

Management of Men Diagnosed With Chronic Prostatitis/Chronic Pelvic Pain Syndrome Who Have Failed Traditional Management

J. Curtis Nickel, MD, FRCSC,* Andrew P. Baranowski, MD,[†] Michel Pontari, MD,[‡] Richard E. Berger, MD,[§] Dean A. Tripp, PhD*

*Department of Urology, Queen's University, Kingston, Ontario, Canada; [†]University College London Hospitals, National Hospital for Neurology and Neurosurgery, Queen Square, UK; [‡]Division of Urology, Department of Surgery, Temple University, Philadelphia, PA; [§]Department of Urology, University of Washington, Seattle, WA

For many patients, the traditional biomedical model that physicians have used to manage chronic prostatitis does not work. This article describes innovative treatment strategies for chronic prostatitis/chronic pelvic pain syndrome, with an emphasis on novel biomedical physical therapy and biopsychosocial approaches to the management of individualized patient symptoms.

[Rev Urol. 2007;9(2):63-72]

© 2007 MedReviews, LLC

Key words: Chronic prostatitis • Chronic pelvic pain syndrome • Physiotherapy • Cognitive-behavioral therapy

Traditionally, chronic prostatitis/chronic pelvic pain syndrome (CP/CPSP) in men (“prostatitis”) was believed to be related to inflammation (usually secondary to infection) localized to the prostate. Treatment consisted of antibiotics and anti-inflammatories and, later, prostate-specific medications such as α -blockers and 5 α -reductase inhibitors. However, these and all the other treatments employed to treat chronic “abacterial prostatitis” and “prostodynia” had never been evaluated or proven to be effective in properly designed clinical trials.

The introduction of an internationally accepted classification system that includes a definition of CP/CPPS and a validated outcome index, the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), stimulated the design and implementation of randomized placebo-controlled trials. These trials, which enrolled comparable subjects and employed similar outcome analyses, allowed researchers and clinicians to objectively evaluate evidence-based efficacy data, as well as compare the various therapies advocated for men diagnosed with CP/CPPS. Evidence-based recommendations can then be based on the assessment of clinical trials that have met the following strict criteria¹:

1. Clearly defined population of CP/CPPS men
2. Randomized placebo-controlled design
3. Validated outcome analyses (NIH-CPSI)
4. Peer reviews (published in a peer-reviewed journal)

Employing these criteria, 12 clinical trials assessing antibiotics (levofloxacin, ciprofloxacin), anti-inflammatories (rofecoxib, zafirlukast), α -blockers (terazosin, alfuzosin, tamsulosin), and other treatments, such as heparinoids (pentosanpolysulfate), phytotherapies (quercetin), allopurinol, 5 α -reductase inhibitors, and other hormone modulators (finasteride, mepartricin), have been rigorously evaluated for comparative efficacy.¹⁻⁵ Table 1 compares the treatment effect (the difference between the change in CPSI score in the treatment group compared with the baseline and the change in the placebo group).⁶⁻¹⁷

On the basis of these analyses, a number of recommendations can be suggested:

- Antimicrobials cannot be recommended for men with longstanding, previously treated CP/CPPS;

Table 1
Randomized Placebo-Controlled Clinical Trials That Employed the CPSI as an Outcome Parameter*

Active Agent	Duration, wk	Patients, n		Treatment Effect
		Active	Placebo	
Levofloxacin ⁶	6	35	45	2.5
Terazosin ⁷	14	43	43	4.1 [†]
Alfuzosin ⁸	24	17	20	6.1 [†]
Tamsulosin ⁹	6	27	30	3.6 [†]
Ciprofloxacin ¹⁰	6	49	49	2.8
Tamsulosin ¹⁰		49		1.0
Tamsulosin + Ciprofloxacin ¹⁰		49		0.7
Rofecoxib 25 mg ¹¹	6	53	59	0.7
Rofecoxib 50 mg ¹¹		49		2.0
Zafirlukast ¹²	4	10	7	0.0
Pentosan polysulfate ¹³	16	51	49	2.7
Finasteride ¹⁴	24	33	31	2.2
Mepartricin ^{*15}	8	13	13	10.0 [†]
Quercetin ^{*16}	4	15	13	6.5 [†]
Allopurinol ^{*17}	12	25	14	3.1

Note: The treatment effect is the change in Chronic Prostatitis Symptom Index (CPSI) from baseline noted in the treatment group compared with the change in CPSI from baseline noted in the placebo group. A treatment effect of approximately 3 is believed to be clinically significant.

*This table has been adapted from Nickel JC¹⁻³ and Dimitrakov JD et al.⁴

[†]P < .05

*Single-center trials. All other are multicenter trials.

however, some clinical benefit may be obtained in antimicrobial-naive early-onset prostatitis patients. (This suggestion is not based on randomized placebo-controlled study data.)

- α -Blockers can be recommended as a first-line medical therapy, particularly in α -blocker-naive men with moderately severe symptoms of a relatively recent onset. α -Blockers must be continued for more than 6 weeks (likely more than 12 weeks). α -Blockers cannot be recommended in men with longstanding CP/CPPS who have tried and failed with α -blockers in the past.

- Anti-inflammatory therapy is not recommended as a primary treatment; however, it may be useful in an adjunctive role in a multimodal therapeutic regime. (This recommendation is not based on randomized placebo-controlled data.)
- At this time, hormonal therapy cannot be recommended as a monotherapy but should be evaluated in selected patients, such as older men with concurrent lower urinary tract symptoms, including those due to benign prostate hypertrophy.
- Although early studies have suggested that allopurinol is effective, it cannot be recommended as a

therapeutic option on the basis of the more recent data.

