Children's Mercy KANSAS CITY

# ADVANCING PEDIATRIC NEPHROLOGY OUTCOMES FOR CHILDREN EVERYWHERE

## A MESSAGE FROM Bradley A. Warady, MD

Division Director, Pediatric Nephrology

The Division of Pediatric Nephrology at Children's Mercy Kansas City is known for consistently setting the bar high when it comes to patient outcomes. Of course, 2021 continued to present Children's Mercy, and all pediatric hospitals, with the challenge of achieving superior patient outcomes while dealing with all of the complexities of the COVID-19 pandemic.

Despite being confronted by this unprecedented challenge, our division and its multidisciplinary team members have worked hard to achieve the clinical excellence that our patients and their families deserve.

Clinical expertise, innovative quality improvement initiatives, highly productive clinical and research collaborations, coupled with a philosophy of shared decision-making with patients and families have all contributed to results that we are very proud to share with you.

## 2021 HIGHLIGHTS

Innovative **Save the Vein quality improvement** initiative to preserve vasculature resulted in placement of **93% of peripheral intravenous lines** in the dominant arm of patients with CKD.

We implemented a quality improvement initiative which **improved vaccination of high-risk** nephrology patients with PPSV23 from 47% to **85%**.

The 3rd edition of **Pediatric Dialysis**, co-edited by Bradley A. Warady, MD, was published in Spring 2021.

Our **graft survival hazard ratio** of 0.41 is second best in the nation and equates to an estimated **59% lower risk** of a transplant failing compared to national averages.

**Tarak Srivastava, MD**, was named a member of the American Pediatric Society.

**Darcy Weidemann, MD, MHS**, serves as Chair of ASPN Workforce Committee.

**Judith VanSickle, MD,** conducted Capitol Hill meetings along with representatives of the American Association of Kidney Patients to address issues pertaining to the Living Donor Protection Act.

**100%** three-year kidney transplant graft and patient survival for the **past seven years.**

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT NEPHROLOGY 2021-22

For **11 consecutive years**, our Division of Pediatric Nephrology has been ranked in the **top 10 nationwide** by U.S. News & World Report.

Vimal Chadha, MD, Pediatric Nephrology, and Sarah Brunner, MD, Pediatric Intensivist, discuss a patient with fellow Nathan LeVoy, MD.

# FY 2021 By the Numbers

## FACULTY

**14** pediatric nephrologists

**3** pediatric nephrology fellows

## NEPHROLOGY CARE TEAM

**6** APRNs **43** RNs

In total, we hold **40** nursing/nurse practitioner certifications.

**2** dedicated social workers

**1** dedicated Child Life specialist

**1** dedicated psychologist

**1** dedicated clinical pharmacologist

**3** dedicated dietitians

**1** dedicated schoolteacher

**9** pediatric kidney transplants

**6,913** outpatient nephrology visits

**4,936** clinic and telemedicine visits

**1,977** outpatient hemodialysis treatments

## CLINICAL OUTCOMES

**100%** three-year kidney transplant graft survival

**100%** three-year kidney transplant patient survival

Hemodialysis catheter-associated blood stream infections:

**0.89/100** patient months

Peritonitis:

**1 infection every 81** patient months

# CLINICAL AND QI INITIATIVES ADVANCE CARE

The Division of Pediatric Nephrology at Children's Mercy Kansas City provides the highest quality care for pediatric patients with kidney and urinary tract disorders. Our outstanding care and leading-edge research has helped us earn recognition as one of the top 10 nephrology programs in the nation by U.S. News & World Report for 11 consecutive years.

Our faculty are recognized as experts and leaders by their pediatric nephrology peers. Through leadership and participation in a variety of national committees and research collaboratives, we are advancing the field of pediatric nephrology and applying what is learned to improve outcomes for patients today and in the future. Utilizing an integrated, collaborative care approach with colleagues in critical care medicine, neonatology, maternal fetal medicine, cardiology, genomics, bioethics and other specialties, we are able to deliver exceptional outcomes for the most critically ill and vulnerable patients.

## Improving Medication Safety

Nephrotoxic medication exposure is a common cause of acute kidney injury (AKI) in hospitalized children. Subsequent to the finding at a single center that strategic interventions could successfully address this issue, a multicenter pediatric institutional collaborative (NINJA; Nephrotoxic Injury Negated by Just-in-time Action) was instituted at nine centers, including Children's Mercy.

