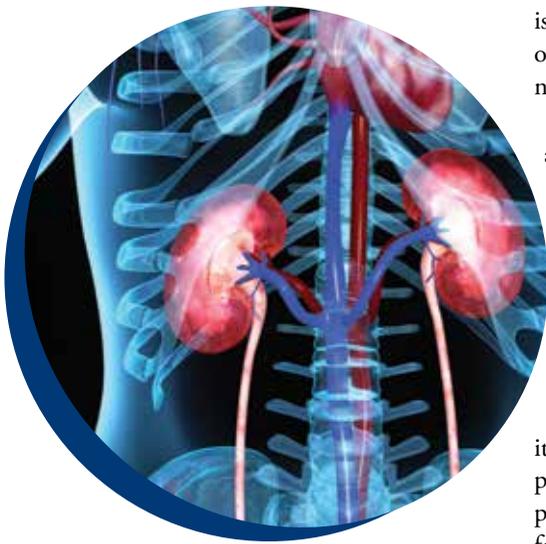


Kidney News

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Basic Science Research Yields Possible New Treatment Targets for AKI



ischemia-reperfusion injury (IRI)—each of which identifies a potentially useful new therapeutic target.

“There is increasing awareness that acute kidney injury is both a major source of immediate morbidity and mortality and has a long-term impact on the development of chronic kidney disease,” said Raymond Harris, MD, FASN, President of the American Society of Nephrology. “Unfortunately, we still lack effective therapies to prevent or treat AKI. Therefore, it is encouraging that these three studies provide important new insights into the pathogenesis and offer potential avenues for prevention and treatment of AKI.”

Possible protective effect of vagal nerve stimulation

Previous research has suggested that ultrasound preconditioning of adrenergic neurons innervating the spleen has an anti-inflammatory effect—including protection against severe sepsis-induced AKI in a mouse model. Those studies identified the cholinergic anti-inflammatory

pathway (CAP) as the central mechanism of protection.

In a new study, Tsuyoshi Inoue, MD, PhD, Chikara Abe, MD, and colleagues at the University of Virginia School of Medicine in Charlottesville sought to build on that knowledge by testing whether similar protective effects could be induced by ultrasound stimulation of the vagus nerve. In their mouse model, vagal nerve stimulation (VNS) ameliorated renal IRI via the same CAP activated by ultrasound. The findings included evidence that vagal efferents were the common pathway activating the CAP.

The results highlight the importance of neuroimmunomodulatory mechanisms of AKI—for example, the “inter-organ crosstalk” by which injury to one kidney affects the response of the other kidney.

“In the setting of multiorgan failure, such neural mechanisms are likely to be even more important,” writes Simon J. Atkinson, PhD, Vice Chancellor of Research at Indiana University–Purdue University, Indianapolis, in an accompa-

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Basic science research into the underlying mechanisms of acute kidney injury (AKI) poses unique challenges, making it difficult to identify promising new targets for prevention and treatment. This month, *The Journal of Clinical Investigation* presents three new and unique basic science studies exploring differing mechanisms of AKI and

Climate Change May Contribute to Rising Rates of Chronic Kidney Disease of Unknown Origin

By Tracy Hampton

Chronic, severe dehydration linked to working in hot, humid climates for long hours may be accelerating rates of chronic kidney disease (CKD). Research published in the *Clinical Journal of the American Society of Nephrology (CJASN)* suggests that a condition

called heat stress nephropathy may represent a disease of neglected populations, but one that may emerge as a major cause of poor kidney health as the climate continues to change (Glaser J, et al. *Clin J Am Soc Nephrol*. doi: 10.2215/CJN.13841215 [published online May 5, 2016]).

Over the next century, climate change and resulting water shortages are likely to affect a wide variety of health issues related to dehydration and heat stress—with risks increasing for cognitive dysfunction, malnutrition, waterborne infectious diseases, CKD, and other conditions. Some health situations, such as a great geographic spread of tropical and infectious diseases, may be more noticeable than gradual changes such as incremental increases in pollen counts that could lead to longer allergy seasons and worse asthma cases. In

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Policy Update

CMS's new pay models: Could MACRA's shift from fee-for-service open up ways for nephrologists to create better care models?

Transforming Medical Education

Look to kidney care as a model

Distinguished Conversations

Sharon Moe, MD, interviews Sharon Anderson, MD, about career-life balance, what it was like to be the first woman president of ASN, and much more

Cancer and the Kidney

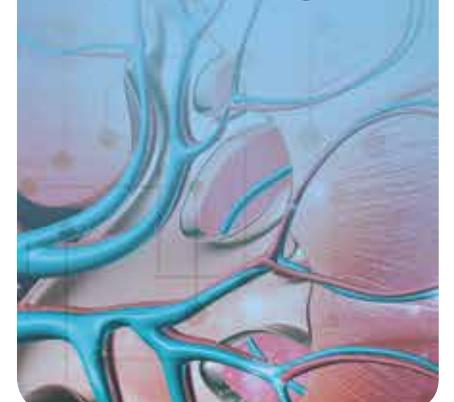
ASN Onco-Nephrology Forum releases new curriculum

Glomerular Diseases

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Findings

Incompatible live-donor kidney transplant improves survival compared with waiting



New Site Extends Kidney News into Digital Space, Expanding Resources, Context

The American Society of Nephrology (ASN) has launched a new website, www.kidneynews.org, that extends *ASN Kidney News* as a digital platform for daily updates on news, context, and resources for all stakeholders in the kidney community.

