JAMA | Review

Prostatitis
A Review

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IMPORTANCE Prostatitis is defined as infection, inflammation, or pain of the prostate gland and affects approximately 9.3% of men in their lifetime.

OBSERVATIONS Acute bacterial prostatitis consists of a urinary tract infection (UTI) that includes infection of the prostate, typically associated with fever or chills and caused by gram-negative bacteria, such as *Escherichia coli, Klebsiella,* or *Pseudomonas*, in 80% to 97% of cases. First-line therapy for acute prostatitis is broad-spectrum intravenous or oral antibiotics, such as intravenous piperacillin-tazobactam, ceftriaxone, or oral ciprofloxacin, which has a 92% to 97% success rate when prescribed for 2 to 4 weeks for people with febrile UTI and acute prostatitis. Chronic bacterial prostatitis is defined as a persistent bacterial infection of the prostate, typically presenting as recurrent UTIs from the same strain. Up to 74% of chronic bacterial prostatitis diagnoses are due to gram-negative organisms, such as *E coli*. First-line therapy for chronic bacterial prostatitis is a minimum 4-week course of levofloxacin or ciprofloxacin. Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) presents as pelvic pain or discomfort for at least 3 months and is associated with urinary symptoms, such as urinary frequency. CP/CPPS is diagnosed when evaluation, including history and physical examination, urine culture, and postvoid residual measurement, does not identify other causes for the symptoms, such as infection, cancer, urinary obstruction, or urinary retention. The National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) measures symptom severity (scale of 0-43), with a 6-point change considered clinically meaningful. First-line oral therapy for CP/CPPS with urinary symptoms is α-blockers (eg, tamsulosin, alfuzosin; ΔNIH-CPSI score difference vs placebo = −10.8 to −4.8). Other oral therapies are associated with modest changes in NIH-CPSI score compared with placebo, including anti-inflammatory drugs (eg, ibuprofen; ΔNIH-CPSI score difference = −2.5 to −1.7), pregabalin (ΔNIH-CPSI score difference = −2.4), and pollen extract (ΔNIH-CPSI score difference = −2.49).

CONCLUSIONS AND RELEVANCE Prostatitis includes acute bacterial prostatitis, chronic bacterial prostatitis, and CP/CPPS, each of which is diagnosed and treated differently. First-line treatments are broad-spectrum antibiotics for acute bacterial prostatitis (such as piperacillin-tazobactam, ceftriaxone, or ciprofloxacin), at least 4 weeks of fluoroquinolones for chronic bacterial prostatitis, and α-blockers for CP/CPPS with urinary symptoms.

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Multimedia

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Prostatitis, defined as infection, inflammation, or pain in the prostate, affects approximately 9.3% of men in their lifetime.[1] The National Institutes of Health (NIH) has defined categories of prostatitis as follows: acute bacterial prostatitis (type I), chronic bacterial prostatitis (type II), chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS; type III), and asymptomatic inflammatory prostatitis (type IV).[2] The first 3 categories of prostatitis are characterized by pelvic pain and urinary symptoms, such as urinary frequency and weak urinary stream, but each condition is diagnosed and treated differently. Asymptomatic inflammatory prostatitis is diagnosed incidentally during the evaluation of other conditions (such as prostate biopsy for cancer) and does not require further evaluation or treatment.[2] This Review summarizes current evidence on the evaluation and management of acute bacterial prostatitis, chronic bacterial prostatitis, and CP/CPPS (**Box**).

Methods

We searched PubMed for publications in English between January 1, 2000, and May 14, 2025, using the *prostatitis* Medical Subject Headings term. We prioritized randomized clinical trials (RCTs), meta-analyses, guidelines, and large population-based observational studies. Additional, relevant studies were identified with targeted searches. Of 2636 studies identified, 83 were included, consisting of 15 clinical trials, 4 meta-analyses, 33 observational or cohort studies

Box. Treatment and Management of Prostatitis

What Is First-Line Treatment for Acute Bacterial Prostatitis?
First-line treatment for acute bacterial prostatitis typically consists of a 2- to 4-week course of empirical broad-spectrum antibiotics, such as piperacillin-tazobactam, ceftriaxone, and ciprofloxacin, with adjustments based on culture result and sensitivity. Multidrug-resistant infections should be considered for men with post–prostate biopsy infections who have a fever and may require empirical antibiotics with broader spectrum, such as meropenem or amikacin.

What Is First-Line Treatment for Chronic Bacterial Prostatitis?
Chronic bacterial prostatitis should be treated with at least 4 weeks of oral fluoroquinolones. Trimethoprim-sulfamethoxazole, doxycycline, and fosfomycin may be considered as alternatives for patients with contraindications or bacterial resistance to fluoroquinolones.

How Is Chronic Prostatitis/Chronic Pelvic Pain Syndrome Managed?
The first-line treatment for men with chronic prostatitis/chronic pelvic pain syndrome and lower urinary tract symptoms is use of α-blockers, such as tamsulosin or alfuzosin. Other therapies, such as pregabalin, pollen extract, and nonsteroidal anti-inflammatory drugs, may be offered after shared decision-making discussions with patients. Multimodal treatment individualized to a patient's symptoms may be beneficial, including specialist referral for comorbid depression or anxiety, pelvic floor myalgia, and nonurologic chronic pain syndromes.

(22 cross-sectional, 11 longitudinal), 5 guidelines, 4 consensus statements, 2 questionnaire validation studies, 12 reviews, 6 US regulatory drug labels, and 2 preclinical studies evaluating antibiotic pharmacokinetics or pathophysiologic mechanisms.

