Conquering Cloacal Exstrophy

John Gearhart dedicates a career to perfecting one of the most complex surgeries for children.

Nursing Beyond the Borders
Through their lens, where they travel and why

Raising Research
Collaborations fuel transformation of All Children’s Hospital
Dear Friend of Johns Hopkins Children’s Center,

I am so pleased to share this edition of our magazine, which presents a rich sampling of the scope and vital importance of our work. The fierce commitment of our staff and supporters to ending children’s suffering remains legendary.

Diminished federal funding, however, poses an ever-growing threat to our ability to develop new therapies and cures. Private philanthropy is fast becoming the chief resource available to our physician scientists for research needed to prevent or render harmless many of the complex maladies you’ll read about in this issue—diseases like diabetes and HIV, antibiotic-resistant infections, immunologic disorders, and birth defects like cloacal exstrophy, among others. Armed with hard-earned knowledge of genetic and molecular causes of many diseases—made possible by your generous funding—we must now drive this profoundly complex information into better therapies and cures. Research is the fuel that will get us there.

So, be a hero. Be inspired. Turn to this issue’s People & Philanthropy section and see how the investments of individuals like Josh Rales and families like the Radmers, Nicholls and Garretts are improving and preserving lives and futures.

Sincerely,

George Dover, M.D.
Director, Johns Hopkins Children’s Center
Given Foundation Professor of Pediatrics
Where Would We Be Without This Place and Its People?

by Courtney Stewart

A team approach to treating pulmonary hypertension saved our twins, Mark and Isabella. Born at 23 weeks gestation, suffering from pulmonary hypertension and heart disease, and weighing less than two pounds, they were medevaced from Atlanta to the Johns Hopkins Children’s Center (thank you, Air Compassion for Veterans!), in November 2012, when they were 5 months-old. In Atlanta, my husband, Mark, and I had the distinct vibe of despair for our children. Even upon our arrival in the pediatric intensive care unit at Johns Hopkins, we experienced the other side of the coin. There was optimism, encouragement and a very disciplined, integrated approach to care for our little guys.

Pulmonary hypertension in preemies requires an incredibly high level of expertise and caution to manage properly. Before we transferred to Johns Hopkins, I Googled pediatric pulmonologist Michael Collaco, who together with pediatric cardiologist John Coulson would manage their care here. I saw that Dr. Collaco had written scholarly articles about pulmonary hypertension and its management in preemies at Johns Hopkins. I was sold.

I liked that care is very family-friendly at Johns Hopkins. Parents are included in the medical rounds. And bedside manner is terrific. Physicians, therapists, nurses all tell you what they’re doing and why, and they listen to you.

Gradually we saw our children improve. Every discipline, whether pulmonary, cardiology, social work or nursing, knew what was going on every step of the way. Isabella would eventually have a hole in her heart fixed in the pediatric cath lab at the hospital, and both were weaned from ventilators and medicines. Today they are happy, healthy toddlers, who like to dance and play and read. Their favorite book is “Chicka Chicka Boom Boom,” which we read to them in the hospital.

We are eternally grateful to Johns Hopkins and those who help support this place. Would the care and big advancements in care our twins so desperately needed have been here without research funding? What about the hospital’s research that showed an integrated approach is critical to saving preemies like ours? I don’t know where we would be today without the wonderful, talented people who make up the Johns Hopkins Children’s Center. Thank you!
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Cover photo by Chris Hartlove
The Director’s View

We’ve Turned Two

As this issue of Hopkins Children’s came off the press, we reached our second year here in our new home, The Charlotte R. Bloomberg Children’s Center. Part of a $1 billion-plus hospital construction project completed in May 2012, the building was designed to launch a new era in pediatric medicine—one that would redefine the hospital experience, push the boundaries of biomedical discovery and sustain our tradition of innovation in clinical care. And it would do all this in a more accessible, family-friendly environment. Did we deliver?

Well, we’re only beginning our toddler years—and in such a short time span hospital data is difficult to measure in a meaningful way—but we decided to take a stab at answering the question. What did we find?

Patients and families, our dramatically improved patient-satisfaction scores tell us, love the building’s naturally lit space and design, our original works of art that stimulate the imagination and soothe the mind, and, thanks to noise-reducing innovations, our quieter and more tranquil environment. Says one parent, “I think the building inspires hope and healing.” Indeed, it has enhanced healing. All single patient rooms have helped bring down our infection rates, new advanced imaging modalities have resulted in more accurate and safer imaging, and our new space has allowed us to implement innovative clinical and treatment protocols designed to improve outcomes and reduce lengths of stay. And with ten customized, dedicated pediatric ORs, we’ve been able to attract top surgical candidates nationwide. Since we opened our new building, we’ve recruited 16 new faculty members across the Department of Pediatrics.

Research? Twice the size of our old unit, our new pediatric clinical research unit has allowed us to see, treat and observe more children more efficiently, which in turn has accelerated the rate of our clinical research. Since May 2012 our scientists have won nearly 100 new highly competitive research grants, allowing us to study a wide range of health issues, including the epigenetics of teen suicide and the prevention of life-threatening bloodstream infections.

So, yes, we’re delivering on our promise but there’s always more work to do. Meanwhile, enjoy this special research issue of our magazine and tell us what you think.
WHEN THE INAUGURAL EDITION of The "Harriet Lane Handbook" was published in 1953, its founding editors could hardly have imagined what it would be 60 years later. They conceived it as a pocket-sized, yet comprehensive “pearl book,” an indispensable resource written by residents for residents of the Harriet Lane Home, the predecessor to the Johns Hopkins Children’s Center. They didn’t know the manual would soar in popularity nationally and internationally as the clinical resource for all clinicians who treat children. Now, in its 20th edition—the book is published every three years to reflect changes in practice—the handbook has a new look and new wings with an app-accessible and interactive digital version. Not bad for a senior citizen.

“At one time the handbook was composed of typewritten chapters with sketches for figures, which would go off to the publisher and come back to us by mail,” says consulting editor Julia McMillan, Executive Vice Chair, Department of Pediatrics. “It’s gotten much more streamlined over the years.”

“The new online platform significantly enhances the digital edition,” adds chief resident Jamie Flerlage, who, with co-chief resident Branden Engorn, edited the book. “Now when you open the chapters you open an interactive book.”

But getting there required new learning. Working on the premier issue of the handbook in the early 1950s, six residents passed notes across a small table in the Harriet Lane Home library. In this 20th edition, the chiefs and residents had to learn html. Gone were Word track changes and overnight express, not to mention scraps of paper.

Like their predecessors, Engorn and Flerlage were most concerned about the accuracy of the handbook’s content and paid steadfast attention to details, particularly with the drug formulary, which is meticulously updated by Johns Hopkins pharmacist Carlton K. K. Lee. After all, the handbook is reputed to be the most trusted resource for pediatricians.

“It keeps us up at night because we have learned that people use the book verbatim,” says Flerlage. The senior residents and their advisers, who are the chapter editors, Flerlage explains, spent endless hours reviewing the guidelines to keep it up-to-date.

The handbook has a new look, too. Replacing Hopkins’ trademark dome on the cover is the multi-colored façade of The Charlotte R. Bloomberg Children’s Center, which opened in 2012.

“We wanted to break the mold for the 20th edition and do something special,” says Flerlage, “so we thought it would be nice to modernize the cover and dedicate it to the new building.”
Conquering Cloacal Exstrophy

by Ekaterina Pesheva

A milestone case, led by pediatric urologic surgeon John Gearhart, illuminates Johns Hopkins’ rich history in redefining the treatment of a devastating birth defect.
On May 5, 2010 — their five-year-wedding anniversary — Meagan Cline, a nurse, and Brandon Cline, a science teacher, went for a routine prenatal ultrasound.

The Mississippi couple, who’d been struggling with infertility, was expecting a child and eager to find out if they were having a boy or a girl. Instead of the baby’s gender, the ultrasound brought a far less welcome revelation: the baby had cloacal exstrophy (CE), a rare birth defect. Children with CE are born with a constellation of gastrointestinal and urinary tract anomalies, including non-fused pelvic bones and open abdominal wall that leave the bladder, intestines, spleen and liver outside the body. Babies with CE can also have short colon, an anus with a missing or blocked opening and, in some 70 percent of the cases, a non-fused spinal column or other spinal defects. In addition to forming outside the abdomen, the bladder is typically split in half.

CE is considered one of the most severe birth defects compatible with life—a mere few decades ago, most babies with CE didn’t survive. Today, the majority of them do, but face years of complex reconstructive surgery—with often uncertain outcomes—to build normal anatomy and restore healthy organ function. The news shook the Clines to the core. “It felt like a punch to the stomach that knocks the wind out of you,” says the child’s father, Brandon.

“Knowing that the child you wanted, hoped for and prayed for so much was going to be born with this condition, not knowing whether he was going to survive and that there’s nothing you could do about it is one of the most helpless feelings,” Meagan says.

After the initial shock wore off, the Clines got to work. They did research relentlessly, devouring articles from medical journals and brushing up on anatomy and physiology. Then something struck them. Every time they typed in “cloacal exstrophy” one name popped up over and over again: John Gearhart.

**Advancing Surgical Repair**

At the crack of dawn on a sweltering morning last June, John Gearhart, the director of pediatric urology at the Johns Hopkins Children’s Center, breezed through the hallway of the pediatric surgery prep area and was promptly swallowed by a set of double doors leading into the operating rooms. On his to-do list for the day: a surgery to relieve kidney obstruction, a hernia repair, two bladder cystoscopies, and an orchiopexy, a procedure to bring down an undescended testis. All of them routine urologic procedures, all of them before noon. It was one of Gearhart’s light OR days. Then it was clinic time.

Gearhart’s first visitors that afternoon were the Clines. A month earlier, their son, Carter, had undergone pelvic reconstruction and bladder closure—back-to-back procedures to repair two of CE’s hallmark defects. During the first surgery, pediatric orthopedic surgeon Paul Sponseller cut Carter’s pelvic bones and inserted metal pins that would slowly pull his separated hip bones closely together over several weeks. A few weeks after his pelvic repair, Gearhart positioned Carter’s bladder deep inside the child’s abdomen, where it should have been in the first place.

A tall Southerner with a larger-than-life personality and contagious laughter, Gearhart is disarmingy casual in his interactions with the Clines. Brandon describes his very first Gearhart encounter as instant doctor-patient chemistry.

“I am sitting in the room waiting to
meet this prestigious doctor and in walks Dr. Gearhart and starts asking me if I knew this person or that person,” Brandon says. “Turns out our families are from the same small town in Kentucky.

“He talked to me like one of my hunting-and-fishing buddies, and immediately I felt ‘OK, we’re going to be all right here,’” Brandon says.

Gearhart’s folksy, relaxed manner and straight talk can quickly melt the suffocating anxiety experienced by parents of children with extrophy facing one of the most complex and rarest conditions in medicine.

“Everyone else we’d seen up to that point was so tentative,” Brandon says. “Dr. Gearhart told us ‘This is what we’ll do, and this is what’s going to happen,’ and we really needed to hear that.”

In the exam room with the Clines that afternoon, Gearhart examined Carter carefully, pressing here, prodding there, firing question after question about his appetite, energy level, fevers. Pleased with Carter’s progress, Gearhart predicted that come Independence Day, the boy would be playing in the pool.

Carter’s pelvic bone reconstruction and bladder closure—considered the pivotal and most complex part of the multi-stage CE repair—were a turning point for the Clines, but his case also marked an important milestone for the Johns Hopkins Children’s Center. That spring, Carter became the 100th patient to undergo CE repair at Johns Hopkins—the highest number of such surgeries performed by any hospital.

Gearhart and Sponseller perform five to seven CE repairs a year. The number may seem misleadingly small until one factors the astonishing rarity of the condition. Estimates vary, but the general agreement is that fewer than one in 200,000 to one in 400,000 babies with CE are born every year in the United States.

“The largest CE repair series ever reported in the medical literature from a single hospital is just about 50. We’ve doubled that!” says Gearhart.

CE repair involves a multi-stage reconstruction over several years and remains one of the most challenging surgeries in modern medicine. The first repair, typically done within a few weeks of birth, involves putting any exposed abdominal organs, such as spleen, liver or intestines inside the abdomen, closing the abdominal hole and sewing the split bladder halves together. Any spinal cord defects, if present, are also repaired at this age. The second step, performed around age 1 or 2, involves cutting and realigning the split sides of the pelvic bone, followed by putting the bladder deep inside the abdomen. Finally, around age 6 or 7, patients undergo a continence procedure, during which surgeons build an
internal urinary reservoir from intestinal tissue that allows children to hold urine, rendering them catheter-free.

Many of the surgical and non-surgical advances in exstrophy repair over the last several decades were spawned at Hopkins, starting in the 1970s with Robert Jeffs, the founding father of pediatric urology at Johns Hopkins, and continuing today under the leadership of Gearhart, one of Jeffs’s disciples. These advances include the development and perfection of the staged approach to exstrophy repair, the introduction of several orthopedic innovations to treat the bony malformations of exstrophy, creation of new imaging modalities and redefining the way pain is managed.

The staged surgical repair, known as the “Jeffs approach,” emerged in the 1970s and was considered experimental well into the 1990s. Today, it is the standard of care for most children with cloacal exstrophy, as well as those with bladder exstrophy—the less-severe form of the condition in which the bladder is the only organ formed outside the body. The beauty of the gradual repair is that it reduces the tension on the abdominal wall muscles caused by abrupt pelvic bone fusion, says Gearhart, allowing the muscles of the pelvic floor to stretch slowly, over several weeks, as the bones are gradually brought closer together.

