Hope and Healing Through Innovation

Children’s Healthcare of Atlanta and Emory University

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Message From Dr. Lucky Jain

Doing everything possible to make anything possible for kids

Dear Colleagues,

As I look across the expanded North Druid Hills campus, and the new Arthur M. Blank Hospital, meet with colleagues at Emory University’s new Health Sciences Research Building II (HSRB-II), and review breakthrough achievements by our clinical and research teams, I am reminded of how much we can accomplish with dedication, collaboration and a willingness to do everything possible to make anything possible for kids.

The Children’s Healthcare of Atlanta and Emory University School of Medicine Department of Pediatrics partnership is stronger than ever, and together, we continue to reach new milestones. Last year alone, Children’s and Emory conducted 59 new clinical trials, enrolled more than 2,600 patients in clinical research, and tracked more than 1,900 hours of patient visits in the Children’s Pediatric Research Unit.

A testament to our progress is the national recognition of our members and programs. Children’s continues to be ranked among the nation’s top pediatric hospitals by U.S. News & World Report for 2023-2024, with four specialties ranked in the top 10, including cancer, gastroenterology and GI surgery, urology and orthopedics.

Together, Children’s and Emory have made incredible strides in our research journey. With the support of multiple grants, we can continue to shape the future of pediatric medicine. These include:

- The principal award by the Pediatric Emergency Care Applied Research Network (PECARN) for the Emergency Medicine research team, recognized as one of only seven nodes in the country to develop best practices in the care for critically ill and injured children
- A $74 million five-year grant for the Atlanta Center for Microsystems Engineered Point-of-Care Technologies, a collaboration between Children’s, Emory and Georgia Tech, to help refine and conduct clinical validation of diagnostic technologies from across the nation, with the objective of accelerating their path to translation and clinical adoption

These grants are part of the $164 million in extramural funding we received during Emory’s 2023 fiscal year—the highest amount ever attained and more than 15% of the $1 billion of total funding achieved by Emory University.

I am proud to share more information about our efforts to advance pediatric care in the 2023 Children’s and Emory Research Report. You’ll see that the unwavering commitment of our clinicians, researchers, educators and support teams truly is making an impact on the lives of kids worldwide, and will continue to do so for generations to come.

Best wishes,

Lucky Jain, MD, MBA
Pediatrician-in-Chief,
Children’s Healthcare of Atlanta
George W. Brumley Jr. Professor and Chair,
Emory University School of Medicine Department of Pediatrics
Children’s Healthcare of Atlanta collaborates with neighboring Atlanta-based academic institutions, Emory University and the Georgia Institute of Technology, to facilitate advanced pediatric care through innovation and discovery.

Egleston Hospital and Emory University first established a pediatric teaching relationship in 1956. This partnership has continued to develop into a hub for leading-edge pediatric research, training and innovation. Today, more than 500 physician-scientists hold appointments at both institutions through a unique employment agreement. Discoveries made in Emory’s labs are translated into lifesaving treatments for patients at Children’s.

Similarly, Children’s providers have access to the latest in technological advancements through the Children’s Healthcare of Atlanta Pediatric Technology Center (PTC), which joins Children’s clinical experts with nation-leading scientists and engineers from Georgia Tech to develop novel technologies for children. The PTC has three key pillars: data science, machine learning and artificial intelligence; patient-centered care delivery; and technologies and devices.

When these three Atlanta pediatric research partners join forces, the outcomes are tremendous, yielding clinical solutions with the potential for public adoption nationwide.
Research by the Numbers

Ranked No. 5
nationally in NIH funding for pediatric departments

$47 million
in funding from NIH

$164 million
in total extramural funding

755 residents and fellows in training

125 new clinical studies opened at Children’s

250 new grant and contract awards totaling $89 million

1,123 hours of CME credits through

152 educational activities for

17,492 participants

2,607 Children’s patients enrolled in clinical studies

1,870 publications in 864 journals

1,986 visit hours in the Children’s Pediatric Research Unit

Our research program has maintained a top 5 ranking for NIH funding since 2016.

Funding Reaches Historic Highs

During fiscal year 2023, Emory’s Department of Pediatrics, which is Children’s primary academic partner, received the highest amount of extramural funding in its history. The once tiny department had only $8 million in total extramural funding in 2005. In the same year, Children’s started planning a path to research excellence. Through this effort and other outstanding commitments, in 2023 the department attained $164 million in funding, exceeding 15% of the total research funding for Emory University. Thirty Children’s and Emory investigators each received $1 million or more in extramural funding:

- Wilbur Lam, $68,799,374
- Eric Sorscher, $6,831,333
- Ann Chahroudi, $4,738,023
- Raymond Schinazi, $3,926,154
- Subramaniam Kugathasan, $3,789,108
- Stefan Sarafianos, $2,883,310
- Douglas Graham, $2,253,066
- Evan Anderson, $2,229,532
- Gregory Melikian, $2,207,765
- Vivien Sheehan, $1,902,315
- Jason Yusteın, $1,829,532
- Saul Karpen, $1,815,913
- David Archer, $1,801,136
- Mehul Suthar, $1,659,037
- Rabindra Tirouvanziam, $1,624,809
- Anne Fitzpatrick, $1,617,276
- Cheng-Kui Ou, $1,563,267
- Renhao Li, $1,559,369
- Harold Trent Spencer, $1,539,371
- Rachel Linne mann, $1,503,447
- Robert Sidonio, $1,480,341
- Soumitri Sil, $1,424,881
- Claudia Morris, $1,416,331
- Dmitry Shayakhmetov, $1,305,211
- Baek Kim, $1,274,491
- Lou Ann Brown, $1,221,391
- Steven Goudy, $1,217,998
- Benjamin Kopp, $1,184,923
- Brian Zanoni, $1,109,353
- Miriam Vos, $1,040,300

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*This data is represents the 2023 calendar year.