Acute Bacterial Prostatitis

Acute bacterial prostatitis is defined as a urinary tract infection (UTI) that includes infection of the prostate gland. It can affect men of any age.[3,4]

Epidemiology and Risk Factors

The age-specific incidence of acute prostatitis is 3.2 to 3.6 per 1000 person-years between ages 20 and 40 years and 5.4 per 1000 person-years between ages 70 and 79 years.[5] Risk factors for acute prostatitis include cystoscopy, urethral catheterization, prostate biopsy, urinary obstruction (eg, benign prostatic hyperplasia, strictures), anal intercourse without condom use, immunosuppression, and neurogenic bladder, defined as dysfunction of the bladder or urethral sphincter related to neurologic disorders (eg, multiple sclerosis, stroke, spinal cord injury).[6]

Pathophysiology and Microbiology

Acute bacterial prostatitis can develop from an infection that ascends the urethra to the prostate, reflux of contaminated urine into the ejaculatory or prostatic ducts, or bacterial seeding of the urinary system during urethral manipulation or prostate biopsy. Gram-negative pathogens are the etiology in 80% to 97% of patients,[3,4,7] including *Escherichia coli* (52%-88% of cases), *Pseudomonas* (3%-16%), *Proteus* (3%-6%), *Klebsiella* (2%-10%), and *Enterococcus* (1%-6%).[3,4,7] Gonorrhea and chlamydia cause less than 1% of cases.[3,4]

Presentation

Men with acute prostatitis typically have fever and chills, pelvic pain, and sudden onset of urinary frequency, urinary urgency, and dysuria. Approximately 10% to 23% of patients experience urinary retention.[3,4,7] Acute prostatitis can develop spontaneously in healthy men or occur after urinary manipulation or prostate biopsy. The latter is associated with bacteremia and multidrug-resistant pathogens.[8]

Differential Diagnosis, Clinical Assessment, and Diagnosis

The differential diagnosis for sudden-onset urinary symptoms in men includes acute bacterial prostatitis, cystitis, pyelonephritis, epididymo-orchitis, and sexually transmitted infections (STIs). Cystitis causes urinary frequency, urinary urgency, and dysuria without fever and chills. Pyelonephritis presents with fever and chills, malaise, and flank pain. Epididymo-orchitis presents with testicular enlargement, induration, and tenderness. A gentle digital rectal examination reveals prostatic edema and tenderness in 77% to 90% of men with acute bacterial prostatitis,[3,4] which distinguishes acute prostatitis from a UTI without prostatitis. Unlike cystitis or STIs, acute bacterial prostatitis is typically associated with fever and chills and malaise. If sepsis is present, flank pain and costovertebral tenderness suggest pyelonephritis over prostatitis.

The evaluation of acute bacterial prostatitis should include a urine culture before antibiotics are administered to identify the bacterial strain responsible for the infection and determine the sensitivity of the bacteria to antibiotics. A definitive diagnosis is based on urine culture. However, UTI may be suggested if the urinalysis is positive for nitrites (sensitivity, 55%-58%; specificity, 90%-94%), leukocyte esterase (sensitivity, 81%-83%; specificity, 67%-71%), or both (sensitivity, 50%-52%; specificity, 93%-97%).[9] For patients with risk factors for STIs, such as at least 2 sexual partners within fewer than 6 months[10] or urethral discharge, urine should be evaluated for gonorrhea and chlamydia.[3] Blood cultures should be obtained for patients with fever because 21% of patients with acute bacterial prostatitis have bacteremia.[11] Prostate-specific antigen (PSA) is not indicated during evaluation. Signs and symptoms of urinary retention, such as urinary urgency, small-volume voiding (<100 mL per void), palpable or tender bladder, or urinary incontinence, should be further evaluated with a postvoid residual measurement obtained through ultrasonography or bladder scan with the patient supine after an attempt to completely void. Approximately 2.7% to 6% of men with acute bacterial prostatitis develop a prostatic abscess,[3,4,7] which should be considered in men who have immunosuppression or HIV, high fever, poor response to appropriate antibiotics, or delayed treatment (>7 days).[12] For these individuals, prostate abscess can be evaluated with a computed tomographic scan.

Treatment for Acute Bacterial Prostatitis

Antibiotics are the primary treatment for acute prostatitis, although the proportion of patients requiring intravenous antibiotics is unknown. To our knowledge, no studies have identified specific factors that determine which patients require intravenous

antibiotics to improve their outcome for acute bacterial prostatitis. Intravenous antibiotics and hospitalization for monitoring for clinical deterioration (eg, hemodynamic instability, persistent or worsening fever, leukocytosis) should be considered for people with sepsis, poor oral intake, recent prostate biopsy, prior multidrug-resistant infection, and infection that is not responding to oral therapy after 48 to 72 hours of antibiotic therapy guided by culture susceptibility data.[13] Oral antibiotics may be considered for men without signs or symptoms of sepsis, nausea or vomiting, recent prostate biopsy, or risk of multidrug-resistant pathogens.

