

Untangling Neural Crest Cell Migration in Hirschsprung Disease

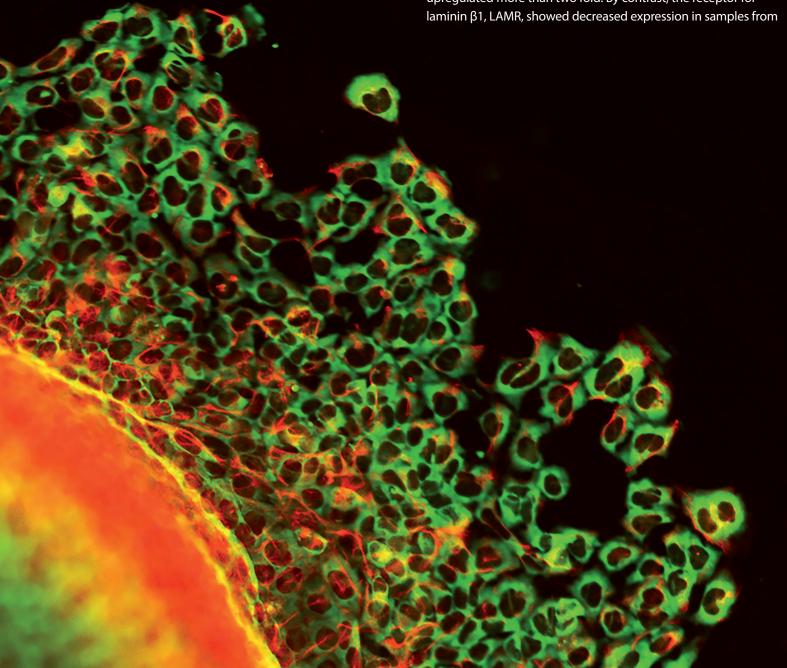
ediatric Surgeon Ankush Gosain, MD, PhD, recently published a study in *The FASEB Journal* delineating interactions between migrating neural crest cells (NCC) and the extracellular matrix in a model of Hirschsprung disease. The results showed that alterations in 37/67 kDa laminin receptor (LAMR) contribute to neural crest cell migration failure in enteric nervous system development. Throughout his career, Gosain has focused his research on determining the mechanisms underlying abnormal development of the enteric nervous system in Hirschsprung disease.

Neurons in the wall of the gastrointestinal tract comprise the enteric nervous system, which controls gut motility, digestion, secretion and absorption. During development, neural crest

cells, the precursors of neurons in the enteric nervous system, migrate throughout the digestive tract to provide innervation. However, in Hirschsprung disease, neural crest cells fail to migrate into the distal colon, resulting in a lack of innervation in this region. This lack of innervation is a common cause of neonatal bowel obstruction, which can progress to bowel distension, Hirschsprung-associated enterocolitis and death.

Gosain and his colleagues specifically focused on abnormalities in how neural crest cells interact with laminin, which is a major component of the extracellular matrix that neural crest cells migrate through in the developing enteric nervous system. The investigators used a mouse model of Hirschsprung disease, the endothelin receptor B knockout mouse, to tease out specific changes in laminin expression.

In the knockout mice, the gene encoding laminin $\beta 1$ was upregulated more than two fold. By contrast, the receptor for laminin $\beta 1$, LAMR, showed decreased expression in samples from



knockout mice and human patients with Hirschsprung disease. Application of exogenous laminin suppressed NCC migration in an organ culture model, whereas YIGSR, a laminin β1 analog, promoted NCC migration. YIGSR also upregulated expression of LAMR and enhanced NCC migration in midgut slice culture. When LAMR expression was silenced, the beneficial effect of YIGSR was abolished. Furthermore, YIGSR application resulted in colonization of the distal colon in 80% of ex vivo organ cultures from endothelin receptor B knockout mice.

These experiments indicate alterations in LAMR contribute to neural crest cell migration failure in enteric nervous system development. The investigators posit that YIGSR may selectively enhance neural crest cell migration with LAMR binding increasing LAMR expression and preferentially promoting migration. These results add to the current body of literature showing that interactions between neural crest cells and the extracellular matrix are involved in enteric nervous system development with the extracellular matrix representing a potential target for intervention in Hirschsprung disease.



The image at left shows a common assay used in the laboratory of Le Bonheur Pediatric Surgeon Ankush Gosain, MD, PhD (above), to study migration of neural crest cells (NCC) during development of the enteric nervous system.



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.

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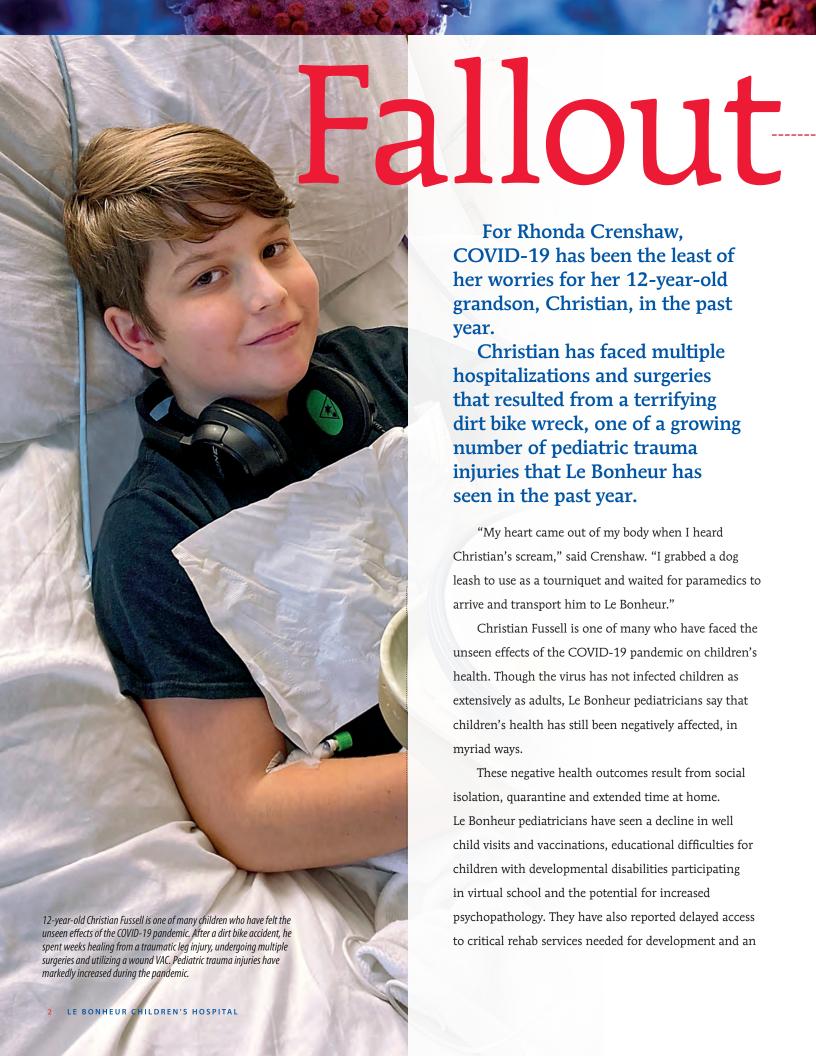








For referrals contact: Le Bonheur Connect at 866-870-5570.



For Rhonda Crenshaw, COVID-19 has been the least of her worries for her 12-year-old grandson, Christian, in the past year.

Christian has faced multiple hospitalizations and surgeries that resulted from a terrifying dirt bike wreck, one of a growing number of pediatric trauma injuries that Le Bonheur has seen in the past year.

"My heart came out of my body when I heard Christian's scream," said Crenshaw. "I grabbed a dog leash to use as a tourniquet and waited for paramedics to arrive and transport him to Le Bonheur."

Christian Fussell is one of many who have faced the unseen effects of the COVID-19 pandemic on children's health. Though the virus has not infected children as extensively as adults, Le Bonheur pediatricians say that children's health has still been negatively affected, in myriad ways.

These negative health outcomes result from social isolation, guarantine and extended time at home. Le Bonheur pediatricians have seen a decline in well child visits and vaccinations, educational difficulties for children with developmental disabilities participating in virtual school and the potential for increased psychopathology. They have also reported delayed access to critical rehab services needed for development and an

A look at the long-lasting effects of COVID-19 on children's health

uptick in trauma cases, particularly all-terrain vehicle (ATV) accidents such as Christian's.

Five Le Bonheur providers discuss the unseen effects of the pandemic that they see regularly, what the long-term effects may be and what can be done to mitigate further health consequences to children.