In March 2023, the largest health sciences research facility in Georgia opened on Emory’s campus adjacent to Egleston Hospital.

The new, eight-story, 350,000-square-foot Health Sciences Research Building II (HSRB-II) boasts two floors with 42,298 square feet of laboratory and office space dedicated to pediatric research. The facility is home to 32 pediatric researchers focusing on child health, such as Children’s Infectious Disease Specialist and Emory Professor of Pediatrics Ann Chahroudi, MD, PhD, whose lab aims to find a cure for HIV, Children’s Cardiologist and Emory Professor of Pediatrics Matthew Oster, MD, MPH, focusing on outcomes data for congenital heart disease, and Manoj Bhasin, PhD, Director of Single-Cell Genomics for the Aflac Cancer and Blood Disorders Center of Children’s and Associate Professor of Pediatrics at Emory, performing large scale analysis of cancer gene-expression data to determine differences in cancers.

In addition to pediatrics, the multidisciplinary team of 1,000 researchers at HSRB-II study a variety of specialty areas, including imaging sciences, biomedical engineering, cardiovascular medicine, inflammation, immunity and immunotherapeutics. They also participate in other innovative collaborative research programs, like the Aflac Cancer and Blood Disorders Center of Children’s operating alongside the Emory Winship Cancer Institute, and the Emory Vaccine Center. Core facilities include advanced imaging (7-T MRI), flow cytometry, high-level containment facilities, an automated biorepository and genomics.

The state-of-the-art HSRB-II building is located next to its sister facility, Health Sciences Research Building I, which opened in 2013, and was designed with sustainability in mind. It uses roughly half the energy of typical research facilities thanks to thoughtful design strategies including: a daylighting approach for all occupied spaces, automated shades for mitigating heat gain, a solar panel array, a microgrid energy management system and a green roof plaza. It also boasts a central atrium awash in natural light with a living five-story green wall, a café, large digital experiential collaboration screens, innovation spaces, and meeting spaces meant to promote collaboration.
Arthur M. Blank Hospital to Open in 2024
With Cell Manufacturing Lab to Follow

The new Arthur M. Blank Hospital will open its doors September 29, 2024, at the site of the Children’s expanded North Druid Hills campus. This 19-story, two-million-square-foot facility represents a major leap forward in Children’s ongoing effort to deliver cutting-edge care, improve outcomes and innovate to meet the pediatric healthcare challenges of tomorrow.

Exemplifying this commitment, the hospital will include a good manufacturing practice (GMP) compliant advanced cell and gene therapy lab scheduled to open in January 2025. The lab will manufacture and deliver cellular therapies to patients through clinical trials offered by the Marcus Center for Advanced Cell and Gene Therapies.

Cell therapy uses cells, derived from a patient or healthy donor, to treat various diseases and conditions. Currently, six cell therapy trials are under way at Children’s and Emory, addressing such areas as the heart, asthma and cancer. With the manufacturing lab in-house at the new Arthur M. Blank Hospital, patient wait times will be reduced by half for some cell treatments, as the cells will not need to be transported from various other locations around the country.

“The Children’s and Emory cell therapy program is the only one in the country offering a full range of cellular therapy treatments, including regenerative medicine, for a broad spectrum of diseases addressing the whole child,” said Edwin Horwitz, MD, PhD, Director of Transplantation Biology and Therapeutics for the Aflac Cancer and Blood Disorders Center and Co-Director of the Marcus Center for Advanced Cell and Gene Therapies alongside H. Trent Spencer, PhD, Co-Director of the Marcus Center for Advanced Cell and Gene Therapies and Director of Gene and Cell Therapy at the Aflac Cancer and Blood Disorders Center. Drs. Horwitz and Spencer are also professors of pediatrics at Emory. Explained Dr. Horwitz, “We’ll have the opportunity for a lot of kids to get novel therapies and provide hope to kids who may not have access to effective treatment.”

Arthur M. Blank Hospital will facilitate the delivery of cutting-edge care to kids and shape the future of pediatric care nationwide. Thoughtfully designed with input from patients, families, staff and community members, this new facility will replace Egleston Hospital and will feature:

- 446 patient beds, 116 more than Egleston Hospital
- Larger private rooms with over 100 square feet of windows providing incredible views
- Convenient amenities for families, including washers and dryers, family lounges and kitchenettes on every floor, with child life activity rooms throughout
- More than 20 acres of greenspace, providing patients easy access to the healing powers of nature
- More than double the conference and simulation space for training
- A Special Care Unit (SCU) within the new Emergency Department for the treatment of patients with potentially highly infectious diseases
- On track to earn Leadership in Energy and Environmental Design (LEED) certification upon opening
Brain

How toddlers look at social information can be an early indicator of autism spectrum disorder (ASD).

That finding from researchers at Marcus Autism Center, a subsidiary of Children’s, led to the development of a breakthrough diagnostic technology that enables clinicians to diagnose autism at a much earlier age. Its first use in a clinical setting took place at Marcus Autism Center in August 2023, following authorization by the U.S. Food and Drug Administration (FDA).

Based on 20 years of research, Ami Klin, PhD, and Warren Jones, PhD, developed and tested EarliPoint Evaluation. The technology tracks the eye movement of young children between the ages of 16 and 30 months as they observe social interactions. This looking behavior serves as an effective and objective biomarker for early signs of autism, according to two safety and effectiveness studies published by Drs. Klin and Jones in the Journal of the American Medical Association (JAMA) and JAMA Open Network, which validate the use of EarliPoint Evaluation for autism diagnosis.

“The published studies show that objective, performance-based biomarkers of children’s looking behavior can help clinicians by reducing the time required for accurate autism diagnosis from multiple hours of assessment to as little as 12 minutes of objective measurements,” said Dr. Klin, Director of the Marcus Autism Center and Division Chief of Autism and Developmental Disabilities at Emory University School of Medicine Department of Pediatrics.

