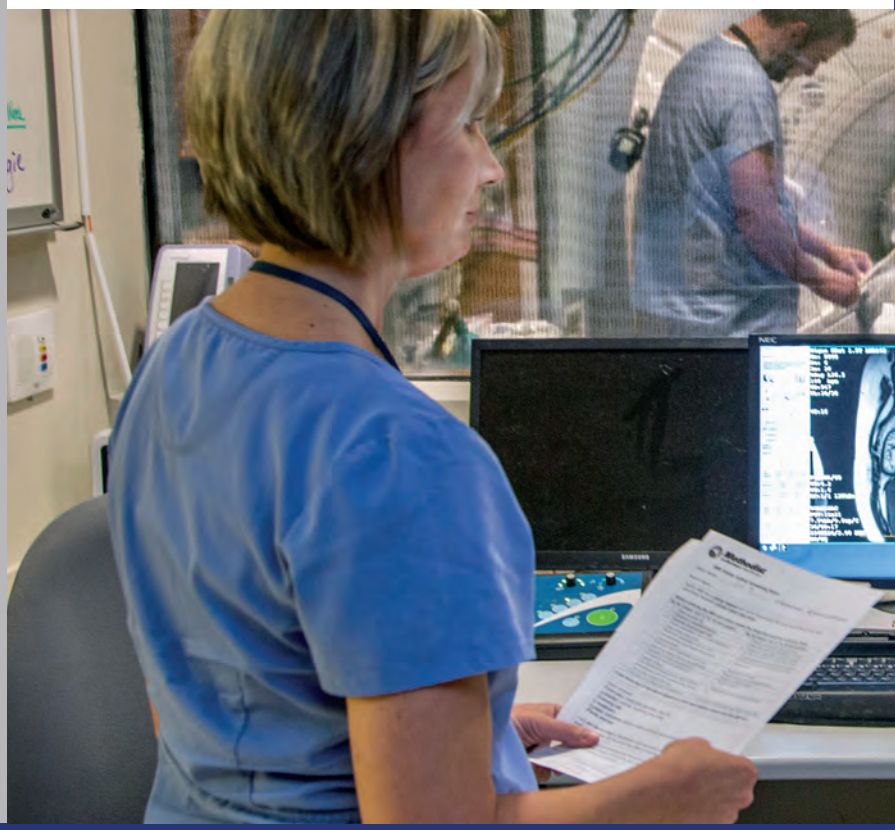
Jeri Thomas, RN
Clinic Coordinator

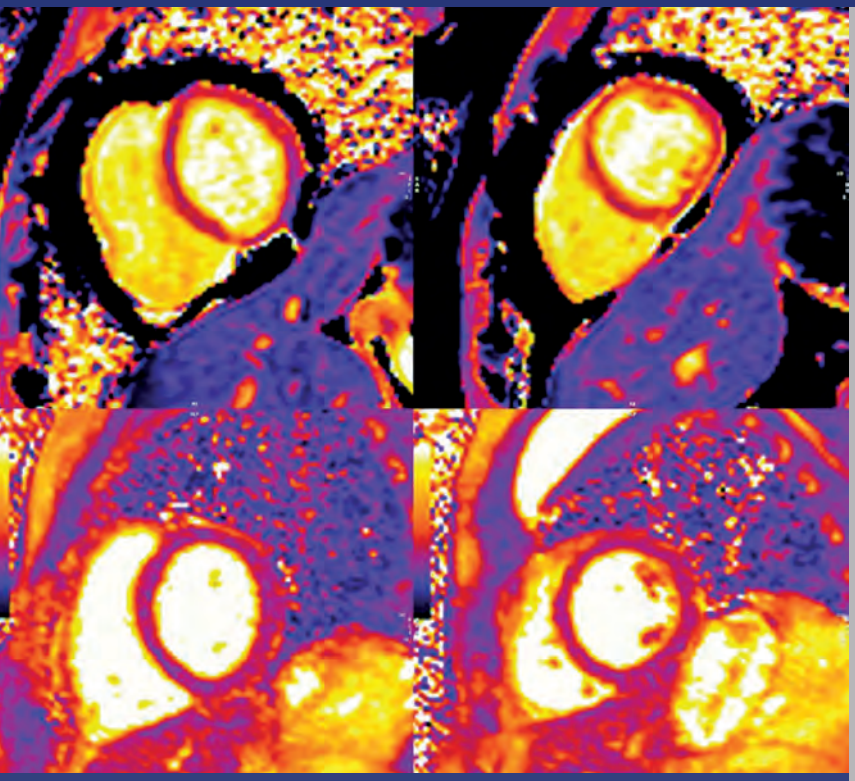
Meanwhile, Pediatric Cardiologist and Cardiac MRI Director Jason Johnson, MD, knows from his work that some children's hearts can tolerate chemotherapy much better than others. He's working with cardiac MRI mapping to better understand each heart's tissue characterization – and hopefully develop prediction models for future cardiomyopathy.

"We don't know why some children suffer heart failure after chemotherapy, but we think mapping can help us predict," Johnson said. "That understanding will lead to better therapies for chemotherapy-induced cardiotoxicity."

Bailey's mom, Kimberly Jessop, is betting on the entire Le Bonheur team and hopes that research will develop better outcomes. She knows that Bailey still has a long road ahead, even if the cancer is gone. But she says that she's grateful to be near a team of doctors willing to research how cancer drugs change the heart and prevent side effects when they are preventable.

"For us, that means a better quality of life for our son and so many others like him," she said. "I wasn't confident that Bailey's heart damage was correctable, but I was confident we were in the best place."





Predicting Heart Failure

Cardiologists at Le Bonheur Children's are using imaging technology to map the heart of patients with chemotherapy-induced cardiomyopathy. Cardiologist Jason Johnson, MD, (below) hopes this work will help physicians better predict heart failure in patients undergoing chemotherapy. Above, a cardiac MRI still-frame collection shows the T1 and T2 mapping at the base and mid axis of a heart patient. The technique allows the heart team to evaluate edema and fibrosis in the heart, a common side effect of chemotherapy.

Cardio-Oncology Research

Physicians at Le Bonheur Children's Hospital and St. Jude Children's Research Hospital are studying how chemotherapy affects hearts of children, adolescents and young adults.

Cardiovascular-hematology-oncology areas of investigation:

- Systolic dysfunction and chemotherapy
- Systolic dysfunction and radiotherapy
- Stress-induced cardiomyopathy
- Cardiovascular biomarkers in patients with cancer
- Diastology in the patient with cancer and hematologic diseases
- Cardiovascular noninvasive imaging in the oncology patient
- Electrophysiology anomalies
- Pericardial disease
- Pulmonary hypertension
- Thromboembolism
- Systemic hypertension
- Cardiac masses
- Primary and secondary prevention of cardiovascular toxicity
- Congenital heart disease in the oncology patient
- Peri-operative evaluation and management of the cardio-oncology patient
- Cardiothoracic surgery in children with cancer
- Genetics of cancer and cardiac toxicity
- Genetic pathways of cancer and cardiac disease
- QOL in children and young adults with cancer
- Invasive/interventional cardiology in patients with cancer

The Faces of Chemotherapy-Induced Heart Failure

Bailey Jessop, Osteosarcoma

Bailey Jessop, 11, had started to walk with a limp. His mom, Kimberly, a physical therapist at Le Bonheur Children's, hoped it was growing pains, but then she noticed that his left knee was significantly larger than the right.

So, she went to see her longtime colleague, Le Bonheur Orthopedic Surgeon William Warner, MD. As they sat in the waiting room, Bailey quietly asked her: "What if it's a tumor?"

He knew.

For the next 10 months, Bailey endured an aggressive chemotherapy protocol to fight osteosarcoma attacking his body. During his treatment at St. Jude Children's Research Hospital, he underwent multiple surgeries to remove part of his femur, replace it with a titanium prosthesis and then later graft his incision. He still faces more surgeries to extend his leg as he grows.

When Bailey was referred to cardiology after an echocardiogram showed heart damage to the lower part of his heart, the Jessops took it stride.

"Our lowest hanging fruit is cancer," Kimberly said. "In the end, he's cancer free and has a lifetime of side effects and surgery."

Bailey, now 15, still receives routine scans at St. Jude Children's Research Hospital and is followed by Le Bonheur Cardiologist Jason Goldberg, MD. Goldberg's ability to relate to Kimberly's skeptical teenager has helped the family navigate this next phase of care.

Before they get down to "heart talk," Goldberg always makes sure to talk to Bailey about climbing, golf or whatever his new hobby might be. "I think he actually doesn't mind going to cardiology," Kimberly said.

"He explains everything about his heart to him directly, instead of just talking to me which is something I love about him," she added. "I am so grateful that doctors are willing to research and help prevent conditions that may be preventable, such as the effect on the heart. For us, that means a better quality of life for our son and for so many others like him."