A key driver diagram was developed by the Children's Mercy NINJA team members, with each medical division informed about the metrics being measured (including the percentage of patients receiving three or more nephrotoxic medications or an IV aminoglycoside for more than three days ["exposed"], and the rate of exposed patients developing AKI. Six divisions were selected for the initial phase of implementation. Daily trigger reports were generated by the EMR and emailed to the clinical pharmacist on the respective medical service who provided valuable education.

The clinical pharmacist reviewed each patient's medication list daily for nephrotoxic medication exposure. If exposed, the pharmacist recommended a daily serum creatinine and alternative, non-nephrotoxic medications, if available.

Over a period of four years, **NINJA has resulted in a 70% decrease in nephrotoxic medication exposure and a 61% decrease in the rate of AKI in all non-ICU inpatients** at Children's Mercy, according to Ricky Ogden, PharmD, MBA, and one of the leaders of the Children's Mercy NINJA team. Of the patients who were exposed, 12.4% developed AKI. Current efforts have focused on sustainability of the results in the medical divisions and expansion of the principles of the project into the intensive care units.

## Preserving Vascular Access

The preferred vascular access for patients who receive hemodialysis is an arteriovenous fistula in the nondominant arm. Prior placement of a peripheral intravenous line can lead to vascular injury and limit options for arteriovenous fistula creation, a particular problem for children with ESKD, who may need HD at some point in their lifetime. We instituted the "Save the Vein" initiative to increase the frequency of PIV line placement in the dominant arm for hospitalized pediatric patients with advanced chronic kidney disease.

At baseline and before institution of this initiative, 47% of all PIV lines and only 25% of those in children under 5 years old were placed in the dominant (preferred) arm. After instituting the initiative following the education of hospital staff and the establishment of an auditing system, **93% of all PIV lines and 94% of those in children under 5 years old were placed in the dominant arm.** In addition, only 10% of PIV lines were placed in the antecubital vein. JoLynn Grimes, RN, nursing lead for "Save the Vein," noted collaboration between nephrology, nursing and the vascular access team was essential to the success of this initiative.

## PPSV23 Immunization Project

Although national guidelines recommend that all children with chronic kidney disease (CKD) and nephrotic syndrome receive PPSV23, an analysis of the Children's Mercy Nephrology ambulatory population revealed that only 47% of eligible patients had received the immunization. The project, led by Darcy Weidemann, MD, MHS, involved children 2-21 years old with nephrotic syndrome, as well as those with CKD stages 2-5, including the dialysis and transplant populations. **Over an eight-month period, the team was able to increase the PPSV23 vaccination rate to 85% through the use of quality improvement methodology, such as multiple Plan-Do-Study-Act cycles.** The intervention with the highest impact was implementation of a prospective "clinic preparation" strategy which included a weekly automated report of eligible immunization opportunities that was shared with the physician and clinic nursing staff and integrated into the clinic workflow.

Judith VanSickle, MD, and patient

# CELLULAR AND ANTIBODY MEDIATED RESPONSE TO THE 3RD COVID-19 VACCINE DOSE IN IMMUNOCOMPROMISED CHILDREN

While vaccines against SARS-CoV-2 have been instrumental in decreasing disease severity and mortality, studies in immunocompromised adults have shown suboptimal response to the two-dose series of COVID-19 vaccinations. This has led to the recommendation for additional vaccine doses for immunocompromised patients under the FDA's emergency use authorization. While recent studies have shown promising results regarding the generation of an immune response following a third vaccine dose in immunocompromised patients, the degree and duration of immunity is unclear, especially in pediatric patients.

To further investigate this important issue, under the leadership of nephrologist Heather Morgans, DO, multiple divisions within Children's Mercy, including Nephrology, Rheumatology, Cardiology, Hepatology/GI, Hematology/Oncology and Infectious Diseases, are actively enrolling patients ages 12-21 years of age who are immunocompromised, have received the first two doses of a COVID-19 vaccine, and plan to receive a third vaccine dose, to enroll in our study of vaccine responsiveness.

The primary aim of the study is to determine the vaccine-induced cellular and antibody mediated immune response to the third COVID-19 vaccine dose by measuring CD4/CD8 assays and quantitative SARS-CoV-2 IgG antibody levels to four viral proteins: SARS-CoV-2 Nucleocapsid proteins, receptor binding domain, spike protein subunit 1 and spike protein subunit 2. Testing of serial blood samples at the time of third COVID-19 vaccination and 3-4 weeks post-vaccination will provide important information on the kinetics and robustness of SARS-CoV-2 antiviral responses. The secondary study aim is to determine the duration of SARS-CoV-2 immunity post-vaccination along with the rate of breakthrough COVID-19 infections in this cohort.



