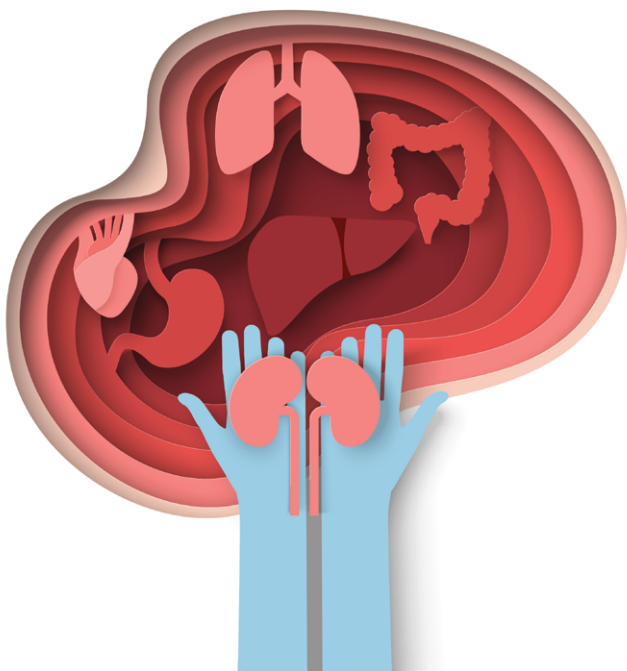


KidneyNews

September 2023 | Vol. 15, Number 9

Legislation Clears the Path for Transplant System Reform

By Bridget M. Kuehn



A July Capitol Hill visit from an ASN delegation highlighted the need to fast-track passage of legislation to reform and modernize the U.S. transplant system. The visit was the latest in years of advocacy by patient and clinician organizations seeking to improve the nation's transplant system and make transplantation more accessible.

The Securing the U.S. Organ Procurement and Transplantation Network (SUS OPTN) Act passed the U.S. House of Representatives and the Senate with bipartisan support in late July (1, 2), 1 week after ASN advocates visited their members of Congress asking for swift enactment of the legislation. ASN and 29 other organizations representing patients with kidney diseases and their clinicians supported the legislation (3). The passage of the SUS OPTN Act provides the Health Resources & Services Administration (HRSA) the ability to fully implement its "OPTN Modernization Initiative," which aims to increase transparency, accountability, competition, and efficiency in the OPTN.

"It just gives HRSA the green light to go ahead with the

Modernization Initiative," said ASN President Michelle Josephson, MD, FASN, professor of medicine and surgery at The University of Chicago Pritzker School of Medicine, IL. "This is step one."

Need for modernization

Roslyn Mannon, MD, chair of ASN's Policy and Advocacy Committee and professor of medicine in the Division of Nephrology and vice chair of research in the Department of Medicine at the University of Nebraska Medical Center in Omaha, remembers that early in her career, many transplant programs were small "mom and pop" operations driven by trailblazers at local hospitals. The National Organ Transplant Act of 1984 established the first national organ recovery and allocation system, and the United Network for Organ Sharing (UNOS) received the first federal contract to operate the OPTN and has operated it ever since (4). Mannon noted the remarkable accomplishments in the field of transplant since then. There are now 56 organ

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Heat, Diet, and Antibiotics Implicated in Rising Pediatric Kidney Stones

By Bridget M. Kuehn

A complex mix of factors, including extreme heat exposure, consumption of processed foods, and antibiotic use, may contribute to rising kidney stone rates in children and adolescents.

A study in *CJASN* identified a 26% increase in kidney stones per 5-year period among 15- to 19-year-olds in South Carolina between 1997 and 2012 (1). This finding was the "canary in the coal mine," alerting scientists to the alarming trend of rising pediatric kidney stones, said Gregory Tasian, MD, MSc, MSCE, a pediatric nephrologist at the Children's Hospital of Philadelphia, PA. The data showed that girls, Black children, and adolescents were disproportionately affected. Since then, data from children's hospitals indicate a nationwide increase of

approximately 6% to 10% per year over the past several decades, according to a recent review of the data by Tasian and colleagues (2).

