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The Role of the Male Urobiome and Dysbiosis in the Pathogenesis of Prostatic Diseases (CP/CPPS and BPH): A Narrative Review.

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Abstract

Background. For decades, the male urinary tract was considered sterile. Next-generation sequencing (NGS) overturned this dogma, revealing a complex urobiome.

Aim. This study aims to summarize literature on the physiological male urobiome and evaluate the impact of its dysbiosis on the pathogenesis of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and benign prostatic hyperplasia (BPH).

Material and methods. A narrative review was conducted using PubMed and Scopus, focusing on contemporary literature (2017–2025). Keywords included: male urobiome, urinary

microbiome, chronic prostatitis, benign prostatic hyperplasia, dysbiosis. Case reports and animal models were excluded, prioritizing human clinical data and NGS-based analyses with rigorous negative controls.

Results. The healthy male urobiome exhibits multi-species diversity (e.g., Corynebacterium, Streptococcus). In CP/CPPS, hidden dysbiosis replaces the sterility concept; anaerobic enrichment directly correlates with pain and inflammation. In BPH, dysbiosis acts as an inflammatory cofactor driving tissue growth. Urobiome destabilization is linked to metabolic syndrome and visceral obesity, generating systemic inflammation and exacerbating lower urinary tract symptoms (LUTS).

Conclusions. Dysbiosis plays a pivotal role in CP/CPPS and BPH pathogenesis. Instead of ineffective empirical antibiotic therapy destroying commensal flora, modern strategies should rely on microbiome modulation (targeted probiotics) and biofilm eradication (bacteriophages for catheter infection prevention).

Keywords: Microbiota; Prostatitis; Prostatic Hyperplasia; Dysbiosis.

1. Introduction

For decades, the male urinary tract was regarded as sterile because routine urine culture was not designed to detect its full microbial diversity (Neugent et al., 2020; Kim & Jung, 2021; Perez-Carrasco et al., 2021; Yu & Jung, 2022; Heidrich et al., 2022). Standard aerobic methods preferentially recover fast-growing cultivable organisms and often miss slow-growing anaerobes and bacteria with complex nutritional requirements (Neugent et al., 2020; Perez-Carrasco et al., 2021). Consequently, lack of growth was long taken as evidence of sterility, although it mainly reflected the limits of culture-based diagnostics (Neugent et al., 2020; Kim & Jung, 2021; Perez-Carrasco et al., 2021; Yu & Jung, 2022; Heidrich et al., 2022).

This view changed with the introduction of culture-independent sequencing, especially 16S rRNA profiling and next-generation sequencing (NGS), together with Expanded Quantitative Urine Culture (EQUC) (Neugent et al., 2020; Kim and Jung, 2021; Perez-Carrasco et al., 2021; Yu &

Jung, 2022; Heidrich et al., 2022). These tools made it possible to identify bacterial DNA and recover viable microorganisms from samples previously classified as culture-negative (Neugent et al., 2020; Kim & Jung, 2021; Perez-Carrasco et al., 2021). The work associated with Alan J. Wolfe and colleagues in 2012–2014 was central to this shift (Pohl et al., 2020; Perez-Carrasco et al., 2021). Yet in men, the field is still evolving rapidly.

Available data show that the male urobiome remains less clearly defined than the female one, and no universally accepted core profile has been established, although *Corynebacterium*, *Streptococcus*, *Staphylococcus* and *Veillonella* are repeatedly reported in healthy men (Pohl et al., 2020; Kim & Jung, 2021; Perez-Carrasco et al., 2021; Yu & Jung, 2022; Heidrich et al., 2022). Interpretation is strongly influenced by sampling method, and catheterized urine appears to reflect the bladder milieu more faithfully than voided specimens (Pohl et al., 2020; Kim & Jung,2021; Perez-Carrasco et al., 2021; Yu & Jung, 2022). Microbial balance is also linked to urothelial barrier integrity and colonization resistance (Lacerda Mariano & Ingersoll, 2020; Jafari & Rohn, 2022).