# RESEARCH COLLABORATIONS advance understanding, improve outcomes

The Division of Pediatric Nephrology at Children's Mercy is committed to advancing understanding of pediatric kidney disease and improving outcomes for all children. Our faculty are involved in a leadership capacity or are actively participating in a variety of national and international research and quality improvement collaboratives including CKiD, SCOPE, NAPRTCS, NINJA, IPPN, PNRC, CureGN, NEPTUNE and IROC. The evidence of our commitment is seen in academic productivity, with 46 peer-reviewed publications this year.

As a comprehensive Pediatric Nephrology center, our research touches on all aspects of care, from bench to bedside, with an emphasis on better understanding disease progression, treatment of acute kidney injury and chronic kidney disease, and improvements in dialysis and transplant care.

**As one of the two clinical coordinating centers for CKiD, we are leaders of this seminal study which is transforming the care of children with CKD.** For 18 years, CKiD has been the preeminent research study advancing the field of pediatric nephrology, and 2021 was no exception.

Over the years, there have been a variety of different glomerular filtration rate estimating equations—and a number of different variables used in the calculation. **By using data from 928 participants in CKiD, the study team published new estimating equations for individuals with CKD from age 1 through 25 years.**[1]

Another CKiD study demonstrated that some cardiovascular risk factors, specifically high blood pressure and high left ventricular mass index, are influenced by socioeconomic status.[2] The study looked at data from more than 600 children and found that the African American population was disproportionately affected by adverse socioeconomic factors, such as maternal health, food insecurity, home income or insurance status. **This study, which was featured as one of the best articles of the year by the *American Journal of Kidney Diseases*, demonstrated how social determinants of health can adversely affect both children and adults, especially those with CKD.**

Likewise, Children's Mercy is a coordinating center for the International Pediatric Peritoneal Dialysis Network. This year, the IPPN published information regarding key factors that influence the morbidity and mortality of the global pediatric peritoneal dialysis population.[3] In addition to reviewing important clinical management and outcome data collected over the course of the registry pertaining to nutritional status, anemia, CKD-MBD, preservation of kidney function and growth, it also highlighted the significant roles that infection and cardiovascular disease play in terms of patient survival.[4] **The international scope of the registry helped assess risk factors related to the geographic location of the patient and the economic status of various regions of the world** and emphasized the importance of global advocacy for children with ESKD on maintenance dialysis.

## In the Lab

Using transgenic TOPGAL mice, **we demonstrated the importance of transcription factor b-catenin in hyperfiltration-mediated injury**. This is downstream of activation of prostanoid receptor EP2 in hyperfiltration-mediated injury, which is being targeted to delay the progression of chronic kidney disease.[5] The manuscript showing mitigation of hyperfiltration-mediated injury by blocking the EP2 receptor will be submitted for publication in 2022.

These are just a few examples of our involvement in meaningful research that is impacting the lives of patients around the world.

## By the Numbers

**46** peer-reviewed manuscripts

**12** published book chapters

**20** international and national presentations

# NOTABLE JOURNAL PUBLICATIONS

[1] Pierce CB, Muñoz A, Ng DK, **Warady BA**, Furth SL, Schwartz GJ. Age- and sex- dependent clinical equations to estimate glomerular filtration rates in children and young adults with chronic kidney disease. *Kidney Int*. 2021;99(4):948-956. doi: 10.1016/j.kint.2020.10.047. Epub 2020 Dec 8. PMID: 33301749.

[2] Sgambat K, Roem J, Brady TM, Flynn JT, Mitsnefes M, Samuels JA, **Warady BA**, Furth SL, Moudgil A. Social determinants of cardiovascular health in African American children with CKD: An analysis of the Chronic Kidney Disease in Children (CKiD) study. *American Journal of Kidney Diseases*. 2021 Jul; 78(1):66-74.

[3] Borzych-Dużałka D, Schaefer F, **Warady BA**. Targeting optimal PD management in children: What have we learned from the IPPN registry? *Pediatr Nephrol*. 2021 May;36(5):1053-1063. doi: 10.1007/s00467-020-04598-0. Epub 2020 May 27. PMID: 32458134; PMCID: PMC8009785.