Bailey Jessop (center) celebrated his 15th birthday (cancer free) in January.

Bailey Jessop (left) and his pediatric cardiologist, Jason Goldberg, MD

"I would never choose this as my story, but I would choose the same care for Bailey every time."

Kimberly Jessop, Bailey's mom

Kimberly is a cancer survivor herself. In 2010, at age 33, she was diagnosed with stage IV melanoma and chronic myelogenous leukemia (CML). A clinical trial for an experimental immunotherapy drug saved her life, so she understands better than most how important research can be.

Her experience helped her prepare and comfort Bailey on the worst days but has also added a layer of gratitude for what her family has endured.

"I would never choose this as my story, but I would choose the same care for Bailey every time," she said. "Good gosh we've been so blessed. I've got both of my kids, and I'm still here."

Amelia Johnson, Acute Myeloid Leukemia

Shortly after 2-year-old Amelia Johnson completed chemotherapy for acute myeloid leukemia, her family learned that she was in heart failure.

Amelia Johnson received a heart transplant after the chemotherapy that saved her life weakened her heart.

It was a blow that her mother, Lisa Akins, remembers well – even 15 years later. Born with Down syndrome, Amelia already had beaten leukemia. But the drug that saved her life also weakened her heart. Amelia would eventually need a new one, doctors told her.

"I just cried and prayed. A bunch of prayers," Lisa said. "There's nothing else you can do. I didn't want her to have to go through something else so terrible."

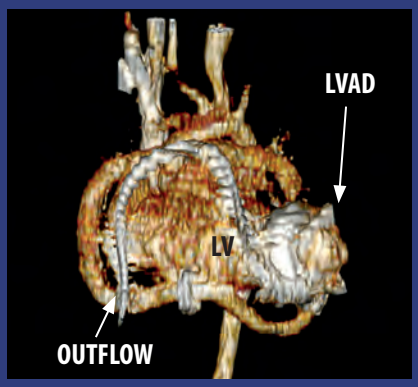
For the next decade, Amelia was hospitalized every time she became sick. In December 2017, Amelia received a ventricular assist device to bridge her failing heart to a transplant. In February 2018, she received a new heart.

> ***"She became very close with her surgeon, Dr. (Umar) Boston. He was amazing. I feel like I owe him my life."***
>
> Lisa Akins, Amelia's mom

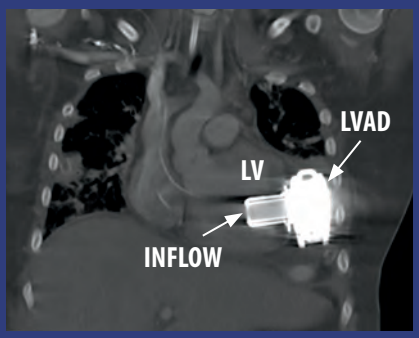
"She became very close with her surgeon, Dr. (Umar) Boston. He was amazing," Lisa said. "I feel like I owe him my life."

Lisa says that Amelia has been out of the hospital and healthy since the transplant. Today, she's a funny high schooler who loves music and loves to dance.

Chemotherapy-induced cardiomyopathy: VAD → Transplant



Amelia Johnson suffered from chemotherapy-induced cardiomyopathy after undergoing cancer treatment. She eventually needed a left ventricular assist device (LVAD) and transplant. Above, a CT chest with 3D reconstruction shows how the LVAD worked to remove blood from the left ventricle (LV) via the LVAD inflow, putting it into the aorta via the LVAD outflow.



A contrast chest CT shows the inflow of the VAD device within Amelia's left ventricle.

Center *of* Attention

Hospital-wide effort reduces CLABSI rate by 44%

In 2017, Le Bonheur Children's had 27 patients contract a central line-associated blood stream infection (CLABSI) during their hospital stay. Infectious Disease Specialist Nick Hysmith, MD, knew that this was 27 patients too many.

"Our standardized infection ratio was too high," said Hysmith. "Patient safety and quality care is our top priority. It was time to develop new strategies for reducing bloodstream infections."

Hysmith and his colleagues set a goal to reduce CLABSIs by 20%, beginning with the reduction of the overall number of central lines used across the hospital. In 2017, the central line standard utilization ratio, or number of patients with central lines, had reached one in four.

By forming a CLABSI Task Force and participating in research in tandem with Critical Care Intensivist Sachin Tadphale, MBBS, MPH, FAAP, and the Bright STAR Collaborative, Hysmith and his team improved patient safety by reducing CLABSIs by 44% over two years.

A Bold Stance

Hysmith's first step was to form a CLABSI Task Force consisting of invested front-line providers from every unit and physicians from the Neonatal Intensive Care Unit (NICU) and Pediatric Intensive Care Unit (PICU) who make real-time decisions.

"Immediately, the task force began identifying the fastest ways to reduce the overall number of central lines as well as providing instruction on appropriate care for the lines that we absolutely need," said Hysmith. "We needed to be bold in our approach to reduce CLABSIs."

The CLABSI Task Force created a rigid criteria for utilization of central lines, including who should have them and when they are necessary. Physicians are now required to put in a daily central line order to document why the line is needed. The task force has also encouraged the use of peripheral IVs by changing tubing and the care of peripheral access points.

For those necessary central lines, the task force created education bundles on the insertion and maintenance of central lines with a goal of compliance above 90%. In

Practical Steps to Reducing CLABSI

Le Bonheur's CLABSI Task Force implemented many new initiatives to lower the CLABSI rate including:

- **Daily central line orders.** Physicians are now required to document necessity of a central line on a daily basis.
- **Chlorhexidine gluconate (CHG) baths.** CHG baths are mandated for all patients in critical care areas (with the exception of the NICU) and patients on medical-surgical floors with central lines.
- **New central line techniques.** Physicians developed a technique to put lines in lower on babies to avoid the line going into the diaper.
- **Reduction in daily cultures.** Previously patients on heart-lung bypass had daily cultures drawn from the line. This as well as other routine lab collection from central lines has stopped.

Infectious Disease Specialist Nick Hysmith, MD, (above) has been working with the CLABSI Task Force to lower CLABSIs by implementing new equipment and procedures for central lines such as the one pictured above.

addition, new products were investigated that might help mitigate the chance of infection.

Finally, an apparent cause analysis was conducted after every CLABSI event. Cause analysis served to reveal irregularities in patient care and other contributions to infection.

"We needed to be bold in our approach to reduce CLABSIs."

Nick Hysmith, MD, Infectious Disease Specialist

"When a CLABSI does occur, we want to take the opportunity to learn from it," said Hysmith. "With cause analysis we can narrow down why they happen and institute new policies to prevent them in the future."

A Collaborative Effort

Patient safety and quality improvements don't occur in a silo. Hysmith and Tadphale understood the importance of collaboration with other children's hospitals around the country to reduce CLABSIs. They joined a group of 15 hospitals as a part of the Blood Culture Improvement Guidelines and Diagnostic Stewardship for Antibiotic Reduction in Critically Ill Children, or the Bright STAR Collaborative. This multi-institutional quality improvement effort out of Johns Hopkins Children's Center was created to optimize blood culture use in PICUs thereby lowering CLABSI risk.

"Any time you enter a central line for a blood culture you increase the risk of infection," said Hysmith. "The Bright STAR Collaborative allowed us to share our efforts with other hospitals and learn from initiatives around the country."

