Bacterial prostatitis

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Purpose of review
The review provides the infectious disease community with a urologic perspective on bacterial prostatitis. Specifically, the article briefly reviews the categorization of prostatitis by type and provides a distillation of new findings published on bacterial prostatitis over the past year. It also highlights key points from the established literature.

Recent findings
Cross-sectional prostate imaging is becoming more common and may lead to more incidental diagnoses of acute bacterial prostatitis. As drug resistance remains problematic in this condition, the reemergence of older antibiotics such as fosfomycin, has proven beneficial. With regard to chronic bacterial prostatitis, no clear clinical risk factors emerged in a large epidemiological study. However, bacterial biofilm formation has been associated with more severe cases. Surgery has a limited role in bacterial prostatitis and should be reserved for draining of a prostatic abscess or the removal of infected prostatic stones.

Summary
Prostatitis remains a common and bothersome clinical condition. Antibiotic therapy remains the basis of treatment for both acute and chronic bacterial prostatitis. Further research into improving prostatitis treatment is indicated.

Keywords
acute bacterial prostatitis, bacterial prostatitis, category I prostatitis, category II prostatitis, chronic bacterial prostatitis, male pelvic pain

INTRODUCTION

Prostatitis is a bothersome condition but carries potential for serious morbidity from sepsis, abscess, or fistula if insufficiently managed. Nearly one in six men report a history of prostatitis, resulting in over $84 million in annual medical expenditure [1,2]. Prostatitis exhibits a bimodal peak of incidence, with men between 20 and 40 years of age or older than 60 years afflicted most commonly [3]. The reasons for this distribution or potential for confounding by sexually transmitted infections are unknown. In over 90% of men with fever and urinary symptoms, prostatitis is the underlying condition in the absence of pyelonephritis symptoms [4]. With that, prostatitis accounts for nearly 8% of urologist visits [5]. Overall, prostatitis remains a common condition and research to improve its management would be beneficial.

This review provides a distillation of notable additions to the literature on prostatitis over the past year. It builds upon the journal's February 2014 review [6▪]. Additionally, it provides a brief overview of prostatitis categorization. To complete this manuscript, a PubMed query for 'prostatitis' was conducted and articles dated between January 2014 and August 2015 were identified among the first 600 search results. The titles of English language articles were examined and those pertaining to non-bacterial prostatitis, chronic pelvic pain, and animal or basic science models were excluded. After this, a total of 38 articles related to acute and chronic bacterial prostatitis were reviewed.

Prostatitis categorization scheme

The National Institutes of Health consensus classification of prostatitis (Table 1) divides the condition into four categories based upon clinical presentation [7]. These include acute (category I) and chronic (category II) bacterial prostatitis, as well as chronic prostatitis/pelvic pain syndrome (category III) and

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KEY POINTS

- Tailoring antibiotic treatment to culture-proven bacterial sensitivity is essential.
- Any chosen antibiotic must penetrate the prostate and reach therapeutic levels.
- Antibiotic resistance is increasingly problematic.
- The indications for surgery in managing prostatitis remain limited and very specific.

asymptomatic inflammatory prostatitis (category IV). To date, no data support the role of 'hidden' infection or atypical organisms in category III or IV prostatitis. As such, there is no role for antibiotic therapy in these conditions, despite many patients strongly believing a true infection exists and seeking out multiple practitioners to diagnose one.

CATEGORY I PROSTATITIS: ACUTE BACTERIAL PROSTATITIS

Acute bacterial prostatitis or National Institutes of Health category I prostatitis (CIP) is defined as an acute urinary tract infection (UTI) with prostatic involvement. Patients are usually febrile and may present with urinary retention. Infection results from bacteria ascending the urethra, reflux of contaminated urine into the prostatic ducts, direct introduction of bacteria during transrectal biopsy or urethral instrumentation, or hematogenous seeding. Causative organisms include *Escherichia coli* in most (65–80%) cases with *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Klebsiella* spp., *Serrita*, and *Enterobacter* spp. comprising the remainder [8–10]. With impaired immunity, other microorganisms like fungi (*Cryptococcus* spp. or *Histoplasma* spp.) and Gram-positive (skin flora) bacteria, as well as *Mycobacterium tuberculosis* may be implicated.

