ASN American Society of Nephrology

KidneyNews

May 2020 | Vol. 12, Number 5

Kidney Transplants Are Cancelled or Rescheduled during COVID-19 Pandemic

By Karen Blum

As the COVID-19 pandemic continues to take hold, kidney transplantation programs across the United States and elsewhere have been canceling or postponing many procedures, moving to telephone or video visits with patients, and emphasizing the importance of handwashing and social distancing in their quest to keep their patients safe.

"There's a lot of unknowns about how SARS-CoV-2 will intersect with organ transplantation," said Ajit Limaye, MD, professor of medicine and director of the transplant infectious disease program at the University of Washington in Seattle, during an international COVID-19 Town Hall webinar sponsored by the United Network for Organ Sharing, the American Society of Transplantation, and other groups.

"A reasonable expectation is that organ transplant patients with immunosuppression might be at increased risk for acquiring the virus," Limaye said. "There are a lot of concerns there may be a higher likelihood of them progressing from infection to more severe disease, perhaps as a result of underlying comorbid conditions as well as the impact of immune suppression." The published data to date on organ transplantation are very limited, he noted.

Meanwhile, many transplantation programs are reducing their operations except for the sickest patients. They're delaying living donor kidney transplantation, being more selective about deceased donor kidneys, screening donor kidneys and recipients for COVID-19, and postponing evaluations of new patients, in addition to offering telephone or telemedicine visits for most patient checkups. The American Society of Transplantation has suggested limiting the recovery of organs to local teams within donor hospitals unless there are extenuating reasons for the transplanting team to perform the recovery, in an effort to help limit exposure to COVID-19 resulting from travel.

The heavy use of resources such as intensive care unit beds and ventilators means that scaling back transplantation activity is inevitable, said Atul Humar, MD, MSc, director of the transplant center at the University Health Network in Toronto. He and his colleagues developed a phased approach to transplant volume reductions (1) to conserve resources while minimizing the waitlist impact, demonstrating what centers could do at 75%, 50%, or

Continued on page 4

NINJA Program Successfully Reduces AKI from Nephrotoxic Medications

By Ruth Jessen Hickman

Exposure to nephrotoxic medications is a major cause of acute kidney injury (AKI) in hospitalized children, increasing the costs and length of hospital stays. In one study of pediatric patients not in the intensive care unit, 86% were exposed to a potentially nephrotoxic medication at some point during hospitalization (1). When children receive three or more nephrotoxic medications in the same day, the rates of AKI double (1). In some patients, the damage is permanent, leading to chronic kidney disease.

Stuart L. Goldstein, MD, director of the Center for Acute Care Nephrology at the Cincinnati Children's Hospital Medical Center, and his colleagues were motivated to do something about the high nephrotoxic burden experienced by their patients.

When they looked at the epidemiology of nephrotoxic medication exposure, they found that patients were having their kidney functions reliably measured by creatinine screening only about 50% of the time. At the time, ne-

Continued on page 3

Inside

ASN American Society of Nephrology

KidneyNews

ASN Kidney News is published by the American Society of Nephrology
1401 H Street, NW, Suite 900, Washington, DC 20005. Phone: 202-640-4660

www.asn-online.org

Postmaster: Please send address changes to *ASN Kidney News*, c/o Customer Service, American Society of Nephrology 1401 H Street, NW, Suite 900, Washington, DC 20005.

Publications mail agreement No. 40624074. Return undeliverable Canadian addresses to PO Box 503, RPO West Beaver Creek, Richmond Hill ON L4B 4R6

ASN Kidney News (ISSN print 1943-8044 and online 1943-8052) is an official publication of the American Society of Nephrology, 1401 H Street, NW, Suite 900, Washington DC 20005, and is published monthly 11 times a year except November. Periodicals postage paid at Washington, DC and at additional mailing offices. Subscription rates: $12 per year. To order, please email bhenkel@asn-online.org. Subscription prices subject to change. Annual ASN membership dues include $12 for *ASN Kidney News* subscription.

★ WINNER OF 2 DESIGN AWARDS ★

WINNER 2019 APEX® AWARDS FOR PUBLICATION EXCELLENCE

GD USA HEALTH + WELLNESS DESIGN AWARDS

CORPORATE SUPPORTERS

ASN gratefully acknowledges the Society's Diamond and Platinum Corporate Supporters for their contributions in 2019.

DIAMOND LEVEL

AstraZeneca

Baxter

FRESENIUS MEDICAL CARE

relypsa
A Vifor Pharma Group Company

TRICIDA

PLATINUM LEVEL

ALEXION®

Mallinckrodt Pharmaceuticals

Otsuka

REATA PHARMACEUTICALS

NINJA Program

Continued from page 1

phrotoxic AKI was viewed as a largely nonmodifiable adverse event for hospitalized patients.

"We felt if we had more reliable kidney function assessment, we could identify acute kidney injury earlier and potentially decrease unnecessary nephrotoxic medication exposure or react to changes in kidney function sooner," Goldstein said.

Goldstein and colleagues developed the Nephrotoxic Injury Negated by Just-in Time Action (NINJA) program in the hopes of decreasing nephrotoxic medication exposure at their center (2). The program leveraged electronic health records to provide notifications to pharmacists who were coordinating with clinical teams. These alerts recommended obtaining daily creatinine levels in all patients not in the intensive care unit who were deemed at high risk for AKI secondary to nephrotoxic medications. Patients were defined as high risk if they had received intravenous aminoglycosides for 3 or more days or were receiving three or more nephrotoxic medications on the same day.

"We know children need to get nephrotoxic medications," said Goldstein. "They are lifesaving. We weren't telling anyone they couldn't give a specific medication. But our overall guiding vision is that children should get the nephrotoxic medications they need for only the duration that they need them."

At Cincinnati Children's, the NINJA program resulted in sustained reductions in nephrotoxic exposures and rates of related AKI. In results reported in 2016, Goldstein and colleagues reported single-center results over a 43-month study period. Overall, the exposure rate to nephrotoxic medications decreased by 38%, and the rate of AKI decreased by 64% (3). Moreover, the team demonstrated that the program had not had a deleterious secondary effect in persistent infections—a potential concern if clinicians had switched to less nephrotoxic but less efficacious medications.

A recent study in *Kidney International* demonstrates the broader potential of the NINJA program through a prospective trial across nine diverse pediatric centers in the United States (4). Details of the program implementation varied, but all included an interprofessional 2-day learning session. At each center, an alert triggered by the electronic health record prompted medication review (and substitution if appropriate) and also assessment of daily creatinine values for high-risk patients.

The primary endpoint was the number of episodes of AKI per 1000 patient hospital days. The centers varied in time to maturity: the speed at which they fully implemented the goals of the NINJA program. AKI was defined by the Kidney Disease Improving Global Outcomes serum creatinine criteria (an increase of 50% or 0.3 mg/dL from baseline). Medications to be included in the algorithm were reviewed and regularly updated by a consensus committee (5).

The authors estimated that over the 2-year study, 242 cases of AKI were prevented. Statistical process control analysis showed that the program yielded a 23.8% decrease in the rates of AKI from nephrotoxic exposure: an improvement in prevalence from 1.7 to 1.3 episodes per 1000 patient hospital days. The analysis also showed a 36.7% reduction in the rates of AKI per exposure to nephrotoxic medication (4).

These decreases were largely driven by the centers with initially higher rates of AKI. Of the six centers that began the initiative with relatively high rates of AKI, five ultimately achieved a significantly lower rate. By contrast, the three centers that started with relatively low rates of AKI did not demonstrate improvements in rates. Eight of the nine centers ended the study clustered around the same rate of AKI (4).

Those rates were exactly what they saw in Cincinnati, Goldstein said. "I think the novel aspect of this quality improvement project is that I think we've demonstrated not only what centers should strive for, but what may be achievable through our intervention in the way that we've designed it." He suggested that future innovations may be necessary to show additional improvements.

Although the original grant sponsoring the NINJA initiative has been completed, the sites continue to gather data. Goldstein and colleagues hope to obtain additional grant funding and use the existing NINJA structure to analyze different potential variables that might lead to even lower rates of AKI, such as specific nephrotoxic medication combinations, current level of kidney function, and genetic predispositions.

The Children's Hospitals' Solutions for Patient Safety is a network of over 135 pediatric hospitals in the United States and Canada aimed at reducing hospital-related medical conditions. Through a grant by the Centers for Medicare & Medicaid Services, it has rolled out NINJA in about 30 hospitals, with the ultimate goal of using NINJA throughout the entire network.

The original algorithm created at Cincinnati Children's Hospital has since been licensed to the VigiLanz digital healthcare intelligence firm, but any electronic health records platform can interface with the NINJA program. Some institutions are assessing the costs of developing their own interface versus adopting the VigiLanz platform.

In adult patients, quality improvement projects focused on preventing AKI have shown mixed results (6–8). Most of them studied the effects of alerting clinicians after patients already had acute kidney damage. By contrast, the NINJA approach is upstream, identifying patients at risk and attempting to lower that risk. Unlike some other interventions, NINJA does not mandate specific clinical action other than surveillance serum creatinine values for high-risk patients.

Currently, other investigators are evaluating the NINJA platform in adult populations. "This has all been demonstrated in the pediatric population," said Goldstein. "There is no reason this should not translate well to hospitalized adults." ■

Ruth Jessen Hickman, MD, is a graduate of the Indiana University School of Medicine. She is a freelance medical and science writer living in Bloomington, Indiana.

References

1. Moffett BS, Goldstein SL. Acute kidney injury and increasing nephrotoxic-medication exposure in noncritically-ill children. *Clin J Am Soc Nephrol* 2011; 6:856–863.
2. Goldstein SL, et al. Electronic health record identification of nephrotoxin exposure and associated acute kidney injury. *Pediatrics* 2013; 132:e756–e767.
3. Goldstein SL, et al. A sustained quality improvement program reduces nephrotoxic medication-associated acute kidney injury. *Kidney Int* 2016; 90:212–221.
4. Goldstein SL, et al. A prospective multi-center quality improvement initiative (NINJA) indicates a reduction in nephrotoxic acute kidney injury in hospitalized children. *Kidney Int* 2020; 97:580–588.
5. Goswami E, et al. Evidence-based development of a nephrotoxic medication list to screen for acute kidney injury risk in hospitalized children. *Am J Health Syst Pharm* 2019; 76:1869–1874.
6. McCoy AB, et al. A computerized provider order entry intervention for medication safety during acute kidney injury: A quality improvement report. *Am J Kidney Dis* 2010; 56:832–841.
7. Colpaert K, et al. Impact of real-time electronic alerting of acute kidney injury on therapeutic intervention and progression of RIFLE class. *Crit Care Med* 2012; 40:1164–1170.
8. Wilson FP, et al. Automated, electronic alerts for acute kidney injury: A single-blind, parallel-group, randomised controlled trial. *Lancet* 2015; 385:1966–1974.

AAKP Addresses Patient Concerns about COVID-19

By Karen Blum

The American Association of Kidney Patients (AAKP) recently held a webinar about coronavirus and kidney patients in partnership with the Centers for Disease Control and Prevention (CDC). Shannon Novosad, MD, MPH, a medical officer with the CDC's dialysis safety team, discussed tips for kidney patients to protect themselves at home, in the community, or in healthcare facilities, including general advice on handwashing and social distancing. She also suggested that patients have a plan in case they become ill and that they have several weeks' worth of medications and supplies. It is important, she added, that they not postpone dialysis treatment.

"Missing dialysis is the worst thing a patient can do," said nephrologist Stephen Fadem, MD, FACP, FASN, a clinical professor of medicine with Baylor College of Medicine in Houston and chair of the AAKP medical advisory board. "Dialysis units have been working on this for a long time. If a dialysis patient has a fever or cough, they should let the unit know, and they will send you to another unit specifically designed to handle this."

Fadem recommends that patients wear masks if they go out, because 20% of people with COVID-19 may be asymptomatic and capable of transmitting the virus. In addition, he said, people with kidney diseases should continue their regular diet and medication regimen, and have at least 2 to 3 weeks' worth of medicines on hand.

"You don't know if your friendly pharmacist is going to be the next guy to get sick," Fadem said. "There have been so many surprises with this disease that the old Boy Scout slogan to be prepared is the best thing I can recommend."

Patients also have been concerned about what to do if they share a home with a sick family member, he said.

"That's the most difficult because most people can't just move out, but the CDC is recommending they isolate as much as possible," he said. This could mean using a separate room or separate part of the house, a separate bathroom, and cleaning every common touchpoint, including doorknobs.

Richard Knight, MBA, AAKP president and a kidney transplant recipient, quarantined himself at home for 2 weeks after a meeting in New York, where he was exposed to someone with COVID-19. Fortunately, he did not become ill himself.

"There's a lot going on in this arena that gives patients concern, but there is hope," Knight said. "We will get through this."

There are things on the horizon that are hopeful, Fadem added. Several centers have been deploying rapid COVID-19 tests and nasal swabs that could make it easier to collect the virus for testing and get better information at the point of service about who has the virus. Tests for antibodies against the virus also are being deployed in some areas, which should give healthcare providers a better understanding about SARS-CoV-2. Some acute therapies and vaccines also are being tested. ■

Kidney Transplantation

Continued from page 1

25% capacity. As of the webinar, his center was operating at 50% volume, doing transplant operations in urgent cases only. For kidney transplantation, they have halted living donor procedures and are doing transplantations only for patients who are highly sensitized and are unlikely to get another offer soon.

"There's a wide variety in the way people are approaching COVID-19, because no one really seems to know what the right answer is," nephrologist Andrew Malone, MB, BCh, an assistant professor of medicine at Washington University School of Medicine in St. Louis, told *Kidney News*. "We're still doing deceased donor transplants for now, but this is in discussion every day. People are thinking of what's the next step in pulling back, although there's an argument that there are a group of patients on the transplant waiting list whose risk–benefit would probably favor going ahead and getting a transplant, especially those who are highly sensitized or who have been waiting a long time."

The University of Maryland School of Medicine in Baltimore, which follows up with about 4000 kidney patients, also has put most kidney transplants on hold, said Matthew Weir, MD, division head of nephrology. Deceased donor operations are proceeding but only in carefully selected cases with a very high likelihood that the kidney will work right away, he said. "We don't want to keep people in the hospital too long," he noted. Donors and recipients are tested for COVID-19 before the operation is performed. If patients still want to see Weir in person, he dons a gown, gloves, and mask for the visit. Other patients are seen by telehealth. One of his dialysis units is now a COVID-positive center.

He did recommend a transplantation for one of his recent patients, a 38-year-old woman who had been on the waiting list for 6 years and had an offer of a 5% Kidney Donor Profile Index kidney.

"She might not get another offer like this for years, let alone any other kidney," Weir said. "I told her with the current testing capabilities, I'd go for it. These are the kinds of questions that come up. It's a very realistic concern and an issue we have to think about."

The University of Alabama at Birmingham has gone to 90-plus percent telemedicine visits for kidney patients, said nephrologist Clifton Kew II, MD, a professor of medicine there. He and his colleagues used to see about 30 patients each morning in clinic—a number that has been slashed to four to six. Transplantations are limited there to deceased donor operations as well, and they're no longer calling in backup patients in case the first intended recipient can't be operated on. In addition, they're trying to reduce hospital lengths of stay after surgery, discharging patients home or to a local hotel sooner.

"We're now doing OK with people with COVID-19, but that could change in 24 hours," Kew said, noting that the previous week the hospital had gone from four to 40 COVID-19–positive patients overnight. "We don't know when a whole flotilla of patients may come in, and we may need that room that transplant patient is in. These are very difficult choices that need to be made, but fortunately for kidneys we do have a luxury, and it's called dialysis."

Physicians who see transplant patients in the office should consider masking them as soon as they arrive, even if they're not sick, and rushing them into a room to avoid having them touch areas that may have been touched by other people, advised Marian Michaels, MD, MPH, a professor of pediatrics and surgery at the University of Pittsburgh School of Medicine

Some hospitals have seen transplant recipients among their COVID-19 patients. During the webinar, participants noted that University of Washington Medicine had five transplant recipients, including one who had received a kidney 20 years prior. The 54-year-old man was an inpatient for 13 days before being discharged home, Limaye said. The ASST Papa Giovanni XXIII hospital in Bergamo, Italy, had six COVID-19 patients who had received heart transplants, said Attilo Iacovoni, MD, FESC, of the heart transplantation unit there. Of those, two were in the hospital, two were being treated on an outpatient basis, and two had died.

"The key message is COVID-19 is very aggressive in immunosuppressed patients, and they could get it easily," Iacovoni said. "If you have an outbreak in your hospital, think twice before treating those with immunosuppression raging."

Unsurprisingly, kidney patients have been placing many calls to their physicians and transplantation centers, wondering what to do. Some have concerns about cold or virus symptoms like runny nose or fever, and others have asked to be prescribed antiviral medications, said Kew.

"Basically, the advice we give to patients is very similar to what is out there for the general population: Stay away from other people, especially if they're sick. Wash your hands. Try to limit contact with others as much as possible," he said. "That's about the best we can do for them."

The American Society of Transplantation has COVID-19 resources on its website, including frequently asked questions for transplantation professionals and for transplant recipients and candidates, and a link to the Town Hall webinar: see https://www.myast.org/covid-19-information. The ASN has compiled additional resources at https://www.asn-online.org/ntds/.

Reference

1. Kumar D, et al. COVID-19: A global transplant perspective on successfully navigating a pandemic [published online ahead of print March 23, 2020]. *Am J Transplant* doi: 10.1111/ajt.15876.

Managing AKI during a Pandemic

By Karen Blum

Renal replacement therapy (RRT) should be initiated for acute kidney injury (AKI) patients who have life-threatening complications and are not responding to medical management, said Anitha Vijayan, MD, FASN, including those with volume overload and respiratory failure, hyperkalemia, or metabolic acidosis. But be wary of aggressive fluid resuscitation, said Vijayan, a professor of medicine at Washington University School of Medicine in St. Louis.

She noted there is no data yet to support early initiation of RRT in COVID patients.

Available RRT modalities that may be employed include continuous renal replacement therapy (CRRT), prolonged intermittent renal replacement therapy (PIRRT), or intermittent hemodialysis, she said. CRRT is the preferred modality in hemodynamically unstable patients, and it is recommended that nephrologists use the established CRRT modality at their home institutions. There is no need to buy a different machine than what your hospital has, but more machines may be needed, according to COVID projections for your city and hospital, Vijayan noted.

PIRRT may be performed either with intermittent hemodialysis or CRRT machines. It can last from six to 12 hours, does not need 1:1 hemodialysis nursing, and allows one machine to be used for two to three patients, Vijayan said. To dose PIRRT, use a 20 mL/kg/hour dose for 24 hours, divided by the number of hours you are planning to treat the patient. Treating 10 hours or fewer allows time for cleaning the machine and using it for additional patients, she said.

Anticoagulation during CRRT/PIRRT in COVID patients with AKI is essential, Vijayan added. If there are no contraindications, use heparin, either via machine circuit or systemically. Citrate may also be used, but its use is nursing-intensive and there is a risk for patient safety. If a center does not already use citrate, Vijayan suggested not starting a new protocol at this time. In addition, hemodialysis catheters normally placed by nephrologists and intensivists may need to be placed by other providers, given shifting workforce needs. She noted the importance of the correct length to ensure adequate blood flow and reduce clotting and suggested creating a cheat sheet to be used by others that includes appropriate lengths.

"This is a critical time everywhere—we're all trying to figure out how to conserve resources," Vijayan said.