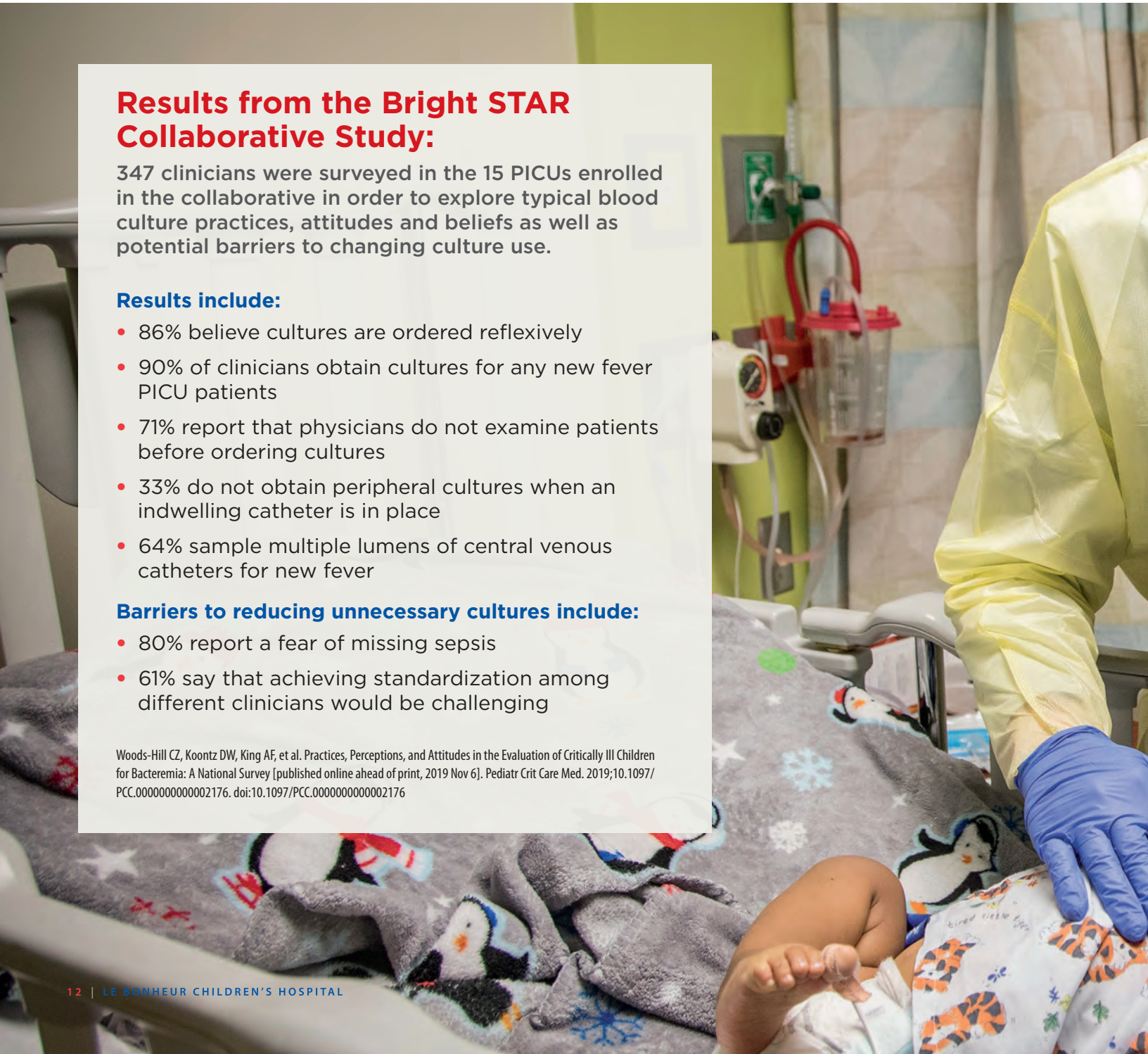
The Bright STAR Collaborative recently conducted a study surveying providers in the 15 PICUs that are part of the collaborative. The study aimed to assess the perceptions of current blood culture practices and identify potential barriers to reducing unnecessary cultures.

According to the study, in addition to the raised risk of infection unnecessary blood cultures cause harm to patients including excessive antibiotics, longer hospital stays and increased cost.

The survey revealed that the barriers to reducing unnecessary blood cultures included variation in blood culture decisions across PICU sites as well as a fear of missing sepsis. Respondents stated that they believed culture use is driven by fear and reflexive habits – diagnostic stewardship is critically needed for blood cultures.

A Dramatic Result

These efforts have already lowered the CLABSI rate at Le Bonheur Children's. Overall blood cultures have been reduced by 66%, which lowers the risk of infection. And at



Results from the Bright STAR Collaborative Study:

347 clinicians were surveyed in the 15 PICUs enrolled in the collaborative in order to explore typical blood culture practices, attitudes and beliefs as well as potential barriers to changing culture use.

Results include:

- 86% believe cultures are ordered reflexively
- 90% of clinicians obtain cultures for any new fever PICU patients
- 71% report that physicians do not examine patients before ordering cultures
- 33% do not obtain peripheral cultures when an indwelling catheter is in place
- 64% sample multiple lumens of central venous catheters for new fever

Barriers to reducing unnecessary cultures include:

- 80% report a fear of missing sepsis
- 61% say that achieving standardization among different clinicians would be challenging

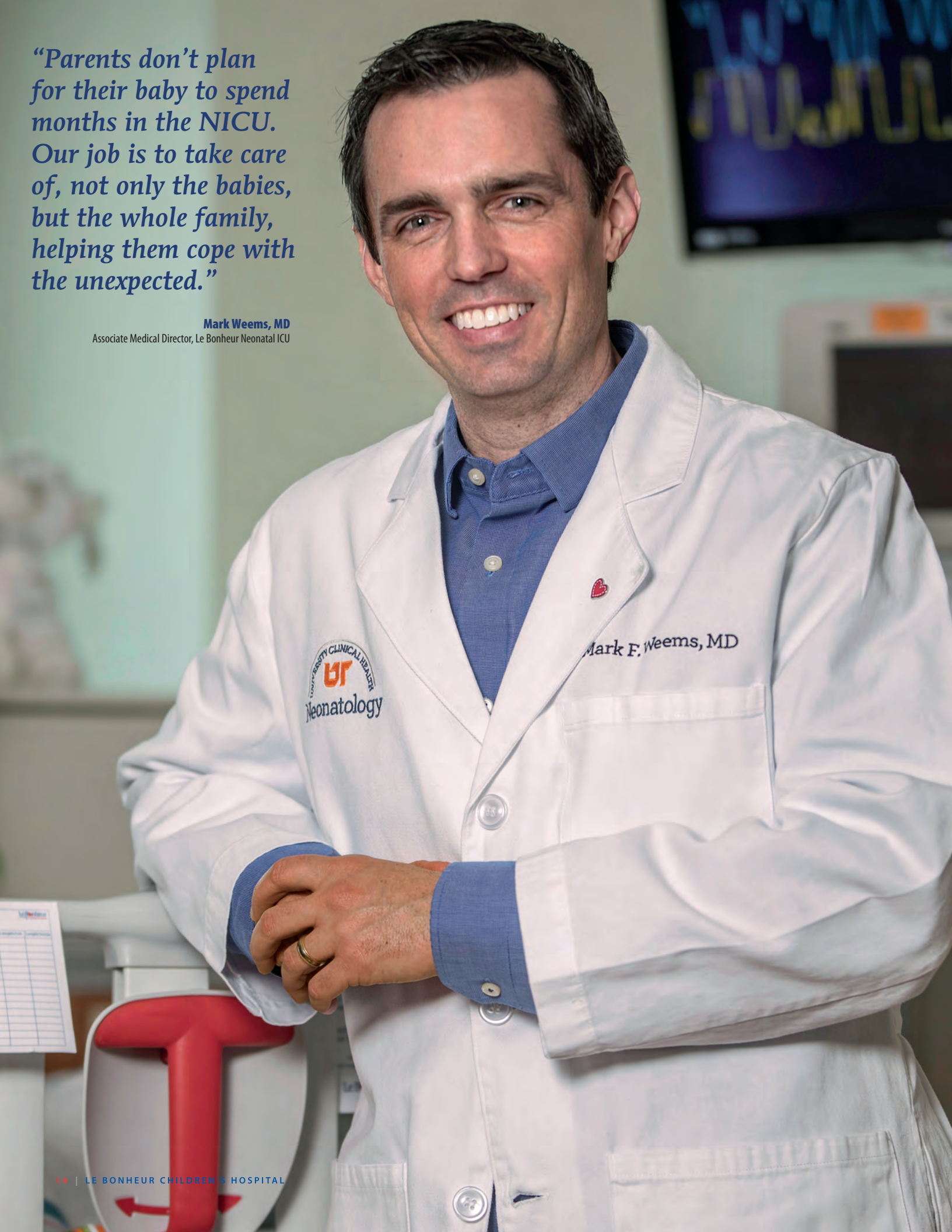
Woods-Hill CZ, Koontz DW, King AF, et al. Practices, Perceptions, and Attitudes in the Evaluation of Critically Ill Children for Bacteremia: A National Survey [published online ahead of print, 2019 Nov 6]. Pediatr Crit Care Med. 2019;10.1097/PCC.0000000000002176. doi:10.1097/PCC.0000000000002176

the end of 2019, the CLABSI rate had dropped by 44% from 2017.

"Le Bonheur is forward-thinking in the consensus not to culture or access lines unless it is absolutely necessary. Now we can proudly say that we are ahead of the game in our safety record and buy-in from physicians," said Hysmith. "We have the lowest blood culture rate of any center in the Bright STAR Collaborative. We are leading the way in keeping children protected from bloodstream infections."

Le Bonheur's CLABSI Task Force consists of frontline providers who meet regularly to evaluate central line use and ways to prevent infections.

Thanks to changes in central line use and care, Le Bonheur has dropped its CLABSI rate by 44% in two years. Left, Infectious Disease Specialist Nick Hysmith, MD, examines Le Bonheur patient Isaias Ortiz.



"Parents don't plan for their baby to spend months in the NICU. Our job is to take care of, not only the babies, but the whole family, helping them cope with the unexpected."

