INTRODUCTION — The prostate is subject to various inflammatory disorders [1]. One of these syndromes is acute bacterial prostatitis, an acute infection of the prostate, usually caused by Gram-negative organisms. The clinical presentation is generally well defined, and antimicrobial therapy remains the mainstay of treatment. Acute bacterial prostatitis will be reviewed here. Chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome are discussed in detail elsewhere. (See "Chronic bacterial prostatitis" and "Chronic prostatitis/chronic pelvic pain syndrome"). Other causes of dysuria in men, including cystitis, urethritis, and epididymitis, are also discussed elsewhere. (See "Acute uncomplicated cystitis, pyelonephritis, and asymptomatic bacteriuria in men" and "Urethritis in adult men" and "Evaluation of the acute scrotum in adults", section on ‘Epididymitis’.)

PATHOGENESIS — Entry of microorganisms into the prostate gland almost always occurs via the urethra. In most cases, bacteria migrate from the urethra or bladder through the prostatic ducts, with intraprostatic reflux of urine (figure 1). As a result, there may be concomitant infection in the bladder or epididymis. Uropathogenic bacterial isolates that cause prostatitis may have a higher accumulation of specialized virulence factors than those involved in cystitis alone [2,3].

EPIDEMIOLOGY — Overall, prostatitis syndromes are a very common presentation in the clinical setting and tend to occur in young and middle-aged men [4]. However, acute bacterial prostatitis accounts for a minority of these cases. In a study of 58,955 ambulatory visits to clinicians by men over the age of 18 years reported to the United States National Ambulatory Medical Care Surveys from 1990 to 1994, 5 percent listed genitourinary tract symptoms as one of the reasons for the visit [5]. Prostatitis was listed as a diagnosis in an estimated two million visits annually. Acute bacterial prostatitis, however, accounted for only 4 percent of prostatitis diagnoses.

Risk factors — Acute prostatitis can occur in the setting of cystitis, urethritis, or other urogenital tract infections. Thus, underlying conditions such as functional or anatomical anomalies (eg, urethral strictures), that predispose to other urogenital infections can increase the risk of prostatitis. Prostate infections following urogenital instrumentation, including chronic indwelling bladder catheterization, intermittent bladder catheterization, and prostate biopsy are well documented [6-8]. As an example, in a retrospective study of 1339 men who underwent transrectal ultrasound-guided prostate biopsy, 28 men (2.1 percent) developed acute prostatitis a mean of three days post-biopsy, despite receiving peri-procedural fluoroquinolone prophylaxis [8].

Lower urinary tract symptoms, including those caused by bacterial prostatitis, also occur more frequently in patients with HIV infection than in the general population [9,10]. Why this occurs is not clear. While immunosuppression associated with HIV certainly increases the risk of prostatitis, HIV-infected men without AIDS-defining illnesses or low CD4 cell counts also report lower urinary tract symptoms more frequently than uninfected patients [9].

Many patients with acute bacterial prostatitis have no clear risk factors. Anecdotally, trauma (eg, bicycle or horseback riding), dehydration, and sexual abstinence have been thought to predispose to prostatitis. However, these factors have not been established by well-controlled studies.

MICROBIOLOGY — The pathogens associated with acute prostatitis reflect the spectrum of organisms causing cystitis, urethritis, and deeper genital tract infections (such as epididymitis). Thus, gram-negative infections, especially with Enterobacteriaceae (typically Escherichia coli or Proteus species), are the most common [11]. As examples, in retrospective studies of men with acute bacterial prostatitis, such pathogens have been identified in positive urine cultures at the following frequencies [12-14]:

- E. coli – 58 to 88 percent
- **Proteus** species – 3 to 6 percent
- Other Enterobacteriaceae (Klebsiella, Enterobacter, and Serratia species) – 3 to 11 percent
- **Pseudomonas aeruginosa** – 3 to 7 percent

Certain gram-positive cocci (including *Staphylococcus aureus*, streptococci, and enterococci) have also been implicated in acute bacterial prostatitis [12,13,15]. Acute *staphylococcal prostatitis*, in particular, may result from bacteremia that accompanies a remote *S. aureus* infection elsewhere. Isolation of *S. aureus* from prostatic secretions should trigger an evaluation for a remote or endovascular staphylococcal infection.

Instrumentation of the prostate has been associated with subsequent acute bacterial prostatitis due to organisms with broad resistance to antibiotics, including fluoroquinolone-resistant *E. coli* and *Pseudomonas aeruginosa* [7,12]. This is likely related to the use of peri-procedural prophylactic fluoroquinolones.

Sexually active men may have sexually transmitted urogenital infections, such as urethritis and epididymitis, which also acutely involve the prostate, in which case *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are important pathogens. (See “Urethritis in adult men.”) This problem tends to occur more often in younger men, but age is not a specific risk factor for these sexually transmitted infections.

In HIV-infected patients, the microbiology typically reflects that seen in the general population; however, involvement with other pathogens, including *Salmonella typhi* and *N. gonorrhoeae*, has also been described [10].

In patients or travelers from regions where *Burkholderia pseudomallei* is endemic (eg, southern and southeast Asia or northern Australia) this uncommon organism has also been described as a cause of acute prostatitis and prostatic abscess [16,17]. (See “Epidemiology, clinical manifestations, and diagnosis of melioidosis”.)

Recurrent infection after completion of therapy is usually caused by the same organism that was found in the original infection [18].

