NewYork-Presbyterian
The University Hospital of Columbia and Cornell

Advances in Pediatric Urology

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SPECIAL EDITION

Increasing Use of Robotics in Pediatric Minimally Invasive Urologic Surgery Improves Care and Outcomes

Physicians at NewYork-Presbyterian Hospital are leaders in the treatment of pediatric urologic disorders. Using minimally invasive, microsurgical, and robotic-assisted surgical approaches, as well as innovative therapeutic regimens, the pediatric urologists at both NewYork-Presbyterian pediatric centers—the Phyllis and David Komansky Center for Children's Health, with faculty from Weill Cornell Medical College; and Morgan Stanley Children's Hospital, with faculty from Columbia University College of Physicians and Surgeons—have amassed extensive experience in treating these often-challenging conditions. Under the direction of Pasquale Casale, MD, at Morgan Stanley Children's Hospital, and Dix P. Poppas, MD, at the Komansky Center for Children's Health, the pediatric urologists are dedicated to advancing the state of the art through considerable clinical and basic science research.

The Komansky Center for Children's Health is recognized worldwide as a leader in the treatment of children with congenital adrenal hyperplasia and has been at the forefront of cutting-edge innovations, such as new drug therapies and surgical approaches, for the treatment of this challenging condition. The multidisciplinary team includes pediatric endocrinologists, urologic surgeons, and other specialists. Dr. Poppas leads the surgical team and, through his focused efforts, has further refined techniques, such as the nerve-sparing clitoroplasty, as well as strategies for the optimization of perioperative stress steroid dosing during urologic procedures.

Recently, the Institute for Pediatric Urology at the Komansky Center for Children's Health received a Center of Excellence designation from the Congenital Adrenal Hyperplasia Research Education & Support Foundation in recognition of its pioneering work in genital reconstruction surgery and hormone replacement therapy, among other approaches. This is the first such center in the United States and establishes a model for other centers to emulate and develop around the country. However, the Hospital's work with congenital adrenal hyperplasia is only part of its extensive efforts at raising the standard of care in pediatric urology across the board.

"We have a long history of being early adopters of new technology," noted Dr. Poppas, who is Chief of Pediatric Urology, Komansky Center for Children's Health, and Vice Chairman of the Department of Urology and Richard Rodgers Family Professor of Pediatric Urology in the James Buchanan Brady Department of Urology at Weill Cornell Medical College. "Here at NewYork-Presbyterian/Weill Cornell, in 1998, we were the first center in New York to perform a laparoscopic nephrectomy and, in 2000, we became the first center in the city to perform a pediatric robotic pyeloplasty. And both campuses, Weill Cornell and Columbia, are strong in robotics."

Innovators in Treatment

According to Dr. Poppas, the Institute for Pediatric Urology has become a leader in the treatment of genital abnormalities (including hypospadias, epispadias, and posterior urethral valves), disorders of sexual development, neurogenic bladder, ureteropelvic junction obstruction, stone disease, vesicoureteral reflux, voiding dysfunction, and other urologic conditions and disorders, thanks to its role in the development of minimally invasive surgical

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Genetics Research Across Medical Specialties Now Yielding Secrets and Improving the Practice of Medicine

The decoding of the human genome and subsequent concerted efforts by physician-scientists to decipher the relationships between specific genes and the diseases they influence have already yielded tremendous advancements in medicine. This work is fostering important strides in understanding and caring for people with diseases affecting all health systems, and much of the laboratory and translational studies, as well as clinical research, are being done at Columbia University College of Physicians and Surgeons, Weill Cornell Medical College, and NewYork-Presbyterian Hospital.

Research abounds in every field. Nephrologists and psychiatrists were interested in the results of a large multinational study in which Columbia University played an important role.[1] The study, led by Ali Gharavi, MD, Associate Director of the Division of Nephrology at NewYork-Presbyterian/Columbia, is the first to link congenital kidney disease, which together with urinary tract defects accounts for about one-fourth of all birth defects in the United States, with neurodevelopmental disorders. The study found that 10% of children born with kidney defects have genomic alterations that have been linked with neurodevelopmental delay and mental illness. The finding is important because it paves the way for identifying subgroups of patients with kidney defects whose treatment will be guided by specific genetic information. The finding also alerts physicians who care for children with congenital kidney disorders that there may be a genetic basis for a neurodevelopmental delay or a mental illness that will occur later in life.

A co-author of this study was Wendy Chung, MD, PhD, Director of Clinical Genetics at NewYork-Presbyterian Morgan Stanley Children's Hospital. Her research interests span multiple areas, including the molecular genetics of obesity and diabetes; congenital heart disease; congenital diaphragmatic hernias; mental retardation; inherited metabolic conditions; and susceptibility to breast and pancreatic cancers. She is Director of the Pediatric Heart Network Genetic Core, the Pediatric Neuromuscular Network Molecular Core, the New York Obesity Center Molecular Genetics Core, and the Diabetes and Endocrine Research Center Molecular Genetics Core.

