Chronic prostatitis and chronic pelvic pain syndrome

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INTRODUCTION

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a clinical syndrome in males defined by pain or discomfort in the pelvic region, often accompanied by urologic symptoms or sexual dysfunction. Despite the use of the term "prostatitis," it is unclear to what degree the prostate is the source of symptoms [1].

A number of other terms have been used to describe the syndrome now commonly called CP/CPPS. These include prostatodynia (painful prostate) and abacterial prostatitis.

The clinical manifestations, evaluation, and management of CP/CPPS will be reviewed here. Acute and chronic bacterial prostatitis are discussed separately. (See "Acute bacterial prostatitis" and "Chronic bacterial prostatitis".)

Chronic pelvic pain in women is also discussed separately. (See "Chronic pelvic pain in adult females: Evaluation" and "Chronic pelvic pain in adult females: Treatment" and "Chronic pelvic pain in nonpregnant adult females: Causes".)

DEFINITION

Research guidelines define chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) as chronic pelvic pain for at least three of the preceding six months in the absence of other identifiable causes, often associated with urinary symptoms and/or sexual dysfunction [2]. CP/CPPS is sometimes referred to as either inflammatory or noninflammatory; however, the

distinction is generally for research purposes only, as there is no evidence that patients in the two subgroups have different symptoms or respond differently to therapy.

EPIDEMIOLOGY

CP/CPPS is a common condition worldwide, affecting approximately 2 to 10 percent of adult men [3]. The prevalence seems to peak in the fifth decade and decline thereafter [4]. Most men diagnosed with "prostatitis" have CP/CPPS rather than acute or chronic bacterial prostatitis [5].

ETIOLOGY

The etiology of CP/CPPS is unknown. Despite the use of the term "prostatitis," it is unclear to what degree the prostate is the source of symptoms [6]. Proposed etiologies include inflammation due to trauma or to normal prostate flora, autoimmunity, neurogenic pain, and the interplay of somatic and psychologic factors [1,7,8]. Psychological stress, including anxiety, appears to be common in men with symptoms of CP/CPPS and may be a contributing factor [9,10].

Many experts believe that CP/CPPS is a noninfectious disorder [11-13]. Although bacterial infection has been suspected, a bacterial etiology has not been identified.

- Studies of *Chlamydia*, *Mycoplasma*, and *Ureaplasma*, which have all been implicated in CP/CPPS, have generally concluded that they are not responsible for CP/CPPS [14-17].
- Several investigators have performed polymerase chain reaction (PCR) testing looking for evidence of bacteria in prostatic tissues, but these have yielded negative results [18,19].
- One study cultured prostatic biopsy specimens obtained via the transperineal approach from men with CP/CPPS and from normal volunteers and found no difference in the number of patients from whom bacteria were cultured (38 versus 36 percent, respectively) [20].

The clinical importance of inflammation is also unclear. There appears to be little relationship between prostatic inflammation on histology and the presence or absence of CP/CPPS symptoms [21,22]. Leukocytes can be found in the prostatic fluid of asymptomatic men, and there is no correlation between the presence of leukocytes and symptoms [1].

CLINICAL MANIFESTATIONS

Symptoms — The primary symptom of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is pain. In a study of 1563 men with CP/CPPS, the most common locations of pain were the perineum (63 percent), testes (58 percent), suprapubic area (42 percent), and penis (32 percent) [23]. Patients also experienced dysuria (43 percent) and pain with ejaculation (48 percent). In our experience, the pain may be sharp or dull and is variable in duration. It does not tend to be colicky (in contrast to pain from renal or ureteral obstruction).

The duration of pain symptoms can be quite variable, from lasting minutes, hours, or days to being constant. Many patients with CP/CPPS also have pain in other regions of the body, which may be part of another chronic pain syndrome such as irritable bowel syndrome, fibromyalgia, or migraine headaches [24].

In addition to pain, many patients have urinary symptoms or sexual dysfunction [25-27]. Urinary symptoms include frequency and urgency [28]. The urgency can be due to a feeling of impending incontinence or due to a painful bladder filling sensation [29]. In reviews of sexual dysfunction in patient with CP/CPPS, the prevalence of ejaculatory pain was 58 percent [30], premature ejaculation 64 percent, and erectile dysfunction between 15.0 to 40.5 percent [31].

