#### RENAL-ELECTROLYTE RESEARCH

# UPDATE

#### **Inside This Edition**

- 1 Message From the Chief
- 2 Fostering Effective Communication Skills for Addressing Serious Illness
- 3 Recent Publications from Division Faculty
- 4 Division Welcomes New Clinical Director
- New Study Seeks to Optimize Chronic Kidney Disease Care
- 6 KO8 Grant Awarded to Chethan Puttarajappa, MD, MS
- 7 Identical Twin Kidney Transplants
  Warrant Gene Sequencing

#### Dear Colleagues,

I am pleased to share with you updates and news from the Renal-Electrolyte Division at UPMC. To begin, it is an honor to announce that **Duncan Johnstone**, **MD**, **PhD**, has joined our Division as its new clinical director and associate division chief. In addition to his research, administrative, and clinical duties, Dr. Johnstone will be leading efforts with faculty and the UPMC Health Plan to develop new models of care for patients with chronic kidney disease. You can read more about Dr. Johnstone further on in this update.

Our Division faculty have been busy with new research, clinical programs, and grants across many of our clinical areas.

Manisha Jhamb, MD, MPH, has new funding from the National Institutes of Health (NIH) (R01DK116957) to develop new models of care for chronic kidney disease patients, including the use of electronic consults for consults that has the potential to dramatically expand our geographic reach to patients in distant regions. Dr. Jhamb also leads a new NIH grant (1U01DK123812) related to pain reduction and opioid medication safety in end-stage renal disease.

**Chethan Puttarajappa, MD, MS**, a transplant nephrologist in our Division, secured a new NIH K08 career development award (1K08DK119576) that will allow him to continue his studies on the utility of virtual crossmatch in deceased-donor kidney transplantation. Several other faculty members also have secured new R01 grants from the NIH recently, and we will be writing more about those in the future.

Please join me in congratulating **Paul M. Palevsky, MD**, who was named president-elect of the National Kidney Foundation this past November. Dr. Palevsky will assume the role of president in October 2020. Dr. Palevsky is the second faculty member from our Division to hold this distinguished position. **Beth Piraino, MD**, previously served as president of the National Kidney Foundation in 2012-2014. Along similar lines, **Linda Fried, MD, MPH**, was appointed to co-chair the programming committee for the American Society of Nephrology annual meeting that will be held in the fall.

Faculty also have been hard at work on developing new clinical centers and subspecialty clinics for our patients. Dr. Johnstone is in the process of establishing a Center for Glomerular Disorders that will help manage this patient population across all of western Pennsylvania. Additionally, Helbert Rondon, MD, MS, FACP, FASN; Evan C. Ray, MD, PhD; and Cary Boyd-Shiwarski, MD, PhD, continue their work to expand our expertise in various electrolyte disorders with their research into hyponatremia, magnesium, and potassium-related research, respectively.

I welcome your inquiries and discussions about these new advances in our Division, and I look forward to hearing from our colleagues around the nation and connecting with you at upcoming conferences and seminars.



Thomas R. Kleyman, MD
Chief, Renal-Electrolyte Division
Sheldon Adler Professor of Medicine
Professor of Cell Biology, Pharmacology, and Chemical Biology





## Fostering Effective Communication Skills for Addressing Serious Illness

Chronic kidney disease (CKD) and end-stage renal disease (ESRD) frequently occur in conjunction with serious conditions such as cancer, cerebrovascular disease, diabetes, heart disease, and liver failure. Although dialysis can improve CKD symptoms such as uremia and fluid overload, the increasing age of patients initiating renal replacement therapy means that many also have comorbidities such as dementia and frailty that are difficult to treat and compromise their quality of life.



Amar D. Bansal, MD, FASN, assistant professor of medicine in the Renal-Electrolyte Division and Section of Palliative Care and Medical Ethics at the University of Pittsburgh

School of Medicine, and associate program director of the Nephrology Training Program, is working at the intersection of nephrology and palliative care to assist his fellow physicians in developing the necessary communication skills to have effective conversations with their peers and with patients and families about just such challenging clinical scenarios. Dr. Bansal's research interests are in communication strategies, directed interventions, and the epidemiology of patients with advanced CKD who opt for renal supportive care.