[4] Ploos van Amstel S, Noordzij M, Borzych-Duzalka D, Chesnaye NC, Xu H, Rees L, Ha IS, Antonio ZL, Hooman N, Wong W, Vondrak K, Yap YC, Patel H, Szczepanska M, Testa S, Galanti M, Kari JA, Samaille C, Bakkaloglu SA, Lai WM, Rojas LF, Diaz MS, Basu B, Neu A, **Warady BA**, Jager KJ, Schaefer F. Mortality in children treated with maintenance peritoneal dialysis: Findings from the International Pediatric Peritoneal Dialysis Network Registry. *American Journal of Kidney Diseases*. 2021 Sep;78(3): 380-390.

[5] **Srivastava T**, Heruth DP, Duncan RS, Rezaiekhaligh MH, Garola RE, Priya L, Zhou J, Boinpelly VC, Novak J, Ali MF, Joshi T, **Alon US**, Jiang Y, McCarthy ET, Savin VJ, Sharma R, Johnson ML, Sharma M. Transcription factor β-catenin plays a key role in fluid flow shear stress-mediated glomerular injury in solitary kidney. *Cells*. 2021 May 19; 10(5):1253. -74. doi: 10.1053/j.ajkd.2020.11.013. Epub 2021 Jan 5. PMID: 33418013; PMCID: PMC8238816.

**Srivastava T**, Joshi T, Heruth DP, Rezaiekhaligh MH, Garola RE, Zhou J, Boinpelly VC, Ali MF, Alon US, Sharma M, Vanden Heuvel GB, Mahajan P, Priya L, Jiang Y, McCarthy ET, Savin VJ, Sharma R, Sharma M. A mouse model of prenatal exposure to Interleukin-6 to study the developmental origin of health and disease. *Sci Rep*. 2021 Jun 24;11(1):13260.

Muff-Luett M, Sanderson KR, Engen RM, Zahr RS, Wenderfer SE, Tran CL, Sharma S, Cai Y, Ingraham S, Winnicki E, Weaver DJ, Hunley TE, Kiessling SG, Seamon M, Woroniecki R, Miyashita Y, Xiao N, Omoloja AA, Kizilbash SJ, Mansuri A, Kallash M, Yu Y, Sherman AK, **Srivastava T**, Nester CM. Eculizumab exposure in children and young adults: Indications, practice patterns, and outcomes – a Pediatric Nephrology Research Consortium study. *Pediatr Nephrol*. 2021 Aug;36(8):2349-2360.

Ashoor I, **Weidemann D**, Elenberg E, Halbach S, Harshman L, Kula A, Mahan JD, Nada A, Quiroga A, Mahon AR, Smith J, Somers M, Brophy PD. ASPN Workforce Summit Action Groups. The pediatric nephrology workforce crisis: A call to action. *J Pediatr*. 2021 Mar 31:S0022-3476.

Darcy Weidemann, MD, MHS

Abraham AG, Xu Y, Roem JL, Greenberg JH, **Weidemann DK**, Sabbisetti VS, Bonventre JV, Denburg M, **Warady BA**, Furth SL. Variability in CKD biomarker studies: Soluble urokinase plasminogen activator receptor (suPAR) and kidney disease progression in the Chronic Kidney Disease in Children (CKiD) study. *Kidney Med*. 2021 Jun 17;3(5):712-721.e1. doi: 10.1016/j.xkme.2021.04.007. PMID: 34693253; PMCID: PMC8515077.

**VanSickle JS, Srivastava T, Monachino P, Alon US**. Rickets, elevated fibroblast growth factor-23 and mild anemia: Questions. *Pediatr Nephrol*. 2021 Aug;36(8):2299. doi: 10.1007/s00467-021-05000-3. Epub 2021 Mar 1. PMID: 33646397.

**VanSickle JS, Srivastava T, Monachino P, Alon US**. Rickets, elevated fibroblast growth factor-23 and mild anemia: Answers. *Pediatr Nephrol*. 2021 Aug;36(8):2301-2304. doi: 10.1007/s00467-021-05012-z. Epub 2021 Mar 1. PMID: 33646398.

**Chadha V**, **Warady BA**. COVID-19 and the multisystem inflammatory syndrome in children: How vulnerable are the kidneys? *Kidney Int*. 2021 Jul;100(1):16-19. doi: 10.1016/j.kint.2021.03.043. PMID: 34154708; PMCID: PMC8221810.