**CLINICAL MANIFESTATIONS** — The clinical presentation of acute prostatitis is generally not subtle. Patients are typically acutely ill, with spiking fever, chills, malaise, myalgia, dysuria, irritative urinary symptoms (frequency, urgency, urge incontinence), pelvic or perineal pain, and cloudy urine. Men may also complain of pain at the tip of the penis. Swelling of the acutely inflamed prostate can cause voiding symptoms, ranging from dribbling and hesitancy to acute urinary retention. In a retrospective review of 614 cases of men who presented to an emergency department in Spain and were diagnosed with acute bacterial prostatitis, irritative symptoms were observed most commonly (93 percent), with obstructive symptoms (poor stream, hesitancy) and fever reported in 25 and 34 percent of patients, respectively [12]. No specific characteristics of urinary symptoms (eg, end-stream dysuria) have been clearly associated with prostatitis.

Rarely, patients lack these local symptoms and present instead with constitutional symptoms or a flu-like illness.

On exam, the prostate is often warm, firm, edematous, and exquisitely tender. Common laboratory findings include peripheral leukocytosis, pyuria, bacteriuria, and, occasionally, positive blood cultures. Inflammatory markers (erythrocyte sedimentation rate, C-reactive protein) may be elevated. Inflammation of the prostate can also lead to an elevated serum prostate specific antigen (PSA) level [19]. Thus, if serum PSA testing for prostate cancer screening is planned, it should be deferred for one month following acute prostatitis. A detailed discussion of the risks and benefits of prostate cancer screening is found elsewhere. (See "Measurement of prostate specific antigen".)

**Complications** — Complications of acute bacterial prostatitis include bacteremia, epididymitis, chronic bacterial prostatitis, prostatic abscesses, and metastatic infection (eg, spinal or sacroiliac infection) [20]. Patients with underlying valvular heart disease or a valvular prosthesis may be at risk for endocarditis when prostatitis is caused by certain bacterial pathogens, particularly gram-positive bacteria. These complications are more likely to occur if diagnosis and antimicrobial therapy is delayed.

**Prostatic abscess** — The incidence of prostatic abscess is currently low with the use of appropriate antibiotic therapy [21]. In a prospective study of transrectal ultrasonography of the prostate in 45 men hospitalized for acute bacterial prostatitis, no lesions with sonographic characteristics of prostatic abscesses were identified, despite detection of
other, often transient, prostatic lesions in almost half of the men [22]. Certain underlying conditions, such as diabetes mellitus or HIV-related immunosuppression, may predispose to the development of prostatic abscesses [23,24].

Signs and symptoms of a prostatic abscess are similar to those of bacterial prostatitis in general, but may persist despite appropriate antibiotic therapy; in addition, fluctuance of the prostate on gentle digital exam can suggest an underlying abscess. On transrectal ultrasound, abscesses appear as hypoechoic or anechoic areas with thick walls or peripheral edema [24,25]. Computed tomography (CT) findings include nonenhancing fluid-density collections that can be multiseptated or rim-enhancing lesions.

**DIAGNOSIS** — The presence of typical symptoms of prostatitis should prompt digital rectal exam, and the finding of an edematous and tender prostate on physical exam in this setting usually establishes the diagnosis of acute bacterial prostatitis. Digital rectal examination should be performed gently; vigorous prostate massage should be avoided since it is uncomfortable, allows no additional diagnostic or therapeutic benefit, and increases the risk for bacteremia. In patients who present with constitutional symptoms only, establishing a diagnosis of acute prostatitis is challenging. Laboratory findings of leukocytosis, pyuria, bacteriuria, or an elevated serum prostate specific antigen (PSA) level can support the diagnosis, and should prompt consideration of digital rectal exam. (See 'Clinical manifestations' above.)

In order to establish the microbial etiology, a urine Gram stain and culture should be obtained in all men suspected of having acute prostatitis. Gram stain of the urine, if positive, can be used as a guide to initial therapy (see 'Antimicrobial therapy' below). Urine culture typically reveals a causative organism in acute prostatitis, unless antibiotics were recently used.

Blood cultures usually are not necessary for microbial diagnosis, and we typically do not perform them for this reason alone. In a retrospective review of 261 men with acute prostatitis in whom urine and blood cultures were collected, blood cultures provided additional microbial information in 14 patients (5 percent) [14]. However, blood cultures are useful to assess for complications in patients with underlying cardiac valvular disease or clinical evidence of impending or severe sepsis.

**EVALUATION**

**Evaluation for complications** — Blood cultures to evaluate for bacteremia are warranted in patients with signs suggestive of severe sepsis (eg, hypotension, hematologic derangements). Additionally, a high level of suspicion for bacteremic complications of acute prostatitis is warranted in patients with underlying conditions that may predispose to them (eg, endocarditis in patients with valvular disease or prostheses).

In particular, when *S. aureus* is recovered from a urine culture, it is important to perform blood cultures to be certain the bacteriuria reflects local infection and not seeding of the prostate or urine in the setting of bacteremia, or even underlying endocarditis. (See "Clinical manifestations of Staphylococcus aureus infection".)

Imaging studies are generally not indicated in acute bacterial prostatitis, unless there is clinical suspicion for a prostatic abscess. In patients who have persistent clinical or laboratory abnormalities despite appropriate antimicrobial therapy, an abscess can be diagnosed radiographically with prostate ultrasonography or computed tomography (CT) scan [26]. (See 'Complications' above.)

**Evaluation for anatomical abnormalities** — Following the acute episode, underlying anatomical abnormalities that may have predisposed to an acute prostatic infection may be sought and, if possible, remedied to decrease the risk of recurrence. Consultation with a urologist for this evaluation may be useful in patients with recurrent infections.

