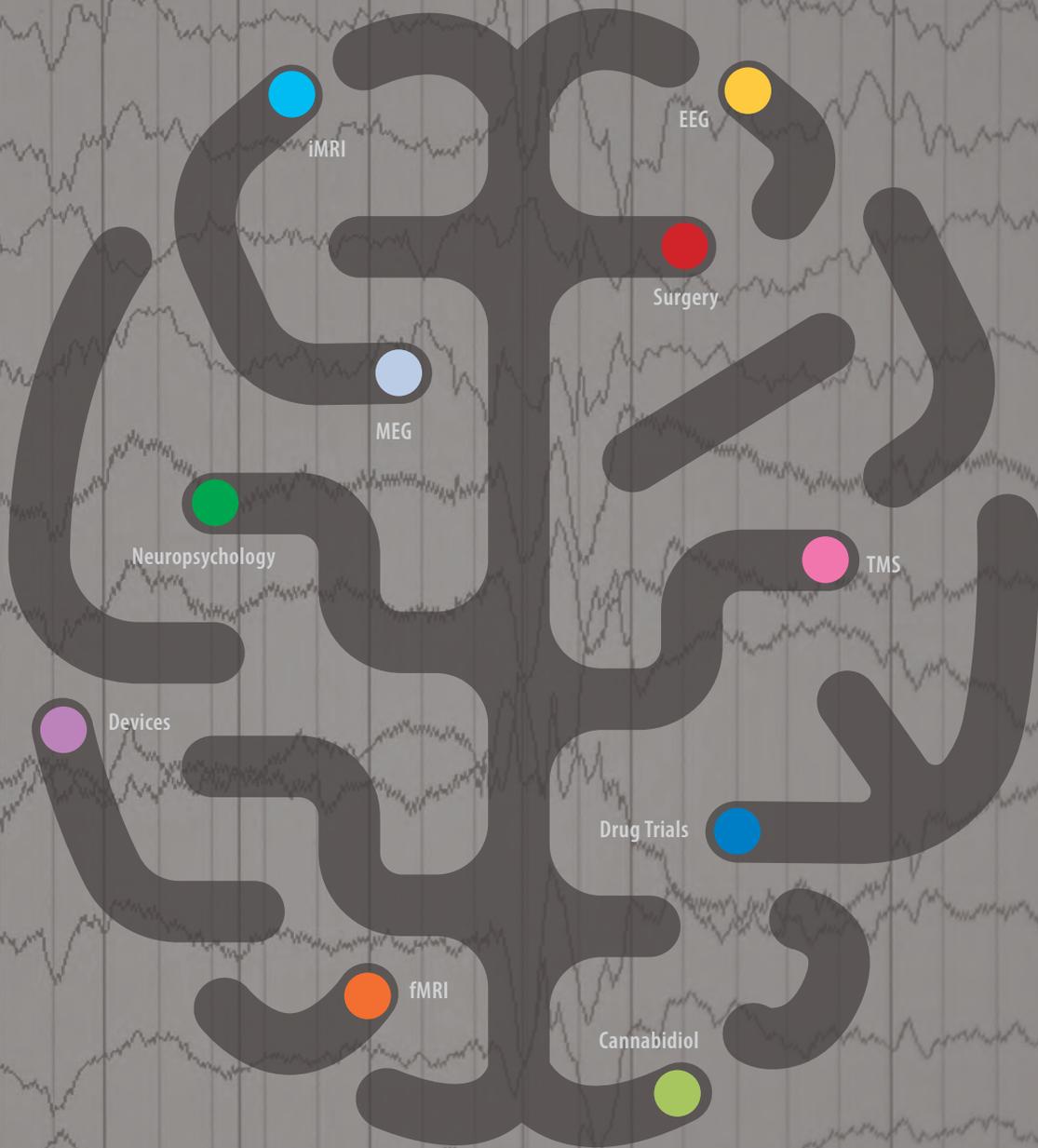


DELIVERING ON A PROMISE



Alternative Path

Finding a new roadmap for epilepsy treatment



+X

A

3 lb

7 lb

9 lb

MODEL TECHNIQUES

Novel 3-D model tests biomechanics of scoliosis bracing

Bracing has been a mainstay of treatment for some patients with idiopathic scoliosis. Although bracing has been shown to halt scoliosis curve progression in a number of published studies, the exact way in which the scoliosis brace transfers force to the growing spine remains a mystery. That's why orthopaedic surgeons at Le Bonheur have joined forces with the BioRobotics Laboratory at the University of Tennessee Health Science Center to test the biomechanics of scoliosis bracing techniques. The team has developed a novel mechanically equivalent analog model of adolescent idiopathic scoliosis, which uses a linkage-based system to simulate 3-D spinal correction. Findings so far have shown that strap material and strap tensioning affect the corrective force applied by the brace — while the order of strap tensioning doesn't seem to matter as much. The team has also developed a new fastening device — the controlled tension unit — which makes the brace less rigid and more comfortable without affecting the strap tension or corrective force.

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



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.



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

In this issue:

2 ALTERNATIVE PATH

Finding a new roadmap for epilepsy treatment

10 STRONGER HEARTS

Two years into ambitious plan, Heart Institute secures top STS rating, 9 super-specialized clinics

14 PROFILE: PATRICIA J. DUBIN, MD

For the new chief of Pediatric Pulmonology, the pursuit of treatments is personal

16 SAFER TRANSFUSIONS

Research looks at lead, mercury levels after blood transfusions in premature infants

