Pediatric Neurosurgery: Minimally Invasive Techniques Bring Maximum Results
When it comes to pediatric neurosurgery, less is better.

That’s the idea behind minimally invasive pediatric neurosurgery, which allows Dr. Lance Governale and other surgeons at Nationwide Children’s Hospital to use the latest endoscopic technology to treat such conditions as craniosynostosis and hydrocephalus in infants.

See the full story on page 8.
Leading Expert to Head Celiac Disease Center

As many as one in 100 children may have celiac disease, a lifelong intolerance to gluten. To continue providing and improving care for these children in a comprehensive manner, the Nationwide Children’s Hospital Celiac Disease Center has appointed Ivor Hill, MD, a pediatric gastroenterologist and national expert in the treatment and research of celiac disease, as its new director. The center, which is part of the Division of Gastroenterology, Hepatology and Nutrition, offers clinical care for pediatric celiac disease, health education services, quality improvement initiatives and targeted research.

“There is a lot of excitement among my colleagues for the improvement initiatives and targeted research,” said Dr. Hill, who joined Nationwide Children’s in May from Wake Forest University and Brenner Children’s Hospital in North Carolina. “I sense a tremendous culture of enthusiasm and support for developing programs that will ultimately benefit children in our region and beyond.”

One of the leading clinicians and researchers in childhood celiac disease, Dr. Hill has been instrumental in raising national awareness of the disease. As chair of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) committee, he helped develop the first evidence-based guidelines on diagnosis and treatment of celiac disease in children. He currently serves on editorial boards for the Journal of Pediatric Gastroenterology and Nutrition and the Journal of Pediatrics and is listed among America’s Top Doctors, America’s Top Pediatricians, Best Doctors in America, Guide to America’s Top Gastroenterologists, and Who’s Who in Medical Science Education. In 2011, he received the Distinguished Service Award from NASPGHAN.

Dr. Hill’s clinical and research interests include multiple gastrointestinal diseases, including infants with chronic diarrhea, effects of glutamine deficiency, gluten peptide toxicity in the pathogenesis of celiac disease and the epidemiology of celiac disease. He has published more than 80 articles in leading peer-reviewed journals and 37 chapters in medical books. He also is a professor of clinical pediatrics at The Ohio State University College of Medicine.

Detail of Cardiac MRI Imaging Offers Valuable Diagnostic Tool

Last year, Nationwide Children’s Hospital performed 160 cardiac MRI scans, giving physicians and surgeons a more comprehensive view of the heart than conventional imaging scans allow. So far, the cardiac MRI team is on track to perform more than 200 scans this year, a number that will only increase as knowledge of the technology’s diagnostic value grows, according to pediatric cardiologist Kan H. Hor, MD, director of Cardiac MRI (cardiology section) in The Heart Center at Nationwide Children’s.

“Cardiac MRI is essentially used to detect all kinds of heart disease, whether it is acquired or congenital,” Dr. Hor says.

The main advantage of cardiac MRI over echocardiogram is the depth of detail it offers, Dr. Hor says. The scans provide a close look at anatomical abnormalities as well as information about cardiac function. For example, doctors can not only see a leaky valve, but also how much it is leaking. They can distinguish old scar tissue on the heart from more recent damage. Cardiac MRI even makes it possible to create 3-D images of blood vessels, a process called magnetic resonance angiography, to give physicians an accurate visual of defects prior to surgery or heart catheterization. And, unlike cardiac catheterization, cardiac MRI is non-invasive.

“What sets it apart from other programs is the focus on family-centered care and a multidisciplinary approach for all children with hearing loss,” he says. The Hearing Program provides hearing testing, specialized speech therapy for children with hearing loss, ear surgery, cochlear implantation and a range of other services. In addition to increasing the number of children the program serves, future plans include adding new clinical services, such as music therapy and a hearing resource center for patients and families, and developing a clinical and basic research program to look into the causes of hearing disorders and the development of new treatments.

“Essentially, cardiac MRI has many capabilities beyond traditional non-invasive techniques,” says Dr. Hor, who joined Nationwide Children’s in February from Cincinnati Children’s Hospital Medical Center, where he was an assistant professor in pediatric cardiology. “It is becoming a widely available diagnostic modality to help us better assess the health status of our patients and provide a better road map for intervention.”

A close collaboration between radiology and cardiology experts is one reason for the cardiac MRI team’s success, says Dr. Hor, whose clinical and research interests include cardiac MRI, cardiac CT angiography, echocardiography and congenital heart disease. Plans to strengthen that partnership, as well as continued efforts to educate physicians about the potential of cardiac MRI for patient care, will likely lead to greater use of the technology, he adds.

“I project that within the next three to five years we will be performing well over 600 cardiac MRI studies a year,” says Dr. Hor, who also is an associate professor of pediatrics at The Ohio State University College of Medicine. “It is an extremely valuable tool.”

Hearing Program Gets New Director, Celebrates 10th Anniversary

When the current Hearing Program at Nationwide Children’s Hospital opened its doors in 2003, the goal was to assemble a team of physicians, surgeons, audiologists, nurses and social workers to provide comprehensive medical care to children with hearing loss—not just during childhood, but throughout each patient’s life. Over the past 10 years, the program’s staff has done that for more than 1,500 children.

Now, even as the staff celebrates their accomplishments, they are looking for ways to expand their services and reach more patients, says Prashant Solanki Malhotra, MD, who joined Nationwide Children’s as the program’s director in April.

“The Hearing Program provides surgical and non-surgical care for deaf and hard-of-hearing children at the highest level,” says Dr. Malhotra, who came to Columbus from the Cleveland Clinic, where he was a surgeon and associate physician staff member of the Head and Neck Institute and the Pediatric Institute.

“When the current Hearing Program at Nationwide Children’s Hospital opened its doors in 2003, the goal was to assemble a team of physicians, surgeons, audiologists, nurses and social workers to provide comprehensive medical care to children with hearing loss—not just during childhood, but throughout each patient’s life. Over the past 10 years, the program’s staff has done that for more than 1,500 children.

Now, even as the staff celebrates their accomplishments, they are looking for ways to expand their services and reach more patients, says Prashant Solanki Malhotra, MD, who joined Nationwide Children’s as the program’s director in April.

“The Hearing Program provides surgical and non-surgical care for deaf and hard-of-hearing children at the highest level,” says Dr. Malhotra, who came to Columbus from the Cleveland Clinic, where he was a surgeon and associate physician staff member of the Head and Neck Institute and the Pediatric Institute.

“When the current Hearing Program at Nationwide Children’s Hospital opened its doors in 2003, the goal was to assemble a team of physicians, surgeons, audiologists, nurses and social workers to provide comprehensive medical care to children with hearing loss—not just during childhood, but throughout each patient’s life. Over the past 10 years, the program’s staff has done that for more than 1,500 children.

Now, even as the staff celebrates their accomplishments, they are looking for ways to expand their services and reach more patients, says Prashant Solanki Malhotra, MD, who joined Nationwide Children’s as the program’s director in April.

“The Hearing Program provides surgical and non-surgical care for deaf and hard-of-hearing children at the highest level,” says Dr. Malhotra, who came to Columbus from the Cleveland Clinic, where he was a surgeon and associate physician staff member of the Head and Neck Institute and the Pediatric Institute.

“When the current Hearing Program at Nationwide Children’s Hospital opened its doors in 2003, the goal was to assemble a team of physicians, surgeons, audiologists, nurses and social workers to provide comprehensive medical care to children with hearing loss—not just during childhood, but throughout each patient’s life. Over the past 10 years, the program’s staff has done that for more than 1,500 children.

Now, even as the staff celebrates their accomplishments, they are looking for ways to expand their services and reach more patients, says Prashant Solanki Malhotra, MD, who joined Nationwide Children’s as the program’s director in April.

“The Hearing Program provides surgical and non-surgical care for deaf and hard-of-hearing children at the highest level,” says Dr. Malhotra, who came to Columbus from the Cleveland Clinic, where he was a surgeon and associate physician staff member of the Head and Neck Institute and the Pediatric Institute.

“When the current Hearing Program at Nationwide Children’s Hospital opened its doors in 2003, the goal was to assemble a team of physicians, surgeons, audiologists, nurses and social workers to provide comprehensive medical care to children with hearing loss—not just during childhood, but throughout each patient’s life. Over the past 10 years, the program’s staff has done that for more than 1,500 children.

Now, even as the staff celebrates their accomplishments, they are looking for ways to expand their services and reach more patients, says Prashant Solanki Malhotra, MD, who joined Nationwide Children’s as the program’s director in April.

“The Hearing Program provides surgical and non-surgical care for deaf and hard-of-hearing children at the highest level,” says Dr. Malhotra, who came to Columbus from the Cleveland Clinic, where he was a surgeon and associate physician staff member of the Head and Neck Institute and the Pediatric Institute.

“When the current Hearing Program at Nationwide Children’s Hospital opened its doors in 2003, the goal was to assemble a team of physicians, surgeons, audiologists, nurses and social workers to provide comprehensive medical care to children with hearing loss—not just during childhood, but throughout each patient’s life. Over the past 10 years, the program’s staff has done that for more than 1,500 children.

Now, even as the staff celebrates their accomplishments, they are looking for ways to expand their services and reach more patients, says Prashant Solanki Malhotra, MD, who joined Nationwide Children’s as the program’s director in April.

