

DELIVERING ON A PROMISE



Viral fix

Memphis researchers are finding better ways to treat RSV

- ▶ ACS accreditation helps trauma team reach an underserved population
- ▶ NIH's Han to lead pediatric obesity program

RSV infects **every** child.
Almost all will get it by
their 2nd birthday.

125,000
U.S. children
are hospitalized
for RSV
each year.

RSV infection
is the **No.1**
cause of
hospitalization
of infants
in the U.S.

25-40%
of children
with RSV
will develop
bronchiolitis
or pneumonia.

RSV causes
10 times
as many
infant
deaths as
influenza.

Of those babies
hospitalized for RSV,
90% are full-term,
healthy babies.

RSV caused **1.5 million**
outpatient visits for
children younger than 5
in the U.S. last year.



Le Bonheur Children's Hospital in Memphis, Tenn., treats more than 250,000 children each year in a 255-bed hospital that features state-of-the-art technology and family-friendly resources. Nationally recognized, Le Bonheur is ranked by U.S. News & World Report as a "Best Children's Hospital."



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

Meri Armour
President and CEO

Jon McCullers, MD
Pediatrician-in-Chief

Mark Williams, MD
Surgeon-in-Chief

Harris Cohen, MD
Radiologist-in-Chief

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

Delivering on a Promise



VIDEO



PHOTO

more content is available at
www.lebonheur.org/promise

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.

In this issue:



4 Viral fix

RSV research opens doors for findings in other respiratory illnesses



10 Raising the game

American College of Surgeons verification helps trauma team reach an underserved population



12 Reconnecting kids to medical homes

Mobile health unit expands pediatric services into region



@lebonheurchild



/lebonheurchildrens



/lebonheurchildrens



Viral fix

Le Bonheur researchers change the course of RSV therapies

It began with a runny nose and watery eyes. Veteran mom Emily Joyner had learned not to overreact: 4-week-old Hayden was a full-term, otherwise healthy baby boy, and this looked like a minor cold. Forty-eight hours later, Hayden was in respiratory failure, as a pediatric Emergency Department team at Le Bonheur Children's Hospital worked to keep him alive.

That was Emily's first introduction to respiratory syncytial virus, or RSV – the most common cause of lower respiratory tract infections in young children in the United States and worldwide. The virus forced Hayden into Le Bonheur's Intensive Care Unit, on a breathing machine for two weeks and hospitalized for three.

"It was the most overwhelming thing I've ever gone through," said Emily. "It went from, 'He has a little

cold; they may give him a breathing treatment,' to 'He can't breathe, and they can't get him stable.'"

Hayden Joyner is one of up to 125,000 children hospitalized in the United States for RSV each year, according to the Centers for Disease Control and Prevention (CDC). In 2013, RSV caused 1.5 million pediatric outpatient visits. While almost every child will get the virus

by his or her second birthday, 25-40 percent of them will also develop bronchiolitis or pneumonia from RSV.



Four-week-old Hayden Joyner (above) was hospitalized for three weeks because of respiratory syncytial virus, or RSV.

Le Bonheur scientists have directed nearly every experimental therapeutic advancement for RSV in the past 15 years.

Scientists at Le Bonheur Children's have been part of virtually every experimental therapeutic advancement,

developmental pathway and antiviral therapy created to tackle RSV in the past 15 years. Today, Le Bonheur labs house the largest collection of human RSV in the United States, and are on the cusp of finding new therapies.

It is the culmination of a growing body of research that could prove life-saving for infants like Hayden.

Laying the foundation

Much of the credit for Le Bonheur's developing research in RSV goes to Infectious Disease Specialist John DeVincenzo, MD, medical director of Le Bonheur's Molecular Diagnostics and Virology Laboratories, and NIH-supported respiratory virus researcher in Le Bonheur's Children's Foundation Research Institute. DeVincenzo came to Memphis from Boston Children's Hospital more than 15 years ago to study respiratory viruses in collaboration with St. Jude Children's Research Hospital.

Today, antiviral development is a main priority of his lab, but his research over time has focused on understanding the pathogenesis of RSV in children, and using that understanding to develop antivirals, vaccines and other prevention strategies. In recent years, his labs have proven the link between the number of viruses in infant lungs and disease dynamics — that the amount of RSV virus a child carries will determine how sick he or she will be.

DeVincenzo also discovered that the faster the amount of virus was reduced in infant lungs, the faster those infants improved — and that the severity of illness was directly proportional to when the virus quantity was highest.



RSV researcher John DeVincenzo, MD, is leading global efforts to find effective RSV antiviral therapies.

“It was very controversial at the time,” DeVincenzo said. “We had a huge gap for four decades (since the last RSV vaccine attempt failed in children), because scientists and doctors thought that the infection first made the infant produce an abnormal amount of inflammation, which in turn made them sick. Because of this erroneous concept, no one believed an

antiviral would work. But once we found a correlation, we shifted our focus to antivirals.”

DeVincenzo's next hurdle was finding a way to test antivirals in humans — without testing them on children. In 2010, he first published findings that showed how an adult version of the virus (specially selected and



Watch a video about Le Bonheur's work treating RSV at www.lebonheur.org/promise



manufactured from a series of more than 200 studied hospitalized Le Bonheur infants) could reliably infect healthy adult volunteers on exposure and safely cause a mild form of RSV illness. His open source model was awarded the best advance in therapeutics and prevention of an infectious disease by the American Society of Microbiology (2007), is now used to test proof-of-concept antivirals, and has allowed for the proper development of investigational agents. All four of his current antiviral programs

will have been tested with the infection model by the end of this spring, a necessary stepping stone toward testing in RSV-infected infants and children themselves.

While each program is at a different stage, it's important to develop them all, he says, because each program targets the virus in a different way.

"Some kids with weakened immune systems will need a combination of antivirals to fight the virus, especially because RSV is always mutating and changing," DeVincenzo said.

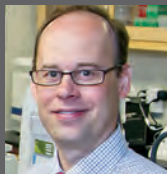
The Investigators:

As Le Bonheur respiratory research grows, a broad range of scientists is working together to lend expertise to a variety of projects tackling RSV, asthma, influenza and more.



Stephania Cormier, PhD, and her six-member research team are learning how early environmental exposure to respiratory viruses like influenza and RSV, allergens and pollutants can predispose or exacerbate asthma in adulthood.

Jon McCullers, MD, and Amali Samarasinghe, PhD, study how the state of allergic airways at the time of influenza virus infections impacts pathogenesis. They have established that acute allergic asthma reduces morbidity and mortality from secondary bacterial infections, and are now working to delineate mechanisms that may be involved in this protection.



Dennis Stokes, MD, MPH, and Christie Michael, MD, are using a CMS Innovation Grant to study how social approaches to asthma can reduce deaths, Emergency Department and urgent care visits, avoidable hospitalizations and asthma exacerbations or episodes.



John DeVincenzo, MD, has spent the past 15 years developing therapeutic and prevention strategies against respiratory syncytial virus.





Another important piece of the puzzle, researchers believe, is understanding the RSV immune response. DeVincenzo works closely with Le Bonheur researcher Young-In Kim Hohamer, PhD, who is developing a tool to measure how much immune response adults and infants have to effectively fight RSV.