By enabling accurate and early diagnosis, EarliPoint Evaluation has the potential to help clinicians change the trajectory of children’s lives.

“If diagnosed earlier, child and family supports can also happen earlier,” said Dr. Jones, Director of Research at Marcus Autism Center and Nien Distinguished Chair in Autism at Emory University School of Medicine Department of Pediatrics. “Currently, only one in four children with autism is identified before age 3. Our hope is that this tool has the potential to help alleviate this enormous public health challenge with earlier diagnoses and treatment.”

Accessible Technology Aids Kids Nationwide

The second generation of the EarliPoint Evaluation tool, which received FDA authorization in July 2023, is small, portable and accessible for clinicians to use in an office setting. It can also be operated remotely anywhere with internet connectivity, enabling providers nationwide to use this technology—even in the most remote communities—to allow for earlier, more equitable and more efficient identification and treatment for ASD.
To use the device, children watch video scenes of social interaction on a portable tablet. As they watch, their looking behavior is monitored moment by moment to determine what social information the children look at and what they don’t. Reviewing the data, clinicians use the personalized, detailed report to provide families with a timely and objective diagnosis, which includes measures of the level of each child’s social disability, verbal ability and non-verbal learning skills.

Clinicians then work with families on an individualized treatment plan. “The implications of these results are that children who face long wait times and multiple referrals before being diagnosed at age 4 or 5 may now be able to obtain a diagnosis before age 3,” said Dr. Jones.

The Marcus Test
EarliPoint Evaluation is also known as “the Marcus Test” to pay homage to Bernie Marcus, founder of Marcus Autism Center, who has provided more than $120 million in philanthropic support for autism research and treatment.

Founded in 1991, Marcus Autism Center is one of the country’s leading centers in research, diagnosis and treatment of autism in children, and is at the forefront of science-based care. Clinicians at Marcus Autism Center have long been focused on addressing one of the key elements of autism in children: diagnosing autism earlier. Early identification and early intervention are important for supporting the health, learning and long-term well-being of all children with autism.

“We are all very grateful to Bernie Marcus for his extraordinary generosity to make this important innovation possible for children and families,” said Donna Hyland, Children’s Chief Executive Officer. “This tool is another example of the wonderful bench-to-bedside clinical expertise we provide to patients in Georgia and throughout the country.”

The translation of this research from laboratory to clinic was made possible by transformational philanthropy from Bernie Marcus and the Marcus Foundation. The technology first received FDA clearance in June 2022. Additional research support was provided by the National Institute of Mental Health, the Joseph B. Whitehead Foundation and the Georgia Research Alliance. The technology is owned by EarliTec Diagnostics Inc. EarliTec develops technologies for early identification and treatment monitoring in autism, and gives revenue to support treatment of children with autism ages 16 to 30 months. The five other specialty centers that participated in the multi-site trial were: Cincinnati Children’s Hospital Medical Center, Southwest Autism Research & Resource Center, Seattle Children’s Hospital, University of Washington, University of California—San Francisco and Rush University.

Children’s Healthcare of Atlanta has intellectual property interests in the EarliPoint device and, along with Drs. Jones and Klin, equity interest in EarliTec Diagnostics Inc. As a result of these interests, Children’s and Drs. Jones and Klin could potentially benefit financially from the sale of the EarliPoint device.
In a pediatric and technological research collaboration between Children’s and Georgia Tech, physical therapists at the Children’s Center for Advanced Technology and Robotic Rehabilitation recruited patients for a study to test the feasibility of robotic exoskeletons in reducing genu recurvatum, or knee hyperextension. The condition’s complex gait pattern has a variety of causes often connected with knee weakness, lack of motor control and spastic movement in children and adolescents.

The study—funded by the Imlay Innovation Fund—was led by Aaron Young, PhD, Associate Professor in the School of Mechanical Engineering at Georgia Tech, and his team. Erin Eggebrecht, DPT, Children’s physical therapist, joined forces with Dr. Young, who leads the Exoskeleton and Prosthetic Intelligent Controls lab at Georgia Tech, to conduct the study.

They tested the robotic exoskeleton device, an external covering providing support for the knee, on kids and teens whose gait was affected by conditions such as stroke, traumatic brain injury, cerebral palsy and spina bifida. These patients experience atypical forces placed on the soft tissues surrounding the knee joint, so early treatment or prevention of knee hyperextension may help prevent further injury.

During the study, five Children’s patients completed three rounds of rehabilitation with the exoskeleton, and pre- and post-assessments were conducted. The team discovered the exoskeleton reduced knee hyperextension and increased swing range of motion, improving their kinematics and ambulation skills. They published the findings in the Institute of Electrical and Electronics Engineers (IEEE) Transactions on Biomedical Engineering (TBME).

“The study demonstrated that a lightweight, low-profile knee exoskeleton for children can address genu recurvatum gait and is a step toward an effective therapy,” said Dr. Young.

With input on specifications from the Children’s physical therapists, Dr. Young is currently working on a version of the device for clinics. In a second study, the team is looking to integrate the exoskeleton into a walking therapy that will focus on therapeutic effects, rather than orthotic effects.
In an effort to strengthen the heart’s ability to pump blood, clinicians and researchers from Children’s, University of Maryland Medical Center and University of Miami launched a novel trial that involved implanting patient-derived stem cells into the hearts of babies with hypoplastic left heart syndrome (HLHS). Now, a research team led by one of the leaders of that study, Michael Davis, PhD, Director of the Emory and Children’s Heart Research and Outcomes Center, is taking their investigation one step further.

Using patient genomic data from the CHILD study, the team has developed a computational model to try to predict what benefits may exist for a small subset of patients receiving the stem cell treatment prior to the trial’s completion.

Babies born with HLHS do not have a functioning left side of the heart. There is a single ventricle doing the work of two ventricles. As a result, it is under a lot of stress and can fail. These babies require surgery shortly after birth, and will undergo three surgeries total over the course of three years, to redirect blood flow through the right side of the heart.