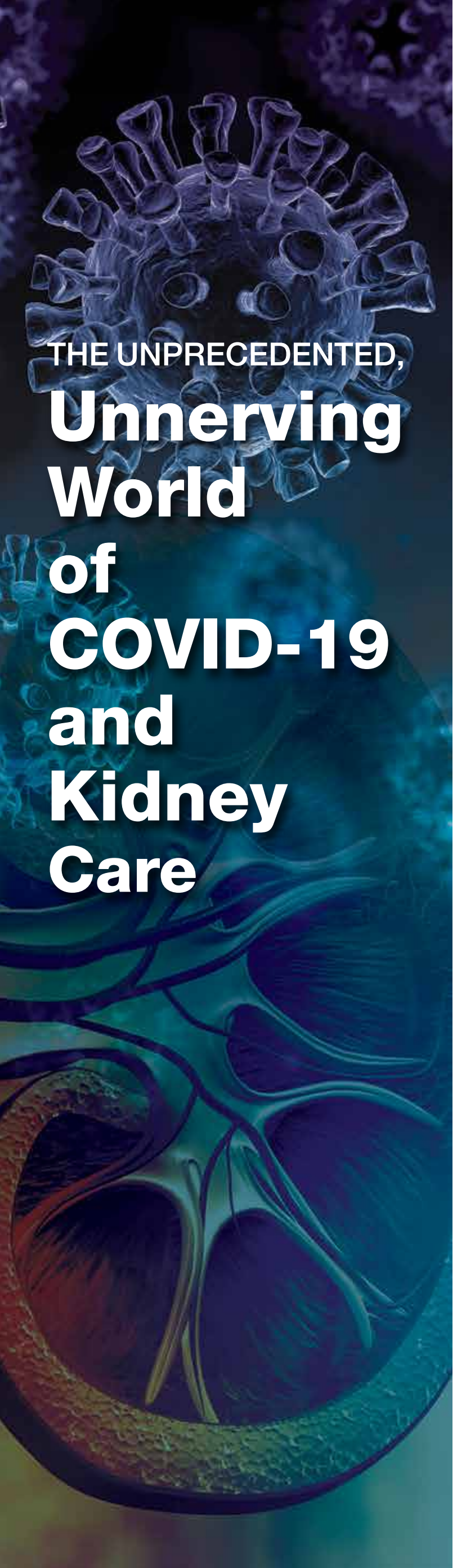
Among the suggestions for conserving resources are the following:

1. For intermittent hemodialysis, consider the shortest duration that achieves metabolic and volume control and minimize 1:1 nurse time in the room.
2. Delay RRT if possible in patients whose COVID tests are pending, which can conserve PPE.
3. Use high-dose diuretics in AKI patients, with binders to lower potassium.
4. Decrease flow rates in CRRT after metabolic control has been achieved to save fluids.
5. Cross-train nephrologists and additional nurses if necessary to help set up or monitor patients undergoing dialysis.

If resources or capacity for acute dialysis and continuous venovenous hemodiafiltration has been exceeded, nephrologists can turn to peritoneal dialysis (PD), said Jeffrey Perl, MD, SM FRCP, an associate professor of medicine at the University of Toronto and St. Michael's Hospital. PD uses less nursing time with direct patient exposure. But there are some concerns to keep in mind, he said: PD has less predictable fluid removal rates, a critical care treatment team may be uncomfortable with the therapy, complications include peritonitis or catheter leaks, and there can be a deleterious impact on respiratory biomechanics in patients on a ventilator.

PD for AKI requires a team approach, buy-in from the care team and nursing expertise, as well as careful, and perhaps more restrictive, consideration of candidates, Perl said.

Vijayan and Perl spoke about their experiences during an ASN webinar about hospital care and treatment options for COVID-19–positive patients.



THE UNPRECEDENTED, Unnerving World of COVID-19 and Kidney Care

By Richard Lafayette

The SARS-CoV-2 virus that causes the disease COVID-19 reached pandemic status in short order and has changed everything in our world. Modern living has been turned upside down in pursuit of efforts to control spread of this virus, identify infected patients, and treat them appropriately. Economies are faltering. Epidemiologists and public health officials are doing their best to find ideal practices while governments impose what they feel are appropriate guidelines and restrictions on populations. How this will evolve and the size of its ultimate impact on our lives is yet to be seen, but it is already certain to have an incredible influence on our health and well-being.

This pandemic has affected kidney care providers and our patients in both specific and general ways. It will continue to influence our daily routines for quite a while. Clearly, patients with chronic kidney disease, not only those with hypertension, diabetes, autoimmune diseases, or those requiring immunosuppressive therapy, are at high risk of severe complications of COVID-19.

We will need to protect our patients from exposure, diagnose and care for them when they get symptoms that may be COVID-19, and ensure that they get appropriate testing and therapy as indicated and available. This has already required huge efforts in just informing ourselves and our patients about this illness and its associated best practices, which are changing on a more than daily basis.

We have been tasked with communicating (in person, by phone, by mail) with employers, families, and community leaders to assure that our patients don't sit in harm's way, often on top of an already maximal work schedule. We continue clinic sessions, rounding in dialysis units, and rounding in hospitals where our skills are desperately needed. However, clinic sessions and dialysis rounds are increasingly being done with virtual visits to limit further spread of the virus. Dialysis patients are highly vulnerable given their general infirmity and need to gather in units. Outbreaks within dialysis units affecting patients and providers are already well reported. Policies are quickly being derived, although they are based on limited data and experience, to maintain their care while limiting the risks of spreading infections.

Inpatient care does not lend itself naturally to virtual visits, but this is being increasingly considered and modeled. However, not only are our kidney disease patients at risk and already needing care for complications of COVID-19 in our hospitals, but the illness carries a risk of acute kidney injury (AKI). Initial reports suggest an AKI rate of 3%–7%, clearly highest among critically ill patients. Urinary abnormalities may be frequent, including proteinuria and hematuria. Kidney imaging may be abnormal. The abnormal imaging and urinary abnormalities suggest direct involvement by the virus, together with risks of sepsis and medication-induced injury. We will certainly learn more with each passing day and each summary report of experiences with this pandemic.

These unprecedented changes to society and to kidney caregivers' workplaces are sure to impose unusual stresses and anxieties on all of us. Caring for our patients—those known to be affected or not—leaves us all vulnerable to infection and its complications. We worry about the very real risks of transmitting illnesses to our family, friends, and community.

As healthcare workers, we have already committed ourselves and are obligated to do our best for our patients and our community. We will harness our best abilities and provide the best care and comfort that we can. We must work together to figure out how to meet this challenge most effectively, advance our understanding of this disease, and become ever more prepared for the next challenge around the corner. Certainly, we hope to see that closing non-essential services and travel, as well as teaching social distancing, reduce the spread of this virus. We also must hope that treatments beyond supportive care, such as remdesevir or hydroxychloroquine and azithromycin, can actually reduce viral growth and improve outcomes. New treatments will arise and ongoing research will pave the way to a more secure future.

We must work together to figure out how to meet this challenge most effectively, advance our understanding of this disease, and become ever more prepared for the next challenge around the corner.

We hope this issue of *Kidney News*, and ongoing updates in *Kidney News* Online as well as future issues will help to inform you and prepare you to deal with COVID-19 and continue your professional life. Please feel free to share your thoughts and experiences with us at *KN*, or in ASN Communities. Be safe and well. ■

Richard Lafayette, MD, FACP is Editor-in-Chief of Kidney News.

Nephrologists Tackle Crisis Planning

By Ruth Jessen Hickman

As dialysis centers prepare for the the need—either current or increasingly likely—for inpatient units to work at surge capacity to manage patients during the COVID-19 pandemic, it's becoming clear that constraints on both personnel and resource supplies may make it impossible to successfully dialyze all patients using standard procedures. In such a scenario, institutions may aim to temporarily adjust their standard of care to provide sufficient treatments to as many patients as possible.

A paper in the *Clinical Journal of the American Society of Nephrology* provides guidance about different strategies and contingency plans that might be employed. Jamie P. Dwyer, MD, is a professor of medicine and director of the Nephrology Clinical Trials Center at Vanderbilt University Medical Center in Nashville, TN, and one of the authors of the study (1). Dwyer and colleagues published the paper to provide practical ideas about how inpatient dialysis units might best maximize their available staff and resources.

Although the incidence and pathophysiology are unclear, acute kidney injury occurs in a significant minority of COVID-19 patients, and many critically ill patients have required renal replacement therapies. In some areas of the country, kidney failure patients with suspected or confirmed COVID-19 infections on maintenance dialysis are being triaged to hospital centers, potentially further increasing the strain on inpatient dialysis units.

Conserving dialysis supplies and equipment

Centers should plan for the possibility that dialysis supplies and equipment may need to be rationed. Dwyer suggested that permissive underdialysis may need to be employed in the inpatient unit, shortening dialysis treatment time to three hours in stable and appropriate patients. If needed, kidney failure patients could be shifted from a schedule of three to two hemodialysis sessions weekly. Such strategies would allow for additional patients to be dialyzed over a given period.

To conserve dialysate supplies, dialysate flow rates could be adjusted to a maximum of 600 mL/min. If dialysis fluids for continuous renal replacement therapy (CRRT) from commercial providers are in short supply, hospital pharmacies could compile replacement fluids via standard recipes. If peritoneal dialysis fluids are available, these may also be utilized as potential replacement fluids. Additionally, fluids and other resources might be available from outpatient dialysis clinics, where needs may be less acute.

A component of resource conservation is reducing the number of patients who might need dialysis. Juan Carlos Q. Velez, MD, is chair of the department of nephrology at Ochsner Medical Center in New Orleans, LA, an epicenter of the outbreak.

"We are trying to be very judicious about who could be managed medically and not just put everyone with acute kidney injury on dialysis," Velez said. "However, when patients become critically ill, dialysis is often an essential component of life support. Fortunately, we have been able to adapt and expand our resources to continue providing optimal care during these challenging times."

Rigorous control of electrolytes and fluid intake in hospitalized patients with kidney failure can help delay the need for dialysis. In some patients with residual kidney function, diuretics may be used to treat volume overload instead of dialysis, and oral alkali replacement and diuretics might be used to manage metabolic acidosis. Novel drugs are now available that can also remove potassium from the body, potentially obviating the need for dialysis.

To help facilitate these strategies, Dwyer strongly recommended early engagement of the hospital system's pharmacy and therapeutics committee. "It is key to make sure that your hospital's pharmacy team knows that these drugs need to be emergently added to the formulary," he said.

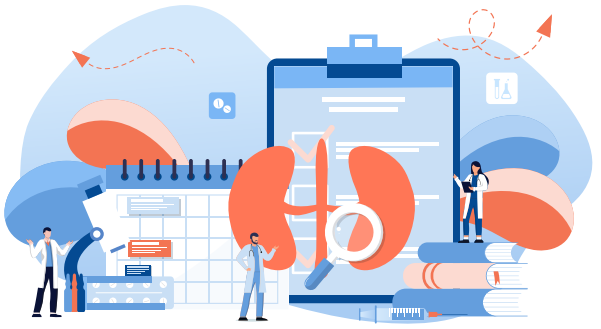
Rethinking and reorganizing dialysis modality

It is also crucial to think about how to best use the available machines for hemodialysis and CRRT if these resources become constrained. "It's important to get a good assessment of the types of devices you have and think about how to use them broadly," said Dwyer.

For example, some centers have dedicated machines that can perform isolated ultrafiltration. Such machines might be designated for patients who need fluid removal but could delay standard dialysis, freeing up the use of full-size dialysis machines. Dwyer suggested that centers may want to look locally to rent, borrow, or buy such machines if available. However, ordered machines may not be available immediately given demand. Additionally, when new machines arrive, it may take several days before they can be safely used.

"If there are unused dialysis machines sitting in an outpatient unit or in a hospital without a lot of COVID patients and a low census, we need to find clever ways to move those over emergently and worry about some of the regulatory concerns and financial constraints later," Dwyer said.

If CRRT machines are limited, standard intermittent hemodialysis machines could be used to perform sustained, low-efficiency dialysis (SLED) using lower dialysate and blood-flow rates to meet the needs of critically ill patients. (SLED is also known as PIRRT, prolonged intermittent renal replacement therapy). Similarly, to ensure that more people receive treatment with existing CRRT machines, one could use CRRT machines running at higher than normally prescribed clearances for 10 to 12 hours.



This method is already being employed selectively at New York University (NYU) in New York City, a current outbreak hotspot, although not all patients can tolerate it, said David M. Charytan, MD, Normal S. Wikler Associate Professor of Medicine and chief of the division of nephrology at NYU.

"For those who can, it relieves nursing issues a bit, because for one patient you have one-to-one nursing for 10 to 12 hours instead of 24," he said. "And you can use one machine to treat two people in the same amount of time you used to treat one."

Dwyer and colleagues noted that critically ill patients already on extracorporeal membrane oxygenation (ECMO) can receive isolated ultrafiltration in a non-traditional way if CRRT machines are in short supply, by adding an in-line hemofilter into the ECMO circuit. Replacement fluid could potentially be added as well, if needed. Although this method would require close monitoring of intake and output volumes and would be more inaccurate than commercially available CRRT, it is an option worth considering.

Urgent start peritoneal dialysis (PD) for acute kidney insufficiency could also be considered to decrease resource drain on inpatient units. However, Dwyer noted that some patients may be too sick to go to the operating room to have surgery. Some centers may have surgeons or interventional radiologists who are able to place a PD catheter at the bedside. Theoretically, nephrologists may be able to perform such placement if absolutely needed, although younger nephrologists currently lack the training to do so. Dwyer said, "I think we need to think broadly about what areas of expertise our colleagues have and remember that acute PD was a thing 30 years ago."

Charytan noted that many centers in New York are preparing to implement urgent start PD. "If our need for renal replacement therapy is double or triple what we normally have to provide, it is hard to see another way," he said. "This can probably help provide adequate if not ideal therapy to many more patients, because the requirement of nurses and the requirements of equipment are less." However, not all centers will have the expertise to implement this efficiently.

A more extreme consideration is continuous arteriovenous hemofiltration, which might be an option for critically ill patients not on ECMO if CRRT machines are lacking. Although many centers lack contemporary expertise with such a setup, some places will have older personnel who may be able to employ the technique if absolutely necessary.

Managing human resources

Human resources may be limited as well. COVID-19 infections may decrease the number of skilled personnel available to dialyze patients. Charytan emphasized the critical importance of skilled nursing personnel to run both ICU and dialysis floors. For example, nurses new to an expanded ICU floor may lack the expertise to perform CRRT. At Ochsner, Velez and colleagues implemented urgent online CRRT training for nurses to help fill some of these needs. Charytan agreed that it may be helpful to think through who might capably run dialysis and assess what training and expert guidance they might need.

Dwyer suggested it may be possible to urgently credential outpatient nurses to work in the inpatient setting, although this would require flexibility from local organizations and potentially advocacy on the part of nephrologists.

Because they spend more time with patients, nurses are at higher risk of infection than physicians, and Charytan emphasized the importance of taking measures to try to keep the nursing staff healthy. Dividing patients and nurses into cohorts and encouraging social distancing at work might help reduce disease spread. To decrease exposure of dialysis nurses, it might be helpful to preferentially use CRRT for patients in the ICU infected with COVID-19. Through telemonitoring, it might be possible to reduce the amount of time nurses need to spend inside patient rooms.

With the use of extension tubing, the CRRT machine could be run outside the patient's room, decreasing nurse exposure. However, Velez noted that this should be weighed thoughtfully, as COVID-19 patients seem to have a higher risk of hypercoagulability, which could be exacerbated by such tubing. Such a measure might make the most sense in institutions that have machines that require more frequent interventions by nurses.

Now is the time to take stock of physical and human resources, Dywer said. "We don't have much time to prepare, which is why getting prepared now, as soon as possible, is mandatory."

Added Velez, "This is a time to be bold and creative and innovative but at the same time be very vigilant for patients, because when you are exploring new territories, the risk for human error increases. We are doing the best we can for our patients, but we have to make sure we don't cause harm and we keep our workforce safe." ■

Ruth Jessen Hickman, MD, is a graduate of the Indiana University School of Medicine. She is a freelance medical and science writer living in Bloomington, IN.

Reference

1. Burgner A, Ikizler T, Dwyer J. COVID-19 and the inpatient dialysis unit: managing resources during contingency planning pre-crisis *Clin J Am Soc Nephrol* 2020. DOI: https://doi.org/10.2215/CJN.03750320

CDC Recommendations for Dialysis Centers Grappling with COVID-19

By Bridget M. Kuehn

Strategies for safely transporting dialysis patients with COVID-19, as well as for discontinuing isolation for staff and patients after infections, were highlighted during an ASN webinar on COVID-19 hosted by Nephrologists Transforming Dialysis Patient Safety.

Infection control strategies

The Centers for Disease Control and Prevention's (CDC) COVID-19 website for dialysis providers now includes more detailed information about screening for COVID-19 and triage of patients upon arrival at dialysis centers, said Shannon Novosad, MD, MPH, medical officer with the Dialysis Safety Team in the Division of Healthcare Quality Promotion at the CDC. She noted that the recommendations haven't changed, but that many centers had questions about them or difficulties following them.

"If the screening and triage is not happening as effectively as it could be, it really kind of sets you up for not being able to implement all of the other recommendations in terms of patient and healthcare [staff] protection," Novosad said.

She emphasized the need for a multilayered approach, with patients who have symptoms calling before arrival to ensure the center is prepared. Some centers are helping to remind patients to call ahead through robocalls or texts a few hours before their scheduled dialysis, Novosad said. Screening and triage should also take place on patient arrival at the door or outside as weather permits. Patients with symptoms should don a mask at arrival.

Given current supply chain difficulties, Novosad recommended that if dialysis centers change disinfectants, they must ensure that the new product's label indicates it is effective against bloodborne pathogens. "We don't want to cause any other inadvertent infections or increase the risk for bloodborne pathogens with the use of these new disinfectants," she said.

The CDC, working with ASN, has created a dialysis facility checklist to help walk leaders through what they may already have in place or additional steps they need to take during the COVID-19 pandemic.

"In communities that have not had a lot of cases yet, this tool could be valuable for thinking through how they are preparing," she said.

Another challenge dialysis centers are grappling with is determining when personnel can return to work or when transmission precautions can be removed after a suspected or confirmed case of COVID-19 in a patient. The CDC has recommendations for centers using a test- or no-test–based strategy.

"In a lot of areas, testing capacity is still not what it should be, and it's really difficult to get sometimes the required number of tests to be able to make some of these decisions," Novosad said. "Even in places where there is more widespread testing available, I think getting dialysis patients to wherever this testing is happening could be very difficult to actually implement in real time."

When tests are available, two negative tests 24 hours apart are recommended before a staff member returns, she said. If no testing is available, employees may return at least 3 days after recovery, defined as the absence of fever without medications, and at least 7 days after the first symptoms appeared. Facilities may want to consider adding more days prior to return for personnel who work with immunocompromised patients.

"If it has been less than 14 days since illness onset, the healthcare providers should consider wearing a face mask at all times within the healthcare facility," Novosad said.

Dialysis centers should also carefully develop strategies for preserving their personal protective equipment (PPE) and tweak them based on their needs. If PPE-preserving strategies are implemented, she emphasized that front line staff should be informed why they are in place and how to most safely follow procedures. She also noted that numerous potential PPE sources are becoming available and urged centers to contact their state public health department for help.

"We all know that PPE shortages are posing a tremendous challenge to our healthcare system," she said. "PPE optimization strategies are really only meant to be options for providing ongoing patient care when supplies are stressed or running low, or in some instances even absent."

Transportation precautions

Safe transportation for dialysis patients during the pandemic is another concern. Only about one-quarter of patients arrive for dialysis via private cars, 7.9% take public transportation or taxis, and 66.8% use a van or ambulance service, according to 2013 data from the US Renal Data Service. Medicare only covers transportation in emergencies. Medicaid does cover transportation.

"It's important that we recognize the patients who have barriers to get to dialysis as otherwise they will end up in the emergency room," said Anitha Vijayan, MD. "This is absolutely not what we want at this time for sure." Vijayan is professor of medicine at Washington University in St. Louis and director of the Acute Dialysis Unit at Barnes-Jewish Hospital.

New York state has provided guidance for its public transport agencies on proper cleaning and disinfection for public transportation, and some dialysis transportation companies have been proactive, she said. For example, LogistiCare has instructed drivers on CDC guidance for cleaning and disinfection, and the company eliminated the need for signatures to verify trips in order to reduce the need to touch devices or pens. They are also transporting confirmed or presumed cases one at a time via ambulance and providing solo van rides for patients at high risk of harm from COVID-19.

If a patient arrives with symptoms after transport or is diagnosed with COVID-19, it is important for the dialysis center to notify the public health department, their transportation company, or the patient's nursing facility immediately, Vijayan noted. This ensures that contact tracing, cleaning, and necessary quarantine precautions are taken for drivers or other patients who may have been exposed.