These observations have clear clinical relevance. In chronic prostatitis/chronic pelvic pain syndrome CP/CPPS, accumulating evidence suggests that some apparently culture-negative cases may represent hidden dysbiosis rather than a truly sterile condition, with microbiota profiles associated with symptom burden and inflammatory phenotypes (Shoskes et al., 2016; Mjaess et al., 2023). In benign prostatic hyperplasia (BPH), chronic prostatic inflammation is a recognized driver of progression, and dysbiotic shifts may contribute to local immune activation, tissue remodeling and lower urinary tract symptoms (LUTS) severity, potentially in conjunction with metabolic disturbances (Kim & Jung, 2021; Yu & Jung, 2022; Mjaess et al., 2023; He et al. 2025). Nevertheless, male-specific reference data remain limited, methodological heterogeneity is substantial and causal inferences remain uncertain (Kim & Jung, 2021; Yu & Jung, 2022; Heidrich et al., 2022; Mjaess et al., 2023).

Research Objective. To summarize the contemporary literature concerning the physiological male urobiome and to critically evaluate the impact of its dysbiosis on the pathogenesis of prostatic diseases, specifically chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and benign prostatic hyperplasia (BPH).

Research Problems. What characterizes the physiological male urobiome, and how does it shift into a dysbiotic state? Furthermore, to what extent does this hidden dysbiosis contribute to local

immune activation, tissue remodeling, and the clinical severity of lower urinary tract symptoms in CP/CPPS and BPH?

Research Hypotheses. We hypothesize that culture-negative cases of CP/CPPS are fundamentally driven by a hidden urobiome dysbiosis rather than true sterility, correlating directly with inflammatory phenotypes. Additionally, we hypothesize that in BPH, urobiome dysbiosis acts as a crucial inflammatory cofactor that, potentially combined with metabolic disturbances, drives prostate tissue proliferation and exacerbates LUTS.

2. Research materials and methods

This study adopts a comprehensive narrative review methodology, which is optimal for synthesizing highly heterogeneous evidence from the intersection of clinical urology, mucosal immunology, and molecular microbiology. Due to the significant methodological diversity across these fields, a rigid systematic review would limit the scope of mechanistic interpretation. The evidentiary corpus for this analysis was established through a structured electronic search of the PubMed and Scopus databases. To ensure high specificity and sensitivity, the search strategy was strictly governed by a combination of standardized Medical Subject Headings (MeSH) and precise keywords, including: *male urobiome*, *urinary microbiome*, *chronic prostatitis*, *benign prostatic hyperplasia*, and *dysbiosis*.

While the primary scope of this extraction strategy was intentionally focused on contemporary literature published between 2017 and 2025, select foundational studies from 2014 and 2016 were also included. The core 2017–2025 timeframe was chosen to reflect the accelerated pace of technological innovation in NGS. These modern genetic tools have revolutionized microbiology, allowing for a much more precise identification of bacteria in low-biomass environments than was previously possible. However, earlier landmark papers were purposefully retained in the evidentiary corpus as they provide critical historical context regarding biofilm-related antibiotic resistance and the initial conceptual shift toward dysbiosis in urological syndromes. To ensure the results represent the highest translational utility for human medicine, strict exclusion criteria were

applied. Case reports were excluded to avoid relying on isolated clinical anomalies, and studies based exclusively on animal models were removed from the final analysis.

The interpretation of urobiome data is inherently constrained by the status of the urinary tract as an extremely low-biomass environment. Consequently, the reliability of these conclusions is strictly dependent on the methodological rigor of the primary research. A critical challenge in NGS is the potential for false-positive identification due to dead DNA contaminants originating from laboratory reagents, a phenomenon known as the "kitome." Therefore, this scholarly inquiry explicitly prioritizes studies that implemented stringent negative controls, ensuring that the discussed microbial signatures reflect true biological presence rather than technical artifacts.