“Some kids with weakened immune systems will need a combination of antivirals to fight the virus, especially because RSV is always mutating and changing.” – John DeVincenzo, MD

And DeVincenzo collaborator and Infectious Disease Specialist Bindiya Bagga, MD, is developing tools to define the mucosal immune response required for effective protection against RSV infection. She is also collaborating with scientists at St. Jude Children’s Research Hospital in a nascent trial of a parainfluenza virus vaccine.



RSV and flu took hold of 4-month-old Chrisiah Cole (above), even after her mom took all the precautions she could think of at home. “I’d rather her be at the hospital and safe because I know she’s in good hands,” mom Cadeidre Cole said.

Scientists at St. Jude are using the Sendai virus particle (SeV), which resembles the physical structure of the human parainfluenza virus Type 1. By genetically engineering SeV to add RSV specific-antigens, Bagga says they are “making headway into RSV” with a prospective vaccine, known as SeVRSV.

Bagga says her interest in RSV research grew from frustrations in the clinical setting. As an infectious disease



Bindiya Bagga, MD, is developing tools to define the mucosal immune response required for effective protection against RSV infection. She also collaborates with St. Jude Children’s Research Hospital scientists in a nascent trial of a vaccine designed to expose children to parts of the RSV virus genetically engineered so as not to be able to fully replicate. Her work is expected to advance the development of RSV vaccine.



Betty Lew, MD, is developing a new class of medicine for asthma, called mannan, that could treat children who don’t respond to steroids or bronchodilators.



Sandra Arnold, MD, and **Jon McCullers, MD**, helped conduct the largest-ever study of the incidence and cause of community-acquired pneumonia in hospitalized children. They expect to begin publishing results this year.



Anami Patel, PhD, serves as technical director of the molecular diagnostic lab, which tests specimens from patients with respiratory symptoms – helping physicians make better clinical decisions.

Young-In Kim Hohamer, PhD, is creating a tool to measure how much immune response adults and infants have to effectively fight RSV. Her work is expected to help other researchers develop better preventions and therapeutic options to fight the virus.



Learn more at www.lebonheur.org/promise

specialist at Le Bonheur, she's grown tired of telling parents of hospitalized children that there's not much she can do to treat the virus.

"The impact of a vaccine would be tremendous,"

Bagga said. "As a parent, you know your kid is going to get infected; it's just a question of when. This is something that can really make a change. It's so translational; it's so real life. You can see the difference that you can make."

DEVELOPING ANTIVIRALS

John DeVincenzo's lab at Le Bonheur Children's Hospital has developed the largest knowledge base in the country showing the dynamics of how RSV grows within human airways and causes human disease. He has led the academic field of antiviral therapy for RSV and is now launching the first set of new RSV antiviral programs since the 1980s, partnering with the biotech and pharmaceutical industries. They include four randomized, placebo-controlled clinical trials, which have been recently completed or are currently underway:

A Phase IIa clinical trial to evaluate AL-8176, a nucleoside analog designed to **inhibit RSV from copying itself by causing chain termination of the virus**. In Phase II, volunteers will be enrolled and inoculated with RSV and then given AL-8176 or a placebo, using the human RSV challenge model developed by DeVincenzo.

A Phase IIa clinical trial of MDT-637, an inhalable molecule that works to **block the RSV from fusing to the human cell membrane within the human respiratory tract**. The experimental therapy is delivered directly to the respiratory tract cell surface via an electrically controlled novel dry power inhaler.

A Phase IIb clinical trial of ALN-RSV01, an **RNA-interference-based experimental therapy to shut down an RSV gene required for the virus to reproduce itself**. DeVincenzo has proven this experimental therapy works to reduce RSV replication in humans experimentally infected with RSV. Now he has conducted a study within adult lung transplant recipients showing that the drug is safe in naturally acquired RSV infections of adults. In the as-yet unpublished placebo-controlled trial, lung transplant patients showed reduced lung disease at 90 and 180 days after receiving the drug (as compared to those receiving placebo).

A Phase IIa clinical trial of GS-5806, an oral drug that **inhibits RSV from entering human respiratory epithelial cells**, is now complete. The drug was shown to safely reduce viral load and clinical illness in healthy adult volunteers, using the RSV experimental challenge model. Results were released at the American Thoracic Society's spring conference.

A widened scope

That push to make research more translational is a big focus for the University of Tennessee Health Science Center Department of Pediatrics Chair Jon McCullers, MD. The relationship between basic and clinical scientists will help move all research forward and bring it to the bedside, he says.

National Institutes of Health-funded researcher Stephania Cormier, PhD, says the relationship between clinical and basic scientists attracted her to Memphis in 2013. After studying the virus in mouse models for years, she wanted to be part of finding better therapeutics and developing safe, effective vaccines. To develop such vaccines requires an understanding of how the infant immune system responds to respiratory tract viral infections like RSV, a major focus of her work.

"Respiratory syncytial virus is the No. 1 cause of bronchiolitis and pneumonia in infants worldwide, and if infants are infected and develop severe bronchiolitis, they go on to develop asthma," Cormier said. "So we're really trying

to figure out what causes them to develop asthma, how to prevent them from developing asthma, and how to



Stephania Cormier, PhD, is studying how environmental factors like pollution and RSV play a role in asthma.

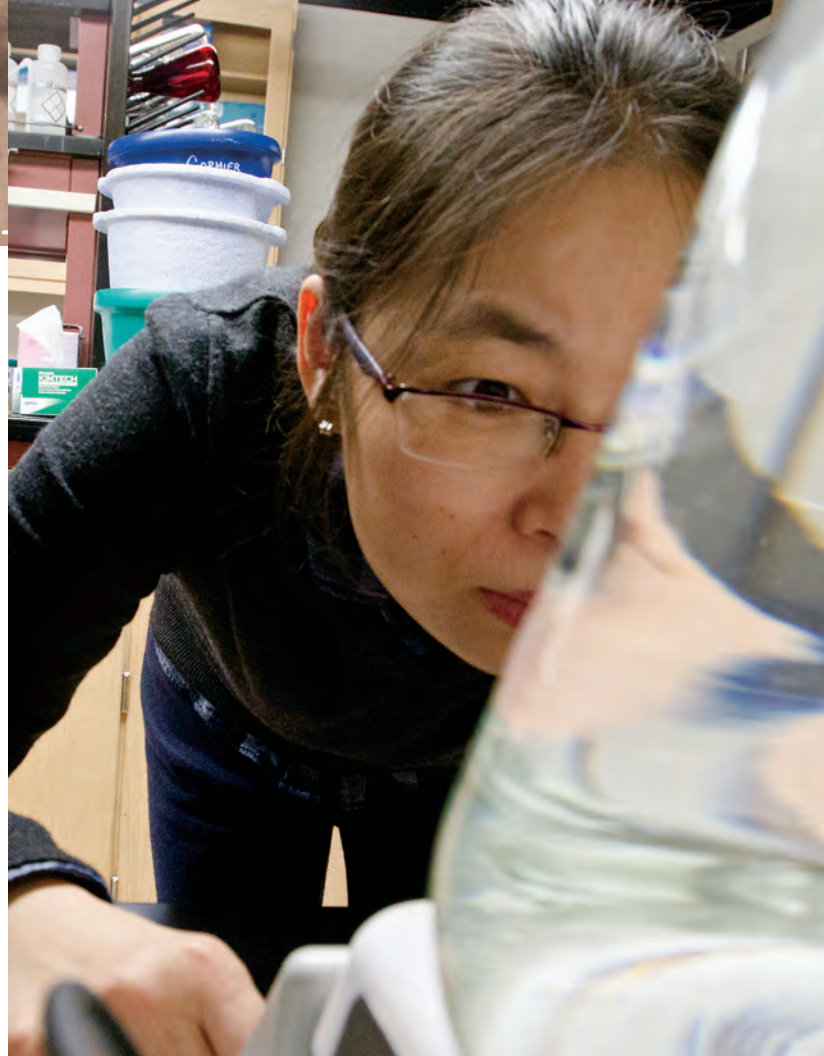
develop vaccines that will prevent them from contracting respiratory syncytial virus in the first place.”