Kidney News has been tremendously successful since launching in 2008. Thanks to its broad scope, *Kidney News* has amassed the largest audience of any ASN publication. Building on that success, this new site uses new digital tools to expand commentary and resources with a focus on developing an interactive presence for everyone interested in and affected by kidney health issues. The thoughtful perspectives and long-form content that have made the print version so popular will continue, while the new digital platform affords the ability to develop online coverage into a diverse resource updated daily, allowing more interactivity, and enabling users to personalize the site according to their interests.

A wealth of new content

Every month, Raymond C. Harris, MD, FASN, will share his thoughts on issues important to nephrology in a new column. Other contributions will reflect the diversity and dynamics of the profession, including a series on the nephrology fellowship experience, interviews with clinicians who will share experiences “from the field,” insights from all members of the kidney care team, and podcast discussions with ASN research grant recipients.

Perspective pieces include a look at gaps in medical education curricula and how nephrology can address them, insights on the leadership qualities physicians need for career success, an up-close look at the advantages of training in smaller fellowship programs, and how priority areas in kidney health differ in various regions of the world. One of the most rapidly changing areas within the kidney community involves public policy. *Kidney News Online* will highlight policy issues relevant to all members of the global kidney community. Marking ASN’s 50th anniversary is a series of contributions from ASN members recalling their observations from the first ASN annual meeting they attended.

The site also contains an archive of past *ASN Kidney News* articles, now available by article (instead of by issue only). The site includes all content from 2014 through the current day, and will continue to build the archive so all past content from *Kidney News* will be easily searchable and accessible. Other resources focus on information key to nephrology professionals, making it easy to find current and relevant information on ICD-10, MACRA, telemedicine,



and other priority areas.

Kidney News Online also offers users the ability to personalize their experience by providing content that matters most to individual users. While access to the site is freely available without login or registration, the site can be integrated with ASN member profiles, or profiles nonmembers set up by registering on the site, allowing users to segment and prioritize new items based on their indicated interest. Those who want to personalize their content can then log in and the displayed content will be automatically updated according to the interest areas selected. Areas of interest can be modified at any time by visiting <http://www.asn-online.org/myasn>.

Serving the readers' interests

The site includes a feedback button on every page, and every section invites readers to send in suggestions for coverage to info@kidneynews.org. Suggestions from readers, combined with closely tracking analytics to see what sections are popular (or not) with users, will guide ASN as it evolves the site to meet the interests of users as well as the rapidly changing worlds of medicine, science, education, and health policy. ●

Climate Change

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this latest *CJASN* research, investigators found that CKD that is not associated with traditional risk factors (CKDu) also appears to be increasing in rural hot communities as worldwide temperature progressively rises.

The researchers believe the risk for heat stress nephropathy—or CKD consistent with heat stress—has increased owing to global warming and an increase in heat waves, and it is having a disproportionate impact on vulnerable populations, such as agricultural workers.

“So far, the profile for impacted communities seems to be extreme heat and heavy labor. As you leave these extremely hot areas, there are far fewer cases recorded to date even though some of the other proposed risk factors remain relatively unchanged,” said lead author Jason Glaser, of La Isla Foundation, in Nicaragua and the US. Decreasing precipitation exacerbates this epidemic by reducing the water supply and water quality as temperatures climb.

“We were able to connect increased rates of chronic kidney disease in different areas to an underlying mechanism—heat stress and dehydration—and to climate,” said senior author Richard Johnson, MD, of the University of Colorado School of Medicine. “A new type of kidney disease, occurring throughout the world in hot areas, is linked with temperature and climate and may be one of the first epidemics due to global warming.”

Mechanistically, dehydration may inhibit an individual’s ability to excrete toxins as effectively as those who are well hydrated, leading to higher concentrations in the blood and kidney. Dehydration also results in the kidney concentrating the urine. While this is a healthy process that is normally protective in the acute setting, repeated dehydration appears to carry a cost to the kidney, according to Johnson. “Specifically, recurrent dehydration can lead to chronic elevations in vasopressin that may induce kidney damage,” he said. “It can also activate processes that lead to fructose generation in the kidney that can cause local oxidative stress. High concentrations of uric acid

can also precipitate in the concentrated urine and may exacerbate injury. These processes may be amplified by rehydrating with drinks high in sugar or high fructose corn syrup.”

Earlier studies by the investigators in Nicaragua and El Salvador revealed a remarkable decrease of kidney function in male sugarcane cutters after high-intensity harvesting in hot conditions (García-Trabanino R, et al. *Environ Res* 2015; 142:746–755; Wesseling C, et al. *Environ Res* 2016; 147:125–132). Other studies have uncovered similar hotspots in other parts of Central America, as well as in South Asia, North and South America, Africa, and the Middle East.

“I don’t think this disease is new—I think it has been with us for some time, and is more recognized due to increasing surveillance but also because the factors that put people at risk are exacerbated by extreme demands at the workplace to meet production needs,” said Glaser. “The result is over 40,000 dead in the last 10 years in Mesoamerica and Sri Lanka alone. Of course, we think that due to surveillance being so inadequate for these

at-risk populations, the disease is much more widespread.”

To address the problem, interventions—such as those proposed in La Isla’s and Solidaridad’s Worker Health and Efficiency (WE) Program (www.weprogram.org)—are needed to improve worksite conditions and ensure adequate hydration. In addition, governments and scientists should work together to conduct epidemiological and clinical studies to document the presence of these epidemics and their magnitude. To this end, the World Health Organization, in collaboration with the Sri Lankan government, called together approximately 45 global experts from various organizations, institutions, and disciplines in late April. Also, Johnson is working with Glaser and others on a simple and practical protocol to estimate distributions of kidney function in rural communities globally. The Disadvantaged populations estimated glomerular filtration rate (eGFR) epidemiology study (DEGREE) will provide key information to inform hypotheses and to guide further research into the sources of CKDu. ●