“Jeffs took a major birth defect which consigned children to a dismal life and devised a three-step technique to repair it, basically altering the lives of thousands of children throughout the world,” Gearhart says.

The Perfectionists

Historically, the rarity of CE and paucity of patients have meant fewer opportunities to study the condition, fewer surgeries and, consequently, more sluggish progress, at least when compared to the pace of advances made in more prevalent conditions such as congenital malformations of the heart, one of the most common birth defects.

As recently as the 1950s and well into the 1960s, physicians considered CE repair medically futile, sending newborns home for end-of-life care. Those who made it through the first year of life were relegated to a reclusive existence. Their bladders were excised, urine and stool-collection bags patched up to their bodies, requiring round-the-clock nursing care. The first cloacal repair leading to long-term survival was performed in 1959 by Peter Rickham, a British physician and pioneer in pediatric surgery who founded the first neonatal surgical unit in the world. Working alongside him was James Herbert Johnston, one of the founding fathers of pediatric urology. In his 1959 address to the British Paediatric Association, Rickham stated that CE was either completely absent from urology textbooks, or, when mentioned, dismissed as untreatable. Rickham made it his mission to change that.

Although a giant leap forward at the
time, early CE repairs were primitive by today’s standards, but the technique improved steadily over the next 20 years. By the mid-1980s long-term survival after CE repair was hovering around 85 percent. Today, nearly every child who undergoes CE surgery survives. Most of those who undergo proper and timely repairs at the handful of institutions in the world with advanced extrophy expertise, can also lead normal lives.

Today, the name of the game is perfection, Gearhart says.

“Today we no longer ask ourselves whether we could or should operate on these children. It’s all about how to do it in a manner that gives them a normal or near-normal physiological function and a healthy life,” Gearhart says.

Gearhart entered medicine just when pediatric urology was coming out of its “dark ages.” As a medical student at the University of Louisville, he became fascinated with embryology and abnormalities of fetal development. He felt that surgery offered a chance to correct nature’s errors: “It became clear to me that surgery offered a chance to correct nature’s errors: “It became clear to me that all major birth defects happen in the first 12-14 weeks of pregnancy, and that there isn’t much we can do to prevent that, but I felt surgery offered a stage to fix these defects.”

By the time Gearhart was out of medical school and entering specialty training, the field was on the cusp of a boom—an “Enlightenment” era of sorts. Gearhart went on to train in England under the extrophy pioneer Johnston and became one of his last residents. In 1984, Gearhart joined Johns Hopkins as a fellow under Jeffs, whom he eventually succeeded as director of pediatric urology. Gearhart performed his first CE repair in 1987, and has led 60 of the more than 100 CE surgeries performed at Hopkins.

Gearhart and Sponseller have restored urinary continence—the definitive marker of normal urinary function and the gold standard for success in CE repair—in some 90 percent of the patients they have treated, an astounding feat given the complexity of the defect and the significant portion of corrective surgeries the two perform. About half of all CE repairs done at Hopkins are corrections of failed surgeries done elsewhere.

Reconstructing the anomalies of CE into a normal anatomy is not unlike piecing a jigsaw puzzle. The various organs and systems affected require a multidisciplinary team of specialists and years to complete. There are few other disorders that demand the breadth and depth of expertise that CE does—urology, general surgery, orthopedic surgery, neurosurgery, gastroenterology, radiology, pain management and nutrition. No two children with CE are alike. The organs involved and the severity of malformations vary greatly from patient to patient. For example, in addition to non-joined pelvic bones, some children also have club feet, tethered spinal cords or hip dislocations. This variance demands surgical timing and technique tailored to each patient’s specific anatomy and overall health. In that sense, CE surgery is not unlike performing a symphony, except each time the piece is slightly different, with fewer or more elements, unexpected twists that require additional instruments or performers and, above all, a highly improvisational approach. “We never really ‘play’ the same piece twice in the exact same way,” Gearhart says.

If Gearhart is the orchestra conductor, then Paul Sponseller, the director of pediatric orthopedics at Johns Hopkins Children’s Center, is the concert master. Sponseller repairs the bone malformations of extrophy and his work lays the foundation for all subsequent soft-tissue and muscle corrections.

Gearhart and Sponseller cut a curious pair. Gearhart is tall, gregarious and voluble. He cracks jokes. Sponseller is a slim, gentle-eyed man of few words and quiet intensity. Over the last 30 years, Sponseller and Gearhart have operated side by side on hundreds of bladder and cloacal extrophy patients. Their work in the OR brings to mind a beautifully synchronized duet, but their partnership goes beyond the OR. The two frequently travel abroad to perform pro-bono surgeries and train colleagues in the latest techniques of extrophy repair.

Children with CE are born with separated and asymmetric pelvic bone due to a missing pubic symphysis, the cartilage that joins the two sides of the pelvic bone in the front. This absent joint leaves the pelvis open, split in half with a gap that can vary from 2 to 6 inches. To close the opening and realign the pelvis, surgeons cut both sides of the pelvic bone in several places, insert surgical pins and slowly pull the two sides together over several weeks. In the late 1980s, Sponseller, working with Jeffs and Gearhart, developed a novel technique that involves cutting the pelvic bone closer to the front rather than in the back. This frontal osteotomy, Sponseller says, allows the pelvic bones to rotate more naturally and eliminates the need to flip patients on their abdomen during surgery. The approach, now standard of care at Hopkins, is catching on elsewhere.

Another one of Sponseller’s innovations is the use of a metal implant to hold the hip bones together in place of the missing joint. Sponseller introduced the metal bar in the 1990s as an alternative to suturing, which, he says, was never strong enough to resist the natural tendency of the pelvic bones to pull back apart after reconstruction. And while surgical steel is decidedly better than sutures, it is less than perfect, Sponseller says. He and his colleagues are on a quest to find a more malleable material that would respond more naturally to changes in a child’s pelvis as it grows. Even though the metal bar works great
in holding the pelvic bones together, it doesn’t have the flexibility of normal cartilage, which allows the pelvic bones to shift gently and separate ever so slightly during movement.

These surgical advances have not occurred in isolation. As is the case with so much of medicine, improvements in one area are often spurred by progress in other specialties and in turn fuel innovation in others. Much of the modern work in extrophy repair would be unthinkable without advances in imaging and pain management (see below).

Imaging has come a long way since plain X-ray films that showed nothing more than a child’s bone defects, which are only one aspect of this multi-organ condition. For example, new imaging techniques now allow for never-before-possible visualization of the layers of muscles that cover the pelvic floor and control bladder and bowel emptying.

Johns Hopkins Children’s Center radiologists have developed a system that allows for unprecedented accuracy and detail in visualizing the soft structures of the abdomen before and after surgery. One such approach combines three-dimensional and two-dimensional visualization to create an image that is greater than the sum of its parts. The 3-D image provides visualization from any angle and any plane, while the 2-D image allows for easy anatomic measurements. Combining the two is something like magic, says pediatric radiologist Aylin Tekes-Brady.

Inspired by Gearhart’s quest to perfect extrophy imaging, Tekes-Brady recently adapted a pre-surgical navigation system used in brain surgeries to map out extrophy repairs before surgery. Images obtained from an MR scan are uploaded into a software program that radiologists use to flag anatomic landmarks for the surgeons before they even enter the OR. “It’s like a GPS for surgical navigation,”

Research at Johns Hopkins Children’s Center, says pediatric anesthesiologist Myron Yaster, has fueled advances in pain management for children who undergo extrophy repair.

In those days, clinicians feared that infants born with extrophies were too sick to tolerate potent opioids, whose side effects are dangerously intensified in ill patients. So under medicine’s basic tenet “First, do no harm,” physicians erred on the side of caution and treated extrophy patients with run-of-the mill pain-killers that did little to nothing to assuage their agony. This was the standard of pain treatment well into the late 1970 and early 1980s.

Things began to change at Hopkins in the 1980s, when Robert Jeffs, Johns Hopkins’ chief pediatric urologist, recognized how essential pain management was to the post-surgical care of his patients. Jeffs introduced pediatric pain specialists formally into the extrophy care team, a tradition continued by John Gearhart.

Around that time, Yaster launched the pediatric pain service at Johns Hopkins, which pioneered new techniques and novel drug-delivery systems for pain management and sedation.

Patient-control anesthesia, or PCA, introduced in the early 1990s, is one of them. PCA allows children to regulate their own intravenous analgesia by pressing a button that delivers an extra shot of pain relief, but is use-
Tekes-Brady says. “You know where you are in three-dimensional space at all times and since so much of our surgeries involve correcting previous surgeries done elsewhere, this visualization gives us extra confidence that we’re doing the right thing in the right spot,” Gearhart says.

**Cellular Cures**

Advances notwithstanding, there’s much more to be done. The holy grail of understanding exstrophy—and indeed, any disorder—lies in decoding the molecular malfunction that fuels abnormal cell behavior and leads to manifest disease. That knowledge, Gearhart says, will illuminate ways to restore normal cell function. One immediate benefit of this knowledge would be to create normal bladder tissue in the lab for use in surgery.

Johns Hopkins biomedical engineer and cell biologist Larissa Shimoda, for example, is working alongside Gearhart and a cadre of pediatric urology fellows to tease out differences in behavior between the cells of normal and exstrophied bladders. A signaling protein known as transforming growth factor-beta (TGF-beta) has emerged as a potent player in the development of exstrophies. TGF-beta is already known for its role in a range of connective tissue disorders such as Marfan and Loeys-Dietz syndromes, genetic conditions marked by blood vessel laxity and dangerous stretching of the aorta, the body’s largest blood vessel. Research conducted by Shimoda and colleagues reveals that abnormal TGF-beta signaling may also lead to anomalous cell development in the bladder.

“We’re essentially learning how cells in the bladder talk to each other,” Shimoda says. “And we’ve learned that cells in exstrophied bladders exhibit a range of abnormalities in that regard.”

Indeed, their work has revealed that cells in exstrophied bladders have low calcium levels and altered functionality, including aberrant migration and growth patterns.

Gearhart and his group recently received a green light from the National Institutes of Health to grow urinary bladder sphincters using undifferentiated cells from a patient’s own tissue. The ability to grow bladder muscle in the lab would also benefit a wider pool of patients, including those with bladder damage following traumatic injuries to the organ, male incontinence following prostate surgery and female incontinence caused by pelvic prolapse, a condition seen in older women who have given multiple births.

Gearhart’s face lights up and his already rapid-fire talk picks up pace ever so imperceptibly when he talks about the scientific advances in exstrophy repair. Yet, he says, even with all the advances in medicine and all the boundary-pushing science, one of the greatest predictors of success remains a child’s family.

“No matter how severe the birth defect, if you have a loving and supportive family, you’re already light years ahead as a surgeon,” Gearhart says.

Case in point—the Cline family and their now-thriving toddler, Carter, whose long-term prognosis is excellent. “Carter is going to be a normal little boy,” Gearhart says. “He’s going to be able to play contact sports, and other than a few bumps on the road, his quality of life is going to be the same as any other boy’s.”

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For more information visit hopkinsmedicine.org and click “Anesthesiology” under “Specialties.”

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Pediatric nurse
Amie Tawney in Carcasse, Haiti.
When Assistant Director of Pediatric Nursing Dawn Luzetsky worked as a clinical instructor, she made a point of asking nurses who were Peace Corps volunteers to join her in the classroom: “I was always in awe of the things they did in such rural, remote places with little or no resources. It takes a special person to do that.” We decided to follow up on her observation with a photo journal snapshot of some of our own “special” Johns Hopkins Children’s Center nurses experienced in so-called “medical missionary” work. Where did they travel? What did they learn? How did the experience enhance their nursing skills? And how did it change them? Through their lens, here are some of the answers.
SANDY DIETZEL: A Bonding Experience

To say pediatric nurse Sandy Dietzel is a veteran when it comes to medical missions would be a gross understatement. In February 2014, she went on her 23rd trip with Operation Smile, adding Honduras to Bolivia, China, Ethiopia, Indonesia, Kenya, Thailand, Peru and Senegal, among other countries she’s traveled. Why so many journeys? “It’s a very bonding experience,” she answers point blank. In the United States, cleft lip and palate patients are treated early in life, avoiding the ostracizing disfigurement and swallowing issues facing many patients in developing nations. “In Honduras,” Dietzel explains, “we operated on a 23-year-old who grabbed my face and said ‘Now I can kiss somebody and get married.’ It’s an immediate difference that improves the quality of their life in such a dramatic way, and you appreciate the difference you can make.”

Dietzel also points to the egalitarian philosophy of the Operation Smile teams: “Everyone is equal, everyone is very flexible, everyone pitches in—you rely on each other so much. You also make life-long friends.” While at Hopkins she cares for infants and toddlers on a medical-surgical unit—overseas she typically fills in as a recovery room nurse for patients young and old, enriching her nursing skills. Her trips also help her to better empathize with the international patients she sees at Hopkins. For example, Dietzel says, she has become more attuned to cultural differences: “In Thailand, you cannot touch the top of a baby’s head. That’s a ‘no-no.’”

