

DELIVERING ON A PROMISE

Research Launchpad

Le Bonheur researchers look for new pediatric discoveries



Le Bonheur trial: *Intravenous indomethacin more effective for hsPDAs*

Intravenous indomethacin is more effective than intravenous acetaminophen in treating hemodynamically significant PDAs (hsPDAs) in very low birth weight (VLBW) infants, according to new Le Bonheur neonatology research published in the *Journal of Perinatology*.

Le Bonheur neonatologists, led by Jennifer M. Davidson, DO, conducted a randomized trial for the treatment of hsPDAs in VLBW infants. Echocardiogram criteria before and after treatment showed that IV indomethacin was more effective.

"We have several options for PDA closure in these very low birth weight infants with varying levels of effectiveness, including intervention by medication therapies," said Davidson.

Commonly used medical therapies are indomethacin and ibuprofen, but these have variable success and notable side effects. Surgical PDA ligation and transcatheter PDA closure can be used if medical therapies fail to close the PDA, but each comes

with risks and lack of access for some hospitals. Studies have shown that, for some neonates, acetaminophen may be equally effective for treating hsPDAs with minimal side effects. Le Bonheur neonatologists wanted to examine this option of IV acetaminophen for treating hsPDA in VLBW infants.

To be included in the trial, infants met specific criteria including gestational age at birth between 22 and 32 weeks, birth weight less than 1500 grams, 21 days of age or younger and no previous pharmacologic treatment for PDA. Infants also had to meet strict echocardiogram criteria including left-to-right ductal flow and two out of three of the following: ductal size greater than or equal to 1.5 mm at smallest diameter, reversal of flow in descending aorta or left atrial size to aortic root ratio greater than or equal to 1.5.

Seventeen infants received 15 mg/kg dose of IV acetaminophen every six hours for 12 doses. Twenty infants received three doses of IV indomethacin every 12 hours with

Le Bonheur Children's Hospital in Memphis, Tenn., treats more than 250,000 children each year in regional clinics and a 255-bed hospital that features state-of-the-art technology and family-friendly resources. Our medical staff of more than 240 physicians provide care in 45 subspecialties.

LE BONHEUR LEADERSHIP

Michael Wiggins, MBA, FACHE – President
Jon McCullers, MD – Pediatrician-in-Chief
Barry Gilmore, MD, MBA – Chief Medical Officer
James "Trey" Eubanks, MD – Surgeon-in-Chief
Harris Cohen, MD – Radiologist-in-Chief



AMERICAN COLLEGE OF SURGEONS
Verified Trauma Center



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

hsPDAs Results:

17 infants received acetaminophen

- 1 (5.9%) had successful treatment with acetaminophen
- 8 (47%) required transcatheter PDA closure

20 infants received indomethacin

- 11 (55%) had successful treatment with indomethacin
- 3 (15%) required transcatheter PDA closure

the amount of medication based on age. Each infant had a follow-up echocardiogram within seven days of the initiation of treatment. Successful PDA treatment was defined as no longer meeting the echocardiogram inclusion criteria for hsPDA.

Results of the study showed that IV indomethacin was more effective in successful treatment of hsPDA. The rate of successful PDA closure was 55% when using IV indomethacin and 6% when using IV acetaminophen.

"Through our study of very low birth weight infants, we were unable to show successful treatment of hsPDA with IV acetaminophen when compared to IV indomethacin in preterm infants born prior to 32 weeks," said Davidson. "In addition, many of our babies in the study treated with acetaminophen required interventional closure later on."

According to Le Bonheur investigators, if acetaminophen continues to be used as a primary treatment of hsPDA, future studies should include a different dosing strategy or route of administration to learn more about its efficacy in PDA closure.

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Research Launchpad

Le Bonheur researchers look for new pediatric discoveries

The Crippled Children's Foundation was in need of a new cause.

Thanks in part to their generosity, polio had been eliminated in the United States, and it was time to point their support in a new direction. So the Children's Foundation of Memphis was born.

Their new cause: The Children's Foundation Research Institute (CFRI) – a partnership between the Children's Foundation of Memphis, University of Tennessee Health

Science Center (UTHSC) and Le Bonheur Children's Hospital. Their goal: to serve the health and well-being of children in the Memphis area.

"Any successful children's hospital has to have the infrastructure to support physician research," said Marie Jackson, senior director of the CFRI. "The Children's Foundation of Memphis allowed us to build out a resource for research on our campus – from outfitting laboratories to providing funding for grants."

The CFRI remains the Children's Foundation of Memphis' primary grantee with continued support for new initiatives and ongoing projects.

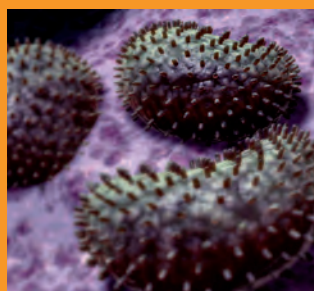
Research at Le Bonheur: In This Issue

The CFRI makes research at Le Bonheur possible. Read more about the ongoing research efforts at Le Bonheur throughout this issue.



At the onset of the COVID-19 pandemic, Le Bonheur researchers sprang into action to begin understanding the effect of this disease on children. Learn about their efforts to unmask this disease on page 8.

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Building on her research into the effects of influenza A (IAV) infection in patients with allergic asthma, Amali Samarasinghe, PhD, showed that IAV directly modulates

eosinophil responses in the airways of mice. View the study results on page 20.

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One of many clinical trials underway in the CFRI is Fenfluramine – a medication for Dravet syndrome. 12-year-old Charlie Byrd is one child who has seen benefits in

seizure control as a part of this trial. Read his story on page 24.

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What medications can be used to heal hemodynamically significant patent ductus arteriosus (hsPDAs)? Neonatologist Jennifer M. Davidson, DO, led a randomized trial that showed intravenous indomethacin to be more effective than acetaminophen in treating hsPDAs. Explore the results of the trial on the inside cover of this issue.



Inside cover



Two physicians – Pediatric Surgeon Ankush Gosain, MD, PhD, and Chief of Cardiology Jeffrey A. Towbin, MD – recently received Research Project Grants from the National Institutes

of Health. Learn more about their research on page 18.

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Chief of Pediatric Neurosurgery Paul Klimo, MD, investigated the efficacy of converting shunts to endoscopic third ventriculostomy (ETV) in children and young adults. This procedure was a godsend for Allie Glozier, a 20-year-old born with hydrocephalus who battled a failing shunt. Read more about her story and the study on page 21.



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Children's Foundation
Research Institute



Memphis provides a unique population in which to conduct research. A large percentage of Memphis children are African-American, a population that has traditionally been underrepresented in research. This affords an opportunity to study the intersection of race and health equity as well as increasing diversity and representation in clinical research. In addition, issues that affect children's health such as childhood asthma, poverty, obesity and adverse childhood experiences (ACEs) are largely prevalent in the city.

Thanks to the CFRI, Le Bonheur has facilitated state-of-the-art biomedical research with the goal of improving the health and well-being of children. From basic to translational to clinical research, the CFRI trains new researchers and supports experienced ones through the course of their projects.

COVID OPPORTUNITIES

The emergence of COVID-19 gave Le Bonheur and the CFRI a unique opportunity to remain committed to their mission by developing new projects to investigate the disease's unique effects on children. Plus, the CFRI had to pivot to adhere to new policies and innovate new methods of delivering care and medication to children involved in research projects.

At the onset of the pandemic, labs were closed and resources were shifted to those working on COVID-19 research. And with reopening, they contend with how to conduct research while navigating regulations to keep everyone safe – cleaning processes, social distancing and more.

“It has affected the basic ways that we execute studies and lab work,” said Jackson. “But it also set

MEET THE CFRI TEAM

Dennis Black, MD
Scientific Director

Stephen Espy, MSCS
Director of the Biomedical Informatics Core

Marie Jackson, PhD, MBA
Senior Director

Thomas Hobson, MME, MHA, MT-BC, CCLS
Business Manager

Billie Masek, MS, MBA
Research Laboratory Manager

Kerry Moore, RN, BS, CCRC
Director of Research and Study Coordinators

Tamekia L. Jones, PhD
Director of the Biostatistics Core

Christopher E. Smith, EMBA, MLS (ASCP)
Director of Finance and Research Lab Operations

Venessa Spearman, MPA
Director of Grant Administration and Contract Development

“It has affected the basic ways that we execute studies and lab work. But it also set us up for a great opportunity to innovate new ways of providing continuity in research.”

Marie Jackson, senior director of the CFRI

us up for a great opportunity to innovate new ways of providing continuity in research.”

The area of greatest concern that arose at the start of the pandemic was how to continue providing medications and follow-up for clinical research participants without requiring in-person contact.

“Our responsibility is to protect those who volunteer

for trials,” said CFRI Director of Research and Study Coordinators Kerry Moore, RN, BS, CCRC. “By using telemedicine and setting up couriers and drive-throughs for obtaining investigational medications, we made sure none of our clinical research participants experienced an interruption in their care.”

