JOHNS HOPKINS
CHILDREN'S CENTER

Pediatrician

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Saving the Child with Short Bowel

A new clinic combines multispecialty medical and surgical services to achieve the best possible outcomes for patients with short gut.

Pediatric surgeon Sam Alaish and pediatric gastroenterologist Darla Shores keep an eye on their young patient Brianna Allen, with her mom Amanda Lafferty.

Pediatric surgeon **Sam Alaish** recalls this decade-old case like it happened yesterday. The 2-year-old was in shock and being rushed to the OR for an emergency laparotomy. Opening the abdominal cavity, Alaish found one of the worst cases of intestinal malrotation with midgut volvulus he would ever see. In such cases, he knew, patients have only six to eight hours before the twisted intestine chokes off its own blood supply, and, by the sight of it, necrosis had already started spreading. He saved what he could but it was too little—the child would require complex, multispecialty care for most of his life.

"You take out what's dead, leave in what's borderline, and come back at a later time to see if it survived to give him his best chance to have the most intestine possible, but we knew he would need TPN (total parenteral nutrition) for a long, long time," says Alaish. "These are kids with severe disease, who need a lot of follow up and multidisciplinary care to optimize their outcomes."

Unfortunately, Alaish adds, there are too few multidisciplinary centers to treat children with short bowel and intestinal failure secondary to congenital conditions like Hirschsprung's disease, gastroschisis, intestinal atresia and necrotizing enterocolitis (NEC), all of which can lead to disabling and even life-threatening complications. Mortality remains high at 7 to 28 percent, and children fortunate enough to survive continue to suffer greater morbidity from both infections and liver failure (*J Surg Res* 2011;170:27-31).

To improve such outcomes, Alaish and pediatric gastroenterologist **Darla Shores** have led development of a new clinic that brings multiple specialists together under one roof to treat such complex patients. "We do know that if you put these very challenging patients in a multi-disciplinary clinic they do better, but not every state has such a clinic for kids," says Alaish.

"We're taking all the bits and pieces that were happening randomly at different clinics and getting everyone in the same area to see patients in a more efficient manner," adds Shores. "All of the specialists come together, agree on one course of action and present a uniform plan to the family, which should improve patient care and patients' quality of life."

In addition to pediatric surgeons, gastroenterologists, gastro-intestinal nurses and pediatric nurse practitioners, clinic staff include a nutritionist, occupational therapist, pharmacist, psychologist and speech pathologist. The strength of Hopkins' long-standing pediatric nutrition program is a value-added feature of the clinic, says Shores, citing the myriad nutritional complications and needs of patients with short bowel. Another value is having pediatric surgeons like Alaish and **David Hackam**, who specializes in treating patients with NEC. Also, all three physicians are aggressively pursuing research to improve existing treatment protocols and to develop new, more effective therapies for short bowel. In fact, to enhance the impact of research for these fragile patients they've created the Center for Intestinal Rehabilitation and Cure Using Science, or CIRCUS.

"The reason I came here," says Alaish, "was to put some science behind our treatments, to measure our outcomes, to see how we're doing and what can we do better." ■

For more information or to schedule an appointment, call 410-614-4615.

David Hackam,
M.D., PH.D.
Pediatric Surgeon-in-Chief
Co-Director, Johns Hopkins Children's Center

Our Story

We all have a story to tell, a life-changing experience that steered us down a certain path in pediatric medicine. Mine, as a newly minted pediatric surgeon, was a premature, extremely ill 2-week-old infant with a distended belly, who was dying in front of our eyes. In the operating room we found pink intestine turned black, the scourge of necrotizing enterocolitis (NEC). He pulled through in that first operation but I had to remove more intestine in another surgery, then another. Then, at 11 months of age, he died, and I remember to this day the shock, the grief and the pain felt by his parents and family, the nurses around them. At that point I decided that this would be my life's work—to understand how we can identify, prevent and treat such devastating diseases.