Sandy Dietzel in her medical-surgical unit and, above, in Senegal, West Africa.
The way pediatric emergency medicine nurse Nayra Zimmermann sees it, her passion for nursing beyond the borders has its origins in Panama—where she grew up. There the importance of family was ingrained in the culture, just as it is in countries like Haiti, Nigeria and Peru, among the places she’s traveled on tropical medicine trips with Johns Hopkins pediatric ED physician Karen Schneider. “Growing up in the Republic of Panama, I saw the need to be with families in true need. And soon after I started doing these trips, I learned that no matter where you go, our friends across the ocean have a sense of family. They’re always struggling and want the best for their kids, so they welcome us and trust us. The family unit does exist everywhere.” The trips, she adds, help her simplify and value her own life—and her basic nursing skills, too. Operating out of rural and remote clinics far removed from the resource-rich world of Johns Hopkins, Zimmermann says, takes one back to one’s roots as a pediatric nurse: “We really get tied up with technology here at Hopkins, and sometimes forget that our eyes and our touch are the best tools in the world. On these trips we really trust the assessment skills we practiced in nursing school, and learn that we are able to apply them anywhere.” Zimmermann adds that participating in medical missions may have saved her marriage, too. How? Her 10 international nursing trips have helped mold her into a more flexible and patient partner, she says with a laugh: “As long as I can work an extra shift in the ED to continue to fund my vacations—and that’s what they really are—I will continue doing it. Needless to say, I’m very thankful for my husband for allowing me to do this, too.”

NAYRA ZIMMERMAN: Connecting with Families

The way pediatric emergency medicine nurse Nayra Zimmerman sees it, her passion for nursing beyond the borders has its origins in Panama—where she grew up. There the importance of family was ingrained in the culture, just as it is in countries like Haiti, Nigeria and Peru, among the places she’s traveled on tropical medicine trips with Johns Hopkins pediatric ED physician Karen Schneider. “Growing up in the Republic of Panama, I saw the need to be with families in true need. And soon after I started doing these trips, I learned that no matter where you go, our friends across the ocean have a sense of family. They’re always struggling and want the best for their kids, so they welcome us and trust us. The family unit does exist everywhere.” The trips, she adds, help her simplify and value her own life—and her basic nursing skills, too. Operating out of rural and remote clinics far removed from the resource-rich world of Johns Hopkins, Zimmermann says, takes one back to one’s roots as a pediatric nurse: “We really get tied up with technology here at Hopkins, and sometimes forget that our eyes and our touch are the best tools in the world. On these trips we really trust the assessment skills we practiced in nursing school, and learn that we are able to apply them anywhere.” Zimmermann adds that participating in medical missions may have saved her marriage, too. How? Her 10 international nursing trips have helped mold her into a more flexible and patient partner, she says with a laugh: “As long as I can work an extra shift in the ED to continue to fund my vacations—and that’s what they really are—I will continue doing it. Needless to say, I’m very thankful for my husband for allowing me to do this, too.”

Nayra Zimmerman outside Johns Hopkins Pediatric Emergency Department and unpacking with colleagues on a medical mission in Nigeria.
Amie Tawney traces her desires to become a nurse back to age 11 when her mother was ill in intensive care, where she wasn’t allowed in. So it was only logical that years later she chose an intensive specialty—neonatal nursing—as a career and an intensive care environment—she wanted to go into the room. She also has this constant need to be challenged, part of her motivation to travel with Health and Education for Haiti volunteers in October 2013 to Carcasse, Haiti, a poor, rural town in southwestern region of the country that has little electricity, no running water and no internet or phone service. Getting there was a journey in itself—a flight to Port-au-Prince, a cab ride to another airport, a puddle jumper to a remote field, and a bumpy, three-hour drive to the village. Housing was a priest’s house, the clinic a dirt floor and canvas canopy, where she saw some 200 pediatric and adult patients daily with conditions ranging from dehydration to malaria, as well as a child with typhoid—the “palest patient” she had ever seen. Much of her work in the clinic was starting intravenous lines, getting fluids into young, dehydrated bodies, and teaching families how to change the IV bags. With no digital readouts to rely on, she had to think outside of the box. “If you don’t have everything at your fingertips, what do you do?” says Tawney. “You’re using your basic skills more often—you can’t rely on an IV pump to tell you how fast the rate should go. I’m like, ‘What’s this drip method again?’” Down time included playing pranks on her teammates, like placing fake spiders in their bunks, listening to the constant skirmishes between goats and stray dogs, and talking about how hot it was. “It is like they say—’hotter than Haiti,’” says Tawney. Is there another trip on the horizon? “Yes, you can get comfortable and bored in a position, and I just have this itch to do something different, to help people who want to be helped,” says Tawney. “They don’t have anything. They are very happy to be seen and they definitely appreciate the care.”

AMIE TAWNEY: Scratching an Itch

Amie Tawney in the NICU and, above, in a clinic in Haiti.
Amy Peters’s older sister, a nurse, inspired her to follow in her footsteps. But it was her best friend in college who triggered her interest in international volunteer work. “After college,” says Peters, “I decided I wanted to do some kind of mission on my own.” And did she—with travels over the past two decades as a pediatric intensive care nurse to places like the Gaza Strip, Kenya, the Philippines and Vietnam. A seasoned nurse with 24 years of experience in pediatric intensive care at Johns Hopkins, Peters is a clinical resource on her unit. Rather than direct hands-on care for patients, she helps new nurses transition to their bedside role. Similarly, on her international trips with Operation Smile, which provides surgical repair of cleft lip and cleft palate, she finds herself educating younger, less experienced nurses: “You provide the same skills but without the things we tend to take for granted here, so you have to think differently and jury-rig things we don’t have.” Much of her time overseas is also spent screening patients and setting up makeshift ORs, while learning the language and culture of the children she treats. Her travels have not been without some troubles along the way, including a bout with malaria in Kenya and gastro-intestinal problems in Venezuela. Then there was the time she had to be escorted in and out of the hospital in the Philippines during civil unrest following contested elections. The rewards? “You become a better nurse by gaining knowledge from other places, and by appreciating the cultures you learn from.”
When Marina Dackman was asked in the fall of 2011 to join a small but highly specialized Johns Hopkins cardiac surgery team traveling to Pavia, Italy, to operate on children with aortic valve disease, she didn’t hesitate. An experienced pediatric intensive care nurse, she knew she would be valued in overseeing with the attending physician the post-operative care of these patients. She also knew she would be challenged, and in her mind that’s what nursing is all about: “If I was to describe the experience I would say ‘awesome and challenging’ to the core, an opportunity to improvise, to think on your feet, to share expertise and meet people from different cultures, and to practice Italian.” What she didn’t anticipate was seeing the image of Johns Hopkins Hospital’s historic “Dome” in a restaurant window one night, what she calls “a special moment.” The image, of course, was not the quintessential Hopkins symbol but the cupola of Pavia’s main cathedral, but it helped solidify why she was there: “I left with a tremendous amount of appreciation for the Hopkins team and the nurses we worked with in Italy. It was a great honor and privilege to be part of this opportunity.”

**Marina Dackman: Finding Hopkins in Pavia**
Elizabeth Foley: A Humbling Experience

Pediatric nurse Elizabeth Foley caught the travel bug early in her career—in 2009 while a student at the Johns Hopkins School of Nursing. There she was offered a 10-day public health nursing experience in Haiti, focusing on education and immunization for adolescents and their families. It was, in her words, “a whirlwind of a trip you can’t put into words” that pushed her, after graduating from nursing school, toward a week-long surgical mission in Guatemala sponsored by the Healing Hands Foundation. In the poor, rural mountain town Patzun, where patients suffer chronic malnutrition and it’s rare for homes to have electricity or water, she joined a team of surgeons, anesthesiologists and other nurses who performed some 70 procedures for conditions ranging from cleft palate to inguinal hernia. At Johns Hopkins, Foley cares for school-age medical and surgical patients. In Patzun, her job was post anesthesia care. The value of the experience? “It’s humbling,” she says. “At Hopkins, with the technology and the assistance from co-workers, we have so many things they just don’t have in developing countries. It’s a good way to keep your career in check. The people I worked with were incredible—everyone was there for one reason, one mission, to get as many surgeries safely done as we could.”

Elizabeth Foley on her medical-surgical unit at far right and in Patzun, Guatemala.
By cultivating clinical investigators and collaborating with Johns Hopkins colleagues up north, All Children’s Hospital aims to have an even bigger impact on children’s health in Florida and beyond.

by Gary Logan
Photography by Allyn DiVito
An experienced and busy pediatric oncologist at All Children’s Hospital (ACH) in St. Petersburg, Fla., Stacie Stapleton often probes her mind for better ways to treat patients with high-grade brain tumors threatening their lives. Treatments like surgery, chemotherapy and radiation therapy bring their own toxic side effects to patients’ health and quality of life. While many of these patients can be treated curatively, some reach a point at which a palliative, symptom-management approach is more appropriate. And that clinical reality led to the latest question poking her brain—at what point?

To get at the answers to what she saw as a qualitative research question, Stapleton realized, she would need to assess perceptions of palliative care among patients, their parents and caregivers. She needed a benchmark, which in her experience in qualitative research—or lack of it—was no small hurdle.

“I’ve done clinical trials and even phase-one trials in the past but I’ve never done qualitative research, which include open-ended questions and surveys regarding quality of life,” Stapleton says. “That’s more of a gray area for me, so I really needed help.”

Help came from Johns Hopkins pediatric investigators Erica Sibinga and Sharon Ghazarian 1,000 miles up the East Coast in Baltimore, Md. As part of a customized team of physician scientists, biostatisticians and epidemiologists, they were tasked with training busy pediatricians like Stapleton in the art of clinical research. Yes, Stapleton and her colleagues had conducted trials through residency and fellowship programs and they were participating in clinical trials at All Children’s, but research has played a small role because their time is almost exclusively dedicated to taking care of patients—a dynamic Johns Hopkins saw as a huge benefit in its integration with All Children’s in 2011. The challenge now was brushing up their research experience and engaging them in leading clinical studies.

“Our job is to help those investigators see that what they do clinically is so amazing and worthy of research, and to help them do the research and push it back into patient care,” says Ghazarian, who provides epidemiology and biostatistical consultation for investigators across Johns Hopkins.

“One of the challenges for very experienced, well-trained clinicians who have lots of ideas, is turning that big question generated from a clinical experience into a question that can actually be answered in a discrete research study,” adds Sibinga.

While Ghazarian and Sibinga have distinct roles at Johns Hopkins—Ghazarian is director of the Biostatistics, Epidemiology And Data Management (BEAD) Core program and Sibinga director of Ambulatory Pediatrics at Johns Hopkins Bayview Medical Center—they are now teammates in Johns Hopkins “Designing Clinical Research (DCR)” program, charged with cultivating clinical investigators and developing the research enterprise at ACH. Moreover, their efforts are central to the transformation of All Children’s from a 259-bed regional Florida children’s hospital known for its exceptional patient care to a pediatric health system known as a national leader in advancing children’s health through research and teaching, as well as patient care.

“I would like people to recognize that we are leaders in transforming care and improving the health of children in Florida and beyond,” says Jonathan Ellen, ACH president and professor of pediatrics and vice dean, All Children’s Hospital, for JHUSOM. “If that’s where we are in 10 years, I’ll be excited.”

But how would All Children’s get there? How would the DCR program and the research collaborations it spawns function and fare?

**Nurturing a Research Environment**

Pediatricians were drawn to All Children’s by its clinical—not research—enterprise. They wanted to deliver first-rate
patient care in a state-of-the-art children’s hospital. While the integration didn’t change these clinical goals, it did add research and teaching to the mix.

So, how do you re-engage such clinically minded pediatricians in research and stimulate collaborations? By invitation, not intimidation, through a partnership rather than a dictatorship, says Johns Hopkins General Pediatrics Division Director Tina Cheng, who is leading the DCR team.

“The fear was we were going to drive a bus full of Hopkins researchers down to St. Petersburg,” says Cheng. “I felt it was really important to identify and collaborate with the people at All Children’s who were already doing research or interested in doing more.”

The blueprint for the plan was distilled from Cheng’s experience in training Johns Hopkins researchers. Ellen knew Cheng well and quickly realized she was a perfect match for All Children’s research-training needs.

“Because of her leadership thinking and sensitivity about how people who are not basic scientists can develop into research teams, I said ‘let’s do this,’” says Ellen. “I knew it would give us a win early on, build some research capacity and create linkage between the two campuses.”

The Baltimore link would be Cheng, Ghazarian, Sibinga and Tracy King—experienced investigators who would work as research mentors with the Stapletons of All Children’s. Those interested were asked to apply with a research question in their area of interest. Members of Cheng’s group would then pair off with ACH researchers and through bi-weekly teleconferences help them refine their research question and mold the methodology of their study.

The formula worked. Stapleton was able to weave her palliative care question into a study design and obtain a grant thanks to guidance from Ghazarian and Sibinga. Now she’s planning an intervention study to assess the impact of palliative care on symptom control.

“It’s been great,” says Stapleton. “I feel like a medical student all over again, learning something quite new.”

All Children’s pediatric oncologist Stacie Stapleton, left, needed epidemiologic help for her palliative care research project and got it from her Baltimore colleague, Sharon Ghazarian.

That’s the idea, fresh ideas and fresh learning, says Ghazarian—and why Stapleton is a “beautiful example” of a pediatrician suited for the program: “She’s taken her experience with brain tumor patients and their families, developed a research program in which she’s learning more about the barriers to palliative care, and is now designing an intervention study to reduce those barriers.”

Similarly, All Children’s neonatologist Fauzia Shakeel wanted to know whether preterm infants who receive higher doses of protein would fare better. And, like Stapleton, she needed help collecting and analyzing quality improvement data. From Cheng and Ghazarian, she got it and more.

“The collaboration was an excellent step toward understanding the progress of developing, designing and executing a project, and writing the manuscript,” says Shakeel, who presented her poster at the annual meeting of the Pediatric Academic Societies.

ACH infectious disease specialist David Berman, concerned about low immunization rates in the St. Petersburg area, wanted to pluck local pediatricians’ beliefs about vaccine refusal by parents. But such a study required a survey design—a new methodology in Berman’s research repertoire. Cheng steered him
toward some resources, helped fine-tune his questions, and kept him on schedule.

