Pediatric
INSIGHTS

SPRING 2017

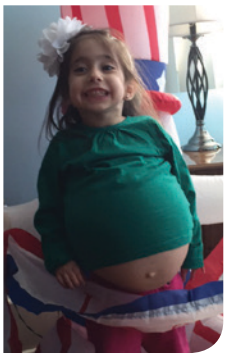
An Update From the Division of Pediatric Nephrology

In This Issue

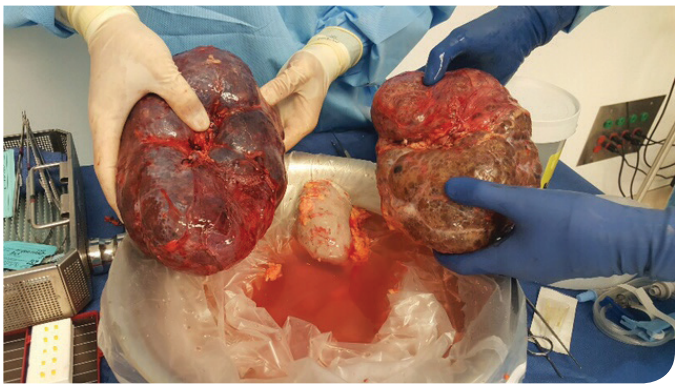
BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT NEPHROLOGY 2016-17

Preemptive Living Donor Kidney Transplantation and Bilateral Nephrectomies in Rare Case of Massive Cystic Kidneys:

Restoring Quality of Life With a 30% Weight Reduction



Polycystic kidney disease is common, but this 4-year-old girl was unlike the others. Shortly after birth, she was diagnosed with polycystic kidney disease, a disease that she shares with her mother and two older sisters. Genetic testing was not consistent with autosomal dominant or autosomal recessive polycystic kidney disease, but the family phenotype was known to cause end-stage renal disease in the late first or second decade of life. It became apparent by two years of age that the patient had a more severe phenotype than her other family members, as her kidneys kept growing at a rapid rate. She also had vesicoureteral reflux into the kidneys, causing frequent episodes of pyelonephritis, and difficult to control hypertension resulting in a dilated cardiomyopathy. Despite these findings, her renal function remained normal. She had a poor quality of life, though, due to her massive abdominal distention, which limited her nutrition, mood, and mobility.



She was a poor candidate for either peritoneal dialysis or hemodialysis due to the patient's massive kidney size and a long geographic distance to our center. "Seeing the decline in the patient's quality of life and knowing the potential complications to her hypertension and infections, we elected to perform simultaneous bilateral nephrectomies and a preemptive living-donor transplant despite her normal renal function," says **Christina Nguyen, MD**, medical director of the Pediatric Kidney Transplant Program at Children's Hospital of Pittsburgh of UPMC.

At the time of her surgery, her renal mass was nearly 10 pounds, almost a third of her weight. The patient was extubated in the immediate postoperative period and was discharged home eight days later without antihypertensive therapy. "Our nephrology team is experienced, and we have the surgical expertise to back it up, so we perform transplants in children that, perhaps, other centers are reluctant to perform. We don't really have many criteria that would exclude a child from getting a transplant," says **Abhinav Humar, MD**, chief of the Division of Transplant Surgery at UPMC.

The patient is now nearly six months posttransplant and thriving in preschool. "With our steroid avoidance immunosuppression protocols, the patient has demonstrated excellent linear growth and weight gain. She is now caught up on developmental milestones and is a completely different child," says Dr. Nguyen. •

Affiliated with the University of Pittsburgh School of Medicine and ranked among the nation's best children's hospitals by *U.S. News & World Report*.

Children's Hospital of Pittsburgh | of UPMC

RESEARCH SPOTLIGHT

Novel Mechanisms Driving Nephronophthisis Induce Genomic Instability

Challenge

Nephronophthisis (NPHP) is the most common genetic cause of childhood kidney failure. Despite the identification of mutations in more than 20 genes that cause the disorder, the precise disease mechanisms remain elusive.

Major Finding

Research conducted by assistant professor **Rannar Airik, PhD**, has expanded our understanding of three important NPHP proteins (CEP164, SDCCAG8, and FAN1) by showing that in addition to their centrosomal and ciliary functions, they also regulate DNA replication, DNA repair, and ploidy.

Significance

Using various kidney injury models, it has been shown that the critical component of the injury is damage to the genomic DNA of the renal epithelial cells. Suppressing proliferation of these cells postinjury through the use of cell cycle inhibitors appears to mitigate overall damage, presumably by giving the injured cells enough time to repair genomic damage before entering the cell cycle.

In contrast to the above models, NPHP offers a genetic model of chronic kidney disease characterized by cell cycle defects and impaired DNA damage response. Thus, it may be possible to mitigate renal disease through interference with drugs that regulate cell cycle progression. Understanding how impaired DNA damage response contributes to renal degeneration and fibrosis opens up new avenues for targeting chronic kidney disease.