19 SEPARATE BUT NEVER APART

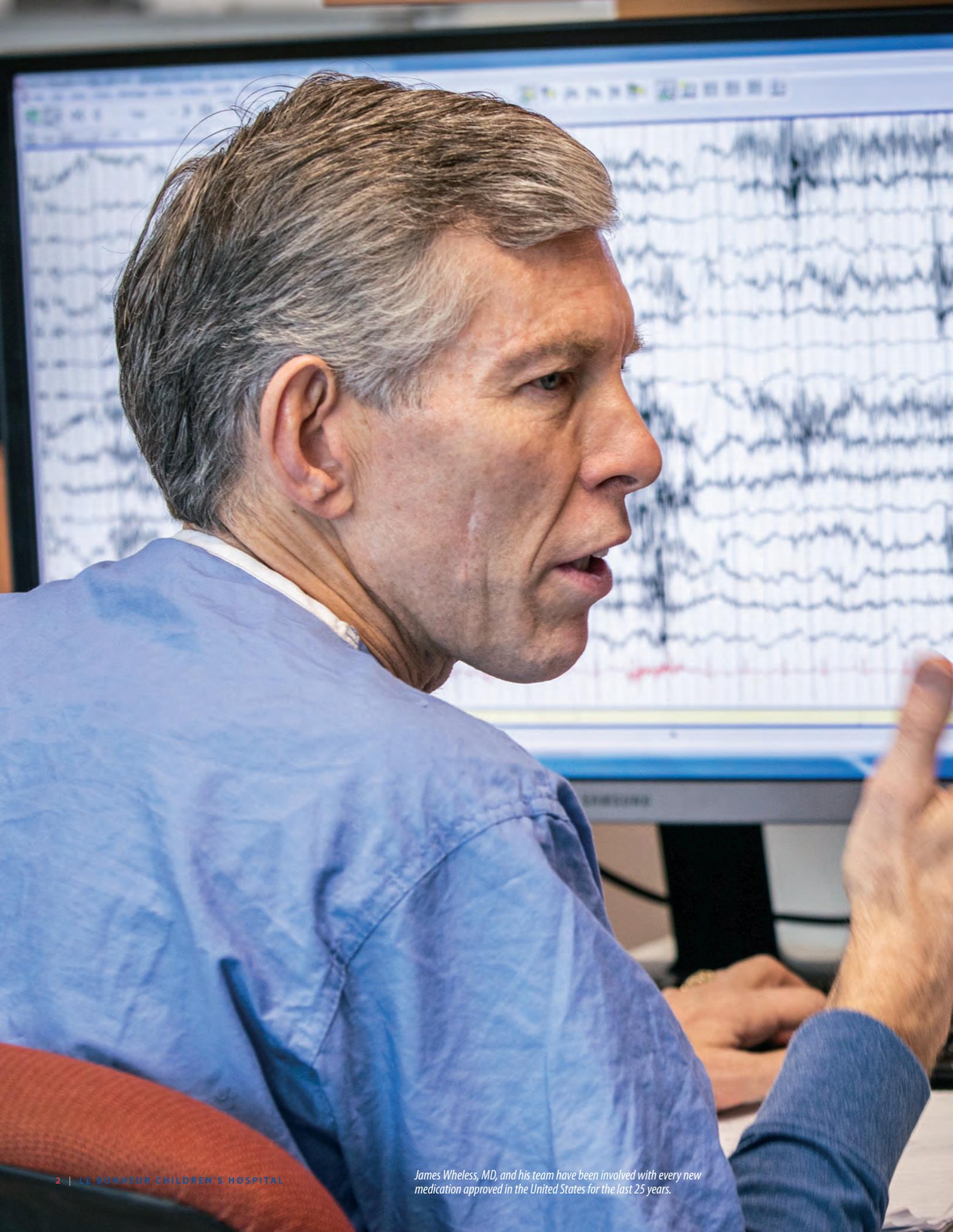
Le Bonheur separates second set of conjoined twins

Delivering on a Promise is a publication of Le Bonheur Children's Hospital, produced by Le Bonheur Marketing & Communications Services. If you have any questions or would like to be removed from our mailing list, please call 901-287-6030 or email info@lebonheur.org.

www.lebonheur.org/promise



For referrals contact:
Le Bonheur Connect at 866-870-5570.



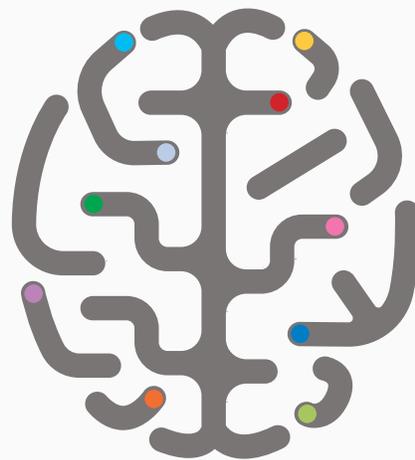
ALTERNATIVE PATH

Finding a new roadmap for epilepsy treatment

When epilepsy medications could no longer control **Payton Stanley**'s seizures, his parents, Stephanie and Robert, were desperate to find alternative treatment options.

Every time **James Sain** would have a seizure, his mom, Michelle, had difficulty administering his emergency medication.

Multiple surgeries and medications did little to slow down **Hannah Lawrence**'s uncontrolled seizures.



As their parents thought they had exhausted nearly all treatment options, these families – and countless others – turned to Le Bonheur Children’s Hospital where physicians and researchers in the Neuroscience Institute offered new and effective methods to treat pediatric epilepsy.

Epilepsy Program Director and Chief Neurologist James Wheless, MD, knows there is no “one size fits all” for managing seizures caused by epilepsy. Discovering the newest therapies and medications is vital to provide the best outcomes possible for children whose ongoing seizures cannot be controlled with medicine, change in diet or surgeries, Wheless said.

“Even though there are more treatment options than ever for kids with epilepsy, we always need to find other options – to come up with new treatments for children when drugs do not help,” he said.

“We need to be on the cutting edge of delivering the best care.”

“We need to be on the cutting edge of delivering the best care.”

James Wheless, MD
Director, Comprehensive Epilepsy Program

For Wheless and his team of pediatric neurologists, that means using state-of-the-art brain-mapping

technology, enrolling patients into various new medication trials and using the new devices to find the right individualized combination of treatment options for each patient.



Neuroscience Institute Co-director James Wheless, MD, right, and his team are working to develop new therapies for kids with epilepsy.



Emergency Nasal Spray

- Rectal emergency Diazepam gel is a standard medication, but for some patients it's ineffective or difficult to administer.
- Diazepam nasal spray drug trial began in October and will last two years.
- Preliminary results are promising – parents say it's cleaner and more convenient.

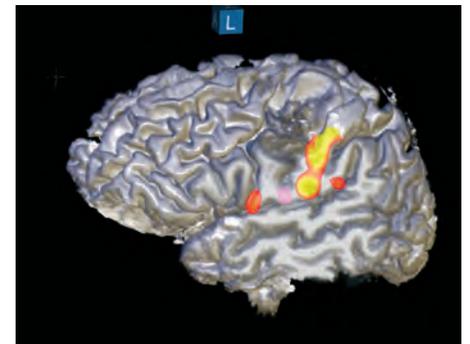
Le Bonheur's two largest drug trials include an emergency nasal spray version of a long-standing seizure drug, Diazepam, and testing of cannabidiol, a compound extract from a cannabis plant. Both trials are offering new options for children with epilepsy.

For others, surgery is an option. Functional MRI (fMRI), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS), single photon emission



Neuroscience Institute Co-director Andrew Papanicolaou, PhD, and his team use tools like functional MRI and transcranial magnetic stimulation to pinpoint areas of the brain causing seizures.

computed tomography (SPECT) and intraoperative MRI (iMRI), give Le Bonheur neurologists tools to map each brain, which are then used to create an intricate roadmap for making surgical decisions.



Brain-mapping technologies help neurosurgeons make surgical decisions. A three-dimensional rendering of MRI with fMRI overlay shows language and motor function.

“Technologies like functional MRI and transcranial magnetic stimulation allow us to pinpoint the exact

areas of the brain causing seizures while also identifying healthy parts of the brain that control other functions such as speech, movement or language,” said Andrew Papanicolaou, PhD, co-director of Le Bonheur's Neuroscience Institute.

