SPRING 2015

DELIVERING ON A PROMISE

Ahead of the curve

Le Bonheur/Campbell Clinic team delivers comprehensive treatments for scoliosis

- Jeffrey A. Towbin tapped new cardiology chief
- Study: E-cigs carry harmful free radicals

THE UNIVERSITY of TENNESSEE HEALTH SCIENCE CENTER

Le Bonheur Children's Hospital

Study: Viral pneumonia most common in children

Pneumonia is the leading cause of hospitalization in children and respiratory viruses continue to be the most common reason children develop pneumonia, according to new results published in *The New England Journal of Medicine*. The results could help with improved strategies to prevent and treat pneumonia.

The study was published last month as part of the Centers for Disease Control and Prevention's Etiology of Pneumonia in the Community (EPIC) Study. Le Bonheur Children's was one of three pediatric sites participating in the study, the largest-ever to investigate community-acquired pneumonia in hospitalized children and adults.

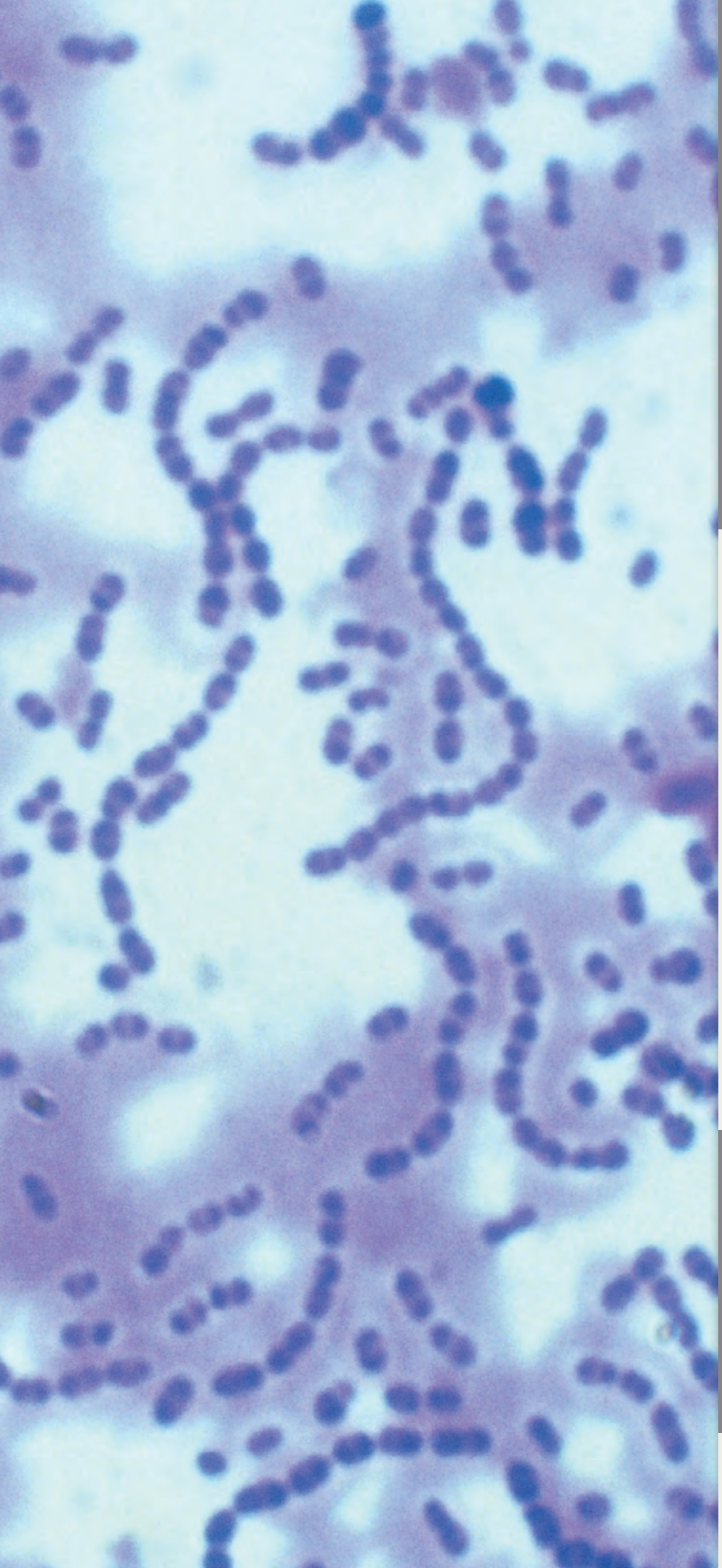
Le Bonheur enrolled 988 children between 2010-2012. The study was conducted by researchers at the CDC, Le Bonheur Children's Hospital, University of Tennessee Health Science Center (UTHSC), St. Jude Children's Research Hospital, University of Utah Health Sciences, Northwestern University Feinberg School of Medicine and Vanderbilt University School of Medicine.

Of the 2,222 children in the study with radiographic pneumonia and specimens available for both bacterial and viral testing, one or more virus was detected in 66 percent of the children. Eight percent had bacteria and 7 percent had bacterial and viral co-detected pathogens.

The study noted that increased influenza vaccination coverage and new respiratory syncytial virus vaccines and/or treatments could reduce the burden of pediatric pneumonia.

"In this study we saw a low prevalence of bacterial infection that reflects the effectiveness of conjugate vaccines targeting the most common bacterial pneumonia pathogens but also, possibly, the low sensitivity of the tests we have to diagnose bacterial pneumonia," said Sandra Arnold, chief of Pediatric Infectious Disease at Le Bonheur and UTHSC and principal investigator for the Le Bonheur site.

"We need better tests to identify the small proportion of children with pneumonia who have bacterial infection so that antibiotics can be appropriately prescribed for these children and avoided in children with viral infection for whom antibiotic therapy is unnecessary. Additional analyses of the EPIC Study data will examine ways to distinguish viral and bacterial pneumonia in children."



Le Bonheur Children's Hospital

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT RANKED IN 7 SPECIALTIES 2014-15

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*
Mark Williams, MD – *Surgeon-in-Chief*
Harris Cohen, MD – *Radiologist-in-Chief*

THE UNIVERSITY of TENNESSEE HEALTH SCIENCE CENTER

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

In this issue:

The cover photo is a 3-D replica of scoliosis, created using CT images.

