Welcome and logistics  
Arlene Chapman, MD  5 min  11:00-11:05
Kidney Stone Program  
Elaine Worcester, MD  5 min  11:05-11:10
Contributions of Urine Sulfate, Titratable Urine Anion and GI Anion to Net Acid Load  
Jenny Huo  12 min  11:10 – 11:22
Evidence for Abnormal Linkage Between Urine Oxalate and Citrate Excretion in Human Kidney Stone Formers  
Megan Prochaska, MD, MPH  12 min  11:22 – 11:34
Oxalobacter formigenes-derived Factors Impacting Hyperoxalemia, Hyperoxaluria, and related Kidney Stones  
Hatim Hassan, MD, PhD  12 min  11:34 – 11:46
Q & A  14 min  11:46 – 12:00

Speakers  
Jenny Huo, BA  
Bio: I worked in the Coe/Worcester lab for a summer while an undergraduate at Smith College. After graduating, I was awarded the post-baccalaureate CRTA fellowship at the NIH/NCI. Currently, I am applying to MD/PhD MSTP programs, and working at the Fred Hutchinson Cancer Research Center in Seattle.

Abstract: Contributions of Urine Sulfate, Titratable Urine Anion and GI anion to Net Acid Load

Models of acid base balance include both exogenous and endogenous acid loads balanced by alkali from the diet, however, relative contributions of these 3 sources acid-base balance have not been well studied. We 52 subjects on free choice diets, and found that endogenous acid production varied directly with age (p<0.03). Endogenous production, measured as titrated urine organic anion, is a significant contributor to total acid production and may be responsible for an increase in acid production with age.
Megan Prochaska, MD, MPH
Instructor of Medicine
Section of Nephrology
University of Chicago Medicine

Bio: I am an Instructor of Medicine at the University of Chicago. I completed medical school and residency at the University of Chicago and nephrology fellowship at the Brigham and Women’s Hospital-Massachusetts General Hospital combined program. I completed my Masters in Public Health at the Harvard T.H. Chan School of Public Health. My primary research interest is focused on kidney stones. My early work was epidemiologic in nature and I am now learning skills in patient-centered mechanistic studies.

Abstract: Evidence for Abnormal Linkage Between Urine Oxalate and Citrate Excretion in Human Kidney Stone Formers

Animal models have demonstrated an interactive relationship between the epithelial anion exchanger SLC26A6 and transporter NaDC-1 that regulates citrate and oxalate homeostasis. This relationship is a potential mechanism to protect against kidney stones as higher urine oxalate is accompanied by higher urine citrate and this is the first large study to explore this relationship in humans. We examined 24-hour urine data on 13,155 kidney stone forming patients from separate datasets at the University of Chicago and Litholink, a national laboratory, and 143 non-kidney stone forming participants. We found that higher urinary oxalate excretion was associated with higher urinary citrate excretion and the magnitude of the effect was larger in non-kidney stone forming participants compared with those who form kidney stones.
Kidney stones (KS) are very common (affecting ~1 in 5 men and ~1 in 10 women), excruciating, and associated with tremendous healthcare cost, chronic kidney disease (CKD), and end stage renal disease (ESRD). Most KS are composed of calcium oxalate and very small increases in urine oxalate concentration significantly increase the risk for stone formation. Besides its critical role in the pathogenesis of KS, emerging data suggests that disturbed oxalate homeostasis contributes to CKD and autosomal dominant polycystic kidney disease progression, CKD - and ESRD-associated cardiovascular diseases, and delayed graft function & poor renal allograft survival. This emphasizes the urgent need for plasma and urinary oxalate lowering therapies, and enhancing the bowel's ability to secrete oxalate may effectively do so. We previously identified Oxalobacter formigenes (Of)-derived factors secreted in its culture conditioned medium (CM) which stimulate oxalate transport by human intestinal Caco2-BBE (C2) cells and reduce urinary oxalate excretion in hyperoxaluric mice by enhancing colonic oxalate secretion. Given their remarkable therapeutic potential, we now identified the small peptides P8 & P9 as the major Of-derived factors, with P8+9 closely recapitulating the CM’s effects, by acting through the oxalate transporters SLC26A2 & SLC26A6 and PKA activation. Importantly, P8+9 also stimulate oxalate transport by human ileal and colonic organoids, confirming that these peptides work in human tissues. Interestingly, this is a prime example of host-microbe interaction where the microbe changes its ecosystem to benefit both host and microbe, by secreting factors stimulating intestinal oxalate secretion, and therefore the microbe potentially serves as an oxalate sensor.