Davis TK, Bryant KA, Rodean J, Richardson T, **Selvarangan R**, Qin X, Neu A, **Warady BA**. Variability in culture-negative peritonitis rates in pediatric peritoneal dialysis programs in the United States. *Clin J Am Soc Nephrol*. 2021 Feb 8;16(2):233-240. doi: 10.2215/CJN.09190620. Epub 2021 Jan 18. PMID: 33462084; PMCID: PMC7863662.

**Morgans HA**, **Chadha V**, **Warady BA**. The role of carnitine in maintenance dialysis therapy. *Pediatr Nephrol*. 2021 Aug;36(8):2545-2551. doi: 10.1007/s00467-021-05101-z. Epub 2021 Jun 18. PMID: 34143302.

Stenvinkel P, Chertow GM, Devarajan P, Levin A, Andreoli SP, Bangalore S, **Warady BA**. Chronic inflammation in chronic kidney disease progression: Role of Nrf2. *Kidney Int Rep*. 2021 May 4;6(7):1775-1787. doi: 10.1016/j.ekir.2021.04.023. PMID: 34307974; PMCID: PMC8258499.

Flynn JT, Carroll MK, Ng DK, Furth SL, **Warady BA**. Achieved clinic blood pressure level and chronic kidney disease progression in children: A report from the Chronic Kidney Disease in Children cohort. *Pediatr Nephrol*. 2021 Jun;36(6):1551-1559. doi: 10.1007/s00467-020-04833-8. Epub 2020 Nov 16. PMID: 33200315; PMCID: PMC8087620.

## Genomic Answers for Kids Advances Rare Disease Research

The Children's Mercy Research Institute has released more than 2,300 pediatric rare disease genomes through its Genomic Answers for Kids (GA4K) program, which makes it one of the largest pediatric rare disease whole genomic datasets ever publicly shared.

To date, more than 3,700 patients have enrolled in the program, which has resulted in more than 18,000 new genomic analyses and more than 600 genetic diagnoses. In addition, the program has advanced research genomic analyses for children of 350 families with more common childhood diseases: cerebral palsy and Down syndrome.

The full pediatric data repository is shared in a real-time web interface through a comprehensive process, which gives researchers and clinicians low-barrier access to processed data with disease prioritized genetic changes.

"Giving access to our data allows researchers to link their own genetic findings so they can accept or reject hypotheses on their gene discoveries," said Tomi Pastinen, MD, PhD, Director, Genomic Medicine Center, Children's Mercy Kansas City. "Data sharing is the only way we'll make headway in the quicker delivery of results that are non-diagnostic today."

The GA4K program has helped hundreds of kids, like Celia, find a genetic diagnosis.

# MEET THE TEAM

## LEADERSHIP

**Bradley A. Warady, MD**
Division Director, Pediatric Nephrology
Medical Director, Dialysis and Transplantation

## MEDICAL FACULTY

**Mohammed Farhan Ali, MD**
Nephrologist

**Uri S. Alon, MD**
Medical Director, Bone and Mineral Disorders Clinic

**Nathan Beins, MD**
Nephrologist

**Douglas L. Blowey, MD**
Medical Director, Children's Mercy Hospital Kansas
Director, Hypertension Clinic

**Vimal Chadha, MD**
Medical Director, Acute Kidney Injury Program

**Nicholas Herrera, MD**
Nephrologist

**Heather Morgans, DO**
Nephrologist

**Sandeep Riar, MD**
Nephrologist

**Nisha Singh, MD**
Nephrologist

**Tarak Srivastava, MD**
Director, Nephrology Research Laboratory

**Judith VanSickle, MD**
Nephrologist

**Darcy Weidemann, MD, MHS**
Associate Director, Pediatric Nephrology Fellowship Program
Medical Director, Quality Improvement

**Laurel K. Willig, MD**
Medical Director, Center for Pediatric Genomic Medicine
Director, Pediatric Nephrology Fellowship Program

## FELLOWS

**Ana Cortez, DO**

**Katherine Kurzinski, MD**

**Benjamin Spector, MD**

Children's Mercy KANSAS CITY

KU SCHOOL OF MEDICINE The University of Kansas

UMKC School of Medicine

in academic affiliation with

**LEARN MORE ABOUT THE DIVISION OF PEDIATRIC NEPHROLOGY.**

**Bradley A. Warady, MD**
Division Director, Pediatric Nephrology
bwarady@cmh.edu • (816) 302-3010

**childrensmercy.org/nephrology**

**FOR CONSULTS, ADMISSIONS OR TRANSPORT CALL:**
**1 (800) GO MERCY**
**1 (800) 466-3729**



22-NEP-2556 01/22