- The early data on herbal therapies, particularly quercetin, are intriguing, but a larger multicenter randomized placebo-controlled trial is required before a recommendation based on a high level of evidence can be made on its use.
- Many other medical therapies have been suggested and tested in small or uncontrolled pilot studies or have not yet been subjected to peer review. Muscle relaxants, cernilton or bee pollen extract, saw palmetto, and corticosteroids have all been suggested and used, but recommendations will have to wait for results from properly designed randomized placebo-controlled trials to be published in peer-reviewed journals.
- A number of uncontrolled clinical studies have suggested that multimodal therapy is more effective than monotherapy in patients with long-term symptoms. Future trials will have to assess such multimodal therapy.
- Surgery, including minimally invasive procedures, cannot be recommended at this time, unless a specific and valid indication exists.

These evidence-based recommendations highlight the fact that the traditional biomedical model of dealing with chronic prostatitis has failed many patients. So where do we go now? The answer will lie in our evolving understanding of the pathophysiology and etiology of CP/CPPS.^{2,3}

It is now apparent that the condition occurs in anatomically and/or genetically susceptible men who suffer from some initiator factor (usually repetitive). These initiators can be infection (urethritis, cystitis, prostatitis), dysfunctional high-pressure voiding (bladder neck, prostate, sphincter, or urethral pathology),

failure to relax the pelvic floor muscles at rest or during voiding, trauma (bicycle seat, prolonged sitting), or allergic phenomenon. This can lead to a self-perpetuating immunologic inflammatory state and/or neurogenic injury, creating acute and then chronic pain. Peripheral and then central nervous system sensitization involving neuroplasticity may lead to a centralized neuropathic pain state, further modulated by upper central nervous system centers.

New avenues of therapy will involve novel diagnostic strategies

New avenues of therapy will involve novel diagnostic strategies leading to neuromodulatory, physical, and cognitive-behavioral therapies.

leading to neuromodulatory, physical, and cognitive-behavioral therapies.¹⁸ Such treatment trials are already ongoing and hold promise for better management of CP/CPPS.

Understanding the Pain in a Patient With CP/CPPS

The primary presenting symptom in all these patients is pain. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.¹⁹ A pain syndrome is usually defined as a group of pain symptoms that characterize a disease state or clinical syndrome. In CP/CPPS, the pain is perceived in the pelvis and, in the absence of classical pathology, is called pelvic pain syndrome.

Actual tissue damage is not usually seen in pain syndromes. In most cases, if not all of the chronic pelvic pain syndromes, the pain is at least partially a function of neuroplasticity in the central nervous system. To understand the justification, a few neuromuscular processes involved in chronic pain have to be defined and understood.²⁰⁻²³

Sensitization is the process by which stimuli are perceived to be greater than before sensitization takes place. If nonpainful stimuli are more intense but not painful, the process is called *hypersensitivity*. If nonpainful stimuli become painful, it is called *allodynia*. Such neurologic processes are difficult to measure or investigate. However, visceral stimulation-response curves, such as the sensory perception associated with visceral distension (eg, urodynamics), may provide some answers. Others have studied the referred cutaneous and muscle

changes using electrical stimulation and quantitative sensory testing.²⁴

Sensitization can involve peripheral nerves in the initial stages of CP/CPPS, or it can be central, as may happen in persistent CP/CPPS. Early peripheral sensitization can be started by a number of known and unknown initiators (such as infection, trauma, dysfunctional voiding, toxins, immunogens) in an anatomically and/or genetically susceptible man.

Central sensitization involves amplification of incoming signals by anatomic and neurochemical mechanisms in the spinal cord or higher central nervous centers before becoming conscious. Changes in the afferent (sensory) nervous system and in the efferent system may also occur. Neuroinflammation occurs when substances are released from nerves, such as substance P, which causes the release of local inflammatory substances from leukocytes and other cells. These substances further amplify inflammation and afferent sensations. Neuroinflammation, and hence changes in nociception, can also spread by antidromic transmission of nerve impulses, which travel down

affected nerves and spread to other branches of the same or synapsing nerves in other areas of the body. There is some evidence that inflammation in one viscus can produce inflammatory changes in another.

Referred pain occurs when pain is felt in a part of the body other than where it originates. Visceral referred pains are thought to happen when the organ is innervated by the same nerves that innervate a somatic dermatome or myotome (eg, as occurs in renal colic going into the testicle or heart pain being felt in the arm), though other mechanisms have been postulated. Convergence occurs when neuronal changes occur in an area of referred pain, which then becomes sensitized and/or in which neuroinflammation occurs. These changes can also spread to adjacent areas in the spinal cord and affect neuronal and ultimately visceral and somatically innervated

structures not initially involved. These processes, which are experimentally well documented, can cause pain originating in a visceral organ to cause muscle pain and spasms.

Conversely, afferent impulses from muscles can cause changes in the spinal cord that affect the physiology of visceral organs. Pain pathways lead to limbic centers in the brain, which

responses, both physical and psychological. The patient's perception and interpretation of the pain can be measured, as can the patient's emotional response and its associated disability. Now a battery of well-researched pain scores is available for general use to measure both the patient's perception of severity and interpretation.²⁵ A summary of these tools can be found

A battery of well-researched pain scores is available for general use.

trigger negative emotions and poor coping mechanisms, which can further affect pain perception and possibly neuromodulation. All or some of these neurological mechanisms may be involved in chronic pain syndromes and CP/CPPS (Figure 1).