"It's important that both the medical directors and the nurse managers familiarize themselves on how the patients are being transported to the dialysis facility," Vijayan said. "It's important that we communicate with them ahead of time to understand what mitigation and containment strategies [transportation companies] already put in place." ■

Suggested Reading

1. ASN NTDS. Webinar: CDC Recommendations and Policy Updates for Current Challenges in the Dialysis Setting. March 26, 2020. https://www.asn-online.org/ntds/resources/Webcast_2020_03_26_COVID-19.mp4
2. CDC. Coronavirus 2019. Dialysis Facilities. Screening and Triage at Intake. https://www.cdc.gov/coronavirus/2019-ncov/healthcare-facilities/dialysis/screening.html
3. CDC. Coronavirus Disease 2019 (COVID-19) Outpatient Dialysis Facility Preparedness Assessment Tool. https://www.cdc.gov/coronavirus/2019-ncov/downloads/COVID-19-outpatient-dialysis.pdf
4. ASN. CMS Announces Relief for Clinicians, Providers, Hospitals and Facilities Participating in Quality Reporting Programs in Response to COVID-19 https://www.asn-online.org/g/blast/files/CMS%20QMVIG%20Updates.pdf
5. White D. *Kidney News* Online. Critical clarification from CMS: PD catheter and vascular access placement is essential https://www.kidneynews.org/policy-advocacy/leading-edge/critical-clarification-from-cms-pd-catheter-and-vascular-access-placement-is-essential

At Home: Considerations in the Care of Patients Receiving Home Dialysis During the COVID-19 Pandemic: A Statement from the ASN COVID-19 Response Team

By Jeffrey Perl, Alan S. Kliger, Martin J. Schreiber, and the Home Dialysis Subcommittee of the ASN COVID-19 Response Team

The world is struggling with the new and uncertain realities of the COVID-19 pandemic, which has challenged all facets of the healthcare system in unprecedented ways. As the initial experience in the United States has taught us, none are more vulnerable to COVID-19–related morbidity and mortality than the ESRD population (1). These individuals carry a high burden of comorbidity, may be immunocompromised, have high rates of healthcare use, and often have a high prevalence of many of the symptoms that overlap with those of COVID-19. Moreover, the risk of viral transmission may be greatest for patients receiving in-center hemodialysis because of the scheduled frequent trips for dialysis treatments within healthcare facilities, limited distancing between patients, and frequent interactions with healthcare workers.

The COVID-19 pandemic will leave a long-lasting mark on . . . home dialysis in the United States, serving as a catalyst for much-needed refinements in the care model.

Taken together, these factors create many challenges in ongoing nationwide efforts to limit the transmission of the SARS-CoV-2 virus. As a result, robust infection prevention and control policies and procedures are needed in the care of ESRD patients and have been developed with guidance from the Centers for Disease Control and Prevention (CDC) and in collaboration with local infection prevention and control authorities. These measures must be implemented and adhered to while being subjected to ongoing revision, both in the face of emerging evidence and in an evolving climate of supply chain disruptions, particularly those resulting from shortages of personal protective equipment (PPE).

By virtue of receiving dialysis treatments at home, both peritoneal dialysis (PD) and home hemodialysis (HHD) patients remain somewhat at an advantage over their in-center hemodialysis counterparts. Home dialysis patients may be better able to adhere to social distancing measures, with fewer interactions with healthcare workers. The COVID-19 pandemic has further underscored the additional potential advantages of increasing home-based ESRD care. It is possible that the long-lasting impact of COVID-19 may serve to further bolster ongoing efforts such as the Advancing American Kidney Health Executive Order in increasing the use of home dialysis in the United States.

Despite the advantages of home dialysis therapy during the COVID-19 pandemic, there are undoubtedly many challenges that patients, care partners, and healthcare providers are facing to ensure that home dialysis treatments remain uninterrupted and that care remains of the highest quality. Efforts to limit healthcare treatment team encounters to minimize the risk of COVID-19 transmission must be carefully balanced against any potential deleterious adverse health consequences that may ensue as a result. In this regard, and in an effort to provide guidance, education, and advocacy for the care of patients receiving home dialysis during this time, the American Society of Nephrology (ASN) COVID-19 Home Dialysis Subcommittee was formed. Composed of representation from the Nephrologists Transforming Dialysis Safety (NTDS) initiative, the CDC, dialysis organizations, home dialysis vendors, nurses, home dialysis patients, and ASN's policy team, our subcommittee operates within a larger ASN-wide effort that is responding to the COVID-19 pandemic across the continuum of kidney care: the ASN COVID-19 Response Team. Among the main purviews of this subcommittee are the following:

1. Advocate for governmental, surgical, and hospital administration policies to ensure that access procedures (i.e., PD catheter insertion, HHD access placement) are not delayed for patients who choose and are in urgent need of home dialysis therapy initiation. Explore the role of percutaneous PD access insertion under the operating room resource limitations imposed by COVID-19.
2. Address potential temporary staffing shortages so as not to limit home dialysis patient training in advocating for policies that expand the eligible pool of nurses able to care for and train patients receiving home dialysis. For example, in the context of the COVID-19 pandemic, advocate for state licensure waivers and waivers by the CMS to temporarily allow registered nurses (RNs) with fewer than 12 months of dialysis experience (but no fewer than 6 months) to be trained and allowed to provide PD training to patients, provided those RNs are working in a facility with at least one RN who has completed at least 12 months of dialysis training.
3. Explore greater use of urgent-start PD and other pathways to allow for a timely transition to home dialysis in an effort to avoid and limit exposure in dialysis facilities.
4. Work with CDC and NTDS to disseminate best demonstrated practices in terms of caring for COVID-19–positive home dialysis patients and reducing the risk of COVID-19 transmission between staff and home dialysis patients and care partners, during clinic visits, laboratory or intercurrent problem visits, patient training, and home visit encounters. These may include appropriate hand hygiene techniques, use of screening measures, use of PPE by patients and facility staff when in the facility and during home visits from dialysis staff, and information regarding testing and care of suspected or confirmed COVID-19–positive patients and/or care partners.
5. Although policies for telehealth have been well established for the care of home dialysis patients, the CMS has made possible significant expansion in the use of telehealth during the COVID-19 pandemic for patients with ESRD. This task force will continue to clarify how these policies apply to telehealth visits for patients receiving home dialysis; what waivers are necessary to support telehealth; which communication means may be used, particularly for patients without internet or smartphone access; and, where possible, advocate for further expanded coverage for telehealth visits while providing guidance and a framework for their optimal conduct.
6. Work with home dialysis vendors to ensure that home dialysis supplies are readily available and are delivered to patients in a way that ensures the safety of patients, their care partners, and delivery personnel.
7. Ensure that education is provided regarding the appropriate disposal of dialysis supplies and dialysis effluent by COVID-19–positive patients performing treatments at home, using the latest available evidence and guidance from the CDC.
8. Address potential and actual PPE shortages by developing mask reuse and conservation strategies for patients who use them during routine PD exchanges and HHD on/off procedures within the home. Reevaluate the policies for the use of masks during routine PD exchanges under constraints of impending or actual mask shortages.
9. In the face of COVID-19, the CMS has already made exceptions in reporting of quality measures and deadlines for a range of programs. Within these policies we seek to provide additional guidance highlighting more judicious use and appropriateness of deferment of various laboratory measures, peritoneal membrane evaluation, and measures of dialysis adequacy (i.e., kt/v urea). We aim to keep the kidney community abreast of any policy changes or infection prevention and control measures that may have a direct impact on the care of home dialysis patients while providing a forum to address questions pertaining to the care of these patients during the COVID-19 pandemic in a timely fashion, using the latest available evidence.

It is our hope that the task force will help facilitate the implementation of and adherence to the best demonstrated practices for the care of home dialysis patients during the COVID-19 pandemic across dialysis facilities in the United States, serving as a resource for credible and time-sensitive information based on sound scientific principles during these challenging times. In addition, the COVID-19 pandemic will leave a long-lasting mark on the home dialysis community in the United States, serving as a catalyst for much-needed refinements in the care model for delivery of home dialysis, future pandemic planning and emergency preparedness, improvement in access to and enhancement of telehealth delivery, and refinement of infection prevention and control measures for home dialysis facilities, all the while improving access to home-based ESRD care.

The authors thank the ASN COVID-19 Response Team Home Dialysis Subcommittee members who contributed to this article: Michael A. Kraus, Kerry A. Leigh, Rajnish Mehrotra, Alicia Neu, Matthew Oliver, Jeffrey I. Silberzweig, Bradley A. Warady, Suzanne Watnick, and Caroline Wilkie.

Jeffrey Perl, MD, SM, FRCP (C), is associate professor of medicine in the division of nephrology at St. Michael's Hospital, University of Toronto. Alan S. Kliger, MD, is NTDS chair and clinical professor of medicine at Yale School of Medicine. Martin J. Schreiber, MD, is chief medical officer, DaVita Home Modalities, DaVita Kidney Care.

Reference

1. Watnick S, McNamara E. On the frontline of the COVID-19 outbreak: Keeping patients on long-term dialysis safe [published online ahead of print March 28, 2020]. *Clin J Am Soc Nephrol* doi: 10.2215/CJN.03540320.

PERSPECTIVE
On the Front Lines of COVID-19

By Edgar Lerma, MD, and Joel Topf, MD

Joel Topf, MD

Kidney News *Editorial Board member Edgar Lerma, MD, interviewed Joel Topf, MD, about his experience on the front lines of the COVID-19 pandemic. Topf is a private practice nephrologist who works primarily at St. John Ascension in Detroit. He is also on the faculty of the St. John Nephrology Fellowship program, where he teaches residents and medical students, using his academic energy to engage them through social media. He is co-creator of NephJC and NephMadness and hosts a nephrology-focused podcast called Freely Filtered.*

How did you get to be on the COVID-19 front lines? Did you volunteer?

I never signed up for this. I was rotating on the Nephrology Consult service during the second half of March. During that time, we saw our first COVID patient and 10 days later our 300th COVID patient. It came very quickly.

Please tell us about your experience.

This is the most challenging medical problem I have ever faced. Because of the avalanche of patients, our normal systems are overwhelmed, so tremendous creativity and innovation are required to adapt to a situation no one has seen before. The way hospitals have responded has been incredible. Our hospital normally has 40 ICU beds. They were able to balloon that up to 100 ICU beds by adapting the cardiac cath labs, the PICU, the PACU, and many other appropriate spaces. It is amazing to witness people shed egos and work together to adapt to some of the most trying times medicine has ever seen.

One of the early things my fellow and I noted was that if we got a patient from positive to negative balance, we would see an improvement in the chest x-ray, oxygenation, and vent settings. This may be just coincidence, but in the absence of clear evidence-based medical guidelines, we fell back on Loeb's Law of Medicine Number One: If what you are doing is working, keep doing it.

We saw success with this strategy in both patients with dialysis-dependent AKI as well as non-dialysis–dependent AKI, where we pushed high-dose loop diuretics to produce and extend negative balance. We stopped being creatinine police and focused on lower oxygen requirements while tolerating modest (or not so modest) rises in creatinine.

We also tried to tailor our orders to keep nurses out of the rooms. So instead of furosemide 80 mg IV q8h, we would start a drip at 10 mg per hour. This was a place where we really appreciated the flexibility of the nursing staff. A lot of the hospital normally restricts where furosemide drips can be run. Many of these regulations make sense where nurses specialize in a single specialty like oncology or orthopedic surgery. But, wisely, nurse managers are realizing that we need to be flexible in implementing regulations designed for an entirely different hospital environment, and we have had little trouble getting these drips approved during the crisis.

The biggest problem I am seeing now is the extended nature of the disease. I am starting to see a lot of patients who emerge from the acute aspect of the disease and are about to go home. And patients ask about elderly family members, is it safe for them to go home? How can I prevent this from affecting more of my family? It feels like an extension of the shelter in place orders we have already implemented. We need places where patients can go after the hospital but while they are still shedding virus. The home may not be ideal.

How does your family feel about you volunteering? What do you do differently when you come home—decontaminate, etc.

This has been very hard on my family. They are very nervous that I could bring SARS-CoV-2 into our house. I always wash before leaving the hospital. I leave all my PPE in the car, and I change clothes as soon as I get home. I then wash my hands and face. I have seen firsthand how this disease just rips through families. This is definitely a concern. We are doing the best we can.

What have you observed about the COVID patients you have encountered with regard to COVID + AKI?

The COVID AKI story is multipronged. One population should be very familiar to anyone who takes care of ICU patients. These patients act like they are septic. They have decreased blood pressure, multi-organ failure, and they develop ATN. But there is another population where a patient's COVID-19 is not that bad, but they have profound AKI. We are seeing patients come in with creatinine of 8 to 18 mg/dL along with hyperkalemia who need to be started on dialysis right away. Usually when we hear about patients arriving with bad AKI we go down to the ER and find a patient who is profoundly volume depleted, but these COVID-19 patients look volume resuscitated, and when you give them fluids they don't get better. It looks to me like there is direct viral damage to the kidney not dependent on multi-organ failure and sepsis. I am not alone with this observation. A lot of people are talking about this. Additionally, the early biopsy and autopsy studies on patients with COVID-19 and AKI are finding evidence of direct viral infection.

What about COVID + ESKD?

We are seeing more and more of our dialysis patients turn positive. And, sadly, I have lost a longtime patient to COVID-19. My dialysis patients all go to DaVita units. DaVita has organized three tiers of dialysis units, one for people with no suspicion for COVID-19, another for people under investigation for possible infection, and a third level for patients with confirmed COVID. I have patients at all three levels. I am impressed with how DaVita has adapted to the challenge of a highly communicable disease and with how they are doing what they need to do to protect our patients. So far (fingers crossed), we have not seen an outbreak in any of the units I go to. They have done a great job of building the airplane while we are flying at 35,000 feet.

What about COVID + transplant?

A number of our transplant patients have been infected with COVID-19 or have become patients under investigation. I am not doing anything too creative. I am stopping the antimetabolite, cutting the CNI in half, and doubling up the steroids to compensate. This seems to be pretty successful. I am seeing transplant patients doing reasonably well without rejection. This protocol came right from the pages of NephJC, which surfaced several early case reports of transplant patients who have developed and recovered from COVID-19. (http://www.nephjc.com/news/covidtx)

As a physician on the front lines, what is your take on the shortage of personal protective equipment (PPE), ventilators, etc.?

This is one of the big problems with the COVID-19 pandemic. I wish there wasn't a shortage. Tragically, the shortage of PPE will mean that doctors and nurses are going to unnecessarily get infected and likely will spread the disease to their families.

I am also concerned about all the emphasis on decontaminating N95 masks. I recognize the need to prevent infections from contact with a mask, but these masks were designed to be used one time. I have found that as I use the masks for a second and third day they lose their shape and no longer seal to my face. I can tell this because on the first day I can wear a mask all day without fogging my glasses, but on the second day I get repeated fogging, and that means the mask isn't sealing to my nose, and that means I'm not being protected by the mask. I worry that attempts to decontaminate a mask by heating it will break down the glue holding it together and make it lose its integrity even faster.

There is a lot of misinformation about COVID-19 out there. What is your take on that?

The rate at which information is coming out about COVID-19 is unprecedented. As of April 8, 2020, there were just over 3000 articles about COVID-19, with 900 of them published just during the previous week. This amazing productivity is being paired with unending public interest, so articles and even pre-prints are finding their way onto CNN, into the *New York Times*, and even the speeches of the president. This means that premature conclusions and sloppy clickbait logic are getting amplified way beyond what we normally see with the traditional publication chain.

One of the early rumors relevant to nephrology was the idea that ARBs and ACEis were harmful in SARS-CoV-2 infection. This was one of the first myth-busting projects that the team at NephJC took on. They analyzed all the relevent publications, going beyond the abstracts and digging into the methods to determine the soundness of the analyses, which turned out to not be so sound. NephJC, along with all the major scientific and professional societies, instructed patients to remain on their RAASi unless instructed by a doctor to stop. There is no compelling data that these drugs are harmful or protective from COVID-19 as of April 9, 2020. This was an example of a group of doctors and scientists coming together in the spirit of cooperation and working to vet the literature of an emerging threat in order to help doctors and patients around the world.

What is your advice to colleagues who are on the front lines and to those who are not?

Be safe out there and do your best. This is the greatest challenge medicine has ever faced, and getting through it will take grit, creativity, flexibility, and all the talents you have developed in your career. This is not a time to close yourself off and try to solve everything yourself. Listen to your peers. Join a physician group, whether it is on Facebook, ASN Communities, or #MedTwitter, because together we know more and can go further than any of us alone.
https://twitter.com/kidney_boy/status/1245717240097443840?s=20

COVID-19: An Asian Perspective

By Vivek Kumar, Vijay Singh, and Vivekanand Jha

Humans face an unprecedented situation today. Human coronavirus disease 19 (COVID-19) has caught everyone, regardless of borders and competence of existing healthcare infrastructures, completely unaware.

The way the disease has spread across the world over 4 months aptly reflects the meaning of "viral" as it is used in social media, where the term frequently describes something that garners immense worldwide publicity within a very short time. The sudden temporal clustering of numerous cases of unexplained rapidly progressive pneumonia leading to respiratory failure baffled clinicians in Wuhan, China, in December 2019. As could be expected, suspicion of some new affliction grew strong as cases started increasing, and patterns became recognizable by early January 2020.

Detailed investigations of this new affliction identified it as a viral pneumonia resulting from a new coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). By this time, the exponential increase in number of cases and pattern of spread among contacts of cases left no doubt that the virus spreads by droplet infection. As new cases continued to pour in, the burden soon overwhelmed existing healthcare facilities. No specific treatment was available, and estimates suggested that millions would be infected. The Chinese government announced a complete lockdown in Wuhan on January 23, 2020, to break the human-to-human chain of transmission. However, by this time, cases had been reported in South Korea, Japan, Thailand, and Singapore. One week later, the World Health Organization (WHO) acknowledged its presence in five WHO regions and declared it a Public Health Emergency of International Concern.

India is the next most populous country in Asia. Approximately 17,000 cases and 550 deaths had been reported in India by April 19, 2020. The initial patients had a history of international travel, but new patients who either are contacts of patients with confirmed cases or have no history of contact or travel are being increasingly recognized. These numbers are to be interpreted cautiously because testing has been limited to cases with a high degree of suspicion on account of a documented history of travel or exposure. Extensive screening, as has been done in countries like South Korea, has not been done in India.

The success of physical distancing, quarantine, and testing in China and South Korea has lessons for all Asian countries. South Korea had brought down the daily number of new cases from 851 in early March, to 18. Singapore has strictly enforced social and physical distancing by imposing legal provisions of fines and imprisonment.

Initially, in India, asymptomatic individuals returning from abroad were advised to self-quarantine at home, and suspected individuals or high-risk individuals were quarantined under Indian government surveillance. Inasmuch as these measures did not seem very effective and suspicion of community spread became higher, the Indian government called for a unique self-imposed home quarantine, referred to as Janata (public) curfew, on March 22, 2020. By this time, COVID-19 had already spread through Europe and the United States, with the WHO declaring that Europe was the new epicenter of the pandemic and the US would follow. In fact, the US, followed by Spain, now has the highest number of reported cases of COVID-19. A quick look at the disease trajectory in late March suggested that India was a close runner-up, with a delay of a few weeks.

At this stage, the Indian government took the unprecedented step of complete nationwide lockdown on all nonessential services. All residents were ordered to stay inside homes, wherever they were, for a 3-week lockdown, which has now been extended by 3 more weeks. The government suspended all modes of public transport, forbad the use of private vehicles except for medical emergencies or by personnel managing essential services, and completely isolated the country from the rest of the world.

Inasmuch as India has a federal structure, some states have instituted additional measures within their jurisdictions to strictly enforce these orders. Simultaneously, the government is expanding the scope of diagnostic testing and increasing diagnostic facilities. Public sector hospitals

China swiftly mobilized its human and material resources toward containing COVID-19, enforcing physical and social distancing. People had to stay inside their homes and could come out only once in a few days in a staggered manner to buy essential commodities. Except for essential services, everything was brought to a halt. Doctors, paramedical personnel, and supplies were brought in from other parts of China. China had recorded approximately 84,000 cases and 4600 deaths resulting from COVID-19 by the third week of April 2020, constituting 3.5% of global cases and 2.8% of reported mortality due to the disease. That country has been able to drastically bring down new indigenous cases, and it now reports new disease mostly in individuals who have recently arrived from abroad. As China is lifting restrictions in Wuhan, the data suggest that continuation until April 2020, followed by staggered removal, would further alter the COVID-19 trajectory, leading to a secondary but smaller epidemic peak by the end of 2020. This could decrease the median number of infections by 92% by mid-2020 and by 24% by the end of 2020.

have stopped elective outpatient clinics and have deferred elective procedures indefinitely. Hospitals are gearing up to screen and create dedicated isolation areas for COVID-19 patients. In view of the shortage of personal protective gear and equipment, efforts have begun to procure them from all sources, initiate or ramp up production in local industries, and rationalize distribution. Central and state governments have started identifying areas beyond hospitals that could be converted into isolation or quarantine facilities if the need arises. These unprecedented steps have been necessitated by a fragile situation, which could go out of control.

