Review Article

The female urinary microbiota, urinary health and common urinary disorders

Linda Brubaker[1], Alan J. Wolfe[2]

[1]Departments of Obstetrics & Gynecology and Urology, [2]Department of Microbiology and Immunology, Loyola University Chicago Stritch School of Medicine, Maywood, IL 60130, USA

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Correspondence to: Linda Brubaker, MD, MS. Departments of Obstetrics & Gynecology and Urology, Stritch School of Medicine Loyola University Chicago, 2160 South First Avenue, Maywood, IL 60153, USA. Email: LBrubaker@luc.edu.

Abstract: This review provides the clinical context and updated information regarding the female urinary microbiota (FUM), a resident microbial community within the female bladder of many adult women. Microbial communities have variability and distinct characteristics in health, as well as during community disruption (dysbiosis). Information concerning characteristics of the FUM in health and disease is emerging. Sufficient data confirms that the microbes that compose the FUM are not contaminants and are cultivatable under appropriate conditions. Common clinical conditions, including urinary tract infection (UTI) and urgency urinary incontinence (UUI), a common form of urinary incontinence (UI), may be usefully reconsidered to determine the role of the FUM. Knowledge of FUM characteristics may help advance prevention, diagnosis and treatment of these conditions and other common lower urinary disorders in women. The FUM appears related to UTI and UUI in adult women. The specific role of the FUM remains to be clarified and requires significant additional work in describing FUM variability and resilience in health. Unique aspects of the FUM prompt re-evaluation of existing nomenclature to more appropriately define health and disease; the concept of dysbiosis may be useful for understanding the interaction of the FUM with other aspects of lower urinary tract physiology, including urothelial signaling. Clinicians, through their clinical laboratories, can adopt enhanced urine culture techniques that more fully describe the living microbes within the FUM. This additional information may provide clinicians and their patients an opportunity to impact clinical care without antibiotic use, if the FUM can be appropriately modified to improve treatment precision for UTI and UUI.

Keywords: Urinary microbiota; urinary microbiome; urinary tract infection (UTI); asymptomatic bacteriuria (ASB); urinary incontinence (UI)

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The discovery of the human microbiome has been a major new frontier for investigators interested in human health and disease. The terms "microbiota" (the microbes themselves) and "microbiome" (the genetic material of those microbes) are becoming part of the clinical lexicon in various aspects of human health and disease. These discoveries are also impacting our understanding of common lower urinary tract disorders, including urinary tract infection (UTI) and urgency urinary incontinence (UUI). This manuscript will highlight the impact of the female urinary microbiota (FUM) as it relates to human health, UTI and UUI.

The FUM in the context of the human microbiota

Researchers working on other human microbial niches

have made tremendous advances. Microbial communities have been described in many parts of the human body. The Human Microbiome Project (HMP) profiled 242 healthy (predominantly young) individuals; samples were collected from 18 body habitats from five major body areas (1). This important work provided an early framework for investigators to characterize human microbial communities in health and disease. Recently, Lloyd-Price et al. described a current understanding of the characteristics of a healthy microbiome (2). Although there are multiple challenges to a dichotomous definition of a "healthy" microbiome, several key observations can be made. First, community characteristics typically rely on attributes of more than a single microbe and commonly feature a "core" set of microbes. Second, while diversity in microbial community characteristics is typical, even within health, the core functions of the 'healthy' microbial community are often quite similar, despite variability in the metagenome of the human microbiome. Thus, even in the absence of disease, microbiomes in many areas of the human body have a large degree of interpersonal diversity (1).

Beyond the simple concept of the presence of a microbe, there are characteristics of a community that are likely associated with a healthy microbiome. For example, descriptors based on the most prevalent microbe (i.e., enterotype or urotype) may help describe a community and distinguish it from another community. Each community also can be described using ecological parameters, including diversity, stability and/or resilience (2).