“Creating a detailed map of



Cannabidiol

- Cannabidiol (CBD) is a compound extract from a cannabis plant.
- Contains less than 1 percent of tetrahydrocannabinol (THC), the chemical responsible for most of marijuana's psychological effects, and does not contain enough to cause psychoactivity.
- Le Bonheur is the only Tennessee hospital studying cannabidiol. The study began in 2015 and is in its third phase.
- Results from the study are promising. For one patient, cannabidiol helped reduce seizure activity from 500 seizures a week to 200.



Brain mapping

- Le Bonheur offers patients the most advanced brain-mapping technology to pinpoint seizure activity while also identifying healthy parts of the brain that controls other functions such as speech, movement or language.
- The hospital is one of the few pediatric centers with a complete complement of this technology under one roof, including:
 - Functional MRI (fMRI)
 - Magnetoencephalography (MEG)
 - Transcranial Magnetic Stimulation (TMS)
 - Single photon emission computed tomography (SPECT)
 - Intraoperative MRI (iMRI)

the brain ensures patients not only receive the best care and treatment, but also allows children to live the best life possible,” he adds.

In addition to drug and surgical options, children with epilepsy also have found success using both vagus nerve stimulation (VNS) and responsive neurostimulation (RNS) devices.

RNS is a relatively new therapy used to treat seizures in adults who have not had their seizures controlled with medication and who are not candidates

for surgery. The device is used in a limited basis in children, primarily in those older than 10 years old, with poorly controlled seizures. Le Bonheur is one of the few children’s hospitals in the country to offer RNS therapy.

“Devices are the second most used way to help children with epilepsy,” Wheless said. “These devices play a critical role. Medicines are still the mainstay for our treatment of epilepsy, but for children and adolescents where medicines don’t work, there are other therapies.”

Nationally, about 800 people have an RNS system. There are approximately 100,000 people worldwide with a VNS device.

Devices

- Vagus nerve stimulation (VNS) is placed beneath the skin of the chest and sends an electrical signal to the brain to prevent or stop seizures.
- 38 VNS devices were implanted in 2016.
- Responsive neurostimulation (RNS) is a new device used in a limited basis in children older than 10 years of age with poorly controlled seizures. The device is implanted in the skull with electrodes placed on the surface of the brain.
- Nationally, about 800 people have an RNS system.
- Le Bonheur was the first children’s hospital in the country to implant RNS.



Learn more at
www.lebonheur.org/promise

EPILEPSY: A TAILORED APPROACH

James Sain, 15: Generalized Tonic-Clonic Seizures *Diazepam emergency nasal spray drug trial*

James and Michelle Sain of Olive Branch, Miss., enrolled their 15-year-old son, James Jr., into the epilepsy nasal spray drug trial after the Sains had complications administering the emergency rectal gel. Michelle said it was difficult to give her son the correct dosage rectally and, at times, wasn't effective at stopping the seizures.

"Sometimes he got nothing from using the gel medication," Michelle said.

The benefit of the nasal spray is three-fold: it's easier, more practical and can be as effective as the rectal gel, said Tracee Ridley-Pryor, MSN, RN, CCRC, Le Bonheur Neuroscience Institute's lead clinical research coordinator.

"It seems more user friendly to administer because of a broader familiarity with intranasal medication," Ridley-Pryor said. "Because the medication is absorbed through the nasal passage, within a minute, often within seconds, the patient will begin to come out of the seizure."

When James Jr. had a seizure in December, Michelle administered the emergency nasal Diazepam, which calmed his seizure activity within minutes.



Payton Stanley, 2: Infantile Spasms, Complex Partial Seizures *Cannabidiol drug trial*

Payton Stanley, 2, is enrolled in a clinical trial of cannabidiol (CBD), a compound extract from a cannabis plant. The year-long trial studies the potential benefits of CBD for children with epilepsy, and Le Bonheur is the only children's hospital in Tennessee to participate.

Prior to taking CBD, Payton — who was diagnosed with infantile spasms and complex partial seizures — would have up to 500 seizures a day, said his mother, Stephanie. When he was 6 months old, the Stanleys of Vinita, Okla., came to Le Bonheur for a lobectomy. In January 2016, the family returned for a hemispherectomy — another attempt to control Payton's ongoing seizures.

The surgeries helped, Stephanie said, but the seizures would always return.

After his hemispherectomy, Le Bonheur neurologists suggested the Stanleys enroll in the hospital's first CBD drug trial. Since taking CBD, Payton's seizure activity has slowed — he's now having fewer than 200 a week — and his family said his personality and cognitive ability also have improved.

"He's more alert. He smiles more and giggles more. He giggles at everything," Stephanie said.



Hannah Lawrence, 22: Complex Partial Seizures *NeuroPace responsive neurostimulation device*

Hannah Lawrence of Brandon, Miss., had her first seizure when she was 13 years old and was transported to Blair E. Baston Children's Hospital in Jackson, Miss., where she was diagnosed with viral encephalitis. Inflammation on her brain left scar tissue and caused uncontrolled seizures.

She came to Le Bonheur in 2007 upon a referral from her pediatric neurologist. At Le Bonheur, Chief Neurologist James Wheless, MD, began exploring various treatment options for Hannah. Because medications did little to stop the seizures, doctors implanted a vagus nerve stimulation (VNS) device. In 2010, Hannah had another surgery, a right temporal lobectomy, to help control the seizures. She underwent another operation in 2013.

While each surgery slowed her seizures, Hannah still couldn't live independently. When Wheless suggested the responsive neurostimulation (RNS) device, the Lawrence family jumped at the opportunity.

RNS is being used in a limited basis in children, primarily those older than 10 years old, with poorly controlled seizures. Le Bonheur is one of the few hospitals in the country to offer RNS therapy for children.

The RNS has dramatically reduced Hannah's seizures, and the care and treatment she received at Le Bonheur has been life changing, her mom, Rhonda, said.

"Hannah can now do things without us like shopping by herself, and we don't have to worry as much," Rhonda said. "The RNS has changed our lives. Independence is important to her."





LE BONHEUR'S COMPREHENSIVE EPILEPSY PROGRAM

By the numbers: 2016

- 505 visits to the Epilepsy Monitoring Unit
- 33 epilepsy-related surgeries
- 38 RNS and 4 VNS devices implanted
- 365 brain-mapping studies, including MEG, TMS and fMRI

Le Bonheur's reputation as one of the country's top epilepsy programs is what attracted the Stanley, Sain and Lawrence families to Memphis. Stephanie and Robert Stanley dream of a day when Le Bonheur neurologists will find a treatment option that will allow Payton to live a seizure-free life –

“Places that have higher volumes typically do better jobs, and Le Bonheur has one of the higher volumes in the country. We have all the sophisticated equipment that most other children's hospitals don't have.”

Frederick Boop, MD
Co-director of the Neuroscience Institute
Chairman of the Department of Neurosurgery for
the University of Tennessee Health Science Center

a day when their son will be able to crawl, sit up, walk and speak.

