

INUS Neuro-Urology News

The Periodical of the International Neuro-Urology Society

Volume 2 • Issue 1 • March 2023 • neuro-uro.org • @Neuro_Urology

From the Editor



Glenn Werneburg, MD, PhD (US)
Editor, Neuro-Urology News

 @gwerneburg

We are pleased to share the latest issue of Neuro-Urology News with you. We thank the readership for its interest and support during the 2022 year. INUS has started off 2023 with a publication (1) calling for a global, resource-independent, consensus guideline for neurogenic lower urinary tract dysfunction (NLUTD). In the paper, the authors emphasize that in this guidance, targeted research addressing the evidence gaps should be called for and pursued. This will allow for the focus to shift to filling the gaps in the evidence.

Authorship included INUS members and experts on NLUTD guidance panels from urologic bodies around the world, including INUS President **Prof. Dr. Thomas Kessler (CH)**, and INUS

Vice-President, **Dr. Blayne Welk (CA)**. As a leading global society with expertise and interest in the diagnosis and management of NLUTD, with representation from areas with varying resources, our society is optimally-suited to lead the charge in the development of this guidance. We look forward to further discussion of these efforts at the upcoming INUS Annual Congress.

Werneburg, G.T., Welk, B., Averbek, M.A., Blok, B.F., Hamid, R., Kennelly, M.J., Liao, L., Musco, S., Vasudeva, P. and Kessler, T.M., 2023. Neuro-Urology: Call for Universal, Resource-Independent Guidance. *Biomedicine*, 11(2), 397.

INUS Calendar

INUS Annual Congress 2023

Athens, Greece
June 8-10, 2023

INUS at ICS 2023

Toronto, Canada
September 27-29, 2023



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Meet the Board Member

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London Health Sciences Center, London, Ontario, Canada
INUS Vice President and Next Generation Officer

As the only neuro-urologist in my urology department, I have focused my clinical research on pilot clinical studies, and collaborative research through the Neuro-genic Bladder Research Group. Being able to work with a large group of like-minded researchers in North America has been a great opportunity and allowed me to share in the wealth of experience and expertise of the other members. As an aside, one of the best things about being a part of INUS is being able to meet with neuro-urologists from around the world! As part of my Masters Degree in Epidemiology, I was introduced to the use of routinely collected data for clinical studies, and have since pursued many studies using this data to conduct primarily pharmacoepidemiology studies in overactive bladder and BPH. I like the immediacy of this research,

where a clinical question can be conceived and studied with minimal cost, and results can be generated in less than a year.

Similar to many urologists in Canada, my practice covers most of functional urology. This includes urethral stricture surgery, neuro-urology, post-prostatectomy incontinence, female incontinence and reconstruction. This combination is necessary as Canada is quite large and healthcare is provided within individual provinces (i.e. patients rarely travel between provinces for elective healthcare, and the distance within provinces often means patients do not wish to travel long distances for appointments). This means that the individual number of patients is often not great enough to sustain a practise focused on only one segment of functional urology.

My wife is a pediatric oncologist, so our life is pretty busy! We have two girls, age 8 and 10, who like to travel (especially if they get to miss some school!) and ski, swim and play soccer. I grew up skiing in the Rocky Mountains of British Columbia, and one of my best INUS memories was the great ski trip Professor Kessler organised in the Swiss Alps after an INUS meeting several years ago.



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Interview with the Expert

Microbiome in neurogenic lower urinary tract dysfunction

Giulia Lane, MD, MS (US)

Assistant Professor, Urology, University of Michigan

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Glenn Werneburg, MD, PhD

Editor, Neuro-Urology News



Dr. Giulia Lane, MD, MS, is a Urologist and Health Services Researcher at the University of Michigan, in Ann Arbor, Michigan, USA. She is trained in Female Pelvic Medicine and Reconstructive Surgery (FPMRS). She completed her undergraduate studies at the University of Texas at Dallas, and Medical School at Texas A&M University. She did her residency at the University of Minnesota, and FPMRS Fellowship at the University of Michigan. She completed her master's degree in Health and Healthcare Research at the University of Michigan.

Dr. Lane's clinical interests include the evaluation and treatment of urinary incontinence, neurogenic lower urinary tract dysfunction, female pelvic floor dysfunction, and urinary tract reconstruction. She is an National Institutes of Health NIDDK K-12 Scholar, and her research is focused on increasing understanding and improving the decision-making between patients and clinicians. She and co-authors from the University of Michigan have recently published a study on the urinary microbiome in individuals with neurogenic lower urinary tract dysfunction. In this month's "Interview with the Expert" we discuss this recent work. The below is our interview, edited for length and clarity.

Dr. Glenn Werneburg: What was known about the urinary microbiome in neurogenic lower urinary tract dysfunction (NLUTD), and what was the impetus for your study?

Dr. Giulia Lane: Most of what we knew about the NLUTD urinary microbiome came to us from the pediatric literature. There was very little known in the adult population. The present study was part of an Explorer Grant, an internal grant from University of Michigan's Microbiome Core to provide new data in an uncharted area of the microbiome. The impetus was to determine whether the adult population with NLUTD had similar urinary microbiota to that described in children, and build on that to look at how different bladder management types may have been associated with differences in the microbiome.