Compared to some other human microbial niches, our knowledge of the FUM is in its infancy; culture-independent data describing the FUM were first published about five years ago (3-5). While much work remains to be done, these seminal studies have helped change the common clinical paradigm that the bladder is a sterile environment and that urinary symptoms/disorders are caused by "invasion" of a single pathogen. Investigators now have the opportunity to consider a wide range of etiologic and therapeutic possibilities that incorporate emerging knowledge about the urinary microbiot and microbiome. An important first step is to understand the characteristics of normal urinary microbiota. As with many human microbial niches, there is a growing awareness of the necessity to carefully describe health populations in order to determine the microbial configurations that relate to clinical conditions of interest.

Despite a lack of a complete understanding of microbial configurations in healthy adults, there is a clear shift to the concept that microbial dysbioses can be associated with a variety of clinical conditions of interest, including inflammatory bowel disease, multiple sclerosis, diabetes, allergies, asthma, autism, and cancer (6-10). Microbial dysbiosis is a useful concept for consideration of human urinary disorders, including UTI and certain forms of urinary incontinence (UI). Recognition that some clinical urinary conditions may result from dysbiosis of the microbial community—instead of or in addition to the invasion of a pathogen—opens investigative possibilities for prevention, diagnosis and treatment.

Based on the 'bladder is sterile' dogma, clinicians and researchers have typically held the concept that human urinary conditions are caused by the additional presence of uropathogenic microbes. However, the loss of "good" bacteria from a healthy urinary bacterial community (i.e., a dysbiosis) could make an otherwise healthy individual vulnerable to urinary conditions.

Research concerning the human gut microbiota has advanced our scientific understanding of the human gut microbiota and allowed that work to meaningfully alter clinical care (11). These advances provide a framework for research in the urinary microbiota. However, there are important differences between the microbiota of the gut and the microbiota of the bladder. The gut microbiota are highly abundant with 10^{12} colony forming units (CFU) per gram of feces (12). The FUM are orders of magnitude less abundant, typically between 10^2 and 10^5 CFU per milliliter of urine (13-17). Gut microbiota are extremely diverse; they typically include hundreds to thousands of different bacterial species (12,18). The typical FUM is considerably less diverse, ranging from one to dozens of species (3,13-17,19,20). The most common microbes that comprise the gut microbiota tend to be distinct from those that comprise the FUM, which are most often members of the genera *Lactobacillus* and to a lesser degree *Gardnerella*, *Streptococcus*, *Staphylococcus* and *Corynebacteria* (13-15,17,19,20). The diversity of the gut microbiota is associated with gut health and disease and this diversity responds to multiple changes within the individual, including diet and drug or antibiotic ingestions (18). It is not yet known whether this is also true of the FUM. There is little longitudinal information concerning FUM stability, variability, and resilience to bladder therapies, including antibiotic usage, surgery or instrumentation (19,21). We also do not know whether the FUM adjusts to liquid or solid oral intake or to other human behaviors.

The relationship between the FUM and the microbiota

of nearby pelvic niches, especially the vagina, also requires study. It is presently unknown whether the bladder and vagina share a common community of microbes or whether different microbes colonize each of these distinct microbial environments. This information will be critical to our understanding of the FUM and its effects upon the bladder, especially since significant overlap exists between the most common bladder genera and those generally associated with vaginal health (*Lactobacillus*) and disease (*Gardnerella*) (13-15,19,20,22).

There is evidence for FUM alterations in two common conditions of clinical interest-UTI and UUI.

The FUM and UTI

Clinicians use a deeply entrenched nomenclature to describe human disease associated with pathogenic organisms. This is especially true in the urinary tract. For example, UTI is a widely used term, both within medicine and in lay communications. It generally refers to a very common, acute, urinary health problem attributed to the presence or predominance of uropathogenic microbes, typically in the urinary bladder. The alternative term "bacterial cystitis" more precisely describes the most common clinical condition. More broadly speaking, UTI also can serve as an umbrella term to describe clinical infections elsewhere within the urinary tract, including the urethra and upper tracts (i.e., the kidney and ureters). These terms may usefully be reconsidered in the context of a microbial dysbiosis. As opposed to overt clinical infection, the concept of a urinary dysbiosis would more usefully describe the clinical spectrum of altered microbial states without symptoms [such as asymptomatic bacteriuria (ASB)].