Dr. Bansal graduated from the New York University School of Medicine in 2010. He completed his residency in internal medicine and fellowships in nephrology and palliative care at the Hospital of the University of Pennsylvania. He joined the University of Pittsburgh School of Medicine in 2017 as an assistant professor of medicine with subspecialties in nephrology and palliative care.

## Talking About Prognosis and Advance Care Planning

Dr. Bansal has developed a new curriculum, with mentorship from colleagues Julie Childers, MD, and Rene Claxton, MD, *Gl Talk*, to teach gastroenterology fellows how to have conversations about goals of care and other clinical scenarios relevant to their practice. In April 2019, he and his colleagues hosted the first one-day communication workshop on this topic.

"Many gastroenterology patients have a heavy symptom burden and are not able to obtain effective treatments, such as liver transplants, whether because of comorbidities or the general shortage of donor organs," says Dr. Bansal. "The goal of this curriculum is to help their physicians become comfortable having difficult conversations with patients and their families about topics such as prognosis, advance care planning, and the end of life."

Dr. Bansal's *GI Talk* curriculum is based on VitalTalk, an evidence-based teaching method that equips clinicians to navigate difficult conversations with patients. "Whether it's serious illness, end-of-life care, or other challenging decision-making, our mission is to teach doctors how to have those conversations effectively," says Dr. Bansal.

#### **Teaching Relevant Clinical Cases**

Dr. Bansal and his colleagues worked for several months to compile clinical cases that were relevant for Gl fellows. The cases were reviewed by gastroenterology faculty to ensure that the content reflected scenarios that gastroenterologists commonly face. To protect patient privacy, professional actors played the roles of standardized patients, and workshop participants took part in encounters with them.

The first case concerned a patient with end-stage liver disease who was no longer a transplant candidate and was dealing with the emotions that this created for his family.

VitalTalk was co-developed by Robert M. Arnold, MD, FAAHPM, Distinguished Service Professor of Medicine, chief of the Section of Palliative Care and Medical Ethics at the University of Pittsburgh School of Medicine, and medical director of the UPMC Palliative and Supportive Institute.

#### **REMAP**

**Reframe** why the status quo isn't working.

**Expect emotion**, respond with empathy.

Map out what's important.

Align with patient values.

Plan to match values.

"We emphasized engaging the patient and family in a meaningful way so that family members didn't feel abandoned or guilty because of the knowledge that their loved one had a short time to live," says Dr. Bansal.

The second case involved an elderly woman with dementia that limited her quality of life and focused on helping the fellows have a conversation with the woman's daughter about whether or not to proceed with the insertion of a feeding tube.

## A Framework for Goals-of-Care Conversations

Workshop participants were introduced to REMAP, a framework for goals-of-care conversations that was developed by University of Pittsburgh palliative care physicians (see box). Two presentations explored using the framework to enable these conversations with patients and families.

In a pre- and post-survey, participants described the workshop as a positive experience. They said that after completing it they felt more confident in carrying out a variety of conversations on specific topics that they are likely to encounter in clinical practice. All seven participating fellows said that they would recommend the training to others and reported feeling strongly that it should be a required part of fellowship training.

Dr. Bansal is optimistic that the *GI Talk* workshop will become an annual event. An abstract he submitted on the overall curriculum design and results of the initial workshop was accepted for presentation at the American Academy of Hospice and Palliative Medicine Annual Assembly in March 2020. He and his colleagues also hope to collaborate on this education model with other institutions.

"I have spoken with potential partners from Massachusetts General Hospital in Boston and the University of Texas Southwestern in Dallas," says Dr. Bansal. "There is national interest in moving the needle on this topic."

#### One Fellow's Experience: "Fluency in Goals-of-Care Conversations Requires Practice"

"Overall I would say it was a positive experience," says Weston Bettner, MD, a third-year gastroenterology fellow in the Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh School of Medicine and one of the seven fellows who participated in the first *GI Talk* workshop.

Dr. Bettner says that he would recommend this training to his colleagues and peers. Role playing in front of one's peers does inherently feel awkward.

