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# Management of Chronic Pelvic Pain in Men

**Learning Objective:** At the conclusion of this continuing medical education activity, the participant will be able to define chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), diagnose CP/CPPS, and employ a multimodal therapy model to treat CP/CPPS.

This AUA Update aligns with the American Board of Urology Module on Core/General Urology. Additional information on this topic can be found in the AUA Core Curriculum sections on Sexual Medicine and Andrology, and Urinary Incontinence and Overactive Bladder.

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**KEY WORDS:** chronic prostatitis, perineal pain, UPOINT classification, CPSI scores

## INTRODUCTION

Male chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS), more frequently diagnosed as CP, accounts for about 90% of all prostatitis cases.[1] The term "prostatitis" itself describes 4 distinct clinical presentations categorized by the National Institutes of Health (NIH) into categories I, II, III, and IV (Figure 1). CP/CPPS belongs to category III–chronic abacterial prostatitis. **Category III is defined by soreness or pain in the pelvic, perineal, or testicular region lasting longer than 3 months, with variable sexual and voiding symptoms, and most distinctively, no identifiable pathology.** A final diagnosis of CP/CPPS is reached when there is no recognizable pathology underlying such symptoms. Category III is subdivided into IIIa, inflammatory CP with pyospermia and/or leukocytes in prostatic secretions, and IIIb, noninflammatory CP with no leukocytes in semen or prostatic secretions.

*Etiology.* CP/CPPS has a median age of presentation of 43 years, with an estimated prevalence of 2%-16% in the US.[1,2] Risk factors for CP/CPPS include urethral catheterization or instrumentation, inadequately treated urinary tract infections (UTIs), pelvic trauma, urethral strictures, and/or psychological stress or depression. **Despite the high prevalence of CP/CPPS, the exact cause is unknown, but it is presumed to be multifactorial, with a combination of factors contributing to the pathology.** Current theories include nano-bacterial colonization, atypical bacterial infection, pelvic floor muscle dysfunction, intraprostatic urinary reflux, elevated intraprostatic pressure due to voiding dysfunction, and endocrine, neuropathic, and autoimmune causes. Associated conditions often include allergies, sinusitis, erectile dysfunction, irritable bowel syndrome, depression, fibromyalgia, fatigue, and neurologic disorders. Due to multiple etiologies and symptoms, the UPOINT (for Urinary, Psychosocial, Organ specific, Infectious, Neurological/systemic, and Tenderness of skeletal muscles) system was developed based on probable etiological mechanisms and clinical phenotypes to improve outcomes by tailoring treatment to the relevant pathology.

| UPOINT Classification | | Shoskes et al.[3] |
|---|---|---|
| **U**rinary | Irritative or obstructive urinary symptoms | 52% |
| **P**sychological | Clinically diagnosed depression, verbalized hopelessness or helplessness | 34% |
| **O**rgan Specific | Prostate tenderness, pain during the voiding cycle, or hematospermia | 61% |
| **I**nfection | Positive culture of expressed prostatic secretion or urine, or concomitant urethritis | 16% |
| **N**eurologic/ Systemic | Pain outside the pelvis, or pain disorders | 37% |
| **T**enderness | Pain on palpitation, or pelvic floor spasm | 53% |

**Figure 2**. UPOINT classification of chronic prostatitis/chronic pelvic pain syndrome and the number of patients positive per domain.

**The UPOINT system divides patients into 6 domains: urinary, psychological, organ-specific, infection, neurologic/systemic, and tenderness (Figure 2).** Twenty-two percent of patients present with a single positive domain, while most patients have 2 positive domains.[3] Though patient age does not influence the number of positive domains, symptom duration and severity are associated with a greater number of positive domains.[3]

*Patient presentation.* **The traditional CP/CPPS patient is an individual who has had pelvic, perineal, or genital pain for at least 3 of the last 6 months.** Pain onset is reported as sudden, and intensity ranges from mild to severe. Though CP/CPPS pain is typically localized to the perineal and genital region, there is often radiating pain to other areas, including the lower abdomen and back, rectum, scrotum, testes, and