**DIFFERENTIAL DIAGNOSIS** — The most common alternate diagnosis to consider in a man who presents with dysuria, frequency, and/or urgency, and who has pyuria and bacteriuria, is an isolated lower urinary tract infection (UTI), or cystitis. UTIs in men generally occur in the presence of a predisposing functional or anatomic abnormality, such as prostatic hypertrophy or genitourinary instrumentation, which increases the risk of infection, although they can also uncommonly occur in otherwise healthy men. While isolated UTIs likely involve some amount of bacterial contamination along the prostatic ducts, this prostatic contamination may remain superficial without overt prostatic inflammation or suppuration. In such cases, fever, chills, and constitutional symptoms are generally absent, and there is no prostatic tenderness on digital rectal exam. Men who lack this evidence of clinically significant prostatic involvement can be managed as having acute uncomplicated or complicated cystitis, depending on the presence of predisposing features, but should be monitored for lack of clinical response, which would warrant reevaluation for the
If available, a Gram stain of the urine can be helpful to further guide the empiric antibiotic choice:

- Patients with gram-negative rods on urine Gram stain should be treated as above.
- Gram-positive cocci in chains usually indicate enterococcal infection, which can be treated with amoxicillin (500 mg orally every eight hours) or ampicillin (2 g intravenously every six hours) if parenteral therapy is indicated. Of note, these regimens are not active against most Enterococcus faecium or other ampicillin-resistant strains. (See "Treatment of enterococcal infections", section on ‘Approach to resistant strains’.)
Further changes to the empiric antibiotic regimen can be made based on susceptibility data of the isolated organism and clinical response. Of note, although nitrofurantoin is commonly used for lower urinary tract infections in women, we avoid this agent in men with prostatitis because of concern about poor tissue penetration and risk of adverse effects from prolonged use.

**Duration of therapy** — Patients initiated on parenteral antibiotics can be switched to oral antibiotics, if drug susceptibility and patient tolerance allow, 24 to 48 hours following improvement in fever and clinical symptoms. Antibiotics should be administered for six weeks to ensure eradication of the infection [28].

Clinical data on the duration of treatment for acute bacterial prostatitis are limited. We favor such a prolonged therapy because of limited antimicrobial penetration into the prostate and the development of protected microcolonies deep within the inflamed gland that may be difficult to reach with antimicrobials. Shorter durations of therapy have been associated with progression to chronic symptoms. (See 'Prognosis' below.)

**Nonantimicrobial therapy** — Rarely, acute urinary retention develops during an episode of acute prostatitis. In this setting, bladder drainage must be done by suprapubic catheterization. Passage of a catheter through the inflamed urethra into the bladder is contraindicated in patients with acute prostatitis.

In a patient with a prostatic abscess, urological referral is indicated if the abscess is persistent after one week or more of antimicrobial therapy. In some cases, ultrasound-guided or surgical drainage may be warranted.

**Monitoring during therapy** — In most cases, fever abates and dysuria disappears within two to six days after the start of therapy. Acute phase reactants (eg, sedimentation rate, C reactive protein) and the PSA, if obtained, return to normal more gradually [19]. Clinical studies using a fluoroquinolone suggest that a negative urine culture at seven days following initiation of therapy predicts cure at the conclusion of the full course of therapy [29]. We typically repeat urine culture at seven days. If it is still positive at that time, alternative therapy should be initiated, based upon in vitro susceptibility tests of the most recent isolate.

Patients with persistently positive urine cultures should be further evaluated and treated for chronic bacterial prostatitis. (See "Chronic bacterial prostatitis".)

**PROGNOSIS** — Progression from acute to chronic bacterial prostatitis or inflammatory chronic pelvic pain syndrome (CPPS) is poorly understood. In a prospective cohort of 437 Korean men who presented with a confirmed diagnosis of acute bacterial prostatitis, 82 percent recovered without subsequent development of chronic infection three months or longer after treatment [30]. Development of chronic bacterial prostatitis or inflammatory CPPS (observed in 1.3 and 10.5 percent, respectively) was associated with higher rates of alcohol consumption, diabetes, voiding symptoms, enlarged prostate volume, catheterization, and short (two weeks) duration of antibiotic treatment.

**INFORMATION FOR PATIENTS** — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- **Beyond the Basics:** Within the inflamed gland that may be difficult to reach with antimicrobials. Shorter durations of therapy have been associated with progression to chronic symptoms. (See 'Prognosis' below.)
- **Nonantimicrobial therapy** — Rarely, acute urinary retention develops during an episode of acute prostatitis. In this setting, bladder drainage must be done by suprapubic catheterization. Passage of a catheter through the inflamed urethra into the bladder is contraindicated in patients with acute prostatitis.
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SUMMARY AND RECOMMENDATIONS

- Acute bacterial prostatitis is an acute infection of the prostate that typically occurs in young and middle-aged men. In most men, it is generally caused by the same organisms that cause urinary tract infections, most commonly gram-negative bacteria, especially Enterobacteriaceae (typically *Escherichia coli* or *Proteus* species). Sexually transmitted pathogens, such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, are possible etiologies in sexually active men, who may have concomitant urethritis or epididymitis. (See 'Epidemiology' above and 'Microbiology' above.)

- Patients with acute bacterial prostatitis are typically acutely ill. The most common symptoms and signs include fevers, chills, dysuria, pelvic or perineal pain, and cloudy urine. Obstructive symptoms, such as dribbling of urine, can also occur. On exam, the prostate is often warm, firm, edematous, and exquisitely tender. Common laboratory findings include peripheral leukocytosis, pyuria, and bacteriuria. (See 'Clinical manifestations' above.)

- Delay of antimicrobial therapy can increase the risk of secondary complications, including bacteremia, prostatic abscess, and metastatic infection (eg, spinal or sacroiliac infection). Certain underlying conditions, such as diabetes mellitus or HIV-related immunosuppression, may also predispose to the development of prostatic abscesses. (See 'Complications' above.)