2.1 AI.

Generative AI was utilized for specific assistance in refining the academic English language of the manuscript, ensuring clarity, consistency, and adherence to scientific writing standards. These tools were used for additional linguistic refinement of the research manuscript, ensuring proper English grammar, style, and clarity in the presentation of results. It is important to emphasize that all AI tools were used strictly as assistive instruments under human supervision. The final selection of literature, interpretation of results, and the formulation of conclusions were determined solely by the authors. The AI tools served primarily to enhance efficiency in linguistic refinement and formatting rather than replacing human judgment in the analytical process.

3. State of knowledge

3.1. The Urobiome Under Physiological Conditions – Male-Specific Features

The application of 16S rRNA gene amplicon sequencing and EQUC has overturned the longstanding paradigm of urinary tract sterility, demonstrating the presence of a resident microbial community in healthy males (Neugent et al., 2020; Pohl et al., 2020; Perez-Carrasco et al., 2021; Saenz et al., 2024). Nevertheless, the male urobiome remains considerably less well characterised than its female counterpart, owing to the paucity of published studies, small cohort sizes, and

methodological heterogeneity (Perez-Carrasco et al., 2021; Saenz et al., 2024). A core male urinary microbiota has not yet been defined (Neugent et al., 2020).

At the phylum level, the urobiome composition of both sexes exhibits similarities, with Firmicutes predominating (65% in males vs 73% in females), followed by Actinobacteria, Bacteroidetes, and Proteobacteria (Perez-Carrasco et al., 2021). Substantial differences emerge at the genus level. In healthy males, the dominant taxa include *Corynebacterium*, *Streptococcus*, *Staphylococcus*, and *Veillonella* (Neugent et al., 2020; Pohl et al., 2020; Perez-Carrasco et al., 2021), whereas the female urobiome is characterised by a marked predominance of *Lactobacillus* (Neugent et al., 2020; Perez-Carrasco et al., 2021; Saenz et al., 2024). Notably, the genus *Pseudomonas* has been reported exclusively in male urine (Perez-Carrasco et al., 2021). Pohl et al., in a study of 14 healthy males and 6 females, confirmed the dominance of *Streptococcus* in males and identified significant sex-based differences in community structure assessed by weighted and unweighted UniFrac beta-diversity metrics ($P \leq 0.031$) (Pohl et al. 2020).

A fundamental distinction of the male urobiome is its multi-taxon profile with higher alpha-diversity, contrasting with the near-monoculture structure of the female urobiome, which is typically dominated by *Lactobacillus crispatus* (Neugent et al., 2020; Pohl et al., 2020; Perez-Carrasco et al., 2021; Saenz et al., 2024). This ecological divergence is attributed in part to anatomical differences, greater urethral length, and the influence of sex hormones – particularly oestrogens, which promote *Lactobacillus* colonisation in women – on the shaping of urogenital ecological niches (Neugent et al., 2020; Saenz et al., 2024).

Interpretation of the male urobiome requires careful consideration of the sampling method employed. Pohl et al. demonstrated that midstream voided and catheterised urine specimens differ significantly in the abundance of *Veillonella* ($P = 0.008$), *Neisseria* ($P = 0.022$), and *Lactobacillus* ($P = 0.041$), although both compartments share the same dominant genera in differing proportions (Pohl et al. 2020). Suprapubic aspiration remains the gold standard for minimising contamination; however, transurethral catheterisation yields largely concordant results and is more widely accepted in male urobiome research (Neugent et al., 2020; Pohl et al., 2020; Perez-Carrasco et al., 2021).

3.2. Urothelial barrier and defense mechanisms

The urothelial barrier represents a highly specialized structural and functional system that protects the lower urinary tract, including the urethra and prostate, against chemical injury and microbial invasion (Jafari & Rohn, 2022). This barrier is formed by umbrella cells with apical uroplakin plaques, tight junctions restricting paracellular permeability, and a glycosaminoglycan (GAG)-rich glycocalyx that limits bacterial adhesion (Jafari & Rohn, 2022).