Human infants who develop severe RSV infection requiring hospitalization often go on to develop asthma that

persists into adulthood. Cormier and her team have developed an infant mouse model system that recapitulates this phenomenon. Her lab seeks to define the immune mechanisms responsible for the development of RSV-induced asthma and identify vaccine strategies and therapeutics to prevent RSV-induced asthma.

In addition to RSV, her lab is also studying how exposure to particulates in the environment can damage young lung cells even more, forcing them to collect in the lining of the lung and thicken. That thickening predisposes children to respiratory conditions like asthma later in life.

As the body of respiratory research at Le Bonheur



grows, studies in other labs begin to intersect – helping investigators understand more dimensions of respiratory infections.

McCullers and Amali Samarasinghe, PhD, for example, are studying co-infections and the role asthma can play in influenza severity. They’ve established that the state of allergic airways at the time of influenza virus infections affects disease, and that acute allergic asthma modifies the response to viruses like influenza. They are working now to determine what mechanisms are involved in this protection.

Additionally, Betty Lew, MD, is trying to develop a new class of asthma medication, mannan, that would provide options for patients who don’t respond to steroids and bronchodilators. And outside the lab, Pulmonologist

Dennis Stokes, MD, MPH, and Allergist-Immunologist Christie Michael, MD, are applying community approaches to reduce deaths, Emergency Department and urgent care



About 125,000 U.S. children are hospitalized for RSV each year. The Joyner family gathers at baby Hayden's bedside during a three-week hospital stay for RSV.

visits, avoidable hospitalizations and asthma exacerbation.

A perfect storm

After more than a decade as scientific director of the Children's Foundation Research Institute – a joint effort between Le Bonheur, UTHSC and the Children's Foundation of Memphis – Dennis Black, MD, is beginning to see what he calls a “perfect storm” of respiratory research efforts. Scientists in niche specialties are working across from one another, lending ideas and expertise to each other's projects.

“All the research today is based on interdisciplinary teams,” Black said. “We want to build a team with areas

PNEUMONIA EPIC STUDY YIELDS EARLY RESULTS

Beyond RSV, asthma and influenza, Le Bonheur was also one of four sites to participate in Centers for Disease Control and Prevention's Influenza Division's Etiology of Pneumonia in the Community (EPIC) Study – the largest-ever study of community-acquired pneumonia in hospitalized children and adults. The project – which was funded for \$3.2 million in Memphis – is the first study of community-acquired pneumonia in children since the pneumococcal vaccine Prevnar was introduced. Le Bonheur enrolled 988 children

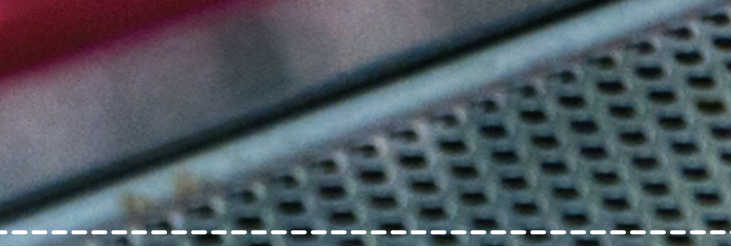
between 2010-2012 and was one of three sites enrolling children.

Preliminary results show that pneumonia remains a common cause of hospitalization in children, predominantly those younger than the age of 5. The study also showed viral causes of pneumonia are most common, and that clinicians need better techniques to distinguish viral and bacterial pneumonia to minimize unnecessary antibiotic use.

“I think we'll get a better understanding of what causes pneumonia in the community and will see that

bacterial pneumonia is relatively uncommon. Non-hospitalized children younger than 5 rarely have bacterial infections,” said Sandra Arnold, MD, principal investigator for the Le Bonheur site. “I hope the data will eventually change how we manage pneumonia and use antibiotics.”

Jon McCullers, MD, chair of the Department of Pediatrics at the University of Tennessee Health Science Center, served as the Memphis principal investigator for the study.



of expertise that complement other areas and get them together to interact. What comes out of that is greater than the sum of the parts.”

The sum, investigators hope, is viable drug therapies and vaccines for a variety of respiratory viruses, and a better understanding of the long-term implications of those viruses.

And for mom Emily Joyner, preventions and better therapeutic options for RSV would put her mind at ease. After a two-week stay in the Intensive Care Unit, she knows any additional virus Hayden contracts this season would be hard for him to fight.

Bindiya Bagga, MD, (above) is developing tools to define the effective immune response to RSV, work that is expected to advance RSV vaccine development. “This is something that can really make a change,” she said.

“We’ve been washing our hands nonstop and making the kids change clothes when they get home from pre-school,” Joyner said. “He’s the third child, and before RSV, we brought him along for pretty much anything. After what we’ve experienced, he won’t be out of the house for a while. He may be in a bubble until he’s 18.”

Family seeks protection from respiratory illness in winter months.

In the winter months, 6-year-old Ellie Sawyer isn’t allowed to sleep over with her friends. She doesn’t spend much time playing in the cove with neighborhood kids. And she lives with an industrial-sized bottle of hand sanitizer.

Those are just some of the precautions Jan and Rob Sawyer have taken to protect their daughter from another trip to Le Bonheur Children’s Hospital, after two bouts with respiratory syncytial virus (RSV) landed her in the Intensive Care Unit.

The Sawyers, who live in the Memphis suburb of Germantown, Tenn., had never heard of RSV when then 2-year-old Ellie first succumbed to the virus. She didn’t respond to steroids or bronchodilators, and her oxygen saturation dropped to the low 70s. After two weeks in the hospital, the Sawyers hoped they’d seen the last of RSV. A year and a half later, Ellie landed back in the ICU.

“I remember our doctor telling us, ‘We don’t know all the



Six-year-old Ellie Sawyer’s parents take extra precautions during winter months to protect her from RSV. Ellie’s two bouts with RSV have landed her in Le Bonheur’s Intensive Care Unit.

features of RSV, but RSV has got your baby again,” Jan said. “It’s amazing how, when your child’s health is at issue, you change.”

Determined to do all they could to protect Ellie, the Sawyers began to take precautions to limit Ellie’s exposure to viruses in the winter.