Mark Weems, MD
Associate Medical Director, Le Bonheur Neonatal ICU

PROFILE: MARK WEEMS, MD

Neonatologist helps families cope with the unexpected

Neonatologist Mark Weems, MD, entered into the medical field differently than most. A film production major at Northwestern University, Weems spent two years in Hollywood before deciding the show business life was not for him. In search of a more fulfilling career, Weems quickly set his sights on returning to school – this time to study medicine.

"I always had medicine in the back of my mind. My grandfather, father and uncles were physicians. But as an undergraduate, when organic chemistry had interfered with my film classes, I dropped it," said Weems.

A Memphis native, Weems and his wife returned home where he enrolled at the University of Tennessee Health Science Center after completing two years of prerequisite classes in California. A rotation at Le Bonheur Children's Hospital inspired him to focus on pediatrics – neonatology, specifically. After a neonatology fellowship in Los Angeles, Weems again returned to Memphis to start his career in Le Bonheur's rapidly expanding Neonatal Intensive Care Unit (NICU), where he serves as the unit's associate medical director.

Today, Weems is one of 15 neonatologists who staff the hospital's 60-bed Level IV NICU. The unit is the region's "safety net" for newborns with complex medical needs, says Weems, caring for patients from a tri-state area.

"Parents don't plan for their baby to spend months in the NICU," said Weems. "Our job is to take care of, not only the babies, but the whole family, helping them cope with the unexpected and often preparing them for the technology we send home with them."

With an average daily census of 53, Le Bonheur's NICU is busy. And with so many patients to care for, so too comes the opportunity for research projects. Specifically: reducing uncontrolled pain in neonates, preserving babies' oral skills and addressing the severe bronchopulmonary dysplasia population in the NICU.

Le Bonheur is currently part of a 34-center national consortium focused on reducing uncontrolled pain in neonates after surgery. Using specific post-operative guidelines, Weems and his colleagues monitor patients' pain levels, scoring based on blood pressure and heart rates, as well as facial expressions. While too little medication causes babies unnecessary pain, too much is also a problem, says Weems, as physicians are understanding more and more about the negative effect of pain therapy and sedation on long-term brain development.

NICU Associate Medical Director Mark Weems, MD, (pictured with Harlynn Johnson, born at 22 weeks) enjoys caring for families in this stage of life.

Preserving oral skills is crucial for babies who can't eat after abdominal surgery. In these cases, Weems and his colleagues encourage a "sham feeding" that still allows parents to feed their baby (bottle or breast feeding). The milk is then removed through a suction tube in the baby's stomach, which allows neonates to develop crucial oral skills needed to feed while waiting for the intestines to recover. In the pilot stage, the study is hypothesized to reduce the time it takes to start feeding by mouth and reduce the need for a gastrostomy tube, especially in infants with gastroschisis.

Another research focus: babies with severe bronchopulmonary dysplasia.

"So many of our babies with lung disease remain in the NICU for one or more years. Many families do not have the resources they need to take care of a tracheostomy at home, and we currently have no long-term care facilities to help these babies transition to home," said Weems.

Neonatologists are working to identify babies at risk for severe lung disease early on – typically any infant born before 26 weeks and those still on ventilator support at 36 weeks. Early identification allows caregivers to better manage the baby's respiratory therapies and work to prevent long-term issues.

Weems is passionate about the work his team is doing.

"I like the stage of life when parents are trying to grow their families. And I get to help when something goes wrong," said Weems.

Mark Weems, MD

Education and Training
University of Southern California – Neonatal-Perinatal Medicine Fellowship
University of California, Irvine – Pediatrics Residency
University of Tennessee Health Science Center – Medical School

Board Certifications
American Board of Pediatrics, Sub-board
Neonatal-Perinatal Medicine

Society Memberships
American Academy of Pediatrics

One in Ten Thousand

Neurologists perform Le Bonheur's first gene therapy infusion for infant with spinal muscular atrophy

Charleigh Jones is the miracle her parents, Charles and Lacey, had prayed for during a two-year infertility struggle. Born happy and healthy, they had no inkling of the disease hiding in Charleigh's genes. She has spinal muscular atrophy (SMA) type 1 — a genetic condition characterized by increasing muscle weakness and early morbidity.

Zolgensma is delivered via intravenous infusion one time in a one-hour period. The drug delivers the missing gene that halts the progression of SMA type 1 for children younger than 2.

As the state of Tennessee was finalizing newborn screening for SMA, 10,000 random samples were pulled for quality assurance testing. Charleigh's was one of them. Diagnosed through the screening with SMA type 1, Le Bonheur neurologists worked with Charleigh's pediatrician to intervene with a brand-new gene therapy to save Charleigh's life.

In December 2019 at 8 weeks old, Charleigh was the first Le Bonheur patient to receive

Neurologist Elena Caron, MD, examines 3-month-old Charleigh Jones during a clinic appointment after she received a Zolgensma infusion to treat her spinal muscular atrophy (SMA) type 1. Charleigh already shows increased muscle strength and control.

an infusion of the newly-approved gene therapy drug Zolgensma. It delivers the gene that Charleigh is missing, stopping SMA in its tracks by preserving motor neuron cells, improving motor function and allowing her to reach childhood milestones like sitting without support.

A Grim Diagnosis

Prior to the screening, no one suspected Charleigh's SMA diagnosis. The state lab contacted Le Bonheur Neurologist Elena Caron, MD, and her team. They alerted Charleigh's pediatrician with the screening results and scheduled Charleigh an appointment two days later.

"We had never even heard of this disease before," said Charles. "Immediately, we started researching and reviewing case studies to understand this disease and what Charleigh's options were."

SMA type 1 is a genetic disease caused by a missing or nonworking SMN1 gene responsible for making SMN protein. This protein is necessary for the survival of motor neuron cells which control muscle function across the body. Without the gene and the subsequent protein, muscular function slowly regresses and eventually ceases. Patients experience progressive muscle weakness including respiratory failure and inability to swallow.

"Born a healthy, vigorous girl, by 5 weeks old her parents started noting weakness in the legs," said Caron. "By the time I saw her in clinic, she was severely weak with progressing arm and neck weakness."

If left untreated, SMA type 1 leads to death or the need for permanent ventilation by the age of 2 in more than 90% of cases.[1] SMA has four types – the most severe and most common being Charleigh's, SMA type 1.

Previously children with SMA type 1 required supportive care – including breathing assistance by a ventilator, a tracheostomy and a gastrostomy tube for nutrition. Untreated infants could not achieve normal developmental milestones such as sitting without support.[2]

"Babies would begin to show symptoms at 2 to 3 months, slowly lose function and eventually be unable to breathe," said Jessica Fleener, clinical director for Le Bonheur's Infant/Toddler and Neuroscience units. "The

[1] Finkel RS, McDermott MP, Kaufmann P, et al. Observational study of spinal muscular atrophy type 1 and implications for clinical trials. Neurology. 2014;83(9); 810-7.
[2] Farrar MA, et al. Emerging therapies and challenges in spinal muscular atrophy. Ann Neurol. 2017;81(3);355-368.

How Zolgensma Works

• *Zolgensma is made of a functional copy of a human SMN gene placed inside a viral vector. The virus used is adeno-associated virus 9, or AAV9, which can travel throughout the body and across the blood-brain barrier to deliver the working gene to the cells where it is needed.*

• *DNA of the virus is removed, and the new SMN gene is put inside.*

• *The vector takes the new, working SMN gene to the motor neuron cells in the body.*

• *When the new gene reaches the motor neuron cells, it tells them to start making SMN protein. This takes place throughout the body.*

• *Motor neuron cells are now able to make SMN protein. Motor neuron cells that have not died may survive, function and be maintained.*

Source: https://www.zolgensma.com/how-zolgensma-works

best we could do was try to make memories during the time parents had with their child."

Hope for Charleigh

Nine days after her diagnosis, Charleigh was at Le Bonheur Children's for her infusion. Time was of the essence – the sooner a child receives the infusion the better the outcome.

Zolgensma protocol calls for a one-time, one-hour intravenous infusion followed by a 24-hour inpatient observation period. The drug was approved by the FDA in May 2019 for children with SMA younger than 2 years. Candidates must meet multifaceted criteria to be eligible for the drug.

Charleigh Jones was kept at Le Bonheur for a 24-hour observation period before returning home to Byhalia, Miss. Since the Zolgensma infusion, she has already seen progression in her muscle control including neck and arm movement.

The drug delivers a new copy of the deleted SMN gene through a viral vector, AAV serotype 9. It provides a functional copy of the SMN gene to a child's neurons to instruct the cells to produce the protein needed to keep anterior horn cells of the spinal cord alive. These cells support motor nerves and connect to muscles for all muscle movement. Delivery of the gene preserves existing motor neuron cells but does not repair ones that have already died.

"I'm thrilled we were able to accomplish this so quickly," said Caron. "It felt like a race against the clock – every day mattered. We had to act as quickly as possible to help achieve the best outcome for Charleigh."

