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# CHRONIC PELVIC PAIN OF BLADDER ORIGIN IN MEN:

## A Revealing Look At The Relationship Between Chronic Nonbacterial Prostatitis and Interstitial Cystitis

**PRESENTED BY**

U.S. Department of Health and Human Services

The Office on Women's Health

**IN COOPERATION WITH**

American Medical Women's Association

American Urogynecologic Society

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# CHRONIC PELVIC PAIN OF BLADDER ORIGIN IN MEN: A REVEALING LOOK AT THE RELATIONSHIP BETWEEN CHRONIC NONBACTERIAL PROSTATITIS AND INTERSTITIAL CYSTITIS

## INTRODUCTION

Chronic prostatitis is a clinically challenging syndrome that urologists are commonly called upon to diagnose and manage. An estimated 50% of all men experience prostatitis-like symptoms at some point during their lifetime; only 5% to 10% of these cases are bacterial in origin.[1-4] The majority (>90%) of men diagnosed with prostatitis have chronic nonbacterial prostatitis (CP)/chronic pelvic pain syndrome (CPPS), characterized by urinary urgency and frequency, pelvic pain, and pain with sexual intercourse and/or ejaculation, all of at least 3 months' duration. Traditionally, management of CP/CPPS has included empiric antimicrobial treatment, alone or in combination with other pharmacologic and nonpharmacologic interventions. However, despite reports of temporary symptomatic relief, these modalities rarely provide patients with long-term remissions. Recently, investigators have raised the possibility that the chronic pelvic pain and urinary symptoms characteristic of CP/CPPS may be associated with chronic pelvic pain (CPP) of bladder origin, or interstitial cystitis (IC). CP/CPPS and IC share similar clinical presentations and similar possible pathologies, and recent data suggest that men with CP/CPPS respond to treatments indicated for IC. Therefore, clinicians should consider IC as a potential cause of chronic pelvic pain in men.

### EDUCATIONAL OBJECTIVES

Upon completion of this program, participants will be able to:

- Differentiate between chronic pain of pelvic origin versus bladder origin
- Discuss the epidemiology and demographics of chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS) and interstitial cystitis (IC)
- Discuss the theories underlying the pathophysiology of IC
- Discuss the impact of IC and CPPS on quality of life
- Understand the evolving roles of the Pelvic Pain Urgency and Frequency Patient Symptom (PUF) Scale, Potassium Sensitivity Test (PST), and other diagnostic tools in identifying patients with IC
- Identify nonpharmacologic and pharmacologic options for the management of IC

### TARGET AUDIENCE

Urologists

This issue of Clinical Courier® is based upon information from a roundtable titled "Chronic Pelvic Pain of Bladder Origin: A Focus on Interstitial Cystitis" presented in February 2004 by the Office on Women's Health of the U.S. Department of Health and Human Services.

## OVERVIEW AND DEFINITIONS

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) developed 4 classifications of prostatitis (Table 1).[5] Categories I and II represent acute or chronic bacterial infections of the prostate and are uncommon, accounting for only 5% to 10% of prostatitis cases.[2-4] Category III prostatitis, CP, is the most prevalent type, accounting for at least 90% of prostatitis cases. Category IV, asymptomatic inflammatory prostatitis (AIP), is diagnosed in patients with no history of genitourinary infection who typically are undergoing evaluation for either prostate cancer or infertility, and who demonstrate high concentrations of leukocytes in their seminal fluid.

**TABLE 1**

**NIDDK/NIH: CATEGORIES OF PROSTATITIS**

| | |
|---|---|
| **Category I:** | **ABP**<br>Acute infection of the prostate |
| **Category II:** | **CBP**<br>Chronic infection and inflammation of the prostate |
| **Category III:** | **CP/CPPS** |
| **IIIA:** | **Inflammatory CP/CPPS**<br>Demonstrable prostatic inflammation but no infection |
| **IIIB:** | **Noninflammatory CP/CPPS**<br>No demonstrable prostatic inflammation or infection |
| **Category IV:** | **AIP**<br>Asymptomatic inflammatory prostatitis |

Category I, acute bacterial prostatitis (ABP), although the least common, is potentially the most severe form of the disease. ABP is diagnosed in approximately 2 of every 10,000 outpatient visits.[6] Men with ABP have an acute urinary tract infection (UTI), along with increased urinary frequency and urgency, nocturia, and acute perineal, suprapubic, and/or genital (especially testicular) pain. They often have fever and/or chills, nausea, vomiting, and burning or painful urination. The urine may be foul smelling, with a decreased force of urinary stream. There may be blood in the urine or semen. If left untreated, ABP can result in confusion, hypotension, and sepsis, and may be fatal. Patients with ABP require aggressive treatment, often including hospitalization, parenteral antimicrobial agents, analgesics, and intravenous fluid.

Please direct all correspondence to:

**SynerMed® Communications**
**Department 131**
**518 Route 513**
**PO Box 458**
**Califon, NJ 07830**




Patients who experience recurrent episodes of a UTI caused by the same pathogen that has entered the prostate are typically diagnosed with Category II, chronic bacterial prostatitis (CBP). CBP manifests with similar symptomatology as ABP, but to a less severe extent: testicular or lower back pain, perineal or pelvic floor pain, and urologic symptoms of frequency, urgency, and pain or burning with urination. Men are frequently asymptomatic between episodes of bacteriuria, although some will continue to experience recurrent low-grade fever, urinary hesitancy, and a decreased urinary stream.

In contrast to ABP, the diagnosis and management of CBP is often challenging. Men with CBP are afebrile, with a predominantly sterile urine culture. They typically report a history of recurrent or relapsing UTIs, epididymitis, or urethritis — primarily with the same organism. A diagnosis of CBP requires localization of bacteria to prostate-specific specimens (including postprostatic massage semen or urine, or expressed prostatic secretions [EPS]). A 10-fold increase in the bacterial count in prostatic specimens compared with urethral specimens is considered confirmatory for CBP.

**Acute and chronic bacterial prostatitis should be treated with antimicrobial agents that can effectively diffuse into prostatic tissue and have broad coverage over gram- and gram+ pathogens.**

As with ABP, CBP is treated empirically with antimicrobial agents, with or without adjuvant therapies. Among the few antimicrobial agents that can effectively diffuse into prostatic tissue and cover both gram-negative and gram-positive pathogens are the fluoroquinolones (ciprofloxacin, levofloxacin, ofloxacin, and norfloxacin) and trimethoprim (TMP) or TMP-sulfamethoxazole (SMX), although SMX alone is not able to penetrate into the prostate.[7] Except for carbenicillin, penicillin derivatives have poor prostate penetration and are rarely used.[4] Treatment duration remains controversial: while bacterial eradication is believed to occur within 28 days, clinicians typically recommend long-duration oral antimicrobial therapy (6 to 12 weeks) in order to prevent recurrences. Suppressive low-dose, long-duration antimicrobial therapy may be indicated for those men with documented bacterial infection who do not respond to the initial course of treatment or for those men who become symptomatic after treatment cessation.