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AHEAD OF THE CURVE

Orthopaedic team delivers comprehensive treatments for scoliosis

One quick growth spurt. That's all it took for 10-year-old Jasmine McGaughy's scoliosis to jump from 19 degrees to an uncomfortable 59 degrees.

Noticing a slight curve, her grandmother, a massage therapist, knew something wasn't quite right with the fifth grader's back.

The family took Jasmine to an orthopaedic surgeon near their hometown of Ripley, Miss. The plan was to monitor Jasmine's scoliosis — at 19 degrees — too minor for any corrective treatments. When her curve progressed to more than 50 degrees in less than a year, the McGaughys were sent to the Pediatric Spine Center at Le Bonheur Children's Hospital and Campbell Clinic Orthopaedics.

When 13-year-old Jasmine McGaughy has adjustments to the Magnetic Expansion Control (MAGEC) device, she describes the sound as a paper shredder. The magnet looks almost like an attachment to a vacuum cleaner, and Orthopaedic Surgeon Jeffrey Sawyer, MD, glides it gently over her back as he watches a screen that tells him how many millimeters he's expanded the rods. The second adjustment has left her a little sorer than the last, but Jasmine's just happy she gets to go back to school in the morning. The now teen dances on her school's pom squad, and she has a performance in two days.

Degrees of scoliosis

A healthy spine has gentle curves to provide strength and support, balancing the weight of everyday movement. In those with scoliosis, most often for reasons unknown, the spine forms an abnormal C- or S-shape.

Types of scoliosis include:

- **Idiopathic:** cause is unknown; this is the most common type (approximately 80-85 percent of cases)
- **Neuromuscular:** secondary scoliosis to a neuromuscular condition, such as cerebral palsy, arthrogryposis or muscular dystrophy
- **Congenital:** caused by vertebrae anomalies present at birth
- **Thoracogenic:** caused by rib abnormalities or thoracic surgery at a young age; scar tissue and/or fused ribs can cause asymmetric growth of the spine

Sub-types include:

- **Early-onset:** any type of scoliosis that presents before age 10
- **Infantile:** occurs in children younger than age 3
- **Adolescent or adult:** occurring in children older than 10

Scoliosis occurs in about 2 to 3 percent of adolescents, but curves range from mild to severe. Though scoliosis is equally common in boys and girls, girls are considered most at risk for curve progression. The most severe curves, greater than 50 degrees, can causes rib and lung issues and make breathing more difficult. These curves will require surgery.

Jasmine and her family became one of the first in the country to receive Magnetic Expansion Control (MAGEC) therapy. Unlike traditional growing rods, where a device is surgically implanted and lengthened every six months in subsequent surgeries, MAGEC allows surgeons to lengthen the device non-invasively – using an external magnet.

It's one of a number of tools and technologies the team is able to offer thanks to a commitment made years ago to build a comprehensive spine program.

REVOLUTIONIZING SCOLIOSIS CARE

Jasmine, now 13, underwent MAGEC implantation in June 2014. Since then, she's had two adjustments, or lengthenings, in clinic – no incisions, no sedation, no recovery time. And no pain.

"We keep asking her if it hurts, and she tells us 'no.' It's amazing," said Jasmine's grandfather, Blake.

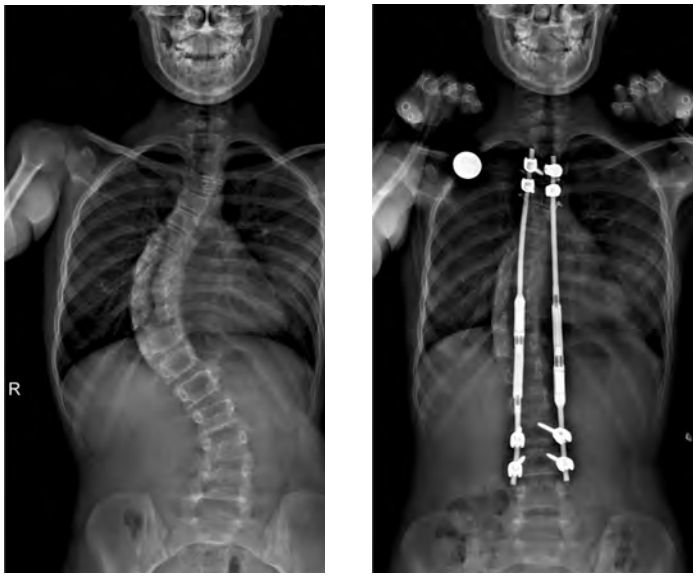
MAGEC is a stark alternative to traditional growing rods, and the Downey family, from Toxey, Ala., knows the difference. Their 9-year-old daughter, Sage, was born with arthrogryposis — a rare neuromusculoskeletal disorder — and had developed neuromuscular scoliosis by the time she was 6 months old. The Downeys first came to Le Bonheur in 2011 when Sage was 5.

Under Orthopaedic Surgeon Dr. Jeffrey Sawyer's care, Sage underwent halo traction and Vertical Expandable Titanium Rib (VEPTR) implantation. Her VEPTR rods were surgically expanded five times.

The Le Bonheur/Campbell Clinic Orthpaedics team, including William Warner, MD, and James Beaty, MD, discuss cases at pre-operative conference.

On May 7, 2014, Sage became the first person in the region to receive MAGEC rods. Her family had followed the new technology as it was first introduced in Europe and Asia and knew MAGEC would be ideal for Sage. Instead of regular

Learn more about MAGEC – lebonheur.org/promise.



Thirteen-year-old Jasmine McGaughy underwent MAGEC implantation last summer. The growing rods have helped straighten her spine. At left, a pre-operative scan shows her 59 degree curve. Today, her curve is 22 degrees (shown at right).

surgical lengthenings like she'd experienced, MAGEC allowed Sawyer to expand Sage's rods in a non-invasive outpatient procedure, as she grew. The technology meant fewer surgeries for Sage.

"We had known about the device's pending approval in the U.S. for a few years and knew we wanted a surgeon who would stay on top of the latest developments in scoliosis treatment," said Janet, Sage's mom.

The Downeys trusted Sawyer, who has spent his career searching for better, less-invasive options for children with scoliosis. Sawyer is a part of a number of study groups focused on best practices for pediatric spine care and has published numerous articles on pediatric spine surgery. He's involved in product development for scoliosis care, as well as surgeon teaching programs for scoliosis patients.

Using an external magnet, Sawyer lengthened Sage's rods for the first time on July 16, a couple months after her conversion.