Administering a rare and expensive drug like Zolgensma requires a team effort across disciplines. Neurology, genetics, nursing and pharmacy all worked together to make sure Charleigh received the infusion as quickly as possible. Now a diagnosis or suspected diagnosis of SMA is considered a medical emergency due to the rapid, progressive and irreversible weakness and the available treatment with good outcomes.

While the infusion will not cure Charleigh of the disease, it will halt her symptoms so that she is able to continue to achieve childhood milestones and preserve her muscle function. Clinical data from the trial of Zolgensma showed unprecedented rates of survival, rapid motor function improvement and milestone achievement.

The Future of SMA Treatment

The state of Tennessee added SMA testing to newborn screenings in January 2020. For the past year, Le Bonheur physicians including Caron, Geneticist Joel Mroczkowski, MD, PhD, and Genetics Nurse Jennifer Smith, MSN, RN, CNL, have worked with the state to streamline SMA newborn screening, including how patients will be referred for treatment once identified.

> ***"It felt like a race against the clock – every day mattered. We had to act as quickly as possible to help achieve the best outcome for Charleigh."***
>
> Elena Caron, MD, Le Bonheur Neurologist

Le Bonheur is a designated treatment site in West Tennessee for children diagnosed with SMA by their newborn screening. After the infusion takes place, children continue with supportive care to complement the effects of the infusion and are followed in Le Bonheur's Muscular Dystrophy Association (MDA) Clinic.

"We anticipate more patients being identified and referred to us through newborn screening," said Caron. "We will continue to follow infants with SMA and provide excellent multidisciplinary care including pulmonology,

neurology, orthopedics, nutrition and physical and occupational therapy."

As for Charleigh, her parents are grateful that their daughter was one in 10,000 chosen for a random screening. It's what made the difference for their little girl. Since her infusion she has already begun to show progress moving her arms and rebuilding the strength in her neck.

"Dr. Caron and the entire Le Bonheur team were wonderful to work with," said Lacey. "Everyone moved quickly so that our little girl could have the best chance possible."

"Dr. Caron and the entire Le Bonheur team were wonderful to work with. Everyone moved quickly so that our little girl could have the best chance possible."

Lacey Jones, Charleigh's mom

Charles and Lacey Jones watch over their daughter, Charleigh, after she received the infusion of Zolgensma. Charleigh is the first infant to receive a gene therapy infusion at Le Bonheur.

AN ALLERGY TREATMENT

Le Bonheur participates in largest peanut oral immunotherapy trial to date

A first-of-its-kind peanut oral immunotherapy, Palforzia (AR101) was recently approved by the Food and Drug Administration (FDA). Le Bonheur was one site in the trial that brought this drug to market, providing a viable treatment for children who have lived years with a peanut allergy.

In this study, peanut allergic patients were given small amounts of peanut protein in the form of a powder. The powder was increased every two weeks until they were eating approximately one peanut's worth. Participants with an allergic response were randomly assigned to receive AR 101, the investigational biologic oral immunotherapy drug (up to 300 mg of peanut protein), or a placebo.

"Over time you can slowly increase that dose in the patient to where they are tolerating an amount they otherwise wouldn't have tolerated prior to the therapy," said Pediatric Allergist/Immunologist Jay Lieberman, MD. "In some patients in the food challenge at the end of the study, say six or 12 months later, they can eat upwards of 10 to 15 peanuts, whereas before they couldn't even eat one."

> *"Over time you can slowly increase that dose in the patient to where they are tolerating an amount they otherwise wouldn't have tolerated prior to the therapy. In some patients in the food challenge at the end of the study, say six or 12 months later, they can eat upwards of 10 to 15 peanuts, whereas before they couldn't even eat one."*
>
> Jay Lieberman, MD, Le Bonheur Allergist/Immunologist

Other therapies being investigated beyond oral immunotherapy include patch immunotherapy, modified allergen therapies and adding a biologic medicine to one of the immunotherapies to improve efficacy or safety.

"There's a lot on the horizon, and it's a good time to be a part of the food allergy community. For so long we haven't had anything to treat these patients, and hopefully soon we'll have more than one option," notes Lieberman.

Previously, the only recommended treatment was avoidance first and

emergency therapy second, specifically in the form of epinephrine, if a reaction occurred.

It is estimated that 1-2% of the population in the United States is peanut allergic with higher numbers in children and adolescents. No known root cause has been identified for peanut allergies, but Lieberman explains there is no single cause — it is a multifactorial disease.

"There's a genetic component, an environmental component and possibly a component of when these foods are introduced into the diet that can play a role into why some kids get peanut allergy and others don't," he explains.

One theory is the hygiene hypothesis. As society becomes more hygienic and has less infectious disease, whether parasitic or bacterial, immune systems may shift to develop more allergies in general, not just peanut allergy. Delayed introduction of peanuts into a child's diet may also play a part.

"Studies have shown that allergic disease in general, meaning developing allergic antibodies to things like dust mites or peanuts, may be more apt to happen in patients who are not exposed to certain infectious agents early on," adds Lieberman.

Thanks to Palforzia, allergists/immunologists like Lieberman now have a proven treatment that they can provide to their peanut allergic patients.

Le Bonheur Children's Hospital PEDS POD

Listen to an interview with Pediatric Allergist/Immunologist Jay Lieberman, MD, about peanut allergy and new immunotherapies at lebonheur.org/podcast.

Allergist/Immunologist Jay Lieberman, MD, led Le Bonheur's efforts in the largest peanut oral immunotherapy trial to date. Here, Lieberman examines patient La'Kayden Smith in allergy clinic.

Le Bonheur Neurologist and Co-director of the Neuroscience Institute James Wheless, MD, provides the latest in treatments for children with Dravet syndrome. The Neuroscience Institute was named a Comprehensive Care Center by the Dravet Syndrome Foundation.

Le Bonheur named a Dravet Syndrome Comprehensive Care Center

The Le Bonheur Neuroscience Institute's Dravet syndrome program was recently named a Dravet Comprehensive Care Center by the Dravet Syndrome Foundation. Le Bonheur's program is one of only 13 in the country certified by the Foundation as a facility with a high level of expertise and resources offering multidisciplinary care for children with this type of epilepsy.

"This designation reflects our continued commitment to providing the best care for children with rare epilepsies," says Chief Pediatric Neurologist and Co-director of the Neuroscience Institute James Wheless, MD. "Our clinicians have an excellent track record of diagnosing and treating every aspect of a child with Dravet syndrome."

Dravet syndrome is a rare form of epilepsy that typically begins in the first year of life and is diagnosed before the pre-school years. It has a genetic cause — mutations in the SCN1A gene.

Le Bonheur's Neuroscience Institute offers a variety of medications for seizures caused by Dravet syndrome as well as multidisciplinary care for cognition, behavior and sleep. The Center is actively engaged in research protocols and clinical trials for seizures, their causes and new treatments.

Le Bonheur is expanding the neuroscience partnership with St. Jude Children's Research Hospital with the launch of a translational neuroscience institute. Research will focus on untreatable epilepsies with genetic causes, such as Dravet syndrome.

"With this partnership we can expand our treatment protocols by offering new treatments for children with genetic epilepsies," said Wheless. "This complements continued participation in clinical trials and our efforts to bring the very best treatments to children."

Dravet Syndrome

ALABAMA FAMILY FINDS EXPERTISE FOR DAUGHTER'S RARE CONDITION IN MEMPHIS

When Charlotte Dalton was 6 months old, she had a seizure that lasted an hour.

"It was the scariest hour of my life," said Charlotte's mom, Gena Dalton.

Before that hour, Charlotte had never shown signs of epilepsy.

Gena started talking to friends and learned of a local child who had brain tumor surgery at Le Bonheur Children's Hospital in Memphis, Tenn.

"On a whim, I called," Dalton said. "I never thought we'd be able to get in, but Karen [Butler, epilepsy coordinator] listened to my story. She said, 'We are going to get this figured out.' We had an appointment within two weeks."

Charlotte spent a week in the Epilepsy Monitoring Unit. Blood work revealed a Dravet syndrome diagnosis, a rare genetic disorder that begins with seizures in infancy and results in developmental disabilities. Dalton, who works as a chemist, had already researched the types of epileptic syndromes, so she knew what might be ahead.

Pediatric Epileptologist Stephen Fulton, MD, worked with the family to develop a plan of care. Dalton said Fulton gave her constant hope despite Dravet's resistance to treatment.

"There was always some sort of plan

Charlotte Dalton

in the works. The doctors and team were always thinking of a way to get around this, to figure out this puzzle," Dalton said.

Dalton says she's impressed at how

"All of my worries were gone. I felt like we were going to come up with a plan. I was at peace."

– Gena Dalton, Charlotte's mom

Fulton has worked with Charlotte's other medical providers back home. When Charlotte landed in the emergency room at a nearby hospital, Fulton talked through Charlotte's care with those physicians. A standard course of treatment to stop a seizure could negatively affect her. When Charlotte failed to qualify for a drug trial at Le Bonheur, Fulton worked with another children's hospital whose qualifications would include Charlotte.