The CFRI has also turned the challenges associated with the pandemic into opportunities for future success. These innovations in remote access through telemedicine and shipping medications have set the stage to expand clinical research beyond Memphis.

Le Bonheur researchers are also joining those around the world to investigate COVID-19, its effects and potential drug therapies through a variety of projects that are underway.

WHAT LE BONHEUR PHYSICIANS SAY ABOUT THE CFRI

*“The resources that the CFRI offers to researchers are excellent. I frequently work with medical students and residents on projects that involve reviewing patient charts and entering data. They do a great job at **teaching these young investigators** about how to use REDCap for building and managing online surveys and databases.”*

Chief of Pediatric Infectious Diseases Sandra Arnold, MD

*“The CFRI makes the process of **starting a research study as smooth as possible**. Whether it be an investigator-initiated study or an industry-sponsored study, they provide the resources necessary to get the study up and running.”*

Allergist/Immunologist Jay Lieberman, MD

*“Without the CFRI, no research would be possible at Le Bonheur Children’s Hospital. They coordinate the complex contracting process, help finalize study budgets and make sure we have all of the necessary research personnel in place to complete the actual study, which **ultimately leads to improved care for our patients**.”*

Neuroscience Institute Co-Director and Chief of Pediatric Neurology James Wheless, MD

THE NEXT GENERATION

The Children's Foundation of Memphis remains integral to supporting the growth of the CFRI — including infrastructure and new initiatives such as the chair of excellence and special programs like the Biorepository and Integrative Genomics (BIG) Initiative and neuroscience research into intractable epilepsy disorders.

And the CFRI's leaders are already looking to the next generation of researchers and of children to benefit from that research.

“Building infrastructure to support growth for researchers is a priority for the CFRI's future. We are poised to continue building off of the great work that our investigators have done for years contributing to pediatric medicine.”

Marie Jackson, senior director of the CFRI

A large focus of the CFRI is training new faculty, says CFRI Scientific Director Dennis Black, MD. He and his



— MISSION OF THE CFRI —

CFRI provides hope to children, families and the community through innovative research to enhance the health of children.

team are able to offer a multitude of guidance and services to facilitate their career growth, whether teaching them how to apply for K-awards, conducting monthly K-RO Club meetings that train junior faculty to successfully write NIH research training and other grants or connecting them with a mentor.

“We want to be smart about our growth – keeping up with the latest innovative techniques and technology



for research,” said Black.

Both Black and Jackson hope to see research initiatives expand to help children beyond the Memphis area and increase the CFRI’s existing footprint.

“Building infrastructure to support growth for researchers is a priority for the CFRI’s future,” said Jackson. “We are poised to continue building off of

the great work that our investigators have done for years contributing to pediatric medicine.”



RESEARCH AWARDS 2020

Le Bonheur researchers have had their hard work recognized by organizations around the country. The awards and achievements so far this year are shown below.

Dennis Black, MD

Scientific Director, Children’s Foundation Research Center

2020 Research Mentor Award

American Gastroenterological Association Institute Council

Section on Obesity, Metabolism & Nutrition

Alicia Diaz-Thomas, MD

Endocrinologist

C-Change Leadership and Mentoring Institute

Fellowship Award

Brandeis University

Ankush Gosain, MD, PhD

Pediatric Surgeon

2019-2020 Mid-Career Award

Society of University Surgeons

Derek Kelly, MD, FAOA

Orthopedist

American-British-Canadian Traveling Fellowship

American Orthopaedic Association

Paul Klimo, MD, MPH

Chief of Pediatric Neurosurgery

Pediatrics Paper of the Year

Congress of Neurological Surgeons

Shalini Narayana, MBBS, PhD

Director, Transcranial Magnetic Stimulation Lab

2020 Infrastructure Grant

American Epilepsy Society

Shyam Sathanandam, MD

2019-2021 Emerging Leader Mentorship Program

Society for Cardiovascular Angiography and Interventions

Ajay Talati, MD

Medical Director, Neonatal Intensive Care Unit

2020 Founders Award

Southern Society for Pediatric Research

Alina Nico West, MD, PhD

2019 Fellowship, Future Leaders Advancing Research in Endocrinology

The Endocrine Society (NIDDK-Supported)

Countering COVID-19

Le Bonheur researchers begin multiple COVID-19 investigation efforts

CIViC-19 study aims to explore clinical, immunological and virological characterization of COVID-19

The rapid appearance of SARS-CoV-2 and its unpredictable clinical impact and outcomes have created opportunities for research into the populations affected by COVID-19. Partnering with the University of Tennessee Health Science Center (UTHSC), Le Bonheur researchers have begun efforts to answer some of the questions that plague medical professionals and pediatric COVID-19 patients. The project is led by Assistant Professor of Pediatrics at UTHSC Heather Smallwood, PhD, who is lead principal investigator, and Le Bonheur Infectious Disease Specialist Nick Hysmith, MD, the clinical director for pediatrics for the study.

“Understanding the relationship between clinical characteristics and what variables influence immune response and severity of the disease are vital to improving diagnosis, prediction and treatment of COVID-19,” said Hysmith.

This study, titled “Clinical, Immunological and Virological Characterization of COVID-19,” or “CIViC-19,” aims to provide a course of action for the clinical and community management of COVID-19. Le Bonheur researchers will manage the pediatric portion of the study, in conjunction with UTHSC researchers who will study adult populations. Their efforts in the study aim to define what characteristics influence the severity of the disease, explore how the virus is shed by infected individuals and identify potential drug treatment opportunities.

The study will rely on the collection of specimens from adults and children to help investigators learn about this virus. Blood draws and stool samples, as well as oral and nasal swabs, will be taken at various intervals from



Pediatric Infectious Disease Specialist Nick Hysmith, MD (above), and Assistant Professor of Pediatrics at the University of Tennessee Health Science Center Heather Smallwood, PhD, are leading the CIViC-19 study, which aims to uncover more about the clinical, immunological and virological characterization of COVID-19.

study participants. This gives Le Bonheur’s researchers the opportunity to better understand whether the virus changes over time and how the body attempts to respond to eliminate the virus.

Team expertise for the study comes from three areas – clinicians with expertise in key patient populations and patient variables, basic researchers in respiratory diseases, immunology and virology and epidemiologists or biostatisticians with expertise in medical informatics.

At the onset of the pandemic, many questions were posed as to how the disease would affect children, specifically populations with weakened immune systems or living with respiratory conditions. Leading Le Bonheur's efforts is Terri Finkel, MD, PhD, vice chair of clinical affairs at Le Bonheur.

"My aim is to connect researchers for collaborative opportunities that come out of our weekly 'think tank' meetings," said Finkel. "More than 50 individuals from Le Bonheur,

UTHSC, St. Jude Children's Research Hospital and other nationally-renowned institutions are joining forces to partner on pediatric COVID-19 research efforts."

Although the pandemic has largely seen the worst outcomes in adults, pediatric cases are still a cause of concern, especially in the Memphis area, according to Le Bonheur COVID-19 census numbers. Le Bonheur researchers have undertaken a variety of investigative efforts to study the

impact of COVID-19 on children and to explore questions related to how asymptomatic children spread the disease, with the aim of providing insight into how COVID-19 spreads in a community.

A better understanding of the disease's effect on children allows Le Bonheur leaders to provide clearer guidance to city leaders, parents and caregivers on how best to keep children safe, whether guiding back-to-school policies or safe return to sports and extracurricular activities.

"This study team builds on existing collaborations and expertise in respiratory viruses, including experience gained during the 2009 H1N1 pandemic," said Hysmith. "Investigators on this team cover a wide range of expertise required to explore the impact of COVID-19 on vulnerable adult and pediatric populations."

"Practically, we hope to be able to help the Memphis area return to normal by providing data-driven management of return-to-work and school policies based on the dynamics of viral shedding and details of how the virus spreads."

Nick Hysmith, MD, Le Bonheur Infectious Disease Specialist

The dataflow and informatics analysis of the project allows investigators to share information quickly and efficiently via preprint publication repositories, including locally with regional COVID-19 response teams and at national and international levels. In addition, rapid reporting will provide a more accurate risk assessment of key populations in Memphis toward better community management of the virus and its spread.

"Practically, we hope to be able to help the Memphis area return to normal by providing data-driven management of return-to-work and school policies based on the dynamics of viral shedding and details of how the virus spreads," said Hysmith.

Finally, the CIViC-19 team aims to provide more efficient clinical management of COVID-19 for local health professionals. To accomplish this, the study will identify what factors predict how severe the disease will be in order to facilitate treatment and intervention as early as possible. For those who have already recovered from the disease, the study seeks to effectively identify who has

The CIViC-19 study consists of four major projects:

Define what clinical and virologic determinants affect COVID-19 presentation

Determine what clinical characteristics and patient variables impact the amount of virus in a patient's system. Do these factors lead to significant differences in symptomology, outcomes or the severity of the disease?