In parallel, the urinary tract hosts a resident microbiota, as demonstrated by culture-independent approaches, indicating that antimicrobial defense involves both epithelial integrity and microbiome-associated mechanisms (Yu & Jung, 2022; Saenz et al., 2024). The protective function of the urinary microbiome is primarily mediated through colonization resistance. Commensal microorganisms compete with uropathogens for adhesion sites on the urothelium and for essential nutrients, thereby restricting pathogen expansion (Saenz et al., 2024). Additionally, selected taxa, including *Lactobacillus* and *Streptococcus* species, produce antimicrobial compounds such as bacteriocins, which directly inhibit the growth of competing microorganisms (Saenz et al., 2024). This ecological competition is particularly relevant in the male urethra, where microbial communities may influence the microbial composition of the prostate and limit colonization by uropathogenic *Escherichia coli*.

Maintenance of homeostasis within the urinary tract depends on dynamic interactions between the microbiota and the mucosal immune system. Urothelial cells express pattern recognition receptors, including Toll-like receptors (TLR2, TLR4, TLR5, and TLR9), enabling the detection of microbial-associated molecular patterns and the initiation of controlled immune responses (Lacerda Mariano & Ingersoll, 2020). This leads to the production of cytokines, chemokines, and antimicrobial peptides, which regulate microbial populations and recruit immune effector cells, such as neutrophils and macrophages (Lacerda Mariano & Ingersoll, 2020). Simultaneously, commensal microbiota contributes to immune modulation by promoting tolerance to non-pathogenic species and preventing excessive inflammatory responses (Saenz et al., 2024).

Additional defense mechanisms include soluble factors such as secretory immunoglobulin A (sIgA), antimicrobial peptides, and iron-binding proteins, which further limit microbial growth (Lacerda Mariano & Ingersoll, 2020). Structural and cellular responses, including urothelial

exfoliation and intracellular bacterial clearance via exocytosis and autophagy, contribute to the elimination of invading pathogens (Jafari & Rohn, 2022). Disruption of these coordinated interactions (dysbiosis) has been associated with altered microbial diversity and the emergence of opportunistic pathogens, including *Gardnerella vaginalis*, *Atopobium vaginae*, and *Anaerococcus vaginalis*, potentially contributing to chronic inflammation and prostatic disease (Saenz et al., 2024).

3.3. CP/CPPS as hidden dysbiosis – pathomechanism

NIH category III CP/CPPS is increasingly recognized as a condition of hidden dysbiosis rather than a sterile disorder. Systematic reviews demonstrate that men with CP/CPPS exhibit distinct microbiota compositions and altered diversity profiles across urinary, seminal, and prostatic compartments compared to healthy controls (Mjaess et al., 2023; Deng et al., 2025). Specifically, Mjaess et al. confirmed that CP/CPPS is associated with significant urinary microbiota remodeling and, in several cohorts, increased microbial diversity (Mjaess et al. 2023). Convergent data also suggest a multisite dysbiotic phenotype involving disturbances in the gut and oral microbiota (Wang et al., 2023; Deng et al., 2025).

The failure of standard culture media to yield pathogens does not equate to microbial absence. NGS have revealed that culture-negative samples often harbor distinct microbial signatures (Shoskes et al., 2016; Mjaess et al., 2023; Deng et al., 2025). Shoskes et al. identified significantly higher phylogenetic alpha-diversity in CP/CPPS patients, with over-representation of 17 bacterial clades, most notably members of the *Clostridia* and *Bacteroidia* classes, alongside a relative depletion of *Bacilli* (Shoskes et al., 2016). However, a precise boundary between healthy, physiological urobiome diversity and a pathological state has not yet been established. Understanding exactly when the natural flora shifts into pathological anaerobic dysbiosis remains a critical challenge for future research. These findings underscore that negative conventional cultures reflect the limitations of culture-dependent detection rather than true sterility.