That path has led me to Johns Hopkins Children's Center and an academic medical center known for its groundbreaking research, world-class clinicians and national centers of excellence. Our aim now is to develop a deeper translational research program to both benefit our patients and help us recruit top pediatric surgeons vital for excellence in pediatric surgery and the treatment of children with complex diseases like NEC. Our vision includes development of six evidence-based surgical centers of excellence in fetal medicine, colorectal/bowel management, short gut/intestinal care, burn/trauma, oncology and vascular anomalies.

This special issue of *Pediatrician* reflects some of our work in these and other areas in pediatric surgery here at Johns Hopkins. We're also reaching out to you, our community pediatricians and pediatric subspecialists, to build our relationship. So please, tell us about your clinical needs and how we can help meet them. And, if you'd like, tell us your story. Thank you and enjoy this issue.

Printing the Heart: An Interview with Narutoshi Hibino, M.D., PH.D.

Pediatric cardiac surgeon and biomedical engineer **Narutoshi Hibino** began his study of tissue engineering in Japan and continued his research in the United States when he arrived at Yale a decade ago. After completing fellowships at the Children's National Medical Center in Washington, D.C., and Nationwide Children's Hospital in Ohio, he joined the faculty at Johns Hopkins Children's Center. There we sat down with him for a brief look back and an update on his current activities.

First off, what was it like undergoing training in Japan?
Japan has a very good medical education system. Starting in high school, students can work in a lab and continue research throughout their education. I used to spend my entire day in the lab. Then, when I became a doctor, I would spend my days doing research and my nights seeing patients. With that hectic schedule, doing surgery was nearly impossible. Since I began working here I've had more opportunities to balance research and clinical work.

How do you approach these very complex patients and their families?
It depends on the child's state of mind. Sometimes you work with a patient who has had heart defects since birth and have no trouble accepting their condition. If you have a patient who recently developed complications, they can harbor confusion because they were healthy before. As a surgeon, I don't always get to interact with my patients but I find it's best to tackle each case individually because while some share similarities, they are also rather unique in some ways. No two kids are alike.

Tell us about your current research.
I began my research studying the cells'role in generating cardiac tissue, but over time my team and I found that we don't need to grow cells when implanting artificial devices such as vessels into the heart because cardiac cells will grow over these new structures. It's incredible. Currently we're focusing on 3-D printing to design and implant artificial vessels into the hearts of patients with congenital heart disease.

How did you get interested in 3-D printing?
3-D printing, which has become popular in medicine lately, gives the surgeon the opportunity to make a model of the patient's heart, and print and implant the new structure in a way that works with the patient's unique anatomy. Surgeons face a real challenge when tailoring unique structures, such as vessels, under the pressure and time constraints of surgery. Our hope is that 3-D printing can help solve those problems.

Does the heart accept that new structure?
Yes, though we are constantly trying to improve printing materials. The plastic in 3-D printing is too hard, not pliable enough. Other materials have proven to have their own limits. We continue to look for the ideal fit.

What's next?
We are trying to bring our vision for medicine closer to the reality of medicine. I hope that in the future we can start generating cardiac tissue, which is far more difficult than 3-D printing. My goal is to improve outcomes and quality of life for my patients, and that's what fuels and inspires the work that I do in my lab day in and day out. ■

Narutoshi Hibino, M.D., PH.D.

A Less Invasive Approach with a Twist

When 4-year-old Kelsey Jenkins was diagnosed with a blockage in the space between her ureter and kidney—the ureteropelvic junction—she was given two operative options at Johns Hopkins Children's Center: an open procedure which requires a long, open-flank incision and a two-to-four-night hospital stay, or a minimally invasive laparoscopic approach that requires three small incisions and a one-night hospital stay. For Kelsey's mom, Nicole Jenkins, the answer was a no-brainer: "The biggest thing for me was the significantly shorter recovery time."

Then, serendipitously, Kelsey's mother learned that a new pediatric urologic surgeon, **Ardavan Akhavan**, was joining Johns Hopkins and bringing with him a minimally invasive approach with a twist—a robot. Akhavan's approach, called a robotic pyeloplasty, not only offered all the benefits of the usual laparoscopic procedure, it also had been shown to offer surgeons a greater range of motion and enhanced visualization for more precise dissection and suturing. Studies have shown that compared with open pyeloplasty, the robotic approach can be done with less post-operative analgesia, less scarring, a shorter hospital stay, and a shorter time to return to normal activities.

