

BLADDER

[Experimental Pain and Auditory Sensitivity in Overactive Bladder Syndrome: A Symptoms of the Lower Urinary Tract Dysfunction Research Network \(LURN\) Study](#)

Steven E Harte, Jon Wiseman, Ying Wang, Abigail R Smith, Claire C Yang, Margaret Helmuth, Karl Kreder, Grant H Kruger, Brenda W Gillespie, **Cindy Amundsen**, Ziya Kirkali, H Henry Lai
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Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN) study participants with OAB symptoms and controls were recruited from six US tertiary referral centers. Quantitative sensory testing (QST) was performed to determine pressure pain sensitivity at the thumbnail bed and auditory sensitivity. Fixed and mixed effect multivariable linear regressions and Weibull models were used to compare QST responses between groups. Pearson correlations were used to assess the relationship between QST measures. Associations between QST and self-reported symptoms were explored with linear regression. 297 participants were analyzed (191 OAB, 106 controls; 76% white, 51% male). OAB cases were older than controls (57.4 vs. 52.2 years, $p=0.015$). No significant differences in experimental thumbnail (nonbladder) pain or auditory sensitivity were detected between OAB cases and controls. Correlations between pressure and auditory derived metrics were weak to moderate overall for both groups, with some significantly stronger correlations for cases. Exploratory analyses indicated increased pressure pain and auditory sensitivity were modestly associated with greater self-reported bladder pain and pain interference with physical function. As a group, no significant differences between OAB cases and controls were observed in experimental nonbladder pain or auditory sensitivity during QST. Associations between QST outcomes and clinical pain raise the possibility of centrally-mediated sensory amplification in some individuals with OAB.

[Interpersonal violence and painful bladder symptoms in community-dwelling midlife to older women](#)

Eva Raphael, Stephen K Van Den Eeden, Carolyn J Gibson, Chris Tonner, David H Thom, Leslee Subak, **Alison J Huang**
Am J Obstet Gynecol. 2021 Sep 20;S0002-9378(21)01045-0. doi: 10.1016/j.ajog.2021.09.017. Online ahead of print.
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The study aimed to determine whether lifetime interpersonal violence exposure and current post-traumatic stress disorder (PTSD) symptoms are associated with prevalence or severity of painful bladder symptoms as well as greater lifetime history of antibiotic-treated urinary tract infections in community-dwelling midlife and older women. We examined cross-sectional data from a multiethnic cohort of community-dwelling women aged 40-80 years enrolled in a northern California integrated healthcare system. Women completed structured self-report questionnaires about their past exposure to physical and verbal/emotional intimate partner violence as well as sexual assault. Symptoms of PTSD were assessed using the PTSD Checklist for DSM-IV, Civilian Version. Additional structured self-report measures assessed current bladder pain, other lower urinary tract symptoms, and history of antibiotic-treated urinary tract infections. Multivariable logistic regression models examined self-reported interpersonal violence exposure history and current PTSD symptoms in relation to current bladder pain and antibiotic-treated urinary tract infection history. In this ethnically diverse, community-based cohort, lifetime interpersonal violence exposures and current PTSD symptoms were independently associated with current bladder pain and lifetime history of antibiotic-treated urinary tract infections in midlife to older women. Findings suggest that interpersonal violence and PTSD symptoms may be under-recognized markers of risk for urologic pain and infections in women, highlighting a need for trauma-informed care of these issues.

[Effect of metabolic syndrome on anatomy and function of the lower urinary tract assessed on MRI](#)