Ellie has stayed out of the hospital since her last bout with RSV, though Jan still travels with a oxygen saturation monitor. The older Ellie gets, the more her parents hope she is prepared to fight a

virus to which she’ll inevitably be exposed. But until then, they’ll do everything they can to protect her.

“All I have to do is picture what she looked like in that big hospital bed, the bluish tint to her face,” Jan said. “That’s all we need to keep doing what we can to keep her safe.”



See more faces of RSV
www.lebonheur.org/promise

RAISING THE GAME

ACS verification helps trauma team reach an underserved population

A push to “raise the game” in pediatric trauma care for Memphis children is helping kids in the most unexpected places – pockets of the rural South where the specialized care was once limited.

In 2011, Le Bonheur began pursuing and later attained American College of Surgeons (ACS) Level 1 pediatric trauma verification, which has translated into a region better prepared for pediatric emergencies.

“Not only did it set us on par with every other pediatric trauma center, it made us raise our game,” said Medical Director of Trauma Services James “Trey” Eubanks, MD.

Le Bonheur has long cared for local children who’ve been in car and ATV accidents, injured on the playing field or burned in house fires. The hospital is designated as a pediatric trauma center in Tennessee, Arkansas and Mississippi. Pursuing ACS verification took the hospital a step further out into the region.

“Though we geographically sit in a large urban city, we are surrounded by a predominately rural and underserved region,” said Le Bonheur President and CEO Meri Armour. “We found that the medical professionals in these areas are equipped to care for adults, but not trained to provide specialized pediatric trauma care.”

As Eubanks’ team began the ACS verification process, the hospital implemented major changes. Today, anesthesiology is in-house 24/7, and the Emergency Department and operating rooms have specialized refrigerators that provide immediate access to blood products. Efforts are better coordinated throughout the hospital – from the moment the patient arrives in the

Le Bonheur educators perform a mock pediatric trauma simulation at the St. Bernards Medical Center in Jonesboro, Ark.

Meet Josiah Crutchfield, a 14-year-old who tore his pancreas while playing football. Hear how the trauma team has him up and exercising again.



www.lebonheur.org/promise



Emergency Department to CT scan to OR to inpatient room. Indirectly, these changes improve the care for children across the hospital.

Another byproduct of raising the level of care has been a 60 percent increase in trauma patient volumes.

“We find most of those patients are coming from those underserved areas and rural communities that don’t have as many physicians or emergency rooms and may not even have a nearby hospital. So I think we’ve done that part of the community a great service,” Eubanks said.



Trauma Clinic Nurse Practitioner Amanda Rotenberry, APN, examines burn patient Destiny Henderson

The team is also making efforts to share its expertise. Outside the hospital, Eubanks’ team is on the road educating emergency room and operating room staff and EMS professionals on topics like how to resuscitate a badly injured patient and techniques for treating minor burns. Part of that training is understanding the level of care each child needs and getting those kids to the best place as soon as possible.

“That first hour after a trauma is the most important. And getting them here as quickly as possible is vital to improving quality and outcomes,” Eubanks said.

Le Bonheur educators work with 28 adult facilities in the region providing mock codes, following up with training after a patient has been transferred and simply being a 24-hour resource.

“I have training in adults and trauma, but I’ve never worked with as many kids as I do now,” said Delta Medical Emergency Department Head Nurse and Educator Jennifer Keith, RN. “The training from Le Bonheur has given us peace of mind. And peace of mind makes us better nurses because we’re not scared.”

After patients are discharged, the trauma team continues to follow them. At the weekly outpatient clinic, general surgeons and nurse practitioners collaborate with physical therapists, occupational therapists and Child Life specialists to help children get back to their normal routines or adjust to life post accident. ACS requires continual tracking and process improvement. Data is collected on each patient, trends are analyzed and care is adjusted across the board.

The trauma team isn’t just analyzing the data on its patients. It’s collaborating with six free-standing children’s hospitals to ask questions about pediatric trauma on a large scale. ATOMAC – a collaboration of hospitals in Little Rock, Oklahoma City, Austin, Dallas, Phoenix and Memphis – is combining research efforts.

“Among the six of us, we see a large

Injury prevention efforts follow trauma trends

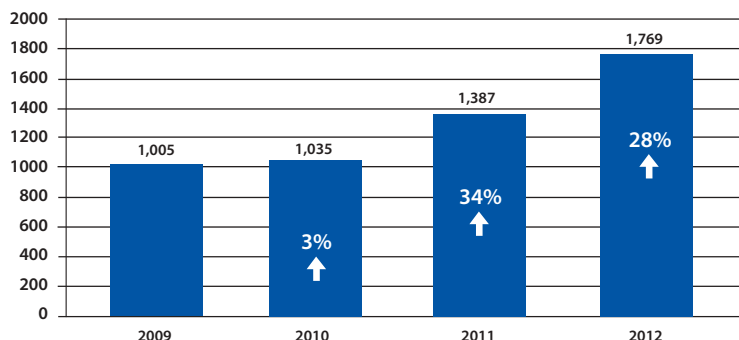
In response to the trends of emergency room visits and trauma cases, Le Bonheur’s Injury Prevention and Safe Kids Mid-South team has designed programs to meet community needs. Spikes in teenage drowning led to a free swim lesson program based at community center and YMCA pools. High infant mortality rates were, in part, tied to babies sleeping on couches and not riding in car seats. Baby safety initiatives ensure that new moms in the highest risk areas have cribs and new car seats. In 26 years, these efforts, led by a former pediatric intensive care nurse, have decreased severe child injury rates by 33 percent regionally.

volume of patients, which allows us to quickly find answers to questions about things that were really difficult to answer or were really rare,” Eubanks said.

The team published in the *Journal of Trauma and Acute Care Surgery* regarding the need for more aggressive screening on blunt trauma in children. Other studies underway include management of blunt spleen and liver injuries and long-term outcomes for brain injury patients.



Trauma Volumes Increase



Since Le Bonheur earned American College of Surgeons pediatric trauma accreditation in 2011, trauma patient volumes have almost doubled.



Le Bonheur expands reach with new mobile unit

Le Bonheur's newest mobile unit is expected to serve more than 4,000 children in Memphis-area and North Mississippi schools.

More than 4,000 children without a primary care provider will have access to a new mobile unit Le Bonheur is sending throughout Memphis and north Mississippi. The unit was built with a \$490,000 grant from the U.S. Department of Health and Human Services-Health Resources and Services Administration (HRSA), Bureau of Primary Health Care, and will begin serving schools in Memphis and Tunica County, Miss., this spring.

The unit will be staffed by a nurse practitioner, two nurses and a data entry clerk and will offer well-child checkups, screenings, sick visits, administration of physician-prescribed medications and referrals to primary and specialty care providers.

“Many children don’t visit their primary care provider frequently enough,” said Cynthia Cross, MD, medical director of Le Bonheur’s mobile health services

and a pediatric hospitalist. “While there are many barriers to obtaining ongoing care, transportation can be particularly difficult. Our new mobile unit allows us to bring care to children. The schools are great with helping us identify children who need our services.”