Diagnosis

Men typically present with systemic symptoms (malaise, fevers, chills, and sweats), evidence of UTI (dysuria, urinary frequency, and urinary urgency), and focal symptoms (pelvic or perineal pressure) suggestive of prostatic involvement. Obstructive urinary symptoms (weak stream, dribbling, and hesitancy) may also present, with urinary retention possible. Commonly, an intervention such as transrectal ultrasound-guided prostate biopsy may precede presentation. A sexual history may indicate the risk of a sexually transmitted infection.

Rectal examination almost always shows a tender prostate. However, caution is warranted during digital rectal examination, as aggressive prostate palpation can release bacteria and inflammatory cytokines triggering an abrupt clinical decompensation, thus contraindicating prostatic massage. Serum laboratory assessment in CIP generally reveals leukocytosis. During infection, prostate-specific antigen is invariably elevated and has no diagnostic value for prostate cancer. Urinalysis and urine culture are essential and blood cultures are indicated for a clinical suspicion of sepsis. All men should have a postvoid residual urine volume measurement, as urinary retention may not be evident. Imaging with computed tomography (CT) scan or ultrasound may reveal an enlarged and inflamed heterogeneously appearing prostate, but is not necessary unless concern for prostatic abscess exists.

Table 1. National Institutes of Health consensus definition and classification of prostatitis

National Institutes of Health consensus definition and classification of prostatitis	
Category I	Acute bacterial prostatitis
Category II	Chronic bacterial prostatitis
Category III	Chronic prostatitis/chronic pelvic pain syndrome
Category IV	Asymptomatic inflammatory prostatitis

Treatment

Successful treatment of CIP rests upon completion of a sufficient course of appropriate antibiotic. The agent used must have demonstrated sensitivity against the infecting organism and also reach therapeutic levels in the prostate. During acute infection with prostatic inflammation, most antibiotics do penetrate the prostate (except nitrofurantoin) [11]. Without evidence of systemic disease or urinary retention, an oral antibiotic for 2–4 weeks is generally sufficient. Typical agents include a fluoroquinolone or trimethoprim-sulfamethoxazole, with the quinolones reaching 3–4 times higher intraprostatic concentrations than beta-lactam antibiotics [10]. Repeat urine culture during therapy to assess for bacterial eradication is necessary, if clinical improvement is not seen, however, all cases of CIP should have a confirmatory urine culture about 1 week following antibiotic completion to ensure bacteriologic cure.

The acutely ill patient warranting hospitalization for prostatitis will present a clinical picture of sepsis or a systemic inflammatory response syndrome. Urinary tract decompression is often required for urinary retention with grossly infected urine via a short-term indwelling urethral catheter,

clean intermittent urethral catheterization, or a suprapubic catheter. Parenteral antibiotic therapy is indicated until clinical stabilization is achieved, with the chosen regimen guided by local antibiogram results. Typical treatment consists of empiric broad coverage with a fluoroquinolone and aminoglycoside, possibly in combination with a penicillin or cephalosporin (second/third generation). Based upon blood and urine culture results, a transition to oral antibiotics can be completed.

Additional treatments to address pain, inflammation, and anatomic complications may be warranted in some patients. In instances of persistent or very slowly improving CIP, the presence of prostatic abscess must be considered. Cross-sectional imaging with CT can be helpful identifying an abscess and facilitating transurethral or transperineal drainage. A transrectal ultrasound may also identify prostatic abscesses, and if done under anesthesia, can accommodate concomitant transrectal drainage. The pain and discomfort accompanying prostatitis is thought to stem from local inflammation. The use of nonsteroidal anti-inflammatory medications can markedly reduce prostatitis-related pain [12]. In addition, the administration of an alfa-1-adrenergic antagonist has also been found to aid in prostatitis-related lower urinary tract symptom relief [13].

New developments

Several reports of imaging in prostatitis have recently been published, likely secondary to increases in the use of multiparametric MRI for prostate cancer diagnosis and active surveillance. A description of Bacillus Calmette–Guerin (BCG) granulomatous prostatitis, secondary to BCG therapy for bladder cancer, highlighted nearly identical imaging characteristics of this condition and prostate cancer [14]. Another study detailed the imaging characteristics that differentiate the lesions [15]. Subsequently, a review of MRI findings in acute and chronic prostatitis, as well as prostate cancer, detailed the challenges of discriminating between these clinical entities [16▪]. Reports of radiotracer imaging in prostatitis were also published, with one describing positron emission tomography (PET)/CT to diagnose and observe CIP resolution [17]. A separate report noted incidental cases of BCG granulomatous prostatitis on PET/CT and reviewed typical PET/CT findings in acute prostatitis [18]. Taken together, these new reports of imaging in prostatitis suggest the incidence of its incidental detection may increase as prostate MRI becomes more common, although true CIP presents as a symptomatic condition.