"It was such a difference," said Janet. "Dr. Sawyer did the expansion in clinic. There was no anesthesia, no incisions. We were eating lunch with Sage an hour later. We couldn't believe it."

The technology is allowing surgeons to improve kids' quality of life, says Sawyer. Historically, patients with severe scoliosis could expect to have multiple surgeries – as often as

A range of options: Treatment for scoliosis

Observation: Some smaller curves can be treated with observation and close follow up to ensure their curve does not progress or cause long-term problems.

Bracing: Bracing is used with moderate curves (about 25 to 40 degrees) to slow or prevent the curves progression, while bones are still growing.

Casting: A long-standing technique, casting is used in children young children and infants to slow the progression of a child's scoliosis. Casting has become re-popularized for infantile scoliosis in recent years. Pictured, Le Bonheur's Mehta casting table helps surgeons build a Risser cast, a type of cast that applies three points of pressure to the curve.

VEPTR, or growing rods: Used in children with more severe curves and those with chest/rib deformities, a Vertical Expandable Titanium Rib (VEPTR) is a metal rod curved to fit the chest that is periodically lengthened to grow with the child and help the spine become straighter. This is also used for children with hypoplastic chest syndromes, such as Jeune syndrome, to increase survival and quality of life.

MAGEC, less-invasive growing rods: Magnetic Expansion Control ® (MAGEC) is an alternative to traditional growing rods, allowing surgeons to straighten and correct the spine gradually and non-invasively. Candidates for the MAGEC device undergo an initial surgery to implant an adjustable magnetized growing rod, which is lengthened externally with a hand-held magnetized device.

Spine Tethering: To stabilize the spine and slow progression, tethers are inserted in the outer curve of the anterior spine, redirecting the growth of the spine straighter while maintaining flexibility.

Spinal Fusion: Surgeons use bone or bone-like material to fuse the affected vertebrae in the back and stabilize the spine.

every six months — to straighten their spine through the course of their treatment. But MAGEC allows patients like Sage and Jasmine to undergo on-going treatment without surgery, overnight hospital stays or even an incision – and with less radiation exposure. In fact, they can return to school the same day as their expansions.

"We know from studies the anxiety level of families increases every time they're in the hospital. With MAGEC, kids can undergo an adjustment without having to stay overnight at the hospital. They can go right back to school and be kids," said Sawyer.

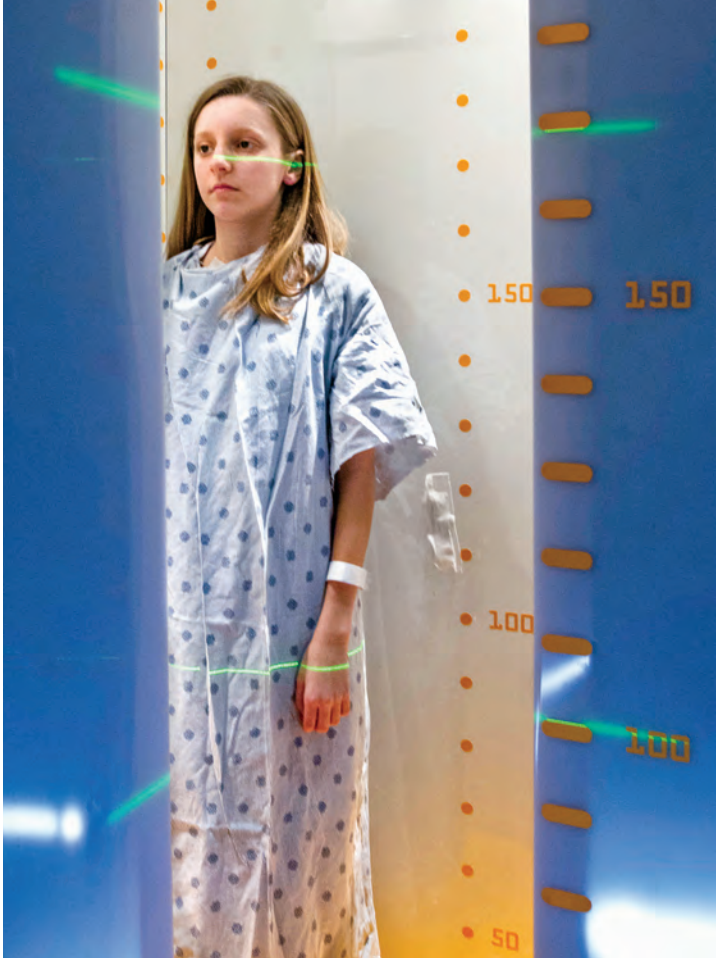
MAGEC also saves families the cost of missed work days. With traditional rods that require frequent surgeries, families often have to take extended time off from work and school.

"Because many of our families travel a distance to see us, parents may miss several days to a week of work twice a year," he said.

BUILDING A COMPREHENSIVE CENTER

Sawyer and the rest of the team surgeons knew they wanted to be one of the first in the country to offer MAGEC. When they formalized the Pediatric Spine Center six years ago, they set out to provide a full range of treatment and care for any child with scoliosis, no matter the severity. Like most surgeons in the field, veteran team member William Warner, MD, has seen scoliosis care evolve tremendously in the last 20 years. Newer techniques have advanced to allow for more secure fixation and better correction.

"In the 1980s, surgical care involved distraction instrumentation that required post-operative bracing or casting – meaning longer recovery time and more



In his career, Jeffrey Sawyer, MD, has seen scoliosis patients who've been exposed to more radiation than survivors of the 1986 Chernobyl disaster. EOS exposes children to 20 times less radiation than traditional imaging. In the early years of scoliosis care, kids averaged 14 X-rays and 0.5 CT scans per year. Thanks to better technology and new protocols, patients today receive, on average, five X-rays per year and almost no CT scans.

Scoliosis patient **Undra "Snoop" Cannon** makes the nurses laugh at every clinic appointment. He loves to make up raps and strike animated poses. Now 10, Snoop underwent VEPTR (Vertical Expandable Titanium Rib) implantation five years ago at Le Bonheur/ Campbell Clinic to correct his curvature. He'll likely receive two more lengthenings before his spinal fusion.

"I'm OK with surgery because it's helping me grow," says Snoop.

Patients like Snoop with early-onset scoliosis are often diagnosed before the age 10 and followed by their doctor for years to monitor the curve's progression.

"One of my favorite parts of my job is getting to follow patients throughout their childhood," says Jeffrey Sawyer, MD.