“We look forward to some normalcy and being able to go out as a family without having to worry about Payton getting sick or having a seizure,” Stephanie said. “We look forward to seeing him continue to develop.”



Payton Stanley, 2, suffers from infantile spasms and complex partial seizures. A cannabidiol trial is helping him find relief.

Epilepsy Monitoring Unit adds new equipment, software

Newly installed software and technology in Le Bonheur Children's Hospital's Epilepsy Monitoring Unit (EMU) will provide pediatric neurologists and nurses better data and information for epilepsy monitoring, brain mapping and other neurological procedures.

The new software, EMU40EX, will be used in the 10-bed EMU and will allow physicians to record and receive a patient's brain activity. The software also provides a faster sampling rate, giving the neurologist a more detailed EEG and enhances subtle abnormalities. More efficient software and hardware will help improve a child's outcome, said Le Bonheur EEG/EMU Manager Penny Taylor.

"It's a better way to diagnose and to treat patients with epilepsy. When you have the latest and the greatest equipment the end result is beneficial to the patient," Taylor said.

In addition to new software, the EMU received three quantum devices, amplifiers and a cortical stimulator, which will be used on patients with intracranial electrodes.

"When you have a child coming in with a long history of epilepsy with no successful treatment they can be referred to Le Bonheur where we have state-of-the-art technology to help treat the patient for their seizures and hopefully become seizure free or decrease their seizure activity," Taylor said.



Stronger Hearts

Two years into ambitious plan, Heart Institute secures top STS rating, 9 super-specialized clinics

After four surgeries at two different children's hospitals, Charlie Hudson's parents were searching for someone who could repair the 2-year-old's tricuspid valve.

Charlie, of Greensboro, N.C., was diagnosed in utero with ventricular septal defect with coarctation of the aortic arch. Now, her damaged valve was affecting her liver, and her spleen had grown enlarged.

Her fifth surgery would require a specialized procedure that few in the country could do: repairing a valve that most surgeons could only replace. Finding the expertise to repair the valve would mean fewer future surgeries for the already fragile child.

"Not only did our little girl need surgery again, but could it even be done," her mom, Nicole, asked.

Their nationwide search led them to Le Bonheur Heart Institute Executive Co-Director Christopher Knott-Craig, MD, a pediatric cardiovascular surgeon whose surgical outcomes earned Le Bonheur a prestigious three-star rating from the



Charlie Hudson, left, and her family traveled from North Carolina to Memphis for a tricuspid valve repair from Chief Cardiovascular Surgeon Chris Knott-Craig, MD.

Society of Thoracic Surgeons (STS) in 2016.

"We knew there weren't a lot of surgeons out there with knowledge on tricuspid valve and repairing it. Most would just go ahead and replace," said Nicole. "He has been repairing valves more so than replacing them, so we went with Dr. Knott-Craig for that option."

Two years after launching an ambitious plan to grow Le Bonheur's Heart Institute, Knott-Craig and his fellow executive co-director, Chief Cardiologist Jeffrey A. Towbin, MD, have expanded nine programs within the Institute,

recruited 10 new faculty members and launched a cardiac genetics research program.

Surgical outcomes continue to be recognized among the best in the country, and both the transplant and mechanical circulatory support programs are growing.

"We know that we are building a program that is ready for the changing needs of children and adults with congenital and acquired heart conditions — and we're focused on offering the best possible care," Towbin said.

SURGICAL SUCCESS

Le Bonheur is one of 11 programs to receive three stars in the latest STS Congenital Heart Surgery Database Feedback Report.

The STS Congenital Heart Surgery Database compiles data from pediatric heart programs across the country and publishes surgical outcomes information twice a year. Participating programs receive a one- to three-star rating semiannually for cardiac





Cardiovascular Surgeon Umar Boston, MD, left, discusses transplant patient Lyric Everhart with Le Bonheur's transplant team.

surgery outcomes in a four-year period.

The ratings are based on STS's mortality risk model, which takes into account the hospital's number of actual mortalities versus expected



Lyric Everhart, 20 months, received a heart transplant at Le Bonheur in late 2016. She was diagnosed with dilated cardiomyopathy weeks before her transplant.

mortalities for a certain illness or condition.

"It's a privilege to be part of developing a program with such world-class results," Knott-Craig said.

The Heart Institute's growth also included the recruitment of Umar Boston, MD, surgical director for both Heart Transplant and Mechanical

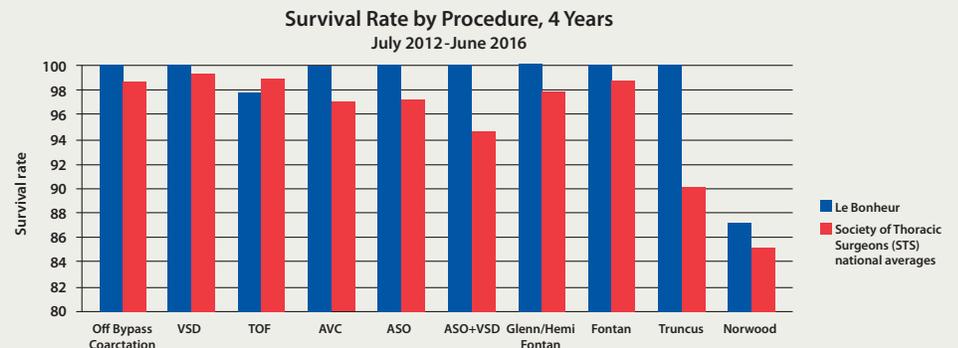
Circulatory Support and Adult Congenital Heart Disease. The hospital performed three heart

transplants for dilated cardiomyopathy in late 2016-17 – all doing well to date.

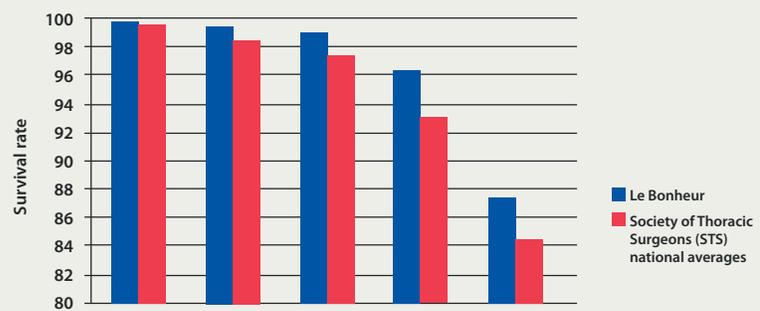
Boston is also working to build the circulatory support program. The Heart Institute currently uses three ventricular assist devices (VAD): the Berlin heart, Centrimag and HeartWare devices. Boston recently placed a VAD in an infant with single ventricle with Glenn circulation. The patient was supported for eight days to allow recovery of his heart and end organs and is recovering well now.

In the catheterization lab, cardiac interventionalists are performing

Surgical outcomes earn national attention



Operative Survival by STAT Category, July 2012-June 2016



Average survival rates for Le Bonheur heart surgeries are higher than national average – especially in most complex procedures.



