

## In This Issue

- Onco-Fertility Preservation for Pediatric Cancer Patients
- Point-of-Care Ultrasound at UPMC Children's
- New Pediatric Research Podcast Series
- Recent Publications
- Upcoming and Recent Research Presentations on the National Stage
- About the Division
- UPMC Physician Resources

UPMC Children's Hospital of Pittsburgh is affiliated with the University of Pittsburgh School of Medicine and nationally ranked in nine clinical specialties by *U.S. News & World Report*.

# Onco-Fertility Preservation for Pediatric Cancer Patients

A relatively common consequence of chemotherapy and radiation treatments for various cancers is permanent infertility through exposure to gonadotoxic agents. This is true in both adults and children, but it is particularly important for children because the survival rates for most childhood cancers now exceeds 85 percent because of the steady improvements in treatment options over many decades.

The treatments for childhood cancers are still toxic, however, and can have lasting consequences.



"Prepubertal boys present a particular challenge with respect to preserving their future fertility when they will require gonadotoxic chemotherapy for some form of cancer or hematologic disorder, or another condition whose treatment would be expected to render them infertile," says **Glenn Cannon, MD**, (far left) chief of the Division of Pediatric Urology at UPMC Children's.

The reason is simple: prepubertal boys have yet to reach a point where their bodies can manufacture viable sperm cells that can be harvested and preserved. To circumvent this challenge, researchers at UPMC, including **Kyle Orwig, PhD**, (above, right) professor of obstetrics, gynecology, and reproductive sciences at UPMC Magee-Womens Hospital, who is also director of research in reproductive endocrinology and infertility, director of the Fertility Preservation Program in Pittsburgh, and principal investigator in the Orwig Laboratory, have developed several novel experimental protocols and clinical trials to help this patient population to possibly retain their future reproductive abilities.

For those individuals who meet the specific criteria for these protocols, the urologic surgical team at UPMC Children's can conduct an open testicular biopsy or a complete simple orchiectomy to derive the necessary tissues from which Dr. Orwig's team can isolate the spermatogonial stem cells and preserve them for future reimplantation when the technology is developed in the future.

"Since the program began in 2011, we have had more than 150 children (boys) from across the United States come to UPMC Children's for spermatogonial stem cell harvest with the future goal of reimplanting those cells once the technology for doing so is proven safe and effective in humans," says Dr. Cannon.

### Important Information for Families and Providers

Children who already have undergone chemotherapy but have not undergone a fully gonadotoxic dose of chemotherapy can still have their spermatogonial stem cells retrieved and preserved.

## Point-of-Care Ultrasound at UPMC Children's

Point-of-Care Ultrasound (POCUS) is a focused ultrasound exam performed directly at the bedside by clinicians. POCUS exams improve the accuracy, quality, and efficiency of clinical care by bringing the diagnostic imaging modality directly to the patient.



The UPMC Children's Hospital of Pittsburgh POCUS program began in 2015. The hospital-wide POCUS program 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**,

and its overall goal 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.

At present, the POCUS program at UPMC Children's encompasses 14 different pediatric subspecialties and receives support from numerous areas within the hospital, including bioengineering, clinical informatics, quality and safety, and others.

**Glenn M. Cannon, MD**, chief of the Division of Pediatric Urology, is a contributing member of the UPMC Children's POCUS team and works

alongside nearly two dozen clinicians and support staff to deliver ultrasound diagnostic capabilities at the bedside across the hospital.

### Further Reading

Marin JR, et al. Pediatric Emergency Medicine Point-of-Care Ultrasound: Summary of the Evidence. *Crit Ultrasound J*. 2016; 8: 16.

10 Important Applications of Point-of-Care Ultrasound in Pediatric Emergency Medicine. Jennifer R. Marin, MD, MSc — Thursday, August 30th, 2018. BeckersHospitalReview.com.

## UPMC Children's Hospital of Pittsburgh Launches New Pediatric Research Podcast Series

UPMC Children's Hospital of Pittsburgh has launched a new medical podcast series for physicians, scientists, and other health care professionals featuring the hospital's leading researchers and clinicians.



Episodes of "That's Pediatrics" will include compelling interviews with scientists at UPMC Children's Hospital who are performing innovative

basic, translational, and clinical research. New episodes will be released every two weeks.