Pain is a sensation that requires perception and is thus associated with interpretation and a range of

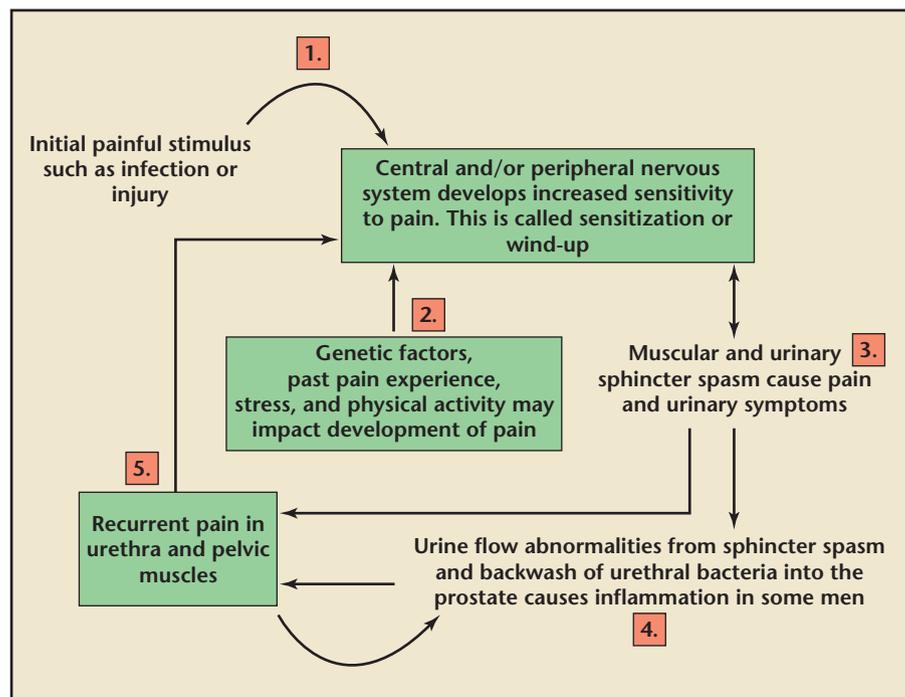
in the International Continence Society guidelines on chronic pelvic pain.²⁶

It is now well accepted that CP/CPPS exists as an entity quite different from the well-defined pain conditions in which the pathology is well understood. Standard urologic investigations may go some way to help define the pain syndromes, and future investigations are likely to better define many of the poorly understood conditions. For example, new conditions are being identified, or old conditions highlighted; pudendal neuralgia is one such condition. The identification of such conditions as defined by differential nerve blocks will move some patients from the pain syndrome group to a well-defined group. In addition to the use of differential nerve blocks to define patients, pain management tools include the intravenous drug challenges that investigate the roles of the sympathetic nervous system, *N*-methyl-D-aspartate, or sodium channels.²⁵

Novel Medical Approaches

The patient diagnosed with CP/CPPS should be initially treated with the standard therapeutic approach, which certainly works for some patients. Once the traditional first-line therapies—antibiotics, α -blockers, and anti-inflammatory medications—fail, there are several other medications to consider.

Figure 1. Possible scheme explaining muscle dysfunction in chronic pelvic pain syndrome. Abnormalities in the pelvic floor musculature can promote abnormal lower urinary tract function and can be a self-promoting phenomenon. A number of pelvic floor neuromuscular abnormalities have been documented in pelvic pain syndromes. Adapted from Berger RE. Physical therapy for CP/CPPS refractory to traditional therapy. Presented at: SIU Meeting; October 2006; Cape Town, South Africa.



Medications to Treat Neuropathic Pain

The predominant symptom of CP/CPPS is pain. Therefore, medications to treat pain specifically may be effective. There is mounting evidence that the pain of CP/CPPS may be neuropathic and associated with central nervous system changes. The presence of central sensitization in patients with CP/CPPS was demonstrated by Yang and colleagues,²⁷ who compared thermal algometry in men with CP/CPPS versus asymptomatic controls. Sensitivity to noxious heat

who are relatively young and working. Starting doses of both amitriptyline and nortriptyline are 10 mg po qhs, working up by 10-mg increments at weekly intervals to a maximum of 75 to 100 mg po qhs. Sedation appears to be less of a problem when the drug is taken at night, and the analgesic effect lasts for 24 hours or so. Other problems include anticholinergic side effects such as dry mouth; these may have a beneficial effect on urinary frequency, though urinary retention can be precipitated in those who are prone to it. Imipramine may

Tramadol, a weak opioid and a mixed serotonin-noradrenaline reuptake inhibitor, has shown efficacy in diabetic neuropathy³⁴ at doses of 50 mg po qid. Side effects include headache, constipation, and somnolence. The maximum dose is 400 mg/d. Slow-release preparations are available. Other opioids may have a role but should only be prescribed by experts trained in their use for chronic pain and using the guidelines available, such as those of the British Pain Society or Australian Pain Society.³⁵

The predominant symptom of CP/CPPS is pain.

stimuli is thought to be a reflection of central sensitization, and men with CP/CPPS reported a higher visual analog scale to short bursts of noxious heat stimuli to the perineum but no difference to the anterior thigh. Thus, these patients have altered sensation in the perineum compared with controls.