"But, as with any skill set, fluency in goals-of-care conversations requires practice.
End-of-life discussions can be particularly challenging. Practicing in a 'safe' environment — where 'failure' simply means restarting the simulated scenario — is ideal before having to do it in the real world, where there are no 'do overs,'" says Dr. Bettner.

Prior to attending the *GI Talk* workshop, Dr. Bettner's formal training in palliative care in medical school and residency was limited.

"In medical school, we had standardized patient interactions, and one session focused on breaking bad news, which involved informing a patient about a new cancer diagnosis," says Dr. Bettner. "In residency, palliative care training was essentially on-the-job training."

Dr. Bettner indicates he learned that while each palliative care discussion is unique, these conversations can be framed in a systematic way, with the aid of tools such as the **NURSE** statements for articulating empathy (**N**aming, **U**nderstanding, **R**especting, **S**upporting, **E**xploring).

"I found it helpful almost immediately in my clinical practice to apply the tools and teaching learned in the workshop in conversations with my patients and their family members," says Dr. Bettner.

#### **Further Reading**

About VitalTalk. https://www.vitaltalk.org/.

Arnold RM, Back AL, Baile WF, Edward KA, Tulsky JA. The Oncotalk/Vitaltalk Model. In Kissane DW, Bultz BD, Butow PN, Bylund CL, Noble S, Wilkinson S, eds. Oxford Textbook of Communication in Oncology and Palliative Care, 2nd ed. 2017. Oxford, UK: Oxford University Press.

Bansal AD, Leonberg-Yoo A, Schell JO, Scherer JS, Jones CA. Ten Tips Nephrologists Wish the Palliative Care Team Knew About Caring for Patients With Kidney Disease. *J Palliat Med.* 2018 Apr; 21(4): 546-551. doi: 10.1089/jpm.2018.0087.

Childers JW, Back AL, Tulsky JA, Arnold RM. REMAP: A Framework for Goals of Care Conversations. *J Oncol Pract.* 2017 Oct; 13(10): e844-e850. doi: 10.1200/JOP.2016.018796.

Responding to Emotion: Articulating Empathy Using NURSE Statements. 2019. VitalTalk. https://www.vitaltalk.org/guides/responding-to-emotion-respecting/.

## **Recent Publications from Division Faculty**

Researchers in the Renal-Electrolyte Division are engaged in a diverse array of basic science, translational, and clinical investigations on numerous aspects of kidney development and disease. Below is a selection of recent high-impact publications from faculty members.

Gliozzi ML, Espiritu EB, Shipman KE, Rbaibi Y, Long KR, Roy N, Duncan AW, Lazzara MJ, Hukriede NA, Baty CJ, Weisz OA. Effects of Proximal Tubule Shortening on Protein Excretion in a Lowe Syndrome Model. *J Am Soc Nephrol.* 2020; 31: 67-83.

Lam DY, Scherer JS, Brown M, Grubbs V, Schell JO. A Conceptual Framework of Palliative Care Across the Continuum of Advanced Kidney Disease. *Clin J Am Soc Nephrol.* 2019; 14: 635-641.

Dalghi MG, Clayton DR, Ruiz WG, Al-Bataineh MM, Satlin LM, Kleyman TR, Ricke WA, Carattino MD, Apodaca G. Expression and Distribution of PIEZO1 in the Mouse Urinary Tract. *Am J Physiol Renal Physiol.* 2019, 317: F303-F321.

Mehran R, Dangas GD, Weisbord SD. Contrast-Associated Acute Kidney Injury. *N Engl J Med.* 2019; 380: 2146-2155.

Cherukuri A, Mehta R, Sharma A, Sood P, Zeevi A, Tevar AD, Rothstein DM, Post-transplant Donor Specific Antibody Is Associated With Poor Kidney Transplant Outcomes Only When Combined With Both T-cell-mediated Rejection and Non-adherence. *Kidney Int.* 2019, 96: 202-210.

Ong J, Kinsman BJ, Sved AF, Rush BM, Tan RJ, Carattino MD, Stocker SD. Renal Sensory Nerves Increase Sympathetic Nerve Activity and Blood Pressure in 2-kidney 1-clip Hypertensive Mice. *J Neurophysiol.* 2019; 122: v358-367.