Category III prostatitis, or CP/CPPS, is defined by the NIDDK as genitourinary/pelvic pain or discomfort, for at least 3 of the last 6 months, in the absence of uropathogenic bacteria localized to prostate-specific specimens on culture through EPS or post-prostatic massage. Men who have leukocytes in EPS, post-prostate massage urine, or semen are diagnosed with Category IIIA, inflammatory prostatitis; men with no evidence of inflammation are diagnosed with Category IIIB, noninflammatory CP/CPPS.[8-10]

**Of the 4 categories of prostatitis classified by the NIDDK, chronic nonbacterial prostatitis (CP/CPPS) is the most prevalent, accounting for 90% of all prostatitis cases.**

The clinical presentation of CP/CPPS is similar to that of CBP and to that of IC, an inflammatory CPPS of bladder origin. IC symptomatology includes chronic pelvic pain (testicular or penile pain, pain in the perineal area, or pain with ejaculation), and urinary symptoms of urgency, frequency, and nocturia. As many as 50% of men with either CP/CPPS or IC have a nonrelaxing pelvic floor upon physical examination, and both CP/CPPS and IC can be associated with pain upon bladder filling.[11,12] In contrast to CBP, there is no defined bacterial etiology associated with either CP/CPPS or IC. Recently, research has demonstrated that at least 60% of men with CP/CPPS have cystoscopically confirmed IC.[13,14] There are currently no objective tests or laboratory analyses available that can facilitate the conclusive diagnosis of either CP/CPPS or IC.

In summary, the NIH consensus classification system improves the diagnostic process and therapeutic management of prostatitis. The system recognizes that prostatitis does not always have a bacterial etiology. However, there is still confusion regarding the overlap between CBP and CP/CPPS, as well as between CP/CPPS and IC. Consequently, many men with CP/CPPS or IC are treated with antimicrobial agents despite the lack of confirmation of a bacterial cause. The need for additional investigation of both CP/CPPS and IC is clearly warranted.

**Most men diagnosed with prostatitis are given empiric antimicrobial therapy, although few have a confirmed bacterial etiology.**

## EPIDEMIOLOGY AND IMPACT ON QUALITY OF LIFE

Prostatitis can affect men of all ages and ethnicities, although it is uncommon among young boys. One in 4 men presenting with urogenital symptoms is diagnosed with prostatitis, which is the most common diagnosis for men under age 50 years who complain of pelvic pain and urologic symptoms (Table 2).[4,15-18] Eight percent of visits to urologists are for prostatitis complaints, and prostatitis symptoms lead to 2 to 7 million medical office visits each year.[15,17] The Health Professionals Follow-up Study found that 16% of healthy adult male medical professionals (without prostate cancer) self-reported a history of prostatitis, and it is estimated that between 9% and 16% of men worldwide have a current or previous diagnosis of prostatitis.[3,15,19-22] Because more than 90% of these cases are urine culture negative, pain of bladder origin may be an important consideration in these patients.[2-4,15]

**TABLE 2**

**MAGNITUDE OF CHRONIC PROSTATITIS[16-18]**

- Overall prevalence – 9%
- ~ 8 million outpatient visits per year
- Among the 5 most common urologic diagnoses in men younger than 50 years of age
- ≥ 90% of chronic prostatitis patients are urine culture-negative
  - Pain of bladder origin can be an important consideration in these patients

The effect of chronic prostatitis on a patient's quality of life (QoL) can be significant. Regardless of the etiology, the illness impact of chronic prostatitis is at least comparable to that of myocardial infarction, angina, or Crohn's disease, and the psychologic consequences of chronic prostatitis are worse than those associated with severe congestive heart failure or diabetes (Figure 1).[23,24] Prompt and accurate diagnosis and treatment can significantly improve the QoL of these patients.

## CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

### Diagnostic Considerations

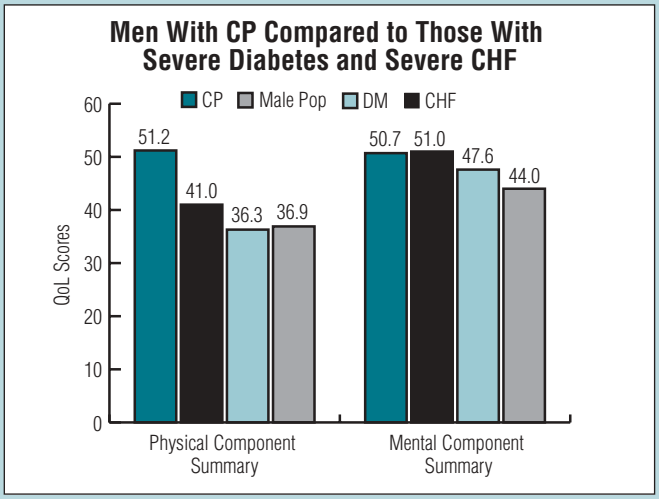
The diagnosis of CP/CPPS involves patient history, physical examination (including a digital rectal examination [DRE]), and urinalysis with culture of midstream urine (Table 3).[25-29] The prostate may or may not have demonstrable tenderness or warmth regardless of etiology. Men with bacterial or nonbacterial chronic prostatitis will have a sterile urine culture unless they have a concomitant acute UTI, and they may or may not have impairment in urinary flow.

### Meares-Stamey 4-Glass Test

Men who present with symptoms characteristic of chronic prostatitis must first be evaluated for the presence of a bacterial etiology. The Meares-Stamey 4-glass lower urinary tract localization test has historically been considered the "gold standard" for diagnosing bacterial prostatitis. The 4-glass test evaluates the presence of bacteria or leukocytes (1+) in four different specimens: (1) the initial voided bladder urine specimen (VB1); (2) midstream second voided bladder urine specimen (VB2); (3) the third voided bladder urine specimen (VB3), which is collected after either EPS or postprostatic massage; and (4) the EPS.[25] Urethritis is diagnosed when bacteria or leukocytes are present in VB1; cystitis is diagnosed when there are bacteria or leukocytes in VB2. Bacterial prostatitis is diagnosed when the bacterial colony in VB3 is at least 10-fold greater than in VB1 or VB2 and/or there are >4 leukocytes/high power field (HPF) in VB1 or VB2.[26] The absence of uropathogenic bacteria and the presence of white blood cells (WBCs) in EPS or VB3 are indicative of prostatic inflammation and a diagnosis of nonbacterial prostatitis. No demonstrable inflammation upon microscopy in otherwise sterile prostate-specific specimens indicates prostatodynia.

**FIGURE 1**

**LOW QoL SCORES IN MEN WITH CHRONIC PROSTATITIS*[24]**




N = 278
DM = diabetes mellitus; CHF = congestive heart failure; CP = chronic prostatitis.
*HRQOL assessed with short form-12 (SF-12, score range, 0-100)/NIH-Chronic Prostatitis Symptom Index

Adapted with permission from Blackwell Publishing. McNaughton Collins M, Pontari MA, O'Leary MP et al. *J Gen Intern Med.* 2001;16:656-662.

**TABLE 3**

**DIAGNOSING CHRONIC PROSTATITIS/ CHRONIC PELVIC PAIN SYNDROME[25-29]**

Clinical presentation
Patient history
Physical examination (with digital rectal exam)
Urinalysis with culture of midstream urine
Lower urinary tract localization test
  Meares-Stamey 4-glass test or
  2-glass premassage and postmassage test
Optional diagnostic tests (as needed)

While the 4-glass test can differentiate between bacterial and nonbacterial prostatitis, it is cumbersome, time-consuming, and therefore rarely used. In a recent national mail survey, 80% of responding urologists admitted they rarely (33%) or never (47%) performed this diagnostic test.[27] It is important to note that the 4-glass test is not effective in diagnosing CP/CPPS. A recent case-control study associated with the NIH Chronic Prostatitis Cohort found that although men diagnosed with CP/CPPS had significantly higher WBC counts in EPS and all segmented urine samples (but not in semen) than did asymptomatic

healthy controls, WBCs were also frequently observed in asymptomatic men.[28] In addition, both groups of men had similar rates of localized uropathogenic and nonuropathogenic bacteria.