Dr. Davis and his team discovered that the cardiac-derived c-kit+ progenitor cells, or CPCs, which were injected into the babies’ hearts during the trial, were effective due to the release of what is known as extracellular vesicles, or nanoparticles, that play a critical role in intercellular communication.

Yet, not all patients exhibited the same level of improvement. To identify contributing factors of cell therapy variability and improve clinical outcomes, the investigators took a machine learning approach by developing a collection of algorithms to attempt to establish patterns from the data and associate those patterns with definitive class samples. They combined the RNA sequencing of CPCs and their vesicles and cardiac-relevant cellular test tube experiments to build a predictive model.

They isolated CPCs from the cardiac biopsies of 29 patients with congenital heart disease and five patients with HLHS from the trial. The team then sequenced the cells and their vesicles and measured various responses from the vesicles.

They found the most important RNA signals involved in reparative outcomes had a significant link to cardiac development and signaling pathways. Furthermore, using a model trained on previously collected CPCs and their vesicles, they were able to predict outcomes for the trial’s clinical samples. Finally, they found that CPCs and their vesicles’ performance in building new blood cells correlated to clinical improvements in right ventricle performance. They published the results in iScience.

“This computational approach may pave the way for personalized medicine and predictive models for pediatric congenital heart disease therapy,” said Dr. Davis, Professor of Biomedical Engineering at Georgia Tech and Emory. “There were changes and we could detect them by sequencing the extracellular vesicles from the cells prior to injection.”
Knee Joint Sound: A Biomarker to Detect Juvenile Idiopathic Arthritis

A study from Children’s, Emory and Georgia Tech shows that sound waves may help diagnose juvenile idiopathic arthritis (JIA), the most common type of arthritis in children younger than 16. It occurs when a child’s immune system attacks the joints, causing swelling, pain and stiffness.

Led by co-principal investigators, Sampath Prahalad, MD, Chief of Rheumatology at Children’s, and Omer Inan, PhD, Professor and Smith Chair in Bioscience and Bioengineering at Georgia Tech, the research team evaluated “joint acoustic emissions” from children’s knees, the most involved joint in the disease, using machine learning algorithms to classify them as active or inactive for JIA. Then they compared them to knee sounds from healthy kids without JIA.

Joint acoustic emissions are sounds from joint surface movement that vary based on the properties of the joint. Different joint diseases change the friction, wear and lubrication properties of interacting surfaces of the joint, affecting their acoustic emissions.

“When machine learning algorithms are applied to analyze these sounds, they can be used as digital acoustic biomarkers,” said Dr. Inan. “The sounds are easy to obtain using non-invasive, inexpensive and compact equipment applied to the surface of the skin.”

During the study at Children’s Center for Advanced Pediatrics, researchers recorded knee sounds for a group of 116 children, 86 of whom had JIA, and 43 who had active knee involvement at the time of the study. All participants performed 10 seated, flexion-extension cycles of the knee, and sounds were recorded using accelerometers attached to the knee.

Sound wave features were used to train a machine learning algorithm to classify JIA and healthy knees. The classifier predicted a joint score between 0 and 1 as the probability of having JIA, and results showed it had more than 80% accuracy. Study findings were published in Pediatric Rheumatology.

“The technology utilizes sound as a digital biomarker for assessing joint health, which clinicians can easily implement in outpatient settings for screening and monitoring diseases,” said Dr. Prahalad, Professor of Pediatrics at Emory. “This tool can aid general pediatricians in making referrals to rheumatologists, prompt early treatment and facilitate decisions on diagnostic tests and treatment adjustments. It represents a potentially inexpensive and easy-to-use screening or disease monitoring tool to help decrease and quantify disease morbidity caused by JIA.”
A study comparing two methods of treatment for infants with neonatal opioid withdrawal syndrome (NOWS) reveals that a non-drug-based approach may be more effective. The study findings were published in the New England Journal of Medicine in an article titled, “Eat, Sleep, Console Approach or Usual Care for Neonatal Opioid Withdrawal,” which was co-authored by Brenda Poindexter, MD, Division Chief of Neonatology at Children’s.

The multicenter study took place at 26 hospitals enrolling more than 1,300 infants born at 36 weeks or older who were diagnosed with NOWS. This disease occurs when an infant withdraws from opioids, such as hydrocodone, oxycodone or heroin, which they are exposed to before birth by their mother.

During the study, at a randomly assigned time, hospitals transitioned from the standard of care—the Finnegan Neonatal Abstinence Scoring Tool (FNAST)—to the Eat, Sleep, Console (ESC) approach. In the three-month transition period, staff members at each hospital were trained to use the new approach. Researchers compared the time from birth to medical readiness for discharge for each care method as a primary measure of effectiveness.

FNAST has been used for the past 50 years to assess opioid withdrawal severity and to help manage care by assessing 21 commonly observed symptoms. However, concerns have been raised about its subjectivity and a possible overestimation of the need for opioid medication.

Conversely, the ESC approach was developed about eight years ago and prioritizes non-drug-based approaches to care, such as a low-stimulation environment, swaddling, skin-to-skin contact and breastfeeding. ESC assessments focus on an infant’s ability to eat, sleep and be consoled. The approach keeps mother and baby together, enabling families to play a larger role in the care and assessment of their infants. Although growing in popularity, this approach had never been tested in a large population until recently.

Results from the trial, funded by the Helping End Addiction Long-Term (HEAL) Initiative of the NIH, showed infants receiving FNAST were ready for discharge after about 15 days, whereas infants receiving the newer ESC approach were ready for discharge after only about eight days. These findings revealed the new method reduced hospital stays by almost half.

“This study provides solid evidence for the effectiveness and safety of ESC, so that it may be used more broadly,” said Dr. Poindexter, Professor of Pediatrics at Emory.

