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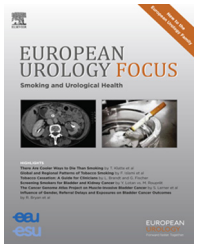

Review – Incontinence

The Urinary Tract Microbiome in Health and Disease

Isabel M. Aragón [a,†], *Bernardo Herrera-Imbroda* [a,†], *María I. Queipo-Ortuño* [b,c], *Elisabeth Castillo* [a], *Julia Sequeira-García Del Moral* [d], *Jaime Gómez-Millán* [e], *Gozde Yucel* [f], *María F. Lara* [a,*]

[a] *Department of Urology, Virgen de la Victoria University Hospital, Malaga, Spain;* [b] *Service of Endocrinology and Nutrition, Biomedical Research Institute,, University of Malaga, Malaga, Spain;* [c] *Biomedical Research Networking Center for Pathophysiology of Obesity and Nutrition, Madrid, Spain;* [d] *Urology Unit, University Hospital Carlos Haya, Malaga, Spain;* [e] *Department of Radiation Oncology, University Hospital Virgen de la Victoria, Malaga, Spain;* [f] *Program in Epithelial Biology, School of Medicine, Stanford University, Stanford, CA, USA*

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Abstract

Context: The urinary tract, previously considered a sterile body niche, has emerged as the host of an array of bacteria in healthy individuals, revolutionizing the urology research field.
Objective: To review the literature on microbiome implications in the urinary tract and the usefulness of probiotics/prebiotics and diet as treatment for urologic disorders.
Evidence acquisition: A systematic review was conducted using PubMed and Medline from inception until July 2016. The initial search identified 1419 studies and 89 were included in this systematic review.
Evidence synthesis: Specific bacterial communities have been found in the healthy urinary tract. Changes in this microbiome have been observed in certain urologic disorders such as urinary incontinence, urologic cancers, interstitial cystitis, neurogenic bladder dysfunction, sexually transmitted infections, and chronic prostatitis/chronic pelvic pain syndrome. The role of probiotics, prebiotics, and diet as treatment or preventive agents for urologic disorders requires further investigation.
Conclusions: There is a microbiome associated with the healthy urinary tract that can change in urologic disorders. This represents a propitious context to identify new diagnostic, prognostic, and predictive microbiome-based biomarkers that could be used in clinical urology practice. In addition, probiotics, prebiotics, and diet modifications appear to represent an opportunity to regulate the urinary microbiome.
Patient summary: We review the urinary microbiome of healthy individuals and its changes in relation to urinary disorders. The question to resolve is how we can modulate the microbiome to improve urinary tract health.

† These authors contributed equally to this work.
* Corresponding author. Department of Urology, Virgen de la Victoria University Hospital, Campus Universitario de Teatinos s/n, 29010 Malaga, Spain. Tel. +34 951032647; Fax: +34 951440263.
E-mail address: mf.lara@fimabis.org (M.F. Lara).

1. Introduction

It is well known that even in a healthy state the body hosts a variety of microorganisms such as bacteria, fungi, viruses, and protozoa. In fact, the body houses approximately ten times more microbial cells than human cells. However, although microorganism residents in the human body have evolved with man, the relationship is not always perfect [1]. The term microbiota refers to microbes living inside and on an individual, while the term microbiome denotes the

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collection of genomes, genes, and products of the microbes present in a particular host [2–4].

The Human Microbiome Project (HMP) was established in 2008 with the aim of developing a comprehensive characterization of the human microbiome and analysis of its role in human health and disease. Initially the HMP did not include investigation of the bladder microbiome. One of the reasons for this was that it was considered unethical to obtain bladder biopsies or suprapubic aspirates from healthy individuals to characterize the bladder microbiome while avoiding sample contamination with microorganisms from the urethra [5]. Moreover, the bladder and urine have long been considered sterile in healthy individuals because of technical difficulties in characterizing the full spectrum of urinary bacterial species using standard microbiological methods. Advances in molecular biology techniques and culture methods have allowed definition of a specific microbiome associated with several body sites previously believed to be sterile, including the urinary tract (UT) [6–10]. The recent identification of a specific microbiome in the UT may have important implications in the maintenance of health and/or the development of certain diseases [10–15]. However, it is difficult to establish a strict relation between the microbiome and health and disease without considering that the human microbiome can change during the life cycle and seasonally, or with environmental changes (infection, treatments, diet, hormone state, or lifestyle) [1,16]. Therefore, these findings opened an emerging research field to explore, especially in the urology context, in terms of future design of treatments/drugs targeting specific microorganisms of the UT. In the present review, we summarize the main recent publications regarding the urinary microbiome (UM) with the aim of evaluating future needs in the field and the option of using probiotics, prebiotics, and diet as a treatment for urinary diseases.