Heart Institute Co-Director Jeffrey A. Towbin, MD, came to Le Bonheur two years ago to build a program focused on improving quality of life for children and adults with congenital heart defects.

transcatheter patent ductus arteriosus (PDA) closures in premature babies, some less than two kilograms. In 2015-2016, the center closed PDAs on 40 children, the most of any center its size.

A NEW DIRECTION

When Towbin came to Le Bonheur from Cincinnati Children's Medical Center two years ago, he made clear his goal — to build a program that would look beyond patient survival and address lifestyle, giving children and adults

with congenital heart defects and heart muscle diseases a great quality of life.

Since his arrival, the Heart Institute has started or expanded the super-specialized programs Towbin set out to establish.

The Heart Institute has added new cardiologists and cardiovascular surgeons to its team and has launched new research, particularly in the area of cardiac genetics.

Enkhasaikhan (Enkhe) Purevjav, MD, PhD, is leading the new Cardiology Genetic Research Laboratory and has

brought new researchers to her lab. Purevjav, who worked with Towbin at Cincinnati Children's, conducts research aimed at discovering and investigating novel genes and gene mutations that contribute to cardiac diseases like cardiomyopathy, heart failure and arrhythmia disorder.

The lab is working to find molecular genetic basis for cardiac diseases and use these discoveries to develop novel, targeted therapies.

Outside of the lab, Le Bonheur continues to participate in several

national registries aimed at improving quality and standards of care for patients with congenital heart disease. They include:

- Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD)
- IMPACT Registry (National Cardiovascular Data Registry)
- Congenital Cardiovascular Interventional Study Consortium (CCISC)
- Scientific Registry of Transplant Recipients
- National Pediatric Cardiology – Quality Improvement Collaborative (NPC-QIC)
- Pediatric Cardiac Critical Care Consortium (PC4)
- Intersocietal Accreditation Commission (IAC)
- American College of Cardiology's Adult Congenital and Pediatric Cardiology, Quality Network (ACPC-QNET)
- Solutions for Patient Safety, Children's Hospital Association
- National Research Corporation (Patient Experience)
- National Database of Nursing Quality Indicators

"We know that better research and quality collaboratives make us better clinicians — and in turn provide better care for our patients," Towbin said.



CARDIAC CLINICAL TRIALS

Le Bonheur's Heart Institute, in conjunction with Le Bonheur's Children's Foundation Research Institute, is currently conducting clinical trials, all aimed at advancing pediatric and adult congenital heart medicine. They include:

We are one of 10 clinical trial sites for a device used to close patent ductus arteriosus (PDA) in extremely premature babies. This includes work in the catheterization lab, where interventionists are closing PDA defects on babies smaller than two kilograms.

A global study for pediatric patients with a single heart ventricle defect, using a blood thinner approved by the FDA for adults. If the medication works, patients would benefit by not having to be treated by Coumadin/Warfarin, resulting in less blood monitoring and fewer food restrictions, thereby improving their quality of life.

Studying transplant patients to learn more about the genetic aspects of heart defects.

Participating in a national study that uses Fitbit technology to record physical activity in patients with a condition that can potentially cause sudden cardiac death.

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

Back in North Carolina, Charlie Hudson is a testament to what a growing program can do for patients. After Knott-Craig successfully repaired her tricuspid valve last year, she has grown into a typical 4-year-old playing with her sister and attending preschool.

"We are so blessed to be able to have found Dr. Knott-Craig and Le Bonheur, a hospital that truly cares for its patients," Nicole said.

Inspirational Drive

For the new chief of Pediatric Pulmonology, the pursuit of treatments is personal

For Le Bonheur's new Chief of Pediatric Pulmonology and Sleep Medicine Patricia J. Dubin, MD, pursuing new treatments for respiratory issues is more than just a passion. It's personal.

As a child, Dubin suffered from severe asthma and was often ill. As she grew older and honed in on a career in medicine, she knew she wanted to find a way to help children with respiratory problems breathe easier. But for Dubin, it was more than her own experience that shaped her future in pulmonology. During her senior year of undergraduate studies, the daughter of a favorite professor, just 10 years old, died. The young girl had cystic fibrosis.

"It had a pretty profound effect on our entire campus, because we all kind of knew this little girl, and that was one of the first exposures that I really had to cystic fibrosis," says Dubin. "When we look at our field, many people think pulmonary evolved out of a need to take care of patients with asthma and other types of breathing disorders, but in large part it evolved around the disease of cystic fibrosis."

Dubin began her medical school training at the University of Rochester School of Medicine and Dentistry, followed by a pediatric residency at Yale New Haven Children's Hospital, where she was able to



Chief of Pediatric Pulmonology and Sleep Medicine,
Le Bonheur Children's Hospital



engage in a fair amount of pulmonary training through the general pediatrics residency. She completed her pediatric pulmonology fellowship at the Children's Hospital of Pittsburgh, where she stayed on for a decade, focused on research and clinical work. She moved to West Virginia University School of Medicine, where she was chief of Pediatric Pulmonology and Sleep Medicine, and served as the director of the Mountain State Cystic Fibrosis Center.

At Le Bonheur, Dubin will focus on developing clinical, research and education programs.

The connection between sleep medicine and breathing disorders drew Dubin's particular interest, something she calls a natural fit for people who think a lot about respiratory problems.

"A good portion of pediatric sleep medicine is secondary to breathing problems," explains Dubin. "When we look at the different kinds of pathology, we think of obstructive sleep apnea or difficulty breathing during sleep. While that is a large part of pediatric sleep medicine, it is not the entire story. There are many other types of disorders."

Dubin will also continue her clinical work with young respiratory patients who seek treatment at Le Bonheur from across the region. Each year, asthma

is the cause of more than 3,500 asthma-related visits to Le Bonheur.

“There are many things that attracted me to Le Bonheur,” says Dubin. “I was attracted to the institutional commitment to community service, clinical program development, research and education.”

She also cites the potential of Le Bonheur’s programs, opportunities for partnering with other research hospitals, and Le Bonheur’s focus on the needs of the community when it comes to respiratory treatment and therapy.

“There is a clear commitment to the Memphis community through the development of programs that address unmet needs for the city and region as well through the development of programs that will garner national attention. The partnership with St. Jude (Children’s Research Hospital) also allows us to focus on respiratory care in oncology and hematology patients.”

“There’s significant asthma in the city and in this area, and so for me the idea of working with our colleagues in allergy and with the CHAMP program (Changing High-Risk Asthma in Memphis through Partnership) to further improve asthma care here was a really appealing opportunity,” continues Dubin. “And there’s a wonderful cystic fibrosis program that I think can continue to grow and become a better resource for this region.”

“I think many of us in medicine are inspired by our personal experiences, and that drives us to do what we do.”

In her words

In the next year, Dubin will lead Pulmonary and Sleep Medicine Program development:

Asthma: Pulmonology will focus on streamlining care and improving clinical outcomes through collaboration with our colleagues in Allergy and the CHAMP program. We will continue to provide excellent care for individuals with asthma and other complicating respiratory comorbidities.

