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New Opioids Research in Pediatric Urology at UPMC Children's

While the COVID-19 pandemic justifiably consumes much of the nation's and world's attention with its rapid, ongoing spread and consequences, the United States is still grappling with another epidemic that continues to inflict a heavy toll on individuals, families, and communities: opioid addiction.

The genesis of the opioid epidemic is years in the making and multifactorial. Finding ways to stem the tide of addiction and unnecessary related deaths must be a concerted effort leveraging smart and effective policies at the governmental level coupled with an evidence-based approach to how and when to most effectively use opioid painkillers for those who genuinely need them while mitigating poor prescribing habits that lead to an overabundance of highly addictive and potentially dangerous narcotics out in the community.

A significant amount of research studying opioids in adult populations has been conducted around the country and at UPMC. UPMC Department of Urology researcher Benjamin J. Davies, MD, has made significant contributions to the science of opioid use and prescribing patterns.

Much less research related to opioids in children has been conducted to date. However, researchers from the Division of Pediatric Urology at UPMC Children's Hospital of Pittsburgh have begun to investigate opioids use in children with two new studies that are nearing completion.

Studying the Effects of a New Pennsylvania Opioids Law

Postoperative opioid over-prescription remains a problem in the United States and has not been well-studied in children. In 2016, Commonwealth of Pennsylvania Governor Tom Wolf signed into law a resolution requiring health care providers to obtain an opioid-specific consent for minors and, except in certain circumstances outlined in the law, limiting the duration of prescriptions to a seven-day supply. A recent study¹ from the Division of



Pediatric Urology at UPMC Children's led by **Janelle Fox, MD, FACS**, demonstrated that the amount of outpatient surgical opiate prescriptions for pediatric urology

patients was dramatically reduced over the four years after the 2016 law was enacted. Physicians decreased the frequency of postoperative narcotic prescriptions by more than 90% and morphine equivalents for each prescription by more than 30%. Variability in prescribing of postoperative narcotics decreased between physicians.

Fertility Preservation for Transgender Pediatric Patients

UPMC is a leading clinical and research center for fertility preservation technologies and protocols and assistive reproduction techniques. UPMC provides the most comprehensive range of fertility preservation options available anywhere in the country, including both standard of care and experimental options.

Fertility preservation options extend to pediatric patients, both male and female, for a variety of indications. The program has provided national and international leadership by offering experimental testicular and ovarian tissue freezing for children — specifically, those children with a clinical cancer diagnosis whose chemotherapy or radiation treatments put them at significant risk for future infertility as a consequence of gonadotoxic therapies.

UPMC Children's Hospital of Pittsburgh, in collaboration with the Center for Fertility and Reproductive Endocrinology at UPMC Magee-Women's Hospital and the Fertility Preservation Program of Pittsburgh of UPMC, which is directed by **Kyle Orwig, PhD**, professor in the Department of Obstetrics, Gynecology, and Reproductive Sciences at UPMC Magee, has been offering these therapies to children and their families for the last decade.

More recently, IRB-approved experimental protocols and related research have commenced applying fertility preservation techniques to transgender male and female patients. UPMC's fertility preservation protocols for transgender pediatric patients are one of only a few in the world at present

with experimental protocols for harvesting and banking tissue from both pre- and peripubertal individuals.

Glenn M. Cannon, MD, chief of the Division of Pediatric Urology at UPMC Children's Hospital of Pittsburgh has collaborated on the first few cases of transgender individuals to take part in the experimental protocols, and he has worked extensively on the protocols for pediatric cancer patients that have been in place for several years.

"For individuals that have reached puberty and can produce sperm, the process is fairly straightforward in obtaining semen samples for cryopreservation. It is best to obtain testicular tissue before individuals undergo estrogen therapy, as this has been shown to be highly detrimental to spermatogenesis, much like chemotherapy or radiation can be for our cancer patients. For prepubertal transgender girls, since they are too young to produce sperm, our protocols can extract spermatogonial stem cells for cryopreservation with the hope that in the future, technologies will be available for these individuals to use their frozen tissues to restore their fertility. Because those technologies do not exist yet, this work is aspirational, but it is the same as with our prepubertal cancer patients who

bank tissues. We are preserving the potential for future fertility," says Dr. Cannon.