This dysbiotic rearrangement extends to other anatomical niches (Wang et al. 2023; Deng et al. 2025). Gut microbiota profiling in CP/CPPS has shown significant shifts, including increased abundance of *Bacteroides*, *Enterobacter*, and *Pseudomonas*, with a concomitant reduction in

beneficial taxa such as *Prevotella*, *Faecalibacterium*, and *Bifidobacterium* (Wang et al., 2023; Deng et al. 2025). Such structured taxonomic shifts substantiate the concept of CP/CPPS as a condition driven by ecological imbalance rather than nonspecific fluctuations, a conclusion further supported by recent evidence of distinct gut microbiome alterations in these patients (Wang et al., 2023; Deng et al., 2025; Khan et al., 2025).

Critically, clinical severity in CP/CPPS appears to be modulated by the specific microbiota profile rather than the mere presence of bacteria (Mjaess et al., 2023). Distinct urinary microbiome patterns correlate with symptom duration, CPSI scores, and specific clinical phenotypes (UPOINT domains) (Shoskes et al., 2016). Communities characterized by a predominance of anaerobic taxa have been associated with higher leukocyte counts, elevated PSA concentrations, greater prostate volume, and more severe pain scores (Shoskes et al. 2016; Mjaess et al., 2023). While both anaerobic- and aerobic-shifted profiles may correlate with different disease expressions, the strongest association with inflammatory burden is reported for anaerobe-enriched signatures (Mjaess et al., 2023). Thus, CP/CPPS represents a chronic inflammatory syndrome where hidden dysbiosis modifies the local immune milieu and clinical disease expression (Shoskes et al., 2016; Mjaess et al., 2023; Wang et al., 2023; Deng et al., 2025).

3.4. BPH – Microbiological Theory of Prostate Growth

One of the mechanisms involved in the development of BPH is an immune response associated with inflammatory processes (Naiyila et al., 2023). Studies suggest that chronic inflammation constitutes a significant factor modulating disease progression, and its potential source is thought to be dysbiosis of the urinary tract microbiome (Yu & Jung, 2022; Naiyila et al., 2023). This may result from bacterial and viral infections, sexually transmitted microorganisms, dietary factors, hormones, or autoimmune mechanisms. Dysbiosis leads to the accumulation of inflammatory cells in the prostate tissues. These include T and B lymphocytes, as well as macrophages, the M2 phenotype of which is considered particularly important (Sheng et al., 2018; Naiyila et al., 2023). It leads to tissue damage, the release of pro-inflammatory cytokines (such as IL-6, IL-8, or TGF-β), and growth factors (Naiyila et al., 2023). These processes promote the proliferation of stromal and epithelial cells, and consequently, prostatic hyperplasia (Naiyila et al., 2023; Wang et al.,

2024). Furthermore, specific pathobionts directly contribute to this pathogenesis; as demonstrated by Jain et al., *Escherichia coli*—a frequent constituent of the BPH-associated tissue microbiota—can directly induce inflammation and DNA damage in prostate epithelial cells, thereby actively exacerbating the hyperplastic process (Jain et al., 2020).

Studies have shown a distinct correlation between urinary tract dysbiosis and changes in the severity of LUTS that accompany patients with BPH; notably, Bajic et al. demonstrated that specific bladder microbiome profiles from catheterized urine significantly correlate with LUTS severity, although definitive causality remains to be established (Bajic et al., 2020). An abnormal microbiome balance activates the immune response, thereby sustaining a vicious circle of inflammation and proliferation of prostatic cells (Yu & Jung, 2022). As further evidence of the importance of the immune mechanism in BPH pathogenesis, Wang et al. (2024) demonstrated an inhibitory effect of the anti-inflammatory factor omentin-1 (ITLN-1) on BPH development by suppressing local inflammation in the prostate. At the same time, this highlights the therapeutic potential of ITLN-1 in the treatment of BPH (Wang et al., 2024).