"Going back to the polio vaccine, Pittsburgh has always been a hub of very innovative research, and in recent years really has become a nexus for some groundbreaking research in pediatric medicine," said

**John Williams, MD**, chief of the Division of Pediatric Infectious Diseases at UPMC Children's and one of the podcast hosts.

"There is a spirit of collaboration here in Pittsburgh that makes it somewhat unique nationally and we really want to explore the

research that is happening here and how we have a real opportunity to change the way pediatric medicine is practiced around the world."

### Current episodes of "That's Pediatrics" include:

"Gene Therapy" with **George Gittes, MD**, director of the Richard King Mellon Foundation Institute for Pediatric Research and co-scientific director, UPMC Children's Hospital

"Don't Rule Out Brain Injuries" with **Rachel Berger, MD, MPH**, chief, Child Advocacy Center, UPMC Children's Hospital



"All About Acute Flaccid Myelitis" with **John Williams, MD**, chief, Division of Pediatric Infectious Diseases, UPMC Children's Hospital

### In addition to Dr. Williams, "That's Pediatrics" hosts are:

**Carolyn Coyne, PhD**, director, Center for Microbial Pathogenesis, UPMC Children's Hospital

**Stephanie Dewar, MD**, director, Pediatric Residency Training Program, UPMC Children's Hospital

**Brian Martin, DMD**, vice president, Medical Affairs, UPMC Children's Hospital

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.

# Recent Publications

Below are select recent publications from Division faculty members.

Jimbo M, Granberg CF, Osumah TS, Bandari J, Cannon GM, Routh JC, Gargollo PC. Discrepancies in Self-Reported and Actual Conflicts of Interest for Robotic Pediatric Urological Surgery. *J Urol*. 2019 Feb; 201(2): 393-399.

Hugar LA, Chaudhry R, Fuller TW, Cannon GM, Schneck FX, Ost MC, Stephany HA. Urologic Phenotype and Patterns of Care in Patients With Megacystis Microcolon Intestinal Hypoperistalsis Syndrome Presenting to a Major Pediatric Transplantation Center. *Urology*. 2018 Sep; 119: 127-132.

Mohapatra A, Chaudhry R, Picarsic J, Schneck FX. A Rare Case of Uterine Torsion With Juvenile Granulosa Cell Tumor in the Pediatric Patient. *Urology*. 2019 Feb 20. pii: S0090-4295(19)30166-9. Epub ahead of print.

Berklite L, Witchel SF, Yatsenko SA, Schneck FX, Reyes-Múgica M. Early Bilateral Gonadoblastoma Associated With 45,X/46,XY Mosaicism: The Spectrum of Undifferentiated Gonadal Tissue and Gonadoblastoma in the First Months of Life. *Pediatr Dev Pathol*. 2019 Jan 15: 1093526618824469. Epub ahead of print.

Benz K, Maruf M, Hatheway C, Kasprenski M, Jayman J, Docimo S, Schneck F, Gearhart J. The Intravesical Phallus in Patients With Cloacal Exstrophy: An Embryologic Conundrum. *J Pediatr Urol*. 2018 Oct; 14(5): 428.e1-428.e5. Epub ahead of print.

Farber NJ, Davis RB, Grimsby GM, Shinder B, Cannon GM Jr, Jacobs MA, Ost MC, Schneck FX, Stephany HA, Gargollo PC, Dwyer ME. Bowel Preparation Prior to Reconstructive Urologic Surgery in Pediatric Myelomeningocele Patients. *Can J Urol*. 2017; 24(5): 9038-9042.

Yecies T, Bandari J, Schneck F, Cannon G. Direction of Rotation in Testicular Torsion and Identification of Predictors of Testicular Salvage. *Urology*. 2018 Apr; 114: 163-166.

Dangle P, Bansal U, Chaudhry R, Cannon GM, Schneck FX, Ost MC. Trends in Urologic Indications for Pediatric Renal Transplantation Over a 27-Year Period — UNOS Database. *Urology*. 2017; Nov 14. Epub ahead of print.

Cannon GM, Ost MC. Robot-Assisted Laparoscopic Extravesical Ureteral Reimplantation for Primary Vesicoureteral Reflux in Children. *J Urol*. 2017; 197(6): 1379-1381.