Peripubertal or adolescent transgender youth initiating gender-affirming hormone treatment may experience impairment of gonadal function, which can lead to infertility. Fertility preservation options are available that may preserve the chance to have a biological child in the future. Through the UPMC Center for Reproduction and Transplantation at Magee-Womens Hospital, the Fertility Preservation Program in Pittsburgh provides the following fertility care services for transgender children and adolescents:

- Semen cryopreservation
- Oocyte cryopreservation
- Testicular tissue freezing (with approval of the Institutional Review Board of the University of Pittsburgh)
- Ovarian tissue freezing (with approval of the Institutional Review Board of the University of Pittsburgh)

For additional information or to refer a patient, please call **412-641-7475** or send an email to **fertilitypreservation@upmc.edu**.

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About the Division of Pediatric Urology

The Division of Pediatric Urology offers diagnostic evaluation and surgical treatment for children with genitourinary disorders, including ureteropelvic junction obstructions (UPJO), vesicoureteral reflux, hydronephrosis, and other conditions. The Division supports robust clinical and research programs, as well as offering an accredited two-year fellowship program featuring an active basic science research laboratory experience.

Our Division is a national leader in providing minimally invasive urologic surgical options for an array of urological conditions. Reconstructive and extirpative techniques can be accomplished laparoscopically, robotically, and endoscopically. Common conditions treated by these modalities include UPJO, duplication abnormalities, reflux disease, and complex stone disease.

Along with our nephrology and nutrition colleagues, we are one of the few pediatric urology divisions in the country that offers a multidisciplinary approach to the treatment of pediatric stone disease.

Disorders of sex development (DSD), formerly termed “intersex conditions,” often require complex surgical reconstruction in addition to input from endocrinologists and psychiatrists.

UPMC Children's Hospital of Pittsburgh is one of the few pediatric hospitals offering a multidisciplinary DSD clinic. Our multidisciplinary Spina Bifida Clinic currently follows more than 400 patients and offers state-of-the-art reconstructive urologic surgery and ongoing care.

The UTI Center at UPMC Children's takes a multidisciplinary approach to addressing and investigating pediatric urinary tract infections (UTIs). This creates a unique setting for providing the highest level of clinical care and research. A resource for families and clinical partners, the Center focuses on UTI and the related conditions of vesicoureteral reflux and bladder and bowel dysfunction. With more than two decades of experience caring for children with UTI, our nationally recognized researchers have changed common practices for treating UTI, improving the lives of children in the process.

Faculty and Staff

Glenn M. Cannon, MD, Division Chief and Associate Professor of Urology

Francis X. Schneck, MD, Clinical Director and Associate Professor of Urology

Rajeev Chaudhry, MD, Assistant Professor of Urology

Janelle Fox, MD, FACS, CSSGB, Assistant Professor of Urology

Katharine Carter, PA-C

Dana Casciato, CRNP

Alyssa C. Messina, CRNP

Kathleen Perich, CRNP

Research Update: Pyeloplasty, Antibiotics, and Ureteral Stent Usage

UPMC Children's Hospital of Pittsburgh Department of Pediatric Urology fellow **Marc A. Colaco, MD, MBA**, is leading the Department's efforts in a multicenter collaborative study called "Is There an Indication for Prophylactic Antibiotics in Children After Pyeloplasty With Ureteral Stent Placement?"



The University of Memphis is the lead site coordinating the study to investigate the use of pre- and postoperative antibiotics and their impact on postoperative urinary tract infection outcomes in cases of pyeloplasty for the correction of ureteropelvic junction obstruction (UPJO), and also the effect on outcomes of pyeloplasty with and without the use of ureteral

stents. UPJO is one of the causes of hydronephrosis, which can lead to permanent kidney damage if left untreated. Vesicoureteral reflux also can be a cause of hydronephrosis in pediatric patients.