Berman’s study has not yet been submitted for publication—free time for a busy clinician is an issue, he says—but one outgrowth of his work has been the formation of a Pinellas County Health Department task force aimed at improving immunization rates. “The experience got me more involved with children’s advocacy,” he says.

Berman’s colleague, Allison Messina, was interested in how ACH staff treat spinal instrumentation patients who develop an infection following surgery. Messina knew that foreign material in the spinal hardware renders such infections hard to clear, but she could not find a clear answer in the literature on how best to treat these patients.

“Most of the studies say you take the instruments out, but we know most people don’t do that because it’s not easy to remove and then you have a child with an unstable spine,” Messina says.

Sibinga helped Messina design her study, make sense of the data and incorporate it into a narrative. “The biggest help was the mentorship,” says Messina. “Erica [Sibinga] helped me put the paper together and present it in a way journals would be receptive to it.”

They were. Messina’s study is now pending publication in The Pediatric Infectious Disease Journal.

With Cheng’s mentorship, All Children’s hospitalist Dipti Amin was able to design her study regarding readmissions in a way that would pass muster with the IRB, receive grant funding and stimulate journal editors’ interest. More importantly, Amin says, the answers to her question—how parents can help reduce readmissions—improved her practice.

“Knowing that unfilled prescriptions can cause readmissions, I now have my team go the extra mile and have medications filled before discharge,” says Amin. “If patients aren’t making follow-up appointments, we ask why?”

The DCR program was working, albeit not without some hurdles—a big one was just getting to know each other.

Cheng and her group knew that achieving successful collaborations meant cultivating long-term relationships.

“We were one of the first groups that came down after the integration, and no one was sure who we were or what we were going to be doing,” says Ghazarian.

“But we’re all flexible and malleable and just sort of moved with the flow.”

Another speed bump—scaling the learning curve and finding free time to do research.

“It’s always a challenge to expand the portfolio of work when you’re serving lots and lots of kids,” says Baltimore collaborator Sara Johnson.

Adds Cheng, “It’s a shift and finding the time is hard.”

But is it a seismic shift? It’s not an issue to which Jon Ellen is insensitive.

“When you’re Johns Hopkins and you come in and start talking about academics, you also need to respect the culture of an organization that already provides great care,” says Ellen. “I’ve made it clear that there is a place here for everyone who contributes to the mission, whether through excellence in research, clinical care or education. The intention is to add to the research leg, not subtract from the value of the other legs.”

Protected time for research?
“Nobody gives it to us here either—they only have it because they have grants,” says Baltimore pediatrician Maggie Moon. “We’re training people how to get grants so it becomes part of the function down there in building a robust research structure.”

Ellen states his world viewpoint—protected time is earned. Well versed in helping young physicians develop as researchers, Ellen has mentored 17 NIH career development award recipients.

“Show me that you have the passion and determination to do research, and show me the results and that you’re being limited by time and not inspiration,” says Ellen. “Then I’ll buy your fire and we’ll talk about what needs to happen to protect you.”

Were members of Cheng’s mentor team feeling the fire? Any “aha” moments early on—or misgivings?

“With the first cohort we did have some concerns, but then we realized they were talking different and thinking different,” says Ghazarian. “They got it.”

**Spawning Collaborations**

Through the DCR program, research seeds were planted and replanted, spawning new collaborative studies. One barometer of change was the whirlwind of literature-search requests arriving at the desk of ACH Medical Library Director Patricia Clark. Her research teaching sessions at hospital units increased dramatically, too.

“Everything stepped up, from the types of searches we were doing to what we were teaching our staff to become self-sufficient researchers,” says Clark. “The day they flipped the switch and gave us access to the Johns Hopkins Welch Library, our little list of databases went way up.”

Another indicator of change was the upsurge in email and Skype communications between Hopkins pediatricians in Baltimore and St. Petersburg. Southwest Airlines likely saw an uptick in bookings on its BWI to Tampa route, too, as practice-related research questions being raised in St. Petersburg—and the collaborations conceived to answer them—began to percolate up and down the East Coast. Hopkins pediatricians suddenly found themselves comparing research notes at 38,000 feet and in hotel lobbies and restaurants in Pinellas County, Fla.

“They’re doing multi-institutional trials, collaborating over the video waves and flight paths,” says Ghazarian.

Examples abound. All Children’s critical care specialist Arabela Stock wanted to identify predictors of outcomes for patients in the hospital’s 146 intensive care units. 

“The fear was we were going to drive a bus full of Hopkins researchers down to St. Petersburg. I felt it was really important to identify and collaborate with the people at All Children’s who were already doing research or interested in doing more.” —TINA CHENG, M.D.
care beds, so she teamed up with Baltimore-based pediatric cardiologist and biomarker investigator Allen Everett. Together they designed a study to identify so-called “electronic markers” of clinical outcomes by acquiring bedside monitoring data and aligning it with patients’ electronic medical records.

“What’s the physiologic signature of someone about to have cardiac arrest, for someone about to go into respiratory failure who needs to be intubated? When can you wean certain patients off narcotics?” says Everett. “The implications are huge.”

“If you can identify physiologic predictors of prematurity, sepsis or sudden cardiovascular collapse, then you can develop algorithms and create interventions to reduce the risk of such outcomes,” adds Stock.

Meanwhile, bricks were being laid for construction of a new research infrastructure at All Children’s to facilitate such studies. A director of research, Neil Goldenberg, was hired from Children’s Hospital Colorado to develop ACH’s new Clinical and Translational Research Organization. Picking up Hopkins’ torch of innovation, Goldenberg incorporated into the organization a framework of seven cores to support all aspects of research. Then he led the creation of iPICS, or Institution-wide Prospective Inception Cohort Study, an innovative research protocol designed to identify key predictors of outcomes in children with a variety of conditions. For good measure, Goldenberg added a Healthy iPICS cohort, too.

For Hopkins pediatric subspecialists north and south, iPICS offered a fertile field to till. Johnson, who focuses on how early life environments may lead to biologic and cognitive changes that affect health later in life, was interested in partnering with All Children’s obstetrician Sheila Devanesan, who was interested in the impact of obesity among pregnant women on birth outcomes (see page 48). Then Johnson learned about Healthy iPICS.

“It’s a pretty cool thing because it allows us to follow a group of healthy children over time and then go back to see how their data differed from kids with conditions like obesity,” says Johnson. “The goal is to better determine why some children remain healthy and others do not.”

Next came epidemiologist/biostatistician Ernest Amankwah, who would help All Children’s clinician researchers formulate study design. All Children’s now had its own Ghazarian.

More bricks were added when All Children’s constructed a biorepository with the capacity to store some 30,000 frozen specimens for researchers like Johnson and Devanesan to study. Next, All Children’s Institutional Review Board (IRB) became an official Johns Hopkins IRB, further expanding collaborative research opportunities between the two campuses.

All of the groundwork and underpinnings pointed to formidable research possibilities in St. Petersburg—and in Baltimore, too. Johns Hopkins Children’s Center Director George Dover saw the potential at a fall 2013 meet-

I would like people to recognize that we are leaders in transforming care and improving the health of children in Florida and beyond. — JONATHAN ELLEN, M.D.
ing with his division chiefs: “My vision is people in St. Petersburg will actually stimulate the folks up here to think about clinical trials we haven’t done.”

Indeed, the research culture being cultivated at All Children’s was sending good vibes north that not only stimulated research collaborations but an array of academic activities. While neonatologists on both campuses began sharing their findings on the use of cooling therapy to protect brain tissue from possible damage at birth, for instance, pediatric neurologists Parrish Winesett in St. Pete and Eric Kossoff in Baltimore were developing a virtual clinic for ketogenic diet patients. A component of iPICS—a pediatric thrombosis program now spans both campuses. All Children’s staff presented at the annual patient safety summit in Baltimore as pediatric cardiologists there presented at All Children’s annual congenital heart symposium. Weekly Pediatric Grand Rounds at both campuses were shared via live videoconference with staff at both campuses. All Children’s could already be called academic—but how was it dealing with the culture shift?

**Blending Cultures**

Pediatrician Maggie Moon tends not to get over the moon when discussing All Children’s transformation. A bioethicist who brings empathy to her role each day, she forecasts a positive shift but not without some bumps along the way.

“Academic medicine is very pushy—it does not allow anyone to stand still for very long,” says Moon. “But people in St. Petersburg have been doing research for a long time. It’s not like they have no track record.”

Moon also notes that the integration is just that—an integration—so the strengths of both institutions will influence each other. “All Children’s reminds us that there’s another way than the East Baltimore way to do things that is functional and fine,” says Moon. “So our style will have to tumble down a bit to incorporate the culture and experience of Florida, which has to be good for us.”

Moon and others also note the obvious—new academic patterns will complement patient care, too. What’s not so obvious is that those patients are opening a window to another academic dynamic—population health.

“All Children’s gives us a greater population of patients to test what we find here with other populations in a completely different environment, which increases the validity and reliability of results,” says Ghazarian. “That’s big!”

So, in Jon Ellen’s mind what does the transformation portend?

“It means we not only offer cooling therapy for fragile prematures but also become known as a thought leader in cooling therapy for fragile premature newborns,” says Ellen. “It means we’ll have an ability to prevent certain outcomes, to not only tell people what we do but actually figure out better ways to do it.”

That impact on pediatric medicine, Ellen and others add, could reach well beyond the Sunshine State. One example—the physiological monitoring collaboration between Everett and Stock, if successful, could reap benefits for pediatric intensive care patients nationwide.

Cultivating thought leaders, advancing and accelerating knowledge, expanding its presence—where will All Children’s go? Will it transform Hopkins pediatrics as a whole?

“It will be interesting to see if this experience leads to a bigger name nationally for Johns Hopkins pediatrics,” says Moon. “If the focus is on enhancing service to children all over the country, that’s a good thing. So maybe it’s time for us to step up and wave our flag harder and higher—we have a good program, good people.”

**Tina Cheng, center, with All Children’s collaborators Dipti Amin, left, and Fauzia Shakeel.**
Neonatologist Frances Northington, with NICU nurse Charlamaine Parkinson, simulates hypothermia therapy for newborns at risk of brain injury.
“When the doctor looked at her he did not think she was alive,” says Wendy Septembre, Hadley’s mom.

But there were signs of life in the limp newborn; she had a strong pulse but was not breathing. Staff were able to revive her after some time and get her to start breathing on her own for the first time ever. Doctors at AAMC knew Hadley needed high-level neonatal intensive care quickly and transferred her to Johns Hopkins Neurosciences Intensive Care Nursery, a unit designed to treat newborns at high risk of brain injury. There neonatologists moved quickly to liberate Hadley’s brain from the ravages of HIE.

“We have a very short time in which we can help rescue the brain and stop the neuronal cell death that begins immediately and escalates rapidly,” explains neonatologist Frances Northington. “We have just minutes to hours to intervene.”

Northington and her team recommended therapeutic hypothermia, or brain cooling therapy, for Hadley. The once-novel treatment, under study at Johns Hopkins since 2000, is now becoming the standard of care for HIE.

How does it work? To cool the baby’s head without cooling off the body, which could result in other problems, Hadley would rest in a radiant warmer to keep her body temperature just slightly below normal as cool water was pumped into a cooling blanket.

“We cool the baby to a temperature of 33.5 Celcius, or 92.3 degrees Fahrenheit, which is fairly cold,” says Northginton. “It interrupts the injurious metabolic processes causing the neurons to die.”

The Septembres were stunned by Hadley’s condition but confident in the treatment. “They explained everything to me, and they were very positive and upbeat about the protocol,” says Sam Septembre.

After three days, Hadley’s body temperature was gradually raised to normal levels. During treatment Hadley did experience a collapsed lung and pulmonary hypertension, but she recovered with no life-limiting, long-term effects.

“I would say to any parent in the beginning stages of this, you just have to have trust in the doctors and the protocol,” says Wendy Septembre.

Says NICU nurse Patrick McGrath, “I’ve seen miracles after miracles happen. I keep on seeing these babies come back and I’m always pleased.”
CALL IT THERAPEUTIC POOP, if you will, but the best hope yet for an effective treatment of childhood infections with the drug-resistant bacterium *C. difficile* may come straight from the gut, according to recent research. Parlaying that research into practice, the Johns Hopkins Children’s Center has launched a fecal transplantation program for patients with recurrent diarrhea caused by what clinicians say is a wily pathogen that is increasingly impervious to drugs and a rapidly growing problem among children and adults.

“Fecal transplantation—or the transfer of ‘good’ bacteria from the colon of one person into the colon of another—should be considered for all children with *C. diff* infections who don’t respond to two standard courses of antibiotics,” says pediatric gastroenterologist Maria Oliva-Hemker.

Such beneficial bacteria work by keeping rogue players in check, Oliva-Hemker explains, so any shifts in gut environment—such as ones caused by antibiotics—can have dire consequences. When good bacteria are killed off by antibiotics, the bad guys multiply causing an imbalance or “dysbiosis,” Oliva-Hemker says. Typically, gut infections caused by one antibiotic are treated with another one to eradicate the overgrowth of harmful pathogens, but drugs often fail to do so fully or permanently because they only treat part of the problem.

“When we administer an antibiotic to treat the *C. diff* infection, we destroy some of the bad bacteria, but that does not address the other half of the problem—the loss of good bacteria that might have led to the infection to begin with, so we never truly restore the balance in the gut and often the diarrhea returns with a vengeance in a matter of weeks,” says pediatric gastroenterologist Suchitra Hourigan.