### 2-Glass Premassage/Postmassage Test

Some clinicians have adopted the simpler and more cost-effective 2-glass premassage and postmassage test (2-glass PPMT) to differentiate between bacterial and nonbacterial prostatitis.[29] Urine is obtained before and after prostatic massage, and is cultured and examined microscopically.[30] According to the 2-glass test, CBP is diagnosed if uropathogenic bacteria are localized to the post–prostatic-massage specimen, and inflammatory CP/CPPS (category 111A) is diagnosed if there are a significant number of WBCs (5 to 10/HPF) in the absence of uropathogenic organisms. Category IIIB noninflammatory CP is diagnosed when there is an absence of both bacteria and WBCs.

Select patients may require additional diagnostic tests, including postvoid residual urine determination, urine flow rate, urodynamic testing, and imaging. Urine cytology may be indicated to rule out carcinoma *in situ* of the lower urinary tract. Cystoscopy, with or without hydrodistention, may also be indicated.

**There is no clear evidence demonstrating the efficacy of antimicrobial therapy for CP/CPPS.**

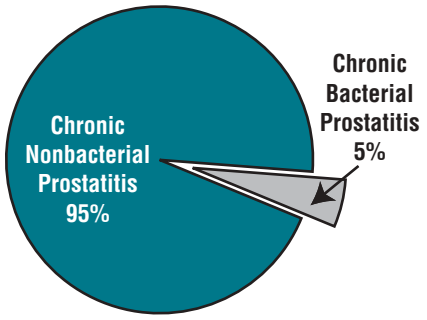
## TRADITIONAL MANAGEMENT

### Antimicrobial Therapy

Prostatitis is frequently treated with antimicrobial agents.[15] Nearly all urologists who responded to a recent national mail survey admitted treating at least 50% of their prostatitis patients with antimicrobials, even though they knew that few of those patients had a bacterial etiology to the prostatitis (Figure 2).[9] Additional courses of treatment or suppressive therapy were recommended for men who either reported initial symptomatic relief but had a recurrence, or did not respond to the initial course of therapy.

**FIGURE 2**

**MAJORITY OF CP/CPPS IS NONBACTERIAL[9]**




Despite its widespread use for chronic prostatitis, there is no clear evidence demonstrating the efficacy of antimicrobial therapy for CP/CPPS. In one study, 50% of men diagnosed with chronic prostatitis had no change in their symptoms after 3 courses of antimicrobial treatment.[31] Another trial involving 80 men with an NIH diagnosis of CP/CPPS, who were randomized to receive either levofloxacin (500 mg/d) or placebo for 6 weeks, found progressive symptomatic improvements in both groups, but no statistically nor clinically significant difference in response between the placebo and antimicrobial therapy.[32] Of concern is the risk of increasing resistance associated with inappropriate use of antimicrobial agents. Escalating rates of antimicrobial resistance have been reported for common uropathogens associated with UTI and bacterial prostatitis, heightening concerns over the potential for greater clinical failure rates.[33] Difficulties in differentiating between bacterial and nonbacterial etiologies support the use of an initial trial of antimicrobial therapy for patients diagnosed with chronic prostatitis; however, long-term antimicrobial therapy is not recommended unless there is clear evidence of bacterial infection.

### Alpha Blockers

Alpha-blocking agents have been used as first-line therapy for chronic prostatitis because they relax the prostate and bladder smooth muscles to improve urine flow and alleviate lower urinary tract symptoms (LUTS).[34,35] Alpha blockers may also alleviate obstructive voiding and urinary retention. The numerous alpha-blockers that have been investigated and/or used to manage CP/CPPS appear to improve symptoms and reduce pain during treatment, but the benefits generally are lost after treatment cessation. The duration of treatment with alpha blockers therefore remains controversial.

### Adjuvant Therapies

A wide range of pharmacologic and nonpharmacologic interventions is used to supplement first-line pharmacologic therapies. Analgesics, including nonsteroidal anti-inflammatory agents (NSAIDs), aspirin, and acetaminophen (with or without codeine) can be used to alleviate pain. The analgesic and sleep benefits of tricyclic antidepressants may be helpful for some patients. Anticholinergic agents may be indicated for men with concurrent overactive bladder (OAB). Some studies have demonstrated improvements in QoL and reductions in pain with finasteride therapy (5 mg once daily for 12 months) among men diagnosed with CP/CPPS; other investigators concluded that the modest benefit obtained with finasteride does not justify its use as monotherapy.[36-38] Men with chronic prostatitis can also benefit from supportive nonpharmacologic measures. Hot sitz baths, hydration therapy, stool softeners, and prostate massage can alleviate pain and urinary symptomatology; anecdotal evidence supports dietary changes to eliminate foods thought to be irritating to the bladder (such as caffeine, foods high in acidity, chocolate, wine).

### Summary

Historically, CP/CPPS has been challenging to manage, and traditional approaches often afford only temporary relief. Antimicrobial therapy, while widespread, may be neither appropriate nor successful, and may contribute to a worldwide increase in antimicrobial resistance. Difficulties in differentiating between CBP and CP/CPPS may support an initial trial of antimicrobial therapy; however, alternate approaches must be considered for the majority of men who fail to respond to antimicrobial treatment. It is important to consider an alternate cause of the symptoms, such as the possibility that the CPP is of bladder origin.

**It is recommended that men with suspected prostatitis who do not respond to an initial course of antimicrobial therapy should be evaluated for IC.**

## INTERSTITIAL CYSTITIS IN MEN

### Overview

IC is a CPPS of bladder origin characterized by voiding symptoms of urinary urgency, frequency, and nocturia, with pelvic pain of at least 3 months' duration. The pain may occur with intercourse or bladder filling, or it may be referred urethral, perineal, lower abdominal, lower back, medial thigh, or postvoid pain. Approximately 70% of patients with IC have a nonrelaxing pelvic floor upon physical examination.[39-41]

Historically, IC has been perceived as a severe disease that affects primarily women. Ninety percent of the 700,000 patients currently diagnosed with IC in the United States are females, and recent research suggests that as many as 2 in 9 women have IC.[42] In men, IC may be commonly misdiagnosed as CP/CPPS. Studies have shown that at least 60% of men diagnosed with CP/CPPS have documented IC.[13,14] In a recent study of 60 men diagnosed with chronic prostatitis and negative urine cultures, 58% of the men had glomerulations upon cystoscopy, indicating severe IC.[43] Other studies indicate that 84% of men with chronic prostatitis who had failed one or more courses of antimicrobial therapy had a positive PST, which is indicative of IC. In light of the high rate of misdiagnosis of IC among both men and women, the true prevalence of this syndrome remains unknown.[44]

**Studies show that at least 60% of men diagnosed with CP/CPPS have documented IC.**

## PROPOSED PATHOGENESIS OF IC IN MEN

Numerous theories have been proposed to explain the pathophysiology of IC, which is believed to have a multifactorial pathogenesis involving specific abnormalities found in the "IC bladder." Theories include the presence of as-yet-undetectable bacteria or unusual organisms in bladder cells and the possibility of a genetic basis for the syndrome, but these hypotheses have never been substantiated. Although some patients with IC do have immunologic abnormalities, there are conflicting data to support autoimmunity as a possible cause of the disease.

The prevailing theory regarding the pathogenesis of IC concerns a glycosaminoglycan (GAG) mucosal barrier deficiency. Alternate hypotheses focus on the presence of Antiproliferative Factor (APF), increased mast cell secretion, and/or neurogenic inflammation with substance P (SP) (Table 4).[45-47] In the healthy bladder, the urothelium has two important roles: it separates urine from extracellular fluid and it acts as an active absorptive epithelium for sodium. The GAG (mucus) layer, composed of lipid and hydrophobically bonded materials, forms a barrier to the luminal membrane that prevents bacteria from adhering to urothelial surfaces and prevents absorption of caustic components of urine into the deeper layers of the bladder wall. In men, the GAG layer extends into the prostatic urethra. With damage or alterations to the GAG layers, transvesical absorption of urea or potassium can occur, resulting in tissue damage and pain.[48] IC and its attendant symptoms are believed to result when damage to the GAG layer alters epithelial permeability; urinary urgency/frequency and pain are the resultant clinical manifestations.