Alex P Tannenbaum, **Matthew D Grimes**, Christopher L Brace, Cody J Johnson, Samuel D Koebe, Lucille E Anzia, Lu Mao, **William A Ricke**, **Diego Hernando**, **Alejandro Roldan-Alzate**, **Shane A Wells**
Urology. 2021 Sep 24;S0090-4295(21)00892-X. doi: 10.1016/j.urology.2021.09.006. Online ahead of print.
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The study aimed to investigate the relationship between metabolic syndrome (MetS) and lower urinary tract symptoms (LUTS) with functional and anatomic changes of the lower urinary tract with MRI. The bladder and prostate of 95 subjects (56M, 39F) were segmented on T2-weighted pelvic MRI using Materialize Mimics 3D software. Bladder wall volume (BWV), post-void residual (PVR) and prostate volume (PV) were quantified from the 3D renderings. LUTS were quantified using validated questionnaires administered at the time of MRI. Wilcoxin ranksum, win ratio and chi-square tests were used to correlate symptom scores, BWV, PVR and PV in patients 1) without vs with MetS, 2) with mild (IPSS or UDI-6: 0-7) vs moderate-severe (IPSS: 8-35 or UDI-6: ≥ 8) and 3) normal vs enlarged prostates ($>40\text{cm}^3$). Multivariate linear regression was used to determine predictors for BWV, PVR and PV. Men with MetS had increased BWV (66.8 vs 51.1 cm^3 , $p=0.003$), higher PVR (69.1 vs 50.5 cc , $p=0.05$) and increased PV (67.2 vs 40.1 cm^3 , $p=0.01$). Women without and with MetS had similar BWV, PVR and LUTS ($p=0.3-0.78$). There was no difference in prevalence of MetS, BWV, PVR or PV in men or women with mild vs moderate-severe LUTS ($p=0.26-0.97$). Men with enlarged prostates were more likely to have MetS ($p=0.003$). There was no difference in BWV, PVR and LUTS for men with normal vs enlarged prostates ($p=0.44-0.94$). In men, BWV was highly correlated with MetS ($p=0.005$) on regression analysis.

[MP44-09 Understanding Prude Belly Syndrome at Single Cell Resolution](#)

Nathalia Amado, Jeremy Mathews, Gervaise Henry, Alexandria Fusco, Thomas Egeland, Alicia Malewska, Brandi Cantarel, **Douglas Strand**, Linda Baker

J Urol. 2021 Sep;206(Suppl 3):e796. doi: 10.1097/JU.0000000000002065.09. Epub 2021 Aug 4.

PMID: 34346772

Prune Belly Syndrome (PBS) is characterized by bladder dysmyogenesis, yielding a dysfunctional compliant thick wall with excess collagen deposition. To dissect the cellular heterogeneity and gene expression networks altered in PBS, we report the cell type composition and transcriptional activity of PBS human bladder by using single cell RNA sequencing (scRNA-seq). Using scRNA-seq, we identified and characterized the disarrayed cell type populations in PBS bladders, generating their unbiased transcriptomic signatures which highlight commonality with neurodegenerative diseases. This PBS transcriptomic map is a step toward potential markers for diagnosis and therapeutic intervention.

[Envisioning treating genetically-defined urinary tract malformations with viral vector mediated gene therapy – Commentary](#)

Douglas B Clayton

J Pediatr Urol. 2021 Aug 17;S1477-5131(21)00374-0. doi: 10.1016/j.jpuro.2021.07.034. Online ahead of print.

PMID: 34483060

Many pediatric urologists are already familiar with the ground-breaking genetic therapies available for devastating monogenic conditions such as spinal muscular atrophy. These expensive yet effective therapies have made waves in both the scientific literature and lay press. The author wonders how many pediatric urologists have stopped to consider whether such gene therapy could be applied to their own specialty.

PROSTATE

[Magnetic Resonance Imaging Features Associated with Histology of Benign Prostatic Hyperplasia Nodules: Generation of a Predictive Model](#)

Jessica C Dai, Tara Nikonow Morgan, Ramy Goueli, Daniel Parrott, Alexander Kenigsberg, Ryan J Mauck, Claus Roehrborn, **Douglas W Strand**, Daniel N Costa, Jeffrey C Gahan

J Endourol. 2021 Sep 22. doi: 10.1089/end.2021.0397. Online ahead of print.