“The Hearing Program provides surgical and non-surgical care for deaf and hard-of-hearing children at the highest level,” says Dr. Malhotra, who came to Columbus from the Cleveland Clinic, where he was a surgeon and associate physician staff member of the Head and Neck Institute and the Pediatric Institute.
Herman Leads National Genomics Organization

Gail E. Herman, MD, PhD, has been appointed president of the American College of Medical Genetics and Genomics (ACMG), a professional organization that represents 1,600 geneticists, genetics counselors and others in the medical genetics field. Dr. Herman, who is a principal investigator in the Center for Molecular and Human Genetics in The Research Institute at Nationwide Children's Hospital, began her two-year term in April.

In addition to her clinical practice, Dr. Herman conducts research on the genetic underpinnings of a number of medical conditions, including autism spectrum disorder. A longtime member of ACMG, she has helped the group develop guidelines and best-practice policies in the field of medical genetics.

“I’ve been doing clinical genetics now for 30 years and while I think we’ve seen exciting new developments and technology before, I think there has never been a time as exciting or as likely to change the field of clinical medical genetics as right now,” Dr. Herman says.

Dr. Herman also is a professor in pediatrics and molecular virology, immunology and medical genetics at The Ohio State University College of Medicine, and a practicing physician in genetics at Nationwide Children’s.

Expansion Enhances Patient Care for Small Baby Program

Bob, an average gestational age of fewer than 25 weeks, the patients in the Small Baby Program at Nationwide Children’s Hospital accurately represent the program’s name, usually weighing in at less than 2 pounds. An expansion underway in the neonatal intensive care unit (NICU) will give these tiny newborns plenty of room to grow in a family-friendly medical unit specially designed to meet the needs of premies.

The project will increase the number of patients the program can accommodate from 10 to 23. The first phase of the construction—the development of 13 private rooms—ended in June and already is making a tangible difference in the patient experience, says Elizabeth Martin, RN, clinical leader of the Small Baby Program.

“Getting the new beds is such an opportunity to really reinforce what we want to see in practice,” Martin says. Family-centered care is a key theme in the unit’s Small Baby Guidelines, including the promotion of Kangaroo Care—regular skin-to-skin contact between parents and premature babies. “We really want to get moms and dads Kangarooing at the bedside,” Martin adds.

“Since we have single rooms now, they can essentially move in. Already they’re raving about how much they like it. Parents can interact with their babies more. They love the privacy.”

The expansion, due for completion by December, will enable the interdisciplinary team to continue applying the Small Baby Guidelines that have already substantially improved mortality, length of stay, oxygen dependency and intraventricular hemorrhage rates among their patient population. Based on standardization of care and incorporation of input from all members of the patient care team, the Small Baby Guidelines developed by NICU staff have resulted in improved outcomes for newborns not just at Nationwide Children’s, but also in hospitals around the country that have adopted the guidelines.

The staff is optimistic about the chance to further improve outcomes for small babies, Martin says. “It’s kind of nice to see where we’ve been and how far we’ve come,” she says, adding that their approach should prompt people to start thinking more positively about the outlook for the tiny patients in the program. “We can do this. It can be done. Prematurity doesn’t have to be bad; a lot of the things we’re doing here are proving that.”

New Patient Simulator Facility Offers On-Site Training Opportunities

A new training facility in Neonatology that features life-size patient simulators and a range of interactive technologies will enable medical teams to train and learn together in an environment that more closely mimics the real-life situations they will face when caring for patients. The on-unit facility, completed in June, includes a control room, full-scale mock-up patient room monitored by video and audio recording devices, and a connected classroom for training and debriefing.

Previously, training took place in a basic classroom off-site, making it difficult for large groups to leave the hospital and limiting the realism of training, says Debbie Dunn, APN, a clinical nurse educator for Neonatal Services who helps organize training.

“We were setting them up on a table in the classroom,” Dunn says. “People were enjoying the simulation of it, but there was still that inability to suspend disbelief.”

Infant and newborn high-fidelity patient simulators are now available to nurses, residents, physicians, respiratory therapists and other medical staff for training sessions. The room offers two neonatal bed units side-by-side, allowing training sessions to run simultaneously, much like real on-unit circumstances.

Expansion Enhances Patient Care for Small Baby Program

The expansion, due for completion by December, will enable the interdisciplinary team to continue applying the Small Baby Guidelines that have already substantially improved mortality, length of stay, oxygen dependency and intraventricular hemorrhage rates among their patient population. Based on standardization of care and incorporation of input from all members of the patient care team, the Small Baby Guidelines developed by NICU staff have resulted in improved outcomes for newborns not just at Nationwide Children’s, but also in hospitals around the country that have adopted the guidelines.

The staff is optimistic about the chance to further improve outcomes for small babies, Martin says. “It’s kind of nice to see where we’ve been and how far we’ve come,” she says, adding that their approach should prompt people to start thinking more positively about the outlook for the tiny patients in the program. “We can do this. It can be done. Prematurity doesn’t have to be bad; a lot of the things we’re doing here are proving that.”

New Patient Simulator Facility Offers On-Site Training Opportunities

A new training facility in Neonatology that features life-size patient simulators and a range of interactive technologies will enable medical teams to train and learn together in an environment that more closely mimics the real-life situations they will face when caring for patients. The on-unit facility, completed in June, includes a control room, full-scale mock-up patient room monitored by video and audio recording devices, and a connected classroom for training and debriefing.

Previously, training took place in a basic classroom off-site, making it difficult for large groups to leave the hospital and limiting the realism of training, says Debbie Dunn, APN, a clinical nurse educator for Neonatal Services who helps organize training.

“We were setting them up on a table in the classroom,” Dunn says. “People were enjoying the simulation of it, but there was still that inability to suspend disbelief.”

Infant and newborn high-fidelity patient simulators are now available to nurses, residents, physicians, respiratory therapists and other medical staff for training sessions. The room offers two neonatal bed units side-by-side, allowing training sessions to run simultaneously, much like real on-unit circumstances.

Expansion Enhances Patient Care for Small Baby Program

The expansion, due for completion by December, will enable the interdisciplinary team to continue applying the Small Baby Guidelines that have already substantially improved mortality, length of stay, oxygen dependency and intraventricular hemorrhage rates among their patient population. Based on standardization of care and incorporation of input from all members of the patient care team, the Small Baby Guidelines developed by NICU staff have resulted in improved outcomes for newborns not just at Nationwide Children’s, but also in hospitals around the country that have adopted the guidelines.

The staff is optimistic about the chance to further improve outcomes for small babies, Martin says. “It’s kind of nice to see where we’ve been and how far we’ve come,” she says, adding that their approach should prompt people to start thinking more positively about the outlook for the tiny patients in the program. “We can do this. It can be done. Prematurity doesn’t have to be bad; a lot of the things we’re doing here are proving that.”

New Patient Simulator Facility Offers On-Site Training Opportunities

A new training facility in Neonatology that features life-size patient simulators and a range of interactive technologies will enable medical teams to train and learn together in an environment that more closely mimics the real-life situations they will face when caring for patients. The on-unit facility, completed in June, includes a control room, full-scale mock-up patient room monitored by video and audio recording devices, and a connected classroom for training and debriefing.

Previously, training took place in a basic classroom off-site, making it difficult for large groups to leave the hospital and limiting the realism of training, says Debbie Dunn, APN, a clinical nurse educator for Neonatal Services who helps organize training.

“We were setting them up on a table in the classroom,” Dunn says. “People were enjoying the simulation of it, but there was still that inability to suspend disbelief.”

Infant and newborn high-fidelity patient simulators are now available to nurses, residents, physicians, respiratory therapists and other medical staff for training sessions. The room offers two neonatal bed units side-by-side, allowing training sessions to run simultaneously, much like real on-unit circumstances.
A Minimalistic Approach to Pediatric Neurosurgery

The field of pediatric neurosurgery has advanced greatly in the past 50 years. Innovations in diagnostic imaging technology and surgical instrumentation have improved patient care beyond measure, saving and improving the lives of thousands of children around the world.

One of the areas most affected by these developments has been minimally invasive neurosurgery, in which endoscopes are used to visualize the delicate structures of the brain, skull base and spinal cord. Highly precise surgical instruments inserted through or around the endoscopes allow neurosurgeons to remove pathologic tissue, correct deformities and repair structural damage caused by disease or trauma. Unlike traditional open neurosurgery, which often requires large incisions and long hospitalizations, minimally invasive procedures need only a few tiny incisions, don’t take as long to perform and often result in a patient discharge within 48 hours or less. The small size of the endoscope means that neurosurgeons can access the surgical site without dissecting large areas of brain tissue or damaging vital anatomical structures.

At Nationwide Children’s Hospital, the neurosurgery team utilizes minimally invasive endoscopy to treat a variety of conditions, ranging from tumors to bone deformities to cerebrospinal fluid blockage. When considering whether to use a minimally invasive technique or a more traditional open approach, neurosurgeons consider many factors. Is the surgical target in a location easily accessible with an endoscope? What other structures is it near? Where are the nerves and blood vessels that must be avoided? Not every patient should have minimally invasive neurosurgery; some conditions are better treated with more traditional approaches. Neurosurgery is all about finding a safe corridor to the target. Whether that is through an open or endoscopic surgery all depends on the fine details.