GENERAL PEDIATRIC HEALTH: WELL-CHILD VISITS AND VACCINATIONS

Missed well-child visits, vaccinations during COVID-19 pandemic require long-term strategies for catch up

Jason Yaun, MD, FAAP

Clinical Director of ULPS General Pediatrics Division Chief of Outpatient Pediatrics Medical Director, Family Resilience Initiative

In the early days of the pandemic, general pediatrician offices — including Le Bonheur's — drastically reduced the number of well-child appointments until more was known about COVID-19. But once proper precautions were established and doctors' offices reopened to a more normal capacity, Le Bonheur Pediatrician Jason Yaun, MD, FAAP, continued to see that parents were hesitant to bring in their children, for fear of the virus.

"While the number of visits in our office are beginning to reach similar levels as last year's, we haven't really seen any catch up from those who missed well-child visits and vaccinations during the beginning of this crisis," said Yaun. "This is something that will have a long-lasting effect on the health and development of children."



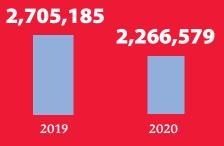
Le Bonheur Pediatrician Jason Yaun, MD, FAAP, works to catch up kids on well-child visits and vaccinations that were missed at the onset of the pandemic.

Yaun and his team continuously look for ways to mitigate this effect. For low-income families, delays exacerbate existing inequities, he said. He has also seen a tremendous gap in immunizations between families who are publicly and privately insured.

"Our initial strategy was to get kids going into kindergarten or seventh grade their required vaccines needed for school entry," said Yaun. "We've had success by setting up clinics in the community, meeting our patients where they

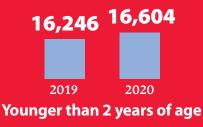
General Pediatrics: Pandemic Impact on Vaccinations

Total Number of Childhood Vaccine Doses as Reported in the Tennessee Immunization Information System (TennIIS)



77 patients Le Bonheur's Community Outreach Clinic

Number of Childhood Vaccines at Le Bonheur's General Pediatrics Clinic by Age Group





44 clinics held in West Tennessee by Le Bonheur's mobile unit

are. Long-term strategies are a must if we're going to catch children up."

But the effects on health go beyond the physical. Middle- and high schoolaged children are facing numerous mental health challenges — whether families are dealing with the death of a loved one, community violence or feelings of isolation. The pandemic can be a type of adverse

"Long-term strategies are a must if we're going to catch children up."

> Jason Yaun, MD, FAAP, Le Bonheur Pediatrician

childhood experience (ACE) for many, which can result in a profound lifelong mental and physical health impact for kids, said Yaun.

Yaun connects patients with therapy and counseling through community

resources, although he continues to see stigma and hurdles for families to get access to the needed mental health care.

> In the meantime, he continues to reassure parents that the doctor's office is safer to visit than the grocery store. And supportive caregivers who demonstrate positive, nurturing interactions can support children and help them build resiliency to mitigate the negative consequences of ACEs.

"With many children on an irregular school schedule, routines, such as sleep schedules, balanced diets and physical activity, are an important, essential component of health," says Yaun. "Continue to talk to children and discuss their social and emotional needs in an open and honest way to support and develop these skills."



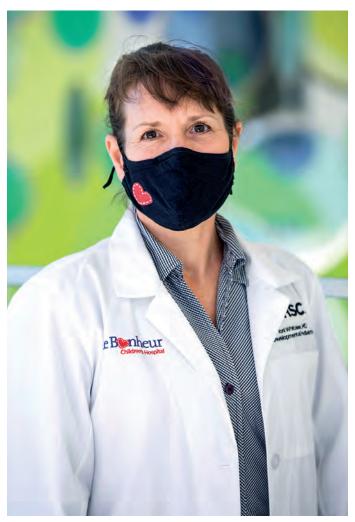
DEVELOPMENTAL HEALTH: VIRTUAL SCHOOL AND SPECIAL NEEDS

Le Bonheur helps schools support children, avoid risks of falling behind in virtual school

Toni Whitaker, MD

Division Chief of Developmental Pediatrics, Le Bonheur and the University of Tennessee Health Science Center Director, Leadership Education in Neurodevelopmental and Related Disabilities (LEND) Program, University of Tennessee Center for Developmental Disabilities

Le Bonheur Developmental Pediatrician Toni Whitaker, MD, is all too aware of the challenges school administrations, teachers and parents face with virtual school and students with special needs.



Le Bonheur Chief of Developmental Pediatrics Toni Whitaker, MD, serves on Le Bonheur and UTHSC's Back-To-School Task Force to provide guidance and support for schools as they help children with special needs.

"We're facing a difficult situation. Schools need to be physically safe and prevent the spread of COVID-19. But simultaneously they are trying to meet the unique needs of kids, especially those with developmental disabilities," said Whitaker.

With many schools remaining virtual for so long, a truth remains: Younger children and children with developmental disabilities don't benefit as well from virtual or online instruction. Both tend to learn at a slower rate and require hands-on guidance and immediate feedback to learn most effectively, said

Whitaker.

Whitaker continues to see discouraged parents resigned to the fact that their children can't learn as well with the circumstances of virtual school.

"We know from time periods where kids don't have instruction, such as the summer,

"We're facing a difficult situation. Schools need to be physically safe and prevent the spread of COVID-19. But simultaneously they are trying to meet the unique needs of kids, especially those with developmental disabilities."

> Toni Whitaker, MD. Le Bonheur Developmental Pediatrician

they lose progress but can often regain it with intensive instruction," said Whitaker. "But we don't have large groups we've followed who have been out of school for this extended period of time, particularly for children with developmental delays or special needs, to really know outcomes."

To support schools and teachers, Le Bonheur formed a Back-to-School Task Force with the University of Tennessee Health Science Center (UTHSC), which provides guidance and information for schools as they safely return to in-person



instruction with a special needs subgroup led by Whitaker.

"School staff who work with these kids daily are the experts in knowing what students with special needs require to learn effectively," said Whitaker. "Our task force wanted to come alongside and provide information and support."

Whitaker has also assisted families of children with developmental disabilities during the pandemic as the ambassador to Tennessee for the Centers for Disease Control and Prevention's (CDC) "Learn the Signs. Act Early." program.

Developmental Pediatrics: Le Bonheur Supports Developmental Health in the Community

30,000+ children assisted by Le Bonheur and partners through the Centers for Disease Control and Prevention's (CDC) "Learn the Signs. Act Early." program

children seen for Early and Periodic Screening, Diagnostic and Treatment (EPSDT) in West Tennessee by Le Bonheur's mobile unit

Le Bonheur and UTHSC Back-to-School Task Force webinars

educators attended Le Bonheur and UTHSC Back-to-School Task Force webinars

March 2020 - present

Using the new CDC grant funding, she will partner with state service agencies to train providers and distribute more than 30,000 free developmental monitoring and developmental promotion resources to families with young children.

Ultimately, Whitaker encourages families and schools to keep an open line of communication so that each can do what's best for the child during a difficult time.

"Families need to interact one-on-one with their child as much as they are able, but also keep in touch with teachers and talk to their child about their experiences," said Whitaker. "Therapy services and availability are evolving so continue to check in for your child's needs."

TRAUMA SERVICES: RISING TRAUMA OCCURRENCES AMONG CHILDREN

Pandemic brings increased trauma cases, gunshot wounds, with potential for generational impact

Regan Williams, MD

Medical Director, Trauma Services

The world slowed down as a result of the pandemic - but Le Bonheur Medical Director of Trauma Services Regan Williams, MD, has experienced the opposite in her patient population: Trauma injuries have risen since the pandemic began.

"When children spend more time at home, trauma cases rise," said Williams. "Typically, cases drop when school starts. But with more children spending large amounts of time at home, sometimes unsupervised, numbers have remained elevated."

She has seen a rise in trauma injuries in four major categories: non-accidental trauma, all-terrain vehicle (ATV) accidents, gunshot wounds and motor vehicle collisions.

But one area has Williams particularly concerned. "Gunshot wounds have seen a concerning increase. Numbers remain high because kids are still



Le Bonheur Medical Director of Trauma Services Regan Williams, MD, continues to see high levels of pediatric trauma since the pandemic began. Gunshot wounds are a particular concern for children in the Memphis area.

at home," said Williams. "This gun violence is turning into a pandemic within a pandemic."

According to Williams' initial data, trauma injuries will continue to rise or stay elevated until children are no longer spending extended periods of time at home. Gun violence in particular has devastating long-term effects on children, says Williams. Children who are victims of violent crime are more likely to end up in jail, be a victim again or be a perpetrator of violent crime.