That was enough for Jenkins, who elected the robotic approach with Akhavan for Kelsey. The result?

"Better than expected," says Nicole Jenkins. "This was great timing with Dr. Akhavan's arrival at Johns Hopkins."

Compared with open pyeloplasty, pediatric surgeon Ardavan Akhavan's robotic approach can be done with less post-operative analgesia, less scarring, a shorter hospital stay, and a shorter time to return to normal activities.

Jenkins was impressed not only with Kelsey's complication-free outcome, but also with Akhavan's way of working with families.

"The moment he took my daughter's case he called us, answered our questions, drew pictures of the procedure for Kelsey, and generally did everything in his power to make sure we understood what was happening with our child," says Jenkins. "He was above my expectations." ■

For more information, call 410-955-3693.

Sparing the Growth Plate in ACL Reconstruction

Pediatric orthopedic surgeon **R. Jay Lee** seemed to be seeing more and more young patients like the 11-year boy with an ACL (anterior cruciate ligament) injury in his exam room. The cause of his injury was an opposing player's football helmet slamming into his knee. His pediatrician immobilized his knee and handed him a pair of crutches and then—especially after the boy stressed that he was anxious to get back on the playing field—referred him to Lee for possible reconstruction of his ACL.

Not too long ago, Lee would have recommended delaying surgery until the patient's growth plates had closed—around age 14 for females and 16 for males. Drilling holes in bones that cross the growth plate—the femur and tibia—can result in serious consequences, including leg-length discrepancy or angular deformity in the leg. However, some studies have shown, conservative management, bracing and delaying ACL reconstruction increases the risk of damage to the menisci and cartilage in the knees of energetic young athletes. After all, how do you keep them off the playing fields?

"We know young patients with ACL tears do have subsequent damage to their knee," says Lee. "We just tell kids to slow down and modify their activities, to pick up biking and swimming, sports that are safe for their knee. But they can't slow themselves down."

Considering these issues, some orthopedic surgeons would modify adult techniques and drill smaller tunnels for smaller ACL grafts, or avoid holes altogether and wrap grafts around the bone. But too often, Lee says, these grafts would tear or fail to completely stabilize the knee.

R. Jay Lee, M.D.

"There were still complications and growth disturbances where the plate would grow at an angled position," says Lee.

New technology and the innovative surgical techniques they've made possible, Lee says, now offer young patients an option for safer reconstruction with less risk of complications and growth plate disturbances. One innovation Lee has taken advantage of is a new drill that employs a retractable drill head that allows him to bore a very narrow tunnel through bone for the best possible placement of the ligament graft.

"Instead of drilling a complete 10 millimeter tunnel, we're able to drill a 2 millimeter tunnel to deploy the drill, which is better for kids because we can minimize any disturbance to the growth plate," says Lee. "Now we're able to reconstruct the ACL with a robust graft that actually replaces the ACL and puts it in the correct spot."

The procedure worked well for Lee's young football player, who is now undergoing physical therapy. He expects to be back on the gridiron soon.

"We've come to appreciate the growth plate more now that we have better equipment and newer technology," Lee concludes. "We're able to avoid the growth centers for our young kids, and we're able to reconstruct the ACL in much younger patients." ■

For more information or patient referrals, call 443-997-2663.

Trying the Sleeve on For Size

Gabrielle Glanville was hardly shy about approaching people, even if others felt uncomfortable approaching her because of her weight, which was over 300 pounds. "People wouldn't approach me but I was very friendly, I didn't let it get the best of me," says Glanville.

But the Maryland teen was worried about her increasing weight and related health problems like diabetes, hypertension and heart disease getting the best of her. Like many overweight and obese young people she tried everything from nutritionists to running clubs to lose weight only to see it return. She needed, she says, a remedy that would force her to lose weight, keep it off and stay healthy.