"There is convincing evidence it is still happening," Tasian said. "If we can understand what is driving these trends, then you can develop interventions that can work on the causal pathway." The cause is likely multifactorial, he continued. About half of an individual's vulnerability to developing kidney stones is genetic, Tasian noted. Additionally, diet and hydration play a role, as do environmental factors, such as heat exposure or other exposures like antibiotics that may alter mineral metabolism by altering the gut microbiome.

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Heat, Diet, and Antibiotics Implicated in Rising Pediatric Kidney Stones

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Effect moderator

There is growing recognition that climate change and more frequent extreme heat episodes are driving increasing rates of kidney diseases in some populations. Emerging evidence demonstrates increased rates of admission for kidney diseases during heat waves (3) and elevated rates of kidney stones (4).

Additionally, scientists have implicated chronic heat exposure in rising rates of kidney disease of unknown origin in young agricultural workers in Central America and other parts of the world (5). Some studies suggest that the roots of the condition may be traced back to childhood (6). Nathan Raines, MD, MPH, an instructor of medicine at Beth Israel Deaconess Medical Center and Harvard Medical School in Boston, MA, and a researcher studying the trend, said that heat is an “effect moderator” in kidney diseases. He described that it likely interacts with genetic factors, agricultural chemical exposures, infections, or other not-yet-identified contributors.

“Heat exposure drives dehydration,” Raines explained. He said dehydration may lead to reduced urine output, which could contribute to stone formation in children, but it is unlikely to cause the condition on its own. Instead, he added, it likely makes the body less able to compensate for other factors that may contribute to stone formation. Rising temperatures may also contribute to drought, reducing water access, said Kari Nadeau, MD, PhD, interim director of the Center for Climate, Health, and the Global Environment and professor and chair of the Department of Environmental Health at the Harvard T.H. Chan School of Public Health, Boston.

Children are especially vulnerable to dehydration, Nadeau said. She explained that children have a faster metabolism than adults and need more water per unit of weight than adults. Their kidneys are also more vulnerable to injury because they are still developing and do not have as much buffer against damage as adult kidneys do. Children also may be less aware of the importance of hydration or the dangers of high temperatures, Nadeau added. “Kids don’t necessarily know to go under a tree right away or go into a cooling room, and they will keep exercising unless someone stops them,” she said.

In addition to driving dehydration, heat stress can cause proteins in the body to degrade, Nadeau explained. Filtering out large amounts of degraded proteins can tax kidneys already struggling with limited water. “It becomes hard for [the kidneys] to function, and you can get kidney stones,” she said. That kind of stress on kidneys early in life may contribute to chronic kidney disease later in life.

Multiplicative effects

Other trends, such as growing consumption of highly processed foods and greater exposure to antibiotics, may interact with factors like heat exposure to propel kidney stone risk in children.

Consuming foods or beverages with very high concentrations of sugar or salt, which is common in many readily available, processed foods, is associated with a higher risk of developing kidney stones, said Kamyar Kalantar-Zadeh, MD, MPH, PhD, professor of medicine at the University of California, Los Angeles (UCLA), and chief of nephrology and hypertension at Harbor-UCLA Medical Center. He explained that diets high in protein, especially processed meats; low in calcium; or high in sugary drinks, may also contribute to kidney stone risk.

Nadeau noted that communities disproportionately affected by food insecurity or scarcity might have less access to affordable, nutritious foods that can help buffer the body

against heat stress. For example, she described that some inexpensive foods, such as potato chips and cookies, might be widely available in stores in California’s Central Valley communities, but the fresh produce grown by workers in the Central Valley may be less accessible. “We need to enable communities to have good, healthy choices,” she said.