Assess the body's immune response to SARS-CoV-2 over time

Following a group of individuals, this will study the excessive immune response some individuals have experienced with COVID-19. Do underlying characteristics such as age, sex or obesity affect the severity of the disease or if they are susceptible to reinfection?

Explore respiratory infection characteristics in COVID-19

Investigate how the lungs and respiratory system respond to SARS-CoV-2. Does this alter the body's immune response to COVID-19 or impact the severity of the disease?

Follow households and learn how COVID-19 and influenza spread

Multiple households will be enrolled in the study to better understand how SARS-CoV-2 is spread in households. Is this household spread dependent on patient variables or the timing of the onset of COVID-19 symptoms?

high antibody levels and could donate plasma for treating COVID-19 positive patients. Testing efficacy will also be explored including greater reliability of swab tests and identifying an effective pin prick antibody test.

Serum biorepository aims to provide public health information

Can you develop immunity to COVID-19?
How does COVID-19 travel through households?
What is the prevalence of asymptomatic positive cases?

These are just a few of the questions that the serum biorepository at the University of Tennessee Health Science Center (UTHSC) hopes to answer. The goal: gather 200,000 serum samples in the Memphis area to test immunity to COVID-19.

Led by Le Bonheur Pediatrician-in-Chief Jon McCullers, MD, the serum biorepository grew out of the need for a more accurate antibody test for SARS-CoV-2. McCullers also serves as senior executive associate dean of clinical affairs and chief operating officer with UTHSC.

Throughout the pandemic, McCullers has led efforts

to provide guidance to city leaders, including creating the “Memphis Roadmap” to provide strategic leadership and developing a drive-through COVID-19 testing center. The natural next step is being a resource for reliable antibody testing in the community.

“Previous tests had a high false positivity rate as it reacts against other human coronaviruses,” said McCullers. “The new test is far more sensitive and will allow us to find the true seroprevalence in the Memphis population.”

Beginning with health care workers in Memphis, the antibody testing will eventually be available to the general public. These serum samples will be held in the biorepository for researchers to access as they explore questions related to immunity and spread of COVID-19, including its effects on children.

“So far pediatrics has not seen as many antibody tests and positive cases,” said McCullers. “This biorepository will allow us to find the seroprevalence in pediatrics and test entire families to see how they are affected.”

From a public health perspective, the biorepository and antibody test will allow research into whether or not COVID-19 patients have immunity to the disease and, if they do, how long that immunity lasts.

“It’s a Herculean challenge, but determining how the antibodies are linked to immunity and the length of immunity would allow us to determine if those who have recovered from the virus are totally immune,” said McCullers. “This would mean that individual wouldn’t need screening or isolation, and we would feel better about our frontline health care workers who have already beaten the disease.”



Le Bonheur Pediatrician-in-Chief and University of Tennessee Health Science Center Senior Executive Associate Dean of Clinical Affairs and Chief Operating Officer Jon McCullers, MD, is leading a serum biorepository with the aim of collecting 200,000 serum samples to test immunity to COVID-19. McCullers has been a guiding voice to Memphis city leadership during the pandemic.

National COVID-19 registries allow for collaboration, potential answers

“Pediatric cases of COVID-19 have been far fewer than adults. Registries are vital to be able to learn about how this disease affects kids,” said Le Bonheur Chief of Pediatric Infectious Diseases Sandra Arnold, MD.

Arnold is one Le Bonheur physician providing and using data from national registries surrounding COVID-19 to better understand the disease and its effects on specific pediatric populations. She coordinates Le Bonheur COVID-19 cases in the Pediatric COVID-19 Case Registry — providing valuable information regarding the disease’s characteristics to physicians around the country.

The Pediatric COVID-19 Case Registry was originally created to record the effects of COVID-19 on compromised or vulnerable children. This population was so small that the registry was opened to any children (20 years and younger) in an effort to follow the disease’s pediatric effect.

With this information, physicians are able to look at symptoms, pre-existing patient conditions and regional effects of the disease — all important for understanding how COVID-19 can affect patients at Le Bonheur.

“We have so much to learn about this disease and contributing to this registry will help us learn more about positive patient cases and provide the best care for our COVID patients,” says Arnold. “We’re able to see the effects of COVID therapies including anti-viral medication or immune modulatory therapy across the country and the effect that they have.”

Other existing national registries also expanded



Chief of Pediatric Infectious Diseases Sandra Arnold, MD, enters information for each of Le Bonheur’s positive COVID patients into the Pediatric COVID-19 Case Registry. Databases like these are essential for the collaboration needed to better understand the effect of COVID-19 on children.

“We have so much to learn about this disease and contributing to this registry will help us learn more about positive patient cases and provide the best care for our COVID patients.”

Le Bonheur Chief of Pediatric Infectious Diseases Sandra Arnold, MD

their datasets to include COVID-related information. Kim Giles, Le Bonheur’s director of Decision Support, has watched these clinical registries add COVID variables to the information collected. This allows the opportunity to evaluate COVID-19’s impact in critical care and corresponding interventions and therapies. It is also valuable to evaluate the effect on high-risk and complex patient populations, such as transplant patients, and diagnosis-specific cohorts, such as children with diabetes and similar chronic conditions.

“This data collaboration is vital to evaluate the impact of COVID-19 on children’s hospitals and advocate based on the national impact,” said Giles.

CALL TO CATH LABS: PRESERVE, PREPARE



Interventional cardiologist publishes guidance for catheterization labs, conservation of resources

Interventional cardiologists should prioritize the conservation of medical resources, minimization of potential COVID-19 exposure and reallocation of resources, according to a paper published in the *Journal of Invasive Cardiology*.

In the article, Le Bonheur Interventional Cardiologist Shyam Sathanandam, MD, suggests that catheterization laboratories should develop strategies for patient care by preserving and repurposing resources in the COVID-19 pandemic.

Sathanandam published the work after issuing a web-based survey to 56 unique U.S. centers, with the objective of describing current practice patterns and recommending potential resource allocation for congenital cardiac catheterization during the COVID-19 pandemic.

“We are faced with a fundamental question,” said Sathanandam, who serves as the medical director of Le Bonheur’s Interventional Cardiac Imaging and Interventional Catheterization Laboratory. “How can we, as pediatric and congenital interventional cardiologists, continue to care for patients who require intervention, while also being good stewards of limited medical resources and maintain an appropriate level of preparedness when we are uncertain about how this pandemic will affect our discipline?”

MEDICAL RESOURCE UTILIZATION AND CASE SELECTION

The majority of survey respondents felt they had sufficient PPE to care for COVID-19 positive patients or PUIs. However, limited access to PPE and ventilators necessitates postponing elective catheterization cases to assist with the preservation of medical resources. The paper recommends using a multi-disciplinary clinical leadership team to triage case priority and timing — at present, only one-half of the reporting U.S. programs employed this strategy to review case selection.

While responding centers have canceled elective procedures with relative uniformity, centers in counties with 2,000 or more COVID-19 cases were more likely to delay certain cases including PDA closures in premature infants, pre-Glenn catheterization and coarctation stenting.

MINIMIZING EXPOSURE

The responses suggest that many programs may not be adequately prepared for a surge of COVID-19 positive patients. Centers located in areas with a higher number of COVID-19 cases have been more involved in a simulation of donning and

doffing PPE equipment than low-prevalence centers (46.7% vs. 10.3%). Only 10.8% had converted a cath lab to a negative pressure room for potential COVID-19 positive patient or PUI. The majority (65%) were only testing for COVID-19 prior to cardiac catheterization if the patient was symptomatic. Only 15% tested all patients prior to aerosol-generating procedures in the cath lab.

CATHETERIZATION CENTERS PREP FOR COVID-19

31% did not allow fellow participation in cardiac catheterization cases.

76% minimized staff exposure through changes to the work and call schedule.

10.8% reassigned staff to provide clinical services outside the typical scope of practice.

41.7% had discussed or planned reassignment.

However, responding centers were employing various strategies to reduce staff exposure to COVID-19.

In addition, many facilities are minimizing staff presence in the cath lab before and after airway manipulation in order to reduce potential exposure.

RESOURCE REALLOCATION AND POTENTIAL REPURPOSING

The primary way responding centers are conserving resources is by decreasing elective cases. “For subspecialists like pediatric interventional cardiologists, this raises the question of how best to utilize our clinical skills if the typical volume of patients with congenital heart disease is reduced,” said Sathanandam.

This decision will vary by pediatric institution and may depend on geographic proximity to and relationship with adult centers. Pediatric interventional cardiologists will likely be deployed for services outside of the cath lab depending on where resources are strained whether inpatient services, ICUs, emergency departments or vascular access teams.