Some of the more common neurosurgical procedures performed endoscopically at Nationwide Children’s are used to treat hydrocephalus, arachnoid or colloid cysts, tumors of the skull base or pituitary and craniosynostosis. A discussion of some of these conditions follows.
HYDROCEPHALUS

The body continuously produces cerebrospinal fluid (CSF), which surrounds the brain and spinal cord. Normally, CSF flows through the ventricles in the brain, exits the brain at the base of the skull, circulates around the brain and spinal cord, and then is reabsorbed into the venous system at the arachnoid granulations.

In hydrocephalus, that flow is blocked and CSF builds up, putting pressure on the brain. Patients can either be born with the condition or develop it. Classically, hydrocephalus is treated by implanting a shunt system, a plastic tube that drains CSF from the brain to another location in the body where it can be absorbed, usually the peritoneal cavity, the right atrium or the pleural cavity. Because shunts can clog or malfunction over time, neurosurgeons attempt to treat hydrocephalus without a shunt when possible.

Depending on the location of the CSF blockage, some patients may be candidates for an endoscopic third ventriculostomy (ETV). During ETV, neurosurgeons create an opening in the third ventricular floor to allow CSF to pass from the inside to the outside of the brain. If successful, this surgery is a permanent correction for hydrocephalus without a shunt when possible.

Studies of the combined ETV-CPC procedure suggest that it is more effective in treating hydrocephalus in infants less than 1 year old than ETV alone. That said, neurosurgeons must always caution their patients’ parents that even if there is 100 percent technical success in the operating room, there is still a 30 to 50 percent chance that the hydrocephalus could return. If that happens, patients will require another surgery to insert a shunt. If the ETV-CPC procedure treats the hydrocephalus for six months, it is likely to treat it in the long term.

Efforts to train current and future neurosurgeons in minimally invasive techniques will no doubt lead to advances in the field itself. The more we do, the more we learn and the more skilled we all become.

— Lance Governale, MD

A HYDROCEPHALUS CASE STUDY:

Eli Fullerton and twin brother Bryce were born prematurely Nov. 14, 2011 at 30 weeks gestation. Two weeks later, Eli developed a fever and had blood in his cerebrospinal fluid (CSF). An ultrasound revealed a grade 3 intraventricular hemorrhage, a condition that arises in some preemies whose fragile blood vessels rupture, allowing blood to enter the ventricles of the brain. In more severe cases, blood clots can form and block the flow of CSF, leading to hydrocephalus.

Eli was transferred to Nationwide Children’s Hospital on Dec. 4. Pediatric neurosurgeon Lance Governale, MD, inserted a temporary shunt to help drain the CSF, a step designed to allow the child to grow before more permanent hydrocephalus treatment can be done. In a minority of cases, the hydrocephalus can resolve on its own and never require permanent treatment. After a period of inpatient observation, Eli went home on Dec. 27 when he met the usual newborn discharge criteria.

After a few months of close monitoring, it became clear that Eli’s hydrocephalus would require additional surgery. On March 13, 2012, Eli underwent a procedure called ETV-CPC (see main article), which not only bypassed the blockage, but also reduced CSF production—without the need for a shunt. The surgery was successful and Eli went home two days later.

Even if this type of surgery goes as planned, there is still a chance that the hydrocephalus could recur. Eli was evaluated by Dr. Governale frequently following the operation. At each follow up, the ETV-CPC appeared to be treating Eli’s hydrocephalus without a shunt and no post-surgical complications were reported.

A little more than a year after his procedure, Eli is a healthy, active, mischievous toddler.
When considering whether to use a minimally invasive technique or a more traditional open approach, neurosurgeons consider many factors. Is the surgical target in a location easily accessible with an endoscope? What other structures is it near? Where are the nerves and blood vessels that must be avoided?

— Lance Governale, MD

TUMORS, PITUITARY LESIONS, COLLOID CYSTS AND ARACHNOID CYSTS

Some brain tumors, pituitary lesions, colloid cysts and arachnoid cysts, depending on their exact location and relationship to surrounding structures, can be resected using minimally invasive techniques. Using an endoscope, the neurosurgeon can access the mass through a small opening in the skull via the ventricular system. Other times, the mass can be accessed through the nose via the air sinuses. With these techniques, brain tissue disruption, incision size, postoperative pain and patient recovery time may all be decreased.

Another condition that may be treatable with minimally invasive techniques is an arachnoid cyst. These CSF-filled sacs form in the subarachnoid or intraventricular spaces. Patients with these cysts sometimes can develop hydrocephalus when the cyst blocks the flow of cerebrospinal fluid through the ventricles. Other times, the cyst can be symptomatic from mass effect on the adjacent brain or skull. Most times, however, these cysts are asymptomatic, incidental findings that require no treatment, referral or follow-up.

For the minority of arachnoid cysts that do require treatment, neurosurgeons attempt to fenestrate the wall of the cyst so the fluid within can drain via normal CSF pathways. If this does not work or is not possible, a shunt may be necessary. Intraventricular arachnoid cysts are usually fenestrated via minimally invasive endoscopic techniques. Ones in the subarachnoid spaces can be fenestrated similarly. However, sometimes an open approach will allow more extensive fenestrations, thus lessening the chance a shunt will be needed, which is the ultimate goal.

In so many of these cases, choosing an open or minimally invasive approach depends almost entirely on where the target is located and what critical structures it is near. This is all part of the art of neurosurgery. It requires seeing the space and how best to access it.

Craniosynostosis is most often repaired with an open surgery that involves an incision from ear to ear and the removal, reshaping and reattachment of affected bones. Otherwise in good health and just over 6 weeks old, James was a candidate for a minimally invasive endoscopic procedure that would correct the problem through just two tiny incisions. Performed by pediatric neurosurgeon Lance Governale, MD, at Nationwide Children’s Hospital on Aug. 10, 2012, the procedure was successful and James went home the following day.

A crucial element to this minimally invasive procedure is the use of a molding helmet, which the child must wear 23 hours a day until his first birthday. The helmet helps direct the skull into the proper shape as the infant’s head grows. James’ parents, Jennifer and Andrew, are devoted fans of The Ohio State University, so his mother painted James’ headpiece to resemble an OSU football helmet.

Frequent evaluations following surgery revealed good progress in head growth. On his first birthday, James received the all-clear from Dr. Governale to remove his helmet for good. James’ parents and Dr. Governale are very happy with James’ head shape, which is now normal.

A CRANIOSYNOSTOSIS CASE STUDY:

When James Vida was born on May 23, 2012, there was a noticeable raised ridge along the top of his head. Initially the shape, which bulged slightly in the front and back, was thought to be the result of a very long labor and difficult passage through the birth canal. But a month later, when James’ head was still misshaped, his pediatrician recommended he have a skull x-ray.

The suture between two of the bones in James’ skull had fused prematurely; a condition called craniosynostosis (see main article). Sutures usually remain open in childhood to allow for the skull and brain to grow normally. In James’ case, the sagittal suture that runs along the top of the head fused too early, forcing the skull to grow in a long and narrow shape.

When considering whether to use a minimally invasive technique or a more traditional open approach, neurosurgeons consider many factors. Is the surgical target in a location easily accessible with an endoscope? What other structures is it near? Where are the nerves and blood vessels that must be avoided?

— Lance Governale, MD

TUMORS, PITUITARY LESIONS, COLLOID CYSTS AND ARACHNOID CYSTS

Some brain tumors, pituitary lesions, colloid cysts and arachnoid cysts, depending on their exact location and relationship to surrounding structures, can be resected using minimally invasive techniques. Using an endoscope, the neurosurgeon can access the mass through a small opening in the skull via the ventricular system. Other times, the mass can be accessed through the nose via the air sinuses. With these techniques, brain tissue disruption, incision size, postoperative pain and patient recovery time may all be decreased.

Another condition that may be treatable with minimally invasive techniques is an arachnoid cyst. These CSF-filled sacs form in the subarachnoid or intraventricular spaces. Patients with these cysts sometimes can develop hydrocephalus when the cyst blocks the flow of cerebrospinal fluid through the ventricles. Other times, the cyst can be symptomatic from mass effect on the adjacent brain or skull. Most times, however, these cysts are asymptomatic, incidental findings that require no treatment, referral or follow-up.

For the minority of arachnoid cysts that do require treatment, neurosurgeons attempt to fenestrate the wall of the cyst so the fluid within can drain via normal CSF pathways. If this does not work or is not possible, a shunt may be necessary. Intraventricular arachnoid cysts are usually fenestrated via minimally invasive endoscopic techniques. Ones in the subarachnoid spaces can be fenestrated similarly. However, sometimes an open approach will allow more extensive fenestrations, thus lessening the chance a shunt will be needed, which is the ultimate goal.

In so many of these cases, choosing an open or minimally invasive approach depends almost entirely on where the target is located and what critical structures it is near. This is all part of the art of neurosurgery. It requires seeing the space and how best to access it.

Craniosynostosis is most often repaired with an open surgery that involves an incision from ear to ear and the removal, reshaping and reattachment of affected bones. Otherwise in good health and just over 6 weeks old, James was a candidate for a minimally invasive endoscopic procedure that would correct the problem through just two tiny incisions. Performed by pediatric neurosurgeon Lance Governale, MD, at Nationwide Children’s Hospital on Aug. 10, 2012, the procedure was successful and James went home the following day.

A crucial element to this minimally invasive procedure is the use of a molding helmet, which the child must wear 23 hours a day until his first birthday. The helmet helps direct the skull into the proper shape as the infant’s head grows. James’ parents, Jennifer and Andrew, are devoted fans of The Ohio State University, so his mother painted James’ headpiece to resemble an OSU football helmet.

