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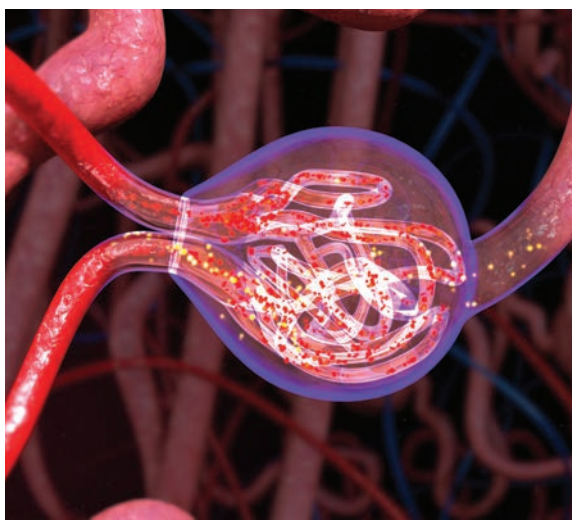
Emerging Work on Boosting Nephron Number Could Aid Kidney Function Preservation in Preemies, Adults

By Bridget M. Kuehn



Advances in neonatal care are boosting survival rates of those born prematurely, but these survivors may later face kidney complications. New insights on how the kidney forms early in life and new tools to help monitor kidney development may one day help improve their health.

As the basic working units of the kidney, nephrons filter the blood, remove and eliminate urine, and help keep nutrients in the body. People have on average about 1 million nephrons per kidney, although the numbers may vary between individuals from 200,000 to about 2 million, said Marva Moxey-Mims, MD, chief of the division of nephrology at Children's National Health System in Washington, DC.

Because nephron formation typically stops by 36 weeks of gestation, babies born earlier may not have a full complement of nephrons, said Moxey-Mims. Some nephrons may still be formed after birth, she noted, but far fewer than if gestation continued. Life-saving treatments, such as certain antibiotics, also may damage the nephrons these premature infants have, she noted.

"We can keep very, very early birth babies alive, but at a cost," said Raphael Kopan, PhD, director of the division of developmental biology at Cincinnati Children's. "The cost will be exacted when they are adults. They are at great risk for end stage renal disease."

Recent findings from a study by Kopan and his colleagues suggest it may be possible to extend the production of nephrons early in life. These findings, along with emerging technologies to help clinicians count nephrons, may lead to new kidney-preserving strategies for both preemies and individuals with other forms of kidney disease.

Extending the clock

Nephrons are under a lot of pressure, and it is normal for some to die over the course of a life. But most people have enough that they can lose some and still eliminate urine effectively. Those born early may not have enough to spare.

"One of the advantages of having so many is that you can lose some of them," said Kevin Bennett, PhD, associate professor of radiology at Washington University in St. Louis.

Pioneering work by nephrologist Barry Brenner showed that those born with fewer nephrons were more likely to develop high blood pressure as adults, eventually leading to kidney failure, Bennett noted.

Understanding why nephrogenesis ends so early in life and what lever turns it off might allow scientists to extend nephron production and boost the number of

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Racial Disparities in Diabetes Complications Are Reduced by Delivering Standardized Care

By Tracy Hampton

Type 2 diabetes and associated chronic kidney disease (CKD) disproportionately affect blacks. Yet when black and white individuals received comparable diabetes care within the context of a clinical trial, black race was not associated with faster development or progression of CKD. The findings are published in the *Clinical Journal of the American Society of Nephrology (CJASN)*.

The prevalence of type 2 diabetes is higher in non-Hispanic blacks than in non-Hispanic whites, and blacks have an elevated risk of diabetes-related complications. In addition, after development of CKD, blacks with type 2 diabetes are more likely to progress to kidney failure.

It has been unclear whether these burdens may be explained by biological factors that influence propensity to CKD and its severity or by differences in type 2 diabetes care.

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Racial Disparities

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To investigate, a team led by Claire Gerber, PhD, MPH, and Tamara Isakova, MD, MMSc, of the Feinberg School of Medicine at Northwestern University, in Chicago, performed a post hoc analysis of a subset of 1937 black and 6372 white middle-aged and older patients with type 2 diabetes who were participating in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. All patients received comparable type 2 diabetes care.

Although people who self-identify as black or African American are underrepresented in pivotal clinical trials for new drug approvals, blacks were adequately represented in the ACCORD trial, comprising 19% of participants. (Blacks constitute 7% of overall clinical trial participants, although they make up 13% of the US population.)

The researchers hypothesized that compared with white participants, black participants with type 2 diabetes who received standardized multifactorial type 2 diabetes care within the context of a randomized controlled trial would have faster kidney function decline and be at greater risk of development and progression of CKD during follow-up. During a median follow-up period of 4 to 5 years, however, black race was not associated with accelerated kidney function decline, and fewer black participants than white participants developed CKD. Specifically, blacks had a 27% lower risk of incident CKD defined by new onset eGFR <60 mL/min/1.73 m^2, eGFR decline by >25%, and slope of eGFR decline faster than -1.6 mL/min/1.73 m^2.

"In spite of blacks having more risk factors for adverse kidney outcomes in our study, we found that comprehensive type 2 diabetes care within the context of a clinical trial eradicated racial disparities in the development and progression of CKD," Gerber said.

At the start of the trial, blacks had higher levels of systolic blood pressure and hemoglobin A1c, as well as more frequent macro- and microalbuminuria. During follow-up, however, there were no racial differences in the development of albuminuria.

Isakova noted that the findings are similar to recent results from the Indian Health Service's first Diabetes Standards of Care implementation effort that delivered comprehensive diabetes care to American Indians and Alaska Natives and eliminated disparities in kidney outcomes in these high-risk populations.

"Taken together, our results and the findings from the Indian Health Service demonstrate that delivery of comparable diabetes care has the potential to achieve equitable health outcomes for all patients with diabetes."

Nilka Ríos Burrows, MPH, MT, of the Division of Diabetes Translation at the Centers for Disease Control and Prevention, in Atlanta, who was a co-investigator in the American Indians and Alaska Natives study, noted that integrating kidney disease prevention and education into routine diabetes care can help prevent or delay kidney problems.

"The diabetes care team can help patients avoid kidney failure by keeping blood pressure and blood sugar under control, using medicines that lower blood pressure and protect the kidneys, and monitoring kidney function," she said. "These and other strategies used successfully by the Indian Health Service contributed to reducing kidney failure from diabetes among American Indians and Alaska Natives and can serve as a model to reduce disparities in other populations."

In an editorial accompanying the *CJASN* study, Katherine Tuttle, MD, FASN, FACP, of Providence Medical Research Center, in Spokane, WA, called for action. She pointed to numerous areas in which blacks in the United States are disadvantaged across social determinants of health: socioeconomic status, psychosocial factors, healthcare access, neighborhood, and environment. She also pointed to barriers to CKD screening among blacks, including lack of knowledge, mistrust, and financial burden. Key facilitators to screening include CKD education, culturally sensitive communication, and better access by convenient screening.

Gerber C, et al. Incidence and progression of chronic kidney disease in black and white individuals with type 2 diabetes. *Clin J Am Soc Nephrol* 2018; 13:884–892.

Bullock A, et al. Vital signs: Decrease in incidence of diabetes-related end-stage renal disease among American Indians/Alaska Natives—United States, 1996–2013. *Morb Mortal Wkly Rep* 2017; 66:26–32.

Tuttle K. Race in America: What does it mean for diabetes and CKD? *Clin J Am Soc Nephrol* 2018; 13:829–830.