2. Evidence acquisition

A systematic literature search was performed using PubMed and Medline databases from inception until July 2016. Papers written in English were selected following the Preferred Reporting Items for Systematic Reviews and Meta-Aaalyses (PRISMA) methodology. A flowchart of the systematic search process is shown in Figure 1. The following keywords were included in this systematic review: "*microbiome, microbiome and bacteriuria*" in combination with "*urinary tract, urinary incontinence, urinary tract infection, cancer, urothelial cancer, bladder cancer, prostate cancer, neurogenic bladder dysfunction, interstitial cystitis, urolithiasis*" and/or "*probiotics, prebiotics, diet, cranberry, pomegranate*". The initial search identified 1419 studies. Only 89 were selected for inclusion in the review.

3. Evidence synthesis

Selected papers were published between 1991 and 2016. Information regarding the UM in healthy individuals was extracted from 11 articles (Table 1). Six articles were

Table 1 – Microbiome composition of urine among healthy individuals

Study population	Main bacterial taxa	Sample collection	Technique used	Ref.
Healthy men aged ~18 yr (n = 9)	*Lactobacillus, Corynebacterium, Escherichia*, and *Streptococcus*	FC urine	16S rRNA GS	[22]
Healthy men (n = 22) age ≥18 yr, median 28 yr	*Lactobacillus, Sneathia, Veillonella, Corynebacterium, Prevotella, Streptococcus, Ureaplasma, Mycoplasma, Anaerococcus, Atopobium, Aerococcus, Staphylococcus, Gemella, Enterococcus*, and *Finegoldia*	FC urine	16S rRNA GS	[23]
Healthy females aged 27–67 yr (n = 8)	*Lactobacillus, Prevotella, Gardnerella, Peptoniphilus, Dialister, Finegoldia, Anaerococcus, Allisonella, Streptococcus*, and *Staphylococcus*	CC MSU	16S rRNA GS	[24]
Healthy males aged 24–50 yr (n = 11) Healthy females aged 22–51 yr (n = 15)	*Lactobacillus, Klebsiella, Corynebacterium, Staphylococcus, Streptococcus, Aerococcus, Gardnerella, Prevotella, Escherichia*, and *Enterococcus*	MSU	16S rRNA GS	[25]
Healthy males aged 14–17 yr (n = 18)	*Corynebacterium, Lactobacillus, Staphylococcus, Gardnerella, Streptococcus, Anaerococcus, Veillonella, Prevotella*, and *Escherichia*	FC urine	16S rRNA GS	[26]
Healthy women (n = 12) age NA	*Lactobacillus, Actinobaculum, Aerococcus, Anaerococcus, Atopobium, Burkholderia, Corynebacterium, Gardnerella, Prevotella, Ralstonia, Sneathia, Staphylococcus, Streptococcus*, and *Veillonella*	CC MSU, SPA, and TUC	16S rRNA GS	[17]
Healthy men aged 39–86 yr (n = 6) Healthy woman aged 26–90 yr (n = 10)	Male and female samples: Firmicutes; female samples: Actinobacteria, Bacteroidetes	CC MSU	16S rRNA GS	[18]
Healthy women (n = 24) age NA	*Lactobacillus, Corynebacterium, Streptococcus, Actinomyces, Staphylococcus, Aerococcus, Gardnerella, Bifidobacterium*, and *Actinobaculum*	TUC	16S rRNA GS and/or EUCT	[21]
Healthy women aged 35–65 yr (n = 58)	*Lactobacillus, Gardnerella, Corynebacterium*, Enterobacteriaceae, *Anaerococcus, Bifidobacterium, Streptococcus, Staphylococcus, Sneathia, Peptoniphilus, Atopobium, Rhodanobacter, Trueperella, Alloscardovia*, and *Veillonella*	TUC	16S rRNA GS and/or EQUC	[19]
Healthy women aged 35–65 yr (n = 60)	*Lactobacillus, Gardnerella, Staphylococcus, Streptococcus, Enterococcus, Bifidobacterium, Atopobium*, and Enterobacteriaceae	TUC	16S rRNA GS and/or EQUC	[20]
Healthy women (n = 10)	*Anoxybacillus, Lactobacillus, Prevotella, Gardnerella, Arthrobacter, Escherichia*, and *Shigella*	TUC	16S rRNA GS	[27]

NA = not available; EUCT = enhanced urine culture technique; EQUC = expanded quantitative urine culture; GS = gene sequencing; FC = first catch; CC = clean catch; MSU = midstream urine; SPA = suprapubic aspirate; TUC = transurethral catheter.

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