The same communities may also be disproportionately affected by climate change-related heat exposure, pollution, and conditions, such as diabetes, that also affect kidney health, she noted. As a result, improving equitable access to social determinants of health is essential. “Climate change is like an X-ray that exposes health inequity,” she added.

Antibiotics may be another potential contributor to pediatric kidney stones. Studies have found that five commonly prescribed antibiotics are associated with an increased risk of kidney stones (7) and that individuals with stones are missing gut bacteria key to human health (8). “Things that change the composition of the microbiome increase the likelihood of forming stones because your gut handles minerals in a different way,” Tasian said.

A complex mix of factors, including extreme heat exposure, consumption of processed foods, and antibiotic use, may contribute to rising kidney stone rates in children and adolescents.

Diagnosis and treatment

One of the challenges of treating kidney stones in children is that they may often go undiagnosed. Physicians may not be expecting to see kidney stones in children or adolescents, Tasian said. Pre-adolescent children may also present with diffuse belly pain instead of the excruciating flank pain, nausea, and vomiting, as experienced by adults during an acute kidney stone event, he explained. “Stones are something you often don’t recognize until you have one of these incredibly painful events; it could be going on for months or years before it’s recognized,” he added.

Physicians typically use computed tomography (CT) scans to diagnose kidney stones in adults. But ultrasound is first used for diagnosing children with kidney stones because it does not expose them to radiation, Tasian said. Ultrasound is not as good at detecting stones as CT, so sometimes a follow-up CT is needed, he expressed.

Two medications—one diuretic and another drug that raises urine pH—have been the frontline therapies for kidney stones for decades, Tasian explained. Both focus on treating the incredibly painful incidence of stones. If a blockage is detected, and surgery is required, a pediatric urologist or surgeon who specializes in treating stones in children is needed because there are unique considerations for treating stones in children, Tasian said.

New therapies are needed to treat stone disease as an ongoing disorder of mineral metabolism, Tasian said. He noted that in children and adolescents, the recurrence rate of kidney stones is 50% (2), and individuals who develop kidney stones also have lower bone density and a higher risk of fracture, hypertension, and heart disease. “We need to shift the paradigm from [the] stone as something that causes episodic events to something that has a continuous and long-term impact on human health,” he continued.

Prevention and policy

Kalantar-Zadeh emphasized the importance of children drinking water and eating fresh fruits and vegetables in reducing the risks of kidney stones. He stressed avoiding processed foods or meats high in salt or other additives. Tasian agreed: “A well-balanced diet high in vegetables and low in sodium—a heart-healthy diet—is helpful for preventing kidney stones and is good for you in general. The more water you drink, the more the urine is dilute, and the less likely stones can form.” Nadeau also recommends rehydrating drinks with electrolytes, such as Gatorade or even milk, to help children who have become dehydrated recover.

Individuals with a history of kidney stones should also seek evaluation and treatment from a urologist or nephrologist to prevent future stones and to help decrease the risk of kidney stones becoming a chronic problem, Tasian said.

Public health measures may also help reverse the trend of rising kidney stones in children and adolescents. Tasian noted that some European countries limit the amount of sodium in processed foods (9). Kalantar-Zadeh recommended that schools restrict access to salty or processed foods or sugary drinks in cafeterias and school vending machines. Raines said schools might also need to implement heat protections for students, for example, ensuring adequate hydration and time for rest, similar to heat protections for workers. Education to help parents understand how heat exposure may contribute to disease mechanisms and how they can prevent it is also essential, Raines continued. Nadeau also recommended more education for physicians and health care professionals on climate change mitigation and adaptation to help them guide patients toward protective measures.

Policies that mitigate rising global temperatures are also urgently needed, Tasian said. “The risk is going to increase as the climate warms,” he added. “More people will be exposed to extreme heat, which we know dramatically increases the risk of presenting with a stone.” ■

Disclaimer: Dr. Raines’ views do not represent the official views of Beth Israel Deaconess Medical Center or Harvard Medical School or of the La Isla Network, a nonprofit organization for which Dr. Raines serves as an advisor.

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