This is similar to other chronic pain syndromes such as complex regional pain syndrome (reflex sympathetic dystrophy) and fibromyalgia, in which patients exhibit heightened responses to noxious heat stimuli in areas of chronic pain compared with controls. Several classes of medications have been found to be useful in treating neuropathic pain, and they may be used alone or in combination.²⁸

Tricyclic antidepressant (TCA) medications have been shown to be effective in treating neuropathic pain.²⁹ Their effects are produced by serotonin and noradrenaline reuptake inhibition. They may also block sodium channels, known to be up-regulated in some neuropathic pains. Nortriptyline may produce less sedation than amitriptyline, which could be important to the many patients

be used if urinary frequency and urgency are particular problems.

The anticonvulsants gabapentin and pregabalin act at the $\alpha 2\delta$ subunit of voltage-gated calcium channels. Pregabalin has a higher affinity for the channel than does gabapentin and is considered by some as the drug of choice because of a superior side-effect profile. Doses of pregabalin starting at 50 mg po tid and going up

Imipramine may be used if urinary frequency and urgency are particular problems.

to 100 mg po tid have been effective in treating neuropathic pain from post-herpetic neuralgia^{30,31} and diabetic neuropathy.³² Doses of up to 450 mg/d were needed to treat fibromyalgia.³³ Common side effects include dizziness and somnolence. The dose should be started at 50 mg tid and increased after 1 week. The drug should be discontinued by tapering off over a period of a number of weeks.

Specialist teams use other anticonvulsants to treat neuropathic pain. It must be remembered, though, that the use of many of these drugs for these indications is "off license."

Medications to Treat Muscle Spasticity

A common observation of men with CP/CPPS is that of discomfort in the perineal area and feelings of spasm in the pelvic floor. Increased muscle tone in the pelvic floor has been observed in studies in men with CP/CPPS compared with controls.³⁶ Men with CP/CPPS also show abnormal electromyographic activity in the perineal muscles.³⁷

Cyclobenzaprine is a medication closely related to the TCAs. This drug has been used for the treatment of

musculoskeletal conditions such as low-back pain, whether spasm has been present or not.³⁸ We have used starting doses of 10 mg po qhs, which can be prescribed up to 3 times per day.

Tizanidine is a centrally acting α_2 -agonist³⁹ shown to be superior to placebo in treating spasticity for several conditions. Doses starting as low as 2 mg po qhs can be used and go up to dosages of 4 to 6 mg tid. Liver function tests must be monitored. Although benzodiazepine-type drugs may be considered, they should be used with caution because of their

addictive properties. Clonazepam has been useful in treating neuro-pathic pain.

Medications Also Used to Treat IC/PBS/BPS

CP/CPPS and interstitial cystitis/painful bladder syndrome/bladder pain syndrome (IC/PBS/BPS) share many similarities, including the presence of pelvic pain and, often, voiding symptoms.⁴⁰ The entrance criteria for the NIH-sponsored Interstitial Cystitis Database and Chronic Prostatitis Cohort Study contain many similarities and allow for men to enter either study. Therefore, medications that are used to treat IC/PBS/BPS may be useful in men with a diagnosis of CP/CPPS.

Montelukast (Singulair®; Merck and Co., Inc., Whitehouse Station, NJ) is a leukotriene antagonist that binds to the cysteinyl leukotriene receptor type 1. It is commonly used for asthma, as it reduces inflammation in the lungs and has been described for the use of IC/PBS/BPS.⁴¹ At doses of 10 mg po qd it has few side effects and anecdotally has been effective in some men with CP/CPPS.

Pentosanpolysulfate (Elmiron®; Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ) is the only oral medication approved by the US Food and Drug Administration for use in IC/PBS/BPS. Its proposed mechanism of action is to repair damage to the glycosaminoglycan layer of the bladder. Trials in men with CP/CPPS have demonstrated that pentosanpolysulfate (900 mg qd) was more likely than placebo to provide relief for CP/CPPS symptoms.⁴²

Surgical Therapies

Incision of the bladder neck has been reported to be effective in men with prostatitis and evidence of bladder neck dyssynergy on videourodynamic studies.⁴³ This represents a very small

and specific group of patients. The diagnosis must be made using videourodynamics, and the risks of retrograde ejaculation must be weighed against the benefits, especially in young men.

Neuromodulation may play a role in treating CP/CPPS. Nine of 10 patients with chronic pelvic pain treated with the InterStim device (Medtronic Inc, Minneapolis, MN) reported improvement after implantation.⁴⁴ This technique has been reported to decrease narcotic use in women with IC/PBS/BPS.⁴⁵ It certainly may be useful in patients with CP/CPPS who

have significant urinary frequency and urgency refractory to standard oral medications. Whether sacral root stimulation, retrograde stimulation, or indeed antrograde stimulation should be employed is being debated.

Injection treatment with local anesthetic and steroid may have a role in some cases. Certainly, injections of the pudendal nerves may be therapeutic, and if not therapeutic, they may have a diagnostic role. There is some evidence that trigger-point injections of muscles may be helpful. For the deep pelvic injections, CT guidance is necessary. If deep pelvic muscle