It is worth noting that dysbiosis and the accompanying inflammatory state are not considered primary causes of BPH; they constitute a cofactor in a multifactorial process. They interact with factors such as aging and hormonal imbalance, in which the most active form of testosterone, dihydrotestosterone (DHT), plays a significant role. DHT is responsible for the function and growth of the prostate gland (Naiyila et al., 2023; Wang et al., 2024). Moreover, disturbed microbiome balance may also have a secondary character in advanced BPH, when urinary retention and impaired bladder emptying occur (Yu & Jung, 2022).

In summary, the microbiological theory of prostate growth does not represent a primary cause but is part of a broader model of BPH pathogenesis. Chronic inflammation—potentially induced by urinary tract dysbiosis—constitutes a supporting factor; however, its role does not surpass fundamental determinants related to age and hormones.

3.5. BPH and the Metabolic Background: The Impact of Visceral Obesity on Urobiome Stability

Modern analysis of BPH pathogenesis highlights the critical role of the urobiome. In healthy men, maintaining physiological microbial homeostasis—dominated by commensal genera such as *Corynebacterium*, *Streptococcus*, *Staphylococcus*, and *Veillonella* (Yu & Jung, 2022)—is strictly correlated with the body's metabolic state.

Epidemiologically, exceeding the European anthropometric threshold for waist circumference (94 cm in men, 80 cm in women) is significantly associated with a shift in systemic homeostasis. Visceral obesity induces low-grade chronic inflammation, elevating pro-inflammatory cytokines such as IL-6 and TNF-alpha (He et al., 2025).

Metabolic Syndrome (MetS) strongly correlates with BPH progression. Cohort studies link MetS to significantly larger Total Prostate Volume (TPV) and Transition Zone Volume (TZV), directly exacerbating LUTS (Chen et al. 2024). Metabolically induced inflammation and accompanying hyperinsulinemia degrade the pelvic microenvironment, triggering urobiome dysbiosis. This paves the way for uropathogens, such as *Escherichia coli*, to invade the urothelium and activate epithelial inflammasomes (e.g., NLRP3). Consequently, the release of pro-proliferative mediators drastically accelerates prostatic glandular and stromal hyperplasia (Yu & Jung, 2022; He et al., 2025).

Accurate urobiome assessment within this context requires rigorous sampling methodology. Compared to Mid-Stream Urine (MSU), catheterized or suprapubically aspirated samples avoid urethral flora contamination, enabling precise identification of the low-biomass bladder dysbiosis associated with advanced BPH (Yu & Jung, 2022; Arican Tarim et al., 2023). In summary, visceral obesity acts as a catalyst for microbiological changes, where systemic metabolic disorders translate into local destabilization of the urothelial barrier and BPH progression (Chen et al. 2024; He et al. 2025).

4. Discussion

4.1. Diagnostic Challenges and Controversies

The diagnostic framework for CP/CPPS is transitioning from conventional culture-dependent methods toward high-sensitivity molecular profiling. Current clinical standards, defined by the European Association of Urology (EAU) guidelines (EAU Guidelines Office 2026), still rely on the Meares-Stamey test and aerobic cultures, which often fail to capture the complex microbial communities identified by modern techniques. Wu et al. (Wu et al., 2020) demonstrated that high-throughput NGS identifies a diverse range of anaerobic and fastidious bacteria in cases previously classified as “culture-negative”. However, the authors emphasized that these findings did not reveal specific potential pathogens, suggesting that the identified DNA might reflect commensal flora or technical artifacts, and that EPS in CP III patients could effectively be sterile.