Empirical antibiotic treatment should be selected according to local antibiotic resistance patterns, a history of a recent prostate biopsy (if performed), and patient-specific culture susceptibility or resistance data during the last 1 to 2 years, if available. A 2024 consensus statement and corresponding systematic review concluded that no high-quality data exist to guide antibiotic selection for acute bacterial prostatitis treatment.[14] When empirical intravenous antimicrobial therapy is warranted, broad-spectrum penicillin, such as piperacillin-tazobactam; third-generation cephalosporins, such as ceftriaxone; and fluoroquinolones, such as ciprofloxacin or levofloxacin, have been recommended.[15] An aminoglycoside, such as gentamicin, may be added if multidrug-resistant infection is suspected.[15] Appropriate empirical oral therapy for acute bacterial prostatitis includes ciprofloxacin, levofloxacin, or trimethoprim-sulfamethoxazole. For febrile infections after prostate biopsy, the American Urological Association recommends carbapenems (eg, meropenem), amikacin, or second- or third-generation cephalosporins (eg, cefuroxime or ceftriaxone, respectively).[16] An analysis of 258 patients admitted to the hospital during 2006 to 2010 for *E coli* bacteremia reported that patients admitted after prostate biopsy (n = 47) had significantly higher resistance to ciprofloxacin (62% vs 14%; $P < .001$) and trimethoprim-sulfamethoxazole (60% vs 26%; $P < .001$) than those with *E coli* bacteremia from other causes.[17] Among patients after prostate biopsy, the study showed low resistance rates to carbapenems (0%), amikacin (0%), and second- or third-generation cephalosporins, such as cefuroxime (15%) and ceftriaxone (11%). After improvement of fever, urinary symptoms, or both, intravenous therapy, if used, can be transitioned to oral antibiotics. Susceptibility testing should be used to narrow the antibiotic spectrum and direct appropriate treatment.

No high-quality data have demonstrated the ideal duration of antibiotics for acute bacterial prostatitis. Typically, 2 to 4 weeks of antibiotics is prescribed.[14] A clinical trial evaluated 72 men with a UTI associated with fever, 65 of whom had transient increases in PSA level or prostate volume, suggestive of prostatitis.[18] Men were randomized to either 2 weeks (n = 38) or 4 weeks (n = 34) of ciprofloxacin. The clinical trial reported clinical cure rates of 92% for 2 weeks vs 97% for 4 weeks of treatment (95% CI for difference, −5% to 15%).[18]

For men with acute bacterial prostatitis and urinary retention due to an inflamed, edematous prostate obstructing the urethra, a urinary catheter is indicated to relieve retention-related discomfort and drain infected urine. A multidisciplinary expert panel on the management of urinary retention in adult inpatients concluded that urinary catheterization was appropriate for postvoid residual measurements greater than or equal to 500 mL for asymptomatic patients and greater than or equal to 300 mL for patients with urinary urgency, small-volume voids (<100 mL per void), suprapubic fullness or discomfort, or acute urinary incontinence.[19] There are no high-quality data available regarding the most optimal method of catheterization (urethral or suprapubic catheterization). Urethral catheterization is typically more practical because suprapubic drainage requires a urologist or interventional radiologist and the procedure is associated with a 0% to 2.7% risk of bowel injury.[20,21]

Chronic Bacterial Prostatitis

Chronic prostatitis is composed of chronic bacterial prostatitis and CP/CPPS. Chronic bacterial prostatitis is defined as a persistent bacterial infection of the prostate despite antibiotic therapy, whereas CP/CPPS is characterized by chronic pelvic pain diagnosed after causes of other symptoms are excluded, such as cancer, UTI, urinary obstruction (such as urethral stricture or benign prostatic hyperplasia), or neurogenic bladder. Chronic bacterial prostatitis composes 4% to 10% of chronic prostatitis diagnoses.[22-24] Remaining episodes of chronic prostatitis are typically due to CP/CPPS.[22,23] Chronic bacterial prostatitis usually presents as recurrent UTIs with bacterial persistence (**Table 1**), defined by multiple urine cultures with susceptibilities that grow the same bacterial strain. Unlike acute bacterial prostatitis, chronic bacterial prostatitis is not associated with fever or chills. Chronic bacterial prostatitis and CP/CPPS may present with chronic pelvic pain; however, in CP/CPPS, UTI is absent.

Epidemiology and Risk Factors

Physician-diagnosed chronic prostatitis is infrequent in patients younger than 50 to 60 years.[5] Risk factors for chronic bacterial prostatitis include prior acute bacterial prostatitis,[5] urethral surgery or catheterization, urinary stasis, unprotected anal intercourse, and genitourinary tuberculosis, which occurs in 2% to 20% of patients with pulmonary tuberculosis.[25]

Pathophysiology and Microbiology

Chronic bacterial prostatitis may be caused by inadequate treatment of acute bacterial prostatitis or poor antibiotic penetration into the prostate from inappropriate antibiotic selection.[6] Up to 85% of bacteria causing chronic bacterial prostatitis produce biofilms, which are bacterial collections making extracellular polysaccharide matrices, conferring protection against antibiotics.[26] Although extensive whole gland inflammation is present in acute bacterial prostatitis, chronic bacterial prostatitis is characterized by patchy, fibrotic areas of chronic inflammation that reduce antibiotic diffusion and focal colonies of bacteria in biofilms that protect against antibiotic penetration.[27] Gram-negative organisms, such as *E coli, Enterobacter, Pseudomonas,* and *Klebsiella,* cause approximately 74% of chronic bacterial prostatitis cases, with *E coli* causing approximately 66% of cases.[23] Although *Enterococcus* can also cause chronic bacterial prostatitis,[28] high-quality data are limited on whether other gram-positive organisms, such as streptococci, reflect actual infections or skin contamination. The ability for *Chlamydia,* a cause of urethritis and STIs, to cause a prostatic infection is uncertain because the detection of chlamydia on prostatic fluid samples may reflect contamination of the prostatic specimen from the urethra rather than prostatic infection by chlamydia. However, treatment of prostatitis attributed to chlamydia is associated with symptomatic improvement and PSA reductions, reflecting decreased inflammation.[29]

Table 1. Presentation, Diagnosis, and Evaluation of Acute Bacterial Prostatitis, Chronic Bacterial Prostatitis, and Chronic Prostatitis/Chronic Pelvic Pain Syndrome

