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Ongoing Research Links Bisphenol A with Negative Health Effects

By Tracy Hampton



disease in children. Still, the risks are far from clear.

In some of the most recent work, researchers found a link between BPA and low-grade urinary albumin excretion in children and adolescents (Trasande L, et al. *Kidney Int* 2013 Jan 9. doi: 10.1038/ki.2012.422). The findings suggest that youngsters who are exposed to BPA, which was once used widely in plastic bottles and is still found in aluminum cans and register receipts, may have an increased risk for the development of heart and kidney disease.

BPA may negatively affect health in a variety of other ways, according to published and ongoing studies. Animal research has linked BPA with early sexual maturation, altered behavior, hyperactivity, and effects on prostate and mammary glands. In humans, the chemical has been linked to cardiovascular disease, diabetes, and male sexual dysfunction (Schechter A, et al. *Environ*

Sci Technol 2010; 44:9425–9430. doi: 10.1021/es102785d).

BPA, disease, and obesity

The latest study by Trasande et al. involved an analysis of data from 710 children and adolescents who participated in the 2009–2010 National Health and Nutrition Examination Survey, which included measurements of urinary BPA and albumin. Compared with children with the lowest amount of BPA in their urine, children with the highest amount had an albumin-to-creatinine ratio that was 0.91 mg/g higher.

The findings may be particularly worrisome for children with poor kidney function.

“While we excluded children with pre-existing kidney disease from our analysis, I am concerned that BPA exposure may have even greater effects on children with kidney disease,” said co-lead author Howard

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Recent studies add growing evidence to the potential dangers of exposure to bisphenol A (BPA). The estrogen-like chemical may be linked to diabetes in adults and to heart and kidney

Ultrasound of Lung Congestion Could Signal ESRD Outcomes

By Eric Seaborg

Pulmonary congestion, even in patients without symptoms of heart failure, could be an important predictor of mortality and cardiovascular risks in hemodialysis patients, a new study shows.

In the multicenter study reported in the *Journal of the American Society of Nephrology*, researchers who used ultra-

sound (US) to categorize patients’ levels of extravascular lung water found that patients with very severe congestion had a four times greater risk of death and a three times greater of cardiac events than patients with mild or no congestion.

“This article is very significant because it points out the relationship

between volume overload and mortality and cardiovascular events,” said Rajiv Agarwal, MD, professor of medicine at the Indiana University School of Medicine, noting that the study did not address causality. “They are simply describing an association between a finding of lung congestion and important outcomes for the patients.”

Led by Carmine Zoccali, MD, of Riuniti Hospitals in Reggio Calabria, Italy, a research team studied 392 Caucasian patients from 11 dialysis units in southern Italy. They classified the subjects according to the New York

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Heart Association (NYHA) scale for heart failure. Using ultrasound examinations performed prior to dialysis, the researchers categorized patients' lung congestion according to the number of "lung comets" or sonographic B-lines found: mild (5 to 15 B-lines), moderate to severe (15 to 60 B-lines) and very severe (more than 60 B-lines). They followed the patients for a median time of 2.1 years to monitor for the study end points of mortality and cardiac events.

"We found that lung ultrasound adds significant prognostic information for death and cardiovascular event to classic risk factors, the NYHA score, and powerful risk factors in [chronic kidney disease] patients, like hypoalbuminemia, hyperphosphatemia, and inflammation," the researchers wrote in "Pulmonary Congestion Predicts Cardiac Events and Mortality in ESRD." "The degree of lung congestion measured by lung ultrasound was a better predictor of the risk of death and cardiac events than symptoms of heart failure as assessed by the NYHA score and provided additional independent information . . . over and above classic risk factors." Plugging the lung congestion estimates into a predic-

tion model based on these other risk factors improved the model's prediction of cardiac events by 10 percent.

B-lines are "probably" good indicators of pulmonary congestion, said Elke Platz, MD, an assistant professor at Harvard Medical School and lead author of a study in the *European Journal of Heart Failure* that demonstrated that B-lines measured by ultrasound are associated with cardiac and pulmonary pressures measured by invasive means.

"We know that B-lines can be detected in acute decompensated heart failure and in patients with ESRD prior to dialysis," Platz told *ASN Kidney News*. "We also know from other studies that in both of these patient populations, the number of B-lines decreases with removal of fluid. What we don't really know is what generates these B-lines, which are essentially sonographic 'reverberation artifacts'."

Agarwal agreed with the authors' assertion of lung congestion as a proxy for general fluid overload, which the authors called "a common modifiable risk factor for the exceedingly high death risk of patients with kidney failure on dialysis."

But W. Charles O'Neill, MD, professor of medicine and director of ultrasonography in the renal division at

Emory University School of Medicine in Atlanta, found the study less persuasive: "It's an interesting finding, but I'm not convinced that it is actually an indicator of interstitial lung water. I think what they are probably looking at is air bubbles within the alveolar fluid, in other words, pulmonary edema, which is in a sense lung water, but it's not interstitial water."

The researchers found very severe congestion in 14 percent of patients, and these patients were at highest risk of mortality and cardiac events. Some 45 percent of patients had moderate to severe congestion, but 71 percent of these patients were asymptomatic or had only slight symptoms of heart failure. Despite their lack of symptoms, they were still at slightly higher risk of mortality and cardiac events compared with patients with mild congestion.

The researchers have previously published studies showing an association of increased lung congestion with problematic symptoms such as increased pulmonary pressure and left atrial volume. They suggest that the use of ultrasound to detect congestion at a preclinical stage could help prevent cardiac events and other problems.

Agarwal said that a reliable measure of fluid accumulation would have great clin-

ical value because it would alert caregivers to the need to reduce fluid volume during dialysis. Fluid accumulation often goes unnoticed despite the possible approaches to measuring it, including relative plasma volume monitoring, physical examination, body impedance analysis, and echocardiographic techniques such as left atrial volume. But Agarwal noted there is no standard reference method, nor have there been studies to show whether any of these methods can improve patient outcomes.

In their paper, Zocalli and colleagues acknowledge that the development of such a biomarker for clinical practice requires significant evidence, including data from clinical trials. But a trial to begin the process, designed and funded by the European Renal Association-European Dialysis Transplantation Association, was launched in September 2012. The LUST study, which stands for Lung Water by Ultrasound-Guided Treatment to Prevent Death and Cardiovascular Complications in High-Risk ESRD Patients with Cardiomyopathy, will test whether a treatment protocol can deliver results. Given this innovation's potential impact on improving patient care, many nephrologists will undoubtedly be eagerly awaiting the results. ●

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