Le Bonheur researchers develop method for re-use of N95 respirators using dry heat kilns

Shortages of N95 filtering face respirators led Le Bonheur researchers to partner with a local small business to develop a method of mass viral decontamination for N95s using a dry heat kiln at a pallet manufacturer. The research provided a design for a wooden container capable of mass reprocessing up to 12,000 N95s in an eight-hour period, as well as qualitative retained filtering efficiency and documentation of influenza A virus inactivation. A pandemic strain of influenza A virus was used to validate decontamination.

N95s are intended to be single-use, but when faced with critical shortages, N95 decontamination for re-use may be an option. Potential choices available for SARS-CoV-2 inactivation include dry or moist heat, vaporized hydrogen peroxide (VHP) and ultraviolet germicidal irradiation (UVGI).

"VHP received emergency FDA approval in this pandemic situation, but it requires costly specialized equipment," said Le Bonheur Medical Director of Infectious Diseases Nick Hysmith,

MD. "Heat treatment is an attractive alternative that is simple, accessible worldwide and relatively inexpensive."

Dry heat kilns, such as those used to heat treat wood packaging material, are required to meet approved standards for products of international trade. Wood packaging material is required to achieve a minimum temperature of 56° C (132.8° F) for a minimum of 30 minutes. Because of this regulation, sawmills, pallet and crating manufacturers and third-party kiln companies are uniquely suited to substitute as decontamination chambers for repurposing N95s as they are distributed globally with large kilns for heat treatment.

In this experiment, Le Bonheur researchers used a high-capacity piggy-back pallet kiln with a gas heating unit capable of producing dry heat up to 200° F. Researchers constructed a wood decontamination dry heat container prototype 4 feet wide, 8 feet long and 3 feet high that could hold up to 400 N95 masks. Each end of the box was open and covered with filter material to maintain airflow without allowing particulate matter to pass through. Fans inside the

N-95 FFR Decontamination Process Flow Using Dry Heat



kiln ensured even heat distribution. Approximately 10 boxes could be placed within the 53-foot-long kiln.

Two H1N1 strains of influenza A virus were used to compare this effect of dry heat kiln treatment on a highly virulent laboratory strain versus a clinically relevant pandemic strain. Virus was added directly to the surface of N95s to mimic real world conditions. For testing, the kiln was programmed to heat to 73.88° C (165° F) for 35 minutes in order to inactivate the virus.

After heat treatment, both strains of influenza A were completely inactivated. The masks showed no observable material degradation, and each passed qualitative seal and fit-testing after reprocessing.

"This decontamination

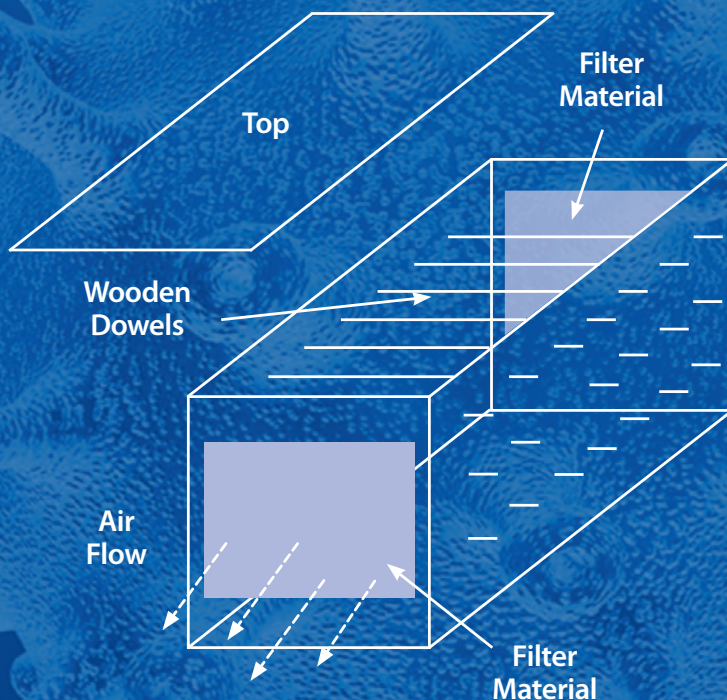


Partnering with a local small business, Le Bonheur researchers developed a method of decontaminating N95 masks using a wood container in a dry heat kiln. This method could reprocess up to 12,000 N95 masks in eight hours.

technique provides a cost-effective and readily accessible method of inactivating virus while also preserving filtering efficiency for up to six cycles, and potentially more," said Hysmith.

Using this method, nearly 12,000 N95s could be repurposed in an eight-hour period for a total approximate cost of \$100.44 in energy consumption. Researchers also developed a hospital workflow that allowed repurposed masks to be returned to the original employee after reprocessing.

"This method will improve children's health care by mitigating PPE shortages during pandemic situations and provide a widely accessible method of reprocessing that can be used by small or rural hospital networks," said Hysmith.



The research provided a design for a wooden container for use in dry heat decontamination.



Researchers developed a design for a wooden decontamination container prototype which was open ended and covered with filter material to maintain airflow. Each box could hold 400 N95 masks, and 10 boxes could be place in each kiln.

PROFILE: TERRI FINKEL, MD, PHD

Renowned rheumatologist and immunologist brings expertise in research, collaboration to Le Bonheur Children's

Terri Finkel, MD, PhD, traces her expansive career back to one main influence: her grandmother.

On the cusp of World War II, Mrs. Berta Helman ran an apron shop in Germany – a business she would lose and restart three times as war chased her family from Germany to Shanghai to America. With each move, determined to support her family, she'd roll up her sleeves, reopen and try again.

"My grandmother showed me it's about finding a solution, not focusing on the problem," remembers Finkel.

That tenacious spirit has served Finkel well as a renowned pediatric rheumatologist and immunologist. Since moving to Memphis this year, she's taken on three leadership roles in Memphis' medical community. At Le Bonheur, she serves as vice chair of Clinical Affairs; at the University of Tennessee Health Science Center (UTHSC), professor and associate chair of Pediatrics; and at St. Jude Children's Research Hospital, an adjunct faculty member.

As Le Bonheur's vice chair of clinical affairs, Finkel will check in regularly with all of Le Bonheur's division chiefs in the Department of Pediatrics, keeping the hospital's many moving parts running smoothly.

She also meets monthly with St. Jude's Chair of Pediatric Medicine, Amar Gajjar, MD, and St. Jude's Physician-in-Chief and Executive Vice President Ellis Neufeld, MD, PhD, discussing joint plans, collaborative research and how to grow the ongoing partnership between institutions.

Finkel's career is a mosaic of research, clinical practice and administrative achievement. She's built a pediatric hospital department from scratch, her autoimmune research is recognized by more than 150 publications, her work was highlighted on the cover of *Rolling Stone* during the height of the HIV epidemic and in 2014, her biography was read into the Congressional Record of U.S. History in honor of her leadership and contributions to health care.

She's tirelessly advanced understanding of the mechanisms underlying immune dysfunction. Her work has received more than \$12 million in research grants since 1990, garnering 10 patents or patents pending.

Finkel primarily investigates how infection sparks autoimmune disease. Within a year of beginning her fellowship in pediatric rheumatology, her findings that developing T-cells are able to receive and transmit cellular signals had been published in *Nature*.

"Many autoimmune diseases we either know, or suspect, to have an infectious trigger," Finkel says. She focuses on identifying the inner workings of that trigger: studying, for example, the interplay between genetics, infection and immune response, which may "switch on" a disease in one person but not another.

Again, Finkel credits her grandmother.

"As a child, she had rheumatic fever that caused severe heart damage in her later life," Finkel says. "Figuring out the

pathogenesis of why she got sick and what to do about it has been a theme in both the clinical work and the research I've done."

Finkel has a knack for connecting not just data, but people, and it's a skill she's used to build partnerships, teaching curriculums and – twice –

hospital departments.

"Sometimes by combining our forces we come up with a better solution," she says. "It's fulfilling to convey the passion that you feel and draw other people into the work."

In 1999, she was recruited as the Joseph Lee Hollander Chair of Pediatric Rheumatology and associate professor of Pediatrics at the University of Pennsylvania School of Medicine, as well as chief of the Division of Pediatric Rheumatology at the Children's Hospital of Philadelphia (CHOP).

Her first day on the job, CHOP's division contained one rheumatologist—herself. By the end of her tenure a decade later, she'd brought in ten faculty members and established one of the nation's top rheumatology fellowships, training seven to eight fellows each year.

Finkel comes from Nemours Children's Hospital in Orlando, Fla., where she was chair of Pediatrics and chief scientific officer. Joining their faculty in 2011 was a gamble. Orlando's first freestanding and academically focused pediatric

"Sometimes by combining our forces we come up with a better solution. It's fulfilling to convey the passion that you feel and draw other people into the work."

Terri Finkel, MD, PhD
Vice Chair of Clinical Affairs, Le Bonheur Children's Hospital

hospital, Nemours was trying to get a foothold alongside two established community hospitals, and so new it hadn't yet opened its doors.