Malaysia, Pakistan, and Indonesia are other large Asian countries that have now reported >5000 cases with similar disease trajectories. Travel restrictions, quarantine of cases and contacts, and partial or full lockdowns have been enforced on similar lines. Nationwide lockdowns or curfews have curbed human movements and are not without undesirable implications. In developing countries like India, most of the population work in unorganized sectors and have been rendered without wages during the lockdown. Ensuring delivery of essential supplies to households when supply chains are disrupted also becomes challenging. It comes as no surprise that chaos and panic could arise, given uncertainties about the future. Governments are trying to support businesses and individuals, stop the spread of misinformation, and educate people about the continued use of measures that enhance the health of the larger public. Another concern is impaired access to care for patients with chronic illnesses and debilities who would otherwise be critically dependent on existing healthcare facilities. The circumstances are highly dynamic and seem to change with each passing day.

Providing maintenance dialysis and caring for patients using maintenance immunosuppressive agents are practical challenges. Several documents have been recently published to guide management. However, resource constraints and the fact that most healthcare expenditures come out of pocket will complicate things in this region, especially when finances will be hit as a result of prolonged lockdowns. Government support and broader public–private sector cooperation will be required to overcome these barriers. In addition to healthcare staff, there is a need to educate patients using dialysis and their caregivers because they frequently visit healthcare facilities. Mobile technology and telemedicine platforms are being used to facilitate clinical decision-making wherever feasible.

Kidney involvement in COVID-19 ranges from asymptomatic abnormalities, such as proteinuria and microscopic hematuria, to dialysis-dependent acute kidney injury (AKI). The prevalence of proteinuria, hematuria, and AKI in a cohort of 701 patients in Wuhan, China, has been reported to be 43.9%, 26.7% and 5.1%, respectively. Importantly, AKI was independently associated with in-hospital mortality. In patients with elevated serum creatinine at admission, the in-hospital mortality was 33.7%. Therefore, nephrologists must be an important part of the core team caring for patients with COVID-19. In addition, given the exponentially increasing burden of COVID-19 and the diversion of resources toward its care and control, nephrologists have been forced to take up the role of front line managers in severely hit areas. Therefore, nephrologists should brace to perform dual roles as nephrologists and physicians.

The South-East Asia regional office of WHO considers the region to be at high risk and highly vulnerable to COVID-19 because of resource constraints, gaps in diagnostic laboratory capacity, lack of proper infection prevention or control practices, and logistics. The WHO has recommended urgent refresher training to healthcare workers, broader intersectoral cooperation, risk communication, community engagement, and international cooperation as important measures to address these deficiencies. In addition to overall burden and mortality statistics, the WHO advises that the percentage of cases among healthcare workers is an important key performance indicator for COVID-19. Isolation of infected patients, tracing followed by quarantine of contacts, and personal protection measures are fundamental to stopping the spread of COVID-19. These measures are directed toward bringing the peak down so that human and material resources can be mobilized to care for patients with COVID-19 in the future. It is important to realize that the diagnostic approach needs to be broad based and that facilities for diagnosis need to be enhanced and made available to make this approach successful. The development of specific drugs or vaccines will be supplemental. There is no doubt that the rapid evolution of COVID-19 across the world and responses to it will have far-reaching implications for the way healthcare is practiced and delivered. ■

Vivek Kumar, MD, is an assistant professor in the department of nephrology at the Postgraduate Institute of Medical Education and Research in Chandgarh, India. Vijay Singh, MSc, PhD, is associated with the department of nephrology at the Postgraduate Institute of Medical Education and Research in Chandgarh, India. Vivekanand Jha, MBBS, MD, DM, PhD, is executive director of the George Institute for Global Health, India; professor of nephrology, University of Oxford; conjoint professor of medicine, University of New South Wales, Sydney; and president of the International Society of Nephrology.

Sweeping CMS Waivers Facilitate Access to Kidney Care

By Nicole Fauteux

Extraordinary times call for extraordinary measures, and at least as far as kidney care is concerned, the federal government is rising to the challenge. In the past month, the Centers for Medicare & Medicaid Services (CMS) has issued an unprecedented set of waivers to facilitate care delivery during the COVID-19 pandemic. The sweeping interim final rule the agency published March 30, 2020, provides a remarkable degree of flexibility in how providers may deliver care to patients insured through Medicare and Medicaid during the current public health emergency (1).

Equally extraordinary, nearly every one of the requests ASN put forward last month in a letter to Health and Human Services (HHS) Secretary Alex Azar is addressed in the new rule (2), paving the way for kidney specialists and the entire kidney care team to continue to provide a high level of care to patients during the pandemic. The government is applying the rule retroactively, as of March 1, 2020, further ensuring continuous care for dialysis patients, who must receive ongoing services despite the need to protect themselves from exposure to SARS-CoV-2.

What's in the rule

The rule aims to mitigate the impacts of the pandemic by giving providers broad flexibility to furnish services in ways that minimize "exposure risks to health care providers, patients, and the community" during the pandemic. To accomplish this goal, the rule:

- authorizes greater use of telehealth and other means of remote communication;
- expands the locations where medical services may be provided;
- changes program requirements that might inadvertently create incentives "to place cost considerations above patient safety;"
- reduces paperwork and other regulatory burdens;
- delays facility inspections;
- removes barriers to health professionals practicing outside the states where they are licensed; and
- extends permission to non-physician licensed practitioners to order home health services.

Expanded telehealth

The expanded use of telehealth could create the biggest change to how providers practice. Under the new rule, nephrologists may conduct all evaluations of in-center and home dialysis patients via telehealth, provided the clinician deems those patients to be in stable condition. Nephrologists may also use telehealth to consult with new patients. To facilitate these virtual encounters while people are self-isolating, CMS specified in the rule that patients and physicians may speak to one another from any location and use non-HIPPA–complaint platforms such as Facetime and Skype.

In its letter to HHS, ASN requested a further relaxation of current telehealth rules in light of the fact that many kidney care patients lack access to two-way video technology. CMS complied, authorizing reimbursement for telephone calls using CPT codes 99441-99443. This is a step in the right direction, but ASN and other physician groups would like to see the agency institute payment parity as well so that telephonic evaluation and management visits are reimbursed at the same level as visits provided in-office or via telehealth. The current policy disproportionately disadvantages physicians who care for the oldest and most vulnerable patients, people who must shelter in place and often lack the technology or know-how to engage in videoconferencing. ASN has also asked CMS to immediately instruct Medicare Administrative Contractors to ensure they follow the latest CMS guidance enabling payment for telephonic visits (3).

Expanded care locations

The rule also authorizes the creation of Special Purpose Renal Dialysis Facilities (SPRDFs) to address access issues and mitigate disease transmission during the pandemic. This authorization allows dialysis centers to establish temporary facilities or provide their services in skilled nursing facilities where patients live in order to reduce the risk of the virus spreading from infected to non-infected individuals. Normally facilities would first need to establish an access need and undergo a federal site survey before establishing an SPRDF. The rule waives these requirements but retains other standards to make sure dialysis provided in alternative locations is both safe and effective. Dialysis facilities must furnish all needed staff, equipment, and supplies in the SPRDF; operate and maintain equipment in accordance with manufacturer recommendations; and follow infection control requirements. Under the rule, physicians who are appropriately credentialed to provide care at a certified dialysis facility may also provide care at designated isolation locations without separate credentials.

Other notable provisions

The CMS rule takes additional steps to streamline care delivery during the pandemic. To provide physicians with greater flexibility, the agency issued a blanket waiver of sanctions under the Stark Law, which prohibits physicians from referring Medicare patients to facilities in which the provider has a financial stake (4). The "on-time" requirement for initial and comprehensive assessments of patients admitted to a dialysis facility has also been waived. Medicare-enrolled providers who hold a valid license in the state where they are enrolled now have the freedom to work across state lines to contribute to relief efforts, assuming they are not affirmatively barred from working in those states.

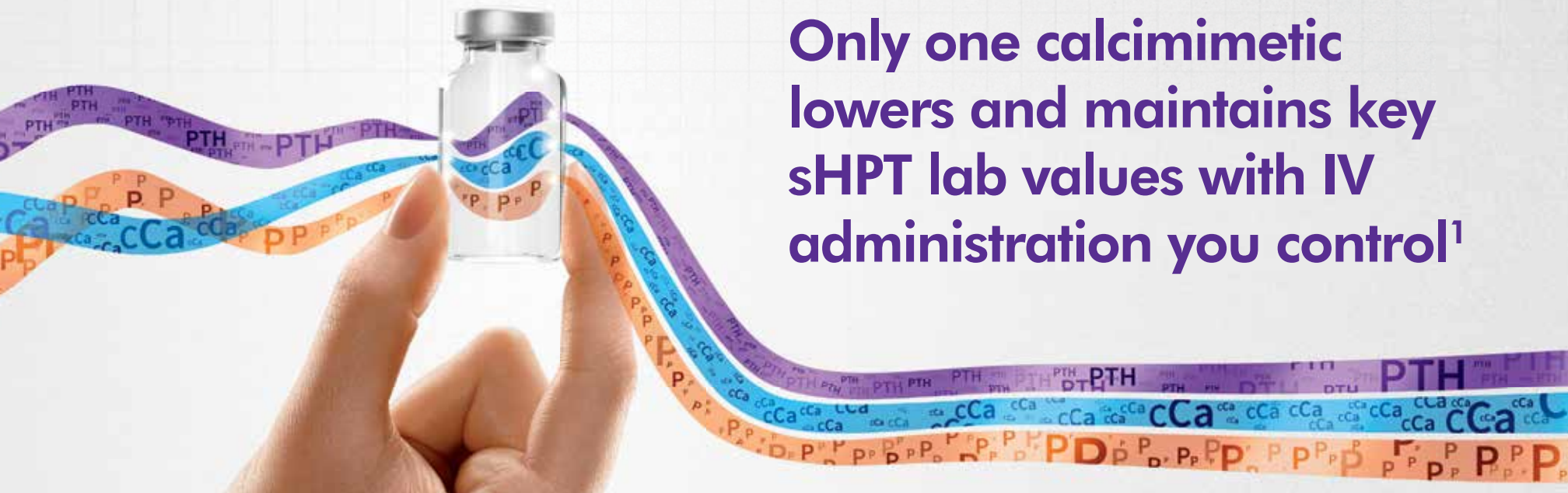
One issue not covered by the rule: vascular access surgery. In recent weeks, some health systems and insurers have postponed peritoneal dialysis catheter placement in the misplaced belief that it is a non-essential or elective surgery. In reality, vascular access surgery is more essential than ever, as the presence of a peritoneal dialysis catheter allows kidney patients to dialyze at home, reducing their risk of exposure to SARS-CoV-2. ASN and other members of the kidney care community approached CMS regarding this concern, and on March 26, 2020, the agency clarified its guidance on deferring nonessential surgical procedures (5). The agency's statement identified arteriovenous fistulas, arteriovenous grafts, peritoneal dialysis catheters, and intravenous catheters as "essential in that establishing vascular access is crucial for End Stage Renal Disease (ESRD) patients to receive their life-sustaining dialysis treatments."

The words "life-sustaining" reflect a critical understanding. While COVID-19 may pose a more immediate threat to life, the disruption of health services caused by the pandemic also poses a serious threat to kidney patients. CMS has taken extraordinary steps to mitigate that disruption, and ASN will urge the agency to continue along this path. As nephrologists are discovering, COVID-19 causes acute kidney injury in a significant number of hospitalized patients who need intensive care (6). That suggests that even more individuals may require renal replacement therapy and other forms of kidney care in the near future. ■

Please note: The information in this article is accurate as of April 20, 2020, but federal regulations and policies are changing on a daily basis. Consult Kidney News *Online and the ASN website for updates.*

References

1. Centers for Medicare & Medicaid Services. Medicare and Medicaid Programs; Policy and Regulatory Revisions in Response to the COVID-19 Public Health Emergency. https://www.cms.gov/files/document/covid-final-ifc.pdf. Accessed Apr. 10, 2020.
2. American Society of Nephrology. Letter to Alex Azar, secretary, Department of Health and Human Services. Mar. 19, 2020. https://www.asn-online.org/policy/webdocs/19.3.20AzarCOVID-19_Letter_Final.pdf. Accessed Apr. 10, 2020.
3. Council of Medical Specialty Societies. CMSS Issues Statement on Temporary Payment Parity for Telephone Visits. https://cmss.org/telephone_payment_parity/. Accessed Apr. 20, 2020.
4. Centers for Medicare & Medicaid Services. Blanket Waivers of Section 1877(g) of the Social Security Act Due to Declaration of COVID-19 Outbreak in the United States as a National Emergency. https://www.cms.gov/files/document/covid-19-blanket-waivers-section-1877g.pdf. Accessed Apr. 10, 2020.
5. Centers for Medicare & Medicaid Services. Statement to ASN on previously released guidance to defer nonessential planned surgical procedures. https://www.kidneynews.org/sites/default/files/Critical_CMS_announcement_3-20.pdf. Accessed Apr. 10, 2020.
6. NephJC. *COVID-19 and AKI FAQs*. http://www.nephjc.com/news/covidaki. Accessed Apr. 10, 2020.



Only one calcimimetic lowers and maintains key sHPT lab values with IV administration you control[1]

Not an actual Parsabiv™ vial.
The displayed vial is for illustrative purposes only.

Measure corrected serum calcium prior to initiation of Parsabiv™. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv™. Measure PTH 4 weeks after initiation or dose adjustment of Parsabiv™. Once the maintenance dose has been established, measure PTH per clinical practice.

Indication

Parsabiv™ (etelcalcetide) is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:

Parsabiv™ has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these populations.

Important Safety Information

Contraindication: Parsabiv™ is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred.

Hypocalcemia: Parsabiv™ lowers serum calcium and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause QT interval prolongation and ventricular arrhythmia. Patients with conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Parsabiv™. Closely monitor corrected serum calcium and QT interval in patients at risk on Parsabiv™.

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to Parsabiv™. Monitor corrected serum calcium in patients with seizure disorders on Parsabiv™.

Concurrent administration of Parsabiv™ with another oral calcimimetic could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to Parsabiv™ should discontinue cinacalcet for at least 7 days prior to initiating Parsabiv™. Closely monitor corrected serum calcium in patients receiving Parsabiv™ and concomitant therapies known to lower serum calcium.

Worsening Heart Failure: In Parsabiv™ clinical studies, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. Closely monitor patients treated with Parsabiv™ for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding: In clinical studies, 2 patients treated with Parsabiv™ in 1253 patient years of exposure had upper gastrointestinal (GI) bleeding at the time of death. The exact cause of GI bleeding in these patients is unknown and there were too few cases to determine whether these cases were related to Parsabiv™.

Patients with risk factors for upper GI bleeding, such as known gastritis, esophagitis, ulcers or severe vomiting, may be at increased risk for GI bleeding with Parsabiv™. Monitor patients for worsening of common Parsabiv™ GI adverse reactions and for signs and symptoms of GI bleeding and ulcerations during Parsabiv™ therapy.

Adynamic Bone: Adynamic bone may develop if PTH levels are chronically suppressed.

Adverse Reactions: In clinical trials of patients with secondary HPT comparing Parsabiv™ to placebo, the most common adverse reactions were blood calcium decreased (64% vs. 10%), muscle spasms (12% vs. 7%), diarrhea (11% vs. 9%), nausea (11% vs. 6%), vomiting (9% vs. 5%), headache (8% vs. 6%), hypocalcemia (7% vs. 0.2%), and paresthesia (6% vs. 1%).

Please see Brief Summary of full Prescribing Information on adjacent page.

IV = intravenous; sHPT = secondary hyperparathyroidism; PTH = parathyroid hormone; P = phosphate; cCa = corrected calcium.

Reference: 1. Parsabiv™ (etelcalcetide) prescribing information, Amgen.

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Visit **ParsabivHCP.com** for more information.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE

PARSABIV is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:

PARSABIV has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with chronic kidney disease who are not on hemodialysis and is not recommended for use in these populations.

CONTRAINDICATIONS

Hypersensitivity

PARSABIV is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred with PARSABIV *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]*.

WARNINGS AND PRECAUTIONS

Hypocalcemia

PARSABIV lowers serum calcium *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]* and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmia.

QT Interval Prolongation and Ventricular Arrhythmia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (0% placebo versus 1.2% PARSABIV). In these studies, the incidence of a maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.8%, respectively *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]*. Patients with congenital long QT syndrome, history of QT interval prolongation, family history of long QT syndrome or sudden cardiac death, and other conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to PARSABIV. Closely monitor corrected serum calcium and QT interval in patients at risk receiving PARSABIV.

Seizures

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to PARSABIV. Monitor corrected serum calcium in patients with seizure disorders receiving PARSABIV.

Concurrent administration of PARSABIV with another oral calcium-sensing receptor agonist could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to PARSABIV should discontinue cinacalcet for at least 7 days prior to initiating PARSABIV *[see Dosage and Administration (2.4) in PARSABIV full prescribing information]*. Closely monitor corrected serum calcium in patients receiving PARSABIV and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of PARSABIV. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with PARSABIV *[see Dosage and Administration (2.2) in PARSABIV full prescribing information]*. Educate patients on the symptoms of hypocalcemia, and advise them to contact a healthcare provider if they occur.

If corrected serum calcium falls below the lower limit of normal or symptoms of hypocalcemia develop, start or increase calcium supplementation (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration). PARSABIV dose reduction or discontinuation of PARSABIV may be necessary *[see Dosage and Administration (2.2) in PARSABIV full prescribing information]*.

Worsening Heart Failure

In clinical studies with PARSABIV, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. In clinical studies, heart failure requiring hospitalization occurred in 2% of PARSABIV-treated patients and 1% of placebo-treated patients. Reductions in corrected serum calcium may be associated with congestive heart failure, however, a causal relationship to PARSABIV could not be completely excluded. Closely monitor patients treated with PARSABIV for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding

In clinical studies, two patients treated with PARSABIV in 1253 patient-years of exposure had upper gastrointestinal (GI) bleeding noted at the time of death while no patient in the control groups in 384 patient-years of exposure had upper GI bleeding noted at the time of death. The exact cause of GI bleeding in these patients is unknown, and there were too few cases to determine whether these cases were related to PARSABIV.

Patients with risk factors for upper GI bleeding (such as known gastritis, esophagitis, ulcers, or severe vomiting) may be at increased risk for GI bleeding while receiving PARSABIV treatment. Monitor patients for worsening of common GI adverse reactions of nausea and vomiting associated with PARSABIV *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]* and for signs and symptoms of GI bleeding and ulcerations during PARSABIV therapy. Promptly evaluate and treat any suspected GI bleeding.

Adynamic Bone

Adynamic bone may develop if PTH levels are chronically suppressed. If PTH levels decrease below the recommended target range, the dose of vitamin D sterols and/or PARSABIV should be reduced or therapy discontinued. After discontinuation, resume therapy at a lower dose to maintain PTH levels in the target range *[see Dosage and Administration (2.1) in PARSABIV full prescribing information]*.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Hypocalcemia *[see Warnings and Precautions (5.1) in PARSABIV full prescribing information]*
- Worsening Heart Failure *[see Warnings and Precautions (5.2) in PARSABIV full prescribing information]*
- Upper Gastrointestinal Bleeding *[see Warnings and Precautions (5.3) in PARSABIV full prescribing information]*
- Adynamic Bone *[see Warnings and Precautions (5.4) in PARSABIV full prescribing information]*

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The data in Table 2 are derived from two placebo-controlled clinical studies in patients with chronic kidney disease and secondary hyperparathyroidism on hemodialysis. The data reflect exposure of 503 patients to PARSABIV with a mean duration of exposure to PARSABIV of 23.6 weeks. The mean age of patients was approximately 58 years, and 60% of the patients were male. Of the total patients, 67% were Caucasian, 28% were Black or African American, 2.6% were Asian, 1.2% were Native Hawaiian or Other Pacific Islander, and 1.6% were categorized as Other.