Neonatal opioid withdrawal syndrome is the most common form of neonatal abstinence syndrome (NAS) whereby a baby experiences withdrawal from any drug. According to the U.S. Centers for Disease Control and Prevention (CDC), about six newborns are diagnosed with NAS for every 1,000 newborn hospital stays.
Study Reveals Fewer Infants Are Dying from Necrotizing Enterocolitis

Research conducted at Children’s and Emory revealed fewer infants are dying from a serious gastrointestinal condition that primarily affects premature babies. Necrotizing enterocolitis (NEC) is the most common cause of death between the ages of 2 weeks and 2 months in extremely preterm infants.

The study, published in JAMA Network Open, found that infant deaths from NEC decreased 7.7% annually between 2007 and 2012, although the death rate has remained virtually unchanged since then at about one infant each day. Also, the study revealed that while racial differences in the death rate have narrowed, Black infants were still 2.5 times more likely to die from NEC than white infants.

Findings from the study and other highlights from the NEC research were presented last spring at the Pediatric Academic Societies (PAS) Conference by the study’s co-authors, Mattie F. Wolf, MD, Children’s Neonatologist and Assistant Professor of Pediatrics at Emory, and Ravi Patel, MD, MSc, Children’s Neonatologist and Professor of Pediatrics at Emory.

“While great strides have been made in understanding, preventing and treating NEC, progress in preventing mortality due to NEC seems to have stalled in recent years, and racial and ethnic disparities still exist,” said Dr. Wolf. She added that further studies are needed to determine the factors leading to these results.

NEC occurs when intestinal tissue is injured or inflamed, which can lead to death of intestinal tissue and sometimes a perforation in the intestine. Bacteria in the intestine can also cause life-threatening infections, sometimes leading to lifelong neurological or nutritional challenges.

The research team examined records from the U.S. Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics’ 2020 Final Multiple Cause of Death Data of more than 88 million live births between 1999 and 2020, during which time 8,951 infants died of NEC.

The National Institutes of Health (NIH) provided funding to support the study.

Research Shows Infants With HIE Should Not Receive Anti-Seizure Medication After Hospital Discharge

Infants with hypoxic-ischemic encephalopathy (HIE), a type of brain injury caused by a lack of oxygen to the brain before or at birth, commonly have seizures. Children’s neonatology researchers found infants with HIE and seizures are at higher risk of death or disability if they continued to receive anti-seizure medication after being discharged from the hospital. They published the findings in the Archives of Disease in Childhood, Fetal Neonatal Edition.

Led by Children’s neonatologists Elizabeth K. Sewell, MD, MPH, Assistant Professor of Pediatrics at Emory, and Ravi M. Patel, MD, MSc, Professor of Pediatrics at Emory, the study revealed that the risk of death or moderate-to-severe disability for infants who continued anti-seizure medication was 44% at 18 to 22 months of age, compared to 28% for infants of the same age who were discharged from the hospital and did not continue taking these medications. The risk remained greater after accounting for potential differences between these groups of patients.

The observational study included 302 HIE patients at 22 academic centers who were enrolled in three National Institute of Child Health and Human Development Neonatal Research Network Trials of therapeutic hypothermia, a common treatment for HIE, which lowers a baby’s body temperature to help reduce the risk of neurological problems.

“This important work provides additional evidence and support for the revised recommendation by the International League Against Epilepsy that advised discontinuation of anti-seizure medication prior to discharge for infants with acute symptomatic seizures,” said Brenda Poindexter, MD, MS, Division Chief of Neonatology at Children’s. “It is wonderful to see our physicians advancing the field and generating critical evidence that supports limiting prolonged exposure to medications that may have adverse effects.”
Children’s Orthopedic and Sports Medicine Surgeons S. Clifton Willimon, MD, and Crystal Perkins, MD, were co-investigators on a study analyzing opioid use in children after common orthopedic surgeries over the course of two years. Findings from the study, published in the Journal of Pediatric Orthopaedics, found that more than half of prescribed opioid pain medication was not used by patients.

“The use and misuse of opioid medications is an epidemic and public health emergency,” said Dr. Perkins, Medical Director for Orthopedic Quality and Outcomes at Children’s. “There are currently no standard guidelines for treating pain related to orthopedic surgeries in the pediatric population, so we hope this study will help establish a baseline to build upon.”

The study analyzed patients between the ages of 5 and 20 undergoing one of seven common orthopedic surgeries between 2018 to 2020, including spine fusion, guided growth, percutaneous pinning of supracondylar humerus fractures, anterior cruciate ligament reconstruction, knee arthroscopy, hip arthroscopy and shoulder arthroscopy. Patients and their families completed a medication logbook to track all doses of pain medication and associated pain scores.
Three-hundred forty-two patients completed the study. A total of 9,867 doses of opioid pain medication were prescribed, which correlated to an average of 29 doses per patient. Researchers observed a total of 4,351 doses of prescribed opioid medication were consumed. This was less than half (44%) of the total prescribed.

“While opioid medication use in children and adolescents after orthopedic surgery was significantly less than the number of tablets prescribed, patients who did use narcotics did so for longer than anticipated, at an average of five days,” said Dr. Willimon.

Fewer than 10% of patients consumed all prescribed opioids, while nonmedical forms of pain management, such as ice treatment, were used by the majority (77%) of patients, though this varied greatly based on a patient’s procedure.

Drs. Willimon and Perkins also observed that when patients used nonsteroidal anti-inflammatory drugs (NSAIDs) to help manage their pain, they used an average of five fewer total doses of the opioid medication as compared to patients who did not use NSAIDs. This was the only independent predictor of reduced narcotic use.

After analyzing the results, the investigators recommend orthopedic surgeons responsibly prescribe pain medications using evidence-based data or the results of their own experience monitoring medication consumption. “Important in the context of the ‘opioid epidemic,’ physicians must counsel patients and families on postoperative pain expectations and appropriate medication use,” added Dr. Willimon.
A Children’s and Emory research team participated in the clinical trial leading to U.S. Food and Drug Administration (FDA) approval of an immunization for respiratory syncytial virus (RSV) infections. The common, highly contagious virus can become life-threatening in babies, especially those born prematurely or with lung and heart conditions, when the typical symptoms of coughing, a runny nose and fever progress to difficulty breathing.

