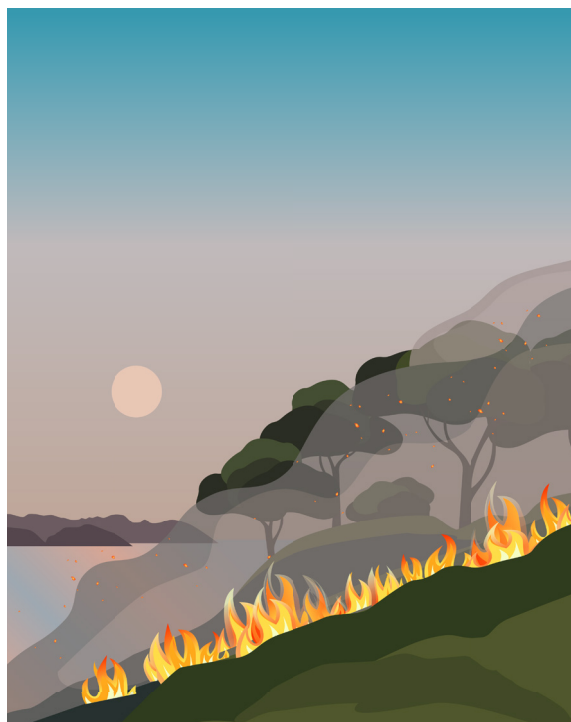


Kidney News

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Exposure to Wildfire Smoke Linked to Higher Death Rates in Patients with Kidney Failure

By Tracy Hampton



Individuals with kidney failure may face a higher risk of dying prematurely if they are exposed to air pollution from wildfires, according to new research published in the *Journal of the American Society of Nephrology*.

Large wildfires are occurring more frequently, and smoke generated from these fires contains high concentrations of fine particulate matter and other forms of pollution. When inhaled, fine particulate matter can travel into the respiratory tract and bloodstream and trigger oxidative stress and inflammation that may contribute to poor health, especially in sensitive populations including the elderly and individuals with chronic health conditions.

Studies have found that air pollution is one of various different environmental factors that can contribute to the development of kidney disease.

Because patients with kidney failure requiring dialysis are a fragile population, often with multiple illnesses such as hypertension and diabetes, investigators examined whether they are especially vulnerable to the health effects of wildfire smoke exposure.

For the study, the team assessed daily exposure of wild-

fire small particulate matter and mortality rates, both on the day of exposure and up to 30 days following exposure, drawing on information from 253 US counties near a major wildfire between 2008 and 2012.

“This study was possible because the US Renal Data System, a registry of patients with kidney failure, included vital records on almost all US patients receiving in-center hemodialysis, as well as the counties of the dialysis clinics,” said lead author Yuzhi Xi, MSPH, of the University of North Carolina at Chapel Hill. “Secondly, we utilized an air quality model to estimate daily exposure to wildfire fine particulate matter across the country at the counties of the dialysis units.”

Among the 268,399 US in-center hemodialysis patient deaths in the five-year period of 2008 to 2012, a total of 48,454 deaths were among patients who were receiving dialysis in the 253 counties. Each 10 $\mu\text{g}/\text{m}^3$ increase in the concentration of wildfire fine particulate matter in the air was associated with a 4% higher death rate on the same day and a 7% higher rate over the next month. On days with wildfire fine particulate matter greater than 10 $\mu\text{g}/$

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Innovators in Bioengineering, Infection Control, and Home Hemodialysis Awarded KidneyX Prizes

By Ruth Jessen Hickman

Bioengineering innovations to decrease failure rates of arteriovenous fistulas and grafts, improved infection control measures in catheter-based and peritoneal dialysis, and a new hemodialysis system designed for home use were the prize-winning “Redesign Dialysis Phase 2” innovations announced at the recent virtual KidneyX Summit.

KidneyX (the Kidney Innovation Accelerator) is a partnership between the American Society of Nephrology and the US Department of Health and Human Services

(HHS) to promote innovations in kidney disease prevention, diagnostics, and treatment. Through a series of monetary prize competitions, KidneyX helps speed the development of new medical products by fostering collaboration among patients, health professionals, industry, innovators, and government experts.

This year’s summit continued the emphasis of the 2019 Redesign Dialysis Phase 1 competition, awarding grants of \$500,000 to each prize winner. The competition received

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COVID-19 has put kidney disease in the spotlight. Will that attract more physicians to the specialty?