- The presence of typical symptoms of prostatitis and the finding of an edematous and tender prostate on physical exam usually establishes the diagnosis. Digital rectal examination should be performed gently; vigorous prostate massage should be avoided since it is uncomfortable, allows no additional diagnostic or therapeutic benefit, and increases risk for bacteremia. Tenderness of the prostate on exam is generally not found in isolated UTIs or other acute causes of dysuria (eg, urethritis, epididymitis) in the absence of coexisting prostatitis. (See 'Diagnosis' above and 'Differential diagnosis' above.)

- A urine Gram stain and culture should be obtained in all men suspected of having acute prostatitis to identify the bacterial etiology. Imaging studies are generally not warranted in acute bacterial prostatitis, unless there is clinical suspicion for a prostatic abscess (ie, when there are persistent clinical or laboratory abnormalities despite appropriate antimicrobial therapy). (See 'Diagnosis' above and 'Evaluation for complications' above.)

- Most cases of acute bacterial prostatitis are caused by gram-negative organisms, and empiric antibiotic therapy should be directed against this class. We suggest empiric treatment with trimethoprim-sulfamethoxazole or a fluoroquinolone (Grade 2C), unless drug resistance is suspected. The choice between these should take into account patient tolerance and regional patterns of Enterobacteriaceae drug resistance. If a urine Gram stain is available and suggests an alternate bacterial cause, initial antibiotic therapy should be directed against the identified class of organism. Parenteral antimicrobial therapy is warranted in patients who cannot tolerate oral medications, demonstrate signs of severe sepsis, or have bacteremia. Further changes to the empiric antibiotic regimen can be made based on susceptibility data of the isolated organism and clinical response. (See 'Antimicrobial therapy' above.)

- Patients initiated on parenteral antibiotics can be switched to oral antibiotics, if drug susceptibility and patient tolerance allow, 24 to 48 hours following improvement in fever and clinical symptoms. We typically use a prolonged antibiotic course (eg, six weeks) to try to ensure eradication of the infection. If the urine culture is still positive at seven days, alternative therapy should be initiated, based upon in vitro susceptibility tests of the most recent isolate. (See 'Duration of therapy' above and 'Monitoring during therapy' above.)

- Adjunctive therapies include management of complications, such as acute urinary retention and prostatic abscesses. Passage of a catheter through the inflamed urethra into the bladder is contraindicated in patients with acute prostatitis. If needed, bladder drainage must be done by suprapubic catheterization. (See 'Nonantimicrobial therapy' above.)
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The prostate gland is a walnut-shaped structure located at the base of the urinary bladder. The prostate gland is composed of both glandular and muscular tissue. Secretions from the prostate, vas deferens and seminal vesicle empty into the prostatic urethra. Graphic 54803 Version 5.0
Chronic bacterial prostatitis

Authors
Alain Meyrier, MD
Thomas Fekete, MD

Section Editor
Stephen B Calderwood, MD

Deputy Editor
Allyson Bloom, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Nov 2014. | This topic last updated: Jun 18, 2014.

INTRODUCTION — The prostate is subject to various inflammatory disorders [1]. One of these syndromes is chronic bacterial prostatitis, which is characterized by chronic or recurrent urogenital symptoms in the setting of documented or suspected bacterial infection of the prostate.

Definitions of inflammatory conditions of the prostate and the syndrome of chronic bacterial prostatitis will be reviewed here. Other prostatic syndromes, including acute bacterial prostatitis and chronic prostatitis/pelvic pain syndrome, are discussed separately. (See "Acute bacterial prostatitis" and "Chronic prostatitis/chronic pelvic pain syndrome".)

DEFINITIONS — While inflammatory or irritative conditions of the prostate are common clinical presentations, they often represent distinct pathogenic processes that may benefit from different management approaches. In order to standardize definitions, improve diagnosis and treatment, and facilitate research, the United States National Institutes of Health (NIH) established an International Prostatitis Collaborative Network to devise a classification approach for prostatitis [2]. The scheme developed by this group is the currently accepted categorization of prostatitis and defines the following syndromes (table 1):

- i. Acute bacterial prostatitis — Acute urogenital symptoms with evidence of bacterial infection of the prostate (see "Acute bacterial prostatitis")

- ii. Chronic bacterial prostatitis — Chronic or recurrent urogenital symptoms with evidence of bacterial infection of the prostate

- iiiA. Chronic prostatitis/chronic pelvic pain syndrome, inflammatory — Chronic or recurrent urogenital symptoms with evidence of inflammation, but not bacterial infection of the prostate (see "Chronic prostatitis/chronic pelvic pain syndrome")

- iiiB. Chronic prostatitis/chronic pelvic pain syndrome, noninflammatory — Chronic or recurrent urogenital symptoms without evidence of inflammation or bacterial infection of the prostate (formerly designated prostatodynia) (see "Chronic prostatitis/chronic pelvic pain syndrome")

- iv. Asymptomatic inflammatory prostatitis — Absence of urogenital symptoms with evidence of inflammation of the prostate found incidentally (eg, biopsy performed for a different purpose)

Evidence of inflammation or bacterial infection is usually determined by the presence of inflammatory cells in, or bacterial growth from, expressed prostatic secretions, post-prostatic massage urine, or seminal fluid. Maneuvers performed in the urology office can help refine the categorization of patients. As an example, including post-massage urine and seminal fluid for the assessment of inflammatory cells effectively doubles the number of people in the inflammatory subset (compared with using purulent prostatic secretions alone) [3].

PATHOGENESIS — The pathogenesis of chronic bacterial prostatitis is the same as in acute infection. Entry of microorganisms into the prostate gland almost always occurs via the urethra. In most cases, bacteria migrate from the urethra or bladder through the prostatic ducts, with intraprostatic reflux of urine (figure 1). Chronic prostatitis may be a complication of acute prostatitis following inadequate and/or too short treatment. (See "Risk factors" below.)