RESEARCH, COLLABORATION IMPROVE SCOLIOSIS CARE

Beyond building a comprehensive center, the Le Bonheur/Campbell Clinic Pediatric Spine Center wanted to contribute to the larger body of knowledge for scoliosis. To stay up-to-date on the latest in the field and expand their expertise, the team:

- **Is a part of several study groups**, like the current multi-center group studying the nuances of Magnetic Expansion Control (MAGEC) and a multi-center retrospective analysis of Vertical Expandable Titanium Rib (VEPTR) surgery infection rates. This allows Le Bonheur/Campbell Clinic to not only help develop care guidelines and protocols, but also to access the latest information on diagnosis and treatment before it even is presented at meetings or published in medical journals.
- Regularly **consults with biomedical engineers** in the industry, offering their insights and experience
- **Publishes and presents peer-reviewed articles about topics**. The team has published several spine-related studies on topics like VEPTR infection rates, VEPTR anchor failure, spondylolysis and spinal cord trauma.
- **Monitors quality measures**, like surgical infection rates – an important measure for any spine program. Surgeons have only seen two infections out of more than 500 cases in the last five years, a rate of about .039 – among the lowest in the country.
- **Trains students from across the country and around the world** through its reputable fellowship program. The Spine Center has trained more than 100 residents, fellows and medical students since its inception. The team has authored numerous textbook chapters.

procedures," said Warner. "And now with better imaging and neuromonitoring techniques certain complex deformities that couldn't be treated in the past can now be fixed."

"We wanted to be able to offer anything and everything in world of pediatric spine care here in Memphis," said Warner, MD. "It can be stressful for families to have to go somewhere far from home to have such a major procedure."

Top-notch technology would play a big role in building a comprehensive center, so the hospital invested in advanced diagnostic and treatment tools and multidisciplinary expertise.

For weeks leading up to a surgery, Jeffrey Sawyer, MD, leaves a 3-D replica of the patient's spine on his desk. Looking at it for a little bit each day helps him know what to expect on the day of the operation, he says.

Physicians also worried about the amount of radiation exposure children with scoliosis received. For children like Jasmine who are diagnosed early in childhood with scoliosis, lifetime radiation exposure poses a significant risk to their health. At nearly each appointment, they receive radiographic scans to monitor their curve's progression or to plan for surgery.

To address those concerns, the center added an EOS imaging system, an ultra-low-dose radiation scanner that can quickly capture two-dimensional computed tomography (CT) images of the spine. EOS imaging exposes patients to about one-tenth of the dose of a plain film X-ray.

From there, the team added technologies like O- and C-arm imaging that provide real-time intraoperative CT imaging and a StealthStation® surgical navigation system to confirm placement of precision hardware in surgery. These tools benefit the more than 200 children who receive spinal surgery each year at Le Bonheur/Campbell Clinic.

The list goes on. The team now offers ScoliScore™ genetic testing for a subset of patients to help predict the progression of idiopathic scoliosis, and three-dimensional printing can allow surgeons to create a real-life replica of a patient's spine using images captured through CT. The 3-D

models help surgeons prepare for surgery by studying the spine's intricate twists and curves.

"We've really created a one-stop shop for all things pediatric spine," said Warner. "As we continue to develop our expertise, we're caring for more and more children from all over the region and beyond."

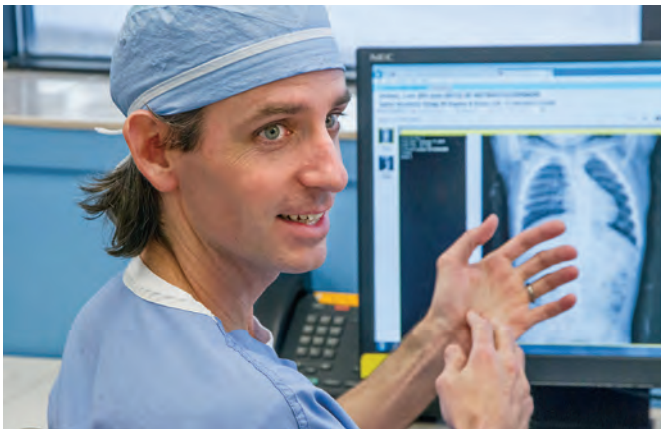
CONTRIBUTING TO THE FIELD

Beyond building a comprehensive center, the Le Bonheur/Campbell Clinic Pediatric Spine Center team wanted to contribute to the larger body of knowledge for scoliosis. That meant sharing its expertise, collaborating with other centers and training students in the field of pediatric spine.

Since the center's inception, the team has trained more than 100 students, residents and fellows, attracting students from across the country and around the world.

Brazilian native Nelson Astur, MD, turned to Le Bonheur/Campbell Clinic when he wanted to improve scoliosis treatment for children in his country. He'd referenced "Campbell's Operative Orthopaedics" throughout his orthopaedic residency in Sao Paulo and applied to the center's Pediatric Spine Research Fellowship program in 2010.

"Spending a one-year fellowship with the Pediatric Spine team was a game-changing experience for my practice. The experience means even more now when I still have the opportunity to collaborate with my mentors to solve cases in Brazil. Even better when this link is still producing research and new projects," said Astur.



Collaboration plays a large role in the success of the Pediatric Spine Center. Surgeon Derek Kelly, MD, joined forces with Medtronic to help local schools identify scoliosis. The hope the program, called Spine Check, will lead to earlier and more effective treatment for children with scoliosis.

The Pediatric Spine Center is also part of several multi-center spine study groups, including a recently formed MAGEC study, as well as a multi-center retrospective analysis of Vertical Expandable Titanium Rib (VEPTR) surgery infection rates. Le Bonheur's Orthopaedic team has published 13 spine-related articles in the last five years. Studies have focused on the efficacy of operative and non-operative treatments for scoliosis, spinal trauma, as well as the safety and effectiveness of diagnostic tools, like EOS imaging.

"Through our research, collaboration and teaching

Noah Anderson , 11, was diagnosed with early-onset scoliosis shortly after birth. His condition was so severe doctors told his family he may never even walk. Today, Noah's spine is getting straighter every year, thanks to the Vertical Expandable Titanium Rib (VEPTR) implant he received almost four years ago. The Andersons travel more than 220 miles from their hometown of Goodlettsville, Tenn., for Noah's regular check-ups at Le Bonheur. He expects to undergo one more lengthening before a final spinal fusion surgery next summer.

efforts, we are able to share our experience and knowledge with other surgeons and centers to help provide the best possible spine care for children in the United States and around the world," said Orthopaedic Surgeon David Spence, MD. "The work also gives us access to the most recent research and outcomes often times before they are published in journals and textbooks."