Table 2
Neuromuscular Findings in Patients With Pelvic Pain

Condition	Parameter Studied	Results*	Study
CP/CPPS	Blinded exam by physical therapist	62 CP/CPPS, 89 control: muscle tone, spasm, and pain	Hetrick DC et al ³⁶
CP/CPPS	Urodynamics	103 men, increased sphincter pressure 73%, decreased flow in 62%	Zermann DH et al ²⁴
Vulvodynia	Surface EMG	25 pts, 25 controls: 9/15 EMG variables different in vulvodynia	Glazer HI et al ⁴⁶
CP/CPPS	Surface EMG	21 pts, 21 controls: differences in hypertonicity, instability, endurance	Hetrick DC et al ³⁷
CP/CPPS	Internal, external tenderness	62 pts, 98 controls: more internal and external tenderness	Berger RE, unpublished
Vulvodynia	Internal, external tenderness	17 pts, 21 controls: more tenderness in vulva and other locations	Giesecke J et al ⁴⁷
Painful bladder syndrome	Cystometry, current perception thresholds, habituation	8 PBS, 10 SUI, 9 asymptomatic: bladder hypersensitivity, no cutaneous sensitization, no habituation in PBS group	Fitzgerald, 2005, AUA abstract
CP/CPPS	Cutaneous heat sensitivity	36 patients, 66 controls: hypersensitivity to heat	Yang CC et al ²⁷

*Results of all studies in table showed statistical significance at $P < .05$ when comparing pretreatment with post-treatment results.
CP/CPPS, chronic prostatitis/chronic pelvic pain syndrome; EMG, electromyography; pts, patients; PBS, painful bladder syndrome; SUI, stress urinary incontinence.

trigger-point injections are of benefit, there is some suggestion that injection of botulinin toxin may provide longer benefit.

Physiotherapy

Perception of pain, no matter what its cause, can lead to both reflex and voluntary muscle contraction, which may result in more pain and dysfunctions. Although the pain of CP/CPPS is poorly understood, nearly all clinicians agree that almost all CP/CPPS patients have some chronic tension and tenderness of the pelvic floor musculature. It is probable that these myofascial abnormalities contribute significantly to the pain of CP/CPPS. This pain could be primarily due to muscle abnormalities from poor posture, chronic stress injuries, or neurologic abnormalities, or to sensitization and convergence from other damaged tissue (Table 2). The recognition of the role of myofascial abnormalities of the pelvis in CP/CPPS has led to several reports of CP/CPPS symptom relief by therapeutic efforts directed at those muscular abnormalities, summarized in Table 3.

Treatment of CP/CPPS with physical therapy is still empiric. In practice, therapeutic interventions are typically carried out by a physical therapist who is skilled in techniques such as connective tissue manipulation and myofascial manipulation or in biofeedback-assisted techniques for pelvic floor reeducation. Anderson and colleagues⁵² reported that moderate or marked improvement in symptoms was noted in 72% of 138 men with CP/CPPS who underwent manual myofascial trigger-point release and paradoxical relaxation training (a form of cognitive therapy).

Although most published studies have shown the benefit of physical therapy interventions, none has been controlled (Table 3).⁴⁸⁻⁵⁷ Physical

Table 3
Physiotherapy Studies on Patients With Pelvic Pain

Condition	Rx	Results	Study
Proctalgia fugax	Pudendal block	55 patients; 65% no symptoms, 25%, decreased symptoms	Takano M ⁴⁸
CP/CPPS/IC	Physical therapy	4/4 cured	Doggweiler-Wiygul R and Wiygul JP ⁴⁹
Adolescent female pelvic pain	Physical therapy	20/21 cured	Schroeder B et al ⁵⁰
CP/CPPS	Biofeedback	33 men: CPSI decreased from 23.6 to 11.4,	Cornel EB et al ⁵¹
CP/CPPS	Myofascial release therapy/paradoxical relaxation therapy	72% clinical success	Anderson RU et al ⁵²
IC	Thiele physical therapy	N = 21: immediate and "long-term" improvement	Oyama IA et al ⁵³
IC	Physical therapy	N = 47: 65% improved EMG, 83% mod./marked improvement	Weiss JM ⁵⁴
IC	Physical therapy	N = 16: O'Leary Sant decreased from 15.75 to 8.5	Lukban J et al ⁵⁵
Vulvodynia	EMG-assisted physical therapy/biofeedback	N = 43: 38 had no long-term (39.5 mo) pain post-treatment	Glazer HI ⁵⁶
IC	Behavioral/PFMT	N = 42: 41 had at least 9 less micturations/d	Chaiken DC et al ⁵⁷

CP/CPPS, chronic prostatitis/chronic pelvic pain syndrome; IC, interstitial cystitis; CPSI, chronic prostatitis symptom index; PFMT, pelvic floor muscle training; EMG, electromyography.

therapy should address most of the following:

1. Education of the patient about pelvic muscle function and pain
2. Education about lifestyle issues that may exacerbate the pain
3. Education about how posture affects the pelvis
4. Education about exercises that may be of benefit and those that may be harmful
5. Specific stress-reduction techniques

6. Manual therapy such as myofascial trigger-point release and joint mobilization
7. Specific exercises to improve strength, relax muscles, and restore balance
8. Exercise aimed at improving core posture and general health and well-being
9. Education about voiding and sexual behaviors that may exacerbate the problem

The NIH has sponsored a multicenter prospective randomized pilot study to compare specific pelvic physiotherapy to a “relaxing” (Swedish) massage therapy to determine the efficacy of a targeted therapy.

A Biopsychosocial Approach

In a recent NIH-sponsored meeting on pelvic pain, more than 50% of the discussion centered on the psychosocial aspects and potential management models for CP/CPPS.¹⁸ As evidenced by the ongoing research with physiotherapy and CP/CPPS, physicians are not only talking but also exploring management options long considered to be outside the traditional “box.”