She was tasked with building Nemours' Department of Pediatrics and Research Institute from virtually the ground up. Her goals? "Build a hospital, staff it and take care of children who weren't there before," she laughs.

Finkel shaped her department into a cutting-edge center for higher level acute care of severely ill children. The staff she recruited fused research and clinical work, both studying and treating rare conditions such as cystic fibrosis, pediatric lupus and spinal muscular atrophy from patients around the world.

Finkel was also Nemours' executive lead on two projects she hopes to bring to Memphis: PedsAcademy, a bedside teaching program for patients, and PEDSnet, an online database and research network of millions of cases.

And though it wasn't part of the plan when she moved to Memphis, Finkel took on additional roles in light of the COVID-19 pandemic: co-leading the build of the UT Community COVID-19 Testing Sites and connecting Memphis medical experts in a COVID-19 research group. The group meets once a week for a "think tank" that's increased from nine initial members to more than 50, representing organizations such as Le Bonheur, St. Jude, UTHSC, the Regional Biosafety Lab, the University of Memphis and Oak Ridge National Laboratory.

Alongside Finkel, her husband, Pediatric Neurologist Richard S. Finkel, MD, has been recruited by St. Jude to lead a pioneering translational neuroscience program.

"What Richard's pursuing [with St. Jude] seeks to do



Terri Finkel, MD, PhD

for children with neurologic diseases what St. Jude has done for children with cancer," says Finkel. "[Studying] not just neuromuscular diseases, but epilepsy, and especially rare diseases in the neurosciences."

Both Le Bonheur and UTHSC will come alongside that effort, and all three organizations plan to form a consortium dedicated to pediatric neuroscience.

Terri Finkel, MD, PhD

Education and Training

National Jewish Center for Immunology and Respiratory Medicine – Basic Immunology and Pediatric Rheumatology Fellowships
University of Colorado Health Sciences Center – Pediatric Residency
Boston Children's Hospital – Pediatric Residency
Stanford University – Doctorate in Biochemistry/Biophysics
Stanford University – Medical School and Medical Scientist Training Program

Board Certifications

Pediatrics
Pediatric Rheumatology

Society Memberships

International Society for Gene Therapy and Molecular Biology
Henry G. Kunkel Society for Translational Immunology, elected membership
NIH/INCHARGE International Working Group
PEDSnet, Steering Board Member
Society for Pediatric Research, elected membership
American Association of Immunologists

Awards and Honors

Colorado Women's Hall of Fame
America's Top Doctors, Castle Connolly
Arthritis Foundation Hero Award
Honorary Master of Arts, University of Pennsylvania
Director, University of Central Florida Research Foundation Board

TOWBIN RECEIVES NATIONAL INSTITUTES OF HEALTH RESEARCH PROJECT GRANT TO STUDY GENETIC CAUSES OF CARDIOMYOPATHY

Le Bonheur Cardiology Chief and Heart Institute Executive Co-director Jeffrey A. Towbin, MD, was awarded a Research Project Grant (R01) from the National Institutes of Health (NIH) with co-principal investigators Enkhsaikhan Purevjav, MD, PhD, and Lu Lu, MD, MS. He is lead principal investigator on the project "Discovery of Modifier Genes in Cardiomyopathy."

The objective of this study is to identify the modifier genes that alter the expression of myopalladin (MYPN), a gene that affects the type and severity of cardiomyopathy – an inherited disease of the heart muscle that may ultimately result in heart failure, transplant or sudden cardiac death in many patients. The project will examine how different genetic backgrounds affect the mutation of the MYPN gene which determines how cardiomyopathy is expressed in children. The study will use systems genetics – an approach to understanding complex diseases by focusing on how genes work together rather than individually.

"Despite decades of research, it's still difficult to predict how cardiomyopathy will present in a clinical setting," said Towbin. "We believe that the likely reason for this is that the interaction of multiple genes – not just a single one – determines the course and severity of the disease."

Previous research published by Towbin and Purevjav has screened adult and pediatric patients with various types of cardiomyopathy and identified MYPN as a strong causal gene associated with a wide variety of severity of cardiomyopathy. Patients had diagnoses ranging from asymptomatic left ventricular hypertrophy (thick heart) to left ventricular dilation and/or dilated atria with a stiff ventricle (restrictive physiology) with progressive heart failure to sudden cardiac death or transplant.

"Symptoms and forms of cardiomyopathy can be highly varied even within the same family who have identical genetic mutations," said Towbin.

Identifying modifier genes is now a crucial goal of research in cardiomyopathies. Results of this study

would change cardiomyopathy care in terms of diagnosis, treatment and genetic counseling.

Towbin is conducting this research in conjunction with co-investigator Robert Williams, PhD, professor and chair of the Department of Genetics, Genomics and Informatics at UTHSC. Williams and Lu are responsible for performing studies and developing technologies necessary to perform the novel collaborative studies in this project.

NIH Research Project Grant (R01) *"Discovery of Modifier Genes in Cardiomyopathy"*

Objective: Identify the modifier genes that alter the expression of myopalladin (MYPN), a gene that affects the type and severity of cardiomyopathy - an inherited disease of the heart muscle that may ultimately result in heart failure, transplant or sudden cardiac death in many patients



Cardiology Chief and Heart Institute Executive Co-director Jeffrey A. Towbin, MD

GOSAIN RECEIVES \$2 MILLION FROM THE NATIONAL INSTITUTES OF HEALTH TO STUDY HIRSCHSPRUNG-ASSOCIATED ENTEROCOLITIS CAUSES

Le Bonheur Pediatric Surgeon Ankush Gosain, MD, PhD, recently received a Research Project Grant (R01) award of more than \$2 million from the National Institutes of Health (NIH) for his project “Dysbiosis in Hirschsprung-Associated Enterocolitis Pathogenesis.”

“This research builds on more than a decade of work supported by the NIH, multiple societies and the generous support from Le Bonheur and the Children’s Foundation Research Institute,” said Gosain.

The objectives of the research project are to establish a causative relationship between dysbiosis – imbalance of the gut microbiome – and Hirschsprung-associated enterocolitis (HAEC) and identify which bacteria are the main drivers of HAEC. Gosain will also test therapeutic targets and examine how neurotransmitters made by bacteria influence the motility of the intestine.

“Our goal is to reach a deeper understanding of the pathophysiology of Hirschsprung-associated enterocolitis as well as the identification of novel treatments and prevention of the disease,” said Gosain.

Gosain’s lab is the only NIH-funded lab in the country to study HAEC.

Hirschsprung disease (HSCR) is a result of the incomplete development of the enteric nervous system, or the “brain of the gut,” which controls motility, water and nutrient absorption and local blood flow. HAEC is a life-threatening complication of HSCR. It affects 30-60% of infants with the disease and is the leading cause of death among these infants.

The cause of HAEC is unknown. Because of this, treatment is limited to targeting acute symptoms rather than the underlying cause. Gosain says the long term goal of his laboratory is to define why and how HAEC develops to prevent and treat it at the source.

The gut microbiome is made of helpful and harmful bacteria. Dysbiosis results when something happens to upset the normal



Pediatric Surgeon and Director of Surgical Research at the University of Tennessee Health Science Center Ankush Gosain, MD, PhD

balance of bacteria leading to loss of beneficial bacteria, increased harmful bacteria and decreased overall diversity of bacteria. All of these can be found in patients with HAEC.

Gosain and his lab want to determine if these changes are a result of HAEC, a cause or a little bit of both.

“Previous studies support this central hypothesis that dysbiotic microbiota drives the development of Hirschsprung-associated enterocolitis,” said Gosain.

Using a mouse model, Gosain will use fecal microbiota transplant to prove this hypothesis. Other goals of the project include determining why HAEC has impaired production and secretion of IgA – the primary antibody targeting bacteria in the gut – and how alterations in bacteria contribute to intestinal stasis.

Gosain is associate professor of Surgery and Pediatrics at UTHSC and director of the Pediatric Surgery Research Laboratory at the Children’s Foundation Research Institute at Le Bonheur.

NIH Research Project Grant (R01)

“Dysbiosis in Hirschsprung-Associated Enterocolitis Pathogenesis”

Objective: Establish a causative relationship between dysbiosis - imbalance of the gut microbiome - and Hirschsprung-associated enterocolitis (HAEC) and identify which bacteria are the main drivers of HAEC

INFLUENZA A VIRUS AND EOSINOPHILS: A CHARGED INTERACTION

Eosinophils residing in the airways of mice respond to influenza A virus (IAV) infection through alterations in surface expression of various markers necessary for migration and cellular immunity responses, according to Le Bonheur research published in the *Journal of Leukocyte Biology*.

Previous research explored the effects of IAV infection in patients with allergic asthma. During the 2009 influenza pandemic, patients hospitalized with influenza experienced lower morbidity if allergic asthma was an underlying condition.

