Gut bacteria byproduct linked to chronic kidney disease for the first time

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Cleveland Clinic researchers have, for the first time, linked trimethylamine N-oxide (TMAO) - a gut metabolite formed during the digestion of egg-, red meat- or dairy-derived nutrients choline and carnitine - to chronic kidney disease.

TMAO has been linked to heart disease already, with blood levels shown to be a powerful tool for predicting future heart attacks, stroke and death. TMAO forms in the gut during digestion of choline and carnitine, nutrients that are abundant in animal products such as red meat and liver. Choline is also abundant in egg yolk and high-fat dairy products.

The research team was led by Stanley Hazen, M.D., Ph.D., Chair of the Department of Cellular & Molecular Medicine for the Lerner Research Institute and section head of Preventive Cardiology & Rehabilitation in the Miller Family Heart and Vascular Institute at Cleveland Clinic, and W.H. Wilson Tang, M.D., Department of Cardiovascular Medicine in the Miller Family Heart and Vascular Institute and Lerner Research Institute. The research will be published online on January 29th and in the January 30th print edition of *Circulation Research* .

According to the Centers for Disease Control and Prevention, more that 20 million Americans are estimated to have chronic kidney disease, many of whom are undiagnosed. It is caused by a gradual loss of kidney function over time. As the disease worsens, waste products can accumulate in the blood and can be fatal without interventions. It has long been known that patients with chronic kidney disease are at an increased risk for cardiovascular disease, but the exact mechanisms linking the two diseases are not known. This newly discovered TMAO link offers further insight into the relationship between cardiovascular disease and chronic kidney disease.

"It's a triple whammy" said Dr Hazen. "Elevated plasma TMAO levels in subjects are linked to future cardiac risks, and in subjects with normal renal function, elevated levels predict long-term future risk for development of chronic kidney disease; animal model studies show that long-term exposure to higher levels of TMAO promotes renal functional impairment and atherosclerosis; and as the kidneys lose function, TMAO isn't eliminated as easily, and levels further rise, increasing cardiovascular and kidney disease risks further."

Drs. Hazen and Tang measured fasting TMAO levels in 521 patients with chronic kidney disease and in 3,166 subjects without chronic kidney disease, following all subjects over five years. They found that TMAO levels were higher in patients with chronic kidney disease, and elevated TMAO levels were associated with greater mortality risk in both subject groups. In animal models, the researchers also found that chronic dietary exposures to choline and TMAO were associated with development and progression of chronic kidney disease. Further studies are needed to determine if dietary interventions can delay disease progression of both chronic kidney disease and associated cardiovascular disease.

"Our studies raise the exciting prospects of nutritional interventions to help retard development and progression of chronic kidney disease. Regrettably, very little is known about diet and renal disease progression," said Dr. Tang.

This research strongly implies the need to focus preventive efforts on dietary interventions and therapeutic targeting of gut microbiota-dependent TMAO pathways, potentially to halt development and progression of chronic kidney disease, as well as cardiovascular disease risks

Provided by Cleveland Clinic