Le Bonheur’s Community Health and Well-Being division has provided school-based health education and primary care services in a six-county area around Memphis since 1995. The hospital’s first mobile unit, Le Bonheur on the Move, provides mobile health services for five counties in rural West Tennessee. Since 2012, the mobile health program has provided care during 2,700 visits and connected more than 300 children to a primary care provider. The mobile unit program receives funding from the Children’s Health Fund.

Han joins Le Bonheur, focuses on pediatric obesity

Pediatric Endocrinologist Joan Han, MD, is director of the new Le Bonheur Healthy Lifestyles Clinic and Metabolic Research Center. She comes from the National Institute of Child Health and Human Development at the National Institutes of Health.

Han has spent her career studying genetic determinants of obesity in the general population and in patients with rare disorders associated with obesity, such as Alström, Bardet-Biedl, Prader-Willi and WAGR/11p deletion syndromes. The hospital's new Healthy Lifestyles Clinic and Metabolic Research Center will care for children who have health complications related to pediatric obesity and is expected to open in the summer. Han will also serve as associate professor of Pediatrics for the University of Tennessee Health Science Center.



Joan Han, MD

NEW RECRUITS



Amanda Adamson, PhD
Neuropsychiatry
Education: University of Mississippi
Fellowship: Children's Healthcare of Atlanta



Abbas Babajani-Feremi, PhD
Clinical Neurosciences
Assistant Professor, The University of Tennessee Health Science Center
Education: University of Tehran, Iran



Kristen Bettin, MD
General Pediatrics
Assistant Professor, The University of Tennessee Health Science Center
Education: The Ohio State University College of Medicine
Residency: The University of Tennessee Health Science Center



Gary Cavender, MD
Pediatric Gastroenterology
Associate Professor, The University of Tennessee Health Science Center
Education: East Carolina University School of Medicine
Fellowship: University of Texas Southwestern Medical Center



Nkiruka Ezenwa, MD
Pediatric Hospitalist
Assistant Professor, The University of Tennessee Health Science Center
Education: College of Medicine, University of Nigeria.
Residency: Bronx-Lebanon Hospital Center/ Albert Einstein College of Medicine



Robert Gold, MD
Interventional Radiology
Professor, The University of Tennessee Health Science Center
Education: University of Manitoba
Fellowship: University of Michigan Hospitals



David Hains, MD
Pediatric Nephrology
Associate Professor, The University of Tennessee Health Science Center
Education: Indiana University School of Medicine
Fellowship: Nationwide Children's Hospital/ The Ohio State University School of Medicine



Tim Jancelewicz, MD
Pediatric Surgery
Assistant Professor, The University of Tennessee Health Science Center
Education: Columbia University College of Physicians and Surgeons
Fellowship: University of California, San Francisco



Jason Johnson, MD, MHS
Pediatric Cardiology
Assistant Professor, The University of Tennessee Health Science Center
Education: Louisiana State University Health Science Center
Fellowship: Duke University School of Medicine



Salil Joshi, MD
Interventional Radiology
Assistant Professor, The University of Tennessee Health Science Center
Education: D.Y. Patil Medical College, India
Fellowship: University of Tennessee Health Science Center



Rana Khaznadar, MD
General Pediatrics
Assistant Professor, The University of Tennessee Health Science Center
Education: University of Texas Medical School at Houston
Residency: The University of Tennessee Health Science Center



Diana Lebron, MD
Pediatric Neurology
Assistant Professor, The University of Tennessee Health Science Center
Education: Robert Wood Johnson Medical School
Fellowship: New York University School of Medicine/Bellevue Medical Center



Brent Logan, MD
Pediatric Endocrinology
Assistant Professor, The University of Tennessee Health Science Center
Education: University of Virginia School of Medicine
Fellowship: University of Virginia Children's Hospital



Elisha McCoy, MD
General Pediatrics
Assistant Professor, The University of Tennessee Health Science Center
Education: The University of Tennessee Health Science Center
Residency: The University of Tennessee Health Science Center



Mark Meredith, MD
Pediatric Emergency Medicine
Associate Professor, The University of Tennessee Health Science Center
Education: University of Mississippi Medical Center
Fellowship: Vanderbilt University Medical Center/Monroe Carell Jr. Children's Hospital at Vanderbilt



Stephen Miller, MD
Pediatric Radiology
Associate Professor, The University of Tennessee Health Science Center
Education: Vanderbilt University School of Medicine
Fellowship: The Hospital for Sick Children, Toronto



Stephanie Payton, MD
Pediatric Hospitalist
Assistant Professor, The University of Tennessee Health Science Center
Education: James H. Quillen College of Medicine, East Tennessee State University
Residency: Medical Center of Central Georgia/Mercer University School of Medicine



Ranjit Philip, MD
Pediatric Cardiology
Instructor, The University of Tennessee Health Science Center
Education: Kasturba Medical College, India
Fellowship: The University of Tennessee Health Science Center



Jorge Salazar, MD
Interventional Radiology
Assistant Professor, The University of Tennessee Health Science Center
Education: The University of Tennessee Health Science Center
Fellowship: The University of Tennessee Health Science Center



Hitesh Sandhu, MBBS
Pediatric Critical Care Medicine
Assistant Professor, The University of Tennessee Health Science Center
Education: Government Medical College, Mysore, India
Fellowship: Children's Hospital of Michigan/ Wayne State University



Mauro Schenone, MD
Maternal Fetal Medicine
Assistant Professor, The University of Tennessee Health Science Center
Education: University of Carabobo, Venezuela
Fellowship: The University of Tennessee Health Science Center



Wednesday Sevilla, MD
Pediatric Gastroenterology
Assistant Professor, The University of Tennessee Health Science Center
Education: University of the Philippines College of Medicine
Fellowship: Children's Hospital of Pittsburgh



Nadeem Shafi, MD
Pediatric Critical Care Medicine
Associate Professor, The University of Tennessee Health Science Center
Education: The University of Tennessee Health Science Center
Fellowship: Baylor College of Medicine



Adeel Siddiqui, MBBS
Pediatric Neuroradiology
Assistant Professor, The University of Tennessee Health Science Center
Education: Hamdard College of Medicine and Dentistry, Pakistan
Fellowship: Beth Israel Medical Center/ The Johns Hopkins Hospital



Akosua Sintim-Damoa, MD
Pediatric Radiology
Assistant Professor, The University of Tennessee Health Science Center
Education: UMCNJ – New Jersey Medical School
Fellowship: Children's National Medical Center



Regan Williams, MD
Pediatric Surgery
Assistant Professor, The University of Tennessee Health Science Center
Education: The University of Tennessee Health Science Center
Fellowship: The University of Tennessee Health Science Center



Jason Yaun, MD
General Pediatrics
Assistant Professor, The University of Tennessee Health Science Center
Education: The University of Tennessee Health Science Center
Residency: The University of Tennessee Health Science Center



Thomas Yohannan, MBBS
Pediatric Cardiology
Instructor, The University of Tennessee Health Science Center
Education: Government Medical College, India
Fellowship: The University of Tennessee Health Science Center

Briefs



EEG lab first in state to earn ABRET accreditation

American Board of Registration of Electroencephalographic and Evoked Potential Technologists (ABRET) recently granted Le Bonheur EEG laboratory a five-year accreditation. The Neuroscience Institute is the only EEG lab in the state of Tennessee to receive this honor.