The concept of treating poop woes with poop is hardly new. The method originated with ancient Chinese healers who gave their diarrhea-ravaged patients “yellow soup,” a concoction of fecal matter and water. Nowadays, fecal transplants are often performed during a colonoscopy, and improvement can be seen in as little as two weeks, as beneficial bacteria start to repopulate the patient’s gut, Hourigan says. Studies in adults show that more than 90 percent of patients are cured following such therapy and, experts say, they have every reason to believe the numbers would be equally impressive in children.
Liver Disease: Stool-Color Chart & App to Speed Up Diagnosis

Fecal color and consistency are well-known markers of digestive health in both children and adults, but paying attention to a newborn’s shade of stool can be a decided lifesaver in babies born with the rare, liver-ravaging disorder biliary atresia, commonly heralded by white or clay-colored stool.

Yet new parents are rarely told to watch out for abnormalities in their baby’s stool. Now, pediatric gastroenterologists from the Johns Hopkins Children’s Center are on a mission to change that by tackling the problem on two fronts.

First, they have designed a simple, one-page stool color chart that Procter & Gamble Baby Care will distribute for free to birthing centers nationwide. In addition, a free mobile app, developed for Johns Hopkins by HCB Health, uses color recognition software to allow parents to snap photos of their baby’s stool and receive feedback within seconds. Parents then have the option of sending the photos to their pediatrician. The app also offers reminder notifications for stool-color checks every two weeks between birth and 2 months of age, the critical window in diagnosing the disease.

Biliary atresia is the leading cause of liver failure in children and the number one reason for liver transplantation in children. Simple interventions, like the stool color chart and the mobile app, can greatly enhance recognition of abnormal stool and even make the difference between life and death in some cases of biliary atresia. A similar stool color chart in Taiwan led to faster diagnosis and improved the five-year survival rate by 33 percent — from 56 percent to 89 percent — according to a 2010 study published in the journal Hepatology.

“The truth is we don’t need an elaborate educational intervention. Something as simple as a tear-off sheet or a quick conversation about what to watch out for can go a long way,” says pediatric gastroenterologist Douglas Mogul.

Mogul believes the mobile app can help ensure timely diagnosis given its convenient automated reminders and the ubiquity of smart phones—a 2013 Pew Research study found that 80 percent of adults ages 18 to 34 have a smartphone.

“Harnessing this simple and free app to help educate people of childbearing age on matters of newborn health is not only logical, it’s essential,” Mogul says.

What does healthy baby stool look like? “Color-wise, anything other than black, red or white/pale yellow is likely to be normal,” Mogul says.

Black stool at any age may signal bleeding in the stomach or another part of the gastrointestinal tract. Red stool indicates bleeding in the lower part of the intestinal tract, while very pale stool in a newborn usually means that bile is building up in the liver due to blockage.

The color chart is available online: hopkinschildrens.org/stoolcolorguide/

The free PoopMD app is available on iTunes and Google Play (for Android devices).
Child Life Protocol Reduces Sedation

by Marjorie Centofanti

MRIs had become a concern for 9-year-old Tyler Freeman, close to a deal-breaker. For him, normal life can hinge on head and spinal scans that can add up to two hours in the MRI suite. Since age 2, when he was first diagnosed with Langerhans cell histiocytosis (LCH), he's undergone up to four MRIs a year to try to keep the rare blood disorder in check.

Scans are crucial for LCH patients. Though the disease can lie dormant, when it's active it sparks painful, eroding tumors. Tyler lost hearing in one ear after LCH claimed its mastoid bone. His skull and spine have also been affected. “Our fear is that it can enter the brain,” says grandmother Patti Freeman.

Yet last summer, the young man balked at undergoing a full MRI without anesthesia, then refused outright. Last February, however, Tyler took to the MRI, apparently without qualms. The presence of Child Life specialist Mollie Young made all the difference.

“A Child Life specialist can use a variety of tools and techniques to soothe a child’s worries and give them much-needed distraction from the actual scan,” says Thierry Huisman, director of Pediatric Radiology at the Johns Hopkins Children’s Center. The approach has dramatically reduced the number of kids needing general anesthesia for MRIs at Johns Hopkins. A recent study Huisman led showed that half of 229 young patients with MRIs lasting an hour or less could forego sedation.

Young was recruited by Huisman as part of his “crusade”—his word—to lessen sedation. Together, they shaped a protocol that tapped Young’s gifts to connect with children and suss out con-

“Knowing temperament is hugely important, along with preexisting fears or past experiences.”

— CHILD LIFE SPECIALIST MOLLIE YOUNG
Pediatric Rounds | Imaging

INCREASINGLY COMMON IN clinics and practically ubiquitous in emergency rooms, CT scans and other imaging tests have revolutionized diagnostics and saved lives, but they have also driven up radiation exposure that can drive up the risk for dangerous mutations that may eventually lead to cancer. Indeed, scientists estimate that up to 2 percent of all cancers in the United States stem from medical radiation, a sobering statistic that has generated a stir among clinicians as well as the lay public.

“A small but growing number of clinicians are now increasingly hesitant to order CT—even clinically justified ones—for fear of exposing kids to unnecessary radiation,” says Thierry Huisman, director of pediatric radiology at Johns Hopkins.

Bringing that thinking back to the middle is at the heart of a radiation-reducing protocol recently developed by Huisman and colleagues. The protocol hinges on pediatric radiologists acting as gatekeepers, proper equipment calibration and parent education. The radiologists must review and question every CT scan ordered and offer advice on radiation-free alternatives.

“A two-minute conversation in the hallway can mean the difference between an ultrasound and a CT,” says Huisman. In a telling example Huisman offers, a 10-year-old boy came to the emergency department hunched over in agony, all signs pointing to appendicitis. The attending physician quickly ordered a CT scan with contrast. But the radiologist on duty, in a corridor consult, advised abdominal ultrasound — when performed by a skilled sonographer, the test is nearly as accurate as CT.

When the child’s sonogram ruled out appendicitis, the attending, once more, ordered a CT scan to verify the diagnosis. And once more, the radiologist offered a radiation-free alternative — magnetic resonance (MR).

“Twice,” adds Huisman, “a well-diagnosed child avoided a CT scan and the significant radiation that comes with it.”

These watchdog services now stand in place throughout the Children’s Center. And because pediatric radiologists are specially trained to interpret ultrasound images, they’re available 24/7 in person or for urgent phone consults.

—MC

Safe-imaging radiologists Melissa Spevak, Thierry Huisman and Aylin Tekes-Brady.
In the lab, pediatric infectious disease specialist Ravit Boger investigates the genetics of Crohn's disease to better understand a protein's role in CMV.
IT WASN’T THAT unusual of a case. The patient had Crohn’s disease, an autoimmune condition marked by painful colon inflammation. A routine gut biopsy revealed the presence of cytomegalovirus (CMV), a common pathogen that causes lifelong infections and can lead to devastating illness in newborns and those with weakened immune systems. Ravit Boger, a pediatric infectious disease specialist who consulted on the case, didn’t think much of it at first. The biopsy result made some sense. Most healthy people carry CMV in their bodies but have no symptoms because their immune systems keep the virus in check, but in people with Crohn’s, CMV might cause infection in the gut because of the immune-suppressive drugs these patients often take that render them prone to infections of all types. So the general wisdom went. Still, the more Boger thought about this patient, the more she felt something didn’t quite add up. She decided to dig deeper.

“I just kept thinking about this patient and the CMV we found in her colon,” Boger recalls. “So I started looking into the genetics of Crohn’s disease.”

Soon, a telling clue emerged. In her research, Boger noticed that people with Crohn’s often carry a defect in the gene that makes a protein known as NOD2. NOD2 is a cell receptor found in certain immune cells and long-known for its role in fighting off bacteria by sensing their presence and alerting immune cells to release chemicals that weaken or destroy these harmful invaders. But CMV is a virus, not a bacterium.

What if this bacterial sensor was also capable of somehow sniffing out CMV? What if people with Crohn’s disease were susceptible to CMV not just because of immunosuppressive therapy but because of this defective protein, Boger wondered. What if the malfunctioning NOD2 found in Crohn’s was also responsible for the uncontrolled CMV infections sometimes seen in these patients?

To test the idea, Boger and fellow researcher Arun Kapoor, Ph.D., took connective cells from human skin and infected them with CMV. The NOD2 receptors of CMV-infected cells showed robust activation, compared with uninfected cells. Next, the investigators compared cells with intact and defective or missing NOD2 receptors. Cells with intact receptors secreted high levels of interferon, a natural antiviral protein, which curtailed viral replication. By contrast, cells with missing or defective NOD2 receptors produced only tiny amounts of interferon and failed to keep CMV in check. When the scientists restored normal NOD2 function, the previously malfunctioning cells were once again able to block viral replication.

NOD2, Boger and colleagues concluded, appears to regulate the body’s immune response to CMV by initiating a chemical signaling cascade that curbs the spread of the virus.

Conducting genetic analysis, the researchers also found that a single misplaced amino acid in the NOD2 gene renders the NOD2 receptor incapable of sensing the presence of CMV. That very same mutation, Boger says, is also commonly found in people with Crohn’s.

The findings, published March 26, 2014 in the open-access journal *PLOS One*, offer what the Johns Hopkins teams says is a first-of-its-kind evidence that a protein that specializes in bacterial detection is also turned on when it comes across a virus from the DNA family. DNA viruses are known for their ability to cause chronic infections.

Boger says the identification of NOD2’s role in CMV may provide new opportunities to modify the body’s immune response to this virus and spur the development of new diagnostic tools and, possibly, a vaccine against this most common congenital infection.

CMV affects one in 150 newborns and causes serious neurologic damage in some of them. Although mostly without symptoms in healthy adults, CMV can cause serious problems in people with certain immune-deficiency disorders, those with advanced HIV, as well as in patients receiving immunosuppressive therapy to treat cancer or prevent organ rejection.
Pamela Frischmeyer-Guerrero, M.D., Ph.D.
Searching for Genetic Links to Allergic Disease

By Jim Duffy and Ekaterina Pesheva

Growing up in the Midwest, Pamela Frischmeyer-Guerrero never had any doubt that she’d find her way to a career in a laboratory.

“During summers in high school I’d sign up for all the science programs at the University of Iowa,” she says. “I was doing research in genetics there as an undergraduate. I guess you could say I’ve followed a pretty linear path.”

Today, that path has Frischmeyer-Guerrero on the faculty at the Johns Hopkins Children’s Center, where she is making groundbreaking discoveries about the genetic and biological processes involved in the development of allergies.

Food allergies now affect 8 percent of U.S. children, with many suffering from sensitivities to multiple types of food. For the environmental allergy hay fever, that number is now 10 percent.

“They deal with these allergies every single day of their lives, and it can be really hard on them,” Frischmeyer-Guerrero says. “Studies show that kids with allergies have lower quality of life even than kids with diabetes.”

One critical observation launched Frischmeyer-Guerrero on her course of investigation in recent years: Why do patients with the rare genetic disorder Loey-Dietz syndrome (LDS) have much higher than normal rates of allergies?

“We think allergies are the result of a complex mix of multiple genetic and environmental factors, right?” she says. “But if we could find a specific genetic pathway to target, without having to wait for all the other complexities about the cause to get sorted out, that would be a huge stride toward developing new treatments sooner.”

The genetic defect in LDS lies in the receptor for a protein called TGF-beta, so that’s where the detective work began. TGF-beta is active on a number of fronts, ranging from how cells communicate with each other to how organs grow.

TGF-beta also controls the maturation of immune cells, so Frischmeyer-Guerrero focused in eventually on a group of cells known as regulatory T cells, which are supposed to keep other immune cells from going into overdrive. In LDS patients, however, those cells were doing the exact opposite—they were secreting allergy-promoting signaling molecules called cytokines.

This discovery of a specific genetic channel linked to allergic disease is believed to be a scientific first. In a 2013 paper in Science Translational Medicine, Frischmeyer-Guerrero identified aberrant TGF-beta signaling as the cause of a complex chain reaction that culminates in allergic disease.

The discovery is already sparking work on treatments.

Frischmeyer-Guerrero, a clinician as well as a researcher, rounds once a week, seeing a lot of patients struggling with allergies. She’s hopeful that her laboratory work will translate one day soon into a better quality of life for them.

“I’ve been interested in the interface between basic science and medicine,” she says. “That’s the career I’ve always wanted, one where I’m sitting at the edge of both and doing translational research that makes a difference.”
THE FIRST TIME pulmonologist Pamela Zeitlin saw cystic fibrosis (CF) patients was back in the mid-1980s, during her residency. At the time, most CF patients never made it out of their teens.

“What a miserable, miserable thing to see,” Zeitlin recalls. “No one understood how the disease worked. All you could really do was treat the symptoms.”

Zeitlin moved on to a postdoctoral fellowship in pediatric pulmonary medicine, where she began studying channels in the body that regulate the movement of chloride ions across cellular membranes. Then, in 1989, Zeitlin saw a new opportunity when the genetic glitch that causes cystic fibrosis was pinpointed in a gene called CFTR, or the cystic fibrosis transmembrane conductance regulator: “This gene is right at the chloride channel, and so ever since I’ve been studying how CF works and what we can do to fix it.”

When CFTR genes malfunction, the body produces thick, sticky mucus that clogs the lungs and obstructs the pancreas. Patients end up short of breath, suffer frequent lung infections, and have trouble breaking down foods. As the disease progresses, they need frequent hospitalizations—perhaps two or three times a year for a week at a stretch.

The progress made in the battle against CF in the years since Zeitlin joined the fight has been steady and impressive. What was once a desperate situation for patients and their families now holds a fair measure of hope that patients can enjoy longer, productive lives. The median life span for CF patients is up into the 40s—and inching up every year. For the first time ever in 2012, the number of adult CF patients outnumbered the number of children with the disease.

