

About the Division

The Division of Pediatric Nephrology at Children's Hospital of Pittsburgh of UPMC provides a full range of services for the evaluation and management of children with simple or complex nephrologic or urologic disorders.

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New Guidelines for the Care of Pediatric High Blood Pressure and Hypertension



Yosuke Miyashita, MD, MPH, assistant professor and director of the Pediatric Hypertension Clinic at Children's Hospital of Pittsburgh of UPMC, was invited to speak at the American Society of Nephrology's 2017 annual meeting — Kidney Week — in New Orleans, Louisiana, on "Advances in Evidence-Based Care of Pediatric Hypertension."

The bulk of his presentation highlighted the American Academy of Pediatrics (AAP) Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents, published on September 1, 2017.

The high blood pressure (BP) guidelines for pediatrics was last updated in 2004, and the 2017 AAP guidelines were based on a comprehensive review of almost 15,000 published articles between 2004 and 2016 to formulate recommendations that provide state-of-the-art evidence-based practice.

Who Should Be Screened?

Dr. Miyashita's presentation on the new guidelines focused on four major areas that every primary care pediatric health care provider and pediatric hypertension (HTN) specialist should be familiar with. These include:

- BP screening
- New diagnostic criteria of HTN
- Wider usage of ambulatory blood pressure monitoring (ABPM)
- Greater emphasis on primary hypertension and its treatment

Since the 2004 guidelines were published, numerous large, long-term longitudinal studies have been published to investigate BP tracking from childhood to young adulthood. "The new guidelines for screening are based on much firmer evidence of the need to screen for high BP in childhood, as these studies showed not only strong BP tracking from childhood to young adulthood, but BP-related target organ changes have also been detected in high BP cohorts," says Dr. Miyashita.

The new 2017 guidelines now recommend BP screening thusly:

- BP should be measured **annually** in children and adolescents ≥ 3 years old
- BP should be checked in all children and adolescents ≥ 3 years old at **every health care encounter** if they have obesity, are taking medications known to increase BP, have renal disease, a history of aortic arch obstruction or coarctation, or diabetes.

New Guidelines

(Continued from Page 1)

- BP should be checked in all children < 3 years old at every health care encounter if they have special circumstances such as a history of prematurity, small for gestational age, very low birthweight, neonatal complication, umbilical artery line use, congenital heart disease, recurrent urinary tract infection, renal disease, and history of solid organ and bone marrow transplant.

New Hypertension Diagnosis Definitions

Traditionally, a pediatric diagnosis of HTN (age 1–17 years old) was defined as BP readings of \geq 95th percentile for age, gender, and height at three different visits. The percentile values were based on approximately 63,000 children and adolescents from the United States. However, Dr. Miyashita points out, “For the new 2017 guideline, the task force took out the BP measurements from overweight and obese children and adolescents because we know that they tend to have higher BP. Thus, the newly created 2017 normalized data table has BP percentile values approximately 2 to 3 mm Hg lower than the 2004 table.”

In addition, BP categories and staging also were updated in the 2017 guideline shown in the tables below. The main reason for this

change is to simplify the HTN diagnosis and to align the definitions for adolescents with the newly published adult HTN definitions. The main differences are highlighted in Table 1 and Table 2.

The Wider Usage of Ambulatory Blood Pressure Monitoring of Ambulatory Screening

The Nephrology Clinic at Children’s Hospital of Pittsburgh of UPMC began using 24-hour ABPM monitoring in 2012 (chp.edu/our-services/nephrology/programs-services/hypertension-clinic). Since the publication of the 2004 guideline, pediatric ABPM studies became one of the more actively published topics, and the 2017 guideline includes more extensive and wider use of ABPM that is more evidence-based. In addition to the traditional indications of ABPM, usage such as white coat hypertension evaluation and HTN treatment efficacy assessment, the new guideline recommends uncovering potential masked HTN in the pediatric patient population with the following listed conditions, as well as more aggressive HTN treatment to preserve renal function in children and adolescents with chronic kidney disease.

These conditions include:

- Chronic kidney disease
- Diabetes mellitus
- Solid organ transplant

- Obesity
- Obstructive sleep apnea
- Post coarctation of aorta repair
- Genetic syndromes such as Turner syndrome and Neurofibromatosis type II
- Former premature neonates

A Greater Emphasis on Primary HTN Evaluation and Treatment

Perhaps one of the more revolutionary changes in the new 2017 guideline compared to the 2004 version is the shift of emphasis to primary HTN from secondary HTN (specific pathology that causes HTN) based on evidence that has been published in the last 12 years. The updated guideline specifically states that patients \geq 6 years old do not require an extensive evaluation for secondary causes of HTN if they have family history of HTN, are overweight or obese, and/or do not have history or physical examination findings suggestive of a secondary cause of HTN. “Traditionally, in pediatrics, providers often had their hypertensive patients undergo extensive medical testing that included blood and urine tests, as well as one or more imaging studies. As we have found out, there are high rates of primary HTN among older children and adolescents. The new guideline will, I hope, change practice to place more emphasis on revising the lifestyle contributions to