### **Division Welcomes New Clinical Director**

The Renal-Electrolyte Division is pleased to welcome our newest faculty member, Director of Clinical Services and Associate Division Chief, **Duncan Johnstone**, **MD**, **PhD**. Dr. Johnstone will work with Divisional and Department of Medicine leadership to oversee the various and expanding clinical activities of the Renal-Electrolyte Division.



Dr. Johnstone completed his undergraduate studies at Harvard University. He earned his medical and PhD degrees at the University of Washington in 2001. Dr. Johnstone completed his residency in internal medicine at Northwestern University, followed by a fellowship in nephrology at the University of Michigan.

Prior to joining the University of Pittsburgh,

Dr. Johnstone held appointments at Temple University. While at Temple University, Dr. Johnstone was an associate professor of medicine, and the Nephrology Fellowship Program director and director of the Outpatient Nephrology Clinic. Dr. Johnstone also served as the chair of the Medication Practices Subcommittee at Temple University Hospital. He joined Temple University in 2012 after previously holding appointments at the University of Pennsylvania. In 2019, Dr. Johnstone was a NephCure® Kidney International-nominated "Nephrotic Syndrome Specialist," and in both 2018 and 2019 he earned a Faculty Teaching Award from Temple University for his educational work in the Nephrology Fellowship Program, where he served as the program director.

#### **Clinical Interests**

Dr. Johnstone's clinical interests focus on glomerular and cystic diseases such as Alport syndrome, FSGS, ADPKD, and other conditions. He also treats patients with genetic and hereditary forms of kidney disease, and drug-induced kidney disease. Additionally, Dr. Johnstone has interests in peritoneal dialysis and improving patient safety in the treatment of renal disorders and injuries.

#### **Research Focus**

During Dr. Johnstone's medical training, his research interests first focused on studies of ion channels in model organisms. His studies then transitioned to examining podocyte biology and the identification of gene variants associated with focal segmental glomerulosclerosis (FSGS). His past research was supported by grants from the National Institutes of Health, the American Heart Association, and NephCure Kidney International.

Dr. Johnstone's research priorities now include clinical studies of FSGS, uremic pruritus, and rare diseases.

A sample of Dr. Johnstone's past published research is included below.

- Canetta PA, et al. CureGN Consortium. Health-related Quality of Life in Glomerular Disease. Kidney Int. 2019 May; 95(5): 1209-1224.
- Selewski DT, et al. CureGN Consortium. Clinical Characteristics and Treatment Patterns of Children and Adults With IgA Nephropathy or IgA Vasculitis: Findings From the CureGN Study. Kidney Int Rep. 2018 Aug 3; 3(6): 1373-1384.
- Trachtman H, et al. DUET Study Group. DUET: A Phase 2 Study Evaluating the Efficacy and Safety of Sparsentan in Patients With FSGS. *J Am Soc Nephrol.* 2018 Nov; 29(11): 2745-2754.