Frequent evaluations following surgery revealed good progress in head growth. On his first birthday, James received the all-clear from Dr. Governale to remove his helmet for good. James’ parents and Dr. Governale are very happy with James’ head shape, which is now normal.
CRANIOSYNOSTOSIS

The sutures of the skull allow brain growth to drive skull growth. In craniosynostosis, one or more of the sutures closes early. The skull then attempts to grow parallel to the fused suture, rather than perpendicular to it. This causes stereotypical head shape abnormalities, usually best viewed from the top of the child’s head.

Sagittal craniosynostosis, the most common non-syndromic form, causes a long and narrow head. Bilateral coronal craniosynostosis causes a rotated appearance to the face with flattening of the forehead on the affected side, elevation of the orbital roof on the affected side and rotation of the nose. Sometimes the anterior fontanel is somewhat displaced to the contralateral side. Metopic craniosynostosis causes a triangular shape to the forehead when viewed from above. Metopic ridging without the triangular shape is a normal variant. Sometimes there is palpable ridging over the fused suture, sometimes not. Sometimes the anterior fontanel is open, sometimes not.

Lambdoid craniosynostosis is a very rare entity and the only one that would cause flattening in the back of the head. The vast majority of posterior flattening is positional plagiocephaly which is purely a cosmetic condition that does not affect brain growth or development. In positional plagiocephaly, the ear and possibly forehead on the side of the posterior flattening is displaced anteriorly, giving the head a parallelogram shape. In the rare case of lambdoid craniosynostosis, the ear and possibly forehead on the side of the posterior flattening is displaced posteriorly giving the head a trapezoidal shape.

If indeed there is a fused suture, ultimately it may cause head growth restriction on the growth curves leading to worrisome increased intracranial pressure (ICP). As such, treatment when craniosynostosis is diagnosed is recommended. The two treatment options are the traditional open approach and the newer minimally invasive endoscopic approach.

The open surgery involves removal of at least half of the bones of the skull, reshaping them and reattaching them in conjunction with a craniofacial plastic surgeon. It is done via a bicoronal incision across the top of the scalp from ear to ear. The surgery lasts approximately four hours; often a blood transfusion is required. Postoperatively, the child is observed in the intensive care unit overnight then spends approximately three days on the regular neurosurgical floor. Periorbital edema usually causes the eyes to swell shut then reopen before discharge. To decrease the surgical risk for this larger surgery, we wait until the child is at least 6 months old. They are very unlikely to experience any ICP sequelae of craniosynostosis before then.

The minimally invasive endoscopic surgery involves excision of the fused suture only. It is done via one or two 2-cm incisions. The surgery lasts approximately one hour; a blood transfusion is only rarely required. Postoperatively, the child typically is observed overnight on the regular neurosurgical floor then is ready for discharge. Usually there is no periorbital edema. Unlike the open procedure, postoperative helmeting is necessary for the minimally invasive surgery to work. The helmet is a hard outer shell with moldable foam on the inside worn 23 hours per day until the child’s first birthday. It does not press the skull into shape, but rather directs the growth of the skull into a more normal shape. Because the helmet relies on the high rate of skull growth in the first year of life, the endoscopic surgery must be done earlier than the open surgery. It can only be done between 2.5 and 3.5 months of age, so early diagnosis and referral is key for it to be an option. It is not an option for syndromic cases.

THE FUTURE OF MINIMALLY INVASIVE PEDIATRIC NEUROSURGERY

Efforts to train current and future neurosurgeons in minimally invasive techniques will no doubt lead to advances in the field itself. The more we do, the more we learn and the more skilled we all become. The development of procedures such as ETV-CPC demonstrate the possibilities for improving patient care that come from looking at what we do from a different viewpoint. Endoscopic third ventriculostomy was once rarely successful in infants. Today, children treated successfully with the combined procedure are living healthy, shunt-free lives.

The first step in any surgical process is determining what is in the best interest of the patient, which begins with the surgical consultation. Accurate and early diagnosis is imperative to successful treatment for all neurological disorders, including hydrocephalus and craniosynostosis. It is only through the support of a comprehensive medical team that includes the surgeons, pediatricians and, most importantly, the parents and patients that we will achieve our ultimate goal of a healthy, happy child.
GI Issues in Children with Autism Require Special Attention

The Centers for Disease Control and Prevention report that one out of every 88 children in the United States has an autism spectrum disorder—a 78 percent increase since 2007. That rise, coupled with research suggesting that these children may be more prone to gastrointestinal (GI) problems, has some clinicians and researchers looking at addressing GI issues as a standard part of comprehensive care for children with autism.

Studies report that as many as one in every three children with autism has a chronic digestive problem. GI issues in children with autism can impact quality of life for both the child and the caregiver, but are often overlooked as crucial contributors to behavior and mood. Often, because of communication difficulties and the hidden nature of many of these complications, the only sign of GI issues is the child’s behavior.

Many autism specialists now acknowledge the importance of looking beyond psychology to treat behavioral problems in children with autism, and examining the occurrence of GI complaints in this population may be a good place to start. Some studies suggest a potential genetic link, while others speculate the cause may be due to alteration of brain-gut interactions. Whatever the connection, treatment options resulting from laboratory research may be a long time coming.

For now, however, there are practical and immediate solutions pediatricians can use to control GI issues and successfully complete toilet training in their patients with autism. These interventions can markedly improve the child’s behavior as well as his or her quality of life—making visits to family and friends easier and relieving some burden from caregivers.

Screening Patients with Autism for GI Problems

Many children with autism have numerous healthcare providers and behavioral specialists working with them on a regular basis. By incorporating screening strategies to address the combination of autism and GI issues into their practice habits, pediatricians can develop a more comprehensive plan for patient care.

The most common GI complaint in children with autism is constipation, but other intestinal problems, such as acid reflux, abdominal pain and diarrhea, can occur. If a patient is having difficulty sleeping, controlling his or her behavior at school or at home, having unexplained changes in behaviors or having any behavioral issues that are not responding to behavioral interventions or existing medication adjustments, pediatricians should assess the patient for GI problems using the following steps:

• First, ask about any changes in behavior and sleeping habits. These may be signs of GI difficulties. For example, does the child get frustrated when brought to the toilet? Does behavior seem to improve after a bowel movement?

• Next, get specific. Ask caregivers in-depth questions about toilet patterns, frequency, consistency and toileting experiences. Inquire about rubbing of the stomach or chest, burping, bad breath suggestive of reflux and other common indicators of GI troubles. For example, does the child push or strain to have a bowel movement?

• If the first two steps suggest an underlying GI problem, empiric treatment of the suspected condition can help determine if a GI problem is contributing to changes in behavior. Begin with over-the-counter or prescription medical treatment for the suspected problem. If after treatment is initiated the behavioral issues appear to resolve, a GI problem was the likely cause of the behavioral disturbances.

Treating GI Problems in Patients with Autism

Although the GI issues in children with autism are not necessarily different from those of other pediatric patients, the standard protocols for GI problems do not always work with autistic patients. Current pediatric GI treatment recommendations are based on non-autistic children, and autistic children do not always respond the same way to such treatments, either behaviorally or medically.

One of the challenging things about working with this population is simply trying to find a medical regimen that works for them. Many children with autism have sensory and control issues and do not want to take medications or follow new routines. Work with patients’ families and caregivers to identify an approach that meets their needs, keeping in mind that it may take a while to find the strategy that works.

Following initiation of a treatment plan, check in with the family to see if the patient has responded to direct treatment of the GI complaint. Determine whether behavior improved, sleep difficulties resolved and if the patient appears to have more normal bowel movements.

When more complicated GI issues are suspected or when pediatricians do not feel comfortable treating the issue without consultation, the patient can be referred to a specialist for medical evaluation and behavioral therapy. Families only seeking assistance with toilet training should be informed that many children with autism must first resolve behavioral issues before toileting habits can be improved. In some cases, progress after treatment initiation is swift and significant; in others, it occurs slowly, over a period of a year or more.

Working to Improve Outcomes

Addressing GI issues in this population would not be complete without searching for ways to improve diagnosis and treatment for all autistic children. This is why patients with autism at the GI Clinic at Nationwide Children’s Hospital are followed over

Autistic children do not always respond the same way to GI treatments, either behaviorally or medically.

—Kent Williams, MD
The eventual goal is to use this data to identify which patients are most likely to respond to treatment.

— Kent Williams, MD

time to track treatment success rates, the number and characteristics of children who respond to treatments and possible predictive factors. The eventual goal is to use this data to identify which patients are most likely to respond to treatment. In time, this and similar research may provide physicians with a stepwise practice tool to address GI issues in children with autism.

Just collecting information on the prevalence of certain GI problems and the effectiveness of treatments—both behavioral and medical—will help specialists and pediatricians better identify problems and take care of patients with autism in the future. This is especially important because of the high need for responsive, precise treatment of GI issues in this population.

While it will be some time before these efforts yield information to guide patient care, pediatricians can still make significant progress with patients by recognizing that GI issues are very common in children with autism and may contribute to changes in behavior. Following the steps outlined here can go a long way toward improving the lives of children with autism and their caregivers.

RELATED PUBLICATIONS


For more information on this topic, please visit NationwideChildrens.org/pd-gastroenterology-hepatology-nutrition.