In mice, the researchers reported that the beneficial effect of

this co-morbidity correlated with a dramatic increase in eosinophils in the airways, a hallmark of allergic asthma. Eosinophils were susceptible to IAV infection and also presented IAV antigens to CD8⁺ T-cells, which are heavily involved in resolving viral infections. This implied that eosinophils actively contribute to the antiviral response during influenza. While once considered to be a cell that degranulated after allergen encounters and incidentally promoted host pathology during allergy, this research expanded the role of eosinophils to that of anti-viral mediators and specifically showed that eosinophils are active participants in the resolution of influenza. Many of the processes that cumulate in eosinophils making this valuable contribution are unclear.

“Very little is known about how eosinophils respond to direct exposure to IAV or the microenvironment in which the viral burden is high,” said Le Bonheur Researcher Amali Samarasinghe, PhD. “We hypothesized that eosinophils would dynamically respond to the presence of IAV through phenotypic, transcriptomic and physiologic changes.”

Researchers investigated eosinophil characteristics in different niches in a mouse model of fungal asthma and influenza, as well as responses to in-vitro IAV exposure. Results of the study showed:

1. Mice with fungal allergic asthma have a lower pro-inflammatory cytokine profile in their lungs during influenza than non-allergic mice.

2. Eosinophil surface antigens are differentially regulated in mice with fungal asthma and influenza.

When influenza was present, eosinophils changed the surface expression of proteins involved in antigen presentation,

activation and survival depending on both niche and allergic environment.

3. Following virus exposure, a discrete subset of eosinophils that decreased their surface expression of Siglec-F were also more active. Siglec-F^{lo} expressors also increased expression of eosinophil survival receptor IL-5R and downregulated CD62L which is associated with activation. The data suggests that subpopulations of eosinophils may have differing functions during IAV infection.

4. IAV exposure alters the eosinophil transcriptome.

IAV-infected eosinophils reduced overall transcriptional activity but up-regulated transcription of mRNAs encoding viral recognition proteins.

5. Eosinophils reduce mitochondrial respiration in response to IAV. Eosinophils had a lowered basal respiration rate and an overall reduction in mitochondrial respiration.

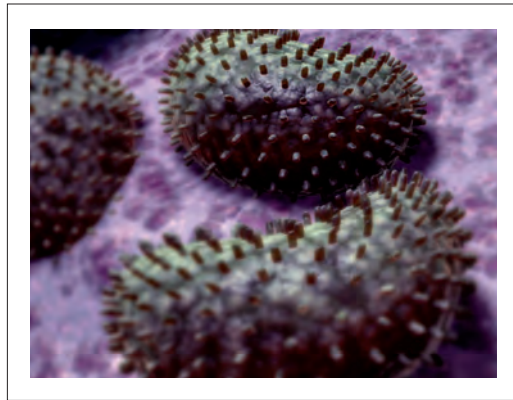
6. Flu-PB-1 pulsed eosinophils promote the generation of cytotoxic CD8⁺ T-cells by causing demethylation of the *Tbx21* locus. IAV-exposed eosinophils can

communicate with CD8⁺ T-cells, resulting in epigenetic changes that allow the differentiation of IAV-specific CD8⁺ T-cells into effector cells.

Overall, mice with fungal asthma that were protected from severe IAV morbidity had reduced levels of cytokines – which can contribute to pathology when present in excess. When exposed to IAV, eosinophils initiate self-preservation mechanisms to survive viral infection, such as conserving energy by reducing transcription activity and mitochondrial respiration. Concurrently, they increase their ability to recognize IAV and induce epigenetic changes in CD8⁺ T-cells that initiate their differentiation into cytotoxic cells known to be a critical component of the antiviral response.

“Our research shows that eosinophils respond dynamically to IAV infection and contribute to antiviral host defense mechanisms during influenza,” says Samarasinghe. “This information is important for selecting effective therapeutics for asthmatics that may benefit from eosinophil presence in airways during IAV infection.”

In addition to Samarasinghe, researchers on the project included Kui Li, PhD, Robert Rooney, PhD, and Heather Smallwood, PhD.



Influenza A virus presence causes alterations to eosinophils in surface expression of various markers necessary for migration and cellular immunity responses according to recent Le Bonheur research.

Pressure Release

Study examines conversion from shunt to endoscopic third ventriculostomy in children, young adults



On Jan. 13, 2000, Allie Glozier (right) and her twin sister, Abbie, were born at 23 weeks, 1 day gestation. Their triplet brother, Caleb, protected in his own amniotic sac, was born five days later.

The Glozier family had become used to the routine. Their daughter, Allie, would become lethargic and develop a headache. The headache would turn to nausea, and they would pack their bags and head to Le Bonheur Children's Hospital, a 90-minute drive from their hometown of Dyersburg, Tenn. Her symptoms were signs that her ventriculoperitoneal shunt (VP shunt) was malfunctioning, and fluid was building up in her brain.

Born prematurely at 23 weeks, 1 day, Allie, now 20, suffers from hydrocephalus, which causes fluid to build up and put pressure on her brain. She received a VP shunt when she was only 3 months old to help fluid drain properly from her brain. A man-made device, shunts can fail for a variety of reasons and often need to be replaced or revised. Allie has undergone 25 shunt revisions in her lifetime.

In March 2019, Allie's shunt failed yet again, but this time Allie and her family received the news that she was a candidate for conversion from her VP shunt to a third ventriculostomy. Endoscopic third ventriculostomies (ETVs) work by creating a bypass (using an endoscope) in the brain for cerebrospinal fluid to flow and eliminate the need for shunts.

ETVs are known to be an effective primary treatment for certain forms of hydrocephalus, but their use in children and young adults with an existing shunt is less known. Le Bonheur participated in a multicenter trial examining the effectiveness of converting pediatric and young adult patients from a shunt to a third ventriculostomy. Results were published in the August 2019 issue of the Congress of Neurological Surgeons

journal, *Neurosurgery*.

"In carefully selected patients, ETV is a durable treatment for many patients, and neurosurgeons need to train or retrain their way of thinking when seeing a shunt malfunction by always asking 'Is this patient a candidate for an ETV?'" said Paul Klimo, MD, chief of Pediatric Neurosurgery at Le Bonheur and senior author of



Allie Glozier, the smallest of the Glozier triplets, weighed only 15 ounces at birth and suffered a grade 4 intracranial hemorrhage.



Chief of Pediatric Neurosurgery Paul Klimo, MD, was senior author of a recent study that evaluated the effectiveness of converting pediatric and young adult patients from a shunt to an endoscopic third ventriculostomy (ETV). He successfully performed the ETV placement for Allie Glozier, a patient with hydrocephalus who experienced 25 shunt revisions in her lifetime.

the study. "If you don't think about doing an ETV, you will never give these kids the opportunity of being shunt-free."

Examining retrospective data from 80 patients (among the three participating centers) who were converted to an ETV showed that, though not all patients will be a candidate for conversion, an ETV should at least be considered in every child who presents with a shunt malfunction or who has an externalized shunt. Researchers defined conversion success



Allie Glozier, now 20, has had no issues since undergoing her ETV placement. She is now studying to become an ultrasound technologist.

as shunt independence at the last follow-up. The overall success rate was 64%, with a median follow-up of two years.

Allie was an ideal candidate for the procedure.

"It appeared that the block in the circulation of Allie's brain fluid was at a narrow channel called the cerebral aqueduct. This choke point prevents

"If you don't think about doing an ETV, you will never give these kids the opportunity of being shunt-free."