Name	Acute bacterial prostatitis	Chronic bacterial prostatitis	Chronic prostatitis/ chronic pelvic pain syndrome
Definition	Acute UTI specifically infecting prostate	Persistent bacterial infection of prostate from same bacterial strain, causing recurrent UTIs	Pelvic pain (≥3 mo) without evidence of infection, cancer, urinary obstruction/retention, neurogenic bladder
Typical symptoms	Abrupt urinary symptoms (dysuria, frequency, urgency) Fever/chills, malaise With or without urinary retention	Recurrent UTIs Asymptomatic or pelvic pain/LUTS between UTIs	Pelvic pain of perineum, suprapubic region, testicle, or penis or pain with voiding or ejaculation With or without LUTS or sexual dysfunction
Diagnosis	Urinalysis: leukocyte esterase and/or nitrites detected UCx: bacterial growth, often gram negative DRE: prostatic tenderness/edema	Identifying persistent bacteria with similar or identical sensitivities on a urine culture compared with prior urine cultures 4- or 2-glass test	No definitive diagnostic test available Exclude treatable alternative conditions (infection, cancer, urinary obstruction/retention, neurogenic bladder) with pathologies with history and physical examination, UCx, and PVR
Evaluation	PVR to evaluate for urinary retention Blood cultures if febrile Pelvic CT for prostatic abscess if immunosuppressed, high fever, poor response to appropriate antibiotics, delayed treatment	PVR to evaluate for urinary retention Pelvic CT for prostatic abscess if immunosuppressed or persistent pelvic discomfort despite appropriate antibiotic therapy	Review of systems LUTS Sexual dysfunction Anxiety, depression, stress, difficulty coping Nonurologic chronic pain syndromes NIH-CPSI score DRE for prostate/pelvic floor tenderness
Microbiology	Primarily gram-negative organisms	Primarily gram-negative organisms	None

Abbreviations: CT, computed tomography; DRE, digital rectal examination; LUTS, lower urinary tract symptoms; NIH-CPSI, National Institutes of Health Chronic Prostatitis Symptom Index; PVR, postvoid residual test; UCx, urine culture; UTI, urinary tract infection.

Presentation

Chronic bacterial prostatitis has a more indolent course than acute bacterial prostatitis and should be considered as a diagnosis for patients with recurrent UTIs with the same organism with similar or identical resistance patterns despite antibiotics.[2,30] Between UTIs, men with chronic bacterial prostatitis may be asymptomatic or may have persistent pelvic pain, lower urinary tract symptoms, or both.

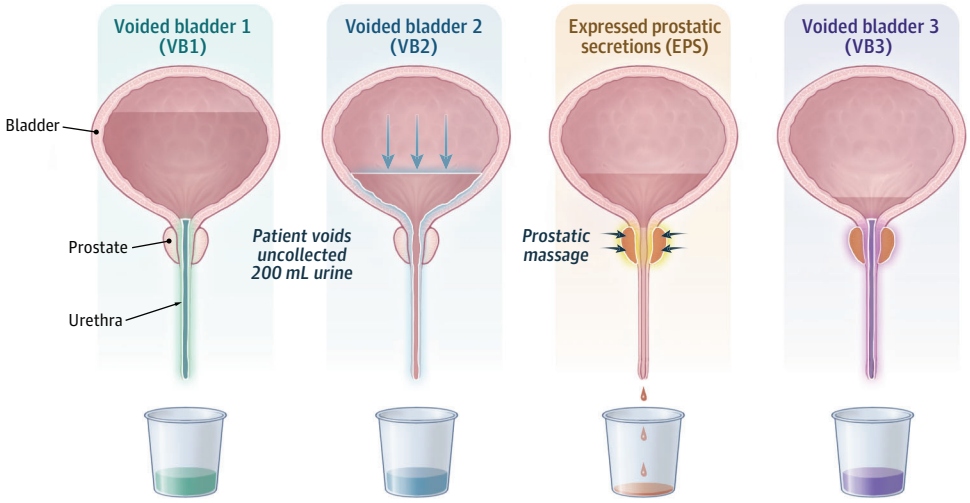
Differential Diagnosis, Clinical Assessment, and Diagnosis

The differential diagnosis includes benign prostatic hyperplasia, urinary retention, urethral stricture, kidney stones, urologic or rectal malignancy, skin or scrotal infection, and STIs. A digital rectal examination may help evaluate for benign prostatic hyperplasia and prostate cancer by assessing for prostatic enlargement and induration or nodularity, respectively. Penoscrotal examination should evaluate for testicular or epididymal tenderness, induration, or swelling, indicating epididymo-orchitis. Postvoid residual measurement via bladder scan or ultrasonography can evaluate for urinary retention. Computed tomography or ultrasonography may help evaluate hematuria, flank pain, or kidney dysfunction and should be considered if history suggests possible kidney or bladder stones or ureteral obstruction. Pelvic computed tomography may help evaluate for prostatic abscess in patients who are immunocompromised or who have persistent pelvic discomfort despite an appropriate course of antibiotics for chronic bacterial prostatitis.[31] Prostate-specific antigen level is unhelpful for diagnosing chronic bacterial prostatitis and may be elevated from prostate inflammation. If PSA testing is indicated for prostate cancer evaluation but infection is suspected, PSA level should be obtained after infection is treated. Testing for gonorrhea and chlamydia, typically with nucleic acid amplification testing in a urine sample, should be considered if urethral discharge or pruritus or dysuria is present.