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Peritoneal dialysis: substantial variation in peritonitis risk



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Innovators Awarded at KidneyX Summit

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deformation of the vein and provides for more effective outward vein growth.” The support also mitigates hyperplasia and turbulence within the vessel.

SelfWrap is designed to slide up the graft or vein before surgically securing the connection between the artery and vein or the graft and vein. After this connection is secured, the SelfWrap is slid down over the junction. The material becomes slightly sticky and viscous at body temperature, allowing it to close without the need for sutures and in a manner that provides a custom fit to the patient’s specific vessel anatomy.

“The wrap provides mechanical support similar in compliance to that of an artery, and is slowly degraded to improve usability and durability, or maturation and patency,” Boire said. Results from sheep studies showed that use of SelfWrap significantly reduced neointimal hyperplasia while promoting outward remodeling of the vessel or graft, potentially leading to reduced infection, thrombosis, and stenosis.

The team is focusing its preclinical development on use in AV fistulas but hopes to receive FDA approval for use in AV grafts as well.

Reducing infection

Two of the KidneyX winners tackled infection prevention as their primary focus, in two quite different contexts: peritoneal dialysis and catheter-based hemodialysis.

Sarah Lee (previous winner, KidneyX Patient Innovator Challenge)

Sarah Lee is CEO of Relavo, a medical device company founded by students at Johns Hopkins University. She and her colleagues created PeritoneX to help prevent infection due to touch contamination in peritoneal dialysis.

Peritoneal dialysis provides better health outcomes, higher patient satisfaction, and improved patient lifestyle, but only 10% of patients needing dialysis are on it because of the inherent risk of peritonitis, which occurs in 30% of patients annually and necessitates hospitalization in 50% of cases, Lee noted. The Advancing American Kidney Health Initiative aims to dramatically increase the percentage of kidney failure patients on home dialysis. This only increases the need to make peritoneal dialysis safer.

PeritoneX is a two-part connection device consisting of a reusable injection-retraction component and a disposable fluid component containing sodium hypochlorite (an established disinfectant in dialysis catheters.)

“Rather than connecting tubes directly, patients will connect them to our device,” Lee said. “They’ll then push a button to release the antimicrobial solution into the connection space, where it will kill any bacteria on the tube surfaces before being automatically retracted.” This maintains a closed system between disinfection and dialysis treatment. In proof-of-concept studies, the device has been shown to exceed industry standards for catheter disinfection.

PeritoneX is compatible with Baxter International peritoneal dialysis supplies, where it can slip seamlessly into the existing setup. Currently no other products on the market aim to reduce risk of peritonitis from peritoneal dialysis, and educational efforts about best practices only slightly decrease rates.

Alexander Yevzlin, MD (previous Phase 1 winner), for NitriCap to reduce catheter infections

Over 110,000 patients in the US use a catheter for vascular access each year, resulting in about 30,000 infections.

In response to this need, Yevzlin, a professor of medicine and director of interventional nephrology at the University of Michigan, and his colleagues developed NitriCap, a disposable hemodialysis cap that secretes nitric oxide gas. The nitric oxide is contained in a stable donor molecule that elutes the gas over three days.

“It’s a very simple, unique extension of a regular cap that fits into the hub of a dialysis catheter that can reduce microbial growth,” Yevzlin said.

Nitric oxide is well known to be a potent antimicrobial and antifungal, but it has a half-life of only seconds, eliminating potential systemic effects. Added Yevzlin, “Nitric oxide is produced as a gas, never enters the body, and disinfects the inside and outside of the catheter as it diffuses harmlessly into the air.”

Studies in sheep demonstrated a more than 100,000-fold reduction in bacteria compared to a control cap. Animal studies also showed that the product prevented the formation of biofilm in all four regions of the catheter. In contrast, commercially available antimicrobial caps using chlorhexidine did not.

“Our patients are constantly living in fear of catheter infection and catheter dysfunction,” Yevzlin said. “We think this device can have a huge impact on our patients’ lives

Shuvo Roy, PhD (previous Phase 1 winner), for a new hemodialysis system for home care

Roy is a professor in the department of bioengineering and therapeutic sciences at the University of California, San Francisco, and technical director of The Kidney Project, an effort focused on creating a small, surgically implanted, bioartificial kidney to treat kidney failure.

Unlike the other awardees, who are producing products that can merge into and improve existing dialysis setups,

Roy and colleagues are developing the iHemo Dialysis System to provide frequent, prolonged hemodialysis sessions with much greater patient ease.