- Singh N, Johnstone DB, Martin KA, Tempera I, Kaplan MJ, Denny MF.
   Alterations in Nuclear Structure Promote Lupus Autoimmunity in a Mouse Model. Dis Model Mech. 2016 Aug 1; 9(8): 885-897.
- Gipson DS, et al. Complete Remission in the Nephrotic Syndrome Study Network. *Clin J Am Soc Nephrol.* 2016 Jan 7; 11(1): 81-89.
- Sorrell SL, Golder ZJ, Johnstone DB, Frankl FEK. Renal Peroxiredoxin 6 Interacts With Anion Exchanger 1 and Plays a Novel Role in pH Homeostasis. Kidney Int. 2016 Jan; 89(1): 105-112.
- George B, Verma R, Soofi AA, Garg P, Zhang J, Park TJ, Giardino L, Ryzhova L, Johnstone DB, Wong H, Nihalani D, Salant DJ, Hanks SK, Curran T, Rastaldi MP, Holzman LB. Crkl/2-dependent Signaling Is Necessary for Podocyte Foot Process Spreading in Mouse Models of Glomerular Disease. J Clin Invest. 2012 Feb; 122(2): 674-692.
- Sampson MG, et al. Nephrotic Syndrome Study Network. Integrative Genomics Identifies Novel Associations With APOL1 Risk Genotypes in Black NEPTUNE Subjects. J Am Soc Nephrol. 2016 Mar; 27(3): 814-823.
- Johnstone DB, Ikizler O, Zhang J, Holzman LB. Background Strain and the Differential Susceptibility of Podocyte-specific Deletion of Myh9 on Murine Models of Experimental Glomerulosclerosis and HIV Nephropathy. *PLoS One*. 2013 Jul 10; 8(7): e67839.
- Johnstone DB, Shegokar V, Nihalani D, Rathore YS, Mallik L, Ashish, Zare V, Ikizler HO, Powar R, Holzman LB. APOL1 Null Alleles From a Rural Village in India Do Not Correlate With Glomerulosclerosis. PLoS One. 2012; 7(12): e51546.
- Zhdanova O, Srivastava S, Di L, Li Z, Tchelebi L, Dworkin S, Johnstone DB, Zavadil J, Chong MM, Littman DR, Holzman LB, Barisoni L, Skolnik EY. The Inducible Deletion of Drosha and microRNAs in Mature Podocytes Results in a Collapsing Glomerulopathy. *Kidney Int.* 2011 Oct; 80(7): 719-730.
- Johnstone DB, Zhang J, George B, Léon C, Gachet C, Wong H, Parekh R, Holzman LB. Podocyte-specific Deletion of Myh9 Encoding Nonmuscle Myosin Heavy Chain 2A Predisposes Mice to Glomerulopathy. *Mol Cell Biol.* 2011 May; 31(10): 2162-2170.
- Arif E, Wagner MC, Johnstone DB, Wong HN, George B, Pruthi PA, Lazzara MJ, Nihalani D. Motor Protein Myo1c Is a Podocyte Protein That Facilitates the Transport of Slit Diaphragm Protein Neph1 to the Podocyte Membrane. *Mol Cell Biol*. 2011 May; 31(10): 2134-2150.
- Garg P, Verma R, Nihalani D, **Johnstone DB**, Holzman LB. Neph1 Cooperates With Nephrin to Transduce a Signal That Induces Actin Polymerization. *Mol Cell Biol.* 2007 Dec; 27(24): 8698-8712.
- **Johnstone DB**, Holzman LB. Clinical Impact of Research on the Podocyte Slit Diaphragm. *Nat Clin Pract Nephrol.* 2006 May; 2(5): 271-282. Review.

## New Study Seeks to Optimize Chronic Kidney Disease Care

Manisha Jhamb, MD, MPH, is working on a new National Institutes of Health-funded RO1 award (RO1DK116957) to improve the care of patients with chronic kidney disease (CKD). Dr. Jhamb is an assistant professor of medicine in the Renal-Electrolyte Division whose clinical research focuses on understanding and improving patient-centered outcomes in patients with chronic kidney disease and end-stage renal disease (ESRD).



Dr. Jhamb is particularly interested in testing the effectiveness of clinical interventions to improve patient symptoms and quality-of-life in CKD and ESRD. Her ongoing studies

are evaluating technology-based collaborative care interventions on symptoms in dialysis patients. Another focus of her research is using health information technology to improve delivery of CKD care, reduce health disparities in CKD, and develop predictive models to identify high-risk CKD patients.

CKD is associated with an unacceptably high human and financial cost. Gaps in CKD care contribute to catastrophic outcomes such as dialysis dependence. Novel system-based interventions are needed to improve CKD care. Real-time risk stratification and population health management using electronic health records can improve CKD care and outcomes in the patients who need it most. This forms the basis of Dr. Jhamb's R01 study.

#### Study Abstract: Kidney-Coordinated HeAlth Management Partnership (Kidney-CHAMP)

Millions of adults have CKD, leading to substantial morbidity, mortality, and health care costs. These effects are concentrated in patients with high-risk disease. Several provider- and system-level barriers lead to well-described gaps in care for these patients that contribute to poor outcomes. Population health management (PHM) improves patient health by aggregating and analyzing data across a population to drive consistent, evidence-based care. CKD PHM using electronic health records (EHRs) can be a sustainable strategy to overcome physicianand system-level barriers. EHR-based PHM could improve the identification of patients with high-risk CKD; increase the use of

evidence-based, widely available, and cost-effective interventions; and enhance medication safety.