Physical examination and laboratory findings — Physical examination features often found in patients with CP/CPPS may include a mildly tender prostate, although in many cases there is no prostate tenderness. Patients may have muscle spasm or myofascial tenderness upon palpation of the perineum, pelvic floor, or pelvic sidewalls.

There are no abnormal laboratory or imaging findings associated with the syndrome, and if found, these would indicate another etiology.

Clinical course — The clinical course of CP/CPPS, with or without treatment, is not well defined [32]. The majority of patients will experience flares (lasting seconds to months), with frequencies ranging from several times per day to once per year or less. Flares may vary in intensity and symptom location. In general, flares occur in a relapsing-remitting pattern where the severity and frequency of flares decreases over many months [33]. Flares may be related to sexual activity [34].

A sense of the clinical course of symptoms is provided by data from the Multidisciplinary Approach to Pelvic Pain (MAPP) study of 424 participants with urologic pelvic pain syndrome, in which symptoms were assessed every two weeks for one year [35]. The percentage of patients who improved was 24.8 percent for pain symptoms and 15 percent for urinary symptoms. The percentages for those whose symptoms became worse were 9.4 percent for pain and 6.1 percent for urinary symptoms. Factors that were predictive of worsening symptoms at one year were widespread pain, the presence of nonurological symptoms, and poorer overall health.

There was no contribution of anxiety, depression, and general mental health to symptom worsening [13].

Similar to other chronic pain syndromes, CP/CPPS may lead to problems with daily activities, depression, and overall quality of life [36]. In addition, there is an association of chronic pelvic pain syndromes with other pain syndromes [37]. Given the overlapping innervation of the bowel and bladder [38], irritation of the bowel can result in lower abdominal pain and urinary symptoms as well. (See "Clinical manifestations and diagnosis of irritable bowel syndrome in adults" and "Clinical features and diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome" and "Clinical manifestations and diagnosis of fibromyalgia in adults".)

DIAGNOSIS

The diagnosis of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is based on the presence of characteristic symptoms of pain or discomfort in the pelvic region, often accompanied by urologic symptoms or sexual dysfunction, for at least three of the preceding six months, after exclusion of other causes of these symptoms.

DIAGNOSTIC APPROACH

As CP/CPPS is a diagnosis of exclusion, the evaluation is designed to rule out identifiable causes of pelvic pain and includes a history, physical examination, urinalysis, urine culture, and, in select cases, diagnostic imaging. A stepwise approach to diagnosis is described below.

Step one: Determine if there is a bacterial infection — All patients should be evaluated for a possible bacterial infection, including acute or chronic bacterial prostatitis, cystitis, urethritis, or epididymitis.

A urinalysis should be performed in all patients, with urine culture as indicated [39]. If the results indicate a bacterial infection, the following alternative or concurrent diagnoses should be considered:

- Chronic bacterial prostatitis – Patients may present with urinary frequency, dysuria, and perineal pain. They may have recurrent urinary tract infections. Features more suggestive of chronic bacterial prostatitis than CP/CPPS include presence of a low-grade fever and rectal examination with prostatic hypertrophy. The diagnosis of bacterial prostatitis requires evidence of a bacterial infection of the prostate. (See "Chronic bacterial

prostatitis", section on 'Clinical presentation' and "Chronic bacterial prostatitis", section on 'Diagnosis'.)

- Acute bacterial prostatitis – Patients with acute prostatitis 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. The prostate is usually severely tender on examination. (See "Acute bacterial prostatitis", section on 'Clinical manifestations'.)

- Cystitis – Patients with cystitis are likely to present with dysuria, urinary frequency, urgency, and/or suprapubic pain. Some patients may have a fever. (See "Acute simple cystitis in adult males", section on 'Clinical manifestations'.)

Other infections to consider include epididymitis and urethritis. Patients with epididymitis will likely have dysuria, fever, and tenderness or swelling of the spermatic cord and epididymis. Patients with urethritis may present with perineal pain and dysuria and have urethral discharge on examination. Patients with either of these conditions should be tested for chlamydia and gonorrhea. (See "Urethritis in adult males", section on 'Clinical manifestations' and "Acute scrotal pain in adults", section on 'Acute epididymitis or epididymo-orchitis'.)