New clinics open for sports cardiology, eosinophilic esophagitis, headaches

Le Bonheur recently expanded outpatient services to meet the needs of patients with complex conditions with three new specialized clinics.

Pediatric headache is a common condition – and one commonly seen by Le Bonheur’s Neuroscience Institute. The hospital recruited Pediatric Neurologist Diana Lebron, MD, last year in an effort to form a designated clinic for patients to receive care in one setting. Lebron specializes in primary and secondary



Diana Lebron, MD

type headaches, including post-traumatic headaches, headaches due to Ehlers Danlos Syndrome, headaches due to idiopathic intracranial hypertension and cervicogenic headaches. The clinic’s goal is to help patients understand and manage their condition through a variety of medications and non-pharmacological treatment options.

The Sports Cardiology Clinic provides specialized care for athletes with suspected, acquired and congenital heart disease. The integrated clinic includes cardiopulmonary stress testing and advanced imaging techniques. Led by Pediatric Cardiologist Alex Arevalo, MD,



Alex Arevalo, MD

the team includes experts from pediatric cardiology, pulmonology, physical therapy, sports nutrition, orthopaedics and sports medicine.



Jay Lieberman, MD

The Eosinophilic Esophagitis Clinic is designed to diagnose and treat children with inflammation of the esophagus, a condition commonly caused by a food allergy, acid reflux or other allergens. Pediatric Allergist Jay Lieberman, MD, and Pediatric Gastroenterologist Cary Cavender, MD, work together to find a cause



Cary Cavender, MD

for the inflammation and determine treatment options.

Greater Mid-South Pediatric Neurology Update set for April 25, 26

Now in its eighth year, the Greater Mid-South Pediatric Neurology Update will be held April 25-26 at The Westin Memphis, Beale Street, Memphis. The seminar encompasses state-of-the-art practices and trends in treating pediatric neurology patients. Topics this year will include neurogenetics, migraines, tuberous sclerosis complex and more.

The event will include the inaugural Kayden R. Vinson Distinguished Scholar Award and Lecture by Pediatric Neurologist Alex Paciorkowski, MD, from the University of Rochester Medical Center. Neuro-ophthalmologist Rod Foroozan, MD, from Texas Children’s Hospital and Baylor University

will also serve as a guest lecturer. For more information or to register, visit www.methodistmd.org.

McCullers reviews influenza and bacterial superinfections in *Nature Reviews Microbiology*

In the April issue of *Nature Reviews Microbiology*, Infectious Disease Specialist Jon McCullers, MD, reviews the co-pathogenesis of influenza viruses with bacteria in the lung. Bacterial superinfection in the lungs of people suffering from influenza is a key element that promotes severe disease and mortality.



Jon McCullers, MD

McCullers analyzes the epidemiology and microbiology of co-infections during the 1918, 1957 and 1968 pandemics as well as the more recent 2009 novel H1N1 virus. This co-pathogenesis is characterized by complex interactions between co-infecting pathogens and the host, leading to the disruption of physical barriers, dysregulation of immune responses and delays in a return to homeostasis.

The net effect of this cascade can be the outgrowth of the pathogens, immune-mediated pathology and increased morbidity.

McCullers calls for large-scale studies involving consortia or clinical networks to unlock the next unanswered questions about co-infections and viruses in order to prevent a loss of life similar to the pandemic of 1918.

“There is increasing recognition that most pneumonia is caused by co-infections rather than a single pathogen, and the most severe disease seen in influenza pandemics is mediated by co-infecting bacteria working with the virus,” said McCullers. “The scientific community must help the world prepare for the next pandemic by understanding a set of key, unanswered questions that are addressed in this review.”

McCullers J. The co-pathogenesis of influenza viruses with bacteria in the lung. Nature Reviews Microbiology. Vol. 12. April 2014.

Of Note

Harris Cohen, MD, radiologist-in-chief for Le Bonheur and chair of Radiology at UTHSC, is the current editor-in-chief of the American College of Radiology Continuous Professional Improvement program.



Harris Cohen, MD

Asim Choudhri, MD, a pediatric neuroradiologist and assistant chairman for Radiology at the University of Tennessee Health Science Center, served on the faculty of the American College of Radiology's review course in neuro-radiology. Choudhri and **Adeel Siddiqui, MD**, also a Le Bonheur neuroradiologist, co-authored chapters in the recently



Asim Choudhri, MD



Adeel Siddiqui, MD

published American College of Radiology's *Reference Guide in Information Technology for the Practicing Radiologist*.

Jay Pershad, MD, medical director of Pedi-Flite and the Transfer Center, was named senior reviewer for the *Annals of Emergency Medicine*, the official publication of the American College of Emergency Physicians.



Jay Pershad, MD

Barry Gilmore, MD, medical director of Emergency Services at Le Bonheur, served as a peer reviewer for "Emergency Department Readiness for



Barry Gilmore, MD

Pediatric Illness and Injury," a study published in the December 2013 issue of *Pediatric Emergency Medicine Practice*.

Mark Corkins, MD, CNSP, chief of Pediatric Gastroenterology at Le Bonheur, recently presented "Right From the Start: Building a Better Eater" and "The Poop Whisperer: Your Digestive Health" at the American Academy of Pediatrics' Healthy Children Conference + Expo. Held March 8-9 in Chicago, the new event designed for parents addressed the latest topics in pediatric health and parenting.



Mark Corkins, MD, CNSP

ARCHIVED PEDIATRIC GRAND ROUNDS

Pediatric Grand Rounds are available online at lebonheur.org/for-providers/continuing-medical-education/. CME credit is offered for each video in the series at no charge. For access to the password, please email physicians@lebonheur.org or call 1-866-870-5570.



Transport nurse: "I feel called"

Helicopter crash leaves lasting mark on Pedi-Flite team

Pedi-Flite Transport Nurse Farrah Anderson, RN, EMT, thinks long and hard about why she climbs into a helicopter every day.

Her friends and colleagues – a Le Bonheur nurse, respiratory therapist and Hospital Wing pilot – died in a helicopter crash in October 2013. They were on their way to pick up a patient. Less than a week later, Anderson and her teammates were back in the air.

"I have a 10-year-old and 12-year-old at home, and ultimately, I answer to them. When I sat down and spoke with my children, I told them that there aren't many of us who do this job and that it is special work – not everyone is going to do what we do," Anderson said.

"I love walking in to pick up a child and hearing the family say, 'I'm so glad to see you. Thank you for coming.' I feel called to do this work . . . I couldn't imagine doing anything else."



Farrah Anderson, RN, EMT

Research Highlights

Researchers at Le Bonheur Children's Hospital and University of Tennessee Health Science Center recently shared their investigations on a variety of pediatric health conditions. Highlights include:

Acute appendicitis: Researchers from the emergency department and pediatric surgery conducted a prospective observational cohort study of 196 patients, evaluating the diagnostic accuracy of a clinical pathway for suspected appendicitis. The protocol combined Samuel's pediatric appendicitis score and selective use of ultrasonography as the primary imaging modality. The clinical pathway demonstrated a high overall diagnostic accuracy of 94%, with a sensitivity of 92.3% (95% CI 83.0%–97.5%) and specificity of 94.7% (95% CI 89.3%–97.8%).