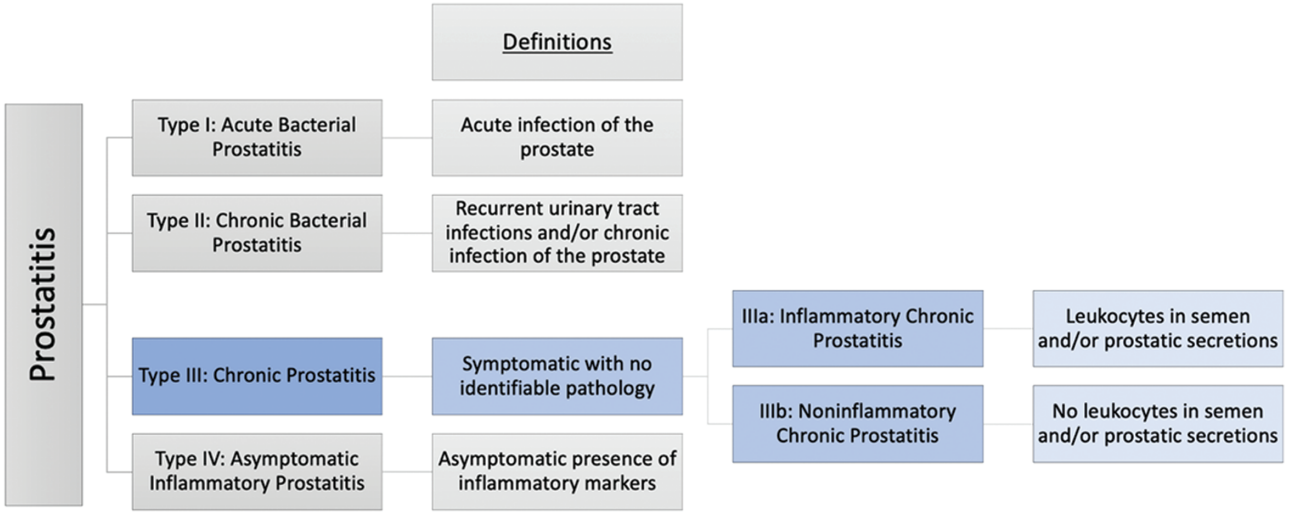



**Figure 1**. NIH classification of prostatitis; the topic of this Update, chronic prostatitis, is highlighted in blue.

**ABBREVIATIONS:** chronic prostatitis (CP), chronic pelvic pain syndrome (CPPS), Chronic Prostatitis Symptom Index (CPSI), digital rectal exam (DRE), expressed prostatic secretion (EPS), lower urinary tract symptoms (LUTS), phosphodiesterase 5 inhibitor (PDE5i), pelvic floor physical therapy (PFPT), urinary tract infection (UTI), voided bladder (VB)

penis. Commonly, voiding and/or sexual dysfunction are also associated with pain. Patients may also report lower urinary tract symptoms (LUTS), such as weak stream, hesitancy, incomplete bladder emptying, interrupted stream, and urinary frequency and urgency. Other systemic symptoms commonly associated with CP/CPPS include depression, anxiety, myalgia, arthralgia, and fatigue. CP symptoms typically fluctuate in an inconsistent relapsing-remitting course, with the timing of flares poorly understood.

## DIAGNOSIS

Diagnosis is complicated by the lack of a known CP/CPPS etiology. **However, good history with a physical exam, including a digital rectal exam (DRE), imaging (especially of the lower abdomen), and laboratory tests (specifically the Meares-Stamey test), can assist in diagnosis.** Pelvic imaging with an MRI can be helpful in very select cases to rule out congenital anatomic abnormalities, spinal dysraphism, and pelvic nerve entrapments.

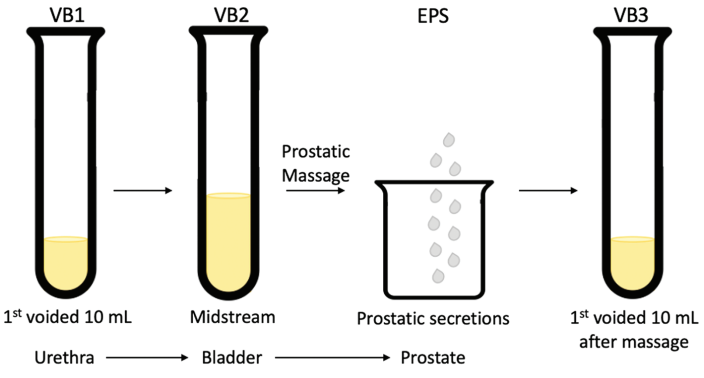
*History.* Most importantly, in diagnosing CP/CPPS, providers must elicit a good history. This must include determining the duration of symptoms, questioning for pain in the suprapubic region, lower back, penis, testes, and/or scrotum, identifying alleviating and exacerbating factors, and checking for systemic symptoms suggestive of infection. A common symptom associated with CP/CPPS, and a strong predictor of quality of life, is the presence of pain or discomfort either during or after ejaculation. It is essential to ask about muscle spasms in the perineal area and any voiding symptoms such as urgency, frequency, hesitancy, and interrupted urinary flow after ejaculation. **Therefore, practitioners should include in their history questions concerning sexual dysfunction, sexually transmitted infections, pelvic floor muscle spasms, recent instrumentations, and LUTS voiding symptoms.** The validated NIH-Chronic Prostatitis Symptom Index (CPSI) questionnaire should be used to assess pain, urinary function, and quality of life.[4]

*NIH-CPSI questionnaire.* The NIH-CPSI is a validated survey consisting of questions regarding pain, urination, the impact of symptoms, and quality of life. It is used for both initial evaluation and treatment follow-up. A 6-point improvement in total score correlates with patient-reported improvement.[4,5] The survey can be found in the article entitled, "The National Institutes of Health Chronic Prostatitis Symptom Index: Development and Validation of a New Outcome Measure," by Litwin et al.[4]

*Physical exam.* The physical exam helps rule out other differential diagnoses such as musculoskeletal inflammation, inguinal herniation, or nerve entrapment. A urologist's physical exam for CP/CPPS should be focused on the genitalia, groin, perineum, coccyx, external anal sphincter, and internal pelvic floor and side walls, with a DRE performed. **Since urine needs to be analyzed before and after a prostatic massage, a urine sample should be collected before carrying out a DRE.** Most CP/CPPS patients will have an unremarkable DRE except for pain; however, the degree of pain does not help differentiate between the various categories of CP/CPPS. During the DRE, the provider should palpate the internal pelvic musculature to assess for muscle spasms, tight knots, or trigger points that can reproduce the pain upon palpation.[6] Following the DRE, the provider, should collect expressed prostatic secretion (EPS) and post-massage urine.