"This gun violence is turning into a pandemic within a pandemic."

> Regan Williams, MD, Le Bonheur Medical Director of Trauma Services

"Le Bonheur only sees children 14 and younger with gunshot wounds. I worry that these children and young

teens who are wrapped up in violence during this pandemic will continue to perpetrate it for years to come," she said.

To mitigate these effects, Le Bonheur worked with the Shelby County Crime Commission, who organizes Walk



CHRISTIAN FUSSELL, 12

All-terrain vehicle accident Hernando, Miss.

dirt bike ride with friends turned into a nightmare for Rhonda Crenshaw when her 12-year-old grandson, Christian Fussell, suffered a traumatic leg injury. After Christian hit a tree, his bike's foot peg created a deep wound that immediately started to bleed heavily.

Christian is one in the ever-increasing number of pediatric trauma cases that Le Bonheur has seen since the onset of the COVID-19 pandemic.

"If this had happened further from our house, he wouldn't have time to get to the hospital and would have bled to death," said Rhonda, who worked for years as a cardiac clinical assistant. "I had to keep my medical brain on to be able to take care of him until the paramedics arrived."

Le Bonheur Medical Director of Trauma Services Regan Williams, MD, says the rise in trauma cases is linked to children spending more time at home, due to quarantine and stay-at-home orders.

"Just because the world slowed down doesn't mean that trauma slowed down," said Williams. "We have seasonal variation every year — cases increasing in summer and decreasing when children return to school. This year we did not see a drop off as many children were still at home doing virtual school."

First on the scene of Christian's accident was neighbor Justin Finger — on off-duty paramedic and former Le Bonheur employee. Christian was rushed to Le Bonheur's Emergency Department by Mississippi's DeSoto County Sheriff's Department. While his prognosis was good, Christian faced a long road to full recovery, including

a wound VAC and 10 outpatient surgeries to progressively close the wound.

Recovery was difficult for Christian. While both grandparents were able to stay with him in the hospital, no visitors could come. And they have continued to limit visitors once home to further reduce risk of any infections.

"Christian is such a people person, and this has been so confining for him," said Rhonda. "We can't let anyone come visit him in the house. We can't afford for him to get any sickness."

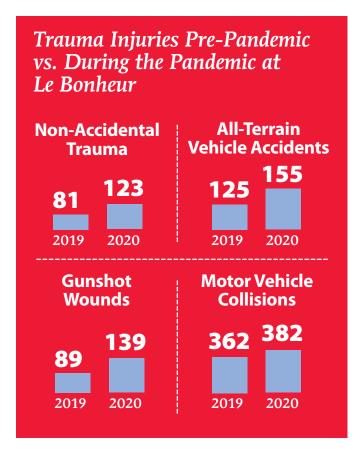
Today, Christian is well on his way to recovery and has had his stitches removed. While he's completing this semester of school at home, he looks forward to going back to school and getting back to his usual activities.

But he did have one special visitor that cheered him up. "The DeSoto County Sherrif's deputies not only saved his life, but they made an effort to make sure he was on his way to healing," said Rhonda. "They gave him a hat and a patch — we will forever be grateful for them, our neighbor Justin and Le Bonheur's fantastic nurses and ED staff."



After a traumatic leg injury, 12-year-old Christian Fussell faced 10 surgeries and a long road to recovery. He is one of the increasing number of pediatric trauma cases that Le Bonheur has seen since the pandemic began. The DeSoto County Sheriff's Department rushed Christian to Le Bonheur and later presented him with a cap and badge for his bravery.

Against Violence events to speak out against the gunshot violence in the city. Williams also represents Le Bonheur and the University of Tennessee Health Science Center as a part of the Memphis Group Violence Intervention Program.



This effort plans to reduce violence in the city through five specific program areas: suppression, intervention, prevention, community mobilization and organizational change.

Williams believes much of the violence and trauma is a result of mental health issues and challenges. Le Bonheur recently partnered with the BRAIN CENTER at the University of Memphis so that all children treated at Le Bonheur's Pediatric Trauma Center can be eligible for free mental health counseling services. Graduate-level students in the Clinical Mental Health Counseling program will provide the counseling.

"The pandemic has helped increase the conversation around mental health and show that the need for mental health support is clear," Williams said. "People are lonely, mad and sad, including children."

PSYCHIATRY: IMMEDIATE AND LONG-TERM MENTAL HEALTH EFFECTS OF PANDEMIC AND ISOLATION

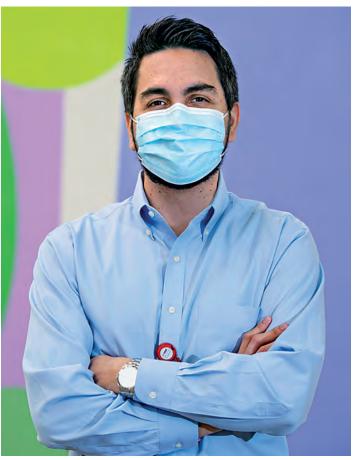
Pandemic stressors historically lead to psychopathology in vulnerable youth

Andres Ramos, MD

Le Bonheur Psychiatrist

Whether it's natural disasters, terrorist attacks or a deadly pandemic, psychopathology in children always follows, according to a wide variety studies conducted in the wake of these disasters.*

"With COVID-19, this is like a second pandemic – a wave of mental illness as a result of the initial pandemic," said Le Bonheur Psychiatrist Andres Ramos, MD.



Le Bonheur Psychiatrist Andres Ramos, MD, is conducting a study on psychopathology by providing a questionnaire in Memphis' Shelby County School system. He aims to identify what stressors in the pandemic are most likely to lead to psychopathology in children.

But kids are resilient, says Ramos. And while he doesn't anticipate a long-lasting issue for masses of children, he admits that certain populations are far more at risk.

"Long-term effects exist for vulnerable kids during this pandemic as it does for any child who undergoes an adverse childhood experience (ACE) or develops post-traumatic stress disorder (PTSD)," said Ramos. "Our hope is to figure out which COVID-related stressors are more likely to lead to

Psychiatry: Mental Health Impact of the Pandemic

of Tennessee children had 2 or more adverse childhood experiences (ACEs) in the last 12 months*

* Source: childrenshospitals.org

Survey of American high school students*



53% said they were "moderately," "very," or "extremely" worried about their mental health



51% experienced anxiety since the beginning of the pandemic



38% reported experiencing depression since the beginning of the pandemic



4% knew of someone with suicidal thoughts

* Source: Survey by Chegg.org in partnership with the Ad Council's Seize the Awkward, the JED Foundation, the American Foundation for Suicide Prevention and the Born This Way Foundation



psychopathology so we can intervene sooner with the children most in need."

To do this, Ramos and his team are planning to conduct a study on psychopathology among Memphis' Shelby County School System youth during the COVID-19 pandemic. The study will screen for PTSD and serious emotional disturbances (SED). SEDs are a wide range of psychopathological conditions, which would be classified as warranting clinical attention.

"The greatest areas of concern are for youth who are already vulnerable. With the COVID-19 pandemic, stressors are amplified in addition to what they already tackle every day."

Andres Ramos, MD Le Bonheur Psychiatrist

The individual stressors caused by the pandemic, from social isolation to sleep problems, are historically noted as leading to mental illness in children. But in the wake of COVID-19, these individual stressors are combined in previously unseen ways, according to Ramos. Social isolation increases risk of depression or anxiety for years after. Disrupted schooling leads young children to deviate from normal developmental milestones. Quarantine and isolation can also

lead to sleep problems, inactivity and increased screen time, which have been shown to make children more vulnerable to psychological distress.

"The greatest areas of concern are for youth who are already vulnerable," says Ramos. "With the COVID-19 pandemic, stressors are amplified in addition to what they already tackle every day."

By determining which of these COVID-related stressors are most impactful to psychopathology, Ramos and his team can lead targeted mental health interventions in children. His team will provide community mental health resources for families engaged with the survey.

Finally, Ramos and psychiatrists have to consider the potential neurobiological effects of the virus itself.

"Coronaviruses are associated with the onset of mood and psychotic disorders," said Ramos. "Inflammatory markers following COVID-19 illness predict depression and anxiety, and the concern is that the inflammation that clears the virus may also put those infected at risk for psychopathology."

Overall, Ramos has hope of what the medical community and society at large can learn from this pandemic about the importance of mental health.

"This season is a humbling experience, but it doesn't have to be a long-lasting psychological injury to children," he says. "It's an opportunity for learning and an evolution in how we think about people and the way circumstances affect mental health."