Cancer-related respiratory disease: Cancer and the treatments it necessitates (e.g. radiation, chemotherapy and bone-marrow conditioning regimens) can cause significant respiratory damage. We will work with our oncology colleagues at St. Jude (Children’s Research Hospital) to develop a better understanding of the impact of cancer therapies on respiratory function as well as approaches to improving outcomes for these children. In patients with brain tumors (CNS tumors), the tumors and the therapies used to treat them can affect the centers in the brain that help control breathing and sleep cycles. We will collaborate with our oncology and neurosurgery colleagues to help develop treatment strategies targeted at these breathing- and sleep-related problems.

Hematology-related respiratory disease: The Memphis region also has a large population of individuals with sickle cell disease. Sickle cell disease is a blood disorder that can cause severe respiratory problems as well as strokes. While outcomes have drastically improved with the use of hydroxyurea therapy, the risks of significant cumulative respiratory and stroke damage over a lifetime remain high. We are developing a program to identify and manage respiratory and sleep complications in sickle cell disease with the ultimate goal of improving outcomes.

Primary Ciliary Dyskinesia: PCD is a respiratory disease that is present at birth and causes permanent and irreversible respiratory damage if not identified early. It is treatable, though not curable. Early identification and intervention markedly improves outcomes. Catherine Sanders, MD, is an expert in PCD and was recently hired to develop and grow our PCD program here at Le Bonheur and the University of Tennessee Health Science Center. Our program will be one of only a handful of nationally recognized pediatric PCD centers in the country.

Medically complex and technology-dependent: Children who require chronic ventilation or airway clearance require individualized treatment plans that fall within a rubric of care. Pulmonology is the primary group responsible for managing their care and partners closely with our intensivists and neonatologists to develop hospital-based, as well as home-based care plans.

Chronic lung disease (CLD) of prematurity, commonly referred to as “BPD”: Infants who are born premature have varying degrees of lung dysfunction that improves over time and with supportive treatment. Consistent and evidence-based care can prevent this vulnerable population from having further complications secondary to acquired infections and environmental exposures. Our group will continue to develop standardized care for the many infants and children with CLD of prematurity through our BPD clinic.

Patricia J. Dubin, MD

Education and Training

Children’s Hospital of Pittsburgh – Pediatric Pulmonology Fellowship
Yale - New Haven Children’s Hospital – Pediatrics Residency

University of Rochester School of Medicine and Dentistry –
Medical School
Mount Holyoke College – Undergraduate Studies





Safer Transfusions

Research studies lead, mercury levels after blood transfusions in premature infants

Small amounts of lead and mercury are delivered to premature infants who have received a blood transfusion, and some of these metals are deposited in body organs, according to research led by Le Bonheur Children's Neonatologist Mohamad T. Elbiad, MD.

The concern with tissue deposition: chronic fetal exposure to heavy metals has been associated with developmental delay. If lead and mercury are being absorbed by the premature babies' organs, is exposure during this critical time enough to cause concern?

"We know that chronic exposure to lead and mercury in utero is associated with developmental delay," said Elbiad. "It is yet unknown if such infrequent exposures in an extremely premature infant will also have similar consequences."

Elbiad's study – supported by the Centers for Disease Control and Prevention, Methodist Healthcare Foundation and The Gerber Foundation – measured the volume of distribution and elimination half-life of lead and mercury based on pre- and post-transfusion levels in premature infants. Initial findings have shown that infants receive enough lead and mercury through the transfusions to cause an increase in their blood's lead and mercury levels. Levels drop back to pre-transfusion levels within two to three days.

"The most likely explanation for this drop back to pre-transfusion levels are either the metals were deposited in certain organs and/or the metals were excreted out of the body," said Elbiad.

Lead levels in the babies' urine – the main route of excretion – were very small compared to levels received with the transfusions, and the team is still working to see if the same is true of mercury levels.

"This tells us that most of the lead received during a transfusion is likely being deposited in organs," Elbiad said.

Elbiad added that metals received through transfusions in term infants and older children is not of concern, as these children rarely receive more than one transfusion in a short amount of time. If they do,

their excretory organs, including the kidney and liver, are much more mature than those of a premature infant.

Blood transfusions are common procedure for premature infants, Elabiad said, because of their finite blood volume and the frequent blood draws needed to



Born at 24 weeks weighing just more than a pound, Malaya Jefferson received multiple blood transfusions in her first few weeks of life. Mohamad T. Elabiad, MD, and his team of researchers are working to determine the long-term effects – if any – of mercury and lead levels received through transfusions.

“We know that chronic exposure to lead and mercury in utero is associated with developmental delay. It is yet unknown if such infrequent exposures in an extremely premature infant will also have similar consequences.”

Mohamad T. Elabiad, MD, neonatologist at Le Bonheur Children’s Hospital

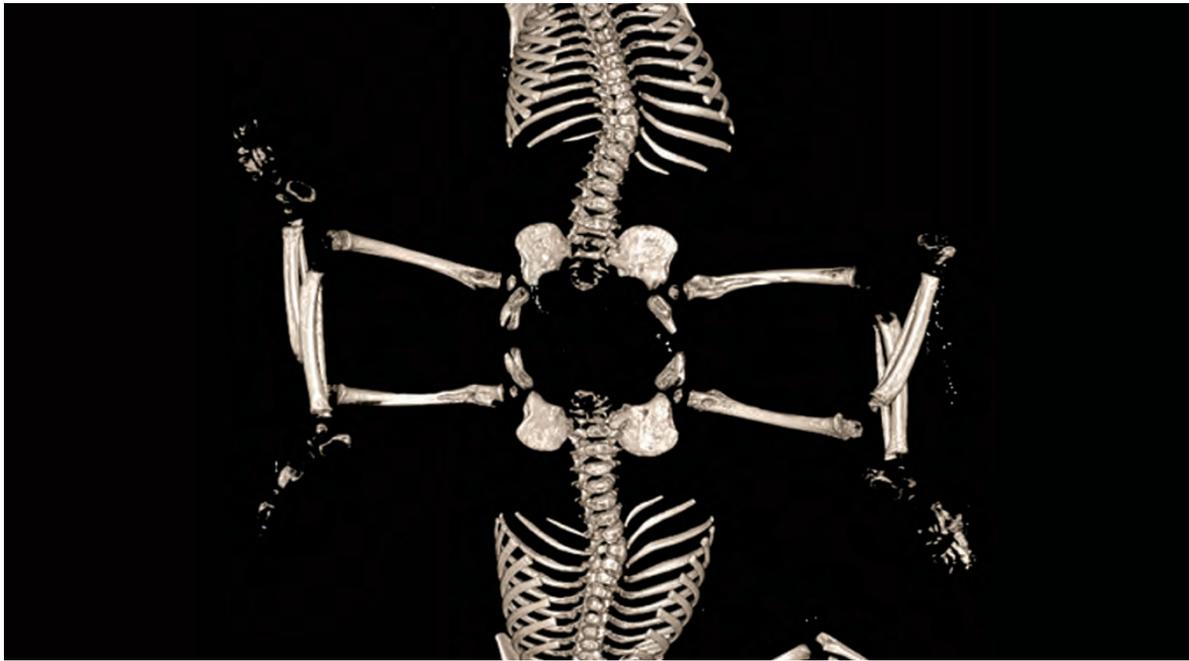
evaluate and assess their condition.