The center's surgeons also collaborate with some of the brightest minds in biomedical engineering. Medical technology companies like Medtronic, Medicrea and Depuy Synthes regularly invite the team to consult on their work. The Pediatric Spine Center has recently partnered with Medtronic on an outreach initiative designed to help local schools identify scoliosis. They hope the program, called Spine Check, will lead to earlier and more effective treatment for children with scoliosis.

True to the Pediatric Spine Center's original vision, the team says it will continue to search for better ways to care for children with scoliosis. Surgeons are working toward using biomechanics to improve bracing outcomes and compliance and studying the biomechanics of multi-rod construct in children with spinal osteotomies. Using EOS, surgeons hope to better understand the 3-D corrections achieved by various spinal deformity implants.

"Personalized care for patients at our spine center provides all the resources for a successful outcome for families facing scoliosis," said Sawyer. "Our work is allowing us to provide the latest, safest and best spine care to our patients and their families."

Scoliosis teen faces fears, helps others

When Sarah Johnson learned she needed surgery to correct her spine's curvature, she elected to have her operation in the winter. A member of her high school's color guard team, Sarah wanted to recover in time to participate in band camp.

When 12-year-old Sarah Johnson of Arlington, Tenn., first learned she likely had scoliosis, she burst into tears. Sarah had seen the disease's effects first-hand. Her grandmother had severe scoliosis and was in constant pain.

After a slight curve in her spine was detected by her pediatrician at a routine visit in 2011, Sarah and her family chose Jeffrey Sawyer, MD, to be her doctor. At their first visit to Le Bonheur/Campbell Clinic's Pediatric Spine Center, an MRI revealed a 33-degree curve. She was fitted for a brace, which she wore consistently for two years.

"Dr. Sawyer helped us find ways to let Sarah still be a normal kid. We'd give her one night off each week from wearing her brace," said Sarah's mom, Lindsay. Sarah usually chose Wednesday nights, when she had youth group meetings at church. She wanted to be able to sit in the beanbag chairs.

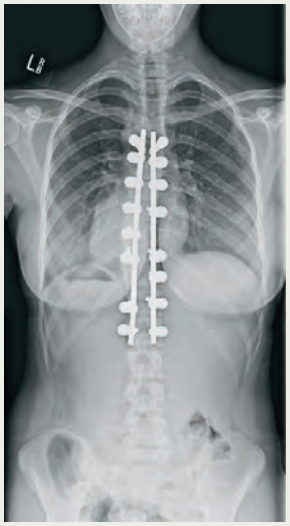
In June 2013, Sarah hit a growth spurt, and her curve progressed to more than 40 degrees. At that point, Sawyer began to discuss surgery with the Johnsons. The brace had done all it could do.

Sarah underwent a spinal fusion the following February. The Johnsons chose to have her operation in the winter, so she'd recover in time for band camp in July. A straight-A student, Sarah kept up with her classwork through a home-bound program for six weeks as she healed.

Now 16, Sarah created a YouTube video for other children with scoliosis. She hopes the video will ease others' fears about scoliosis and surgery.

"Even though Sarah is the patient, the whole family plays a role in ensuring the best possible outcome. When it came time for surgery, Sarah and her family learned a lot about the procedure, asked many good questions and were extremely well-prepared," said Sawyer. "Now Sarah helps educate other patients and their families about the procedure and what to expect."

Pre-op 50°



Post spinal fusion 12°

Watch Sarah's story –
www.lebonheur.org/promise

Young hearts inspire cardiologist to find research answers

Pediatric Cardiologist Jeffrey A. Towbin, MD, dreams of a day when there are no transplant doctors – when scientists so clearly understand the causative genes and proteins for cardiomyopathies that they are able to develop targeted therapies to protect children from heart failure and sudden death.

It's what drives him to the bench.

Towbin, a pediatric cardiologist and cardiac researcher, recently became executive co-director of the Heart Institute and chief of Cardiology at Le Bonheur Children's Hospital. He serves as chief of Cardiology at St. Jude Children's Research Hospital and chief of Pediatric Cardiology at the University of Tennessee Health Science Center as well. He also serves as vice chair of Strategic Advancement and will hold the St. Jude Chair of Excellence in Cardiology at Le Bonheur.

Executive Co-Director, Heart Institute at Le Bonheur Children's Hospital
Chief of Cardiology, St. Jude Children's Research Hospital
Chief of Pediatric Cardiology, University of Tennessee Health Science Center

Vice Chair of Strategic Advancement, Le Bonheur Children's
St. Jude Chair of Excellence in Cardiology, Le Bonheur Children's

He comes to Le Bonheur from Cincinnati Children's Hospital Medical Center, where he successfully built one of the country's largest and most well respected pediatric cardiology programs.

"Dr. Towbin is a pioneer in advancing the field of cardiac research and what we know about cardiovascular disease in children," said Chris Knott-Craig, Chief of Cardiovascular Surgery and executive co-director of the Le Bonheur Heart Institute. "His expertise will help the Le Bonheur Heart Institute advance our mission of finding better ways to diagnose and treat complex pediatric heart diseases, especially those with heart failure and malignant disease."

Towbin has spent his career studying heart disease and heart failure. His research has been funded continuously since 1987 and he has trained more than 50 post-doctoral and 20 pre-doctoral students – many of whom now have high level academic faculty positions.

His laboratory research team has been a leader for many years in the field of gene discovery and mechanisms of cardiomyopathies, arrhythmias, sudden cardiac death, vascular disorders and congenital heart disease – as well as viral causes of

myocarditis, cardiomyopathies, transplant rejection and transplant coronary disease.

He has co-authored more than 475 publications in high-impact journals, served as a principal mentor for multiple K-Grant-funded trainees and has been a member of multiple T32 training grants. In 2007 he received the American College of Cardiology (ACC) Distinguished Scientist (Basic Science) Award, and in 2013, he was awarded the American Heart Association's Basic Research Prize.

Towbin pioneered the concept of pathway-focused candidate gene analysis using his "final common pathway hypothesis," and calls his work in understanding how heart muscle turns into heart muscle disease, or cardiomyopathy, his most important research work to date.

"Many years ago, my lab was able to identify a major gene for muscular dystrophy, the dystrophin gene, as a cause of just heart disease instead of heart and muscle disease," he said. "We've used that to enable us to understand what other genes and proteins might be causative of cardiomyopathies, heart failure and sudden death."