Step two: Evaluate for other conditions — Certain historical and examination features are suggestive of alternative diagnoses including:

- Sensation of incomplete bladder emptying, suggestive of lower urinary tract disease (see "Lower urinary tract symptoms in males")

- Hematuria, which may be suggestive of many other diagnoses, including urogenital cancer (see "Etiology and evaluation of hematuria in adults")

- Lower-extremity paresthesias or weakness, suggestive of neurologic disease affecting the bladder such as spinal cord injury and lumbar spinal stenosis (see "Chronic complications of spinal cord injury and disease", section on 'Urinary complications' and "Lumbar spinal stenosis: Pathophysiology, clinical features, and diagnosis", section on 'Clinical presentation')

- Testicular masses or tenderness, suggestive of orchitis or testicular tumor (see "Acute scrotal pain in adults", section on 'Acute epididymitis or epididymo-orchitis' and "Clinical manifestations, diagnosis, and staging of testicular germ cell tumors", section on 'Clinical manifestations')

- Groin lymphadenopathy (suggestive of inflammation or malignancy in the penis or scrotum)
- Abdominal masses or hernias

Step three: Confirm findings consistent with CP/CPPS — If there are no findings suggestive of alternative diagnoses, those consistent with CP/CPPS should remain. (See 'Clinical manifestations' above.)

Symptoms include pain for three of the last six months, located in the perineum, testes, suprapubic area, or penis. Patients may also experience dysuria or pain with ejaculation. In addition, some patients may have urologic symptoms or sexual dysfunction.

Physical examination findings include a prostate that may be mildly tender or non-tender and muscle spasm or myofascial tenderness upon palpation of the perineum, pelvic floor, or pelvic sidewalls.

The urinalysis and culture should not indicate an infectious process, unless there is an alternative diagnosis or concurrent condition.

There is some overlap in presentation with interstitial cystitis/bladder pain syndrome (IC/BPS). This is another symptom-based syndrome whose diagnosis is made when there is pain attributed to the bladder, such as with bladder filling, and/or pain relieved by bladder emptying in the absence of other pathologic conditions [40]. There are no pathognomonic biological markers or pathology for either CP/CPPS or IC/BPS, as both are symptom complexes. The same symptoms may coexist in one individual. In the Multidisciplinary Approach to Pelvic Pain (MAPP) study sponsored by the National Institutes of Health (NIH), at baseline 42 percent of males enrolled with a working diagnosis of CP/CPPS also met criteria for a diagnosis of IC/BPS [41]. (See "Interstitial cystitis/bladder pain syndrome: Clinical features and diagnosis".)

Urine and laboratory studies — As noted above, all patients should have a urinalysis and culture. (See 'Step one: Determine if there is a bacterial infection' above.)

A prostate-specific antigen (PSA) test is not indicated for the assessment of CP/CPPS. If a PSA is measured and found to be elevated, the elevation should not be ascribed to CP/CPPS [42]. (See "Measurement of prostate-specific antigen".)

A urine cytology may be indicated if the patient has persistent dysuria [43]. (See "Overview of the initial approach and management of urothelial bladder cancer", section on 'Diagnosis'.)

Limited role for diagnostic imaging — Imaging studies are appropriate in certain patients:

- Patients with concomitant abdominal pain may require imaging to exclude an intraabdominal process.
- Testicular pain should be evaluated with a scrotal ultrasound, especially in patients with focal tenderness on examination or evidence of a mass. (See "Nonacute scrotal conditions in adults".)
- A bladder ultrasound or catheterization may be performed to check a post-void residual in patients who report a sensation of incomplete bladder emptying. (See "Clinical manifestations and diagnosis of urinary tract obstruction (UTO) and hydronephrosis".)
- Lumbar radiculopathy can produce pelvic pain, so patients with signs and symptoms suggesting radiculopathy (eg, lower-extremity paresthesias or weakness) may require imaging of the spine with magnetic resonance imaging (MRI). (See "Acute lumbosacral radiculopathy: Pathophysiology, clinical features, and diagnosis", section on 'Neuroimaging'.)

Referral to urologist — Patients who are found to have hematuria or an elevated PSA, and those who do not respond to initial treatment, should be referred to a urologist. Other indications for referral to a urologist include urinary retention, testicular mass, and abnormal prostate examination.

MANAGEMENT

Our approach — A number of medications and nonpharmacologic therapies including physical therapy and psychological support are available. There is no uniformly accepted treatment regimen and the approach to each patient is tailored to their predominant symptoms. Many treatments are used in combination, and monotherapy is generally considered to be less effective [44]. Some patients are treated initially with medications, others with nonpharmacologic interventions. Patient preference is an important determinant of treatment choice.