**TABLE 4**

**INTERSTITIAL CYSTITIS: THEORIES OF PATHOGENESIS[45-47]**

- Mucosal barrier GAG deficiency
- Presence of APF
- Mast cell inflammation
- Neurogenic inflammation with substance P

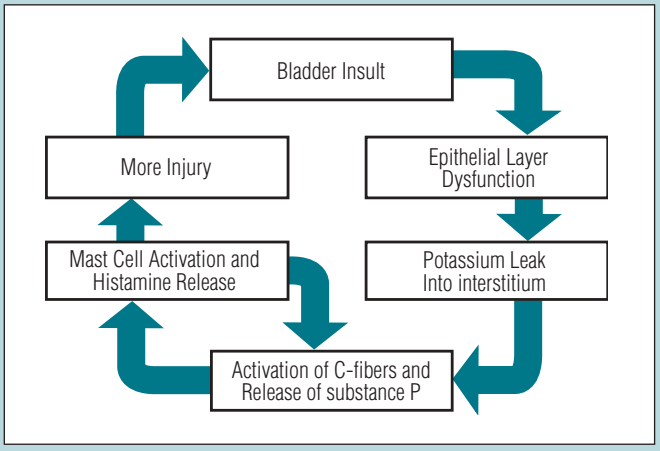
Another theory currently considered examines the role of mast cells in IC. Mast cells are found in the detrusor layer and, to a lesser extent, in the lamina propia and bladder epithelium.[47] Inside the mast cells are granules containing histamines that can cause inflammation. It is thought that degranulated mast cells abnormally release histamines, which may in turn cause the initial insult or damage to the GAG layer. Mast cells appear to play a role in the pathogenesis of other inflammatory and neuroendocrine conditions, including irritable bowel disease and multiple sclerosis.[49]

Patients with IC have been found to have increased levels of pain-carrying nerves called C-fibers that carry and release the neuropeptide SP from sensory nerve endings, transmitting pain information and stimulating inflammation.[46] IC patients have increased levels of SP, which has been shown to trigger mast-cell activation and secretion, particularly in the bladder submucosa.[46]

In summary, it is theorized that an initial bladder insult causes a deficiency in or dysfunction of the protective mucosal surface GAG layer that allows potassium to leak into the interstitium, activating C-fibers and releasing SP (Figure 3).[50] SP may activate mast cells that release histamines, resulting in additional injury to the bladder and continuously triggering the cycle that results in the inflammation, pain, and urologic symptoms characteristic of IC. Research has identified a lower urinary dysfunctional epithelium (LUDE) in the urethra, bladder, and prostate of men diagnosed with IC, CP/CPPS, or prostatitis.[44,51,52] Consequently, the pathophysiology of IC and prostatitis may be similar, as are the symptomatic presentations. It has therefore been recommended that patients with unresolved CP/CPPS should be evaluated for pelvic pain of bladder origin, specifically IC.

**FIGURE 3**

**VICIOUS CYCLE OF INTERSTITIAL CYSTITIS[50]**






**The clinical presentations of IC and CP/CPPS are nearly identical, and both conditions may share a similar pathophysiology.**

## DIAGNOSING IC IN MEN WITH CHRONIC PROSTATITIS

### Clinical Presentation

IC presents with clinical manifestations that are nearly identical to those of CP/CPPS (Table 5).[53] Several recent studies of IC in men found that the average age at diagnosis was 44 years, with a range of 2.5 to 7.8 years from onset of symptoms until accurate diagnosis.[54,55] One study found that men were most commonly initially referred to urologists for treatment of prostatitis (54%), BPH (23%), or epididymitis (10%), and had concurrent hypertension (30%), asthma (7.5%), or irritable bowel syndrome (4%).[54] Early manifestations of IC included mild symptoms of dysuria, suprapubic discomfort, urgency/frequency, and nocturia. Over a brief period of time, the severity of the symptoms dramatically increased, and the men began experiencing pain with sexual activity.[54]

**TABLE 5**

**INTERSTITIAL CYSTITIS AND CHRONIC PROSTATITIS MAY BE NEARLY IDENTICAL IN CLINICAL PRESENTATION[53]**

| Symptom | IC | Chronic Prostatitis |
|---|---|---|
| Voiding symptoms (frequency, urgency, nocturia) | ✓ | ✓ |
| Food often affects symptoms | ✓ | ✓ |
| Pain (generalized*, pelvic, with intercourse, on bladder filling, and postvoid) | ✓ | ✓ |
| Glomerulations often noted upon hydrodistention | ✓ | ✓ |

*Perineal, medial thigh, rectal, lower back, lower abdomen.

Adapted with permission from Eisenberg ER, Moldwin RM. Etiology: where does prostatitis stop and interstitial cystitis begin? *World J Urol.* 2003;21:64-69.

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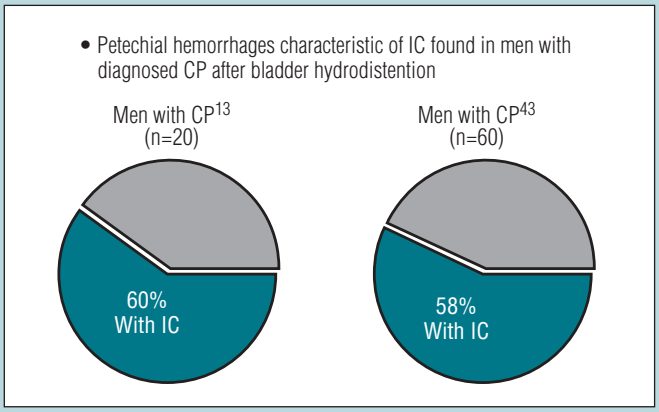
Research has shown that 45% of men diagnosed with CPPS have pain with bladder filling, a symptom characteristic of IC.[53] Studies demonstrated that approximately 60% of men diagnosed with and treated for chronic prostatitis were found upon bladder hydrodistention to have petechial hemorrhages (glomerulations) characteristic of IC (Figure 4).[13,43,51,56] In light of the many similarities in clinical presentation, IC should be suspected in all men presenting with the signs and symptoms of CP/CPPS.

**FIGURE 4**

**CYSTOSCOPIC FINDINGS INDICATE INTERSTITIAL CYSTITIS IN CHRONIC PROSTATITIS PATIENTS[13,43]**




## Traditional Approaches

In addition to symptomatic presentation, IC in men should be considered after a negative urinalysis and sterile culture rule out UTI. As with CP/CPPS, men with IC will have testicular pain and tenderness during a DRE, in the absence of objective findings. Additional diagnostic tests might include bacterial localization studies, potential urinary markers, cystoscopy (with hydrodistention), and the PST. Symptom questionnaires can also assist in the diagnostic process (Table 6).[51-61] Men with CBP or CP/CPPS are traditionally treated with empiric antimicrobial agents; it is recommended that those men who do not respond to an initial course of antimicrobial therapy be evaluated for IC before initiating additional courses.