Historically, clinical practice has entailed using antibiotics immediately before surgery and in the post-procedural period until the removal of the patient's stent (if a stent is used) several weeks after surgery. However, with the continued push toward more judicious use of antibiotics, in part to combat the development and spread of antibiotic resistant bacteria, this pathway needs to be studied to ensure patients are receiving only the antibiotics they need when it is most effective to do so in order to achieve optimal surgical outcomes. The same is true for the use of ureteral stents during pyeloplasty.

The purpose of this multicenter study is to determine if the use or non-use of antibiotics has any effect on postoperative infection rates. The participating centers in the study all use varying protocols for

prophylactic antibiotic use in cases of pyeloplasty. The use of ureteral stents also differs from one institution to the next. By combining data from multiple institutions that use varying protocols for their pyeloplasty cases, outcomes can be compared to assess which protocols and standards of care perform better. This research may contribute to future clinical guidelines and standards of care for pyeloplasty in pediatric patients.

"There's a bit of an old dogma in place when it comes to the use of antibiotics with pyeloplasty, and there isn't a lot of data available in the literature to guide clinical practice or inform changes that may be beneficial to patients and institutions alike. Since these cases are not that common, it is very difficult for a single institution to have enough case volume to power a study on their own. Hence the need for a collaborative multi-institution trial such as this one," says Dr. Colaco.

More About Dr. Colaco

Dr. Colaco is a second-year fellow in the Department of Pediatric Urology at UPMC Children's. He earned a dual MD/MBA degree from the University of Medicine and Dentistry of New Jersey – Robert Wood Johnson Medical School and The State University of New Jersey – Rutgers Business School. Dr. Colaco then completed his residency training at Wake Forest Baptist Health prior to beginning his pediatric urology fellowship at UPMC Children's.

New Opioids Research in Pediatric Urology at UPMC Children's *Continued from Page 1*

These changes in practice pattern were durable, with narcotic utilization continuing to decrease in the three years following the mandate. This finding could have a beneficial effect on states who do not have such legislation in place.

New PA Law and Opioid Use in Inpatient Pediatric Urologic Surgery

In a companion study to their outpatient opioids research, Dr. Fox and Division colleagues investigated how the 2016 Pennsylvania law affected the use of opioids after major inpatient pediatric urologic

surgeries. Little data currently exist on minimal narcotic utilization in these procedures. The new study will be one of the first to describe how the new Pennsylvania regulations have affected the utilization of opioids and the use of multimodal pain control methodologies for inpatient pediatric urologic surgery. Data collection and analysis have been completed, and Dr. Fox and her collaborators are currently preparing a manuscript for publication.

Acknowledgement: The research team would like to thank Christopher Myers, systems analyst expert at UPMC Children's Data

Warehouse, for his essential work in helping to analyze the more than 4,000 surgical cases upon which the new research is based.

Reference

- ¹ Villanueva J, Grajales V, Colaco M, Ayyash O, Chaudhry R, Schneck F, Cannon G, Fox J. Government Mandated Consent Dramatically Reduces Pediatric Urologist Opioid Utilization for Outpatient and Minor Emergency Surgeries. *J Urol*. 2020 Aug 4. Epub ahead of print.

New Research Shows Efficacy for Postoperative Use of POCUS in Cases of Pyeloplasty

New research from the Department of Pediatric Urology at UPMC Children's Hospital of Pittsburgh published in August in the *Journal of Pediatric Urology* showed a number of efficacious outcomes related to the use of point-of-care ultrasound (POCUS) in the postoperative period for cases of pyeloplasty.



The research was led by former Department fellow Jeffrey Villanueva, MD. **Glenn M. Cannon, MD**, chief of Pediatric Urology at UPMC Children's was Dr. Villanueva's mentor on the research project.