Zeitlin attributes this progress in part to innovations aimed at keeping the side effects of CF in check. New and improved nebulizers make it easier to cough mucus out of the body and get rid of dangerous bacteria. Hypertonic saline treatments also help prevent lung infections.

The latest source of hope is ivacaftor, the first drug that actually attacks the underlying workings of the disease. However, it only works in cases that involve a handful of genetic mutations like G551D that are quite rare among CF patients.

“Many patients are doing amazingly well with this drug,” Zeitlin says. “We predict it’s going to make a big difference when it comes to extending their lives.”

Nearly 90 percent of the mutations that cause CF take the form Delta F508. A number of studies are now looking at ways of combining ivacaftor with other drugs in ways that will help these patients.

Zeitlin has been involved in every step of this journey. She has studied CF treatments in animal models, developed a CF cell line that’s now shared around the world, and participated in a number of studies evaluating an array of novel treatments, including ivacaftor.

“I’ve seen this go from a disease where there were no treatments to a point where we’re starting to really make a difference,” Zeitlin says. “It’s a very hopeful time in cystic fibrosis.”

Innovative treatments aimed at keeping the side effects of CF in check, notes pediatric pulmonologist Pam Zeitlin, are lengthening the life span of patients.
During her residency rotation, pediatric emergency medicine physician Leticia Manning Ryan was surprised to see so many fractures. One patient in particular, a 1-year-old with a distal femur fracture, proved to be a career-shaping case. As Ryan was presenting her patient, the attending held up a hard copy of the child’s X-ray and made a secondary diagnosis—rickets—pointing to some bowing, osteopenia and metaphyseal fraying consistent with the condition. Later, Ryan included the image in a research project to evaluate the ability of pediatric residents to diagnose fractures.

“Interestingly, this case stumped both the residents and the attendings, with only 15 percent of each picking up on the rickets,” Ryan says. “We felt this serves as a reminder to evaluate appropriately for non-traumatic medical etiologies of fractures.”

The case also made her wonder what happens to children with fractures in which the underlying cause is not recognized—and also how suboptimal bone health may contribute to fractures in children. Her curiosity ignited a series of retrospective studies on the relationship between bone health and pediatric fractures, with a focus on forearm fractures, which account for 25 percent of all pediatric fractures.

Interestingly, in her review of 929 consecutive cases of isolated forearm fractures in Washington, D.C., she found that more than a third of the fractures were severe enough to warrant sedation and orthopedic reduction—or realignment—yet more than 50 percent resulted from minor trauma. Indeed, nearly a quarter of the fractures occurred after a fall from standing height (J Trauma 2010 Oct;69).

“I would sometimes see two children of the same gender, similar ages and from the same neighborhood, have comparable minor falls and one would have a fracture and the other would not,” says Ryan. “Why?”

Was bone mineral density (BMD) a factor? Studies in New Zealand and the United States, Ryan says, have shown that otherwise healthy children with forearm fractures have lower BMD than children without forearm fractures.

“While it may not seem earth-shattering that lower bone mineral density is associated with increased fracture risk, I don’t think this association has been fully recognized in children,” says Ryan. “Also, these findings have not been incorporated into our clinical approach to fracture evaluation and management.”

With that goal in mind, Ryan began to investigate the relationship between forearm fractures and vitamin D deficiency in African American children, who may be at significant risk for bone health deficits.

Indeed, in her study of 150 otherwise healthy African-American 5-to-9-year-olds, Ryan found that BMD and vitamin D deficiency, as well as overweight status, were all associated with forearm fracture risk (Journal of Pediatric Orthopedics 2010 March;30(2):106-109).

“Our results add to the growing body of evidence suggesting that a forearm fracture is a marker of children with suboptimal bone health in the sense that they have significantly lower BMD than fracture-free peers,” Ryan said.

Next steps, Ryan said, include unraveling just how lower bone mineral density leads to fractures, designing interventions to improve bone health in these children, and developing a screening protocol to identify children with fractures related to bone health.
WORKING WITH MICE and human blood and liver samples, Johns Hopkins Children’s Center investigators have identified a previously unsuspected liver hormone as a critical player in the development of type 2 diabetes, a condition that affects nearly 26 million people in the United States and is a leading cause of heart disease and stroke, as well as kidney, nerve and eye damage. The study shows that the hormone, kisspeptin 1, or K1—up until now known for its regulation of puberty and fertility—also slows down the production of insulin, the sugar-regulating hormone secreted by the pancreas, and in doing so fuels the development of type 2 diabetes. The findings provide what researchers consider a missing link in understanding the origins of type 2 diabetes. Two critical hormones, glucagon and insulin, must work in synchrony to maintain healthy sugar levels in the bloodstream. Secreted when sugar levels drop down, glucagon causes the liver to release its strategic reserves of glucose into the bloodstream. Insulin acts as an antidote to glucagon and helps the body lower blood sugar by transporting it out of the bloodstream and into organs and tissues as fuel. In type 2 diabetes, pancreatic cells secrete too little or no insulin at all, leading to a dangerous buildup of sugar in the blood. The prevailing wisdom has been that exposure to chronically elevated glucagon and blood sugar take a gradual toll on the pancreas, its overworked beta cells slowly decreasing insulin output until they stop making insulin altogether. The new findings, however, show that the pancreatic cells don’t just get tired—their function is directly suppressed by K1. “Our findings,” says lead investigator and endocrinologist Mehboob Hussain, M.D., “suggest that glucagon issues the command, but K1 carries out the orders, and in doing so appears to be the very cause of the declining insulin secretion seen in type 2 diabetes.” —EP

Newborn Brain Injury: How Boys and Girls Recover

PHYSICIANS HAVE LONG known that oxygen deprivation to the brain around the time of birth causes worse damage in boys than girls. Now Johns Hopkins Children’s Center researchers in an animal study have revealed one possible reason—gender-specific mechanisms of brain repair. Inherent differences in the way newborn brains react to the sex hormone estradiol may be behind the sex-specific response to brain damage and cell repair. “Our observations reveal intriguing differences in the way male and female brains respond to injury following oxygen deprivation and in the manner in which they recover following such injury,” says lead investigator and neonatologist Raul Chavez-Valdez. Neurons in male and female brains, he adds, undergo different type of cell death following oxygen deprivation that may be due to the presence of certain receptors that trigger sex-specific pathways of cell demise. —EP

Sickle Cell Disease: Better, Less Costly Care

THE BENEFITS OF hydroxyurea treatment in people with sickle cell disease are well known—fewer painful episodes, blood transfusions and hospitalizations. Recent research reveals that by preventing such complications, the drug can also considerably lower the overall cost of medical care in children with this condition. The cost-benefit analysis, believed to be the first of its kind in pediatric patients, showed that children whose standard care was augmented with daily hydroxyurea incurred, on average, $3,000 less in medical costs per year, compared with children who got standard therapy plus placebo. “Our main goal is to find better treatments, but in a time when we are trying to curb health care spending while improving patient outcomes this is really welcome news,” says pediatric hematologist James Casella. Although proven valuable in therapy of sickle-cell disease, hydroxyurea remains woefully underused in the treatment of people with this condition. The new findings should encourage more physicians to consider adding hydroxyurea to their patients’ therapeutic regimens. —EP

James Casella, M.D.
A child had been born to a mother who didn’t know she was infected with HIV. At high risk of having the infection herself, the young patient was started on a drug regimen to mitigate the damage, hopefully to prevent her from getting HIV entirely. Her doctor, Hannah Gay at University of Mississippi Medical Center, took an unusual step: she started the baby just 30 hours after birth on full-blown therapeutic doses of antiretroviral medicines, not the much smaller prophylactic doses typically used in cases like this. When the toddler’s test results came back positive for the immune-ravaging virus, the baby girl was kept on antiretroviral medicines, with a plan for life-long treatment for her HIV infection.

Here’s where things get really different: When the child stopped showing up for routine appointments, her doctor found out that her mother hadn’t given her any antiretroviral drugs for months—usually a recipe for failure. But the girl’s disease hadn’t rebounded, as doctors would expect. In fact, tests showed that her HIV infection didn’t seem to be there anymore at all. It was a case that Persaud, a pediatric HIV researcher and clinician, had been waiting and working toward for a long time.

Specializing in pediatrics was an easy choice for Persaud when she was in medical school in the mid-1980s. “Kids got better a lot more than adults did after being hospitalized,” she says.

But there was a notable exception to children’s resiliency in the early days of Persaud’s training. Working toward her M.D. degree at New York University School of Medicine, Persaud and her colleagues were on the front lines of the emerging HIV-AIDS epidemic, though they didn’t know that’s what it was at the time. Children were dying in droves. “It was dreadful,” Persaud remembers. “We attended so many funerals.”

It wasn’t until the advent of the first antiretroviral drugs in the mid-1990s that doctors gained the upper hand on HIV-AIDS, helping adults and children live longer by introducing first one drug, then multidrug regimens. By that time, Persaud had married, traveled with her husband to Kenya for his work in public health for Johns Hopkins, had her first child, then come back to Hopkins with her family for her husband to start a new position.

Interviewing for a junior faculty position at Hopkins while eight months pregnant with her second child, fresh from years of little clinical or laboratory research, and with no connections at Hopkins, Persaud worried that no one would take her seriously. But one Hopkins faculty member chose to take a chance on Persaud: Robert Siliciano, whose research had identified why the immune system can’t wipe out lingering HIV in adults, even as antiretroviral drugs kept the virus in check. Siliciano’s lab had shown that the virus hides out in immune cells known as resting memory T cells, forming a formidable reservoir that the typical immune response can’t reach. This reservoir is a major roadblock to an HIV cure.

No one knew whether it existed in children, whose immune systems are immature and work differently in some ways from adults. Siliciano and Persaud decided to work together to answer this question. “It was a perfect opportunity to have an expert on pediatric HIV working with our lab on viral reservoirs,” Siliciano says.

“"We’re claiming it’s a case of HIV remission, but obviously it’s something that needs to be replicated.”

— DEBORAH PERSAUD, M.D.
The finding was encouraging, yet heartbreaking as well. Though the reservoir represented a new target for attacking HIV, it also meant that kids who had established reservoirs had the same burden as adults: the need to take antiretroviral medications for life. “It’s more problematic than treating adults for life,” Siliciano says. “You need to start giving these very powerful drugs in infancy, and no one knows what the fallout will be.”

Despite these significant consequences, it held little interest with the National Institutes of Health at the time, thus stymieing funding to investigate them much further. Persaud kept researching reservoirs among her many projects, showing later that they were still present even in children who were treated from infancy up to five years. But reservoirs often took a backburner to other, better funded projects.

Fast-forward to early last year. When Gay, the pediatrician from the University of Mississippi Medical Center, got the child’s mysterious test results, she contacted Katherine Luzuriaga, an immunologist at the University of Massachusetts Medical School, who, in turn, contacted Persaud. By then, Persaud was leading the HIV Cure Committee of the International Maternal, Pediatric Adolescent AIDS Clinical Trials (IMPAACT) network, a research consortium that was critical in spearheading the earliest clinical trials of mother-to-child transmission and early treatment of infants 15 years ago.

Together, the physicians and their colleagues tried to explain what the toddler’s test results meant from every possible angle. They confirmed that the patient didn’t have any unusual genetic traits that might make her resistant to the virus. They also showed that her mother’s virus has the usual virulence, so the child’s should have, too. The researchers established that the child and mother were definitely genetically related, so the unusual test results didn’t come from any “switched at birth” scenario. Persaud also used her assay to look for any trace of HIV reservoirs present, but the child didn’t seem to have any.

The only circumstance they could imagine was the aggressive treatment she received soon after she was born. Receiving therapeutic doses of antiretroviral medications from the start most likely blocked establishment of the reservoirs that make HIV incurable.

“We’re claiming it’s a case of HIV remission,” she adds, “but obviously it’s something that needs to be replicated.”

In the coming months, the team and colleagues from across IMPAACT will begin the first clinical trial to examine whether they can replicate the Mississippi baby case in more children.

At the time this article was written, the Mississippi child remains off antiretroviral therapy, with no signs that her HIV will return. This viral remission is something, Persaud says, that she and other HIV researchers were unsure if they’d ever see in their lifetimes.

“Who would have thought we’d ever be at this point where we’d be contemplating lifelong HIV remission?” Persaud says. “It’s pretty remarkable, but we still have a lot of work to do.”
Joshua Rales and pediatric immunologist Jerry Winkelstein have worked arm-in-arm to further Pediatric Allergy & Immunology’s fellowship training program.
Endowing a Legacy of Excellence in Immunology

by Wendell Smith

AROUND THE TIME that pediatric immunologist Jerry Winkelstein was considering his retirement from Johns Hopkins, businessman Joshua Rales was considering his immunologist’s legacy. A new patient of Winkelstein’s, Rales was impressed by his physician’s thoroughness, warmth and clinical acumen in treating his immunodeficiency disorder.

“I was very impressed with Johns Hopkins in general and Jerry in particular,” says Rales, founder and managing partner of RFI Associates, a Maryland-based real estate investment company. “He was clearly a kind human being and devoted to his patients. His wonderful demeanor put you at ease, and he took terrific clinical care of you. So I asked him, ‘How are you going to protect your legacy, this great division you created?’”

Winkelstein was intrigued. He had spent 35 years building the Division of Pediatric Allergy and Immunology at the Johns Hopkins Children’s Center and its fellowship training program. Most of the trainees in the three-year program had gone on to careers in academic medicine, with many becoming leading figures in the field. One of these fellows was Robert Wood, who succeeded Winkelstein as division director and is a world-renowned food allergy and asthma expert.