Continued on Page 5

TABLE 1: 2004 Guidelines
BP Categories and Hypertension Staging — Children Age 1 to 17

Normal	< 90th percentile for age, gender, height
PreHTN	90th – 95th percentile or > 120/80
Stage I HTN	\geq 95th – 99th percentile + 5 mm Hg
Stage II HTN	\geq 99th percentile + 5 mm Hg

TABLE 2: 2017 Guidelines
BP Categories and Hypertension Staging

	Ages 1 to 12	Ages \geq 13
Normal	< 90th percentile	< 120/80
Elevated BP	90th – 95th percentile or \geq 120/80 – 95th percentile (whichever is lower)	120-129/< 80
Stage I	95th – 99th percentile + 12 mm Hg, or 130-139/80-89 (whichever is lower)	130-139/80-89
Stage II	\geq 99th percentile + 12 mm Hg, or \geq 140/90 (whichever is lower)	\geq 140/90

The Impact of Pretransplant Psychosocial Risk Factors and Posttransplant Correlations



Christina R. Nguyen, MD, (left) assistant professor of medicine and medical director of pediatric kidney transplant at Children's Hospital of Pittsburgh of UPMC, is conducting new research on the role of pretransplant psychosocial risk factors on long-term renal transplantation outcomes. Dr. Nguyen, along with her colleague and study collaborator **Beth Logan, PhD**, are working to identify in those patients deemed at high risk for complications and poor outcomes what pretransplant factors are actually the most responsible or factor heavily in posttransplant outcomes.

"In our program, we know these children perform significantly better and have better outcomes with a transplant as opposed to remaining on long-term renal replacement therapy."

There are a number of known factors that drive declines in patient health posttransplant and contribute to suboptimal outcomes in the one to three years following transplantation. These factors include patients not following up with care and appointments, lack of adherence to medication regimens and dietary plans, and others. "In our program, we know these children perform significantly better and have better outcomes with a transplant as opposed to remaining on long-term renal replacement therapy. Some of the behavioral and noncompliance issues don't disappear completely, but they are not problematic for our program and the patients in the posttransplant environment," says Dr. Nguyen.

In discussions with psychologists and social workers who are part of the transplant team, Dr. Nguyen became immediately curious to find out exactly which psychosocial high-risk behaviors actually matter in terms of a patient's posttransplant outcome and long-term health. There are many reasons why someone could be deemed too high risk for a transplant, but without knowing for sure which factors are more important

in influencing negative outcomes, patients who could benefit from a transplant and successfully negotiate the posttransplant world may be getting left behind, so we decided to investigate this in detail within the confines of our own transplantation program at Children's Hospital," says Dr. Nguyen.

Dr. Nguyen began the study looking at all kidney transplants at Children's Hospital over a five-year period, from 2009 to 2014 (70 total cases). The study team reviewed social work assessments, psychology assessments, and nephrology assessments at the time of the patients' transplant evaluation. Assessments were scored using several instruments — the Pediatric Transplant Rating Instrument and the Stanford Integrated Psychosocial Assessment for Transplant — and then these score results were analyzed in comparison to how well the patient fared after transplant.

"We looked at patient posttransplant results at one and three years from the transplant, as these are typically the most used time-frames to assess outcomes," says Dr. Nguyen. In the posttransplant period, Dr. Nguyen's team examined if patients had suffered rejection, if they lost their kidney, or if they died. Other factors considered to be high-risk behaviors were measured, including missing scheduled labs, and too much variability in their immunosuppression drug levels.

Continued on Page 4

New Faculty Profile — Paul Fadakar, MD



Paul Fadakar, MD, is the Division of Pediatric Nephrology's newest faculty member, having joined the Division in August as an Assistant Professor of Pediatrics. Dr. Fadakar completed his fellowship training at Children's Hospital of Pittsburgh of UPMC, following his general pediatrics residency and medical school training at Connecticut Children's Medical Center and the University of Connecticut School of Medicine, respectively.

"My first-ever visit to Pittsburgh was for my fellowship interview, and I was immediately impressed with the program, the hospital, and with Dr. Bates, the division chief. His passion for the training program at Children's was so clear and focused, it was a big reason I wanted to come here to train, and now I find myself privileged to be part of the Division faculty," says Dr. Fadakar.