ABOUT THE AUTHOR:

Kent Williams, MD, is a pediatric gastroenterologist at Nationwide Children’s Hospital and an assistant professor of clinical pediatrics at The Ohio State University College of Medicine. Dr. Williams’ clinical interests involve all aspects of pediatric gastroenterology, with a special interest in GI disorders in children with autism spectrum disorders. As an investigator in the Research Institute at Nationwide Children’s and OSU, he conducts basic and translational research into the mechanisms that cause functional gastrointestinal disorders, such as abdominal pain, constipation and reflux, in children with autism. In 2012, Dr. Williams became co-chair of the Autism Treatment Network’s gastrointestinal committee, a national work group that is responsible for developing guidelines and recommendations for treatment of GI issues in children with autism spectrum disorders.

What happens when a patient is referred to Nationwide Children’s Hospital?

When a pediatrician cannot find an effective treatment or is uncertain of how to proceed, the GI Clinic and the Bowel Management Clinic, cooperative specialty clinics at Nationwide Children’s, can help. Specialists and staff at these clinics are accustomed to treating coexisting conditions and have experience working with children with autism.

Referrals and Consultations
Online: NationwideChildrens.org
Fax: (614) 722-4000
Phone: (614) 722-6200 or (877) 722-6220

Physician Direct Connect Line for 24-hour urgent physician consultations: (614) 355-0221 or (877) 355-0221

AFTER THE REFERRAL

Patients and their families meet Dr. Kent Williams and his staff in the GI Clinic. Families can expect:

• Questions about behavior, toileting habits and attempted treatments
• Diagnostic testing to determine the true cause of the problem
• Medical treatment, if necessary

AFTER MEDICAL EVALUATION AND TREATMENT

Some patients may benefit from behavioral therapy in the Bowel Management Clinic, which addresses behavioral and cognitive issues surrounding autism and GI problems. Families can expect:

• An initial meeting to set realistic expectations and assess opportunities for intervention
• Evaluation of sensory and anxiety issues to enable treatment success
• Consultation with specialists to build a customized behavioral intervention plan
• Toilet training or reward system programs
Robot-Assisted Laparoscopic Surgery Offers Less-Invasive Treatments

In January, Nationwide Children’s Hospital launched a Robot-Assisted Laparoscopic Surgery program, which utilizes advanced robotics technology to give surgeons greater precision, dexterity and visualization than possible with conventional laparoscopic tools. The da Vinci Surgery System features four arms and wrists—only steadier—and allow surgeons to control a camera and place sutures, reconstruct tissues and perform other tasks that are far more difficult to complete in traditional laparoscopy. With the aid of 3-D technology built into the console, surgeons have a view of the surgical site that is far closer than human vision allows.

Daniel Herz, MD, joined Nationwide Children’s in January to lead the program. When Dr. Herz began performing robot-assisted surgery in 2004, he learned the craft on the first generation of robotic equipment. Today, the technology is more precise, the surgical tools are smaller and more flexible and the high-definition monitors offer far superior visualization than ever before. Since Dr. Herz’s arrival at Nationwide Children’s, he and others on the robotics team have performed nearly 70 procedures, a number he expects to grow as more surgeons are trained to use the system. We met with Dr. Herz to talk about the program and the future of robot-assisted surgery at Nationwide Children’s.

What are the benefits to robot-assisted surgery? Compared to standard laparoscopic procedures, robot-assisted surgery shares the same benefits in minimizing the invasiveness of the operation, which leads to less time under anesthesia and a faster recovery. But the robotic technology dramatically expands the surgeon’s natural abilities. The robotic arms and instruments allow for the same dexterity that once was possible only through open surgery, and the range of motion is far better than the human hand can do on its own. The equipment’s movement is precise and not at the mercy of the natural tremor of human hands. And the 3-D visualization and high-definition monitoring possible with this technology is superior to anything we’ve seen in the laparoscopic surgical field. Overall, the primary benefit of the robot is that it makes each surgeon a ‘top gun’ and allows more surgeons to perform these procedures safely.

What kinds of questions do parents often have about performing robot-assisted surgery on their children? I think many people hear the phrase “robotic surgery” and imagine a machine wielding a scalpel doing surgery on their son or daughter. I like to emphasize the robot-assisted part—the surgery is performed by the surgeon, not the robot. The robot is not autonomous; it doesn’t move unless we direct it to. I try to explain that the robot is just another tool we have at our disposal—granted, a very high-tech tool—but a tool nonetheless. In general, I find that parents are mostly concerned with the fact their child has to have surgery, and once I explain how the system works, they are comfortable with it.

What kind of procedures can be performed with robot-assisted surgery? We use robot-assisted surgery to treat a variety of conditions. Among the most common is urinary reflux, in which urine from the bladder is able to flow back up into the kidney through the ureter. To correct the problem, we perform a ureteroneocystostomy, or ureteral reimplantation, which changes the position of where the ureter attaches to the bladder and prevents this back-up. Another procedure we perform often with the robot is pyeloplasty, a treatment for a congenital defect called ureteropelvic junction obstruction. About one in every 1,500 children has this condition, in which the urinary tract is blocked at the junction where the ureter meets the renal pelvis.

We have had great success using the robotic technology for partial or complete nephrectomy, which removes part or all of a damaged or diseased kidney. We are also able to treat complicated pyeloplasty failures with a procedure called ureterocolicostomy. Once only possible through an open surgery that involved a 10- to 20-centimeter incision, we now perform this operation through robot-assisted laparoscopy that requires three incisions, each only about 5 millimeters long. Bladder neck reconstruction or bladder neck sling, both used to treat incontinence caused by a variety of conditions, also are much easier robotically and are very rarely attempted by traditional laparoscopy any longer.

In addition, our General Surgery team has recently begun to utilize robotic technology, and has performed such procedures as choledoectomy to remove a diseased gallbladder; ileocecectomy to treat appendicitis or Crohn’s disease; j-pouch procedures for ulcerative colitis or colon cancer patients; and bariatric surgeries such as gastric sleeve.

How are surgeons trained to use the robotic equipment? We have developed a rigorous training program that involves completion of computer simulation modules, dry and wet lab training sessions, and a period of proctoring for the first five to 10 surgeries depending on individual surgeon progress. Before any new surgeon’s “first case” or before performing a new type of surgery, a dry run is planned and performed. The

It is my belief that, based on our unrelenting focus on safety of robot-assisted surgery and the rigorous training program surgeons must complete before performing robot-assisted surgery at Nationwide Children’s, our program will serve as an example for other children’s hospitals to follow.

—Daniel B. Herz, MD
Robot-assisted minimally invasive surgery

Minimally invasive 3-D robotics technology enables surgeons to perform operations with just a few small incisions instead of through open surgery, resulting in less pain and a shorter recovery. Approved in 2000 by the Food and Drug Administration, the da Vinci Surgery System was the first to be used for general laparoscopic surgery. Nationwide Children's Hospital is one of nearly 1,400 hospitals in the nation that utilizes the technology.

Surgical applications

Surgeons at Nationwide Children's use the robotic equipment to perform a range of procedures in urology and general surgery, including operations to treat such problems as urinary reflux, birth defects in the urinary tract, kidney disease, Crohn’s disease and appendicitis.

Vision cart

The vision cart is the hub for various parts of the surgical system. The consoles, robotic arms and monitors in the operating room feed into the vision cart, which connects to a central computer system that collects data on instrumentation and surgeons’ movements.

Robot-assisted surgery

A surgeon, entire robotic surgery team, director of robot-assisted surgery, and the robotic surgery and surgical team coordinators are present for all of these events. The purpose of this is to discuss logistics, equipment and specific safety concerns before the morning of the surgery. During this period, emphasis is placed on learning to use visual cues to compensate for the lack of tactile or haptic feedback that the surgeon has in open or pure laparoscopic surgery. Understanding the limitations, power and precision of robotic instruments is also emphasized at this stage.

We have partnered with our anesthesia colleagues to avoid inadvertent movement while the robot is docked and the robotic instruments are engaged within the patient. We have specific protocols to avoid injury from positioning and inadvertent collisions of the robotic arms with the patient’s limbs, face or head.

Three additional surgeons at Nationwide Children’s have completed the robotic training program and are now performing surgeries using this technology. Another two surgeons are currently in training.

The use of this technology is not without controversy.

What can you tell us about concerns regarding the da Vinci system and where things stand?

Earlier this year, the Food and Drug Administration launched an investigation into the safety of the robot. Though the agency won’t release specific numbers, officials say there have been numerous complaints regarding the 11-year-old technology.

The agency is looking into these complaints and in a statement outlined plans to discuss the matter with surgeons.

For more information on this topic, please visit NationwideChildrens.org/pd-robot-assisted-surgery.

Daniel B. Herz, MD, is a member of the Section of Pediatric Urology and director of Robotic-Assisted Laparoscopic Surgery at Nationwide Children’s Hospital. He previously served as Director of Pediatric Urology at Children’s Hospital at Dartmouth, and associate professor of surgery and pediatrics at Dartmouth Medical School. Certified by the American Board of Urology in both urology and pediatric urology, Dr. Herz received his medical degree from SUNY Health Science Center at Brooklyn (Downstate Medical Center) and completed his urological residency at University of Pittsburgh Medical Center. He completed a two-year clinical and research fellowship in pediatric urology at the Hospital for Sick Children, University of Toronto.

