



Letter to the Editor

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Commentary on “The Urine Microbiome of Healthy Men and Women Differs by Urine Collection Method”

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To the editor,

I read with great interest the article titled “The Urine Microbiome of Healthy Men and Women Differs by Urine Collection Method” published by Pohl et al. in the *International Neurourology Journal* in March 2020 [1]. The authors concluded that the urinary microbiome differed according to urine collection methods and that sex differences in the core microbiome exist.

When I analyzed articles that studied urinary microbiome in healthy individuals, or healthy controls in case-control studies, most studies showed similar results (Table 1). *Lactobacillus* was the predominant genus in the urinary microbiome in females, whereas a more heterogeneous group of microbiomes was shown in males [2-23]. The study by Wolfe et al. [5] was the only study that compared different urine collection methods, and they concluded that the best methods are suprapubic aspiration and transurethral catheterization.

There are still clear limitations in the study of the human urinary microbiome. Due to the heterogeneous design of urinary microbiome studies, it is difficult to make comparisons between studies and to draw conclusions. There are differences according to the urine collection method, 16s rRNA analysis tools, statistical methods, and the taxonomic database on which the reporting of genera or species is based. These heterogeneous study designs cause discrepancies in results. In addition, as the authors clearly pointed out, many other factors can influence the urinary microbiome, such as age, sex, dietary habits, infections and antimicrobial use, hormonal status, and regional variation.

Several points should be considered in future studies involv-

ing the urinary microbiome. First, a larger sample size is needed. Second, standardization of methodology and reporting is necessary to facilitate comparisons between studies. Third, more studies on the normal urinary microbiome and factors influencing its composition are needed. Age, sex, and urine collection methods are known factors, but many other factors likely exist. One point to consider in this regard is that it may be impossible to define a “universal norm” regarding the urinary microbiome. Rather than defining a universal norm, identifying the normal urinary microbiome in each individual and using it as a personalized reference for future disease may be a more reasonable approach. Fourth, the connection between dysbiosis and disease should be more clearly identified. When this connection is found, it may become possible to use the urinary microbiome in diagnosis or treatment. Lastly, studies have suggested that the overall composition and richness of the microbiota play an important role in modulating vaccine response [24]. In this regard, the effects of the urinary microbiome on vaccinations for urinary tract infection may be an interesting topic for future studies.

• **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

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Table 1. Articles that studied the urinary microbiome in healthy individuals, or healthy controls in case-control studies