**TABLE 6**

**DIAGNOSING INTERSTITIAL CYSTITIS IN PATIENTS WITH CHRONIC PROSTATITIS[51-61]**

- History
  - Question: Could the bladder be the origin of pain?
    - Voiding symptoms, painful voiding
    - Location and occurrence of pain
    - Painful intercourse/painful ejaculation
- Physical Examination
  - Tenderness with DRE
  - Testicular pain in absence of objective findings
- Diagnostic Tests
  - Urinalysis/culture (rule out UTI)
  - Bacterial localization studies
  - Optional
    - PST
    - Intravesical anesthetic challenge
- Symptom Questionnaires
  - NIH-CPSI
  - O'Leary-Sant ICSI
  - PUF

## Cystoscopy With or Without Hydrodistention

Cystoscopy, with or without hydrodistention, is a common procedure in urologic practice and is frequently performed to rule out carcinoma *in situ* of the bladder. Early studies utilized cystoscopy with hydrodistention to identify the presence of a Hunner's patch, a finding indicative of severe IC. When combined with hydrodistention, cystoscopy can add certainty to a presumptive diagnosis of IC. Nevertheless, cystoscopic/hydrodistention findings do not definitively diagnose IC, as the presence of glomerulations is uncommon and not specific for IC, and does not influence therapeutic management strategies.[57] The absence of definitive histologic findings in 60% of IC patients minimizes the utility of bladder biopsy for confirming IC.[57]

## Evolving Diagnostic Tests

*Potassium Sensitivity Test (PST)*

A good predictor of IC is the PST, which detects abnormal bladder epithelial permeability by identifying those patients who respond with pain or urgency following the instillation of potassium chloride (KCl) into the bladder.[48] The PST can be performed by urologists or nonurologists on an outpatient basis. The procedure involves the very slow (over 2 to 3 minutes) introduction of 40 mL of room-temperature sterile water (or normal saline solution) into the bladder through a thin catheter. The patient is asked to rate his baseline pain perception and degree of urgency upon bladder filling using a 0- to 5-point scale (with 5 indicating the most severe pain). After the water has been retained for up to 5 minutes, it is emptied through the catheter; then 40 mL of 0.4M KCl solution is instilled. The patient is then asked to evaluate the level of pain and/or urgency with the KCl instillation. Any increase of >2 points over baseline for pain or urgency indicates a positive PST. The KCl solution can be retained in the bladder for up to 5 minutes (unless severe pain occurs), after which the catheter is removed and the patient is asked to urinate before re-evaluating the level of pain/urgency. A patient is considered to have a negative PST if he has no pain or urgency response to the procedure; patients who respond to the introduction of water or who report discomfort with the KCl solution are considered likely to have IC. The procedure may cause immediate discomfort or flare-ups of the disease that quickly subside.

A positive PST indicates abnormal epithelial permeability and is a sign that the chronic pelvic pain is of bladder origin.[52,58] However, a positive PST is not sufficient to conclusively diagnose IC, since other bladder diseases (such as acute bacterial cystitis and radiation cystitis) can cause a positive PST. Similarly, a negative PST does not conclusively rule out IC, as false negatives may occur in patients who have recently undergone heparin and/or dimethyl sulfoxide (DMSO) treatment or hydrodistention, or are currently taking pain medications. While fewer than 3% of healthy individuals demonstrate a positive PST, nearly 80% of patients with IC have a positive PST.[51]

**A positive PST indicates abnormal epithelial permeability and is a sign that the pelvic pain may be of bladder origin.**

In summary, the PST is a sensitive diagnostic tool that identifies patients with abnormal epithelial permeability indicative of IC. The PST, in combination with patient history, negative laboratory analyses, and a physical examination, can identify a high percentage of men with IC.

*Intravesical Anesthetic Challenge*

An evolving diagnostic tool that may also afford patients temporary symptomatic relief is the intravesical anesthetic challenge. Preliminary research has found that bladder instillation of an anesthetic solution utilizing 40 cc of 0.5% bupivacaine/2% lidocaine jelly (1:1) leads to significant improvements in pain among patients with IC. Patients who respond favorably to the intravesical anesthetic challenge most likely have pain of bladder origin indicative of IC.[59]

## Symptom Questionnaires

Several symptom questionnaires have been developed to identify patients with suspected CP/CPPS or IC and/or to assess the impact of symptoms or progress of treatment. The NIH Chronic Prostatitis Symptom Index (NIH-CPSI) is a validated outcome measure developed by the NIH Chronic Prostatitis Collaborative Research Network to assess the symptoms associated with CP. This 1-page, 43-point scale examines the 4 domains associated with CP: pain or discomfort (4 questions), urinary function (2 questions), impact of symptoms (2 questions), and effect on quality of life (1 question).[60] The NIH-CPSI can be easily self-administered, and has been found to be a reliable, highly responsive measure of prostatitis symptoms.[61]

The PUF Patient Symptom Scale is an 8-question symptom scale that measures the presence and severity of symptoms associated with IC, and the degree to which the patient is bothered by the symptoms (Table 7). The PUF gives equal weight to the 3 primary symptoms of IC: urinary frequency, urinary urgency, and pelvic pain. Two additional questions focus on symptoms that are associated with sexual activity. The maximum score on the PUF is 35. High symptom, "bother," and total scores (10 points or higher) indicate a high probability that the patient has IC. In contrast, the overwhelming majority of healthy patients have low PUF scores (< 2 points).

**The PUF Patient Symptom Scale is a 5-minute self-administered questionnaire that measures the presence and severity of IC symptoms.**

Recent studies have shown that a high PUF score is strongly indicative of IC: patients with a PUF score >5 had a 55% chance of having IC, and patients who scored >10 points had a 74% likelihood of IC.[42] The PUF can distinguish IC from other abdomenopelvic conditions, including UTI and urinary incontinence, and is therefore a useful screening tool. As such, it has been recommended that the PUF should be administered to all men who manifest symptoms characteristic of CP/CPPS, and that any patient with a PUF score >5 points should be suspected of having IC and assessed and treated appropriately.

**TABLE 7**

**PELVIC PAIN AND URGENCY/FREQUENCY PATIENT SYMPTOM SCALE (PUF)[89]**

Patient's Name:_____ Today's date: _____

Please circle the answer that best describes how you feel for each question.

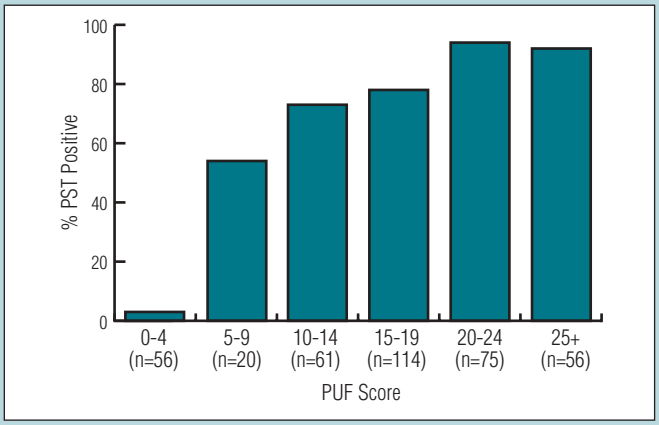
| | | 0 | 1 | 2 | 3 | 4 | SYMPTOM SCORE | BOTHER SCORE |
|---|---|---|---|---|---|---|---|---|
| 1 | How many times do you go to the bathroom during the day? | 3-6 | 7-10 | 11-14 | 15-19 | 20+ | | |
| 2 | a. How many times do you go to the bathroom at night? | 0 | 1 | 2 | 3 | 4+ | | |
| | b. If you get up at night to go to the bathroom, does it bother you? | Never bothers | Occasionally | Usually | Always | | | |
| 3 | Are you currently sexually active? YES____ NO____ | | | | | | | |
| 4 | **a. IF YOU ARE SEXUALLY ACTIVE,** do you now or have you ever had pain or symptoms during or after sexual activity? | Never | Occasionally | Usually | Always | | | |
| | b. If you have pain, does it make you avoid sexual activity? | Never | Occasionally | Usually | Always | | | |
| 5 | Do you have pain associated with your bladder or in your pelvis (vagina, labia, lower abdomen, urethra, perineum, penis, testes, or scrotum)? | Never | Occasionally | Usually | Always | | | |
| 6 | a. If you have pain, is it usually | | Mild | Moderate | Severe | | | |
| | b. Does your pain bother you? | Never | Occasionally | Usually | Always | | | |
| 7 | Do you still have urgency after you go to the bathroom? | Never | Occasionally | Usually | Always | | | |
| 8 | a. If you have urgency, is it usually | | Mild | Moderate | Severe | | | |
| | b. Does your urgency bother you? | Never | Occasionally | Usually | Always | | | |
| | | | | | | | SYMPTOM SCORE (1, 2a, 4a, 5, 6a, 7, 8a) | |
| | | | | | | | BOTHER SCORE (2b, 4b, 6b, 8b) | |
| | | | | | | | TOTAL SCORE (Symptom Score + Bother Score) = | |