“RSV is the leading cause of hospitalization in U.S. infants,” said Christina Rostad, MD, Pediatric Infectious Disease Specialist at Children’s and sub-investigator on the study. “For decades, researchers have been working on developing safe and effective RSV vaccines that could protect the youngest infants during their time of greatest vulnerability to severe RSV disease.”

Children’s and Emory clinical researchers, led by Evan Anderson, MD, a former Children’s physician and Emory professor, participated in a pivotal phase 3 global clinical trial for the infant immunization nirsevimab, an antibody to protect infants for an entire RSV season with a single injection dose. The trial studied more than 3,000 term and late pre-term infants who were randomly assigned to treatment and control groups. In the treatment group, infants received nirsevimab at the start of the RSV season (which starts during the fall and peaks in the winter) and were followed for 150 days.

Results showed the occurrence of medically attended RSV-associated lower respiratory tract infection, such as pneumonia or bronchiolitis often leading to an emergency department visit, was 76% lower with nirsevimab than with a placebo. The incidence of hospitalization for RSV-associated lower respiratory tract infection was similarly almost 80% lower with nirsevimab compared to a placebo. These results were consistent throughout the 150-day period after the dose was administered and across geographic locations and RSV subtypes.

Due to these findings published in the New England Journal of Medicine, the FDA approved nirsevimab in July 2023 for all infants under 8 months of age entering their first RSV season, and for children up to 2 years of age who are vulnerable to severe RSV disease through their second RSV season.

“We are thrilled about the recent FDA approval of this immunization, which will offer protection from RSV disease to the youngest infants and alleviate fears of many parents and families,” said Dr. Rostad, who is also Associate Professor of Pediatrics at Emory.
A Children’s, Emory and Georgia Tech team led by cystic fibrosis (CF) researcher Marvin Whiteley, PhD, identified a new gene and potential biomarker associated with the severe worsening of a chronic lung infection into an acute, life-threatening infection in kids with CF.

Their findings, published in Nature, revealed that the gene, named sicX by the research team, can serve as both a target for treating a chronic lung infection caused by the bacterium Pseudomonas aeruginosa (P. aeruginosa), as well as a biomarker for predicting when that infection exacerbates into its more deadly acute form.

“Since the 1980s, researchers have questioned why the acute worsening of a P. aeruginosa infection occurs,” said Dr. Whiteley, a microbiologist and Associate Director of the Emory and Children’s Center for Cystic Fibrosis and Airways Disease Research, a Georgia Research Alliance Eminent Scholar at the Georgia Tech School of Biological Sciences, and Adjunct Professor of Pediatrics at Emory. “Exacerbations often result in a decline in health and can be fatal. Finding answers for them is very important.”

Typically, a CF infection caused by P. aeruginosa is chronic and is managed with a strict therapeutic regimen. But if the bacteria enter a patient’s bloodstream, the infection can become an acute, life-threatening condition.

With funding from the U.S. Cystic Fibrosis Foundation, Dr. Whiteley and the research team found that P. aeruginosa uses oxygen as a cue to determine whether to stay locally in chronic infection or cause an exacerbation. P. aeruginosa responds to low oxygen with production of the sicX gene that prevents the bacterium from entering the bloodstream to cause such a reaction.

As Dr. Whiteley explained, “The most immediate opportunity for clinical application is using the sicX as a diagnostic tool. The gene can serve as a biomarker for predicting when a child with this type of CF infection will transition to an acute exacerbation.”

In the future, Dr. Whiteley and his team plan to study whether the amount of sicX can predict when an acute exacerbation will occur by developing a point-of-care analysis to detect sicX levels in the lungs of CF patients. They also hope to work with other researchers to apply their findings toward treatment.

“Pseudomonas aeruginosa is one of the leading pathogens infecting the lungs of CF patients,” said Nael A. McCarty, PhD, Marcus Professor of Cystic Fibrosis at Emory, and Director of the Emory and Children’s Center for Cystic Fibrosis and Airways Disease Research. “Most patients are chronically infected before they reach age 10, and the bacteria linger in a chronic infection, often becoming resistant to antibiotics. In response to unknown triggers, infection can ramp up causing a rapid decline in lung health during an acute pulmonary exacerbation.” The gene identified by Dr. Whiteley may play an important role in controlling this pathway that leads to worse lung disease, and thus may also be a target for therapeutic design.”
Children’s and Emory were awarded a four-year $2.8 million grant to lead one of six national research node centers for the Pediatric Emergency Care Applied Research Network (PECARN), the first federally funded pediatric emergency medicine research network established in 2001. The grant is the second awarded to Children’s and Emory after receiving an initial grant to join the network in 2019. Since then, it has been a top enrolling site, and the only site representing the Southeast.

With this grant, Children’s and Emory will now lead the node of PECARN including Brown University/Hasbro Children’s Hospital and the University of California, San Francisco/UCSF Benioff Children’s Hospital (Oakland) called the San Francisco-Oakland, Providence, Atlanta Research Collaborative, or SPARC. Claudia R. Morris, MD, Children’s Pediatric Emergency Medicine Physician and Professor of Pediatrics and Emergency Medicine at Emory, will serve as the node’s principal investigator. She is the Co-Chair of the Emory and Children’s Center for Clinical and Translational Research and holds the Wilbur Fisk Glenn Jr. Distinguished Faculty Chair for Clinical and Translational Research. Mark Griffiths, MD, Children’s Pediatric Emergency Medicine Physician and Associate Professor of Pediatrics and Emergency Medicine at Emory, is the site Hospital Emergency Department Affiliate (HEDA) principal investigator. Emergency departments at all three Children’s campuses facilitate PECARN trials, evaluating about 250,000 ill or injured children annually.