Table 2 shows common adverse reactions associated with the use of PARSABIV in the pool of placebo-controlled studies. These adverse reactions occurred more commonly on PARSABIV than on placebo and were reported in at least 5% of patients treated with PARSABIV.

Table 2: Adverse Reactions Reported in ≥ 5% of PARSABIV-Treated Patients

Adverse Reaction*	Placebo (N = 513)	PARSABIV (N = 503)
Blood calcium decreased[a]	10%	64%
Muscle spasms	7%	12%
Diarrhea	9%	11%
Nausea	6%	11%
Vomiting	5%	9%
Headache	6%	8%
Hypocalcemia[b]	0.2%	7%
Paresthesia[c]	1%	6%

*Included adverse reactions reported with at least 1% greater incidence in the PARSABIV group compared to the placebo group

[a] Asymptomatic reductions in calcium below 7.5 mg/dL or clinically significant asymptomatic reductions in corrected serum calcium between 7.5 and < 8.3 mg/dL (that required medical management)

[b] Symptomatic reductions in corrected serum calcium < 8.3 mg/dL

[c] Paresthesia includes preferred terms of paresthesia and hypoesthesia

Other adverse reactions associated with the use of PARSABIV but reported in < 5% of patients in the PARSABIV group in the two placebo-controlled clinical studies were:

- Hyperkalemia: 3% and 4% for placebo and PARSABIV, respectively.
- Hospitalization for Heart Failure: 1% and 2% for placebo and PARSABIV, respectively.
- Myalgia: 0.2% and 2% for placebo and PARSABIV, respectively.
- Hypophosphatemia: 0.2% and 1% for placebo and PARSABIV, respectively.

Description of Selected Adverse Reactions

Hypocalcemia

In the combined placebo-controlled studies, a higher proportion of patients on PARSABIV developed at least one corrected serum calcium value below 7.0 mg/dL (7.6% PARSABIV, 3.1% placebo), below 7.5 mg/dL (27% PARSABIV, 5.5% placebo), and below 8.3 mg/dL (79% PARSABIV, 19% placebo). In the combined placebo-controlled studies, 1% of patients in the PARSABIV group and 0% of patients in the placebo group discontinued treatment due to an adverse reaction attributed to a low corrected serum calcium.

Hypophosphatemia

In the combined placebo-controlled studies, 18% of patients treated with PARSABIV and 8.2% of patients treated with placebo had at least one measured phosphorus level below the lower normal limit (i.e., 2.2 mg/dL).

QTc Interval Prolongation Secondary to Hypocalcemia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (0% placebo versus 1.2% PARSABIV). The patient incidence of maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.8%, respectively.

Hypersensitivity

In the combined placebo-controlled studies, the subject incidence of adverse reactions potentially related to hypersensitivity was 4.4% in the PARSABIV group and 3.7% in the placebo group. Hypersensitivity reactions in the PARSABIV group were pruritic rash, urticaria, and face edema.

Immunogenicity

As with all peptide therapeutics, there is potential for immunogenicity. The detection of anti-drug binding antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to etelcalcetide with the incidence of antibodies to other products may be misleading.

In clinical studies, 7.1% (71 out of 995) of patients with secondary hyperparathyroidism treated with PARSABIV for up to 6 months tested positive for binding anti-etelcalcetide antibodies. Fifty-seven out of 71 had pre-existing anti-etelcalcetide antibodies.

No evidence of altered pharmacokinetic profile, clinical response, or safety profile was associated with pre-existing or developing anti-etelcalcetide antibodies. If formation of anti-etelcalcetide binding antibodies with a clinically significant effect is suspected, contact Amgen at 1-800-77-AMGEN (1-800-772-6436) to discuss antibody testing.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no available data on the use of PARSABIV in pregnant women. In animal reproduction studies, effects were seen at doses associated with maternal toxicity that included hypocalcemia. In a pre- and post-natal study in rats administered etelcalcetide during organogenesis through delivery and weaning, there was a slight increase in perinatal pup mortality, delay in parturition, and transient effects on pup growth at exposures 1.8 times the human exposure for the clinical dose of 15 mg three times per week. There was no effect on sexual maturation, neurobehavioral, or reproductive function in the rat offspring. In embryo-fetal studies, when rats and rabbits were administered etelcalcetide during organogenesis, reduced fetal growth was observed at exposures 2.7 and 7 times exposures for the clinical dose, respectively.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

There were no effects on embryo-fetal development in Sprague-Dawley rats when etelcalcetide was dosed at 0.75, 1.5, and 3 mg/kg/day by the intravenous route during organogenesis (pre-mating to gestation day 17) at exposures up to 1.8 times human exposures at the clinical dose of 15 mg three times per week based on AUC. No effects on embryo-fetal development were observed in New Zealand White rabbits at doses of etelcalcetide of 0.375, 0.75, and 1.5 mg/kg by the intravenous route (gestation day 7 to 19), representing up to 4.3 times human exposures based on AUC. In separate studies at higher doses of 4.5 mg/kg in rats (gestation days 6 to 17) and 2.25 mg/kg in rabbits (gestation days 7 to 20), representing 2.7 and 7 fold clinical exposures, respectively, there was reduced fetal growth associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption.

In a pre- and post-natal development study in Sprague-Dawley rats administered etelcalcetide at 0.75, 1.5, and 3 mg/kg/day by the intravenous route (gestation day 7 to lactation day 20), there was a slight increase in perinatal pup mortality, delay in parturition, and transient reductions in post-natal growth at 3 mg/kg/day (representing 1.8-fold human exposures at the clinical dose of 15 mg three times per week based on AUC), associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption. There were no effects on sexual maturation, neurobehavioral, or reproductive function at up to 3 mg/kg/day, representing exposures up to 1.8-fold human exposure based on AUC.

Lactation

Risk Summary

There are no data regarding the presence of PARSABIV in human milk or effects on the breastfed infant or on milk production. Studies in rats showed [^{14}C]-etelcalcetide was present in the milk at concentrations similar to plasma. Because of the potential for PARSABIV to cause adverse effects in breastfed infants including hypocalcemia, advise women that use of PARSABIV is not recommended while breastfeeding.

Data

Presence in milk was assessed following a single intravenous dose of [^{14}C]-etelcalcetide in lactating rats at maternal exposures similar to the exposure at the human clinical dose of 15 mg three times per week. [^{14}C]-etelcalcetide-derived radioactivity was present in milk at levels similar to plasma.

Pediatric Use

The safety and efficacy of PARSABIV have not been established in pediatric patients.

Geriatric Use

Of the 503 patients in placebo-controlled studies who received PARSABIV, 177 patients (35.2%) were ≥ 65 years old and 72 patients (14%) were ≥ 75 years old.

No clinically significant differences in safety or efficacy were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old). No differences in plasma concentrations of etelcalcetide were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old).

OVERDOSAGE

There is no clinical experience with PARSABIV overdosage. Overdosage of PARSABIV may lead to hypocalcemia with or without clinical symptoms and may require treatment. Although PARSABIV is cleared by dialysis, hemodialysis has not been studied as a treatment for PARSABIV overdosage. In the event of overdosage, corrected serum calcium should be checked and patients should be monitored for symptoms of hypocalcemia, and appropriate measures should be taken *[see Warnings and Precautions (5.1) in PARSABIV full prescribing information]*.

AMGEN®

PARSABIV™ (etelcalcetide)

Manufactured for:
KAI Pharmaceuticals, Inc., a wholly owned subsidiary of Amgen, Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799

Patent: http://pat.amgen.com/Parsabiv/

Positive Trends in Kidney Transplantation in the United States

By Uday Nori

In July 2019, President Trump signed an executive order to launch Advancing American Kidney Health. This event underscored the importance and the urgency of recognizing kidney disease as a national priority. One of the three goals of this order is to double the number of kidneys available for transplantation by 2030. Although this idea might appear to be impracticable at the outset, the data presented in this brief report suggest that the process is already well under way.

Since 2014, the majority of the kidney transplantation centers across the United States have reported record increases in the volume of kidney transplantations. Several reasons are thought to be responsible for this heartening trend, but the principal mover seems to be the increased use of deceased donor organs (Figure 1). These data are also supported by the decreasing number of patients on the waiting list since 2014.

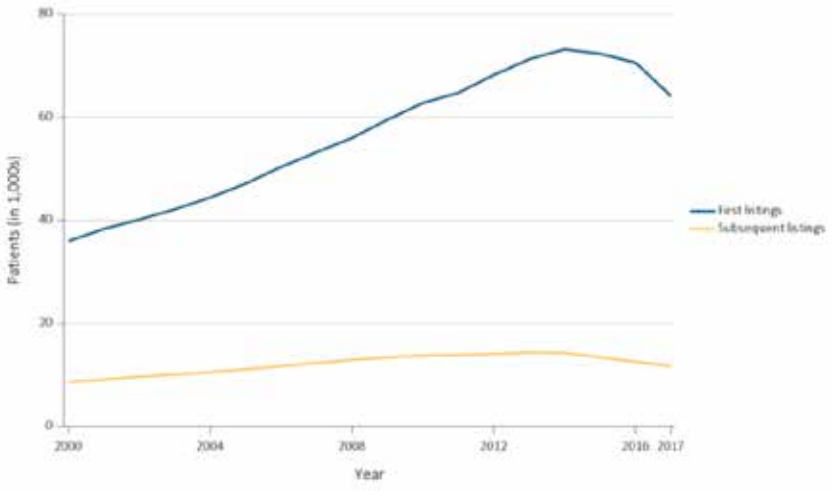
It is the opinion of this author that the following advances have played a large role in the increased transplantation rates:

1. The new Kidney Allocation System implemented in December 2014 has significantly improved the number of African American patients receiving transplants. The other components of the Kidney Allocation System that improved access to transplantation are awarding additional points to patients with very high plasma renin activity, using high Kidney Donor Profile Index kidneys, and including the preregistration dialysis time in the candidates' waiting time.
2. In 2013, the US Public Health Service published new guidelines for reducing the transmission of HIV, hepatitis B virus, and hepatitis C virus (HCV) through organ transplantation. This allowed transplantation centers to streamline the process of consenting and of providing posttransplantation surveillance in a systematic way. As can be seen in Figure 2, an increasing number of organs procured from these "increased-risk" donors have been successfully transplanted. The unfortunately high incidence of opiate overdose–related deaths in the United States, despite the attendant risk of infection transmission, fueled the use of organs with the help of these guidelines.
3. Transplantation of HCV-positive donor kidneys into HCV-negative recipients was previously thought to be unethical. The availability of direct-acting antiviral agents with high HCV cure rates has opened up the possibility of using those organs. After the 2017 publication of the first successful case series in the *New England Journal of Medicine*, several centers in the United States, including ours, have started performing these transplantations. Given the medicolegal implications of such practice, some centers have institutional review board–approved protocols and require informed consent from interested recipients. The success of this novel practice is substantial, with the likely number of such organs transplanted in 2019 in the several hundreds.

Among many new initiatives being brought into practice, the Organ Procurement and Transplantation Network is working on increasing organ use. More information can be found at https://unos.org/news/improvement/10-things-unos-is-doing-to-increase-organ-utilization/. ■

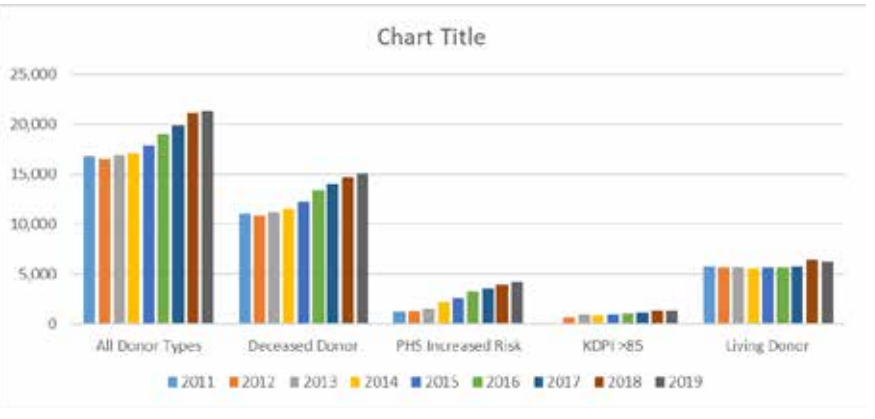
Uday Nori, MD, is associate professor of medicine and program director of the nephrology fellowship program at The Ohio State University Wexner Medical Center. He is a member of the Kidney News *editorial board.*

Figure 1. Deceased donor kidney transplantation waiting list trends



Reprinted with permission from the United States Renal Data System.

Figure 2. Transplantation trends by year and category



Abbreviations: KDPI, Kidney Donor Profile Index; PHS, US Public Health Service.

Reprinted with permission from the Organ Procurement Transplantation Network (accessed on December 16, 2019).

Nursing Care in the COVID-19 Pandemic

Interview with Nurse Leaders Liz McNamara and Diane Morris

By Tamara Kear and Glenda Payne

Nurses and patient care technicians are on the front lines in the multiple short-term and long-term dialysis units that are caring for patients who may have COVID-19. Dialysis patients and staff have been hit hard by this virus, with more than 6000 patients and more than 700 staff members receiving positive test results as of April 21, 2020. More than 790 dialysis patients have died as a result of COVID-19.

Seattle was the initial locus of the virus, and the first death in the United States was that of a dialysis patient. New York City then became the "leader" in this horrible "contest," with the most cases identified.

Nurse leaders in Seattle and New York City were asked to respond to questions about their experience, challenges, and advice for others. Liz McNamara, MN, RN, is vice president of patient care services and chief nursing officer for Northwest Kidney Centers in Seattle; Diane Morris, MS, MR, CNN, is director of nursing and clinical services for the Rogosin Institute in New York City.

We understand that the first patient death in the United States occurred in a patient at one of your dialysis centers. Had the patient been in a dialysis center during the period when he would have been contagious? How did your staff become aware of the patient having COVID-19?

McNamara: The first patient who died had last undergone dialysis in the outpatient facility 7 days before he died; so yes, we did provide care within the 14-day window. He was only symptomatic the last day he received dialysis with us, but he did report that he had been feeling unwell for 2 or 3 days prior. He died on a Friday night, and the clinic was closed on Saturday. We crafted an all-staff message that was texted out to ask all recipients to check their e-mail and to let all Northwest Kidney Center (NKC) staff know that the reported death was an NKC patient. We (leadership) went to the unit early Sunday morning and talked with the affected staff directly. The leadership also spoke with each patient individually that Sunday. I felt it imperative that patients hear from us directly rather than hear the news in the media.

How have your staff reacted to the need to care for patients with COVID-19?

McNamara: It has really ebbed and flowed. Many staff are quite frightened, because there is not much in the media about the mild cases and patients who do well. This type of disease was pretty new to outpatient dialysis. Both our chief medical officer and I have daily phone calls for the staff and physicians. We give updates from the county and the local hospitals, and then we field questions. This was very powerful in the early days. I have done calls with each unit and also with our acute care services division.

Morris: The staff have been very anxious for their own safety and the safety of their families. The concerns regarding limited personal protective equipment (PPE) add to their worries. We asked for volunteers from the staff to care for the known COVID-19–positive patients, and in each of our units, staff members volunteered.

How have you isolated COVID-19–positive patients? Are they in the same dialysis facility as COVID-19–negative patients, on different shifts, or in a different facility?

McNamara: We have 19 clinics, and all but three of them have a private room. We are not cohorting COVID-19–positive patients in one unit but have stood up the ability to perform dialysis to patients in modified contact/droplet precautions in each clinic. We plan to continue to provide patients care in their home units where they know the staff and are most comfortable.

Morris: The majority of the Rogosin Institute dialysis units have an open fourth shift on Tuesdays, Thursdays, and Saturdays. We have elected to keep the patients under investigation (PUIs) and COVID-19–positive patients in their respective dialysis units and segregate them on the fourth shift. We are keeping a distance of 6 feet between machines and patients, and the groups (i.e., COVID-19–positive patients and PUIs) are separated from each other. We are also planning on the possibility of cohorting patients from various facilities into a selected location by borough should there be a surge of COVID-19–positive patients needing dialysis.

What would cause you to transfer a COVID-19–positive patient to the hospital?

McNamara: The only reason we would send either a COVID-19–positive patient or a PUI to the hospital is if they are clinically ill enough to go.

Morris: We have asked patients to call before coming to dialysis if they have fever, cough, or respiratory distress. If the distress is severe, we instruct them to call 911 from home, and go to the hospital. If the patients do not have respiratory distress, we tell them to come to dialysis. These patients are met at the door, and a surgical mask is placed on them. Their temperature and symptoms are assessed. A patient who is a PUI will be diverted to a shift caring for PUIs, or if the symptoms warrant it (fever, cough, or respiratory distress), the patient is sent to the hospital.

Do you dedicate staff to the care of only COVID-19–positive patients?

McNamara: No; with the use of proper PPE there is no reason to do that.

Morris: We are seeing COVID-19–positive patients returning from the hospital before their test results are negative. We have dedicated staff to care for these patients.

What strategies have you put in place to deal with the psychosocial needs of both patients and staff?

McNamara: This is really an evolving issue. We have created patient letters and walked through how to have the conversation with a patient with our staff. For our staff we have provided our usual employee assistance program resources, along with some supplies that may be hard for them to get, like toilet paper, cleaning products, and a weekly treat delivery. This is an area we are continuing to work on.

Morris: We have seen a lot of anxiety among staff because they are fearful they will catch COVID-19 or infect their families. We have a psychologist on staff who has put together a program of Zoom support calls for the staff to ask questions and express their fears. We also have a yoga therapist who works with our patients and provides a daily meditation for the staff through Zoom. As part of the Rogosin employee benefit package, the staff also have access to counseling and telemedicine. Our unit managers have also been active in supporting the staff, especially when they have child care or transportation issues. Additionally, our nurse managers and administrators are conducting daily huddles with the staff to answer any questions or concerns they may have. The social workers and the psychologist have provided support for the patients. The patients have not expressed the degree of anxiety about the virus that I expected. I suspect they see the dialysis unit as a safe place where they receive care by well-trained staff, so they feel well cared for during treatment.

If you are experiencing a shortage of PPE, what is in short supply, and what measures are you taking?

McNamara: Surgical masks are of concern. We are wearing them longer than we normally would. We have been working to actively source more masks, and several of our dialysis partners have been helping us. We are having hand sanitizer made. We are accepting hand-sewn masks from the community but are using those for our patients and saving the medical-grade masks for our staff. We have also created NKC bandanas for our patients to use, which can be used in place of or in addition to the hand-sewn masks. We also offer these to our transport drivers as a thank-you.

Morris: We have experienced difficulty in obtaining surgical masks, N95 masks, shoe covers, impermeable gowns, thermometer probe covers, and disposable thermometers. We were able to obtain nondisposable face shields for all the staff members, and we have distributed face masks to wear under the shields as an added layer of protection. We have asked staff to conserve the face masks. We continue to take the temperatures of staff, patients, and their companions daily on entry to the dialysis unit building.

What are the biggest challenges you are facing during this pandemic?

McNamara: The biggest challenge right now is supplies. We started actively conserving supplies early on, but surgical masks and disposable gowns are at the top of my concern list. Hand sanitizer as well. We are working with a compounding pharmacy to actually make our own! The other challenge has been all the different sources of information. At the end of February, the World Health Organization came out and very clearly stated that COVID-19 was spread primarily by droplets and was not airborne like tuberculosis. Canada followed suit, as did our local healthcare systems here in Seattle. We have followed that guidance, knowing the potential of airborne organisms, with highly aerosolized generating procedures. It is matching the PPE to the exposure risk. The CDC has not officially stated the route of transmission, so there is a lot of confusion, and with all the different media reports, that has been tough. I will say that our local county public health department and the CDC team that worked on site with us for the first 2 weeks of March have been amazingly supportive.

Morris: The conservation of PPE and managing staff anxiety have been the biggest challenges.

Do you feel you have all the resources you need to care for your patients?