"I reached a point where I knew things had to change not because of how I looked but because of how I felt physically," says Glanville. "My blood pressure and cholesterol were fine but I knew I'd have problems later on if I didn't lose weight."

That's when Glanville, 16 at the time, learned about Johns Hopkins Center for Bariatric Surgery and bariatric surgeon **Kimberley Steele**, who offers weight loss surgery for adolescents. Criteria for teens, Steele explains, include a BMI over 35 with severe medical comorbidities, BMI over 40 with less-severe obesity related conditions, and a failed supervised six-month diet and exercise program. Pediatric patients, she adds, go through rigorous educational, nutritional and psychiatric evaluations, as well as anesthesia, medical and surgical consultations to help determine whether they are candidates for surgery. A strong supportive family environment is also a must.

The center offers such pediatric patients three surgical options, all laparoscopic—adjustable gastric band, vertical sleeve gastrectomy, and gastric bypass. The band and sleeve are so-called "restrictive" weight loss procedures in that they limit the amount of food patients can eat at any one time. In the sleeve approach, which Glanville opted for, three-quarters of the stomach is removed, reducing its typical watermelon size to that of a banana. Also, because there's no cutting or rerouting of the small bowel, bile and pancreatic fluid allow food to be completely digested and absorbed in the bowel.

The results? The evidence is still scarce because bariatric surgery has only recently been offered to adolescents, Steele notes, and most long-term studies have focused on obese adults, with around 80 percent of patients losing and keeping weight off (*Obesity Surgery* 2006 Aug;16(8):1032-1040). To date there is one large longitudinal study tracking outcomes in adolescent patients for longer than a year (*JAMA Pediatri*. 2014;168(1):47-53).

"The nice thing about surgery is the weight loss is maintained and sustained," says Steele. "Patients who stick with it, are compliant, see their primary care physician and follow nutritional guidelines following surgery do great."

Glanville, now 125 pounds lighter and a freshman in college, agrees: "I'm very much more active now, feeling healthier and freer, like a weight has been lifted off of me." ■

For more information, contact the Johns Hopkins Center for Bariatric Surgery at 410-550-0409 or email bariatric surgeon Kimberley Steele: ksteele3@jhmi.edu.

An Endoscopic Approach for Craniosynostosis

In the past, children with prematurely fused skull sutures had just a single option available to them: an operation involving an ear-to-ear incision done when they're 9 to 12 months old, the age when they're more likely to withstand the procedure. Today, however, says pediatric neurosurgeon **Edward Ahn**, it's possible using endoscopic techniques to perform the same procedure through a one-inch incision. The only real impediment to making sure children receive this significantly safer and less invasive option, says Ahn, is for prospective patients to be referred before they reach 3 months of age.

Developed in the early 2000s, the endoscopic version involves making a small incision where the skull bones are fused. By inserting an endoscope and tools, surgeons can excise the problematic bone section. Ahn and his colleagues recently introduced an ultrasonic bone cutter, which provides better protection against blood loss since many bleeds come from skull bones themselves. Minimizing blood loss—the riskiest part of the operation—is especially important because even a small amount of lost blood is proportionally large for these tiny patients.

Pediatric neurosurgeon Edward Ahn notes that the endoscopic technique can only be offered to infants up to 3 months of age. After that, patients have fewer treatment options

Although the traditional operation usually necessitates blood transfusions for all patients, with the newer procedure only a fifth will require a transfusion. Additionally, patients who have the newer operation typically spend only a single night at the hospital, compared with up to a week for the traditional procedure.

