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BLADDER

Considerations for integrated cognitive behavioural treatment for older adults with coexisting nocturia and insomnia

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Nocturia and chronic insomnia disorder are common conditions that frequently coexist in older adults. Existing medication treatments for each condition have risks, particularly in older adults. While treatment guidelines recommend starting with behavioural therapy for each condition, no existing program simultaneously addresses nocturia and insomnia. Existing behavioural interventions for nocturia or insomnia contain concordant and discordant components. An expert panel (including geriatricians with sleep or nocturia research expertise, sleep psychologists and a behavioural psychologist) was convened to combine and reconcile elements of behavioural treatment for each condition. Concordant treatment recommendations involve using situational self-management strategies such as urge suppression or techniques to influence homeostatic drive for sleep. Fluid modification such as avoiding alcohol and evening caffeine and regular self-monitoring through a daily diary is also appropriate for both conditions. The expert panel resolved discordant recommendations by eliminating overnight completion of voiding diaries (which can interfere with sleep) and discouraging routine overnight voiding (a stimulus control strategy). The final product is an integrated cognitive behavioural treatment that is delivered by advanced practice providers weekly over 5 weeks. This integrated program addresses the common scenario of coexisting nocturia and chronic insomnia disorder.

Distinguishing Features of the Urinary Bacterial Microbiome in Patients with Neurogenic Lower Urinary Tract Dysfunction

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We aimed to characterize the urinary microbiome of catheterizing patients with neurogenic lower urinary tract dysfunction (NLUTD) and to evaluate differences based on type of bladder management or frequency of urinary tract infections. This is a prospective, cross-sectional study of urine samples from asymptomatic, catheterizing patients with neurogenic lower urinary tract dysfunction who used either clean intermittent catheterization or indwelling catheters. Patients without symptoms of urinary tract infection provided a catheterized urine sample for urinalysis, culture and bacterial community microbiome analysis. Enterobacteriaceae and Escherichia were the most abundant genera in the urinary microbiome of patients with neurogenic lower urinary tract dysfunction. Urinary microbiome diversity varied based on bladder management type. Future clinical correlations between microbiome of neurogenic patients and clinical presentation may help guide treatment strategies.

Impact of Sleep Disturbance, Physical Function, Depression, and Anxiety on Male Lower Urinary Tract Symptoms: Results from the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN)

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The impact of non-urologic factors on male lower urinary tract symptoms (LUTS) remains unclear. We investigated cross-sectional and longitudinal associations among anxiety, depression, physical function, sleep quality and urinary symptom sub-domains. Data from 518 men in the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN) study were analyzed to identify associations between PROMIS depression, anxiety, sleep disturbance, and physical function measures and LUTS sub-domains, as derived from the AUA-Symptom Index and LUTS Tool. Multivariable linear regression was used to assess the relationships between PROMIS measures and LUTS sub-domains at baseline and at 3- and 12-month follow-up. Urinary symptom sub-domains are independently associated with modifiable clinical variables including sleep quality and depression at all time points, but these variables do not predict the degree of improvement in LUTS following urologic evaluation and treatment over the medium-term. Bidirectional assessment and randomized experiments may improve our understanding of these relationships.

Male Lower Urinary Tract Dysfunction: An Underrepresented Endpoint in Toxicology Research

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Lower urinary tract dysfunction (LUTD) is nearly ubiquitous in men of advancing age and exerts substantial physical, mental, social, and financial costs to society. While a large body of research is focused on the molecular, genetic, and epigenetic underpinnings of the disease, little research has been dedicated to the influence of environmental chemicals on disease initiation, progression, or severity. Despite a few recent studies indicating a potential developmental origin of male LUTD linked to chemical exposures in the womb, it remains a grossly understudied endpoint in toxicology research. Therefore, we direct this review to toxicologists who are considering male LUTD as a new aspect of chemical toxicity studies. We focus on the LUTD disease process in men, as well as in the male mouse as a leading research model. To introduce the disease process, we describe the physiology of the male lower urinary tract and the cellular composition of lower urinary tract tissues. We discuss known and suspected mechanisms of male LUTD and examples of environmental chemicals acting through these mechanisms to

contribute to LUTD. We also describe mouse models of LUTD and endpoints to diagnose, characterize, and quantify LUTD in men and mice.

Pre-natal vs Post-natal Presentation of PUV: A Multi-institutional Experience

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The objective of this study was to compare the outcomes of prenatally versus postnatally diagnosed posterior urethral valves (PUV) at two large pediatric centres in North America to ascertain if the prenatal diagnosis of PUV is associated with better outcomes. All patients with PUV were identified at 2 large pediatric institutions in North America between 2000-2020 (The Hospital for Sick Children [SK] and Children's Hospital of Philadelphia [CHOP]). Baseline characteristics and outcome measures were compared between those diagnosed prenatally vs. postnatally. Main outcomes of interest included progression of chronic kidney disease (CKD), the need for renal replacement therapy (RRT) and bladder function compromise as determined by need for clean intermittent catheterization (CIC). Time-to-event analyses were completed when possible. This study represents the largest multi-institutional series of patients with PUV and failed to identify any difference in the outcomes of prenatal versus postnatal detection of PUV. A multidisciplinary approach with standardization of the treatment pathways will help in understanding the true impact of prenatal/ early detection on outcomes of PUV.