Perhaps no area of medicine has been as affected by research into the genetic foundations of disease as much as oncology. Researchers, led by Antonio Iavarone, MD, Professor of Pathology and Neurology at Columbia's Institute for Cancer Genetics at the Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian/Columbia, conducted genetic analyses of patients with glioblastomas, searching for evidence of gene fusions.[2] They found them, with the most common being fusions involving the fibroblast growth factor receptor (*FGFR1* or *FGFR3*) and transforming acidic coiled-coil (*TACC1* or *TACC3*) genes. The protein produced by the fusion of *FGFR-TACC* disrupts the mitotic spindle, causing aneuploidy, and from there tumorigenesis. The finding is important because it provides researchers with a protein target for pharmaceutical research for a cancer that is especially difficult to treat.

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Gastroenterologists have been interested in recent work performed by Manish Shah, MD, Director of Gastrointestinal Oncology at Weill Cornell Medical College, who with his colleagues elucidated the heterogeneity of gastric cancer, dividing it into 3 types.[3] The first type, noncardia gastric cancer, is linked to environmental factors such as high dietary salt and tobacco use; clinical factors such as *Helicobacter pylori* infection and use of nonsteroidal anti-inflammatory drugs; and genetic factors including immune regulatory single-nucleotide polymorphisms. A second type, diffuse gastric cancer, is associated with *CDH1* mutation and family history and has no known environmental or clinical factors. The third type, proximal gastric cancer, is caused by tobacco and alcohol use; has no known genetic link; and is associated with obesity, high body mass index, and gastroesophageal reflux disease. Dr. Shah's work has alerted those performing drug clinical trials that testing should be based on these subtypes and not on gastric cancer as a whole. Because of the genetic differences in subtypes, the effects of drug therapy may vary significantly between groups.

The field of clinical genetics is rapidly changing and improving the practice of medicine. As the field of genetics continues to grow so too the physician-scientists at Columbia University College of Physicians and Surgeons, Weill Cornell Medical College, and NewYork-Presbyterian Hospital will continue to be at the forefront of integrating genetics into all specialties.

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approaches to these disorders. For example, surgeons at the Institute for Pediatric Urology are in the process of publishing the results of a study assessing the use of a subinguinal technique for hernia repair; the approach has a lower complication rate than standard inguinal approaches and is more effective.

Dr. Poppas and his team are also leaders in the use of the extravesical surgical correction of vesicoureteral reflux. This minimally invasive approach is performed entirely outside of the patient's bladder to correct reflux in patients with single- and double-collecting systems and is routinely performed bilaterally without postoperative voiding dysfunction. Its use leads to fewer postoperative complications, such as hematuria and bladder spasms. The surgery takes less than 30 minutes per side and all patients are discharged on the day of surgery. To date, Dr. Poppas said, the procedure has a 98% success rate.

Finally, the team has been active in the refinement of a microsurgical approach to the treatment of adolescent varicoceles. Although the procedure has been used extensively in adult patients for more than 2 decades, the Institute was the first to make the approach the standard of care in children. To date, the surgery, which is performed through a 1.2-cm incision, has a complication rate of less than 1%.

The Institute also has a state-of-the-art pediatric voiding dysfunction center, the Linda and Carl Seaman Pediatric Urodynamics Unit, operated under the leadership of Carlos Medina, MD, who is also Assistant Professor of Urology at Weill Cornell Medical College. The Unit specializes in the management of complex neuropathic voiding dysfunction caused by cerebral palsy, myelodysplasia, and other neurologic and/or spinal cord disorders as well as radiation therapy for cancer. Dr. Medina also heads the Institute's Pediatric Stone Unit, which uses a number of innovative technologies, including percutaneous nephrolithotomy, a minimally invasive technique designed to remove kidney stones too large for more traditional procedures such as ureteroscopy.

Additionally, the Institute has established a dedicated laboratory for basic research in pediatric urology, under the leadership of Diane Felsen, PhD. At present, Dr. Felsen and her team are working on developing a synthetic nonbiodegradable hydrogel bladder augmentation patch for use in children with poorly compliant, high-pressure bladders who fail other forms of medical management. They have already developed a prototype for the patch and hope to begin studies of its safety and efficacy in animal models in the coming year.

"This could be a new option for patients at high risk for chronic kidney failure because the pressure in their bladder will ultimately be transmitted to their kidneys," Dr. Poppas said. "The current approach for these patients is ileal augmentation cystoplasty, which is an open, abdominal procedure. Patients who undergo this procedure are at high risk for infections, bladder stones, and other metabolic disturbances. This synthetic patch would eliminate these adverse outcomes and allow the augmentation procedure to be done extraperitoneally, with fewer complications."