CP/CPPS outcomes of pain and disability have recently been examined using a biopsychosocial model with physical, cognitive-behavioral, and environmental predictors.^{58,59} North American men enrolled in the NIH-funded Chronic Prostatitis Cohort Study completed surveys describing

their pain and pain-related disability (N = 253). Assessments included demographics, urinary symptoms, depression, pain, disability, catastrophizing (ie, a pervasive negative cognitive orientation to pain that may involve excessive rumination about pain, magnification of the threat value of pain sensations, and feelings of low ability to manage pain: feeling helpless), patients’ perceptions of control over pain, pain-contingent resting, social support, and solicitous responses from a significant other.

The results show that urinary symptoms were elevated in those reporting greater pain, but that elevated depression and helplessness catastrophizing were even stronger predictors of high pain reported by these men. Further, when the pain reports are broken down into their affective and sensory pain components, varied results are present that may be useful in guiding psychological therapeutic approaches. For example, higher levels of affective pain (ie, pain described in

terms of emotional descriptors such as “sickening” and “fearful”) were significantly associated with greater depression, but elevated helplessness catastrophizing was the strongest predictor. The helplessness expressed by these men is an important clinical feature of affective pain because its impact is significant when other variables such as demographics, urinary status, and other environmental predictors are included in the analyses.

Completing a similar analysis for sensory-type pain (ie, pain described in terms of physical sensations such as throbbing, sharp, aching) was also associated with elevations in urinary symptoms. Again, helplessness catastrophizing was a stronger predictor.

In regard to CP/CPPS disability, worse urinary symptoms and pain predicted greater disability, but greater pain-contingent resting (ie, reporting the use of sedentary behaviors such as sitting in a chair as a method of coping with the pain) was

Main Points

- In chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), pain is perceived in the pelvis and, in the absence of classical pathology, is called *pelvic pain syndrome*.
- If nonpainful stimuli are more intense but not painful, the process is called *hypersensitivity*. If nonpainful stimuli become painful, it is called *allodynia*.
- *Referred pain* occurs when pain is felt in a part of the body other than where it originates.
- Pain is a sensation that requires perception and thus is associated with interpretation and a range of responses, both physical and psychological.
- Tricyclic antidepressant medications have been shown to be effective in treating neuropathic pain.
- The anticonvulsants gabapentin and pregabalin have the potential to alleviate the neuropathic pain associated with CP/CPPS.
- CP/CPPS has many similarities to interstitial cystitis/painful bladder syndrome/bladder pain syndrome, including the presence of pelvic pain and, often, voiding symptoms.
- Incision of the bladder neck has been reported to be effective in men with prostatitis and evidence of bladder neck dyssynergy on videourodynamic studies.
- Neuromodulation may play a role in treating CP/CPPS.
- Recognition of the role of myofascial abnormalities of the pelvis in CP/CPPS has led to several reports of symptom relief by physiotherapy.
- Cognitive-behavioral interventions are successful in other chronic pain states, and an NIH-sponsored pilot program is evaluating their use in CP/CPPS management.

the strongest predictor. Taken together, these data suggest that a biopsychosocial intervention in regard to CP/CPPS pain is warranted and that cognitive-behavioral variables such as depression, coping mechanisms, and catastrophizing are evidenced as targets for change.

Cognitive-behavioral interventions, some of which address catastrophizing and the other psychosocial parameters associated with the pain, disability, and quality of life of men with CP/CPPS, are successful in symptom relief in other chronic pain states.⁶⁰ Responding to the present state of affairs and the request for innovative empiric psychological treatment options, the NIH has sponsored the development of a CP/CPPS cognitive-behavioral intervention, which is to be evaluated in a pilot program in 2007. This Cognitive Behavioral–Symptom Management Program (CB-SMP) will be unique to CP/CPPS management because it is based on CP/CPPS research,^{58,59,61} is specific to the pain-related fears and cognitions of each patient based on assessments they complete, and is to be delivered by trained clinical urology nurses using a patient workbook to increase quality assurance.

Conclusion

The optimal response to the limited symptom-relief profile of biomedical treatment options for the patients suffering from CP/CPPS is to continue to critically evaluate novel biomedical treatments. But we must also develop and investigate physical therapy and biopsychosocial approaches to managing individual patient symptoms. The new management model presented in this article should bring hope for CP/CPPS providers and refractory patients. ■

References

- Nickel JC. The three A's of chronic prostatitis therapy; antibiotics, alpha-blockers, and anti-