GW: How did you design this study, and what did you hypothesize?

GL: This is a cross-sectional study. We recruited individuals with NLUTD using indwelling or intermittent catheterization who presented to our clinic for either routine care or as part of our onabotulinumtoxinA clinics. We obtained their urine by clean catheterization. Individuals with symptomatic evidence of urinary tract infection (UTI) were excluded. We hypothesized that there would be differences in the catheter modalities: intermittent versus indwelling catheters, for example. We also hypothesized that there would be differences between individuals with frequent symptomatic UTIs versus no UTIs, and in people undergoing interventions such as onabotulinumtoxinA.

GW: What were your findings, and what were the main implications?

GL: A total of 95 patients were included in the study. We had a high number of sequence reads per sample, considering the low-biomass nature of the urinary tract. This is distinct from prior literature of non-NLUTD individuals, who generally have a lower biomass. The most abundant bacterial taxa were the Proteobacteria, Enterobacteriaceae, and Escherichia. The microbial abundance was independent of whether a patient had a history of recurrent urinary tract infection. The main takeaway from this portion of the study, is that bacteria traditionally classified as uropathogens, may not necessarily be contributing to pathology or symptoms. Just because these bacteria are present, does not mean they warrant treatment. This is in line with the guidance that emphasizes that asymptomatic bacteriuria generally does not require antibiotics.

We also found that individuals with catheters had a higher abundance of Pseudomonas. This is a tenacious microbe, creating sediment and associated with biofilms. We also found that men had a greater abundance of Aerococcus than women. Aerococcus is an underreported pathogen, but has been associated with urosepsis. It generally does not get speciated, and sensitivities are infrequently reported. Whether individuals with Aerococcus are at increased risk for UTI and urosepsis is a viable area for future investigation.

People with indwelling catheters had greater diversity than those without catheters. Individuals who had a history of onabotulinumtoxinA bladder injection had less diverse microbiota. This could relate to the onabotulinumtoxinA, or could relate to their receipt of antibiotic prophylaxis.

GW: Do you think the gut microbiome may also differ between those with NLUTD and healthy controls?

GL: While we haven't looked at that, I would suspect differences. The difference may not be due to NLUTD itself, but rather may be consequences of the differences in interventions of these patients. Those with NLUTD may have decubitus ulcers for which they may receive antibiotics, or they may receive frequent antibiotic prophylaxis for urologic interventions, and this history may influence the gut microbiome. The differences may be due to the differences in antibiotic exposure or other history, rather than the neurologic etiology itself.

GW: What were the limitations of the study?

GL: Microbiome research is challenging, and there are many potential confounders and artifacts. The urine is often a low biomass environment, potentially amplifying these artifacts. We are fortunate that we have a microbiome core, and a microbiologist collaborator, to help us identify and include series of controls to limit the influence of the low biomass. The other major limitation is that our study is cross-sectional. In the future, I want to determine whether these differences are preserved over time or are transient. I'm also interested in how the microbiome may change pre- and post-injury, or with change in bladder management strategy. The data from this study were deposited in a publicly-accessible repository. Other groups can evaluate

our results and metadata, and compare these with other datasets to perform secondary analyses.

GW: Do you think the urinary microbiome might change based on etiology of NLUTD – multiple sclerosis versus spinal cord injury, for example?

GL: We did perform an exploratory analysis to try to answer this, but we did not find an effect. I don't think the neurologic etiology is a major driver. I think other factors, such as frequency of contact with the healthcare system, bladder management strategy, antibiotic exposures, and others, are more likely to be drivers.

GW: Do you think that, with our increasing understanding of the microbiome composition and its relationship with NLUTD and other pathology, we may soon be able to modulate the microbiome to reduce infection risk?

GL: We looked at individuals who were on antibiotic prophylaxis and non-antibiotic prophylaxis, but we did not find that either of these were associated with differences in diversity. In one way, our study suggests that we may be able to modulate the microbiome through choice of bladder drainage strategy: indwelling versus intermittent catheterization. We don't yet know how microbial diversity in these populations relates to clinical outcomes. While we didn't see clinical differences in UTI, we know that people who undergo intermittent catheterization have preserved kidney function over time, and we are interested in whether the microbiome may contribute to this.

GW: What advice do you have for junior INUS members who are interested in embarking on careers as physician-scientists?

GL: There is a lot of dogma that we

should carefully evaluate. I suggest seeking to assess why we hold particular beliefs. Is there evidence to support our clinical practice, or is there room for discovery in an area? Junior INUS members can consider keeping track of their ideas. I keep a journal where I write my research ideas. Maintain curiosity, but sort through ideas and triage them to maximize your research efficiency. For example, maintain a theme – either a methodology or a particular disease state to avoid spreading yourself too thin without a clear story or theme linking research.

Further Reading

Lane, G., Gracely, A., Bassis, C., Greiman, S. E., Romo, P. B., Clemens, J. Q., ... & Cameron, A. P. (2022). Distinguishing features of the urinary bacterial microbiome in patients with neurogenic lower urinary tract dysfunction. *The Journal of Urology*, 207(3), 627-634.