The large, pioneering, and internationally respected transplant programs at Children's Hospital and the broader UPMC system were

another attracting feature, and for his fellowship research Dr. Fadakar chose to become involved in translational work studying transplant immunology at the Thomas E. Starzl Transplantation Institute. Dr. Fadakar's work involved ongoing projects in the lab of Dr. Diana Metes investigating the role of T follicular helper cells in antibody-mediated rejection in renal transplant recipients.

Clinically, Dr. Fadakar retains his interest in transplantation but is still active as a general nephrologist as well. Another area of interest

for Dr. Fadakar is in patients with idiopathic nephrotic syndrome. "These patients can be very challenging to treat because some of them do not respond to conventional therapies," says Dr. Fadakar.

With respect to future work, Dr. Fadakar sees himself being involved in outcomes research and quality improvement initiatives related to various aspects of nephrology and kidney transplantation.

Impact of Pretransplant Psychosocial Risk Factors (Continued from Page 3)

"What we found was that the patients who had high-risk factors pretransplant actually outperformed our patients who were never flagged as having risk factors to begin with. This was quite unexpected."

Part of the reason driving the outcome was significant psychosocial interventions for the high-risk patients prior to and immediately after transplant. Patients had lower rates of rejection, fewer missed labs, and less immunosuppression variability. "Our transplant psychologist and social worker performed assessments frequently before and after surgery. Patient interventions would vary, of course, depending on the need, but placement in therapy, social support services, community services, and financial support services are routinely recommended and provided."



Dr. Nguyen and her study colleague **Beth Logan, PhD**, who is the transplant psychologist in the Division, are currently preparing a manuscript for publication with the

detailed findings of their initial study.

Another line of research Drs. Nguyen and Logan are preparing to pursue — one that has not garnered much attention or study to date — is the prevalence of posttraumatic stress disorder (PTSD) in pediatric renal transplant patients and their family members.

References and Further Reading

Dr. Nguyen has published numerous works on renal failure and pediatric kidney transplantation. Below is a selection of past papers for further reading.

Nguyen C, Shapiro R. Is Routine Ultrasound Necessary Following Renal Transplantation in Children. *Pediatr Transplant*. 2012; 16(6): 523-524.

Nguyen C, Shapiro R. Alemtuzumab Induction in Pediatric Kidney Transplantation. *Pediatr Transplant*. 2013; 17(4): 319-320.

Nguyen C, Shapiro R. Progressive Multifocal Leukoencephalopathy (PML) After Transplantation. *Pediatr Transplant*. 2011; 15(2): 126-127.

Nguyen C, Shapiro R. New Immunosuppressive Agents in Pediatric Transplantation. *Clinics (Sao Paulo)*. 2014; 69: 8-16.

Nguyen C, Shapiro R. Renal Failure and Transplantation Following Nonrenal Solid Organ Transplantation. *Curr Opin Organ Transplant*. 2012; 17(5): 525-530.

New Guidelines

(Continued from Page 2)

primary HTN, and on preventing our patients from undergoing unnecessary medical tests. This also may have a positive effect on more cost-effective practice as a whole,” says Dr. Miyashita. The new guideline provides a clear table for primary care providers on the timing of specific BP measurements, such as lower extremity BP measurements, as well as when to institute treatments and referral to a HTN specialist (Table 3). At all stages (elevated BP, stage I and II HTN), lifestyle modification counseling is a highly important aspect.

Insert Modified Stage-Specific Evaluation Recommendations

As Dr. Miyashita points out, the changes in treatment or therapy modalities between the old and new guidelines do not vary significantly with lifestyle modifications and first line pharmacologic interventions. However, several new additions are important to highlight. The new guidelines specifically call out adoption of the DASH diet and its variants, as well as stress reduction within the lifestyle modifications. Both Dr. Miyashita and Jessica Kirin, RD, LD, a registered dietitian who works extensively with patients in the Division, underscore how clearly the new guideline emphasizes lifestyle interventions,

regardless of underlying cause or level of HTN; this emphasis comes from an understanding in the literature (for both adults and children) of the importance and effectiveness these lifestyle changes can have in regulating and reducing BP.

“In our program, the DASH diet, and variants to it that we have adapted, have been part of our standard course of intervention. It is one of the interventions specifically studied in children and has been shown to be effective. But remember, everything we do needs to be, and is, individualized and continually reinforced. By making small, incremental changes, we can increase the likelihood of adoption and success with lifestyle changes,” says Ms. Kirin.

Future Needs and Challenges

Widespread adoption and acceptance of the new guidelines will take time to disseminate and propagate throughout the health care continuum. However, Dr. Miyashita is optimistic that this new guideline will lead to better detection and proper diagnosis of HTN in pediatrics, and be a foundation for better long-term longitudinal studies to eventually show that detecting and improving HTN starting in childhood will have a direct impact on reducing cardiovascular burden that afflicts many Americans. As for the more immediate future, Dr. Miyashita anticipates,

“There may be a big increase in demand of ABPM usage due to the new 2017 guideline recommending its wider use. Our division offers one of the largest ABPM programs in the country, and plans are in progress to expand it even further. This puts our program ahead of the curve and in a good position to meet expected demand.”