*Laboratory tests.* While a thorough history and physical exam form the cornerstone of CP/CPPS diagnosis, lab tests may be ordered when the differential remains broad. **Providers should collect and culture urine samples from before and after prostatic massage by ordering the Meares-Stamey 4-glass test; however, due to the practical limitations in obtaining an EPS in all patients, the 2-glass test may be sufficient.**[7] A previous study has demonstrated the 2-glass test to be 91% sensitive and specific compared to the 4-glass test.[7] The 4-glass test consists of 4 fluid samples: voided bladder (VB) 1, which is the first 10 cc of voided urine representing urethral bacteria, VB-2, which is a midstream collection representing bladder urine, at least 4 drops of postprostatic massage EPS, and VB-3, which is the first 10 cc of postprostatic massage voided urine (Figure 3). The 2-glass test consists of 2 urinary samples: VB-2, a midstream bladder urine, and VB-3, a postmassage voided urine. To note, EPS can be evaluated in the office via microscopy while VB specimens must be sent to lab.

Inflammatory CP/CPPS (CP/CPPS IIIA) is diagnosed when there are greater leukocytes in the EPS or VB-3 than VB-1 or VB-2. At the same time, noninflammatory CP/CPPS (CP/CPPS IIIB) is diagnosed when no pyuria or bacteriuria is observed. Both tests have variable interpretations of white blood cell counts, can fail to identify difficult-to-culture organisms, and can result in difficulties with interpreting bacterial localization, as asymptomatic individuals often have uropathogens. To note, we do not routinely use the Meares-Stamey 4-glass test or the 2-glass test to differentiate between IIIA and IIIB as this may not provide clinically relevant information pertinent to management. Differentiation is best reserved for specific patients, including those with recurrent UTIs, or for research purposes. There is little evidence for using seminal culture in evaluating a CP/CPPS




| Classification | Specimen | VB1 | VB2 | EPS | VB3 |
|---|---|---|---|---|---|
| Type IIIA | WBC | - | - | + | + |
| | Culture | - | - | - | - |
| Type IIIB | WBC | - | - | - | - |
| | Culture | - | - | - | - |

**Figure 3.** The Meares-Stamey 4-glass test procedure and interpretation. EPS indicates expressed prostatic secretion; VB, voided bladder; WBC, white blood cell.

patient.[6] Further, there is limited evidence associating CP/CPPS with prostate cancer, and therefore obtaining a PSA at the time of diagnosis is not indicated unless warranted by other patient-specific factors.[8]

*Imaging*. Though pelvic imaging is considered optional, urologists may choose to obtain a CT or MRI to rule out other differentials of pelvic pain, such as cysts, cancers, calculi, and pudendal neuralgia. Lumbosacral spine MRIs should also be considered to evaluate spinal pathology. However, transrectal ultrasonography is not warranted unless there's a high suspicion of obstructed seminal vesicles or prostate abscesses.

*Other evaluations*. Young men with chronic LUTS are often misdiagnosed with CP/CPPS. Though challenging to differentiate, various video urodynamic findings, including decreased peak and mean urinary flow rates, elevated maximal urethral closing pressure, incomplete funneling of the bladder neck, and urethral narrowing at the level of the external urethral sphincter, support a CP/CPPS diagnosis.[9] Prostate biopsies are not recommended. If other etiologies are indicated, a cystoscopy may be performed.

*Differential diagnosis*. The following conditions can mimic CP/CPPS: benign prostatic hyperplasia, varicocele, seminal vesicle obstruction, bladder calculus, bladder cancer, bladder neck contracture, primary bladder neck obstruction, overactive bladder, interstitial cystitis, primary voiding dysfunction, prostate abscess, prostate cancer, prostate cyst, radiation cystitis, tuberculosis of the prostate, urethral stricture, urethritis, urethral diverticulum, diabetes mellitus, and pudendal nerve entrapment, to name a few.

## TREATMENT

**Effective treatment requires multimodal therapy targeted to the positive UPOINT categories. Efficacy is gauged primarily on symptom relief.**[10] Treatment options often include antibiotics, alpha-blockers, phosphodiesterase 5 inhibitors (PDE5is), anti-inflammatories, 5-alpha-reductase inhibitors, neuromodulators, pelvic floor physical therapy (PFPT), cognitive behavior therapy, and surgery (Figure 4). Conservative measures, including diet modifications, myofascial physical therapy, and acupuncture, are part of first-line therapy.