Ashley Saucier, Eunice Y. Huang, Chetachi A. Emeremni, and Jay Pershad. *Pediatrics* 2014; 133:e88–e95

Blunt cerebrovascular injury: Researchers found blunt cerebrovascular injury (BCVI) in Level 1 pediatric trauma centers is diagnosed less frequently than in adult centers, and pediatric surgeons should be more vigilant about screening pediatric patients with high-risk criteria for BCVI. Le Bonheur's trauma division studied, in a retrospective cohort study, all pediatric patients younger than 15 years admitted with blunt trauma to one of six American College of Surgeons-verified Level 1 Trauma Centers. The Abbreviated Injury Scale (AIS) helped identify patients with blunt injuries to the head, face or neck. From this subset, researchers analyzed demographics, mechanism of injury, Injury Severity Score (ISS), presence of injuries considered high risk for BCVI based on the Memphis criteria (anisocoria, basilar skull fracture, cervical spine fracture, neck soft tissue injury, LeFort II or III fracture and neurological exam unexplained by brain imaging), angiography results, presence of stroke, presence and characteristics of BCVI and treatment methods used.

Azarakhsh N, Grimes S, Notrica DM, Raines A, Garcia NM, Tuggle DW, Maxson RT, Alder AC, Recicar J, Garcia-Fillon P, Greenwell C, Lawson KA, Wan JY, Eubanks JW 3rd. *J Trauma Acute Care Surg.* 2013 Dec;75(6):1006–11; discussion 1011–2. doi: 10.1097/TA.0b013e31829d3526.

Malnutrition in hospitalized patients: Using Healthcare Cost and Utilization Project (HCUP) data, researchers found that 3.2 percent of all U.S. hospital discharges (including patients of all ages) in 2010 had a malnutrition diagnosis (as defined by a composite variable using ICD-9 codes). Those with malnutrition were older, had longer lengths of stay, incurred higher costs and were more likely to have 27 of the 29 comorbidities assessed in HCUP.

Corkins MR, Guenter P, Dimaria-Ghalili RA, Jensen GL, Malone A, Miller S, Patel V, Plogsted S, Resnick HE; the American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr.* 2013 Nov 18.

Seizures: Pediatric emergency medicine specialists recently reviewed protocols and current practice for managing patients who present to the emergency department with various seizure types, from first-time afebrile seizures to status epilepticus.

Szlam S, Meredith M. Shake, rattle and roll: An update on pediatric seizures. *Pediatr Emerg Care.* 2013 Dec; 29(12):1287–91; quiz 1292–4. Doi: 10.1097/PEC.0000000000000046.

Attention deficit hyperactivity disorder: Researchers evaluated the efficacy and safety of modafinil for treating adults with attention deficit hyperactivity

disorder (ADHD). They found that modafinil, a psychostimulant thought to improve attention capacity, was well tolerated but not effective in alleviating symptoms of ADHD in adults. Investigators used a range of doses and a placebo.

Arnold VK, Feifel D, Earl CQ, Yang R, Adler LA. A 9-week, randomized, double-blind, placebo-controlled, parallel group, dose-finding study to evaluate the efficacy and safety of modafinil as treatment for adults with ADHD. *J Atten Disord.* 2014 Feb; 18(2):133–44. Doi: 10.1177/1087054712441969. Epub 2012 May 22.

Radiation exposure in patients with scoliosis:

Le Bonheur/Campbell Clinic's pediatric orthopaedic team studied the amount of radiation exposure for patients undergoing VEPTR (Vertical Expandable Prosthetic Titanium Rib) treatment for early-onset scoliosis. Researchers found that patients with congenital scoliosis received greater amounts of radiation than patients with neuromuscular scoliosis – and that surgeon experience is correlated with decreased levels of radiation exposure. The surgeons retrospectively reviewed charts for 24 patients (121 surgical procedures and 962 radiographs).

Cannon TA, Neto NA, Kelly DM, Warner WC Jr, Sawyer JR. Characterization of radiation exposure in early-onset scoliosis patients treated with Vertical Expandable Prosthetic Titanium Rib (VEPTR). *J Pediatr Orthop.* 2013 Oct 29.

Spiral femur fractures: The ability of different specialists to reproducibly classify femoral shaft fractures in children younger than 3 years is highly variable, and classification of such fractures is an important part of evaluating young children for possible non-accidental trauma. Campbell Clinic and Le Bonheur clinicians looked at classification of femoral shaft fractures according to three groups with varied training and background: orthopaedic surgeons, emergency room physicians and musculoskeletal radiologists. Results showed that intra-observer reliability was stronger than inter-observer reliability, perhaps suggesting the characterizing features of each fracture are not shared amongst the different specialties.

Thompson NB, Kelly DM, Warner WC Jr, Rush JK, Moisan A, Hanna WR Jr, Beaty JH, Spence DD, Sawyer JR. Intraobserver and interobserver reliability and the role of fracture morphology in classifying femoral shaft fractures in young children. *J Pediatr Orthop.* 2013 Oct 29.

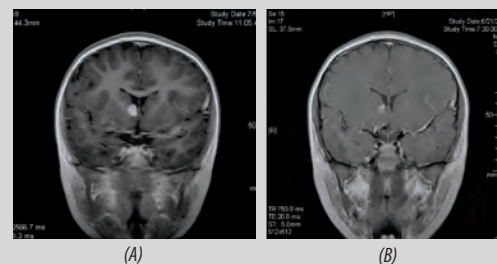
Stents in interventional cardiology: Interventional cardiologists Shyam Sathanandam, MD, and B. Rush Waller, MD, are testing options to develop an ideal neonatal stent. Children require multiple surgical procedures to relieve fixed narrowings caused by stents implanted as an infant. If the small diameter stent can be longitudinally fractured, or “unzipped,” in the catheterization lab, then the narrow blood vessel can be re-dilated. Researchers performed feasibility studies that described the technique of unzipping small diameter stents. They found that small diameter stents can be unzipped and stainless steel stents of a

closed cell design were best suited for unzipping. As a next step, they are testing this technique in a growing swine model. Several stents were implanted in different blood vessels of newborn piglets. The stents will be unzipped after the swine have grown and will undergo microscopic analysis. They also have other neonatal swine models with narrowing in several blood vessels in which they are planning to do the same with a newly conceptualized stent design.

Researchers include Sathanandam S, Haddad L, Philip R, Subramanian S, Wright D, Waller B, Gillespie M and Rome J.

Tuberous sclerosis complex: Neuroscientists reviewed the timing and use of neurosurgery versus pharmacotherapy for the treatment of subependymal giant cell astrocytomas (SEGAs) in patients with tuberous sclerosis complex (TSC). SEGAs are slow-growing brain tumors associated primarily with TSC. Usually located in the ventricles, the tumors can lead to increased intracranial pressure if they grow too large. Surgery to remove a tumor has been the mainstay of treatment but can be associated with postoperative morbidity and mortality. The recent development of mammalian target of rapamycin inhibitor everolimus that targets the pathway affected by TSC1/TSC2 mutations offers a novel pharmacotherapeutic option for these patients.