Towbin says he finds inspiration for his research work at the bedside: the initial questions come from caring for his patients. To find solutions, he goes to the research bench to identify the genetic basis of disease. Today, his work has helped families better understand their risk for developing cardiomyopathy, and he hopes it leads to the development of targeted therapies for those patients.

"It would be fantastic if no one had to say they were transplant doctors because we were better able to take care of patients with cardiomyopathies and heart failure, so they don't have to go down that final path of needing a heart transplant," Towbin said. "That's really been the goal set and why I went to the bench in the first place."

At Le Bonheur, Towbin plans to recruit a large cadre of faculty to develop several novel clinical and research programs to the already excellent heart care provided at Le Bonheur, and enhance the training of pediatric and congenital cardiologists. He also plans to develop a new cardio-oncology specialty, in partnership with St. Jude Children's Research Hospital.

"I hope to accomplish the building of a nationally recognized destination program with world-class expertise and help the field to expand into new areas of care based on the paradigm we develop," he said.

Jeffrey A. Towbin

Education and Training
- University of Cincinnati, University of Cincinnati – Children's Hospital, pediatrics
- Baylor College of Medicine, Texas Children's Hospital, pediatric cardiology

Recent Experience
- Executive Co-Director, The Heart Institute, Kindervelt-Samuel Kaplan Professor and Chief, Pediatric Cardiology (2009-2015)
  Director, Heart Failure Services and Cardiovascular Genetics (2009-2011)
  Cincinnati Children's Hospital Medical Center
- Chief, Pediatric Cardiology, Texas Children's Hospital, Baylor College of Medicine (2003-2009)
  Director, Heart Failure and Cardiovascular Genetics, Texas Children's Hospital (2003-2009)

Clinical and Research Focus
- diagnostic and therapeutic advancements for cardiomyopathies and sudden death
- heart failure
- mechanical circulatory support
- heart transplantation
- cardiovascular genetics

TOXIC RADICALS

Study finds free radical toxins, harmful aerosols in e-cigarettes

Electronic- or e-cigarettes release damaging free radical toxins during the vaporization process, and exposure to e-cigarette aerosols can cause airway inflammation and compromise the immune system, according to new research published in the open-access journal *PLOS ONE*.

A team of researchers at the Children's Foundation Research Institute at Le Bonheur Children's Hospital joined scientists at Johns Hopkins School of Public Health to study the health effects of e-cigarette vapors in mice.

In the study, mice were divided into two groups: one group was exposed to clean air and the other group was exposed to e-cigarette aerosol for two weeks at levels similar to those of a human smoking or "vaping" an e-cigarette.

Researchers found the e-cigarette creates combustion particles that contain 7 x 10e11 free radicals per puff and that a two-week exposure produced a significant increase in oxidative stress and moderate macrophage-mediated

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

inflammation in mice. These mice showed significantly impaired immune responses to both bacteria and viruses. In fact, mice exposed to e-cigarette vapors were less able to clear the bacteria, Streptococcus pneumonia, from their lungs. In response to Influenza A infection, e-cigarette-exposed mice displayed increased amounts of virus in their lungs and enhanced virus-induced illness including weight loss and mortality.

Le Bonheur researcher Stephania Cormier, PhD, and her team measured the free radical content of e-cigarette exposure using electron paramagnetic resonance spectroscopy. Free radicals are especially reactive molecules that can damage cells, proteins and DNA, causing disease. The free radicals produced by "vaping" are typically associated with combustion processes. They are especially dangerous because they are stabilized on the surface of the particles formed during the vaporization process, persisting in the environment for days to months, and in biological solutions for hours.

"We know that e-cigarette users inhale more puffs compared to regular cigarette users in order to get the same amount of nicotine," Cormier said. "Because of that, users are exposed to higher levels of these damaging free radicals."

Cormier leads one of only a few labs in the world to study free radicals – which are often found in homes with gas, wood or kerosene-burning stoves. She leads a National Institute of Environmental Health Sciences Superfund Research Program to study the how environmentally persistent free radicals are formed and affect human respiratory and cardiac health.

Cormier said she became interested in studying the effects of e-cigarettes on airway function and pulmonary immune responses after a friend starting using e-cigarettes as he tried to stop smoking. Her expertise on pollutants that are released into the air during the combustion process made her well suited for the work.

"We know that e-cigarette users must inhale more puffs compared to regular cigarette users in order, to get the same amount of nicotine. Because of that, users are exposed to higher levels of these damaging free radicals."

