Podium Lecture

AB006. The urinary microbiome in health and disease

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Abstract: Lower urinary tract symptoms (LUTS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) are common problems in men of all ages. The human microbiome is the totality of microbes, their genetic contents, and their interactions within an ecosystem or body habitat. Recent studies using culture-independent approaches have provided evidence for a unique human urinary tract microbiome. Common constituent organisms of the purported urinary microbiota include *Lactobacillus*, *Streptococcus*, *Corynebacterium*, *Gardnerella*, and numerous other common bacterial species. Certain characteristic patterns have been noted in the putative urinary microbiota of patients with urologic disease, including but not limited to benign prostate hyperplasia (BPH), LUTS, and CP/CPPS. Whether a causal relationship exists between the microbiome and urologic disease remains to be elucidated. However, studies have linked alterations in the urinary microbiome to urge incontinence, neurogenic bladder, sexually transmitted infections, urological cancers, and certain painful bladder syndromes such as interstitial cystitis and CPPS. The gut microbiome may also play an important role in urinary symptoms, either indirectly by mediating host pathways or perhaps directly by altering the phylogenetic makeup of the urinary microbiome. The mechanisms of microbiome influence on LUTS is unclear but purported mechanisms include intracellular bacterial colonization of the urothelium, modulation of host inflammatory responses (e.g., prostaglandin E2 and cyclo-oxygenase expression), and epigenetic influences (e.g., methylation of specific genes in urothelial cells). Patients with neurogenic bladder dysfunction and urge urinary incontinence are more likely to host potentially pathogenic bacteria (e.g., *Klebsiella*, *E. Coli*, *Bacteroides*, *Gardnerella*, and *Enterococcus)* and less likely to have *Lactobacillus* and *Corynebacterium* species as constituents of their microbiome. Variations in microbiota have also been linked to differences in outcomes from pharmacotherapy (e.g., women with urge incontinence and less microbial diversity are more likely to respond to therapy with anticholinergics). Bladder sensation at urodynamics and incontinence are positively associated with presence of low level bacteriuria in women. Several small studies have investigated the urinary microbiome as a mediator of LUTS. Women with acutely worsened symptoms from pelvic pain are more likely to have yeast species identified in mid-stream urine. Men with chronic pelvic pain are more likely to harbor *Burkholderia Cenocepacia* in their initial voided urine although no differences were noted in mid-stream nor post-prostate massage urine. There tends be marked heterogeneity of the microbiome within groups, although this heterogeneity appears even more pronounced in patients with pelvic pain syndromes. Genes relevant to sporulation and chemotaxis are more heavily activated in pelvic pain patients whereas glycolysis, phosphotransferase, and pyruvate metabolism are less active when compared to healthy controls. Additional work will be required to carefully elucidate the presence, location, and scope of the putative urinary microbiome. Aside from taxonomic classification, assessment of functional gene assays will be essential; the presence of specific species may be less relevant than the presence of specific genes that up- or down-regulate host pathways that are germane to inflammation, nociception, infection-resistance, and other factors.

Keywords: Chronic prostatitis; sexual dysfunction; prostate-pelvic syndrome; urinary symptoms

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