Mastering Robotic-Assisted Surgery

Urologists at Morgan Stanley Children's Hospital have contributed significantly to the study of the use of robotics in pediatric urologic surgery, and continue to develop new surgical approaches using robotic technology. In general, the application of camera-guided robotic technology to the field of pediatric urology enables surgeons to perform complex procedures with smaller incisions, which result in minimal scarring. Smaller incisions also lessen the inflammatory response throughout the body, which can lead to better healing. Together with his team, Dr. Casale, Chief of Pediatric Urology at Morgan Stanley Children's Hospital and Professor of Urology at Columbia University College of Physicians and Surgeons, established a Pediatric Robotic Surgery Center, which has "an expertise that is world renowned and unparalleled both nationally and internationally." The Pediatric Urology team also has established a Stone Center with the collaborative efforts of Nephrology and Radiology.

Dr. Casale—a world leader in and pioneer of minimally invasive surgery in children—and his team have developed and mastered many minimally invasive techniques. Their expertise in endourology, laparoscopy, robotics, and stone disease has opened new horizons for complex pediatric urologic disorders. Dr. Casale's current work has included a study of the use of robotic-assisted laparoscopic bladder diverticulectomy in children with symptomatic congenital bladder diverticula, which was published in September in the *Journal of Endourology*. For the study, Dr. Casale and his team performed robot-assisted surgery on 14 children, including 6 who also had a history of diurnal enuresis, using a transperitoneal approach. The mean operative time (including cystoscopy) was 132.7 minutes and the average hospital length of stay was 24.4 hours. None of the patients had intraoperative or postoperative complications and all patients had normal results on voiding cystourethrography on follow-up, with no evidence of a diverticulum. Additionally, all 6 of the patients with diurnal enuresis experienced a resolution of symptoms within 3 months following surgery.[1]

Dr. Casale and his team also have worked extensively with extravesical robotic-assisted laparoscopic ureteral reimplantation to determine whether postoperative voiding dysfunction can be avoided with pelvic plexus visualization and to assess the efficacy of this approach for the treatment of vesicoureteral reflux (VUR). In a study, published in the journal *Urology* last spring, the researchers followed 150 patients who underwent bilateral extravesical robotic-assisted laparoscopic ureteral reimplantation using the da Vinci Surgical System. All 150 patients had primary VUR of at least grade 3 bilaterally, with 127 having parenchymal defects found on renal scans. The operative success rate was 99.3% for VUR resolution on voiding

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cystourethrography. Overall, the study found that the bilateral nerve-sparing robotic-assisted extravesical reimplantation approach demonstrates the same success rate as the traditional open approaches, with minimal morbidity and no voiding complications.[2]

"This success rate coupled with no voiding complications has never been achieved in any other technique," Dr. Casale said. "The team believes that identification of the nerves during the procedure is made possible with robotics, and is paramount in avoiding the debilitating complication of urinary retention."

Dr. Casale and his team also specialize in pediatric genitourinary reconstructive surgery and stone disease. While researching kidney stone disease in children, Dr. Casale found that some children's kidneys behave differently from each other. For example, the right kidney will have elevated levels of calcium, whereas the left kidney remains normal. This finding is changing the treatment of kidney stone disease because it has always been hypothesized that both kidneys behave the same way. Not only has this enabled the use of laparoscopic and/or endoscopic surgical approaches that focus only on the affected kidney, but nonsurgical therapy can be administered as well to help prevent kidney stones in some children who had no other treatment options before this discovery.

Morgan Stanley Children's Hospital also has a nationally and internationally renowned Center for Urodynamics and Incontinence, which is a referral center for complex voiding dysfunction and spinal abnormalities, including pediatric dysfunctional voiding especially in myelomeningocele, cerebral palsy, obstructive uropathy, such as posterior urethral valves, and other neurologic disorders, such as traumatic spinal injury and pediatric peripheral neuropathies.

The team is very active in basic science research. Sarah Lambert, MD, Attending Surgeon at Morgan Stanley Children's Hospital and Assistant Professor of Urology at Columbia University College of Physicians and Surgeons, is currently working in the Developmental Biology Laboratory under the leadership of Cathy Mendelsohn, PhD, a recognized expert in the embryonic development of the lower urinary tract. The other arm of the basic science work is a collaborative effort between Dr. Casale and Jessica Kandel, MD, Interim Surgeon-in-Chief at Morgan Stanley Children's Hospital and R. Peter Altman Professor of Surgery and Pediatrics at Columbia University College of Physicians and Surgeons, as well as Elisa Konofagou, PhD, Director of the Ultrasound Elasticity Imaging Laboratory at Columbia University. All 3 are working on a study (using animal models) evaluating the safety and efficacy of high-frequency ultrasound for obstructive uropathy in fetal and pediatric interventions.

"In addition to our clinical expertise, the Pediatric Urology team at Columbia University is dedicated to clinical and basic science research," Dr. Casale said. "In our clinical research, outcomes, quality, and safety are being monitored through the prospective database and studied to ensure the best possible outcomes for patients in many categories, including convalescence, morbidity, and complications, while maintaining proven high success rates for minimally invasive and reconstructive surgery."

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