Stephania Cormier, PhD

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

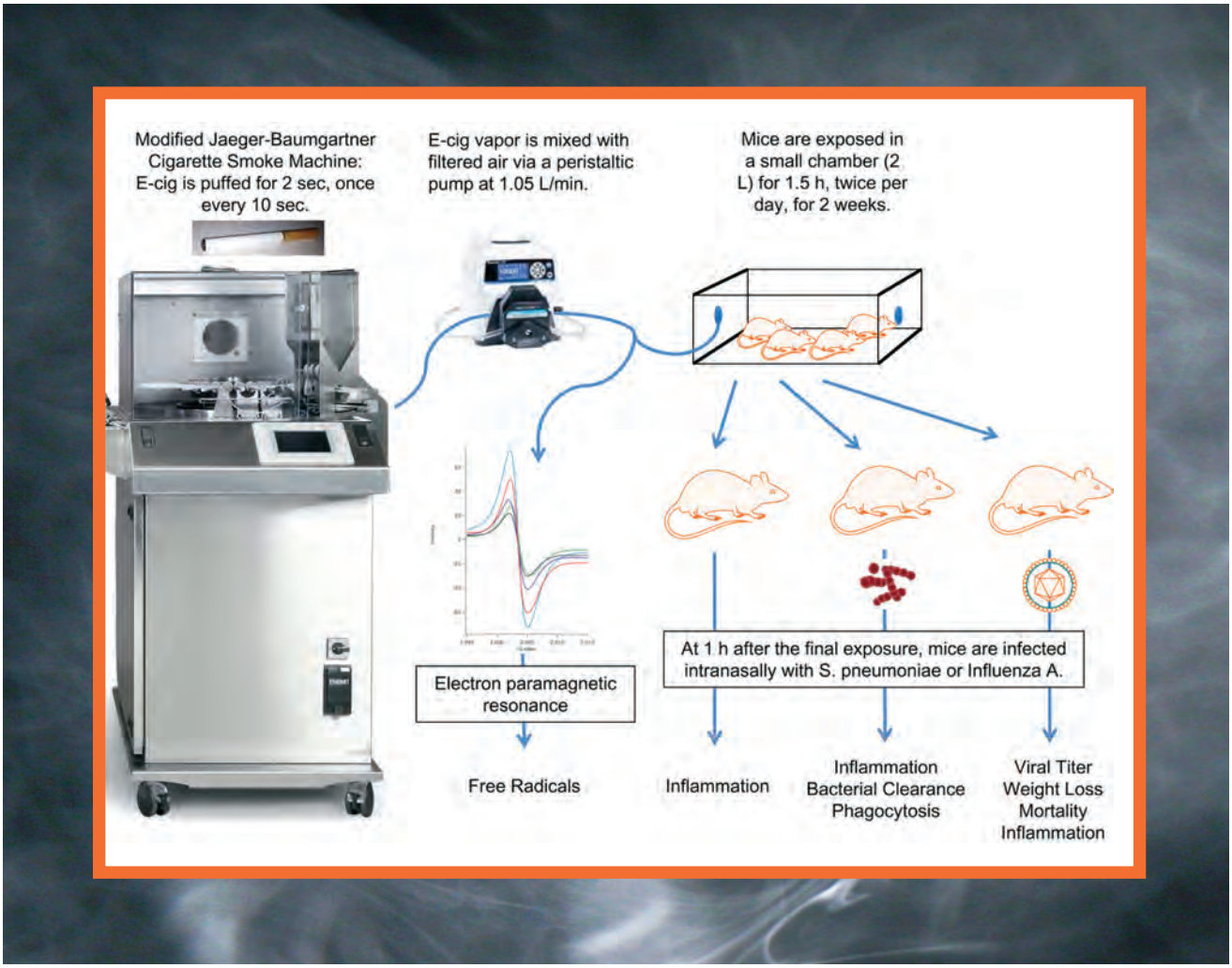


Figure 1. Schematic of our E-Cig exposure model
doi: 10.1371/journal.pone.0116861.g601

E-cigarettes are also of interest to her, she says, because they are largely marketed to young adults and teens – with candy and fruit-flavors. The American Academy of Pediatrics (AAP) has called for the Food and Drug Administration to oversee the unregulated e-cigarettes. The AAP and the American Association of Poison Control Centers have called on Congress to pass the Child Nicotine Poisoning Prevention Act, which would require child safety packaging for liquid nicotine containers and for other purposes.

In November 2014, the Centers for Disease Control and Prevention (CDC) reported that fewer U.S. high school students are smoking traditional cigarettes, but current use (use on one or more days in the past 30 days) of e-cigarettes by high school students tripled to 4.5 percent in 2013 from 1.5 percent in 2011. The CDC also reported that 22.9 percent of high school students said they were currently using tobacco.

"I hope that this study shows consumers that e-cigarettes are not a healthful alternative to regular cigarettes. They are not a way to quit. I think they are going to cause a lot of health problems for teens and young adult users," said Cormier.

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

Let's talk

Le Bonheur school-based program helps push county teen birth rate down 32 percent

In 2010, a television story about an influx of pregnant teens in one Memphis high school made national news. The teen birth rate in Shelby County at that point was nearly twice the national average. Nearly 2,300 babies were born to teens ages 15-19.

Around the same time, Le Bonheur Community Health and Well-Being received a five-year, $4 million grant from the state's Office of Adolescent Health to address teen pregnancy. Using evidenced-based, medically accurate curriculum developed by leading pregnancy prevention researcher Loretta Jemmott, PhD, the program based at Le Bonheur Children's Hospital has contributed to a 32 percent decrease in the county's teen birth rate.

Now in its fifth year, Be Proud! Be Responsible! Memphis! educators have taught more than 12,000 teens, male and female, in Shelby County about safe sex practices and attitudes.

Tennessee still ranks among the top 10 states with the highest teen birth rates, expressed as the number of births

per 1,000 females aged 15–19. Shelby County rates, which includes Memphis, are among the highest in the state.

Children born to teen moms are more likely to live in poverty and have a low birth weight, behavioral issues and lower academic and intellectual achievement. These children are also less likely to have a primary care doctor, receive proper nutrition and cognitive stimulation and graduate from high school.

"Teen pregnancy has long-term effects on the community. If the hospital can be part of reducing the number of teen pregnancies in our community, that translates to better long-term physical, social and emotional outcomes for children in Memphis," said Le Bonheur President and CEO Meri Armour.

Be Proud! Be Responsible! Memphis! is a six-module, two-week interactive program designed to educate adolescents ages 13 to 18 about safe sex practices and attitudes. The Le Bonheur-based team partners with community centers, churches and Shelby County Schools.

Be Proud! Be Responsible! Memphis! is a six-module, two-week interactive program designed to educate adolescents ages 13 to 18 about safe sex practices and attitudes. The Le Bonheur-based team partners with community centers, churches, charter schools and Shelby County Schools. Teens are encouraged to develop a sense of pride, self-confidence and self-respect through sexual disease education, safe sex practices and life skills-building activities. The program empowers youth to build and maintain healthy relationships throughout their entire lives.

Program Manager Jeremy Sanders says much of the program's success has to do with the diverse team of educators. The nine educators are all graduates of Memphis City Schools and once lived in the targeted zip codes. One is the child of a parent who died of AIDS and another is the single mom of twins. All are college educated, and several have master's degrees.

Peer mentor Jennifer Taylor, who previously worked as a Child Life specialist at Le Bonheur, spends the first few sessions making her students feel comfortable with her.

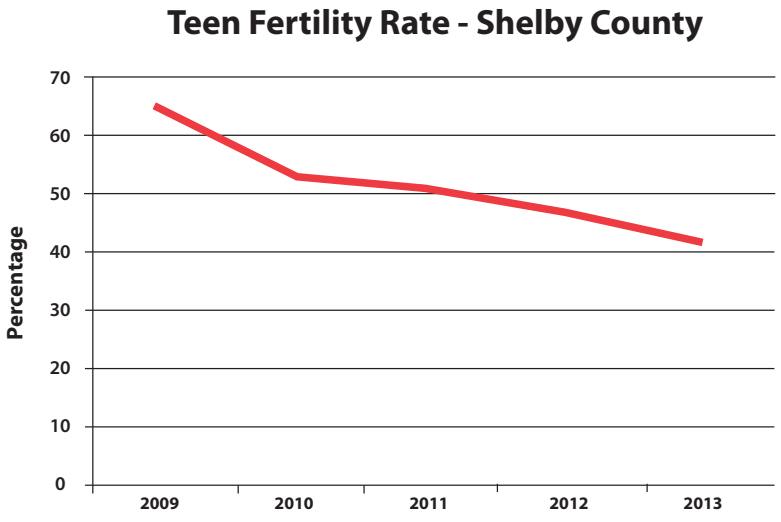
"They're trying to get to know me. I want them to know we're open for discussion," she said. "A lot of these kids don't understand risky behaviors. They're getting information from their friends, and clearly the information is not correct."