Guided by the UPOINT classification, providers should prescribe patients with CP/CPPS a multimodal protocol with minimal drug and antibiotic usage to limit adverse effects. The distinction between inflammatory CP/CPPS and noninflammatory CP/CPPS is not required for an empiric treatment protocol. Further, mild central nervous system analgesics, such as sertraline or fluoxetine, may be utilized to reduce associated CP/CPPS pain. Providers should obtain information about modifiable factors such as diet, environment, and sexual habits and counsel patients accordingly. The NIH-CPSI questionnaire and voiding diaries should be used to monitor patient response to the treatment regimen closely. A multidisciplinary team consisting of a urologist, pain control specialist, physiotherapist, psychologist, cognitive behavioral therapist, and a sexual health counselor is often required for effective CP/CPPS treatment.

### *Medical therapy*

Antibiotics: Treatments for antibiotic-naïve patients may include antibiotics. **Providers should reassess patients 2 to 4 weeks after initiating therapy. Continued treatment with antibiotics is warranted if pretreatment cultures are positive or the patient reports symptom improvement with treatment.**[11] It is not recommended to re-treat with the same antibiotic if the initial therapeutic course fails. Further, if the patient's symptoms have persisted over 6 weeks with no documented UTI, urologists should avoid antibiotics

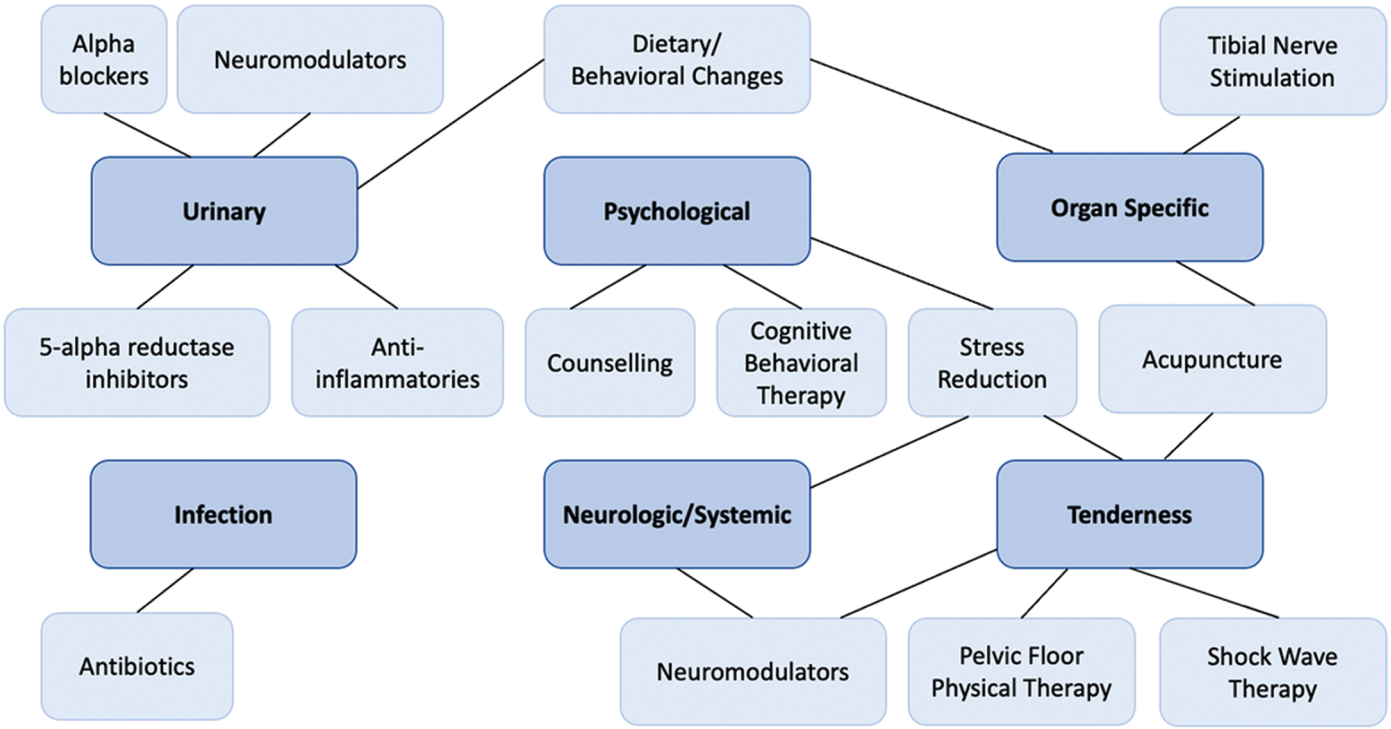



**Figure 4**. Treatment modalities based on UPOINT classification.

altogether.[12,13] However, patients who have demonstrated improvement with antibiotic treatment in the past may be prescribed additional courses upon symptom relapse. The most commonly used antibiotics in CP/CPPS are TMP-SMX (trimethoprim/sulfamethoxazole) or fluoroquinolones such as ciprofloxacin or levofloxacin, due to their good prostatic penetration.[12-16] However, urologists should be aware of the anti-inflammatory properties of some antibiotics and the potential for a placebo effect along with toxicity associated with long-term usage of fluoroquinolones, including but not limited to tendon rupture, peripheral neuropathy, and aortic rupture.