The relationship between the urinary microbiota and prostatic disease is increasingly viewed as a "key for the lock" (Mjaess et al., 2023). Furthermore, research indicates a distinct link between the microbiome profiles of urine and prostatic tissue. Specifically, Hurst et al. provided fundamental evidence for the presence of microbes directly within prostate biopsies across various patient risk groups (Hurst et al., 2022). Confirming these microbial signatures is crucial for definitively rejecting the dogma of prostatic sterility, serving as a starting point for further analyses on the role of dysbiosis in urological diseases (Hurst et al., 2022). While liquid fractions provide a non-invasive window into the prostatic environment, the interpretation of these signals requires high precision to account for low microbial biomass and susceptibility to the "kitome"—contaminating DNA within laboratory reagents (Heidrich et al., 2022; Hurst et al., 2022). Without rigorous negative controls and specific primer selection, molecular findings may reflect environmental noise rather than true pathology (Heidrich et al., 2022).

It must be objectively acknowledged that expressed prostatic secretion (EPS), the most frequently studied fraction, is inherently burdened by the risk of urethral contamination. As highlighted by Pohl et al. (Pohl et al., 2020), the composition of the male urinary microbiome varies significantly depending on the collection method, with voided specimens being highly susceptible to external noise. Therefore, the gold standard for confirming the presence of a biofilm strictly within the

glandular tissue remains more invasive procedures, such as analysis of tissue obtained through biopsy or transurethral resection of the prostate (TURP), which effectively bypass the urethral conduit (Pohl et al., 2020; Wu et al., 2020). The current discrepancy between observed prostatic inflammation and the lack of detectable pathogens in expressed prostatic secretion (EPS) represents a significant knowledge gap. Future studies must definitively determine whether bacteria hide deeper within tissues as hard-to-detect biofilms, which would make analyzing EPS alone insufficient.

4.2. Clinical and Therapeutic Implications

Modern urology, driven by NGS, is moving away from the simplistic "one pathogen – one antibiotic" model toward a complex understanding of the urogenital ecosystem. The discovery that the bladder and prostate are not sterile (Pohl et al., 2020) has revolutionized the treatment of CP/CPPS and BPH (Table 1).

Table 1. Key Next-Generation Sequencing (NGS) studies in prostatic diseases and the microbiome profiles.

Study & Year	Disease	Method	Conclusions
Bajic et al., 2020	BPE/LUTS	catheterized urine sample	Microbiome correlates with LUTS severity, but there is no proof of causality
Khan et al., 2025	CP/CPPS	fecal sample	Gut dysbiosis in CP/CPPS
Wu et al., 2020	CP/CPPS	EPS / prostatic fluid	No potential pathogens were identified in diagnosed patients with CP III. The EPS

			may be free from bacteria before and after infection
Jain et al., 2020	BPH	TURP	BPH tissue harbors distinct microbiota (incl. Escherichia coli); bacteria may drive inflammation and DNA damage
Hurst et al., 2022	Prostatic diseases	urine sample	Demonstrates a distinct link between urinary and prostatic microbiomes, confirming the presence of microbes directly within prostate tissue and supporting the rejection of the sterility dogma.
Pohl et al., 2020	Healthy	Urine sample: midstream vs catheter	Lactobacillus/Streptococcus dominant; composition differs by collection site

BPH – benign prostatic hyperplasia; BPE – benign prostatic enlargement; CP/CPPS – chronic prostatitis/chronic pelvic pain syndrome; LUTS – lower urinary tract symptoms; EPS – expressed prostatic secretion; TURP – transurethral resection of the prostate. In urinary studies, microbiome composition varies significantly depending on the collection method (midstream vs. catheter vs. suprapubic), with different dominant genera identified between urethral and bladder

samples. This demonstrates that urobiome NGS results are highly sensitive to sampling technique, contributing to discrepancies between studies.

Traditional Methods: The use of prolonged empirical antibiotic therapy in CP/CPPS has proven to be largely ineffective because bacteria often form biofilms that impair antibiotic penetration and activity. While planktonic bacteria are eradicated, those residing within the biofilm are protected by its extracellular matrix, promoting recurrence. It has been shown (Bartoletti et al., 2014) that despite bacterial eradication in 58.6% of patients, only 9.5% achieved sustained symptom improvement, indicating a poor correlation between microbiological and clinical outcomes. Furthermore, long-term antibiotic therapy disrupts the healthy microbiota, potentially worsening the patient's condition with no clinical benefit.