McNamara: I think all of us wish we could have additional staff when they may be needed. The only other resource I worry about is the supplies.

Morris: We do have the resources we need, but we have been very careful to conserve them because we have experienced great difficulty in finding sources from whom we can purchase PPE.

If necessary, has the local or federal government provided you with the resources you need to provide safe care to your patients and a safe work environment for your staff?

McNamara: The King County public health department has been a great source of information, and I am still in contact with our CDC colleagues who came on site early in the pandemic.

Morris: We participate in a weekly webinar from the New York state department of health on COVID-19 updates.

The state department of health staff have also been available by phone to answer our questions. Unfortunately, no outpatient testing is available to us. We have applied to the New York City office of emergency management for surgical masks and hope to receive a shipment soon.

Are you facing any staffing concerns with staff having to be quarantined? If so, how are you dealing with those staffing shortages?

McNamara: The guidelines around quarantine changed during about our second week. We actively screen all of our healthcare workers for symptoms every day when they come in to work. This is a symptom screen (cough, shortness of breath, sore throat) and temperature that is documented daily. Staff who are asymptomatic can work. If they experience symptoms they must go home.

Morris: We have faced staff shortages but have managed to staff the dialysis unit normally. We have discussed contingency plans in the event the staff shortages worsen, and we may consider shortening the dialysis day to be able to cover with a single shift of staff.

Have you experienced an increase in patient absences resulting from fear of contracting COVID-19? If so, what measures have been taken to combat those fears?

McNamara: We have not seen an uptick. We are really giving our patients messages about what they can do for staff, and the number-one thing is to come to dialysis. We want them to feel safe with us.

Morris: Interestingly, we have not seen an increase in patient absences except for hospitalized patients. Again, I suspect patients see the dialysis unit as a safe place where they receive care by well-trained staff, so they feel safe and well cared for during treatment.

What about home patients?

McNamara: Our home patients have been faring well. The home program is now scheduling virtual visits with them, and we are doing some online education for choices classes so we can continue to help patients choose home or go home. The mask supply has affected our PD patients, so we are having them reuse their masks for multiple days. We have also created NKC bandanas that patients can wear to extend the life of their masks.

Morris: We are seeing home patients by videoconference or phone if the patients cannot manage Zoom. We have mailed their medications to them. The PD patients are using a community laboratory to have their blood drawn. We are completing training with those who had started. We have patients with PD catheters who are receiving flushes, but we have not yet determined a training schedule for them. We will continue to offer new patients modality options, but we will delay the start of training until this crisis is over.

Do you feel your emergency preparedness plan prepared you for this pandemic? Explain.

McNamara: Yes; we immediately stood up our emergency operations command center, and having worked together in that structure before really helped us. Although this is different from our last emergency related to heavy snowfall in 2019, many of the issues were the same: transportation, missed treatment follow-up, staff coverage. Within that structure, the leaders continue to meet daily and to provide a daily communication update that goes to all staff, including our physicians and nurse practitioners.

Morris: The emergency preparedness plan has been effective in guiding staff and patient communication. It provides the units with a framework in which to operate if we have staffing shortages. We're considering adding the difficulty in obtaining PPE supplies in a pandemic scenario, along with cohorting affected patients and other pandemic scenarios, to our hazard vulnerability assessment tool.

Is there anything else you would like to share?

McNamara: This is an unprecedented time in healthcare, and being at the forefront of an evolving pandemic has been both challenging and rewarding. I see our nurses shine every day, using those skills and keeping our patients safe. I do think that much of what we have stood up will continue: the extra environmental cleaning, and the screening during our next flu season. Modified contact droplet precautions may indeed have a positive impact on our regular virus season.

Morris: I would like to thank Liz McNamara and the team at Northwest Kidney Centers for freely sharing their experience with COVID-19 early in this epidemic. Their information was invaluable in allowing the team at Rogosin to prepare our units for the epidemic in New York City.

We thank Liz McNamara and Diane Morris for sharing their experiences. Both Northwest Kidney Centers and the Rogosin Institute are independent small chains. The two largest dialysis providers, Davita and Fresenius Medical Care, have received waivers from the Centers for Medicare & Medicaid Services to allow them to establish designated isolation centers, which are paired centers where one will accept COVID-19–positive patients and the other will accept COVID-19–negative patients as a way to segregate these groups of patients. These centers are open to all providers who agree to participate. Also, daily calls are conducted by the Kidney Community Emergency Response Coalition. These calls offer the opportunity to ask for help with supplies, including PPE.

For direct care staff seeking more information and support, the American Nephrology Nurses Association (ANNA) has developed a COVID-19 webpage (https://www.annanurse.org/article/coronavirus) on the ANNA website to share innovative measures being taken to provide the safest and most efficient care to these patient populations. The webpage is updated several times daily with the latest evidence, policies, and advocacy opportunities. ANNA's virtual community, known as Open Forum, is another way information and best practices are shared. ANNA is also sharing continuing education content at no cost to members and nonmembers to expand knowledge and science during this unprecedented time.

ANNA recognizes that nephrology nurses are providing care to patients under unconventional circumstances in an environment where there has been an increase in acute kidney injury cases related directly to COVID-19. Tamara Kear, ANNA's chief executive officer, reports that ANNA has been working with other associations and healthcare organizations to provide resources to nurses and other healthcare providers caring for patients with kidney failure, those receiving dialysis, and those receiving continuous renal replacement therapy. ANNA is proud of all members who are providing direct and indirect patient care during this challenging time. ■

Tamara Kear, PhD, RN, CNN, FAAN, is executive director of the American Nephrology Nurses Association, Pitman, New Jersey. Glenda Payne, MS, RN, CNN, is the principal and chief compliance officer of the National Dialysis Accreditation Commission, Glen Ellyn, Illinois.

Key Practices

- Screen everyone, staff and patients, each time they enter the unit—by phone if possible, or at the entrance.
- Restrict visitors.
- Isolate COVID-19–positive patients as much as possible.
- Reinforce education of staff on the importance of PPE, strict adherence to hand hygiene, and cleaning surfaces between patient treatments. Identify champions to troubleshoot areas where compliance seems to lag.
- Hold leadership rounding in the unit; talking to staff lends credibility to promises of support.
- Data are helpful—share your own numbers constantly with staff.

Creativity and Safety Paramount in Caring for Kidney Failure Patients with COVID-19

By Karen Blum

Good communication, creative use of resources, and protecting dialysis and other hospital staff are all keys to success in caring for COVID-19-positive patients with end-stage kidney disease and acute kidney injury in the hospital, according to Michele H. Mokrzycki, MD, MS, professor of medicine at Montefiore Medical Center and Albert Einstein College of Medicine in the Bronx,.

The pandemic developed in New York very quickly, Mokrzycki said, from a few international travelers to hotspots to many communities. As of late spring, her hospital had admitted 829 patients with COVID-19. The nephrology service cared for 47 hemodialysis patients with COVID, 8.5% of whom died; 109 AKI patients with COVID, of whom 31% died; and 24 kidney transplant patients with COVID, of whom 17% died.

At Montefiore, an outdoor tent is set up to triage emergency department patients, including kidney failure patients with fever, respiratory symptoms, or known COVID exposure. Those with confirmed COVID are masked and evaluated. If they need to be admitted, they are placed on a COVID floor and receive bedside hemodialysis or continuous renal replacement therapy (CRRT). Those considered persons under investigation (PUI) are masked and isolated for testing; if admitted, they're placed on a PUI floor.

COVID-19 and PUI patients with a fever, hepatitis B, or who are intubated receive bedside hemodialysis in their room using a portable machine with reverse osmosis hooked up to the wall plumbing. Nurses managing them wear full personal protective equipment (PPE). Machines are cleaned and disinfected but not dedicated to particular patients. Tubing and dialyzers are discarded in hazardous waste bins. COVID-19 and PUI patients who are no longer coughing, are seven days out from the onset of symptoms, or are 72 hours fever-free can be safely transported to the inpatient

Continued on page 18 >

Creativity and Safety

Continued from page 17

dialysis unit, where COVID-19 patients are cohorted on the last shift.

COVID-19 and PUI patients in the intensive care unit receive either CRRT, continuous venovenous hemodiafiltration (CVVHD) or sustained low efficiency dialysis (SLED), or intermittent hemodialysis, depending on their acuity level, Mokrzycki said. Staff use extra-long tubing so they can sit outside the room. Again, machines are cleaned and disinfected but not dedicated to particular patients, and tubing and dialyzers are discarded. To optimize the use of CVVHD for two to three patients a day, she said, treatment times may be shortened to eight hours and high dialysate flow of 30-40 mL/kg/hour may be used.

To protect healthcare providers, patients remain masked during RRT procedures, and droplet precautions are maintained. Dialysis staff use full PPE and extra-long tubing, and direct exposure with patients is limited. Some use baby monitors to observe patients during hemodialysis treatments from the doorways. Limited nephrology staff who are rounding enter patient rooms for physical exams, use full PPE in patient rooms, and wear masks the entire time in the hospital.

Staff shortages a challenge

One of the biggest challenges, Mokrzycki said, is providing dialysis treatments with ongoing staff shortages owing to illness or quarantine. Pre-COVID, the team was doing about 8–12 sessions per day. "That has increased two- to threefold and has really put a strain on our nursing staff," she said.

The medical center has made several adaptations in response to the growing number of COVID patients requiring RRT, Mokrzycki said. These adaptations include reducing hemodialysis frequency to twice a week, shortening treatment times, initiating more AKI patients on urgent or acute peritoneal dialysis and creating a peritoneal dialysis rounding service, as well as using palliative care consultants where appropriate. Key to their success has been establishing several COVID task forces among the nephrology division, ICU teams, and hospital administration, with frequent communication, she said.

Mokrzycki spoke about her experiences during an ASN webinar about hospital care and treatment options for COVID-19–positive patients. ■

Dialysis Companies Join to Create Contingency Plans During COVID-19 Crisis

By Ruth Jessen Hickman

Dialysis patients pose a major challenge for limiting the spread of the SARS-CoV-2 virus, as they normally receive thrice weekly dialysis in often densely populated outpatient centers. They may have compromised immune systems, and many have additional health comorbidities that put them at risk of poor outcomes from COVID-19 (1).

Early in the pandemic, many symptomatic dialysis patients positive for COVID-19 were transferred to hospitals to reduce the risk of spread at outpatient dialysis units (1). It became clear, however, that triaging all such patients to hospitals might unnecessarily strain inpatient dialysis units, which might already be working past normal capacities treating people with kidney involvement from COVID-19 (2).

Outpatient dialysis units around the country instituted measures to try to protect their patients and workers, such as screening staff and patients entering clinics. Dialysis organizations such as Fresenius Medical Care North America also started developing isolation units and shifts that could be used to separate people positive for COVID-19 as well as those with high risk of exposure from the general dialysis population.

In March, several dialysis companies began communicating about how they might work together to protect dialysis patients and staff. As the virus spread around the country, the companies accelerated their efforts and worked with the Centers for Medicare & Medicaid Services to establish how a collaboration might best be implemented.

On March 31, official news of the collaboration was released. Participating dialysis organizations included Fresenius, DaVita Inc., U.S. Renal Care, American Renal Associates, and several others. The idea was to create a nationwide contingency plan that could be used to help maintain continuity of care for all dialysis patients during the COVID-19 pandemic.

Under the plan, patients would ideally be seen at isolation centers sponsored by the individual organizations, but if needed, patients could be transferred to isolation units at other dialysis companies. "Having this safety net assures us that we can continue to treat our patients, maintaining continuity of care at another provider should a particular clinic or geographic region need additional options," said Craig Smith, RN, vice president of clinical administration at American Renal Associates.

"The contingency plans are designed to ensure there is capacity among our centers to safely isolate and treat COVID-19–positive patients in the outpatient setting, particularly in communities hardest hit by the virus," said Jeff Giullian, MD, chief medical officer for DaVita. "We believe it's our duty as clinical leaders to push for more collaboration across the industry to help optimize patient care during this unique time."

Individual clinics made plans detailing the number of patients they can safely isolate while preventing cross-contamination. These plans include designating areas within specific clinics and designing dedicated shifts or days devoted to patients positive for COVID-19 and persons potentially infected. In some cases, entire clinics have been designated to treat such patients, and other clinics have been identified that might be converted to COVID-19 clinics if necessary.

Collaboration to help areas with worst outbreaks

The collaborative effort allows the organizations to collectively brainstorm about how to best meet the needs of patients and providers, and it helps the industry rapidly respond in areas of the country with the worst outbreaks.

"Our biggest goal of this collaboration is to keep dialysis patients out of the hospital whenever possible, freeing up limited hospital resources and limiting the spread of COVID-19," said Robert Kossman, MD, chief medical officer for Fresenius Medical Care North America.

Added Mary Dittrich, MD, chief medical officer for U.S. Renal Care, Inc.: "The dialysis providers involved are focused on ensuring there are enough nurses, social workers, dietitians, care technicians, and available space to provide uninterrupted care to all dialysis patients—including those who are or may be infected with COVID-19—in a manner that does not unnecessarily expose the hundreds of thousands of other patients who entrust them with their care."

Patients with mild or moderate symptoms of COVID-19 are dialyzed in these designated centers, while only patients with severe symptoms are sent for hospital evaluation and treatment. The outpatient organizations are planning to have capacity to meet the needs of all patients who can safely be dialyzed on an outpatient basis.

Members of the collaboration developed a centralized admissions process that permits any provider to call a single number to initiate a placement in an isolation clinic. They also developed a set of best practices covering such topics as admissions, transportation, telemedicine, and medication management. Under the agreement, the attending nephrologist continues to manage care of the patient, even if the patient is treated by another provider for purposes of cohorting.

All the organizations have been working with the US Department of Health and Human Services and the Centers for Disease Control and Prevention to ensure they are following updated guidelines regarding infection prevention and control. Measures to reduce potential spread of the virus include screening all people entering the facilities, requiring the use of masks for all patients and more elaborate personal protective equipment for staff, limiting visitors, instituting rigorous cleaning processes, and keeping patients at least six feet apart.

To date, dialysis companies participating in the collaboration for the most part have been able to treat their patients independently, without relying significantly on the developed contingency plans.

The members of the dialysis collaborative continue to communicate daily to review COVID-related needs, updates, potential issues, and patient transfers. "It is through effective, ongoing communication about the needs in different communities across the country that we can continue to enact plans that help all of our patients maintain safe, uninterrupted dialysis treatments," said Guillian. ■

Ruth Jessen Hickman, MD, is a graduate of the Indiana University School of Medicine. She is a freelance medical and science writer living in Bloomington, IN.

References

1. Rabb H. Kidney diseases in the time of COVID-19: major challenges to patient care. *J Clin Invest* 2020 Apr 6. doi: 10.1172/JCI138871.
2. Burgner A, Ikizler TA, Dwyer JP. COVID-19 and the inpatient dialysis unit: managing resources during contingency planning pre-crisis. *Clin J Am Soc Nephrol* 2020 Apr 3. doi: 10.2215/CJN.03750320.

Patient Organizations Engage on All Levels of COVID-19 Advocacy and Education

By Eric Seaborg

Like every corner of the medical community, kidney patient advocacy groups have mobilized in response to the COVID-19 pandemic. The many responses include direct monetary grants to patients; education for patients about the virus and how they can react; increased efforts for communication, networking, and counseling; and mobilization for political activity.

With the flurry of activity, patients with internet access may be receiving more information and support than ever.

The American Kidney Fund (AKF) opened applications for its Coronavirus Emergency Fund (https://www.kidneyfund.org/news/akf-launches-coronavirus-emergency-fund-to-help-low-income-dialysis-and-transplant-patients.html) on March 23 to provide $250 grants to any US dialysis patients or recent kidney transplant patients who demonstrate financial need. The fund aims to help "low-income patients who are experiencing financial shocks related to food, transportation, medications, and medical supplies," according to Alice Andors, AKF's senior director of communications. AKF reallocated $300,000 from its 2020 budget to the fund, which "was depleted on the first day when we received nearly 2000 applications for assistance. We have received 6000 applications and we have funding for fewer than half, resulting in a shortfall of about $1 million. We are issuing urgent appeals to individuals, corporations, associations, and foundations, but contributions are not keeping pace with the need in our patient community." (ASN has contributed to the fund.)

Educational efforts

Many patient organizations have amplified their educational outreach in creative ways.

The National Kidney Foundation (NKF) created a new website "dedicated to information for patients on COVID-19 and kidney disease (https://www.kidney.org/covid-19)," said Julie Kimbrough, vice president of marketing, communications, and public affairs. "There are many hyperlinks within the site dealing with everything from dialysis, [to] transplant, nutrition, etc."

Home Dialyzors United added a link at the top of its homepage to a "Coronavirus Updates" page (https://www.homedialyzorsunited.org/coronavirus-news), which provides a compendium of links to articles, information, and webinars available from a wide variety of websites.

"It's clear that patients and caregivers are hungry for fact-based information that provides important information in an approachable and straightforward manner," Andors said. "We created special webpages for news and updates (KidneyFund.org/coronavirus) and for general educational information (https://KidneyFund.org/covid-19/). These pages have quickly become among the most-visited pages on our website."

Webinars and interaction

In addition to the relatively passive informational webpages, many organizations are using the internet for webinars and interactive educational activities.

The Dialysis Patient Citizens (DPC) Education Center may have been the first in the kidney community to offer a patient-directed COVID-19 webinar, with speakers from ASN and the Centers for Disease Control and Prevention (CDC), said Kathi Niccum, EdD, education director of the DPC Education Center. Their second webinar on April 7 included three nephrologists, two of whom shared the experiences of their dialysis units in the Bronx, New York. (https://www.dpcedcenter.org/education-webinar/the-covid-19-explosion-lessons-from-new-york-what-kidney-patients-should-know/)

"NKF has been hosting weekly 'Facebook Live' [events] with our nationally recognized medical leadership team answering questions from patients and their families in real-time," said Kimbrough. A recent event featured nephrologist Holly Kramer, MD, NKF president, with previous events archived at the organization's Facebook page. (https://business.facebook.com/nationalkidneyfoundation/videos/774335743092951/)

NephCure Kidney International Foundation (NKI) is also streaming physician-hosted webinars live on Facebook, with the first topic being IgA nephropathy and future topics including genetic testing, diet and nutrition, clinical trial education, and different disease states, according to Kristen Hood, MSN, RN, director of clinical outreach. Hood is hosting Facebook Live events every other Friday called "Chats with Nurse Kristen." The first was on telemedicine, covering topics such as what telemedicine is and how patients need to prepare for a visit.

AKF held a "Kidney Chat" webinar (https://www.kidneyfund.org/training/webinars/kidney-chat-ask-a-nephrologist-about-covid-19.html) on April 14 during which a nephrologist answered questions submitted by viewers.

Emotional/coping support

But in addition to simply providing information, some organizations are attempting to provide emotional support and tips on coping during a trying time.

> **We have been very engaged in collecting patient experiences, like what people are seeing or feeling in practical terms, [such as] experiencing difficulties getting medications, difficulties with coordinating dialysis visits, concerns whether their facility has masked and gloved healthcare workers. —Paul T. Conway, AAKP chair of policy and global affairs**

"We serve a community of rare kidney disease patients, from teenagers through adult patients," NephCure's Hood said. "There is a wide variety of needs among the different ages, so we have developed programs for each. We have been doing a four-part series on resilience with a renowned doctor of communication and relationships. We have a Monday motivational series on Facebook Live led by a patient." The leader takes participants through a series of deep breathing and stretching exercises that help with anxiety and coping. There is a support group called NephCure Quaranteens for teenagers from 13 to 17 that meets by Zoom and is moderated by an NKI staff member. Teenagers hear news stories, but may not understand everything, so the group provides a place to discuss their anxieties, their worries, and how life is going, Hood said.

There are similar Zoom support meetings for parents, moderated by a staff member, and for adult patients, moderated by their peers.

Hood said NKI has canceled all of its in-person meetings, but they could well be reaching more people by "changing things to a virtual platform and streaming things onto Facebook Live. It gives us more touch points, especially for the patients who weren't able to travel to our in-person events [because of] work, their disease state, or dialysis schedules."

The DPC Education Center holds monthly patient webinars, with the March and April events focusing on COVID-19. "The May 28 webinar will address the mental health needs of kidney patients during this stressful time. It will be presented by the American Psychological Association, with whom we have a partnership to educate dialysis patients and their families on the psychological aspects of managing kidney disease," Niccum said.