Urologic procedures may incite UTIs and prostatitis. A case report detailed a case of *Salmonella typhimurium* prostatitis in a spinal cord injury patient performing clean intermittent urethral catheterization and discussed the role of perineal colonization and bacterial seeding in such a setting [19]. A comparison of the clinical details in a series of CIP after transrectal prostate biopsy described a higher incidence of sepsis and antibiotic-resistant bacteria in the postbiopsy prostatitis group [20▪▪]. Current guidelines recommend under 24 h of periprocedural antibiotic prophylaxis for prostate biopsy [21]. Another series noted all cases of postbiopsy prostatitis were caused by drug-resistant *E. coli* and treatment with an intravenous third-generation cephalosporin or imipenem was effective for these [22]. A comparative analysis of transrectal and transurethral procedures found similar results, but *Pseudomonas* spp. were far more common in transurethral procedures [23▪].

Lastly, several case reports on CIP were recently published. One was that of a *Stapylococcus aureus* prostatic abscess diagnosed by CT and MRI in an immunocompetent host with the classic clinical picture of persistent prostatitis and worsening infectious symptoms [24]. The remaining reports highlighted acute *Coccidioides* fungal prostatitis and acute *Raoultellaplanticola* bacterial prostatitis in hosts immune compromised secondary to corticosteroids and immunosuppression for renal transplant, respectively [25,26]. A review on diagnosis and treatment of prostatic tuberculosis, with an emphasis on drug-resistance in Eastern Europe and Central Asia, was also completed [27].

CATEGORY II: CHRONIC BACTERIAL PROSTATITIS

Recurrent UTIs with the same organism suggest a persistent source of urinary tract bacterial seeding. Chronic bacterial prostatitis or category II prostatitis (CIIP) is defined as recurrent UTIs with the same organism in prostatic secretions during asymptomatic periods [7]. Only 10% of men with CIP will eventually develop CIIP [28]. Similarly, CIIP comprises just 10% of all prostatitis cases [29]. CIIP may also impair fertility per its association with impaired semen quality and a higher prevalence of premature ejaculation with *Chlamydia trachomatis* infection [30,31]. Causative organisms include *E. coli* in most cases with *P. aeruginosa*, *P. mirabilis*, *Klebsiella* spp., and *Enterobacter* spp. leading to others [32].

Diagnosis

A recent consensus guideline reviews patient evaluation and management in CIIP [33▪▪]. The history is

that of intermittent symptomatic episodes that resemble CIP, but generally without fever, which resolve with antibiotic treatment. The crux of CIIP diagnosis is the 'two glass test,' where a clean catch urine specimen is obtained prior to examination and a second specimen of expressed prostatic secretions is collected during prostatic massage or within the first urination following this [34]. These specimens are then sent for culture to screen for infection and identify the causative agent. No hard evidence exists for a diagnostic cutoff in colony count for symptomatic patients. Semen or ejaculate culture may increase the number of bacteria detected, but decreases the specificity for true uropathogens secondary to skin contaminants [35]. Transrectal ultrasound may be helpful to identify heavy prostatic calcification, which may serve as a nidus for recurrent infection.

Treatment

The basis of CIIP treatment is antibiotics. Unlike CIP, the ability of antibiotics to penetrate the noninflamed prostate is crucial in drug selection. Generally, antibiotics with a high pKa (acid dissociation constant) and increased lipid solubility have superior prostatic penetration. The quinolones, sulfas, macrolides, and tetracyclines typically exhibit these features [36]. If indicated, sexually transmitted infection with *C. trachomatis*, should be treated [37]. In all cases, the optimal duration of antibiotics is at least 2–4 weeks, with up to 6 weeks or repeated treatment courses often needed [32,38]. However, despite prolonged administration of optimal agents, a 25–50% recurrence rate exists [39,40]. If the source of prostatic infection cannot be eliminated, long-term low-dose antibiotic therapy may suppress symptomatic recurrences, but long-term data on this approach are lacking [32,36].