Initial pharmacologic treatment

- In most patients, we use an alpha blocker (either receptor specific or nonspecific) in combination with a shorter course of an antiinflammatory medication [45]. A reasonable option is tamsulosin 0.4 mg daily for six weeks and ibuprofen 400 mg three times daily for one week.

- Antiinflammatory medications can also be used alone, as can medications for neuropathic pain (eg, pregabalin) [45-48].

- In patients with voiding difficulties, we consider use of 5-alpha-reductase inhibitors. However, while these agents are commonly used in older men, they are not recommended in young men who are still trying to have children given the effects on semen volume. We also typically reserve 5-alpha-reductase inhibitors for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) for men with a prostate-specific antigen (PSA) level of at least 1.4 ng/mL [49].

- Treatment for sexual dysfunction in men with CP/CPPS includes the use of phosphodiesterase-5 inhibitors, which are discussed elsewhere. (See "Treatment of male sexual dysfunction".)

In a meta-analysis of 19 trials, patients using either antiinflammatories or alpha blockers were more likely to have a treatment response than those using placebo (risk ratio 1.7, 95% CI 1.4-2.1; and 1.4, 95% CI 1.1-1.8, respectively [45]. Post-treatment chronic prostatitis symptom index scores were also reduced with alpha blockers and to a lesser extent with antiinflammatories (mean difference compared with placebo of -10.8 and -1.7, respectively).

The best evidence for 5-alpha-reductase inhibitors comes from an analysis from the REDUCE trial, which administered dutasteride in an attempt to prevent prostate cancer and found that more men with CP/CPPS symptoms improved with dutasteride than with placebo (46 versus 35 percent) [50].

Limited role for antibiotics

- In patients who have a negative urine culture and features consistent with CP/CPPS, we do not treat with antibiotics. We are aware that there are many providers who would do so, based on limited and conflicting available evidence [51-53]. However, although some trials have shown improvement in symptoms after antibiotic treatment, certain antibiotic classes such as quinolones and tetracyclines have antiinflammatory and analgesic properties which may account for symptom improvement regardless of infection [54,55]. Although we do not favor this approach, it is not unreasonable to offer a course of antibiotics (four weeks' duration) despite a negative urine culture as a one-time trial intervention.

- In patients with a positive urine culture and symptoms consistent with cystitis, we treat with a seven-day course of antibiotics. (See "Acute simple cystitis in adult males" and "Acute simple cystitis in adult males", section on 'Treatment'.)

- Patients with a history of recurrent positive urine cultures and features consistent with chronic bacterial prostatitis should be treated accordingly. (See "Chronic bacterial prostatitis", section on 'Diagnosis' and "Chronic bacterial prostatitis", section on 'Antibiotic therapy'.)

- Patients with findings consistent with acute bacterial prostatitis, urethritis, or epididymitis should be treated accordingly. (See "Acute bacterial prostatitis", section on 'Management' and "Urethritis in adult males", section on 'Management' and "Acute scrotal pain in adults", section on 'Management'.)

Nonpharmacologic therapies — Patients may be interested in nonpharmacologic therapies for CP/CPPS, either alone or in combination with other treatments. Several have been evaluated, with varying results.

We utilize physical therapy in many patients. Those patients found to have pelvic floor muscle spasm on examination may benefit from physical therapy aimed at achieving myofascial trigger point release [56,57]. Patients who experience pain with ejaculation are also good candidates for physical therapy. This therapy is usually performed by a physical therapist rather than a urologist or primary care clinician.

In patients in whom psychological symptoms are prominent, a cognitive behavioral program specifically targeting CP/CPPS can improve both symptoms and quality of life [58-60]. This approach addresses approaches to pain, urinary difficulties, depressive symptoms, social support, sexual functioning, and overall quality-of-life issues. There are no randomized trials examining a behavioral counseling approach, and further studies are needed to determine which patients with CP/CPPS might benefit from this type of program.

Acupuncture has shown benefit in small studies [61,62]. In a 2018 systematic review, acupuncture reduced symptoms compared with a sham procedure (National Institutes of Health [NIH] Chronic Prostatitis Symptoms Index [NIH-CPSI] -5.79, 95% CI -7.32 to -4.26) and compared with standard medical therapy (-6.05, 95% CI -7.87 to -4.24) [63]. In a subsequent trial among 440 men with moderate to severe CP/CPPS comparing acupuncture with sham acupuncture (20 sessions over eight weeks), those receiving treatment had a greater reduction in symptoms (at least a 6-point reduction on the NIH-CPSI) at 8 weeks (60.6 versus 36.8 percent, adjusted odds ratio [AOR] 2.6, 95% CI 1.8-4.0) and at 32 weeks (61.5 versus 38.3 percent, AOR 2.6, 95% CI 1.7-3.9) [64].