Next Steps

Using transgenic mice combined with renal injury models, Dr. Airik continues to investigate the molecular mechanisms of nephronophthisis and how DNA damage affects renal homeostasis and regeneration capacity. •

Rannar Airik, PhD
Assistant Professor of Pediatrics
University of Pittsburgh

PROGRAM COLLABORATIONS

The Pediatric Kidney Transplant Program will be participating in the newly formed learning network, Improving Renal Outcomes Collaborative (IROC). Through this unique learning health system network, the transplant program will partner with patients who have received a kidney transplant and their families to achieve health, longevity, and quality of life equivalent to the general population. Using Quality Improvements methods, IROC Centers will test clinical practice changes with their patients and families and identify best practices that improve care and outcomes in kidney transplant recipients. Currently, the Children's Hospital Pediatric Kidney Transplant Program is one of 17 transplant centers across the country to participate. •

Kidney Transplant Survival Rates

1 Year	100%	National Average	97%
3 Years	100%	National Average	92%

Kidney Transplant Volumes

Transplant Type	2016	Program Inception Through 12/31/2015
Living-Donor Kidney	11	208
Deceased-Donor Kidney	8	312
Subtotal	19	520

FELLOWSHIP HIGHLIGHTS

The Division of Pediatric Nephrology at Children's Hospital of Pittsburgh of UPMC — one of the largest in the country — offers a three-year ACGME-accredited fellowship program that features outstanding opportunities in both clinical care and research initiatives.

- Our robust inpatient, consult, and outpatient services allow direct patient contact across a wide spectrum of cases.
- The fellowship also offers diverse opportunities for clinical, translational, and basic research. It is one of only a handful in the country that has an NIH T32 fellowship training grant. There are currently six NIH-funded investigators within the division working on areas that include fluid management, renal development (genetic and epigenetic), vesicoureteral reflux, obstructive nephropathy, polycystic kidney disease, tubular toxicity of albuminuria, transplant immunology/infection, podocyte biology, epithelial cell polarization, protein trafficking in epithelial cells, pyelonephritis, and neonatal hydronephrosis.
- Fellows have the opportunity to work with more than 30 NIH-funded investigators across the University of Pittsburgh.
- Our fellowship program has trained seven graduates who are located at many prestigious programs across the country. •

DIVISION NEWS

Carlton M. Bates, MD
Chief, Division of Pediatric Nephrology

Activities at the International Pediatric Nephrology Association Congress in Brazil:

- Moderator of a session titled "Congenital Anomalies of the Kidney and Urinary Tract"
- Moderator of a poster walk
- Delivered the "State of the Art" closing plenary session talk titled "From Tubes to Cysts: Novel Mechanisms Driving Pathology in Polycystic Kidney Disease"

Jacqueline Ho, MD
Assistant Professor of Pediatrics

- Delivered a talk at the International Pediatric Nephrology Association Congress titled "The Long and Short of MicroRNAs in the Developing Kidney"
- Member of the ASPN program and research committees
- Moderating a session at the ASN titled "Recent Advances in Pediatric Nephrology"
- Presenting Renal Grand Rounds at Northwestern University in December: "Small RNAs and Small Kidneys"

Emily Joyce, MD
Pediatric Nephrology Fellow — Third Year

Abstracts at the American Society of Nephrology:

- Joyce EL, Fuhrman DY, Priyanka P, Kellum JA. November 2016. AKI Outcomes in Young Adults. American Society of Nephrology, Kidney Week, Chicago, Illinois
- Joyce EL, Nguyen CR. October 2016. Improving Adolescent Health in Renal Transplant Patients. Quality Week, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania

Agnieszka Swiatecka-Urban, MD
Associate Professor of Pediatrics
Associate Professor of Cell Biology

- Chair, Potassium in Childhood Health and Disease Workshop at the 2016 Pediatric Academic Societies/American Society of Pediatric Nephrology (PAS/ASPN) Annual Meeting, Baltimore, Maryland
- Chair, 3rd Annual Nephrotic Syndrome Symposium: Clinical Challenges and Evidence-based Management, Pittsburgh, Pennsylvania, 2016
- Program Committee, PAS/ASPN, 2017-18
- Champion and Organizer, The Future of Nephrology: Tissue Regeneration, 3D Printing, and the Wearable Kidney Workshop at the 2017 PAS/ASPN Meeting, San Francisco, California
- Workshop and abstract reviewer, PAS/ASPN, 2017-18
- Planning Committee, the National Kidney Foundation Kidney Gala, Pittsburgh, Pennsylvania, 03/11/2017

One Children's Hospital Drive
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Pittsburgh, PA 15224

Save the Date

4th Annual Nephrotic Syndrome Symposium

Thursday, Sept. 28, 2017 • Pittsburgh, Pa.

Mark your calendar for the **4th Annual Pittsburgh Nephrotic Syndrome Symposium: Focus on Evidence-Based and Personalized Approach**, scheduled for Sept. 28, 2017, in Pittsburgh, Pennsylvania. This CME-accredited conference is a forum for scientists and physicians who are interested in advancing a cure for nephrotic syndrome through cutting-edge research and innovative clinical practice.

The conference is sponsored by the University of Pittsburgh School of Medicine Center for Continuing Education in the Health Sciences, the Division of Pediatric Nephrology at Children's Hospital of Pittsburgh of UPMC, the Pittsburgh Center for Kidney Research, and the Renal-Electrolyte Division at the University of Pittsburgh School of Medicine. For more information, visit **chp.edu/nss**. •

ABOUT CHILDREN'S HOSPITAL OF PITTSBURGH OF UPMC

Children's Hospital of Pittsburgh of UPMC 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.

Children's is consistently recognized for its research and clinical achievements, including ranking 10th among children's hospitals and schools of medicine (FY15) in NIH funding for pediatric research, and being named to the 2016-17 *U.S. News & World Report* Honor Roll of America's Best Children's Hospitals.