“When Josh brought up the issue of preserving one’s legacy, I’d never thought about it in terms of fundraising,” says Winkelstein. “But it became apparent to me that one of the biggest threats to our division and its ability to bring about critical advances in the field of allergy and immunology would be the loss of funding for our fellowship training program. Its survival was too dependent on federal funds.”

Since 1980, the National Institutes of Health (NIH) had awarded annual training grants to fund the fellows. While the Johns Hopkins pediatric program has been fortunate enough to maintain its NIH funding, the overall number of grants was already in decline by 2004, as Winkelstein approached retirement, a trend that is likely to persist in an era of ongoing budget cuts, rendering alternative sources of funding increasingly critical.

To begin creation of the private allergy and immunology fellowship fund Winkelstein now envisioned, Rales donated $10,000 and said that he would match whatever Winkelstein could raise. “We wanted to help ensure that America’s leading hospital could continue to improve treatments and advance science in these areas,” says Rales. “I’ve seen dramatic improvements in my own care over the years, with new developments in the field here, and wanted to see that they continued for others, too.”

Once challenged, Winkelstein wrote to his former fellows, seeking their support. Within a year, they’d raised enough money to fund at least one three-year fellowship position. At Rales’s suggestion, the new fund was named for Winkelstein.

“It’s a tremendous cause,” said Bradley E. Chipps, at the time. The program’s first pediatric allergy, immunology and pulmonology fellow, he was among the first to contribute to the fund: “Hopkins taught me how to incorporate medical literature in my daily practice. You need this analytic approach to treat immunologic disorders. Jerry was a terrific mentor.”

Another supporter and former fellow, Scott Sicherer added, “The fellowship provided me with lifetime mentors and colleagues who are also friends, and continues to produce the best of the best in pediatric allergy.”

Rales, who has ever since supported the Winkelstein Fellowship Fund in Pediatric Immunology in the Eudowood Division of Allergy and Immunology, upped the ante in the fall of 2013. Rales pledged $50,000 if the now-retired Winkelstein could match it by year’s end.

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“Josh put it to me this way, ‘Let me help you raise $100,000,’” says Winkelstein, who wrote another letter to former fellows and current faculty. Funds totaling more than $50,000 poured in over the next three months, enriching the fund by more than $100,000.

“Thirty-five years later, I feel very fortunate to have been a small part of what has grown into one the finest allergy divisions in the world,” says former fellow Ken Schuberth.

Says Rales, “Jerry has become a very successful steward and fundraiser. He has built up a fund to help support the fellows he believes are crucial to breaking new ground and help more patients. My foundation stepped up its gift last year because we thought it prudent and appropriate to help maintain the caliber of people and research at Johns Hopkins.”

Current Winkelstein Fellow Mark Gorelik, who is studying the mechanisms of desensitization in peanut allergy and working on mouse models of asthma, adds, “My mentorship and guidance here have been second to none. I am deeply appreciative for the funding and support.”

Winkelstein hopes the fund will grow with additional philanthropy to become an endowment, with funds sufficient to cover the salaries of all the fellows. For now, he says, it remains a safety net. “With the NIH’s budget shrinking for activities like research, it’s increasingly important for institutions to find alternative sources for funding, such as philanthropy, to drive their basic mission of research and training,” he says.

“Terrific people like Josh Rales are stepping up and making a substantial difference in some of the most important programs that Hopkins houses,” says Wood, a contributor to the Winkelstein fund. “Our fellows are critical to advancing our understanding of how the immune system works.”

With his support for the division, Rales joins generations of generous donors, chief of which is The Hospital for the Consumptives of Maryland (Eudowood) Foundation. Its board has also long supported the Johns Hopkins divisions of pediatric infectious diseases, pediatric pulmonology and neonatology.

“We are indebted to individuals like Rales and our Eudowood board members who have been such stalwart supporters of our mission,” says Johns Hopkins Children’s Center Director George Dover. “Countless children have a chance for long and healthy adulthoods because of what they all make possible here at Johns Hopkins. It’s a simple fact.”

For their part, pediatric allergy and immunology faculty and trainees continue to develop and deliver life-saving and life-altering therapies to more than 2,500 patients each year for the treatment of primary immunodeficiencies and environmental and food allergies.

Primary immunodeficiency disorders—also called primary immune disorders or primary immunodeficiency—weaken the immune system, allowing repeat infections and other health
problems to occur more easily. Many people with these inherited conditions are born missing some of the body’s immune defenses, which leaves them more susceptible to germs that can cause infections. In its lab and clinics, division specialists provide diagnoses and long-term management for patients of all ages.

Most of today’s allergy and immunology faculty members are former fellows. They are investigating the basic mechanisms of milk, egg, peanut, and tree nut allergies, and the effectiveness of immunotherapy in potentially curing them. In other research, they are studying the role of cockroach and mouse allergens in flare-ups among inner-city children with asthma. Former fellows Satya Naivety and Justin Sripak were among the investigators who, in 2013, showed that some children treated for milk allergies with progressively higher doses of milk, a method known as oral immunotherapy, lose tolerance over time, while others remained symptom free long-term.

“Many children were still clearly better off with treatment,” says lead investigator and former fellow Corinne Keet, a pediatric allergist in the division.

In this challenge to preserve all that the division has become, “Josh Rales opened my eyes to my responsibility to sustain what we’ve developed here and then to make it happen,” says Winkelstein. “I’ve learned from him some of the ways in which you can effect success in fundraising. You have to get people involved, to recognize the importance of your mission, and to understand how the funds will be used.”

This voyage of philanthropy has solidified his own devotion to Johns Hopkins. “Johns Hopkins allowed me to practice medicine the way I thought it should be practiced and gave me the opportunity to explore research in my chosen field of immunology,” says Winkelstein, who, too, was an immunology fellow, as well as a pediatric resident, at Johns Hopkins. “I feel a responsibility now to see that this division on which so many children and families depend can continue its research and training.”

At Johns Hopkins, Rales is one of many adults whose condition is best managed by pediatric specialists. Today, in the care of pediatric immunologist Howard Lederman, who is director of the division’s immunodeficiency clinic, pediatric immunology laboratory and A-T clinical center, Rales can extol with confidence the soundness of the institution and its mission: “There’s nothing like personal experience at this place to recognize its greatness.”

To learn how you can become involved with our philanthropic effort and further Dr. Winkelstein’s legacy in Pediatric Allergy and Immunology, please contact Maureen Royer, 410-361-6396, mroyer2@jhu.edu.
Fruits of a Pediatric Diabetes Nurse Educator Endowment

IN THE PEDIATRIC DIABETES Clinic at the Johns Hopkins Children’s Center, James Conway, 12, is learning how to use his new insulin pump. The size of a small pager, it will replace the older, larger one in the belt clip. He’s introduced to a small continuous glucose monitoring sensor. Worn on the body, typically on the abdomen, it checks blood sugar every five minutes.

Pediatric diabetes nurse educator Loretta Clark tells him and his mother, Denise Conway, “It will transmit the same information wirelessly so we can see what’s going on and help you manage.”

Teaching patients and families how to manage diabetes and all its related and ever-changing technology is what Clark does. A disease of numbers, diabetes requires close scrutiny of multiple factors in a patient’s life. Diabetes management, Clark says, is “more of an art than a science. There are so many daily variables that make blood sugar change. Every minute of the day, blood sugar is going up and down. Families need the skills and confidence to manage this.”

A disorder of the immune system, Type 1 diabetes is due to a loss of pancreatic insulin secretion, affecting several metabolic functions, most notably glucose metabolism. Type 1 usually appears suddenly in childhood and is life-long. While the disorder can be controlled with insulin, such management requires vigilance and a strict regimen of care.

Clark is available to families on a fulltime basis thanks to an endowment created in 2007 with gifts from Richard and Kathryn Radmer and the Nicholls Family Foundation to ensure that the education and support the pediatric nurse provided to them and their own families would be available to those who followed. Clark is the inaugural recipient of the Pediatric Diabetes Nurse Educator Endowment at Johns Hopkins.

“Loretta has been a vital lifeline for us,” says Tom Johnson, whose sons, Nick and James, were diagnosed with type 1 diabetes at the ages of 2 and 12, respectively. “She is at the vanguard of diabetes care and urges us ever onward to adopt the newer therapies. She has helped our now teenage sons learn to manage their condition. When you’re dealing hourly, daily with pumps, insulin, syringes, measuring and worry for your kids and your own proficiencies, the diabetes nurse educator has to be someone who does it all—who is a nutritionist, endocrinologist, technologist, coach and cheerleader. Loretta is all of these, and more.”

Today, Clark and fellow pediatric diabetes nurse educator Kimber-Lee Abel care for more than 400 children in the clinic, leading the education and training so critical to the health and lives of children with diabetes. In partnership with pediatric endocrinologists like Leslie Plotnick, co-founder with Clark of the Pediatric Diabetes Clinic at Johns Hopkins Children’s Center, the nurse educators work around the clock with families to help them manage and cope with the endless schedule of measuring, dosing and calculating.

While the technology to help diabetes patients is improving, the sheer number of children with type 1 or type 2 diabetes—the latter chiefly associated with diet and lifestyle—are increasing. Virtually unseen in children a few decades ago, cases of type 2 are shadowing the rising rates of obesity in kids, now at epidemic levels. The diabetes clinic at Johns Hopkins Children’s Center is always full.

“We need more nurse educators,” says Plotnick, the clinic’s director, “and more endowments to fund them. The need is critical.”

“We endocrinologists would have no time to follow more than a handful of diabetes patients without the consistent expertise of our nurse educators.”

– LESLIE PLOTNICK, M.D.
Pediatric nurse educator Loretta Clark teaches patients like James Conway how to use the latest technology to manage their diabetes.

Because there’s no “cure” for diabetes, the best therapies are still primarily those that control symptoms, hopefully mitigating some of the disease’s profound consequences, which include kidney and nerve damage, heart disease and stroke. “We endocrinologists would have no time to follow more than a handful of diabetes patients, without the consistent expertise of our nurse educators, given the incredible complexity in managing this illness,” she continues. “But it can be managed well, if done properly.”

Stacie Peddy knows both the challenge and power of proper management. “We called Loretta at least once a day in the first months after our daughter, Brynn, was diagnosed with type 1 at Johns Hopkins,” says Peddy, a pediatric cardiac intensivist at Children’s Hospital of Philadelphia, and a former resident and fellow at Johns Hopkins. “We’d fax her Brynn’s blood glucose levels and she’d tell us how to tweak things. It was overwhelming for me, and I’m a physician. I don’t know how Leslie could do what she does without her nurse educators. Brynn is doing beautifully today.”

To help ensure that young patients’ diabetes is safely managed when they are away from home and parents and in school, Clark and Abel offer education and guidance to school nurses.

Also, with Plotnick and a team of pediatric endocrinologists, nutritionists and psychologists, they focus on diabetes prevention.

—WS

To learn how you can become involved with our philanthropic effort in pediatric diabetes, including endowment of a nurse educator, please contact Maureen Royer, 410-361-6396, mroyer2@jhmi.edu
SARA JOHNSON WONDERS what kinds of experiences in utero might affect behavior, learning and the response to stress in an individual after birth. “Experiences powerfully shape who we become,” says the assistant professor of General Pediatrics and Adolescent Medicine at Johns Hopkins Children’s Center, “even those of our parents.”

Johnson is working to understand how social experiences—whether family relations, life events or neighborhood characteristics—shape the biology of child development, including behavior. Does fetal exposure, too, to a mother’s high level of long term stress or unremitting adversity affect self-regulatory development in childhood, in adolescence and over a lifetime?

In studies at the Johns Hopkins Children’s Center in Baltimore and in one proposed at All Children’s Hospital Johns Hopkins Medicine in St. Petersburg, Fla., Johnson and her colleague Janet DiPietro at the Johns Hopkins Bloomberg School of Public Health are studying such correlation and causation. They are identifying stressors in the lives of pregnant women, and then, using fetal actocardiograph, which tracks fetal heart rate and movement, to monitor the fetus’s neurological and behavioral development. “We want to know how their brains are developing,” says Johnson, “and what sorts of exposures have the biggest effects.”

They are re-examining these children at the age of 5 to see how experiences in utero shape behavioral development, as well as health conditions like asthma and obesity, which are traced to stress.

A better understanding of biological influences on behavior could one day lead to preventive measures, both in pregnant women and childhood, to foster better regulatory development, including better impulse control and decision-making. “Does a fetus get the message, by exposure to a mother’s stress, that their world will be a harsh place, and that they should accordingly develop more quickly, more hastily?” Johnson asks.

The answer, she continues, could lead to a new emphasis on reducing in-utero exposure to certain chronic stressors that keep the body’s stress response turned on, as well as disease prevention.

For example, Johnson says, asthma, the most common chronic childhood disease, is influenced by a complex interplay of inflammation, immunity and the body’s stress response. So, could asthma be prevented by predicting which babies are the most susceptible and intervening early, before birth?

“I think we’re in the dawn of a new era in which we can,” says Johnson. “We’re in the era of epigenetics, of understanding and mitigating the impact of a child’s environment on his genes, and eventually his or her health in adulthood.”

An era that philanthropy will usher in, says Johns Hopkins Children’s Center Director George Dover. “Philanthropy is critical to sustain studies like Sara’s that will enable us increasingly to prevent early in life many of the chronic illnesses that strike in childhood and beyond.”

Sara Johnson received her M.P.H., Ph.D., in public health from the Johns Hopkins Bloomberg School of Public Health, where she holds a joint appointment in Population Health. She can be reached at sjohnson@jhsph.edu

To learn how you can become involved with our philanthropic effort and further studies like Dr. Johnson’s, please contact Maureen Royer, 410-361-6396, mroyer2@jhmi.edu.
Garrett was a descendant of a long succession of champions of child health whose unwavering support of the Johns Hopkins Children’s Center has fueled both clinical achievements and scientific advances.