The diagnostic criteria for UTI continue to be debated. Excellent recent reviews highlight the history of the clinical evolution of screening techniques and diagnostic tests for uncomplicated UTI (23). These evaluations have centered on the (I) detection of organisms associated with human disease; and (II) the host response.

A simple patient history is the most common screening evaluation for a UTI diagnosis. The typical symptoms of an uncomplicated UTI in women are the abrupt onset of urgency, frequency and dysuria. Clinicians also rely on urinary dipsticks to assess nitrates and/or leukocytes, although these are relatively limited screening assessments. Due to the cost of formal urine cultures, most clinical settings rely on a phased assessment, often called reflex cultures. Only samples with a high likelihood of a positive result are formally subjected to culture and sensitivity testing.

Most clinical laboratories rely on standard urine culture methods that were designed to detect common, fast growing aerobic uropathogens, especially uropathogenic *Escherichia coli* (UPEC). These methods generally do not detect slow growing, anaerobic and fastidious (i.e., those with special nutrient requirements) bacteria. Fortunately, culture-independent methods, most notably *16S rRNA* gene sequencing, have demonstrated that standard urine culture protocols do not detect the majority of bacteria present in urine samples (4,5). While the earlier study used voided urines, our later study collected urine through direct suprapubic aspiration from the bladder. Since this method of collection bypasses the vagina, the bacteria detected by 16S rRNA sequencing in the aspirated urine samples could not be due to vulvo-vaginal contamination. Since samples obtained by transurethral catheter resembled those obtained by suprapubic aspirate and since catheterization is less intrusive than aspiration, we have used catheterized urine for the bulk of our subsequent studies (5).

Although DNA sequencing detected the presence of bacterial DNA in the bladder (3,5), it did not determine whether the bacteria were alive. To make this determination, our team and another developed enhanced urine culture techniques (16,24). These techniques utilize appropriate culture conditions to determine whether the bacteria detected by 16S rRNA sequencing grow in culture. Compared to our clinical microbiology laboratories standard urine culture protocol, simple refinements provide a more complete description of the bladder microbiota. These refinements include increased urine volume, increased duration of incubation, the use of diverse growth media and a range of atmospheric conditions.

Recently, we recommended a streamlined version of our enhanced quantitative urine culture (EQUC) protocol (14). The most important parts of this streamlined EQUC are increased urine volume (100 μL instead of the standard 1 μL), incubation in a 5% CO_2 incubator (instead of the standard ambient atmospheric conditions), incubation for 48 hours (instead of the standard 24 hours), and the inclusion of colistin-nalidixic acid (CNA) agar in addition to the standard blood and MacConkey agars. Exclusion of any of these four refinements leads to substantial loss of bacterial detection, including known and suspected uropathogens (14). This streamlined EQUC protocol is both feasible for clinical microbiology laboratories and informative to clinicians, who would have access to more

information concerning the composition of an individual patient's FUM.

To appropriately treat clinical conditions of interest, clinicians will need to determine the clinical relevance of the more complete microbial information provided by 16S rRNA sequencing and streamlined EQUC. The diagnosis of "asymptomatic bacteriuria" (ASB) is an illustrative example. An ASB diagnosis is variably defined for clinical purposes and used to describe a variety of important clinical situations that may warrant treatment. It is generally used to indicate colonization by a known uropathogen of the urinary tract in an individual without symptoms typical of acute bacterial cystitis, although the specific symptoms are not defined (25,26). Although up to 10% of all women may be diagnosed with ASB, the diagnosis of ASB has special relevance during pregnancy and in certain elderly patients. In pregnancy, for example, there is a greater chance of progression to poor clinical outcomes, including pyelonephritis and preterm labor and delivery (27). The goal of an ASB diagnosis is to prevent future clinical problems. The emerging information concerning the FUM, however, complicates the ASB diagnosis. What does the term ASB mean if the bladders of most women contain bacteria, including previously undetected or under-appreciated uropathogens? Increased knowledge of the roles played by the newly detected microbes may allow more personalized and precisely targeted treatment.