The Daltons continue to make the three and half hour drive from Huntsville, Ala., to Memphis because of the connection Charlotte has made with the hospital.

"Le Bonheur is warm and inviting. They treat us like family. Charlotte feels comfortable and doesn't fight when it's time for bloodwork. The care is top notch," Dalton said.

Making frequent trips to Memphis is a little easier on the family, Dalton says, because they can stay for free at FedEx-FamilyHouse. The 75-room residence is across the street from the hospital. Thanks to the support of donors, there is no fee for families who travel long-distances for care at Le Bonheur.

"There are so many things families like ours have to worry about," Dalton said. "We don't have to worry where we're going to stay in Memphis. We can rest after a long trip at FedExFamilyHouse. There are always homemade snacks and meals provided by volunteers."

Charlotte is in the second grade and enjoys interacting with her peers at school. She loves to go camping and swimming – activities now possible because she has better seizure control.

New Options for TSC

Nephrologist and robotic surgeon develop novel procedure to decorticate kidney cysts and prolong kidney function

Ryan and Brittany Schwaigert knew early that their son Greyson had polycystic kidney disease (PKD). After being diagnosed with tuberous sclerosis complex (TSC) type 2, Greyson's kidney ultrasound revealed so many cysts that Brittany describes them as looking like popcorn.

Greyson Schwaigert and his mom, Brittany

Until recently, children with PKD like Greyson only had one option for managing cysts: an mTOR inhibitor medication. Now, surgeons can remove the cysts and keep them from returning, thanks to a new decortication procedure developed by Le Bonheur Nephrologist John Bissler, MD.

"Previously, there was nothing we could do for PKD but watch the kidneys slowly fail," said Bissler. "After research in

Robotic Surgeon Joseph Gleason, MD, (far left) performs a kidney cyst decortication procedure using Le Bonheur's robotic technology. During this surgery, he is able to treat as many cysts as needed on a child's kidneys.

the lab, we developed this procedure to drain cysts and ultimately prolong kidney function for kids like Greyson."

THE DANGERS OF POLYCYSTIC KIDNEY DISEASE

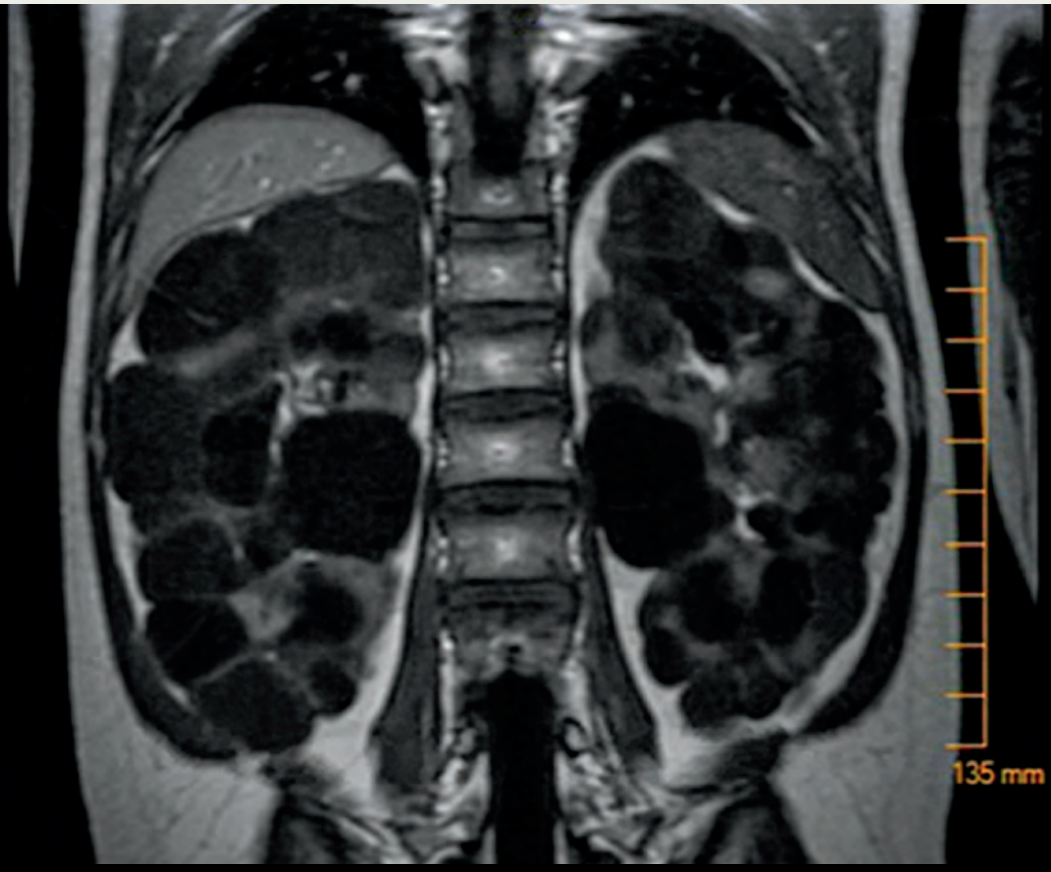
All it takes is a few cells with a deleted TSC gene to instruct the formation of kidney cysts. Bissler's recent research, "Tuberous sclerosis complex exhibits a new renal cystogenic mechanism" published in *Physiological Reports*, has uncovered the process by which these mutant cells communicate to healthy cells to produce cysts. This causes several types of cystic disease and benign tumors on the kidneys that can drastically affect the health of a child with TSC for a lifetime.

"Renal disease is the leading cause of death for TSC populations," said Bissler. "We also know that PKD causes a plethora of additional health risks for those with TSC."

"Previously, there was nothing we could do for PKD but watch the kidneys slowly fail. After research in the lab, we developed this procedure to drain cysts and ultimately prolong kidney function."

– John Bissler, MD, Le Bonheur Nephrologist

In addition to high morbidity, kidney cysts cause high blood pressure, urinary concentration defect, ambulation delays, the possibility of renal hemorrhage and eventually kidney failure. Before developing this procedure, Bissler's course of treating PKD included mTOR inhibitors to slow cyst growth and



Greyson Schwaigert was one of a handful of children with tuberous sclerosis and polycystic kidney disease to undergo kidney cyst decortication. Pictured above are Greyson's kidneys before his procedure. Robotic Surgeon Joseph Gleason, MD, was able to remove cysts and drain 800 mL of fluid from Greyson's abdomen.

Benefits of decortication procedure:

- **Remove cysts**
- **Prohibit cyst regrowth**
- **Reduce medication**
- **Lower blood pressure**
- **Improve balance and movement**
- **Prolong kidney function**

Robotic Surgeon Joseph Gleason, MD, (middle) and Nephrologist John Bissler, MD, (right) confer before conducting a kidney cyst decortication procedure. Together, they have created a new procedure to treat polycystic kidney disease.

constant blood pressure medications. Lesion growth is continually monitored with MRI.

But for Bissler, these treatments were not enough to provide the quality of life he sought for his patients. Too many families had passed through his clinic feeling desperate, abandoned and that nothing else could be done for their children. He wanted to find a better option.

A SURGICAL PARTNERSHIP

Bissler joined Medical Director of Robotic Surgery Joseph Gleason, MD, to develop a procedure to "de-roof," or decorticate, kidney cysts to drain fluid, relieve pressure and prevent cysts from returning.

"Decorticating the cysts is a laparoscopic surgery that requires only one to two hours and three small incisions to approach both kidneys," says Gleason. "It's a safe, straightforward operation with a uniformly easy recovery."

During the surgery, Gleason laparoscopically cuts out tissue from the top of each cyst to remove the fluid – simply draining the fluid without tissue removal would allow opportunity for the cyst to regrow. Any fluid not drained is reabsorbed by the abdomen. Gleason is able to decorticate multiple cysts in a single procedure.

The goal of kidney cyst decortication: to mitigate the detrimental effects of PKD including lowering blood pressure, reducing protein in the urine, improving balance and movement and ultimately prolonging kidney function thereby delaying the need for kidney transplant.

In the procedures completed so far, patients have seen improvements in these areas with a recovery time as short as a few days.

Nephrologist John Bissler, MD, (left) consults with Robotic Surgeon Joseph Gleason, MD, during a recent kidney cyst decortication. Gleason conducts the procedure robotically using just three small incisions to access both kidneys.

"Greyson was able to bounce back from this surgery incredibly quickly," said Brittany. "Within 72 hours he was back to his normal self, and we couldn't be happier with how this procedure turned out."

Nephrologist John Bissler, MD, is finding new ways to treat children with tuberous sclerosis complex and polycystic kidney disease. His recent research unveiled the cellular process by which mutant cells communicate to healthy cells to produce these cysts.