It’s important to note that the FDA itself has said that it is uncertain whether the rise in reported adverse events is not simply related to an increased awareness or willingness to report such events among doctors and hospitals. Not to sound too much like a cliché, but those who do robotics are pioneering a new era—one that will see robotics replace not only most if not all laparoscopy, but much of open surgery as well. With this type of challenge there are going to be mishaps and missteps. We keep patient safety at the forefront here at Nationwide Children’s, and do not succumb to market pressures or company advertising or aggressive marketing—that is the cornerstone of our program. It is my belief that, based on our unrelenting focus on safety of robot-assisted surgery and the rigorous training program surgeons must complete before performing robot-assisted surgery at Nationwide Children’s, our program will serve as an example for other children’s hospitals to follow.

RELATED PUBLICATIONS


Monitoring and Modulating Immune Function in Critically Ill Children

Each year, more than 225,000 children in the U.S. are hospitalized following a traumatic injury, according to the Centers for Disease Control and Prevention. As if the damage from the trauma weren’t bad enough, studies have found that in some cases, the body’s immune system shuts down as a result of the injury, leaving patients at higher risk for hospital-acquired infections. When the immune system loss is severe or prolonged, the condition is called immunoparalysis—a potentially life-threatening problem.

What causes the immune system to fail in these cases is a mystery. Dr. Mark Hall, MD, has spent nearly 15 years trying to solve. A critical care specialist and director of the Immune Surveillance Laboratory at Nationwide Children’s Hospital, Dr. Hall is painting a clearer picture of this phenomenon in pediatric patients—work that could redefine how physicians think about and treat immune dysfunction in critically ill patients. We asked Dr. Hall to explain the problem and his research.

What do scientists know about the link between traumatic injury and problems with immune function? Our studies suggest that innate immune function, which is responsible for protecting the body by identifying and killing pathogens, can be impaired following critical injury, which we think is somehow linked to an innate immune cell called a monocyte. Monocytes recognize microbes such as bacteria, engulf and kill them, then display their remains on the cell surface with the aid of a class of receptors that include Human Leukocyte Antigen (HLA)-DR. Immune cells called lymphocytes detect these microbe remnants and activate the adaptive immune system, which allows the body to effectively battle the infection. In addition, activated monocytes should robustly produce the chemical tumor necrosis factor (TNF)-alpha. This pro-inflammatory cytokine, while harmful in excess, is important for making the local environment favorable for fighting infection.

For reasons we don’t yet fully understand, in some trauma patients, monocytes produce much less TNF-alpha than they normally would when stimulated. Similarly, the monocytes can show reduced expression of HLA-DR molecules, which impairs the cell’s ability to activate lymphocytes. This state represents a form of immune suppression that places patients at high risk for new infection and death. Perhaps contrary to what one might think, this state can occur even in the presence of clinical signs and symptoms of hyperinflammation (fever, hemodynamic instability and capillary leak). We think that the monocytes are shutting themselves down in response to an overwhelming inflammatory stimulus and the system is unable to turn itself back on. Just why that happens is something we’re still investigating.

In the past, treatment of critical illness or traumatic injury has included an aggressive anti-inflammatory regimen to treat the kinds of symptoms you described. However, studies increasingly show that this approach isn’t working and can, in fact, further weaken immune function in some patients. Why does this happen?

Inflammation is a natural part of the body’s immune response to trauma and disease, but in many critically ill patients, the inflammatory response can rage out of control, causing organ failure. In the 1980s and 1990s, multiple therapies aimed at reducing inflammation reached phase III clinical trials in adults with severe sepsis and septic shock. Nearly all of these studies failed to demonstrate a survival benefit, suggesting that perhaps reducing inflammation is not the appropriate therapeutic goal in all cases.

We think it’s possible that an overactive inflammatory response may actually trigger a compensatory overactive anti-inflammatory response, or immunoparalysis. Since anti-inflammatory drugs also inhibit immune function, these medications may prevent the body from re-starting its immune system, perpetuating the state of immunoparalysis. Unfortunately, current clinical practice for critically ill patients does not include measurement of immune function. We believe in these cases, it is essential to find out whether the patient’s immune system is functioning properly. If it is, anti-inflammatories may be able to do their job without causing further harm. But if the immune system isn’t working, anti-inflammatory therapies may not be the best course of action.

How can you measure immune function?

One of the major missions of our laboratory over the past decade has been the development and testing of protocols that allow for rapid, reliable measures of immune function in critically ill children. With the support of the National Institutes of Health and the Research Institute at Nationwide Children’s Hospital, we have evaluated TNF-alpha production capacity and other tests of immune function in hundreds of critically ill children across a broad range of diagnoses. We have also tested healthy children so that we can identify normal values for these assays. The result of this work is that we have been able to identify thresholds of immune function below which patients are at high risk for the development of new infection and death.

Among the most exciting parts of our immune monitoring program is the fact that we can provide same-day results, with our immune function testing taking about six hours to complete. In addition, these tests require only a very small amount of blood, so they are suitable for our smallest patients. The program has gained national and international attention, and we now provide test kits to researchers around the world for the study of immunoparalysis in a variety of patient conditions. Their work, along with studies in our lab, is answering a lot of questions about immunoparalysis, but there is still a lot we don’t know.

Is immunoparalysis reversible?

We believe it is, and to test that theory, we are conducting a phase IV clinical trial of a drug called GMS-CSF, which was approved by the Food and Drug Administration in 1991 to stimulate white blood cell growth in bone marrow transplant patients. A number of small studies, mostly in adults, suggest the drug can reverse immunosuppression in critical illness, but ours is the first to study its use in pediatric trauma patients. In partnership with the Surgical Intensive Care Unit at The Ohio State University Wexner Medical Center, we plan to enroll more than 100 patients age 1 to 21 who are admitted to the ICU following a traumatic injury. We will measure immune function in these patients in the days following their injury. If a patient’s TNF-alpha production capacity drops below a certain level, they will receive GMS-CSF. The first step is to figure out what dose will effectively reverse critical injury-induced immune suppression. The next step will be to conduct a blinded, randomized, placebo-controlled clinical trial to see if improving immune function results in decreased risk for the development of new infection. If that trial is successful, it could move immune monitoring and modulation out of the research realm and closer to routine bedside care.

We have also tested healthy children so that we can identify normal values for these assays. The result of this work is that we have been able to identify thresholds of immune function below which patients are at high risk for the development of new infection and death. Among the most exciting parts of our immune monitoring program is the fact that we can provide same-day results, with our immune function testing taking about six hours to complete. In addition, these tests require only a very small amount of blood, so they are suitable for our smallest patients. The program has gained national and international attention, and we now provide test kits to researchers around the world for the study of immunoparalysis in a variety of patient conditions. Their work, along with studies in our lab, is answering a lot of questions about immunoparalysis, but there is still a lot we don’t know.

Is immunoparalysis reversible?

We believe it is, and to test that theory, we are conducting a phase IV clinical trial of a drug called GMS-CSF, which was approved by the Food and Drug Administration in 1991 to stimulate white blood cell growth in bone marrow transplant patients. A number of small studies, mostly in adults, suggest the drug can reverse immunosuppression in critical illness, but ours is the first to study its use in pediatric trauma patients. In partnership with the Surgical Intensive Care Unit at The Ohio State University Wexner Medical Center, we plan to enroll more than 100 patients age 1 to 21 who are admitted to the ICU following a traumatic injury. We will measure immune function in these patients in the days following their injury. If a patient’s TNF-alpha production capacity drops below a certain level, they will receive GMS-CSF. The first step is to figure out what dose will effectively reverse critical injury-induced immune suppression. The next step will be to conduct a blinded, randomized, placebo-controlled clinical trial to see if improving immune function results in decreased risk for the development of new infection. If that trial is successful, it could move immune monitoring and modulation out of the research realm and closer to routine bedside care.

Studies of immunoparalysis from our lab and others have offered vital insight into immune function in the critically ill patient and the importance of considering immunotherapy alongside other therapies to prevent and treat secondary infection.

— Mark W. Hall, MD
Immune function

**INNATE IMMUNE SYSTEM**

The innate immune system is the body’s first line of defense, comprising the cells and molecules that recognize and respond to bacteria, viruses and other pathogens.

- **Phagocytes such as monocytes** engulf the pathogens and kills them.

- **Monocytes** mature into macrophages when foreign pathogens enter the body, the immune system recruits them.

- The macrophage engulfs the pathogens and breaks them into pieces inside the cell.

- The remains are displayed on the cell’s surface with the aid of a class of receptors that include Human Leukocyte Antigen (HLA)-DR. A pro-inflammatory cytokine is secreted to help stimulate the immune system to fight the infection.

**ADAPTIVE IMMUNE SYSTEM**

Unlike the innate immune system, the adaptive system always requires the detection of a specific antigen, to which they recognize and respond.

- The cells of the adaptive immune system are called lymphocytes. The two primary types, B cells and T cells, carry receptor molecules that recognize specific targets.

- Activated B cells secrete antibody molecules that bind to antigens and destroy the invader or mark it for attack by other cells.

- Activated T cells recognize their targets by binding to antigen present on the surface. Individual T cells are able to recognize only certain antigens that match their type of receptor.

- Cytotoxic T cells destroy infected cells by releasing cytotoxic proteins and cytokines. Perforin makes a hole in the membrane of the infected cell. The cytokines enter the cell through this hole and destroy the cell and the pathogen inside.

When you began this work nearly 15 years ago, you were among the first to suggest that immunoparalysis in critically ill children was a problem. What’s different today?