UTIs are very common, especially in women, and UTIs are more common than ASB. International Classification of Disease (ICD) codes are used in calculations of economic cost for individuals and health systems. Such calculations suggest that UTI is a costly health condition in the US, mostly based on the frequency that UTIs occur. In non-institutionalized elderly populations, UTIs are the second most common form of infection, accounting for nearly 25% of all infections (28). The estimated annual cost of community-acquired UTI is significant, at approximately $1.6 billion (28). UTIs affect more women than men. Based on ICD coding, UTI is estimated to account for nearly 7 million office visits and 1 million emergency department visits, resulting in 100,000 hospitalizations populations (29). Even a short-term acute UTI can adversely affect quality of life; however, in the elderly, UTIs are associated with a significant detriment to morale and the quality of life for affected women (30).

The frequent diagnosis of UTI is of interest to researchers who concentrate on metrics for health quality. Although the scientific literature has not reached consensus, there is a growing sense that at least a portion of UTI events may be preventable. The emerging knowledge regarding the human urinary microbiome has potential to advance UTI prevention efforts. In addition, the knowledge that certain microbes, including beneficial ones, exist in the healthy human bladder may move clinicians away from over-zealous antibiotic use in an erroneous effort to sterilize the bladder. It is widely recognized that antibiotic administration may be life saving for certain conditions; yet, overuse of antibiotics is a major health and environmental concern. In the US, nearly all UTIs are treated with prescription, oral antibiotics. Abbo and Hooten have contributed useful guidance for clinicians seeking to improve prescription of UTI-related antibiotics (31). Their suggested guidelines include limiting *antimicrobials* to only appropriate use, selection of the appropriate antimicrobial treatment or an appropriate duration, and emphasis on short-course therapy when clinically appropriate. In light of the improved detection and description of the FUM, these common-sense recommendations are likely to require additional nuance, as the symptoms and clinically important tests for UTI are refined. If beneficial members of the FUM protect women against UTI, and there is some preliminary evidence that they do (19,21), then improper use of antibiotics may be detrimental, at least for some individuals. The existence of the FUM also challenges UTI researchers to reassess their results in animal models that were designed with the assumption that the animal's bladder was sterile. Other evidence suggests that previously undetected uropathogens lurk below the usual uropathogens (5,14). Treatment with antibiotics designed to defeat UPEC for example, could, in some patients, select for other typically undetected uropathogens, perhaps setting the stage for chronic conditions.

The FUM and UI

The FUM also may hold clues for some forms of UI, a common condition in adults; the International Continence Society proposed standardized nomenclature for UI (32). The most common forms of UI in women are UUI and stress urinary incontinence (SUI); these conditions commonly coexist. Although many affected women do not seek treatment, both UUI and SUI are treatable. Because of substantial symptom overlap with UTI, UI is a diagnosis of exclusion; thus, the traditional evaluation for UI includes assessment for UTI. Many clinicians use simple screens, such as urinary dipstick assessment for leukocytes and/

or nitrates; other centers use reflex or routine standard urine cultures, as discussed earlier. A clinician may select a diagnosis of UTI based on clinical assessment without testing and/or the results screening or diagnostic testing for UTI.

Early research on the FUM of women affected with UUI has raised several clinically relevant questions concerning the characteristics of the UUI urinary microbiota. UUI is a common disorder, affecting many adult women who experience bothersome urinary urgency, frequency and urgency incontinence. Symptoms of UUI are highly variable within individuals and among affected women. Persistence of UUI symptoms is common, despite treatment. FUM research raises the question of whether UUI is caused or influenced by any specific microbe; this includes the possibility that a microbe (or community of microbes) can be protective or contribute to symptoms. Evidence to date suggests that a variety of "good" bacteria exist within a healthy FUM (13).