On the day of discharge, patients who have the endoscopic surgery are fitted for a helmet, which they wear 23 hours a day for the next six to nine months, a treatment that molds the head into a natural shape as it grows. When children are finished with the helmet, Ahn says, they rarely need additional treatment. This period is pivotal to

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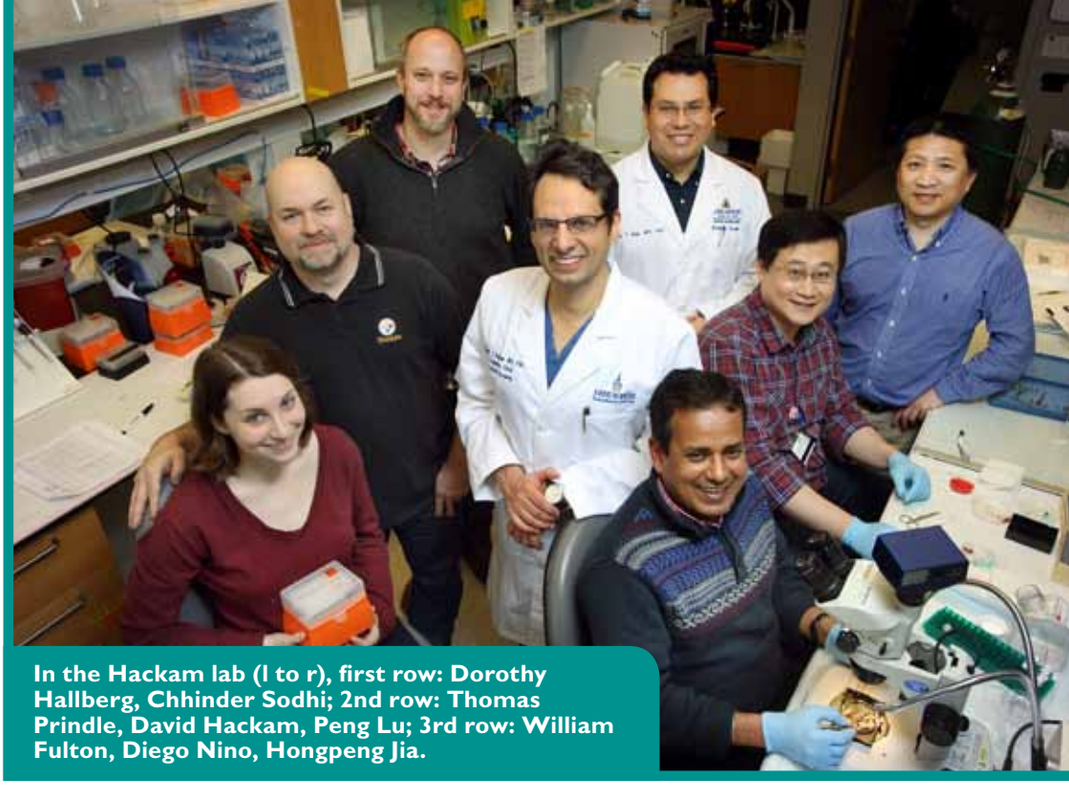
An Artificial Intestine for NEC Patients?



In the Hackam lab (l to r), first row: Dorothy Hallberg, Chhinder Sodhi; 2nd row: Thomas Prindle, David Hackam, Peng Lu; 3rd row: William Fulton, Diego Nino, Hongpeng Jia.

Therapy for necrotizing enterocolitis, or NEC, is limited to surgery that leaves patients with insufficient intestine—short bowel syndrome—and at risk of long-term complications. Unable to absorb enough nutrients, these children require feeding support for life—and many transplantation and immune-suppressive therapy that pose long-term risks. If ever a disease needed a lab, Johns Hopkins pediatric surgeon **David Hackam** felt, NEC was it.

Through simulating NEC in mouse models and employing genetic and pharmacologic approaches to prevent its course, Hackam and his colleagues have made some significant inroads. For NEC to develop, explains Assistant Professor of Surgery **Chhinder Sodhi**, three factors must come into play—premature birth, hypoxia, and a bacterial infection. In that perfect storm, Hackam's group identified a specific molecule that attracts gram-negative bacteria in the gut—toll like receptor 4 (TLR4)—which is highly expressed in the initiation of the disease. Expression of TLR4 is necessary for the development of the intestines, Sodhi explains, but high expression of it halts blood flow to the intestines and normal development in its tracks, resulting in NEC. The Hackam lab had its treatment target.