Elabiad and his research team will next focus on evaluating markers of the brain or kidney’s exposure to these metals post-transfusion. If organ deposition is confirmed, screening blood donors for lead and mercury levels will help reduce the amount of heavy metals given during a transfusion, says Elabiad.

Pharmacokinetics of Lead and Mercury in Premature Infants After Blood Transfusions

10 infants, mean birth weight of 688±125g

Lead	
Pre-transfusion (mean levels)	Post-transfusion (mean levels)
0.39±0.16 µg/dL	0.61±0.24 µg/dL (collected at a mean time of 5.1±1.1 hours)
	0.47±0.13 µg/dL (collected at a mean time of 17.8±3 hours)
<i>The volume of distribution and elimination half-life of lead were 99ml and 137 hours, respectively.</i>	
Mercury	
Pre-transfusion (mean levels)	Post-transfusion (mean levels)
0.60±0.18 µg/L	0.72±0.23 µg/L (collected at a mean time of 5.1 hours)
	0.61±0.17 µg/L (collected at a mean time of 17.8 hours)
<i>The volume of distribution and elimination half-life of mercury were 87ml and 292 hours, respectively.</i>	



SEPARATE BUT NEVER APART

Le Bonheur separates second set of conjoined twins

A team of Le Bonheur pediatric surgeons and specialists separated 12-month-old ischiopagus conjoined twin girls in November. The 18-hour procedure involved a team of more than 20 surgeons and physicians from five subspecialties.



Conjoined twins Testimony (left) and Miracle (right) Ayeni were separated on Nov. 7 at Le Bonheur Children's Hospital.

The girls, Miracle and Testimony Ayeni, are now undergoing rehabilitation at Le Bonheur Children's after a successful separation surgery. They were

discharged Jan. 10 after nearly seven months in Memphis.

The Ayeni twins were born in Enugu State, Nigeria, on Nov. 16, 2015, via a caesarian. The girls, who were diagnosed as conjoined in utero, shared a large intestine, two

bladders and a pelvis. In early 2016, the Nigerian-based Linking Hands Foundation sought Le Bonheur's help on behalf of the Ayenis.



Watch a video about the Ayeni case at www.lebonheur.org/promise

The surgery was Le Bonheur's second separation of conjoined twins in the past five years. A team of specialists from the areas of anesthesia, child life, critical care, pediatric surgery, orthopaedics, nursing, plastic surgery, radiology, rehabilitation therapy, social



The Ayeni Family came to Le Bonheur from Nigeria in June 2016, hoping surgeons could separate conjoined twins Miracle (left) and Testimony (right).

work, spiritual care and urology met weekly for four months prior to the surgery to plan the separation.

More than 20 physicians and surgeons were involved in separation – and another 100 nurses and other clinicians were involved in their care.

“I know they will walk, I

Le Bonheur surgeons, nurses and technicians flip Miracle and Testimony Ayeni during their separation surgery. “Team Miracle” wore green scrubs hats while “Team Testimony” wore pink to differentiate themselves.



know they will do everything,” said Mary Ayeni, the twins’ mother. “God used the hospital to save the lives of Miracle and Testimony.”



Mary and Sam Ayeni rejoice after seeing their daughter, Miracle, for the first time following separation surgery.

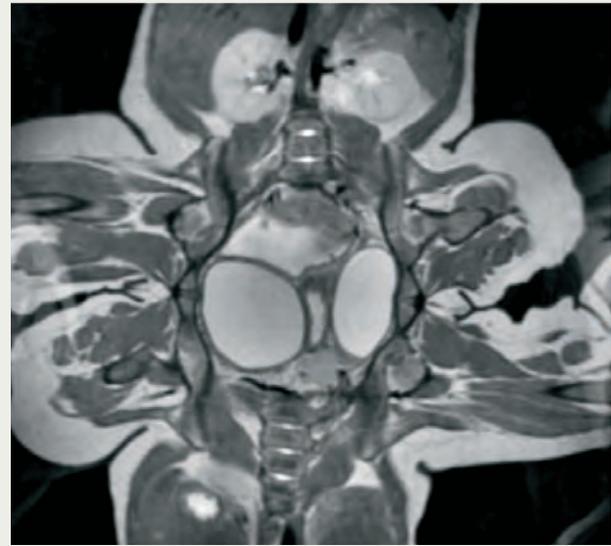


Miracle and Testimony Ayeni

12-month-old ischiopagus conjoined twins



Miracle and Testimony Ayeni, 12-month-old conjoined twins, shared one intestine, two bladders and a pelvis.



Surgeons separated the large intestine and conjoined bowel and divided and reassigned ureters.

- Born Nov. 16, 2015, via caesarian in Enugu State, Nigeria.
- Weighed 11 pounds at birth.
- Ischiopagus twins, conjoined at the lower half of body. They shared one large intestine, two bladders and a pelvis. Each twin had two legs and were joined end to end.
- Spent four months at Le Bonheur Children's undergoing physical and occupational therapy while a team of surgeons, physicians, nurses and other staff met weekly to plan for separation.
- During separation, surgeons separated the large intestine and conjoined bowel, divided and reassigned ureters and divided and reconstructed each girl's pelvis.

MIRACLE AND TESTIMONY AYENI: *AT LE BONHEUR*



July-October 2016: Le Bonheur physicians perform tests and scans to learn more about where Miracle and Testimony are conjoined and which organs the girls share. The twins begin physical and occupational therapy to meet developmental goals while their surgical team begins to meet weekly to discuss separation plan.



June 27, 2016: Ayeni family arrives at Le Bonheur, connected through the Nigerian-based Linking Hands Foundation. Family begins living at Le Bonheur's FedExFamilyHouse.



Oct. 3, 2016: Plastic surgeons insert four tissue expanders that will help grow excess skin and cover their wounds after separation.



Miracle (left) and Testimony (right) Ayeni stayed at Le Bonheur for two months following separation. They continue to receive outpatient rehabilitation at Le Bonheur.

Jan. 10, 2017: Miracle and Testimony are discharged. The family stays at FedExFamilyHouse while the girls continue outpatient rehabilitation.

Nov. 7-8, 2016: Miracle and Testimony are separated in a 18-hour procedure that involves more than 20 physicians. They leave the OR wearing external fixators designed to stabilize their pelvis bones.



Dec. 20, 2016: Orthopaedic surgeons remove the external fixators, as their pelvis bones have stabilized. Twins begin more intensive physical therapy.