From an early study that sought to describe FUM variability in women seeking UUI treatment, we reported an association between symptom severity and FUM diversity, including the number and identity of detected bacteria. We also observed evidence of a protective relationship between UTI and the pre-treatment FUM after urinary tract instrumentation (19,21). In another study, our group compared the baseline FUM of women with and without symptoms of UUI. We found statistical associations between symptoms of UUI and several bacterial species, including several uropathogens that are not detected by standard urine culture procedures. Intriguingly, *Lactobacillus crispatus* was associated with non-symptomatic controls, while *Lactobacillus gasseri* was associated with UUI symptoms. This is an intriguing observation, as both species are common members of the vaginal microbiota and both are considered to be protective in that niche. This result suggests that these two species play different roles in the bladder (13). Finally, we detected differences in the response to an oral UUI medication that associated with baseline FUM diversity and baseline identity of certain FUM members. Specifically, women who responded to oral UUI medication had less FUM diversity than did women who did not respond or responded only to increased medication doses (15). Fast accumulating evidence suggests that FUM heterogeneity may provide insight into etiology, prevention and treatment of UUI. Another key concept is the personal variability of the FUM in health and disease. This variability provides an opportunity for more personalized, precise interventions. Using models from other human microbial niches, modulation of community characteristics is biologically plausible and a reasonable investigative approach.

Although the information to date is limited, SUI does not appear to have a similar association with the FUM (20). This resonates with clinicians who observe that SUI symptoms are more predictable for affected patients and that SUI symptoms respond more predictably to first-line treatments, such as surgery. In this study of women seeking treatment for SUI, we found a statistical association between FUM diversity and UUI symptoms (20), as we had observed previously (13,19). We also observed an association between hormone status and FUM diversity. This is an intriguing observation, as associations between hormone status and the vaginal microbiota have been reported (33-36).

Concluding remarks

The recent confirmation that the FUM exists—that there is a resident community of bacteria in the adult bladder—challenges the scientific community to understand these microbiota in health and disease. This will require researchers to address basic questions about normal FUM characteristics: how does the FUM get established and maintained? What are the community characteristics of a healthy FUM? How stable is the FUM? Does it respond to diet and other behaviors? Is it resilient in the face of perturbations, such as antibiotics, instrumentation, surgery or other therapies? What roles do members of the FUM play? Which microbes are beneficial? Which ones are detrimental? Do unrecognized uropathogens lurk within the FUM? How do members of the FUM interact with the urothelium? Most importantly from a clinical perspective, it is important that we learn whether the urinary microbiota can be clinically modified to prevent lower urinary tract disorders, especially common conditions, such as UTI and UUI.