“Rob was a remarkable, insightful man and a very generous and enthusiastic supporter of our mission to protect the lives and futures of children,” says Johns Hopkins Children’s Center Director George Dover. “We shall miss him. His leadership and instincts were impeccable. He, his family and all who have shepherded the Garrett Fund over successive generations deserve our enduring gratitude.”

Established in 1936 by the will of Mary Frick Garrett Jacobs, in memory of her first husband, Robert Garrett—former president of the Baltimore and Ohio (B&O) Railroad and a trustee of the Johns Hopkins University, the Garrett Fund has long supported the pediatric surgical program at Johns Hopkins. In the early 1940s, the fund helped support the seminal research of surgeon Alfred Blalock, who, with pediatric cardiologist Helen Taussig and surgical technician Vivien Thomas pioneered a life-saving cardiac procedure for children born with a devastating heart defect. Together they transformed the field of pediatric cardiology. The first director of pediatric surgery as a specialty at Johns Hopkins, Alex Haller, M.D., who was appointed in 1965, and his successors have held the position of the Robert Garrett Professor of Pediatric Surgery at the Johns Hopkins Children’s Center. The fund was also instrumental in the eventual establishment of the nation’s first pediatric shock trauma program in 1973.

In addition to its enduring stewardship of the pediatric surgical program at Johns Hopkins, the Garrett Fund and its board have helped ensure the continued development of the Johns Hopkins Children’s Center, founded as the Harriet Lane Home for Invalid Children in 1912. In the 1950s, under the leadership of Rob Garrett’s father, Harrison Garrett, the Garrett Fund board joined forces with the boards of The Hospital for the Consumptives of Maryland (“Eudowood”) and The Harriet Lane Home for Invalid Children of Baltimore City to underwrite construction of Johns Hopkins’ Children’s Medical and Surgical Center building, completed in 1964. In 2003, under Rob Garrett’s leadership, the Garrett Fund joined forces again with those two boards and others, to help finance construction of today’s state-of-the-art Charlotte R. Bloomberg Children’s Center building, which opened in 2012.

The Garrett family itself has been affiliated with Johns Hopkins since the 1800s. John Work Garrett, Rob Garrett’s great-great-grandfather, was instrumental in persuading Johns Hopkins to earmark his fortune of $7 million for the establishment of Johns Hopkins University in 1876. John Work Garrett’s daughter, Mary Elizabeth Garrett, played a key role in the creation of the Johns Hopkins School of Medicine.

Born in Morristown, N.J., in 1937, the son of the late Grace and Harrison Garrett of Baltimore, Rob Garrett was a member of the distinguished Baltimore family that has been one of the most generous supporters of Johns Hopkins for many generations. A graduate of the Gilman School, Princeton University, and the Harvard Business School, Garrett spent three years in Germany as a First Lieutenant in the U.S. Army. He then moved to New York City in 1965 where he pursued a career in investment banking, which included reactivating his family’s 150-year-old merchant banking firm, Robert Garrett & Sons. Throughout his career, Garrett served on multiple boards, including those of The Abell Foundation, Continental Airlines, C.R. Gibson, the Adirondack Council, the New York Botanical Garden, and the Johns Hopkins Children’s Center, where he was a member of its National Advisory Board.

At the time of his death, Rob Garrett was a founding member of Media Advisory Partners, a financial advisory firm. Rob Garrett is survived by his wife of 48 years, Jacqueline Marlas Garrett; sons Robert Garrett, Jr. and Johnson Garrett; four grandchildren; brothers Thomas Harrison Garrett, M.D., and James Rea Garrett, and a sister, Julia Garrett Fox.
Honors and Awards

**Robert Cooke,** M.D., the former director of the Johns Hopkins Children’s Center and fourth director of the Department of Pediatrics at Johns Hopkins, died in his Martha’s Vineyard, Mass., home Feb. 2, 2014. He was 93. Cooke, who joined Johns Hopkins in 1956, would preside over the opening of its Children’s Medical and Surgical Center in 1964. A prolific academician and bioethicist, he was an ardent and tough advocate for child health, a political power broker who shaped child health policy on a national scale. He was the catalyst behind Head Start, the federal program that provides academic and social services to millions of low-income children and their families each year.

Cooke’s friendship with the Kennedy family—he was senior medical adviser to President John F. Kennedy and family pediatrician to the president’s sister, Eunice Kennedy Shriver, an early advocate for people with mental retardation—allowed him to shape U. S. public health policy on mental disabilities. In 1961, Cooke chaired a task force to study child development whose report called on the White House to form a federal agency that would study developmental disorders. That document became the blueprint for the National Institute of Child Health and Human Development (NICHD), the federal agency within the National Institutes of Health that studies maternal, fetal and child health and issues treatment guidelines. Much of what is considered standard practice in the care and treatment of premature babies, newborn screening and childhood immunizations is based on NICHD-funded research, and the creation of the agency paved the way for the study of mental retardation and developmental disabilities as a pediatric sub-specialty.

At Johns Hopkins, Cooke recruited a cadre of young physicians who later became luminaries in their specialties. Much of his scientific work focused on understanding metabolic dysfunction and nutritional deficiencies of early childhood.

**Maureen Royer** is the new senior director of development for the Johns Hopkins Children’s Center. Royer leads the campaign for Johns Hopkins Children’s Center, a component of Johns Hopkins University’s current $4.5 billion campaign. Royer, who joined Johns Hopkins last spring, most recently served as director of development for children’s health in the Department of Pediatrics at the University of California, San Francisco.

**Maria Trent** one of the country’s 100 most influential African-Americans for 2013. A nationally renowned expert on teen reproductive health, fertility, polycystic ovary syndrome, adolescent obesity, and sexually transmitted infections and pregnancy prevention.

**David Matthew (Matt) Norvell** is Johns Hopkins’ first pediatric chaplain. The new chaplaincy is endowed by the Bunting Family Foundation. Norvell joined Johns Hopkins in 2008 as a specialist in palliative care and a member of the Harriet Lane Compassionate Care Program at the Johns Hopkins Children’s Center.

Last December, the prestigious science journal *NATURE* named Johns Hopkins pediatric HIV expert Deborah Persaud “One of 10 People Who Mattered in 2013” for her work in providing “the strongest evidence yet that infants born with HIV can be cured.”

In Memoriam

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Listening to his mother and grandfather discuss the possibility of establishing a fund at Johns Hopkins in his great-grandfather’s name, 10-year-old Jacob Rose offered his support of $10. As the conversation continued, Jacob upped his contribution to $20.

“Jacob really decided this for us,” says grandfather Joel Brenner, director of Pediatric Cardiology at Johns Hopkins. “He loves his great-grandfather and is someone who readily spends his money on others.”

The Sam Brenner Family Fund in the Department of Pediatrics at Johns Hopkins was established a year later, in 2012, and Jacob became its founding donor.

Designed to illuminate ethics in children’s health care, the fund seemed a fitting tribute, says Joel Brenner, to an honorable man, who celebrated his 90th birthday that June of 2012 and had led an equally honorable professional life in New York’s diamond industry, where integrity and ethical conduct are mandatory.

“We all grew up admiring our father, and striving to follow his example,” says Brenner, Sam Brenner’s oldest son. “We were thrilled to show him that who he has strived to be and exemplify throughout his life has been meaningful for his children and grandchildren.”

The inaugural lecture of the Sam Brenner Family Fund was held Sept. 11, 2013 during Pediatric Grand Rounds at the Johns Hopkins Children’s Center and featured Mark Mercurio, director of the pediatric ethics program at Yale University. Sam Brenner, who was celebrating his 91st birthday year, was in the audience.

As it continues to grow, the family fund will enable the Department of Pediatrics to invite speakers to Johns Hopkins for biennial lectures and symposia to discuss developing work in pediatric ethics in today’s evolving world of high tech medical care and changing cultural and economic realities. The fund will also help to support the Department of Child Life at the Johns Hopkins Children’s Center.

“I hope very deeply that our family will be involved in and dedicated to these goals for generations to come,” said Joel Brenner. “From Jacob’s initial gift has come a lot of good will and generosity, and for our family a very strong sense of legacy.”

—WS
HI, I’M BACK. Yes, I know it’s been 12 months since my last column, so there’s much to share—including developments in our “Family as Faculty” initiative where we take on the role of our doctors’ teachers.

What is it? In the truest terms it’s putting members of our Pediatric Family Advisory Council (PFAC) in the same settings as clinical staff at the Johns Hopkins Children’s Center, and once there having them share their personal story in a constructive, educational way with the goal of improving the patient experience. Examples include parent advisors Stefanie Fay and Robert Hicks speaking at new nurses orientations, parent advisor Lisa Jones participating in a daylong grief and bereavement workshop for residents, and parent advisors Carol Davenport and Jane Webster participating in a Bloomberg School of Public Health panel discussion on patient- and family-centered care in maternal and fetal medicine. By hearing the parent’s point of view in such circumstances, staff can better empathize and communicate with parents in an array of interactions.

Similarly, PFAC members are increasingly engaging staff—and future staff—in a variety of activities. Parent advisors Anne Wills and Debbie Burton, for instance, are members of a search committee interviewing candidates for the new pediatric-surgeon-in-chief position at the Children’s Center. Also, they and other parent advisors will be included in the vetting of new division directors and other senior leadership positions. Parents helping to choose the doctors who will care for their children? What a novel idea!

Other examples include parent advisor Sue Mead’s participation in an MRI anesthesia workgroup, and parent advisor Bob Seipel as a member of the new patient-centered-care design team. PFAC members are pollinating the parent’s perspective across the institution and, as Johns Hopkins Children’s Center Director George Dover likes to say, “gradually changing our culture.”

We are not, however, keeping the value of our PFAC members within the walls of the hospital. This August, two of our parent advisors and one of our staff advisors will be in Vancouver representing the Children’s Center at the annual meeting of the Institute for Patient- and Family-Centered Care. We share what we learn and bring back new learning, as well.

We’re busy in other areas, too. At the end of last year we produced our 2013 annual report, covering our involvement in a number of Children’s Center initiatives; email me if you’d like a copy. Now we’re moving forward in 2014, incorporating a family history tool in our “Your Voice Matters” parents journal, adding more parent audio vignettes to our “We’ve Been There, Too” web page, and tailoring our in-room TigreNet system to be consistently user friendly across hospital units. And, hopefully soon, I’ll be sharing our work in a new information technology initiative called Yammer.

Well, enough yammering for now. Until next time, remember, your voice matters.

Pamela Griffin, Parent Advisor on Staff at Hopkins Children’s Center, can be reached at HopkinsChildrensFAC@jhmi.edu
At Johns Hopkins, Dr. (Robert) Greenberg is my “preferred” anesthesiologist because with me, you really have to know how to do things just right, like how to get a breathing tube down my throat. It can be difficult because, given my scoliosis, my esophagus and nasal passages don’t line up. Dr. Greenberg once said he treated me like a NASA mission.

I’m a complicated patient. I was born in Colorado in 1999 with a dislocated knee and long fingers and toes. I had a bilateral inguinal hernia, and needed eye and dental surgeries. I had my first cervical spine surgery a few months later. I saw lots of doctors. They thought I might have Beal’s contractual arachnodactyly syndrome, or possibly Ehlers-Danlos syndrome or Shprintzen-Goldberg syndrome. You learn these things.

Noting my fast heart beat and heart complications that included a dilated aorta and a mild mitral valve prolapse, my cardiologists suspected another syndrome, Marfan, and said I should see the country’s top expert, Dr. (Hal) Dietz at Johns Hopkins. In 2003, I did. Dr. Dietz was doing research on a Marfan cousin, but had not yet created a test for it. He put me on a different medicine, and took a skin biopsy for banking.

In 2006, we got the call. Dr. Dietz had developed a skin test for the new syndrome he’d identified, and I had it—a connective tissue disorder called Loeys-Dietz syndrome. He said I had to take care of my heart because this syndrome can cause an aneurysm or, worse, a tear of the wall of the aorta. And that’s exactly what happened a year later, but I survived.

Over the years, I’d travel to see him. In 2010, he noticed that my scoliosis, another consequence of Loeys-Dietz, was getting worse and squishing my heart and lungs. Just before Dr. (Paul) Sponseller could place growing rods in my spine to correct the scoliosis and make room for my organs, I arrested and they had to stabilize me. I spent a lot of time in the Johns Hopkins PICU.

Today, my mother and sister and I live in Maryland to be near Johns Hopkins. I continue to get better with physical therapy and follow-ups with my doctors. I like school, astronomy and building model airplanes. My dream future includes taking over the Loeys-Dietz research that Dr. Dietz has begun and finishing it. He has to retire one day. Until then, I like to look at the sky and wonder about what we can’t see or know now, but will in the future.

Like a NASA Mission

by Trey Price
In the spirit of their late mentor, friend and colleague Richard Talamo, MD, a dedicated pediatric physician, professor and researcher, Ron and Ginger planned a bequest to support innovative ideas for advancing cures and treatment of diseases affecting children.

What will your legacy be?

To learn how you can make a bequest to the Johns Hopkins Children’s Center or a gift that also provides income to you, contact the Office of Gift Planning today. We look forward to creating a plan that achieves your goals, and to welcoming you into the Johns Hopkins Legacy Society.

“These are the values that Johns Hopkins lives by and why we were inspired to include the Children’s Center in our will.”

Ron Berninger, PhD, and Ginger Berninger, PhD
Johns Hopkins Legacy Society Ambassadors