Dr. Miyashita says, “We have begun the discussion with our colleagues at the Heart Institute at Children’s Hospital of Pittsburgh of UPMC to create a collaborative and streamlined program for HTN and preventive cardiology care that includes clinical, research, and educational components. I am excited that we are entering a new phase in our approach to state-of-the-art care for children and adolescents in western Pennsylvania that could make positive long-term impacts in their health.” The Heart Institute efforts in this collaboration will be led by new recruit Brenda Mendizabal, MD, who recently joined the Institute after completing a unique, preventive cardiology/hypertension fellowship offered by Cincinnati Children’s Hospital Medical Center and the American Heart Association.

References and Further Reading

Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics*. 2017; 140(3): e20171904.

TABLE 3: Stage-Specific Evaluation Recommendations

BP Category	BP Measurement Scale	Lifestyle Counseling	UE and LE BPs	ABPM	Diagnostic Evaluation	Initiate Treatment	Consider Referral
Elevated BP	Initial	x					
	2nd Measurement in 6 months	x	x				
	3rd Measurement in 12 months	x		x	x		x
Stage I HTN	Initial	x					
	2nd Measurement in 1 to 2 Weeks	x	x				
	Third Measurement in 3 months	x		x	x	x	x
Stage II HTN	Initial	x	x				
	2nd Measurement in 1 Week or Refer	x		x	x	x	x

Kidney Week 2017 — Division Recap

The Division of Pediatric Nephrology offered numerous presentations, posters, abstracts, and oral presentations at last year's American Society of Nephrology annual meeting. Highlights from the meeting include:

Presentations

- Recent Advances That Should Drive Improvements in Evidence-Based Care of Children With Hypertension. *Yosuke Miyashita.*

Posters

- Deletion of Sirtuin-5 (SIRT5) Protects Mice Against Ischemia-Reperfusion Kidney Injury. *Eric S. Goetzman; Katherine V. Maringer; Sivakama S. Bharathi; Elina Mukherjee; Sunder Sims-Lucas.*
- Hypoxia-Regulated MicroRNA-210 Expression and Role in Nephrogenesis. *Shelby L. Hemker; Andrew S. Clugston; Yu Leng Phua; Jacqueline Ho; Dennis Kostka.*
- AKI Associated with Antibiotic Exposure in Critically Ill Children. **Emily L. Joyce;** *Priyanka Priyanka; John A. Kellum.*
- Anks6^{-/-} Mice Have Laterality Defects and Develop Renal Cystic Disease. **Rannar Airik;** *Merlin Airik; Nathan Allen Herdman.*
- The Cure Glomerulonephropathy (CureGN) IgA Nephropathy and IgA Vasculitis Pediatric Cohort. *Agnieszka Swiatecka-Urban, et al.*

- Mild Chronic Prolonged Hyponatremia at Admission Is Associated with Long Term Mortality in Patients with Hip Fracture Repair. *Juan Carlos Ayus; Nora Fuentes; Michael L. Moritz; Alan S. Go; Armando Luis Negri.*

Oral Abstracts

- Bioengineering a Kidney in Secondary Lymphoid Tissues: A LTBR Dependent Pathway for Ectopic Organogenesis. *Maria Giovanna Francipane; Bing Han; Leif Oxburgh; Sunder Sims-Lucas; Carlton M. Bates; Eric Lagasse.*
- Loss of Dicer Activity in the Peri-Wolffian Duct Stroma Leads to Increased Rates of Vesicoureteral Reflux. *Melissa J. Anslow; Jacqueline Ho; Carlton M. Bates; Andrew J. Bodnar; Sunder Sims-Lucas.*
- HIF Regulation of Nephron Progenitor Metabolic State Mediates Cell Fate Decisions. *Anjana Murali; Kasey Cargill; Elina Mukherjee; Zubaida R. Saifudeen; Sunder Sims-Lucas.*
- Endothelial Marker Expressing Stromal Cells Are Important Regulators of Recovery From AKI. *Katherine V. Maringer; Elina Mukherjee; Sunder Sims-Lucas.*



About Children's Hospital of Pittsburgh of UPMC

Regionally, nationally, and globally, 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. With generous community support, Children's Hospital has fulfilled this mission since its founding in 1890. Children's is named consistently to several elite lists of pediatric hospitals, including ranking No. 9 in the prestigious *U.S. News & World Report* annual Honor Roll of America's Best Children's Hospitals for 2017-2018 and ranking 10th among children's hospitals and schools of medicine in funding for pediatric research provided by the National Institutes of Health (FY2016).