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Footnote

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References

1. Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. Nature 2012;486:207-14.
2. Lloyd-Price J, Abu-Ali G, Huttenhower C. The healthy human microbiome. Genome Med 2016;8:51.
3. Fouts DE, Pieper R, Szpakowski S, et al. 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. J Transl Med 2012;10:174.
4. Siddiqui H, Nederbragt AJ, Lagesen K, et al. Assessing diversity of the female urine microbiota by high throughput sequencing of 16S rDNA amplicons. BMC Microbiol 2011;11:244.
5. Wolfe AJ, Toh E, Shibata N, et al. Evidence of uncultivated bacteria in the adult female bladder. J Clin Microbiol 2012;50:1376-83.
6. Bäckhed F, Fraser CM, Ringel Y, et al. Defining a healthy human gut microbiome: current concepts, future directions, and clinical applications. Cell Host Microbe 2012;12:611-22.
7. Hsiao EY, McBride SW, Hsien S, et al. Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. Cell 2013;155:1451-63.
8. Petersen C, Round JL. Defining dysbiosis and its influence on host immunity and disease. Cell Microbiol 2014;16:1024-33.
9. Trompette A, Gollwitzer ES, Yadava K, et al. Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis. Nat Med 2014;20:159-66.
10. Garrett WS. Cancer and the microbiota. Science 2015;348:80-6.
11. Shreiner AB, Kao JY, Young VB. The gut microbiome in health and in disease. Curr Opin Gastroenterol 2015;31:69-75.
12. Guarner F, Malagelada JR. Gut flora in health and disease. Lancet 2003;361:512-9.
13. Pearce MM, Hilt EE, Rosenfeld AB, et al. The female urinary microbiome: a comparison of women with and without urgency urinary incontinence. MBio 2014;5:e01283-14.
14. Price TK, Dune T, Hilt EE, et al. The Clinical Urine Culture: Enhanced Techniques Improve Detection of Clinically Relevant Microorganisms. J Clin Microbiol 2016;54:1216-22.
15. Thomas-White KJ, Hilt EE, Fok C, et al. Incontinence medication response relates to the female urinary microbiota. Int Urogynecol J 2016;27:723-33.
16. Khasriya R, Sathiananthamoorthy S, Ismail S, et al. Spectrum of bacterial colonization associated with urothelial cells from patients with chronic lower urinary tract symptoms. J Clin Microbiol 2013;51:2054-62.
17. Karstens L, Asquith M, Davin S, et al. Does the Urinary Microbiome Play a Role in Urgency Urinary Incontinence and Its Severity? Front Cell Infect Microbiol 2016;6:78.
18. Lozupone CA, Stombaugh JI, Gordon JI, et al. Diversity, stability and resilience of the human gut microbiota. Nature 2012;489:220-30.
19. Pearce MM, Zilliox MJ, Rosenfeld AB, et al. The female urinary microbiome in urgency urinary incontinence. Am J Obstet Gynecol 2015;213:347.e1-11.
20. Thomas-White KJ, Kliethermes S, Rickey L, et al. Evaluation of the urinary microbiota of women with uncomplicated stress urinary incontinence. Am J Obstet Gynecol 2016. pii: S0002-9378(16)30522-1.
21. Brubaker L, Nager CW, Richter HE, et al. Urinary bacteria in adult women with urgency urinary incontinence. Int Urogynecol J 2014;25:1179-84.
22. Ravel J, Brotman RM. Translating the vaginal microbiome: gaps and challenges. Genome Med 2016;8:35.
23. Stapleton AE. Urine Culture in Uncomplicated UTI: Interpretation and Significance. Curr Infect Dis Rep 2016;18:15.
24. Hilt EE, McKinley K, Pearce MM, et al. Urine is not sterile: use of enhanced urine culture techniques to detect resident bacterial flora in the adult female bladder. J Clin Microbiol 2014;52:871-6.
25. Glaser AP, Schaeffer AJ. Urinary Tract Infection and Bacteriuria in Pregnancy. Urol Clin North Am 2015;42:547-60.
26. Schnarr J, Smaill F. Asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy. Eur J Clin Invest 2008;38 Suppl 2:50-7.

27. Ipe DS, Sundac L, Benjamin WH Jr, et al. Asymptomatic bacteriuria: prevalence rates of causal microorganisms, etiology of infection in different patient populations, and recent advances in molecular detection. FEMS Microbiol Lett 2013;346:1-10.
28. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med 2002;113 Suppl 1A:5S-13S.
29. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Dis Mon 2003;49:53-70.
30. Eriksson I, Gustafson Y, Fagerström L, et al. Do urinary tract infections affect morale among very old women? Health Qual Life Outcomes 2010;8:73.
31. Abbo LM, Hooton TM. Antimicrobial Stewardship and Urinary Tract Infections. Antibiotics (Basel) 2014;3:174-92.
32. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/ International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. Neurourol Urodyn 2010;29:4-20.
33. Brotman RM, Shardell MD, Gajer P, et al. Association between the vaginal microbiota, menopause status, and signs of vulvovaginal atrophy. Menopause 2014;21:450-8.
34. Cribby S, Taylor M, Reid G. Vaginal microbiota and the use of probiotics. Interdiscip Perspect Infect Dis 2008;2008:256490.
35. Devillard E, Burton JP, Hammond JA, et al. Novel insight into the vaginal microflora in postmenopausal women under hormone replacement therapy as analyzed by PCR-denaturing gradient gel electrophoresis. Eur J Obstet Gynecol Reprod Biol 2004;117:76-81.
36. Heinemann C, Reid G. Vaginal microbial diversity among postmenopausal women with and without hormone replacement therapy. Can J Microbiol 2005;51:777-81.

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