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REHABILITATION SERVICES: BARRIERS IN ACCESS TO CARE

Backlog of rehab referrals to Le Bonheur reflects lack of access to in-person care

Danielle Keeton, MA, CCC-SLP

Director, Le Bonheur Outpatient Rehabilitation & Developmental Services

Le Bonheur's Outpatient Rehabilitation Services is facing a backlog of hundreds of children who could face long-term consequences to their development without rehab intervention, according to Danielle Keeton, MA, CCC-SLP, director of the department.

Keeton and her team of occupational, physical and speech therapists see multiple factors related to the pandemic that could lead to negative developmental outcomes for children



Director of Le Bonheur Outpatient Rehabilitation and Developmental Services Danielle Keeton, MA, CCC-SLP, has seen an increase in the backlog of patients in need of in-person therapy. Because of virtual school, access to in-person services has been limited for many children and families.

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FRANNIE CROWLEY, 3

Diagnosis: Congenital limb differences and heart defects Services: Occupational and physical therapy

hree-year-old Frannie Crowley has been a
Le Bonheur patient since before she was born.
Diagnosed at 20 weeks gestation, Frannie was
born with limb differences and heart defects, which led to
multiple procedures and stays in the hospital.

Continuous occupational and physical therapy has

always been critical for Frannie's development. And the COVID-19 pandemic was not going to stop the need for her to continue reaching milestones. She was one of the fortunate children who have been able to continue rehab services in spite of the pandemic, thereby avoiding delays in her development.

"Frannie's limb differences mean that in order to meet milestones, she has to learn to do everything differently," said Frannie's mom, Hannah.

"Our therapists have worked on everything from practicing falling to using utensils to creating adaptive equipment. She met milestones later than some kids, but not that much later, thanks to our therapy team."

The arrival of COVID-19 threatened to interrupt
Frannie's therapy — a vital part of keeping her
development on track and teaching her how to do
everyday tasks. When the pandemic hit, she saw an
occupational therapist once a week and a physical
therapist every other week. On top of that, her physicians
had concerns about the impact that contracting COVID-19
could have on Frannie's health with her existing heart
condition. All of this meant switching to telehealth rehab
for nearly three and a half months.

"Because of COVID, we have tried to set up as much of a hybrid model of virtual and in-person therapy as we can," said Danielle Keeton, MA, CCC-SLP, Le Bonheur's director of Rehabilitation and Developmental Services. "Success of virtual therapy is very dependent on the individual needs of the child and family."

Telehealth rehab for Frannie looked a bit different from usual therapy services. Therapists spent more time talking through her needs and modeling activities for Hannah to replicate with her daughter. Telehealth therapy allowed her

to keep her development on track during the pandemic.

"Frannie is a hard worker, and she didn't lose any progress by using telehealth rehab," said Hannah. "They continued to give us ideas to work on the skills she needs to develop."

In May 2020, when elective surgeries were reinstated at Le Bonheur, Frannie underwent a pollicization surgery to create a thumb, giving her better grip and control. Telehealth therapy for surgery recovery was no longer a viable option. It was vital that her therapy services resume in-person

Three-year-old Frannie Crowley works with Occupational Therapist Hillary Carden to gain strength in the new thumb that surgeons created for her. Frannie was one of many children who used telehealth rehab during the pandemic.

in order for her new thumb to heal and develop the strength she needed to use it properly.

"Telehealth was fine, until it wasn't fine anymore," said Hannah. "If we weren't able to be in person for therapy, she definitely would not have progressed learning to use her thumb."

In June, Frannie was able to return to in person therapy, with Le Bonheur following all precautions for social distancing, cleaning and masking. Hannah says they have felt safe both at the doctor's office and at therapy. It mitigated the risks for Frannie's development and progress to halt during the COVID-19 pandemic.

"We love Le Bonheur very much and are so thankful for Frannie's therapists," said Hannah. "The therapists from Le Bonheur have been on top of it and work hard to get us the services we need. Frannie is excited to go to therapy — they know what she likes and make therapy fun for her."

- especially families with TennCare, Tennessee's Medicaid program for children, who depend on Le Bonheur's services.

The largest hurdle is the sheer number of children in need of rehab. A marked increase in trauma cases as a result of the pandemic increased the number of children who need immediate rehabilitation services. And when Memphis' Shelby County Schools were following a 100% virtual model, children lost access to in-person therapy through school. Many of these children are covered by TennCare. According to Keeton, physicians refer to Le Bonheur's rehab services in droves because it is difficult for families to find rehab centers where TennCare is accepted.

"Without access to care, some children will see a loss in function. We won't know all of the impact of missed developmental milestones for several years."

> Danielle Keeton, MA, CCC-SLP Le Bonheur Outpatient Rehabilitation & Developmental Services Director

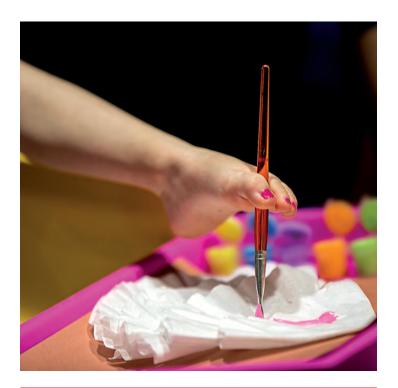
School therapists continue to provide services through telehealth. While highly effective for many kids, it requires large amounts of caregiver participation.

"We provide telehealth therapy services in our own school-based and early intervention programs, and it works very well. Only sometimes do acute needs require in-person evaluation, hands-on attention and specialized equipment to see progress," said Keeton. "This is especially true for children with caregivers who, for very legitimate reasons, are unable to participate in telehealth sessions. We see parents juggling so many priorities right now."

On top of this backlog: concern for missed developmental red flags that could lead to substantial future impacts.

"Without access to care, some children will see a loss in function," said Keeton. "We won't know all of the impact of missed developmental milestones for several years."

Child care centers, schools and pediatrician offices



Rehab Services: Telehealth Appointments

16,540 total telehealth rehab appointments conducted through Le Bonheur since April 2020

serve as safety nets to catch children early who need therapy intervention for development. Closed child care centers, virtual school and missed doctor's appointments mean that these preventative measures are missed.

But Keeton sees the pandemic as a wake-up call to the barriers that families and children have to access care, with so many depending on Le Bonheur's limited resources without access to in-person therapy options through the school system.

"These inequities and social barriers to care have always been present, but the pandemic has raised more community awareness of the unmet support for families who have children with special needs," said Keeton. "The success of a child is always about the success of the family."

ANNOUNCEMENT

Biorepository and Integrative Genomics Initiative partners with biotechnology company to sequence 25,000 DNA samples

s research into genetic causes of disease began to grow, Le Bonheur Pediatrician-in-Chief Jon McCullers, MD, knew it was time to start building a pediatric DNA biorepository.

So in 2015, Le Bonheur's Children's Foundation Research Institute (CFRI) created the Biorepository and Integrative Genomics (BIG) Initiative and began collecting DNA samples from hospitalized children at Le Bonheur with the consent of their parents.

"We knew then that changes in genes impact health and cause disease. We began collecting DNA samples in the hope that at some point we would be able to sequence the DNA and use it for research," said McCullers.

Five years and more than 10,000 DNA samples later, this dream is becoming a reality. Le Bonheur



Le Bonheur Genetics Chief Chester Brown, MD, PhD, says that targeted genetic therapies are the future of medicine. Obtaining genetic information from Le Bonheur's biorepository samples is foundational for research into these new possibilities.



More than 10,000 pediatric DNA samples from consenting participants are currently included in the Biorepository and Integrative Genomics Initiative.

and the University of Tennessee Health Science Center (UTHSC) recently signed an agreement with a leading biotechnology company to obtain genetic information from 25,000 DNA samples in the next five years with the option to increase that number to 100,000. This partnership is a step forward to support research to better understand the genetic contributions to disease and the ultimate goal of precision medicine.

Precision medicine uses genetic and other important health information to either correct or reduce the effects of genetic abnormalities or to understand which therapies will be most effective.

Research into this field requires a diverse team — physicians who understand the most important medical questions, researchers who know how to analyze the DNA to answer those questions and laboratories with the capability to generate the data on a large scale and help develop new medical therapies.

"Genetic data from the biorepository will provide the foundation for research that can change the way we practice medicine to provide more precise therapies," "Genetic data from the biorepository will provide the foundation for research that can change the way we practice medicine to provide more precise therapies."