PMID: 34549591

Histologic phenotypic variation of benign prostatic hyperplasia (BPH) has been hypothesized to underlie response to medical therapy. We evaluate pre-operative magnetic resonance imaging (MRI) of robotic simple prostatectomy (RASP) specimens and determine imaging features associated with histologic phenotype. All patients undergoing RASP from 11/2015 to 11/2019 with a multiparametric MRI ≤ 1 year prior to RASP were included. Patients without identifiable BPH nodules on histologic specimens were excluded. Histology slides were obtained from whole mount adenoma specimens and corresponding MRI were reviewed and graded independently by a blinded expert in BPH histopathology (DWS) and an experienced radiologist specializing in prostate imaging (DNC), respectively. Each nodule was assigned a phenotypic score on a 5-point Likert scale (1=predominantly glandular, 5 = predominantly stromal) by each reviewer. Scores were compared using the sign test and univariate analysis. Signal intensity relative to background transition zone and nodule texture were noted on T2, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced imaging (DCE) sequences. Univariate and multivariate stepwise linear regression analysis were conducted to identify MRI features associated with histology score. All analyses were performed using Statistical Analysis System (SAS, v. 9.4). There is strong correlation between MRI features and the histologic phenotype of BPH nodules. MRI may provide a non-invasive method to determine underlying BPH nodule histology.

STONES

[Quality of Life of Urolithiasis Patients During the COVID-19 Pandemic: A Multi-Institutional Cross-Sectional Study](#)

Victor Kf Wong, Naeem Bhojani, Vincent Bird, Nicole Streeper, Stephen Y Nakada, **Kristina L Penniston**, Ben H Chew

J Endourol. 2021 Sep 25. doi: 10.1089/end.2021.0298. Online ahead of print. PMID: 34569279

In this multi-institutional study, we investigated whether the fear of COVID-19 affects the QOL of urolithiasis patients during the COVID-19 pandemic using the Fear of COVID-19 Scale (FCV-19S) and the Wisconsin Stone Quality of Life (WISQOL) questionnaires. Patient-reported data collection occurred between April-October 2020 during the COVID-19 pandemic where many procedures (radiological or surgical) and visits were either delayed or cancelled. The scores generated from patient-reported responses to questionnaires were correlated and then further sub-analyzed dependent on categorical responses related to procedural delays or care and were analyzed via the Student's T-test. A single factor analysis of variance (ANOVA) was performed to analyze varying QOL scores across the FCV-19S quartiles. Results 400 respondents participated in this study. Overall mean total standardized FCV-19S and WISQOL scores (both transformed to min-max 0-100) were 34.3 and 70.3 respectively. A significant inverse correlation ($r=-0.265$, $p<0.0001$) was demonstrated suggesting greater COVID-19 fear may result in lower stone-related quality-of-life. A significant difference in fear and QOL scores was observed between the sexes, with women having more COVID-19 fear (35.8 vs. 28.6, $p<0.01$) and lower stone-related QOL (64.2 vs. 75.2, $p<0.01$). Quartile ANOVA analysis revealed significant mean difference in WISQOL scores across all FCV-19S score quartiles ($p<0.05$).

[Is It Time to Retire the Low-Oxalate Diet? Yes](#)

Kristina L Penniston

J Endourol. 2021 Sep 14. doi: 10.1089/end.2021.0581. Online ahead of print. PMID: 34520254

The low-oxalate diet (LOD) for kidney stone prevention should be retired for the following reasons. Firstly, effects of the LOD on 24-hour urinary stone risk parameters and on the oxalate degradation capacity of the gut microbiome are inadequately characterized. Additionally, effects on nutrient quality and density and on nutritional status are virtually unknown. Effects of an LOD on general health has also not been explored. Finally, as there are other effective means to reduce both hyperoxaluria and CaOx stone formation, reliance on an LOD should be limited if not retired.

[Is it time to retire the low-oxalate diet? No!](#)

Joseph Crivelli, Kyle Wood, Dean Assimos

J Endourol. 2021 Aug 19. doi:

10.1089/end.2021.0576. Online ahead of print.

PMID: 34409855

The low-oxalate diet (LOD) for kidney stone prevention should not be retired. Dietary oxalate intake contributes significantly to urinary oxalate excretion, and this is a factor that is within calcium oxalate stone forming patients' control. In light of the important role of dietary oxalate and the rising incidence and prevalence of kidney stone disease in the United States³, now is not the time to retire the low-oxalate diet. We describe dietary oxalate's relationship to urinary oxalate and calcium oxalate kidney stone formation, and the critical role of the low-oxalate diet in kidney stone prevention.