- inflammatories: what is the evidence? *BJU Int.* 2004;94:1230-1233.
- Nickel JC. Chronic prostatitis/chronic pelvic pain syndrome: a decade of change. *AUA Update Series.* 2006. [Lesson 34].
- Nickel JC. CP/CP/CPPS: The biomedical model has failed! So what's next? *Contemporary Urol.* 2006;July:30-39.
- Dimitrakov JD, Kaplan SA, Kroenke K, et al. Management of chronic prostatitis/chronic pelvic pain syndrome: an evidence-based approach. *Urology.* 2006;67:881-888.
- Shaeffer AJ, Anderson RU, Krieger JN, et al. The assessment and management of male pelvic pain syndrome, including prostatitis. In: McConnell J, Abrams P, Denis L, et al., eds. *Male Lower Urinary Tract Dysfunction, Evaluation and Management.* 6th International Consultation on New Developments in Prostate Cancer and Prostate Disease; Paris: Health Publications; 2006:341-385.
- Nickel JC, Downey J, Clark J, et al. Levofloxacin treatment for chronic prostatitis/chronic pelvic pain syndrome (CP/CP/CPPS) in men: a randomized placebo controlled multi-center trial. *J Urol.* 2003;169:614-617.
- Cheah PY, Liong ML, Yuen KH, et al. Terazosin therapy for chronic prostatitis/chronic pelvic pain syndrome: a randomized, placebo controlled trial. *J Urol.* 2003;169:592-596.
- Mehik A, Alas P, Nickel JC, et al. Alfuzosin treatment for chronic prostatitis/chronic pelvic pain syndrome: a prospective, randomized, double-blind placebo controlled, pilot study. *J Urol.* 2003;169:425-429.
- Nickel JC, Narayan P, MacKay J, et al. Treatment of chronic prostatitis/chronic pelvic pain syndrome with tamsulosin: a randomized double blind trial. *J Urol.* 2004;171:1594-1597.
- Alexander RB, Probert KJ, Schaeffer AJ, et al. Chronic Prostatitis Collaborative Research Network. Ciprofloxacin or tamsulosin in men with chronic prostatitis/chronic pelvic pain syndrome: a randomized, double-blind trial. *Ann Intern Med.* 2004;141:581-589.
- Nickel JC, Pontari M, Moon T, et al. A randomized, placebo controlled multi-center study to evaluate the safety and efficacy of rofecoxib in the treatment of chronic non-bacterial prostatitis. *J Urol.* 2003;169:1401-1405.
- Goldmeier D, Madden P, McKenna M, Tamm N. Treatment of category IIIA prostatitis with zafirlukast: a randomized controlled feasibility study. *Int J STD AIDS.* 2005;16:196-200.
- Nickel JC, Forrest JB, Tomera K, et al. Pentosan polysulfate sodium therapy for men with chronic pelvic pain syndrome: a multicenter, randomized, placebo-controlled study. *J Urol.* 2005;173:1252-1255.
- Nickel JC, Downey J, Pontari MA, et al. A randomized placebo controlled multicentre study to evaluate the safety and efficacy of finasteride for male chronic pelvic pain syndrome (category IIIa chronic nonbacterial prostatitis) *BJU Int.* 2004;93:991-995.
- De Rose AF, Gallo F, Giglio M, et al. Role of mepartricin in category III chronic nonbacterial prostatitis/chronic pelvic pain syndrome: a

- randomized prospective placebo-controlled trial. *Urology.* 2004;63:13-16.
- Shoskes DA, Zeitlin SI, Shahed A, et al. Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial. *Urology.* 1999;54:960-963.
- Ziaee AM, Akhaviadegan H, Karbakhsh M. Effect of allopurinol in chronic nonbacterial prostatitis: a double blind randomized clinical trial. *Int Braz J Urol.* 2006;32:181-186.
- Nickel JC, Pontari M, Berger R. Changing paradigms for chronic pelvic pain: a report from the Chronic Pelvic Pain/Chronic Prostatitis Scientific Workshop October 19-21, 2005, Baltimore, MD. *Rev Urol.* 2006;8:28.
- Merskey H, Bogduk N. *Classification of Chronic Pain.* Seattle, WA: IASP Press; 1994.
- Giamberardino MA. Visceral pain. *Pain Clin Updates.* 2005;13:1-6.
- Loeser JD, Melzack R. Pain: an overview. *Lancet.* 1999;353:1607-1609.
- Cervero F, Laird JM. Visceral pain. *Lancet.* 1999;353:2145-2148.
- Ashburn MA, Staats PS. Management of chronic pain. *Lancet.* 1999;353:1865-1869.
- Zermann DH, Ishigooka M, Doggweiler R, Schmidt RA. Neurourological insights into the etiology of genitourinary pain in men. *J Urol.* 1999;161:903-908.
- Baranowski AP. Pharmacological diagnostic tests. In: Breivik H, Campbell W, Eccleston C, eds. *Clinical Pain Management—Practical Applications and Procedures.* London: Arnold; 2003.
- Hanno P, Baranowski AP, Rosamilia A, et al. International Continence Society guidelines on chronic pelvic pain. International Consultation on Incontinence (ICI): 2005. Reported at: Changing paradigms for chronic pelvic pain: a report from the Chronic Pelvic Pain/Chronic Prostatitis Scientific Workshop; October 19-21, 2005; Baltimore, MD.
- Yang CC, Lee JC, Kromm BG, et al. Pain sensitization in male chronic pelvic pain syndrome: why are symptoms so difficult to treat? *J Urol.* 2003;170:823-827.
- Gilron I, Watson CP, Cahill CM, Moulin DE. Neuropathic pain: a practical guide for the clinician. *Can Med Assoc J.* 2006;175:265-275.
- McQuay HJ, Tramer M, Nye BA, et al. A systematic review of antidepressants in neuropathic pain [see comment]. *Pain.* 1996;68:217-227.
- Sabatowski R, Galvez R, Cherry DA, et al. Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: results of a randomized, placebo-controlled clinical trial. *Pain.* 2004;109:26-35.
- Dworkin RH, Corbin AE, Young JP Jr, et al. Pregabalin for the treatment of postherpetic neuralgia: a randomized, placebo-controlled trial [see comment]. *Neurology.* 2003;60:1274-1283.
- Rosenstock J, Tuchmen M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain.* 2004;110:628-638.
- Bouchelouche K, Nordling J, Hald T, Bouchelouche P. Treatment of interstitial cystitis with montelukast, a leukotriene D(4) receptor antagonist. *Urology.* 2001;57(suppl 1):S118.