Paul Klimo, MD
Le Bonheur Chief of Pediatric Neurosurgery

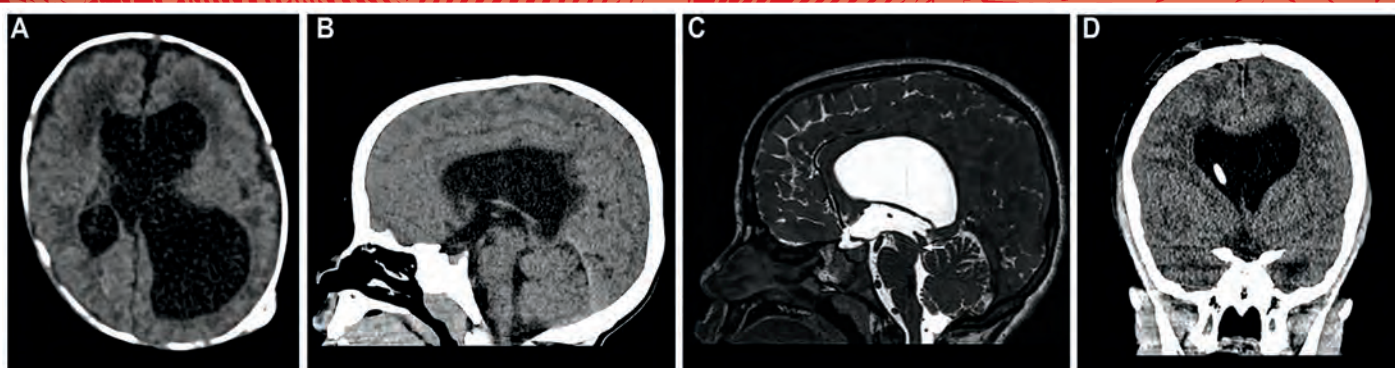
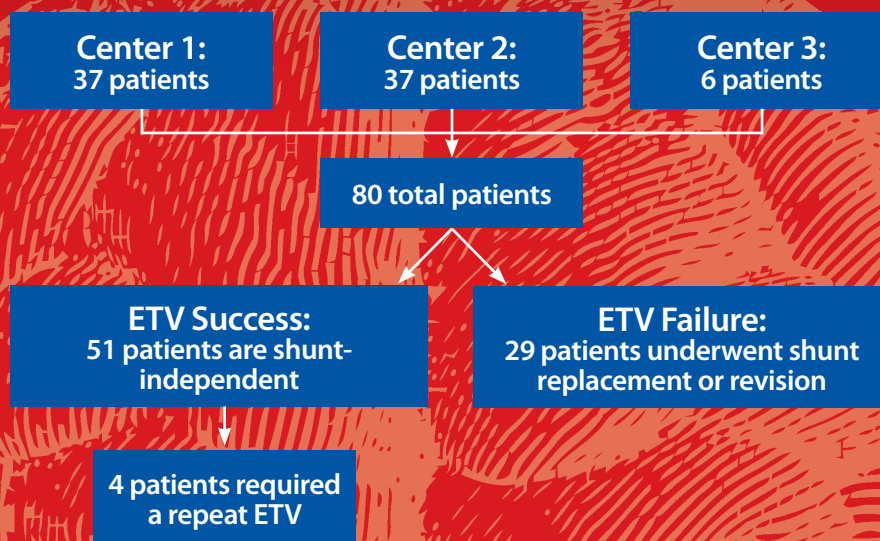
fluid from flowing from the top of the brain to the bottom; patients with an obstructed aqueduct are typically ideal candidates for an ETV," said Klimo.

Allie underwent an ETV in March 2019 and has had no issues since the procedure. A first-year student studying to become an ultrasound technologist, Allie is relieved to be free of the headaches and lethargy that would inevitably come every year, when her shunt began to fail.

"It's a godsend," said her mom, Diana. "We have had no problems."

STUDY PATIENTS AND OUTCOMES:

Effectiveness of Converting Pediatric and Young Adult Patients from a Shunt to a Third Ventriculostomy



A representative example of a patient with posthemorrhagic hydrocephalus who successfully underwent an endoscopic third ventriculostomy after presenting with a shunt malfunction. **A**, An axial CT scan without contrast demonstrated posthemorrhagic hydrocephalus of prematurity in a male infant who was born at 24 weeks gestation and had a Grade III germinal matrix hemorrhage. A ventricular access device was placed and later converted to a ventriculoperitoneal shunt. **B**, A sagittal reconstruction of a CT scan without contrast performed for symptoms of a shunt malfunction demonstrated enlarged lateral and third ventricles without enlargement of the fourth ventricle, suggesting obstructive hydrocephalus. **C**, A sagittal FIESTA MRI sequence demonstrates narrowing of the inferior third of the cerebral aqueduct inferior bowing of the third ventricle floor and anterior displacement of the lamina terminalis. An endoscopic third ventriculostomy was therefore performed. **D**, A coronal CT scan without contrast obtained almost 6 years later, when the patient presented to the emergency room bradycardic and obtunded with several days of headaches, emesis and sunsetting eyes. His Ommaya reservoir was immediately accessed for 30cc of CSF with rapid neurologic improvement. He was then taken emergently to the operating room, and his ETV was successfully repeated.

Dravet on Trial

One family's journey with drug trials for Dravet syndrome

"I'm the type of mom that if there's a cure for my son and I have to go to Antarctica to get it, I'm going tomorrow," says Crystal Byrd, mother to 12-year-old Charlie who was diagnosed with Dravet syndrome at 2 years old.

So now Crystal and Eric Byrd of West Liberty, Ky., gladly make the nine-hour journey to Le Bonheur so that Charlie can participate in the Fenfluramine trial for Dravet syndrome — the only medication that has been successful in keeping his seizures under control.

Tracee Ridley-Pryor, DNP, APRN, PMHNP-BC (far right), oversees the trials for Dravet syndrome ensuring that Le Bonheur's epilepsy patients can participate in the latest therapies available.



Charlie began to have seizures after his first round of childhood vaccinations. Thinking they were febrile seizures, the Byrds weren't concerned until his seizures started again just a few months later. This time, they were referred to a local epileptologist for diagnosis and treatment.

The symptoms were clear and a genetic test confirmed – Charlie had Dravet syndrome.

But standard epilepsy treatments weren't controlling Charlie's seizures. After three years on various medications, Crystal and Eric knew their son needed more specialized care. Researching online, Crystal found eight hospitals recommended by the Dravet Foundation – the Byrds chose Le Bonheur.

"It was perfect," says Crystal of their first experience. "Le Bonheur was such a different and more welcoming atmosphere. We wanted to stay forever!"

Neurologist Stephen Fulton, MD, worked steadily to get Charlie the treatment that would be most effective. His seizures stabilized, and he was able to avoid hospitalization. However, as he grew older, his seizure pattern changed, and the increasing medication dose was no longer effective in seizure control.

So in 2013, Charlie underwent surgery for a vagus nerve stimulation (VNS) implant. He responded well – his mood improved, but he was still having nocturnal seizures, which pose the highest risk of death for someone like Charlie.

So Fulton decided that it was time to try to get Charlie into a brand new drug trial – ZX-008 (fenfluramine hydrochloride) oral solution.

"Charlie's seizures were extremely difficult to control and quite dangerous," says Fulton. "Therapies are now much more targeted to underlying causes of disease. It was an easy decision to talk to his family about the potential for current trials for Dravet syndrome that are much more efficacious than previous therapies."

At first, the Byrds came to Le Bonheur twice a month in order to kick off participation in the trial. Various tests, including blood work, EKGs, ECHOs and more, helped determine if Charlie could qualify and established a baseline for his health and seizure

patterns. Crystal also had to track everything on behalf of the drug trial – when he had seizures, what kind of seizures he had, when he received medication and any other health concerns.

"Every clinical drug trial requires a review of inclusion and exclusion criteria to guide the selection of the patients that are eligible to participate," says Tracee Ridley-Pryor, DNP, APRN, PMHNP-BC.

Ridley-Pryor is director of Pediatric Neurology Research for the University of Tennessee Health Science Center Pediatric Neurology and oversees the current trials for Dravet syndrome while also investigating new trials for current and future patient participation.

"The most rewarding part of my role is witnessing the patients make strides that their parents weren't even sure were attainable."

Beginning at the lowest dose, Charlie has slowly increased his medication so that he now takes the maximum dosage permitted. He has not experienced any side effects during his three years on the trial and had a 90% reduction in his seizures – where he used to have 24 to 30 seizures a month, he now has one or two.

"We are so thankful for Dr. Fulton," says Crystal. "At first the trial was overwhelming, but we know we have a knowledgeable health care team with

Charlie's best interest at heart, who will be on top of all the details of the trial."

But Crystal is holding out hope for one more drug for Charlie – a DNA therapy drug that could potentially address his Dravet syndrome at the genetic level. This drug would correct the genetic mutation that leads to the seizures and other symptoms Charlie and other children like him have to wrestle with.

"Someday his disease may not affect anybody, but we'll never get there if we don't have people actively engaging in trials like these," says Crystal. "I wouldn't recommend a drug trial just anywhere, but at Le Bonheur the communication and support are incredible. Sometimes you get scared, but I know that I have somebody who I can talk to who will return my calls and concerns within minutes."



The Byrd family makes a nine-hour journey in order for 12-year-old Charlie to participate in a trial for Dravet syndrome. This has been the only medication that has successfully reduced his seizures.

COVID-19: *Innovation Under Pressure*

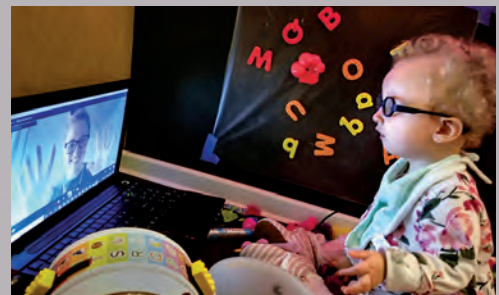
The onset of the COVID-19 pandemic forced health care institutions to change the way they deliver care and innovate new ways to meet the unusual demands created in a space of social distancing, masks and PPE shortages. Le Bonheur providers and Associates used new tactics to ensure the safest care for children in need.

Tech Talk

Telehealth services inside and outside the hospital allow continuity of care



Pediatric Pulmonologist Tonia Gardner, MD, is one of many providers at Le Bonheur who complete more than 2,400 telehealth visits each week in an effort to limit unnecessary exposure. Telehealth allows children not to miss critical appointments while providing the safest possible environment for patients and providers.