Apart from antibiotic bacterial eradication, nonsteroidal anti-inflammatory medications can reduce discomfort and local symptoms. Additionally, there are some data that alfa-1-adrenergic antagonists may expedite symptom resolution and reduce bacteriologic recurrence [41]. Given the often frequent and prolonged antibiotic courses, the authors feel probiotic use may reduce the risk of antibiotic-related diarrhea. The role for surgery in CIIP is limited. The transurethral elimination of prostatic tissue, by various techniques, may resolve elevated postvoid residual urine volumes and eradicate bacteria-harboring intraprostatic stones, removing these risks for infection. Otherwise, in very rare situations, where recurrent life-threatening sepsis develops, radical prostatectomy, which includes seminal vesicle removal, can be discussed.

New developments

Clarifying risk factors for CIIP may improve its treatment. A large epidemiological analysis using the Health Professionals Follow-Up Study cohort found no associations between lifestyle risk factors and chronic prostatitis/chronic pelvic pain syndrome [42▪]. Although in a group of 50 chronic spinal cord injury patients, asymptomatic bacterial prostatitis was unrelated to recurrent UTIs upon routine urologic evaluation [43]. An investigation of rapid diagnosis using prostatic fluid leukocyte CD64 expression compared to bacterial cultures showed promise in expediting laboratory confirmation of prostatitis per the authors' interpretation of the data [44].

High recurrence rates suggest incomplete bacterial elimination occurs with CIIP treatment. In 34 spinal cord injury patients with CIIP only two had bacterial eradication [45]. This suggests interventions should be limited to symptomatic cases. Certain bacterial virulence factors may predispose to persistent prostatic infection. One study cultured prostatic bacterial isolates for quantitative assessment of biofilm production and found biofilm producing bacteria were positively associated with symptom severity and negatively with improvement upon treatment [46▪▪]. Another study identified seminal vesiculitis using single photon emission computerized tomography and found typical CIIP organisms in percutaneous aspirates [47▪]. This suggests the seminal vesicles may sequester bacteria causing recurrent prostatic infections.

Antibiotics remain the foundation of CIIP treatment. The tolerability and efficacy of daily 500 mg levofloxacin for 4 weeks was recently validated in Saudi Arabian patients [48]. The comparative effectiveness of the newer macrolide roxithromycin relative to ciprofloxacin and aceclofenac was also demonstrated [49]. Nutriceutical supplementation (*Serenoarepens*/*Lactobacillus sporogens*/arbutin) with prulifloxacin antibiotic therapy was found to be superior to the antibiotic alone for bacteriologic cure and symptoms [50]. Otherwise, rifaximin with probiotic VSL#3 was found superior to no treatment for reducing the progression of bacteriologically cured CIIP in men with irritable bowel syndrome, based upon the benefit of probiotics observed in the latter condition [51].

A pair of case reports on drug-resistant bacterial prostatitis treated with fosfomycin detailed the related pharmacokinetics of each [52]. Commentary accompanying this provided insight into using fosfomycin for UTI [53]. Another study assessed intraprostatic, urinary, and serum concentrations of fosfomycin after oral administration, which identified reasonable levels in the normal prostate

without inflammation [54▪▪]. A similar study described the pharmacokinetics and pharmacodynamics of piperacillin–tazobactam by measuring serum and prostate tissue levels at transurethral prostate resection [55]. It found that isolates of *E. coli, Klebsiella* spp., *and Proteus* spp. would be sufficiently treated but *P. aeruginosa* would not, according to minimum inhibitory concentrations.

Along with medical treatment, surgical intervention was studied for CIIP treatment. One study found better prostatitis symptom improvement from antibiotic, anti-inflammatory, and alfa-1-adrenergic antagonist therapy with circumcision compared with medical therapy alone [56]. Another described transurethral resection of the prostate to eliminate 'as much infected tissue as possible' as beneficial, but only 57% of the participating 21 patients were cured and 9.5% experienced postoperative complications [57]. The role of surgical treatment for CIIP remains limited.

CONCLUSION

Acute and chronic bacterial prostatitis have clear diagnostic criteria and are often amenable to antibiotic therapy. Surgical intervention is rarely utilized, and only for limited specific indications. The majority of men with prostatitis-like symptoms do not have a true infection (category III or IV prostatitis) and no evidence supports antibiotic therapy in such cases.

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Conflicts of interest

There are no conflicts of interest.

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