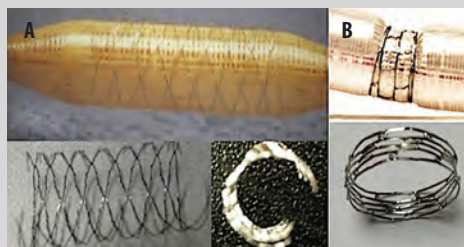
Wheless J, Klimo P. Subependymal giant cell astrocytomas in patients with tuberous sclerosis complex: Considerations for surgical or pharmacotherapeutic intervention. *J Child Neurol.* Published online at jcn.sagepub.com.



Response of a subependymal giant cell astrocytoma tumor to treatment with everolimus. Patient has well-controlled partial seizures and normal intelligence. Initial magnetic resonance imaging (MRI) was done as routine surveillance study. (A) Coronal T1 fluid-attenuated inversion recovery plus contrast MRI demonstrating right-side subependymal giant cell astrocytoma (longest diameter 11.34 mm) in a 5-year-old male patient. (B) Coronal T1 contrast MRI showing decreased tumor size (longest diameter 6.16 mm) after treatment with everolimus, taken nearly 12 months after the first MRI.

Pre-surgical brain mapping: Noninvasive functional neuroimaging methods including Magnetoencephalography (MEG), functional Magnetic Resonance Imaging (fMRI) and Transcranial Magnetic Stimulation (TMS) can replace what long has been the gold standard in neuroimaging, authors suggest in a recent issue of *Epilepsia*. Invasive pre-surgical brain mapping approaches of direct cortical stimulation and the Wada procedure long have been used in surgical planning to prevent or reduce morbidity and optimize the therapeutic effects of surgery. The advent of non-invasive functional imaging provides equally trustworthy results.

Papanicolaou A, Rezaie R, Narayana S, Choudhri A, Wheless J, Castillo E, Baumgartner J, Boop F. Is it time to replace the Wada test and put awake craniotomy to sleep? *Epilepsia*.



A. Serial dilation with incremental balloon sizes leads to unzipping of the stent without shortening. B. Dilation with a large diameter balloon leads to “napkin-ringing” of the stent.

Pediatric asthma in our community

3,500 visits to Le Bonheur each year make asthma the hospital's most common diagnosis.

In Tennessee, asthma cases (adults and children) lead to **\$41.4 million in health care costs**.

Asthma causes 10.5 million **missed schools days** and 14.2 million **missed days of work** in the United States.

Shelby County has **one of the highest rates of asthma-related hospitalizations in the state** of Tennessee.

Children affected by asthma:

- 15 percent in Arkansas
- 13.7 percent in Mississippi
- 10 percent in Tennessee

* Data from Centers for Disease Control and Prevention and state health departments.



Allergy Immunology Fellow David Petty, MD, teaches high-risk asthma patients enrolled in the CHAMP program how asthma affects their bodies.

continued from back cover

CHAMP is funded by a three-year \$2.9 million Health Care Innovation grant by the Centers for Medicare and Medicaid (CMS). Its chief aims are to:

- Improve health of children with high-risk asthma by reducing emergency department and hospital visits
- Lower overall asthma-related health care costs
- Improve the health care experience for patients and families
- Improve the quality of life for children with asthma

“In order to follow through with the education and plans of care, families need support to overcome the barriers that get in the way of following medical advice,” said Christie Michael, MD, medical director for CHAMP and an allergist-immunologist.

To address those barriers, CHAMP has employed coordinators and community health and asthma care workers to support families in their homes and communities, providing environmental interventions, reinforcing asthma education and helping to navigate psycho-social issues. For example, the team works directly with patients’ school nurses, ensuring they have the medications and information they need to treat asthma emergencies. CHAMP also works closely with the patient’s primary care physician to provide the most up-to-date information on the patients they serve.

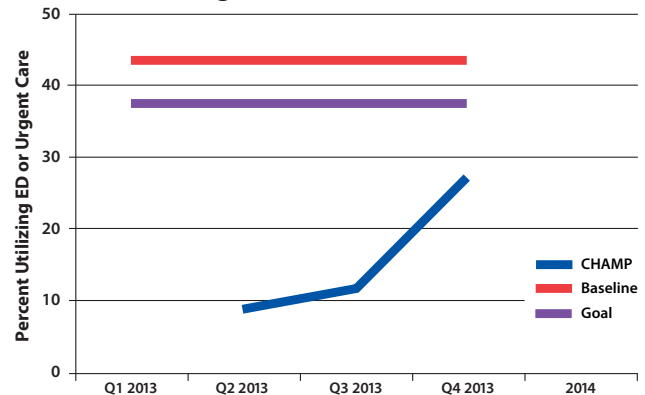
“CHAMP is here to help connect the dots in the community,” said Michael.

The program continually tracks 54 data variables in an asthma registry to ensure it is making progress on goals. It estimates a cost savings of more than \$4 million by June 2015 and has already seen reduced Emergency Department and urgent care use.

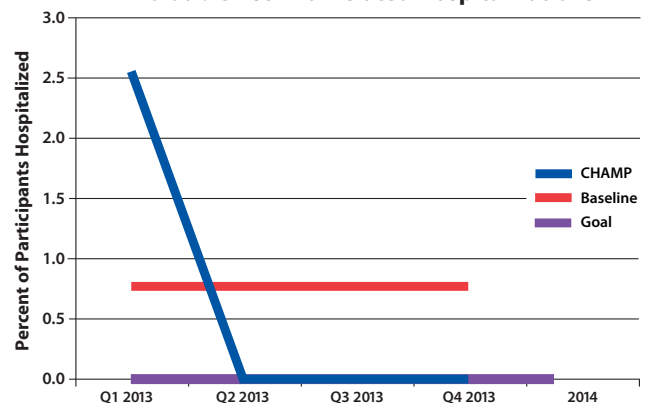
“For many of these children, their asthma keeps them from being normal kids,” said Dennis Stokes, MD, MPH, medical director of Pulmonology and co-principal

investigator on the project. “Helping kids to overcome potential limitations of asthma enables them to be more active and attend school more often, which helps to prevent the common co-morbidities of obesity and diabetes. CHAMP is truly an innovative program and is changing our care model for kids with asthma.”

Asthma-Related Emergency Department and Urgent Care Visits in Past 6 months



Avoidable Asthma-Related Hospitalizations



Breathing easy

Federally funded program removes barriers for asthma patients, reduces health care costs

Hospitalizations and Emergency Department visits for high-risk asthma patients are down for children enrolled in a new Le Bonheur program geared at helping improve quality of life and lowering health care costs.

The CHAMP (Changing High-Risk Asthma in Memphis through Partnership) program has enrolled 200 high-risk asthma patients since its inception in 2013. Of those enrolled in the program, hospitalizations are down from 9 percent from the year before enrollment to 5.4 percent in the program's fifth quarter. The program has also reported zero avoidable asthma-related hospitalizations and no asthma-related deaths.

continued on page 17