Total score ranges are from 1 to 35.
A total score of 10-14 = 74% likelihood of positive PST; 15-19 = 76%; 20+ = 91% Potassium Positive



**FIGURE 5**

**HIGHER PUF SCORES CORRELATE WITH INCREASED PST-POSITIVE REACTION[42]**




N=334 urologic patients, 48 controls.
Adapted with permission from Elsevier, © 2002. Parsons CL, Dell J, Stanford EJ, et al. *Urology.* 2002;60:573-578.

Studies have recently found a significant correlation between high PUF scores and a positive PST in men with prostatitis (Figure 5), as well as in gynecologic patients with pelvic pain.[42] In a study of 382 individuals screened with both

the PUF and PST, 84% of patients with a PUF score >15 had a positive PST, whereas fewer than 2% of patients who had a PUF score <4 had a positive PST.[42] This high correlation supports use of the PUF as an initial screening tool, reserving the PST for those patients whose symptoms are suggestive of IC but who have lower PUF scores (2 to 5 points).

### Summary

The past decade has facilitated a greater understanding of the IC disease process that recognizes the rarity of Hunner's ulcers, especially in mild-to-moderate disease, and the lack of evidence for their use in diagnosis. The introduction of new diagnostic measures (such as the PST and intravesical anesthetic challenge) and questionnaires (most notably the PUF) allow clinicians to more easily and reliably diagnose patients suspected of having IC.

## MANAGEMENT OF IC

### Traditional Approaches

IC is often initially misdiagnosed as CP/CPPS in men and treated with empiric antimicrobial agents, alpha blockers, and a variety of adjuvant therapies.[15] However, at least half of patients with CP fail to respond to 3 courses of antimicrobial therapy, primarily owing to the absence of a bacterial etiology underlying the symptoms, and possibly because many of the men may, in fact, have IC instead of (or in addition to) CP/CPPS.[31]

Men with either CP/CPPS or IC will respond to adjuvant nonpharmacologic interventions such as diet modification and behavior therapies. Although bladder-training techniques, supplemented with relaxation and distraction techniques and pelvic floor relaxationeast moderate disease.[62]

### FDA-Approved Pharmacologic Therapies

*Pentosan Polysulfate Sodium*

Pentosan polysulfate sodium (PPS) is the only oral drug approved by the Food and Drug Administration (FDA) for the management of IC.[63] It is also indicated for the treatment of bladder pain and urinary tract irritation. PPS is believed to act primarily by replenishing the defective GAG layer and inhibiting inflammatory processes. PPS may act as a buffer to control cell permeability and prevent solutes from reaching epithelial cells. PPS may also have a stabilizing effect on mast cells.

PPS is a heparinoid compound similar in chemistry and structure to the naturally occurring GAG produced in the urinary epithelium.[45] It appears to work slowly and methodically to repair the damaged epithelium. The current FDA-recommended dosage is 300 mg/d taken as a 100-mg capsule 3 times daily; to enhance compliance, an evolving regimen (not approved by the FDA) recommends patients take two 100-mg capsules twice daily. Patients with mild disease are instructed to take PPS for a minimum of 2 to 4 months; however, treatment durations of at least 6 months are necessary to afford symptomatic relief to patients with moderate disease, and patients with severe disease may require PPS treatment for at least 1 year.[64] PPS is well tolerated, with no known drug-drug interactions and no impact on coagulation profiles. Side effects have been reported to be infrequent, mild, and transient, and can include minor gastrointestinal discomfort, localized alopecia, and headache.[63] Approximately 1% of patients experience slight liver function changes that resolve spontaneously and have not been associated with jaundice or other clinical signs or symptoms. Because of its good safety profile, clinicians frequently recommend that all patients with IC receive PPS treatment for a minimum of 6 months.

PPS has been found effective in reducing pain and urinary symptoms in male and female patients with IC. Initial studies demonstrated statistically significant improvements in pain, urinary urgency, urinary frequency, and nocturia; PPS led to significant subjective improvement in average voided volumes, but had no significant impact on average number of daily voids.[65] Similar research found that more than twice as many patients with long-term IC (>1 year) who received PPS (100 mg tid X 3 months) had moderate improvement relative to baseline (28% vs 13% for placebo), with reduced pain (27% PPS vs 14% for placebo) and reduced pressure to urinate (22% PPS vs 11% for placebo).[66] There was a greater increase in bladder capacity (volume per void) among PPS recipients, and a significantly greater number of PPS recipients reported good or better overall improvement (26% PPS vs 11% for placebo).

Additional research has demonstrated that improvement of symptoms increases with duration of use. In a long-term, open-label study involving more than 2800 patients with IC, PPS treatment for 3 months led to at least moderate improvement in pain relief for approximately 50% of the patients. Maximum benefit in pain and urgency that persisted for at least 3 years was noted after PPS therapy that had lasted for 6 to 11 months.[67] Similar results were noted in a dose-ranging study of PPS, in which there was minimal difference on exit scores between the 3 trial doses of PPS (300 mg/d, 600 mg/d, or 900 mg/d), but clear demonstration of the benefits of long-term PPS therapy. This study also demonstrated that treatment with PPS dramatically reduces potassium sensitivity as measured by the PST.[68]

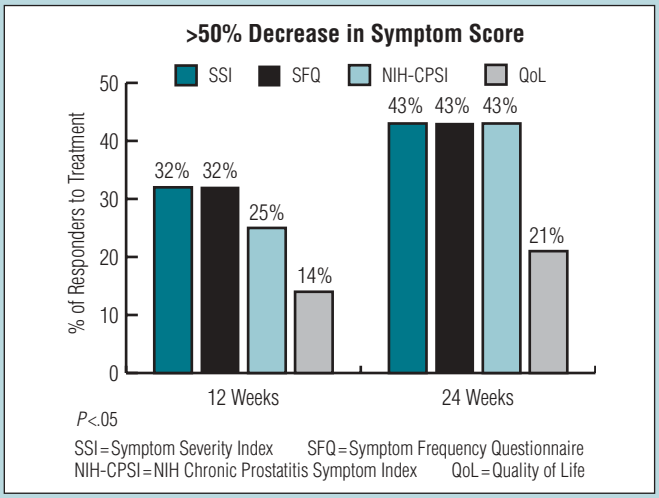
**PPS, the only oral drug approved for the management of IC, has been shown to reduce pain and improve QoL in men diagnosed with CP/CPPS.**