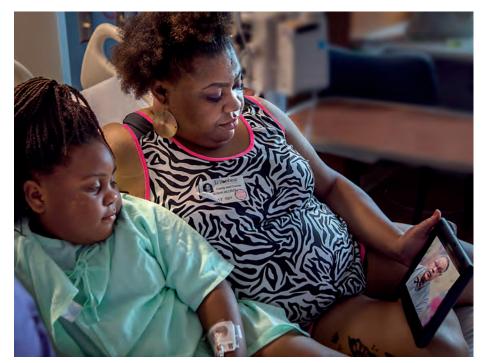
Le Bonheur Genetics Chief Chester Brown, MD, PhD

said Le Bonheur Genetics Chief Chester Brown, MD, PhD.

Le Bonheur's biorepository is one of only a handful in the country devoted to pediatrics. In addition, Memphis' pediatric population provides a unique opportunity to focus on minority health issues and disparities. Forty-five percent of the biorepository samples are from African-American children — a unique feature compared to other pediatric biorepositories in the country.

BIG collects leftover samples that would otherwise be thrown out from Le Bonheur patients

in the inpatient, outpatient and Emergency Department settings. Appropriate consent is obtained and education provided for parents and caregivers to understand how their child's sample will be used to contribute to the future of medicine.



Each parent and child who consents to adding their DNA to the BIG repository watches a short video explaining that their DNA will be used to help make new medical discoveries for children.

But the pediatric biorepository is just the beginning for DNA sequencing and research at Le Bonheur.

"The second phase of our biorepository is to go statewide and get to 100,000 individual samples as a part of the

University of Tennessee 100,000 genomes project,"

said McCullers. In addition, Le Bonheur is partnering with a local

While all samples are de-identified for research purposes, each sample connects to the patient's

electronic medical record (EMR) through a secured process. This includes a longitudinal health record of every patient, so researchers know a child's health conditions, but not who they are. This sample can be traced back to a patient in the event that any beneficial therapies are discovered that pertain to that individual.

BIG BY THE NUMBERS

70% of all screened participants enroll **10,000+** DNA samples **125** samples added per week 45% of samples are African American

BIG RESEARCH AREAS OF **INTEREST INCLUDE:**

Asthma Cystic Fibrosis Down Syndrome Duchenne Muscular Dystrophy Hirschsprung Disease Prader-Willi Syndrome **Tourette Syndrome Tuberous Sclerosis** Complex Type I Diabetes Obesity

adult hospital. Regional One Health, to start an adult biorepository that will be housed at Le Bonheur.

"DNA sequencing will give us insight into diseases that are not just a one gene model but have effects from multiple genes," said Brown. "Our ultimate goal is to provide higher quality care for our patients tailored to the individual."

Meeting the Need for School Nurses

School nurse pilot aims to improve health, reduce absenteeism



t the start of the school term, a teacher at A.B. Hill Elementary noticed a neck rash on one of the students. In previous years, without a full-time school nurse on staff, the teacher might have called the child's parents to let them know or might have sent the child home, typically the only methods of recourse when presented with health issues in the classroom.

But this year, the teacher had a better option. The student saw Le Bonheur school nurse Patricia McGraw, who had recently joined the elementary school team as part of a pilot project seeking to determine if dedicated school nurses could improve the health of children in Memphis and Shelby County and reduce rates of chronic absenteeism.

Nurse McGraw identified the rash as possible Acanthosis Nigricans, a sign of diabetes in children. She connected with the student's parents to help them understand the issue and seek additional care. After receiving a formal diabetes diagnosis and insulin prescription, McGraw initiated diabetic teaching with the child back at school.

It's one of dozens of examples illustrating the impact made by nurses in the pilot program, a partnership initiated in the 2019-2020 school year by Le Bonheur Children's Hospital, Shelby County Schools and Urban Child Institute.

Less than a year into the pilot, initial results show an 85% return to class by children who saw their school nurses, better management of chronic conditions and increased referrals for health issues likely to have gone unnoticed without professional evaluation.

The five schools chosen by Memphis' Shelby County School system to participate in the pilot — A.B. Hill Elementary, Riverview K-8, Hamilton K-8, Hamilton High School and Magnolia Elementary — are known as "feeder schools," meaning they involve family members in multiple grades. Five comparison schools were also chosen for evaluation purposes.

The concept of school nursing has existed for a century; but uniformity among states and school districts varies greatly, as do the laws governing school health services. Some school districts in the rural Mid-South, such as Tipton County, provide a nurse in every school, while others such as Shelby County provide, on average, a nurse in each school for only four hours a week. The current Tennessee ratio equates to one nurse per 3,000 students.

As part of this pilot, one Le Bonheur nurse is embedded in each of the five schools, while a nurse practitioner and social worker rotate among the schools. They function as staff members, actively working with students, teachers and families to keep children healthy, safe and ready to learn.

Services include:

- · Providing care or first aid for sick and injured students and staff
- Helping parents and health care providers obtain necessary health information
- · Administering medications as ordered by the physician and

necessary for school attendance

- Assisting with state-mandated school health screenings
- Helping families find other specialized doctors and nurses when needed
- Ensuring students have the required vaccines and physical exams for school
- Providing staff emergency first aid and CPR training
- Helping families learn to care for chronic diseases like asthma and diabetes, when needed
- Providing weekly support from a licensed social worker and nurse practitioner

Outcomes indicated success, according to research by Debra Bartelli, DrPH, Research Associate Professor, Division of Epidemiology, Biostatistics, and Environmental Health & Director of Undergraduate Programs at The University of Memphis.

Teachers overwhelmingly agree that the program has improved the health of students in their school and say that with a nurse in the schools, they have more time to teach. Principals also strongly endorse that the program has resulted in an increased number of children returning to the classroom after seeing the nurse for health concerns.

Based on this early success, the Shelby County Schools leadership team is interested in expanding the school nurse



program in an additional five schools. The ultimate goal is to provide a nurse in every Shelby County school.

Le Bonheur School Health Services Director Cindy Hogg said the pilot has also highlighted the value of relationship building, an intangible core aspect of community outreach work.

"One thing we've seen is the trust parents have for our nurses," she said. "This is really important when it comes to children who have chronic conditions like asthma, and the result is that our nurses are able to partner with families when making the call about whether these children can stay in school or need to seek higher levels of care."

Teacher Response

SHELBY COUNTY SCHOOLS NURSE PILOT PROJECT PRELIMINARY EVALUATION FINDINGS, UNIVERSITY OF MEMPHIS

Response from Le Bonheur School Health Services pilot participants 88% of teachers responded

- 95.7% agree that the program has improved the health of their students
- 90.6% agree that having the nurse in the school allowed them to spend more time teaching
- 96.1% agree that the nurse had a positive impact on the overall well-being of students
- 95.3% agree that the nurse had a positive impact on overall well-being of students with chronic conditions
- 86.8% agree the nurses had a positive impact on improving academic performance for students

Response from five control schools

42% of teachers responded

- 66.1% agree that school nurses improved the health of their students
- 70.5% agree that having the nurse in school allowed them to spend more time teaching
- 62.5% agree that the nurse had a positive impact on the overall well-being of students
- 65.4% agree that the nurse had a positive impact on overall well-being of students with chronic conditions
- 52.2% agree that the nurses had a positive impact on improving academic performance for students

The American **Academy of Pediatrics** (AAP) recommends that each school has its own full-time nurse due to the increase of chronic conditions in children, including asthma. The increased survival of pre-term infants and children born with congenital anomalies has resulted in more children with disabilities and chronic diseases. The number of children with behavioral issues has also



In the initial responses from the pilot schools, 90.6% agreed that having the nurse in the school allowed them to spend more time teaching, and 86.8% agreed that the nurses had a positive impact on improving academic performance for students.

increased. Caring for these children in school requires the services of a professional registered nurse.

Since program implementation in the pilot schools, approximately 2,750 nurse visits were completed. The COVID-19 pandemic and early school closures cut those numbers short, though when school returns in person, the role of the school nurse is sure to be even more critical to community health. And during this time, nurses have kept in contact with students known to have chronic conditions to ensure proper case management. They've also participated in efforts such as creating pop-up food pantries to help families experiencing food insecurity.

"We can focus on children's health needs and the educators can focus on educating, which takes a huge weight off of their shoulders," said Charnece Brown, Le Bonheur school nurse supervisor. "With a rotating system, there is not as much continuity of care and many gaps. Although they are wonderful professionals, it's rare that school staff has a health care background. As a result, many health care needs can be left untreated."

The difference a school nurse makes can be seen with another anecdote, this time from pilot school Hamilton K-8 and a sixth-grader experiencing frequent nosebleeds.