Roy pointed to evidence that patients receiving more frequent and prolonged hemodialysis treatments have better survival rates, better overall health, and fewer dietary restrictions. Currently only about 2% of people on dialysis receive such treatment. Existing bulky hemodialysis systems approved for home use require complex tasks such as vascular cannulation, and they pose risks such as exsanguination.

With iHemo, a compact hemodialyzer (HemoCartridge) is surgically implanted inside the patient’s abdomen. It is constructed from silicon nanopore membranes that allow it to work under normal cardiac perfusion pressures, without the need of a mechanical blood pump or systemic anticoagulation therapy. The hemodialyzer connects to the blood vessels on one side, creating a permanent blood circuit inside the patient’s body. On the other side, it connects to catheters leading to an external pump.

“From the viewpoint of patients, iHemo fundamentally simplifies the procedure of hemodialysis,” said Roy. “The only external component is a compact pump to recirculate dialysate. No blood ever leaves the body, and patients never have to insert needles into a fistula or graft. Instead, they connect dialysis tubing to a catheter to conduct their treatments.”

Looking ahead

All the recipients emphasized how important these prizes are for furthering their work. The money allows the teams to push their development forward while they raise additional funds from investors.

“This award will help us advance our prototypes to clinically relevant devices that we can test in preclinical disease models and ultimately in clinical trials,” Roy said. “We also hope that the KidneyX award will garner more interest from industry and the investor community to support new innovations to treat kidney failure and kidney disease, because such interest has been significantly lacking for quite some time. It has taken the vision of HHS and ASN to step up.”

KidneyX will soon open two more prize competitions: an artificial kidney prize and a competition for solutions to address challenges caused by the COVID-19 pandemic.

“I hope that KidneyX plays a catalytic function, that we’ll get a self-sustaining innovation ecosystem where we are getting new products on the market constantly and are constantly improving patient care,” Patel said. “Ultimately the measurement of success of KidneyX is not in the programs we create . . . it’s whether we create health and wellness for the people for whom we are innovating.” ■

Exposure to Wildfire Smoke

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m³, exposure to the pollution accounted for 8.4% of daily mortality, but this percentage varied from 3.0% to 20.5% across counties depending on the exposure level.

The investigators did not find a significant association with specific causes of death, including cardiac-, vascular-, or infection-related mortality, but they did observe a strong association with deaths related to “other” causes (listed as other, unknown, un-listed other, and missing), which accounted for over 40% of deaths.

“The findings highlight the impact of air pollution exposure in individuals receiving hemodialysis, and they support the need for more research to develop and implement interventions to manage exposure during wildfire smoke episodes in this population,” said senior author Ana Rap-

pold, PhD, of the US Environmental Protection Agency.

Ziyad Al-Aly, MD, FASN, who is chief of research and education for the Department of Veterans Affairs Health Care System in St. Louis and was not involved with the study, noted that the findings lend support to results from previous research. “This paper is yet another piece of evidence that air pollution is an important driver of poor health outcomes, and the study’s link between exposure to wildfire smoke and death is alarming,” he said.

Al-Aly and his colleagues recently integrated all available epidemiological evidence to characterize an exposure-response model of ambient fine particulate matter and the risk of chronic kidney disease, uncovering an increase in risk with increasing air pollution concentrations. The authors of the *BMJ Global Health* study estimated that in 2017, there were 3,284,358 incident and 122,409,460 prevalent cases of chronic kidney disease in the world that were attributable to fine particulate matter, as well as 211,019 deaths due to chronic kidney disease from this

form of air pollution. The burden varied by geography and was disproportionately borne by disadvantaged countries.

“Patients and clinicians should be cognizant that poor air quality, especially spikes in levels of fine particulate matter in the setting of wildfires, may be deleterious to human health and especially for our patients with end stage kidney disease on dialysis,” Al-Aly said. “The wider policy implications of this body of research are clear: poor air is hazardous to human health, and it tends to disproportionately affect the sick and the poor. Effort to halt climate change and improve air quality is important to the health and well-being of all of us, and especially the most vulnerable among us.” ■

The article, titled “Mortality in US Hemodialysis Patients Following Exposure to Wildfire Smoke,” appeared online at <https://jasn.asnjournals.org/content/early/2020/07/15/ASN.2019101066> on July 16, 2020, doi: 10.1681/ASN.2019101066