22-month-old Mary Kate Webb participates in telehealth physical and speech therapy with Le Bonheur therapists. She has Wolf-Hirschhorn syndrome and suffers developmental delays from her diagnosis. Missing therapy appointments would put her at risk for falling behind. Within days of the first reports of COVID-19 in Tennessee, therapists were able to expand telehealth services to ensure that children like Mary Kate don't miss vital therapy sessions and can continue their progress.



Parties, concerts and game shows are just a handful of activities that the Child Life team provides on a daily basis to help bring a bit of normalcy to the hospital setting. But the implementation of social distancing and need to avoid unnecessary exposure has changed their approach. Le Bonheur's Child Life team has looked to technology to help them provide normalcy for children during COVID-19, moving in-person programming to the hospital's closed-circuit TV channel, creating a virtual Easter egg hunt and providing interaction with special visitors via video chat.

Caring for the Community

Community-based health workers meet vital needs during COVID-19

Children living with chronic conditions like diabetes and asthma were on the minds of Le Bonheur's community health workers when COVID-19 emerged. Their concern: would children already living with food insecurity have access to the nutrition they needed to stay healthy during a pandemic?



Access to nutritious food can mean the difference between children staying safe at home and having to be hospitalized. Community health workers have made no-contact deliveries of food and necessary supplies to families – more than 300 and growing – and children like Carter Evans (left).



COVID-19 has intensified an urgent need for support for many expecting mothers in the Memphis area. A Le Bonheur community outreach program, Nurse-Family Partnership (NFP) is stepping in to help hundreds of new and expecting moms and their babies. Community Health Nurse Beth Pletz (left) is able to continue providing medical and social support to new moms like Dominique Jones (right) and bring her vital food and supplies. Partnerships with organizations like Slingshot Memphis also allow the NFP team to use impact funds to provide support for clients' utility bills as many have lost jobs but still have bills accruing.

Procuring PPE

New PPE construction and reprocessing techniques mitigate shortages



At the onset of the outbreak, Le Bonheur leaders took a proactive approach to calculate PPE stockpiles and how long it would last. Face shields were identified as a critical need. Le Bonheur Chief Medical Officer Barry Gilmore, MD, and Surgeon-in-Chief Trey Eubanks, MD, partnered with University of Memphis Mechanical Engineering Assistant Professor Ebrahim Asadi, PhD, who runs a 3D printing lab. The U of M converted its lab to create face shield frames 24 hours a day. The U of M made its first delivery of 50 new face shields, which can be easily cleaned and reused, to Le Bonheur at the end of March.



N95 respirators have been in short supply since the beginning of the COVID-19 pandemic. Medical Director of Infection Prevention Nick Hysmith, MD, and Manager of Infection Prevention Don Guimera knew

that drastic measures were needed to optimize and maintain a consistent supply of disinfected N95s. Working with the Methodist Healthcare system, Guimera and Hysmith created a hospital workflow process for the decontamination and reuse of N95 masks using hydrogen peroxide vapor in line with the Centers for Disease Control and Prevention guidelines.



10 Years in a Row!

Le Bonheur Children's Hospital has been named a Best Children's Hospital for 2020-2021 by *U.S. News & World Report*. This is the tenth consecutive year Le Bonheur has been included in the prestigious list with recognition in eight specialties.

The annual Best Children's Hospitals rankings recognize the top 50 pediatric facilities across the U.S. in pediatric specialties. Le Bonheur was recognized in eight specialties – cardiology and heart surgery, gastroenterology and GI surgery, neonatology, neurology and neurosurgery, nephrology, orthopedics, pulmonology and urology.

"I am thrilled that for the tenth consecutive year, Le Bonheur has been recognized as a Best Children's Hospital by *U.S. News & World Report*," said Le Bonheur President Michael Wiggins. "This honor is a sign of our dedication to providing the best health care for children. This means that families can count on us to provide safe and effective care for all children who need us."

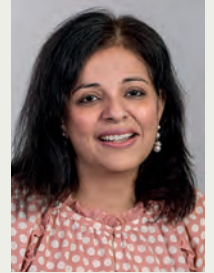
Le Bonheur
Children's Hospital
Where Every Child Matters



Briefs

Bagga appointed Vice Chair of Southeast Region of the Association of Pediatric Program Directors

Bindiya Bagga, MD, was appointed vice chair of the Southeast Region of the Association of Pediatric Program Directors. Bagga is the Le Bonheur site director for the University of Tennessee Health Science Center's Pediatric Infectious Disease Fellowship Program. She is also associate director of Le Bonheur's Infectious Disease Program and medical co-director of Antimicrobial Stewardship.



Bindiya Bagga, MD

Dormois named 2020 Ronald Bell Mentor of the Year

Larry Dormois, DDS, MS, was named the 2020 Ronald Bell Mentor of the Year by the Foundation of the College of Diplomates of the American Board of Pediatric Dentistry. This award recognizes someone who has been instrumental in mentoring pediatric dentistry residents and new pediatric dentists. Dormois is associate professor of Pediatric Dentistry at the University of Tennessee Health Science Center.



Larry Dormois, DDS, MS

Le Bonheur Children's Outpatient Center – Jackson named a "2019 Business of the Year"



Le Bonheur Children's Outpatient Center in Jackson, Tenn., was named a 2019 Business of the Year (category of 1-49 employees) at the annual celebration for the Jackson Chamber of Commerce. The celebration highlighted businesses that made an extra effort to achieve excellence through high standards, professional accomplishments and community contributions.

McCullers receives Dream Hero Award

Pediatrician-in-Chief Jon McCullers, MD, was selected as a 2020 Dream Hero Award recipient by the Legacy of Legends Community Development Corporation. The organization is dedicated to decreasing adverse childhood experiences (ACEs), gang and youth violence, family violence and poverty in Memphis. He was recognized for his contributions to Legacy of Legends' fundraising efforts and work to reduce ACEs.



Jon McCullers, MD

Le Bonheur Pediatrics recognized as a Patient-Centered Medical Home

All six of Le Bonheur Pediatrics primary practice locations have been awarded the National Committee for Quality Assurance Patient-Centered Medical Home (PCMH) designation.

Practices with this designation employ a model of care that puts patients at the forefront to build better relationships between patients and their clinical care teams,

improve quality and patient experience and increase staff satisfaction while reducing health care costs.



Neuro Symposium postponed to 2021

The Pediatric Neurology Symposium has been postponed to 2021 due to the COVID-19 pandemic. Please save the date for April 30 – May 1, 2021 at The Westin Beale Street, Downtown Memphis.

If you had already registered for this year's symposium, please contact cme@mlh.org to have your registration fee refunded or moved to the 2021 date.

Researchers published in American Thoracic Society's Research News Quarterly "COVID Collection"

Le Bonheur Researcher Amali Samarasinghe, PhD, coordinated the "COVID Collection" feature in the latest issue of the American Thoracic Society's *Research News Quarterly*. Samarasinghe serves as a Research Advocacy Committee member for the American Thoracic Society. The series discussed first research efforts, clinical and scientific discoveries and questions concerning COVID-19 as well as the impact of the disease on clinical research and training. Articles from Le Bonheur researchers and physicians included:



- "Encounters of the COVID Kind" by Amali Samarasinghe, PhD
- "A City's Response to COVID-19: The Memphis Roadmap" by Jon McCullers, MD, and Terri Finkel, MD, PhD
- "Clinical Research in the Era of COVID-19" by Patricia Dubin, MD, and Nicholas Hysmith, MD
- "Chronic Lung Disease and COVID-19: A Complicating Duo?" by Amali Samarasinghe, PhD

To read the full articles, visit lebonheur.org/news.

COVID-19 Resources for Providers and Patients

Le Bonheur has multiple resources for providers including information related to COVID-19 and MIS-C to share with patients and families.

- Visit lebonheur.org/for-providers for the latest policies, procedures and guidelines regarding COVID-19 and MIS-C including frequently asked questions for providers.
- Email providerquestions@lebonheur.org for any questions regarding COVID-19, patient admission, referrals or other inquiries.
- Visit lebonheur.org/coronavirus for an up-to-date list of resources for patients including public testing locations, community resources and sources for trusted information regarding the pandemic.



Countering COVID-19

How does COVID-19 affect children? How does the disease spread among households? What are the risks for immuno-compromised children?

These questions are just a few that Le Bonheur investigators hope to answer through their research into the SARS-CoV-2 virus and COVID-19. Research projects include:

- "Clinical, Immunological and Virological Characterization of COVID-19" study in partnership with researchers from the University of Tennessee Health Science Center
- Development of a serum biorepository with the goal of reaching 200,000 samples to better understand COVID-19 immunity
- COVID-19 registries for children especially within high-risk and complex patient populations

Learn more about these research projects, registries and partnerships on page 8.