NKF's Kimbrough said: "We're holding our annual spring clinical meetings (https://www.kidney.org/springclinical/program) as a live-virtual event instead of the in-person gathering that brings together thousands of nephrology healthcare professionals all under one roof." The live meeting was to have featured the 10 winners of the KidneyX: Patient Innovator Challenge (https://www.kidney.org/news/25-people-win-kidneyx-patient-innovator-challenge-ideas-to-improve-patients-lives), but instead NKF invited the winners to film a one-minute smartphone video explaining their innovation and how it helps patients.

Political advocacy

Kidney patient organizations have also entered the fray in the political arena.

Paul T. Conway, chair of policy and global affairs for the American Association of Kidney Patients (AAKP), said that during congressional deliberations about coronavirus relief legislation "we were hearing a tremendous amount from our patients and our patient ambassadors all over the country that this is not a partisan issue [so Congress should] come together in a bipartisan manner and pass this relief legislation. So we organized that voice in our action center, and did a letter campaign to Congress where people could contact their elected representatives."

"AAKP has invested a lot of money over the past four or five years in our platforms, not just social media, but action and education centers," he said. "Over the past six weeks we have had a number of online campaigns that increased engagement, [and] have brought the patient voice directly into many of the deliberations on policy and legislation. And we have exceeded every target and every [patient participation] record we've ever had."

He noted that March was National Kidney Month when "historically, hundreds of kidney patients and their families travel to the nation's capital to discuss policies related to patient care and medical innovation with White House and congressional officials. As an alternative, AAKP is encouraging patients to expand their engagement with key federal policymakers through AAKP's virtual and social media platforms."

AKF's Andors said: "We have activated our 14,000-member advocacy network of AKF ambassadors to contact their members of Congress in support of S. 3571, the Banking for All Act, to ensure that Americans who do not have bank accounts—like many of the end

Continued on page 20

Patient Organizations Engage

Continued from page 19

stage renal disease patients AKF helps financially—can access their stimulus funds through the establishment of free 'FedAccounts.'"

Patient care advocacy

Several patient care organizations, including NKF, DPC, AAKP, AKF, and Renal Support Network, have been engaging with the US Department of Health and Human Services as part of stakeholder discussions about COVID-19–related issues kidney patients are facing. ASN is also part of those discussions.

"AKF has been "engaged with policymakers to ensure that the needs of kidney patients are considered in emergency orders and legislation," Andors said. "Per HHS' request, we submitted proposals that address current COVID-19–related issues that the dialysis and kidney transplant communities are facing."

DPC's Niccum said that her organization has also "provided feedback to HHS.

Said AAKP's Conway: "We have been very engaged in collecting patient experiences, like what people are seeing or feeling in practical terms, [such as] experiencing difficulties getting medications, difficulties with coordinating dialysis visits, concerns whether their facility has masked and gloved healthcare workers. We have been working closely with HHS as part of some of their work groups and the [Centers for Medicare & Medicaid Services (CMS)] in letting them know what patient concerns are. [We have] deployed flash surveys and tracking surveys to get the pulse of patients and track what they are saying."

As part of this engagement AAKP told CDC, "you are pumping guidance out to medical facilities and hospitals and care providers, but the patient is lost in the equation," Conway said. AAKP worked with CDC on a webinar for patients on "what they need to know to protect themselves and also what they need to ask" that attracted more than 5000 views on AAKP's YouTube channel. (https://www.youtube.com/watch?v=xwU5FZ9HpK4&feature=youtu.be)

Conway said the current crisis has highlighted some narrower issues as well, such as the decision by CMS to cease coverage of a pill therapy for iron deficient anemia, which now requires patients to go to a medical facility for infusions. "No one wants to go get their treatment and expose themselves," Conway said. "We have been educating CMS that this is a huge fear of patients, and they ought to revisit their decision. It is a Food and Drug Administration–approved pill."

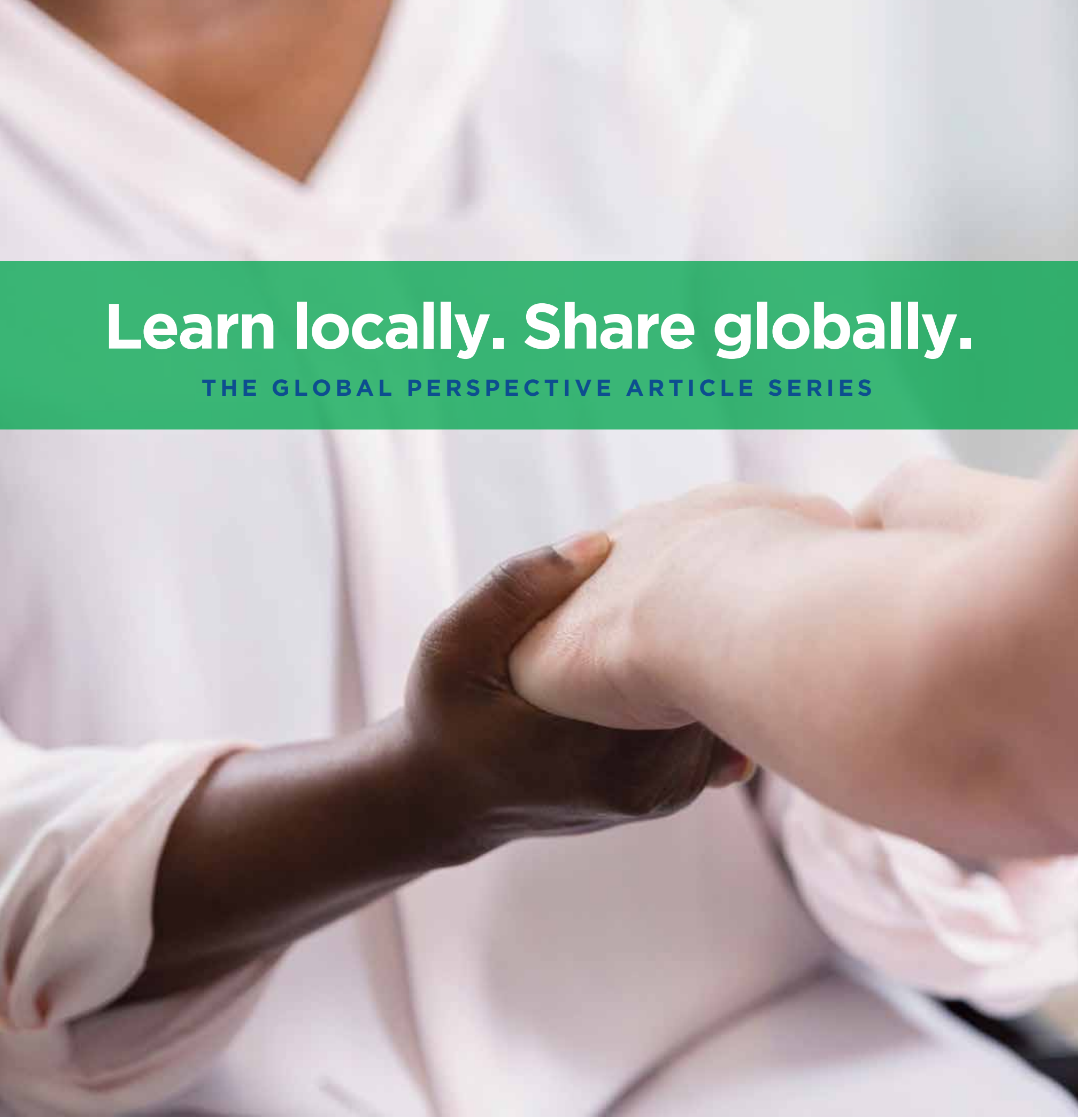
Andors noted, "AKF has joined broad coalitions of patient advocacy groups that support implementing special enrollment periods in the ACA marketplace and in Medicare; providing personal protection for healthcare workers; providing additional funds to states for healthcare costs; providing financial protections to people diagnosed and treated for COVID-19; and expanding eligibility for the paid family and medical leave program to individuals at high risk for complications from COVID-19 and working members of their households."

On a broader scale

NKF has also been advocating for kidney patients in the court of public opinion. The organization wrote an "open letter to America's hospitals and health systems" saying that "we are deeply troubled by news reports that some health systems and state governments are considering crisis-management policies that would deprive certain patients—including patients with end stage renal disease—of life-saving interventions for COVID-19, including ventilation." The letter notes that ESRD "is not a 'terminal' condition and should not be treated as such. We call on all health systems to recognize that ESRD patients have the same inherent worth as any other patient and should be afforded the same level of care." (https://www.kidney.org/sites/default/files/20200402open-letter-treating-covidesrd-patients.pdf)

With the conditions and challenges constantly changing, organizations are monitoring developments and blogging to keep patients informed.

"We conducted an informal survey of patients and caregivers to better understand what they are experiencing to inform our response and updates to our resource pages and blog. Our Kidney Today blog (https://www.kidneyfund.org/kidney-today/) and our advocacy blog (https://www.kidneyfund.org/advocacy-blog/) have been posting almost daily on various topics relating to COVID-19, including the government's response, patient experiences, and more," AKF's Andors said. ■



Learn locally. Share globally.

THE GLOBAL PERSPECTIVE ARTICLE SERIES

Kidney360's ongoing series of Global Perspective articles focuses on how different countries address vital issues affecting kidney diseases such as: dialysis management, treatment, patient education, funding, challenges unique to various cultures, and more. Staying connected and up-to-date with how the rest of the world fights kidney diseases benefits us all. Read the articles at Kidney360.org, the open-access journal of ASN.

AMERICAN SOCIETY OF NEPHROLOGY · ASN ·

Kidney360

www.Kidney360.org

Higher Mortality in Kidney Transplant Recipients Versus Matched CKD Patients

Beyond the first year, kidney transplant recipients (KTRs) have an excess risk of mortality, compared to matched chronic kidney disease (CKD) patients who do not undergo kidney transplantation, reports a preliminary study in *Nephrology Dialysis Transplantation*.

The analysis included patients from two French multicenter prospective cohorts: 340 KTRs and 605 nontransplant CKD patients. The groups were matched on a propensity score incorporating six outcome-dependent variables assessed at cohort enrollment, including estimated glomerular filtration rate (eGFR). Mean eGFR at inclusion was 42 and 41 mL/min/1.73 m^2, respectively. All-cause mortality was compared between groups, with cardiovascular events as a secondary outcome.

As expected, patients receiving a kidney transplant were younger: median age 60 years, compared to 66 years in the nontransplant CKD group. Patients in the KTR group may have had a longer duration of CKD. Median duration of follow-up was 2.03 versus 2.92 years, respectively.

All-cause mortality was 9% in the KTR group versus 7% in the CKD comparison group. On univariate analysis, KTRs were at significantly higher risk of death: hazard ratio (HR) 1.70. Other factors associated with mortality were older age, diabetes, history of cardiovascular (CV) disease, and lower eGFR at inclusion. Proteinuria was not a significant factor.

The association between KTR status and death remained significant on multivariate analysis: HR 2.7. The two groups were similar in terms of CV event rate and risk of death due to CV events: 29.0% in the KTR group and 22.5% in non-transplant CKD patients. There was a possible increase in the risk of death due to infection among KTRs: 19.4% versus 10.0%.

Kidney transplantation leads to prolonged survival, compared to dialysis. However, KTRs remain at higher risk of death than healthy people, especially in the first year after transplantation. Most studies of the effects of kidney transplantation on mortality and CV events have compared KTRs with the general population or with wait-listed dialysis patients.

The new analysis suggests that KTRs have a 2.7-fold increase in all-cause mortality beyond the first year posttransplant, compared to matched nontransplant CKD patients. The incidence of CV events is similar between groups, but KTRs may be at higher risk of severe infections. The researchers conclude: "In view of the excess mortality after kidney transplantation, preventing CKD and slowing its progression remain an absolute priority" [Cheddani L, et al. Higher mortality risk among kidney transplant recipients than among estimated glomerular filtration rate–matched patients with CKD—preliminary results. *Nephrol Dial Transpl* 2020; DOI: 0.1093/ndt/gfaa026]. ■

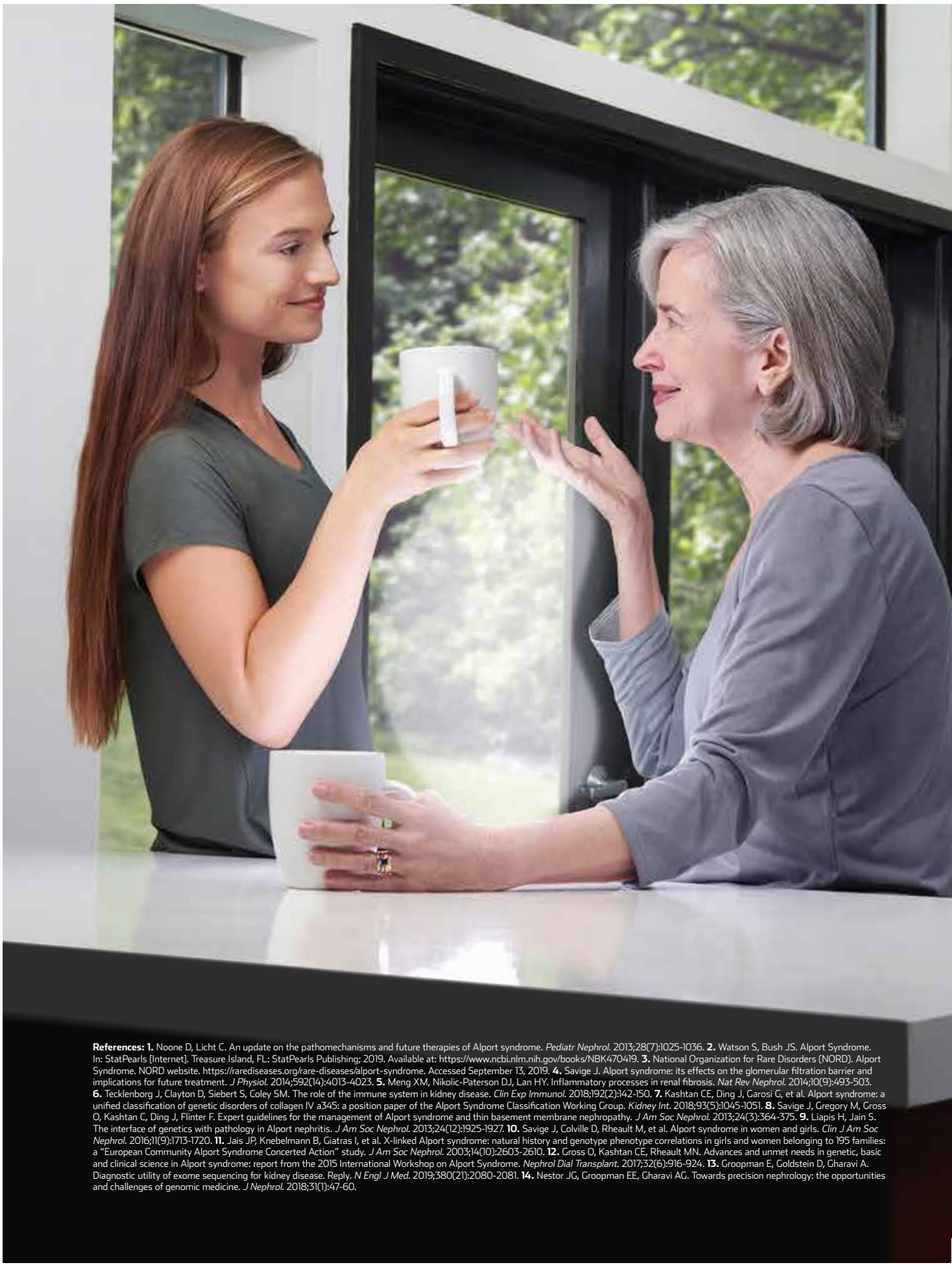
ACEIs/ARBs Have Continued Benefits in Patients with Falling eGFR

For patients whose estimated glomerular filtration rate (eGFR) declines to less than 30 mL/min/1.73 m^2, continuing treatment with renin-angiotensin system blockers has continued cardiovascular benefits, suggests a study in *JAMA Internal Medicine*.

Using data from a large integrated healthcare system in Pennsylvania, the researchers identified approximately 163,000 patients who started angiotensin-converting enzyme inhibitor (ACE) or angiotensin receptor blocker (ARB) therapy between 2004 and 2018. Of these, nearly 11,000 patients subsequently had a drop in outpatient eGFR to less than 30 mL/min/1.73 m^2. After elimination of patients who discontinued ACEI/ARB therapy before the drop in kidney function (and other exclusion criteria), the study population included 3909 patients: 61.6% female, mean age 73.7 years. Of these, about 31.6% discontinued ACEIs/ARBs within 6 months after the reduction in eGFR.

On propensity score matching, the researchers identified 1205 patients who discontinued ACEI/ARB therapy and 1205 controls who continued on treatment. The main outcome of interest was the association between ACEI/ARB discontinuation and mortality over the subsequent 5 years. Analyses were adjusted for patient characteristics at the time of the drop in kidney function.

In the overall study population, median follow-up was 2.9 years. Mortality was 35.1% for patients who discontinued ACEIs/ARBs and 29.4% for controls who continued therapy. The increase in mortality associated with discontinuation remained



References: 1. Noone D, Licht C. An update on the pathomechanisms and future therapies of Alport syndrome. *Pediatr Nephrol.* 2013;28(7):1025-1036. **2.** Watson S, Bush JS. Alport Syndrome. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2019. Available at: https://www.ncbi.nlm.nih.gov/books/NBK470419. **3.** National Organization for Rare Disorders (NORD). Alport Syndrome. NORD website. https://rarediseases.org/rare-diseases/alport-syndrome. Accessed September 13, 2019. **4.** Savige J. Alport syndrome: its effects on the glomerular filtration barrier and implications for future treatment. *J Physiol.* 2014;592(14):4013-4023. **5.** Meng XM, Nikolic-Paterson DJ, Lan HY. Inflammatory processes in renal fibrosis. *Nat Rev Nephrol.* 2014;10(9):493-503. **6.** Tecklenborg J, Clayton D, Siebert S, Coley SM. The role of the immune system in kidney disease. *Clin Exp Immunol.* 2018;192(2):142-150. **7.** Kashtan CE, Ding J, Garosi G, et al. Alport syndrome: a unified classification of genetic disorders of collagen IV a345: a position paper of the Alport Syndrome Classification Working Group. *Kidney Int.* 2018;93(5):1045-1051. **8.** Savige J, Gregory M, Gross O, Kashtan C, Ding J, Flinter F. Expert guidelines for the management of Alport syndrome and thin basement membrane nephropathy. *J Am Soc Nephrol.* 2013;24(3):364-375. **9.** Liapis H, Jain S. The interface of genetics with pathology in Alport nephritis. *J Am Soc Nephrol.* 2013;24(12):1925-1927. **10.** Savige J, Colville D, Rheault M, et al. Alport syndrome in women and girls. *Clin J Am Soc Nephrol.* 2016;11(9):1713-1720. **11.** Jais JP, Knebelmann B, Giatras I, et al. X-linked Alport syndrome: natural history and genotype phenotype correlations in girls and women belonging to 195 families: a "European Community Alport Syndrome Concerted Action" study. *J Am Soc Nephrol.* 2003;14(10):2603-2610. **12.** Gross O, Kashtan CE, Rheault MN. Advances and unmet needs in genetic, basic and clinical science in Alport syndrome: report from the 2015 International Workshop on Alport Syndrome. *Nephrol Dial Transplant.* 2017;32(6):916-924. **13.** Groopman E, Goldstein D, Gharavi A. Diagnostic utility of exome sequencing for kidney disease. Reply. *N Engl J Med.* 2019;380(21):2080-2081. **14.** Nestor JG, Groopman EE, Gharavi AG. Towards precision nephrology: the opportunities and challenges of genomic medicine. *J Nephrol.* 2018;31(1):47-60.

significant in the propensity-matched analysis: 40.0% versus 34.0%, hazard ratio (HR) 1.39. Discontinuation was also associated with an increased risk of major adverse cardiovascular events: HR 1.37.