The goal of this research was to determine if follow-up ultrasound imaging by urologists is efficient, cost-effective, and safe, and that quality and diagnostic determinants are equal to imaging procedures conducted in the radiology department.

Performing point-of-care ultrasound imaging for pyeloplasty patients in the clinic as opposed to complete retroperitoneal ultrasound (CRUS) in the radiology department can cut down on the amount of time patients need to spend in the hospital and clinic, but only if it is possible to maintain similar levels of quality and detection rates of the patient's hydronephrosis status.

The retrospective analysis examined a cohort of 45 patients who had a previous pyeloplasty procedure for a ureteropelvic junction obstruction (UPJO).

During patient-follow up, which for this cohort was a mean period of 29 months, there were 67 POCUS and 73 CRUS imaging procedures performed. Dr. Villanueva and colleagues research examined the incremental length of time needed during patient visits for CRUS, cost analysis on the additional charges to payers between CRUS and POCUS imaging, and the detection rates of instances of hydronephrosis — whether they were improving, stable, or becoming worse.

"In our study, we did not find any difference in rates relative to hydronephrosis detection. Our analysis showed that CRUS patients spend on average an additional two hours more in the hospital for their visit, and there was a related increase in charges to payers approaching \$84,000. It would appear, that with the appropriate training, POCUS imaging for pyeloplasty patient by the urologist can be done accurately and efficiently. That's not to say that POCUS can or should replace CRUS in every instance for every patient, but it does appear to be a viable option with benefits to patients, health care systems, and insurance payers," says Dr. Cannon.



More About the POCUS Program at UPMC Children's

UPMC Children's Hospital of Pittsburgh has one of the most extensive point-of-care ultrasound (POCUS) programs in the United States. Begun in 2015, the hospital-wide POCUS program encompasses 14 subspecialties. The Division of Pediatric Urology is one of the 14 subspecialties taking part in the program and has an extensive patient data history on its use that is being used for ongoing research projects.

The hospital-wide POCUS program at UPMC Children's Hospital is one of only a handful in existence in the United States. The program is currently led by emergency medicine physician and Point-of-Care Ultrasound Medical Director **Jennifer Marin, MD, MSc**. The goal of the POCUS program is to improve patient care across a mix of diverse clinical specialties by standardizing the performance of point-of-care diagnostic and procedural ultrasound for many conditions and care scenarios.

Reference

Villanueva J, Pifer B, Colaco M, Fox J, Chaudhry R, Schneck FX, Cannon GM. Point-of-Care Ultrasound Is an Accurate, Time-Saving, and Cost-Effective Modality for Postoperative Imaging After Pyeloplasty. *J Pediatr Urol*. 2020 Aug; 16(4): 472.e1-472.eg.

UPMC Children's Hospital of Pittsburgh Pediatric Research Podcast Series

UPMC Children's Hospital of Pittsburgh "That's Pediatrics" podcast series features interviews with the hospital's leading researchers and clinicians.

Episodes featuring pediatric urology faculty include compelling interviews with scientists at UPMC Children's Hospital who are performing innovative basic, translational, and clinical research. Subscribe to "That's Pediatrics" in iTunes or Google Play Music to have new episodes automatically download to your phone for free when they become available.



About UPMC Children's Hospital of Pittsburgh

Regionally, nationally, and globally, UPMC Children's Hospital of Pittsburgh is a leader in the treatment of childhood conditions and diseases, a pioneer in the development of new and improved therapies, and a top educator of the next generation of pediatricians and pediatric subspecialists. With generous community support, UPMC Children's Hospital has fulfilled this mission since its founding in 1890. UPMC Children's is recognized consistently for its clinical, research, educational, and advocacy-related accomplishments, including ranking 15th among children's hospitals and schools of medicine in funding for pediatric research provided by the National Institutes of Health (FY2019) and ranking on *U.S. News & World Report's* Honor Roll of America's Best Children's Hospitals (2020–21).