PDE5is: PDE5is represent a new development in the treatment of CP/CPPS. These drugs, such as sildenafil and tadalafil, are commonly used to relieve erectile dysfunction and LUTS in men with benign prostatic hyperplasia.[17,18] Previous studies have evaluated the role of PDE5i in CP/CPPS, for example, by showing improvement in International Prostate Symptom Score amongst men with LUTS on daily sildenafil.[19] **A recent prospective study demonstrated everyday use of tadalafil resulted in significant improvement in all domains investigated by the NIH-CPSI; this is one of the first studies to show sustained long-term relief of symptoms following CP/CPPS treatment.[20]** The authors postulate an improved response to tadalafil, as opposed to other PDE5is, such as sildenafil and vardenafil, due to tadalafil's much higher sensitivity for PDE-11, which is vastly expressed in the prostate.[20,21]

Alpha-blockers: The prostate and bladder neck are rich in alpha-adrenergic receptors. Therefore, alpha-blockers may induce bladder neck relaxation and improve urinary symptoms. A meta-analysis investigating the effectivity of alpha-blockers reported improvements in CPSI scores with alpha-blocker use compared to placebo; however, this improvement was more significant in voiding symptoms than pain.[22] Considering the side effect profile of alpha-blockers, including hypotension, dizziness, fatigue, and weak force of ejaculation, their use necessitates a careful balance of pros and cons. **Therefore, alpha-blockers are only recommended in patients with voiding symptoms and, even then, should be combined with other forms of therapy.[6,11] Preference for alpha-blockers should be given to those patients at risk of LUTS, including patients with post-void residuals higher than 200 mL indicating urinary retention.** Alpha-blockers have minimal ejaculatory side effects but are contraindicated with moderate hepatic insufficiency or with cytochrome P450 3A4 inhibitors.[23] To note, a recent randomized clinical trial demonstrated no benefit of alfuzosin compared to placebo in CP/CPPS alpha-blocker–naïve patients with no documented history of UTI.[24]

Anti-inflammatory Agents: Anti-inflammatory agents, including nonsteroidal anti-inflammatory drugs, corticosteroids, and immunosuppressive drugs, have been used to treat CP/CPPS.[25] While higher IL-1 beta and lower HSP70 levels are observed in patients with CP/CPPS symptoms, anti-inflammatories have failed to show significant positive clinical results.[6] Daily dosed rofecoxib did demonstrate symptom relief at higher doses, but it also carried an increased cardiovascular risk, negating any symptom benefit.[26] Another study looking at celecoxib demonstrated short-term symptom improvement; however, any difference between placebo and agent disappeared within 2 weeks of treatment cessation.[6,27] Oral prednisone therapy has also not shown any benefit.[6,28] In contrast, herbal anti-inflammatories such as bioflavonoids, cernilton, and saw palmetto had demonstrated efficacy in CP/CPPS.[6,29-32]

5-Alpha-reductase Inhibitors: Older men with increased PSA and enlarged prostates have benefited from long-term therapy with 5-alpha-reductase inhibitors such as mepartricin or finasteride and have demonstrated improvements in CPSI scores.[11,33] Currently, these agents are not recommended as first-line choices.

Neuromodulators: Neuromodulating medications have been well studied in neuropathic pain. Recent research is beginning to illuminate their role in treating CP/CPPS. A placebo-controlled trial of amitriptyline treatment demonstrated improvement in pain and urinary frequency symptoms.[34] Relatedly, a trial of gabapentin, amitriptyline, or both showed similar symptom alleviation during treatment across the cohorts and improved long-term pain scores in the gabapentin or the gabapentin plus amitriptyline cohorts.[35] A pregabalin trial also demonstrated improvements in CPSI and global pain scores.[36]

*PFPT.* Patients with refractory CP/CPPS often have pelvic floor muscle dysfunction and benefit significantly from PFPT.[6,37] PFPT includes paradoxical relaxation, myofascial release, and stretching exercises.[6] Greater clinical experience in PFPT is correlated with better patient outcomes post-therapy.[38] **Providers should refer patients to specialized centers with highly trained PFPTs.** Understandably, many patients live far away from such centers, and repeated trips to PFPT may be cumbersome. However, a recent study revealed a significant reduction in CPSI scores in most patients receiving short courses of intensive PFPT sessions.[39] Moreover, 88% of patients have had a greater than 25% improvement in pelvic pain symptom survey sexual scores post-PFPT, and 50% have had at least a 50% improvement in these scores.[6,37] **Hence, PFPT may reduce pain and improve sexual function in those with CP/CPPS.**

*Psychological support and cognitive behavioral therapy.* Coping mechanisms influence patients' reactions to and treatment for pain. Therefore, cognitive behavioral therapy and/or psychological support are needed in addition to medical and physical therapy to improve patient outcomes.[6] This is a field of active ongoing research but should be part of all patient discussions and treatment strategies.[40]