EPIDEMIOLOGY — Overall, prostatitis is a very common presentation in the clinical setting and tends to occur in young and middle-aged men. In a study of 58,955 ambulatory visits to clinicians by men over the age of 18 years reported to the United States National Ambulatory Medical Care Surveys from 1990 to 1994, 5 percent listed genitourinary tract symptoms as a reason for the visit [4]. Extrapolation of the data estimated that the diagnosis of
prostatitis was associated with two million visits annually. However, actual bacterial infections of the prostate account for a minority of these cases [2].

In a retrospective study of 409 men with prostatitis syndromes, bacterial cultures of prostatic fluid were positive only in 10 percent [5]. The observed prevalence of bacterial prostatitis may be underestimated, as most studies infrequently evaluate for atypical organisms, such as Ureaplasma urealyticum, which in the above study was cultured in 20 percent of prostatic fluid samples. However, the role of atypical bacteria, like Ureaplasma in genitourinary infections, is not fully defined since it can be isolated from asymptomatic men as well [6].

**Risk factors** — The risk factors for the development of chronic bacterial prostatitis have not been clearly defined. Chronic bacterial infection of the prostate can develop following an episode of acute prostatitis. In a retrospective review of 480 patients with acute prostatitis, the 49 men (10 percent) who developed chronic infection were more likely to have a history of prior manipulation of the urinary tract, voiding symptoms, diabetes, and smoking, and on average had higher prostate volumes [7]. Furthermore, men who had been treated for acute prostatitis, but did not develop chronic prostatic symptoms, had received a longer treatment duration compared with men who developed chronic prostatic infection (average 36.5 versus 27.5 days). However, it is unknown whether these factors contribute independently to the development of chronic infection.

The presence of prostate stones may also contribute to the persistence of infection. In one study of men with chronic bacterial prostatitis, patients with prostate stones were more likely to experience relapse following antimicrobial therapy than patients without stones [8]. Otherwise, the risk factors for chronic infection appear to be similar to those observed for acute infection. (See "Acute bacterial prostatitis", section on 'Risk factors'.)

**MICROBIOLOGY** — Gram-negative rods are the most common etiologic agents, with Escherichia coli causing approximately 75 to 80 percent of episodes [9]. Enterococcus faecalis, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, and other gram-negative bacilli are the next most commonly reported organisms [10-12]. Staphylococcus aureus and streptococcal species are occasional pathogens. The isolation of other gram-positive organisms, such as coagulase negative staphylococci and corynebacteria from prostatic fluid, is of uncertain clinical significance as illustrated by studies in which isolation of these organisms was neither associated with inflammatory cells in prostatic secretions nor reproducible even in the absence of antibiotic therapy [13,14].

Fastidious sexually transmitted organisms, such as Chlamydia trachomatis, have also been associated with chronic prostatic infection, although this attribution remains speculative. C. trachomatis has been isolated from the prostate and in such cases appears to reside in prostate tissue as opposed to represent a contaminant from the urethra [15,16]. Some studies have shown that men with chronic prostatitis without a clear bacterial etiology had detectable chlamydial antigen in urine or prostatic secretions more frequently than men with pelvic pain but no signs of prostatic inflammation (21 to 25 versus 0 to 6 percent, respectively) [17-19].

Rarely, fungi or Mycobacterium tuberculosis may be involved in chronic prostatitis [20,21]. Patients with underlying immunosuppression may be more likely to have prostatic involvement with atypical organisms. As an example, in a series of patients with HIV-related immunosuppression and a history of treated cryptococcal meningitis, Cryptococcus neoformans could be isolated from prostatic secretions at a time when the organism was absent in blood or cerebrospinal fluid [22].

**CLINICAL PRESENTATION** — The presentation of chronic bacterial prostatitis can be quite subtle. Classically, men present with symptoms of recurrent urinary tract infection (frequency, dysuria, urgency, perineal discomfort, and perhaps a low-grade fever) with repeated isolation of the same organism from the urine. However, this presentation is reported by the minority of patients [11].

Some men may be asymptomatic and have only incidentally noted persistent or recurrent bacteriuria. Other symptoms can include pain (in the perineum, lower abdomen, testicles, penis, and with ejaculation), bladder irritation, bladder outlet obstruction, and sometimes blood in the semen. Sexual dysfunction may accompany chronic bacterial prostatitis, although it does not clearly occur more commonly than in men of a similar age without prostatitis [23-25].

On rectal examination, there may be prostatic hypertrophy, tenderness, edema, and nodularity. However, the prostate exam is frequently normal.
Laboratory findings that suggest inflammation or infection, such as elevated serum leukocytes or inflammatory markers, may be absent. In an analysis of participants in a trial of treatment for documented chronic bacterial prostatitis, an elevated prostatic specific antigen (>4 ng/mL) was detected in only about 25 percent [26].

**DIAGNOSIS** — The diagnostic standard for bacterial prostatitis is the finding of bacteria at higher levels in prostatic fluid compared with urethral and bladder specimens. However, maneuvers to express prostatic fluid can be cumbersome and are rarely performed in clinical practice. Instead, chronic bacterial prostatitis is often presumptively diagnosed and empirically treated with antimicrobials when men present with chronic (eg, longer than three months) or recurrent urogenital symptoms, particularly if bacteriuria is also present. Because of the insensitivity of these clinical findings and the therapeutic implication of a prolonged course of antibiotics, we favor obtaining prostatic specimens for analysis and culture to confirm the prostate as the site of infection in men with chronic symptoms of prostatitis, incidental bacteriuria, or recurrent urinary tract infections in the absence of other risk factors, such as bladder catheterization. In most cases, this is best performed in an urologist’s office, where there is a greater level of experience in obtaining prostatic secretions and thus a greater likelihood of a microbial diagnosis.