The 4-glass test involves culturing 4 urinary specimens and is the criterion standard for the diagnosis of chronic bacterial prostatitis (**Figure**). The test is currently infrequently performed because it is difficult to carry out but may be used to distinguish chronic bacterial prostatitis from CP/CPPS.[32-34] Before testing, a clean-catch midstream urine culture should be sterile because acute infections can confound test interpretation.[30] With a full bladder, the patient voids, and the first 10 mL of urine is collected as a urethral specimen (voided bladder 1). After approximately 200 mL of urine is voided but not collected, a second 10 mL is collected (voided bladder 2). Prostatic massage is then performed for approximately 1 minute, compressing each prostate lobe laterally to medially and from base to apex. After massage, expressed prostatic secretions spontaneously exit the meatus and are obtained. The patient then voids again, with the first 10 mL (voided bladder 3) collected as a prostatic specimen.[35] Voided bladder specimens 1 through 3 and expressed prostatic secretions are sent for culture. Microscopy of specimens has not been shown to affect clinical management.[1] Routine STI testing of 4-glass specimens is not supported by high-quality evidence.

Chronic bacterial prostatitis is diagnosed in patients with recurrent UTIs when expressed prostatic secretions and voided bladder 3 (prostate) cultures grow bacteria, whereas voided bladder 1 and 2 (urethra/bladder) cultures are sterile (Figure). If voided bladder 1, 2, or both cultures show bacterial growth, expressed prostatic secretions, voided bladder 3, or both cultures must have 10 times higher

Figure. The 4-Glass and 2-Glass Tests for Localizing Prostatic Pathogens



4-Glass test culture results

Diagnosis		First voided 10 mL urine (urethral)	Premassage midstream 10-mL specimen (bladder)	EPS postmassage (prostate)	First 10 mL urine voided postmassage (prostate)
Chronic bacterial prostatitis	Bacterial growth only from prostatic specimens or greatest in prostatic specimens	Negative or, if positive, less bacterial growth than EPS/VB3	Negative or, if positive, less bacterial growth than EPS/VB3	**Positive**	**Positive**
Chronic prostatitis/ chronic pelvic pain syndrome (CP/CPPS)	No bacterial growth in any specimen	Negative	Negative	Negative	Negative
Urethritis or urethral colonization	Bacterial growth greatest in urethral specimen	**Positive with greatest bacterial growth**	Negative or, if positive, less bacterial growth than VB1	Negative or, if positive, less bacterial growth than VB1	Negative or, if positive, less bacterial growth than VB1
Cystitis	Bacterial growth greatest from bladder specimen or significant bacterial growth in all specimens	**Positive**	**Positive, typically with greatest bacterial growth compared with other specimens**	**Positive**	**Positive**

2-Glass test culture results

Diagnosis		Premassage midstream 10-mL specimen (bladder) VB2	First 10 mL urine voided postmassage (prostate) VB3
Chronic bacterial prostatitis	Bacterial growth only in prostatic specimen or greatest in prostatic specimen	Negative or, if positive, less bacterial growth than VB3	**Positive**
CP/CPPS	No bacterial growth in any specimen	Negative	Negative

The 4-glass test begins with a full bladder. Ten milliliters of urine is voided, collecting any bacteria localized in the urethra (VB1 specimen). The specimen is cultured. The patient is then asked to void approximately 200 mL to wash out possible urethral organisms. Afterward, a 10-mL midstream void is collected, representing bladder urine (VB2 specimen), which is cultured. The prostate is massaged with a gloved finger inserted into the rectum. Secretions from the prostate that spontaneously exit the meatus are collected as EPS and cultured. Bacteria growing in an EPS culture originate from the prostate. Residual prostatic fluid remains after massage. The patient voids 10 mL after massage to collect residual fluid or organisms originating from the prostate (VB3 specimen). The specimen is cultured. If bacteria are found in VB1, VB2, or both, cultures from EPS, VB3, or both must have 10 times greater bacterial counts to be diagnostic of chronic bacterial prostatitis.

bacterial counts to diagnose chronic bacterial prostatitis. Chronic prostatitis symptoms with negative culture results in all 4 specimens may suggest CP/CPPS. Urethritis or asymptomatic urethral colonization is suggested with significant growth in only voided bladder specimen 1 and minimal to no growth in the other 3 specimens.[36] Cystitis is suspected if voided bladder specimen 2 has significantly more growth, such as at least 10 times higher bacterial counts, than other cultures or if all specimens have bacterial growth; however, acute cystitis should be ruled out with a preprocedural urine culture and treated before the 4-glass test is performed. When chronic bacterial prostatitis is suspected but testing is confounded by cystitis, the 4-glass test should be repeated after β-lactam or nitrofurantoin therapy. These medications do not penetrate the prostate, which causes a possible false-negative result on repeat testing.[30]

A 2-glass test, which consists of only voided bladder specimens 2 and 3, collected before and after prostatic massage, has been proposed as an alternative to the 4-glass test because it is easier to collect (Figure). In the setting of recurrent UTIs, a 2-glass test requires greater than or equal to 10 times more bacteria in the voided bladder 3 specimen than the voided bladder 2 specimen to diagnose chronic bacterial prostatitis.[37] The 2-glass test

has sensitivity of 44% to 54% and specificity of 100% compared with the 4-glass test but has 96% to 98% accuracy.[37] Semen culture may increase the sensitivity of pathogen detection when added to a 4-glass test; however, organisms in a semen culture may reflect skin contamination.[38]

Treatment

Acute bacterial prostatitis is associated with a diffusely inflamed prostate gland that is permeable to antibiotics commonly used for UTI treatment such as penicillins and cephalosporins.[39] In contrast, few antibiotics adequately penetrate prostatic tissue to effectively treat chronic bacterial prostatitis. Because active transport mechanisms of antibiotics into the prostate gland are lacking, prostatic diffusion is highest when antibiotic agents attain high plasma concentration, have high lipid solubility, and have minimal protein binding.[39] Fluoroquinolones (such as levofloxacin or ciprofloxacin), trimethoprim-sulfamethoxazole, doxycycline, and fosfomycin can penetrate noninflamed prostatic tissue.[40]

Fluoroquinolones, such as ciprofloxacin and levofloxacin, are first-line therapy for chronic bacterial prostatitis because they are effective against multiple infectious causes of prostatitis, including *E coli, Pseudomonas,* and *Klebsiella*. There are insufficient data to determine the optimal duration of therapy. A minimum of 4 weeks of fluoroquinolones is recommended for chronic bacterial prostatitis.[15,35,41] Trimethoprim-sulfamethoxazole, doxycycline, or fosfomycin may be used for 4 to 6 weeks if fluoroquinolone alternatives are necessary; however, there are no high-quality data to support these treatments. Fosfomycin may be considered for multidrug-resistant pathogens.