*Additional therapies.* Many modifiable risk factors are associated with CP/CPPS. **These factors are categorized into diet (excessive dieting, hot pepper and other spicy foods, alcohol consumption, coffee intake, and bowel dysfunction), sexual habits (excessive sex, delaying ejaculation, and coitus interruptus), sedentary lifestyle, and perineal trauma (pelvic floor muscle tenderness, excessive sitting, and traumatic sports).[41,42]** Associated lifestyle adjustments require open communication and support from partners and family and can result in a significant reduction of CP/CPPS symptoms.[10,43,44]

Further, recent studies have revealed long-lasting symptom alleviation with trials of percutaneous tibial nerve stimulation,[10,43-46] acupuncture,[10,43,44,46,47] or perineal extracorporeal shock wave therapy.[10,44,46] As data regarding these treatments

continue to emerge, providers should consider them an adjunct to first-line medical therapy.

*Surgery.* It is the authors' opinion that bladder outlet procedures should be considered for men over the age of 50, where bladder outlet due to benign prostatic hyperplasia is also thought to be present.

## CONCLUSION

In conclusion, CP/CPPS is a set of symptoms rather than a single disease entity with a broad range of etiologies, treatment modalities, and prognosis. Although CP/CPPS remains an elusive diagnosis for practitioners and patients, significant progress has been made in its evaluation and treatment. As research and clinical evidence continue to elucidate the pathophysiology of CP/CPPS, practitioners must employ multidisciplinary, multimodal treatment plans that provide patients with superior overall outcomes. Treatment of CP/CPPS involves a multimodal approach consisting of antibiotics alpha-blockers, PDE5is, anti-inflammatories, 5-alpha-reductase inhibitors, neuromodulators, PFPT, cognitive behavior therapy, and/or surgery. Conservative measures, including diet modifications, myofascial physical therapy, and acupuncture, are considered part of first-line therapy.

### DID YOU KNOW?

- Male CP/CPPS, more commonly known as CP, is defined by discomfort or pain in the pelvic, perineal, or testicular region lasting longer than 3 months, with variable sexual and voiding symptoms, and no identifiable pathology.
- For effective diagnosis of CP/CPPS, providers must elicit a good history, including information on sexual dysfunction, sexually transmitted infection history, pelvic floor muscle spasms, recent instrumentation, and voiding symptoms, along with performing a DRE and the Meares-Stamey 4-glass or 2-glass test.
- Providers should administer the NIH-CPSI questionnaire during each visit to evaluate and track domains of pain, urination, the impact of symptoms, and quality of life.
- Patients should be classified and treated according to their symptoms as categorized by the UPOINT classification system.

## REFERENCES


1. Habermacher GM, Chason JT, Schaeffer AJ. Prostatitis/chronic pelvic pain syndrome. *Annu Rev Med.* 2006;57:195-206.
2. Clemens JQ, Meenan RT, O'Keeffe Rosetti MC, Kimes T, Calhoun EA. Prevalence of and risk factors for prostatitis: population based assessment using physician assigned diagnoses. *J Urol.* 2007;178(4 Pt 1):1333-1337.
3. Shoskes DA, Nickel JC, Dolinga R, Prots D. Clinical phenotyping of patients with chronic prostatitis/chronic pelvic pain syndrome and correlation with symptom severity. *Urology.* 2009;73(3):538-542.
4. Litwin MS, McNaughton-Collins M, Fowler FJ Jr, et al. The National Institutes of Health Chronic Prostatitis Symptom Index: development and validation of a new outcome measure. Chronic Prostatitis Collaborative Research Network. *J Urol.* 1999;162(2):369-375.
5. Propert KJ, Litwin MS, Wang Y, et al. Responsiveness of the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI). *Qual Life Res.* 2006;15(2):299-305.
6. Polackwich AS, Shoskes DA. Chronic prostatitis/chronic pelvic pain syndrome: a review of evaluation and therapy. *Prostate Cancer Prostatic Dis.* 2016;19(2):132-138.
7. Nickel JC, Shoskes D, Wang Y, et al. How does the pre-massage and post-massage 2-glass test compare to the Meares-Stamey 4-glass test in men with chronic prostatitis/chronic pelvic pain syndrome?. *J Urol.* 2006;176(1):119-124.
8. Liu Y, Mikrani R, Xie D, et al. Chronic prostatitis/chronic pelvic pain syndrome and prostate cancer: study of immune cells and cytokines. *Fundam Clin Pharmacol.* 2020;34(2):160-172.
9. Hafez H. Urodynamic evaluation of patients with chronic pelvic pain syndrome. *UroToday.* 2009;2(3).
10. Khattak AS, Raison N, Hawazie A, Khan A, Brunckhorst O, Ahmed K. Contemporary management of chronic prostatitis. *Cureus.* 13(12):e20243.
11. Pena VN, Engel N, Gabrielson AT, Rabinowitz MJ, Herati AS. Diagnostic and management strategies for patients with chronic prostatitis and chronic pelvic pain syndrome. *Drugs Aging.* 2021;38(10):845-886.
12. Nickel JC, Downey J, Clark J, et al. Levofloxacin for chronic prostatitis/chronic pelvic pain syndrome in men: a randomized placebo-controlled multicenter trial. *Urology.* 2003;62(4):614-617.
13. Magri V, Trinchieri A, Pozzi G, et al. Efficacy of repeated cycles of combination therapy for the eradication of infecting organisms in chronic bacterial prostatitis. *Int J Antimicrob Agents.* 2007;29(5):549-556.
14. Magri V, Montanari E, Škerk V, et al. Fluoroquinolone-macrolide combination therapy for chronic bacterial prostatitis: retrospective analysis of pathogen eradication rates, inflammatory findings and sexual dysfunction. *Asian J Androl.* 2011;13(6):819-827.
15. Doiron RC, Shoskes DA, Nickel JC. Male CP/CPPS: where do we stand?. *World J Urol.* 2019;37(6):1015-1022.
16. Gorpynchenko I, Nurimanov K, Poroshina T, Savchenko V, Drannik G, Shulyak A. Antibiotic therapy effectiveness as an outcome predictor of complex treatment in chronic prostatitis/chronic pelvic pain syndrome. *Cent European J Urol.* 2021;74(2):241-248.
17. Gacci M, Andersson KE, Chapple C, et al. Latest evidence on the use of phosphodiesterase type 5 inhibitors for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia. *Eur Urol.* 2016;70(1):124-133.
18. Salonia A, Rigatti P, Montorsi F. Sildenafil in erectile dysfunction: a critical review. *Curr Med Res Opin.* 2003;19(4):241-262.