The Kidney-Coordinated HeAlth Management Partnership (Kidney-CHAMP) study (R01DK116957) is testing the effectiveness of a multifaceted EHR-based PHM intervention to improve the delivery of evidence-based CKD care in high-risk patients in the primary care setting. Specifically, it targets: 1) timely identification of high-risk CKD; 2) implementation of remote nephrology guidance (e-consult) to improve evidence-based CKD care; 3) opportunities for pharmacist-led medication safety reviews; and 4) access to standardized CKD patient education. A novel aspect of this study is the delivery of evidence-based nephrology guidance to primary care providers using Targeted Automated electronic Consults (TACo) which are targeted to the high risk patients and use an opt-out approach. This 42-month pragmatic, cluster-randomized, controlled trial in ~1,700 high-risk CKD patients from 330 primary care physicians (PCPs) will evaluate the intervention's effects on kidney disease progression, key processes of care such as hypertension control, avoidance of nephrotoxic medications, and health care utilization costs.

Dr. Jhamb has an ancillary study to Kidney-CHAMP (OPTIMIZE; R18DK118460) that will qualitatively identify barriers and facilitators of the intervention's effectiveness and response heterogeneity in diverse settings and with diverse patient and provider groups. Participants in the study will be selected using purposive sampling from the PCPs and patients who are randomized to the intervention arm in the Kidney-CHAMP study. Semi-structured interviews will be conducted to elicit key physician and patient level predictors that underlie the effectiveness of the intervention in diverse settings. This will allow for refinements of CKD phenotypes and transportability of the intervention in heterogeneous populations. These deliverables would strengthen future trials and specifically address disparity in CKD care by interviewing patients from vulnerable groups including minorities, low socioeconomic status, and those with multimorbidity. Dr. Jhamb's study is highly complementary and valuable to the evaluation of the Kidney-CHAMP intervention. The proposed qualitative work will further refine future efforts to improve the intervention's implementation, dissemination, and use in real practice and diverse health care settings.



## KO8 Grant Awarded to Chethan Puttarajappa, MD, MS

**Chethan Puttarajappa, MD, MS**, a transplant nephrologist in the Renal-Electrolyte Division, secured a National Institutes of Health K08 career development award (1K08DK119576) that will allow him to continue his renal transplantation research.



Dr. Puttarajappa's K08 award, "Utility of Virtual Crossmatch in Deceased Donor Kidney Transplantation," seeks to improve organ utilization along with maximizing function and

longevity of transplanted kidneys to allow more patients with end-stage kidney disease to benefit from kidney transplantation. This research will use a combination of health services research methods and decision analysis to identify optimal crossmatch strategies in deceased donor kidney transplantation (DDKT).

#### **Grant Abstract**

The 2014 kidney allocation system (KAS) gave high priority to highly sensitized (i.e., higher calculated panel reactive antibody or PRA) waitlisted candidates and allowed for wider sharing of kidney donor profile index > 85 kidneys, resulting in increased shipping of organs, higher non-local kidney transplant surgeries, and increased cold ischemia time

(CIT). To assess donor-recipient compatibility and avoid immediate transplant rejection, a physical cell-based crossmatch (XM) is routinely performed prior to KT. Physical XM has the risk of false positive results and may increase cold ischemia time (CIT), particularly for organs imported from a non-local Organ Procurement Organization. Virtual crossmatch (VXM) allows for rapid assessment of donorrecipient compatibility by comparing donor and recipient human leukocyte antigen (HLA) information. VXM has the potential to decrease CIT in DDKT, which will reduce delayed graft function rates and improve transplant outcomes. Reducing false positive XM and CIT could also reduce organ discard and improve organ utilization.

Specific aims of Dr. Puttarajappa's research are:

1) Evaluate the current crossmatch practices in DDKT among different donor and recipient subgroups, along with assessing perceptions of transplant professionals regarding VXM;

2) Explore whether the use of VXM is associated with lower CIT and DGF, and whether this is different before and after the introduction of KAS; and 3) Explore whether

routine application of VXM prior to DDKT has the potential to improve patient outcomes.