CP/CPPS

Chronic prostatitis/chronic pelvic pain syndrome is characterized by urogenital pain or discomfort, typically lasting at least 3 months. It is associated with urinary symptoms, such as urinary frequency, and is diagnosed after exclusion of other causes of symptoms, such as urethritis, cancer, UTI, urethral stricture, or neurogenic bladder (Table 1).[2]

Epidemiology and Risk Factors

Ninety percent of people with chronic prostatitis symptoms have CP/CPPS.[24] Approximately 267 000 men in the United States receive a diagnosis of CP/CPPS annually.[42] Risk of this condition increases after age 50 years.[5,42] Other risk factors for CP/CPPS are unclear.

Pathophysiology

Although the disease is named chronic prostatitis, only 33% of patients with CP/CPPS have histopathologic inflammation in the prostate,[43] and presence of prostatic inflammation is not associated with worse symptom severity or quality of life.[44] The pathophysiology of CP/CPPS remains unclear. Alternative biologic pathways may contribute to CP/CPPS symptoms. For example, when exposed to high-temperature stimuli at the perineum, men with CP/CPPS perceive greater heat sensation compared with healthy control participants, suggesting that the sensory nervous system may contribute to CP/CPPS symptoms.[45] Men with CP/CPPS are more likely to have chronic pain syndromes (eg, fibromyalgia [4%], chronic fatigue syndrome [3%], irritable bowel syndrome [22%]), reflecting increased pain sensitivity outside the pelvis.[46]

Presentation

Chronic prostatitis/chronic pelvic pain syndrome presents as pain localized to the perineum, suprapubic region, testicle, and penis or pain with ejaculation or voiding.[47] Many men with CP/CPPS report urinary frequency (63%-84%) or weak urinary stream (49%-73%),[48] erectile dysfunction (15%-41%), premature ejaculation (64%-77%), and ejaculatory pain (58%-74%).[1,49]

Clinical Assessment and Diagnosis

The duration, severity, and localization of pelvic pain should be characterized, and patients should be evaluated for urinary symptoms, sexual dysfunction, and chronic pain syndromes, such as fibromyalgia or irritable bowel syndrome. Quality of life and functional impairment from CP/CPPS should be assessed. Men with CP/CPPS have higher rates of depression or anxiety and panic disorder than unaffected men (13% vs 4%).[50]

Validated questionnaires for CP/CPPS include the NIH Chronic Prostatitis Symptom Index (NIH-CPSI),[1,34,41] a 13-item questionnaire assessing pelvic pain, urinary symptoms (frequency, sense of incomplete emptying), and quality of life.[51] Scores range from 0 to 43 and consist of 3 subscores: pain (0-21), urinary symptoms (0-10), and quality of life (0-12). Higher scores indicate worse symptoms. A 6-point NIH-CPSI change in score on the 0- to 43-point scale is considered the minimum clinically important difference.[52,53]

Patients with CP/CPPS should be evaluated for signs and symptoms of UTI, urinary retention, inguinal hernia, skin or genital infections, and malignancy. Physical examination of the penis, scrotum, and inguinal region should assess for masses, bulges, erythema, edema, or tenderness. Areas of focal pain should be examined for edema, erythema, and tenderness that suggests soft tissue infection. Digital rectal examination should assess the prostate for nodularity, which may suggest cancer, and tenderness. The pelvic floor musculature, palpated lateral to the prostate and along the rectal wall, should be palpated for tenderness. A 2- or 4-glass test may be performed to differentiate CP/CPPS from chronic bacterial prostatitis.[34] Urinary urgency, small-volume voids (<100 mL per void), or a palpable or tender bladder should prompt a postvoid residual measurement to assess for urinary retention. Elevated postvoid residual measurement or urinary incontinence in the setting of neurologic disease may indicate neurogenic bladder, defined as dysfunction of the bladder or urethral sphincter related to neurologic disorders, such as multiple sclerosis, stroke, or spinal cord injury. Urine culture should be performed to rule out UTI. Prostate-specific antigen testing is not indicated but should be conducted if the digital rectal examination identifies nodularity or induration and should be conducted for patients with indications for prostate cancer screening based on age or history. If PSA level is obtained, elevations should not be attributed to CP/CPPS and should be further evaluated.[54] Testing for STIs may be performed if the patient has risk factors (eg, ≥2 sexual partners within ≤6 months),[10] urethral discharge or pruritus, or dysuria. Routine imaging is unnecessary for CP/CPPS diagnosis.