19. Sairam K, Kulinskaya E, McNicholas TA, Boustead GB, Hanbury DC. Sildenafil influences lower urinary tract symptoms. *BJU Int.* 2002;90(9):836-839.

20. Pineault K, Ray S, Gabrielson A, Herati AS. Phosphodiesterase type 5 inhibitor therapy provides sustained relief of symptoms among patients with chronic pelvic pain syndrome. *Transl Androl Urol.* 2020;9(2):391-397.

21. Fujishige K, Kotera J, Yuasa K, Omori K. The human phosphodiesterase PDE10A gene genomic organization and evolutionary relatedness with other PDEs containing GAF domains. *Eur J Biochem.* 2000;267(19):5943-5951.

22. Yang G, Wei Q, Li H, Yang Y, Zhang S, Dong Q. The effect of alpha-adrenergic antagonists in chronic prostatitis/chronic pelvic pain syndrome: a meta-analysis of randomized controlled trials. *J Androl.* 2006;27(6):847-852.

23. Michel MC. Alpha1-adrenoceptors and ejaculatory function. *Br J Pharmacol.* 2007;152(3):289-290.

24. Nickel JC, Krieger JN, McNaughton-Collins M, et al. Alfuzosin and symptoms of chronic prostatitis–chronic pelvic pain syndrome. *N Engl J Med.* 2008;359(25):2663-2673.

25. Anothaisintawee T, Attia J, Nickel JC, et al. Management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. *JAMA.* 2011;305(1):78-86.

26. Nickel JC, Pontari M, Moon T, et al. A randomized, placebo controlled, multicenter study to evaluate the safety and efficacy of rofecoxib in the treatment of chronic nonbacterial prostatitis. *J Urol.* 2003;169(4):1401-1405.

27. Zhao WP, Zhang ZG, Li XD, et al. Celecoxib reduces symptoms in men with difficult chronic pelvic pain syndrome (Category IIIA). *Braz J Med Biol Res.* 2009;42(10):963-967.

28. Bates SM, Hill VA, Anderson JB, et al. A prospective, randomized, double-blind trial to evaluate the role of a short reducing course of oral corticosteroid therapy in the treatment of chronic prostatitis/chronic pelvic pain syndrome. *BJU Int.* 2007;99(2):355-359.

29. Shoskes DA, Zeitlin SI, Shahed A, Rajfer J. Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial. *Urology.* 1999;54(6):960-963.

30. Wagenlehner FME, Schneider H, Ludwig M, Schnitker J, Brähler E, Weidner W. A pollen extract (Cernilton) in patients with inflammatory chronic prostatitis-chronic pelvic pain syndrome: a multicentre, randomised, prospective, double-blind, placebo-controlled phase 3 study. *Eur Urol.* 2009;56(3):544-551.

31. Cai T, Verze P, La Rocca R, Anceschi U, De Nunzio C, Mirone V. The role of flower pollen extract in managing patients affected by chronic prostatitis/chronic pelvic pain syndrome: a comprehensive analysis of all published clinical trials. *BMC Urol.* 2017;17(1):32.

32. Zhang K, Guo RQ, Chen SW, et al. The efficacy and safety of serenoa repens extract for the treatment of patients with chronic prostatitis/chronic pelvic pain syndrome: a multicenter, randomized, double-blind, placebo-controlled trial. *World J Urol.* 2021;39(9):3489-3495.

33. Nickel JC, Roehrborn C, Montorsi F, Wilson TH, Rittmaster RS. Dutasteride reduces prostatitis symptoms compared with placebo in men enrolled in the REDUCE study. *J Urol.* 2011;186(4):1313-1318.