Research has demonstrated the efficacy of PPS in men diagnosed with CP/CPPS, possibly suggesting that these men have IC and were initially misdiagnosed. In an early double-blind study, 24 men diagnosed with CP/CPPS were randomized to receive either placebo or PPS (200 mg).[69] After 3 months, PPS was found to afford a modest benefit, particularly on systemic effects such as arthralgia and myalgia. Phase II and phase III studies have examined the efficacy of PPS in men diagnosed with inflammatory CP/CPPS.[10,70] In the prospective phase II study, 32 men with CP/CPPS Category IIIA were given 100 mg of pPS 3 times daily for 6 months.[10] The men had been symptomatic for an average of 9.2 years, suggesting at least moderate disease. They completed the NIH-CPSI and Subjective Global Assessments at study initiation and after 3 and 6 months of treatment. After only 12 weeks of PPS therapy, 41% of the men reported either "moderate" or "marked" improvement on the Subjective Global Assessment, and 25% of men reported >50% decrease in symptom scores on the NIH-CPSI (Figure 6).[10] After PPS treatment for 24 weeks, 43% of men experienced >50% decrease in symptom scores on the NIH-CPSI. The authors concluded that PPS benefits men with CPPS by reducing symptoms and improving QoL.[10]

The subsequent phase III trial randomized 100 men with CPPS to receive PPS 300 mg tid (n=51) or placebo (n=49) for 16 weeks during the initial double-blind phase, with an optional additional 16-week open-label phase.[70] As with the phase II trial, the Subjective Global Assessments and the NIH-CPSI were administered at baseline and again at weeks 4, 8, 12, and 16. By week 12, patients receiving PPS reported a significant reduction in pain and a significant improvement in QoL (Figure 7).[70] There was also a significant difference in favor of PPS among percentage of responders (defined as patients who were moderately or markedly better on Clinical Global Improvement assessments). As with the earlier trial, PPS was found to be both safe and effective for patients with CP/CPPS.

**FIGURE 6**

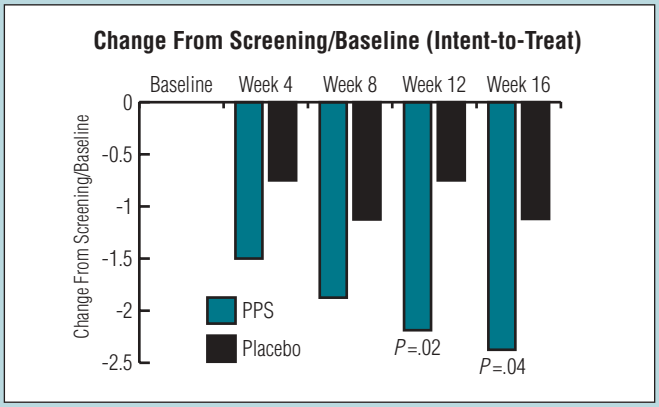
**IMPROVEMENT OF SYMPTOMS WITH PPS[10]**




Adapted with permission from Nickel JC, Johnston B, Downey J, et al. *Urology*. 2000;56:413-417.

**FIGURE 7**

**SIGNIFICANT IMPROVEMENT IN QoL AT WEEK 12 IN PPS PATIENTS[70]**

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*Intravesical DMSO*

Intravesical instillation of DMSO is the only other treatment indicated for the management of IC. DMSO is an anti-inflammatory analgesic with muscle-relaxing properties that is believed to increase reflex firing of pelvic nerve efferent axons and bladder capacity.[71,72] Research suggests that DMSO releases nitric oxide from afferent neurons and may inhibit mast cell secretion.[73,74] DMSO has no known effect on the underlying cause(s) of IC.

**Intravesical instillation of DMSO is the only other treatment indicated for the symptomatic relief of patients with IC.**

Intravesical instillation of DMSO can be administered by a clinician in the office or by motivated patients at home.[75] The treatments are administered either once weekly or every other week for 6 to 8 weeks per course, and patients often report a response to the treatment within 3 to 4 weeks after completion of the first course. The procedure involves the instillation of 50 mL of an aqueous solution (50%) of DMSO through a catheter into the bladder, where the solution is retained for 15 to 20 minutes before being expelled. Patients with severe disease may not initially be able to retain the solution for the recommended duration.

DMSO treatments appear to afford at least moderate symptom relief and an increase in bladder capacity.[72,74,76] In a trial comparing intravesical administration of placebo versus DMSO every 2 weeks for 2 sessions (4 treatments in all), 93% of DMSO patients compared with 35% of placebo patients reported objective improvement, and 53% of DMSO versus 18% of placebo patients experienced marked improvement.[76] Eighty percent of patients with ulcerative IC who were treated with DMSO experienced an increase in bladder capacity, and 75% of them reported satisfactory symptomatic relief.[72] The procedure is safe but can be painful, and can leave a garlic-like taste and/or odor on the breath or skin for up to 72 hours after treatment.[77] Patients receiving DMSO therapy are advised to have blood testing, including kidney and liver function tests, every 6 months. Remissions are rarely complete, and additional treatment courses can decrease the duration of remissions.[78,79]

## Second-Line Therapeutic Interventions

*Oral Agents*

The same adjuvant therapies that are used to manage CP/CPPS may also provide supplemental relief to patients with IC. Analgesics can alleviate mild discomfort, although NSAIDs release histamines and can exacerbate IC symptoms. Men with severe and/or long-standing disease may require opioid analgesics, at least during the initial treatment stages. Patients with concomitant OAB or with severe urgency/frequency may benefit from anticholinergics and/or antispasmodic agents, particularly hyoscyamine sulfate. Antihistamines, particularly hydroxyzine hydrochloride (25 to 75 mg), can be administered in the evening for patients with an allergic component to their IC. Hydroxyzine (75 mg/d for 3 months) has been shown to alleviate IC symptoms in 55% of IC patients with a history of allergy.[80]

Antidepressants, particularly tricyclic antidepressants (TCAs) such as amitriptyline, decrease norepinephrine and serotonin reuptake in the central and peripheral nervous system to provide pain relief. Treatment with amitriptyline resulted in pain reduction in 60% to 90% of patients with IC.[81] TCAs also inhibit histamine secretion from mast cells. When administered in the evening (at a dosage that is slowly titrated upward from 10 to 150 mg), the anticholinergic properties of amitriptyline can reduce nocturia and urinary frequency.[81] Amitriptyline has been causally associated with drowsiness, constipation, and cardiac irregularities and should be cautiously recommended.

*Intravesical Agents: Heparin*

Intravesical administration of heparin (10,000 units in 10 mL of sterile water 3 times per week for 3 months), although not approved by the FDA, has been used in both monotherapy and combination therapy with generally favorable results. Heparin is a mucopolysaccharide found naturally in the GAG epithelium; its antiadherence action protects the bladder mucosa against bacterial invasion.[82] As with the heparinoid agent PPS, intravesical instillation of heparin is believed to correct the underlying GAG defect associated with IC.