34. Harati Y, Gooch C, Swenson M, et al. Double-blind randomized trial of tramadol for the treatment of the pain of diabetic neuropathy [see comment]. *Neurology*. 1998;50:1842-1846.
35. Nickel JC. Opioids for chronic prostatitis and interstitial cystitis: lessons learned from the 11th World Congress on Pain. *Urology*. 2006;68:697-701.
36. Hetrick DC, Ciol MA, Rothman I, et al. Musculoskeletal dysfunction in men with chronic pelvic pain syndrome type III: a case-control study. *J Urol*. 2003;170:828-831.
37. Hetrick DC, Glazer H, Liu YW, et al. Pelvic floor electromyography in men with chronic pelvic pain syndrome: a case-control study. *NeuroUrol Urodyn*. 2006;25:46-49.
38. Chou R, Peterson K, Helfand M. Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review. *J Pain Symptom Manage*. 2004;28:140-175.
39. Wagstaff AJ, Bryson HM. Tizanidine. A review of its pharmacology, clinical efficacy and tolerability in the management of spasticity associated with cerebral and spinal disorders. *Drugs*. 1997;53:435-452.
40. Pontari MA. Chronic prostatitis/chronic pelvic pain syndrome and interstitial cystitis: are they related? *Curr Urol Rep*. 2006;7:329-334.
41. Bouchelouche K, Nordling J, Hald T, Bouchelouche P. The cysteinyl leukotriene D4 receptor antagonist montelukast for the treatment of interstitial cystitis. *J Urol*. 2001;166:1734-1737.
42. Nickel JC, Forrest JB, Tomera K, et al. Pentosan polysulfate sodium therapy for men with chronic pelvic pain syndrome: a multicenter, randomized, placebo controlled study. *J Urol*. 2005;173:1252-1255.
43. Kaplan SA, Te AE, Jacobs BZ. Urodynamic evidence of vesical neck obstruction in men with misdiagnosed chronic nonbacterial prostatitis and the therapeutic role of endoscopic incision of the bladder neck. *J Urol*. 1994;152:2063-2065.
44. Siegel S, Paszkiewicz E, Kirkpatrick C, et al. Sacral nerve stimulation in patients with chronic intractable pelvic pain. *J Urol*. 2001;166:1742-1745.
45. Peters KM, Konstand D. Sacral neuromodulation decreases narcotic requirements in refractory interstitial cystitis. *BJU Int*. 2004;93:777-779.
46. Glazer HI, Jantos M, Hartmann EH, Swencionis C. Electromyographic comparisons of the pelvic floor in women with dysesthetic vulvodynia and asymptomatic women. *J Reprod Med*. 1998;43:959-962.
47. Giesecke J, Reed BD, Haefner HK, et al. Quantitative sensory testing in vulvodynia patients and increased peripheral pressure pain sensitivity. *Obstet Gynecol*. 2004;104:126-133.
48. Takano M. Proctalgia fugax: caused by pudendal neuropathy? *Dis Colon Rectum*. 2005;48:114-120.
49. Doggweiler-Wiygul R, Wiygul JP. Interstitial cystitis, pelvic pain, and the relationship to myofascial pain and dysfunction: a report on four patients. *World J Urol*. 2002;20:310-314.
50. Schroeder B, Sanfilippo JS, Hertweck SP. Musculoskeletal pelvic pain in a pediatric and adolescent gynecology practice. *J Pediatr Adolesc Gynecol*. 2000;13:90.
51. Cornel EB, van Haarst EP, Schaarsberg RW, Geels J. The effect of biofeedback physical therapy in men with chronic pelvic pain syndrome type III. *Eur Urol*. 2005;47:607-611.
52. 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;174:155-160.
53. Oyama IA, Rejba A, Lukban JC, et al. Modified Thiele massage as therapeutic intervention for female patients with interstitial cystitis and high-tone pelvic floor dysfunction. *Urology*. 2004;64:862-865.
54. Weiss JM. Pelvic floor myofascial trigger points: manual therapy for interstitial cystitis and the urgency-frequency syndrome. *J Urol*. 2001;166:2226-2231.
55. Lukban J, Whitmore K, Kellogg-Spadt S, et al. The effect of manual physical therapy in patients diagnosed with interstitial cystitis, high-tone pelvic floor dysfunction, and sacroiliac dysfunction. *Urology*. 2001;57(suppl 1):121-122.
56. Glazer HI. Dysesthetic vulvodynia. Long-term follow-up after treatment with surface electromyography-assisted pelvic floor muscle rehabilitation. *J Reprod Med*. 2000;45:798-802.
57. Chaiken DC, Blaivas JG, Blaivas ST. Behavioral therapy for the treatment of refractory interstitial cystitis. *J Urol*. 1993;149:1445-1448.
58. Tripp DA, Nickel JC, Landis JR, et al, and CPCRN Study Group. Predictors of quality of life and pain in chronic prostatitis/chronic pelvic pain syndrome: findings from National Institutes of Health Chronic Prostatitis Cohort Study. *BJU Int*. 2004;94:1279-1282.
59. Tripp DA, Nickel C, Wang Y, et al, and Chronic Prostatitis Collaborative Research Network (NIH-CPCRN) Study Group. Catastrophizing and pain-contingent rest as predictors of patient adjustment in men with chronic prostatitis/chronic pelvic pain syndrome. *J Pain*. In press.
60. Turk DC, Okifuji A. Psychological factors in chronic pain: evolution and revolution. *J Consult Clin Psychol*. 2002;70:678-690.
61. Smith KB, Pukall CF, Tripp DA, Nickel JC. Sexual and relationship functioning in men with chronic prostatitis/chronic pelvic pain syndrome and their partners [published online ahead of print December 21, 2006]. *Arch Sex Behav*. 2007;36:301-311.