PECARN aims to develop and conduct studies with the goal of preventing and reducing morbidity and mortality in the sickest of ill and injured children seen in emergency departments. It forms an infrastructure for clinical investigators from each node to ask questions that are a priority in pediatric emergency medicine. If the network approves a researcher’s idea, they have a high likelihood of securing federal funding to support their study. Participating in this network establishes a pipeline of additional federally funded grants of more than $2 million per year for clinical trials and pediatric emergency medicine research. More than 18 Children’s and Emory investigators are involved in PECARN studies that include other disciplines such as pediatric nephrology, critical care, asthma, trauma and neurology.
Developing and Testing the First At-Home Oral Therapy Targeting Acute Forms of Leukemia

Building on three decades of work that led to the development of an oral drug to treat two forms of leukemia, a Children’s and Emory research team has launched a phase 1 clinical trial to determine the maximum tolerated dose of the therapy, establish its safety profile and determine side effects in adolescents.

Melinda G. Pauly, MD, Pediatric Hematologist/Oncologist and Medical Director of the Aflac Cancer and Blood Disorders Center, is leading the 45-patient trial of MRX-2843, an oral therapy that inhibits the growth of leukemia cells in relapsed acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) at the Aflac Cancer and Blood Disorders Center. Simultaneously, as the first cancer trial at Children’s and Emory to open for adults and children at the same time, an MRX-2843 trial in adult patients is being led by William G. Blum, MD, Director of the Acute Leukemia Program at the Emory Winship Cancer Institute. A trial in adults and children is also taking place at Memorial Sloan Kettering Cancer Center and University of North Carolina at Chapel Hill.

Douglas K. Graham, MD, PhD, Chief of the Aflac Cancer and Blood Disorders Center, discovered the MerTK gene and his research has validated it as a target for leukemia therapy. Working with Deborah DeRyckere, PhD, Assistant Professor of Pediatrics at Emory and scientists from the University of North Carolina at Chapel Hill, Dr. Graham developed MRX-2843 to specifically target these leukemia cells and stop their growth. His preclinical work showed that blocking MerTK with MRX-2843 effectively kills leukemia cells, especially in combination with chemotherapy. Preclinical findings have also shown the drug can activate the immune system to combat the leukemia cells.

“Historically, new therapies are tried in adults first, but this will give children with relapsed and resistant acute AML and ALL the opportunity to access the drug sooner, hopefully improving their quality of life with an oral medicine taken at home,” said Dr. Pauly.

The MRX-2843 trial is being supported by the Peach Bowl LegACy Fund, along with Swim Across America. The Peach Bowl LegACy Fund was created in 2019 with a $20 million gift from Peach Bowl Inc. and it funds the most promising clinical drug trials for children with cancer. It is named for Anna Charles “AC” Hollis, a former patient of Dr. Pauly and the daughter of Peach Bowl Inc. executive Benji Hollis.
“From first discovery through all the different steps of drug development, every physician involved in research has an ultimate dream their work will have a positive impact on patients and improve outcomes,” said Dr. Graham, Chief of the Division of Pediatric Hematology/Oncology and BMT at Emory. “When you work in team science, you pass the baton on to the next person. Dr. Pauly is extremely well qualified to run the clinical trial. Our next step will be to extend this therapy to all ages of children who have leukemia that is not responding to standard treatment protocols.”

A retrospective study led by first author Xu Ji, PhD, Assistant Professor of Pediatrics at Emory, shows Medicaid expansion under the Affordable Care Act (ACA) is associated with improved overall survival among young adults with cancer.

Dr. Ji and her team observed that Medicaid expansion through the ACA was shown to improve insurance coverage and early diagnosis of cancer in young adults. Therefore, they wanted to determine whether these improvements translated to survival benefits.

Using the National Cancer Database, they identified more than 345,000 young adults from ages 18 to 39 years diagnosed with cancer from 2010 to 2017. Researchers then analyzed changes in two-year overall survival before and after Medicaid expansion in states that underwent the expansion compared to states that did not.

Results, published in the Journal of Clinical Oncology, showed that among all young adults, the two-year overall survival increased more in Medicaid expansion states than in non-expansion states. The expansion-associated survival benefit was concentrated in female breast cancer patients and in patients with stage 4 disease. In addition, greater survival benefit associated with Medicaid expansion was observed among racial and ethnic minoritized groups compared to non-Hispanic white peers.

“Medicaid expansion under the ACA was associated with an improvement in overall survival among young adults with cancer, with survival benefits most pronounced among patients of under-represented race and ethnicity and patients with high-risk diseases,” said Dr. Ji, who conducted the study with co-investigators Ann Mertens, PhD, Research Director of the Cancer Survivor Program at the Aflac Cancer and Blood Disorders Center, and Sharon Castellino, MD, Director of the Leukemia and Lymphoma Program at the Aflac Cancer and Blood Disorders Center. Both Drs. Mertens and Castellino are Professors of Pediatrics at Emory.

The ACA is the comprehensive healthcare reform law enacted in March 2010 with the goal of making affordable health insurance available to more people, expanding the Medicaid program to cover all adults with incomes below 138% of the federal poverty level (not all states have expanded their Medicaid programs) and supporting innovative medical care delivery methods to lower healthcare costs overall, according to the U.S. Department of Health and Human Services.
A skin patch has the potential to mitigate the effects of food allergies in young children, according to findings from an international multicenter clinical trial led at Children’s and Emory by researcher Brian Vickery, MD.

Results from the phase 3 EPITOPE trial, published in the New England Journal of Medicine, found that DBV Technologies’ Viaskin™ Peanut patch, used daily for 12 months, desensitized toddlers to peanuts, decreasing their chance of experiencing allergic reaction after an accidental peanut exposure. No approved treatment options exist for peanut-allergic children under 4 years of age, so the patch has the potential to help modify their food allergy by desensitizing the immune system to an allergen.