Nov. 16, 2016: Miracle and Testimony celebrate their 1st birthday at Le Bonheur.



MIRACLE AND TESTIMONY AYENI: *SEPARATION SURGERY*

NOV. 7

7:05 a.m. Anesthesia induction begins and intravenous lines are inserted.



9:43 a.m. Twins are rolled onto their backs; team applies sterile drapes

10 a.m. Pediatric surgery divides colon and separates the conjoined bowel



3:16 p.m. Girls are separated, and Testimony is moved to Operating Room 6.



8:45 a.m. Orthopaedics team marks posterior tibial arteries; general surgery team marks abdominal incisions.

9:06 a.m. Twins are rolled onto their stomachs; urology team places foley catheters; pediatric surgery marks spots to create anus and rectum.



11:15 a.m. Plastic surgery and urology teams make incisions to access the ureters.

12:10 p.m. Urology team mobilizes and divides the ureters.

2 p.m. Orthopaedics teams divides the two shared pubic bones.

2-3 p.m. Urology and pediatric surgery teams complete soft tissue dissection.

MIRACLE

3:50 p.m. Plastic surgery team removes Miracle's right tissue expander and makes incisions for osteotomies.

5 p.m. Orthopaedics team completes reshaping of Miracle's pelvic bone.

5:55 p.m. Pediatric surgery team completes creation of anus and rectum.

7 p.m. Urology team completes ureter to bladder connection.

8:30 p.m. Orthopaedics team begins pin placement and external fixator to hold pelvis in place.

9:15 p.m. Pediatric surgery team closes the perineum.

11:40 p.m. Plastic surgery team completes removal of tissue expanders, placement of patch between the pubic bones in the midline and abdominal wall reconstruction.

12:06 a.m. Orthopaedics team completes readjustment of the external fixator. Surgery is complete. Miracle is transported to the Pediatric Intensive Care Unit.

TESTIMONY

3:15 p.m. Team begins incisions to reshape Testimony's pelvis.

5:56 p.m. Orthopaedics team completes reshaping of pelvic bone.

7:30 p.m. Urology team completes the new connection between Testimony's ureter and her other ureter.

8:15 p.m. Pediatric surgery team completes colon to small intestine connection.

9:30 p.m. Orthopaedics team completes placement of pins and an external fixator to hold pelvis in position.

12:25 a.m. Plastic surgery team closes the perineum and abdominal wall after removing tissue expanders.

12:55 a.m. Orthopaedics finishes readjusting the external fixator, and surgery is complete. Testimony is moved to Pediatric Intensive Care Unit.

Tuberous Sclerosis team presents at international TSC conference in Lisbon

Eight members of Le Bonheur's Tuberous Sclerosis Complex (TSC) team attended the recent International TSC Research Conference in Lisbon Dec. 3-6. The team delivered eight podium and three abstract presentations. Le Bonheur's multidisciplinary TSC program – led by John Bissler, MD, and James Wheless, MD — is recognized as a Center of Excellence by the TS Alliance.



Gosain receives grant for Hirschsprungs Disease Research

Ankush Gosain, MD, PhD, FACS, FAAP, associate professor in the University of Tennessee Health Science Center Department of Surgery and director of Pediatric Surgery Research at the Children's Foundation Research Institute of Le Bonheur Children's Hospital, has been awarded a \$785,220 grant to continue research for the treatment of a birth defect that can affect the colon of newborns. The grant is funded by the National Institute of Diabetes and Digestive and Kidney Diseases.



Ankush Gosain, MD, PhD, FACS, FAAP

"This project came from the patients that I saw during my pediatric surgery training," Gosain said. "Before that, during my PhD work, I became really interested in the idea that the nervous system and the immune system can interact and influence each other's behavior. I had studied that interaction in the skin, as part of wound healing, and how the nervous system controls immune cells and how that impacts healing."



Orthopaedic team co-hosts inaugural surgical techniques lab

Two-day course maximizes hands-on time

Pediatric Orthopaedic Surgeon Jeffrey Sawyer, MD, and Todd Milbrandt, MD, of Mayo Clinic hosted the inaugural Pediatric Orthopedic Surgical Techniques Lab, a two-day intensive cadaveric lab, designed for senior residents, pediatric orthopaedic fellows and new attendings. The course, held at the Medical Education & Research Institute in Memphis, was sold out at 32 participants.

"Our goal was to develop a course with minimal lecture and maximal hands-on time in the lab. We are also using this course to test new educational techniques for adult learners," said Sawyer.

Topics covered upper extremities, spine, hip and lower extremities, including trauma, deformity and sports.

Choudhri named chief of Neuroradiology

Asim Choudhri, MD, was recently named chief of Pediatric Neuroradiology at Le Bonheur Children's Hospital. Choudhri is board certified by the American Board of Radiology with a subspecialty of neuroradiology. He specializes in neuroradiology, spine imaging, functional neuroradiology, head and neck imaging and non-invasive neurovascular imaging.



Asim Choudhri, MD

New study published on abusive head trauma



Paul Klimo, MD

A majority of children who suffer from abusive head trauma (AHT) are African American males younger than 6 months old, according to a new study led by Scott Boop, MPH, and Le Bonheur Neurosurgeon Paul Klimo, MD. The study was published in the *Journal of Neuroscience*.

The study was conducted from 2009-2014, and all cases of AHT were patients at Le Bonheur Children's Hospital. AHT was identified as a skull fracture or intracranial hemorrhage in a child younger than 5 years old with suspicious mechanisms or evidence of other intentional injuries, such as retinal hemorrhages or soft-tissue bruising. Injuries were categorized as Grade 1 (skull fracture only), Grade II (intracranial hemorrhage or edema not requiring surgical intervention) or Grade III (intracranial hemorrhage requiring intervention or death due to brain injury).

The study identified 213 AHT cases. Approximately 55 percent of cases involved children 6 months or younger; 61 percent were males; 47 percent were African Americans; and 82 percent were publicly insured. The injuries resulted in 101 procedures being performed on 58 children, with the most common procedure being bur hole placement for treatment of subdural collections and decompressive hemicraniectomy. The annual incidence rates more than doubled between 2009 and 2014. In 2009, 19.6 cases per 100,000 in the population under 5 years of age were reported. In 2014, that number increased to 47.4 cases reported in children younger than 5 years old.

The study also showed seasonal peaks in January, July and October. The total hospital charges were \$13,014,584, with a median cost of nearly \$28,000.

Separate but never apart

Le Bonheur separates second set of conjoined twins

Miracle and Testimony Ayeni, 12 months, were separated at Le Bonheur Children's Hospital on Nov. 7 in an 18-hour procedure that involved more than 20 physicians from five subspecialties. Born Nov. 16 in Enugu State, Nigeria, the twins shared one large intestine, two bladders and a pelvis. Miracle and Testimony were discharged on Jan. 10 after nearly seven months at Le Bonheur and continue to receive physical and occupational therapy. Read more about the case on page 19.