The program has proven effective in reducing teen pregnancy and increasing education about HIV, and sexually transmitted infections for both genders and for all races and ethnicities in youth ages 13 to 18.

One of the challenges is getting teens to understand that you don't have to have sex.

"Many teens believe that I'm dating this person and that the natural progression in order to keep this relationship is to have to sex. Through our program, they realize you don't have to have sex, and in many cases the other person didn't want to either," Sanders said.

Post-surveys show increases in overall knowledge, pregnancy prevention, risk of unplanned pregnancy and confidence in negotiating safer sex. Evaluations are insightful. One teen wrote she learned, "A person doesn't have to look sick to have a disease." Another learned, "You could have HIV/AIDS for up to 10 years and never know it."



The teen birth rate is expressed as the number of births per 1,000 females aged 15–19.

Briefs

Eubanks named Surgery chief

James "Trey" Eubanks, MD

Pediatric Surgeon James "Trey" Eubanks, MD, was recently named chief of Pediatric Surgery for Le Bonheur and the University of Tennessee Health Science Center. Eubanks has worked at Le Bonheur since 2002 and also serves as the hospital's medical director for Trauma Services.

Bissler honored for Tuberous Sclerosis Complex work

John Bissler, MD

John Bissler, MD, chief of Pediatric Nephrology at Le Bonheur, recently received Tuberous Sclerosis Complex International's research award for his work with Chinese patients with tuberous sclerosis complex (TSC). Bissler received the award at the 2014 International Research Conference on TSC/LAM in Beijing.

National Green & Healthy Homes Initiative to support Le Bonheur's high-risk asthma patients

Le Bonheur Children's has been selected as one of five health care organizations to receive services addressing the medical, housing/environmental and medical-legal needs of asthma patients and families. The services are provided through a federal grant awarded by the Corporation for National and Community Service (CNCS) to the Green & Healthy Homes Initiative (GHHI) and Calvert Foundation. Through the project, Le Bonheur's CHAMP (Changing High-Risk Asthma in Memphis through Partnership) program will receive technical assistance over a seven-month period to assess the feasibility of using an innovative, Pay for Success model to address conditions that contribute to asthma. The GHHI/Calvert Foundation program is also conducting asthma-related projects in Massachusetts, Michigan, New York and Utah. Le Bonheur launched CHAMP in 2013 thanks to a $2.9 million Health Care Innovations award from the Centers for Medicare and Medicaid. The program works to improve the health and quality of life for Memphis children with high-risk asthma. The new GHHI and Calvert Foundation initiative, in partnership with Habitat for Humanity and other community partners, will augment CHAMP's existing medical services with assistance focused on reducing in-home asthma triggers.

Le Bonheur-designed, cost-effective diagnostic pathway for suspected appendicitis reduces misdiagnoses, radiation exposure

Study in Journal of the American College of Surgeons *determines cost effectiveness of diagnostic strategies*

A pathway combining the use of the Pediatric Appendicitis Score (PAS) and selective ultrasonography (USG) to diagnose pediatric appendicitis improves diagnostic accuracy over USG alone at a moderate increase in cost to the hospital, while decreasing radiation exposure associated with excessive CT use. These findings were the result of a Le Bonheur Children's study comparing hospital costs for diagnostic strategies for suspected appendicitis to be published in the April 2015 issue of the *Journal of the American College of Surgeons*.

The study utilized a cost-effectiveness analysis technique to model possible costs associated with different methods of diagnosing pediatric appendicitis, such as using emergency department clinician judgment alone, USG on all patients, CT on all patients, overnight observation with surgical evaluation without studies and the combined use of PAS and selective USG. Findings showed that although using USG for every patient is the most cost-effective method amongst the methods compared, it has a 2 percent higher diagnostic error rate than use of PAS and selective USG. Using a combination of PAS and selective USG is slightly more expensive than using USG alone, but the combination improves diagnostic accuracy, reducing the chance for an even costlier misdiagnosis.

The combined use of PAS and selective USG for suspected appendicitis is a novel diagnostic pathway, designed and tested by Le Bonheur Children's Emergency Department, Radiology and Surgery teams. Le Bonheur previously published a study aimed at determining the safest and most accurate pathway for diagnosing appendicitis in children in the journal *Pediatrics* in January 2014. The study found that using PAS and selective USG exposes children to less radiation than other currently used strategies and very accurately diagnosed appendicitis, yielding a sensitivity of 92 percent and specificity of 95 percent. For more information about the pathway, visit www.lebonheur.org/appendicitis.

Pershad J, Waters TM, Langham MR Jr, Li T2, Huang EY. Cost-Effectiveness of Diagnostic Approaches to Suspected Appendicitis in Children. J Am Coll Surg. 2014 Dec 20. pii: S1072-7515(14)01911-5. doi: 10.1016/j.jamcollsurg.2014.12.019. [Epub ahead of print]

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Surgeon finds Guatemala mission field

Le Bonheur and Campbell Clinic orthopaedic surgeon William Warner, MD, joined a team from Dell Children's Hospital's Surgical Outreach Program recently to care for children in Guatemala City, Guatemala.

Warner helped care for more than 30 cases during the five-day trip. Children were prescreened before the surgical team arrived, and then treated for an array of conditions, including dislocated hips, club feet, benign tumor resections and tendon transfers. Warner's wife, Pathologist Susan Warner, MD, joined him on the trip and scrubbed in during surgeries.

"I have always wanted to do this and participate in this sort of mission work, " Warner said. "When the opportunity came, we knew we were ready to help."

The trip was part of a group put together by Dell Children's Hospital to work at the Moore Pediatric Surgical Center in Guatemala City. The center is operated by the Shalom Foundation in Franklin,Tenn. Patients are brought to the center and evaluated before surgical teams arrive. The center's follow-up program with local physicians ensures patients receive post-operative care.