[Early-Onset Kidney Stone Disease- Consequences and Opportunities](#)

Gregory E Tasian, Michelle R Denburg, Jonathan S Ellison

JAMA Pediatr. 2021 Sep 7. doi:

10.1001/jamapediatrics.2021.2966. Online ahead of print.

PMID: 34491264

Historically, nephrolithiasis affected older adult men but now is increasingly occurring earlier in life. Early-onset kidney stone disease has also increased among all Black youths, predominantly among Black females. The prevalence of nephrolithiasis in the United States increased from 5% (in 1988 to 1994) to 9% (in 2007 to 2010); among all age groups, the greatest increase in the annual incidence of nephrolithiasis is among adolescents. This earlier age at

onset has increased the number of children presenting to the emergency department, admitted to the hospital, and requiring surgery, effects compounded by a 50% recurrence rate of symptomatic stone events within 5 years of diagnosis. The rapid emergence of nephrolithiasis as a disease of childhood has revealed deficiencies in our understanding of the epidemiology of the disease and exposed critical gaps in the evidence informing treatment decisions. This Viewpoint explores these deficiencies and proposes a framework to address these gaps in order to improve outcomes for this vulnerable population

[Forty Years of Oxalobacter formigenes, a Gutsy Oxalate-Degrading Specialist](#)

Steven L Daniel, Luke Moradi, Henry Paiste, Kyle D Wood, Dean G Assimos, Ross P Holmes, Lama Nazzal, Marguerite Hatch, John Knight

Appl Environ Microbiol. 2021 Aug 26;87(18):e0054421. doi: 10.1128/AEM.00544-21. Epub 2021 Aug 26.

PMID: 34190610

Oxalobacter formigenes, a unique anaerobic bacterium that relies solely on oxalate for growth, is a key oxalate-degrading bacterium in the mammalian intestinal tract. Degradation of oxalate in the gut by *O. formigenes* plays a critical role in preventing renal toxicity in animals that feed on oxalate-rich plants. The role of *O. formigenes* in reducing the risk of calcium oxalate kidney stone disease and oxalate nephropathy in humans is less clear, in part due to difficulties in culturing this organism and the lack of studies which have utilized diets in which the oxalate content is controlled. Herein, we review the literature on the 40th anniversary of the discovery of *O. formigenes*, with a focus on its biology, its role in gut oxalate metabolism and calcium oxalate kidney stone disease, and potential areas of future research. Results from ongoing clinical trials utilizing *O. formigenes* in healthy volunteers and in patients with primary hyperoxaluria type 1 (PH1), a rare but severe form of calcium oxalate kidney stone disease, are also discussed. Information has been consolidated on *O. formigenes* strains and best practices to culture this bacterium, which should serve as a good resource for researchers.

[Variations of stress field and stone fracture produced at different lateral locations in a shockwave lithotripter field](#)

Gaoming Xiang, Xiaojian Ma, Cosima Liang,

Hongyang Yu, Defei Liao, Georgy Sankin,

Shunxiang Cao, Kevin Wang, Pei Zhong

J Acoust Soc Am. 2021 Aug;150(2):1013. doi: 10.1121/10.0005823.

PMID: 34470261

During clinical procedures, the lithotripter shock wave (LSW) that is incident on the stone and resultant stress field is often asymmetric due to the respiratory motion of the patient. The variations of the LSW-stone interaction and associated fracture pattern were investigated by photoelastic imaging, phantom experiments, and three-dimensional fluid-solid interaction modeling at different lateral locations in a lithotripter field. In contrast to a T-shaped fracture pattern often observed in the posterior region of the disk-shaped stone under symmetric loading, the fracture pattern gradually transitioned to a tilted L-shape under asymmetric loading conditions. Moreover, the model simulations revealed the generation of surface acoustic waves (SAWs), i.e., a leaky Rayleigh wave on the anterior boundary and Scholte wave on the posterior boundary of the stone. The propagation of SAWs on the stone boundary is accompanied by a progressive transition of the LSW reflection pattern from regular to von Neumann and to weak von Neumann reflection near the glancing incidence and, concomitantly, the development and growth of a Mach stem, swirling around the stone boundary. The maximum tensile stress and stress integral were produced by SAWs on the stone boundary under asymmetric loading conditions, which drove the initiation and extension of surface cracks into the bulk of the stone that is confirmed by micro-computed tomography analysis.