Table 2. Summary of Oral Therapies for Chronic Prostatitis/Chronic Pelvic Pain Syndrome[a]

Therapy	Examples	Mechanism of action	Summary of efficacy	Adverse effects
Antibiotics[a]	Levofloxacin 500 mg daily Ciprofloxacin 500 mg twice a day	Possible anti-inflammatory effect or treatment of undetected organisms	Only 2 of 4 meta-analyses found significant association with change in NIH-CPSI score, with variable clinical significance (ΔNIH-CPSI score difference, −9.7 to −2.43)	Levofloxacin and ciprofloxacin[55-57]: Tendinopathy/tendon rupture (0.14%-0.4%) Nausea (3%-7%), diarrhea (5%), vomiting (2%-5%) Headache (6%) QT-interval prolongation Contraindicated with aneurysm
α-Blockers	Tamsulosin 0.4 mg daily Alfuzosin 10 mg daily	Relaxation of prostatic and bladder neck smooth muscle	Meta-analyses: significant association with change in NIH-CPSI score (difference from placebo, −10.8 to −4.8)	Tamsulosin and alfuzosin[58,59]: Dizziness, orthostatic hypotension (6%-17%) Ejaculatory dysfunction (up to 18%)
Anti-inflammatory drugs	NSAIDs: diclofenac 50 mg 3 times a day, ibuprofen 400 mg 4 times a day	Reduction in prostatic inflammation	Meta-analyses: associated with significant but small improvement (ΔNIH-CPSI score difference, −2.5 to −1.7)	NSAIDs: nephrotoxicity (1%-5%),[60] peptic ulcer disease, platelet inhibition
Pregabalin	Pregabalin 50-200 mg 3 times a day	Neuromodulation of pain pathways	RCT did not meet primary end point, but more responders with pregabalin (31.2% vs 18.9% in placebo; *P* = .02)	Pregabalin[61]: Dizziness (30%) Sedation (23%) Weight gain (9%) Blurred vision (7%) Peripheral edema (6%) Seizure with rapid discontinuation Suicidal thoughts/behavior (0.4%)
Pentosan polysulfate	Pentosan polysulfate 100 mg 3 times a day	Protective effect on bladder epithelium, possible anti-inflammatory	RCT: more patients with moderate/marked improvement (36.7% vs 17.8% in placebo; *P* = .04)	Pentosan polysulfate[62,63]: Reversible alopecia (4%) Nausea (4%), diarrhea (4%) Vision change secondary to macular eye disease with long-term use (0.6%-5.4%)
Phytotherapy	Quercetin 500 mg twice a day Pollen extract RCT: 2 capsules (each containing 63 mg extract) every 8 h	Possible anti-inflammatory effect or smooth muscle relaxation	Quercetin RCT: 67% response rate (vs 20% in placebo; *P* = .001) Pollen extract (*Secale cereale*) RCT: change in NIH-CPSI score difference = −2.49 (*P* = .013)	Quercetin[64]: headache (3%), rash (3%), paresthesia (3%) Pollen extract[65]: gastrointestinal upset (1%)

Abbreviations: NIH-CPSI, National Institutes of Health Chronic Prostatitis Symptom Index; NSAID, nonsteroidal anti-inflammatory drug; RCT, randomized clinical trial.

[a] High-quality evidence does not support that antibiotics have a clinically important effect on symptoms, and guidelines do not recommend antibiotics.

Treatment

The American Urological Association guidelines for CP/CPPS recommend initial nonsurgical therapy based on shared decision-making.[34] Nonsurgical therapy consists of α-blockers, such as alfuzosin, nonopioid analgesics, such as ibuprofen, and neuropathic medications, such as pregabalin (**Table 2**),[55-65] and multimodal therapy is often needed. Referral to the appropriate specialist is advised for psychosocial impairment and chronic nonurologic pain, such as fibromyalgia or irritable bowel syndrome. Pelvic floor myalgia or tenderness, observed in 27% to 64% of men with CP/CPPS, may be treated with physiotherapy.[66,67]

Antibiotics

Recent American Urological Association guidelines do not recommend antibiotic therapy as a treatment option for CP/CPPS.[34] High-quality data supporting antibiotics to treat CP/CPPS are lacking despite that antibiotics are commonly used in clinical practice. A network meta-analysis of 13 RCTs (n = 1352 people with CP/CPPS) reported that antibiotics (ciprofloxacin, levofloxacin, or tetracycline) were associated with a mean NIH-CPSI score difference of −9.7 over placebo (*P* < .001).[68] A Cochrane review (5 RCTs; 372 participants) concluded that antibiotics compared with placebo were associated with NIH-CPSI score improvements of −2.43 (95% CI, −4.72 to −0.15), below the minimum clinically important difference of 6.[69] A meta-analysis of 2 RCTs of ciprofloxacin and levofloxacin (n = 167 with CP/CPPS) did not find a significant difference in change in NIH-CPSI score between antibiotics and placebo (NIH-CPSI score mean difference = −1.80; 95% CI, −5.88 to 2.27).[70] Another meta-analysis of 4 trials (n = 245 with CP/CPPS) that compared antibiotics (levofloxacin, ciprofloxacin, mepartricin, or tetracycline) with placebo found that antibiotic therapy was not associated with significant improvement in NIH-CPSI score (mean difference = −7.82; 95% CI, −15.64 to 0.01).[71] To minimize antibiotic resistance and adverse effects, antibiotics should not be prescribed unless a culture result is positive.