The group has also found that amniotic fluid, which contains the wound-healing protein epidermal growth factor or EGF, inhibits TLR4 signaling, which could lead to development of a drug inhibiting TLR4 activity and preventing NEC inflammation in premature infants. In the womb, Sodhi notes, normal birth babies bathe in and drink amniotic fluid while premature babies do not. Lab members have also found protection against NEC in breast milk, which is not readily available to premature infants. They showed that NEC did not develop in mice fed with infant formula containing sodium nitrate, a compound known to improve blood flow and found in breast milk.

"NEC often develops within the first two weeks of life, usually after milk feeding has begun and the infant's immature bowels are prone to infection," says Sodhi. "The premature infant's difficulty with blood and oxygen circulation also increases their risk of NEC. Without the breast milk and amniotic fluid, you have high levels of TLR4."

In another preventive strategy, the group is also searching for diagnostic markers in, among other places, the mother's stool. Another goal is identification of mutations in the TLR4 gene that cause higher signaling and expression. "We're studying all of the genes in the TLR4 pathway, taking them away and putting them back, to correct the signaling," says Sodhi.

In yet another approach, what Hackam calls his lab's "most exciting work," he and his team are collaborating with Cornell scientist John March to create an artificial intestine for NEC patients. They've mastered a way to culture intestinal stem cells but they've been unable to create a structure where the cells can grow—but Hackam is determined to find such a scaffold.

"Surgeons can't operate in silos and by necessity," says Hackam. "These infants, born with intestines that don't work, are left without a gut. They can wait for an intestinal transplant, but why not develop an artificial intestine? There's a clear, unmet need for it."

This research initiative, funded by a $500,000-plus grant from The Hartwell Foundation, also dovetails with studies by Hopkins pediatric plastic surgeon **Anand Kumar** in the plastics stem cell lab. There Kumar and his colleagues are investigating muscle stem cell biology for regenerative applications for bone defects of the skull and face for cleft lip and palate, and craniosynostosis patients.

"These children have too much or too little bone and we don't have great places to get bone grafting materials," says Kumar. "We're working constantly to engineer bone."

In Hackam's mind, that's one more illustration of the continuing influence of science on surgery. ■

An Endoscopic Approach for Craniosynostosis

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successful outcomes, he adds, and it's why the endoscopic surgery is only available to patients no older than 3 months. After that, the head is less malleable, requiring patients to have the riskier open surgery.

Besides age, Ahn says, there are few factors that disqualify potential patients from the endoscopic technique. Although it's been used most often to correct only fused sagittal sutures, he and other neurosurgeons are now using it for patients with more than one fused suture and even more complex craniofacial syndromes.

The endoscopic technique also offers cosmetic advantages, Ahn adds, making scars essentially invisible compared to the obvious marks left behind after a bilateral craniotomy. Often, parents bring their children back to visit, with their boys sporting short haircuts—something that would have been a rarity in the past.

"The biggest compliment to me," says Ahn, "is when parents say their friends are amazed after they describe what their child went through as a baby, because they never would have known." ■

An Effective Distraction for Neonatal Airway Obstruction

One of the most exciting technical advances in pediatric craniofacial surgery at Johns Hopkins today is distraction osteogenesis, which eliminates the need for bone grafting and replaces it with bone generation. By moving bones slowly over time, the technique avoids soft-tissue damage and promotes bone formation with no permanent hardware. In treating neonatal airway obstruction, in which an infant's jaw is so small that the tongue is pushed against the back of the throat, explains pediatric craniofacial surgeon **Anand Kumar**, surgeons manipulate the jawbone and insert a device to gradually move it forward, bringing the tongue along with it. The device is initially adjusted, followed by a three-month healing period, and then removed to allow the patient to heal hardware-free. Traditional treatments have included the use of breathing and feeding tubes, but distraction can eliminate these. It is also decreases tissue damage, the need for secondary bone grafting procedures, and blood loss during surgery. "The neonatal airway distraction program," says Kumar, "has really changed many lives." ■

3-D models take the guesswork out for craniofacial surgeons Richard Redett, Amir Dorafshar and Anand Kumar.

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