Rather than experiencing the old hallway head-tilt, this student saw his Le Bonheur school nurse. The nurse watched the child for several days and found his blood pressure to be extremely high for his age. The nurse notified his parents, who took the student to a physician's office, where the child was determined to have hypertension.

Thus, not only could the child return to class, he was able get treatment for the underlying issues that were taking him out in the first place.

PROFILE: DENNIS BLACK, MD

Children's Foundation Research Institute Scientific Director exudes passion for research, music

ennis Black, MD, shares a near-equal love for science and rock and roll. He's an accomplished researcher, award-winning physician and an avid vinyl record collector. He spent his days in high school and college working at the local radio station, while also taking all the necessary courses for a career in medicine.

Today, Black is scientific director of the Children's Foundation Research Institute (CFRI), a pediatric gastroenterologist and co-owner of Memphis-based music label, Black and Wyatt Records. He's a man who certainly proves the expression, "There's more than meets the eye."

Black grew up in Covington, Tenn., a small

city 40 miles north of Memphis. The town's family practitioner sparked Black's interest in medicine.

"As a kid, I was always fascinated going to his office," said Black. "His tools and instruments. The thoughtful way he could examine a patient and come up with a diagnosis."

His career as a pediatric gastroenterologist and researcher has taken him from Memphis for medical school, pediatric and gastroenterology (GI) training to Chicago, Ill., to Little Rock, Ark., and back to Memphis. As a clinician he specializes in pediatric liver diseases and was part of the team responsible for the very first living donor liver transplant in a pediatric patient in the country in 1989 at the University of Chicago.

As a scientist, Black has taken a fascination to studying lipids and understanding how they are absorbed in children and neonates. He has focused on apolipoprotein A-IV and



Scientific Director, Children's Foundation Research Institute
Vice President of Research, Le Bonheur Children's Hospital
J.D. Buckman Professor of Pediatrics, The University of Tennessee Health Science Center
Vice Chair for Research, UTHSC Department of Pediatrics

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demonstrated a role for this protein in facilitating fat absorption in the neonatal small intestine. He also showed that genetically altering the structure of the protein could significantly enhance fat absorption, which may lead to a therapy to improve fat absorption in infants with intestinal failure. The research side of medicine, in particular, is Black's passion and has earned him more than \$8 million in funding for his research from organizations like the National Institutes of Health (NIH) and the Food and Drug Administration (FDA).

"I love the process of coming up with a research idea, setting up and designing the experiment, carrying out the experiment and getting results," said Black. "And

when your hypothesis is validated, there's a huge satisfaction."

His latest research project funded by the FDA Office of Orphan Product Development, published in *Hepatology Communications*, evaluated the use of ursodeoxycholic acid in the treatment of primary sclerosing cholangitis (PSC), a rare liver disease. That work earned him the Gerard Odell Prize for Excellence in Hepatology Research from the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition and could make way for promising new drugs that can treat PSC, for which transplantation is the only cure.

It was research that drew Black and his family — wife, Pediatrician Gail Beeman, MD, and their three children — back to Memphis, where his medical career first began. He was recruited in 1999 to serve as scientific director for the Children's Foundation Research Institute, then called the Crippled

Children's Foundation Research Center. He is also vice president of Research at Le Bonheur and the J. D. Buckman endowed

professor of pediatrics at the University of Tennessee Health Science Center (UTHSC).

Memphis, known for its music, has been the perfect place for Black to nurture his two passions: research and music. He started a vinyl-only record label in 2018 with colleague Pediatric Nephrologist Robert Wyatt, MD. The label, Black and Wyatt Records, was created to give a platform to local



In addition to his career as a researcher and physician, Dennis Black, MD, is co-founder of the vinvl-only record label Black and Wyatt Records. He established the label in 2018 with colleague Pediatric Nephrologist Robert Wyatt, MD, to highlight local Memphis talent.

musicians and support the Memphis music scene. The label has released eight records, and two more releases are planned by the end of the year. The record company has been more of a spare-time hobby than a business, but one that has been a real joy for Black and Wyatt and a boost for local Memphis talent.

And as for research: Black and other leaders have worked hard to transform the CFRI — a collaboration among Le Bonheur, UTHSC and the Children's Foundation of Memphis - into a world-class organization with 30,000 square feet of lab and research space. Last year, CFRI investigators received more than \$9 million in NIH and other external funding, and faculty members assisted by CFRI published more than 217 papers with 39% appearing in the top 25% of high-impact journals.

"We used to have two floors of laboratory space in the Le Bonheur West Tower for the research center and that was all," said Black. "We've recruited top notch researchers, more than doubled our faculty and now have a dedicated tower on

> (Le Bonheur's) campus for research efforts."

In 2010, Le Bonheur leaders and major long-time CFRI supporter, the Children's Foundation of Memphis, made a commitment to invest in research expansion renovating its seven-story West Tower, purchasing state-of-the-art equipment and hiring the human resources needed to support researchers, including experts in biomedical informatics

and biostatistics.

It's created an atmosphere of learning and discovery that Black loves.

Black was awarded the Department of Pediatrics annual Excellence in Mentorship Award in 2017 and the American Gastroenterological Association Institute Council Section on Obesity, Metabolism and Nutrition Research Mentor Award in 2020.

"I enjoy helping young researchers and physicians. Getting to know them and mentor them along the way in their projects," said Black. "I tell my students, 'There aren't many professions out there where you can take something you're really interested in and are supported to delve deeper into it.' To be successful (with research), it has to be more than a passing interest. There has to be a fire in your belly."

Education and Training

The University of Tennessee Health Science Center -Medical School

Le Bonheur Children's Hospital – Internship, Residency and Pediatric Gastroenterology Fellowship

Board Certifications

American Board of Pediatrics, Sub-board Gastroenterology

Society Memberships

American Gastroenterological Association, American Heart Association, American Pediatric Society, Society for Pediatric Research, American Association for the Study of Liver Diseases, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

Dennis Black, MD

Awards and Honors

Alpha Omega Alpha Honor Society

J.P. Quigley Award in Physiology Merck Medical Publications Book Award

Special Achievement Award, The University of Tennessee Health Science Center

Special Achievement Award, Mid-South Chapter of the American Liver Foundation

The University of Tennessee Health Science Center College of Medicine Outstanding Alumnus of the Year Award The University of Tennessee Health Science Center Department of Pediatrics Etteldorf Alumni Award

Excellence in Mentorship Award, The University of Tennessee Health Science Center Department of Pediatrics and Le Bonheur Children's Hospital

Gerard Odell Prize for Excellence in Hepatology Research, North American Society for Pediatric Gastroenterology, **Hepatology and Nutrition**

American Gastroenterological Association Institute Council Section on Obesity, Metabolism and Nutrition Research Mentor Award



PILOT STUDY: SHAM FEEDING IN POST-OPERATIVE NEONATES MAY ENHANCE ORAL DEVELOPMENT, **DECREASE MATERNAL STRESS LEVELS**

Tham feeding may enhance oral skill development in neonates after bowel surgery and decrease stress levels in mothers, says research published by Le Bonheur Neonatologist Mark Weems, MD, in the American Journal of Perinatology.

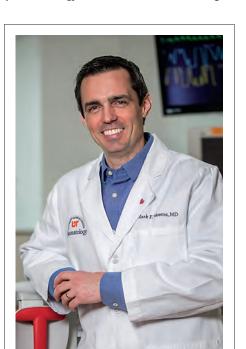
This research marks the first time that sham feeding post-operative neonates has ever been described in published literature. The research is a result of a pilot study developed to test whether sham feeding would be feasible in this population, identify any safety hazards and assess the impact on mothers.

The novel sham feeding protocol used in the study was developed collaboratively between Le Bonheur's neonatology and pediatric surgery divisions. Sham feeding is the process of offering an oral feeding followed by the removal of the feed before digestion. In the study, all 15 infants enrolled were able to sham feed with just four infants experiencing minor complications. Mothers reported a decrease in stress and 100% satisfaction with sham feeding.

"Neonates who have abdominal surgery often have a considerable delay until they are able to initiate

oral feeding," said Weems. "This delay during a time that is critical for development of oral skills is further complicated by negative oral feeding stimuli, such as prolonged airway management and nasogastric tubes, which may negatively impact long-term outcomes."

The mothers of these children can also suffer from psychological morbidity from the stress of their stay in the Neonatal Intensive Care Unit (NICU), which can interfere with infant bonding and breastmilk supply and lead to longer NICU stays. Furthermore, mothers who cannot feed their babies often begin to feel helpless, said Weems. Le Bonheur neonatologists introduced sham feeding to attempt to mitigate these negative effects.