Some things have changed, but some have stayed the same. In 2000, I gave my first national talk on the idea that immunoparalysis is associated with adverse outcomes in critically ill kids. It was a new idea then. Just this past January, I was asked to be part of a multi-expert panel at a Society of Critical Care Medicine Congress on immune monitoring and modulation in critical illness—which the organizers still considered a relatively new concept. The focus on anti-inflammatory therapies to reduce the pro-inflammatory response in critical illness has been quite persistent. The viewpoint that the anti-inflammatory response can be harmful is still gaining momentum.

That said, we have made progress. Studies of immunoparalysis from our lab and others have offered vital insight into immune function in patients with influenza and respiratory syncytial virus. We also plan to expand our ongoing project, and we have other studies under way to explore immunoparalysis and mortality in critically ill children with influenza—a multicenter study. Critical Care Medicine. 2013 Jan, 41(1):224-36. PMID: 23222596.

**RELATED PUBLICATIONS**


For more information, visit NationwideChildrens.org/pd-mark-hall.
Researchers at Nationwide Children’s Hospital will use a $6.3 million grant to further their study of pediatric sarcomas, a rare form of disease that affects bone or soft tissue and accounts for 11 percent of all childhood cancers. The project is funded by the National Institutes of Health and the National Cancer Institute.

“The ultimate goal of this project is to develop novel therapeutic approaches for advanced childhood sarcoma,” says Peter Houghton, PhD, lead researcher on the grant and director of the Center for Childhood Cancer and Blood Diseases in The Research Institute at Nationwide Children’s.

While more than 70 percent of children with sarcoma are cured, the outcome is still poor for those with advanced or metastatic disease. Specifically, the five-year, event-free survival rates are 30 percent or less in children with advanced or metastatic Ewing sarcoma, osteosarcoma or rhabdomyosarcoma. Intensive chemo-radiotherapy has not significantly altered this outcome, making the search for effective new therapies a critical pursuit.

Each of the three sarcomas targeted by this grant has distinct characteristics requiring in-depth analysis of disease pathways and treatment opportunities. "The projects will characterize the interrelationship of these pathways and identify combinatorial inhibitory approaches most likely to yield biologic activity in the clinical setting," says Dr. Houghton, who has spent nearly three decades studying pediatric cancer to bring knowledge from the laboratory to the bedside.

The grant comes on the heels of a series of publications by Dr. Houghton and colleagues that examines the molecular and genetic underpinnings of sarcomas. One such study, published in June in Cancer Research, explored the connection between DNA repair pathways and the potency of radiation therapy.

When cancer cells are bombarded by radiation, many die. However, some are able to withstand the assault and repair DNA damage. An early step in the DNA repair pathway is activation of a checkpoint that halts the cell cycle and allows cells to repair damage before they divide.

The recent study found that one important protein in this repair pathway, FANC D2, was regulated by a signaling process called TORC1. Inhibition of TORC1 led to a rapid loss of FANC D2 in cultured cells and in cancers in mice. Without FANC D2, anticancer treatments, such as focused beam radiation therapy, were dramatically enhanced because cells could no longer repair the DNA.

Although further studies are necessary, Dr. Houghton says that these data suggest that drugs that inhibit TORC1 signaling may improve the effectiveness of radiation therapy in clinical practice. "Enhancing radiation therapy could increase cure rates for childhood cancers, or allow lower curative doses of radiation that would spare normal tissues and reduce the long-term side effects of therapy," says Dr. Houghton.

Experts in sarcoma biology, cellular signaling pathways and drug development from Nationwide Children’s and The Ohio State University will collaborate on the grant to find answers to the questions raised by this study and related pediatric sarcoma research.

In this image of rhabdomyosarcoma cells from Dr. Houghton’s research laboratory, red staining identifies the insulin receptor and green staining highlights the location of cells insulin-like growth factor-1 (IGF-1) receptors.
New Technology Could Improve Diagnosis and Prognosis of Brain Injuries in Infants

In preterm infants, brain injury and abnormal brain development are leading predictors of cerebral palsy, cognitive impairments, and attention and behavioral disorders. However, current ultrasound and standard MRI diagnostic methods used in most children’s hospitals are subjective and lack the ability to sensitively identify premature babies at risk of disability or delay.

To address the problem, Nehal Parikh, DO, MS, a principal investigator in the Center for Perinatal Research in the Research Institute, and his colleagues are developing advanced automated imaging methods to create a more accurate picture of neonatal brain development and brain injury.

Although many hospitals have the capacity to perform advanced MRIs, only a handful of them use the machines and customized imaging programs to study neonatal brain development and injury. According to Dr. Parikh, this can lead to missed diagnoses.

“In about 20 to 40 percent of babies with developmental problems, we can’t see anything on the conventional, structural images,” Dr. Parikh says. “They primarily pick up the more severe findings, such as hemorrhages and cystic lesions, whereas advanced MRI can give us information about those things as well as delayed development, more diffuse but subtle non-cystic injury and other types of newer abnormalities that we’re still learning about.”

With his advanced imaging programs, Dr. Parikh is able to objectively visualize subtle structure, volume, metabolite and diffusion abnormalities in the brain that, in preliminary studies, are directly correlated to developmental delays common in premature infants. If further research confirms the connection, regular use of advanced MRIs for brain injury detection in this population could help clinicians identify babies in need of targeted, aggressive interventions that could minimize future developmental delays.

In a recent series of publications, Dr. Parikh and his team evaluated the application of their imaging technology in clinical pilot studies and larger correlational investigations. Studying brain structure, development and the progression of injuries may offer information about the causes of such injuries—allowing physicians the opportunity to try to prevent them in the first place. Dr. Parikh hopes to develop standardized diagnostic and prognostic tests and tools that would enable doctors to incorporate advanced MRI technologies into premie care across the country.

“I was fortunate to recognize very early in my training that we’re doing a great job of keeping these babies alive,” Dr. Parikh says, “but if we can figure out why these injuries are happening and in whom they’re happening, we can intervene early, and perhaps we can reduce the morbidity and improve the quality of life of these babies as well as their families.”

Brain imaging from Dr. Parikh’s research laboratory’s advanced MRI work displays automated segmentation of voxel-wise matter signal abnormalities. Novel image analysis programs allow the team to detect subtle brain injuries previously unobserved by clinicians.

Injury Study Leads to New Child-Resistant Spray Bottle Design

Three years ago, Lara McKenzie, PhD, led a study of how many children are injured or poisoned by household cleaners each year. The numbers were astonishing. During just one year of the study, nearly 12,000 kids age 6 and younger in the U.S. were hurt when they came in contact with or ingested a cleaning product. About 40 percent of the injuries involved cleaners packaged in spray bottles. Drawn to the brightly colored levers, a child grabs the bottle, turns it toward him so he can easily press the lever with his thumbs—and sprays himself in the face.

It was one of many studies Dr. McKenzie has done in her position as a principal investigator in the Center for Injury Research and Policy in The Research Institute at Nationwide Children’s Hospital. But this time, something was different. This, Dr. McKenzie and her team thought, was an injury they could prevent.

“We immediately began to think about what we could change about the spray bottle that would make it not work for a child, but work normally for adults and automatically go back to a locked position after it’s used,” Dr. McKenzie recalls.

Working with faculty in the design and mechanical engineering departments at The Ohio State University, Dr. McKenzie and team members senior research associate Kristin Roberts and research associate Nick Nelson developed a crude mock-up of a spray bottle that requires an adult-size hand to operate and automatically locks after it is sprayed. The first model was a normal spray bottle retrofitted with a lever in front and one in back, both made of cardboard and duct tape. For the sprayer to work, both levers had to be pressed at the same time, a motion that requires dexterity, strength and long fingers—three things children don’t have.

When the mock-up was filled with water and given it to several children to try, none could get the sprayer to work. The next step was to build an actual prototype, which has a two-stage trigger mechanism and an automatic lock. Preliminary testing of the device found that children were unable to press both levers to make the spray bottle work. The nozzle is the same size as on regular spray bottles and would cost only pennies more to produce, Dr. McKenzie says. Parents are pending on the design, and Nationwide Children’s is working to license the technology and bring it to market.

“In our field, we try to help parents use existing countermeasures for safety, and I have first-hand experience of how difficult it can be to do all the things we recommend parents do to keep their children safe,” says Dr. McKenzie, the mother of 2-year-old triplets. “This is the first time I’ve been able to take data I’ve collected for a study and use it to create a technology to prevent those injuries. It feels great to be able to do that.”

This prototype of a new child-resistant spray bottle features a two-stage trigger mechanism and automatic lock.
Children with Anxiety Disorders More Likely to Have Painful Stomach Problems

Children with anxiety or depression are more likely to suffer from painful stomach problems and migraine-like headaches, according to a new study by researchers at Nationwide Children’s Hospital. The findings could help clinicians develop treatment plans that better address both the psychological and physical ailments of their patients.

Some studies suggest that as many as 60 percent of school-age children experience recurrent abdominal pain symptoms at least once a week, a striking figure that caught the eye of Desale yacob, MD, an attending pediatric neuro-gastroenterologist in the Division of Gastroenterology, Hepatology and Nutrition at Nationwide Children’s and lead author of the new research.

Predominant functional gastrointestinal disorders—FGID for short—are defined as persistent and recurring in the GI tract. They are not caused by tumors or biochemical abnormalities, making them harder to detect with CT scans, ultrasounds, blood-work or other conventional tests. Of the more than 20 different disorders in this group, the most common are irritable bowel syndrome, characterized by recurrent abdominal pain associated with either diarrhea or constipation, and functional dyspepsia, which is marked by abdominal pain and symptoms of nausea, vomiting or early satiety.