Probiotic Therapy and the Gut-Prostate Axis: Probiotic intervention represents a paradigm shift, focusing on modulating the urogenital microbiome rather than solely aiming for bacterial eradication. By introducing specific bacterial strains, probiotics compete for ecological niches and regulate systemic inflammatory pathways. This mitigates uropathogen translocation, while the "gut-prostate axis" attenuates localized prostatic inflammation. Recent evidence (Vocca et al., 2025) demonstrates that microbial restoration correlates with symptom relief and a significant reduction in CPSI scores. Consequently, targeted probiotics serve as a crucial adjunctive modality to enhance recovery and prevent the symptomatic recurrences associated with conventional treatment failures.

Bacteriophages: The clinical utility of bacteriophage therapy in urology requires a distinction between prophylactic interventions and the resolution of established glandular dysbiosis. Currently, phages are ineffective against the complex polymicrobial biofilms characteristic of CP/CPPS in the prostate tissue. However, a recent study (Sanchez et al. 2022) demonstrated that specific phage cocktails are highly effective in protecting silicone surfaces from *Escherichia coli* biofilm formation. This finding is of high clinical relevance for patients with severe BPH, where chronic catheterization often results in refractory catheter-associated urinary tract infections (CAUTI). Thus, while phages cannot yet cure multi-species tissue dysbiosis, they represent a validated strategy for preventing catheter colonization.

4.3. Limitations and Future Research Perspectives

The male urobiome still holds many unknowns. Further multicenter studies utilizing rigorous sampling methods are essential to definitively establish the causal relationships between the urobiome, metabolism, and the pathogenesis of prostatic diseases.

5. Conclusions

The introduction of modern molecular methods into urological diagnostics has irreversibly altered the paradigm of the urinary tract. The traditional approach based on standard aerobic cultures is giving way to a comprehensive analysis of the microbial ecosystem. Based on this literature review, the following key conclusions can be drawn:

1. Overturning the sterility dogma: The application of NGS and EQUC has definitively dispelled the historical myth of physiological sterility in the male urinary tract. The healthy male urobiome is characterized by a specific, multi-species diversity, and recognizing this physiological norm is an essential starting point for understanding prostate pathology.
2. Hidden dysbiosis in CP/CPPS: In NIH category III, cases previously defined as "abacterial" actually represent states of hidden dysbiosis. The inability to detect pathogens in standard cultures is merely a result of methodological limitations. Taxonomic shifts, including the promotion of multi-species anaerobic communities, directly correlate with the severity of inflammation, pain intensity, and clinical symptom burden in patients.
3. The urobiome and metabolic background in BPH: The pathogenesis of BPH is closely linked to dysbiosis, which acts as a key inflammatory cofactor. This phenomenon is drastically exacerbated by systemic metabolic disorders. Exceeding a healthy waist circumference—defined in the European population as a maximum of 94 cm for men and 80 cm for women—is considered a key factor contributing to chronic low-grade inflammation. This cascade degrades the pelvic microenvironment, paves the way for uropathogen invasion, and ultimately stimulates the pathological proliferation of glandular and stromal prostate tissue.

4. Evolution of therapeutic strategies: The accumulated evidence necessitates a radical shift in the clinical approach. Chronic, empirical antibiotic therapy represents a dead end—it demonstrates low efficacy in penetrating biofilms while simultaneously destroying protective commensal flora. Modern urology must rely on targeted modulation of the gut-prostate axis (e.g., via probiotic therapy) and the prevention of biofilm formation (e.g., using bacteriophages on catheters). However, the exact mechanisms and clinical efficacy of these therapies require further investigation.

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