The efficacy and safety of intravesical heparin monotherapy has been demonstrated in numerous studies. Early research found that more than half (56%) of IC patients receiving heparin treatment experienced clinical remissions after 3 months that were maintained with ongoing therapy (up to 9 months).[83] Other research found intravesical heparin (25,000 units twice/week for 3 months) afforded 75% of women with IC or frequency/urgency syndrome a >50% improvement in symptom scores that was confirmed by urodynamic studies.[84] Heparin has also been shown to augment the benefits of DMSO treatment: the addition of heparin to DMSO reduced the relapse rate and extended remissions.[71,85]

*Intravesical Anesthetic Solutions: "Therapeutic Cocktails"*

The most recent additions to the IC therapeutic armamentarium are intravesical anesthetic solutions. These solutions, which are similar to those used in the intravesical anesthetic challenge, combine 16 mL of 2% lidocaine, 3 mL of

8.4% sodium bicarbonate, and either PPS (1 or 2 100-mg capsules dissolved in 10 mL buffered normal saline) or heparin (10,000 to 40,000 units) as the active agent.[83,86,87] The addition of sodium bicarbonate to the solution significantly increases absorption of the anesthetic (lidocaine); cost-conscious patients may prefer the cost savings of PPS over heparin in these solutions.[88]

The procedure involves instilling the solution into the bladder through a small catheter, where it is retained for up to 30 minutes. It can be performed by patients at home, and is particularly beneficial for patients who are beginning oral PPS therapy or for men/women with severe disease.[51,86] The anesthetic instillations often provide immediate relief of the urgency/pain associated with IC that can last for a few hours up to a few days. Recent research demonstrated that 85% of patients with IC had sustained pain relief when treated 3 to 7 times per week for at least 2 weeks.[86]

### Surgery

Surgery for treatment of IC remains a last resort and is not always successful. Surgery to remove Hunner's ulcers can eliminate or dramatically reduce symptoms in the short run, but symptoms often recur within 1 to 2 years. Bladder augmentation reduces urinary frequency but does not influence pain and can result in incontinence. Patients with severe disease who have failed all other forms of treatment may eventually require cystectomy.

## SUMMARY

The management of chronic nonbacterial prostatitis has traditionally been challenging and frustrating for both patient and clinician. Long-term empiric antimicrobial therapy is neither appropriate nor effective for this nonbacterial condition; nevertheless, it is frequently recommended as first-line treatment. Many patients who present with urinary frequency/urgency and pelvic pain have IC and may be misdiagnosed with CP/CPPS. Managing these patients requires appropriate IC therapy. The recent approval of PPS affords patients an oral therapeutic intervention that provides symptomatic relief while replenishing the damaged urothelium, and may be a preferable alternative to intravesical DMSO instillations. Adjuvant therapies and the anesthetic intravesical solutions can augment and/or speed symptomatic relief.

## CONCLUSIONS: THE MANY SIMILARITIES BETWEEN IC AND CP/CPPS

Both CP/CPPS and IC are common conditions affecting men of all ages. These conditions are characterized by symptoms of urinary urgency and frequency, nocturia, pelvic pain, and pain associated with sexual activity in the absence of other defined bladder pathology. Both conditions can significantly impair the patient's QoL, and the absence of disease markers or specific histologic changes have historically made both conditions difficult to diagnose.

It has been suggested that many men diagnosed with CP/CPPS may, in fact, have another condition underlying their symptomatic presentation, one in which the bladder and not the prostate is the source of the pelvic pain and urinary symptoms of urgency/frequency. Support for this hypothesis is increasing, as research demonstrates that a majority of men initially diagnosed with CP/CPPS are found to have positive PST and high PUF scores, both indicative of IC. In addition, a majority of men diagnosed with CP/CPPS respond to treatment indicated for IC. Clinicians are aware of the difficulties in distinguishing between a diagnosis of CBP, CP/CPPS, and IC; therefore, men who present with symptoms suggestive of chronic prostatitis are usually given an initial course of empiric antimicrobial therapy. However, an alternative cause of the symptoms, such as IC, should be considered for nonresponders to antimicrobial treatment. The PUF can be easily administered during the initial diagnostic process to help identify those patients with a high likelihood of IC. The more invasive PST can be reserved for those patients who have inconclusive scores on the PUF. When a man presents with symptoms suggestive of chronic prostatitis, the diagnosis of CPP of bladder origin, or IC, should be considered.

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IMPORTANT CME MATERIALS ENCLOSED

# CHRONIC PELVIC PAIN OF BLADDER ORIGIN IN MEN: A REVEALING LOOK AT THE RELATIONSHIP BETWEEN CHRONIC NONBACTERIAL PROSTATITIS AND INTERSTITIAL CYSTITIS

**CME POSTTEST/REGISTRATION/EVALUATION (04-726H)**

**Release date: October 2004**
**Expiration Date for credit: October 31, 2005**

**Instructions:**
Please mark your answers on the CME Registration/Posttest Answer Form/Evaluation.

This activity should take approximately 1 hour to complete. The participant should, in order, read the objectives and newsletter, answer the 10-question multiple-choice posttest, and complete the Program Evaluation. If you wish to receive CME credit, please mail or fax a copy of your completed answers to:

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Expiration date for credit: October 31, 2005

**POSTTEST/ASSESSMENT** (Circle the single most appropriate answer below.)

1. What percentage of prostatitis cases have a bacterial etiology?
   a. 5% to 10%
   b. 25%
   c. 48%
   d. 90%

2. According to worldwide estimates, what percentage of men have a current or previous diagnosis of prostatitis?
   a. 2% to 7%
   b. 8%
   c. 9% to 16%
   d. 25%

3. A man presenting with chronic pelvic pain, pain with bladder filling, urinary urgency/frequency, and nocturia should be suspected of having:
   a. Chronic bacterial prostatitis
   b. Chronic nonbacterial prostatitis
   c. Interstitial cystitis
   d. All of the above
   e. None of the above

4. Psychologic consequences of chronic prostatitis are:
   a. At least comparable to those of Crohn's disease
   b. Worse than those of myocardial infarction
   c. Worse than those of congestive heart failure
   d. Similar to those associated with diabetes

5. The prevailing theory regarding the pathogenesis of IC in men concerns:
   a. The presence of as-yet-undetectable bacteria/unusual organisms
   b. Immunologic abnormalities
   c. Defect in the mucosal GAG barrier
   d. The presence of antiproliferative factor

6. When used alone, which of the following can conclusively diagnose IC?
   a. Cystoscopy with hydrodistention
   b. PST
   c. PUF questionnaire
   d. All of the above
   e. None of the above

7. Which diagnostic assessment has been considered the gold standard for bacterial prostatitis?
   a. Cystoscopy with hydrodistention
   b. Urinalysis with culture
   c. Meares-Stamey 4-glass test
   d. 2-glass PPMT

8. What is the likelihood of IC with a PUF score of >15?
   a. 43%
   b. 55%
   c. 68%
   d. 84%

9. Which of the following is an appropriate first-line agent for the management of IC?
   a. Fluoroquinolone
   b. Finasteride
   c. Alpha-blocking agent
   d. PPS

10. In a phase III trial, oral PPS was shown to have what effect on men with CP/CPPS, when compared with placebo?
    a. Significant decrease in number of daily voids
    b. Significant improvement in amount of voids
    c. Significant reduction in pain
    d. All of the above

**PROGRAM EVALUATION**

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The Dannemiller Memorial Educational Foundation would appreciate your comments regarding the quality of the information presented. Later, via email, we would also like to send you a website link to a follow-up survey regarding the material presented. May we contact you? (Please check one.)

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1. The program objectives were fully met.
   Strongly Agree Agree Disagree Strongly Disagree

2. The quality of the educational process (method of presentation and information provided) was satisfactory and appropriate.
   Strongly Agree Agree Disagree Strongly Disagree

3. The educational activity has enhanced my professional effectiveness and improved my ability to treat/manage patients.
   Strongly Agree Agree Disagree Strongly Disagree NA

4. The educational activity has enhanced my professional effectiveness and improved my ability to communicate with patients.
   Strongly Agree Agree Disagree Strongly Disagree NA

5. The information presented was *without* promotional or commercial bias.
   Strongly Agree Agree Disagree Strongly Disagree

   (When answering this question, please refer to the following guidelines set forth by the ACCME regarding commercial bias and fair balance: *Discussion of commercial products must be free of bias for or against any one product and must present objective information about each product discussed: only generic names of therapeutic options should be used, however if trades names are used, those of several companies must be discussed in the activity.*)

6. Comments/suggestions regarding *this* material. _____

_____

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_____