**Obtaining and testing prostatic specimens** — Prostatic specimens can be obtained by collecting expressed prostatic fluid and a urine sample expressed following prostatic massage. For primary care doctors and internal medicine subspecialists, obtaining fluid or tissue from the prostate is difficult and semen cultures are not standard. Thus, referral to an urologist can be helpful for men with long-standing or refractory prostatic symptoms to obtain such specimens for diagnosis.

The classic method for localizing pathogens in the lower urinary tract and thus evaluating for bacterial prostatitis is the Meares-Stamey four-glass test [9]. It involves first cleaning the periurethral area and then collecting the first 5 to 10 mL void of urine (VB1, urethral sample) and a midstream sample (VB2, bladder sample). The patient should stop voiding before the bladder is empty and the prostate is then digitally massaged by applying gentle pressure moving from the superior portion to the apex for about one minute. Any prostatic secretions that are expressed (EPS, prostatic sample) and the first 5 to 10 mL of subsequently voided urine (VB3, prostatic sample) are collected (figure 2). (See "Sampling and evaluation of voided urine in the diagnosis of urinary tract infection in adults").

The finding of pathogens on culture of prostatic samples (EPS and VB3) exclusively or at a level 10 times higher than in urethral and bladder samples (VB1 and VB2) is diagnostic of bacterial prostatitis. For the test to be interpretable, the colony count in VB2 must be less than $10^5$/mL, since bladder bacteriuria prevents identification of the frequently small number of organisms from the prostate. Chronic prostatitis is suspected when VB3 has more than 12 leukocytes per high power field; more than 20 leukocytes per high power field is generally diagnostic unless leukocytes were also present in VB2 [23].

Although the four-glass test is described extensively in the literature, it appears to be infrequently used in practice. In one survey of urologists in which 64 percent responded, 33 and 47 percent, respectively, said that they never or rarely performed the four-glass test [27]. Furthermore, the results of the test apparently did not influence the use of antibiotics, since urologists who used the test routinely did not differ in antibiotic prescribing from others who used it less often.

A simpler, "two-glass" method, in which cultures from only the post-prostatic massage urine (VB3) are compared with the pre-massage bladder urine sample (VB2), has been suggested as an alternate method, with a 100 percent positive and 96 percent negative predictive value when compared with the four-glass test [28]. Although this test has slightly lower sensitivity than the four-glass test, it is a preferred alternative compared with not performing any cultures of prostatic samples.

**Evaluating the microbial etiology** — Cultures of post-prostatic massage urine or expressed prostatic secretions are almost always positive in chronic bacterial prostatitis (table 1) and thus reveal the bacterial etiology. The repeated isolation of the same organism from urine cultures over time also suggests the etiologic agent. However, sexually transmitted organisms that may play a role in chronic bacterial prostatitis, such as C. trachomatis, will not grow in routine culture. Thus, in men who are sexually active and have clinical evidence of chronic prostatitis, but negative results of urine and prostatic secretion cultures, nucleic acid amplification testing for C. trachomatis on urine or urethral swabs can be diagnostically useful [15,16]. (See 'Microbiology' above and 'Clinical manifestations and diagnosis of Chlamydia trachomatis infections', section on 'Diagnosis of chlamydial infections'.)

**DIFFERENTIAL DIAGNOSIS** — The main differential diagnosis to consider in a patient with symptoms and signs consistent with chronic bacterial prostatitis is chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), in whom the
symptoms may be the same, but there is no clear evidence of a bacterial infection (see 'Definitions' above). This distinction is not always readily established; however, as cultures of prostatic specimens are infrequently performed in clinical practice and atypical, fastidious pathogens have been implicated as occasional causes of chronic bacterial prostatitis. (See 'Microbiology' above and 'Evaluating the microbial etiology' above.)

Furthermore, some patients with CP/CPPS respond to antibiotic therapy despite lack of a clear bacterial infection [29]. Thus, an initial antimicrobial course is often given to patients with symptoms of prostatitis to treat a potential bacterial infection, and the diagnosis of CP/CPPS is entertained among those patients who do not respond or relapse and continue to have no clear evidence of infection. (See "Chronic prostatitis/chronic pelvic pain syndrome", section on 'Differential diagnosis' and "Chronic prostatitis/chronic pelvic pain syndrome", section on 'Management'.)

Noninflammatory disorders of the prostate, bladder, and urinary tract can also lead to persistent irritative (urgency, frequency, nocturia) and obstructive (slow stream, hesitancy, dribbling) urinary symptoms that can be seen with chronic bacterial prostatitis. The evaluation of men with lower urinary tract symptoms is discussed in detail elsewhere. (See "Lower urinary tract symptoms in men'.)

**MANAGEMENT** — Prolonged antibiotic therapy (eg, at least six weeks) with an agent that has good penetration into the prostatic tissue is generally necessary for treatment of chronic bacterial prostatitis. Nevertheless, the infection frequently recurs. A fluoroquinolone is generally the drug of choice for both initial and recurrent episodes, if organism susceptibility and patient tolerance allow. Trimethoprim-sulfamethoxazole is an adequate alternative regimen.

**Antimicrobial penetration into prostatic tissue** — The barrier between the microcirculation and the prostate gland stroma limits drug entry to passive diffusion, which only permits non-protein-bound, lipophilic antimicrobial agents to reach therapeutic levels within the gland. In addition, the low pH of prostatic fluid permits antibiotics with alkaline pKₐ's (such as fluoroquinolones and sulfonamides) to achieve high concentrations in prostatic tissue more readily than antibiotics with acidic pKₐ's. However, antibiotic prostatic penetration in the setting of inflammation occurs more readily [30]. Nevertheless, ideal choices for therapy of bacterial prostatitis include those agents that have optimal prostatic penetration.

In addition to fluoroquinolones and sulfonamides, other agents with good to excellent penetration into prostatic fluid and tissue include tetracyclines and macrolides [31].