Study	No.	Sex	Age	Urine collection	Microbiome
Siddiqui et al. [2] (2011)	8	F	27-67 yr	CCU	<i>Lactobacillus</i> , <i>Prevotella</i> , <i>Gardnerella</i> , <i>Peptoniphilus</i> , <i>Dialister</i> , <i>Finegoldia</i> , <i>Anaerococcus</i> , <i>Allisonella</i> , <i>Streptococcus</i> , <i>Staphylococcus</i>
Wolfe et al. [5] (2012)	12	F	NA	CCU, TUC, SPA	<i>Lactobacillus</i> , <i>Actinobaculum</i> , <i>Aerococcus</i> , <i>Anaerococcus</i> , <i>Atopobium</i> , <i>Burkholderia</i> , <i>Corynebacterium</i> , <i>Gardnerella</i> , <i>Prevotella</i> , <i>Ralstonia</i> , <i>Sneathia</i> , <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Veillonella</i>
Fouts et al. [3] (2012)	11	M	24-50 yr	MSU	<i>Corynebacterium</i> , <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Lactobacillus</i> , <i>Gardnerella</i> , <i>Veillonella</i>
	15	F	22-51 yr		<i>Lactobacillus</i> , <i>Corynebacterium</i> , <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Prevotella</i>
Nelson et al. [4] (2012)	18	M	14-17 yr	FCU	<i>Corynebacterium</i> , <i>Lactobacillus</i> , <i>Staphylococcus</i> , <i>Gardnerella</i> , <i>Streptococcus</i> , <i>Anaerococcus</i> , <i>Veillonella</i> , <i>Prevotella</i> , <i>Escherichia</i>
Lewis et al. [6] (2013)	6	M	39-83 yr	CCU	<i>Firmicutes</i>
	10	F	26-90 yr		<i>Firmicutes</i> , <i>Actinobacteria</i> , <i>Bacteroidetes</i>
Hilt et al. [7] (2014)	24	F	NA	TUC	<i>Lactobacillus</i> , <i>Corynebacterium</i> , <i>Streptococcus</i> , <i>Actinomyces</i> , <i>Staphylococcus</i> , <i>Aerococcus</i> , <i>Gardnerella</i> , <i>Bifidobacterium</i> , <i>Actinobaculum</i>
Pearce et al. [8] (2014)	58	F	35-65 yr	TUC	<i>Lactobacillus</i> , <i>Gardnerella</i> , <i>Corynebacterium</i> , <i>Enterobacteriaceae</i> , <i>Anaerococcus</i> , <i>Bifidobacterium</i> , <i>Streptococcus</i> , <i>Staphylococcus</i> , <i>Sneathia</i> , <i>Peptoniphilus</i> , <i>Atopobium</i> , <i>Rhodanobacter</i> , <i>Trueperella</i> , <i>Alloscardovia</i> , <i>Veillonella</i>
Karstens et al. [9] (2016)	10	F	58 (mean)	TUC	<i>Anoxybacillus</i> , <i>Lactobacillus</i> , <i>Prevotella</i> , <i>Gardnerella</i> , <i>Arthrobacter</i> , <i>Escherichia</i> , <i>Shigella</i>
Thomas-White et al. [10] (2016)	60	F	35-65 yr	TUC	<i>Lactobacillus</i> , <i>Gardnerella</i> , <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Enterococcus</i> , <i>Bifidobacterium</i> , <i>Atopobium</i> , <i>Enterobacteriaceae</i>
Wu et al. [15] (2017)	25	F	26 (mean)	TUC	<i>Lactobacillaceae</i> , <i>Prevotellaceae</i> , <i>Enterobacteriaceae</i> , <i>Veillonellaceae</i> , <i>Tissierellaceae</i> , <i>Bifidobacteriales</i>
Gottschick et al. [12] (2017)	49	F	19-62 yr	MSU	<i>Lactobacillus crispatus</i>
Abernethy et al. [11] (2017)	20	F	28-43 yr	TUC	<i>Lactobacillus acidophilus</i>
Wang et al. [14] (2017)	21	F	43 (mean)	MSU	<i>Lactobacillus</i> , <i>Varibaculum</i> , <i>Porphyromonas</i> , <i>Prevotella</i> , <i>Bacteroides</i>
Rani et al. [13] (2017)	5	F	27-63 yr	MSU	<i>Proteobacteria</i> , <i>Firmicutes</i> , <i>Actinobacteria</i> , <i>Bacteroidetes</i>
	3	M			
Wu et al. [18] (2018)	18	M	55.5 (mean)	MSU	<i>Escherichia-Shigella</i> , <i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Aeromonas</i> , <i>Acinetobacter</i> , <i>Bacteroides</i> , <i>Lactobacillus</i>
Komesu et al. [17] (2018)	84	F	53 (mean)	TUC	<i>Lactobacillus</i> , <i>Gardnerella</i> , <i>Tepidimonas</i> , <i>Prevotella</i>
Bucevic Popovic et al. [16] (2018)	19	M	61-82 yr	MSU	<i>Firmicutes</i> , <i>Actinobacteria</i> , <i>Bacteroidetes</i> , <i>Proteobacteria</i>
Meriwether et al. [21] (2019)	18	F	33.7 (mean)	MSU	<i>Lactobacillus</i> , <i>Prevotella</i>
Bresler et al. [19] (2019)	20	F	48 (mean)	MSU	<i>Lactobacillus</i>
Kassiri et al. [20] (2019)	10	M	3 mo-8 yr	TUC	<i>Staphylococcus</i> , <i>Varibaculum</i> , <i>Peptoniphilus</i> , <i>Actinobaculum</i>
Xie et al. [23] (2020)	21	M	44.2 (mean)	NA	<i>Acinetobacter</i> , <i>Prevotella</i> , <i>Oscillospira</i> , <i>Parabacteroides</i> , <i>Fusobacterium</i>
Liu et al. [22] (2020)	9	M	58.9 (mean)	TUC	<i>Gardnerella</i> , <i>Pontibacter</i> , <i>Sphingomonas</i> , <i>Prevotella</i> , <i>Propionibacterium</i>
	3	F			

CCU, clean catch urine; TUC, transurethral catheter; SPA, suprapubic aspirate; MSU, midstream urine; FCU, first catch urine; NA, not available.

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