POSITIVE RESULTS

Bissler and Gleason have performed this procedure on seven patients with several more already planned for 2020. Thanks to decortication, parents are able to take action for their children instead of waiting, watching and fearing the worst outcomes.

For Greyson, the new procedure was a definite success. The effects were immediate — he has cut his blood pressure medicine in half and has an easier time playing and moving. His parents don't worry about the risk of a ruptured cyst, and his stomach is no longer distended.

"With Dr. Gleason's reputation and role as chief of robotics and our implicit trust in Dr. Bissler as a world-renowned nephrologist, we knew we had a dream team," said Brittany. "We've lived Greyson's whole life with PKD as a weight upon us. It's a relief that we no longer have to worry about the immediate risks of his kidney cysts."

Case Study: *Greyson Schwaigert*

When Greyson was 6 months old, Ryan and Brittany Schwaigert saw an ultrasound with cysts that looked like popcorn crowding their son's kidneys.

When he was 11 years old, they found themselves making a decision that could impact him well into adulthood. Should they proceed with a new procedure – kidney cyst decortication?

"Greyson has the polycystic variety of tuberous sclerosis which means cysts on his kidneys are hampering their ability to function properly," said Nephrologist John Bissler, MD. "He also has autism and sensory processing difficulties which would make dialysis difficult and unpleasant. Cyst decortication was the best option for him."

Although his kidney function had been fine up to this point, controlling his blood pressure was difficult – Greyson had doubled his blood pressure medication in the past year and was on his third medication.

"The option for this procedure took us by surprise, but we knew we wanted to be as aggressive as possible," said Greyson's mom, Brittany. "It was also important to address this pre-puberty before it would become more difficult to control."

After speaking with another mom whose child was one of the first to undergo cyst decortication, Ryan and Brittany knew that this was the right choice for Greyson.

"I never want to put Greyson through anything that he doesn't have to do," said Brittany. "But we trust Dr. Bissler implicitly and know that he wants to do whatever is best for Greyson."

During the procedure, Medical Director of Robotic Surgery Joseph Gleason, MD, removed 800 mL of fluid from Greyson's abdomen. The change was visible and immediate as they watched Greyson's stomach deflate and blood pressure drop when they began to drain cysts.

The Schwaigerts were back home the same day as surgery, and Greyson was back to his normal self within 72 hours of surgery. Bissler has cut his blood pressure medication in half.

"Greyson will continue to have yearly imaging follow-up to track the results of the surgery and the development of any new cysts," said Bissler. "Any small cysts that were not decorticated will continue to be controlled by medication."

The Schwaigerts hope that the procedure will delay Greyson's need for a kidney transplant. With the alleviation of pressure on his kidneys, the normal tissue will now be better able to function at full capacity. The Schwaigerts also feel less of the weight of polycystic kidney disease hanging over their heads. No longer must they worry that activities like playing with the dog or an accidental fall will lead to a ruptured cyst and hemorrhaging.

As a result of his tuberous sclerosis diagnosis, 11-year-old Greyson Schwaigert lives with polycystic kidney disease. He recently underwent an innovative cyst decortication procedure to prolong the life of his kidneys and improve his overall quality of life.

"Le Bonheur's Tuberous Sclerosis Clinic is truly the best in the world – all of the doctors, nurses and staff are incredible," said Brittany. "With this under-publicized disease we feel so incredibly lucky to have this clinic in our backyard. It has changed Greyson's life."

"Le Bonheur's Tuberous Sclerosis Clinic is truly the best in the world – all of the doctors, nurses and staff are incredible. With this under-publicized disease we feel so incredibly lucky to have this clinic in our backyard. It has changed Greyson's life."

– Brittany Schwaigert, Greyson's mom

Next Gen Impact

18-year evaluation of nurse-led early intervention program shows significant outcomes for participants

Improved math scores. Better emotional intelligence. Increased receptive language. Improved working memory. More high school honors graduates.

These are among the cognitive function and academic performance findings of an 18-year follow-up study of Nurse-Family Partnership (NFP) participants in Memphis, according to a recent report published in the journal *Pediatrics*. The study evaluated 18-year-old youth born to high-risk mothers with limited psychological resources to cope with poverty.

This new evidence signals that the national program, which pairs first-time moms with home-based, personal nursing care from pregnancy through the first two years of a child's life, may positively influence a child into adulthood.

An additional *Pediatrics* study, over the same 18-year period, found that NFP saved the government $17,310 per family in public-benefit costs, resulting in a net savings of $4,732 (in 2009 dollars) after accounting for the cost of NFP. This is a 9% reduction in public benefit expenditures over the 18-year period.

These studies represent the largest, with 742 women (228 nurse-visited; 514 control), and longest (18 years) evaluations of the program to measure youth cognitive development, academic performance and cost savings per family to the government.

On the heels of these two new studies, the Tennessee Department of Human Services announced in January an award of approximately $4.6 million in four years to the NFP program at Le Bonheur Children's Hospital to expand its services.

"If a mother is supported in her pregnancy, the outcome of that investment will change a generation," said Le Bonheur Community Outreach Maternal Child Director Sandra Madubuonwu, who is in charge of the hospital's NFP program.

With the new $4.6-million investment, Madubuonwu's team will double and expand to serve approximately 200 additional families. Since 2010, more than 900 mothers and babies have completed the program in Memphis.

Nurse-Family Partnership pairs first-time moms with home-visitation nurses from pregnancy to her child's second birthday.

POSITIVE OUTCOMES

NFP changes the future for the most vulnerable babies born into poverty by giving a first-time mom trusted support through nurse home visitations from pregnancy through her child's second birthday. The program is backed by over 40 years of scientifically-proven outcomes for mom and baby and currently serves over 38,000 moms in 41 states, the U.S. Virgin Islands and many Tribal communities.

The Memphis studies, which began in 1990, enrolled primarily African-American women living below the federal poverty level. Researchers found that nurse-visited youth were three times as likely to graduate with honors compared to the control group. Also, at age 18, the proportion of nurse-visited youth receiving supplemental security income (SSI) for disability was 64.2% lower than that of the control group. Moreover, girls born to mothers participating in NFP, as a trend, had fewer convictions at age 18 than girls in the control group.

Nurse-visited women, compared with women in the control group, had no increase in partnered relationships but had increased cohabitation (as a trend), marriage and confidence in the ability to manage challenges in their lives. Although the program had no effects on income, nurse-visited women earned more than women in the control group during years four and five after the first child's birth.

Nurse-Family Partnership resulted in:

- Savings of **$17,310** per family in public-benefit costs
- Net savings of **$4,732** after program cost
- **9%** reduction in public benefit expenditures

Previous program studies have shown reductions in first-born disability and rates of low birth weight in second births. Of Le Bonheur program participants, 89% of babies are born full-term, 75% of mothers initiate breastfeeding and 97% of toddlers are current with immunizations.

This latest study notes that nurse-visited mothers had more limited psychological resources (the ability to manage challenges in their lives) than the control group, and yet, children in the program outperformed those in the control group on many important cognitive and academic measures.

The findings suggest that nurse-visited mothers, like current program participant Charol Hewitt, truly change the life course for their children.

"The only thing I don't like about this program is that more mothers don't have access to it," said Hewitt.

A BEACON OF TRUTH

When Hewitt was 24-weeks pregnant, she attended a community baby shower where she learned about the program and decided to enroll. A few weeks later, the expecting mom from Whitehaven met Nurse Stephanie Washburn.

"It's so different when you to go to the OBGYN, as soon as I got there the questions I had would just fly out of my head," she said. "But when Stephanie visited, in my most comfortable place, my home,

I felt like I could ask her more. I had a lot of questions about childbirth."

Hewitt said that as a Southern woman with a large family, her nurse served as a beacon of truth in a sea of superstition and old-wives tales.

"The greatest support I received from NFP was facts," she said. "The readings and materials we received from the program I actually use when parenting," she said.

Washburn's first visits with Hewitt revealed blood pressure issues missed in previous office appointments. Washburn counseled Hewitt and her husband, Chris, through the pregnancy and helped them create a birth plan.

"Stephanie gave me that support and knowledge that other moms go through this. It's joyful, but it's also demanding and takes so much from us."

– Charol Hewitt, participant

Hewitt said that after watching several birthing videos with Stephanie and completing her hospital preparation checklist, by the time she went into labor on June 18, 2018, she felt calm and prepared to meet her son, Gavin.

"I remember when I first held him, I looked into his eyes, and I just saw all this personality," she said. "Now that he has grown more and is more expressive, I think 'Yep, I saw all this personality when you were just a little bitty baby.' He's this incredible person that I can't believe I carried in my belly."

Gavin, whom Hewitt calls her "sonshine," is a thriving 18-month old who loves to laugh and practice on his kid-size drum set.