Researchers elsewhere had identified a possible link between FGIDs and such emotional disorders as anxiety and depression. To investigate this further, Dr. Yacob’s team conducted psychological screenings of 67 children age 6 to 18.

Nearly half of those patients were found to suffer from anxiety or depression. Of that group, 52 percent were found to have abdominal pain of the FGID variety, while 57 percent had experienced a migraine-like headache at least once in the past month. These findings were significantly higher when compared to the children who screened negative for depression and anxiety. The study, which was published in a recent issue of The Journal of Pediatrics, points to the need for a comprehensive treatment plan for children with this combined diagnosis, Dr. Yacob suggests.

“Our approach to patients with FGID is always multifaceted, and cognitive and behavioral therapies are key components of the plan,” says Dr. Yacob, who also is an assistant professor of clinical pediatrics in The Ohio State University College of Medicine. “They become even more important when the child has a history of depression and anxiety.”

The new research will build on findings from a small study conducted at Nationwide Children’s Hospital. The likely culprit: easy access to prescription and over-the-counter drugs found in the home.

The study, published in May in Pediatric Emergency Care, examined accidental poisonings in young children from medication, household cleaners and other toxins in Ohio, Kentucky, Louisiana, North Carolina and Texas. The total number of poisonings from all substances rose by 12 percent, largely due to increased in-home pharmaceutical ingestion, says Henry Spiller, MS, FAACt, lead author of the study and director of the center. In addition, the effects of pharmaceutical poisonings were more likely to cause serious medical problems than those of other toxins.

While there was a 10 percent increase in the number of serious medical outcomes related to non-medication poisonings in children, there was a 98 percent increase in serious health outcomes, such as seizures or death, related to medications.

“I suspect the increase of pharmaceutical-related poisonings is due to the increase of medications like dietary supplements, antipsychotics, cardiovascular drugs and other medications in the home,” Spiller says. The number of poisonings due to dietary supplements and herbs increased by 274 percent during the study period. Exposures to electrolytes and minerals, vitamins, anesthetics, antihistamines and topical medications also represented a substantial portion of the increase in medication-related poisonings. “Parents may forget that supplements and nonprescription pills can be just as dangerous as prescription pills, especially if their child ingests many of them.”

Cough and cold medication was the only pharmaceutical category that saw a decline in cases over the study period, although these over-the-counter medications still resulted in 17.6 percent of all fatal poisonings—matched only by opiate or narcotic analgesics.

“Childhood poisoning remains common, increasingly involves medications in the home and is causing more hospitalizations,” Spiller says, adding that he is optimistic about the ability to prevent childhood poisoning, particularly when it involves family medications. “We hope that education is the key. Pediatricians should remind parents that child-resistant bottles are not child-proof and to keep medications locked up and out of site, where children cannot access them.”

Physicians can obtain free poison education materials to distribute to families by calling the American Association of Poison Control Centers at 1-800-222-1222.

Study to Examine Antibiotic-Only Appendicitis Treatment

A new study at Nationwide Children’s Hospital on the effectiveness of using antibiotics alone to treat early appendicitis in children could allow patients to avoid a surgery many may not need. The $1.6 million project also will explore the impact that involving children and their parents in medical decision-making may have on a child’s response to treatment.

Appendicitis, caused by a bacterial infection in the appendix, affects more than 80,000 children to the operating room each year. In as many as half of those cases, the condition may have been treatable with antibiotics alone, according to Katherine J. Deans, MD, MHSc, and Peter C. Minneci, MD, MHSc, co-directors of the Center for Surgical Outcomes Research at Nationwide Children’s and leaders of this new study, which is funded by the nonprofit Patient-Centered Outcomes Research Institute.

“The idea that surgery is the only treatment for appendicitis goes back to 50 or 60 years ago when high-resolution imaging studies were unavailable for early diagnosis and antibiotics were less effective in treating intra-abdominal infections,” Dr. Deans says. That’s not the case today, thanks to access to ultrasound and CT scans and a wide range of antibiotics, allowing physicians to more accurately diagnose and treat appendicitis early.

The new research will build on findings from a small pilot study launched last year by the pair, who also are principal investigators in The Research Institute at Nationwide Children’s and assistant professors of surgery and pediatrics at The Ohio State University College of Medicine. Preliminary data suggest that, when caught early, appendicitis can be treated with antibiotics, making surgery unnecessary. The results are similar to those from a series of European studies performed in adults.

Participants will be recruited through the emergency room and randomly assigned to one of two groups. Both will discuss appendicitis and treatment options with a physician, but one group will also receive an iPad equipped with an interactive educational app offering information about appendicitis and the different treatment options.

Participants will then opt for surgery or a course of IV antibiotics alone. Patients in the latter group will be admitted to the hospital for at least 24 to 48 hours. If their condition doesn’t improve, they will have surgery. Participants will be followed until age 18 to ensure that appendicitis does not recur in the group that chose antibiotic therapy.
As a medical student, my education on intimate partner violence (IPV) was limited to resources available in the community (which were few) and reasons why physicians don’t talk to their patients about IPV (which were many). As a resident, IPV was presented almost exclusively as an adult issue that affected grown women. During a rotation at our community shelter to learn more about the “adult issues” of IPV, however, I remember my first day turning the corner and being greeted by a child running full speed with an arm full of books. Naive as it was, my first thought was: What is a child doing in a shelter for victims of IPV? They never taught us that victims have children.

But they do, of course…15 million children by recent estimates. Rates of IPV, in fact, are disproportionately higher in homes with young children. Once rarely ever mentioned as a consequence of IPV, the effects of childhood exposure to IPV (and other toxic stressors) are now a foremost area of medical and behavioral health research. We now know that the infant brain exposed to IPV develops with a different architecture than the infant not exposed to violence. This abnormal brain development is the nidus for a cascade of cognitive and developmental problems that can ultimately lead to early mortality, with a host of social, medical and behavioral health consequences in-between.

It is important to acknowledge with colleagues that IPV is not an inherently easy subject to discuss. As pediatricians, however, we discuss the most sensitive of subjects with our patients and their families, from delivering a diagnosis of cancer in a child to obtaining the most personal of sexual histories from teenagers. Why should the issue of IPV be any more difficult? I think it is equally important to recognize that screening is not a one-time discrete event, but rather an ongoing conversation between the pediatrician and the caregiver. “Caregivers lie to me,” I’m often told. Perhaps, but by initiating a discussion on IPV, you have told the caregiver that your office is a safe place to discuss the topic if and when she is comfortable doing so.

Remember—with our relatively frequent contacts in the context of well-child and sick visits, we are in a unique position of having ongoing discussions with the caregiver.

The American Academy of Pediatrics advises pediatricians that “the abuse of women is a pediatric issue.” If we know that IPV is frighteningly common and we know that the adverse effects on the child are innumerable and undeniable, I argue that it is no longer acceptable for pediatricians to simply ignore the issue. When discussing IPV screening by pediatricians, it is time for the conversation to shift from, Why don’t I ask? to How could I not?

Jonathan D. Thackeray, MD, is clinical director of the Center for Family Safety and Healing at Nationwide Children’s Hospital and assistant professor of clinical pediatrics at The Ohio State University College of Medicine. This essay was originally published in the May 2013 issue of Contemporary Pediatrics and is reprinted with permission.

2013 Pediatric Update: Pediatric Specialty Focused on Primary Care Regional Conference
September 14, 2013
Our Lady of Bellefonte Hospital, Ashland, KY

Global Conference on Child Injury Prevention
September 19-20, 2013
Hilton Easton, Columbus, OH

31st Annual Pediatric Infectious Diseases Pearls Conference and 5th Annual Allergy, Immunology Dermatology Pearls Conference
September 26, 2013, 8 a.m. – 4:30 p.m.
Nationwide Children’s Hospital, Stecker Auditorium, Columbus, OH

Tri-State Craniofacial Conference
October 4, 2013
Nationwide Children’s Hospital, The Ohio State University, Columbus, OH

Sports Medicine and Orthopedics Conference
November 22, 2013
Nationwide Children’s Hospital, Stecker Auditorium, Columbus, OH

For more information or to register for these or other courses and conferences, please visit NationwideChildrens.org/Courses-Conferences
Nationwide Children's Hospital has again been ranked in all 10 specialties in *U.S. News & World Report's* 2013-14 Best Children's Hospitals rankings. This is the eighth consecutive year Nationwide Children's has been ranked in all 10 specialties, including four specialties ranked in the top 10. Nine out of 10 specialties at Nationwide Children's were ranked in the top 15.

The rankings feature the top 50 hospitals in each of 10 pediatric specialties. Best Children's Hospitals annual release also provides unparalleled quality-related information, including survival rates, adequacy of nurse staffing, procedure volume and much more. This year, *U.S. News* surveyed 110 pediatric centers to obtain such data as availability of key resources and ability to prevent complications and infections. The hospital survey made up 75 percent of the rankings. A separate reputational survey in which 1,500 pediatric specialists — 150 in each specialty — were asked where they would send the sickest children in their specialty made up the remaining 25 percent.

“While rankings are certainly not the reason for our work, they are an external validation of our staff’s commitment to delivering outstanding care and quality,” says Steve Allen, MD, chief executive officer of Nationwide Children’s. “These results are another way that we demonstrate our belief that everything matters.”