Le Bonheur Neonatologist Mark Weems, MD, recently published the first literature to ever describe sham feeding for post-operative neonates. The pilot study showed that sham feeding may be beneficial for oral skill development in neonates after bowel surgery and decrease stress levels in mothers.

"Post-operative delay in enteral feeding contributes to prolonged hospital stay, prolonged exposure to parenteral nutrition and increased risk of infection," said Weems. "Sham feeding is one place where we may be able to offer an

intervention for better outcomes."

In the pilot study, 15 patients admitted to the Le Bonheur NICU were enrolled for sham feeding after assessment for feeding readiness by a speech therapist. Infants were sham fed first by bottle and then at the mother's breast. Gastrointestinal suction remained on for the duration of the feed and for five minutes after the feed ended. An eight-question survey was administrated to mothers in the study to assess maternal stress and satisfaction with sham feeding.

Of the 15 patients, all were able to safely sham feed after surgery with a total of 312 sham feeds. After the satisfaction survey, all mothers reported a reduction in stress with sham feeding, and 86% reported that sham feeding improved the mother-infant relationship. All reported that they would recommend sham feeding.

The pilot study identified areas for additional research around sham feeding to:

- Determine the risks and benefits of sham feeding in post-operative infants
- Evaluate if sham feeding improves the development of oral skills when compared to non-nutritive sucking
- Assess the impact of sham feeding on postpartum depression and prolonged breastfeeding
- Test specific hypotheses in larger groups of infants with specific surgical diagnoses

"Our study demonstrates that sham feeding in neonates after abdominal surgery is feasible," said Weems. "Ultimately we may be able to improve long-term outcomes for both the mother and infant."

A SHOULDER TO LEAN ON

Neonatologist, social work team develop NICU screening program to connect parents with mental health support



Le Bonheur Neonatologist Jennifer M. Davidson, DO (far left), and social workers (second from left to far right) Toya Pride, LCSW, Tanekia Jones, LMSW, Jacqueline Thomas, LCSW, and Barbara Williams, LMSW, created the NICU Perinatal Mental Health Screening Initiative. This effort helps to identify parents in need of mental health intervention to the benefit of the parents as well as the health of the neonate.

One in seven new moms experience postpartum depression or anxiety. One in 10 new dads have parallel symptoms.

Observing the effect that parental mental health has on the physical health of a neonate, Le Bonheur Neonatologist Jennifer M. Davidson, DO, realized that the Neonatal Intensive Care Unit (NICU) at Le Bonheur Children's had a chance to intervene early in a child's life.

"We have always acknowledged the stress in a stay in the NICU," said Davidson. "The NICU has a unique opportunity to provide mental health support for parents to the benefit of the children in the unit."

Mental health struggles can be a driving factor that keeps parents from visiting their child in the NICU. The more a parent is present during a NICU stay, the better the long-term outcomes for the child. Davidson believes that by intervening in a parent's mental health, Le Bonheur can positively affect the physical health of a child for years to come.

Working closely with nurses, child life

specialists and lactation consultants, Davidson and the NICU social work team developed the NICU Perinatal Mental Health Screening Initiative to identify parents in need of intervention and provide needed mental health support with the ultimate goal of improving health outcomes for neonates.

BUILDING A PROGRAM

Le Bonheur's Social Work team consists of professionally trained and licensed master social

workers who help patients and families with a variety of issues that may arise as a result of a child's illness. Prior to the implementation of the formal program, the social work team provided mental health screening throughout the hospital — but only if the parent was referred. They noted a trend — the vast majority of referrals were coming from the NICU. In 2019 alone, social workers screened more than 120 neonatal parents.

"Parents with newborns in the NICU face



Jennifer Davidson, DO, and the NICU social workers meet weekly to discuss mental health screening results and parents who may need to be referred to a higher level of mental health support.

unique challenges and stressors including, but not limited to, postpartum mental health struggles. We knew that we needed a formal structure to provide these parents with the best support we could offer," said Davidson.

The NICU Perinatal Mental Health Screening Initiative was implemented in February 2020, and social workers now screen all mothers who have a baby in the NICU with a stay in the hospital longer than two weeks, using a standardized depression screening tool. This screening identifies possible mental health diagnoses, what interventions would be most beneficial and whether the parent is open to receiving help.

Subsequent interventions and support fall on a three-tier continuum. Parents who need the lowest level of support are provided with typical NICU support such as social work and child life to cope with stressors present at home or related to the birth of their child. The second tier consists of more focused social work support and education. Parents have a brief consultation with Licensed Psychologist Carlos Torres, PhD, where they are given coping strategies to apply to their situation. And the highest level is clinical support including one-on-one counseling and frequent follow up with Torres. Medication support is provided when needed, and the team continues to track any cognitive or behavioral symptoms.

"We are always asking the question 'Does this mom have good support?" says Davidson. "Social support is key for parents with mental health struggles. We can ensure that parents who need it are connected with others whether through individual counseling or parent support groups."

The hospital also has a general parent support group that meets weekly. Caregivers who want social support and connection discuss the emotional burdens associated with having a sick child in the hospital. Plans are in place to start a support group specifically for NICU parents.

Support doesn't end when a child is discharged from the NICU. Social workers create a discharge plan for parents to ensure continuity of care including connecting parents to a community provider for counseling when needed.

LASTING CHANGE

One of the roadblocks that Davidson and her team uncovered was the stigma toward mental health that still exists in the South — and the unique issues that Memphis families face in that regard.



Mental health intervention for parents can directly impact the health of the neonate. By improving parental mental health, Le Bonheur neonatologists hope to decrease the length of hospital stays, increase parent visits and increase bonding between parent and child.

"Philosophies around strength and what that looks like can be a hindrance to getting parents the support they need. We're working to break down beliefs and fight against the stigma of mental health," said Davidson.

Success in the fight to provide mental health support leads to more than just improved parental mental health — it's a chain reaction delicately interconnected with the child's physical health.

The better the parent's mental health, the more often they visit his or her child in the NICU. And the more time a parent spends in the NICU with his or her child, the better the child's long-term outcomes.

Over time, Davidson hopes to affect change in the physical health of NICU babies by decreasing the length of hospital stays and increasing parent visits thereby increasing bonding between a parent and child.

"We're trying to help parents be present more often," said Davidson. "Integrated behavioral health is embedded in what we do at Le Bonheur, and the NICU strives to start this chain reaction from a baby's first days of life."

Early PDA closure

may improve outcomes in preterm infants

Le Bonheur cardiologists evaluate the benefits of PDA closure prior to 4 weeks of age

Extremely low birth weight (ELBW) infants with moderate to large patent ductus arteriosus (PDA) may benefit from transcatheter PDA closure (TCPC) in the first four weeks of life, according to research published by Le Bonheur Cardiologist Ranjit Philip, MD, and Medical Director of Interventional Cardiac Imaging and Interventional Catheterization Laboratory Shyam Sathanandam, MD. Early PDA closure may prevent early onset pulmonary vascular disease, promote growth and facilitate faster weaning off supplemental oxygen and ventilator support.

"The primary objective of this study was to describe changes in hemodynamics, respiratory support and growth associated with TCPC in ELBW infants," said Philip. "We also wanted to describe clinical outcomes in early versus delayed PDA closures to identify factors associated with worse clinical outcomes."



The study followed 100 infants with a hemodynamically significant PDA (hsPDA) who were born at less than 27 weeks gestation, weighed less than 1 kg at birth and were referred for possible TCPC. The infants were separated by age into those who underwent TCPC at younger than 4 weeks (group 1), 4-8 weeks (group 2) and older than 8 weeks of age (group 3).

A hemodynamic assessment was completed as part of the procedure and included baseline pulmonary to system flow ratio, pulmonary artery systolic pressure (PASP), degree of shunting and pulmonary vascular resistance. To assess respiratory outcomes of these infants, a respiratory severity score (RSS) was calculated by a product of the mean airway pressure and the fractional inspired oxygen with a lower score denoting less respiratory support.

"The presence of moderate to large PDA in ELBW preterm infants is associated with poor respiratory outcomes and an increased mortality," said Philip. "Our study aimed to determine if early PDA closure demonstrated a reduction in these adverse outcomes."

While all infants were on mechanical ventilator support at the time of TCPC, baseline RSS was highest for infants in group 3. Although younger and smaller, infants in group 1 were able to extubate sooner compared to group 3 and reach an RSS of less than two (denoting minimal support) significantly faster than those with late PDA closure.

Pulmonary hypertension (PHT) also influenced RSS. Those with PHT were referred for PDA closure later and consequently had a higher pre-procedure RSS. This group took a longer time to return to baseline RSS following TCPC in comparison to infants without PHT.