Hugar SB, Kadow BT, Davis A, Ranganathan S, Reyes-Mugica M, Schneck FX, Picarsic J. Pediatric Testicular Hemangioma in a 10-Year Old: A Rare Entity That May Mimic Malignancy With Appraisal of the Literature. *Urology*. 2018; Jan 3. Epub ahead of print.

Chaudhry R, Theisen KM, Dangle PP, Schneck FX. Congenital Aphallia: Novel Use of Acellular Dermal Matrix During Scrotal Flap Phalloplasty. *Urology*. 2017; 105: 167-170.

Chaudhry R, Theisen KM, Dangle PP, Schneck FX. Percutaneous Stone Surgery in Spina Bifida Patients — Are Stone-Free Rates Worth the Risk? *J Endourol*. 2017 Apr; 31(S1): S81-S86. Epub ahead of print.

Dangle PP, Lee A, Chaudhry R, Schneck FX. Surgical Complications Following Early Genitourinary Reconstructive Surgery for Congenital Adrenal Hyperplasia-Interim Analysis at 6 Years. *Urology*. 2017; 101: 111-115.

## Onco-Fertility Preservation *Continued from Page 1*

“This is important for families to know because many families do not necessarily learn about these fertility preservation options until after their child has received at least one dose of chemotherapy that may be gonadotoxic. Sometimes this is the case because the child does not reside locally in our immediate area or simply because their treatment needed to begin immediately,” says Dr. Cannon.

### Reimplantation Under Ultrasound Guidance

The fertility preservation program at UPMC has reached a level of maturation that is now close to the point where it can begin to reimplant spermatogonial stem cells back into pediatric patients who have successfully undergone chemotherapy for their original disease process.

Clinical trials with Dr. Orwig’s group are currently ramping up in adult subjects to determine the safety and efficacy of the reimplantation protocol before the program can apply for and receive IRB approval to begin the treatment in pediatric patients. However, with Dr. Orwig’s past studies and clinical trials in various model systems, it is fully expected that these initial human trials will be successful, thereby opening the door to the first reimplantations in pediatric patients in the near future.

The reimplantation procedure involves an ultrasound-guided needle injection into the remaining testis, into which the previously preserved spermatogonial stem cells are injected. The ultrasound-guided procedure

also uses a microbubble contrast agent to aid in ensuring adequate and complete distribution of the spermatogonial stem cells throughout the entire testis.

### The Future Is Approaching Fast

The ultimate measure of the success of this novel approach to fertility preservation will be paternity: that these boys will grow up and father children of their own.

“It will take many years to determine success by that measure, but in the more immediate future, it is our firm belief that within the next five years we will be able to reimplant cells into adolescents who underwent the harvest procedure when they were younger and restore their fertility potential.

## Upcoming and Recent Research Presentations on the National Stage

### AUA 2019

At the upcoming American Urological Association (AUA) annual meeting in May, Division faculty, including second-year fellow **Mary Killian, MD**, will be presenting a new research abstract titled "Socioeconomic Factors in the Presentation and Progression of Posterior Urethral Valves."

### Fall 2018 Societies for Pediatric Urology (SPU) Congress

The Fall 2018 SPU Congress saw several moderated poster presentations by Division faculty. Posters presented included the following studies.

#### *The Effect of Oral Steroids on Postoperative Complications in Proximal Hypospadias Repair: A Prospective, Randomized, Placebo-Controlled Trial*

**Mary Killian, MD, Rajeev Chaudhry, MD, Patrick J. Fox, MD, Michelle J. Barlas, PharmD, Heidi A. Stephany, MD, Pankaj Dangle, MD, Moira Dwyer, MD, Glenn M. Cannon, MD, Francis X. Schneck, MD.**

**Background:** Proximal hypospadias is a complicated diagnosis with the treatment being equally problematic. Complication rates for proximal hypospadias repairs reach as high as 50 percent in the literature. Here we present preliminary data on a novel therapy to attempt to reduce complications and improve wound healing in proximal hypospadias repair.

**Methods:** We obtained IRB approval and designed a randomized, double-blind, placebo-controlled trial. Patients with proximal hypospadias (proximal shaft, penoscrotal, or scrotal) undergoing single-stage or staged repairs were prospectively enrolled after obtaining informed consent. Patients received either methylprednisolone (1.5 mg/kg/day divided into two doses) or placebo for five days postoperatively. Urethral stents were kept for seven to 10 days postoperatively. Patients had scheduled follow-up at six weeks, six months, and annually thereafter. The primary outcome was postoperative complication rate, while secondary outcomes included compliance with and safety of the medication.