α-Blockers

In RCTs, α-blockers, such as tamsulosin[72,73] and alfuzosin, improved symptoms in people with CP/CPPS compared with placebo.[74] However, a trial of 272 men with CP/CPPS randomized to 12 weeks of alfuzosin or placebo reported no significant differences in the primary outcome (≥4-point reduction in NIH-CPSI score; 49.3% in each group; $P = .99$) at 12-week follow-up.[75] A second RCT of 196 men with CP/CPPS who were randomized to tamsulosin, ciprofloxacin, both drugs, or placebo reported no difference in NIH-CPSI score (primary outcome) between the tamsulosin groups (tamsulosin alone and tamsulosin + ciprofloxacin) vs the no tamsulosin groups (placebo and ciprofloxacin alone) (−4.4 vs −4.8; $P > .2$) at 6-week follow-up.[76] A meta-analysis of 8 RCTs (n = 770 with CP/CPPS) reported that, compared with placebo, α-blockers were associated with a statistically significant NIH-CPSI score change (mean difference = −4.8; 95% CI, −7.1 to −2.6); however, the effect size was below the 6-point minimum clinically important difference threshold.[70] A network meta-analysis of 8 RCTs with 395 participants who had CP/CPPS concluded that α-blockers (terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin) compared with placebo were associated with a mean difference NIH-CPSI score change of −10.8 ($P < .001$).[68] A 2020 Cochrane review of 18 RCTs with 1524 patients with CP/CPPS concluded that α-blockers compared with placebo were associated with an NIH-CPSI score mean difference of −5.01 (95% CI, −7.41 to −2.61), which was smaller than the 6-point minimum clinically important difference threshold. In this study, α-blockers were associated with increased risk of adverse effects (eg, dizziness, orthostatic hypotension) (placebo: 94 per 1000 persons; α-blockers: 56 more per 1000 persons [95% CI, 8-126]).[69] Although data supporting α-blocker monotherapy are inconsistent, men with bothersome lower urinary tract symptoms may experience benefit, but people without improvement after 4 to 6 weeks should discontinue α-blocker therapy.[1,41]

Anti-Inflammatory Drugs

Anti-inflammatory drugs, such as glucocorticoids,[77] zafirlukast,[78] rofecoxib,[53] and diclofenac,[79] have typically not improved symptoms in patients with CP/CPPS. Compared with placebo, anti-inflammatory drugs were associated with statistically significant but not clinically significant symptom improvement in a network meta-analysis including 5 RCTs (evaluating celecoxib, glycosaminoglycan, quercetin, pollen extract, and tanezumab vs placebo) with 191 men with CP/CPPS (NIH-CPSI score mean difference = −1.7; $P = .03$) and a 2020 Cochrane review of 7 RCTs comparing anti-inflammatories (prednisone and nonsteroidal anti-inflammatory drugs, including ibuprofen, diclofenac, celecoxib, dexketoprofen, and thiocolchicoside) with placebo among 372 men who had CP/CPPS (NIH-CPSI score mean difference = −2.5; 95% CI, −3.74 to −1.26).[68,69] These improvements were below the minimum clinically important threshold of 6.[68]

Analgesic Therapy

Narcotics should be avoided for patients with CP/CPPS to prevent addiction and other adverse effects. Acetaminophen or short-term nonsteroidal anti-inflammatory drugs, such as ibuprofen for 4 to 6 weeks, may be considered.[41] An RCT evaluated 6 weeks of pregabalin (n = 218) vs placebo (n = 106) in men with CP/CPPS.[80] The primary outcome, defined as a greater than or equal to 6-point decrease in NIH-CPSI score at 6 weeks, was not significantly different between pregabalin and placebo (47.2% vs 35.8%; $P = .07$).[80] The secondary outcome of NIH-CPSI score improvements, however, was significantly better with pregabalin vs placebo (mean NIH-CPSI score difference = −2.4; $P = .01$). Another secondary outcome, the rate of men reporting moderate or marked improvement on the Global Response Assessment questionnaire, was better with pregabalin vs placebo (31.2% vs 18.9%; $P = .02$).

Phytotherapies

Phytotherapies, such as quercetin (an antioxidant with anti-inflammatory properties) and pollen extract, are plant-based remedies. A trial of 30 men with CP/CPPS reported higher 1-month response (defined as 25% improvement in NIH-CPSI score) with quercetin vs placebo (67 vs 20%; $P = .001$).[64] Pollen extracts may have anti-inflammatory effects and cause smooth muscle relaxation.[81] In a placebo-controlled trial of 139 patients with CP/CPPS, the NIH-CPSI pain subscore and total score improvements were significantly greater with pollen extract *(Secale cereale)* compared with placebo (difference = −1.58 [$P = .009$] and −2.49 [$P = .013$], respectively) at 12 weeks.[65] Although phytotherapies are promising, their adoption into practice is limited by the small body of evidence, absence of Food and Drug Administration regulation, and concerns about supplement purity and potential contamination.

Pentosan Polysulfate

Pentosan polysulfate, an oral therapy for interstitial cystitis, has potential to reduce bladder pain and inflammation because it forms a protective layer over the bladder epithelium. An RCT of 100 men with CP/CPPS reported no significant differences in the primary end point of Clinical Global Improvement score (scale: −3 [markedly worse] to 3 [markedly better]; response defined as 2 or greater) at 16 weeks (1.0 vs 0.6; $P = .11$).[82] However, pentosan polysulfate had higher response rates than placebo (36.7% vs 17.8%; $P = .04$).[82] Patients should be cautioned that pigmentary maculopathy, consisting of difficulty reading, difficulty seeing in low-light environments, or blurred vision, was reported in approximately 0.6% to 5.4% of patients exposed to pentosan polysulfate at 7 years.[62,83]

Limitations

This review has several limitations. First, a formal quality assessment of evidence was not performed. Second, relevant studies may have been missed or omitted. Third, procedural interventions for prostatitis were not discussed.

Conclusions

Prostatitis includes acute bacterial prostatitis, chronic bacterial prostatitis, and CP/CPPS, each of which is diagnosed and treated differently. First-line treatments are broad-spectrum antibiotics for acute bacterial prostatitis (such as piperacillin-tazobactam, ceftriaxone, or ciprofloxacin), at least 4 weeks of fluoroquinolones for chronic bacterial prostatitis, and α-blockers for CP/CPPS with urinary symptoms.

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