Groah, S. L., Pérez-Losada, M., Caldovic, L., Ljungberg, I. H., Sprague, B. M., Castro-Nallar, E., ... & Pohl, H. G. (2016). Redefining healthy urine: a cross-sectional exploratory metagenomic study of people with and without bladder dysfunction. *The Journal of Urology*, 196(2), 579-587.

Fouts, D. E., Pieper, R., Szpakowski, S., Pohl, H., Knoblach, S., Suh, M. J., ... & Groah, S. L. (2012). Integrated next-generation sequencing of 16S rDNA and metaproteomics differentiate the healthy urine microbiome from asymptomatic bacteriuria in neuropathic bladder associated with spinal cord injury. *Journal of Translational Medicine*, 10(1), 1-17.

Forster, C. S., Panchapakesan, K., Stroud, C., Banerjee, P., Gordish-Dressman, H., & Hsieh, M. H. (2020). A cross-sectional analysis of the urine microbiome of children with neuropathic bladders. *Journal of Pediatric Urology*, 16(5), 593-e1.



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SUFU Recap

The Society for Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) 2023 meeting took place in Nashville, Tennessee, USA from March 7-11, 2023. The meeting was organized by the clinical program committee members **Drs. Quentin Clemens, Ariana Smith, Donna Deng, and Ekene Enemchukwu**, and basic science program committee members **Drs. John Speich and Michel Pontari**. The meeting was a great success, and included an excellent series of keynote lectures, panels, workshops, videos, and breakout sessions.

The Basic and Translational Science portion of the Scientific Program commenced on Tuesday, March 7. This portion of the meeting included a series of sessions with a focus on neuro-urology. The first session was entitled “Advances in Neural Engineering” and included talks on catheter-free closed loop neuromodulation by **Dr. Margot Damaser**, neuromodulation via interfacing with the peripheral nervous system by **Dr. Tim Bruns**, and computational modeling to understand and design neuromodulation by **Dr. Zachary Danziger**. **Dr. Janet Keast** then gave a compelling keynote lecture on multi-scale mapping of the pelvic visceral nervous system. The following day included an excellent panel on advances in imaging moderated by **Dr. Rose Khavari**. Panelists included **Dr. Becky Clarkson**, who discussed imaging the role of the brain in continence, **Dr. Alejandro Roldan-Alzate** who discussed non-invasive assessment of the lower urinary

tract using MRI-urodynamics, and **Dr. Wouter Everaerts** who discussed videocystometry to study bladder function in rodent models. Basic science abstracts were presented in the form of podium and poster presentations. The grand prize winner was **Dr. Margot Damaser** for her work on measuring bladder pressure and volume using a catheter-free wireless intravesical sensor in felines.

The Clinical portion of the Scientific Program began on Thursday, March 9. A machine learning panel moderated by **Dr. Jason Van Batavia** included discussion by **Dr. Stephen Zderic** on the application of machine learning for prediction of hydronephrosis in individuals with spina bifida. Later, a panel moderated by **Dr. Jaspreet Sandhu** focused on complex abdominal reconstruction. **Dr. Rose Khavari** discussed the types, indications, and techniques for continent catheterizable channel creation, **Dr. O. Lenaine Westney** discussed ureteral stricture workup and management following diversion, and **Dr. John Stoffel** discussed the evaluation and treatment of stoma complications. An interesting series of case discussions were presented by the panel.

A neuromodulation and neuroimaging podium session highlighted the top submitted abstracts in these areas on Friday, March 10. Highlights included work from **Dr. Evgeniy Kreydin's** group including the comparison of bladder-related brain activity between basal ganglia and the pons in individuals with

lower urinary tract dysfunction, presented by **Dr. Luis Morales Ojeda**, and pre-treatment micturition-associated brain activity and its prediction of response to transcutaneous electrical spinal cord neuromodulation in stroke survivors, presented by **Dr. Veronica Stefania Montero Arcila**. The afternoon started off with an engaging panel on the recent developments in sacral neuromodulation featuring discussion on coding changes by **Dr. Elizabeth Brown**, technological advancement by **Dr. Christopher Chemansky**, patient selection by **Dr. Benjamin Brucker**, and technical considerations and programming by **Dr. Bradley Gill**. Friday ended with a breakout session in advanced urodynamics moderated by **Dr. Stephen Kraus** with a panel including **Drs. Christopher Elliott, Ricardo Gonzalez, and Priya Padmanabhan**. The meeting concluded with a video session. One of many highlights was a case of robotic-assisted laparoscopic ileocecal augmentation cystoplasty (Indiana augment) for neurogenic bladder presented by **Dr. Connie Wang**. The meeting wrapped up on Saturday, March 11, with a breakout session on complex cases moderated by **Dr. Anne Cameron**, and an engaging and informative panel on pelvic floor considerations following radical cystectomy in females, moderated by **Dr. Ariana Smith**, with panelists including **Drs. Polina Reyblat, Lee Richter, and Sandip Vasavada**.