**Results:** Twenty-two patients were prospectively enrolled in the study. Fourteen patients (64 percent) were penoscrotal, six patients (27 percent) were proximal shaft, and two patients (9 percent) were scrotal. Eighteen patients (82 percent) underwent single-stage repairs, while four patients (18 percent) underwent staged repairs. Median age at surgery was 8.5 months (IQR 7.2-11.2). Thirteen patients (60 percent) were in the prednisone arm and nine patients (40 percent) in the placebo arm. There was one complication in the prednisone group (8 percent), and two complications in the placebo group (24 percent) ( $p = 0.5$ ), for a total complication rate of 14 percent among both cohorts. Complications were noted as early as 10 days and up to 6 weeks postoperatively, and included one glans dehiscence and two urethrocutaneous fistulae. The patient with the complication in the prednisone arm also had early dislodgement of urethral catheter. There was a 95 percent compliance rate with medication; one patient only completed 9/10 doses. There were no adverse events with the medication.

**Conclusion:** This is the first randomized, placebo-controlled trial evaluating the effect of postoperative steroids on proximal hypospadias repair. While the results do not reach significance, we had a low overall

complication rate with only one complication in the prednisone arm. There were no adverse events from the medication, and all patients tolerated it well. We plan to continue enrolling patients and look to long-term follow-up to better assess the outcomes.

#### *Delayed Presentation of Posterior Urethral Valves*

**Mary Killian, MD, Rajeev Chaudhry, MD, Francis X. Schneck, MD, Glenn M. Cannon, MD, Omar Ayyash, MD, Patrick J. Fox, MD.**

**Background:** Posterior urethral valves (PUV) are the most common cause of congenital lower urinary tract obstruction. Even with early treatment in the newborn period, children experience long-term effects. Historically, approximately 10 percent of patients have presented with a delayed diagnosis of posterior urethral valves. We reviewed our cohort of patients with a diagnosis of posterior urethral valves to assess patients with a late presentation.

**Methods:** In accordance with institutional review board approval, we performed a retrospective review of all patients seen in the pediatric urology clinic with a diagnosis of posterior urethral valves between the years of 1988 and 2017. Patient charts were then reviewed and classified by the age of diagnosis. Late presentation was defined as an age at diagnosis of six months or greater. The clinical characteristics of these patients were analyzed and compared with patients with an antenatal or immediate postnatal diagnosis of posterior urethral valves.

**Results:** Thirty-two percent of the patients were delayed presentation of PUV. When compared with patients diagnosed prior to six months, these patients were noted to have a lower peak creatinine (0.5 versus 1.35 [ $p < 0.01$ ]). The delayed presentation patients were also less likely to have a postoperative VCUG or require a vesicostomy. While a higher percentage of delayed presentation patients underwent repeat ablation (12 percent versus 6 percent), this was not statistically significant. The majority of patients in both groups were noted with type 1 PUV, but there were more (18 versus 3) type 3 PUV noted in the early diagnosis group. No patients in the delayed presentation group underwent a transplant within the follow-up period.

**Conclusion:** Our results demonstrate a larger percentage of patients with delayed presentation of PUV. These patients appear to have a less severe form given their lower peak Cr at time of diagnosis, as well as the fact that none of the patients has required a renal transplant. Longer-term follow-up will be needed to assess the continued renal function in both groups.

### 2018 NSUA Participation

Division faculty presented three posters at the 2018 Northeastern Section American Urological Association Meeting:

- Robotic Ureteropyelostomy for a Lower Pole Ureteropelvic Junction Obstruction in a Partially Duplicated Kidney
- Delayed Presentation of Posterior Urethral Valves
- The Effect of Oral Steroids on Postoperative Complications in Proximal Hypospadias Repair: A Prospective, Randomized, Placebo-Controlled Study



## ABOUT THE DIVISION

The Division of Pediatric Urology offers diagnostic evaluation and surgical treatment for children with genitourinary disorders, including ureteropelvic junction obstructions, 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.



Drs. Rajeev Chaudhry, Francis Schneck, and Glenn Cannon in the operating room.

### Faculty and Staff

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Division Chief and Associate  
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### 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 (FY2018).