34. van Ophoven A, Pokupic S, Heinecke A, Hertle L. A prospective, randomized, placebo controlled, double-blind study of amitriptyline for the treatment of interstitial cystitis. *J Urol.* 2004;172(2):533-536.

35. Sator-Katzenschlager SM, Scharbert G, Kress HG, et al. Chronic pelvic pain treated with gabapentin and amitriptyline: a randomized controlled pilot study. *Wien Klin Wochenschr.* 2005;117(21-22):761-768.

36. Pontari MA, Krieger JN, Litwin MS, et al. Pregabalin for the treatment of men with chronic prostatitis/chronic pelvic pain syndrome: a randomized controlled trial. *Arch Intern Med.* 2010;170(17):1586-1593.

37. Anderson RU, Wise D, Sawyer T, Chan C. Integration of myofascial trigger point release and paradoxical relaxation training treatment of chronic pelvic pain in men. *J Urol.* 2005;174(1):155-160.

38. Polackwich AS, Li J, Shoskes DA. Patients with pelvic floor muscle spasm have a superior response to pelvic floor physical therapy at specialized centers. *J Urol.* 2015;194(4):1002-1006.

39. Anderson RU, Wise D, Sawyer T, Glowe P, Orenberg EK. 6-Day intensive treatment protocol for refractory chronic prostatitis/chronic pelvic pain syndrome using myofascial release and paradoxical relaxation training. *J Urol.* 2011;185(4):1294-1299.

40. Urits I, Callan J, Moore WC, et al. Cognitive behavioral therapy for the treatment of chronic pelvic pain. *Best Pract Res Clin Anaesthesiol.* 2020;34(3):409-426.

41. Gallo L. Effectiveness of diet, sexual habits and lifestyle modifications on treatment of chronic pelvic pain syndrome. *Prostate Cancer Prostatic Dis.* 2014;17(3):238-245.

42. Herati AS, Shorter B, Srinivasan AK, et al. Effects of foods and beverages on the symptoms of chronic prostatitis/chronic pelvic pain syndrome. *Urology.* 2013;82(6):1376-1380.

43. Zhang J, Liang C, Shang X, Li H. Chronic prostatitis/chronic pelvic pain syndrome: a disease or symptom? Current perspectives on diagnosis, treatment, and prognosis. *Am J Mens Health.* 2020;14(1):1557988320903200.

44. Hu M, Wazir J, Ullah R, et al. Phytotherapy and physical therapy in the management of chronic prostatitis–chronic pelvic pain syndrome. *Int Urol Nephrol.* 2019;51(7):1081-1088.

45. Cohen JM, Fagin AP, Hariton E, et al. Therapeutic intervention for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS): a systematic review and meta-analysis. *PLoS One.* 2012;7(8):e41941.

46. Franco JV, Turk T, Jung JH, et al. Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome. *Cochrane Database Syst Rev.* 2018;2018(5):CD012551.

47. Chang SC, Hsu CH, Hsu CK, Yang SSD, Chang SJ. The efficacy of acupuncture in managing patients with chronic prostatitis/chronic pelvic pain syndrome: a systemic review and meta-analysis. *Neurourol Urodyn.* 2017;36(2):474-481.

# Study Questions Volume 42 Lesson 21

1. A 45-year-old male patient presents with sudden onset, chronic perineal pain exacerbated during sexual function over the past 5 months. There is no history of UTI. What should be included in a differential diagnosis list?
   a. Acute bacterial prostatitis
   b. Chronic bacterial prostatitis
   c. Chronic prostatitis/chronic pelvic pain syndrome
   d. Asymptomatic inflammatory prostatitis

2. A 52-year-old patient diagnosed with chronic prostatitis reports worsening nocturia, increased frequency of urination, and abdominal pain on palpation. During assessment, he states "Doc, we've tried everything, it just feels like nothing is helping. I don't know what to do anymore." How many UPOINT domains does this patient have?
   a. 1
   b. 2
   c. 3
   d. 4+

3. When should the digital rectal examination be performed on chronic prostatitis/chronic pelvic pain syndrome patients during a Meares-Stamey 4-glass test?
   a. Before collecting VB1
   b. After collecting VB1
   c. After collecting VB2
   d. After collecting VB3

4. A 65-year-old patient presents with a diagnosis of chronic prostatitis/chronic pelvic pain syndrome with pelvic pain lasting over a year. He has no other symptoms. His past medical history includes 4 weeks of ciprofloxacin for CP with no alleviation of symptoms and atrial fibrillation. What treatment may be prescribed?
   a. Antibiotics: TMP-SMX, 180 mg twice daily for 4 weeks
   b. Alpha-blockers: tamsulosin, 0.4 mg daily for 12 weeks
   c. Anti-inflammatory: celecoxib, 25 mg daily for 4 weeks
   d. Phosphodiesterase 5 inhibitors: tadalafil, 5 mg daily

5. A patient is diagnosed with chronic pelvic pain, perineal pain, and erectile dysfunction. He has no voiding symptoms. Which treatment option is most beneficial?
   a. Pelvic floor physical therapy
   b. Antibiotics
   c. Alpha-blockers
   d. 5-Alpha-reductase inhibitors