Sitz baths have anecdotally been reported to provide some relief of pain, although there have been no studies on efficacy for chronic symptoms.

In a trial among 231 males with CPPS, an 18-week program of aerobic exercise resulted in improvement in pain, quality of life, and overall symptom scores compared with stretching and nonaerobic exercise [65].

Follow-up — Regardless of treatment, patients are usually seen in follow-up every three to four months until they have improved and stabilized. The NIH-CPSI can be used to follow symptoms (ie, pain, voiding, and quality of life) and measure response to treatment [30]. A modified version of the NIH-CPSI is the Genitourinary Pain Index (GUPI), which adds questions on pain with bladder filling and bladder emptying [66].

Treatment for patients refractory to initial therapy — If initial treatment does not provide adequate symptomatic improvement, patients should be referred to a urologist for further evaluation and management. In patients with continued pain and voiding symptoms, it is reasonable to continue an alpha blocker beyond the initial treatment duration. Such patients should be reevaluated after three months of continued alpha-blocker therapy.

Other therapies — Although used less commonly, there are other therapies with potential benefit:

- Tricyclic antidepressants (eg nortriptyline, amitriptyline) may have modest benefit in patients with CP/CPPS [67,68].
- Phytotherapies that may be effective include cernilton (pollen extract) and quercetin (bioflavonoid) [69,70].
- Extracorporeal shockwave therapy – In a systematic review that included three small studies of extracorporeal shockwave therapy, symptoms measured by NIH-CPSI were reduced by 6.17, although the effect was not necessarily sustained [63].
- Surgical intervention for CP/CPPS is reserved only for those patients with a specific indication (eg, urethral stricture, bladder neck obstruction) [71].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Chronic prostatitis, interstitial cystitis, and chronic pelvic pain syndrome".)

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.)

- Basics topics (see "Patient education: Chronic prostatitis and chronic pelvic pain syndrome (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a clinical syndrome defined primarily by pelvic pain with or without urinary symptoms. It is the most common diagnosis in men presenting with prostatitis; acute and chronic bacterial prostatitis are less common. (See 'Definition' above.)

- The etiology of CP/CPPS is unknown. Despite the use of the term "prostatitis," it is unclear to what degree the prostate is the source of symptoms. (See 'Etiology' above.)

- CP/CPPS is a diagnosis of exclusion. Patients should have a physical examination directed at identifying other etiologies of pelvic pain. A urinalysis should be performed in all patients, with urine culture as indicated. Diagnostic imaging is used in selected patients. (See 'Diagnostic approach' above.)

- In patients with CP/CPPS, we suggest against antibiotic therapy (**Grade 2C**). However, given that some patients appear to benefit from antibiotic treatment, a single course of antibiotics may be a reasonable alternative. In addition, antibiotic therapy is warranted in patients with objective evidence of alternative or concurrent diagnoses characterized by bacterial infection (eg, cystitis, bacterial prostatitis, urethritis, epididymitis). (See 'Limited role for antibiotics' above.)

- In most patients, we suggest combination therapy with an alpha blocker and an antiinflammatory agent (**Grade 2C**). A reasonable option is tamsulosin 0.4 mg daily for six weeks and ibuprofen 400 mg three times daily for one week. (See 'Initial pharmacologic treatment' above.)

  Alternative treatment approaches are also reasonable. Antiinflammatory medications alone and 5-alpha-reductase inhibitors also appear to have modest but lesser effects on symptoms in some patients. Physical therapy aimed at myofascial release may have benefit in patients with pelvic floor muscle spasm. A cognitive behavioral treatment program may be beneficial in some patients with concomitant psychosocial problems. Benefit has also been suggested with acupuncture and extracorporeal shock wave therapy. (See 'Management' above.)

- Patients whose symptoms persist despite these initial treatments, or who are found to have abnormalities such as hematuria or an elevated prostate-specific antigen (PSA), should be referred to a urologist. (See 'Referral to urologist' above.)

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Topic 6880 Version 46.0

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