Risk of developing kidney failure was about 7% in both groups. The presence of baseline diabetes had a modifying effect on the association between ACEI/ARB and risk of kidney failure: estimated HR 1.56 in patients with diabetes versus 0.61 in those without. Discontinuation of ACEI/ARB therapy was associated with a lower risk of hyperkalemia: HR 0.65. Analysis of ACEI/ARB discontinuation after eGFR decrease by 40% or more also showed significant increases in the risk of death or cardiovascular events: HR 1.53 and 1.40, respectively.

Patients with lower eGFR are more likely to experience adverse effects of ACEI/ARB therapy. As kidney disease progresses, treatment discontinuation becomes increasingly common. However, there are conflicting data on the risks versus benefits of ACEI/ARB discontinuation in patients with advanced CKD.

Continuing ACEI/ARB therapy after a decline in eGFR is associated with lower mortality and a lower rate of cardiovascular events, with no increase in kidney failure, the retrospective study suggests. The findings are robust on sensitivity analyses and similar for patients with an eGFR under 30 mL/min/1.73 m^2 or a decline of 40% or more. "The findings suggest that continuing ACE-I or ARB therapy in patients with declining kidney function may be associated with cardiovascular benefit without excessive harm of ESKD," the investigators conclude [Qiao Y, et al. Association between renin-angiotensin system blockade discontinuation and all-cause mortality among persons with low estimated glomerular filtration rate. *JAMA Intern Med* 2020; DOI:10.1001/jamainternmed.2020.0193].

DMV Video Increases Organ Donor Registrations

A video played at Alabama Department of Motorized Vehicles (DMV) facilities—specifically targeting African Americans—resulted in a modest but significant increase in organ donor registrations, reports a study in *Transplantation*.

The 10-minute video was created by a professional film company experienced in producing motivational "call to action" videos. The video built on previous research with African American DMV patrons and was developed with input from members of the community. Topics included medical mistrust, the need for donor organs, and stories shared by organ donor and recipient families. The video also featured brief promotional clips by well-known local figures, such as elected officials and football coaches.

In an interrupted time series design, the video was played in six DMV facilities, in cycles of 2 months on and 2 months off over 1 year. Evaluation included assessment of the video's impact on organ donor registration rates.

The analysis included nearly 163,000 patron visits during the 12-month study period; about 55% of patrons were Caucasian and 40% African American. Overall donor registrations increased by an average of 2.3% during times the video was on. Rates were 51.1% with the video on versus 48.4% with the video off; increases varied by site, from 1.98% to 3.35%.

On multivariable analysis, the video-on condition was significantly associated with donor registration: odds ratio (OR) 1.09. Other independent factors included female sex (OR 1.29), Caucasian race (OR 4.48), and younger age (OR 0.982 per year). Even though the video was tailored to African Americans, there was no evidence of an incremental effect in this group. In exit interviews with African American patrons, only 16% said they watched the video and could identify its main message.

Efforts are needed to increase organ donor registration, particularly among potential African American donors. Baseline data suggest that only 28% of African Americans in Alabama are registered organ donors, compared to 64% of Caucasians. Nationwide, DMV locations are a major portal for organ donor registration.

A video played in Alabama DMV locations resulted in a modest but significant increase in organ donor registrations. The findings suggest similar effectiveness in African American and Caucasian DMV patrons. The authors plan refinements to the video approach, particularly marketing-based promotion with frequent and unambiguous calls to action [DuBay D, et al. A video intervention to increase organ donor registration at the department of motorized vehicles. *Transplantation* 2020; 104:788–794].

Fellows Corner

Residents' Perception of Nephrology
A Call for Action

By Ali Mehdi and Georges N. Nakhoul

Ali Mehdi

It comes as no surprise to anyone within the nephrology community that interest in a career in nephrology has declined drastically over the past decade, particularly among United States allopathic medical graduates. According to the American Society of Nephrology Data Brief regarding the 2020 nephrology fellowship match, 39% of nephrology fellowship positions went unfilled, with only 41% of available tracks filling (1). Only 69 United States allopathic medical graduates matched into nephrology, corresponding to a 14% decline from the previous year's match. This trend is of particular concern, given the increasing prevalence of patients with kidney disease in the United States.

In response to this challenge, the American Society of Nephrology has launched multiple initiatives aimed at a better understanding of the observed trend and ultimately rekindling interest in the field. Other groups have also attempted to understand the attitudes and opinions of medical students and residents as they pertain to the field of nephrology. Most of these studies, however, were survey-based and lacked a clear theoretic framework or a rigorous qualitative methodology.

To shed more light on the subject, our group aimed to identify the factors influencing subspecialty career decisions among internal medicine residents at a large residency program. We used a qualitative research design consisting of semistructured interviews with 10 internal medicine residents (2). The interview questions were guided by the Professional Identity Formation framework, which aims at capturing key elements contributing to the formation of professional identity (3). Inasmuch as interest in nephrology was the main focus of our study, the residents were specifically asked about their perceptions of nephrology as a career and their educational experiences with nephrology through medical school and residency. The open-ended nature of the interview process allowed for rigorous theme identification, which is at the core of qualitative research. The interviews were recorded and transcribed verbatim. Two authors with training in qualitative research independently analyzed the data using thematic analysis. The factors influencing career decisions were grouped into three categories: personal attributes, social factors, and subspecialty-specific factors. Nephrology-specific factors were grouped on the basis of whether they were cited positively or negatively. The frequency with which these factors were cited was tracked as a surrogate of their perceived impact.

Personal or family experiences were frequently cited factors in subspecialty career decisions. The importance of role models and career mentors was also particularly evident. Of particular interest was the impact of early exposure to, and quality of instruction in, a particular field in the preclinical and clinical years of medical school. Comments spanning intellectual challenges, topic difficulty, autonomy, and overall performance in a particular block or rotation seemed to be influential in subspecialty decision-making. As anticipated, an array of subspecialty-specific factors was cited, including type of practice, pathology breadth and complexity, work-life balance, academic prospects, job market and compensation, field innovation, and patient population. Table 1 details the social and subspecialty-related factors cited by residents, which may shed some light on the dwindling interest in nephrology.

Figure 1 highlights the most frequent factors mentioned negatively or positively in relation to nephrology. Lack of exposure in the clinical and preclinical years of medical education was the most frequent negative factor cited by nine of the 10 residents. The quality of instruction in those years was frequently cited negatively as well. The patient population, particularly patients with ESKD receiving dialysis, was a frequently mentioned deterring aspect of the field. This appeared to be closely linked to the perceived lack of innovation and inability to make a difference, both of which were also frequently cited. Compensation, however, was mentioned by only three of the 10 residents. Interestingly, complexity of the field, which came up frequently as a negative factor, was also the most highly cited positive aspect. Other positive factors mentioned included the breadth of pathology and the perception that nephrology is a "smart" or "brainy" specialty.

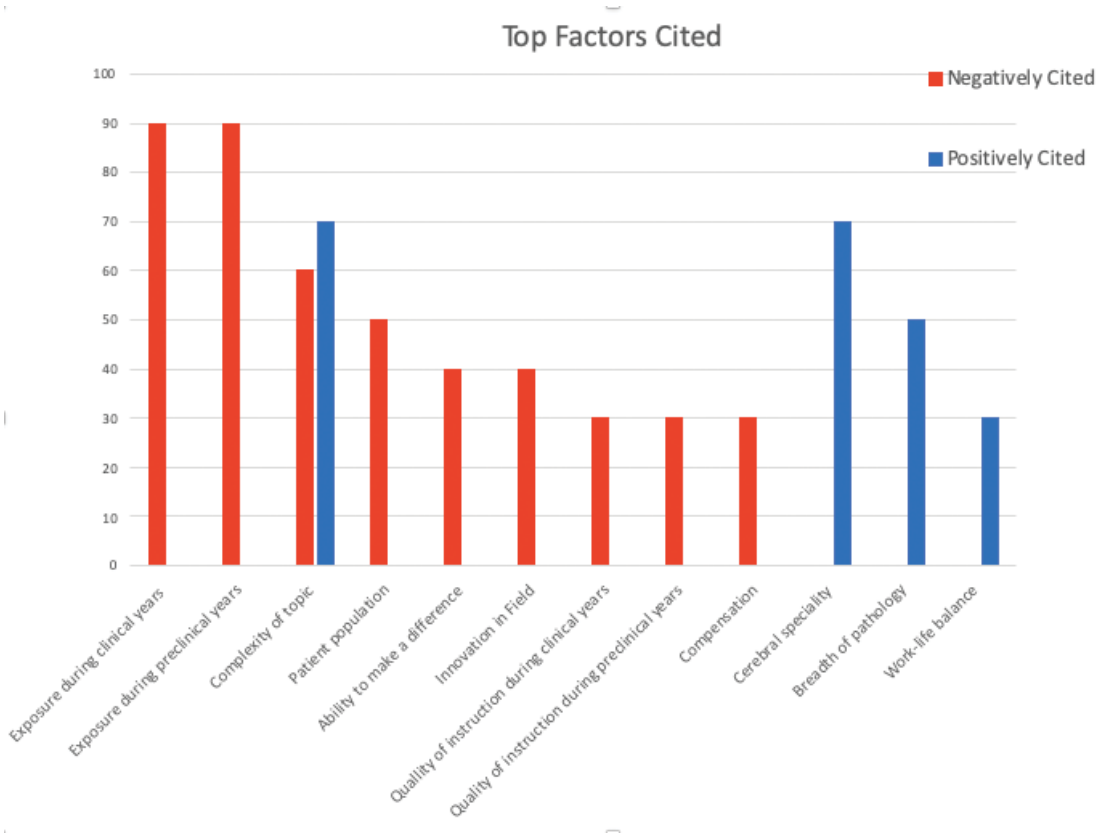
This study adds to the available literature and offers more insight into residents' perceptions of nephrology. Of particular importance was the strong signal pointing toward exposure to nephrology and the quality of instruction in the preclinical and clinical years being a negative factor or deterrent away from nephrology. As shown in Table 1, the importance of these formative years was clearly highlighted as an important factor in subspecialty career decisions in general. The quality of teaching, learning environment, performance, and overall experience in a particular subspecialty block or clinical rotation appeared to be important in guiding career decisions. Indeed, early exposure has been reported as an important career-affecting factor in other specialties, including geriatrics and rheumatology (4, 5). We believe that this highlights an area of opportunity that the nephrology community has to commit to. Educators within nephrology have to place themselves in a position to be involved in medical school curricula, at both the preclinical and the clinical years. The quality of instruction is also vital, and, as content experts, nephrology educators need to take charge of shaping the educational experience in ways that reach the next generation of learners. Innovative instructional strategies need to be used to facilitate delivery of the potentially complicated nephrology concepts. In addition, the early clinical years, both in medical school and in residency, appear to be of particular importance in the choice of a subspecialty. Nephrology educators have to realize this fact and strive to stay involved directly with our learners. Through early interactions with medical students and residents, we hopefully can project not only our nephrology pearls but also our passion and enthusiasm for the field.

These are exciting times in nephrology. The momentum

Table 1. General factors influencing subspecialty decision-making

Social factors	*Subspecialty factors*
Role models/mentors	Field-related factors Innovation in the field Social aspect (teamwork) Breadth of pathology
Formal learning (preclinical) Exposure Topic difficulty Intellectual challenge Quality of instruction Experience/performance on block	Lifestyle-related factors Work-life balance Stress level/acuity Workload
Clinical years Exposure Environment Quality of instruction Experience/performance on rotation Autonomy on rotation	Job-related factors Prestige/influence Compensation Job market Academic prospects Opportunity for procedures
	Patient-related factors Patient population Longitudinal care/continuity Inpatient vs. outpatient focus Practice focus: narrow vs. wide Ability to make a difference

Figure 1. Factors cited positively or negatively in relation to nephrology and their relative frequencies (percentage of residents mentioning the factor). Factors cited by two or fewer residents are not presented.



to advance the field has never before been like this. It is clear, however, that our learners do not appreciate the change. The perceived lack of innovation in the field and inability to "make a difference" were both highly cited as negative factors. The negative perception of our patient population was also frequently cited. This too is an area of opportunity that the community can potentially seize through early interactions with medical students and learners. The community needs to showcase the momentum and drive for nephrology innovation. We need to alleviate the stigma associated with our patient population: one that is driven by the inpatient-heavy nature of our training process, wherein our sick dialysis patients with frequent readmissions bias our learners' perceptions.

This study was a single-center qualitative interview-based study aimed at uncovering themes pertaining to residents' perceptions of nephrology. We are using the themes uncovered to guide a survey that we plan to institute at a national level. We are hopeful that the insight thus gained will inform societal and national interventions aimed at rekindling the interest in nephrology and ultimately help sustain the future of our specialty.

Ali Mehdi, MD, MEd, and Georges N. Nakhoul, MD, Med, are associated with the department of nephrology and hypertension, Glickman Urological and Kidney Institute, Cleveland Clinic, and the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University.

References

1. https://asndataanalytics.github.io/AY-2020-Nephrology-Match/#part1.
2. Nakhoul G, et al. Residents' perception of the nephrology specialty. *Kidney Int Rep* 2020; 5:94–99.
3. Cruess RL, et al. A schematic representation of the professional identity formation and socialization of medical students and residents: A guide for medical educators. *Acad Med* 2015; 90:718–725.
4. Blachman NL, Blaum CS, Zabar S. Reasons geriatrics fellows choose geriatrics as a career, and implications for workforce recruitment. *Gerontol Geriatr Educ* 2019; 19:1–8.
5. Kolasinski SL, et al. Subspecialty choice: Why did you become a rheumatologist? *Arthritis Rheum* 2007; 15:1546–1551.

FDA Clears Tablo Home Dialysis Device

By Bridget M. Kuehn

The US Food and Drug Administration cleared Outset Medical's Tablo device for home dialysis in March. It was previously cleared for in-center and hospital use.

The clearance will give patients a second option for home hemodialysis in addition to Fresenius' NxStage System One device, which has been available since 2017. The clearance was based on a 30-patient, multicenter trial that met its endpoints for safety and efficacy and in patients who received home dialysis with the device 4 times a week for 32 weeks after an in-center lead-in and transition period. The news comes at a time when demand for home dialysis is high as a result of the COVID-19 pandemic. The desire to stem the spread of the virus among the high-risk dialysis population has created a need for more options that allow patients with the virus or those at high risk to isolate themselves from others.

"[COVID-19] really has put a spotlight on the need to increase our capacity to treat patients in isolated environments," said Leslie Trigg, CEO of Outset Medical. "Giving patients and providers a second choice for a home hemodialysis device can only help increase the amount of isolation dialysis treatment that's available."

Currently, only about 12% of the more than 500,000 US dialysis patients receive their treatments at home, according to Outset Medical. But even before the COVID-19 pandemic, there was growing interest in increasing access to home hemodialysis. The Advancing American Kidney Health (AAKH) initiative created by executive order in July 2019 is expected to help increase the number of patients on home dialysis. The AAKH will create payment incentives to increase patient access to home dialysis and kidney transplants.

Richard Crawford, a dialysis patient who participated in the Tablo trial, said he was very excited about the device finally being available. Crawford said he likes the device because it was easy to set up in just 20 minutes compared to 4 hours with other home dialysis devices he has used and didn't require help from his family to set up. He and his nephrologist agreed his clearance was better on the device, he said.

"It will provide self-empowerment and make it easier for families," he said. The device requires only an electrical outlet and uses tap water, so it also requires less storage space at home. Crawford said he hopes to be able to get the device for home use now that it is available.

Trigg said Outset Medical plans a "thoughtful, more measured rollout" of the Tablo for home use. They will start by working with nephrologists who are already using the device, which was previously cleared for use at dialysis centers and in hospitals. They plan to provide a 24-7 support system for home patients.

The home rollout of Tablo is also being balanced against a surge in demand for the device for hospitals, according to a press release from Outset Medical. Because the device is so portable and nurses can be trained to use it in a matter of hours, hospitals are using it to expand the availability of dialysis. It is being used for isolation dialysis, acute dialysis needs, and in parts of the hospital where it isn't normally available.

"Tablo has definitely been pressed into service all across the country," Trigg said. "You don't often get an opportunity like this maybe in your entire career to get to be a part of something that really, really deeply matters." ■

References

1. FDA: March 2020 510(K) Clearances https://www.fda.gov/medical-devices/510k-clearances/march-2020-510k-clearances
2. Plumb TJ, et al. *Hemodial Int* 2020; 24:22–28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7027451/
3. White House. Executive Order on Advancing American Kidney Health. July 10, 2019. https://www.whitehouse.gov/presidential-actions/executive-order-advancing-american-kidney-health/
4. Outset Medical. Tablo® Hemodialysis System receives FDA clearance for home dialysis. April 1, 2020. https://www.outsetmedical.com/news/tablo-hemodialysis-system-receives-fda-clearance-for-home-dialysis/

Cricket Assists Cigna in Kidney Care

Cricket Health, a company that aims to provide cost-effective integrated nephrology and dialysis, has begun to leverage its high-tech approach to kidney care by helping major insurer Cigna identify patients who may need further care.

Cigna was a supporter of Cricket's vision and plans and, along with other funding entities, invested in Cricket Health. Cigna's contribution was part of a $24 million funding round in 2018.

Now Cricket, which bills itself as an evidence-based firm, will use its technology expertise to identify and assist patients who have early to late kidney disease. Cricket attracted early investors and supporters because the company had designed a machine-learning algorithm that now will work to identify which Cigna customers might need attention.

Cricket's algorithm relies on claims data; thus, there is no need for electronic health records or clinical test data. Using claims data lets Cricket run continuous risk assessment monitoring of Cigna's patient population inexpensively, the company noted in a media release.

Noted Cricket Health cofounder and Chief Executive Officer Arvind Rajan: "Directing patients toward home care options when possible will be especially critical as more Americans are urged to stay home to prevent the spread of the novel coronavirus." Rajan, speaking to https://www.fiercehealthcare.com/special-report/cricket-health, added that the current health crisis "has underlined the importance of the Cricket model of care even more sharply."

That model begins with Cricket's algorithm to identify potential kidney health problems. Identified patients would become part of a nephrology practice that provides several alternatives, including remote care, in-person care, and at-home care.

For patients identified as part of the Cigna California work, Cricket Health plans to deploy a care management team with the goal of reducing hospitalizations and managing progression of disease; helping patients whose disease is progressing to understand treatment, including from conservative care, dialysis in appropriate locations, and transplantation; and encouraging patients to select the best care options for themselves and their families.

"Cigna has been an industry leader in adopting data to improve early detection and treatment for other chronic diseases," Rajan said. "Together, we will apply the same evidence-based, multidisciplinary approach to chronic kidney disease and end stage renal disease." ■

Are you a fellow and have a tip or idea you'd like to share with your fellow peers and the broader kidney community?

Send your idea to the Kidney News Fellows Corner column at kidneynews@asn-online.org

KidneyNews Free Subscriber Service Request Card

☐ **I wish to start/renew a FREE* subscription to Kidney News**

7-digit number label (Required for change of name/address only)

Name

Address

City State Zip

Telephone Fax

Email Address

Signature Date

Title/Position
- ☐ Physician
- ☐ Researcher
- ☐ RN, CNN, NM, LPN, APN, PA
- ☐ Dialysis Center Director
- ☐ Administration
- ☐ Clinic Manager/Coordinator
- ☐ Social Work
- ☐ Other

Specialty Area
- ☐ General Nephrology
- ☐ Transplantation
- ☐ Dialysis
- ☐ Laboratory
- ☐ Other

Institution
- ☐ Hospital <100 beds
- ☐ Hospital 100-250 beds
- ☐ Hospital 251-500 beds
- ☐ Hospital > 500 beds
- ☐ Dialysis Center
- ☐ Clinical Lab
- ☐ Other

Please Circle Degree:

MD MD/PhD DO
PhD MBA RN MS
BS Other_____

ASN American Society of Nephrology

Return the completed form to:
Bob Henkel, 1401 H Street NW, #900, Washington, DC 20005
or Fax: 202-403-3615 or Email: bhenkel@asn-online.org

Index to Advertisers

MAYO CLINIC LABORATORIES

COMPLEX CASES. DEFINITIVE ANSWERS.

RPCWT | Renal Pathology Consultations

Mayo Clinic board-certified pathologists specialize in non-neoplastic kidney diseases and provide your practice with 24/7 clinical support.

Helping you be the hero your patients need.

mayocliniclabs.com/renal
855-516-8404