Fosfomycin also appears to achieve reasonable intraprostatic concentrations in uninflamed prostate. In a prospective pharmacokinetic study of 26 healthy men undergoing a transurethral resection of the prostate for benign prostatic hyperplasia, serum, urine, and prostatic tissue, fosfomycin concentrations were assessed following a single 3-g oral fosfomycin dose within 17 hours of surgery [32]. The mean overall prostate fosfomycin level was 6.5 mcg/g (range, 0.7-22.1 mcg/g), with therapeutic concentrations detectable up to 17 hours following the dose. Only one patient had a mean prostatic fosfomycin concentration of <1 mcg/g, whereas the majority (70 percent) had concentrations ≥4 mcg/g. Further data are warranted before fosfomycin can be routinely recommended for use in prostatic infections, as tissue levels after multiple doses and in the presence of inflammation or microabscesses remain to be determined.

**Initial antibiotic therapy** — For men with an initial episode of chronic bacterial prostatitis caused by a susceptible organism, we suggest antibiotic treatment with a fluoroquinolone. In cases of patient intolerance or bacterial drug resistance, antimicrobial choice should be guided by susceptibility testing. Fluoroquinolones are generally given for at least six weeks. Courses exceeding this duration may be warranted for patients who have a relatively difficult to treat organism or who cannot tolerate first-line therapy and need other agents. Patients should be counselled about and monitored for potential adverse effects associated with such prolonged use of antibiotics. (See"Fluoroquinolones", section on 'Adverse reactions' and "Trimethoprim-sulfamethoxazole: An overview", section on 'Adverse effects and precautions'.)

The selection of agents and duration of therapy for chronic bacterial prostatitis have not been extensively studied using comparative trials with antimicrobial agents from varying classes. Moreover, studies of antimicrobial treatment of chronic prostatitis often include men with inflammatory chronic prostatitis/chronic pelvic pain syndrome, in which an infectious etiology is not clearly established. (See 'Definitions' above.) Nevertheless, in studies restricted to men with documented chronic bacterial prostatitis, various fluoroquinolone regimens (eg, levofloxacin 500 mg PO every 12 hours or levofloxacin 500 mg PO daily) have six-month clinical cure rates of about 60 to 70 percent when given for four weeks or longer [33-37]. Shorter courses of higher doses of fluoroquinolones have been associated with an increased likelihood of relapse [38]. A longer course of six or more weeks may be needed to achieve clinical cure with other agents, such as trimethoprim-sulfamethoxazole [9,11].
The rising rate of resistance of Enterobacteriaceae to fluoroquinolones and trimethoprim-sulfamethoxazole (see “Acute uncomplicated cystitis and pyelonephritis in women”, section on ‘Antimicrobial resistance’) and the frequency of allergies or intolerance to these agents complicate treatment decisions for chronic bacterial prostatitis. There are limited data on management of such cases. Based on biological plausibility, some experts use a prolonged course of other antimicrobials (including tetracyclines, macrolides, and cephalosporins) chosen based on susceptibility results and monitor closely for clinical response and relapse. In some cases, the resistance pattern may only leave intravenous agents as effective options. In cases of complicated drug resistance or intolerance, consultation with an expert in the treatment of prostatitis is advised.

Of note, although nitrofurantoin is commonly used for lower urinary tract infections in women, we avoid this agent in men with prostatitis because of concern about poor tissue penetration and risk of adverse effects from prolonged use.

Doxycycline and azithromycin are effective agents against C. trachomatis and are the agents of choice in prostatic infections associated with this organism [39,40]. In a trial of 89 men with chronic prostatitis and laboratory evidence of C. trachomatis infection, men randomly assigned to azithromycin (500 mg daily for three days each week for three weeks) had higher rates of bacterial eradication (80 versus 39 percent) and clinical cure (69 versus 34 percent) compared with those who received ciprofloxacin (500 mg twice daily for 20 days) [41].

Management of recurrences — Chronic bacterial prostatitis often recurs and is usually treated with an additional course of antibiotics. Fluoroquinolones generally remain the treatment of choice for recurrent bacterial prostatitis, even if this class of drug was used for the initial treatment course, unless a resistant organism is suspected or detected. If the first course was four weeks or less, a longer second course of at least six weeks is recommended.

The efficacy of fluoroquinolones in recurrent chronic bacterial prostatitis has been suggested by several small studies [42-44]. In one study of 33 men who had failed therapy with trimethoprim, TMP-SMX, or norfloxacin, and were then retreated with ciprofloxacin (500 mg twice daily) for two to four weeks, the following results were noted [42]:

- Of 26 patients with E. coli as the pathogen, 17 were cured at greater than one year follow-up. In another two patients, a second treatment course with ciprofloxacin was successful. Two patients withdrew from therapy due to adverse drug reactions.

- Therapy was successful in two of five with pathogens other than E. coli.

Furthermore, failures of initial fluoroquinolone therapy are not necessarily due to bacterial resistance and instead can also be related to underlying prostate disease, incomplete adherence, drug interactions that reduce fluoroquinolone bioavailability, or to some other less understood component. Thus, in patients who have relapsed or failed to respond following a course of a fluoroquinolone, causes of impaired bioavailability of the fluoroquinolone should be sought and, if possible, remedied. (See “Fluoroquinolones”, section on ‘Drug interactions’.)

However, prolonged use of fluoroquinolones has been associated with several serious side effects, including Clostridium difficile associated diarrhea, central nervous system toxicity, and tendinopathy. As examples, tendinitis and tendon rupture have been reported in patients receiving prolonged fluoroquinolone therapy, especially in patients >60 years of age [45]. Among patients in this age group, those receiving glucocorticoids are at the highest risk. (See “Fluoroquinolones”, section on ‘Adverse reactions’.)