Sandra Madubuonwu, Le Bonheur Community Outreach Maternal Child Director, delivers remarks at an annual graduation ceremony for Nurse-Family Partnership families.

FRONTLINE CARE

Hewitt's transition to motherhood wasn't without its challenges. Hewitt said her 15 minutes with a lactation specialist at the hospital did little to help when she got home and experienced latching issues.

Washburn came over and provided "hands-on, frontline care" that made a difference in her decision to breastfeed, Hewitt said. And when Hewitt began crying "for no reason" after she came home with Gavin, she recognized the signs of post-partum depression she had discussed with Washburn beforehand.

Gavin Hewitt, 18-months-old

"I was able to identify it, able to coach myself through it and express, 'Hey – I need a break,'" she said. "Stephanie gave me that support and knowledge that other moms go through this and it doesn't make me a bad mom. You feel so guilty for being depressed during a time when we are supposed to be so happy. It's joyful, but it's also demanding and takes so much from us."

Hewitt's health and coping skills have since transcended her own family. When her nail technician told her about a new mom who was exhibiting severe signs of post-partum depression, Hewitt gave Washburn a call. Together, they found resources to offer the new mom in Hewitt's social circle.

Study Design

"Prenatal and Infancy Nurse Home Visiting and 18-Year Outcomes of a Randomized Trial" (Memphis 18-Year Youth Study) and "Prenatal and Infancy Nurse Home Visiting Effects on Mothers: 18-Year Follow-up of a Randomized Trial" published in *Pediatrics* on November 20, 2019

- **Beginning in 1990, this study enrolled primarily African-American women with high-risk characteristics: 85% were living in households below the federal poverty level and in highly-disadvantaged neighborhoods in Memphis, Tenn.**
- **Both studies had high retention rates, which contribute to the validity of the findings. The mother study completed assessments of 85% of those mothers that were still alive at their first child's 18th birthday; while the youth study completed assessments on 90% of the children still alive at age 18.**
- **The follow-up studies are the most recent reports from a series of randomized, clinical trials of Nurse-Family Partnership (NFP) in the past four decades. Families in these trials are being followed to estimate NFP's long-term effects—far beyond when the program ends at the first child's second birthday.**
- **These studies have found the NFP is successful in reducing welfare use, improving maternal life course, improving a child's cognitive development and academic achievement, reducing juvenile crime and improving birth outcomes.**

Huang elected to American College of Surgeons' Board of Governors

Eunice Huang, MD

Eunice Huang, MD, professor of Surgery and Pediatrics at the University of Tennessee Health Science Center, has been elected to a three-year term as the Surgical Specialty Society Governor from the American Academy of Pediatrics. As a governor, she will facilitate communication between the Fellows of the College and the members of the Board of Governors.

University of Tennessee Health Science Center opens Pediatric Dental Clinic at Le Bonheur

The new dental clinic provides comprehensive pediatric dental care for patients in the hospital, as well as children from Midtown, Downtown and surrounding areas. For more information, contact (901) 448-5437, or visit uthsc.edu/dentistry/lebonheur.

Cystic Fibrosis Center receives full re-accreditation from the Cystic Fibrosis Foundation

The University of Tennessee Cystic Fibrosis Care and Research Center, a pediatric and adult clinic, recently received full re-accreditation from the Cystic Fibrosis Foundation. The multidisciplinary clinic provides comprehensive care for CF and ensures smooth transition from pediatric to adult care.

Black honored with American Gastroenterological Association Research Mentor Award

Dennis Black, MD, received the 2020 American Gastroenterological Association Institute Council Section on Obesity, Metabolism & Nutrition (OMN) Research Mentor Award. This annual award recognizes outstanding contributions to the mentoring and training of new investigators in the field. The award will be presented during Digestive Disease Week in May 2020.

Heart Transplant Program named a Cigna Program of Excellence

Le Bonheur's Heart Institute Transplant Program was recently recognized as a Program of Excellence as a part of Cigna's LifeSOURCE Transplant Network. Programs of Excellence meet or exceed the LifeSOURCE Performance Guidelines for Quality Inclusion.

Pediatricians receive leadership appointments

Emilee Dobish, MD

Jason A. Yaun, MD, FAAP

Hospitalist Emilee Dobish, MD, was elected vice president of the Memphis Pediatric Society. Pediatrician Jason A. Yaun, MD, FAAP, was elected vice president of the Tennessee Chapter of the American Academy of Pediatrics (TNAAP).

Fetal Center named a member of NAFTNet

Le Bonheur's Fetal Center was recently named a member of the North American Fetal Therapy Network (NAFTNet). This association consists of medical centers with established expertise in fetal surgery and other forms of multidisciplinary care for complex disorders of the fetus.

Le Bonheur Children's Hospital

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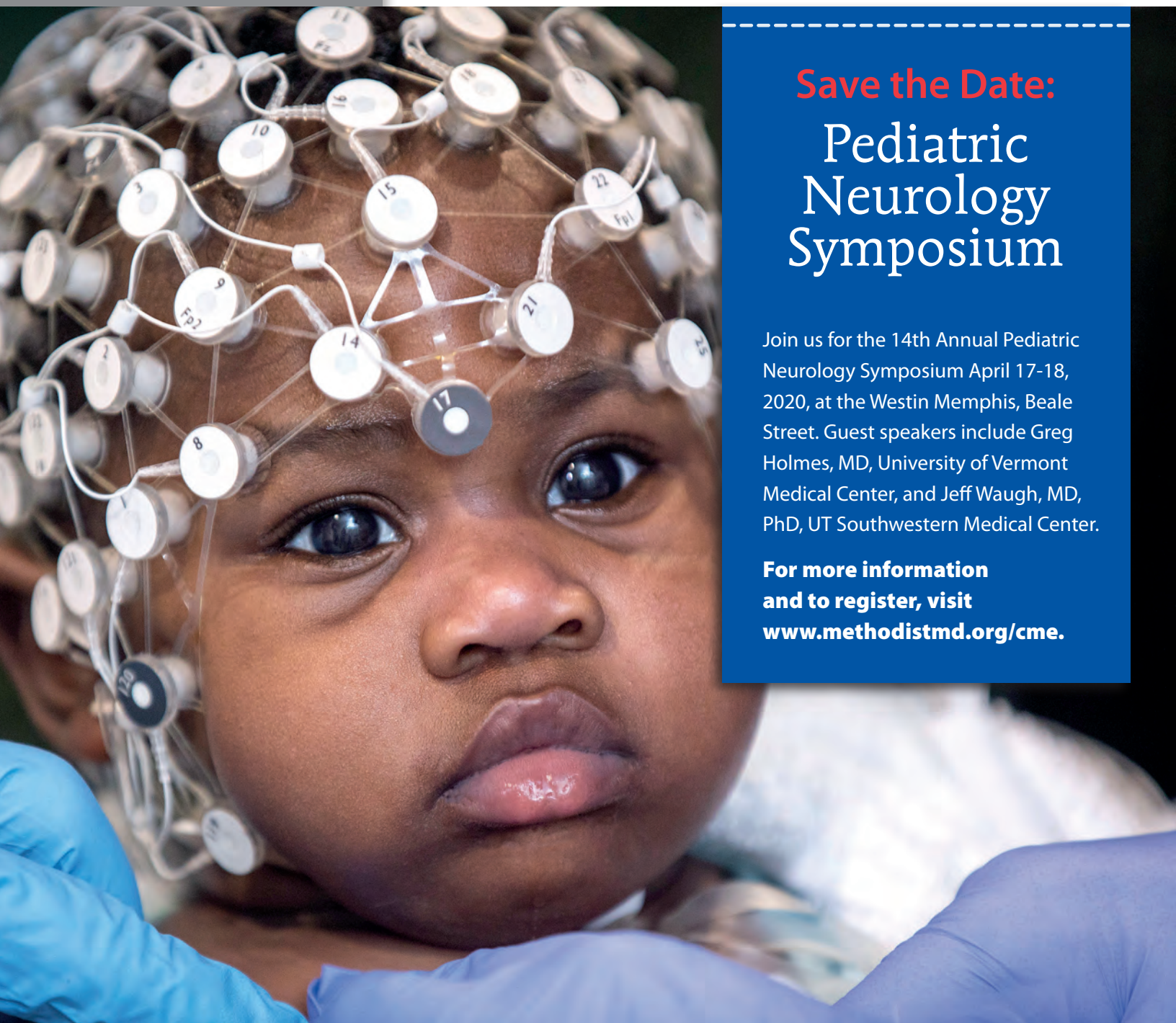

Save the Date:

Pediatric Neurology Symposium

Join us for the 14th Annual Pediatric Neurology Symposium April 17-18, 2020, at the Westin Memphis, Beale Street. Guest speakers include Greg Holmes, MD, University of Vermont Medical Center, and Jeff Waugh, MD, PhD, UT Southwestern Medical Center.

For more information and to register, visit www.methodistmd.org/cme.