Dr. Puttarajappa's research aims to identify situations in DDKT where a VXM alone can be used to safely proceed to transplantation without a physical XM. Modeling results will aim to quantify risks and benefits of omitting a physical XM in specific scenarios that differ in key patient and immunological risk categories. Additionally, findings on national crossmatch practice variation and perceptions of the transplant community towards VXM will help direct future research, changes to histocompatibility testing protocols, and health policy surrounding kidney transplantation.

Dr. Puttarajappa will be mentored in his research by kidney transplant outcomes research expert **Sundaram Hariharan, MD**; mathematical modeling and decision analysis experts Kenneth Smith, MD, MS, and Mark Roberts, MD, MPP; and survey methodology and donor research mentor Howard Degenholtz, PhD.

## **UPMC Physician Resources**

For the latest news, events, videos, and free CME courses presented by UPMC clinicians and researchers, visit **UPMCPhysicianResources.com/Kidney**.

#### **Current CME Courses Include:**

Preventing the "Crash": The Internist's Guide to Managing Advanced Stage Kidney Disease

Presented by James R. Johnston, MD

High Risk Kidney Donor: New Paradigms in Transplantation Presented by Amit D. Tevar, MD, FACS

Is My Patient a Candidate? Advanced Age/Frailty, Obesity, Recurrent Disease, Malignancy, Noncompliance, Advanced CV Comorbidity

Presented by Christine Wu, MD

**BKV, CMV, and EVB (PTLD): Bench to Bedside Updates** *Presented by Chethan Puttarajappa, MD, MS* 

Updates in Diagnosis and Management of Rejection in Renal Transplantation

Presented by Rajil Mehta, MD, FASN

**Disorders of Sodium and Potassium in the Elderly** *Presented by James R. Johnston, MD* 

**Kidney Transplantation for the Pediatric Patient** *Presented by Armando Ganoza, MD* 

#### Video Rounds

**Video Rounds** is a series of short, informative, and educational videos created for physicians and covering a variety of medical and surgical disciplines. Current topics in nephrology and kidney transplantation include:

Hyponatremia Treatment - Helbert Rondon, MD

Renal Palliative Care - Jane Schell, MD

Kidney Transplantation - Sundaram Hariharan, MD

Acute Kidney Injury and Critical Care Nephrology – John Kellum, MD

Evaluating Medications That Induce Hyperkalemia – Thomas Kleyman, MD

## Identical Twin Kidney Transplants Warrant Gene Sequencing

Using U.S. transplant registry data, clinical researchers at the University of Pittsburgh School of Medicine found that kidney transplants between identical twins have high success rates, but also high rates of immunosuppressant use.

Among 143 patients who received a kidney from their identical twin in the U.S. from 2001 to 2017, about half were on immunosuppressant drugs a year after the operation. Yet, survival rates were about the same regardless of whether patients were on immunosuppressants or not. The researchers propose guidelines for genetic testing and continued management of identical twin transplants. The paper¹ was published in the *American Journal of Transplantation* in October. 2019.

"Once you confirm that the organ donor and recipient are identical, that's really a best-case scenario," says lead author **Dana Jorgensen, PhD, MPH**, an epidemiologist at UPMC. "It's almost like getting a transplant from yourself because the tissue would be almost identical."

Twin transplants have a long history. In the 1950s, before the age of immunosuppressants, doctors tried kidney transplantation first with identical twins because the odds of rejection are close to zero.

Back then, doctors would graft a piece of skin from one twin to another to see whether the twins were, indeed, a perfect match before attempting to transplant a whole organ. Today, gene sequencing allows physicians to say with near certainty whether a pair of twins is identical or not, and the researchers recommend using this test when preparing a transplant between suspected identical twins.

Although the researchers were surprised to see such a high rate of immunosuppressant use among the twins sampled for this study, Jorgensen pointed out that in many of these cases the physician may not have been confident that the twins were actually identical.

"One of the big things we noticed in researching this is that the patient will think they're an identical twin, but they've never been tested, so they don't know for sure," says Dr. Jorgensen. "Maybe doctors put these patients on immunosuppressants just in case."