In cases of bacterial resistance, patient intolerance, or concerns about prolonged use of fluoroquinolones, trimethoprim-sulfamethoxazole is an alternative. As above, a longer duration of therapy (at minimum, six weeks) may be needed to achieve clinical cure.

Fosfomycin may be a potential option for the treatment of multidrug-resistant gram-negative prostatitis, as the drug appeared in one study to achieve reasonable intraprostatic concentrations in the uninflamed prostate following a single 3-g oral dose [32], but further data are warranted.

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5 th to 6 th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10 th to
12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

● Basics topic (see "Patient information: Prostatitis (The Basics)"

SUMMARY AND RECOMMENDATIONS

● Prostatitis can be divided into the following categories (table 1) (see 'Definitions' above):
  
  • I. Acute prostatitis
  
  • II. Chronic bacterial prostatitis
  
  • IIIA. Chronic prostatitis/pelvic pain syndrome, inflammatory
  
  • IIIIB. Chronic prostatitis/pelvic pain syndrome, non-inflammatory
  
  • IV. Asymptomatic inflammatory prostatitis

● Overall, prostatitis is a very common presentation in the clinical setting and tends to occur in young and middle-aged men. However, actual bacterial infections make up a minority of these cases. Gram-negative rods and Escherichia coli in particular, are the most common etiologic agents of chronic bacterial prostatitis. Other organisms, including enterococci, staphylococci, streptococci, and Chlamydia trachomatis have also been associated with chronic prostatic infection. (See ‘Epidemiology’ above and ‘Microbiology’ above.)

● Drug entry into the prostate is limited. Fluoroquinolones and sulfonamides achieve the highest concentrations in prostatic tissue; tetracyclines and macrolides can also reach therapeutic levels in the prostate. (See ‘Antimicrobial penetration into prostatic tissue’ above.)

● The clinical presentation of chronic bacterial prostatitis is typically subtle. Classically, men present with symptoms of recurrent urinary tract infection with repeated isolation of the same organism from the urine. However, some men may be asymptomatic with only persistent or recurrent bacteriuria. Other lower urinary tract symptoms include pain and irritative and obstructive symptoms. (See ‘Clinical presentation’ above.)

● In clinical practice, chronic bacterial prostatitis is usually presumptively diagnosed in men with chronic or recurrent urogenital symptoms and/or persistent bacteriuria. Ideally, bacterial infection of the prostate should be confirmed with comparative analysis of cultures from prostatic secretions and urine obtained prior to and following prostatic massage (figure 2). (See ‘Diagnosis’ above and ‘Obtaining and testing prostatic specimens’ above.)

● The bacterial etiology can usually be identified through culture of urine or expressed prostatic secretions. In sexually active men with suspected chronic bacterial prostatitis, but no bacterial organism on routine culture, nucleic acid amplification testing for C. trachomatis on urine or urethral swabs should be performed. (See ‘Evaluating the microbial etiology’ above.)

● The main differential diagnosis to consider in a patient with symptoms and signs consistent with chronic bacterial prostatitis is chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS). An initial antimicrobial course is often given presumptively to patients with symptoms of prostatitis without a documented bacterial infection, and the diagnosis of CP/CPPS is then entertained among those patients who do not respond or relapse and continue to have no clear evidence of infection. (See ‘Differential diagnosis’ above and "Chronic prostatitis/chronic pelvic pain syndrome".)
• For patients with an initial episode of chronic bacterial prostatitis, we suggest treatment with a fluoroquinolone as long as organism susceptibility and patient tolerance allow (Grade 2C). **Trimethoprim-sulfamethoxazole** is an alternative option. Fluoroquinolones are typically given for at least six weeks for probable or documented chronic bacterial prostatitis. Longer courses may be indicated for patients who are infected with a relatively difficult to treat organism or are given a nonfluoroquinolone antibiotic for therapy. Shorter courses (eg, two to four weeks) are sometimes used when the diagnosis is uncertain and the possibility of CP/CPPS is being entertained. Documented C. trachomatis infections can be treated with **doxycycline** or **azithromycin**. (See 'Initial antibiotic therapy' above.)

• Recurrences of chronic bacterial prostatitis are common and warrant a second course of antibiotics. Possible causes of treatment failure, including antibiotic resistance, incomplete adherence, and impaired drug absorption, should be evaluated. For men with a recurrent episode of chronic bacterial prostatitis, we suggest treatment with a fluoroquinolone regardless of the initial antibiotic choice unless there is suspicion of a resistant organism or poor drug bioavailability (Grade 2C). **Trimethoprim-sulfamethoxazole** is an alternate agent. If the initial course of therapy was less than six weeks, a longer subsequent course is indicated. (See 'Management of recurrences above'.)

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**REFERENCES**


Topic 86802 Version 6.0
### Classification of prostatitis with prostatic localization studies

<table>
<thead>
<tr>
<th>Category</th>
<th>Mid-stream urine (VB2)</th>
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<td>Culture</td>
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<td>CP/CPPS, noninflammatory</td>
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<tr>
<td>Asymptomatic inflammatory prostatitis*</td>
<td>−</td>
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<td>+</td>
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The prostate gland is a walnut-shaped structure located at the base of the urinary bladder. The prostate gland is composed of both glandular and muscular tissue. Secretions from the prostate, vas deferens and seminal vesicle empty into the prostatic urethra.
**Four-glass test**

The diagnosis of chronic prostatitis is made by analyzing specimens obtained following prostatic massage. The periurethral area is cleaned and the patient allowed to void. The initial 5 to 10 mL (VB1) and a midstream specimen (VB2) are obtained for quantitative culture. The patient should stop voiding before the bladder is empty and the prostate should then be massaged. Any prostatic secretions that are expressed (EPS) should be cultured, as well as the first 5 to 10 mL of subsequently voided urine (VB3).