Dr. Vickery, site principal investigator in the global study and Director of the Food Allergy Program at Children’s, said the new treatment approach, if approved for clinical use, could be a game-changer for children suffering from peanut allergies.

“Because the patch dose is given on the skin and not as a shot or an oral treatment, the approach is very patient-friendly,” explained Dr. Vickery, Professor of Pediatrics at Emory. “Young peanut-allergic children currently have no treatment options, and often struggle with staying safe during routine daily activities. If approved, the patch may help them be safer in their normal daily activities and hopefully improve quality of life.”

Viaskin is a new form of epicutaneous immunotherapy, or EPIT, a potential new class of treatment that uses the immune properties of the skin. It begins with a small dose that is increased over time by wearing the patch for longer periods of the day, until a maintenance dose is reached, at which point each patch is worn 24 hours and replaced daily. Viaskin does not require physical activity restrictions and is not disrupted by illness, as required for oral and other forms of immunotherapy.

The Food Allergy Program is housed in the Center for Advanced Pediatrics at Children’s North Druid Hills campus, home to the future Arthur M. Blank Hospital. Its clinical research program is critical to the institutions’ continued effort to learn more about all food allergies and develop new treatments for them.
Advancing the Pediatric Research Enterprise

The Children’s and Emory pediatric research enterprise is on track to complete a bold five-year strategic growth plan. Research programs in critical areas such as Infectious Diseases and Emergency Medicine are expanding, and many leverage new and innovative research modalities to address outcomes, behavioral and mental health, and diversity and inclusion. Fourteen new investigators have been successfully recruited and 25 medical residents and pediatric subspecialty fellows will follow at the start of the academic year.

With the opening of Emory’s second Health Sciences Research Building, our pediatric research footprint has grown and increased access to innovative support infrastructure. The building features the Raymond F. Schinazi Family Innovation Floor, which includes start-up “incubator” space, a 3-D printing and micro-machining area, extended reality and artificial intelligence technologies.

Furthermore, Emory’s Department of Pediatrics achieved a new record in extramural funding in 2023 allowing for an expansion of research programs such as:

- A reimagined Pediatric Technology Center supporting collaborative activities and pediatric innovation and discovery efforts with the Georgia Institute of Technology
- A growing Children’s Health Informatics Core (CHIC) leveraging vast clinical data to expand our expertise in improvement science and outcomes research
- Increased access to cellular and gene therapy research with the introduction of GMP manufacturing capabilities for cell and gene therapies at the new Arthur M. Blank Hospital

Also in 2023, a nationwide search began for a new Chief Research Officer (CRO) at Children’s and Executive Vice Chair for Research at Emory School of Medicine. Kristy Murray, DVM, PhD, an experienced leader, researcher and teacher with great expertise in research administration and a true passion for helping kids, was successfully recruited. Dr. Murray comes to Children’s and Emory from Baylor College of Medicine and Texas Children’s Hospital, where she was Vice Chair for Research in the Department of Pediatrics, Director of the William T. Schearer Center for Human Biology, Assistant Dean for Faculty and Academic Development in the School of Tropical Medicine and Professor of Pediatrics and Molecular Virology and Microbiology. Dr. Murray begins her new role at Children’s and Emory on April 1, 2024.

Clinton Joiner, MD, PhD, brought excellent leadership to the role of Chief Research Officer and, while he is stepping back in this capacity, he will remain at Children’s to continue his clinical work and research as Director of Hematology in the Aflac Cancer and Blood Disorders Center. Many transformational milestones were achieved during Dr. Joiner’s time as CRO, creating a strong foundation for programs to continue to grow and mature.
Notable National Awards and Distinctions

Sharon Castellino (Hematology/Oncology)—Exceptional Women in Medicine, Castle Connolly

Brian Costello (Emergency Medicine)—Fellow, Academy of Wilderness Medicine

Anne Gill (Radiology)—Board of Directors, Society for Pediatric Interventional Radiology

Ammar Kheder (Neurology)—Adelyn Stroup Lectureship in Pediatric Epilepsy, Johns Hopkins

Allen Ligon (Cardiology)—President, Pediatric Interventional Cardiology Early Career Society

Katherine Pickard (Psychology)—American Pediatric Society and Society for Pediatric Research Frontiers Program, 2023

Brenda Poindexter (Neonatology)—President Elect, Society of Pediatric Research

Nikhila Raol (Otolaryngology)—Fulbright Scholar Award

Edward Richer (Radiology)—Assistant Editor, American Journal of Roentgenology

Zahidee Rodriguez (Cardiology)—National Compassionate Caregiver of the Year, Schwartz Center for Compassionate Healthcare

Jana Stockwell (Critical Care)—Barry A. Shapiro Memorial Award for Excellence in Critical Care Management, Society for Critical Care Medicine

Wilbur Lam (Hematology/Oncology)—Member, National Academy of Medicine, and Member, National Academy of Inventors

Dr. Lam is the second Children’s and Emory physician elected to the National Academy of Medicine following Barbara Stoll, MD, former Chief Academic Officer for Children’s and Pediatrics Department Chair for Emory. He receives the honor "for outstanding contributions in point-of-care, home-based, and/or smartphone-enabled diagnostics that are changing the management of pediatric and hematologic diseases, as well as the development of microsystems technologies as research-enabling platforms to investigate blood biophysics; and leading national/NIH efforts to assess diagnostic tests (including those for COVID-19) for the entire country."

As the third Children’s and Emory physician elected to the National Academy of Inventors, Dr. Lam has made several key discoveries, including microvasculature-on-chip microdevices that function as in vitro models of blood diseases, a smartphone ear scope that has since been acquired and is now being produced and sold, a single drop of blood anemia test that was just cleared by the FDA for home use and a smartphone app that uses fingernail selfie photos of anemia patients to determine the level of hemoglobin in their blood, replacing the need to draw blood.