Finally, age at PDA closure affected weight gain for these infants. Specifically between four and eight weeks, the weight gain for infants in group 1 was much more rapid than those in group 3 who still had the PDA at this age.

"Growth during the four to eight week period is important for the overall outcomes of these ELBW infants," said Philip. "This further supports the notion that earlier PDA closure would be beneficial for ELBW infants."

The study's results raise questions regarding when, how and whether a PDA should be closed in ELBW infants. Based on this study, benefits of early closure in ELBW include rapid improvement of respiratory status and normal weight gain. Delayed PDA closure

and PHT are risk factors for worse respiratory outcomes.

In terms of how closure is performed, the study shows that TCPC can be performed with good success with no significant adverse events while also obtaining invaluable information on hemodynamic significance. And finally, this is the first published study of PDA closure whose hemodynamics were measured prior to closure.

"When we first started offering this novel procedure, the



Le Bonheur Cardiologist Ranjit Philip, MD, recently studied early transcatheter PDA closure (TCPC) in extremely low birth weight (ELBW) infants. Results showed that ELBW infants may benefit from TCPC in the first four weeks of life.

infants were usually older and more critical. Since January 2016, with our growing experience in TCPC, younger and smaller infants are being referred," said Philip. "As our team has gotten more comfortable with the procedure and post-procedure care, ELBW infants are referred for TCPC between the second and third week of life."

Philip and the Le Bonheur cardiologists work closely with neonatology teams at Le Bonheur and referring centers in order to provide excellent care for ELBW infants with hsPDAs and determine the best course of treatment for each patient.

The study concluded that it may be beneficial to close hsPDAs in the first four weeks of life before the onset of elevated pulmonary vascular resistance in ELBW infants with the additional benefits of faster weaning off ventilator and oxygen support and better weight gain. Researchers concluded that additional RCTs are needed to examine the short- and long-term benefits for ELBW infants, evaluating no intervention versus TCPC and long-term neurodevelopmental outcomes.



Le Bonheur Cardiologist Jason Johnson, MD. MHS (left), and Le Bonheur Neonatologist Mark Weems, MD (right), moderated the International PDA Symposium in October 2020.

Le Bonheur holds virtual International PDA Symposium for 1,700 registrants

In October 2020, Le Bonheur's Heart Institute hosted the International PDA Symposium virtually for 1,700 registrants from around the world. The goal of this symposium is to facilitate building a consensus in management of PDA in preterm infants.

Speakers covered topics ranging from trend in management of preterm infants with PDA to ongoing PDA trials to transcatheter PDA closure in premature infants. This is the third year that Le Bonheur's Heart Institute has held the International PDA Symposium.

To view the recording of the symposium, visit pdasymposium.org.

Brown named to list of inspiring black scientists

Le Bonheur Genetics Chief Chester Brown, MD, PhD, was recently named among the "1,000 Inspiring Black Scientists in America" by the journal Cell Mentor. This list was compiled by The Community of Scholars members of the group Persons Excluded because of their Ethnicity or Race (PEER).



Chester Brown, MD, PhD

Nuclear medicine receives three-year reaccreditation from American **College of Radiology**

N COLLEGE OF A A recent review awarded the nuclear medicine department a three-year reaccreditation term from the American College of Radiology (ACR). The ACR gold seal of accreditation represents the highest level of image quality and patient safety awarded only to facilities meeting ACR Practice Parameters and Technical Standards after a peer-review evaluation.

Hysmith, McCullers, Weatherspoon named Health Care Heroes by the **Memphis Business Journal**

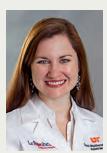
Le Bonheur Director of Infection Prevention Nick Hysmith, MD, Le Bonheur Pediatrician-in-Chief Jon McCullers, MD, and Le Bonheur Pediatric Neurologist Sarah Weatherspoon, MD, were recently named Health Care Heroes by the Memphis Business Journal (MBJ). Each year the MBJ recognizes individuals and organizations for their contributions to improving health care in the Mid-South.



Nick Hysmith, MD



Jon McCullers, MD



Sarah Weatherspoon, MD

Sawyer elected to presidential line of POSNA

Le Bonheur and Campbell Clinic Orthopedist Jeffrey R. Sawyer, MD, was elected to the presidential line of the Pediatric Orthopaedic Society of North America (POSNA). He currently serves on the POSNA Board of Directors as vice president.



Jeffrey R. Sawyer, MD

Rebolledo named to American College of Cardiology subcommittee

Le Bonheur Cardiologist Michael Rebolledo, MD, MBA, MPH, was selected by the American College of Cardiology as a member of the Adult Congenital and Pediatric Cardiology (ACPC) Quality Network Subcommittee. This subcommittee focuses on outpatient pediatric cardiology quality measures.



Michael Rebolledo, MD, MBA, MPH

Lieberman receives multiple leadership appointments

Le Bonheur Allergist/Immunologist Jay Lieberman, MD, was named chair of the Food Allergy Committee and vice chair of the Annual Program Committee for the American College of Allergy, Asthma and Immunology. He was also elected as a board member of the American Board of Allergy and Immunology.



Jay Lieberman, MD

Le Bonheur Pediatric & Adolescent **Sleep Disorders Center receives** reaccreditation

The American Academy of Sleep Medicine (AASM) recently granted the Le Bonheur Pediatric & Adolescent Sleep Disorders Center a five-year reaccreditation. This sleep facility accreditation includes accreditation for all types of sleep testing, including in-center polysomnography, multiple latency testing, maintenance of wakefulness testing and home sleep apnea testing.



Cystic Fibrosis Center receives Outstanding Care Center Partnership Award

The University of Tennessee Cystic Fibrosis Care and Research Center at Le Bonheur was recognized with the Outstanding Care Center Partnership Award at the North American Cystic Fibrosis Conference. This award recognizes

exceptional collaborative work with the local cystic fibrosis community through outreach and education.



Samarasinghe awarded research grant from the American Lung Association

Le Bonheur Researcher Amali Samarasinghe, PhD, was awarded the Charles and Amelia Gould Innovation

award amounting to \$75,000 for two years through the American Lung Association's Awards and Grants Program. Samarasinghe's research is focused on eosinophils, cells important to the development of asthma, and how they respond to influenza virus and Stretococcus pneumoniae bacteria when exposed to both agents simultaneously.



Amali Samarasinghe, PhD

Le Bonheur's Children's Foundation Research Institute joins the I-ACT for Children Site Network



The Children's Foundation Research Institute (CFRI) at Le Bonheur was recently accepted to the Institute for Advanced Clinical Trials (I-ACT) for Children Site Network. This is a globally collaborative research network that enables regulatory-grade scientific data to support the safe and effective use of new medicines and devices in children.



Le Bonheur begins COVID-19 vaccinations

Le Bonheur recently received the first shipments of COVID-19 vaccine and began vaccinating staff, providers and physicians. Individuals at Le Bonheur are vaccinated on a priority basis until all who choose to get the vaccine receive it. This is the next critical step in the fight against the COVID-19 pandemic.

Pictured above is Le Bonheur Hospitalist Cynthia Cross, MD, the first front-line provider at Le Bonheur Children's Hospital to receive a COVID-19 vaccine.



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Le Bonheur's Heart Institute Earns Accreditation from the Adult Congenital Heart Association

he Mid-South Adolescent and Adult Congenital Heart Disease
Program at Le Bonheur's Heart Institute earned accreditation from the
Adult Congenital Heart Association (ACHA), a nationwide organization
focused on connecting patients, family members and health care providers
to form a community of support and a network of experts with knowledge
of congenital heart disease (CHD). The accreditation recognizes expertise in
serving adults with CHD, structural heart conditions present at birth.

"Le Bonheur is dedicated to providing the best health care for children including those going into adulthood with congenital heart disease," said Le Bonheur Cardiologist and Medical Director of Adult Congenital Heart Disease B. Rush Waller, III, MD. "Our ACHD program's purpose is to ensure

that patients with heart disease have easy access to lifelong care from cardiologists who are specially trained to care for their unique issues. We are very excited about this accreditation for our program."

Le Bonheur received accreditation by meeting ACHA's criteria, which includes medical services and personnel requirements, and going through a rigorous accreditation process, both of which were developed over a number of years through a collaboration with doctors, physician assistants, nurse practitioners, nurses and ACHD patients. The Le Bonheur cardiologists in this program are also all board certified in adult congenital heart disease. Le Bonheur is one of 40 ACHA ACHD accredited programs throughout the United States.