Doctors also tend to use immunosuppressants for patients with glomerulonephritis — inflammation of the kidneys' tiny filters — due to fears that the disease would recur in the transplanted kidney. Transplanted kidneys did tend to fare slightly worse in patients with glomerulonephritis, the study showed, but there were not enough cases to draw conclusions about the benefits of immunosuppression for these patients.



"Long-term immunosuppressant use leaves patients vulnerable to infections, cancer, diabetes, and high blood pressure, so it's best to avoid them for identical twin transplants

if possible," says **Sundaram Hariharan, MD**, professor of medicine in the Renal-Electrolyte Division and medical director of kidney and pancreas transplantation at UPMC, and senior author on the study.

"If you ask me, I'm very comfortable withholding immunosuppressants from a patient who receives a kidney from their identical twin," says Dr. Hariharan, who also is the Robert J. Corry Chair of Surgery at the University of Pittsburgh. "Every transplant patient will have surveillance to quickly

detect potential organ rejection. They can be put on immunosuppressants later if the need arises."



Renal-Electrolyte Division faculty member **Christine Wu, MD**, also contributed to the study. Dr. Wu is an associate professor of medicine, and she currently serves as the

Transplant Nephrology Fellowship program director. Her clinical and research interests lie in the selection of kidney transplant recipients and wait list management, kidney transplantation in the elderly, and the impact of co-morbidity on transplant outcomes.

#### References

<sup>1</sup> Jorgensen DR, Wu CM, Hariharan S. Epidemiology of End-Stage Renal Failure Among Twins and Diagnosis, Management, and Current Outcomes of Kidney Transplantation Between Identical Twins. *Am J Transplant*. 2019; doi: 10.1111/ajt.15638. Epub ahead of print.





#### ABOUT THE UPMC RENAL-ELECTROLYTE DIVISION

The Renal-Electrolyte Division is devoted to clinical care and academic excellence, and training the next generation of nephrologists.

Our multidisciplinary approach provides the highest quality care for patients with complex kidney and electrolyte disorders.

- Inpatient services at UPMC Presbyterian focus on patients with acute kidney injury, chronic kidney disease, end-stage kidney disease, and patients awaiting or who have received kidney transplants. Our on-site dialysis center performs nearly 10,000 dialysis treatments a year in various settings.
- Outpatient services are provided at our specialized kidney and multidisciplinary clinics treating a variety of kidney and hypertensive disorders.
- The Pittsburgh Center for Kidney Research, one of eight nationwide NIDDKsupported George M. O'Brien Kidney Research Core Centers, supports more than 110 investigators and provides funding for pilot projects.

Thomas R. Kleyman, MD
Professor of Medicine

Chief, Renal-Electrolyte Division

Address correspondence to:

A915 Scaife Hall 3550 Terrace St. Pittsburgh, PA 15261 Phone: 412-647-3118 Fax: 412-647-6220 Email: kleyman@pitt.edu

For consults and referrals, please call UPMC's 24-hour physician OnDemand service at **1-866-884-8579**.

A \$20 billion health care provider and insurer, Pittsburgh-based UPMC is inventing new models of The largest nongovernmental employer in Pennsylvania, UPMC integrates 89,000 employees, 40 hospitals, 700 doctors' offices and outpatient sites, and a nearly 3.6 million-member Insurance Services Division, the most recent fiscal year, UPMC contributed \$1.2 billion in benefits to its communities, including more care to the region's most vulnerable citizens than any other health care institution, and paid \$587 million in federal state, and local taxes. Working in close collaboration with the University of Pittsburgh Schools of the Health sciences, UPMC shares its clinical, managerial, and technological skills worldwide through its innovation and commercialization arm, UPMC Enterprises, and through UPMC International. U.S. News & World Report consistently ranks UPMC Presbyterian Shadyside on its annual Honor Roll of America's Best Hospitals and ranks UPMC Children's Hospital of Pittsburgh on its Honor Roll of America's Best Children's Hospitals For more information, go to UPMC.com.

To learn more about the UPMC Renal-Electrolyte Division, please visit **UPMCPhysicianResources.com/Kidney**.