A tRNA modifying enzyme as a tunable regulatory nexus for bacterial stress responses and virulence

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Post-transcriptional modifications can impact the stability and functionality of many different classes of RNA molecules and are an especially important aspect of tRNA regulation. It is hypothesized that cells can orchestrate rapid responses to changing environmental conditions by adjusting the specific types and levels of tRNA modifications. We uncovered strong evidence in support of this tRNA global regulation hypothesis by examining effects of the well-conserved tRNA modifying enzyme MiaA in extraintestinal pathogenic Escherichia coli (ExPEC), a major cause of urinary tract and bloodstream infections. MiaA mediates the prenylation of adenosine-37 within tRNAs that decode UNN codons, and we found it to be crucial to the fitness and virulence of ExPEC. MiaA levels shifted in response to stress via a post-transcriptional mechanism, resulting in marked changes in the amounts of fully modified MiaA substrates. Both ablation and forced overproduction of MiaA stimulated translational frameshifting and profoundly altered the ExPEC proteome, with variable effects attributable to UNN content, changes in the catalytic activity of MiaA, or availability of metabolic precursors. Cumulatively, these data indicate that balanced input from MiaA is critical for optimizing cellular responses, with MiaA acting much like a rheostat that can be used to realign global protein expression patterns.

Urinary tract infections in cystic fibrosis patients

Seth A Reasoner, Kyle T Enriquez, **Benjamin Abelson**, Steven Scaglione, Bennett Schneier, Michael G O'Connor, Gerald Van Horn, **Maria Hadjifrangiskou**

Improved understanding of non-respiratory infections in cystic fibrosis (CF) patients will be vital to sustaining the increased life span of these patients. To date, there has not been a published report of urinary tract infections (UTIs) in CF patients. We performed a retrospective chart review at a major academic medical center during 2010-2020 to determine the features of UTIs in 826 CF patients. We identified 108 UTI episodes during this period. Diabetes, distal intestinal obstruction syndrome (DIOS), and nephrolithiasis were correlated with increased risk of UTIs. UTIs in CF patients were less likely to be caused by Gram-negative rods compared to non-CF patients and more likely to be caused by Enterococcus faecalis. The unique features of UTIs in CF patients highlight the importance of investigating non-respiratory infections to ensure appropriate treatment.

KIDNEY

GWAS in Mice Maps Susceptibility to HIV-Associated Nephropathy to the Ssbp2 Locus

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To gain insight into the pathogenesis of collapsing glomerulopathy, a rare form of FSGS that often arises in the setting of viral infections, we performed a genome-wide association study (GWAS) among inbred mouse strains using a murine model of HIV-1 associated nephropathy (HIVAN). We first generated F1 hybrids between HIV-1 transgenic mice on the FVB/NJ background and 20 inbred laboratory strains. Analysis of histology, BUN, and urinary NGAL demonstrated marked phenotypic variation among the transgenic F1 hybrids, providing strong evidence for host genetic factors in the predisposition to nephropathy. A GWAS in 365 transgenic F1 hybrids generated from these 20 inbred strains was performed. hese findings demonstrate the utility of GWAS in mice to uncover host genetic factors for rare kidney traits and suggest Ssbp2 as susceptibility gene for HIVAN, potentially acting via the LDB1-LMX1B transcriptional network.

Snapshots of nascent RNA reveal cell- and stimulus- specific responses to acute kidney injury

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The current strategy to detect acute injury of kidney tubular cells relies on changes in serum levels of creatinine. Yet serum creatinine (sCr) is a marker of both functional and pathological processes

and does not specifically assay tubular injury. In addition, sCr may require days to reach diagnostic thresholds, yet tubular cells respond with programs of damage and repair within minutes or hours. To detect acute responses to clinically relevant stimuli, we created Rosa26-floxed-stop uracil phosphoribosyl-transferase (Uprt) expressing mice and inoculated 4-thiouracil (TU) to tag nascent RNA at selected time points. Cre-driven TU-tagged RNA was isolated from whole kidneys and demonstrated that volume depletion and ischemia induced different genetic programs. Even lineage related cell types expressed different genes in response to the two stressors. TU-tagging also demonstrated the transient nature of the responses. Because we placed Uprt in the ubiquitously active Rosa-26 locus, RNAs from many cell types can be tagged in vivo and their roles interrogated under various conditions. In short, TU labeling identifies stimulus-specific, cell-specific, and time-dependent acute responses that are otherwise difficult to detect with other technologies and are entirely obscured when sCr is the sole metric of kidney damage.

PATIENT-CENTERED RESEARCH

Assessing the impact of decision aid use on post prostatectomy patient reported outcomes

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The purpose of this study was to evaluate whether completing a decision aid, Personal Patient Profile - Prostate (P3P), prior to prostatectomy, affects self-reported bother from post-prostatectomy urinary incontinence and erectile dysfunction. This retrospective analysis included data from men with newly diagnosed clinically localized, very low to intermediate risk prostate cancer who elected for prostatectomy within the Michigan Urological Surgery Improvement Collaborative (MUSIC) between 2018-21. Multivariable logistic regression models were used to estimate the association between P3P use and bother from post prostatectomy erectile dysfunction and urinary incontinence as measured by the Expanded Prostate Cancer Index Composite (EPIC-26). Within the stated limitations of this study, we find that use of a decision aid for localized prostate cancer was associated with decreased odds of men being bothered from sexual dysfunction but not urinary incontinence at 6 months post prostatectomy.

-Muen Wang, Jennifer Allmaras, MPH, 3/6/2022

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