KIDNEY

[Iron deficiency exacerbates cisplatin- or rhabdomyolysis-induced acute kidney injury through promoting iron-catalyzed oxidative damage](#)

Shifeng Zhao, Xueqiao Wang, Xiaoqing Zheng, Xiu Liang, Zhigang Wang, Juanlian Zhang, Xudong Zhao, Shougang Zhuang, Qihui Pan, Fenyong Sun, Wenjun Shang, **Jonathan Barasch**, Andong Qiu
Free Radic Biol Med. 2021 Sep;173:81-96. doi: 10.1016/j.freeradbiomed.2021.07.025. Epub 2021 Jul 21.
PMID: 34298093

Iron deficiency is the most common micronutrient deficiency worldwide. While iron deficiency is known to suppress embryonic organogenesis, its effect on the adult organ in the context of clinically relevant damage has not been considered. Here we report that iron deficiency is a risk factor for nephrotoxic intrinsic acute kidney injury of the nephron (iAKI). Iron deficiency exacerbated cisplatin-induced iAKI by markedly increasing non-heme catalytic iron and Nox4 protein which together catalyze production of hydroxyl radicals followed by protein and DNA oxidation, apoptosis and ferroptosis. Crosstalk between non-heme catalytic iron/Nox4 and downstream oxidative damage generated a mutual amplification cycle that facilitated rapid progression of cisplatin-induced iAKI. Iron deficiency also exacerbated a second model of iAKI, rhabdomyolysis, via increasing catalytic

heme-iron. Heme-iron induced lipid peroxidation and DNA oxidation by interacting with Nox4-independent mechanisms, promoting p53/p21 activity and cellular senescence. Our data suggests that correcting iron deficiency and/or targeting specific catalytic iron species are strategies to mitigate iAKI in a wide range of patients with diverse forms of kidney injury.

ERECTILE DYSFUNCTION

[Erectile dysfunction resulting from pelvic surgery is associated with changes in cavernosal gene expression indicative of cavernous nerve injury](#)

Guillermo Villegas, Moses Tarndie Tar, Kelvin Paul Davies
Andrologia. 2021 Sep 12;e14247. doi: 10.1111/and.14247. Online ahead of print. PMID: 34514620

Pelvic surgery, even without direct cavernous nerve injury, carries a high risk of post-operative erectile dysfunction. The present studies were aimed at identifying molecular mechanisms by which pelvic surgery results in erectile dysfunction. As a model of pelvic surgery, male Sprague-Dawley rats underwent pelvic laparotomy, avoiding direct cavernous nerve injury. A second group of animals, serving as a model of direct cavernous nerve injury, underwent bilateral transection of the cavernous nerve. Cavernosometry demonstrated,

that even in the absence of direct nerve injury, the pelvic surgery model exhibited significant erectile dysfunction 3 days post-operatively. Gene expression profiling also demonstrated that even in this animal model of nerve-sparing pelvic surgery, the profile of differentially expressed genes in cavernosal tissue was indicative of cavernous nerve injury. In addition, although 6 hr after surgery there were significant changes in circulating cytokine/chemokine levels, an inflammatory response in the major pelvic ganglion, cavernous nerve and cavernosal tissue was only observed 3 days post-surgery. Our results validate a rat model of pelvic surgery exhibiting erectile dysfunction and suggest systemic release of cytokines/chemokines following surgical trauma might mediate a pathological inflammatory response in tissues distal to the site of surgical trauma, indirectly resulting in cavernous nerve injury and erectile dysfunction.

- Jennifer Allmaras, MPH, 9/28/2021

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